November 2020

Harnessing the Immune System to Cure Neurodegeneration

ALECTOR

Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, 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,” “target,” “will” or the negative of these terms or other similar expressions.

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: the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results; the timing and focus of our future clinical trials, and the reporting of data from those trials; our plans relating to commercializing our product candidates, if approved; the expected potential benefits of strategic collaborations with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise; our estimates of the number of patients who suffer from the diseases we are targeting; our ability to expand our product candidates into additional indications and patient populations; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates; our plans relating to the further development and manufacturing of our product candidates, including additional indications we may pursue; our continued reliance on third parties to conduct additional clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and trials; our plans and ability to obtain or protect intellectual property rights; the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing; our financial performance; and the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements. 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, as discussed in greater detail in our filings with the Securities and Exchange Commission (SEC), including without limitation in our Quarterly Report on Form 10-Q, as filed on November 10, 2020 with the Securities and Exchange Commission (“SEC”). 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. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

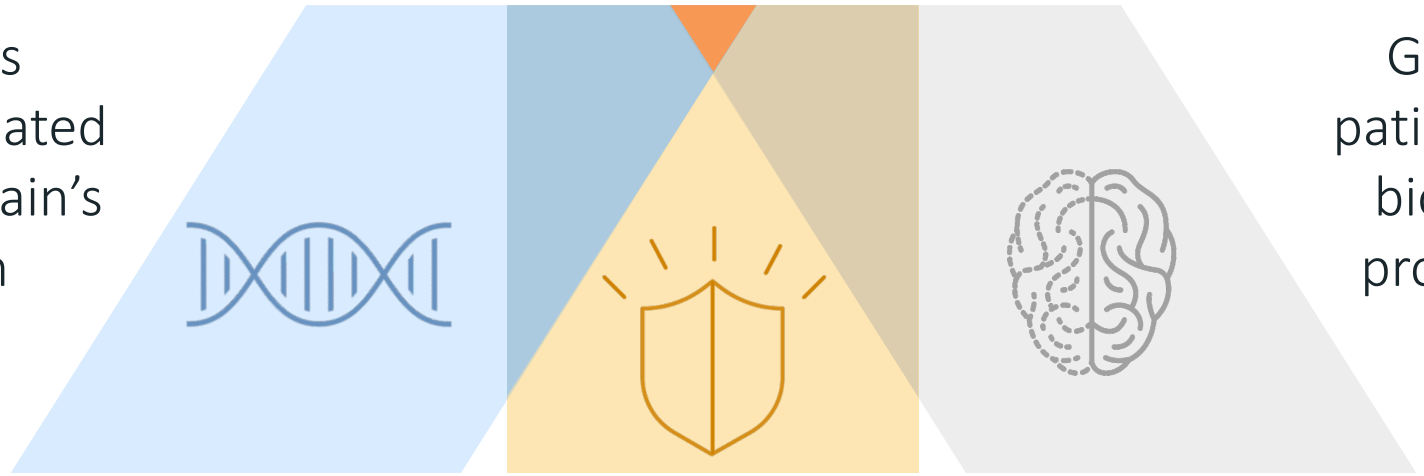
In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

Pioneering immuno-neurology

IMMUNO NEUROLOGY

Recruiting the brain's immune system
to cure neurodegeneration

Our therapeutics
are genetically validated
regulators of the brain's
immune system



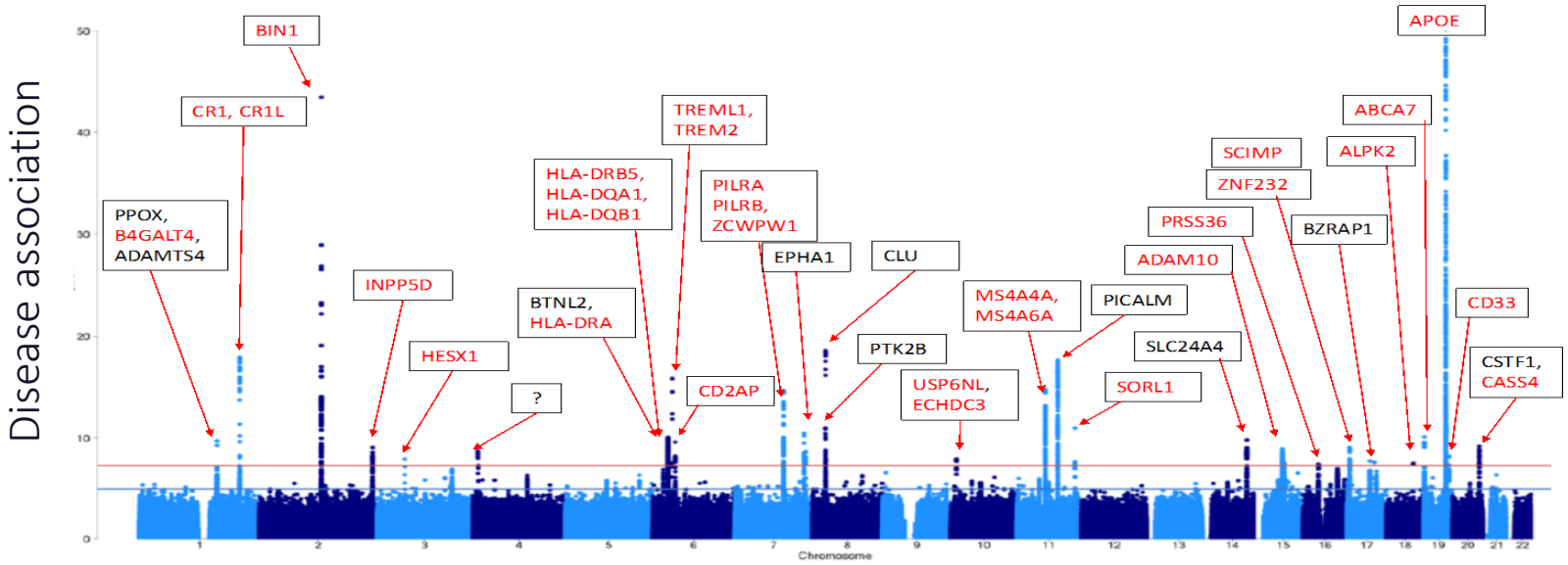
Genetically defined
patient populations and
biomarkers enhance
probability of success

Human Genetics Immunology Neuroscience

Human genetics has enabled a new therapeutic strategy

22/29

of AD risk genes are microglia specific (red)

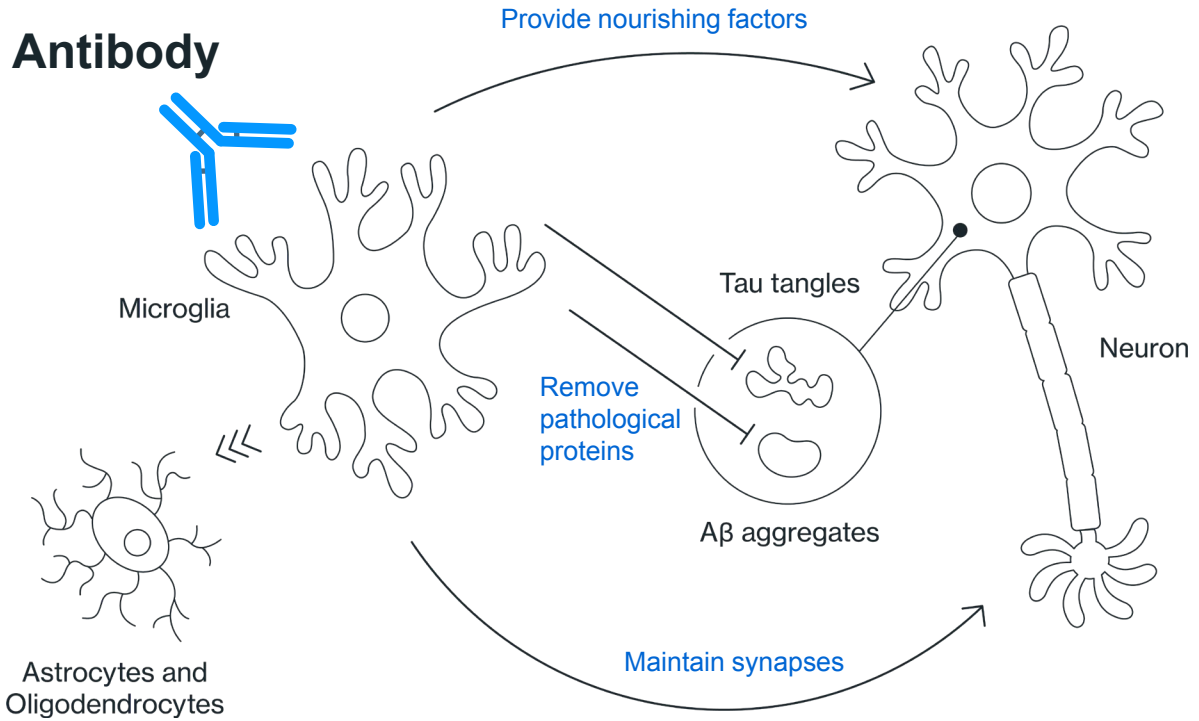


Annotated from Nature Genetics 2019 Mar;51(3):404-413

Our differentiated approach: Combining human genetics with our understanding of immunology and neurodegeneration

Our therapies are designed to restore the function of the microglia to treat these multiple parallel pathologies in order to slow or stop the progression of neurodegenerative disease

Alector's Immuno-Neurology Approach



Rapidly translating scientific leadership into emerging portfolio of first-in-class programs

Multiple first-in-class clinical programs

- Advanced **4 candidates** into the clinic since our founding
- **Advanced AL001 from preclinical to a Ph 3 study** in less than two years
- **Two** immuno-neurology programs for **Alzheimer's disease**, advancing to Ph 2
- **3 additional clinical ready** programs progressing forward

Robust discovery pipeline

- >120 immune system targets
- Progressed **14 programs** into R&D development
- **>200 patent applications**, 38 patent families and 6 issued U.S. patents

Current cash and equivalents of $461.7M* expected to fund operations through 2022

ALECTOR

*As of 3Q 2020
** FIH: first-in-human trials

Robust portfolio of product candidates targeting the innate immune system

PROGRAM	CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Progranulin	AL001	FTD-GRN					
	AL001	FTD-C9orf72					
	AL101	Neurology					
TREM2	AL002	Alzheimer's disease (AD)					abbvie
SIGLEC3	AL003	Alzheimer's disease (AD)					abbvie
MS4A4A	AL014	Alzheimer's disease (AD)					
SIRP-alpha	AL008	Cancer					Innovent
Multi-Siglec	ADP009	Cancer					
Research pipeline	ADP012						
	ADP016						
	ADP017						
	ADP023						
	ADP026						
	ADP122						
	ADP022						

