February 5, 2026

Analyst Call

Enzyme TransportVehicle™ Highlights from the 2026 WORLD*Symposium*™

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements do not relate strictly to historical or current facts and they may be accompanied by such words as “anticipate,” “believe,” “could,” “estimate,” “expected,” “forecast,” “intend,” “may,” “plan,” “potential,” “possible,” "future," “will” and other words and terms of similar meaning. All statements other than statements of historical facts contained in this presentation, including, without limitation, statements regarding future results of operations and financial position of Denali Therapeutics Inc. (“Denali” or the “Company”); Denali’s business strategy and business plans, expected progress and expansion, and expected key milestones for Denali's therapeutic portfolio in 2026 and beyond; Denali’s ability to execute on its tailored manufacturing and commercial strategies and accelerate commercial launch readiness; the potential for Denali's product candidates to treat various neurodegenerative diseases including MPS I (Hurler Syndrome), MPS II (Hunter Syndrome), MPS IIIA (Sanfilippo Syndrome), PD, ALS, AD, FTD-*GRN*, UC, Gaucher's Disease, Pompe Disease, and related peripheral inflammatory diseases; planned preclinical studies and clinical trials and the expectations regarding the timing and availability of results and data from such studies and trials; plans, timelines, expectations related to Denali's TransportVehicle™ (TV) platform, its therapeutic and commercial opportunities, and the potential of TV-supported programs to be best-in-class; plans, timelines, and expectations related to the ETV franchise and ETV-enabled programs, including ETV:GAA, ETV:GCase, and ETV:IDUA, their therapeutic and commercial potential, and the timing and likelihood of planned regulatory filings; plans, timelines, and expectations relating to DNL310 (ETV:IDS), including the Phase 2/3 COMPASS study and its ability to support global approvals, and the timing, likelihood, and scope of regulatory approvals and commercial launch; plans, timelines, and expectations related to DNL126 (ETV:SGSH), including the timing and availability of data from the Phase 1/2 study and likelihood and pathway of regulatory approval; plans, timelines, and expectations related to the OTV and OTV-enabled programs, including DNL628 (OTV:MAPT) and OTV:SNCA, their therapeutic and commercial potential, the timing of study initiation and the availability of data, and the timing and likelihood of planned regulatory filings; plans, timelines, and expectations relating to DNL921 (ATV:Abeta), including its therapeutic potential, the timing and likelihood of clinical proof of concept, and the timing of planned regulatory filings; plans, timelines, and expectations relating to DNL151; plans and expectations regarding DNL593 (PTV:PGRN), the ongoing Ph1/2 study, and the timing and availability of data; plans, timelines, and expectations related to DNL952 (ETV:GAA), including the timing and availability of data; plans and expectations regarding Denali's global organization and clinical and manufacturing operations, its projected cash runway and likelihood of receipt of milestone payments, and its likelihood of achieving operational efficiencies; the expected timing and likelihood of success of Denali's commercial growth; and the potential market opportunities for each of Denali's programs, are forward-looking statements. Denali has based these forward-looking statements largely on its current expectations and projections about future events, and forward-looking statements regarding potential outcomes should not be interpreted as guarantees of future performance.

These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including but not limited to: the risk of the occurrence of any circumstance that could give rise to the termination of Denali’s agreements with its collaborators; Denali’s and its collaborators’ ability to complete the development and, if approved, commercialization of its product candidates; Denali’s and its collaborators’ ability to enroll patients in its ongoing and future clinical trials; Denali’s ability to manufacture and supply product candidates at clinical and commercial scale, including through its internal manufacturing capabilities and its reliance on third parties for the manufacture and supply of its product candidates; Denali’s dependence on successful development of its blood-brain barrier platform technology and TV-enabled product candidates; Denali’s and its collaborators’ ability to conduct or complete clinical trials on expected timelines; the predictive value of Denali's biomarker selection; the occurrence of significant adverse events, toxicities or other undesirable side effects; the extent to which preclinical and early clinical results (including safety-related findings) predict later-stage outcomes; the uncertainty that product candidates will receive regulatory approval or be commercialized; Denali’s ability to continue to create a pipeline of product candidates or develop commercially successful products; Denali’s ability to obtain, maintain, or protect intellectual property rights related to its product candidates; Denali's achievement of planned milestones and realization of value; Denali’s ability to realize anticipated financial resources, including receipt of contingent royalty financing and milestone payments; implementation of Denali’s strategic plans for its business, product candidates, and blood-brain barrier platform technology; and other risks. In light of these risks, uncertainties and assumptions, the forward-looking statements in this presentation are inherently uncertain and may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should not rely upon forward-looking statements as predictions of future events. Information regarding additional risks and uncertainties may be found in Denali’s most recent quarterly and annual reports filed with the Securities and Exchange Commission on Forms 10-Q and 10-K, respectively, as well as Denali’s future reports to be filed with the SEC. Denali does not undertake any obligation to update or revise any forward-looking statements, to conform these statements to actual results or to make changes in Denali’s expectations, except as required by law.

