Prospective Observational Study to Assess the Long-term Safety of Olipudase Alfa Effect in Pediatric Patients Less Than 2 Years of Age with Acid Sphingomyelinase Deficiency: Study Design

Pablo Bianculli[1], Sefika Uslu Cil[2], Daniel Lewi[3], Kathleen Coolidge[3], Femida Gwadry-Sridhar[3], Judy Hull[2], Antonio Oliveira-dos-Santos[4]

[1]Sanofi, Buenos Aires, Argentina; [1]Sanofi, Cambridge, MA, USA; [3]Pulse Infoframe, London, ON, Canada; [4]Sanofi, Sao Paulo, Brazil

BACKGROUND

Acid Sphingomyelinase Deficiency (ASMD)

- Rare genetic disorder characterized by deficient activity of lysosomal enzyme, acid sphingomyelinase
- Sphingomyelin accumulation in cells leads to progressive disease manifestations

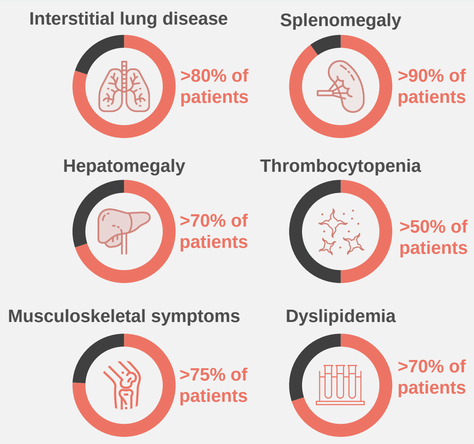
Olipudase Alfa

- A recombinant human acid sphingomyelinase (rhASM) approved for treatment of non-central nervous system manifestations of ASMD in pediatric and adult patients
- U.S. Food and Drug Administration requested additional data on olipudase alfa in ASMD patients < 2 years of age

Challenges in ASMD Study Design

- Low incidence is a barrier to studying subpopulations within pivotal clinical studies, particularly children diagnosed very early in life and needing treatment
- Enrollment and follow-up of patients with ultra-rare diseases present significant challenges
- Need to balance demands of study visits/sufficient data collection with minimizing burden on patients and caregivers

Common ASMD Disease Manifestations[1-3]



STUDY OBJECTIVES

Primary Objective

Characterize long-term safety and immunogenicity of olipudase alfa in real-world clinical practice in the United States for pediatric patients with ASMD <2 years of age at time of treatment initiation, and patients with ASMD type A without age restriction

Secondary Objective

Evaluate the relationship between anti-olipudase alfa antibodies and safety

ELIGIBILITY CRITERIA

Inclusion Criteria

- ASMD type A/B or B and <2 years of age at time of treatment initiation or ASMD type A without age restriction
- Weight ≥ 2 kg*
- ASMD diagnosis determined in peripheral leukocytes, cultured fibroblasts, or lymphocytes and/or by genotype determination
- Signed informed consent by participant's parent(s)/legal guardian(s)
- Eligible to start olipudase alfa enzyme replacement therapy or has received the first dose of olipudase alfa (and no more), and has retrievable clinical, laboratory, and anti-drug antibody data.

Exclusion Criteria

- Investigational drug within 30 days or 5 drug half-lives before study enrollment
- Determined by the Investigator to be unsuitable for participation due to medical or clinical conditions or potential risk of noncompliance with study procedures
- Immediate family member of employees of the study site or other individuals directly involved in study conduct

*The USPI for olipudase alfa specifies this minimum weight for infants receiving olipudase alfa.

