UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 24, 2024

PASSAGE BIO, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-39231	82-2729751
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

One Commerce Square 2005 Market Street, 39th Floor Philadelphia, PA	19103
(Address of principal executive offices)	(Zip Code)

(267) 866-0311
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value Per Share	PASG	The Nasdaq Stock Market LLC (Nasdaq Global Select Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On October 24, 2024, Passage Bio, Inc. (the "***Company***") presented a scientific presentation at the European Society of Gene & Cell Therapy 31st Annual Congress (the "***ESGCT Presentation***").

The Company also issued a press release on October 24, 2024, related to the ESGCT Presentation.

A copy of the press release and ESGCT Presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K.

The information in this Item 7.01, including Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, shall not be deemed to be "filed" for purposes of Section 18 of the Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended (the "***Securities Act***"). The information contained in this Item 7.01 and in the accompanying Exhibits 99.1 and 99.2 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Passage Bio, Inc. press release dated October 24, 2024
99.2	ESGCT Presentation
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PASSAGE BIO, INC.

Date: October 24, 2024

By: /s/ Kathleen Borthwick
Kathleen Borthwick
Chief Financial Officer

Passage Bio Presents Preclinical and Interim Clinical Data for PBFT02 in FTD-GRN at the European Society of Gene & Cell Therapy (ESGCT) 31st Annual Conference

Preclinical data demonstrated that an AAV1 vector achieved superior human progranulin levels in the CSF as compared to AAV5 and AAVhu68 (an AAV9 variant)

Nonclinical data showed PBFT02 improved lysosomal histopathology and reduced neuroinflammation in Grn knockout mice, and achieved widespread vector distribution throughout the nervous system in non-human primates

Company delivered data during an oral presentation on Thursday, October 24 at ESGCT

PHILADELPHIA, October 24, 2024 — Passage Bio, Inc. (Nasdaq: PASG), a clinical stage genetic medicines company focused on improving the lives of patients with neurodegenerative diseases, today announced the company delivered preclinical and interim clinical data as part of an oral presentation at the European Society of Gene & Cell Therapy (ESGCT) 31st Annual Congress being held October 22-25, 2024, in Rome, Italy.

Details of the oral presentation are below:

Abstract Title:	Non-clinical and early clinical development of PBFT02, an AAV gene therapy for frontotemporal dementia with *GRN* mutations (FTD-*GRN*)
Session:	7d: CNS gene therapy
Date & Time:	Thursday, October 24 from 9:00 a.m.-11:00 a.m. CEST (3:00 a.m.-5:00 a.m. ET)
Presenter:	Sue Browne, Ph.D., Chief Scientific Officer

Today's oral presentation at ESGCT outlined the robust preclinical data generated in the development of PBFT02, including studies that informed vector and dose selection and demonstrated the positive effects of elevating progranulin levels *in vivo*. Additionally, the presentation highlighted interim safety and biomarker data from the upliFT-D clinical trial, which validate the preclinical findings and position PBFT02 as a potential best-in-class progranulin-raising therapy.

“We are excited to share a detailed overview of the preclinical studies that support our PBFT02 program and informed our clinical development strategy,” said Will Chou, M.D., president and chief executive officer of Passage Bio. “These strong preclinical results gave us confidence in choosing the AAV1 vector and ICM administration as a differentiated approach to administer our gene therapy to patients in our ongoing upliFT-D clinical study. It’s also encouraging to see these preclinical findings translate into the clinic, with interim PBFT02 data demonstrating a well-tolerated safety profile and consistent, durable increases in CSF progranulin levels. We remain committed to advancing PBFT02 in FTD and look forward to exploring its therapeutic potential in additional neurodegenerative diseases that could benefit from elevated progranulin levels.”

Data Summary

- Capsid comparison study in non-human primates (NHPs) showed the AAV1 vector achieved superior human PGRN levels in the CSF as compared to AAV5 and AAVhu68 (an AAV9 variant) following intra-cisterna magna (ICM) administration
- Dose escalation study in *Grn* knockout mice showed PBFT02 improved lysosomal histopathology and reduced neuroinflammation throughout the brain following intra-CSF delivery, including evidence suggesting that higher levels of PGRN may provide additional benefits
- NHP biodistribution study showed ICM administration of PBFT02 achieved high levels of gene distribution throughout the nervous system, including vector delivery to the cortical and sub-cortical brain regions affected in FTD, and to the spinal cord
- PBFT02 was well tolerated in NHPs, and ICM administration resulted in dose-dependent PGRN elevations in NHP CSF
- Interim safety and biomarker data from the upliFT-D clinical study demonstrated that Dose 1 of PBFT02 was generally well-tolerated after ICM administration and led to consistent, durable increases in levels of CSF progranulin in all treated Cohort 1 patients, with elevated CSF progranulin levels sustained up to 12 months post-administration

Additional details on the meeting can be found at the ESGCT 31st Annual Congress website, and a copy of the oral presentation deck will be available on the Investor Events and Presentations page of the Passage Bio corporate website.

