New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	**Xenpozyme™ (olipudase alfa-rpcp) [Genzyme Corporation]**
Dosage Formulations:	Lyophilized powder for reconstitution, administered as an intravenous injection.
FDA Approval Date: **FDB File Date:**	FDA: August 31, 2022 FDB: September 11, 2022
Indication:	Treatment of non-central nervous system (CNS) manifestation of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.
Mechanism of Action:	ASMD is a lysosomal storage disease that results from reduced activity of the enzyme acid sphingomyelinase (ASM), caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 gene. ASM degrades sphingomyelin to ceramide and phosphocholine. The deficiency of ASM causes an intra-lysosomal accumulation of sphingomyelin (as well as cholesterol and other cell membrane lipids) in various tissues. Xenpozyme provides an exogenous source of ASM.
Dose/ Administration:	• Before initiating Xenpozyme obtain baseline transaminase levels in all patients within 1 month prior to treatment initiation. • Verify pregnancy status in females of reproductive potential. • Consider pretreatment with antihistamines, antipyretics, and/or corticosteroids. • The recommended adult and pediatric dosages of Xenpozyme for the dose escalation and maintenance phases are based on body weight as follows for patients with a body mass index (BMI): ○ Less than or equal to 30: dose is based on actual body weight (kg) ○ Greater than 30: dosage is based on adjusted body weight (kg) calculated by (actual height in m)^2 x 30. • Adult Dosing ○ The recommended starting dose of Xenpozyme in adults is 0.1 mg/kg, administered every two weeks via intravenous infusion. ○ In order to reduce the risk of hypersensitivity and infusion-associated reactions or elevated transaminase levels, the manufacturer provides the following dose escalation regimen:

Adult Patients (18 years and older)[a]	
First dose (Day 1/Week 0)	0.1 mg/kg
Second dose (Week 2)	0.3 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.6 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	1 mg/kg
Seventh dose (Week 12)	2 mg/kg
Eighth dose (Week 14)[b]	3 mg/kg (recommended maintenance dose

[a]Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)^2 x 30
[b]The dose escalation phase includes the first 3 mg/kg dose.

○ Maintenance Phase: the recommended maintenance dosage of Xenpozyme in adults is 3 mg/kg via intravenous infusion every two weeks.

• Pediatric Dosing
○ The recommended starting dose of Xenpozyme in pediatric patients is 0.03 mg/kg.
○ In order to reduce the risk of hypersensitivity and infusion-associated reactions or elevated liver enzyme elevations, the manufacturer provides the following dose escalation regimen:

Pediatric Patients (0 to 17 years)[a]	
First dose (Day 1/Week 0)	0.03 mg/kg
Second dose (Week 2)	0.1 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.3 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	0.6 mg/kg
Seventh dose (Week 12)	1 mg/kg
Eighth dose (Week 14)	2 mg/kg
Ninth dose (Week 16)[b]	3 mg/kg (recommended maintenance dose)

[a]Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)^2 x 30
[b]The dose escalation phase includes the first 3 mg/kg dose.

  - Maintenance Phase: the recommended maintenance dosage of Xenpozyme in pediatric patients is 3 mg/kg via intravenous infusion every two weeks.
- Missed Doses: a dose is considered missed when it is not administered within 3 days of the scheduled date. When a dose of Xenpozyme is missed, the manufacturer provides the following guide for resuming therapy:

Consecutive Missed Doses	Escalation Phase	Maintenance Phase
1 missed dose	• First dose after a missed dose: Administer last tolerated dose • Second and subsequent doses after missed dose: Resume dose escalation at next infusion according to Table 1 for adult patients or Table 2 for pediatric patients	First and subsequent doses after missed dose: Administer maintenance dose
2 consecutive missed doses	• First dose after missed dose: Administer 1 dose below last tolerated dose • Second and subsequent doses after missed dose: Resume dose escalation according to Table 1 for adults or Table 2 for pediatric patients	• First dose after missed dose: Administer 1 dose below the maintenance dose • Second and subsequent doses after missed dose: Resume the maintenance dose
3 or more consecutive missed doses	First and subsequent doses after missed doses: Resume dose escalation at 0.3 mg/kg and follow Table 1 for adults or Table 2 for pediatric patients	First and subsequent doses after missed doses: Restart dosing at 0.3 mg/kg and follow Table 1 for adult patients or Table 2 for pediatric patients

