AVIADOBIO

# Frontotemporal dementia with progranulin mutations research (FTD-GRN)

## AVIADOBIO: CHASING CURES. DELIVERING HOPE.™

At AviadoBio, we are relentlessly chasing cures by translating groundbreaking science and precision delivery into potentially life-changing medicines for people living with neurological disease, beginning with frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS).

### OUR FOCUS

AviadoBio is on a mission to transform the lives of people living with neurodegenerative disorders by developing and delivering potentially transformative gene therapies for neurological diseases such as FTD and ALS.

### OUR PLATFORMS

AviadoBio is focused on targeted and precise drug delivery and dosing for maximal biodistribution to the brain and spinal cord with a favorable safety profile. We believe delivery to be the game-changer in overcoming challenges with existing treatment pathways.

## WHAT IS FRONTOTEMPORAL DEMENTIA?

Frontotemporal Dementia (FTD) is a devastating form of early-onset dementia that varies in each individual. Symptoms of FTD can include changes in personality or uncharacteristic behaviors, progressive loss of language, loss of executive function and cognitive abilities, apathy, and reduced mobility.[1-3] FTD causes a substantial reduction in life expectancy, and on average people with FTD die 3-13 years from diagnosis.[4-7]

FTD can be separated into familial and sporadic FTD.[8] Sporadic FTD is more common and occurs when no genetic cause for FTD is known. However, FTD is highly heritable, and a strong family history is found in approximately 30-50% of all FTD patients.[5,8,9] Mutations in progranulin (GRN) account for about 10% of all FTD cases and approximately 22% of familial cases of FTD.[8]

Access to genetic counseling and testing is an important step for patients with FTD to determine if their disease is the result of a genetic mutation. While there are currently no approved disease-modifying treatments for FTD, learning whether FTD is caused by a genetic mutation may help clinicians to determine if patients are eligible for any clinical trials.

## WHAT IS A PROGRANULIN MUTATION?

This is a mutation in the GRN gene. Genes are instructions that tell the body's cells what to do. Sometimes, genes contain errors called mutations.

The GRN gene tells the body to make progranulin, which is a protein that plays an important role in the healthy functioning of cells in the brain. When there is a mutation in the GRN gene, the body may not make enough progranulin, which can lead to cell death in the brain and the symptoms of FTD.

Mutated gene

Gene with no mutation

## WHAT IS AVB-101?

AVB-101 is an investigational one-time therapy designed to deliver a functional copy of the progranulin (GRN) gene directly to the brain, thereby potentially restoring progranulin levels and stopping disease progression in patients with FTD-GRN. It is delivered directly into the brain using a neurosurgery procedure. AVB-101 has been granted orphan designation by the U.S. Food and Drug Administration and the European Commission.

## ASPIRE-FTD CLINICAL TRIAL FOR FTD-GRN

All clinical trials have specific eligibility criteria for participants to ensure that research is well-controlled. For FTD clinical trials, this may include a specific genetic profile for FTD, how quickly the disease is advancing, and how far the disease has already progressed. People with more advanced FTD may be excluded from the opportunity to participate in certain trials. Not all patients will qualify for all studies.

If you are interested in participating in a study, it is critical that you speak to your neurologist to learn more about opportunities that might be best for you.

ASPIRE·FTD

**ASPIRE-FTD** is a Phase 1/2 open-label, multi-center study designed to evaluate the safety and preliminary efficacy of AVB-101 in patients with FTD-GRN. Individuals may be eligible to participate if diagnosed with FTD-GRN (confirmed with a genetic test), among other criteria.

For more information about the ASPIRE-FTD study and to find clinical trial sites, visit: aspire-ftd.com and clinicaltrials.gov/study/NCT06064890.

## WHY IS SURGERY NEEDED TO DELIVER AVB-101?

AVB-101 is designed to be delivered directly to a part of the brain called the thalamus. The thalamus is a key hub for connectivity in the brain with widespread projections across the brain including the cortex – a key area affected in FTD-GRN. Gene therapy aims to deliver functional gene copies to deficient cells. By increasing levels of progranulin in cortical brain tissue, AviadoBio hopes to restore physiological function to patients with FTD due to progranulin mutations (who are relatively deficient in progranulin).

With central nervous system diseases like FTD, the blood-brain barrier can be a hurdle for gene therapy delivery. The blood-brain barrier is a layer of cells between the blood vessels and the brain that protects the brain from harmful outside substances while letting through nutrients that the brain cells need.

The neurosurgery procedure to deliver AVB-101 aims to bypass the blood-brain barrier, thereby limiting the treatment to only the brain itself, where it is needed the most. At the same time, this reduces the amount of dose required and potential exposure in other parts of the body.

## MEETING AN URGENT NEED FOR FTD RESEARCH

While an FTD diagnosis can be devastating for many families, there is much reason for hope. Researchers are working relentlessly to find potential new treatments for FTD with multiple clinical trials underway.

There is an urgent need for collaboration between researchers, clinicians, patients, advocates, and families to courageously explore new approaches to tackling FTD, including innovative and targeted delivery approaches.

A strong family history is found in approximately 30-50% of all FTD patients[5,8,9], and much of the current research focuses on genetic FTD, especially FTD-GRN. People living with FTD are an essential part of the research process to help discover new treatments. Without these individuals and their families, clinical research cannot advance.

Participating in a clinical trial can be a big decision for people with FTD and their families. While study participants may not directly benefit from an investigational treatment in a clinical trial, participating in research may help some people feel like they are contributing to a larger body of research for future generations who might be affected by FTD.

### REFERENCES


1. Pressman PS and Miller BL. Biol Psychiatry 2014;75:574–81;
2. Young JJ et al. Ther Adv Psychopharmacol 2018;8:33–48;
3. Hogan DB et al. Can J Neurol Sci 2016;43 Suppl 1:S96–109;
4. Onyike CU and Diehl-Schmid J. Int Rev Psychiatry. 2013;25(2):130–137;
5. Riedl L et al. Neuropsychiatr Dis Treat. 2014;10:297–310;
6. Onyike CU. Neuroepidemiology. 2011;37:166–167;
7. Kansal K et al. Dement Geriatr Cogn Disord. 2016;41:109–122;
8. Greaves CV and Rohrer JD. J Neurol 2019;266:2075–86;
9. Kuang, L., et. al. Human Molecular Genetics, 2020;29(4):624-634


AVIADOBIO.COM



@AviadoBio AviadoBio