About PBFT02

PBFT02 utilizes an AAV1 viral vector to deliver, through ICM administration, a functional *GRN* gene that encodes for PGRN. This vector construct and delivery approach aim to elevate PGRN levels in the central nervous system to alter the course of neurodegenerative diseases. Interim clinical data from the upliFT-D Phase 1/2 study in FTD-*GRN* participants shows that ICM administration of PBFT02 resulted in robust PGRN elevations in the CSF.

The potential clinical benefit of PBFT02 is supported by extensive preclinical studies. In non-human primates, a single ICM administration of PBFT02 led to broad vector distribution throughout the CNS, and robust, dose-dependent elevations in PGRN levels in CSF. An NHP study also demonstrated that AAV1 was particularly proficient at transducing ependymal cells. In a murine FTD model, PBFT02 administration improved lysosomal function and reduced neuroinflammation.

About Passage Bio

Passage Bio (Nasdaq: PASG) is a clinical stage genetic medicines company on a mission to improve the lives of patients with neurodegenerative diseases. Our primary focus is the development and advancement of cutting-edge, one-time therapies designed to target the underlying pathology of these conditions. Passage Bio's lead product candidate, PBFT02, seeks to treat neurodegenerative conditions, including frontotemporal dementia, by elevating progranulin levels to restore lysosomal function and slow disease progression.

To learn more about Passage Bio and our steadfast commitment to protecting patients and families against loss in neurodegenerative conditions, please visit: www.passagebio.com.

Forward-Looking Statements

This press release contains “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; our expectations about our collaborators’ and partners’ ability to execute key initiatives; and the ability of our product candidates to treat their respective target CNS disorders. 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, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; 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; 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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Non-clinical and early clinical development of PBFT02, an AAV gene therapy for FTD with *GRN* mutations (FTD-*GRN*)

SE Browne, YG Ni, KJ Quadrini, T Voss, MS Forman, J Chavez, N Miller, C Hinderer, JM Wilson

ESGCT **OR070**, 24 October 2024

Disclosures

- Sue Browne, Ph.D, Yan Yi, Ph.D and Juan Chavez, MD, Ph.D are employees of Passage Bio, Inc. (the “Company”) and have certain equity interests in the Company
- James Wilson, MD, Ph.D is a paid advisor to the Company and has certain equity interests in the Company.
- James Wilson, MD, Ph.D and Christian Hinderer are inventors on patents that have been licensed to the Company and for which they may receive payments.

FTD-*GRN*: A Devastating Adult Disease

Frontotemporal Degeneration, FTD

- Rapidly progressive, fatal, neurodegenerative disease affecting the frontal and temporal lobes of the brain
- Common cause of early-onset dementia
  - Onset typically between ages of 40 and 65 years

FTD-*GRN*

- 5 to 10% of FTD is caused by mutations in the ***granulin*** **(*GRN*)** gene
  - Haploinsufficiency reduces brain **progranulin** to 30-50% of normal
- Prevalence in EU + US is ~18,000
- **No approved disease-modifying therapy**

Loss of inhibition

Apathy

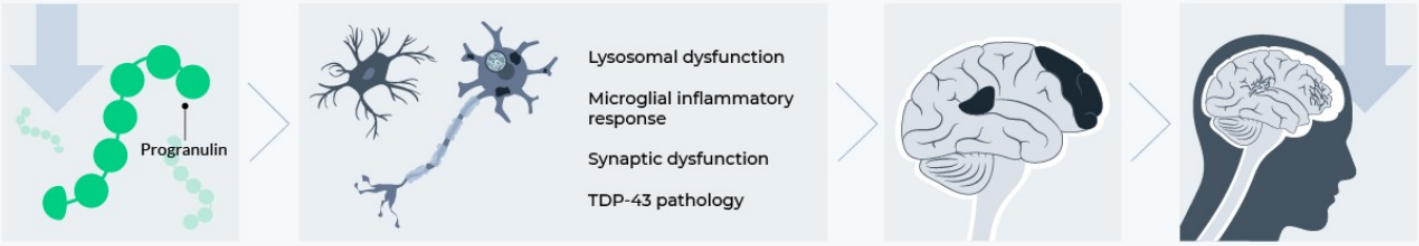
Social withdrawal

Hyperorality (mouthing of objects)

Ritualistic compulsive behaviors

Progranulin (PGRN) Deficiency is the Defining Characteristic of FTD-*GRN,* Leading 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

