Corporate Presentation

August 12, 2026

Forward Looking Statements

This presentation contains forward-looking statements about Spruce Biosciences, Inc. ("we," or the "Company"). All statements other than statements of historical facts contained in this presentation are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including statements about our strategy, our expectations regarding the timing and achievement of our product candidates' development activities and ongoing and planned clinical trials, the timing or likelihood of regulatory filings and approvals for any of our product candidates, amount and sufficiency of our cash and cash equivalents to achieve our projected milestones and to fund our planned operations, and plans and expectations for future operations. These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2025 and other filings with the SEC, including, but not limited to: our limited operating history; our expectation that we will incur net losses for the foreseeable future, and that we may never be profitable; our ability to continue as a going concern; our need for additional funding and related risks for our business, product development programs and future commercialization activities; the timing and success of clinical trials we conduct; the ability to obtain and maintain regulatory approval of our product candidates; the ability to commercialize our product candidates; our ability to compete in the marketplace; risks regarding our license agreements; and our ability to obtain and maintain intellectual property protection for our product candidates. We operate in a competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as otherwise required by securities and other applicable laws.

Industry and Market Data

Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently verified, and make no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which they are being studied. Caution should be exercised when comparing data across trials of different products and product candidates. Differences exist between trial designs and patient populations and characteristics.

Our Commitment to Patients

"We are inspired by **Liv**, living with Sanfilippo Syndrome Type B (MPS IIIB). "

*Her **courage** in facing a relentlessly-progressive condition challenges us to move faster and think bolder — because for patients like Liv, time is everything!*

Spruce Bio: Global Neuroendocrine Biopharma Company

Advancing a Differentiated Pipeline of Potentially First-to-Market and Best-in-Class Programs

Tralesinidase Alfa Enzyme Replacement Therapy (TA-ERT) for Sanfilippo Syndrome Type B (MPS IIIB), granted Breakthrough Therapy Designation by U.S. FDA

BLA-Ready Program

Expected BLA Filing Anticipated in Q4 2026

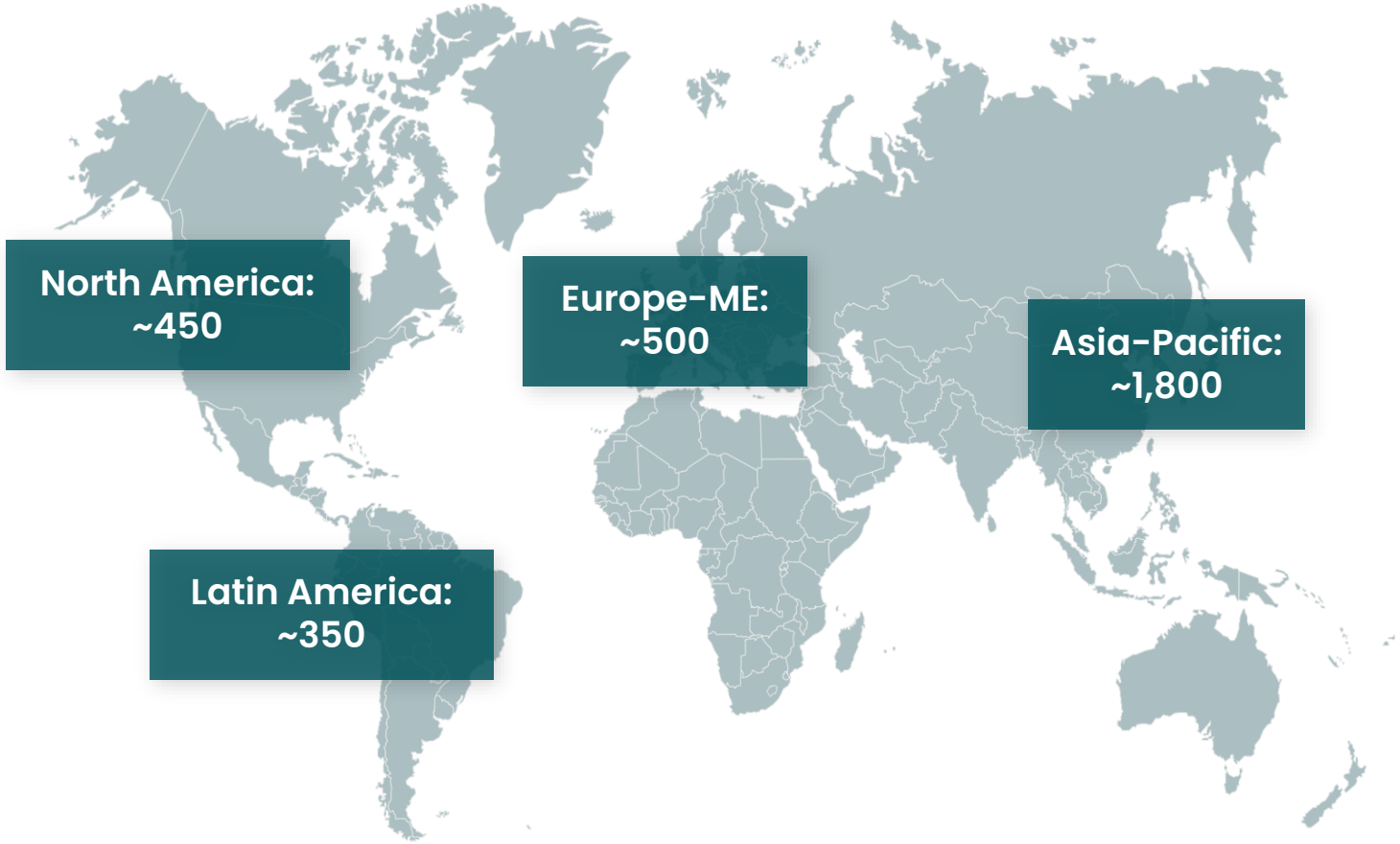
- TA-ERT Significantly Reduces and Durably Normalizes CSF HS-NRE[1] over Five Years
- U.S. FDA Alignment on CSF HS-NRE[1] as a Potential Valid Surrogate for Accelerated Approval
- TA-ERT Stabilizes Cognition and CGMV[2] Relative to Declines in Untreated Children
- PRV Eligibility Upon U.S. FDA Approval
- First-to-Market Potential | IP Exclusivity to 2038 | Orphan Drug Designations in US + EU

SPR202: Novel Anti-CRH Monoclonal Antibody (mAb)

- CRH Antagonist mAb for Congenital Adrenal Hyperplasia

1. Cerebral spinal fluid heparan sulfate non-reducing end.
2. Cortical grey matter volume.

Estimated More Than 3,000 MPS IIIB Patients in Key Commercial Territories



- Incidence varies across regions (0.5 to 4 per 100k live births)[1,2,3]
- ~90% of all incident cases are non-attenuated (severe and rapidly-progressing)[4,5]
- Non-attenuated Sanfilippo B lifespan = 20 years [6]
- Highest concentration of patients in Southern Europe, Turkey, and LATAM

Sources: [1] Rouse, Courtney J.1; Jensen, Victoria N.1; Heldermon, Coy D.2,*. Mucopolysaccharidosis type IIIB: a current review and exploration of the AAV therapy landscape. Neural Regeneration Research 19(2):p 355-359, February 2024. [est. incidence of 1/200,000 births * ~3.6 MM Us Census estimate of ages 0-1 in 2024]. 2 Chien, et al. Newborn Screening for Morquio disease and other lysosomal storage disease: results from the 8-plex assay from 70,000 newborns, Orphanet Journal of Rare Diseases (2020) 15:38 [3]Blackswan Analysis ISOPR Poster, 2019. [4]Estimate from 901-201 clinical trial recruitment (5 of 60 screens attenuated), [5]Valstar, JIMD 2010, [6]Lavery, OJRD 2017

"North America" = United States and Canada. "Europe-ME" = Italy, Spain, France, Germany, Turkey, Saudia Arabia, and Greece. "Asia-Pacific" = China, Japan, South Korea, and Australia. "Latin America" = Argentina and Brazil. Estimates assume an incidence of 0.5 per 100,000 live births and a lifespan of approximately 20 years of age.

