Twelve-Month Results from the INFRONT-2 Phase 2 Open-Label Study of latozinemab (AL001) in Frontotemporal Dementia Patients with a *C9orf72* Mutation

March 15, 2022

All authors are equity stakeholders in Alector, Inc and/or employees of Alector, LLC

Agenda and Speakers

Topic	Speaker
Rationale for Targeting PGRN in FTD-*C9orf72* Population	• **Sara Kenkare-Mitra, Ph.D.** • President & Head of R&D
Overview of 12-Month INFRONT-2 Phase 2 Data from Symptomatic FTD-*C9orf72* Cohort	• **Sam Jackson, M.D.** • Interim Chief Medical Officer
Closing Remarks and Q&A	• **Arnon Rosenthal, Ph.D.** • Chief Executive Officer and Co-Founder • **Sam Jackson, M.D.** • **Marc Grasso, M.D.** • Chief Financial Officer • **Sara Kenkare-Mitra, Ph.D.**

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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.

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Rationale for Targeting PGRN in FTD-*C9orf72* Population

Sara Kenkare-Mitra, Ph.D.

President and Head of R&D

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12-month data from **symptomatic FTD-*C9orf72* cohort** in INFRONT-2 Phase 2 study

Successfully elevated progranulin **above physiological levels**

Data supports opportunity to **expand PGRN franchise** into additional neurodegenerative indications

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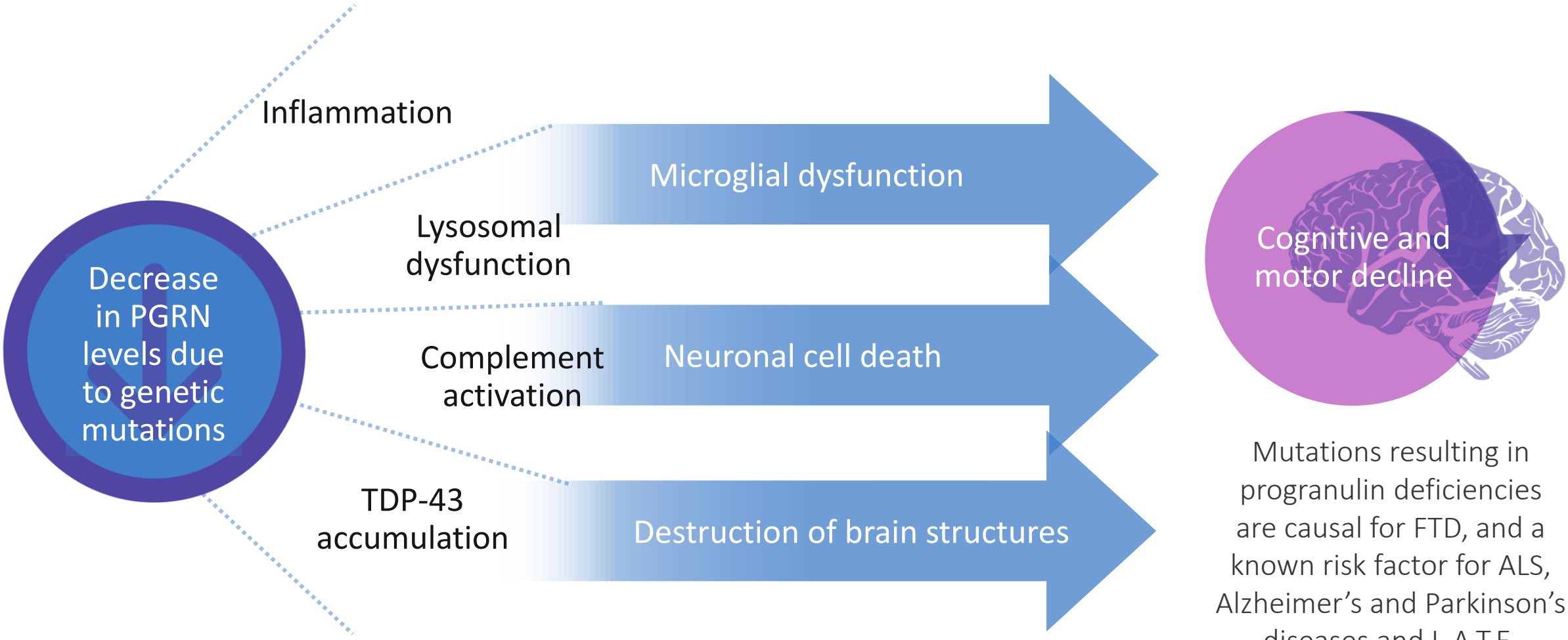
The role of progranulin in neurodegeneration



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

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

Genetics

Progranulin polymorphisms:

- Exacerbate *C9orf72* FTD and ALS[1]
- Associated with accelerated disease progression and earlier age of onset in ALS[2]

Mechanistic

C9orf72 repeats cause[3]:

- TDP-43 aggregation
- Microglia pathology

Therapeutic

PGRN may counteract:

- TDP-43 pathology[4]
- Microglia pathology
- Lysosomal pathologies that typify ALS and FTD-*C9orf72*

References: 1. Balendra R, Isaacs AM. Nat Rev Neurol. 2018;14(9):544-558. 2. van Blitterswijk M, Mullen B, Wojtas A, et al.. Mol Neurodegener. 2014;9:38. K. Sleegers, N. Brouwers, S. Maurer-Stroh, et al. Neurology Jul 2008, 71 (4) 253-259. 3. Balendra R, Isaacs AM. Nat Rev Neurol. 2018;14(9):544-558. 4. Beel S, Herdewyn S, Fazal R, et al. *Mol Neurodegener*. 2018;13(1):55.

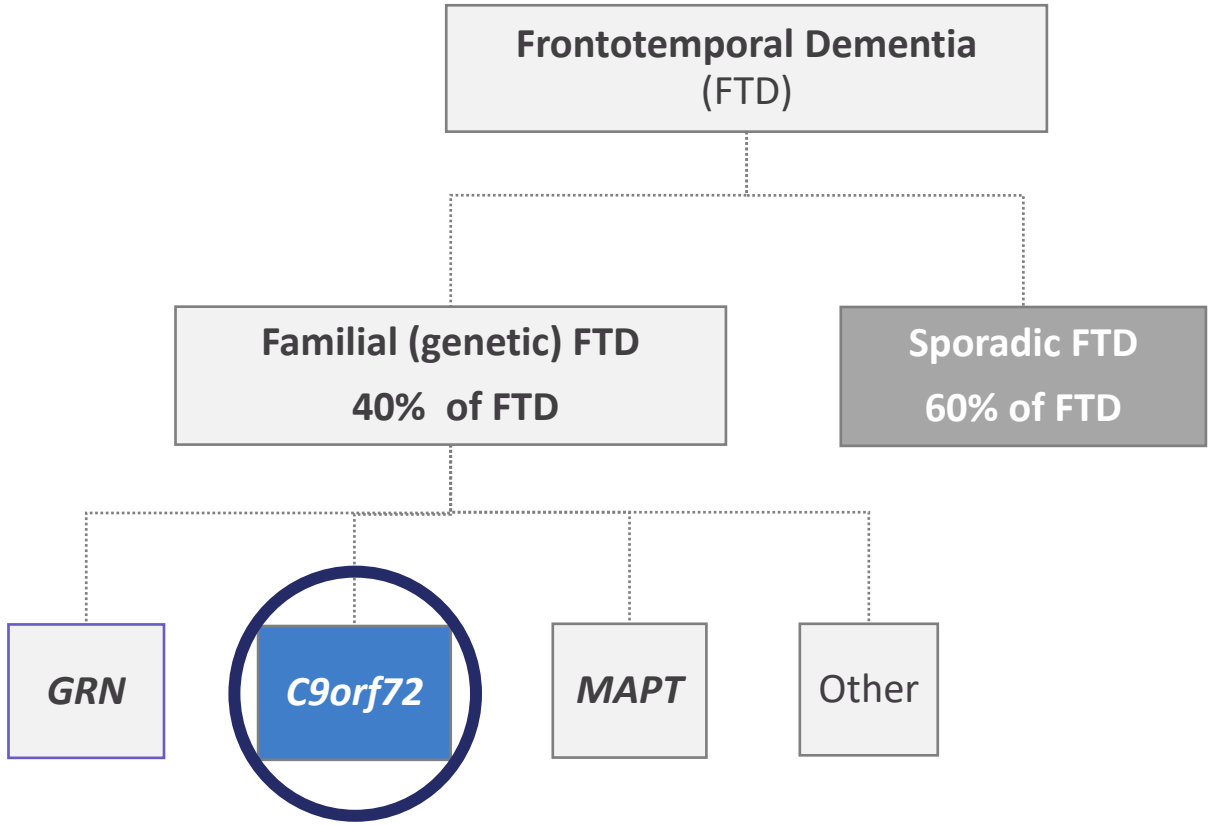
12-Month INFRONT-2 Phase 2 Data from Symptomatic FTD-*C9orf72* Cohort