The product candidates being developed by Denali are investigational and their safety and efficacy profiles remain unestablished. Denali's product candidates have not been approved by any health authority for any use.

Accuracy of Data. This presentation contains statistical data based on independent industry publications or other publicly available information, as well as other information based on Denali’s internal sources. Denali has not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, Denali makes no representations as to the accuracy or completeness of that data.

Leading a New Era of BBB-Crossing Therapeutics

Key Messages

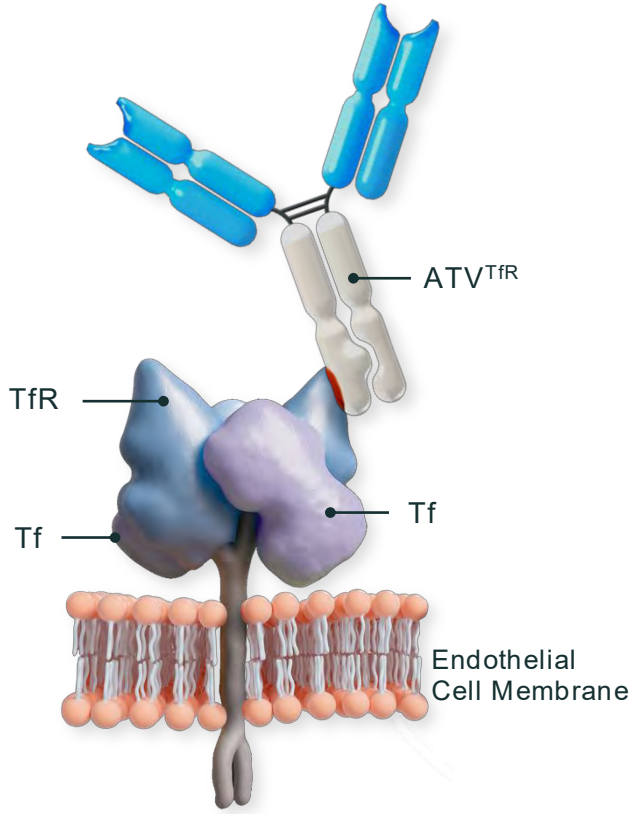
Ryan Watts, Ph.D.
Chief Executive Officer

Our Purpose

Deliver the power of biotherapeutics to the whole body, including the brain, transforming life for people living with serious diseases

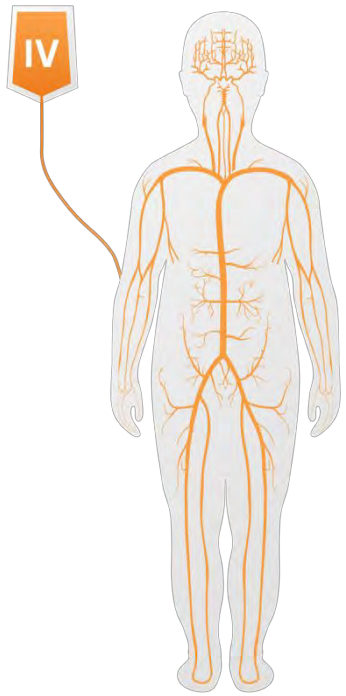
DENALI

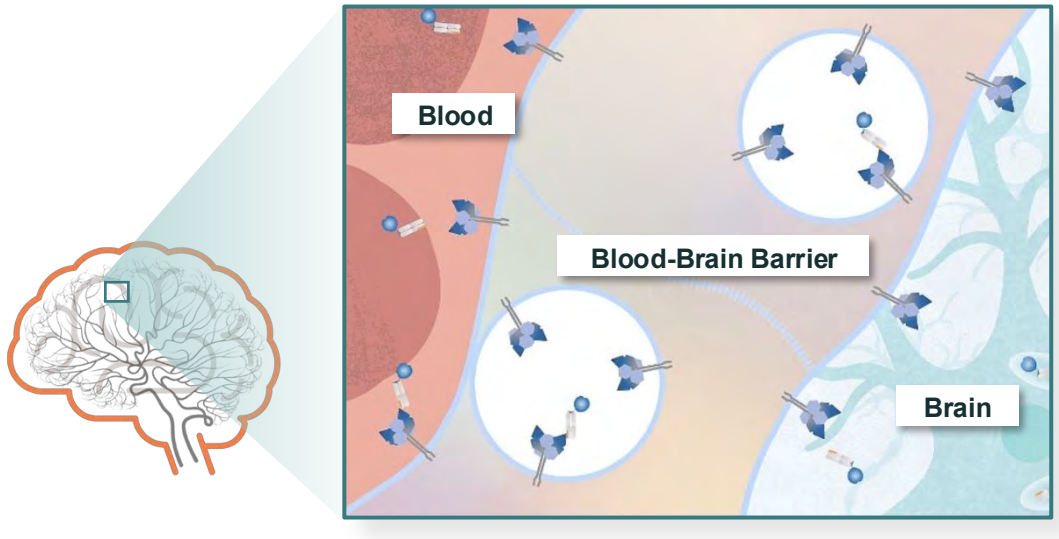
Treating the Whole Body, Including the Brain

