Olezarsen

An **Investigational Medicine** Designed to Target Severely Elevated Triglycerides

Disease Background

Severe hypertriglyceridemia (sHTG) is a condition in which a person's triglyceride levels are dangerously high.[1] Although a healthy triglyceride level for adults is typically below 150 mg/dL, people living with sHTG have levels greater than 500 mg/dL.[2]

Familial chylomicronemia syndrome (FCS) is a rare, genetic, life-threatening form of sHTG that prevents the body from digesting fats and severely impairs the body's ability to remove triglycerides from the bloodstream.[1,3] This condition leads to a build-up of large triglyceride-containing particles in the blood called chylomicrons, which can result in severe health complications, including acute pancreatitis (AP).[1,4] People living with FCS have triglyceride levels greater than or equal to 880 mg/dL.[4]

Overview

Olezarsen is an investigational RNA-targeted **LIgand-**C**onjugated **A**ntisense (LICA) medicine being studied in patients with severely high triglycerides, including FCS and sHTG.**

There is a significant need among people living with these diseases, which can cause intense physical pain, negative impacts on quality of life and other chronic health issues or life-threatening complications, such as AP.[5]

Olezarsen is designed to specifically enter liver cells and inhibit the body's production of a protein called apoC-III, with the goal of reducing triglyceride levels. By reducing triglyceride levels, the hope is to reduce the risk of recurrent AP and other disease complications.[6,7]

Previous studies have validated apoC-III as a potential target in lowering triglyceride levels.[6]

Olezarsen is an investigational medicine for which the safety and efficacy have not been evaluated by any regulatory body.

Phase 3 Clinical Development Program

The olezarsen clinical program includes three pivotal Phase 3 investigational clinical trials:

Balance — a pivotal Phase 3 study in people with FCS

The global, multicenter, randomized, double-blind, placebo-controlled **Phase 3 Balance study** showed a statistically significant reduction in triglyceride levels with the olezarsen 80 mg monthly dose at six months compared to placebo ($p<0.001$); triglyceride lowering continued to improve at 12 months.

- The Balance study enrolled 66 patients aged 18 and older with confirmed FCS and a triglyceride level ≥880 mg/dL, inclusive of both those with and without a prior history of AP.
- Study participants were randomized in a 1:1:1 ratio to receive olezarsen 80 mg or 50 mg or placebo via subcutaneous injection once every four weeks for 53 weeks.
- The Balance study also provided exploratory data for patient-reported outcomes such as abdominal pain, diarrhea, difficulty in thinking, fatigue and health-related quality of life.[5,8,9]

Eligible study participants have enrolled in ongoing open-label extension studies.

CORE and CORE2 — two pivotal Phase 3 studies in people with sHTG

The global, multicenter, randomized, double-blind, placebo-controlled **Phase 3 CORE and CORE2 studies** in patients with sHTG are evaluating the effect of olezarsen on the percent change in fasting triglycerides from baseline at six months in more than 1,000 sHTG patients.

- The studies are also evaluating the percent change from baseline in triglycerides at month 12, the proportion of patients who achieved fasting triglycerides less than 500 mg/dL, as well as clinically important secondary endpoints.
- Study participants are randomized 2:1 to receive olezarsen 50 mg or 80 mg or placebo via subcutaneous injection once every four weeks for 53 weeks.

These studies are ongoing to evaluate olezarsen as a potential treatment option for people living with FCS or sHTG. Olezarsen is an investigational medicine for which the safety and efficacy have not been evaluated by any regulatory body. If approved, olezarsen would be the first available treatment in the U.S. for FCS.

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