- In the event of a severe hypersensitivity reaction (e.g., anaphylaxis) or a severe infusion-associated reaction, immediately discontinue Xenpozyme administration and initiate appropriate medical treatment. In the event of a mild to moderate hypersensitivity or infusion-associated reaction, consider temporarily holding or slowing the infusion rate, and/or reducing the Xenpozyme dose. If dose is reduced, re-escalate following dose escalation described above.
- If transaminase levels are elevated above baseline and > 2 times the upper limit of normal (ULN) prior to the next scheduled administration, the Xenpozyme dose can be adjusted or treatment can be temporarily withheld until the liver transaminase return to the patient's baseline value.
- Using aseptic technique each Xenpozyme vial (20 mg) is reconstituted with 5.1 mL of sterile water for injection resulting in a 4 mg/mL solution. Xenpozyme is then diluted in 0.9% sodium chloride in a syringe or infusion bag depending on the volume of infusion.

Disease State Clinical Highlights:	• Niemann-Pick disease (NPD) is a group of autosomal recessive disorders associated with splenomegaly, variable neurologic deficits, and the storage of lipids including sphingomyelin and cholesterol. NPD is further classified as type A (NPD-A), type B (NPD-B), or type C (NPD-C). NPD-A and NPD-B are allelic disorders caused by pathogenic variants in the sphingomyelin phosphodiesterase-1 gene (*SMPD1*) resulting in a deficiency of acid sphingomyelinase activity. Build-up of excess sphingomyelin leads to clinical manifestations of the disease due to build-up of this lipid throughout the body. NPD-C is caused by pathogenic variants in the *NPC1* or *NPC2* genes, differentiating itself from NPD-A and NPD-B. ASMD refers to both NPD-A and NPD-B.
	• NPD-A (infantile neurovisceral ASMD) is the acute, more severe neuronopathic form and presents with hepatosplenomegaly, feeding difficulties, lung disease, and loss of early motor skills in the first few months of life. Rapid, progressive, and profound loss of neurologic function often leads to death by two to three years of age.
	• NPD-B (chronic visceral ASMD) presents later in life and is less severe compared to NPD-A, with a good prognosis for survival into adulthood. Hepatosplenomegaly occurs during infancy or childhood, which can result in thrombocytopenia and leukopenia. Other systemic manifestations include short stature, delayed skeletal maturation, respiratory issues, and abnormalities of the retina. Intellectual deficiencies have also been reported.
	• Type A/B (chronic neurovisceral ASMD) is another classification known as intermediate phenotype. Patients have symptom onset in early childhood and slower progression of mild neurologic symptoms than patients with NPD-A. According to one study of patients with NPD type A/B, median age of death for patients with chronic neurovisceral disease was 8 years versus 23.5 years for patients with chronic visceral disease.
	• Combined prevalence for NPD-A and NPD-B is 1 in 250,000. Incidence of NPD-A is highest among Ashkenazi Jews, affecting 1 in 40,000 individuals.
	• Diagnosis of NPD-A and NPD-B is suspected when the following clinical features are observed:
	  ○ Hepatosplenomegaly
	  ○ Interstitial lung disease
	  ○ Macular cherry red spot
	  ○ Developmental delay
	• Diagnosis is confirmed via molecular genetic testing detecting both disease-causing alleles in *SMPD1* or by testing residual acid sphingomyelinase activity in peripheral blood leukocytes or cultured skin fibroblasts. If the residual acid sphingomyelinase activity is < 10% compared to control, diagnosis of ASMD is confirmed.

Drug Clinical Highlights:	• Xenpozyme is the first and only FDA-approved medication for ASMD. It received Fast Track Review, Breakthrough Therapy, Priority Review, and Rare Pediatric Disease designations by the FDA.
	• Xenpozyme is not expected to cross the blood-brain barrier or modulate CNS manifestations of ASMD.
	
	<u>Contraindications</u>: none
	
	<u>Warnings/Precautions</u>:
	• Hypersensitivity reactions including anaphylaxis
	  ○ Prior to Xenpozyme administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during Xenpozyme administration.
	  ○ Hypersensitivity reactions, including anaphylaxis, have been reported in Xenpozyme-treated patients. One 18-month-old patient experienced an anaphylactic reaction during the sixth infusion. Additionally, a 16-month-old patient with ASMD type A experienced two anaphylactic reactions during the fifth and sixth infusions in the dose escalation period. In both of these patients anti-olipudase alfa-rpcp IgE and IgG antibodies were detected.