Portfolio optimized for enhanced clinical success

Each development program incorporates:

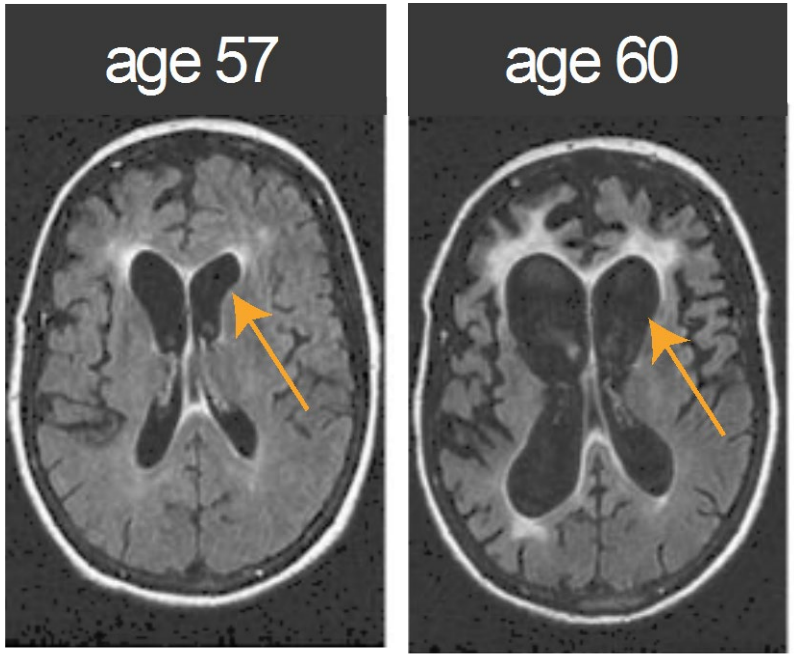
Proven, genetically validated targets

Biomarkers

Defined patient populations

FTD-*GRN* represents our initial indication from our first-in-class progranulin program

MRI of frontal and temporal atrophy in FTD



- Frontotemporal dementia (FTD) is a devastating and rapidly progressive form of dementia
- Early onset under the age of 60
- Life expectancy 7 - 10 years
- 170,000 FTD patients in (US + EU)
  - 15,000 patients with PGRN mutations (FTD-GRN)

Image source: Brain, Volume 129, Issue 11, 1 November 2006, Pages 3103–3114.
Note: Arrows added to MRI image of brain pointing to enlarged ventricles, a sign of brain atrophy.

AL001 scientific rationale: PGRN deficiency causal for FTD

Homozygous mutations (100% LOF)

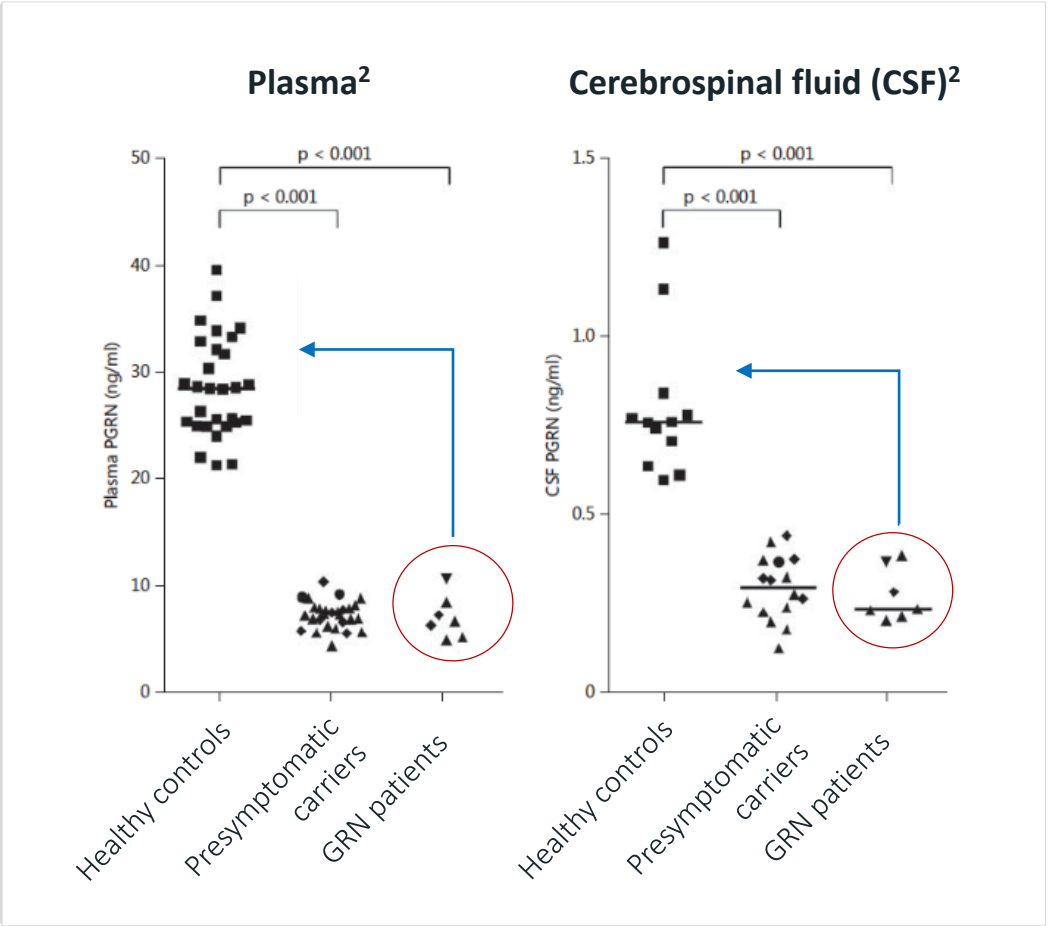
- 100% decrease in PGRN levels
- Dementia, vision loss, epilepsy, death[1]

Heterozygous mutations (50% LOF)

- >50% decrease in PGRN levels
- FTD with >90% penetrance
- Dementia, death within 7 - 10 years

Regulatory mutations (~20% LOF)

- ~20% decrease in PGRN levels
- Risk factor for Alzheimer's[3], Parkinson's diseases[3]



Note: LOF - loss of function.

(1) Sci Transl Med. 2017 Apr 12;9(385)
(2) Dement Geriatr Cogn Disord Extra 2016;6:330-340;
(3) Eur J Neurol. 2013 Dec;20(12):1571-3; Gene. 2014 Jun 1;542(2):141-5

AL001 for FTD-*GRN*: Targeting progranulin to restore function of microglia

MECHANISM OF ACTION

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

PHASE 1/2 DATA

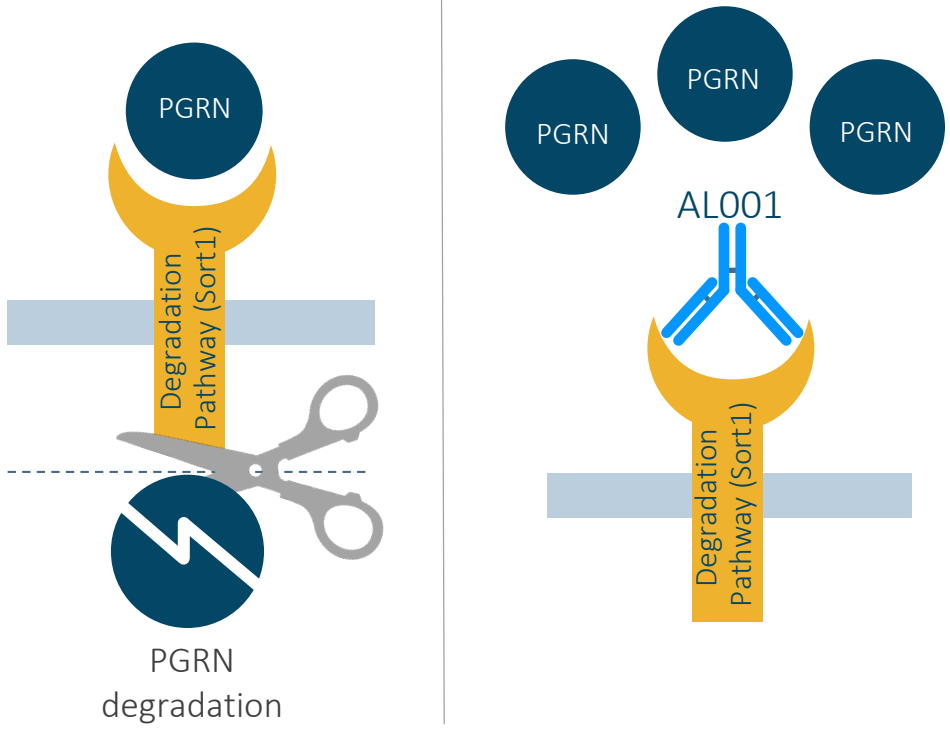
- AL001 was safe and well tolerated in healthy volunteers and patients and showed target engagement and restoration of PGRN

STATUS

- Pivotal Phase 3 study initiated in July 2020

REGULATORY

- Orphan Drug and Fast Track Designation



AL001 Phase 1 study design

In the Phase 1 study, AL001 was generally safe and well tolerated with no SAEs or DLTs reported

Phase 1a Dose Escalation (N = 50)

Healthy Volunteers	AL001 dose escalation 1 dose	N = 50

STUDY OBJECTIVES: Safety and tolerability, Pharmacokinetic (PK), and pharmacodynamic (PD) markers in blood and CSF

Phase 1b Open Label (N = 14)

Asymptomatic FTD-*GRN*	AL001 60 mg/kg 1 dose	N = 6
Symptomatic FTD-*GRN*	AL001 30 mg/kg q2w x 3 doses	N = 8