Our approach: **AAV gene therapy to deliver functional PGRN to the brain**

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

PBFT02 Development Pathway

- Transgene cassette design
- Dose ranging in granulin-deficient mice
- Vector selection in NHPs
- Clinical lead biodistribution, safety, toxicology in NHPs

Penn GENE THERAPY PROGRAM

Discovery | Pre-clinical | IND

- Ph 1/2 clinical study in FTD-*GRN*

PassageBio

Phase 1/2 | Pivotal | Filing/Comm

upliFT-D

Abbreviations: NHP, non-human primate

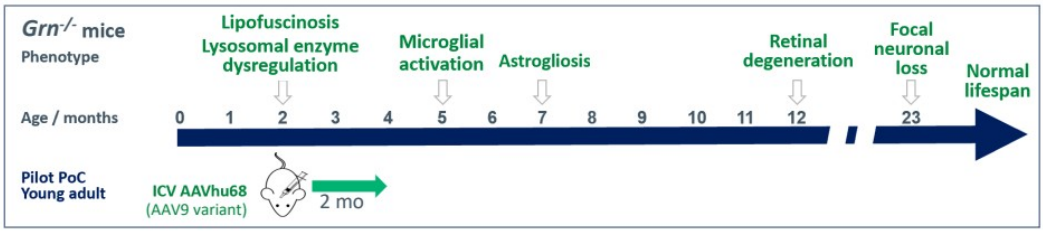
Discovery & Lead ID

h*GRN* Transgene Cassette Optimized

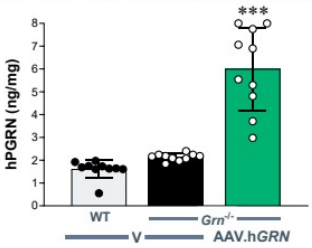
- Codon-optimized sequence of the human *GRN* gene under the control of the ubiquitous CB7 promoter
- Designed to deliver functional *GRN* genes encoding PGRN to brain and spinal cord
- Ability to transduce multiple CNS cell types

Proof of Concept: h*GRN* Transgene Delivery Improved Lysosomal Function in PGRN-Deficient Mice

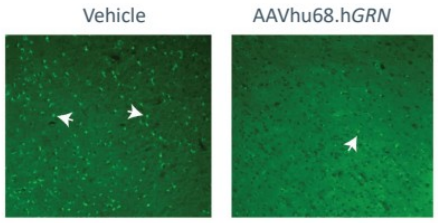
Efficacy in *Grn* knockout mice after tool AAVhu68.h*GRN* vector ICV administration to CSF



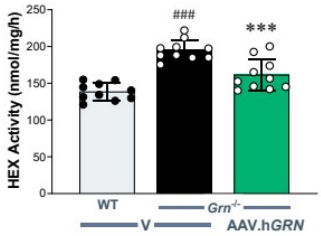
hPGRN Expressed in Brain of *Grn*$^{-/-}$ mice



Reduced Lipofuscin Fluorescence in Thalamus



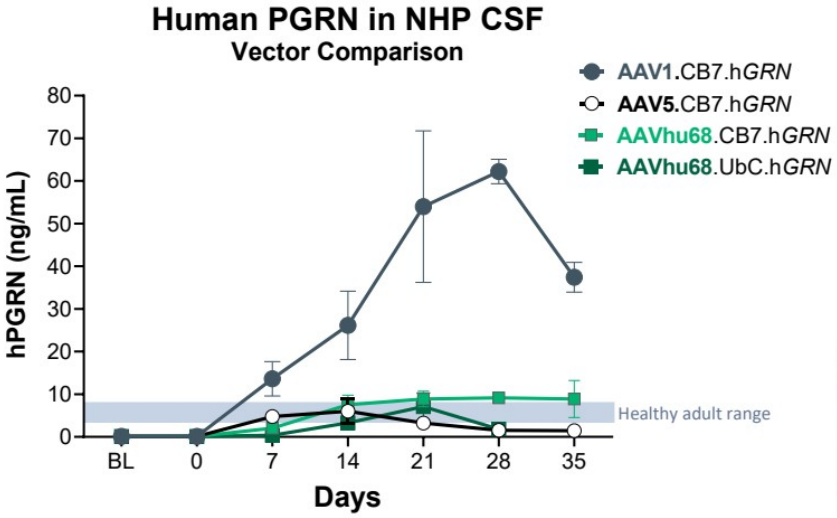
Reduced Brain Hexosaminidase Activity



7 Tissue collected 60 days post-ICV administration. N = 10/gp ### $p < 0.005$ vs WT + V control; *** $p < 0.005$ vs GRN-/-+ V , one-way ANOVA + Tukey's multiple comparisons test

Abbreviations: CSF, cerebrospinal fluid; *GRN/Grn,* granulin gene; ICV, Intra-cerebroventricular; PBS, phosphate-buffered saline; V, Vehicle. *Reference:* Hinderer et al., *Annals Clin Trans Neurology.* 2020.