Ultra Rare Disease Products Command Premium Pricing with Limited Restrictions

- **Premium Pricing & Reimbursement:** High unmet need and measurable clinical benefit support favorable payer coverage and sustainable pricing models
- **Small patient numbers results in low overall payer burden:** Multiple approved MPS and other rare disease products confirm long-term potential
- **Broad Access:** Payors unlikely to restrict access in rare pediatric disease population with high unmet medical need

Product	Indication[1]	Approval[1]	Incidence[2]	Estimated Annual Cost (30kg – 80kg)[3]
Mepsevii®	MPS VII	2017	1 in 1M	~$750K-$2.8M
AVLAYAH®	MPS II	2026	1 in 160K (males)*	~$811K-$2.2M
Vimizim®	MPS IVA	2014	1 in 200K	~$600K-$2.4M
Strensiq®	HPP	2015	3 in 100K	~$600K-$2.4M
Naglazyme®	MPS VI	2005	1 in 250-600K	~$450K-$1.6M
Elaprase®	MPS II	2006	1 in 160K (males)*	~$480K-$1.3M
Brineura®	CLN2	2017	0.5 in 100K	~$840k

**MPS II (Hunter Syndrome) exclusively affects males*

Sources: 1. Approval Dates & Indications: U.S. Food and Drug Administration (FDA), *Drugs@FDA* Database (www.fda.gov); 2. National Organization for Rare Disorders (NORD); Christina L. Grant, Jaime López-Valdez, Deborah Marsden, Fatih Ezgü, Mucopolysaccharidosis type VII (Sly syndrome) - What do we know?, Molecular Genetics and Metabolism, Volume 141, Issue 3, 2024, 108145, ISSN 1096-7192.; *https://hppregistry.com/physicians/what-is-hpp#:~:text=1-6,%20penetrance,%20and%20clinical%20presentation. 3. Micromedix/Redbook March 2026; https://www.fiercepharma.com/pharma/fda-approves-denali-hunter-syndrome-drug-breaking-streak-rare-disease-rejections#:~:text=Denali%20itself%20faced%20a%20delay,vary%20based%20on%20body%20weight.*

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

- Autosomal recessive disorder affecting 1 in 200,000 newborns [1,2]
- A deficiency in alpha-N-acetylglucosaminidase (NAGLU) leads to lysosomal accumulation of Heparan Sulfate (HS)[3]
- 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

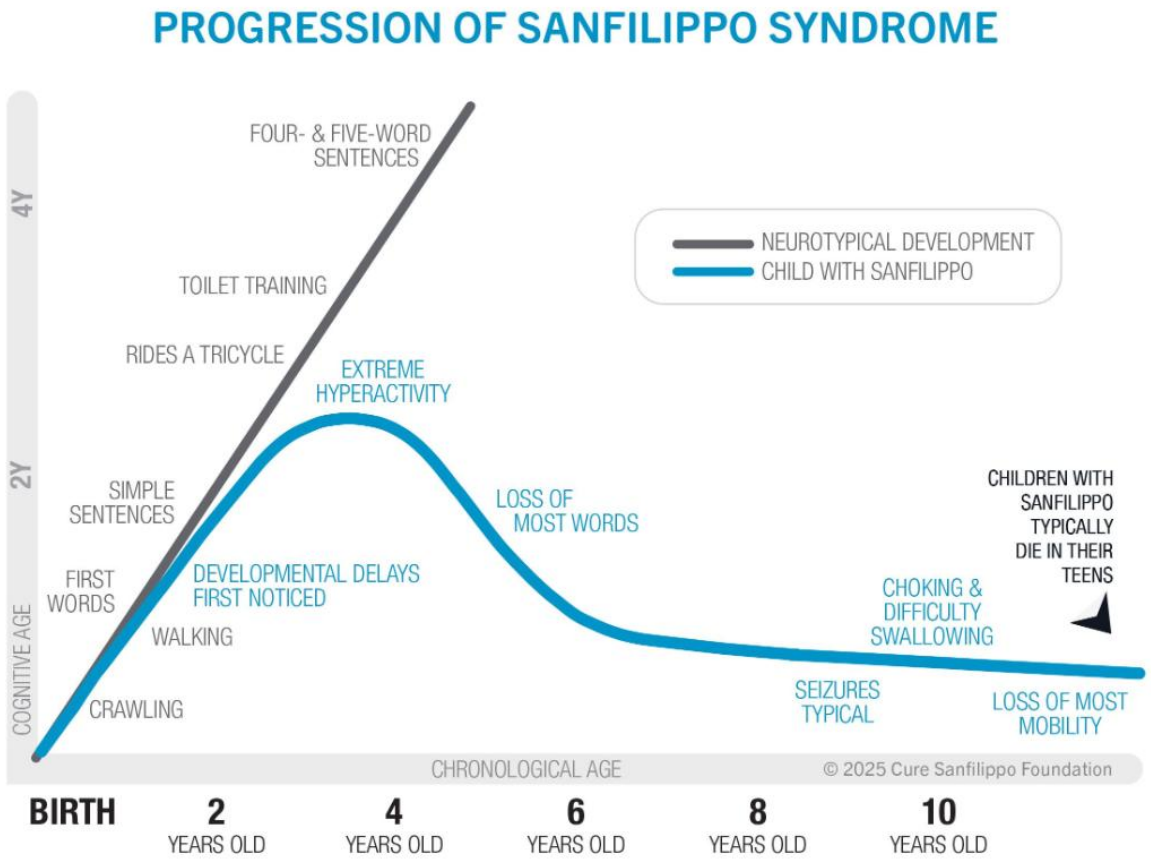
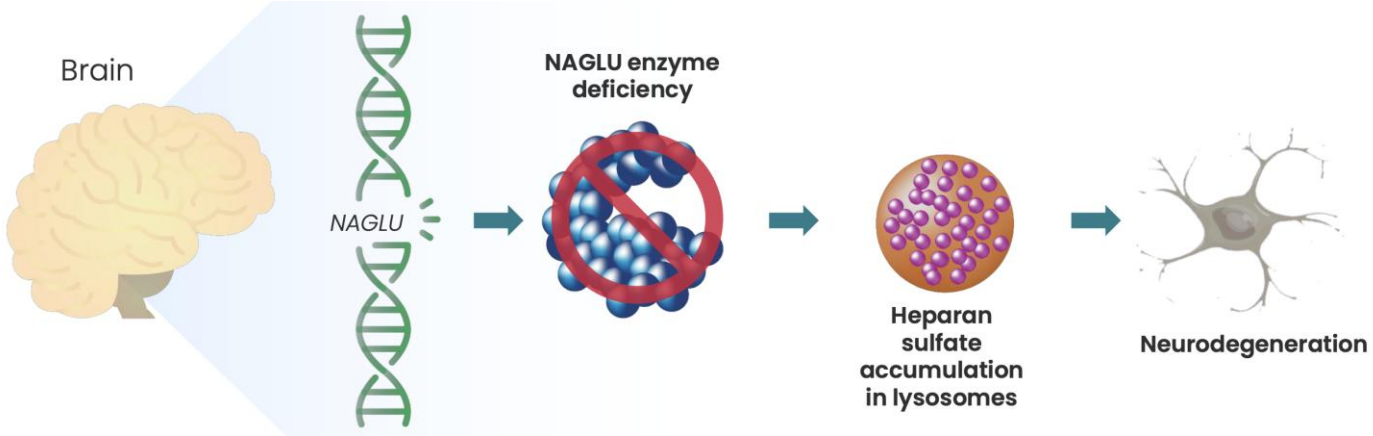


Figure represents studies of disease impact in rapidly-progressing forms of Sanfilippo Syndrome.