Sam Jackson, M.D.

Interim Chief Medical Officer

Frontotemporal dementia is a rapidly progressive form of dementia with no approved treatment

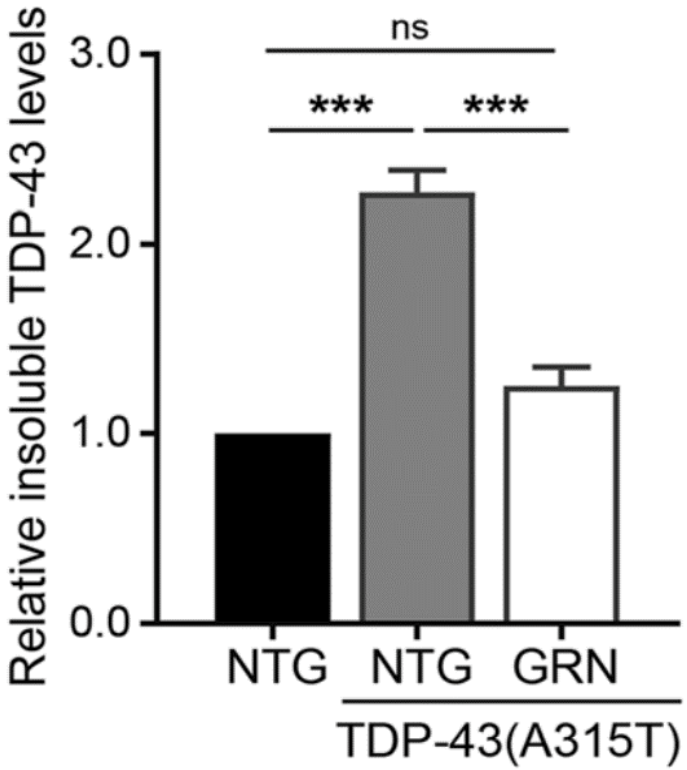
- Most common form of dementia under age 60[1]
- Patients present with compulsive behavior, lack of restraint, apathy, anxiety, and aphasia[2]
- Life expectancy after diagnosis is 7 - 10 years[3]
- *C9orf72* repeat expansion mutations are the most common genetic cause of FTD[4]
- *C9orf72* repeat expansion mutations cause FTD (and ALS) and lead to TDP-43 pathology[5]
- Human genetic and preclinical studies support progranulin elevation as a therapeutic strategy in FTD-*C9orf72*[4,5]



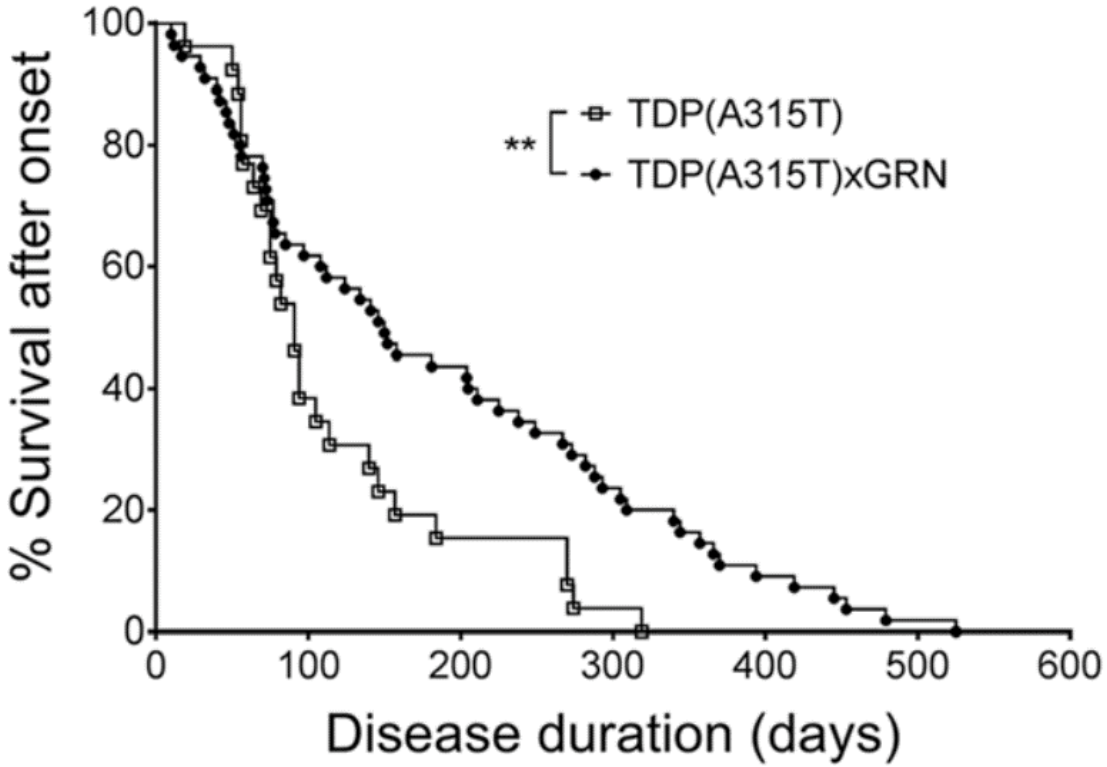
References: 1. Perry DC, Miller BL. Neurol. 2013;33(4):336-341. 2. Finger EC. 2016;22(2 Dementia):464-489. 3. Moore KM, Nicholas J, Grossman M, et al. Lancet Neurol. 2020 Feb;19(2). 4. Greaves CV, Rohrer JD.. J Neurol. 2019;266(8):2075-2086. 5. Balendra R, Isaacs AM. Nat Rev Neurol. 2018;14(9):544-558.
FTD- frontotemporal dementia, ALS- amyotrophic lateral sclerosis