DATA COLLECTION

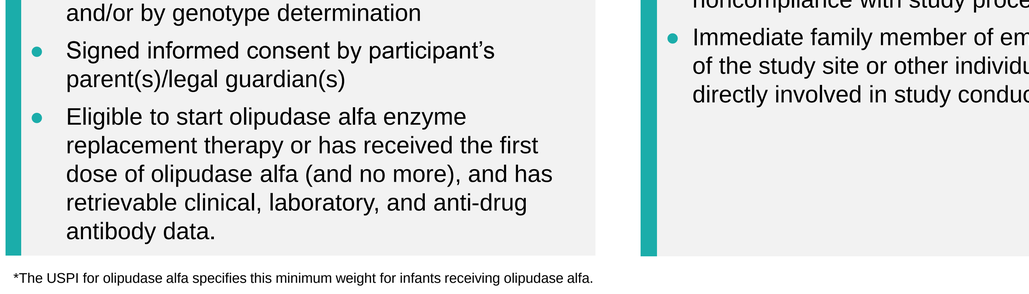
Data

- Demographics
- Confirmation of ASMD diagnosis
- Medical history
- Prior and concomitant medications
- Weight, height/length, vital signs
- Physical examination
- Olipudase alfa infusion information
- Adverse events
- Labs (hematology, chemistry, liver function)
- Anti-drug antibodies

Timepoints

At every infusion of olipudase alfa (every 2 weeks) during dose escalation phase

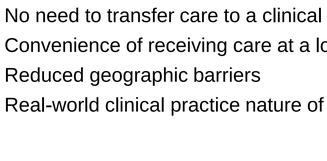
Every 3 months during dose escalation phase (up to 24 months) and at 36 months



STUDY DESIGN

Multicenter, Open Label, Observational Study of Olipudase Alfa Treatment in Young Children with ASMD

Population



3 to 10 children <2 years old with ASMD in the United States

Recruitment | Enrollment | Data Collection

Decentralized/hybrid process facilitated by investigators and through Pulse *healthie*™*2.0* platform after diagnosis of ASMD and consultation with investigator

Follow-up

1-3 years

Total study duration: 5 years

Currently enrolling in the United States (ClinicalTrials.gov: NCT06192576)

DECENTRALIZED RECRUITMENT

Decentralized study design was developed to minimize burden of clinical visits for assessments and data collection using digital technology for remote collection of clinical data and pre-specified laboratory tests

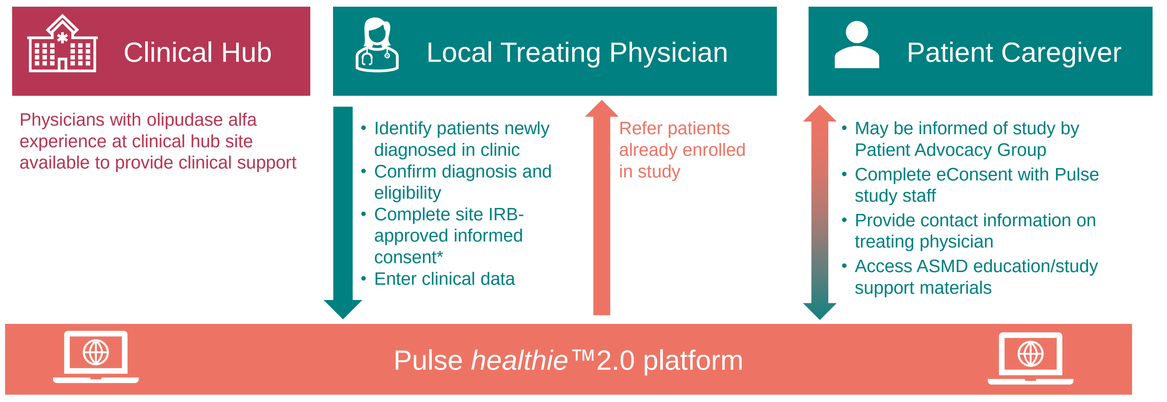
Advantages

- More efficient than opening multiple study sites and waiting for new incident diagnoses or referrals
- Faster enrollment
- No need to transfer care to a clinical research site
- Convenience of receiving care at a local facility
- Reduced geographic barriers
- Real-world clinical practice nature of data collected

