# upliFT-D: A Clinical Trial of Gene Therapy (PBFT02) for Frontotemporal Dementia With Progranulin Gene Mutations (FTD-*GRN*)

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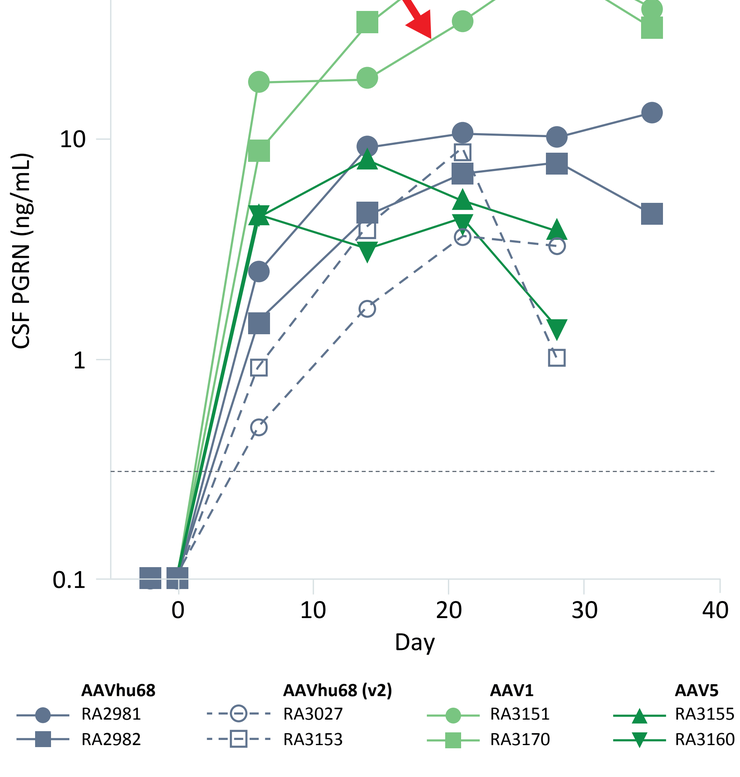
## Background

- In up to 10% of patients with **frontotemporal dementia (FTD)**, the disease is caused by changes or mutations in a gene called ***GRN*** that makes a protein called **progranulin (PGRN)**.[1]
- Most *GRN* mutations lead to insufficient PGRN in the brain to ensure proper function.[2]
- To increase the levels of PGRN in the brain, a potential new gene therapy called **PBFT02** has been developed by Passage Bio, Inc.[3,4]
- PBFT02 is a one-time gene therapy that delivers a healthy working copy of the *GRN* gene to the brain, which then makes more PGRN, reducing or eliminating the protein deficiency in patients with FTD-*GRN*. [3,5]
- Gene therapy offers a way to deliver a healthy working copy of the gene using an envelope called the **adeno-associated virus (AAV) vector** (a way to deliver genetic material into cells).[4]

## Preclinical Evidence

- Passage Bio tested several AAV vectors for *GRN* gene delivery and selected the one that led to the greatest increase in PGRN levels (**Figure 1**).[6]
- When PBFT02 was tested in monkeys it was shown that the delivery of a functional human *GRN* gene to the brain resulted in a substantial increase of PGRN levels in cerebrospinal fluid surrounding the brain[6] (**Figure 1**, red arrows).

**Figure 1 Production of PGRN Following the Administration of AAV Vectors Carrying the Human *GRN* Gene to the Monkey Brain[6]**

