The Promise of FTD Research Trials: What Should I Know About Current Drug Studies?

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Chief Scientific Officer

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Current interventional trials in genetic & sporadic FTD

**FTD-GRN (Progranulin)**
- Latozinemab (AL001), Phase 3, Alector/GSK
- PR006, Phase 1/2, Prevail Therapeutics/Eli Lilly
- PBFT02, Phase 1/2, Passage Bio
- TAK-459/DNL359, Phase 1/2, Denali Therapeutics/Takeda
- AVB-101, Phase 1/2, AviadoBio (*not yet recruiting*)

**FTD-C9orf72**
- WVE-004, Phase 1/2, Wave Life Sciences
- TPN-101, Phase 2, Transposon Therapeutics

**Sporadic FTD**
- NIO752, Phase 1, Novartis
- Verdiperstat, Phase 1, Investigator-sponsored
- Oxytocin, Phase 2, Lawson Health Research Institute
- Low-dose lithium, Phase 2, Columbia University
ClinicalTrials.gov is a searchable database of clinical studies conducted in the US and around the world.

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 434,068 research studies in all 50 states and in 221 countries.

See listed clinical studies related to the coronavirus disease (COVID-19).

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your health care provider and learn about the risks and potential benefits.

e.g. FTD, PPA, progranulin, GRN, C9orf72

e.g. NCT04374136, PROCLAIM, FOCUS-C9, AL001, DNL593
<table>
<thead>
<tr>
<th><strong>Sponsor:</strong></th>
<th>The entity running the trial, usually a company or a university</th>
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<tbody>
<tr>
<td><strong>Development Stage</strong></td>
<td>Phase 1, 2 or 3 in the process for FDA approval (+ trial name)</td>
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<tr>
<td><strong>ClinicalTrials.gov identifier:</strong></td>
<td>Enter this number at <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a> to see the specific details of the trial</td>
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<tr>
<td><strong>Enrollment criteria:</strong></td>
<td>Criteria that interested individuals must meet in order to qualify to participate in the trial</td>
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<td><strong>Experimental drug:</strong></td>
<td>The name of the experimental drug</td>
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<td><strong>Delivery method:</strong></td>
<td>How the experimental drug will be administered to the participant (by mouth, injection, infusion, etc.)</td>
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<td><strong>Placebo-controlled?:</strong></td>
<td>Will some participants receive a placebo instead of the experimental drug?</td>
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<td><strong>Length of trial:</strong></td>
<td>How long participants will be monitored</td>
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<td><strong>Locations:</strong></td>
<td>Countries where clinical trial sites are planned or actively recruiting participants</td>
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<tr>
<td><strong>How to contact:</strong></td>
<td>Phone number and website to contact the sponsor</td>
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Explanation of how the experimental drug targets processes that have led to FTD:

Adapted from the National Institute on Aging
Current clinical trials for FTD caused by mutations in progranulin (GRN)

- **INFRONT-3**
  - Latozinemab (AL001), Phase 3, Alector/GSK (Antibody)
- **PROCLAIM**
  - PR006, Phase 1/2, Prevail Therapeutics/Eli Lilly (Gene replacement)
- **upliFT-D**
  - PBFT02, Phase 1/2, Passage Bio (Gene replacement)
- **TAK-594/DNL593**, Phase 1/2, Denali Therapeutics/Takeda (Protein replacement)
- **AVB-101**, Phase 1/2, AviadoBio (*not yet recruiting*) (Gene replacement)

All of these trials require participants to know they carry a mutation in progranulin in order to enroll.
Four experimental therapies for FTD-GRN are currently in clinical trials

<table>
<thead>
<tr>
<th>Company</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Approval</th>
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<td>alector gsk</td>
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<td>UPFRONT-3</td>
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<td>Lilly Prevail</td>
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<td>Denali Takeda</td>
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Not listed above: A Phase 1/2 trial of AVB-101 from AviadoBio is expected to start soon
**Sponsor:** Alector Therapeutics  
[alector.com](http://alector.com) / Partnered with Glaxo Smith Kline

**Development Stage:** Phase 3 (INFRONT-3)

**ClinicalTrials.gov identifier:** NCT04374136

**Enrollment criteria:** Known GRN mutation carrier
- May be **asymptomatic**
- If **symptomatic**, must have one or more of the criteria for the diagnosis of possible behavioral variant FTD, or a diagnosis of Primary Progressive Aphasia

**Experimental drug:** Latozinemab (AL001)

**Delivery method:** Intravenous (IV) infusion every 4 weeks

**Placebo-controlled:** Yes

**Length of trial:** Up to 96 weeks, with optional open label extension

**Locations:** 54 sites in the US, Canada, Australia, Argentina, Europe and Western Asia

**How to contact:** 650-826-2454; clinicaltrials@alector.com

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**Latozinemab (AL001) increases progranulin levels by blocking progranulin degradation**

Progranulin is degraded in cells as part of its life cycle. Latozinemab increases the half-life of progranulin by blocking sortilin, a degradation receptor, in order to restore progranulin to normal levels.

