

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

**THIS WAY
FORWARD**
TO TRANSFORM TOMORROW

BRADLEY, living with ASMD.

**HELP PATIENTS WITH ASMD RECLAIM THEIR POTENTIAL WITH XENPOZYME—
PROVEN TO DEMONSTRATE MULTISYSTEMIC IMPROVEMENTS¹**

ASMD—historically known as Niemann–Pick disease types A, A/B, and B—is caused by reduced activity of the enzyme acid sphingomyelinase (ASM). Insufficient ASM activity causes an accumulation of sphingomyelin, which can lead to multisystemic damage, morbidity, and early mortality.²



XENPOZYME targets the underlying cause of ASMD. As an enzyme replacement therapy, XENPOZYME provides an exogenous source of ASM.¹



The safety and efficacy of XENPOZYME were evaluated in 3 clinical trials including adult and pediatric patients with ASMD.¹



XENPOZYME is administered in 2 phases: (1) dose escalation, followed by (2) maintenance phase,* with an option of home infusion during the maintenance phase.¹

*3 mg/kg is the target maintenance dose, which can be administered following the dose escalation schedule.¹

ASMD=acid sphingomyelinase deficiency.

INDICATION

XENPOZYME[®] (olipudase alfa-rpcp) is indicated for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

IMPORTANT SAFETY INFORMATION

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with XENPOZYME have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical monitoring and support measures, including cardiopulmonary resuscitation equipment, should be readily available during XENPOZYME administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue XENPOZYME immediately, and initiate appropriate medical treatment. In patients with severe hypersensitivity reactions, a desensitization procedure to XENPOZYME may be considered.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including Boxed WARNING.

ASMD IS PROGRESSIVE AND CAN PUT PATIENTS AT RISK FOR LONG-TERM, MULTIORGAN DAMAGE³

THE MULTISYSTEMIC SIGNS AND SYMPTOMS OF ASMD CAN BE PROGRESSIVE AND POTENTIALLY LIFE-THREATENING^{2,3}

IN PATIENTS WITH ASMD TYPES A/B AND B:



>90% OF PATIENTS HAVE SPLENOMEGALY²

The degree of splenomegaly has been shown to correlate with hepatomegaly, growth, lipid profile, and hematologic parameters. However, spleen volume showed only weak negative correlations with measures of pulmonary function and did not correlate with exercise tolerance. Increased spleen volume can also lead to **hypersplenism** with increased risk for **bleeding** and **splenic ruptures**.^{2,4-6}



>80% OF PATIENTS HAVE INTERSTITIAL LUNG DISEASE (ILD)²

Abnormal DLco* can be an indicator of ILD. ILD may **impair daily exercise**, and **respiratory disease is a leading cause of death**. A proportion of patients with ILD may progress to **oxygen dependence** and **pulmonary failure**.⁷⁻⁹



>70% OF PATIENTS HAVE HEPATOMEGALY²

Hepatomegaly is associated with **liver fibrosis**, which may progress to **cirrhosis** and even **liver failure** in some patients with ASMD.³



>50% OF PATIENTS HAVE THROMBOCYTOPENIA²

Patients with thrombocytopenia may experience serious bleeding events such as **subdural hematoma**, **hematemesis**, and **hemothorax**. **Anemia** and **leukopenia** may also be present. Patients may also experience **fatigue**.^{3,10}



>50% OF PATIENTS HAVE PEDIATRIC GROWTH DELAY¹¹

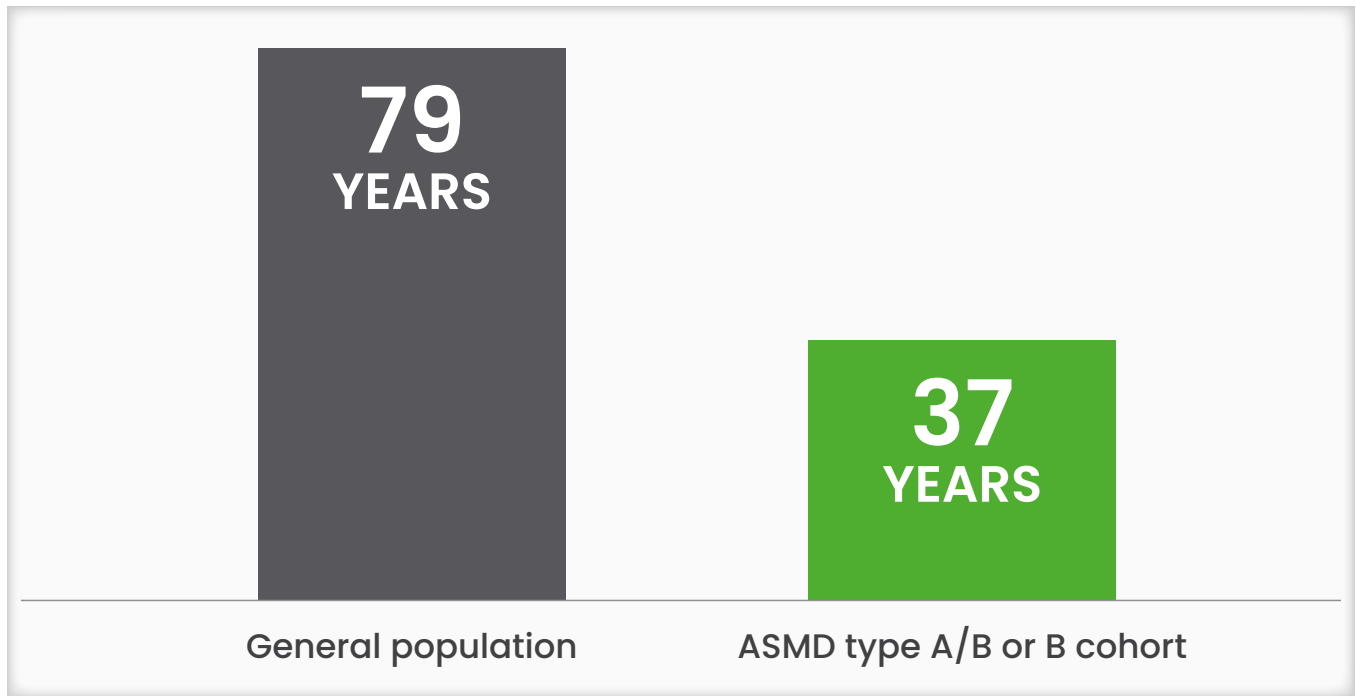
Children and adolescents may experience **delayed bone age**, **short stature**, **low weight**, and **delayed puberty**. Both pediatric and adult patients may experience **joint and limb pain**.⁵

