

# Long-term Administration of Tralesinidase Alfa Enzyme Replacement Therapy (TA-ERT) Results in Profound and Durable Reduction of Heparan Sulfate (HS) and Stabilization of Cognitive Function, Adaptive Behavior, and Cortical Gray Matter Volume (CGMV) in Patients with Sanfilippo Syndrome Type B (MPS IIIB)

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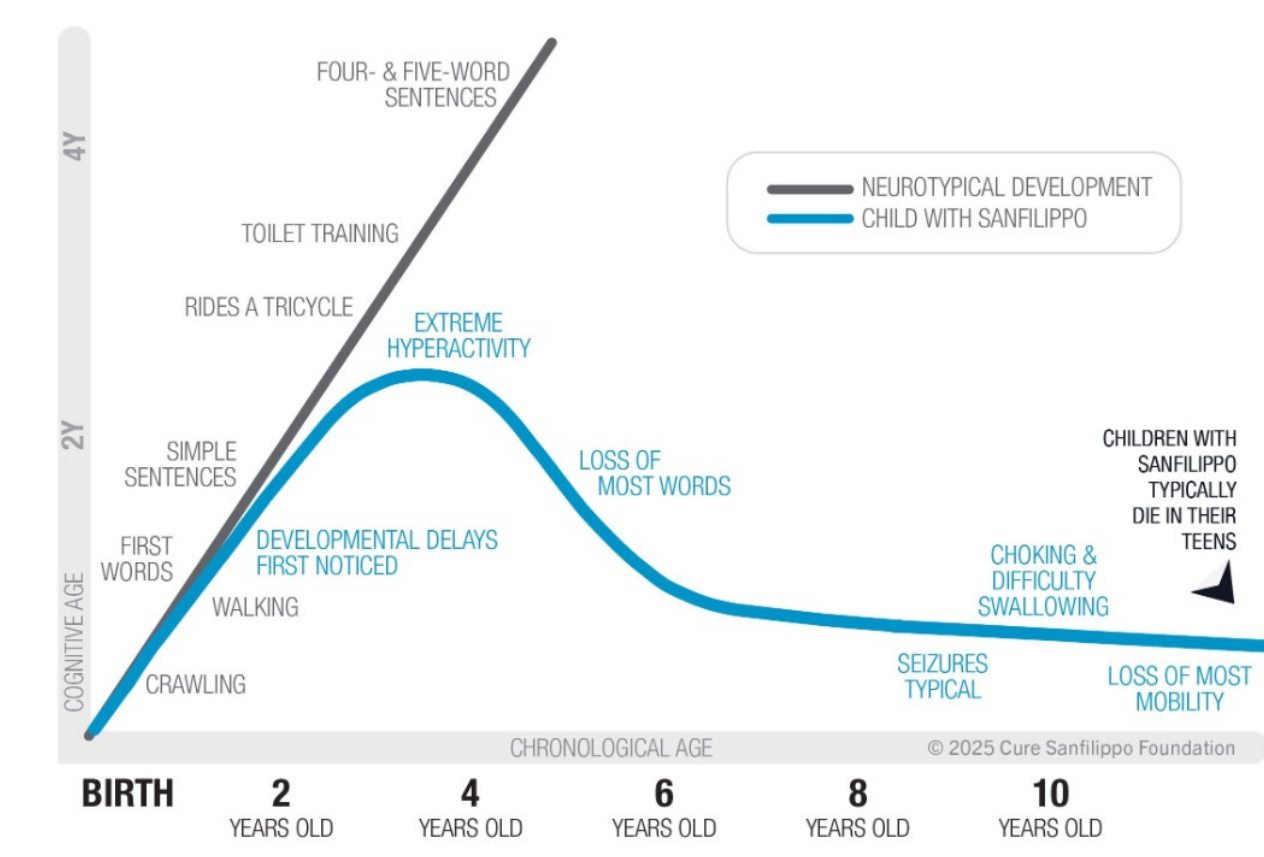
## INTRODUCTION

### Mucopolysaccharidosis IIIB (MPS IIIB): Progressive Fatal Neurodegenerative Pediatric Disorder

- Autosomal recessive disorder affecting 1 in 200,000 newborns<sup>1,2</sup>
- A deficiency in alpha-N-acetylglucosaminidase (NAGLU) leads to lysosomal accumulation of heparan sulfate (HS)<sup>3</sup>
- HS buildup impairs neuronal development ultimately leading to neurodegeneration and death
- No FDA-approved therapies and limited palliative care
- Heavy burden on caregivers: severe sleep disruptions, hyperactive/impulsive actions requiring constant supervision, progressive communication barriers

