What will happen in this study?
continued

You will attend monthly follow-up visits for approximately two years.

After you're randomized, you will receive an aflibercept injection at your first follow up visit regardless of your group assignment.

Beginning on the 3rd month, you will either receive an aflibercept or sham injection based on your randomly assigned group. If needed, you may be given aflibercept instead of sham based on the study requirements and the health of your study eye. Both groups will be checked to see if you need an aflibercept injection at visits where aflibercept and sham injections aren't already scheduled.

You may be compensated for travel expenses related to your study visits, with options including reimbursement for travel to and from the study center or transportation services arranged by the study center. All reimbursements and transportation services will be available based on the rules and guidelines in your area. Talk to the study center to learn more about your options.

How are the study injections given to participants?

- **Aflibercept and 4D-150 are given as IVT injections through the white part of the eye**
- **A sham injection is given by pressing a needleless syringe against the eye to mimic the sensation of an injection**
- **Each injection will be provided while you are awake, laying down, and without sedation. You will be given numbing gel and/or an eye injection to prevent pain. The injection will take less than 10 seconds.**

What risks are involved?

There are possible risks involved with any clinical study. The study doctor will review the risks with potential participants or caregivers, and participants will be closely monitored throughout the study.

Why should I join this study?

Being part of this study is voluntary. You may choose not to join, or you may leave this study at any time. Your participation may help determine if 4D-150 may help other people with wet AMD in the future. Current treatments for diseases or conditions are only available because of clinical study volunteers.

Thank you for your interest in the 4FRONT-1 study.

For more information, please visit **www.4FRONTClinicalStudies.com** or scan the QR code.

4FRONT-1 | 4DMT

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Bringing wet AMD into focus

At the 4FRONT of wet AMD research

Now enrolling: the 4FRONT-1 study for adults with wet age-related macular degeneration (wet AMD)

4FRONT-1

Why is the 4FRONT-1 study important?

The current treatment for wet AMD is an anti-vascular endothelial growth factor (anti-VEGF) therapy. VEGF is a protein that can cause abnormal, leaky blood vessels to grow in the eye, which may lead to vision loss. Approved anti-VEGF treatments, also known as aflibercept IVT eye injection, find these unhealthy VEGF proteins and block them.

Many people with wet AMD need treatment in the form of eye injections every 4 or 8 weeks to maintain their vision or prevent vision loss. These repeated injections may be difficult for some people with wet AMD and their caregivers. The appointments can be lengthy, and many people also need someone to accompany them to their appointments, adding to the challenge. Traveling to and from the clinic, scheduling visits, and managing discomfort after injections can make this treatment difficult to keep up with over time.

The 4FRONT-1 study is a Phase 3 clinical study testing an investigational gene therapy (also known as the "study drug") called 4D-150 to see if it is effective, safe, and if it reduces the number of anti-VEGF injections needed by people with wet AMD. Study volunteers can help us learn more about this investigational gene therapy.

What is a Phase 3 clinical study?

A Phase 3 clinical study tests how well a study drug works, and the safety of the study drug compared to either the natural course of a disease, or in this case, compared to the current standard of care treatment. The 4FRONT studies will assess how well 4D-150 works compared to standard treatment in people with wet AMD.

What is 4D-150?

4D-150 is an investigational gene therapy that is being tested in a clinical study and has not been approved by health regulatory agencies. It is designed to help the cells in the eye continuously produce their own proteins, which act like tiny helpers that treat wet AMD—potentially reducing the need for frequent injections.

What is gene therapy?

Genetic medicine is the use of genetic materials, such as deoxyribonucleic acid (DNA; which **genes** are made of), to possibly treat or prevent disease. **Gene therapy**, a type of genetic medicine, works by giving cells a healthy copy of a gene that isn't working properly. This helps the cells make the proteins or molecules needed to treat certain conditions, like wet AMD.

How does gene therapy work?

Gene therapy uses something called a vector, which is like an envelope, to deliver a specific message.

Viruses can be used as vectors because they are good at getting into cells. The part of the virus that causes sickness is removed so it cannot make you sick or multiply. The vector carries the healthy gene and is injected into the eye. It travels to part of the eye called the retina, where the target cells are. Once delivered, the new gene begins working. It makes a protein, called anti-VEGF, which may help alleviate the disease symptoms and hopefully help reduce the number of anti-VEGF injections needed to treat people with wet AMD. Gene therapy may be permanent and irreversible.

Who can participate in the 4FRONT-1 study?

You may qualify if you meet the following*:

- Are at least 50 years of age
- Have wet AMD
- Have not received wet AMD treatment in the affected eye
- Be able and willing to attend all study visits and perform study examinations throughout the 24-month (2-year) duration

*Additional study requirements will be reviewed by the study doctor to confirm if a person is eligible to participate

How long will this study last?

Participants will be in this study for approximately 24 months (2 years). At the end of the study, participants may be asked to participate in a separate long-term follow-up study. The study doctor will provide more information prior to the last visit.

What will happen in this study?

If you decide to participate, you'll attend up to 3 screening visits at your study center to confirm eligibility. During these visits, you'll complete several assessments to ensure you qualify to move forward. If eligible, you'll receive initial anti-VEGF injections (also known as aflibercept).

About a week after your second aflibercept injection, you'll return for your next visit and be randomly assigned to either the 4D-150 study drug group or the standard of care treatment group. If you are randomized to the 4D-150 study drug group, you will receive 4D-150 at the visit. If you are randomized to the standard of care treatment group, you will receive a sham injection (an injection simulation without a needle). This is a double-masked study, meaning neither you nor your study doctor will know your group assignment.