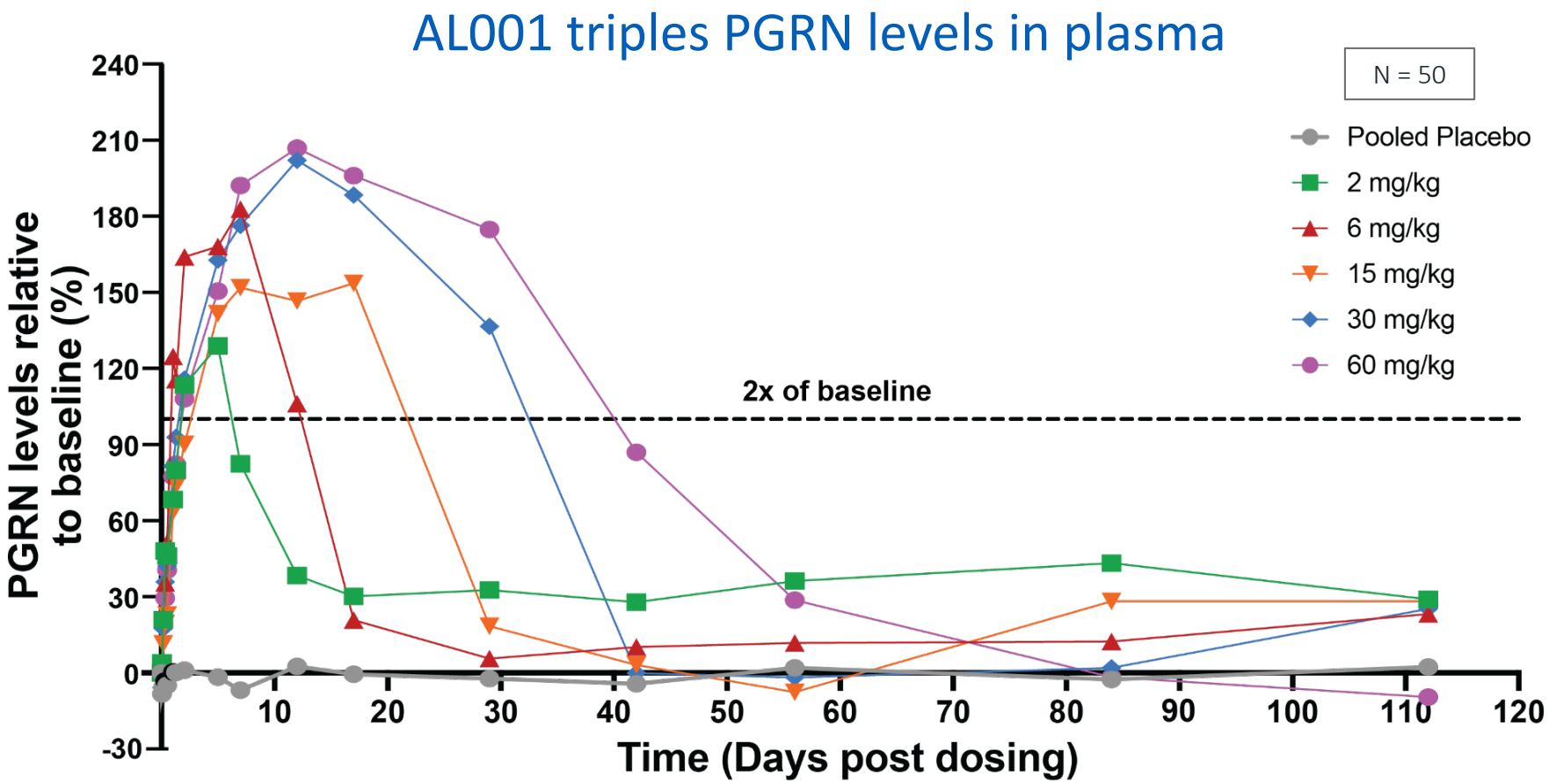
PRIMARY ENDPOINT: Safety and tolerability

SECONDARY ENDPOINT: Pharmacokinetic (PK)

EXPLORATORY: Pharmacodynamic (PD) markers in blood and CSF

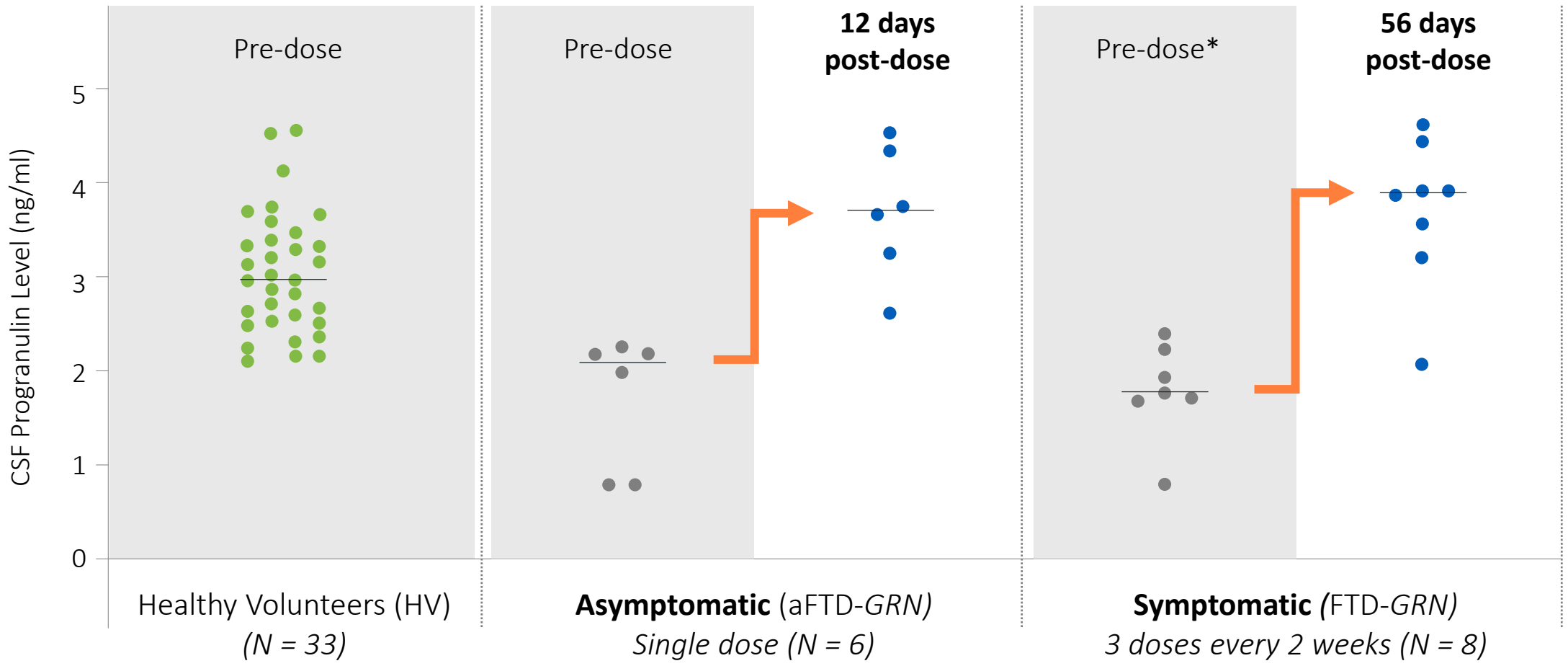
AL001 increased plasma progranulin in healthy volunteers

AL001 was generally safe and well tolerated



Phase 1 data shows AL001 restores PGRN levels back to the normal range

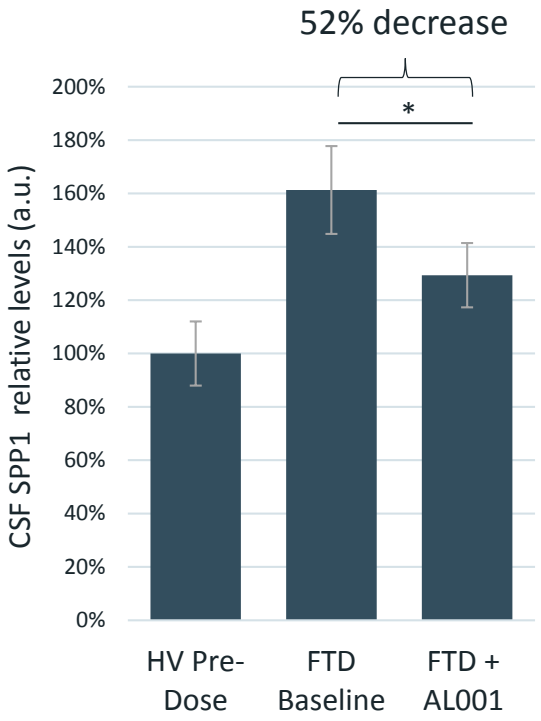
Sustained increase in CSF PGRN in AL001 Phase 1b study



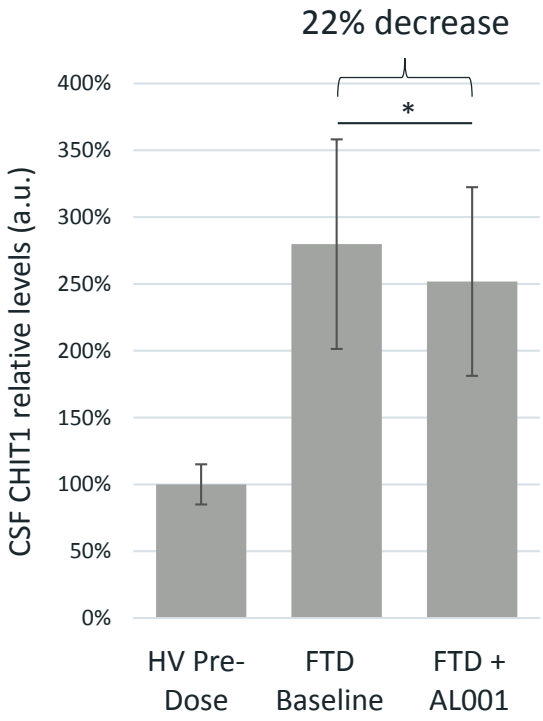
Individual dots represent individual subjects. Horizontal line represents the median.
* One symptomatic subject did not have a reportable CSF PGRN baseline level which complied with Core lab SOP and was therefore excluded.