Sources: 1. Disease modeling for Mucopolysaccharidosis type IIIB using patient derived induced pluripotent stem cells Huang et al. -Experimental Cell Research 2021; 2. IQVIA MPS-IIIB Global Patient Mapping Report, 2022. Proprietary analysis al. -Cell Death & Disease 2018; 3. https://curesanfilippofoundation.org

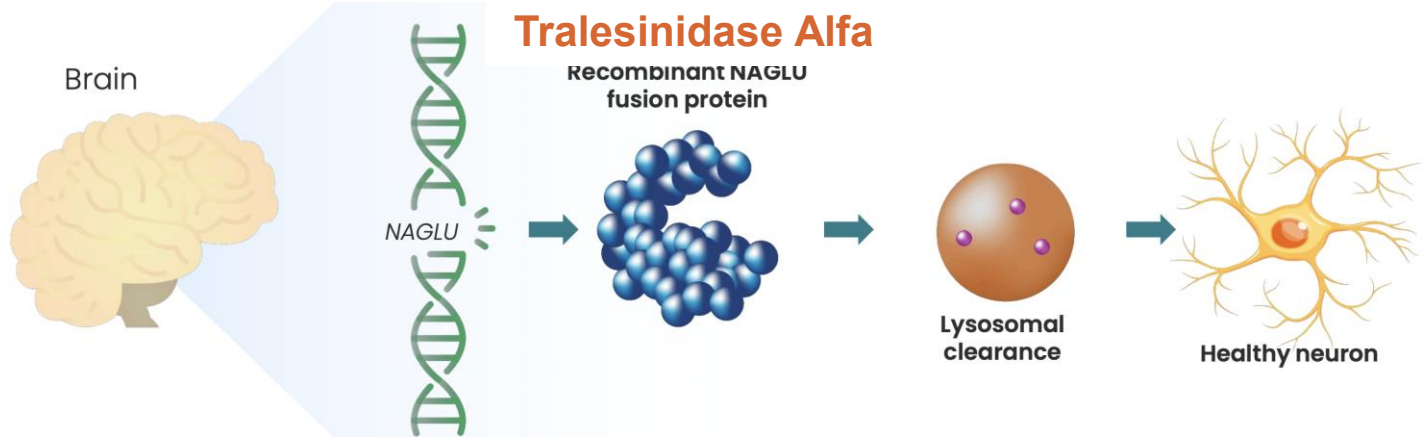
MOA: TA-ERT as Enzyme Replacement Therapy

TA-ERT is a recombinant human NAGLU fusion protein (rhNAGLU) delivered directly to the CNS to reduce the accumulation of HS in lysosomes and stabilize progressive neurodegeneration.



Heparan Sulfate accumulation is the underlying pathophysiology of MPS IIIB

- A deficiency in alpha- N-acetylglucosaminidase (NAGLU) leads to lysosomal accumulation of Heparan Sulfate (HS)3
- HS buildup impairs neuronal development ultimately leading to neurodegeneration and death



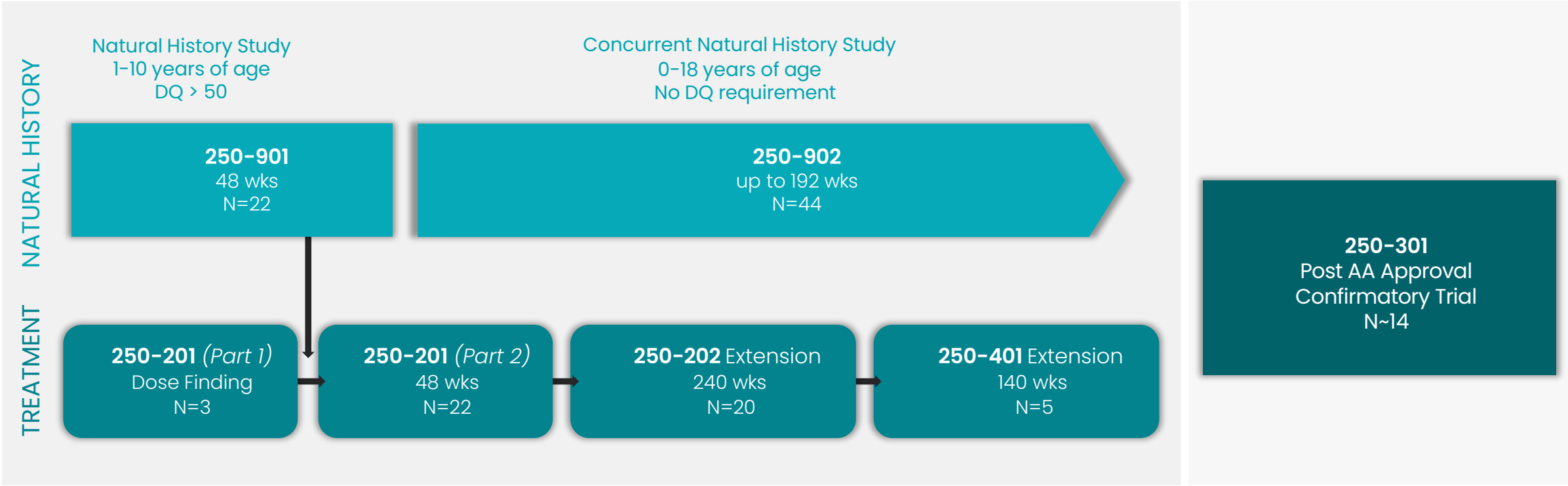
TA-ERT Is an enzyme replacement therapy administered directly to the brain by Intracerebroventricular (ICV) infusion

TA-ERT Anticipated Development Roadmap

No further clinical or non-clinical studies are expected to be required for BLA submission in Q4 2026

COMPLETED STUDIES SUPPORTING AN ACCELERATED APPROVAL (AA[3])

PLANNED STUDY FOR FULL APPROVAL



Accelerated Approval Request to be Based on Reduction in HS Biomarker[1, 2]

Confirmatory Trial Anticipated to Support Full Approval

Sources: 1. Community consensus for Heparan sulfate as a biomarker to support accelerated approval in Neuronopathic Mucopolysaccharidoses Muenzer et al. -Molecular Genetics and Metabolism 2024 2. FDA Guidance to Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products 2019 3. Data from completed studies 250-201, 250-202 and 250-401 expected to provide sufficient data for BLA filing in Q4 2026.