- Mild to moderate hypersensitivity reactions occurred in 10 (33%) adult patients treated with Xenpozyme and 4 (50%) pediatric patients in clinical trials.

- Infusion-associated reactions (IARs):
  - Antihistamines, antipyretics, and/or corticosteroids may be given prior to Xenpozyme administration to reduce the risk of IARs.
  - IARs occurred in approximately 75% of pediatric and 50% of adult patients treated with Xenpozyme. The most frequent IARs in:
    - ≥ 10% of adult patients were headache, pruritis, vomiting, and urticaria.
    - ≥ 20% of pediatric patients were urticaria, erythema, headache, nausea, pyrexia, and vomiting.
  - Acute phase reaction (APR), an acute inflammatory response accompanied by elevations in inflammatory serum protein concentrations, was observed in one adult and one pediatric patient. The most common symptoms associated with APRs were pyrexia, vomiting, and diarrhea.
- Elevated transaminase levels
  - Elevated transaminase levels were reported in 4 (13%) adults and 1 (13%) pediatric patient treated with Xenpozyme during the dose escalation phase. At the time of the next scheduled infusion, these elevated transaminase levels generally returned to levels observed prior to the Xenpozyme infusion.
  - Assess ALT and AST within one month prior to initiation of Xenpozyme, within 72 hours prior to any infusion during dose escalation, or prior to the next scheduled Xenpozyme infusion upon resuming treatment following a missed dose.
- Risk of fetal malformations during dosage initiation or escalation in pregnancy
  - There is no evidence that olipudase alfa-rpcp crosses the human placenta. However, there is evidence that early embryonic exposure to a metabolite of sphingomyelin (ceramide) or the S1P receptor modulator fingolimod can produce exencephaly in chicks and mice. Xenpozyme dosage initiation or escalation, at any time during pregnancy, is not recommended as it may lead to elevated sphingomyelin metabolite levels that may increase the risk of fetal malformations.
  - Verify the pregnancy status in females of reproductive potential prior to initiating Xenpozyme treatment.

<u>Pregnancy/Lactation</u>:

- Based on findings from animal reproduction studies, Xenpozyme may cause embryo-fetal harm when administered to a pregnant female. Xenpozyme dosage initiation or escalation at any time during pregnancy is not recommended.
- There are no data on the presence of Xenpozyme in human milk, the effects on the breastfed infant, or the effect on milk production.

<u>Clinical Studies</u>

- ASCEND (NCT02004691): multicenter, randomized, double-blinded, placebo-controlled, repeat-dose phase II/III trial in adult patients with ASMD. Patients received Xenpozyme or placebo as an intravenous infusion once every 2 weeks. Trial consisted of two parts: a randomized placebo-controlled, double-blinded primary analysis period (PAP) which lasted to Week 52, followed by an extension treatment period (ETP) for up to 4 years. Patients randomized into the placebo arm in the PAP crossed over to receive Xenpozyme in the ETP.
  - Key Inclusion Criteria
    - Participant aged at least 18 years
    - Documented deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes; and a clinical diagnosis consistent with Niemann-Pick disease type B.
    - Participant has diffuse capacity of the lung for carbon monoxide (DLco) ≤ 70% of the predicted normal value
    - Participant has a spleen volume ≥ 6 multiples of normal (MN) measured by magnetic resonance imaging (MRI); participants who have had partial