Early management and ongoing monitoring for disease progression are critical for optimizing patient outcomes.^{3,5}

*DLco below the predicted reference range (75% to 140% of predicted).⁷
DLco=diffusing capacity of the lungs for carbon monoxide.



LIFE EXPECTANCY AT BIRTH FOR THE ASMD COHORT AND GENERAL POPULATION IN THE US IN 2018¹²

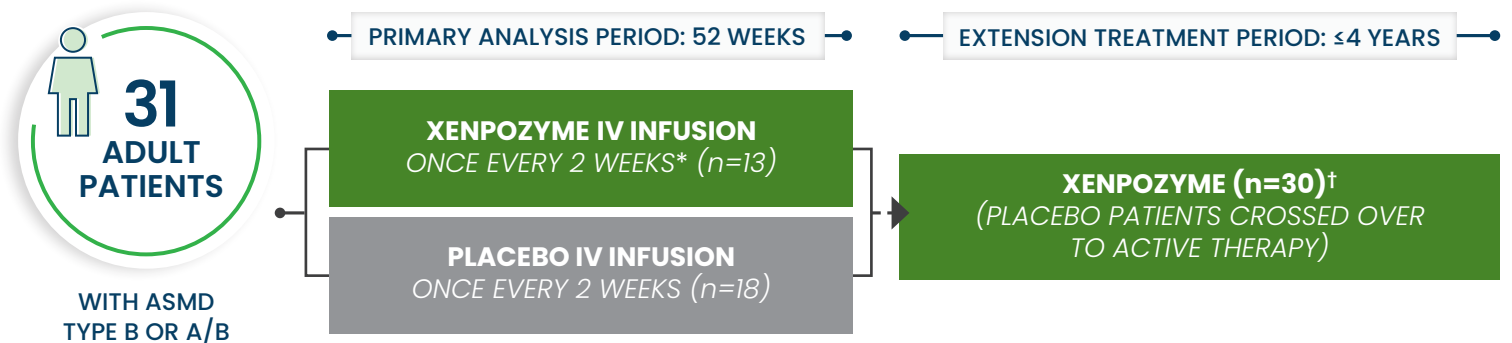


This observational, multicenter, retrospective cohort study included medical chart records retrieved from 25 medical centers in the US. The study included pediatric, adolescent, and adult patients (n=110) with ASMD non-type A (including type B, type A/B, or unspecified), surviving or deceased, with retrievable information from the US hospital medical records and the first date of evidence of ASMD, defined as either first symptom onset or a diagnosis of ASMD types B or A/B (whichever came first) between January 1, 1990, and February 28, 2021. Eligible medical chart records were abstracted to collect the evaluation criteria, including demographics, medical and developmental history, and mortality data, and characterized using descriptive statistics. Life expectancy at birth was computed as the area under the survival curve.¹²

The multisystemic impacts of ASMD are far-reaching and potentially life-threatening in both adult and pediatric patients.¹³

CLINICAL TRIAL IN ADULT PATIENTS
A MULTICENTER, RANDOMIZED, DOUBLE-BLINDED TRIAL¹

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg



[†]17 out of 18 patients previously receiving placebo and 13 out of 13 patients previously treated with XENPOZYME in the primary analysis period started or continued treatment with XENPOZYME, respectively, for up to 4 years.

KEY EFFICACY ENDPOINTS AT WEEK 52: MEAN PERCENT CHANGE FROM BASELINE (VS PLACEBO)	
➤ DLco (% predicted)	➤ Liver volume (MN)
➤ Spleen volume (MN)	➤ Platelet count (10 ⁹ /L)

*Patients received XENPOZYME via a dose escalation regimen over a minimum period of 14 weeks from 0.1 mg/kg to a target dose of 3 mg/kg.
MN= multiples of normal.

A systemic treatment for a multisystemic disease.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

See Boxed WARNING. Prior to XENPOZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

- If a *severe* hypersensitivity reaction occurs, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe hypersensitivity reactions.
- If a *mild or moderate* hypersensitivity reaction occurs, consider temporarily holding the infusion, slowing the infusion rate, and/or reducing the XENPOZYME dose.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

IN ADULT PATIENTS

XENPOZYME ACHIEVED RAPID*, SIGNIFICANT, AND SUSTAINED IMPROVEMENTS ACROSS KEY MULTISYSTEMIC SIGNS AND SYMPTOMS OF ASMD¹

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

AT WEEK 52, XENPOZYME DEMONSTRATED:

21%
($P=0.0003^{\dagger}$)

SIGNIFICANT IMPROVEMENT IN LUNG FUNCTION[‡]
($n=12$) vs PLACEBO ($n=17$)



39%
($P<0.0001^{\dagger}$)

SIGNIFICANT REDUCTION IN SPLEEN VOLUME
($n=13$) vs PLACEBO ($n=17$)



25%
($P<0.0001^{\dagger}$)

SIGNIFICANT REDUCTION IN LIVER VOLUME
($n=12$) vs PLACEBO ($n=17$)



16%
($P=0.0280^{\dagger}$)

SIGNIFICANT INCREASE IN PLATELET COUNT
($n=13$) vs PLACEBO ($n=16$)



BRADLEY, living with ASMD

AT WEEK 104, XENPOZYME DEMONSTRATED SUSTAINED IMPROVEMENTS IN MULTIPLE ORGANS^{1,14}

Patients previously in the XENPOZYME arm during PAP continued experiencing improvements in all key endpoints compared to baseline:

- 34% improvement in lung function[‡] ($n=5$)
- 32% reduction in liver volume ($n=9$)
- 48% reduction in spleen volume ($n=9$)
- 24% increase in platelet count ($n=9$)

*At Week 26: first post-dose endpoint assessment (vs baseline).

