PassageBio

Corporate Presentation

November 2025

Nasdaq: PASG

Forward-Looking Statement

This presentation includes “forward-looking statements” within the meaning of, and made pursuant to the safe harbor provisions of, the Private Securities Litigation Reform Act of 1995, including, but not limited to: our expectations about timing and execution of anticipated milestones, including the progress of clinical studies and the availability of clinical data from such trials; timing of feedback from regulatory authorities; the potential of our product candidates versus other treatment options and clinical candidates; our expectations about cash runway; and the ability of PBFT02 to treat FTD-*GRN* or FTD-*C9orf72*. These forward-looking statements may be accompanied by such words as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “might,” “plan,” “potential,” “possible,” “will,” “would,” and other words and terms of similar meaning. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our ability to develop and obtain regulatory approval for our product candidates; the timing and results of preclinical studies and clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, the timing of and our ability to obtain and maintain regulatory approvals; our expectations about the willingness of healthcare professionals to use our product candidates, the timing, or amount, the occurrence of adverse safety events; the risk that positive results in a preclinical study or clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; failure to protect and enforce our intellectual property, and other proprietary rights; our dependence on collaborators and other third parties for the development and manufacture of product candidates and other aspects of our business, which are outside of our full control; the timing, or amount, of receipt of any potential future milestone and royalty payments; risks associated with current and potential delays, work stoppages, or supply chain disruptions; and the other risks and uncertainties that are described in the Risk Factors section in documents the company files from time to time with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. Passage Bio undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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REDEFINING THE COURSE OF NEURODEGENERATIVE CONDITIONS

Advancing potential best-in-class, one-time progranulin raising FTD-*GRN* gene therapy

Exploring benefits of elevated progranulin in multiple adult neurodegenerative diseases

Established suspension-based PBFT02 manufacturing process to support late-stage development

Cash runway expected into 1Q 2027*

* Based on cash, cash equivalents and marketable securities as of September 30, 2025.

Validating the Therapeutic Potential of PBFT02

Urgent Patient Need in FTD-*GRN*

Genetic form of FTD caused by *GRN* mutations, which lead to progranulin (PGRN) deficiency

No approved disease-modifying therapies

Fast Track and Orphan Drug Designation

upliFT-D

Promising data from initial clinical study of PBFT02 in FTD-*GRN*

Differentiated, Potential Best-in-Class Profile

One-time, gene replacement therapy

Proprietary AAV1 construct

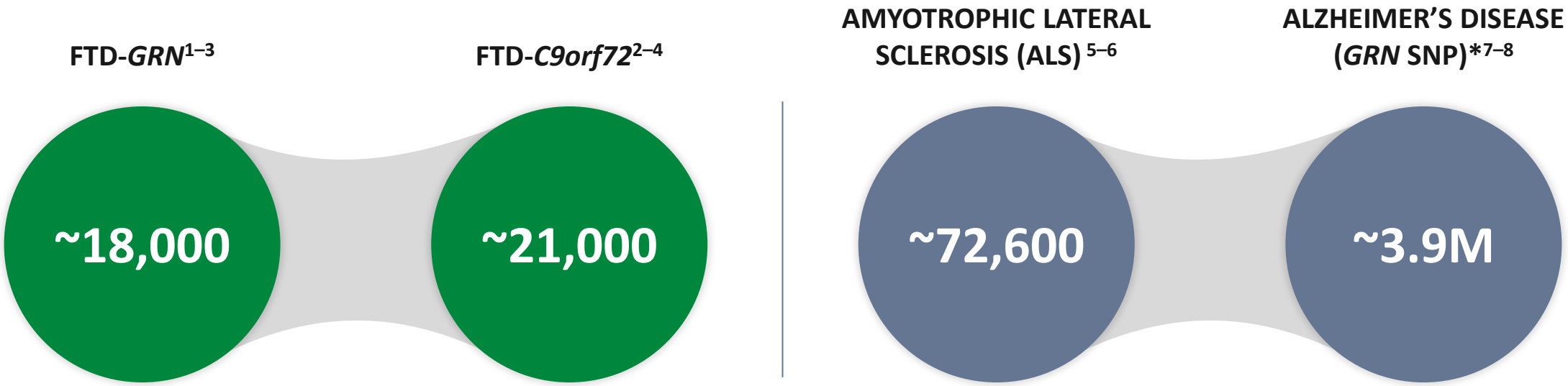
Nonsurgical injection directly to cerebrospinal fluid (CSF)

Durable, elevated CSF PGRN levels*

* Based on interim data.

Significant Market Opportunity for PBFT02 Across Multiple Neurodegenerative Diseases

Estimated Prevalence (US and EU)



Current clinical programs

* rs5848 single nucleotide polymorphism (SNP)

1. Greaves CV, et al. *J Neurol* 2019; 266:2075-2086. 2. Galvin JE, et al. *Neurology* 2017; 89:2049-2056. 3. Onyike CU, et al. *Int Rev Psychiatry* 2013; 25:130-137. 4. Moore KM, et al. *Lancet Neurol* 2020; 19: 145–156. 5. Brown et al. *Neuroepi* 2021; 55:342-353. 6. CDC ALS Registry Dashboard. 7. Sheng J, et al. *Gene* 2014; 141-145. 8. Alz Assoc. 2023 Alzheimer's Disease Facts and Figures. *Alzheimers Dement* 2023;19.

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PBFT02

Frontotemporal Dementia

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FTD: A Devastating Adult Disease

OVERVIEW

- Fatal adult-onset neurodegenerative disease affecting the frontal and temporal lobes of the brain, characterized by a decline in behavior, language and executive function
- One of the most common causes of early-onset dementia worldwide, disproportionately affecting individuals aged 40-65 years

CLINICAL SYMPTOMS

Disease progression is rapid and degenerative, including loss of speech, loss of expression, behavioral changes and immobility

Loss of inhibition

Apathy

Social withdrawal

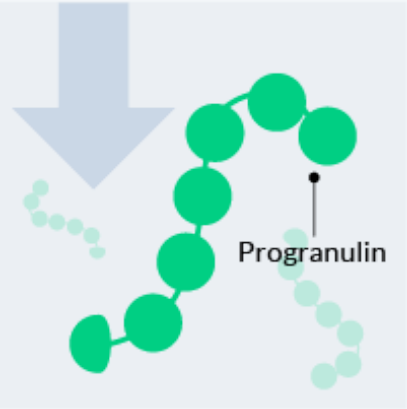
Hyperorality (mouthing of objects)

Ritualistic compulsive behaviors

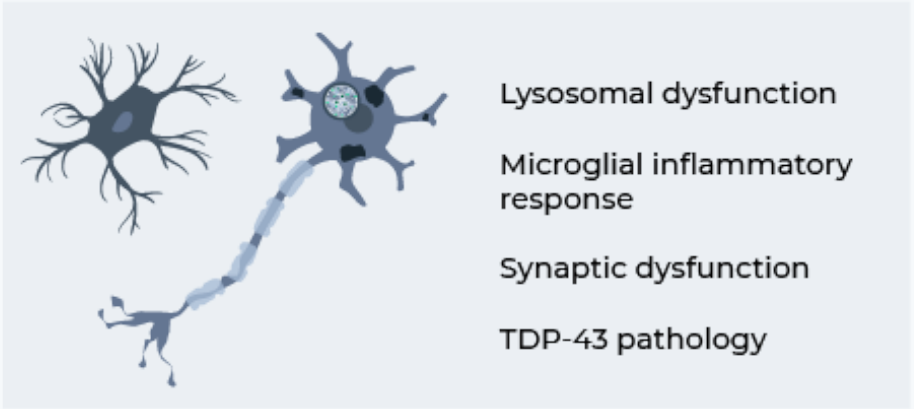
On average, people with FTD live 8 years after the onset of symptoms