AAV1 Selected as Vector Serotype after a Capsid Comparison Study in NHPs



- Superior hPGRN levels in CSF after **AAV1** compared to **AAV5** and **AAVhu68** (AAV9 variant)
  - Clinical delivery route, ICM
- **AAV1.*hGRN*** selected as clinical candidate, **PBFT02**

PBFT02 taken into IND-enabling studies

- Dose escalation in mice
- Safety, tolerability, and biodistribution in NHPs

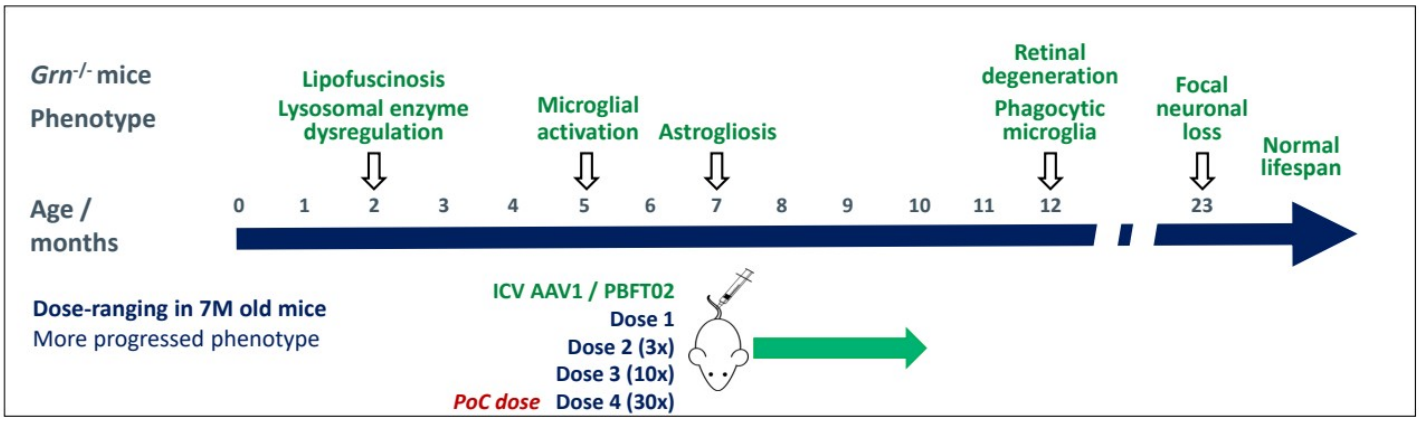
Rhesus macaques (n=2/group) ICM-delivered AAV.hPGRN (3.3 x 10^{11} GC/g brain), day 0
Size and duration of elevation muted by immune response to human PGRN.

8 *Shading:* Healthy adult human sample range, n = 61 (Passage Bio data)

Abbreviations: CSF, cerebrospinal fluid; ICM, intra-cisterna magna; hGRN, human granulin gene; NHP, non-human primate; PGRN, progranulin. *Reference:* Hinderer et al., *Annals Clin Trans Neurology.* 2020

Non-clinical

PBFT02 Dose Selection: Efficacy in *Grn*$^{-/-}$ Mice



- Assayed four PBFT02 doses
  - Starting from 1/30 lower than dose used in prior mouse proof of concept (PoC) study

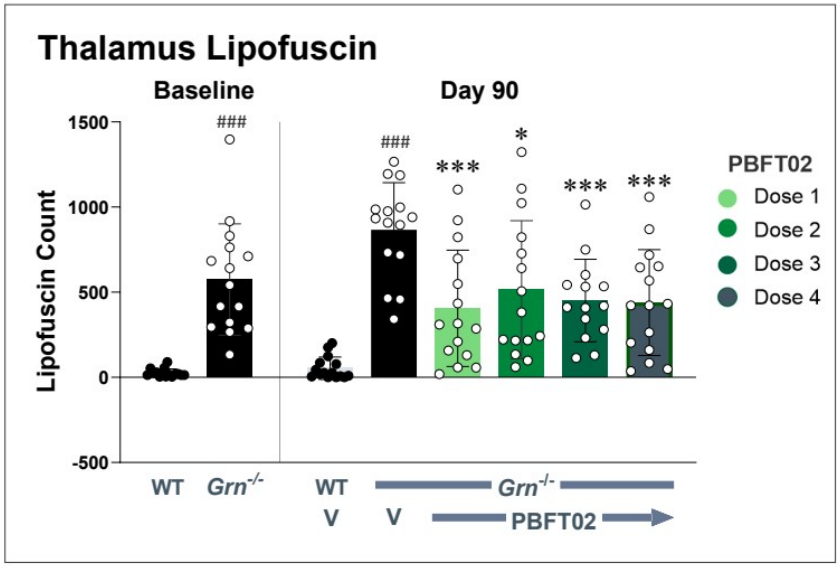
Abbreviations; *GRN,* granulin gene; ICV, Intra-cerebroventricular; M, month. *Reference:* Hinderer et al., *Annals Clin Trans Neurology*. 2020