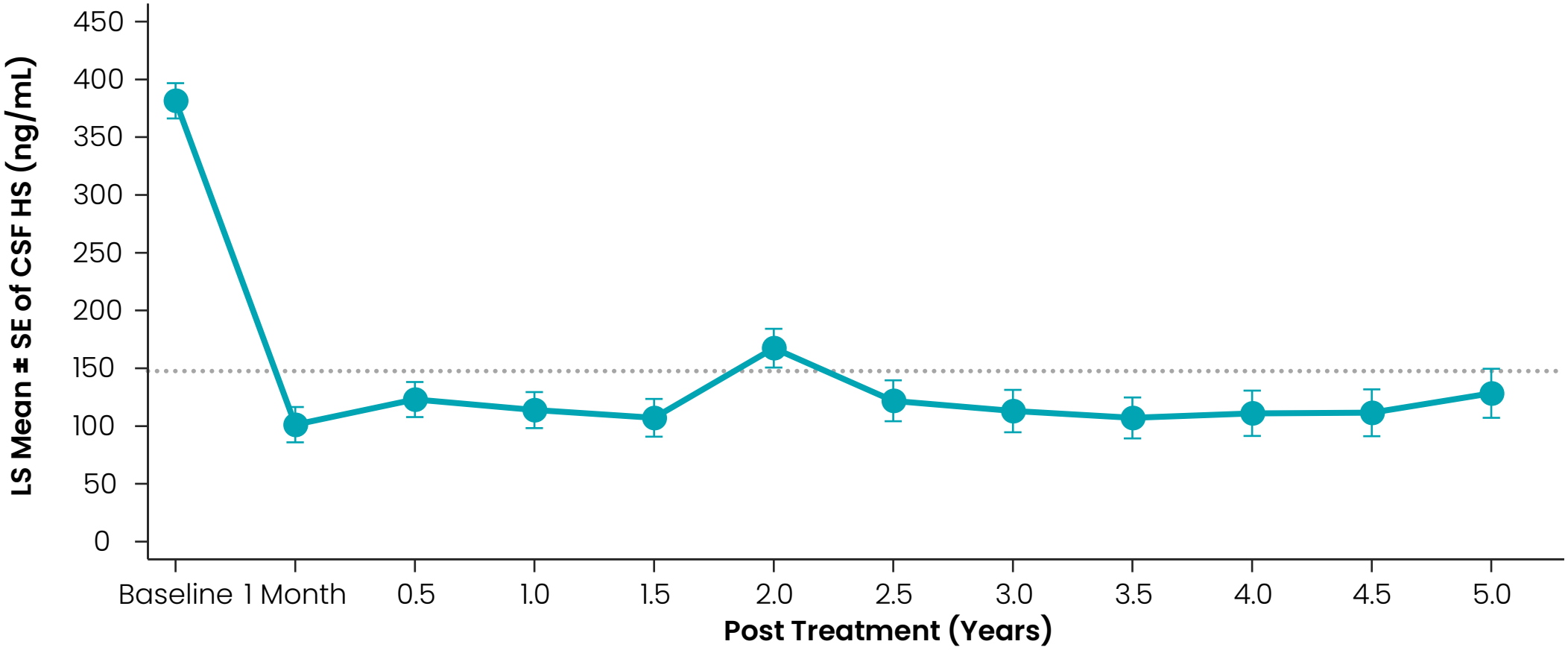
Baseline Demographics and Characteristics in Untreated (Study 902) and Treated (Study 201 + EXT) Participants

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

[a]n=31 for Bayley-III Cognitive Raw Score.

Bayley-III=Bayley Scales of Infant and Toddler Development, Third Edition; DQ=development quotient; NH=natural history; SD=standard deviation.

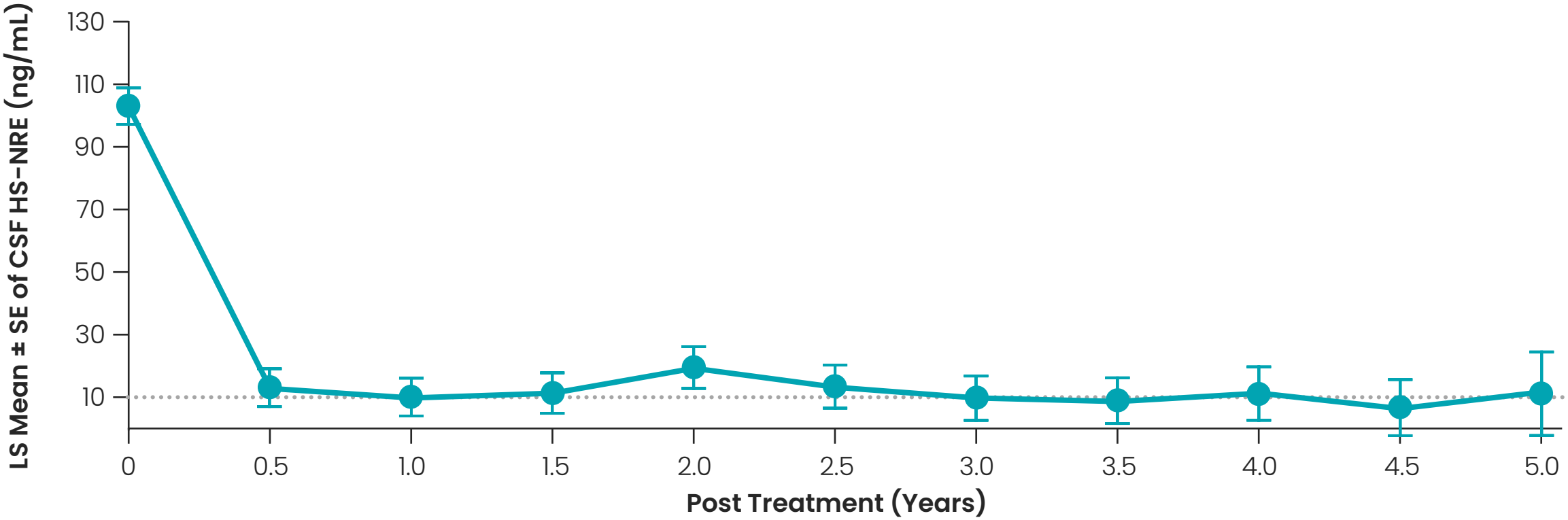
TA-ERT Rapidly and Durably Normalized CSF HS Over Five Years



	Baseline	1 Month	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
n	22	22	22	21	19	18	16	15	16	13	12	11
LS Mean	381.5	101.1	122.9	113.9	107.1	167.4	121.8	113.0	107.0	111.0	111.4	128.2

Dashed line represents ULN (150 ng/mL) for CSF HS; LS mean based on mixed-model repeated measures (MMRM) 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.