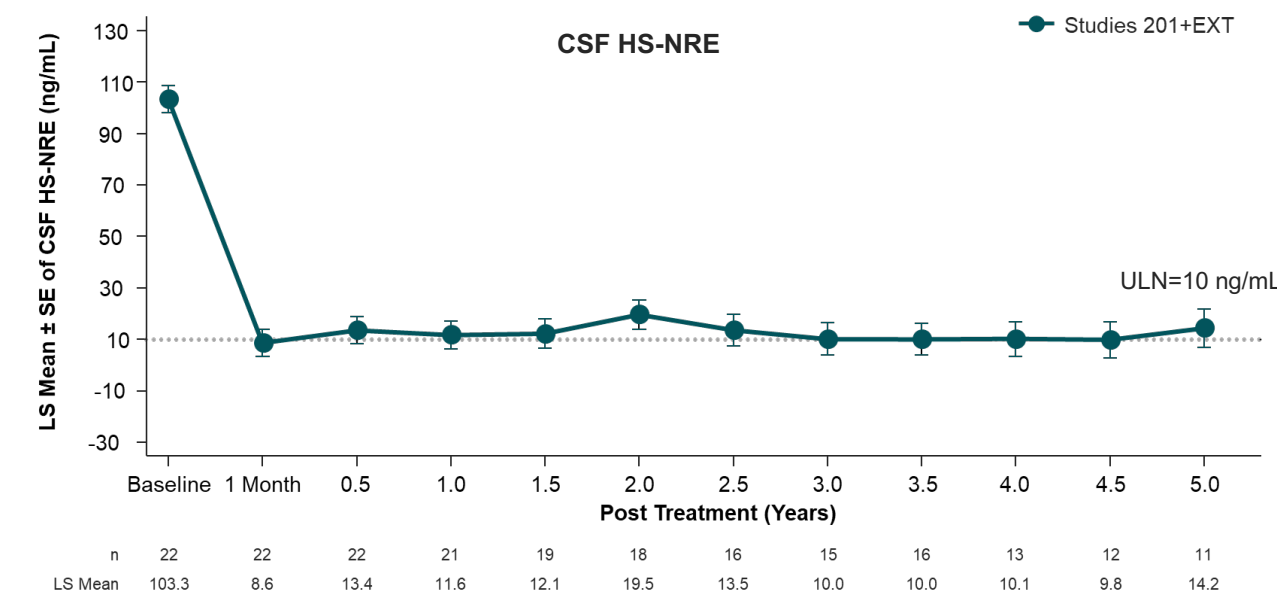
Sources: 1. Disease modeling for Mucopolysaccharidosis type IIIB using patient derived induced pluripotent stem cells. Huang et al. *Exp Cell Res*. 2021;407(1):112785; 2. IQVIA MPS-IIIB Global Patient Mapping Report, 2022. Proprietary analysis al. -Cell Death & Disease 2018; 3. <https://curesanfilippo.org>.