Overexpression of PGRN rescues a mouse model of TDP-43 pathology

PGRN reduces TDP-43 aggregation in a mouse model of TDP-43 pathology



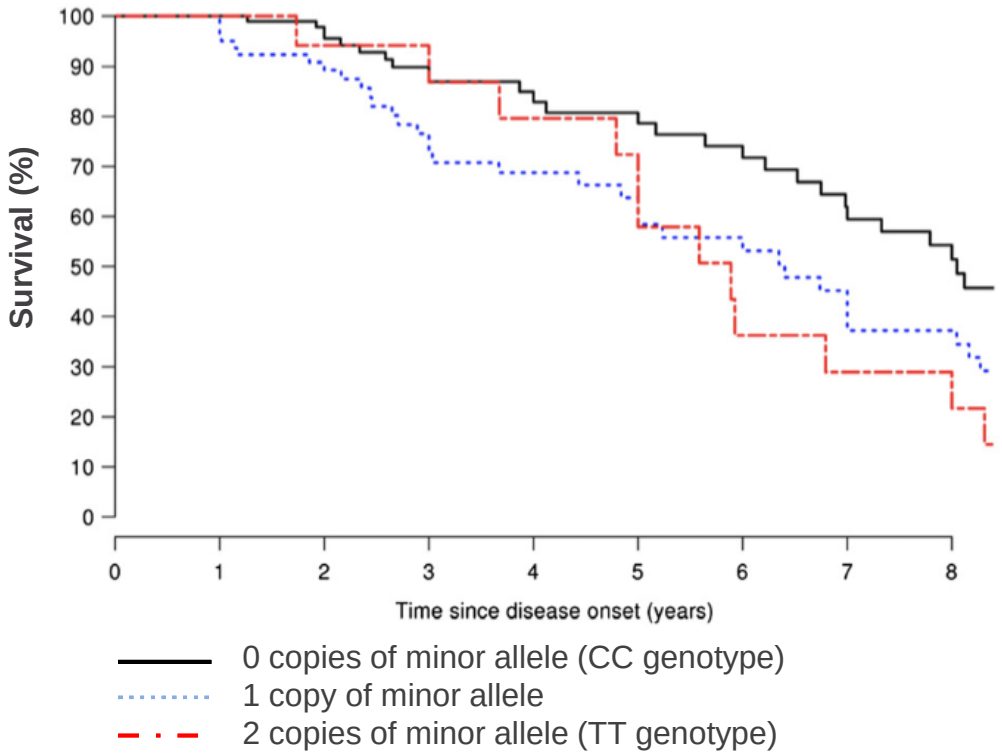
PGRN prolongs survival of TDP-43 overexpression mouse model



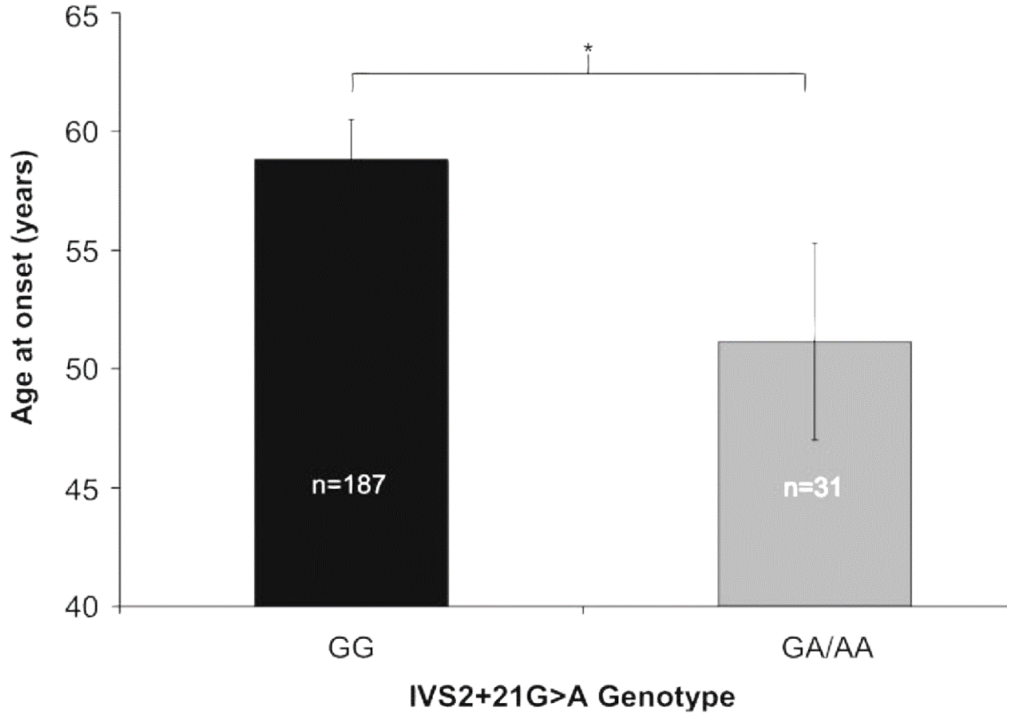
References: Beel S, Herdewyn S, Fazal R, et al. *Mol Neurodegener*. 2018;13(1):55.
PGRN- Progranulin, NTG- Non transgenic, GRN- Granulin, TDP-43- TAR DNA-binding protein 43

PGRN deficiency in humans exacerbates FTD and ALS

PGRN deficiency is associated with decreased survival after onset in FTD and ALS caused by *C9orf72* repeat expansion mutations



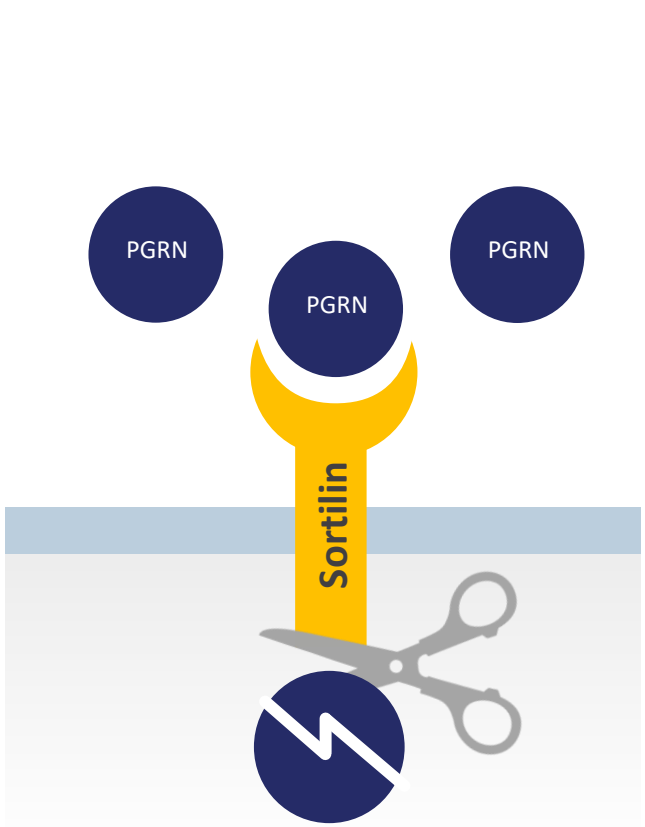
Earlier age of onset in ALS with PGRN missense mutations in idiopathic ALS



