

December 7, 2022

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

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Chief Scientific Officer



BLUEFIELD
PROJECT

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](#).

Find a study (all fields optional)

Status ⓘ

Recruiting and not yet recruiting studies
 All studies

Condition or disease ⓘ (For example: breast cancer)

X

Other terms ⓘ (For example: NCT number, drug name, inve
Name of a Disease or Medical Condition. Known synonyms automatically included

X

Country ⓘ

X

[Search](#) [Advanced Search](#)

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

e.g. NCT04374136, PROCLAIM, FOCUS-C9, AL001, DNL593

Explanation of the template to describe each clinical trial:

Sponsor: The entity running the trial, usually a company or a university

Development Stage Phase 1, 2 or 3 in the process for FDA approval (+ trial name)

ClinicalTrials.gov identifier: Enter this number at www.clinicaltrials.gov to see the specific details of the trial

Enrollment criteria: Criteria that interested individuals must meet in order to qualify to participate in the trial

Experimental drug: The name of the experimental drug

Delivery method: How the experimental drug will be administered to the participant (by mouth, injection, infusion, etc.)

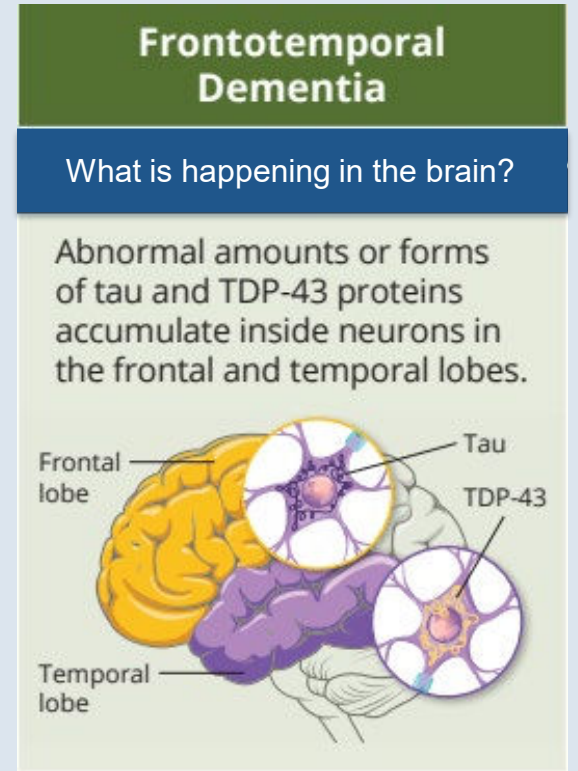
Placebo-controlled?: Will some participants receive a placebo instead of the experimental drug?

Length of trial: How long participants will be monitored

Locations: Countries where clinical trial sites are planned or actively recruiting participants

How to contact: Phone number and website to contact the sponsor

Explanation of how the experimental drug targets processes that have led to FTD



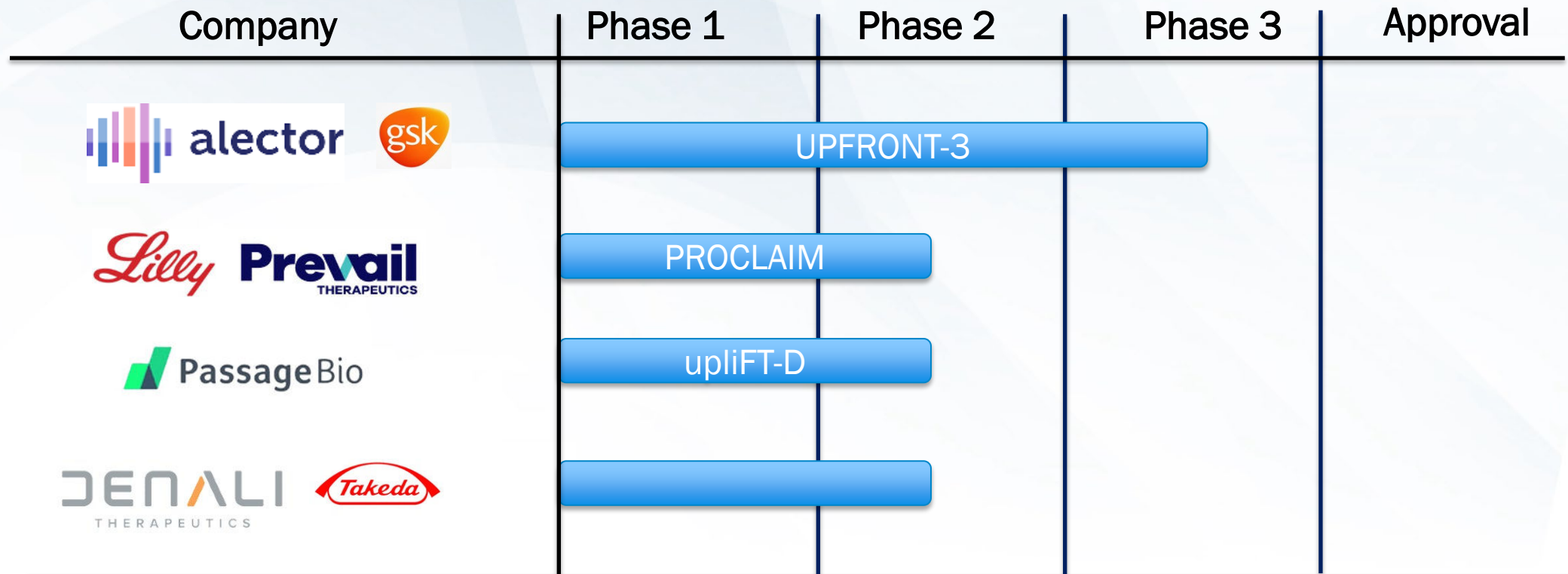
Adapted from the National Institute on Aging