Figure 1: Progression of Sanfilippo Syndrome

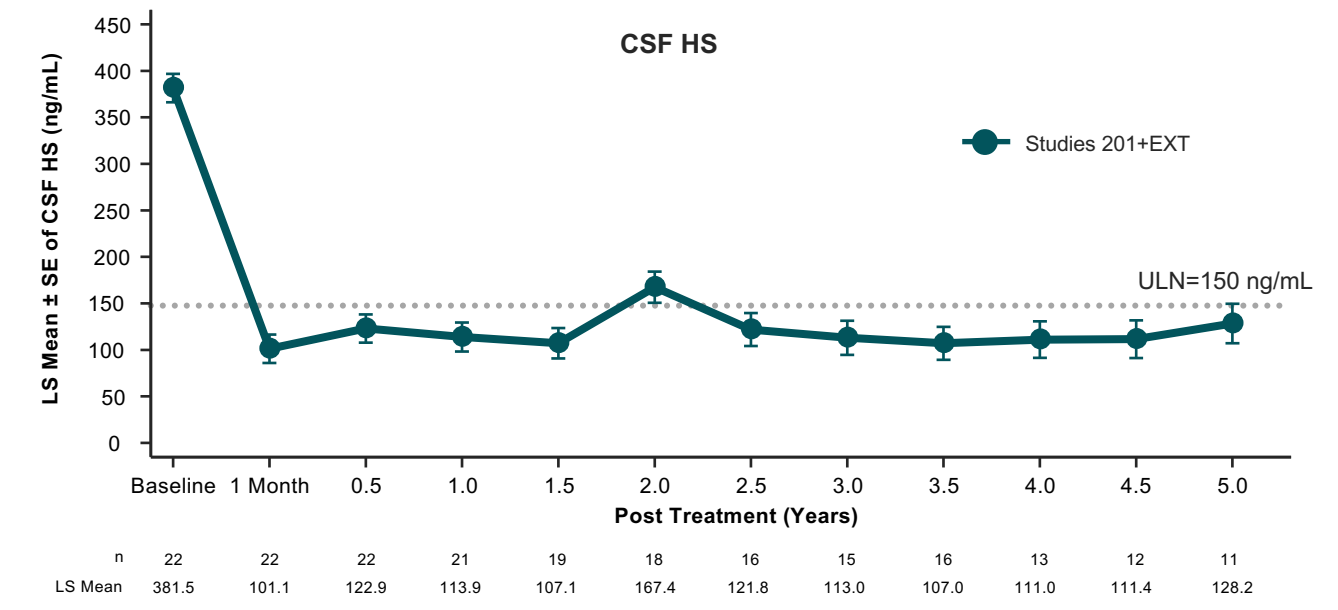


## RESULTS

Figure 4: TA-ERT Rapidly Normalizes CSF Heparan Sulfate



Dashed line represents ULN (10 ng/mL) for CSF HS-NRE; LS mean based on mixed-model repeated measures analysis with study visit as covariate. Note: Data are shown for up to 5 years, but 2 subjects were on treatment for up to 6 years. CSF HS-NRE levels were averaged over each 0.5-year interval. CSF= cerebrospinal fluid; EXT=extension; HS-NRE=heparan sulfate-nonreducing end; LS=least squares; ULN=upper limit of normal. Source: Integrated Figure 5.3.5.3.1-2.1.5.1 and 5.3.5.3.1-2.1.5.2



Dashed line represents ULN (150 ng/mL) for CSF HS; LS mean based on mixed-model repeated measures analysis with study visit as covariate. Note: Data are shown for up to 5 years, but 2 subjects were on treatment for up to 6 years. CSF HS levels were averaged over each 0.5-year interval. CSF= cerebrospinal fluid; EXT=extension; HS=heparan sulfate; LS=least squares; ULN=upper limit of normal. Source: Integrated Figure 5.3.5.3.1-2.1.5.1 and 5.3.5.3.1-2.1.5.2