PBFT02 Improved Lysosomal Function in the Brain

Dose ranging in *Grn*$^{-/-}$ mice after intra-CSF delivery

Lipofuscin deposition in brain was reduced by ICV PBFT02

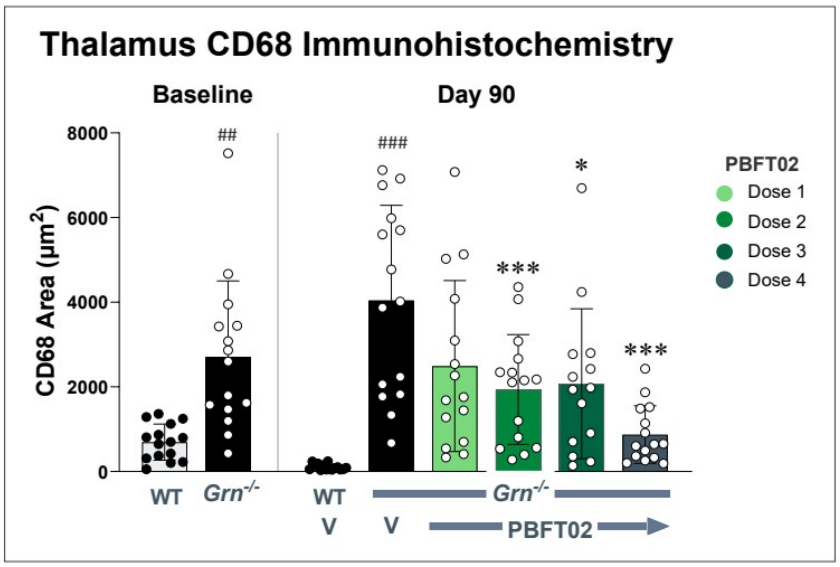
- Partially reversed existing pathology
- Also effective in cortical and sub-cortical regions after ICV administration



10 *Grn*$^{-/-}$ and WT mice (n=14-15/gp) ICV-administered PBFT02 or vehicle (V). Baseline controls are untreated mice on Day 1. Bars: mean +/- SEM.
$p < 0.005$ vs WT control; * $p < 0.05$, *** $p < 0.005$ vs *Grn*-/- + V , one-way ANOVA then Tukey's multiple comparisons test. *Abbreviations*; *Grn*, granulin gene; ICV, Intra-cerebroventricular; V, vehicle; WT, wildtype

Neuroinflammation Reduced in the Brain after PBFT02

Dose ranging in *Grn*$^{-/-}$ mice after intra-CSF delivery

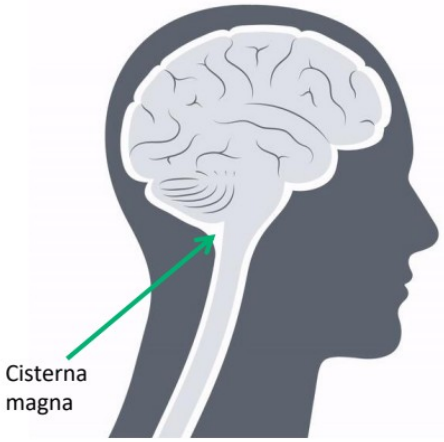


Activated microglia reduced in both cortical and sub-cortical brain regions after ICV PBFT02

- From combined mouse data, Dose 1 established as minimum effective dose
- Dose 2, 3 and 4 equivalents taken forward into NHP studies

11 *Grn*$^{-/-}$ and WT mice (n=14-15/gp) ICV-administered PBFT02 or vehicle (V). Baseline controls are untreated mice on Day 1. Bars: mean +/- SEM.
$p < 0.01$; ### $p < 0.005$ vs WT; * $p < 0.05$, *** $p < 0.005$ vs *Grn*$^{-/-}$ + V , one-way ANOVA then Tukey's multiple comparisons test. *Abbreviations; GRN,* granulin gene; ICV, Intra-cerebroventricular; V, vehicle; WT, wildtype

Intra-Cisterna Magna (ICM) Administration of PBFT02 Enables PGRN Delivery Throughout CNS



