

Sanofi's venglustat earns Breakthrough Therapy designation in the US for type 3 Gaucher disease

Paris, March 18, 2026. The US Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to venglustat, a novel, investigational oral glucosylceramide synthase inhibitor (GCSI), for the treatment of neurological manifestations of type 3 Gaucher disease (GD3), a rare lysosomal storage disorder.

The designation is based on data from the LEAP2MONO phase 3 study (clinical study identifier: [NCT05222906](#)) in which patients receiving venglustat demonstrated statistically significant improvements in neurological symptoms measured by a global test score that included assessments for ataxia (mSARA) and cognition (RBANS) compared with patients receiving the enzyme replacement therapy (ERT), imiglucerase ($p=0.0179$). In the study, venglustat was well tolerated overall with no new safety signals compared with previous studies. The most commonly reported adverse events were headache (14.3% in the venglustat arm versus 18.2% in the ERT arm), nausea (14.3% versus 4.5%), spleen enlargement (14.3% versus 0), and diarrhea (14.3% versus 0).

Gaucher disease (GD) is a rare inherited lysosomal storage disorder that results from a deficiency of an enzyme called glucocerebrosidase, leading to the accumulation of sugar-and-fat molecules called glycosphingolipids (GSL) in the spleen, liver, bone marrow, and lungs. There are three major forms of the disease: GD1, characterized by lack of central nervous system (CNS) involvement; GD2, marked by rapid neurological decline and severe neurocognitive symptoms; and GD3, marked by slower and more variable progression and symptom severity.

In people with GD3, accumulation of GSLs in the CNS can result in neurological symptoms, in addition to the systemic manifestations seen in GD1, such as liver and spleen enlargement, anaemia, low platelet counts, and bone disease. Systemic manifestations of GD3 are treated with ERT but there are no approved treatments for the neurological symptoms. Venglustat works by reducing the abnormal accumulation of GSLs. It is designed to cross the blood-brain barrier to target the underlying pathology causing the neurological effects of GD3.

*"This regulatory milestone recognizes the significant unmet medical need for people living with type 3 Gaucher disease, particularly those experiencing progressive neurological deterioration," said **Karin Knobe**, Global Head of Clinical Development, Rare Diseases at Sanofi. "The positive LEAP2MONO findings are an encouraging step forward in the research and development process, and we will continue collaborating with the FDA to advance this potential treatment option."*

Venglustat was previously granted fast-track designation from the FDA for its potential use in GD3 as well as orphan designation for GD3 in the US, EU and Japan. Sanofi will pursue global regulatory filings for venglustat in GD3 during 2026.

FDA Breakthrough Therapy designation is designed to expedite the development and review of medicines in the US that target serious or life-threatening conditions. Medicines qualifying

for this designation must show preliminary clinical evidence that the drug may demonstrate substantial improvement on clinically significant endpoints over available medicines.

About the LEAP2MONO study

The LEAP2MONO phase 3 study was a double-blind, double-dummy, active-comparator, two-arm study that evaluated the efficacy and safety of once daily oral venglustat versus intravenous ERT every two weeks in adults and pediatric patients aged 12 and older with GD3. Forty-three patients were randomized [1:1] to receive venglustat and placebo infusion or ERT and placebo tablet. Patients must have been treated with ERT for at least three years and achieved therapeutic goals for systemic disease manifestations. The primary endpoints for the study were change in SARA modified total score and change in RBANS total scale index score for patients receiving venglustat versus those receiving ERT from baseline to week 52. Systemic key secondary endpoints include percent change in spleen volume, liver volume and platelet count and change in hemoglobin levels. Biomarker key secondary endpoints include percent change in cerebrospinal fluid and plasma GL1 and lyso-GL1. The LEAP2MONO study is ongoing and results from its open-label phase will be presented in the future when available.

About venglustat

Venglustat is a novel, investigational oral glucosylceramide synthase inhibitor (GCSi), designed to cross the blood-brain barrier (i.e., brain-penetrant), that has the potential to slow the progression of GD3 by inhibiting the abnormal GSL accumulation and its physio-pathologic consequences. GSLs are cellular building blocks whose abnormal accumulation is implicated in several rare diseases leading to both cell dysfunction and disease progression.

About Sanofi

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