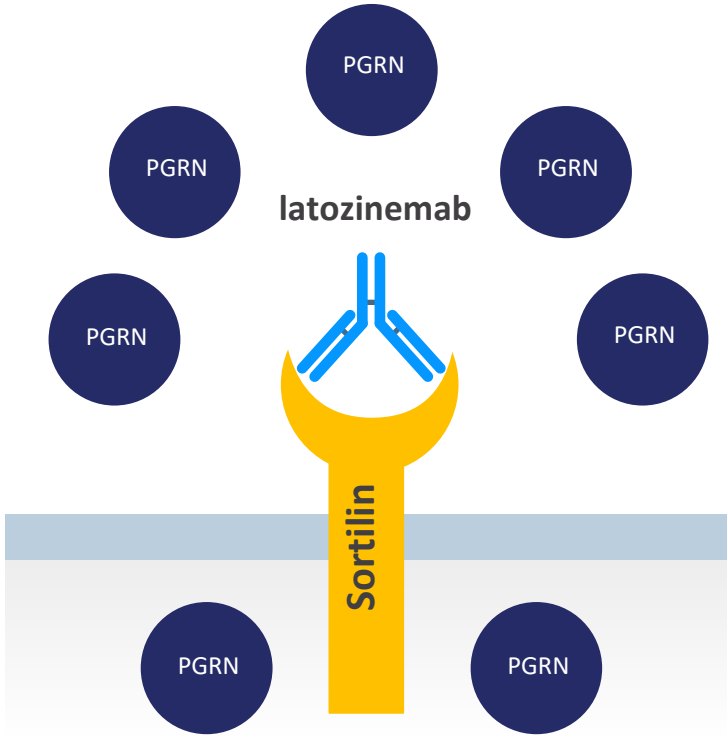
References: van Blitterswijk M, Mullen B, Wojtas A, et al.. Mol Neurodegener. 2014;9:38. (Left); Permission granted by the publisher. All rights reserved. © 2022. K. Sleegers, N. Brouwers, S. Maurer-Stroh, et al. Neurology Jul 2008, 71 (4) 253-259.Right)

Latozinemab (AL001) increases PGRN levels by blocking PGRN degradation

Latozinemab increases the half-life of PGRN by blocking a PGRN degradation receptor

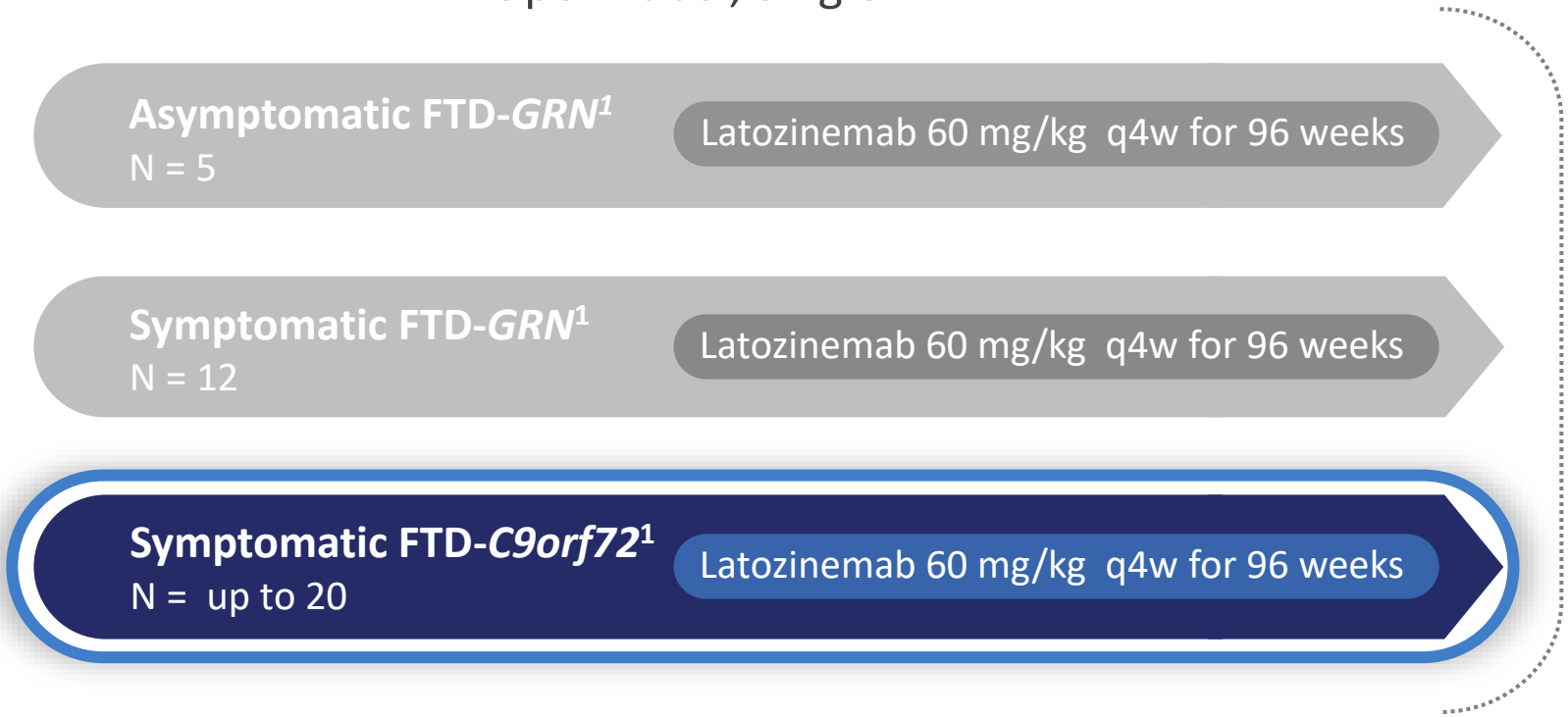


PGRN degradation



INFRONT-2: A Phase 2 open-label study evaluating latozinemab treatment in three different FTD patient cohorts

Open Label, Single Arm



Primary Endpoint:

- Safety and tolerability

Secondary Endpoints:

- PK, PD

Exploratory Endpoints:

- Clinical Outcome Assessment (CDR® plus NACC FTLD-SB[2])
- CSF, plasma & imaging biomarkers

Twelve-month biomarker and clinical data presented today is from symptomatic FTD-*C9orf72* 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 is well tolerated in INFRONT-2 FTD patients