AL001 counteracts disease protein signature by normalizing inflammatory and lysosomal biomarkers and demonstrates a decrease in NfL in Phase 1b

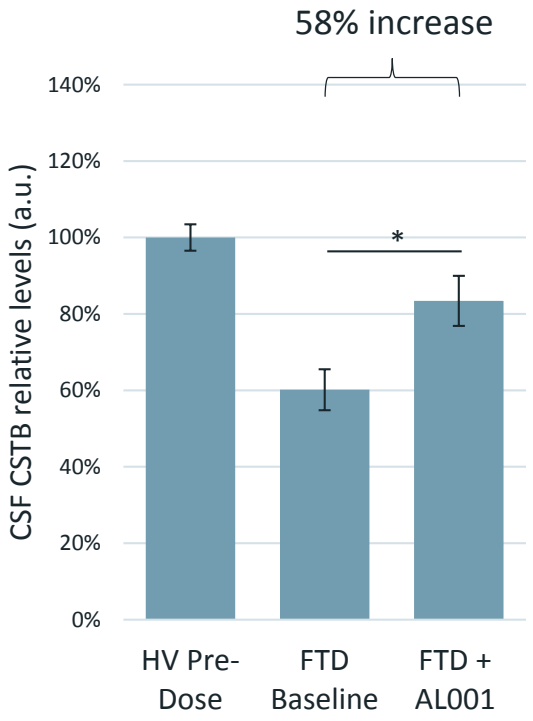
AL001 reduced CSF Osteopontin (SPP1), a marker of inflammation



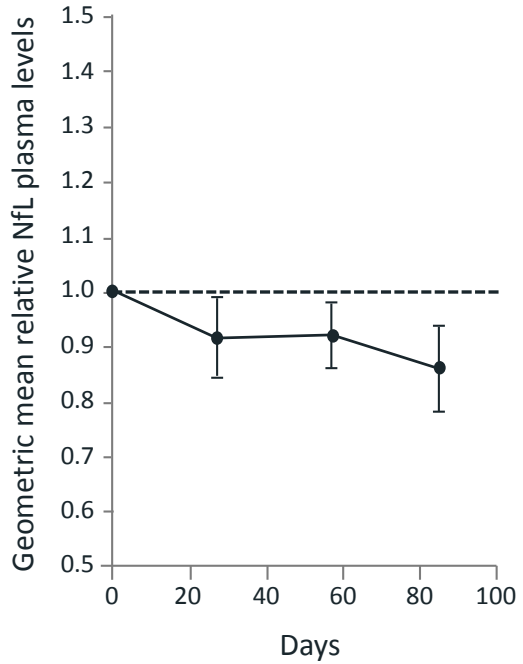
AL001 reduced CSF Chitotriosidase (CHIT1), a marker of gliosis



AL001 increased CSF Cathepsin B (CTSB), a marker of lysosomal function

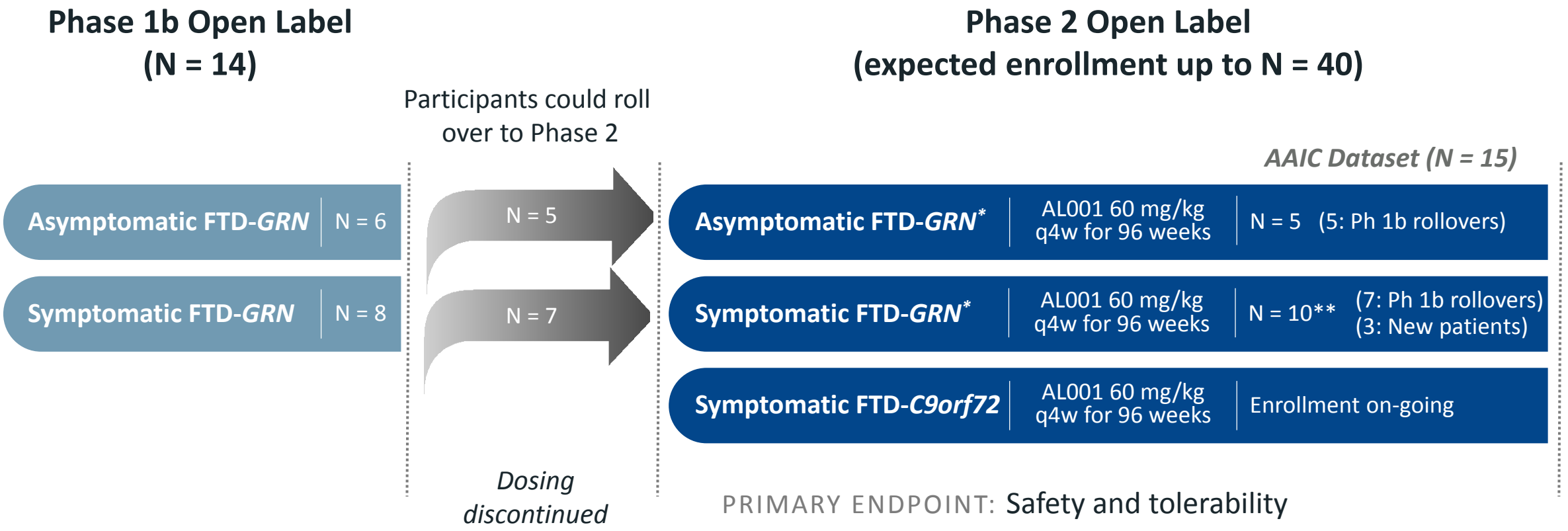


Trend in reduction of plasma Neurofilament (NfL) levels from baseline in Phase 1b[1,2]



Note: * represents p<0.05
NfL = Neurofilament light chain
1 Alector Research and Development Day presentation, December 13, 2019
2 SEM: standard error of the mean

AL001 Phase 1b participants had the option to rollover into Phase 2



PRIMARY ENDPOINT: Safety and tolerability

SECONDARY ENDPOINT: PK

EXPLORATORY: PD markers in blood and CSF, volumetric MRI (vMRI), Clinical Outcome Assessments

ALECTOR

* Asymptomatic and Symptomatic FTD-*GRN* enrollment closed.

** Due to COVID-19 mediated site closures, 2/10 patients missed a dose and biomarker evaluations.

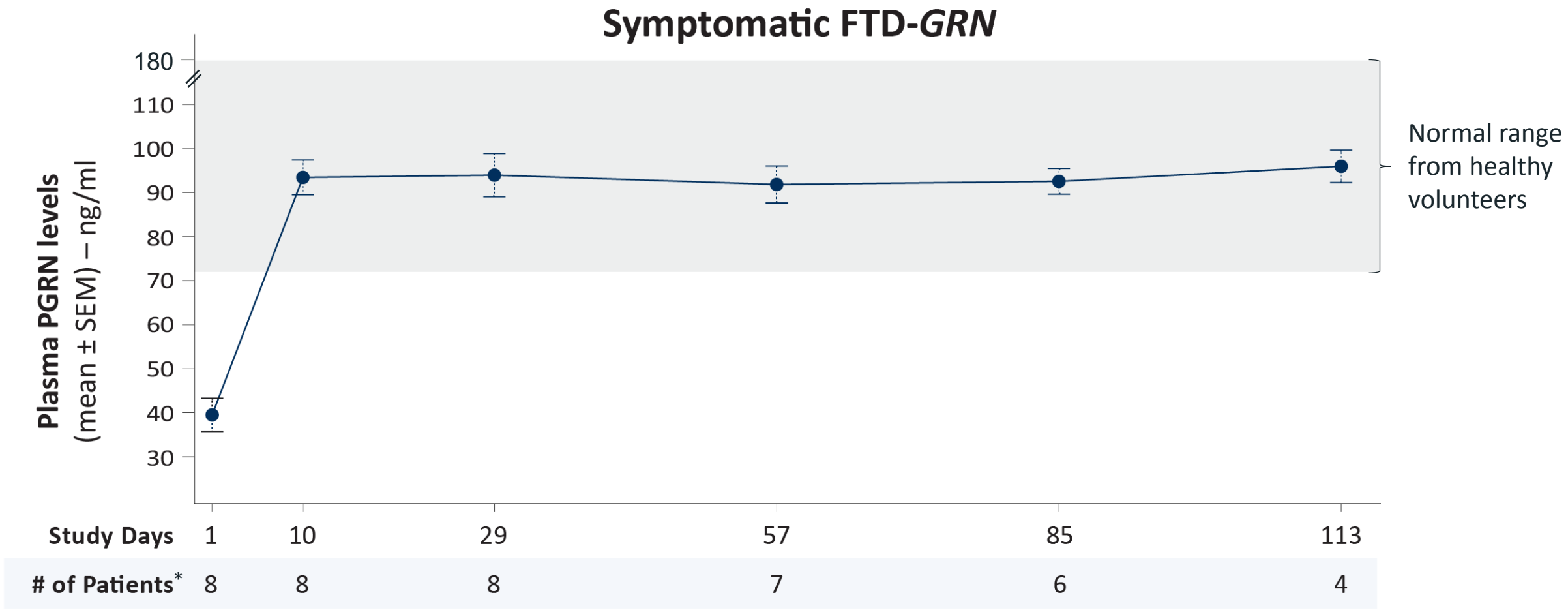
AL001 Phase 2: Generally safe and well tolerated in FTD-*GRN* participants

	aFTD-*GRN* (N=5) | n (%)	**FTD-*GRN* (bvFTD and PPA)** (N=10) | n (%)	**Total** (N=15) | n (%)
Any TEAE	4 (80.0)	4 (40.0)	8 (53.3)
Any Severe TEAE	0	1* (10.0)	1* (6.7)
Any Treatment-Related TEAE	1 (20.0)	0	1 (6.7)
Any Treated-Related Severe TEAE	0	0	0
Any SAE	0	1* (10.0)	1* (6.7)
Any TEAE Leading to Study Drug Discontinuation	0	1* (10.0)	1* (6.7)
Any TEAE Leading to Study Discontinuation	0	0	0

** One participant had an unrelated severe SAEs (deep venous thrombosis) with onset date ~7 weeks after the last dose that led to treatment discontinuation. All other TEAEs were mild in severity.*

Data cut-off: 13 April 2020
Note: aFTD = asymptomatic carriers of a GRN mutation causative of FTD; bvFTD = behavioral variant FTD; PPA = primary progressive aphasia, TEAE = Treatment Emergent Adverse Event

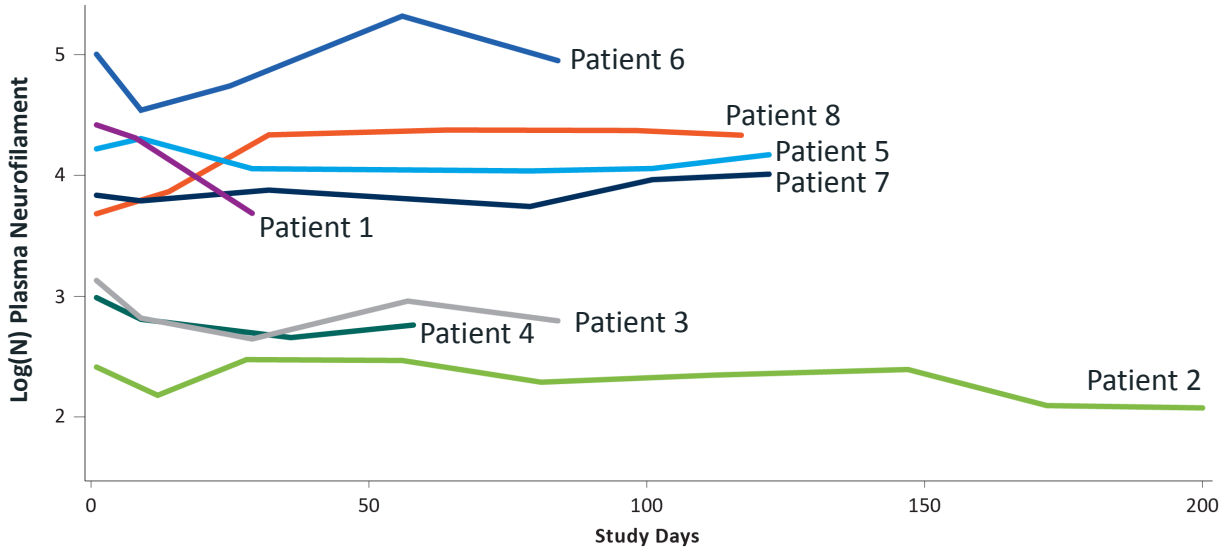
Phase 2 data shows plasma PGRN restored to normal in FTD-*GRN* participants



Data cut-off: 14-May 2020
SEM: standard error of the mean
Solid circles represent the mean and the dashed bars represent the standard error of the mean.
*Due to COVID-19 mediated site closures, 2/10 patients missed a dose and biomarker evaluations.