Progranulin Deficiency is the Defining Characteristic of FTD-*GRN* and Leads to Neurodegeneration

Progranulin is critical to maintaining CNS cell homeostasis



Decrease in PGRN levels



Neuronal dysfunction, pathological changes, and inflammation

Vulnerability of neurons in affected regions

Neurodegeneration

Rhinn H et al. *Trends Pharmacol Sci.* 2022, 43:641-652

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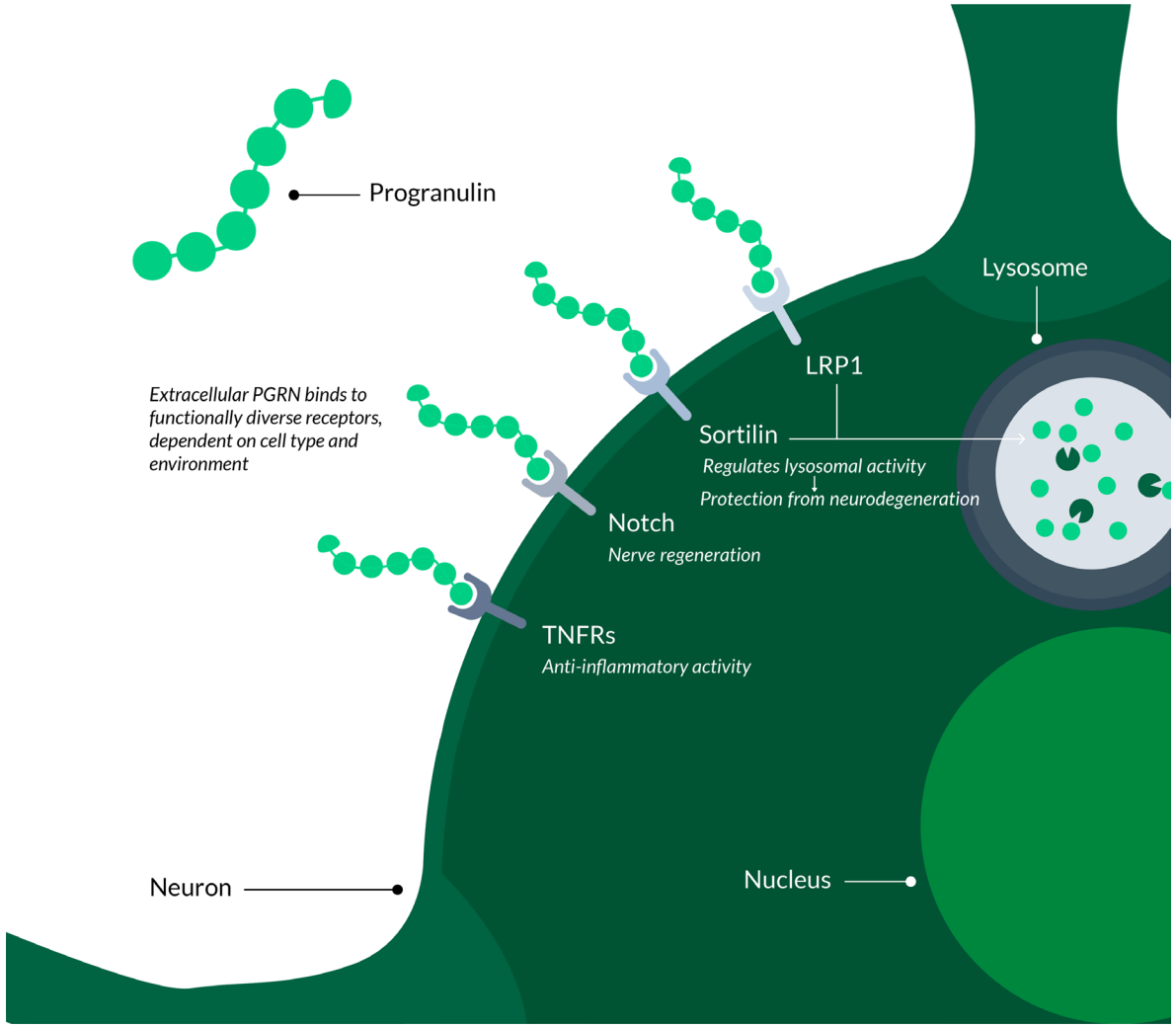
Elevated PGRN Increases Potential for Improved Cellular Function

- Progranulin is a secreted protein that binds to cell membrane receptors to affect multiple intracellular pathways
  - Major role is regulating intracellular lysosomal activity
  - Extracellular PGRN is endocytosed via multiple receptors
- Driving elevated PGRN levels in the extracellular space increases the amount of PGRN available to enter target CNS cells
- Able to leverage cross-correction mechanism: secreted PGRN can be taken up by non-transduced cells



Paushter et al. *Acta Neuropathol*. 2018;136:1-17. Rhinn et al. *Trends Pharmacol Sci.* 2022; 43:641-652.