[†]P value is nominal.

[‡]As measured by DLco.

PAP=primary analysis period.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Infusion-Associated Reactions

Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of infusion-associated reactions (IARs). However, IARs may still occur in patients after receiving pretreatment.

- If severe IARs occur, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe IARs.
- If a mild or moderate IAR occurs, the infusion rate may be slowed or temporarily withheld, and/or the XENPOZYME dosage may be reduced.

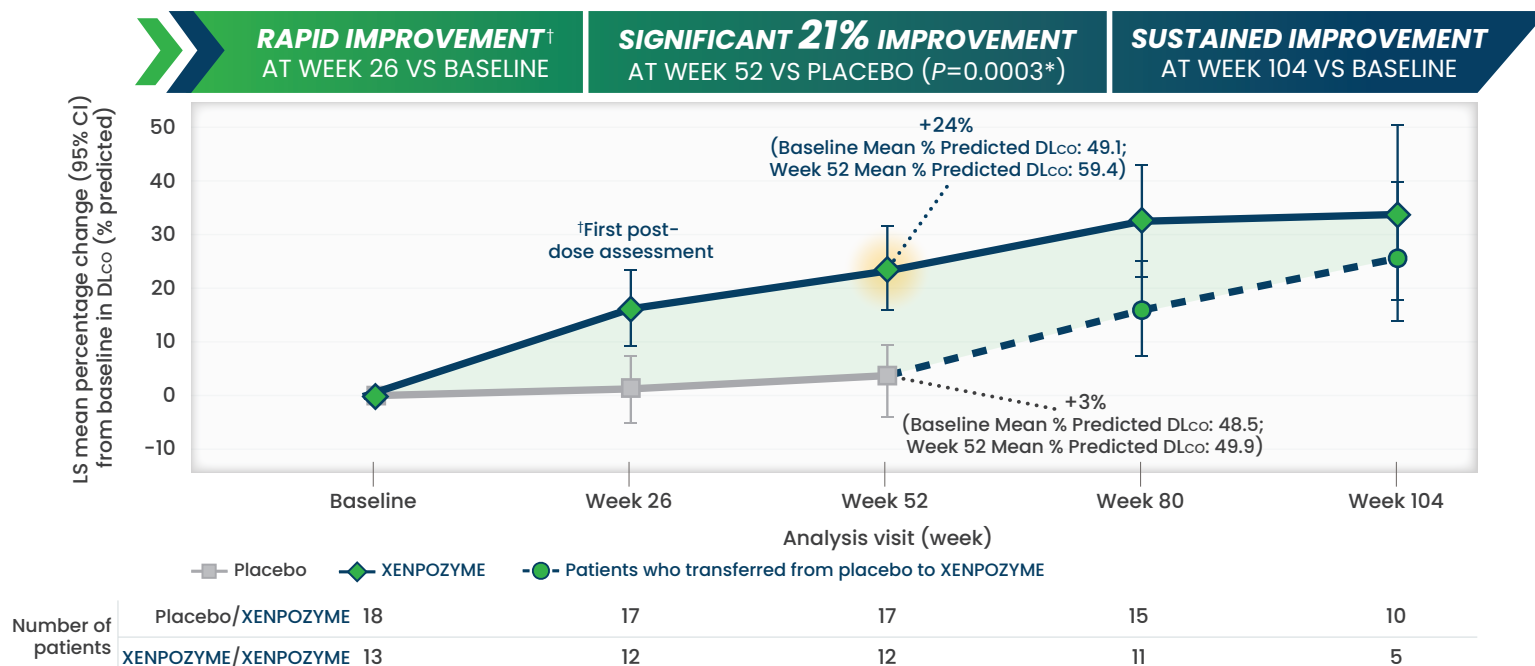
Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

IN ADULT PATIENTS

XENPOZYME SIGNIFICANTLY IMPROVED LUNG FUNCTION VS PLACEBO AT WEEK 52 ($P=0.0003^*$)¹

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

KEY ENDPOINT: MEAN PERCENT CHANGE IN % PREDICTED DL_{CO}



After Week 52, all patients received XENPOZYME. Vertical bars represent the 95% confidence intervals (CI) for the least squares (LS) means. The LS means and 95% CIs are based on a mixed model for repeated measures approach, using data up to Week 104.¹

*P value is nominal.¹

Patients previously in the XENPOZYME arm during PAP continued experiencing improvement in lung function at Week 104 vs baseline, with a mean percent increase of 34% predicted DL_{CO}.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Infusion-Associated Reactions (continued)

Acute phase reactions (APRs), acute inflammatory responses accompanied by elevations in inflammatory serum protein concentrations, have been observed. Most APRs occurred at 48 hours post infusion during the dose escalation period. APRs were managed similar to other IARs.