Six out of eight participants in Phase 2 showed a decrease in NfL at their last measured timepoint

Natural Log of Plasma Neurofilament Level Over Time Symptomatic FTD-*GRN* (N=8*)



Plasma NfL levels – Symptomatic FTD-*GRN* (N=8*)

	Plasma NfL (pg/mL)			
Patient	Baseline	Last Measured Timepoint	% Change in NfL from Baseline	Last Measured Timepoint
1	82.9	39.9	(52%)	Day 29
2	11.2	8.0	(29%)	Day 200
3	22.9	16.4	(28%)	Day 85
4	19.8	15.8	(20%)	Day 58
5	68.0	64.8	(5%)	Day 122
6	148.8	141.2	(5%)	Day 85
7	46.3	55.1	19%	Day 122
8	39.7	76.1	92%	Day 117

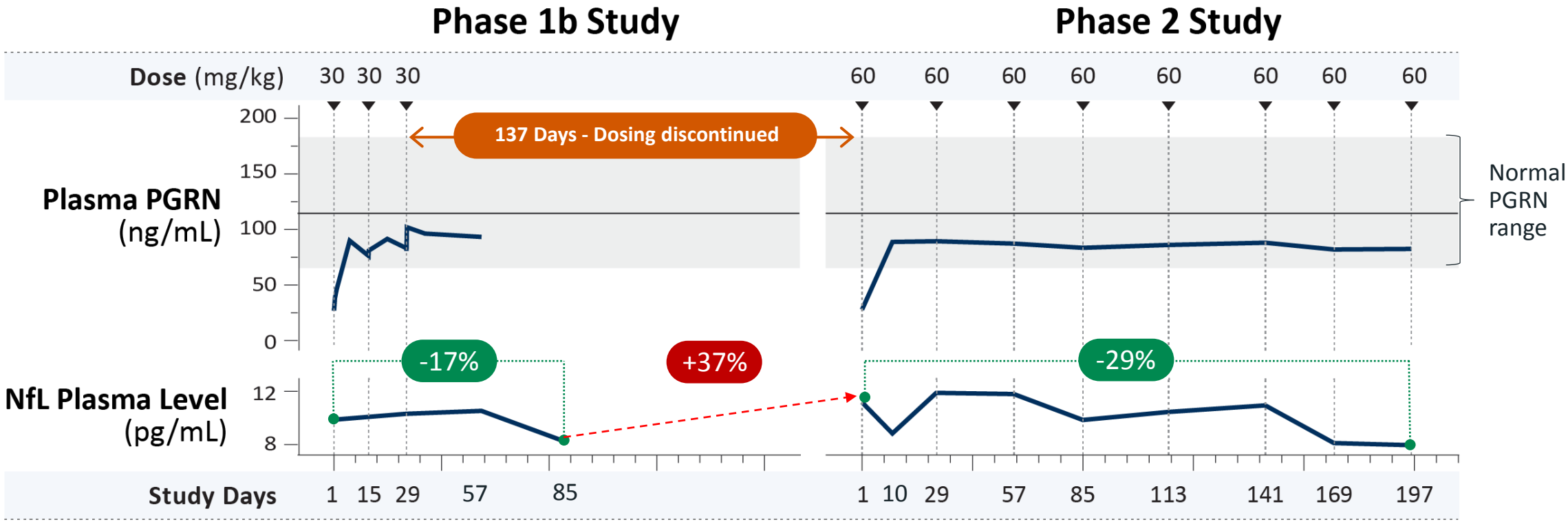
ALECTOR

Phase 2 data cut-off: 14-May-2020
*Due to COVID-19 mediated site closures, 2/10 patients missed a dose and biomarker evaluations.

AL001 case study: 47yo FTD-*GRN* patient with primary progressive aphasia

197 days of uninterrupted dosing shows a decrease in NfL

- Patient enrolled and completed Phase 1b, PGRN levels normalized and NfL decreased
- Patient had a 137-day gap between last dose in Phase 1b and enrollment in Phase 2, during which NfL increased by 37%
- After being on drug for 197 days in the Phase 2, without interruption, patient's NfL decreased by 29%

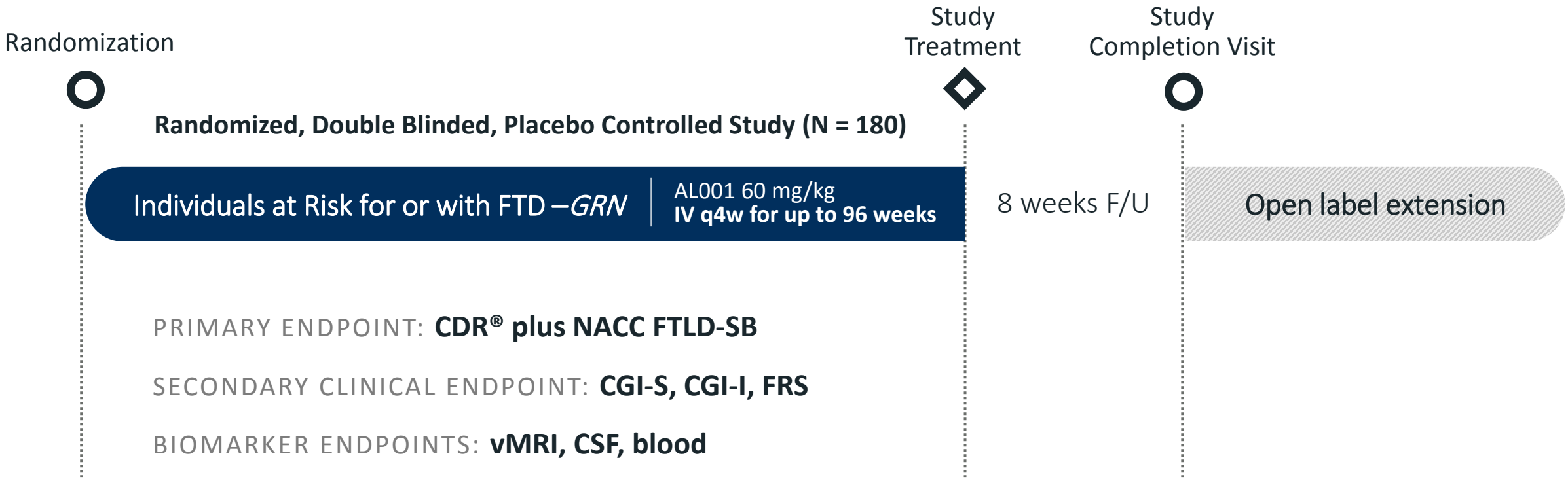


AL001 program next steps

- FTD-C90rf72 patients will **continue the enrollment in Phase 2** (up to 20 total)
- **Present additional data** from the Phase 2 trial of AL001 in pre-symptomatic and symptomatic FTD-GRN participants and an additional cohort of FTD-C9orf72 patients in 2021
- Continue to **execute INFRONT-3 pivotal Phase 3**

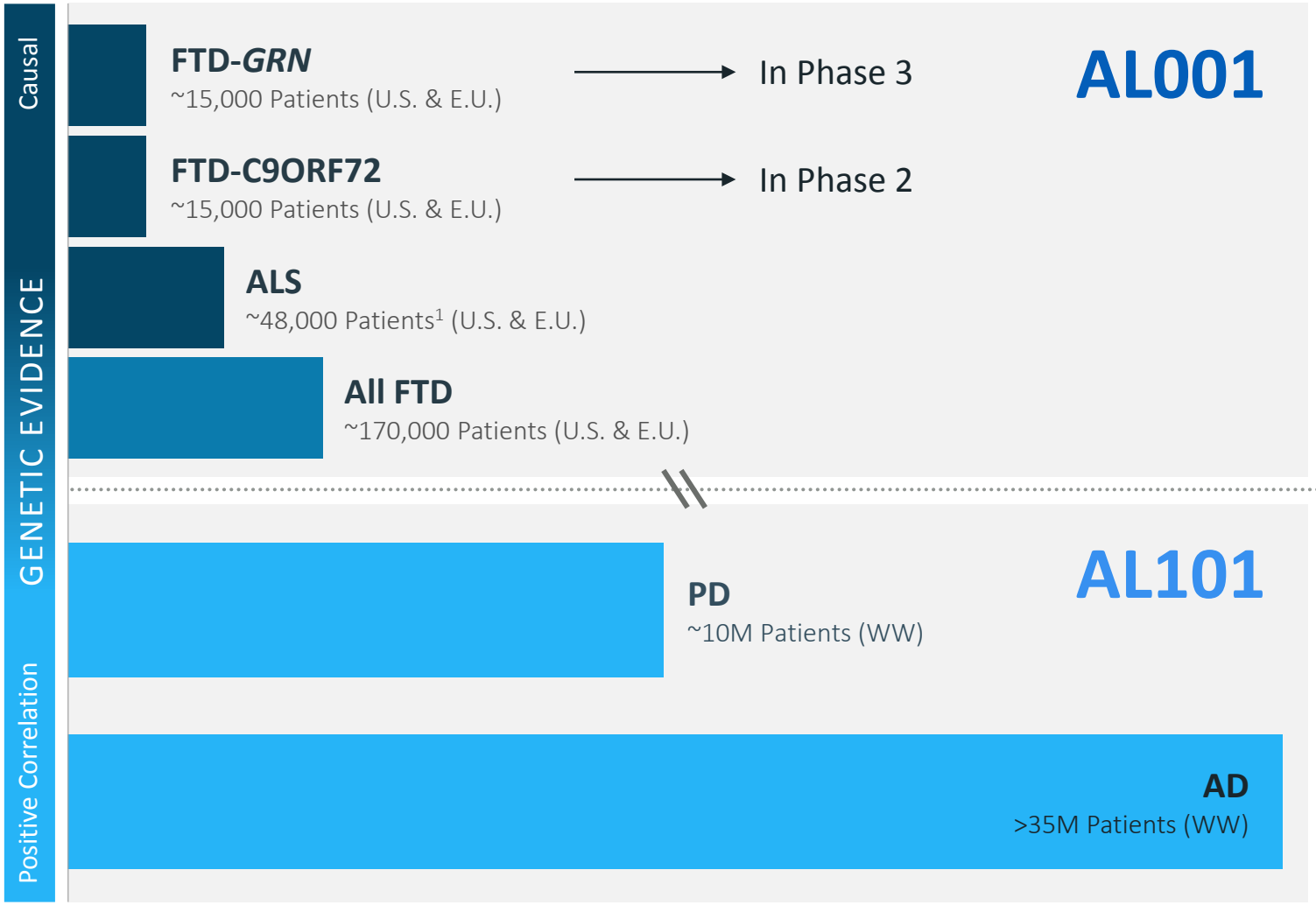
AL001 next steps: Pivotal Phase 3 study initiated in July 2020

Approximately 50 clinical centers, including GENFI and ALLFTD registry sites, will be included in the global Phase 3 study



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

Targeting PGRN beyond FTD-*GRN*: Indication expansion



Note: Figure not to scale.