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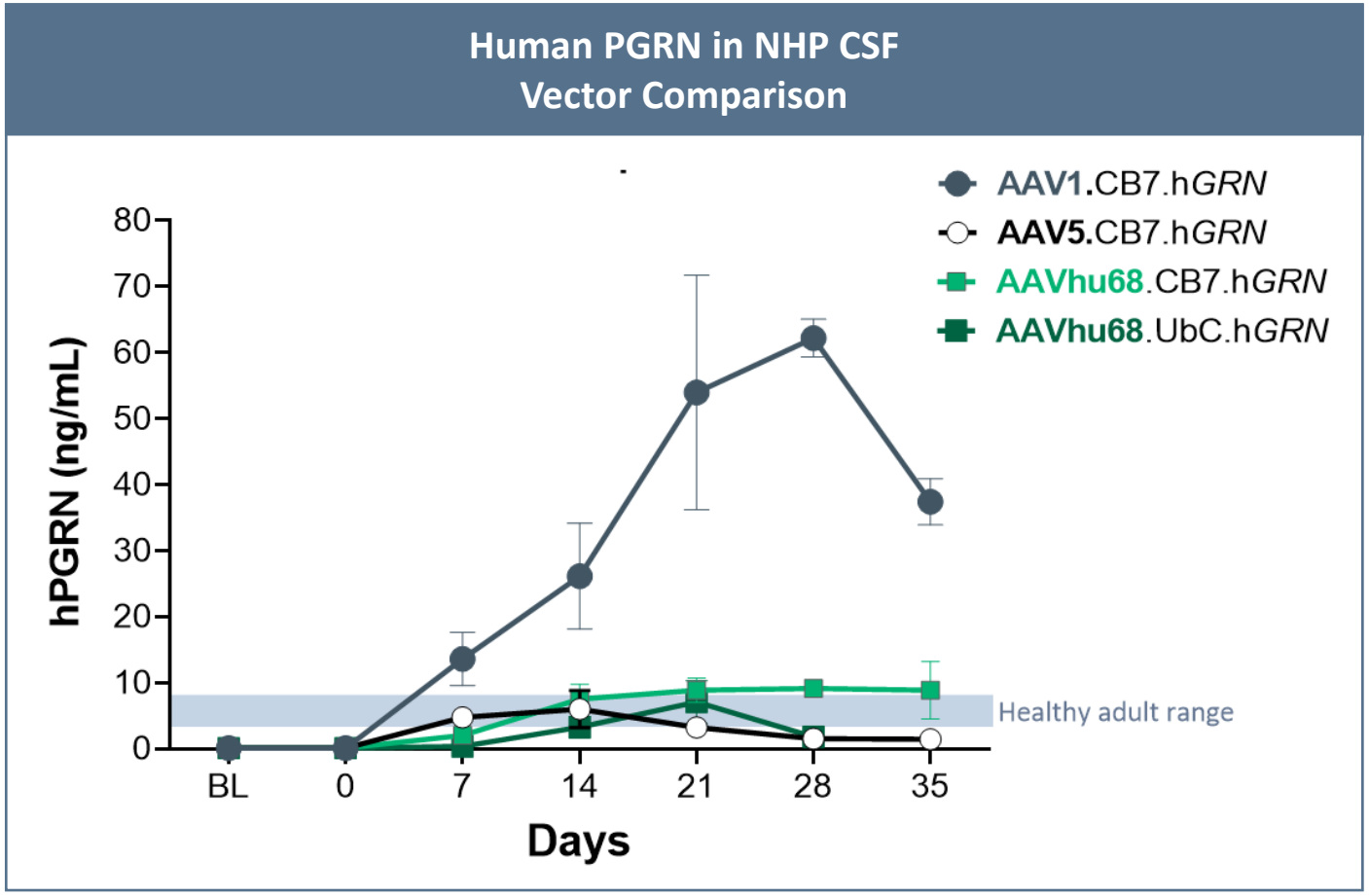
Preclinical NHP: AAV1 Achieved the Highest Levels of CSF PGRN

- AAV1 resulted in superior CSF hPGRN levels, 5x higher than AAV5 and AAVhu68 (an AAV9 variant) vectors, after ICM administration



Rhesus macaques (n=2/gp) ICM-delivered AAV.hPGRN (3.3 x 10^{11} GC/g brain), day 0

*Size and duration of elevation muted by immune response to human PGRN. *Shading:* Healthy adult sample range for CSF PGRN, n = 61 (Passage Bio data)

CSF, cerebrospinal fluid; GC, genome copies; ICM, intra-cisterna magna; NHP, non-human primate. *Reference:* Hinderer et al., *Ann Clin Trans Neurol.* 2020; 7:1843-1853

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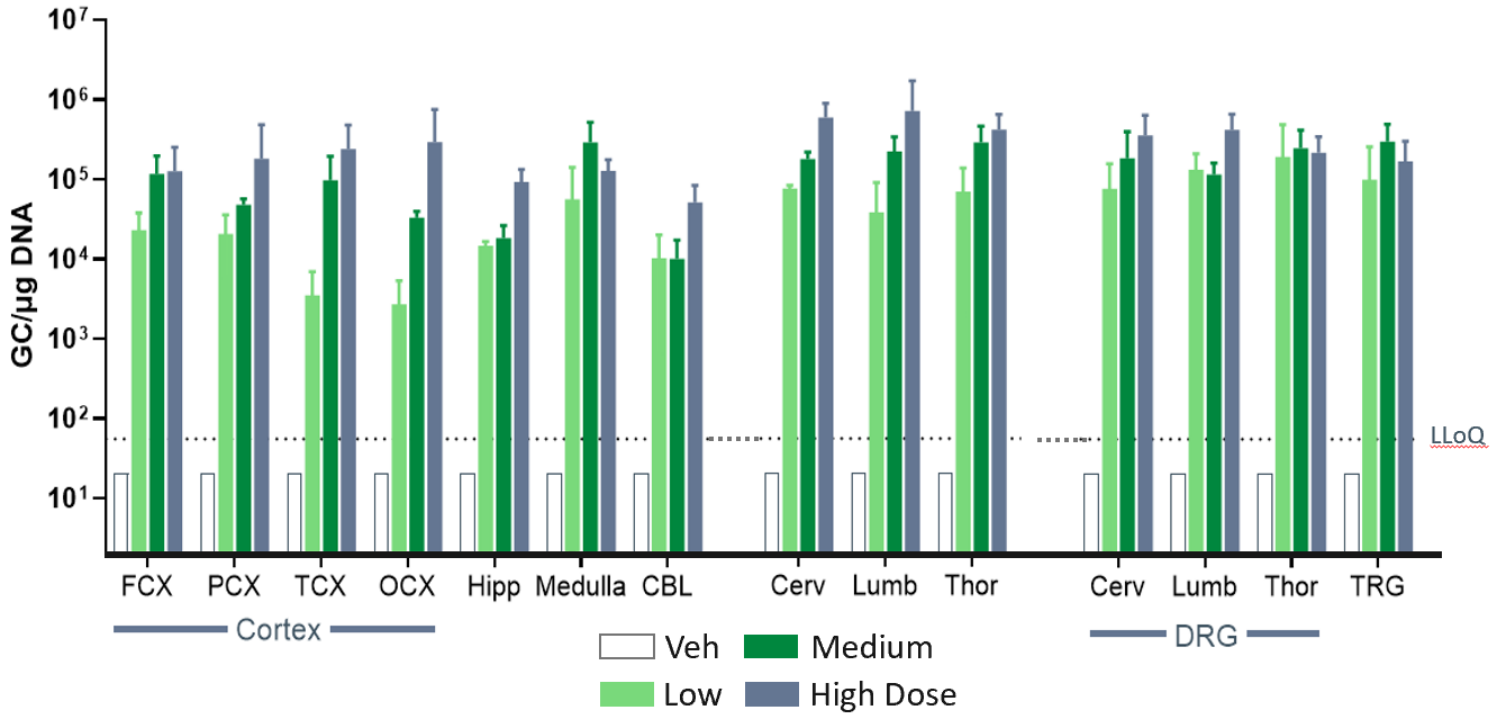
Preclinical NHP: ICM Administration of PBFT02 Led to Broad Distribution of Vector Throughout Brain/Spinal Cord

