Xenpozyme™ (olipudase alfa-rpcp) – New orphan drug approval

- On August 31, 2022, the FDA announced the approval of Sanofi's Xenpozyme (olipudase alfa-rpcp), for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

- ASMD is caused by the lack of an enzyme needed to break down a complex lipid, called sphingomyelin, that accumulates in the liver, spleen, lung, and brain. Patients with ASMD have enlarged abdomens that can cause pain, vomiting, feeding difficulties, and falls. The most severely affected patients have profound neurologic symptoms and rarely survive beyond two to three years of age. Other patients may survive into adulthood but die prematurely from respiratory failure.

    — It has been estimated that there are fewer than 120 patients diagnosed with ASMD in the U.S. Approximately two-thirds of patients with ASMD in the U.S. are pediatric.

- Xenpozyme is an enzyme replacement therapy that helps reduce sphingomyelin accumulation in the liver, spleen, and lung. Xenpozyme is the first approved medication to treat symptoms that are not related to the central nervous system in patients with ASMD.

- The efficacy of Xenpozyme for the treatment of non-central nervous system manifestations of ASMD has been evaluated in 3 trials in patients with ASMD. Trial 1 was a randomized, double-blinded, placebo-controlled, repeat-dose trial in 31 adult patients with ASMD (clinical diagnosis consistent with ASMD type B and A/B). Patients received either Xenpozyme or placebo. Key efficacy endpoints included assessment of % predicted diffusion capacity of the lungs for carbon monoxide (DLco), spleen volume, liver volume, and platelet count.

    — At week 52, an increase of 20.9% in the mean percent change in % predicted DLco was observed in the Xenpozyme-treated patients compared to the placebo-treated patients ($p = 0.0003$). A reduction in spleen volume of 39.4% was observed in the Xenpozyme-treated patients compared to the placebo-treated patients ($p < 0.0001$).
    — A 24.7% decrease in mean liver volume and a 15.6% increase in mean platelet count were also noted in the Xenpozyme-treated patients compared to the placebo-treated patients at week 52 ($p < 0.0001$ and $p = 0.0280$, respectively).

- Trial 2 was an open-label, repeated-dose trial of Xenpozyme in 8 pediatric patients aged < 18 years with a clinical diagnosis consistent with ASMD type B and A/B. Exploratory efficacy endpoints related to organomegaly, pulmonary and liver functions, and linear growth were evaluated at week 52.

    — Treatment with Xenpozyme resulted in improvements in mean percent change in % predicted DLco, spleen and liver volumes, platelet counts, and linear growth progression (as measured by height Z-scores) at week 52 as compared to baseline. Refer to the drug label for full results.

- Additionally, the 8 pediatric patients 2 to < 12 years of age from Trial 2 continued treatment in an open label long term trial (Trial 3) and were treated with Xenpozyme for 2.5 to 3.2 years.

    — Efficacy analyses showed continued improvements in the 3 patients evaluated for % predicted DLco, 6 patients evaluated for platelet counts, and all 8 patients evaluated for spleen and liver volumes, compared to baseline, during the additional 6 months extension.

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In addition, the height Z-score increased by 1.3 from baseline when evaluated through 24 months of Xenpozyme treatment.

- Xenpozyme carries a boxed warning for severe hypersensitivity reactions.
- Additional warnings and precautions for Xenpozyme include infusion-associated reactions, elevated transaminases levels, and risk of fetal malformations during dosage initiation or escalation in pregnancy.
- The most common adverse reactions in adult patients (≥ 10%) with Xenpozyme use were headache, cough, diarrhea, hypotension, and ocular hyperemia.
- The most common adverse reactions in pediatric patients (≥ 20%) with Xenpozyme use were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.
- The recommended starting dose of Xenpozyme in adults is 0.1 mg/kg via intravenous (IV) infusion. To reduce the risk of hypersensitivity and infusion-associated reactions or elevated transaminase levels, the dose should be escalated following instructions in the drug label. The recommended maintenance dosage of Xenpozyme in adults is 3 mg/kg every 2 weeks.
- The recommended starting dose of Xenpozyme in pediatric patients is 0.03 mg/kg via IV infusion. To reduce the risk of hypersensitivity and infusion-associated reactions or elevated transaminase levels, the dose should be escalated following instructions in the drug label. The recommended maintenance dosage of Xenpozyme in pediatric patients is 3 mg/kg every 2 weeks.
- Sanofi plans to launch Xenpozyme in the coming weeks. Xenpozyme will be available as a 20 mg lyophilized powder in a single-dose vial for reconstitution.