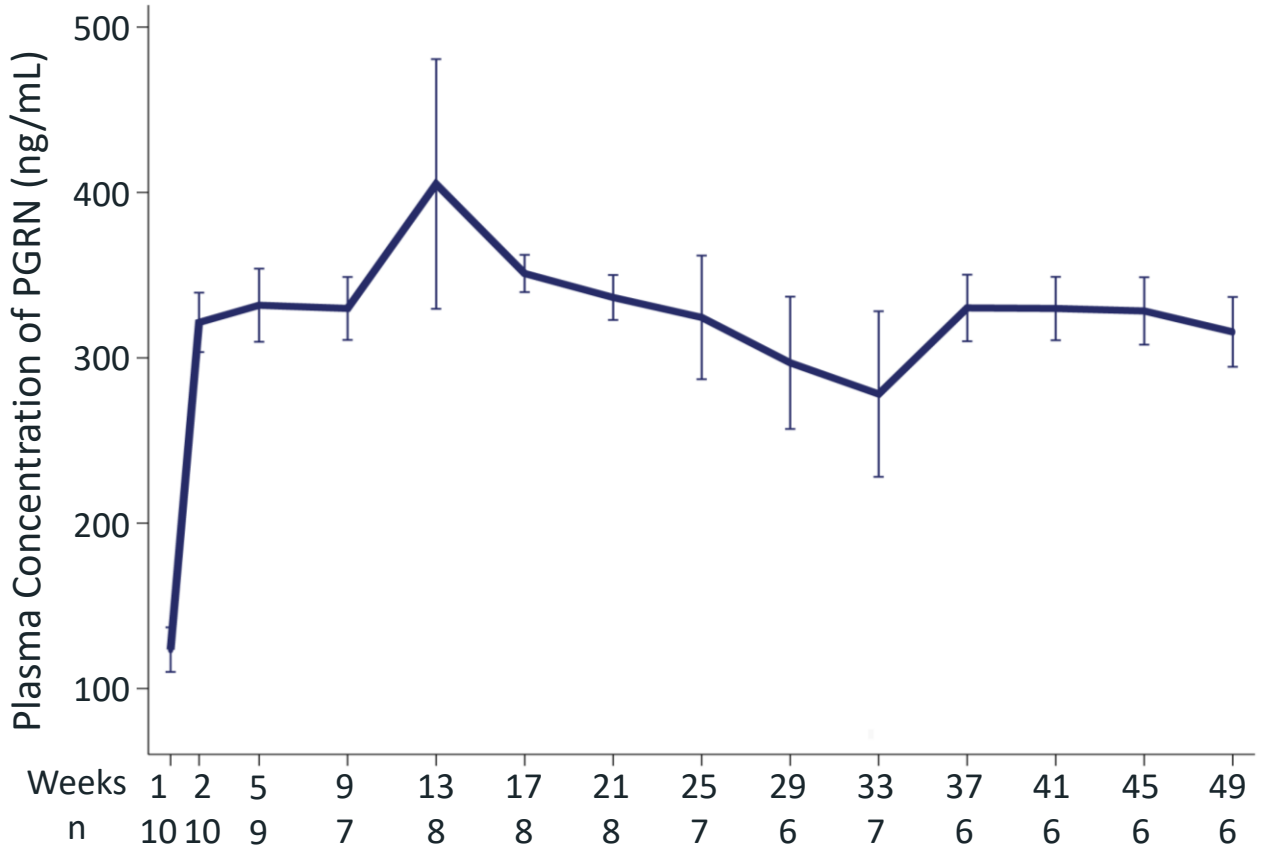
	aFTD-*GRN* (N=5) n (%)	FTD-*GRN* (N=12) n (%)	FTD-*C9orf72* (N=11) n (%)	Total (N=28) n (%)
Any TEAE	5 (100)	11 (92)	10 (91)	26 (93)
Any treatment-related TEAE[1]	2 (40)	3 (25)	7 (64)	12 (43)
Any SAE[2]	0	3 (25)	0	3 (11)
Any treatment-related SAE	0	0	0	0
Any TEAE leading to study drug discontinuation	0	0	0	0

Data cut: Electronic data capture extraction Jan 2022, TEAE = treatment emergent adverse event; SAE = serious adverse event
1. 4 most common AEs(>10%)- Fall, rash, UTI, HA (total population)
2. SAEs observed in study: pelvic venous thrombosis, syncope, pneumothorax

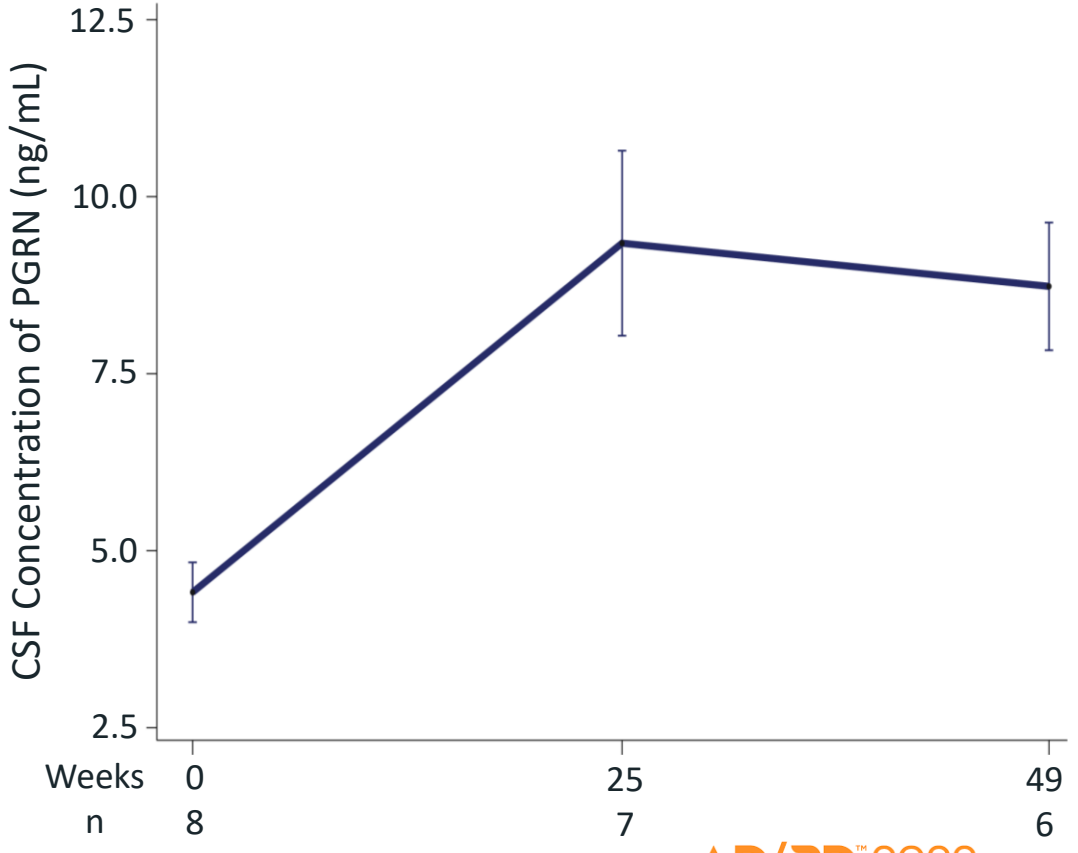
INFRONT-2: Latozinemab elevates PGRN in plasma and CSF in symptomatic FTD-*C9orf72* participants throughout treatment

TARGET ENGAGEMENT

PGRN plasma concentration



PGRN CSF concentration



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

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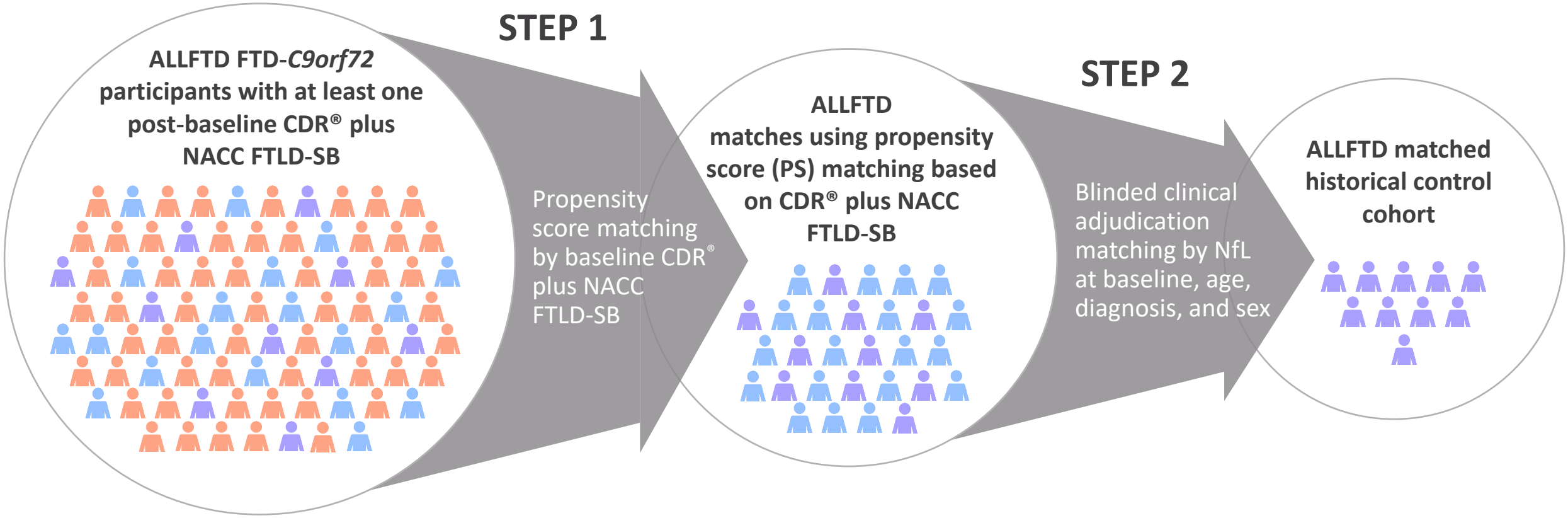
Blinded matching strategy to develop historical control cohort with ALLFTD