Vector Biodistribution in NHPs 90 days post-ICM PBFT02



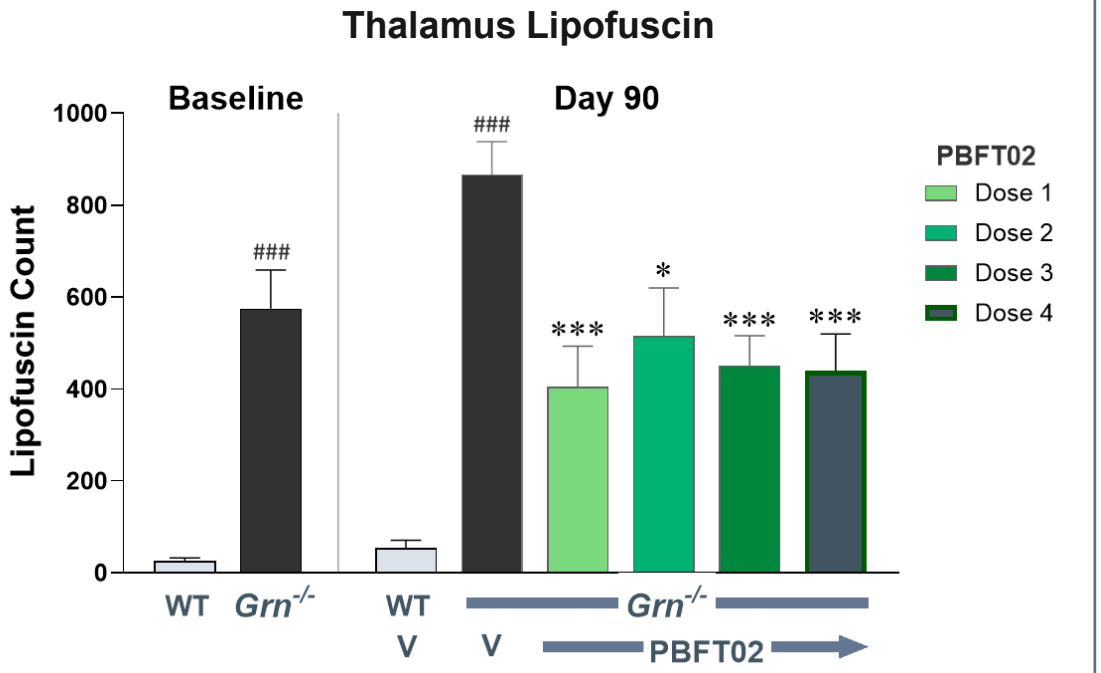
- Robust, dose-dependent vector delivery to cortical and sub-cortical brain regions affected in FTD
- NHP low dose, equivalent to clinical Dose 1 of PBFT02 in upliFT-D study, resulted in ~10^4 GC/µg DNA in all sampled areas throughout the brain

n=3/gp. Data are mean +/- SEM.

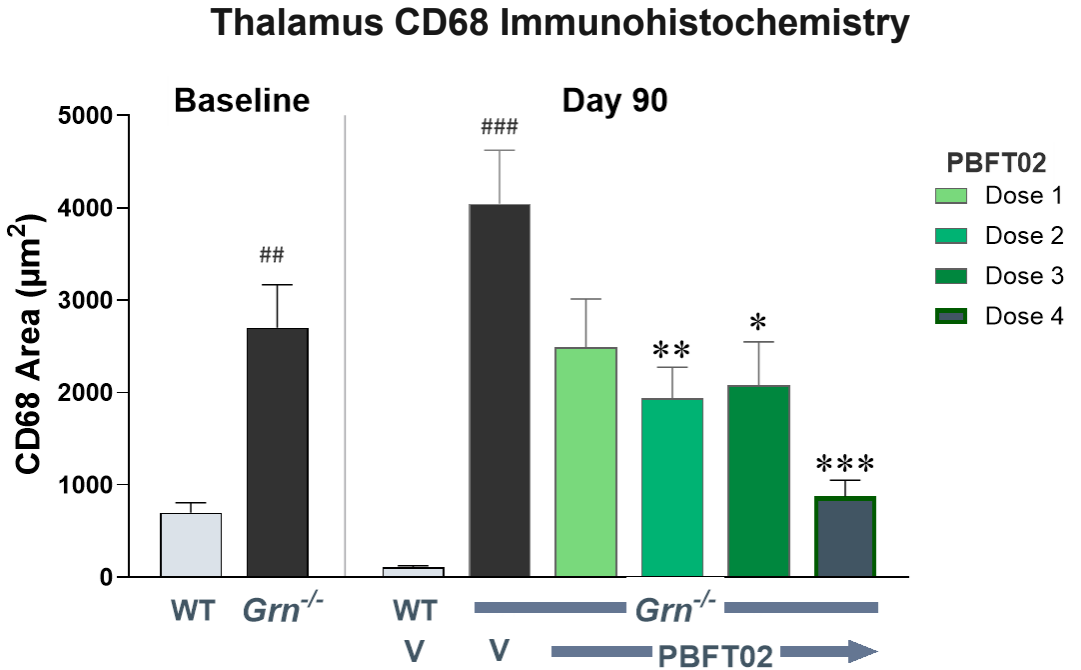
CBL, cerebellum; Cerv, cervical; DRG, dorsal root ganglion; FCX, frontal cortex; GC, genome copies; Hipp, hippocampus; ICM, intra-cisterna magna; LLoQ, lower limit of quantitation; Lumb, lumbar; OCX, occipital cortex; PCX, parietal cortex; TCX, temporal cortex; Thor, thoracic; TRG, trigeminal root ganglion; Veh, vehicle

Preclinical *Grn*$^{-/-}$ Mice: Expression of hPGRN Improved Lysosomal Dysfunction and Neuroinflammation in the Brain

PBFT02 reduced lipofuscin deposition at all doses, suggesting improved lysosomal dysfunction



Dose-dependent elevations in CSF PGRN after PBFT02 led to progressive reductions in microglial activation



Greatest pathological benefit was associated with the highest PGRN levels in the CSF

Lipofuscin deposition and microglial activation are hallmark pathologies seen in FTD; Improvements in both measures were seen in cerebral cortex, thalamus, and hippocampus after PBFT02 administration

Grn$^{-/-}$ and WT mice (n=14-15/gp) ICV-administered PBFT02 or vehicle (V). Baseline controls were untreated mice on Day 1. Bars: mean +/- SEM.

$^{\#\#}p < 0.01$, $^{\#\#\#}p < 0.005$ vs WT control; $^{*}p < 0.05$, $^{***}p < 0.005$ vs *Grn*$^{-/-}$+ V , one-way ANOVA followed by Tukey's multiple comparisons test.

Grn, granulin gene; ICV, Intra-cerebroventricular; PGRN, progranulin; WT, wildtype