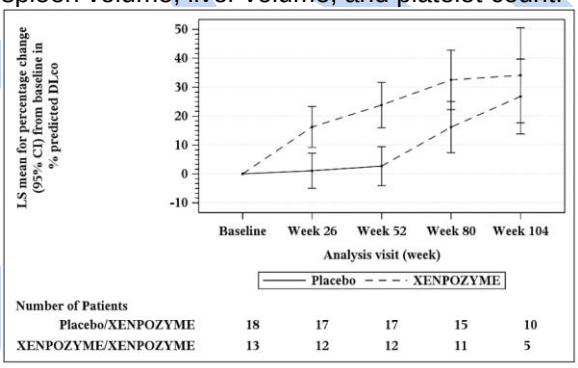
splenectomy allowed if the procedure was performed ≥ 1 year before screening/baseline and the residual spleen volume is ≥ 6 MN
    - Participant has a splenomegaly-related score (SRS) ≥ 5
    - Female participants of childbearing potential must have a negative serum pregnancy test
- Key Exclusion Criteria
    - Participant has a medical condition, including significant intercurrent illness; significant cardiac disease; active hepatitis B or hepatitis C, or infection with human immunodeficiency virus (HIV); malignancy diagnosed within the past 5 years, or any other serious medical condition that may preclude participation in the study.
    - Participant has a platelet count < 60,000/microliter based on the average of 2 samples.
    - Participant has an international normalized ratio (INR) > 1.5
    - Participant has ALT or AST > 250 IU/L or total bilirubin > 1.5 mg/dL.
    - Participant has had a major organ transplant
    - Participant requires use of invasive ventilator support or noninvasive ventilator support while awake for longer than 12 hours daily.
- Key Baseline Characteristics
    - 87% White, 7% Asian, 7% other. 32% identified as Hispanic/Latino, 65% as non-Hispanic/Latino, and 3% were not reported.
    - Five males and 13 females (median 34 years, range 18 to 66) were included in the placebo arm.
    - Eight males and 5 females (median 34 years, range 20 to 59) were included in the Xenpozyme arm.
- Primary Outcome Measures:
    - Percent predicted DLco at baseline and Week 52: the DLco test is one of the most clinically valuable tests of lung function. It measures the ability of the lungs to transfer gas from inhaled air to the red blood cells in pulmonary capillaries.
    - Spleen volume: assessed at baseline and Week 52 by abdominal MRI to quantitate the degree of splenomegaly in MN.
- Secondary Outcome Measures:
    - Liver volume: assessed at baseline and Week 52 by abdominal MRI to quantitate the degree of hepatomegaly in MN.
    - Percent change from baseline in platelet counts at Week 52.

	Placebo	Xenpozyme	Difference [95% CI]
DLco			
n	18	13	
Mean % predicted DLco at baseline (SD)	48.5 (10.8)	49.1 (9.7)	NA
n	17	12	
Mean % predicted DLco at Week 52 (SD)	49.9 (11.1)	59.4 (9.6)	NA
n	17	12	
LS Mean Percent change in % predicted DLco at Week 52 (SE)	3.0 (3.3)	23.9 (3.8)	20.9 (5.0)[a] [10.6, 31.2]
Spleen volume			
n	18	13	
Mean spleen volume (MN) at baseline (SD)	48.5 (10.8)	49.1 (9.7)	NA
n	17	12	
Mean spleen volume (MN) at Week 52 (SD)	49.9 (11.1)	59.4 (9.6)	NA
n	17	12	
LS Mean Percent change in Spleen Volume (in MN) at Week 52 (SE)	3.0 (3.3)	23.9 (3.8)	-39.4 (4.0)[b] [-47.6, -31.2]

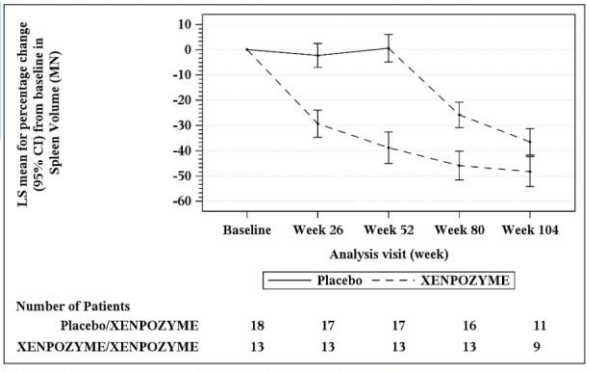
Liver volume			
n	18	13	
Mean liver volume (MN) at baseline (SD)	1.6 (0.5)	1.4 (0.3)	NA
n	17	12	
Mean liver volume (MN) at Week 52 (SD)	1.6 (0.5)	1.0 (0.2)	NA
n	17	12	
LS Mean Percent change in Liver volume from baseline to Week 52 (SE)	-1.8 (2.7)	-26.5 (3.2)	-24.7 (4.2)[b] [-33.4, -16.1]
Platelet count			
n	18	13	NA
Mean platelet count (109 /L) at baseline (SD)	115.6 (36.3)	109.3 (30.6)	
n	16	13	NA
Mean platelet count (109 /L) at Week 52 (SD)	120.2 (43.2)	126.4 (29.0)	
n	16	13	
LS Mean Percent change in Platelet Count from baseline to Week 52 (SE)	2.7 (4.5)	18.3 (5.0)	+15.6 (6.7)[c] [1.8, 29.4]

Nominal p value: [a]p value=0.0003; [b]p value <0.0001; [c]p value=0.0280

- Seventeen out of 18 patients previously receiving placebo and all patients previously receiving Xenpozyme (in the PAP) started or continued treatment with Xenpozyme for up to 4 years. At Week 104, patients initially randomized to placebo and had received Xenpozyme for 52 weeks demonstrated improvements in % predicted DLco, spleen volume, liver volume, and platelet count. Patients previously receiving Xenpozyme demonstrated continued improvement in % predicted DLco, spleen volume, liver volume, and platelet count.