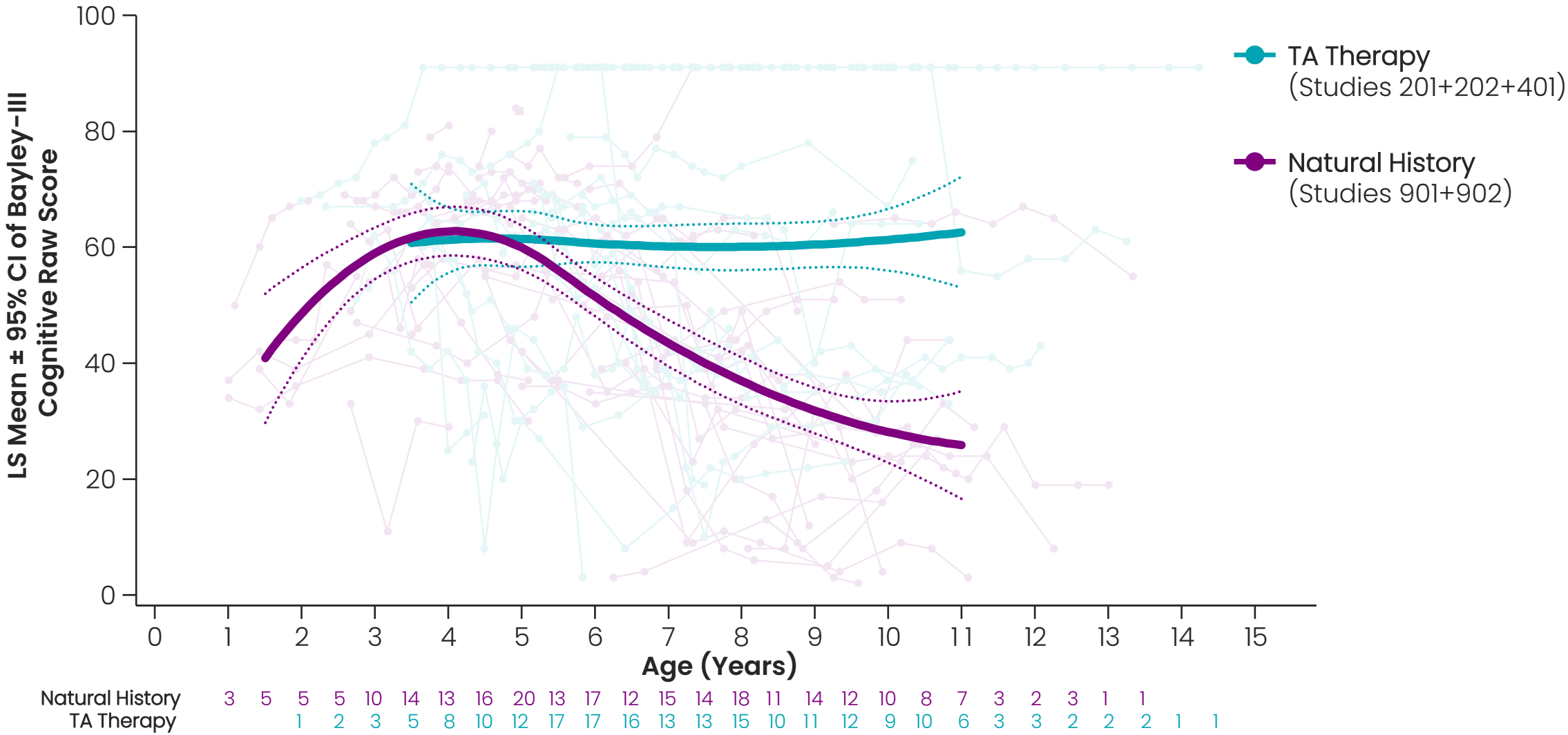
TA-ERT Rapidly and Durably Normalized CSF HS-NRE Over Five Years



n	22	20	21	17	17	15	15	14	10	9	4
LS Mean	103.3	13.5	10.5	11.7	19.9	13.8	10.2	9.4	11.5	7.1	11.6

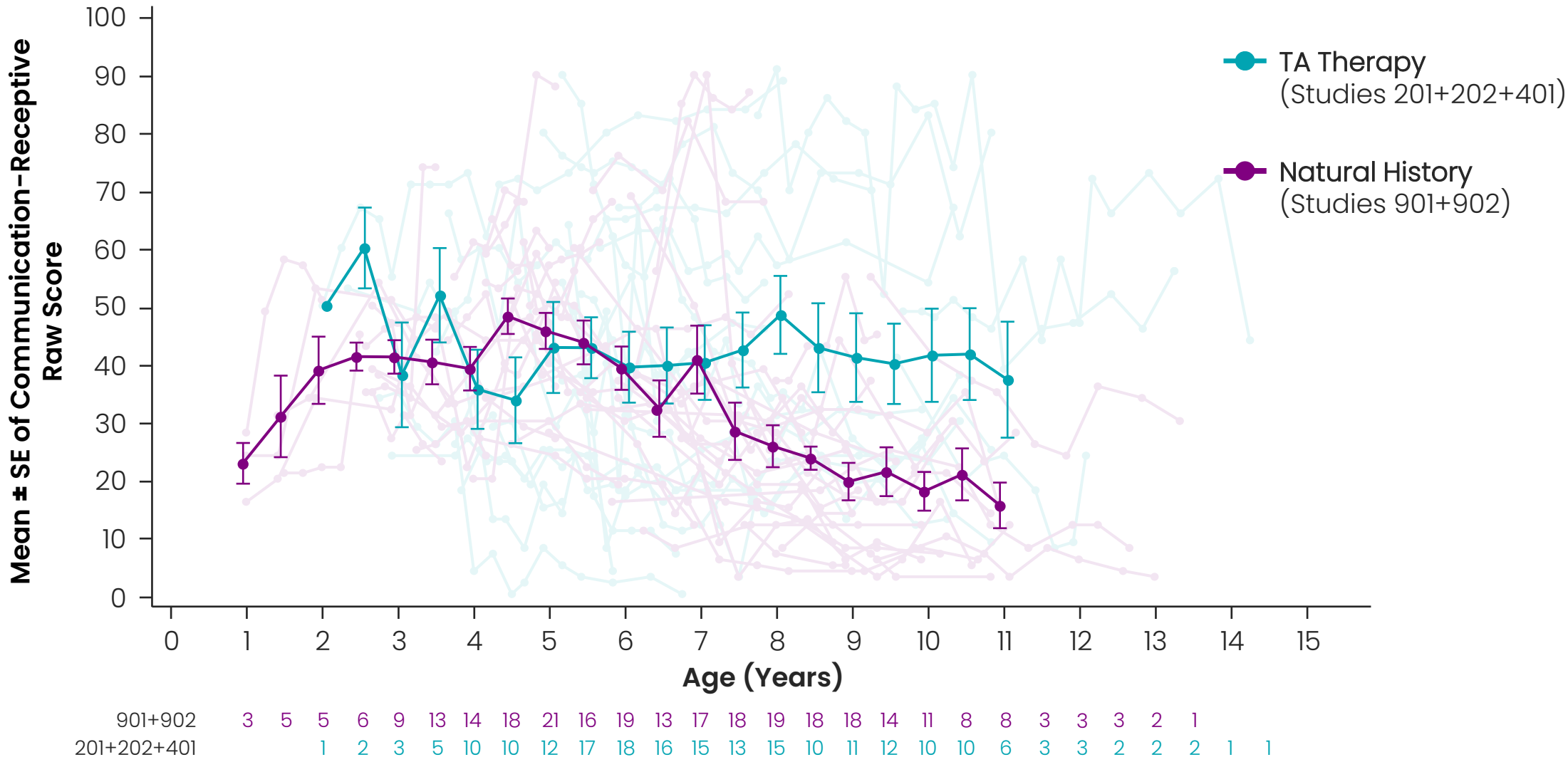
Dashed line represents ULN (10 ng/mL) for CSF HS-NRE; LS mean based on mixed-model repeated measures (MMRM) analysis with study visit as covariate
Note: data are shown for up to 5 years, but 2 subjects were on treatment for up to 6 years. CSF HS-NRE levels were averaged over each 0.5-year interval.