Rate of disease progression is primarily driven by CDR® plus NACC FTLD-SB at baseline



CDR® plus NACC FTLD-SB at baseline 0-22
N=84

CDR® plus NACC FTLD-SB 2.5-12
N=29

CDR® plus NACC FTLD-SB 2.5-12

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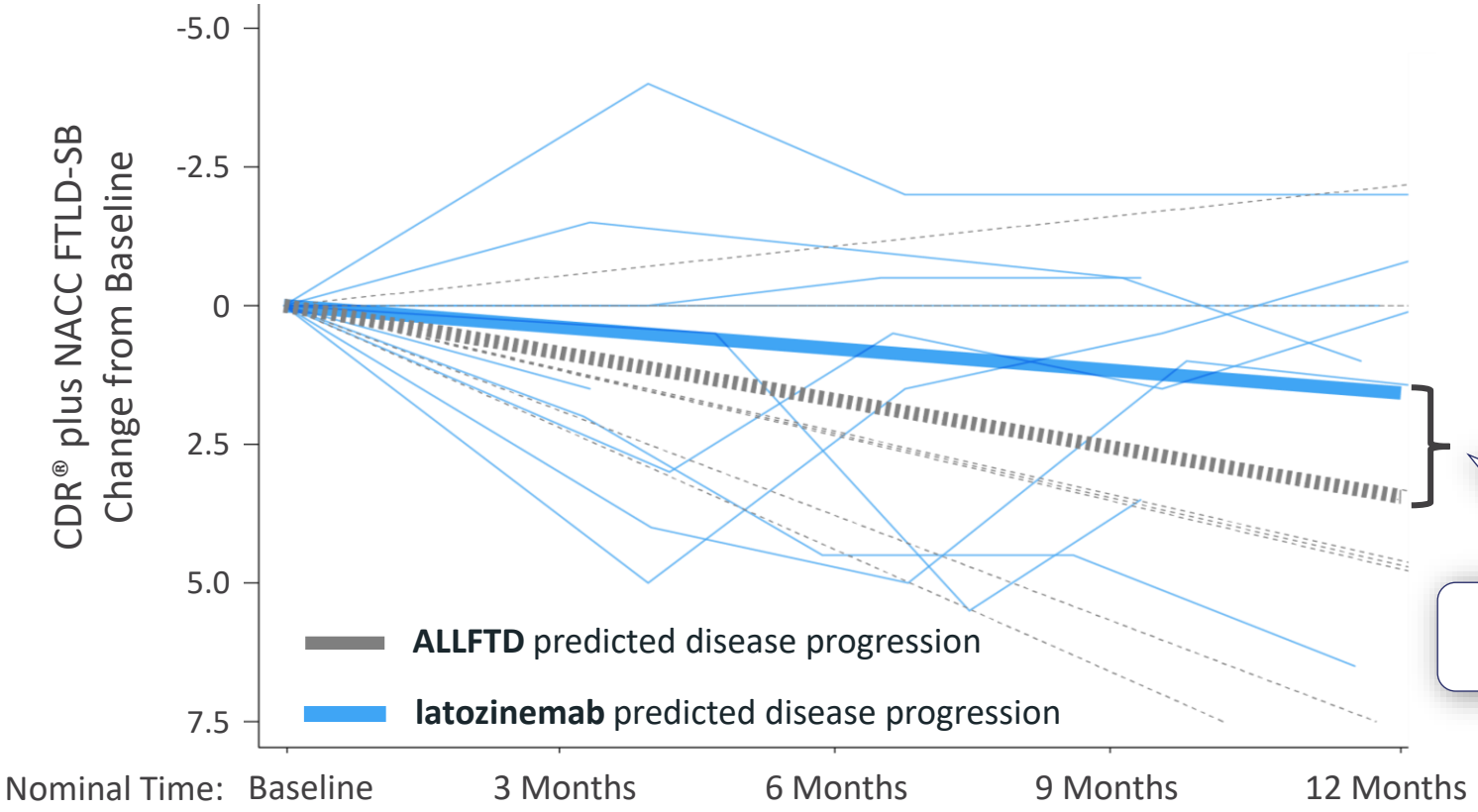
Comparable baseline characteristics between INFRONT-2 Phase 2 participants and ALLFTD matched historical controls

Baseline characteristics		latozinemab (N=10)	ALLFTD – Matched Historical Controls (N=10)
CDR® plus NACC FTLD-SB	**Mean (SD)**	**6.8 (3.31)**	**7.2 (3.48)**
	Min, Max	**2.5, 12.0**	**02.0, 12.5**
Age (Years)	Mean (SD)	61.8 (9.51)	61.3 (11.76)
	Min, Max	41, 75	33, 72
Sex	Male	6 (60%)	6 (60%)
	Female	4 (40%)	4 (40%)
Neurofilament (pg/mL)	N	10	9
	Mean (SD)	33.0 (28.25)	38.6 (24.81)
	Min, Max	9.1, 102.3	12.6, 91.3
Diagnosis	bvFTD	10 (100%)	8 (80%)
	PPA	0	0
	Both	0	0
	Other (FTD/ALS and MCI)	0	2 (20%)

When compared to the ALLFTD matched historical controls, latozinemab-treated FTD-*C9orf72* participants experience a ~54% annual delay in disease progression

