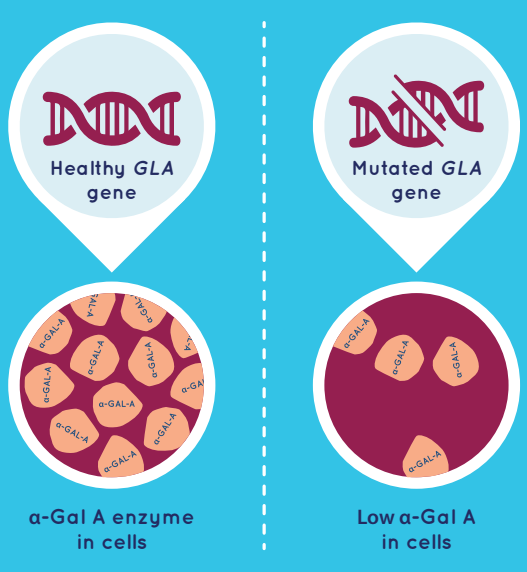
The STAAR Clinical Trial

STAAR

A Phase 1/2 dose-ranging, multicenter study designed to investigate the safety and tolerability of **ST-920**, an investigational gene therapy, to treat adult patients with classical Fabry disease.

What is Fabry disease?

- Fabry disease is a rare, X-linked lysosomal storage disorder caused by a mutation in the *GLA* gene, resulting in an absence or deficiency of the enzyme α-galactosidase A (α-Gal A). This enzyme is responsible for breaking down fatty substances called globotriaosylceramide (Gb3) and lyso-Gb3.
- Gb3 builds up in the bodies of people living with Fabry disease, leading to dysfunction in the skin, eye, kidney, heart, brain and peripheral nervous system. Symptoms vary widely from patient to patient and can range in severity.
- The current standard of care for Fabry disease is enzyme replacement therapy (ERT), which aims to replace the missing α-Gal A enzyme in the blood through regular infusions, usually once every two weeks.



About ST-920

ST-920 is a gene therapy product candidate that aims to provide stable, long-term production of α-Gal A at therapeutic levels in Fabry disease patients by delivering a healthy copy of the *GLA* gene to the liver. The corrective gene is delivered through a deactivated virus called AAV2/6, which targets the liver and provides cells the instructions for α-Gal A enzyme production. This technology is proprietary to Sangamo; ST-920 uses the same AAV6 capsid as another Sangamo liver-targeted gene therapy for hemophilia A (SB-525), which was generally well-tolerated and resulted in dose-dependent and sustained increases in FVIII levels in a Phase 1/2 study. Peer-reviewed pre-clinical studies in mice and non-human primates have suggested that producing the α-Gal A enzyme through the liver may limit the effects of neutralizing antibodies to the enzyme. It is unknown if this potential benefit for patients will be demonstrated in human studies.

STAAR Study Design

Primary Endpoint

Incidence of treatment-emergent adverse events (TEAEs) during 12 months after ST-920 infusion

- Additional safety evaluations will include routine hematology, chemistry and liver tests, vital signs, ECG and ECHO, serial alpha fetoprotein (AFP) testing and liver MRI to monitor for any liver mass formation

Secondary Endpoints

Change from baseline at specific time points during the follow-up period:

- α-Gal A activity in plasma
- Gb3 and lyso-Gb3 plasma levels
- Frequency of ERT
- Estimated glomerular filtration rate (eGFR) calculated by creatinine levels in blood
- Vector clearance (measured by level of vector genome in blood, saliva, urine, stool and semen)

Key Exploratory Endpoints

- Left ventricular mass (measured by cardiac MRI)
- Quality of life, Fabry symptoms and neuropathic pain scores
- Immune response to AAV and to α-Gal A

Eligibility (screening up to 8 weeks)

- The study includes men aged 18 years and older with a diagnosis of classical Fabry disease; patients will be enrolled from 10-15 clinics in the United States and United Kingdom.
- Patients can continue on ERT during the study.

Key exclusion criteria include:

- Known to be unresponsive to ERT
- Neutralizing antibodies to AAV2/6
- eGFR ≤ 60 ml/min/1.73m2
- Contraindication to use of corticosteroids for immunosuppression
- Non-classical Fabry disease

Baseline stage (up to 12 weeks)

Tests and procedures (e.g., blood and urine samples) conducted to determine Fabry disease symptoms and patients' baseline levels for heart, kidney, liver and lung function

Administration (up to 2 days)

- **One-time intravenous infusion** of ST-920 (no further treatment with ST-920 will be given throughout the study duration)
- The infusion will be administered in the hospital. An additional hospital stay of approximately 24 hours will be required for monitoring.
- Patients may have to start taking steroid medication to prevent and treat potential allergies and minimize detrimental immune reaction to ST-920. This medication will be taken in gradually decreasing doses when liver enzymes have come back to acceptable levels.

The study has oversight of a Safety Monitoring Committee (SMC). Because of monitoring and necessary dosing interval between patients, time between start of cohort and SMC will be a minimum of 3 months.

Follow-up stage (12 months)

- Every **2 weeks** for 8 weeks
- Then every **4 weeks** for the remainder of the follow-up period
- **Potential ERT withdrawal** after ST-920 dosing in a controlled and monitored fashion, at the discretion of the patient and physician
- Patients are also eligible and encouraged to participate in a **4-year follow-up study**

Learn more about the STAAR study at https://staarclinicalstudy.com

Sangamo THERAPEUTICS

References:

National Organization for Rare Disorders. *Fabry Disease*. Retrieved from https://rarediseases.org/rare-diseases/fabry-disease/

Goker-Alpan O, et al. (2020, February). *A Phase I/II multicenter gene therapy clinical study for Fabry disease*. Poster session presented at the WORLDSymposium, Orlando, FL.