Figure 5: TA-ERT Stabilized Cortical Grey Matter Volume Through 240 Weeks

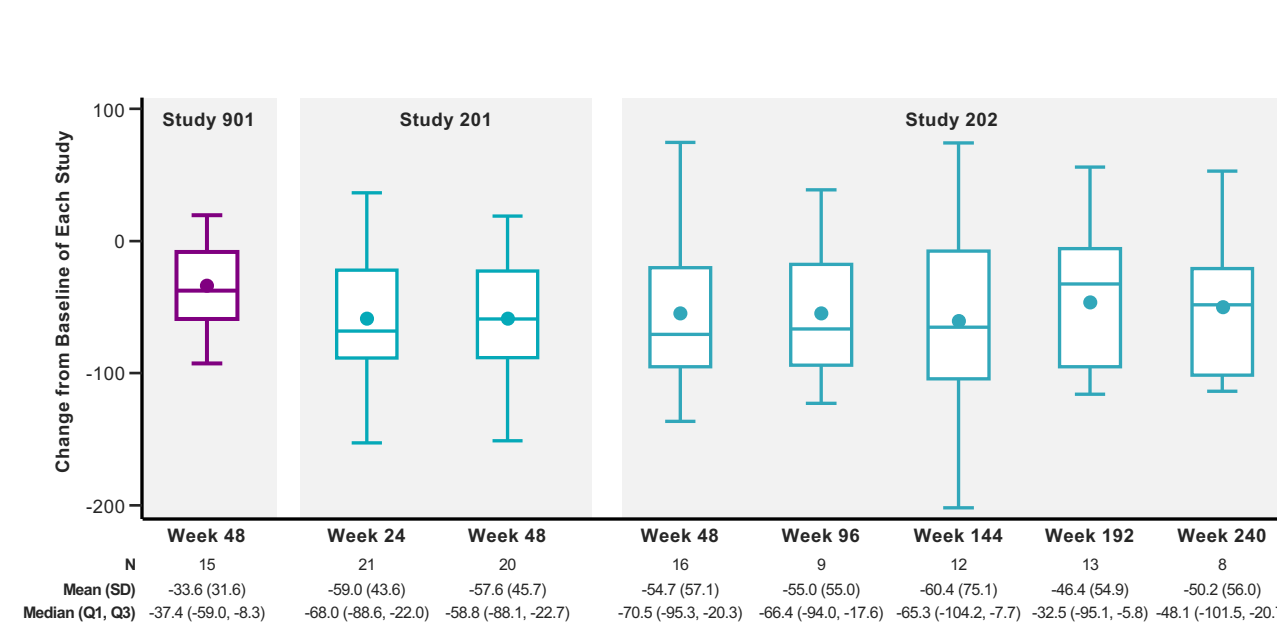


Figure 6: Meaningful Correlation Between Changes from Baseline in Cognition and Expressive Communication