The vertical bars represent the 95% CIs for the LS means.
The LS means and 95% CIs are based on a mixed model for repeated measures approach, using data up to Week 104. Patients in placebo/XENPOZYME group received placebo by Week 52 and switched to XENPOZYME thereafter.



The vertical bars represent the 95% CIs for the LS means.
The LS means and 95% CIs are based on a mixed model for repeated measures approach, using data up to Week 104. Patients in placebo/XENPOZYME group received placebo by Week 52 and switched to XENPOZYME thereafter.

- ASCEND-Peds (NCT02292654): multi-center, open-label, repeated dose trial in pediatric patients aged < 18 years with a clinical diagnosis of ASMD type B and A/B. Patients were administered Xenpozyme intravenously once every 2 weeks for 64 weeks.
  - Key Inclusion Criteria
    - Documented deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes.
    - Spleen volume ≥ 5 MN measured by MRI; participants who had partial splenectomy were allowed if the procedure was performed ≥ 1 year before screening and the residual spleen volume was ≥ 5 MN.
    - Participant height was -1 Z-score or lower
    - Negative serum pregnancy test in female participants of childbearing potential.
  - Key Exclusion Criteria
    - Participant has any of the following medical conditions: active hepatitis B or hepatitis C infection, HIV infection, cirrhosis, significant cardiac disease, malignancy within the previous 5 years (except basal cell carcinoma), acute or rapidly progressive neurological abnormalities, delay of gross motor skills, or major organ transplant.
    - Participant requires use of invasive ventilator or noninvasive ventilatory support while awake for > 12 hours a day.
    - Platelet count < 60,000/microliter based on average of 2 samples
    - ALT or AST > 250 IU/L or total bilirubin > 1.5 mg/dL
    - INR > 1.5
  - Key Baseline Characteristics
    - Seven participants were 2 to <12 years of age, one patient was < 2 years old
    - All patients were White and of non-Hispanic/Latino ethnicity.
    - Both sexes were equally represented.
  - Primary Outcome Measure: exploratory efficacy endpoints related to organomegaly, pulmonary and liver functions, and linear growth were evaluated at Week 52. These included % predicted DLco score, spleen volume, liver volume, platelet count, and height Z-score.

	Baseline Values	Week 52 Values
Mean % predicted DLco (SD) LS mean Percent change in % predicted DLco* (SE) 95% CI	(n=3) 48.5 (8.1)	(n=3) 70.9 (13.7) 45.9 (22.7) -12.5, 104.3
Mean spleen volume (MN) (SD) LS Mean Percent change in Spleen Volume (in MN) (SE) 95% CI	(n=8) 8.3 (5.6)	(n=8) 9.50 (2.4) -46.7 (3.6) -55.5, -37.9
Mean liver volume (MN) (SD) LS Mean Percent change in Liver Volume (in MN) (SE) 95% CI	(n=8) 2.5 (0.5)	(n=8) 1.6 (0.3) -38.1 (2.9) -44.1, -32.0
Mean platelet count (109 /L) (SD) LS Mean Percent change in Platelet Count (SE) 95% CI	(n=8) 136.7 (33.2)	(n=7) 184.5 (54.2) 37.6 (13.7) 8.5, 66.7
Mean height Z-scores (SD) LS Mean Change in height Z-scores (SE) 95% CI	(n=8) -1.9 (0.8)	(n=7) -1.5 (1.0) 0.5 (0.1) 0.2, 0.8