All of these trials require participants to know they carry a mutation in progranulin in order to enroll

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*)

Four experimental therapies for FTD-GRN are currently in clinical trials



Not listed above: A Phase 1/2 trial of AVB-101 from AviadoBio is expected to start soon

Sponsor: **Alector Therapeutics**
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

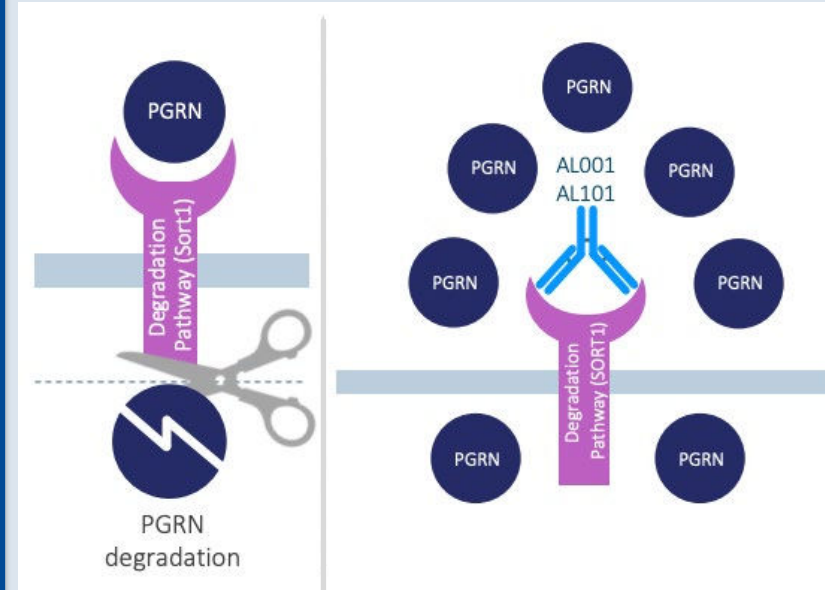
Placebo-controlled: Yes

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