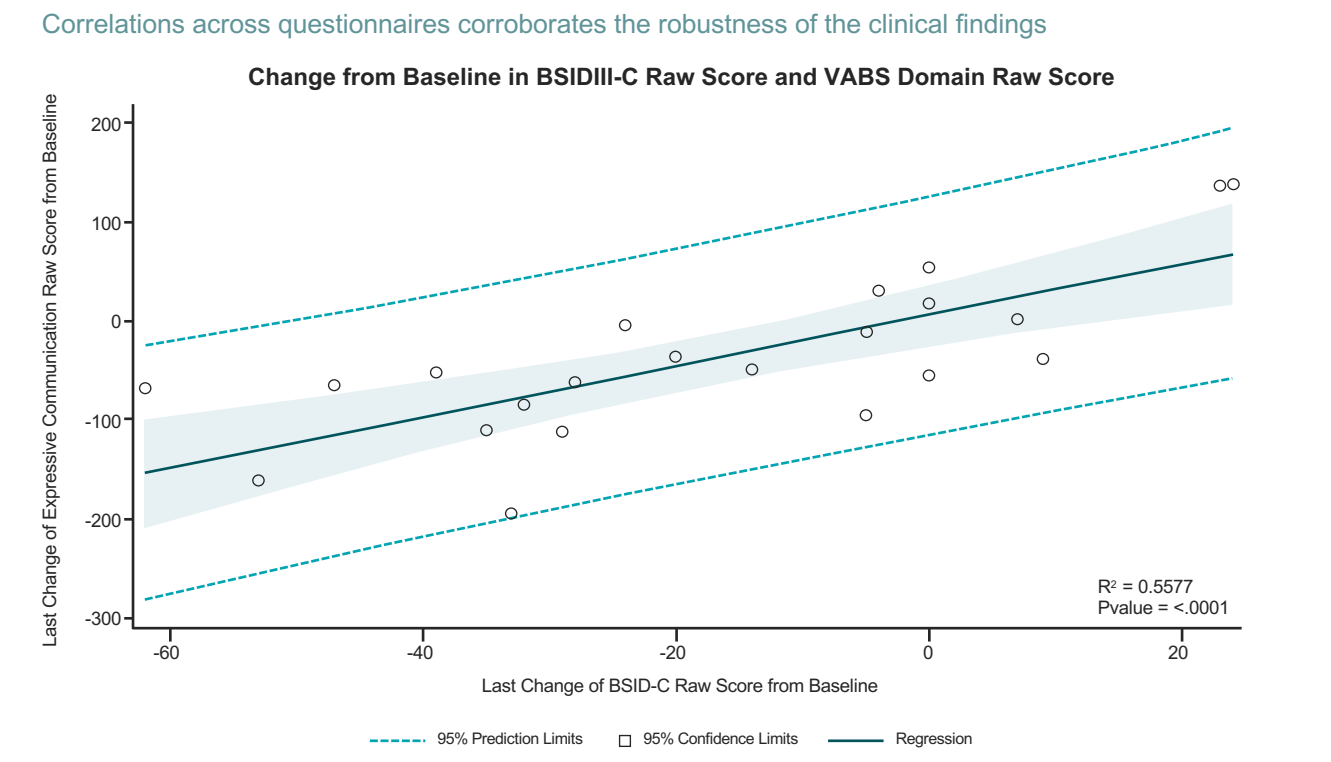
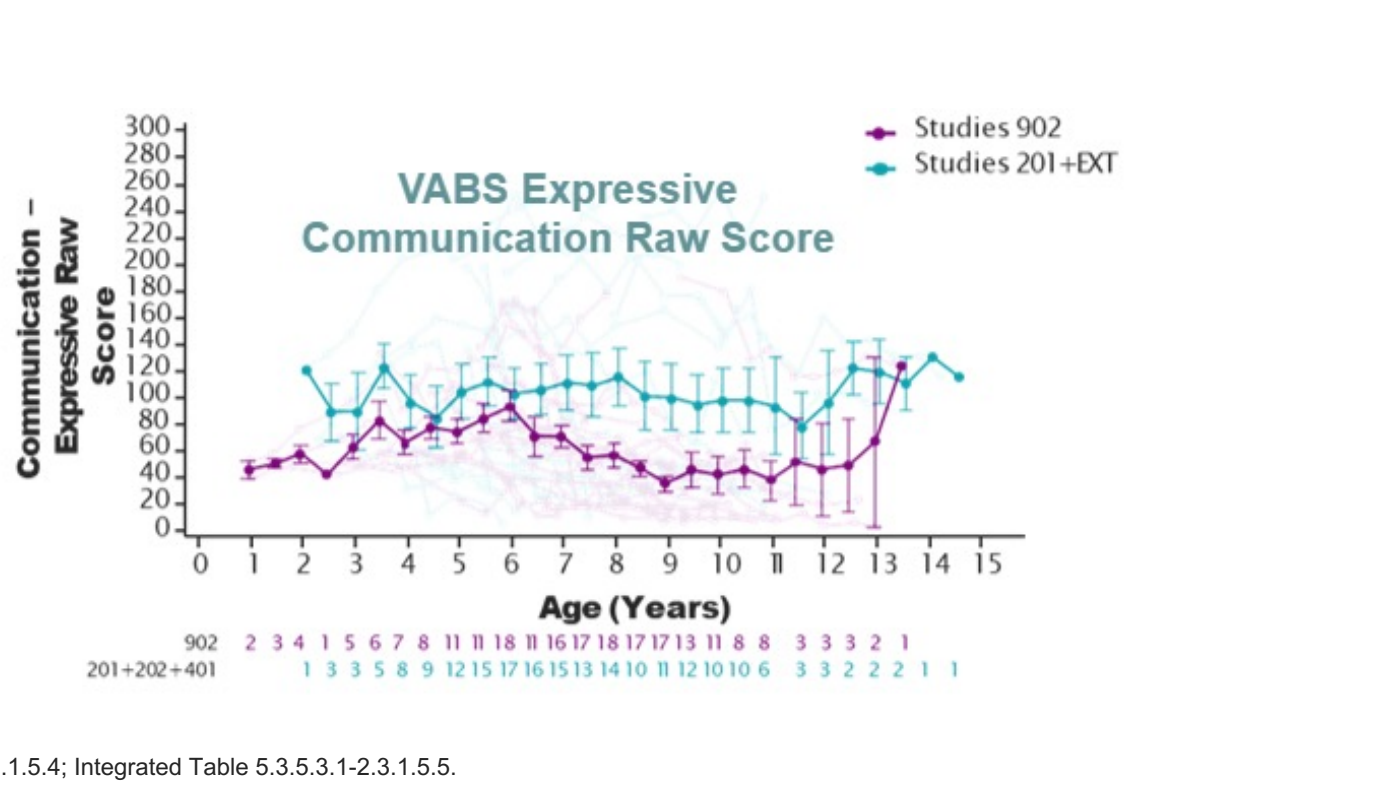