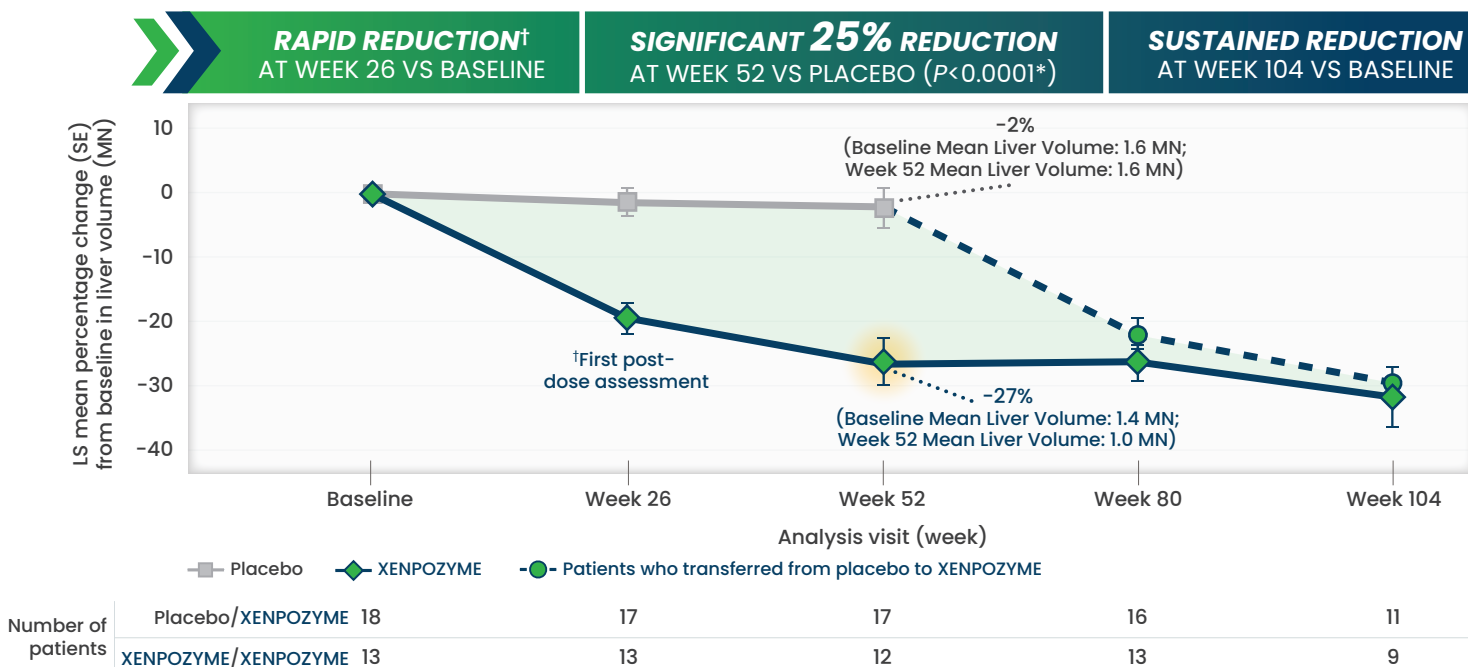
Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

IN ADULT PATIENTS

XENPOZYME SIGNIFICANTLY REDUCED HEPATOMEGALY VS PLACEBO AT WEEK 52 ($P < 0.0001^*$)^{1,14}

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

KEY ENDPOINT: MEAN PERCENT CHANGE IN LIVER VOLUME



After Week 52, all patients received XENPOZYME. Vertical bars represent the standard errors (SE) for the LS means. The LS means and SE are based on a mixed model for repeated measures approach, using data up to Week 104.¹

*P value is nominal.¹

TRANSAMINASE EXPLORATORY ENDPOINT¹⁴

- Reductions in transaminase levels were seen in adult patients treated with XENPOZYME at Week 52.
- Compared to baseline, after 52 weeks of treatment with XENPOZYME:

MEAN ALT DECREASED 37% **MEAN AST DECREASED 36%**

- Because liver function tests were an exploratory analysis, results require cautious interpretation.

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

Patients previously in the XENPOZYME arm during PAP continued experiencing reduction in liver volume (MN) at Week 104 vs baseline, with a mean percent reduction of 32%.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy

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. The decision to continue or discontinue XENPOZYME maintenance dosing in pregnancy should consider the female's need for XENPOZYME, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal ASMD disease. Verify pregnancy status in females of reproductive potential prior to initiating XENPOZYME treatment. Advise females of reproductive potential to use effective contraception during XENPOZYME treatment and for 14 days after the last dose if XENPOZYME is discontinued.