How Decentralized Recruitment Works

- Establish sites with prior experience in olipudase alfa treatment
- Additional treating sites (i.e., local investigators) considered to facilitate enrollment
- Single collection platform:
  - Eligibility • Enrollment
  - Clinical & laboratory data
  - Educational materials about ASMD & olipudase alfa
- Emulate usual care as closely as possible (including home infusion)

Decentralized Recruitment Process



*if different than eConsent on Pulse Platform

HYBRID ENROLLMENT

3 Ways Patients Can Enroll in the Study

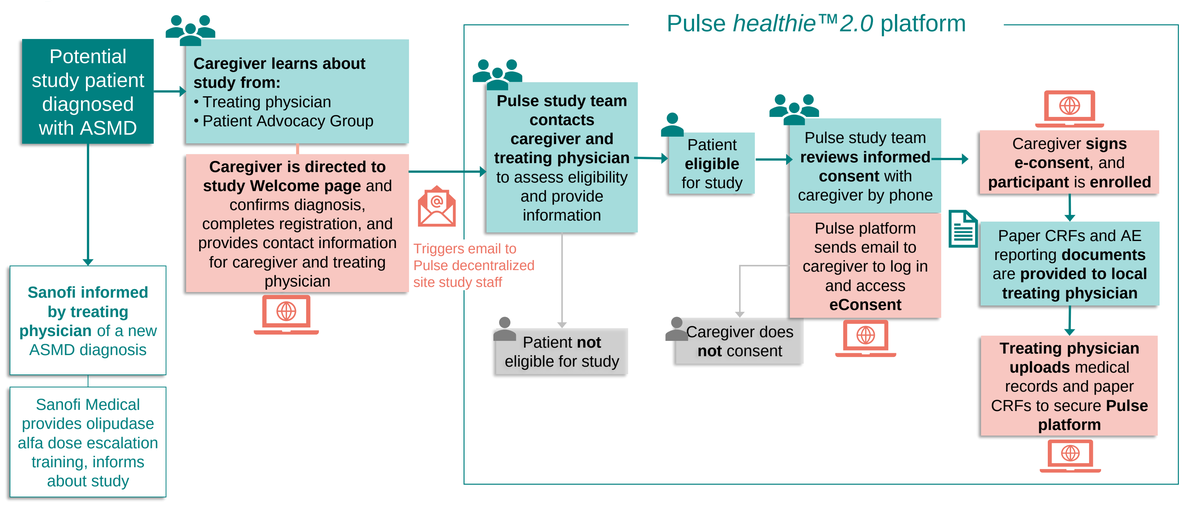
Site-based enrollment

- At clinical hub site with ASMD specialists who have olipudase alfa experience
- Through their local treating physician's office

Online enrollment

- On the Pulse platform (data collection website for this study)

Hybrid Enrollment Process



REFERENCES

1. McGovern MM et al. Orphanet J Rare Dis. 2017;12:41
2. Cox GF et al. JIMD Rep. 2018;41:119–29.
3. Pokrzywinski R et al. Scientific Reports 2021;11:20972

ACKNOWLEDGMENTS

This study (NCT06192576) is sponsored by Sanofi. The authors thank the trial participants, their families, and Sanofi employees involved in the trials, data analyses, and presentations. Medical writing and graphics support was funded by Sanofi and provided by Laurie LaRusso (Chestnut Medical Communications). The text, figures, and tables in this presentation cannot be reproduced without the explicit permission of the authors and Sanofi.

DISCLOSURES

Pablo Bianculli, Sefika Uslu Cil, Judy Hull, and Antonio Oliveira-dos-Santos are employed by Sanofi and may hold stock in the company. Daniel Lewi, Kathleen Coolidge, and Femida Gwadry-Sridhar are employed by Pulse Infoframe, which was contracted by Sanofi to administer the real-world evidence platform utilized in this study.

Presented at WORLDSymposium 2025. San Diego, California, USA, Feb 3-7, 2025