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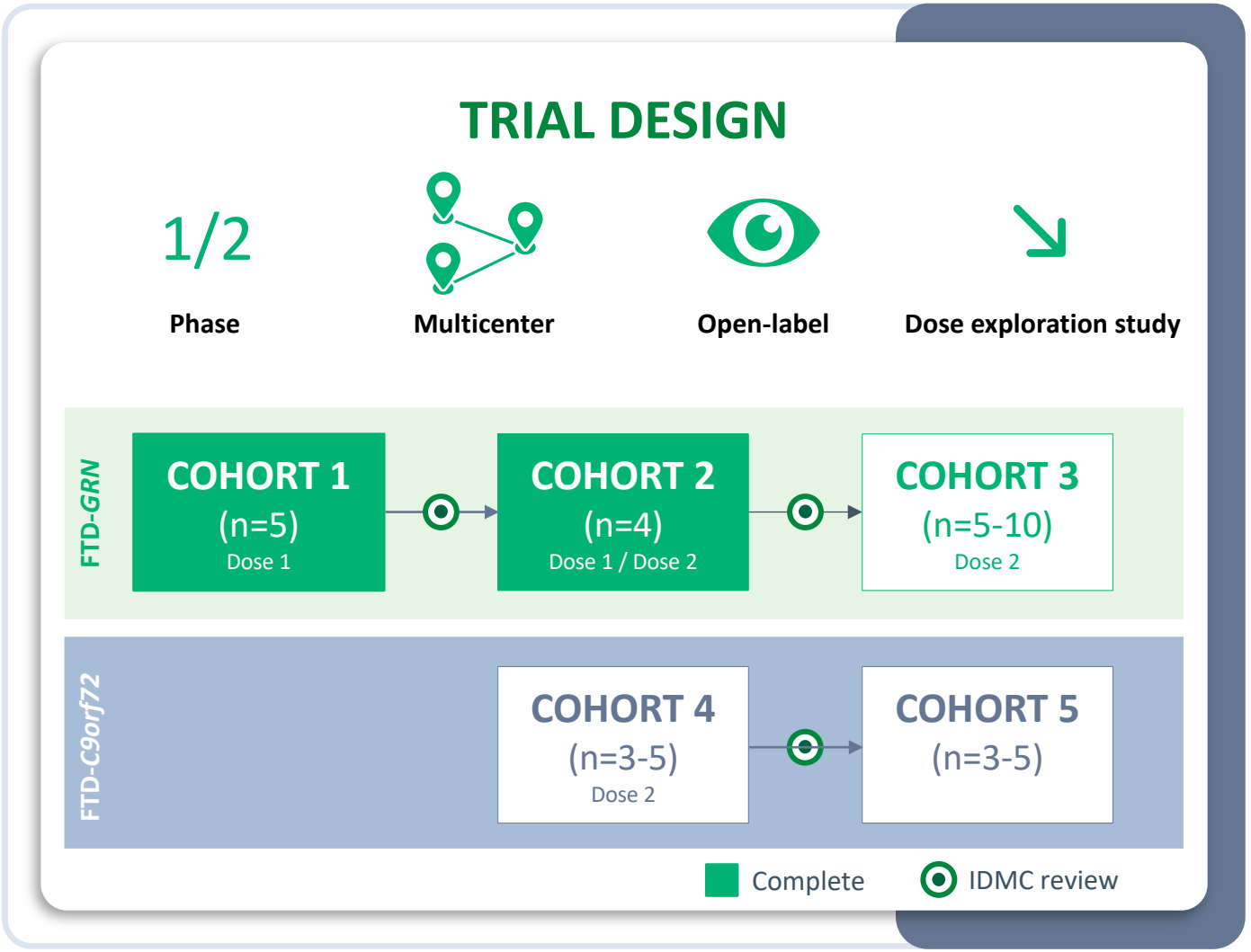
upliFT-D: Global Phase 1/2 Trial with PBFT02

Currently enrolling patients in Cohort 3 and Cohort 4



DURATION

2 years; with additional 3 years of follow-up for safety and durability of effect

PRIMARY ENDPOINTS

Safety and tolerability

SECONDARY ENDPOINTS

Biomarkers

- Progranulin (CSF, plasma)
- vMRI
- Retinal nerve fiber layer and retinal lipofuscin deposits via OCT
- NfL (CSF, plasma)

Clinical

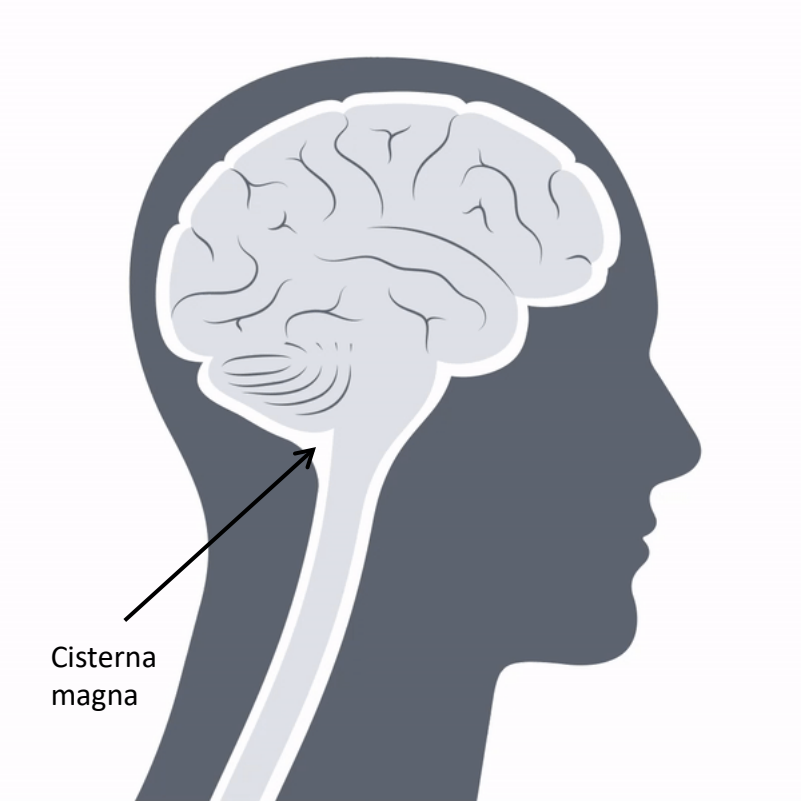
- CDR + NACC FTLD sum of boxes

EXPLORATORY BIOMARKERS

- Cathepsin D (CSF)
- GFAP (CSF, plasma)
- LAMP 1 (CSF)
- Lys-GL1 (CSF)

Dose 1: 4.5e13 GC
Dose 2: 2.2e13 GC

Intra-Cisterna Magna (ICM) Administration



- Directly deliver vector into the CSF via a single injection
  - Allows for broad CNS biodistribution[1]
  - Lower doses compared to IV systemic delivery
  - Reduced impact of neutralizing antibodies
- Brief (<60 min), non-surgical, CT-guided procedure for precise delivery to the cisterna magna
  - Procedure avoids penetration of brain tissue

1. Hinderer et. al, *Hum Gene Ther*. 2018; 29:15-24.

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Key Baseline Demographics for FTD-*GRN* Participants*

Dose 1 (n=7); Dose 2 (n=1)

(n=8)	Mean / % / n	Range
Age (yrs)	64.4	51-72
Sex	M: 50% F: 50%	
FTD-*GRN* phenotype (n)	bvFTD: 5 PPA: 3	
Disease duration at baseline (yrs)	2.9	1 - 5
PGRN, CSF (ng/mL)	2.1	1.5 - 2.9
PGRN, plasma (ng/mL)	36.6	22.4 - 89.0
NfL, plasma (pg/mL)	51.9	12.4 - 111
Clinical Dementia Rating Scale[1], Global (%)	1: 50% 2: 50%	
Clinical Dementia Rating Scale[1], Sum of Boxes	10.3	5 - 17

*Data as of June 15, 2025

[1]CDR® +NACC FTLD.

bvFTD, behavioral variant; IvPPA, logopenic variant primary progressive aphasia; svPPA, semantic variant PPA; nfvPPA, nonfluent variant PPA.

upliFT-D: PBFT02 Interim Safety Profile

PBFT02 Interim Safety Highlights*
FTD-GRN Patients (Dose 1 n=7; Dose 2 n=1)

- In 5 of 8 patients, all treatment emergent AEs were mild to moderate in severity
- 3 of 8 patients experienced a total of 4 SAEs