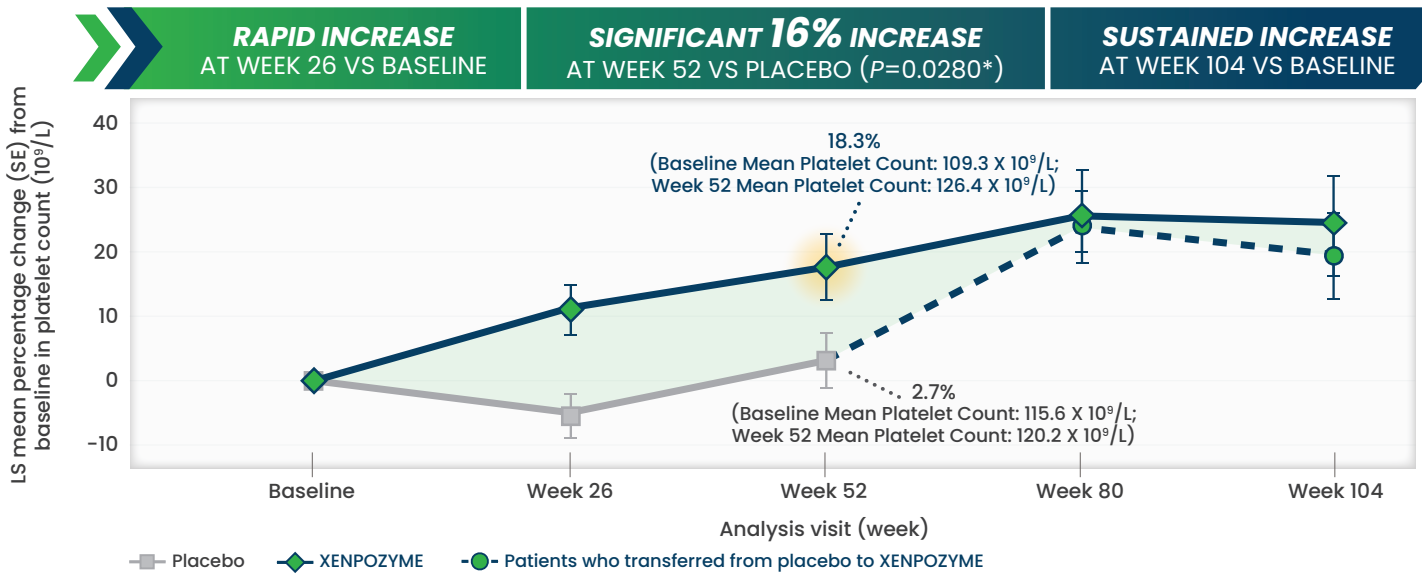
Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

IN ADULT PATIENTS

XENPOZYME SIGNIFICANTLY RAISED PLATELET COUNT VS PLACEBO AT WEEK 52 (P=0.0280*)^{1,14}



KEY ENDPOINT: MEAN PERCENT CHANGE IN PLATELET COUNT



Number of patients	Placebo/XENPOZYME	18	15	16	15	15
	XENPOZYME/XENPOZYME	13	13	13	12	9

After Week 52, all patients received XENPOZYME. Vertical bars represent the SE for the LS means. The LS means and SE are based on a mixed model for repeated measures approach, using data up to Week 104.¹

*P value is nominal.¹

Patients previously in the XENPOZYME arm during PAP continued experiencing an increase in platelet count (10⁹/L) at Week 104 vs baseline, with a mean percent increase of 24%.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

- Most frequently reported adverse drug reactions in adults (incidence ≥10%) were headache, cough, diarrhea, hypotension, and ocular hyperemia.
- Most frequently reported adverse drug reactions in pediatric patients (incidence ≥20%) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

**ADVERSE REACTIONS OCCURRING AT >10% IN ADULT PATIENTS WITH ASMD
 DURING THE 52-WEEK PRIMARY ANALYSIS PERIOD**

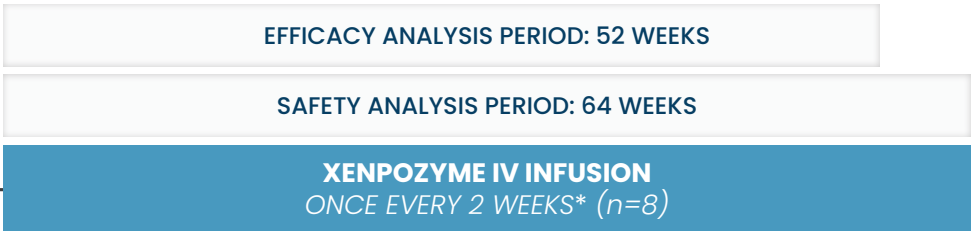
ADVERSE REACTION	XENPOZYME n=13	PLACEBO n=18
Headache	7 (54%)	8 (44%)
Cough	4 (31%)	2 (11%)
Diarrhea	2 (15%)	2 (11%)
Hypotension	2 (15%)	2 (11%)
Ocular hyperemia	2 (15%)	1 (6%)

➤ 30 adult patients treated with XENPOZYME with a median exposure of 2.5 years were included in the pooled safety analysis from 3 clinical trials.

No patients in the adult trial discontinued treatment due to adverse events.



WITH ASMD
 TYPE B OR A/B



The trial population included pediatric patients in the following age ranges:

- > 7 patients, 2 to <12 years old
- > 1 patient, <2 years old

Eight pediatric patients from this trial continued in a long-term, open-label extension trial and were treated for 2.5 to 3.2 years.

EXPLORATORY EFFICACY ENDPOINTS AT WEEK 52 (CHANGE FROM BASELINE)	
> DLco (% predicted)	> Platelet count (10 ⁹ /L)
> Spleen volume (MN)	> Height Z-scores
> Liver volume (MN)	

*Patients received XENPOZYME via a dose escalation regimen over a minimum period of 16 weeks from 0.03 mg/kg to a target dose of 3 mg/kg. All but 1 patient completed the dose escalation up to the maintenance dose of 3 mg/kg within 22 weeks.



LUKE, living with ASMD, and his mom, Nicole.

PEDIATRIC PATIENTS IN A LONG-TERM TRIAL¹

TRIAL DESIGN
> 8 pediatric patients from the open-label pediatric trial continued treatment in an open-label, Long-Term Trial.
• Patients ranged from 2 to <12 years of age and were treated for 2.5 to 3.2 years.
> XENPOZYME was administered at 3 mg/kg once every 2 weeks by IV infusion.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

See Boxed WARNING. Prior to XENPOZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

- If a *severe* hypersensitivity reaction occurs, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe hypersensitivity reactions.
- If a *mild or moderate* hypersensitivity reaction occurs, consider temporarily holding the infusion, slowing the infusion rate, and/or reducing the XENPOZYME dose.











Please see **Important Safety Information** and full **Prescribing Information** for complete details, including **Boxed WARNING**.