- On-going Phase 2 study includes FTD-*C9orf72* cohort
- Additional indications include ALS and/or all FTD patients regardless of mutation

- Ongoing Phase 1 study assessing the safety and tolerability in healthy volunteers with data expected in 2021.

1. Nat Commun. 2016 Aug 11;7:12408.

Alzheimer’s disease represents a significant unmet need

No disease modifying therapeutics available

Most common form of dementia[1]

Initial onset in patients **over 65**[2]

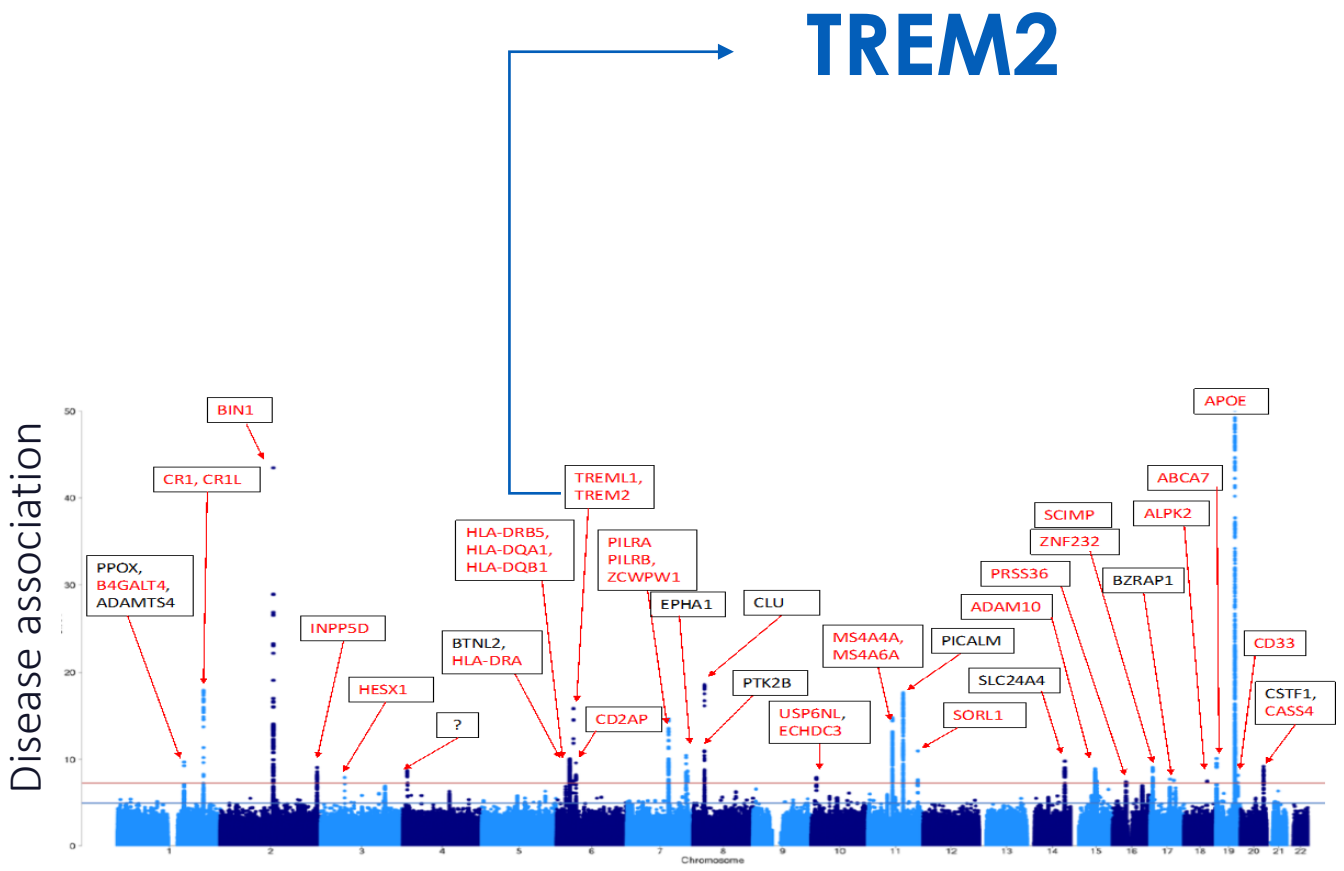
~5.7 million[2] cases in the U.S. in 2018 with projections to rise to nearly **14 million in 2050**[2]

6th[3] leading cause of death in the U.S.

Past development programs focused on single pathology of disease, such as beta amyloid and tau proteins, which did not yield success.

1. Wilson RS, Segawa E, Boyle, PA, Anagnos SE, Hizel LP, Bennett DA. The natural history of cognitive decline in Alzheimer’s disease. Psychol Aging 2012;27(4):1008-17.
2. Alzheimer's Association, "2018 Alzheimer's Disease Facts and Figures"[Alzheimer’s Association]
3. NIH National Institute of Aging, “Alzheimer's Disease Fact Sheet”

TREM2 has the strongest genetic links to Alzheimer's disease after only APOE4



- TREM2 homozygous loss of function may cause neurodegeneration by age 40, with a lifespan of ~10 years following diagnosis
- TREM2 heterozygous loss of function increases risk for AD by 3x
- A SNP (rs9381040) associated with increased TREM2 expression is protective against AD

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

AL002 for AD: Targeting TREM2 to recruit microglia to counteract disease pathologies

MECHANISM OF ACTION

- Antibody designed to activate TREM2 and enhance microglia activity

PHASE 1 DATA

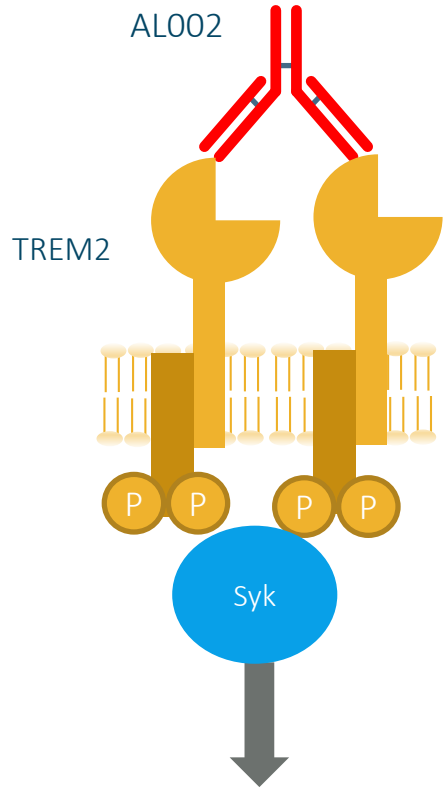
- AL002 successfully achieved its primary and secondary endpoints in the Phase 1 study

STATUS

- Initiating Phase 2 in 2020

PARTNER

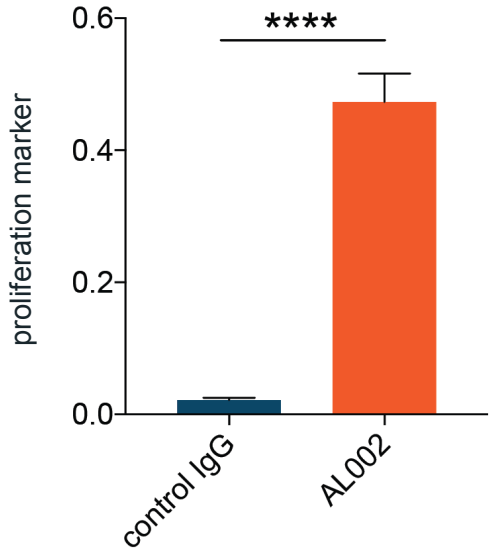
- Global 50/50 profit and cost share partnership with AbbVie



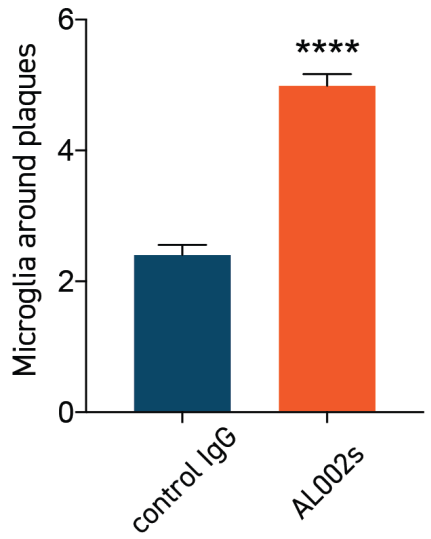
Improve survival, proliferation, function of microglia

AL002 recruits microglia to counteract pathologies in AD mouse model

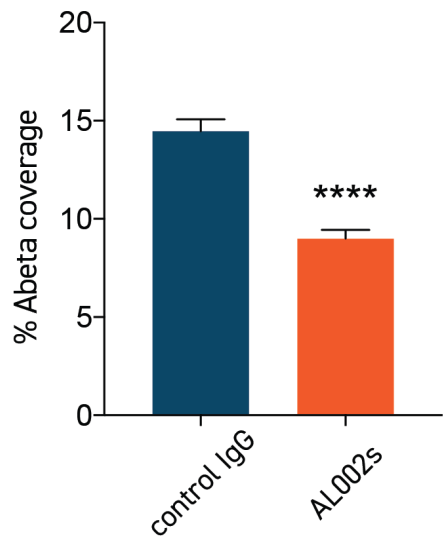
AL002 strongly increases a marker of microglial proliferation



AL002s recruit microglia to plaques[1]



AL002s reduces area occupied by plaques[1]