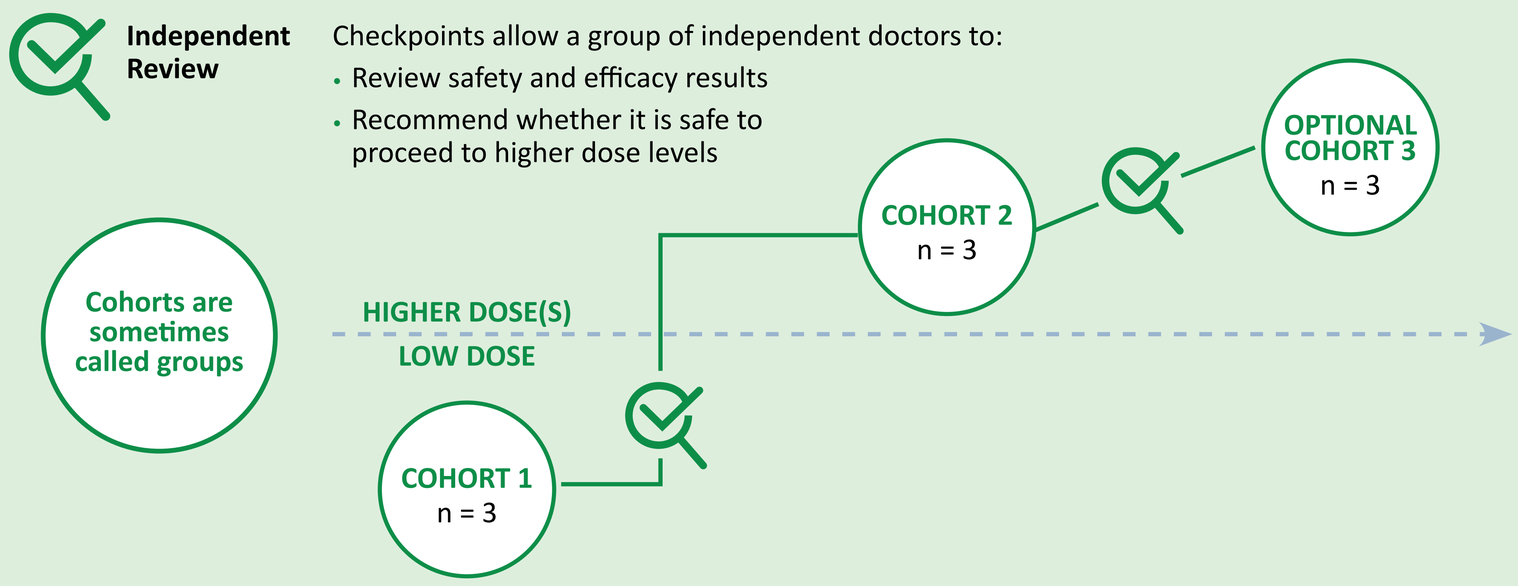



## upliFT-D – A First-in-Human Clinical Trial

### Trial Design

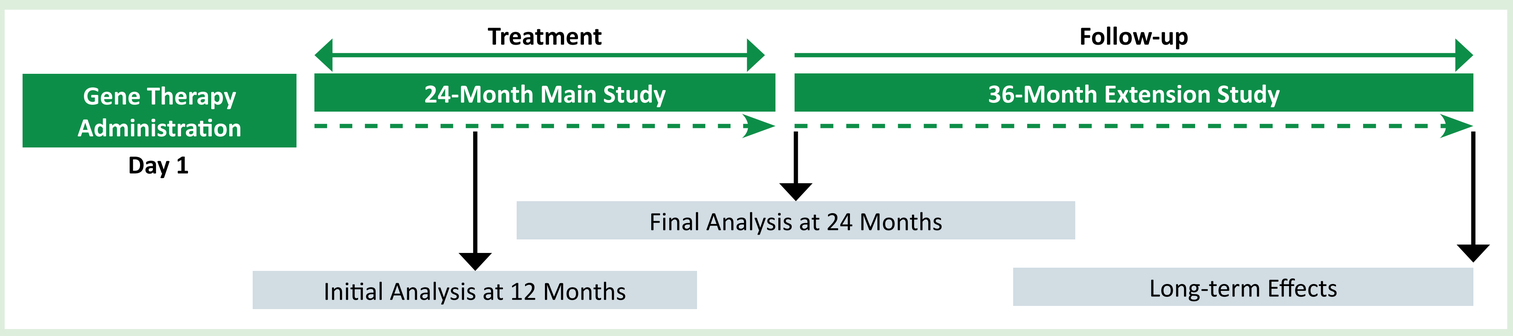
- **All patients** will receive **treatment** in the upliFT-D trial (**Figure 2**).[5,7]
- **Cohort 1**: patients will receive a low dose of PBFT02; **Cohort 2**: patients will receive a higher dose of PBFT02; and **Cohort 3**: an optional third dose level may be studied, depending on the results from the first 2 groups.[5,7]

**Figure 2 The upliFT-D Trial Design[5,7]**




- Patients will be followed for up to 5 years, including a 2-year main study and a 3-year safety extension study (**Figure 3**).[8]

**Figure 3 Treatment Duration[8]**




### Goals of the Clinical Trial

- The upliFT-D clinical trial[5] is designed to provide information about the safety, effectiveness, and appropriate dosing of PBFT02 gene therapy in patients with FTD-*GRN* (**Figure 4**).[7]
- Safety and efficacy will be monitored with different types of tests.

**Figure 4 Data Collection in the upliFT-D Clinical Trial[5,7]**

**SAFETY**

Is the treatment…

- Safe?
- Causing side effects? If so, what are they?

**EFFECTIVENESS**

Does the treatment…

- Help improve cognitive functions?
- Help improve behavioral and language symptoms?

**DOSING**

Do different doses…

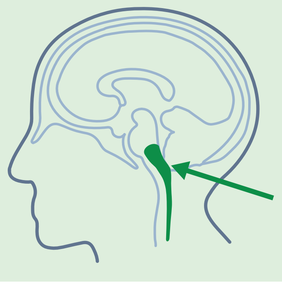
- Change the effectiveness of the potential treatment?
- Change the type and intensity of side effects?

### Key Eligibility Criteria[5,7]

- To be eligible to join this clinical trial, participants must:
  - be aged **35 to 75 years**
  - have a diagnosis of FTD with **a confirmed *GRN* mutation**
  - have **mild FTD symptoms**
  - have **no complicating medical conditions** and
  - be living in the community.
- There are other criteria that must be met in order to join this clinical trial.[5]

### How will gene therapy be administered?

- Participants will receive a **single injection** of the PBFT02 gene therapy into a region called the **cisterna magna**,[5,7] which is the space between the brain and the spinal cord; the injection will be administered by an interventional radiologist or a neurosurgeon.[9]



## Additional Information for Patients and Caregivers

- Patients with FTD may be eligible for enrollment in clinical trials of investigative therapies, so an early diagnosis is critical. Caregivers should reach out to their health care professional to learn more.

## Links to Resources

- If you would like to learn more about FTD or the upliFT-D clinical trial, please visit: ftdclinicaltrial.com.
- Please contact Passage Bio to learn more about the upliFT-D clinical trial: https://passagebioclinicaltrials.com/Frontotemporal-Dementia/#contactForm.

## References

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## Disclosures

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