IN PEDIATRIC PATIENTS

XENPOZYME ACHIEVED SUSTAINED IMPROVEMENTS ACROSS KEY MULTISYSTEMIC SIGNS AND SYMPTOMS OF ASMD¹

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

EXPLORATORY EFFICACY ENDPOINTS

	Baseline Mean	Week 52 Mean	LS Mean Change
 Lung function	n=3 48.5% predicted DLco	n=3 70.9% predicted DLco	 45.9% Change in % predicted DLco
 Spleen volume	n=8 18.3 MN	n=8 9.5 MN	 -46.7% Change in spleen volume (MN)
 Liver volume	n=8 2.5 MN	n=8 1.6 MN	 -38.1% Change in liver volume (MN)
 Platelet count	n=8 136.7 x 10 ⁹ /L	n=7 184.5 x 10 ⁹ /L	 37.6% Change in platelet count (10 ⁹ /L)
 Height Z-scores	n=8 -1.9	n=7 -1.5	 0.5 Change in height Z-score

TRANSAMINASE EXPLORATORY ENDPOINT¹⁴

- › Reductions in transaminase levels were seen in pediatric patients treated with XENPOZYME at Week 52.
- › Compared to baseline, after 52 weeks of treatment with XENPOZYME:

MEAN ALT DECREASED 53%  **MEAN AST DECREASED 47%** 

- › Because liver function tests were an exploratory analysis, results require cautious interpretation.

PEDIATRIC PATIENTS EVALUATED IN A LONG-TERM TRIAL EXPERIENCED CONTINUOUS IMPROVEMENTS¹

- › Over the course of the Long-Term Trial in pediatric patients, compared to baseline, XENPOZYME continued to improve lung function, reduce spleen volume, reduce liver volume, raise platelet count, and improve growth patterns.
- › XENPOZYME continued to improve growth patterns in pediatric ASMD patients with growth delay.
 - Height Z-score increased by 1.3 from baseline when evaluated through 24 months of treatment with XENPOZYME.
 - Bone age was delayed by a mean of 26.4 months at baseline.
 - After 24 months of treatment with XENPOZYME in the Long-Term Trial, bone age improved to within a mean of 12 months of chronological age.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Infusion-Associated Reactions

Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of infusion-associated reactions (IARs). However, IARs may still occur in patients after receiving pretreatment.

- If *severe* IARs occur, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe IARs.
- If a *mild or moderate* IAR occurs, the infusion rate may be slowed or temporarily withheld, and/or the XENPOZYME dosage may be reduced.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

ADVERSE REACTIONS OCCURRING AT >20% IN XENPOZYME-TREATED PEDIATRIC PATIENTS WITH ASMD IN THE OPEN-LABEL PEDIATRIC TRIAL* AND A LONG-TERM TRIAL FOR AN OVERALL OBSERVATION PERIOD OF 2.5 TO 3.2 YEARS

ADVERSE REACTION	XENPOZYME n=8
Pyrexia	8 (100%)
Cough	6 (75%)
Diarrhea	6 (75%)
Rhinitis	6 (75%)
Abdominal pain	5 (63%)
Vomiting	4 (50%)
Headache	4 (50%)
Urticaria	4 (50%)
Nausea	3 (38%)
Rash	3 (38%)
Arthralgia	3 (38%)
Pruritus	2 (25%)
Fatigue	2 (25%)
Pharyngitis	2 (25%)

- 8 pediatric patients treated with XENPOZYME with a median exposure of 2.7 years were included in the pooled safety analysis from 3 clinical trials.
- Treatment-related serious adverse reactions, hypersensitivity reactions including anaphylaxis, and infusion-associated reactions (IARs) occurred within 24 hours of infusion and were observed in a higher percentage of pediatric patients than in adult patients.
- Serious adverse reactions of anaphylactic reaction were reported in 2 (25%) pediatric patients treated with XENPOZYME.

Abdominal pain includes abdominal pain and abdominal pain upper. Fatigue includes fatigue and asthenia. Rash includes rash and erythema.

The use of XENPOZYME in pediatric patients is supported by evidence from an adequate and well-controlled trial in adults with supportive efficacy, safety, and tolerability data in pediatric patients.

*Duration of treatment in the open-label trial was 64 weeks. All patients continued into the Long-Term Trial.



No patients in the pediatric trial permanently discontinued treatment due to treatment-related adverse events.

XENPOZYME REQUIRES 2 DOSING PHASES:



DOSE ESCALATION

- An initial dose escalation phase is necessary for XENPOZYME.
- The recommended starting dose is 0.1 mg/kg for adult patients and 0.03 mg/kg for pediatric patients (under age 18).
- Dose escalation takes at least 14 weeks for adults and at least 16 weeks for pediatric patients.
 - In the clinical trial in pediatric patients, all but 1 patient completed the dose escalation up to the maintenance dose of 3 mg/kg within 22 weeks.
- Initial dose escalation should take place in a clinical setting.
- If doses are missed, re-escalation may be necessary.



MAINTENANCE

- The maintenance phase of XENPOZYME can take place every 2 weeks, after the patient has successfully completed the dose escalation regimen.
- **XENPOZYME target maintenance dose: 3 mg/kg**



XENPOZYME is administered every 2 weeks, with an option for home infusion during the maintenance phase, if recommended by the treating physician.