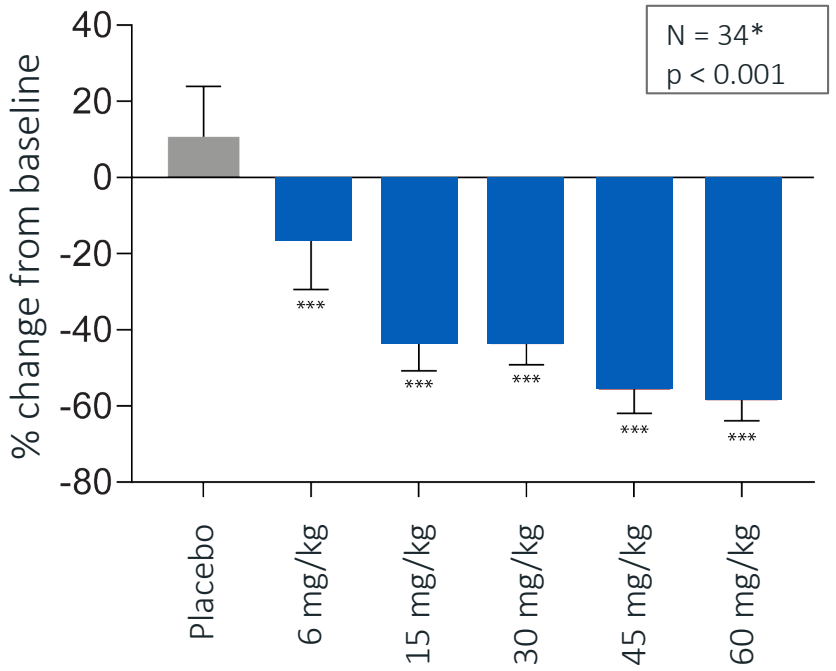


**** indicates a p-value < 0.0001 by T-test.
(1) Data generated by D. Wilcock, University of Kentucky

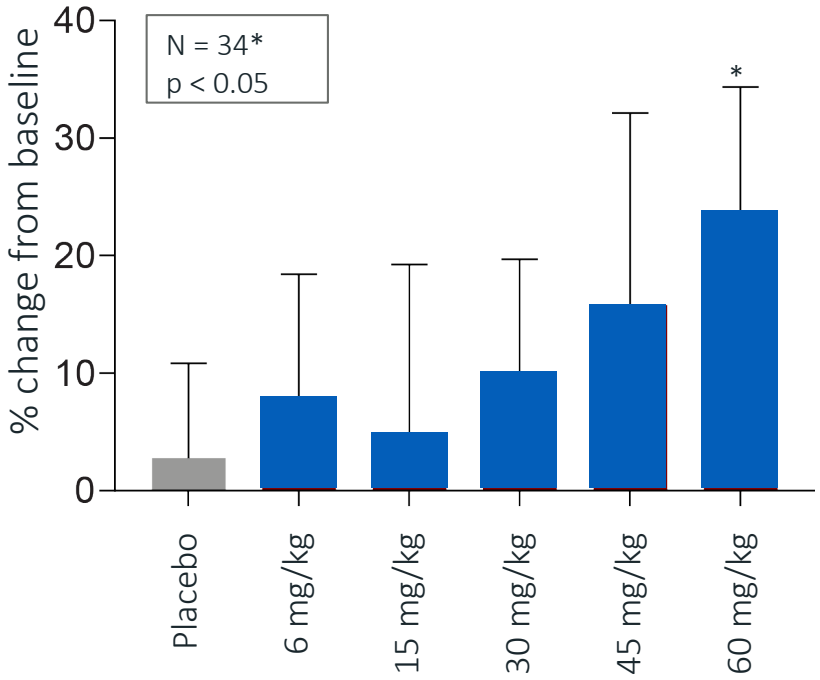
Target engagement and proof-of-mechanism in CSF achieved in Phase 1

AL002 was found to be generally safe and well-tolerated in 34 healthy volunteers

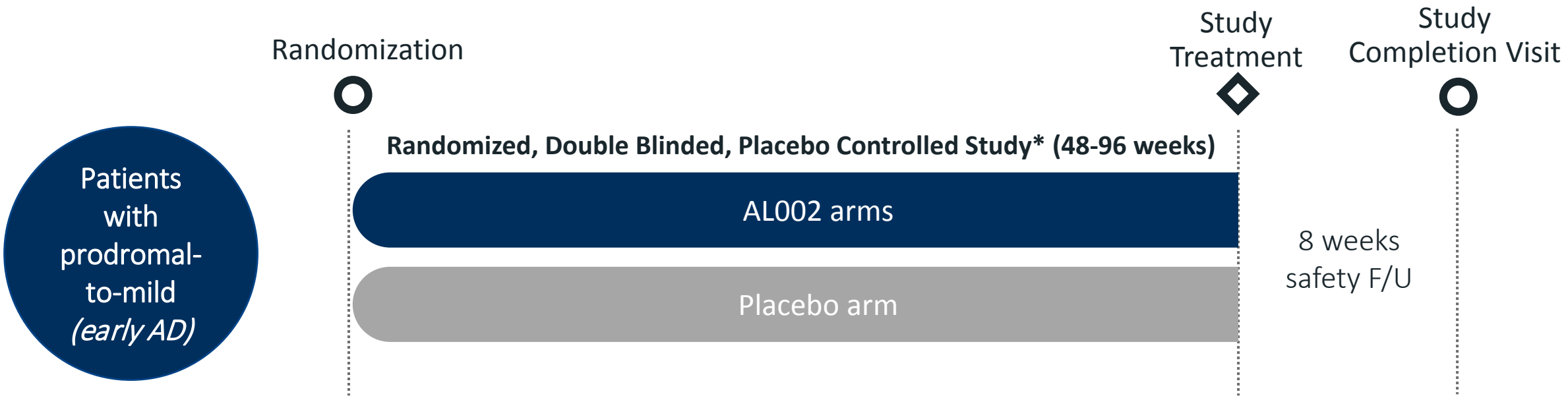
Dose-dependent reduction in soluble TREM2



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



AL002 next steps: Initiate Phase 2 in 2020



PRIMARY ENDPOINT: **CDR-SB**

SECONDARY CLINICAL OUTCOME ASSESSMENTS:

RBANS, ADAS-Cog13, ADCS-ADL-MCI

ALECTOR

* Number of active arms could change during the study

AL003 for AD: Increase activity of microglia by blocking SIGLEC 3

MECHANISM OF ACTION

- SIGLEC 3 is inhibitory receptor expressed on microglia
- AL003 blocks SIGLEC 3 in the same manner of a PD-1 inhibitor to allow immune system to work at fully capacity

PHASE 1A DATA

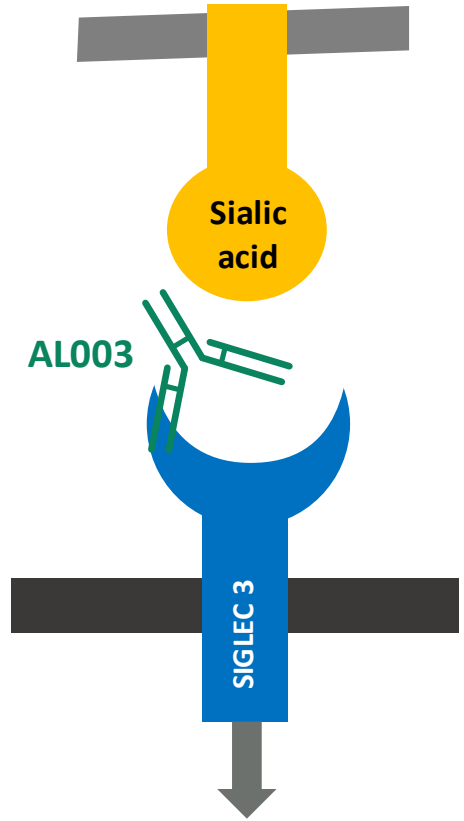
- AL003 successfully achieved its primary and secondary endpoints in the Phase 1a study

STATUS

- Phase 1b ongoing with data expected in 2021

PARTNER

- Global 50/50 profit and cost share partnership with AbbVie



Increases function by releasing inhibition on microglia

SIGLEC 3 mutation a risk for Alzheimer's disease

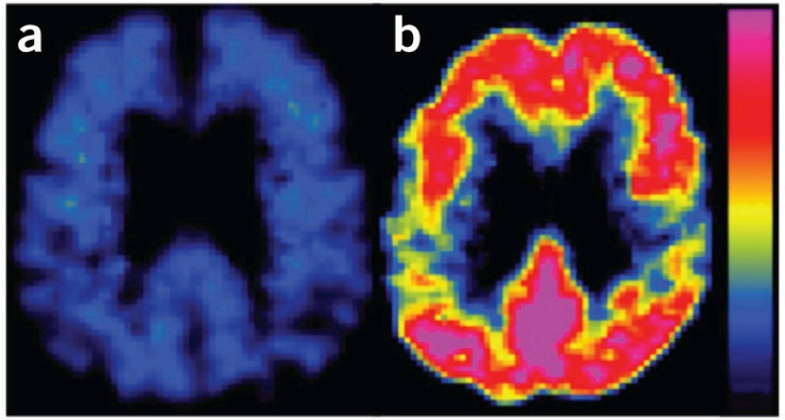
SIGLEC 3 is an inhibitory receptor for microglia

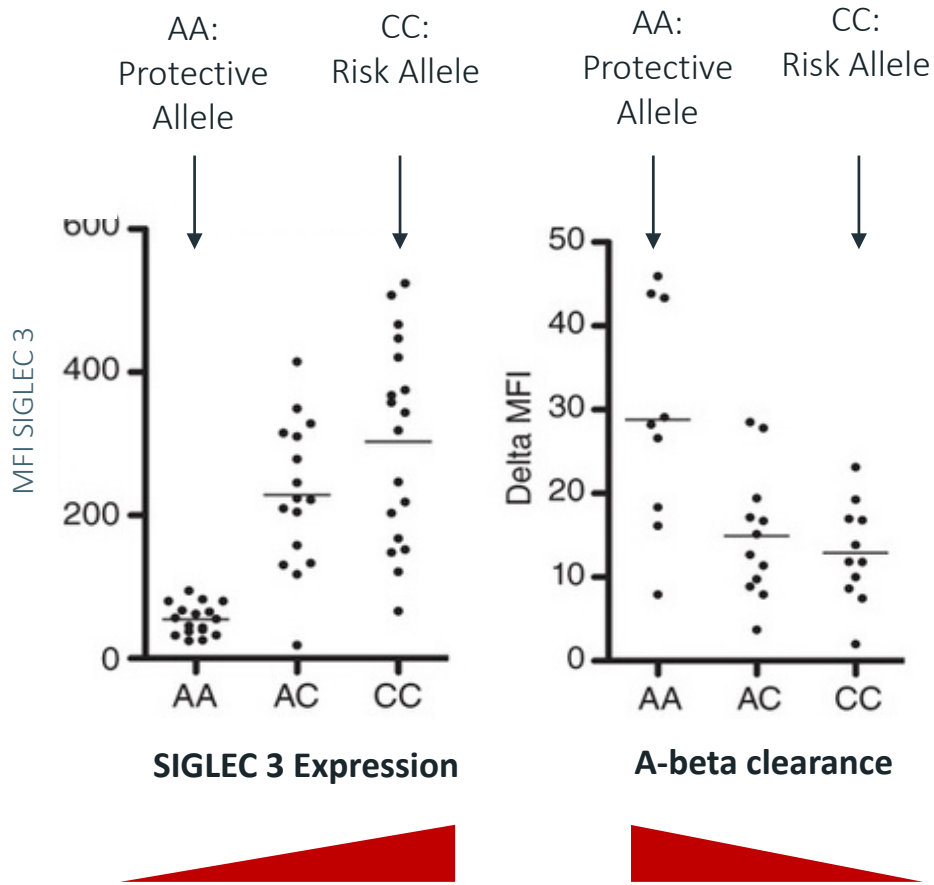
Prevalent risk allele in AD*:

- Reduces ability to clear A beta plaques**
- Leads to a smaller brain volume***

Protective SIGLEC 3 variant
low A-beta

Risk SIGLEC 3 variant
high A-beta



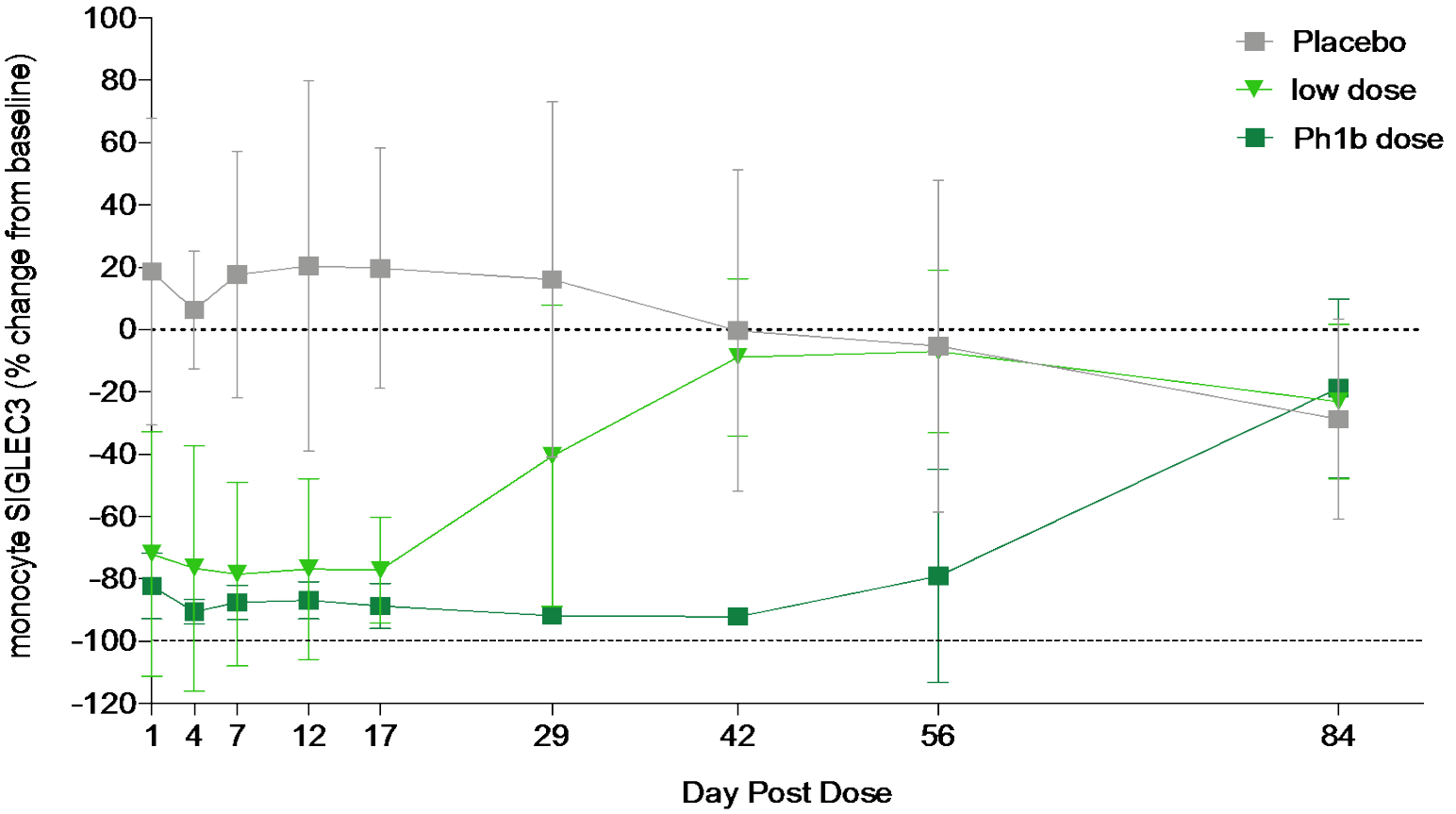


*Neurobiol Aging. 2015 Apr;36(4):1765.e7-1765.e16.
**Nature Neuroscience volume 16, pages 848–850 (2013).
***Neurobiol Aging. 2015 Apr;36(4):1765.e7-1765.e16

Target engagement and proof-of-mechanism in CSF achieved in Phase 1a

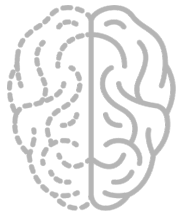
AL003 was found to be generally safe and well-tolerated in 21 healthy volunteers

AL003 demonstrated long lasting peripheral target engagement



The Phase 1b portion of the study continues to enroll with data expected in 2021

Latest prioritized product candidates moving towards the clinic



AL014
for AD

- Designed to counteract the risk variants of MS4A4A and to functionally convert the risk variants of MS4A4A to the protective variant
- Goal: mimic and exceed the beneficial activity of the protective MS4A4A variant, which may potentially decdecrease the progression of AD
- First-in-human study expected to initiate in the next 12-18 months

AL008
Oncology

- Novel antibody targeting the CD47-SIRP-alpha pathway
- Unique dual mechanism of action that relieves immune suppression (a “don’t eat me signal”) while also engaging Fc gamma to drive anti-tumor immunity

ADP009
Oncology

- First-in-class multi-Siglec inhibitor that recruits innate immune cells to activate adaptive immunity

In 2021, we will continue to advance Alector's broad clinical pipeline

AL001	• Continue progressing Phase 3 study of AL001 in FTD-*GRN* • Phase 2 results in FTD-*GRN*
AL002	• Continue progressing Phase 2 study of AL002 in AD (initiation expected in 2020)
AL003	• Phase 1b results from AL003 in AD
AL101	• Phase 1 results of AL101 in healthy volunteers
AL014	• Initiation of Phase 1 FiH study of AL014

Current cash and equivalents of $461.7M* expected to fund operations through 2022

ALECTOR

*As of 3Q 2020
** FIH: first-in-human trials

“At Alector we envision a world where dementia and neurodegeneration are illnesses of the past, just as smallpox and polio have become.”

Arnon Rosenthal, PhD

Chief Executive Officer, Co-Founder

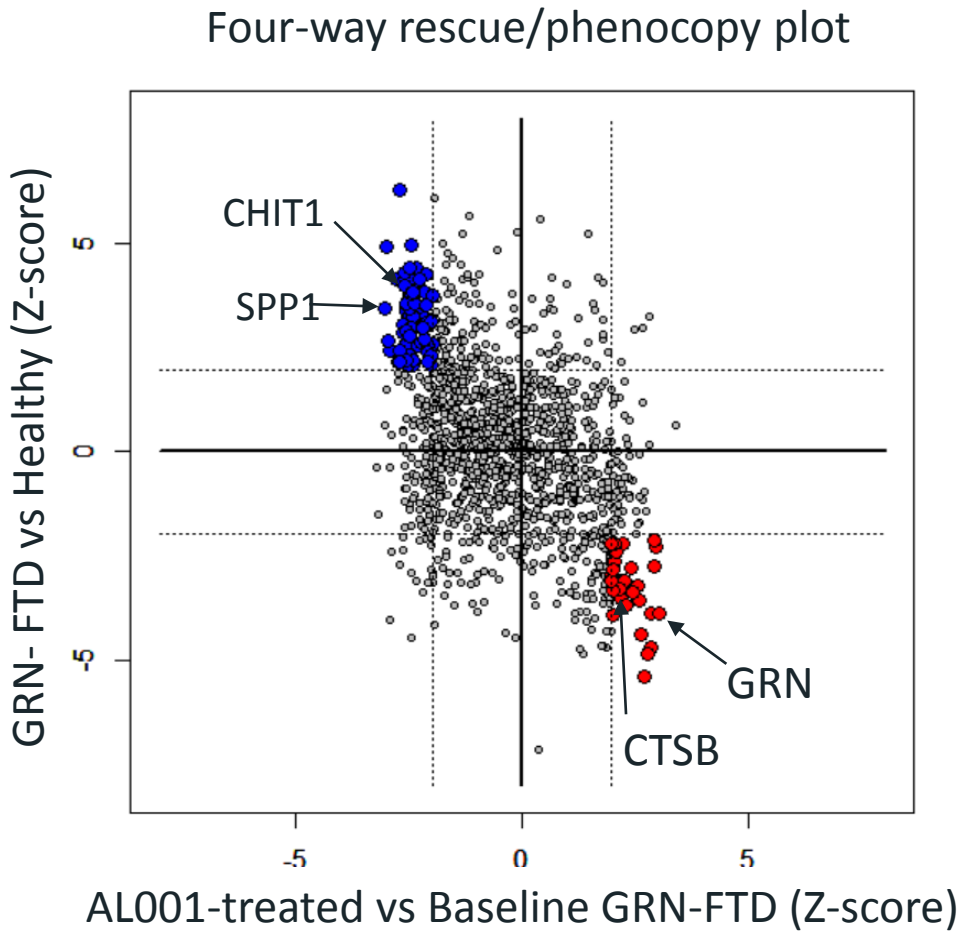
ALECTOR

November 2020

Harnessing the Immune System to Cure Neurodegeneration

ALECTOR

AL001 counteracts the disease protein signature in FTD patients in Phase 1b



- AL001 reduces inflammatory markers of disease (blue)
- AL001 increases proteins associated with lysosomal function (red)