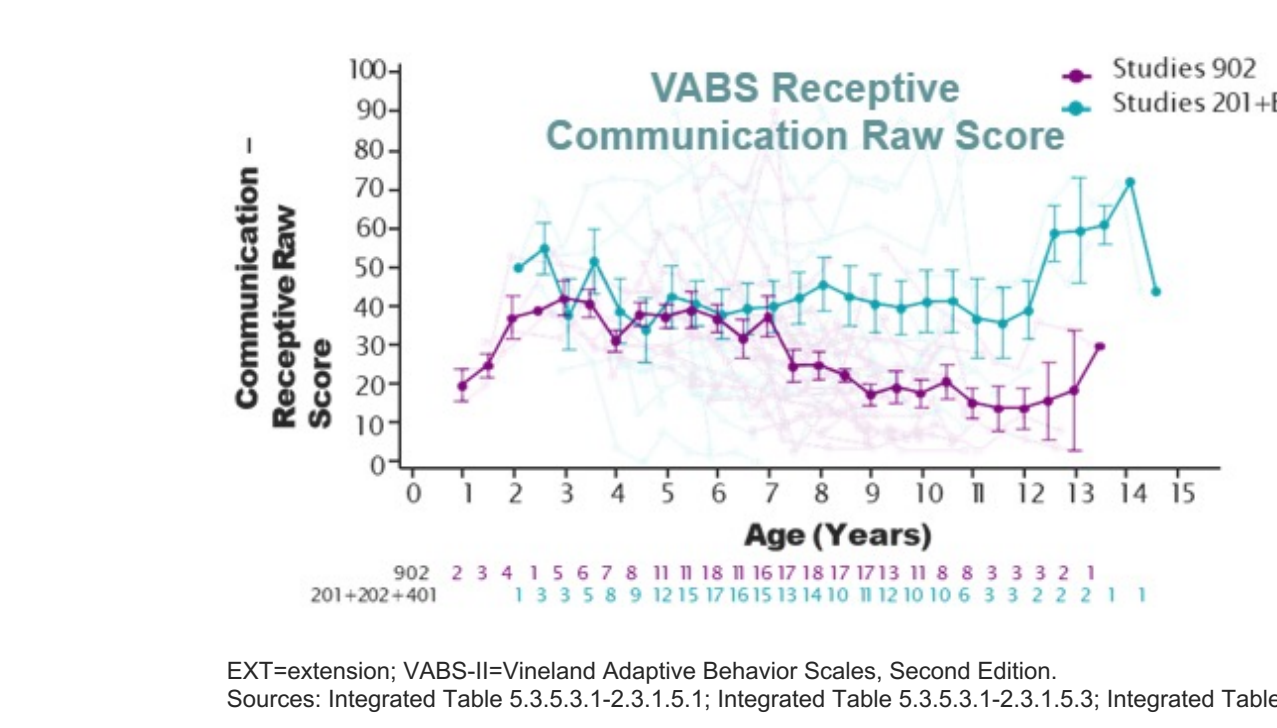
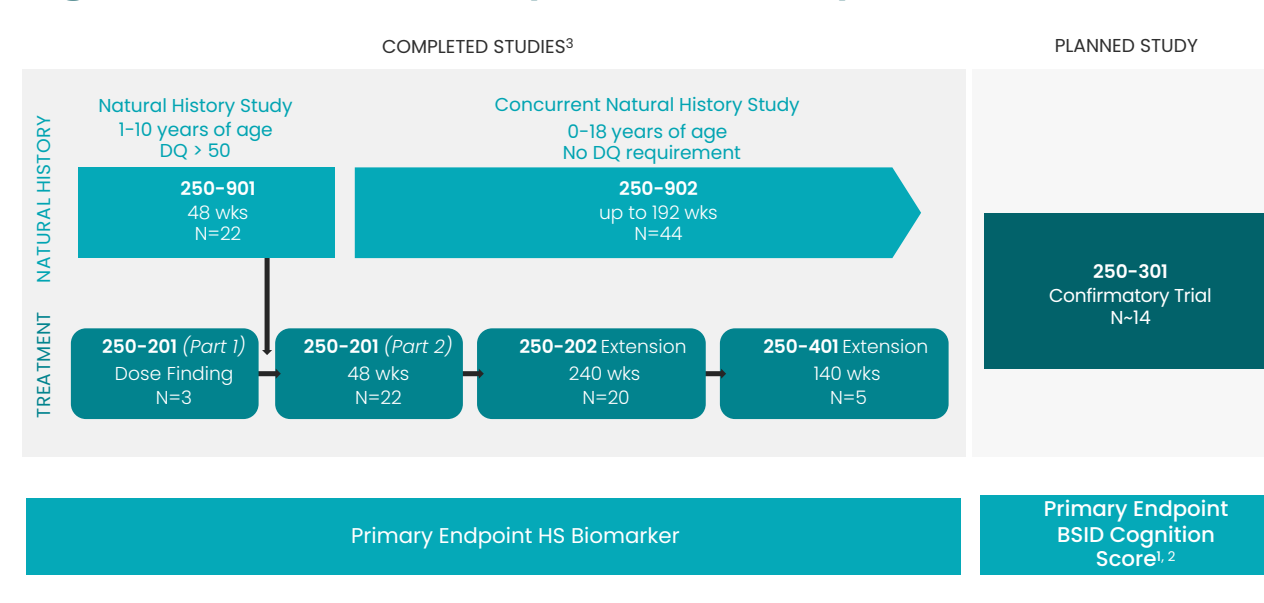