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

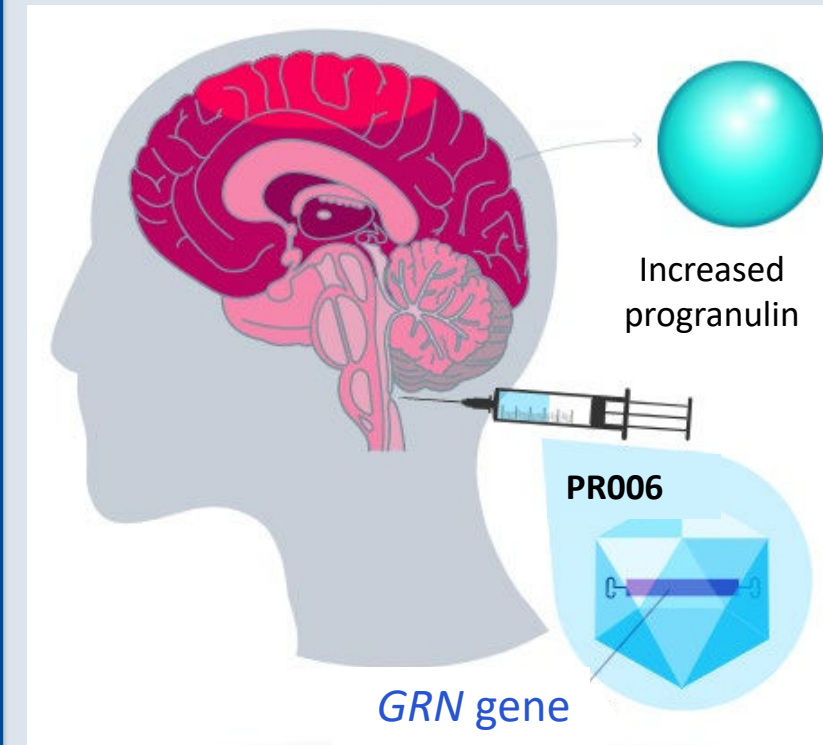
Placebo-controlled: No

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

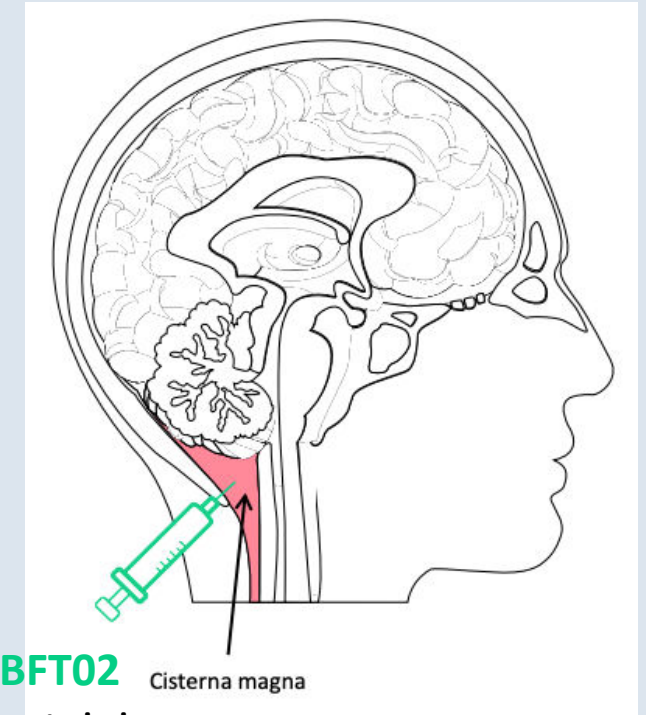
Placebo-controlled: No

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



PBFT02 Cisterna magna
containing
healthy
GRN gene

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

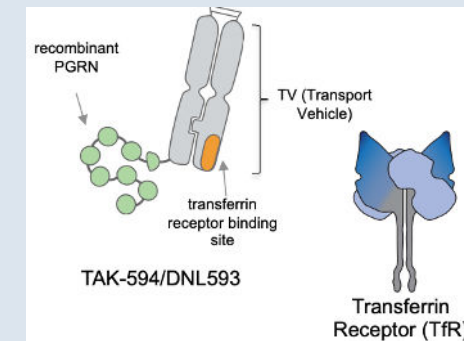
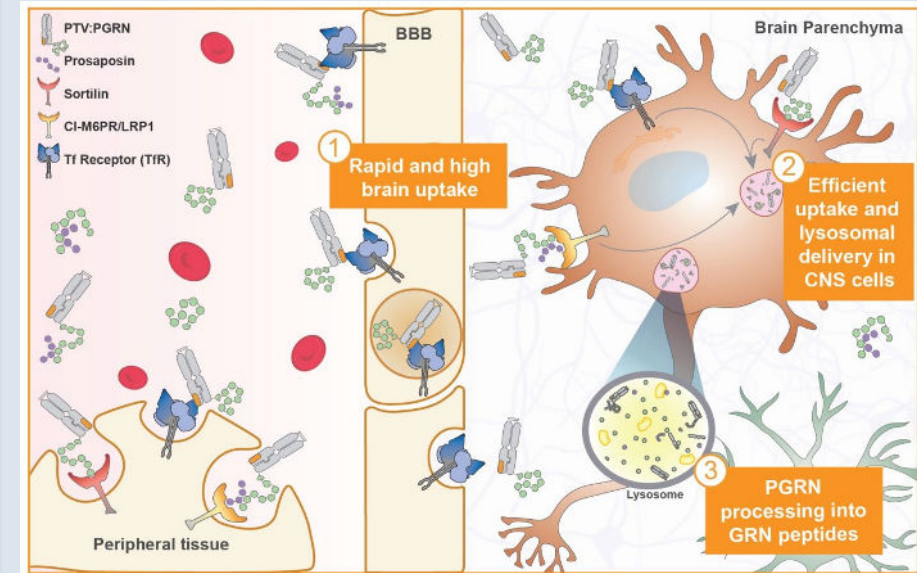
Placebo-controlled: Yes