	• Eight pediatric patients from ASCEND-Peds continued treatment in an open label long-term trial (NCT02004704) and were treated with Xenpozyme for 2.5 to 3.2 years. Efficacy analysis 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. The height Z-score increased by 1.3 from baseline when evaluated through 24 months. Bone age, as assessed by hand x-ray, was delayed by a mean of 26.4 months at baseline in the 7 pediatric patients enrolled in ASCEND-Peds with a bone age measured at Month 24. • Adverse Events ○ Anaphylactic reactions were reported in 2 (25%) of Xenpozyme-treated pediatric patients ○ Most frequently reported adverse drug reactions in adults (≥ 10%) were headache, cough, diarrhea, hypotension, and ocular hyperemia. ○ Most frequently reported adverse drug reactions in pediatric patients (≥ 20%) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.
Price Per Unit (WAC):	• $7,142 per vial • Estimated annual cost for first year of therapy (70 kg participant): $1,728,364.00 • Estimated annual cost for maintenance therapy (70 kg participant): $2,042,612.00
Therapeutic Alternatives:	• Xenpozyme represents the first FDA-approved treatment for ASMD. • Management of NPD-A involves supportive care. Infants may benefit from physical and occupational therapy, periodic nutritional assessment, feeding tube for nutrition, and sedatives for sleep difficulty and irritability. • Management of NPD-B includes surveillance and periodic assessments of growth in height, weight, nutrition, activity level, bleeding, shortness of breath, abdominal pain, neurologic function, and lab values. Patients with symptomatic pulmonary disease may benefit from supplemental oxygen. Bleeding due to thrombocytopenia may require blood transfusions. Cholesterol-lowering therapy may also be required for adults with hyperlipidemia.
Prior Authorization Approval Criteria:	**Must meet the following criteria:** <u>Initial Therapy</u>: • Documented diagnosis of ASMD (NPD-B or NPD-A/B) (ICD10 E75.241, E75.244) confirmed by: ○ Molecular genetic testing confirming biallelic pathogenic variants in *SMDP1* gene **OR** ○ Documentation of deficient acid sphingomyelinase activity in peripheral leukocytes, cultured fibroblasts, or lymphocytes **AND** • Participant has clinical manifestations of ASMD defined by ONE of the following: ○ Baseline DLco ≤ 70% of predicted normal **OR** ○ Spleen volume ≥ 6 MN for adults or ≥ 5 MN for participants < 18 years of age **OR** ○ Height ≤ -1 Z score **AND** • Baseline platelet count > 60 × 10^3/μL **AND** • Baseline INR < 1.5 **AND** • Baseline AST/ALT < 250 IU/L **AND** • Baseline total bilirubin < 1.5 mg/dL **AND** • Participant is not currently pregnant **AND** • Participant lacks history of major organ transplant **AND** • Participant lacks acute or rapidly progressive neurologic abnormalities • Initial approval for 1 year

	Continuation of Therapy:
	• Compliance to prescribed drug therapy **AND**
	• Documented benefit of therapy including one of the following:
	  ○ Reduced liver volume from baseline
	  ○ Reduced spleen volume from baseline
	  ○ Improved platelet count from baseline
	  ○ Improved DLco score from baseline
	
	Additional Provider Diagnostic/Monitoring Criteria, if desired:
	• Xenpozyme has not been studied in patients with significant cardiac disease, active hepatitis B or hepatitis C infection, and HIV infection.

Implication to State Medicaid Program:	• LOE: 2034-2036
	• Sanofi/Genzyme estimates that there are approximately 2,000 patients in the United States, Europe, and Japan currently with ASMD.
	• Trappsol® Cyclo™ (Cyclo Therapeutics) is an investigational intravenous infusion currently in a Phase III trial for NPD-C.
	  ○ Trappsol Cyclo works by replacing the defective NPC1 protein thereby facilitating the transport of accumulating cholesterol out of cellular lysosomes.
	  ○ Estimated completion date of December 2023.
	• IB1001 (IntraBio) is currently in Phase III trials for NPD-C.
	  ○ Observational studies suggest a symptomatic and neuroprotective disease-modifying effect in NPD-C.
	  ○ Phase II trial found statistically significant improvement in symptoms, function, and quality of life for pediatric and adult patients.
	  ○ Phase III trial started in June 2022, with an estimated completion date of August 2023.
	  ○ If approved, would be first FDA-approved treatment for NPD-C.
	• Arimoclomol (Orphazyme) is another pipeline agents for the treatment of NPD-C. In June 2021, Orphazyme announced that the New Drug Application for arimoclomol received a complete response letter (CRL) from the FDA. The CRL cited the need for additional qualitative and quantitative evidence to further substantiate the validity and interpretation of the outcomes studied, despite positive late-phase data. There is currently no timeline regarding potential resubmission to the FDA.

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