Dose 1

  - Patient 1: asymptomatic venous sinus thrombosis (VST) and hepatotoxicity, leading to a revised immunosuppression regimen in all subsequent patients**
  - Patient 7: asymptomatic VST, completely resolved prior to day 30 following treatment with anticoagulants. No evidence of hepatotoxicity, immune response or other laboratory abnormalities

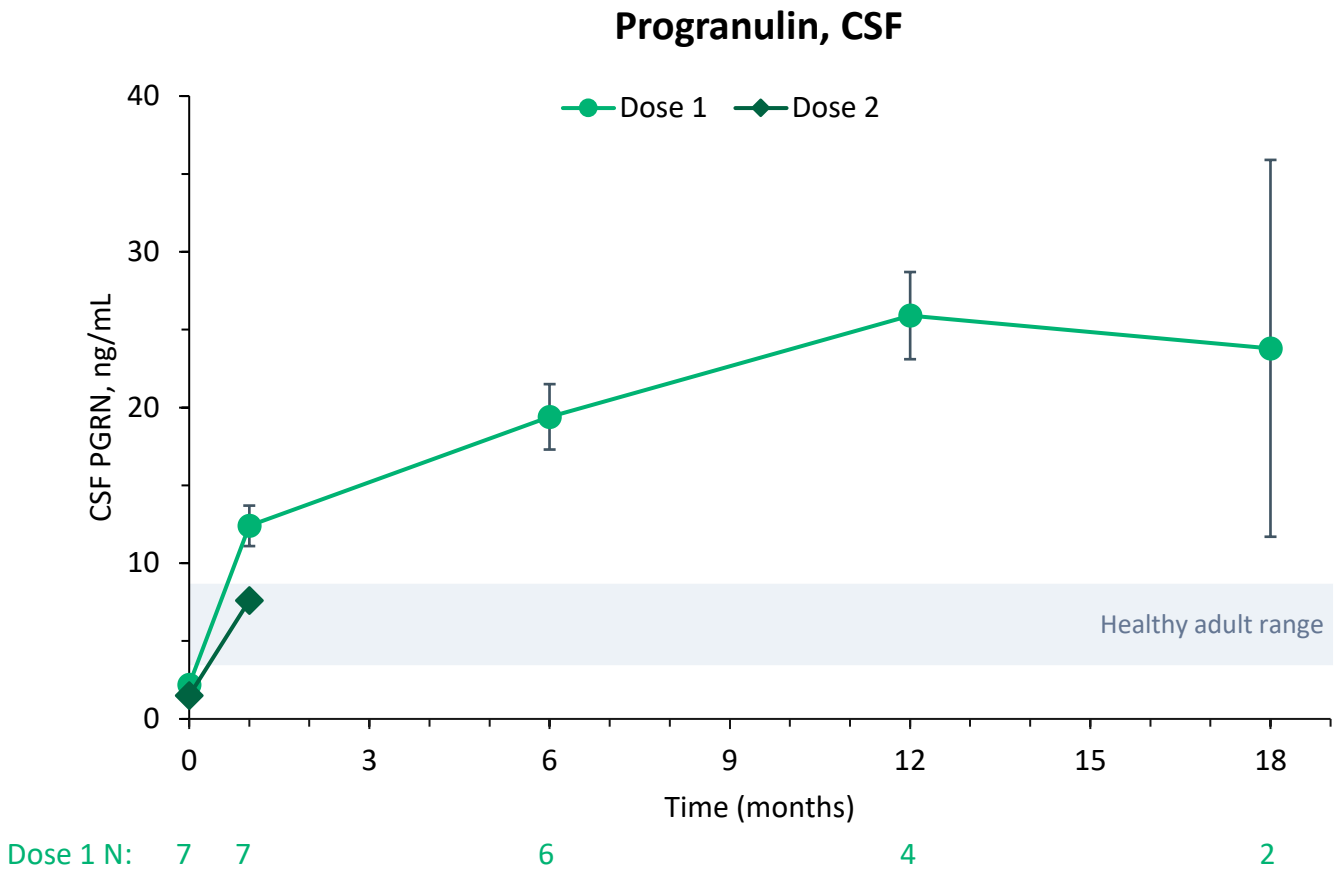
Dose 2

  - Patient 8: pulmonary embolism (PE) in setting of a concurrent systemic infection. PE responded to treatment with anticoagulants

- No evidence of DRG toxicity
- No complications during ICM administration

*Data as of June 15, 2025
**Patient 1 received oral prednisone 60 mg daily through day 60; subsequent patients received a revised immunosuppressive regimen of 1g methylprednisolone IV daily to day 3, followed by oral prednisone 60 mg to day 60, then taper
AE, adverse event; DRG, dorsal root ganglion; ICM, intra-cisterna magna; PE, pulmonary thromboembolism; SAE, serious adverse event; VST, venous sinus thrombosis.

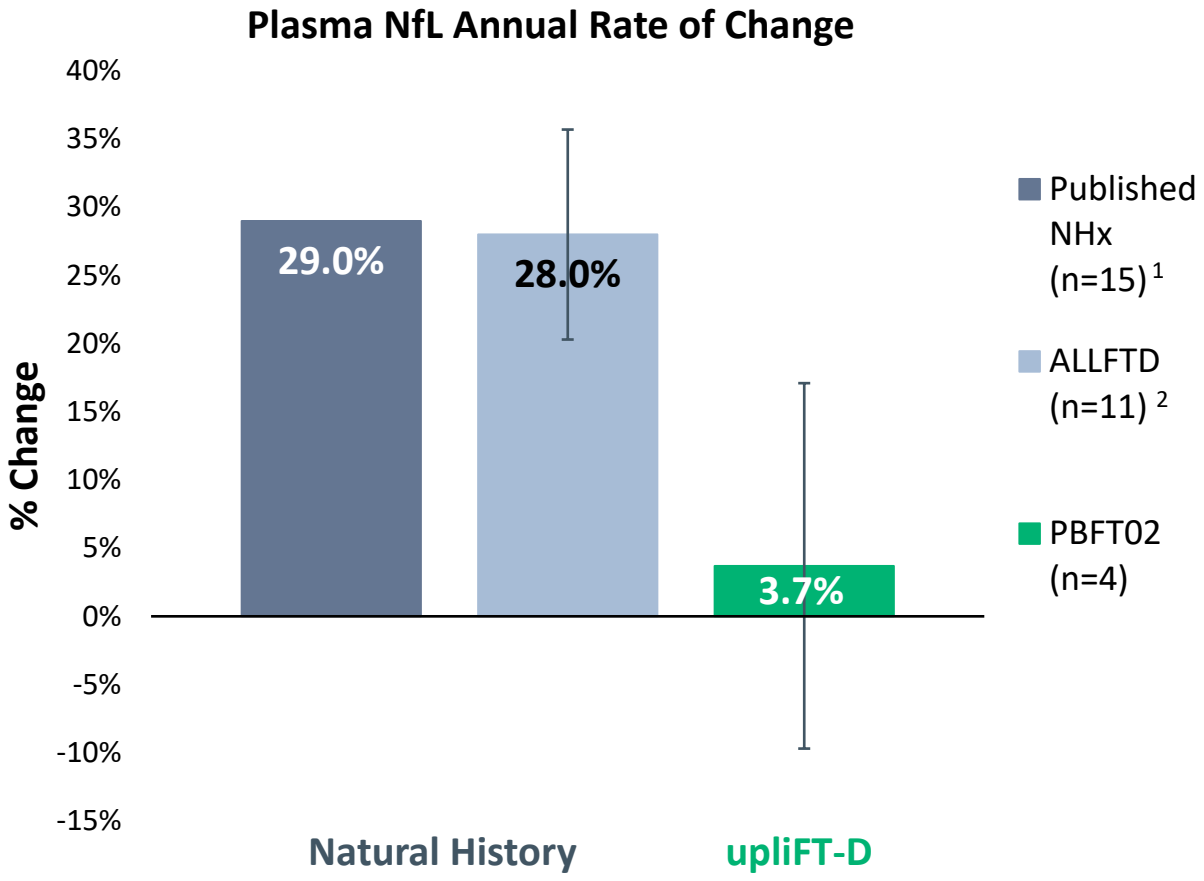
PBFT02 Generated Robust, Durable Increases in CSF PGRN in FTD-*GRN* Patients