Figure 7: Tralesinidase Alfa Stabilizes Communication in VABS-II



## METHODS

Figure 2: TA-ERT Development Roadmap



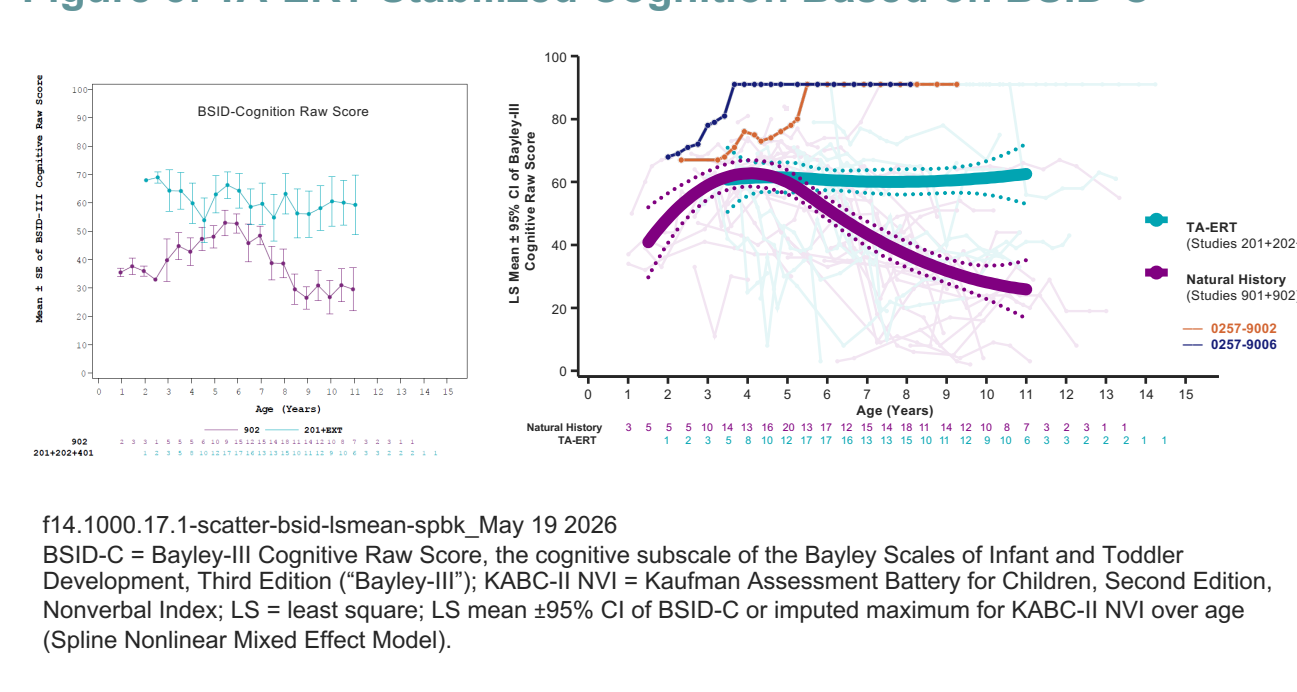
BLA= Biologics License Application; DQ=development quotient. Sources: 1. FDA Guidance to Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products 2019; 2. Community consensus for Heparan sulfate as a biomarker to support accelerated approval in Neuropathic Mucopolysaccharidoses. Muenzer, et al. *Mol Genet Metab*. 2024;142(4):108535; 3. Data from completed studies include 250-201, 250-202 and 250-401.