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

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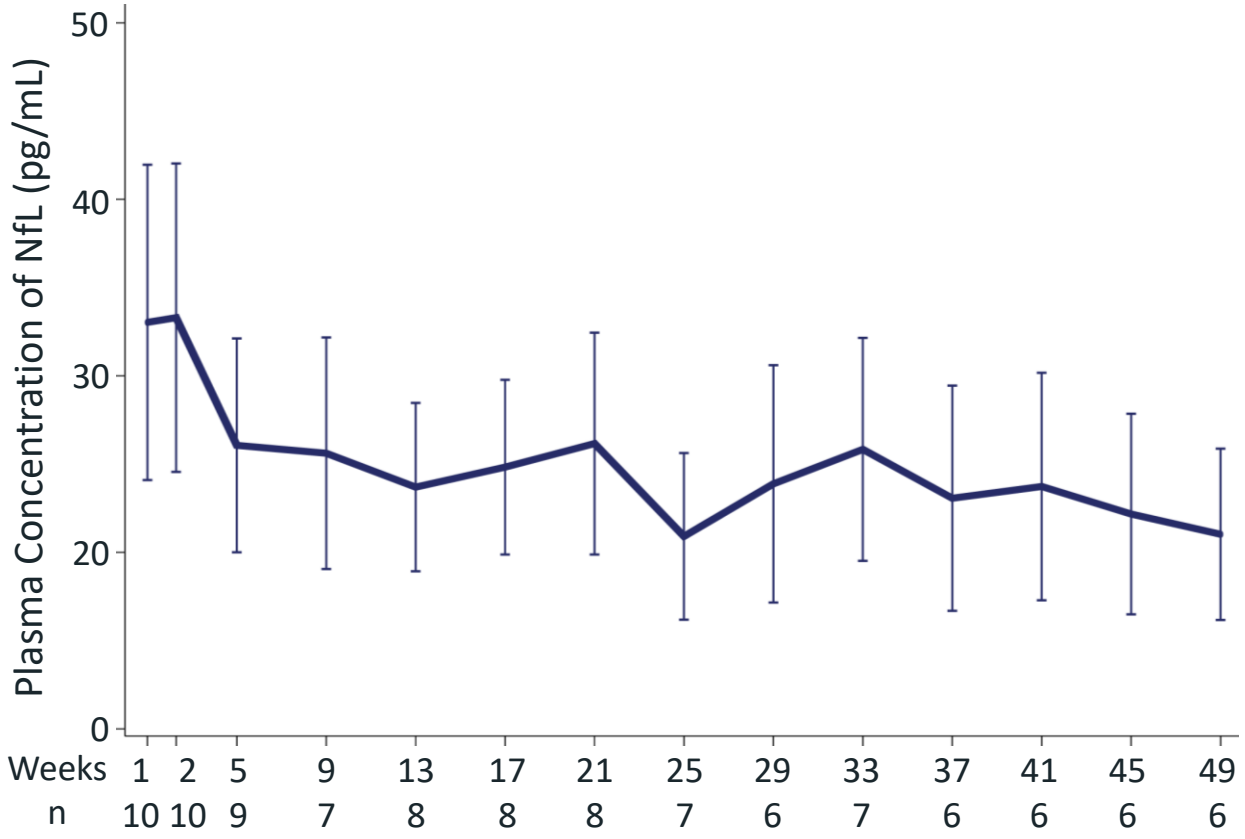
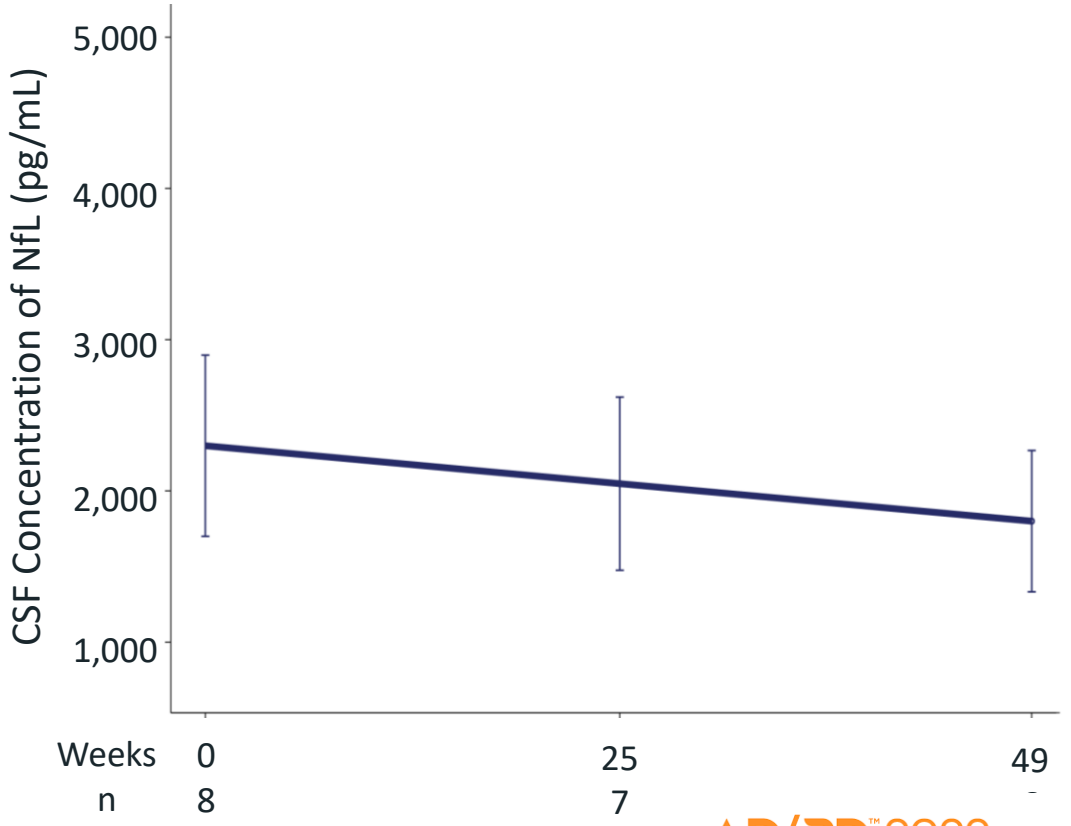
INFRONT-2: NfL levels in plasma and CSF are stable over 12 months in latozinemab-treated FTD-*C9orf72* participants

EXPLORATORY BIOMARKER – Neurofilament Light (NfL)