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

TAK-594/DNL593 increases progranulin levels by delivering the progranulin protein across the blood brain barrier



From Denali's November 2022 FPI presentation

Both of these trials require participants to know they carry a *C9orf72* expansion in order to enroll

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*)

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

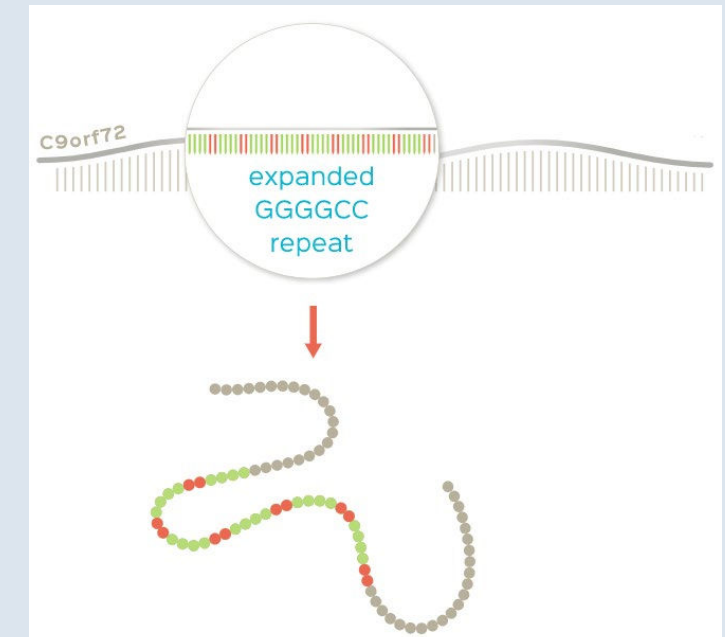
Placebo-controlled: Yes

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



WVE-004 is designed to affect multiple drivers of toxicity

Variant-selective oligonucleotide, lowering V1 & V3 in preclinical studies¹

Preserves *C9orf72* protein expression; does not exacerbate potential loss-of-function driver of disease

Reduces toxic gain-of-function drivers of disease (RNA foci, DPRs)