STEPS TO TAKE PRIOR TO TREATMENT INITIATION

- **Verify pregnancy status in females of reproductive potential.**
 - XENPOZYME dosage initiation or escalation, at any time during pregnancy, is not recommended.
 - Advise female patients of reproductive potential to use effective contraception during treatment with XENPOZYME and for 14 days after the last dose if XENPOZYME is discontinued.
- **Consider administering pretreatment medication.**
 - Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of IARs. However, IARs may still occur in patients after receiving pretreatment.
- **Assess baseline transaminase (ALT and AST) levels** in all patients within 1 month prior to treatment initiation.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

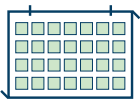
Infusion-Associated Reactions (continued)

Acute phase reactions (APRs), acute inflammatory responses accompanied by elevations in inflammatory serum protein concentrations, have been observed. Most APRs occurred at 48 hours post infusion during the dose escalation period. APRs were managed similar to other IARs.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

TRANSAMINASE LEVELS SHOULD BE ASSESSED TO MANAGE THE RISK OF TRANSIENT TRANSAMINASE ELEVATIONS PRIOR TO AND DURING DOSE ESCALATION, OR UPON RESUMING TREATMENT FOLLOWING A MISSED DOSE

XENPOZYME may be associated with transaminase elevations within 24 to 48 hours after infusion. Transaminase elevations generally returned to pre-infusion levels at the time of the next scheduled infusion.



Within 1 month prior to treatment initiation:

- Assess baseline ALT and AST levels.



During dose escalation or upon resuming treatment following a missed dose:

- Assess transaminase levels 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.
 - If transaminase levels are elevated above baseline and >2 times the ULN, the XENPOZYME dose can be adjusted (prior dose repeated or reduced) or treatment can be temporarily withheld until the liver transaminases return to the patient's baseline value.
 - If either the baseline or pre-infusion transaminase level (during the dose escalation phase) is >2 times the ULN, repeat assessment of transaminase levels within 72 hours after the end of the infusion to monitor trends in transaminase elevations.



During the maintenance phase:

- Transaminase testing is recommended to be continued as part of routine clinical management.

ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Elevated Transaminase Levels

XENPOZYME may be associated with elevated transaminases (ALT, AST, or both) within 24 to 48 hours after infusion. Levels generally returned to levels observed prior to the XENPOZYME infusion. To manage the risk of elevated transaminase levels, assess ALT and AST:

- within one month prior to initiation of XENPOZYME,
- within 72 hours prior to any infusion during dose escalation, which includes the first 3 mg/kg dose, or prior to the next scheduled XENPOZYME infusion upon resuming treatment following a missed dose.

Upon reaching the recommended maintenance dose, transaminase testing is recommended to be continued as part of routine clinical management of ASMD.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

MONITORING INFUSION-ASSOCIATED REACTIONS (IARs) AND HYPERSENSITIVITY¹

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg



TRINA, living with ASMD.



OBSERVE PATIENTS CLOSELY DURING AND FOR AN APPROPRIATE PERIOD OF TIME AFTER THE INFUSION, BASED ON CLINICAL JUDGMENT

During and after the infusion:

- In the event of a **severe** hypersensitivity reaction or a **severe** IAR, immediately discontinue XENPOZYME administration and initiate appropriate medical treatment.
- In the event of a **mild to moderate** hypersensitivity reaction or IAR, consider temporarily holding or slowing the infusion rate, and/or reducing the XENPOZYME dose. If dose is reduced, re-escalate according to the dose escalation regimens for adult and pediatric patients, as applicable.
- Consider testing for IgE ADA, serum tryptase, and complement activation in patients who experience anaphylaxis.

ADA=antidrug antibody; IgE=immunoglobulin E.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy

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. The decision to continue or discontinue XENPOZYME maintenance dosing in pregnancy should consider the female's need for XENPOZYME, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal ASMD disease. Verify pregnancy status in females of reproductive potential prior to initiating XENPOZYME treatment. Advise females of reproductive potential to use effective contraception during XENPOZYME treatment and for 14 days after the last dose if XENPOZYME is discontinued.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with XENPOZYME have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical monitoring and support measures, including cardiopulmonary resuscitation equipment, should be readily available during XENPOZYME administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue XENPOZYME immediately, and initiate appropriate medical treatment. In patients with severe hypersensitivity reactions, a desensitization procedure to XENPOZYME may be considered.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

See Boxed WARNING. Prior to XENPOZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

- If a *severe* hypersensitivity reaction occurs, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe hypersensitivity reactions.
- If a *mild or moderate* hypersensitivity reaction occurs, consider temporarily holding the infusion, slowing the infusion rate, and/or reducing the XENPOZYME dose.

Infusion-Associated Reactions

Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of infusion-associated reactions (IARs). However, IARs may still occur in patients after receiving pretreatment.

- If *severe* IARs occur, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe IARs.
- If a *mild or moderate* IAR occurs, the infusion rate may be slowed or temporarily withheld, and/or the XENPOZYME dosage may be reduced.

Acute phase reactions (APRs), acute inflammatory responses accompanied by elevations in inflammatory serum protein concentrations, have been observed. Most APRs occurred at 48 hours post infusion during the dose escalation period. APRs were managed similar to other IARs.

Elevated Transaminase Levels

XENPOZYME may be associated with elevated transaminases (ALT, AST, or both) within 24 to 48 hours after infusion. Levels generally returned to levels observed prior to the XENPOZYME infusion. To manage the risk of elevated transaminase levels, assess ALT and AST:

- within one month prior to initiation of XENPOZYME,
- within 72 hours prior to any infusion during dose escalation, which includes the first 3 mg/kg dose, or prior to the next scheduled XENPOZYME infusion upon resuming treatment following a missed dose.

Upon reaching the recommended maintenance dose, transaminase testing is recommended to be continued as part of routine clinical management of ASMD.

Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy

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. The decision to continue or discontinue XENPOZYME maintenance dosing in pregnancy should consider the female's need for XENPOZYME, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal ASMD disease.

Verify pregnancy status in females of reproductive potential prior to initiating XENPOZYME treatment. Advise females of reproductive potential to use effective contraception during XENPOZYME treatment and for 14 days after the last dose if XENPOZYME is discontinued.