*From Alector’s November 2022 corporate presentation*
Sponsor: Prevail Therapeutics
prevailtherapeutics.com / A subsidiary of Eli Lilly and Co.

Development Stage: Phase 1/2 (PROCLAIM)

ClinicalTrials.gov identifier: NCT04408625

Enrollment criteria: Known GRN mutation carrier
• Must have a clinical diagnosis of FTD

Experimental drug: PR006

Delivery method: Single intra-cisterna magna injection

Placebo-controlled: No

Length of trial: 12 months plus 4 years long term follow-up (5 years total)

Locations: 7 sites in the US, Australia, Belgium, Spain and the United Kingdom

How to contact: 917-336-9310; prevail_patients@lilly.com

PR006 increases progranulin levels by delivering a healthy GRN gene into the brain

Adapted from prevailtherapeutics.com
Sponsor: Passage Bio
passagebio.com

Development Stage: Phase 1/2 (upliFT-D)

ClinicalTrials.gov identifier: NCT04747431

Enrollment criteria: Known GRN mutation carrier
  • Must have a clinical diagnosis of FTD

Experimental drug: PBFT02

Delivery method: Single intra-cisterna magna injection

Placebo-controlled: No

Length of trial: 24 months plus 4 years long-term follow-up (5 years total)

Locations: 9 sites in the US, Canada, Brazil, Italy, Portugal and the United Kingdom

How to contact: 267-866-0113; patientservices@passagebio.com

PBFT02 increases progranulin levels by delivering a healthy GRN gene into the brain

From Passage’s November 2022 corporate presentation
Sponsor: Denali Therapeutics
denalitherapeutics.com /partnered with Takeda

Development Stage: Phase 1/2

ClinicalTrials.gov identifier: NCT05262023

Enrollment criteria:
- Known GRN mutation carrier
  - Must have a clinical diagnosis of FTD

Experimental drug: TAK-594/DNL593

Delivery method: Intravenous (IV) infusion

Placebo-controlled: Yes

Length of trial: 6 months, with optional 18 month open-label extension

Locations: 4 sites in Spain, with more to be added (not yet in US)

How to contact: patients@dnli.com
Current clinical trials for FTD and ALS caused by expansions in **C9orf72**

- **FOCUS-C9**
  - WVE-004, Phase 1/2, Wave Life Sciences (Antisense oligonucleotide)
- **TPN-101**, Phase 2, Transposon Therapeutics (Small molecule)
- **Latozinemab (AL001)**, Phase 2, Alector/GSK (*no longer recruiting*)
- **LAM-002A**, Phase 2, AI Therapeutics (*no longer recruiting*)

Both of these trials require participants to know they carry a **C9orf72** expansion in order to enroll.
Sponsor: Wave Life Sciences
wavelifesciences.com

Development Stage: Phase 1/2 (FOCUS-C9)

ClinicalTrials.gov identifier: NCT04931862

Enrollment criteria: Must have GGGGCC [G4C2] repeat expansion in the first intronic region of the C9orf72 gene and be:
- Diagnosed with FTD, or
- Diagnosed with ALS, or
- Diagnosed with mixed phenotype (FTD and ALS)

Experimental drug: WVE-004

Delivery method: Intrathecal (IT) infusion every 4 weeks

Placebo-controlled: Yes

Length of trial: 24 weeks

Locations: 17 sites in Canada, Australia, New Zealand and Europe (not yet in US)

How to contact: 855-215-4687; clinicaltrials@wavelifesci.com

WVE-004 selectively blocks the mutant C9orf72 gene from making harmful proteins

From wavelifesciences.com
**Sponsor:** Transposon Therapeutics  
transposonrx.com

**Development Stage:** Phase 2

**ClinicalTrials.gov identifier:** NCT04993755

**Enrollment criteria:** Hexanucleotide repeat expansion in *C9orf72* gene, and
- Diagnosed with FTD, or
- Diagnosed with ALS, or
- Diagnosed with mixed phenotype (FTD and ALS)

**Experimental drug:** TPN-101

**Delivery method:** Capsule, taken once daily by mouth

**Placebo-controlled:** Yes

**Length of trial:** 24 weeks, with a 24 wk open label extension

**Locations:** 19 sites in US and Europe

**How to contact:** 310-261-5312; clinicaltrials@transposonrx.com

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**TPN-101 blocks disease-causing production of the LINE-1 gene**

Loss of nuclear TDP-43 during FTD leads to harmful LINE-1 expression.