First Dose 2 patient (Patient 8) increased from 1.5 ng/mL at baseline to 7.6 ng/mL at M1, approaching the upper healthy adult range

Data as of June 15, 2025. Mean +/- SEM
Shading: Healthy adult sample range for CSF PGRN (range: 3.28 – 8.15 ng/mL, mean: 4.76 ng/mL, n = 61) (Passage Bio data)
Dose 1: 4.5e13 GC; Dose 2: 2.2e13 GC
CSF, cerebrospinal fluid; M, month

Plasma NfL Showed Early Evidence of Improvement in a Disease Progression Biomarker vs. Natural History



- Plasma NfL is the only FTD-*GRN* disease progression biomarker with longitudinal natural history data available[1,3]
- PBFT02-treated patients with 12 months follow-up (n=4) had a reduced annual rate of change in plasma NfL compared to published natural history data

Note: annual rate of increase in plasma NfL in a healthy adult sample reported to be ~4%[1]

Data as of June 15, 2025. Mean +/- SEM

PBFT02 patients (n=4, Dose 1): Baseline plasma NfL (neurofilament light chain) range: 39.6 to 45.6 pg/mL. Average time since diagnosis 2.3 years.

[1] Published natural history. Chart (left): 15 symptomatic, untreated FTD-*GRN* patients; mean years since diagnosis: 2.9; Note (right): 65 healthy adults. (Saracino et al, *J Neurol Neurosurg Psych* 2021; 92:1278-1288).

[2] Passage Bio analysis of ALLFTD natural history sample comprised of individuals with a pathogenic *GRN* mutation and a CDR+NACC FTLD global score between 0.5 and 2, inclusive.

[3] van der Ende et al, *Lancet Neurol* 2019; 18:1103-11.

PBFT02 Offers Best-in-Class Therapeutic Potential

	PBFT02		
Product Candidate	AAV1 gene therapy delivering *GRN*	AAV9 gene therapy delivering *GRN*	AAV9 gene therapy delivering *GRN*
Stage of Development	Phase 1/2	Phase 1/2	Phase 1/2
Route of Administration	ICM (Non-surgical, 1 hour procedure)	ICM	Intrathalamic (Neurosurgery, lengthy procedure)
CSF PGRN Level at 12m[1]	***26 ng/mL*** ***(mean; n=4)***	~4-8 ng/mL (n=7 higher dose)[2]	-
Durability of CSF PGRN Elevation[1]	***Durable at 18 m*** ***(n=2)***	Declining from 2 to 12 m (n=7 higher dose)[2]	-

PBFT02 uniquely positioned to offer a one-time therapy capable of achieving highest progranulin levels

[1] Clinical evidence based on public disclosure. Results are derived from different clinical trials at different points in time. No head-to-head trials have been conducted among the results shown. Comparing the results from different trials may be unreliable due to different protocol designs, trial design, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that may not be the same between trials.

[2] Lilly/Prevail AD/PD Mar 2024 presentation and abstract.

PBFT02: Summary of Approach

- AAV delivery of functional *GRN* gene to **express new PGRN, increasing levels both intra- and extra-cellularly**
  - Preserves all natural pathways to properly traffic PGRN intracellularly where it is needed
- ICM route of administration enables **low doses of AAV and broad CNS biodistribution**
  - Non-surgical, brief procedure (< 60 minutes)
- Promise of a **one-time therapy** for patients
  - Durable elevation of CSF PGRN[1]

A Novel and Potentially Transformative Therapy for FTD-*GRN* Patients

[1] Interim data from upliFT-D as of June 15, 2025.

Looking Ahead

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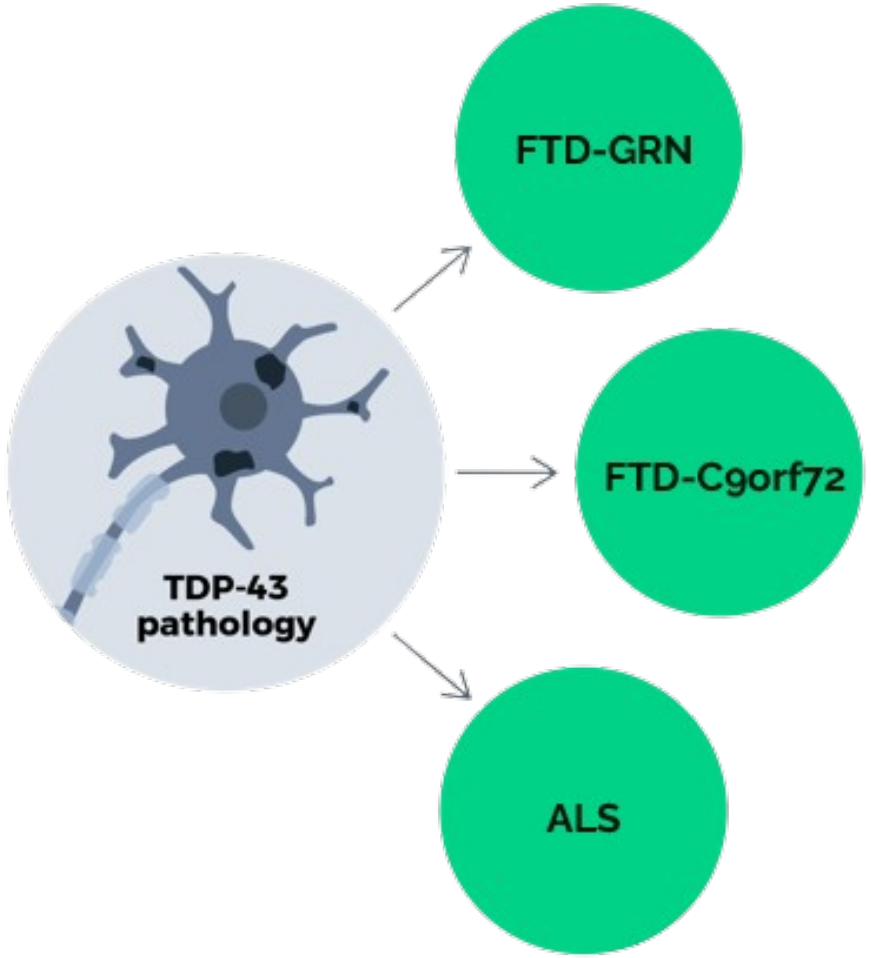
PBFT02 has Potential to Correct Underlying Pathology in FTD-*GRN*, FTD-*C9orf72* and ALS