NfL Plasma Concentration



NfL CSF Concentration



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

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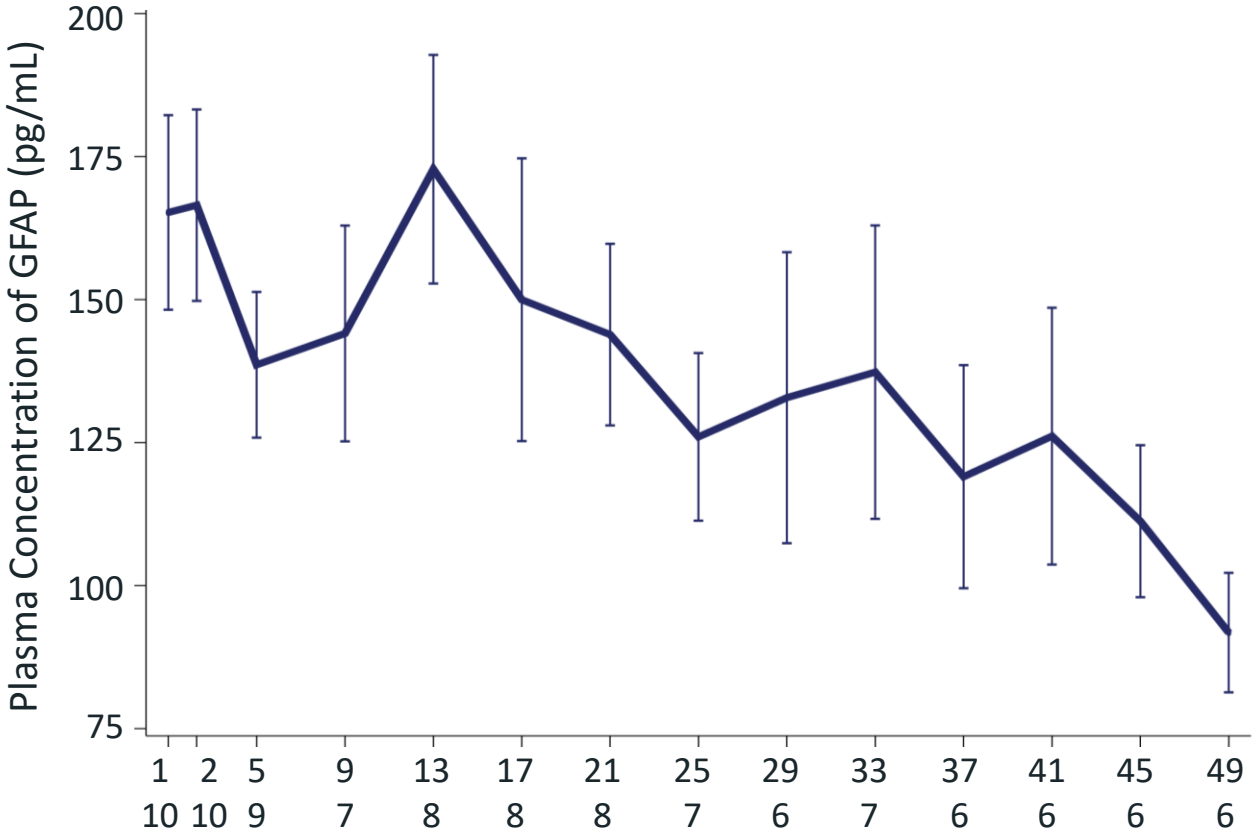
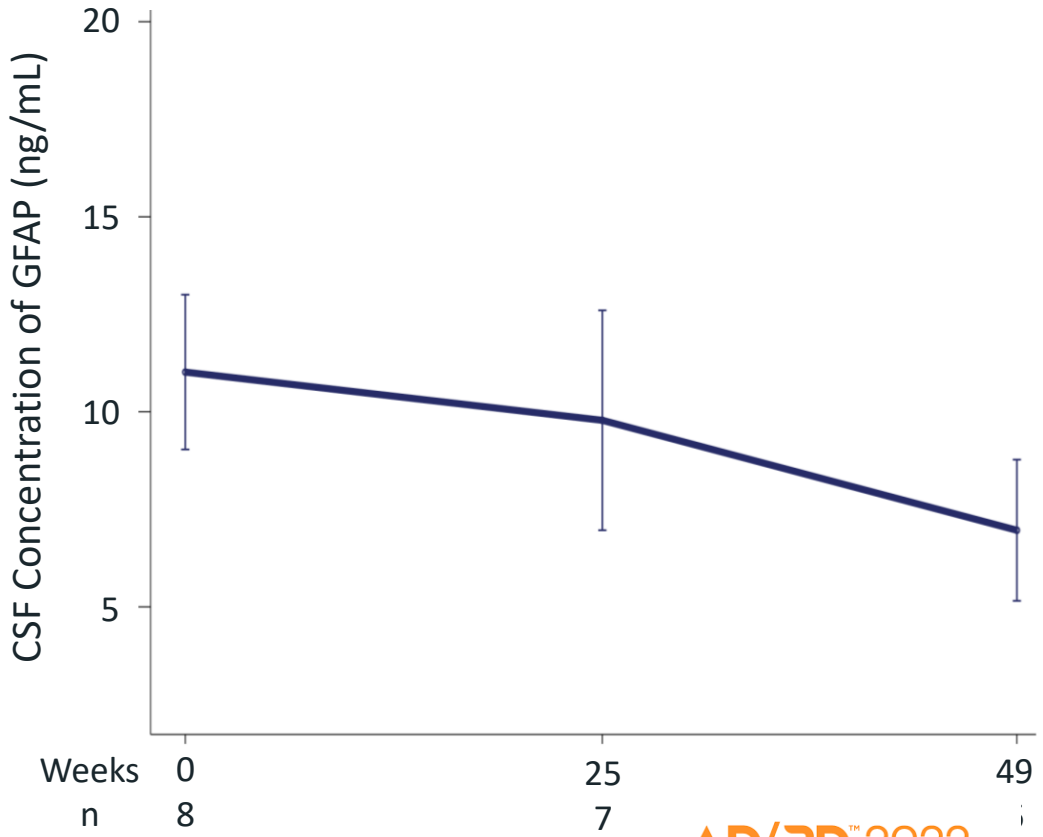
INFRONT-2: GFAP levels in plasma and CSF are decreased over 12 months in latozinemab-treated FTD-*C9orf72* participants

EXPLORATORY BIOMARKER – Glial Fibrillary Acidic Protein (GFAP)

GFAP Plasma Concentration



GFAP CSF Concentration



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

Summary

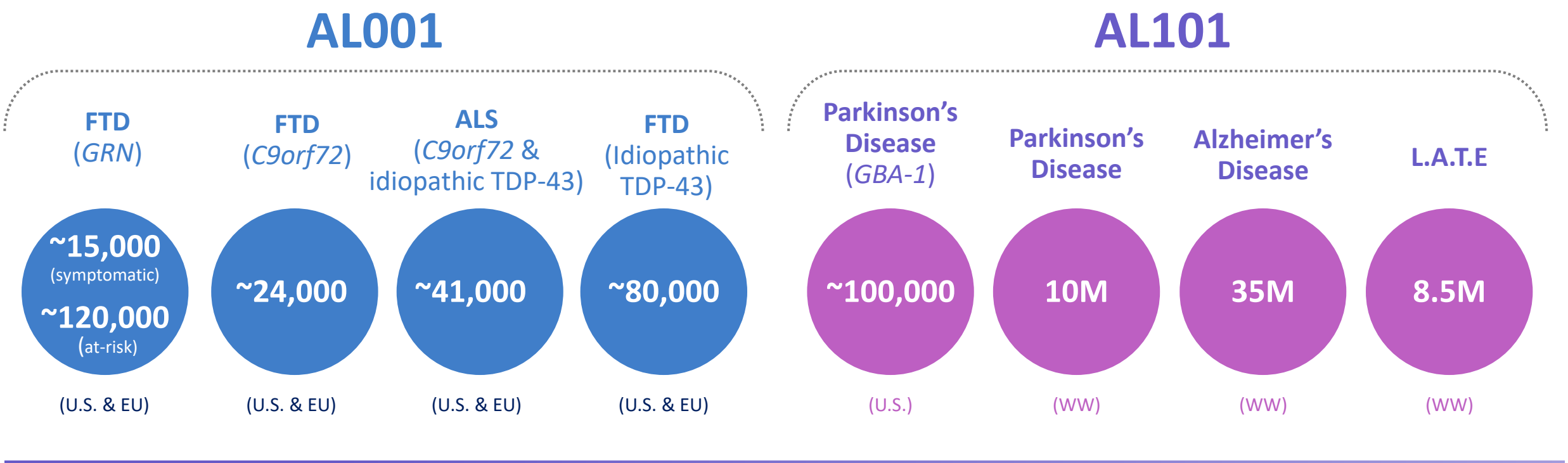
- Human genetics and preclinical studies provide scientific rationale for studying latozinemab in FTD-*C9orf72*
- Latozinemab demonstrated target engagement with an increase in PGRN in all patients and is well tolerated in participants treated for a median duration of 12 months
- We observed a trend toward benefit with a ~54% annual delay in disease progression in FTD-*C9orf72* patients treated with latozinemab
- Biomarker results support a trend towards clinical benefit:
  - Plasma and CSF NfL levels are stable after latozinemab treatment
  - Plasma and CSF GFAP levels are decreased after latozinemab treatment
- First example of elevation of PGRN above normal levels associated with potential benefit

Closing Remarks

Marc Grasso, M.D.

Chief Financial Officer

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

Q&A