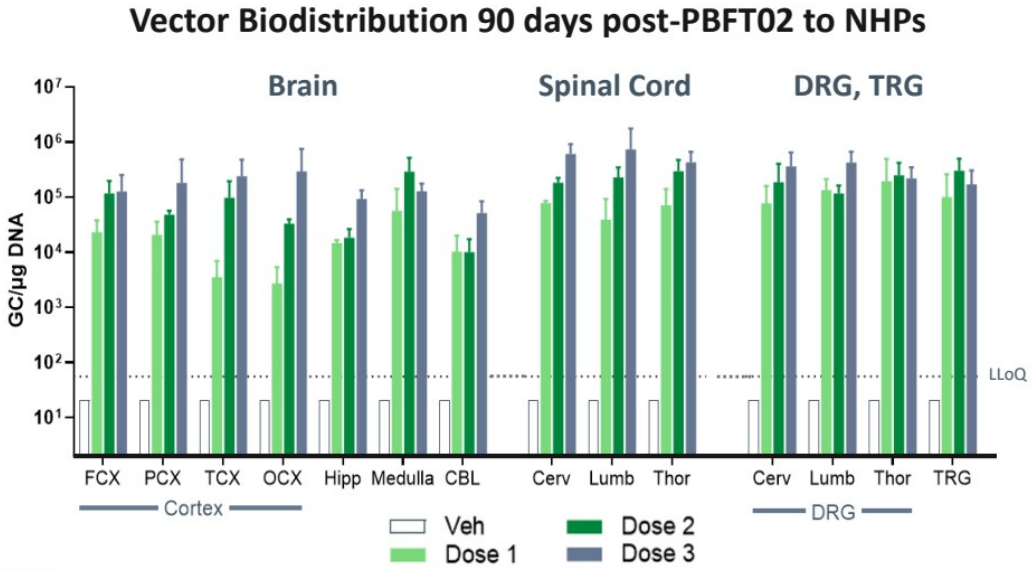
- Directly delivers vector into the CSF via a single infusion, to reach CNS, PNS, and peripheral tissues[1]
  - Allows for broad CNS biodistribution
  - Lower doses compared to IV systemic delivery
  - Reduced impact of neutralizing antibodies
- Brief, < 1 h, non-surgical, CT-guided procedure
  - Infusion catheter **does not** enter brain tissue
- **Expressed PGRN directly impacts transduced cells**
- **Secreted PGRN cross-corrects proximal cells**

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; h, hour; ICM, intra-cisterna magna; IV, intra-venous; PNS, peripheral nervous system; PGRN, progranulin.

Reference: [1]Hinderer et al, *Human Gene Therapy*. 2018, 29:15-24

ICM Administration to NHPs Achieved High Levels of Gene Distribution Throughout the Nervous System

- Robust vector delivery to cortical and sub-cortical brain regions affected in FTD
- NHP PBFT02 dose 1 (equivalent to upliFT-D clinical Dose 1) resulted in ~10e^4 GC/ug DNA throughout the brain

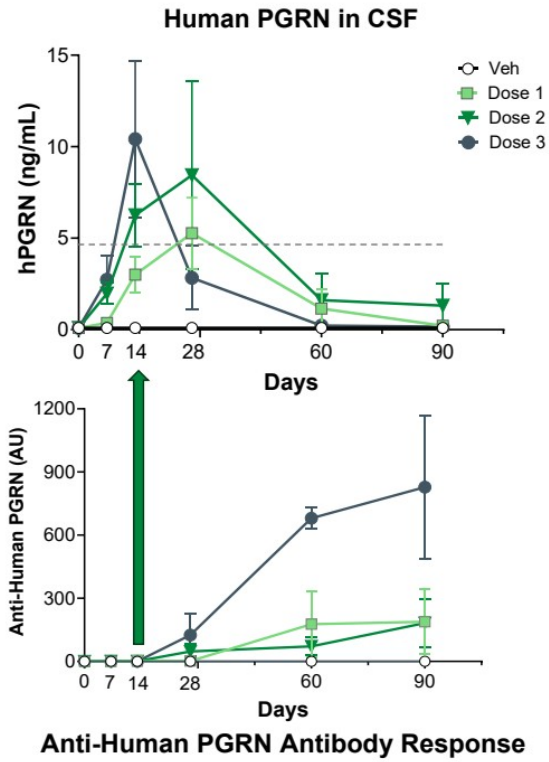


PBFT02, n=3/group; Veh, n=2/group. Data are mean +/- SEM.

