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 life-changing medicines for people living with frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS).

OUR FOCUS

Targeted and precise drug delivery and dosing for maximal biodistribution to the brain and spinal cord with a favorable safety profile.

OUR PLATFORMS

Designing next-generation gene therapy constructs and delivery platforms optimized for delivery route, target tissue, safety, and treatment effect.

WHAT IS FRONTOTEMPORAL DEMENTIA?

Frontotemporal Dementia (FTD) is a devastating form of early-onset dementia and is characterized by a rapid decline in executive function (attention control, working memory, problem-solving, etc.), behavior and/or language,[1] and typically leads to death within 7 to 13 years of symptom onset and 3 to 10 years from diagnosis.[2,3] People with FTD experience severe personality changes, behavioral disturbance, loss of language, apathy, and reduced mobility.[4]

FTD can be separated into familial and sporadic FTD. Sporadic FTD is more common and occurs when only one person in a family has FTD. While some familial FTD has no known cause, a strong family history is found in about one-third of cases. The majority of inherited FTD is accounted for by autosomal dominant disease-causing mutations in three genes, including the GRN (progranulin) gene.[5]

Access to genetic counseling 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 opens doors to patients and enables their clinicians to help determine if they 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, adeno-associated virus-based (AAV) gene supplementation therapy for FTD patients with disease-causing mutations in the GRN gene. Designed as a one-time therapy to potentially halt disease progression, it delivers a functional copy of the GRN gene to restore progranulin levels in the brain. 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 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, which has extensive connections to other parts of the brain, including the frontal and temporal lobes, which are critical in frontotemporal dementia.

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.

With central nervous system diseases like frontotemporal dementia, 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.

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 about one-third of FTD cases, 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.

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