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

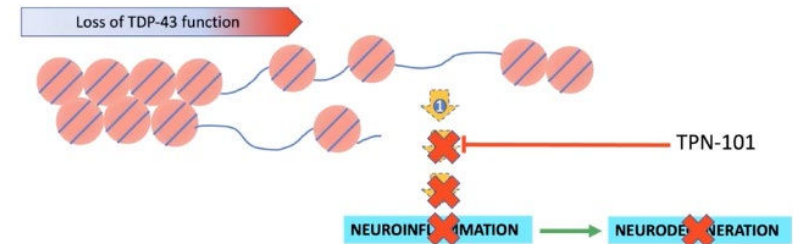
Placebo-controlled: Yes

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

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

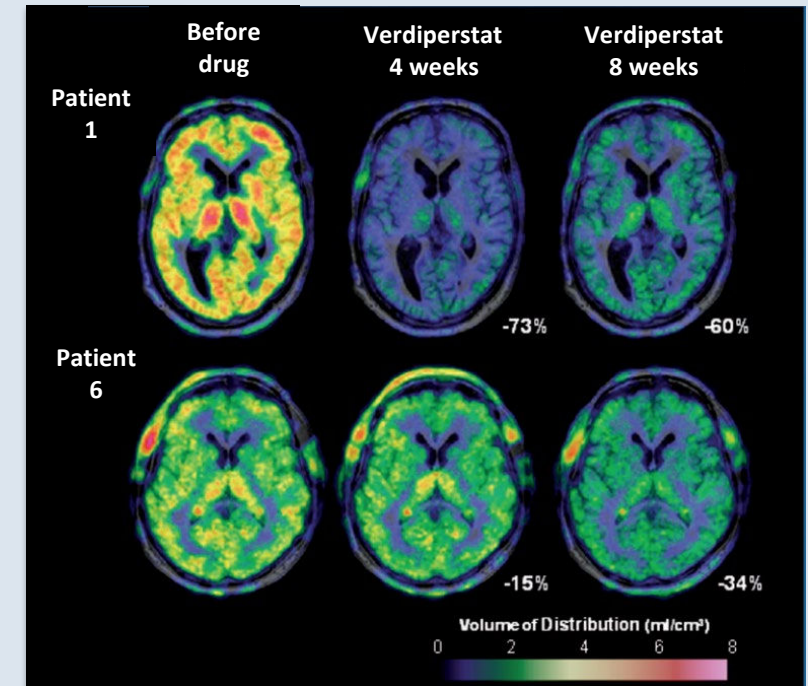
Placebo-controlled: Yes

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



Jucaite, A. *et al.* Effect of the myeloperoxidase inhibitor AZD3241 on microglia: a PET study in Parkinson's disease. *Brain* **138**, 2687–2700 (2015).

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

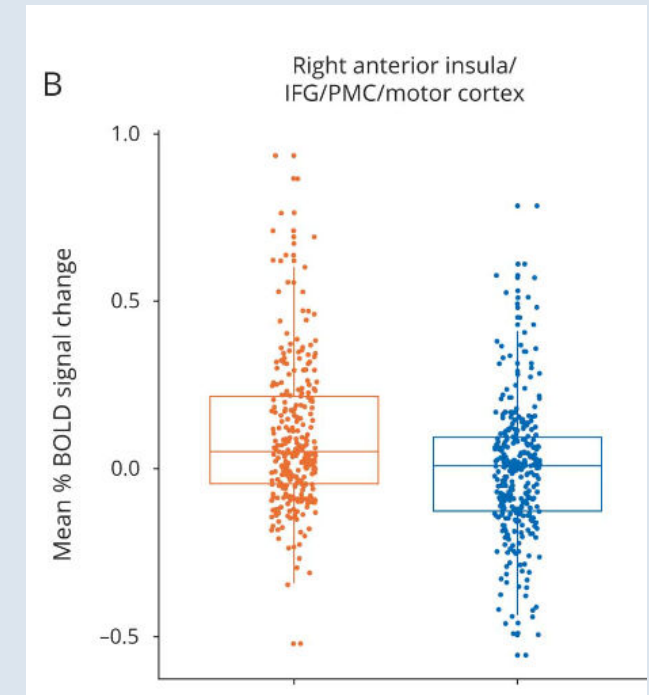
Placebo-controlled: Yes

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



Oliver, L. D. *et al.* Neural effects of oxytocin and mimicry in frontotemporal dementia: A randomized crossover study. *Neurology* **95**, e2635–e2647 (2020).

Sponsor: Columbia University

Dr. Ted Huey

Development Stage: Phase 2

ClinicalTrials.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

The image shows the homepage of the FTD Disorders Registry. At the top left is the logo, which consists of a cluster of colorful hexagons next to the text 'FTD DISORDERS REGISTRY'. To the right of the logo is the website URL 'www.ftdregistry.org'. In the top right corner, there are links for 'NEWS' and 'CONTACT US', and a 'Participant Login' button with an orange arrow icon. Below the header is a dark blue navigation bar with white text for the following menu items: 'WHY JOIN', 'FIND A STUDY', 'WAYS TO HELP', 'FOR RESEARCHERS', 'FTD RESOURCES', and 'ABOUT US'. The 'FIND A STUDY' item is circled in orange. The main content area features a large photograph of a woman and a young girl smiling together. To the left of the photo, the text reads: 'IN THE WORLD OF FTD, EVERY STORY ADVANCES THE SCIENCE. Starting with yours.' To the right of the photo, the text reads: 'TOGETHER WE CAN FIND A CURE FOR FTD'. Below this is a paragraph: '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.' At the bottom right, there is a yellow button with the text 'JOIN THE REGISTRY' and an orange arrow icon. Below the button, there is a privacy statement: 'Your privacy is important! We promise to protect it. We will not share your contact information.' and a link: 'Read Full Privacy Statement'.

FTD DISORDERS
REGISTRY

www.ftdregistry.org

NEWS | CONTACT US

→ Participant Login

WHY JOIN

FIND A STUDY

WAYS TO HELP

FOR RESEARCHERS

FTD RESOURCES

ABOUT US

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

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[Read Full Privacy Statement](#)

Thank you!

Contact me at laura.mitic@bluefieldproject.org



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