TA-ERT Stabilized Cognition Based on BSID-C



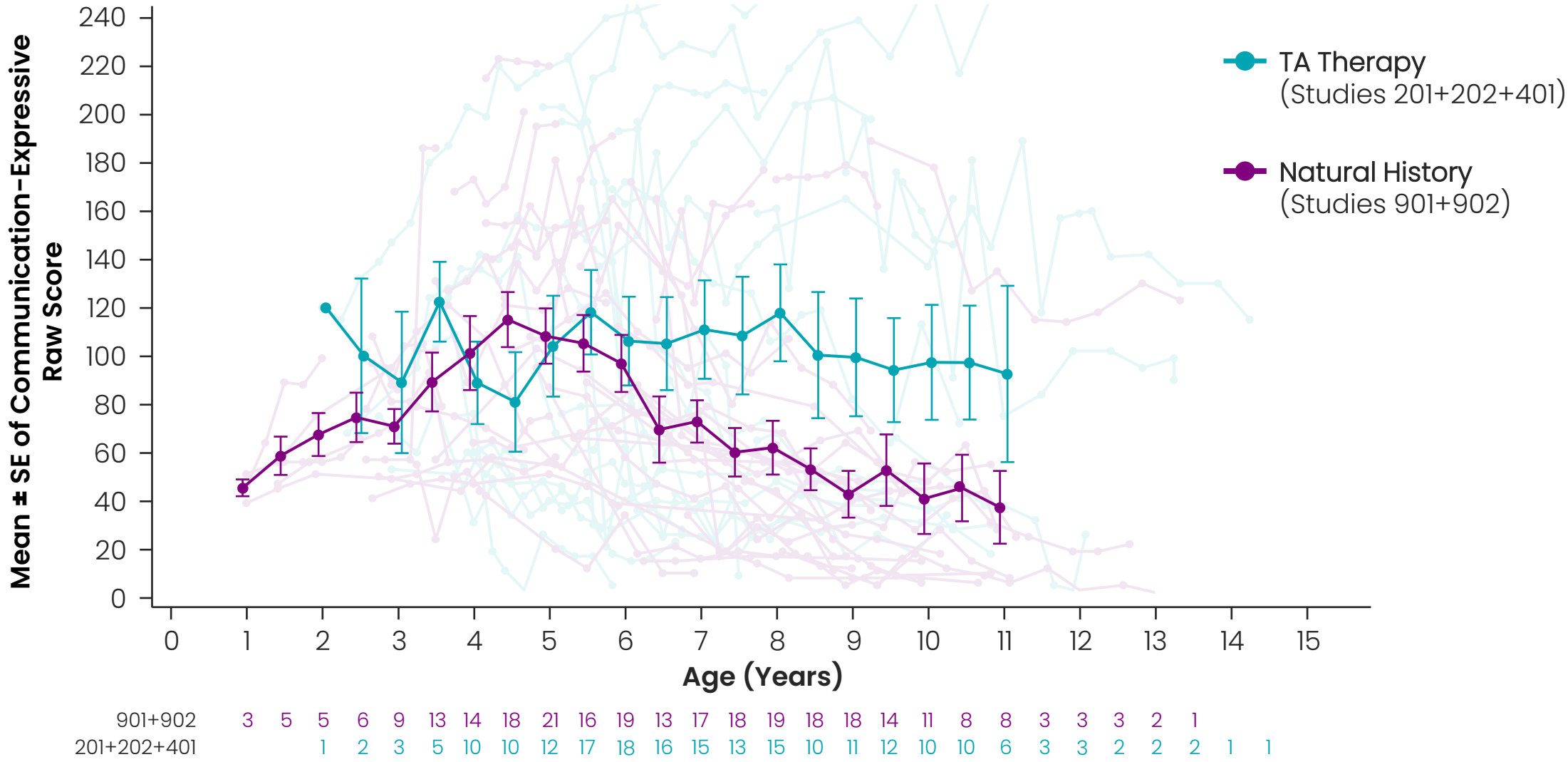
BSID-C = Bayley-III Cognitive Raw Score, the cognitive subscale of the Bayley Scales of Infant and Toddler Development, Third Edition ("Bayley-III"); CI = confidence interval; KABC-II NVI = Kaufman Assessment Battery for Children, Second Edition, Nonverbal Index; LS = least square; LS mean ±95% CI of BSID-C or imputed maximum for KABC-II NVI over age (Spline Nonlinear Mixed Effect Model).

TA-ERT Stabilized Receptive Communication Skills Based on VABS-II



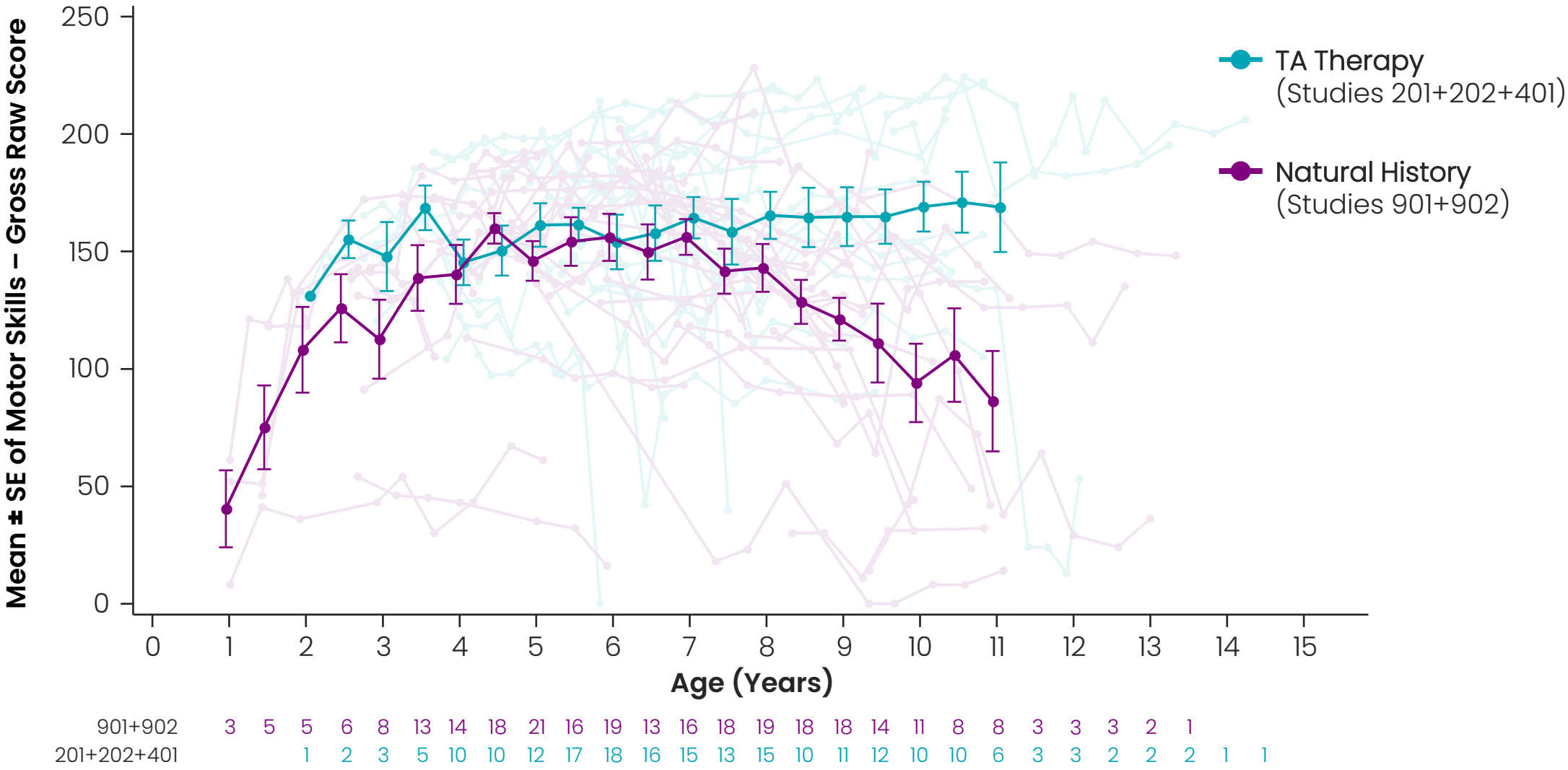
VABS-II=Vineland Adaptive Behavior Scales, Second Edition.