TDP-43 pathology is a hallmark of multiple neurodegenerative diseases[1]

- TDP-43 mislocalizes from nucleus to cytoplasm and forms inclusion bodies

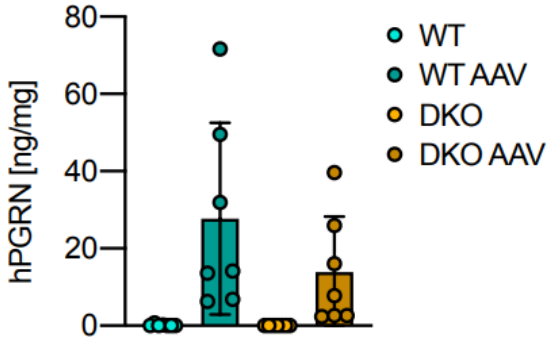


1. Rhinn H et al. *Trends Pharmacol Sci.* 2022; 43:641-652

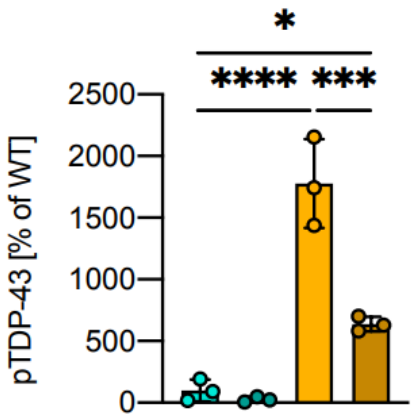
Elevated PGRN Ameliorates TDP-43 Pathology in Preclinical Models

TDP-43 pathology due to lysosomal dysfunction (*GRN/ TMEM106* double knockout, DKO) reduced by AAV.hPGRN[1]

AAV delivered hPGRN to mouse brain

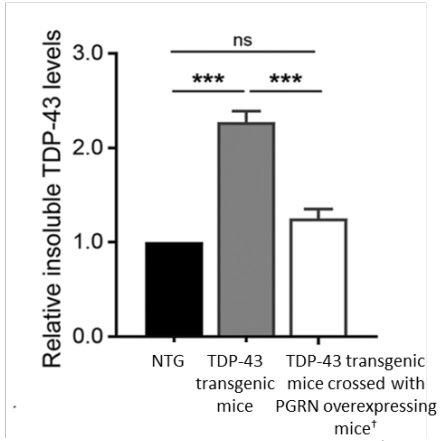


TDP-43 pathology in DKO mice reduced by AAV.hPGRN

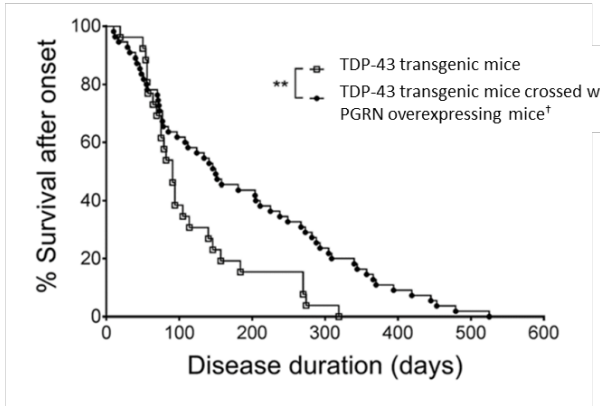


Elevated PGRN ameliorated TDP-43 pathology and disease course in a preclinical model[2]

Elevated PGRN reduced insoluble TDP-43 in mouse spinal cord



Elevated PGRN extended survival of TDP-43 mutant mice



† *PGRN increased to >2x endogenous levels*

- Elevated PGRN also prevented degeneration of large axon fibers in TDP-43 mice
- PGRN neuroprotection from pleiotropic effect, not single pathway

1. Reich et al. *Sci Transl Med.* 2024; 16(750); 2. Beel et al. *Mol Neurodegen.* 2018: 13:55.; Laird et al. *PLoS One* 2010; 5:e13368.
DKO, double gene knockout; *GRN,* granulin gene; PGRN, progranulin; TDP-43, transactive response DNA binding protein 43 kDa

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Critical Manufacturing Milestones Achieved to Enable Late-Stage Development

Functional Potency Assay	Developed assay and reached alignment with FDA on suitability of assay for PBFT02 release
Robust Manufacturing Process	Completed development of high-productivity, suspension-based manufacturing process *Single production lot estimated to yield >1,000 doses[1] with >70% full capsids*
Process Comparability Plan	Aligned with the FDA on an analytical approach to establish comparability of suspension-based process

[1] Estimated yield based on Dose 2

Plan to Initiate Discussions with the FDA on a Registrational Study Design in 1H 2026

Rationale for a single-arm registrational study

- FTD-*GRN* is a rapidly progressing disease with no approved disease-modifying therapies and a substantial unmet clinical need
- Multiple recent gene therapy precedents demonstrate FDA receptivity to a single-arm registrational approach
- Existing, well structured FTD natural history studies with >300 FTD-*GRN* patients

Upcoming Milestones and Corporate Updates

TIMING	MILESTONE
1H 2026	Report updated interim safety and biomarker data from Dose 2 in 1H 2026
1H 2026	Seek regulatory feedback on registrational trial design in FTD-*GRN* in 1H 2026

PIPELINE

- Advancing Huntington's disease preclinical program

BALANCE SHEET

- Cash balance of ~$53 million as of 9/30/25*
- Cash runway into 1Q 2027

* Based on cash, cash equivalents and marketable securities

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REDEFINING THE COURSE OF NEURODEGENERATIVE CONDITIONS

Advancing potential best-in-class, one-time progranulin raising FTD-*GRN* gene therapy

Exploring benefits of elevated progranulin in multiple adult neurodegenerative diseases

Established suspension-based PBFT02 manufacturing process to support late-stage development

Cash runway expected into 1Q 2027*

* Based on cash, cash equivalents and marketable securities as of September 30, 2025.

Thank You

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Focused Pipeline Addressing Rare and Prevalent Neurodegenerative Indications

Program	Indication	US/EU prevalence	Discovery	Preclinical	Phase 1/2	Pivotal
PBFT02	Frontotemporal dementia - *GRN*	*18,000*[1-3]				upliFT-D
	Frontotemporal dementia - *C9orf72*	*21,000*[2-4]				upliFT-D
	Amyotrophic lateral sclerosis	*72,600*[5-6]				
	Alzheimer's disease with *rs5848 SNP*	*3.9M*[7-8]				
Unnamed	Huntington's disease	*60,000*[9]				

1. Greaves CV, et al. *J Neurol* 2019; 266:2075-2086. 2. Galvin JE, et al. *Neurology* 2017; 89:2049-2056. 3. Onyike CU, et al. *Int Rev Psychiatry* 2013; 25:130-137. 4. Moore KM, et al. *Lancet Neurol* 2020; 19: 145–156. 5. Brown et al. *Neuroepi* 2021; 55:342-353. 6. CDC ALS Registry Dashboard. 7. Sheng J, et al. *Gene* 2014; 141-145. 8. Alz Assoc. 2023 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2023;19. 9. Crowell et al. *Neuroepi*. 2021; 55:361-368

Demonstrated Leadership

Deep experience in rare disease, CNS disorders and genetic medicines

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