Table 1: Baseline Demographics and Characteristics in Natural History (Study 902) and Treated (Study 201 + EXT) Participants

	No DQ Inclusion Criterion	DQ>50 Inclusion Criterion
	Study 902 (NH) N=32 <sup>a</sup>	Study 201+EXT N=22
<b>Age (years)</b>		
Mean (SD)	5.81 (2.20)	4.96 (2.03)
Median	6.08	5.08
<b>Sex n (%)</b>		
Male	17 (53.1)	13 (59.1)
<b>DQ (AEq/age)</b>		
Mean (SD)	26.0 (20.4)	55.4 (21.1)
Median	22.5	51.6
<b>Bayley-III Cognitive Raw Score</b>		
Mean (SD)	41.9 (17.76)	69.6 (15.20)
Median	40.0	69.0

<sup>a</sup>n=31 for Bayley-III Cognitive Raw Score. AEq=age equivalent; Bayley-III=Bayley Scales of Infant and Toddler Development, Third Edition; DQ=development quotient; EXT=extension. Table 5.3.5.3.1-2.2.1 (for 202) and Table 5.3.5.3.1-2.2.2.

Figure 3: TA-ERT Stabilized Cognition Based on BSID-C



f14\_1000.17.1-scatter-bsid-ismean-spbk\_May 19 2026 BSID-C = Bayley-III Cognitive Raw Score. The cognitive subscale of the Bayley Scales of Infant and Toddler Development, Third Edition ("Bayley-III"); KABC-II NVI = Kaufman Assessment Battery for Children, Second Edition, Nonverbal Index; LS = least squares; LS mean ±95% CI of BSID-C or imputed maximum for KABC-II NVI over age (Spline Nonlinear Mixed Effect Model).

### TA-ERT Safety and Immunogenicity Profile

- 22 patients enrolled with some followed up to 6 years
- 3 most common TEAEs were vomiting, pyrexia, upper respiratory infection
- 3 most common TESAEs were vomiting, device related infection, and pleocytosis
- 4 discontinuations: 3 due to hydrocephalus and 1 following infection
- Study drug-related adverse events occurred at a rate of 0.068 per infusion with serious adverse events occurring at a rate of 0.004 per infusion
- Device-related adverse events occurred at a rate of 0.014 per infusion with serious adverse events occurring at a rate of 0.005 per infusion
- Hypersensitivity related adverse events occurred at <0.01 per infusion and none were severe or serious<sup>1</sup>
- Anti-drug and neutralizing antibodies were detected but without impact to CSF TA-ERT exposure or CSF HS/HS-NRE levels<sup>2</sup>

CSF=cerebrospinal fluid; HS=heparan sulfate; HS-NRE=heparan sulfate-nonreducing end; SAE=serious adverse event; TEAE=treatment-emergent adverse event; TESA=serious adverse event. Event rate is the number of events divided by the number of infusions of study drug. Sources: 1. Internal data on file from 250-201 clinical study report; 2. A phase I/II study on intracerebroventricular tralessinidase alfa in patients with Sanfilippo syndrome type B Muschol, et al. *J Clin Invest*. 2023;133(2):e165076. T 14.3.1.5; 14.3.1.29; T14.3.1.11; T14.3.1.13; 14.3.1.23; 14.3.1.17; 14.3.1.21; ISS Pre-final Outputs 26Apr2026.

## CONCLUSIONS

- Weekly intracerebroventricular 300-mg TA-ERT administration rapidly and durably normalized CSF HS and HS-NRE, the pathogenic glycosaminoglycans causing neurotoxicity in patients with MPS IIIB
- The totality of the evidence suggest a meaningful positive effect of TA-ERT on cognitive outcomes as measured by BSID-C cognition and on measures of adaptive behavior, as well as magnetic resonance imaging stability in CGMV, and somatic reductions in liver and spleen size
- TA-ERT safety profile was consistent with that expected of an intracerebroventricular-administered drug
- Early diagnosis and treatment of MPS IIIB remain important therapeutic goals

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**References:**  
1. Internal data on file from 250-201 clinical study report  
2. Muschol N, Koehn A, von Cossel K, et al. A phase I/II study on intracerebroventricular tralessinidase alfa in patients with Sanfilippo syndrome type B. *J Clin Invest*. 2023;133(2):e165076.

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