Abbreviations: 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; NHP, non-human primate; OCX, occipital cortex; PCX, parietal cortex; TCX, temporal cortex; TRG, trigeminal root ganglio; Thor, thoracic; Veh, vehicle

PBFT02 Dose-Dependently Increased PGRN in NHP CSF

- Human PGRN was detected in NHP CSF shortly after ICM PBFT02 administration
- Dose-dependent increases in PGRN seen up to day 14
- Thereafter, an immune response to the human protein in NHPs attenuated PGRN levels
  - Not relevant when dosing FTD-*GRN* haploinsufficient individuals



14 PBT02, n=3/group; Veh, n=2. Data: mean +/- SEM. Dashed line is mean healthy adult human PGRN (n=61)

Abbreviations: AU, arbitrary units; CSF, cerebrospinal fluid; ICM, intra-cisterna magna; NHP, non-human primate; PGRN, progranulin; SEM, standard error of mean; Veh, vehicle

PBFT02 was Well Tolerated in NHPs

Followed for 90 days after a single ICM delivery of one of 3 doses

Assessments	Observations in NHPs
Abnormal clinical, neurological, or behavioral signs	None
Blood and CSF clinical pathology	Mild and transient increases in CSF leukocytes only
DRG, TRG, sensory nerve histopathology	Typically minimal to mild • Consistent with NHP AAV responses • No clinical correlates observed
NOAEL	Not reached

Dose 1 equivalent taken forward into a Ph1/2 clinical study, upliFT-D

Abbreviations: CSF, cerebrospinal fluid; DRG, dorsal root ganglion; ICM, intra-cisterna magna; NOAEL, no observed adverse effect level; TRG, trigeminal root ganglion

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

- Phase 1/2 multi-center, open label dose-escalation study
- Primary endpoints: Safety and tolerability

Dosing Complete **Enrolling**

Progress

- FTD-*GRN* Cohort 1 (n = 5) dosing complete
- Longest followed 12 months

Dose 1: 3.3e10 GC/g estimated brain weight. ⊙ IDMC review

*Revised steroid regimen: 1 g methylprednisolone IV daily to day 3, then 60 mg oral prednisone to day 60; Participant 1 received 60 mg oral prednisone to day 60 and had 2 SAEs. Safety cut-off: 08/20/2024

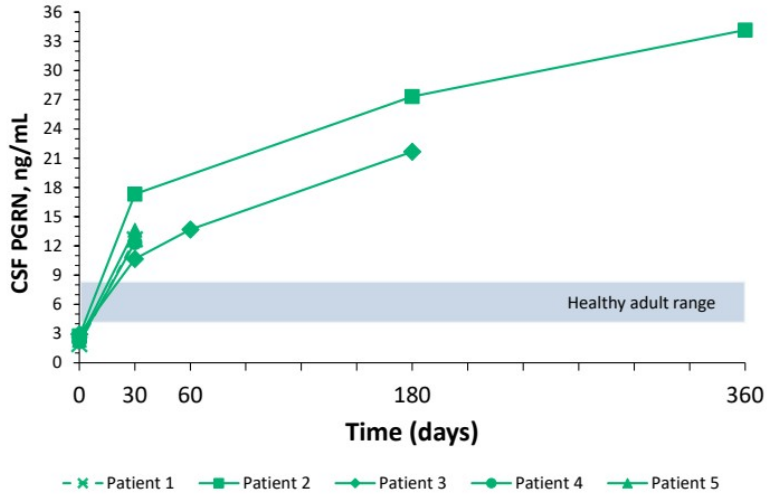
Abbreviations: DRG, dorsal root ganglion ICM, intra-cisterna magna; SAE, severe adverse event

Safety Observations

- All four Cohort 1 participants who received a revised immunosuppression regimen* had no SAEs or significant immune responses
- No patients showed evidence of DRG toxicity, as measured by nerve conduction studies
- No complications of ICM administration

Find more information on the upliFT-D trial here

Cohort 1 Interim Data: PBFT02 Administration Leads to Robust and Sustained Increases in CSF PGRN



- Continued elevation of CSF PGRN at 6 M (n=2) and 12 M (n=1)
  - Rate of increase slowing over time
- Consistent response across all five treated patients
- Plasma PGRN remained below healthy adult control levels
- Potential for best-in-class profile

Shading: Healthy adult human sample range of PGRN levels in CSF, n=61 (Passage Bio data)
Abreviations: CSF, Cerebrospinal fluid; M, month; PGRN, progranulin

PBFT02 Preclinical and Clinical Development Summary

Strong preclinical profile of PBFT02, a gene therapy to elevate PGRN in FTD-*GRN*