TA-ERT Stabilized Expressive Communication Skills Based on VABS-II



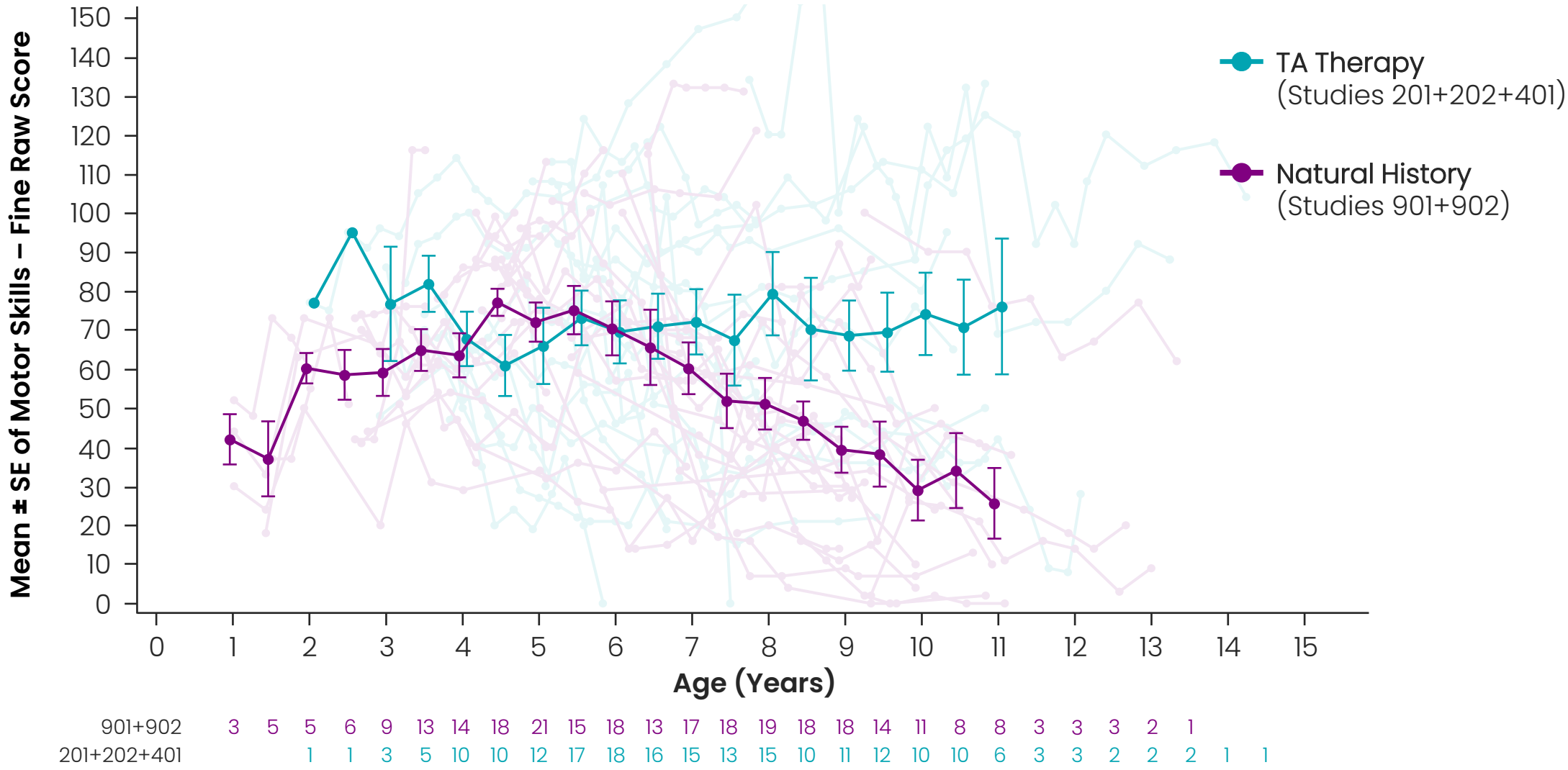
VABS-II=Vineland Adaptive Behavior Scales, Second Edition.

TA-ERT Stabilized Gross Motor Skills Based on VABS-II



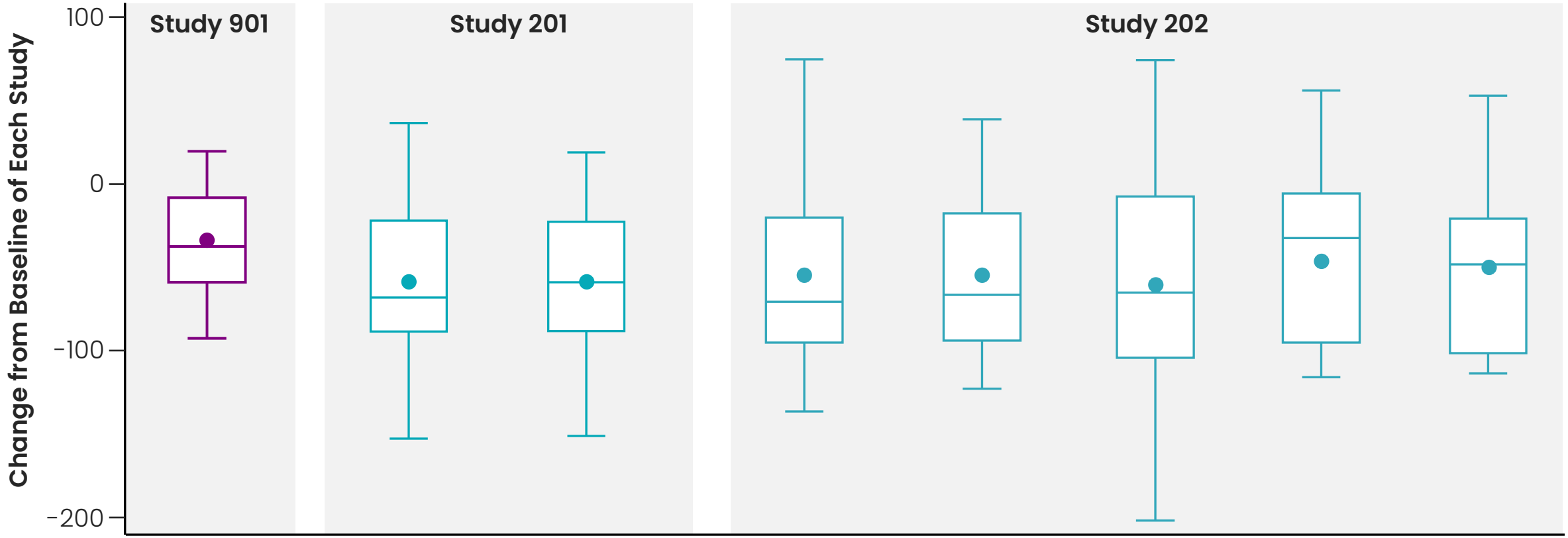
VABS-II=Vineland Adaptive Behavior Scales, Second Edition.