Preclinical evidence shows blocking LINE-1 production with **TPN-101 mitigates neurotoxic pathology.**

*From May 6, 2022 NEALS webinar, “A Phase 2a Study of TPN-101 in Patients with C9ORF72 ALS/FTD*
There are currently no treatment trials specifically for FTD caused by mutations in *MAPT*, but efforts for future trials are in development.
Current clinical trials for sporadic (i.e. non-genetic) FTD

• PSP
  • NIO752, Phase 1, Novartis (Antisense oligonucleotide)

• Semantic dementia
  • Verdiperstat, Phase 1, Investigator-sponsored (Small molecule)

• FTD
  • Oxytocin, Phase 2, Lawson Health Research Institute (Hormone nasal spray)

• bvFTD or sv-PPA or nfv-PPA with behavior
  • Low-dose lithium, Phase 2, Columbia University (Small molecule)
Sponsor: Novartis  
https://www.recruiting-trials.novartis.com/clinicaltrials/study/nct04539041

Development Stage: Phase 1

ClinicalTrials.gov identifier: NCT04539041

Enrollment criteria: PSP diagnosed for less than 5 years with a current classification of probable PSP Richardson syndrome, a progressive supranuclear palsy rating scale (PSPRS) score < 40 and MOCA score > 17 at screening

Experimental drug: NIO752

Delivery method: Intrathecal (IT) infusion 4x over 3 months

Placebo-controlled: Yes

Length of trial: 12 months

Locations: 12 sites in the US, Canada, Germany and the UK

How to contact: 888-669-6682; novartis.email@novartis.com

NIO752 is an antisense oligonucleotide that reduces production of tau (MAPT) protein.
Sponsor: University of California, San Francisco
Dr. Peter Ljubenkov

Development Stage: Phase 1

ClinicalTrials.gov identifier: NCT05184569

Enrollment criteria: Diagnosed with semantic dementia (semantic variant primary progressive aphasia, svPPA)

Experimental drug: Verdiperstat

Delivery method: Tablet, taken twice daily by mouth

Placebo-controlled: Yes

Length of trial: 24 weeks

Locations: 1 site at University of California, San Francisco (additional sites in US to open shortly)

How to contact: 415-514-5745; taylor.sulse@ucsf.edu
415-476-0661; mary.koestler@ucsf.edu

Verdiperstat irreversibly inhibits myeloperoxidase to reduce neuroinflammation

Sponsor: Lawson Health Research Institute
Dr. Elizabeth Finger

Development Stage: Phase 2

ClinicalTrials.gov identifier: NCT03260920

Enrollment criteria: Diagnosis of FTD

Drug: Syntocinon (Oxytocin)

Delivery method: Intranasal spray

Placebo-controlled: Yes

Length of trial: 20 weeks

Locations: 11 sites in Canada and the US

How to contact: Contact individual sites as listed on clinicaltrials.gov or on ftdregistry.org

Oxytocin increases neural activity in brain areas associated with emotions and empathy

**Sponsor:** Columbia University  
Dr. Ted Huey

**Development Stage:** Phase 2  
**Clinical Trials.gov identifier:** NCT02862210

**Enrollment criteria:** Diagnosed with bvFTD or sv-PPA or nfv-PPA with behavior

**Drug:** Low-dose lithium  
**Delivery method:** Tablet, taken 1-4x daily depending on dose

**Placebo-controlled:** Yes  
**Length of trial:** 12 weeks  
**Locations:** 1 site at Columbia University

**How to contact:** 212-304-7943; cs4125@cumc.columbia.edu  
212-305-1134; edh2126@columbia.edu

Lithium carbonate will be compared to placebo in the treatment of agitation, aggression, and inappropriate repetitive behaviors in people diagnosed with FTD.
Stay informed about clinical research via the FTD Disorders Registry

www.ftdregistry.org

IN THE WORLD OF FTD, EVERY STORY ADVANCES THE SCIENCE.
Starting with yours.

TOGETHER WE CAN FIND A CURE FOR FTD

The FTD Disorders Registry is a powerful tool in the movement to create therapies and find a cure. Together we can help change the course of the disease and put an end to FTD.

JOIN THE REGISTRY

Your privacy is important! We promise to protect it. We will not share your contact information.

Read Full Privacy Statement
Thank you!
Contact me at laura.mitic@bluefieldproject.org

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