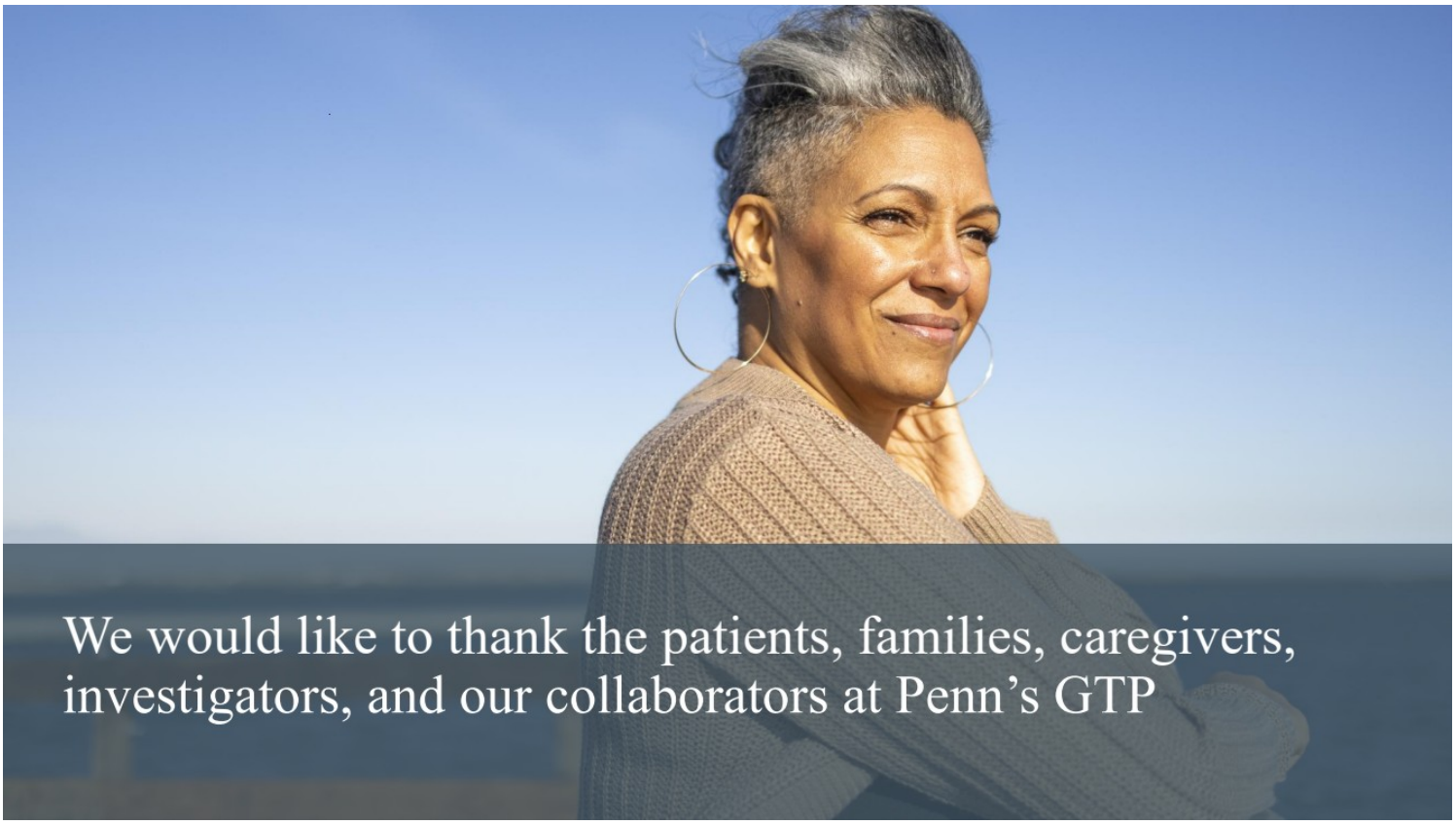
- PBFT02 improved lysosomal histopathology and neuroinflammation in *Grn*$^{-/-}$ mice
- Broad transduction across the brain and spinal cord in NHPs after ICM administration into the CSF
- Well-tolerated in NHPs with no clinical adverse effects

PBFT02 shows clinical potential as a one-time, CSF-delivered gene therapy approach

- Consistent, durable elevation of CSF PGRN at 6-months and 12-months
- Dose 1 well-tolerated among all Cohort 1 patients who received the revised steroid regimen*
- Continuing to assess Dose 1 in Cohort 2, given the robust effects on PGRN expression

*Revised steroid regimen: 1 g methylprednisolone IV daily up to day 3, followed by 60 mg oral prednisone to day 60. Safety cut-off: 08/20/2024

Abbreviations: CSF, cerebrospinal fluid; *GRN*/*Grn*, granulin gene; ICM, intra-cisterna magna; NHP, non-human primate; PGRN, progranulin


We would like to thank the patients, families, caregivers,
investigators, and our collaborators at Penn’s GTP