ADVERSE REACTIONS

- Most frequently reported adverse drug reactions in adults (incidence $\geq 10\%$) were headache, cough, diarrhea, hypotension, and ocular hyperemia.
- Most frequently reported adverse drug reactions in pediatric patients (incidence $\geq 20\%$) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.

Please see full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

XENPOZYME: THE FIRST AND ONLY DISEASE-SPECIFIC TREATMENT FOR ASMD¹

IN ADULT PATIENTS



➤ XENPOZYME achieved rapid*, significant, and sustained[†] improvements across key efficacy endpoints that were assessed at Week 26, Week 52, and Week 104, including¹:

- Lung function as measured by DLco
- Spleen volume
- Liver volume
- Platelet count

See the data on pages 5–9.

IN PEDIATRIC PATIENTS



➤ XENPOZYME achieved sustained[†] improvements across key multisystemic signs and symptoms of ASMD.¹

➤ The use of XENPOZYME in pediatric patients is supported by evidence from an adequate and well-controlled trial in adult patients with supportive efficacy, safety, and tolerability data in pediatric patients.¹

See the data on page 12.



- The most common adverse drug reactions in adult patients (incidence $\geq 10\%$) were headache, cough, diarrhea, hypotension, and ocular hyperemia.¹
- The most common adverse drug reactions in pediatric patients (incidence $\geq 20\%$) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.¹

PATIENT SUPPORT WITH CARECONNECT PERSONALIZED SUPPORT SERVICES

careconnect[™]
PERSONALIZED SUPPORT SERVICES

CareConnect can help eligible patients with starting treatment, insurance changes, transition of care, and resource connections.

Visit [CareConnectPSS.com](https://www.careconnectpss.com) to learn more.

*At Week 26: first post-dose endpoint assessment (vs baseline).

[†]At Week 104 (vs baseline).

INDICATION

XENPOZYME[®] (olipudase alfa-rpcp) is indicated for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

IMPORTANT SAFETY INFORMATION

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with XENPOZYME have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical monitoring and support measures, including cardiopulmonary resuscitation equipment, should be readily available during XENPOZYME administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue XENPOZYME immediately, and initiate appropriate medical treatment. In patients with severe hypersensitivity reactions, a desensitization procedure to XENPOZYME may be considered.

Please see [Important Safety Information](#) and full [Prescribing Information](#) for complete details, including **Boxed WARNING**.

FOR MORE INFORMATION ON XENPOZYME, VISIT [XENPOZYME.COM/HCP](https://www.xenpozyme.com/hcp)

Xenpozyme[®]
(olipudase alfa-rpcp)
For Injection, 20 mg

References: **1.** XENPOZYME. Prescribing Information. **2.** McGovern MM, Avetisyan R, Sanson B-J, Lidove O. Disease manifestations and burden of illness in patients with acid sphingomyelinase deficiency (ASMD). *Orphanet J Rare Dis.* 2017;12(1):41. **3.** Geberhiwot T, Wasserstein M, Wanninayake S, et al. Consensus clinical management guidelines for acid sphingomyelinase deficiency (Niemann-Pick disease types A, B and A/B). *Orphanet J Rare Dis.* 2023;18(1):85. **4.** Arslan N, Coker M, Gokcay GF, Kiykim E, Onenli Mungan HN, Ezgu F. Expert opinion on patient journey, diagnosis and clinical monitoring in acid sphingomyelinase deficiency in Turkey: a pediatric metabolic disease specialist's perspective. *Front Pediatr.* 2023;11:113422. **5.** Wasserstein M, Dionisi-Vici C, Giugliani R, et al. Recommendations for clinical monitoring of patients with acid sphingomyelinase deficiency (ASMD). *Mol Genet Metab.* 2019;126(2):98-105. **6.** McGovern MM, Wasserstein MP, Giugliani R, et al. A prospective, cross-sectional survey study of the natural history of Niemann-Pick disease type B. *Pediatrics.* 2008;122(2):e341-e349. **7.** Jones SA, McGovern M, Lidove O, et al. Clinical relevance of endpoints in clinical trials for acid sphingomyelinase deficiency enzyme replacement therapy. *Mol Genet Metab.* 2020;131(1-2):116-123. **8.** Faverio P, Stainer A, De Giacomo F, et al. Molecular pathways and respiratory involvement in lysosomal storage diseases. *Int J Mol Sci.* 2019;20(2):327. **9.** von Ranke FM, Pereira Freitas HM, Mançano AD, et al. Pulmonary involvement in Niemann-Pick disease: a state-of-the-art review. *Lung.* 2016;194(4):511-518. **10.** Platelet disorders: symptoms. National Heart, Lung, and Blood Institute. Updated March 24, 2022. Accessed February 1, 2024. <https://www.nhlbi.nih.gov/health/platelet-disorders/symptoms> **11.** Cox GF, Clarke LA, Giugliani R, McGovern MM. Burden of illness in acid sphingomyelinase deficiency: a retrospective chart review of 100 patients. *JIMD Rep.* 2018;4:119-129. **12.** Pulikottil-Jacob R, Dehipawala S, Smith B, et al. Survival of patients with chronic acid sphingomyelinase deficiency (ASMD) in the United States: a retrospective chart review study. *Mol Genet Metab Rep.* 2023;38:101040. **13.** Cassiman D, Packman S, Bembi B, et al. Cause of death in patients with chronic visceral and chronic neurovisceral acid sphingomyelinase deficiency (Niemann-Pick disease type B and B variant): literature review and report of new cases. *Mol Genet Metab.* 2016;118(3):206-213. **14.** Data on file, Sanofi.

© 2024 Sanofi. All rights reserved. CareConnect Personalized Support Services is a trademark of Sanofi or an affiliate. Sanofi and Xenpozyme are registered trademarks of Sanofi or an affiliate.

MAT-US-2205983-v5.0-06/2024

sanofi