TA-ERT Stabilized Fine Motor Skills Based on VABS-II



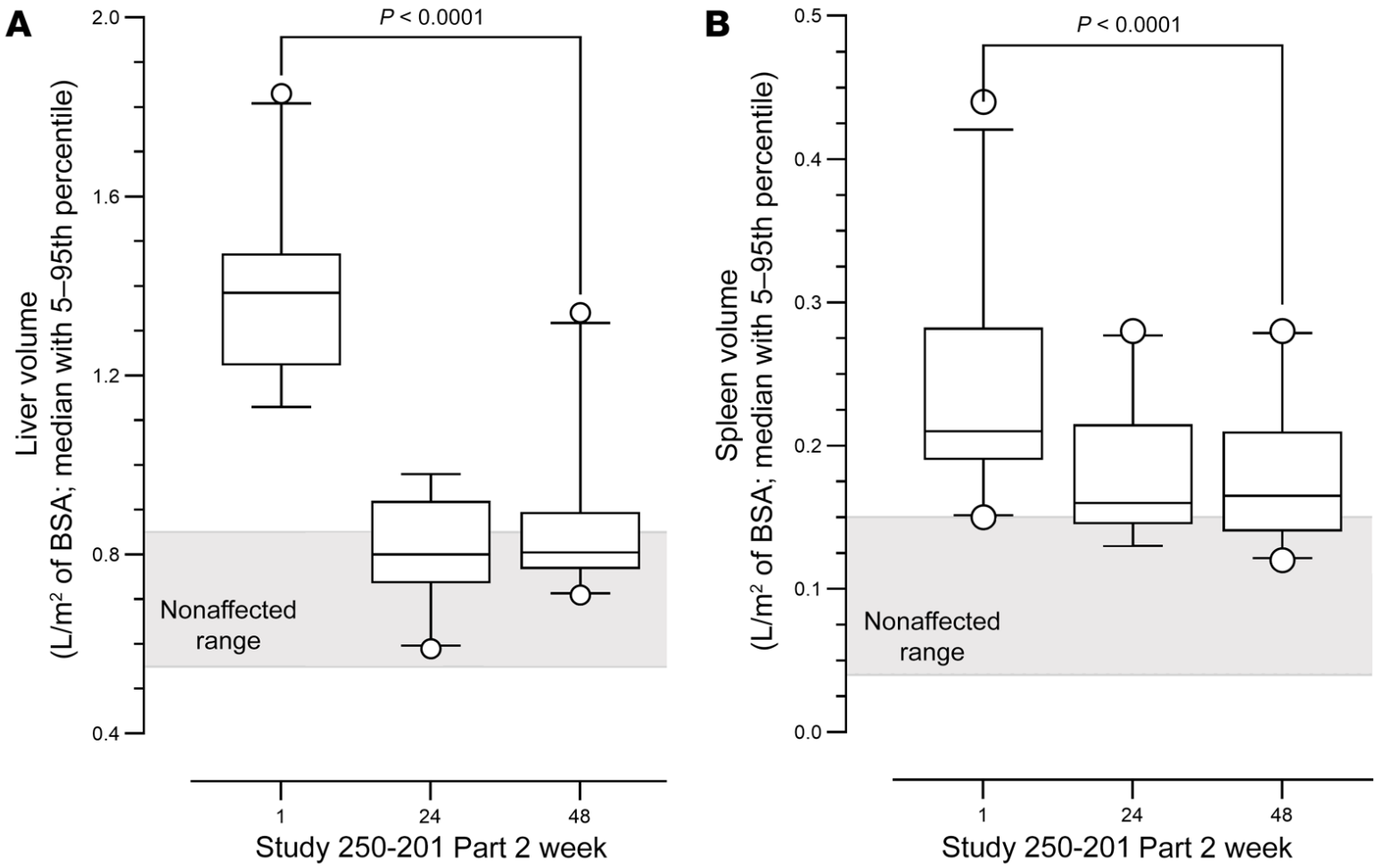
VABS-II=Vineland Adaptive Behavior Scales, Second Edition.

TA-ERT Stabilized Cortical Grey Matter Volume (CGMV)



	Week 48	Week 24	Week 48	Week 48	Week 96	Week 144	Week 192	Week 240
N	15	21	20	16	9	12	13	8
Mean (SD)	-33.6 (31.6)	-59.0 (43.6)	-57.6 (45.7)	-54.7 (57.1)	-55.0 (55.0)	-60.4 (75.1)	-46.4 (54.9)	-50.2 (56.0)
Median (Q1, Q3)	-37.4 (-59.0, -8.3)	-68.0 (-88.6, -22.0)	-58.8 (-88.1, -22.7)	-70.5 (-95.3, -20.3)	-66.4 (-94.0, -17.6)	-65.3 (-104.2, -7.7)	-32.5 (-95.1, -5.8)	-48.1 (-101.5, -20.7)

TA-ERT Normalized Liver and Spleen Volume



Liver (A), spleen (B) were measured by magnetic resonance imaging at Week 1 (Baseline) and Weeks 24 and 48. Liver and spleen volumes were adjusted for body surface area. BSA=body surface area. Boxes represent the 5th to 95th percentiles with the median; dots represent values outside the 5th to 95th percentiles.

TA-ERT Safety Profile and Immunogenicity

- 22 patients enrolled with follow up lasting up to 6 years with ~6,000 TA doses administered
- 4 discontinuations occurred (3 due to hydrocephalus and 1 following infection)
- Most common Treatment-Emergent Adverse Events were vomiting, pyrexia, and upper respiratory infection. Most common Treatment-Emergent Serious Adverse Events were vomiting, device-related infection, and pleocytosis
- 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[1]
- 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[1]
- Hypersensitivity related adverse events occurred at <0.01 per infusion and none were severe or serious[1]
- Anti-drug and neutralizing antibodies were detected but did not affect CSF TA-ERT exposure or CSF HS/HS-NRE levels[2]

Source: [1] Internal data on file from 250-201 clinical study report; [2] J Clin Invest. 2023 Jan 17;133(2):e165076.

Financial Snapshot

Capital Structure and Financials as of June 30, 2026

Capital Structure	Shares
Common Shares Outstanding[1]	2,874,013
Restricted Stock Units	127,084
Common Stock Options[2]	49,174
Common Stock Warrants[3]	233,147
Fully Diluted Shares Outstanding[4]	3,283,418

Cash and Debt	000's
Cash & Cash Equivalents[5]	$96,295
Debt[6]	$16,600

TA-ERT Exclusive Worldwide License Terms with BioMarin Pharmaceutical, Inc.

Term	
Milestones[7]	$125,500,000
Royalties on Worldwide Net Sales[8]	High Single – Low Double Digit %

1. Common shares outstanding as of August 10, 2026.
2. Weighted-average exercise price of $213.26 per share and weighted-average remaining contractual term of 6.4 years as of June 30, 2026.
3. 169,147 common stock warrants Issued in connection with February 2023 private placement financing with an exercise price of $297.02 per share plus 64,000 common stock warrants issued in connection with the Avenue Capital debt facility with an exercise price of $50.00 per share.
4. Fully diluted shares outstanding includes all potentially dilutive securities and is not calculated in accordance with the Treasury Stock Method.
5. Cash and cash equivalents as of June 30, 2026. Excludes gross proceeds of $5.5 million from the August 2026 private placement.
6. Principal loan balance ($15.0 million) plus the final balloon payment ($1.6 million) under the Avenue Capital debt facility as of June 30, 2026.
7. Up to $125.5 million in total milestones, including up to $25.5 million due upon the achievement of certain development and regulatory milestones and up to $100 million due upon the achievement of certain sales milestones.
8. Subject to the applicable royalty term and certain customary reductions and floors.

spruce BIOSCIENCES