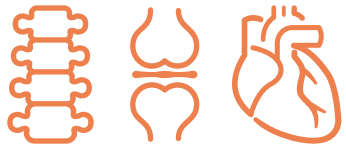


Transferrin receptor (TfR) is highly expressed at the blood–brain barrier for natural iron transport

Our **TransportVehicle™** leverages TfR to enable **brain delivery** of biotherapeutics



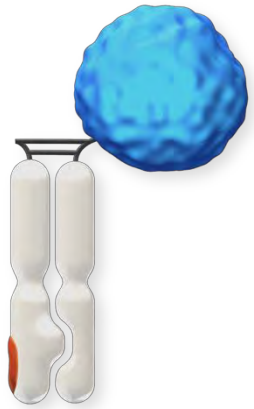




TfR may also facilitate delivery into tissues such as **bone**, **cartilage**, and the **heart**

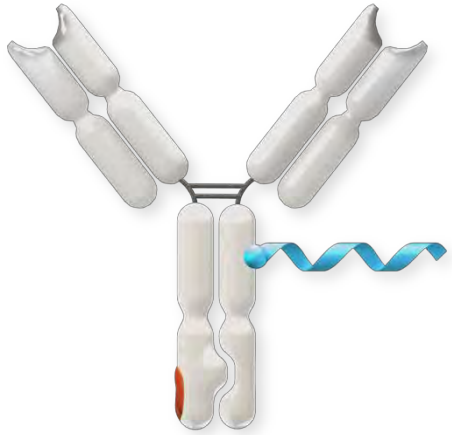
TransportVehicle™: Enabling a New Class of Biotherapeutics

Enzyme TV
(ETV)



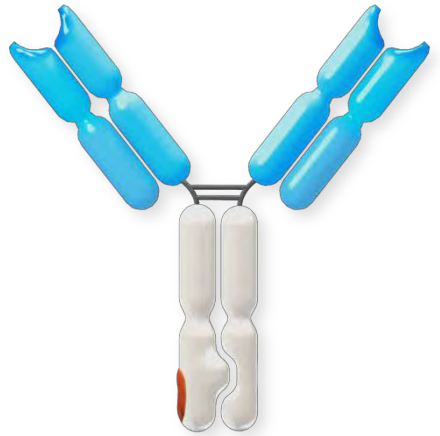
Enzyme replacement therapy for the body and brain

Oligonucleotide TV
(OTV)



Genetic medicines for the brain, delivered systemically

Antibody TV
(ATV)

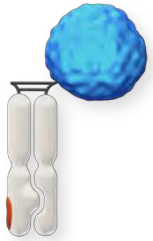
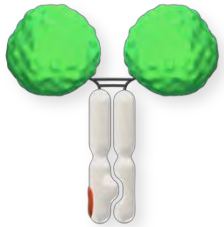
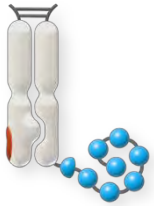
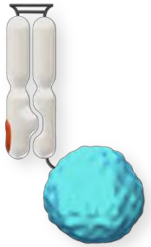
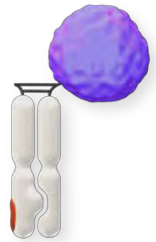
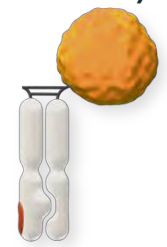


Brain-penetrant immunotherapy for a wide range of diseases

Our TransportVehicle™ (TV) Platform enables TfR-mediated brain biodistribution and enhanced tissue delivery of biotherapeutics throughout the body with systemic administration

TfR – Transferrin receptor

Building the Enzyme TransportVehicle™ (ETV) Franchise

	Tividenofusp alfa (ETV:IDS; DNL310)	ETV:SGSH (DNL126)	PTV:PGRN (DNL593)	ETV:GAA (DNL952)	ETV:GCase (DNL111)	ETV:IDUA (DNL622)
						
	MPS II (Hunter syndrome)	**MPS IIIA** (Sanfilippo syndrome)	**FTD-*GRN*** (Frontotemporal dementia-granulin)	**Pompe Disease**	**Parkinson's and Gaucher**	**MPS I** (Hurler syndrome)
Patients WW[1]	**~2,000**	**~1,500+**	**~25,000+**	**~5,000 – 10,000**	**~300,000+ (GBA-PD) ~10,000 – 15,000 (GD)**	**~1,500+**
Status	Phase 2/3 BLA filing[2]	Phase 1/2	Phase 1/2	Phase 1	IND-enabling	IND-enabling

We are developing the next generation of enzyme replacement therapies designed to treat brain and body manifestations of serious genetic diseases

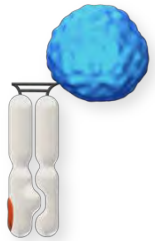
WW – Worldwide; **BLA** – Biologics License Application; **IND** – Investigational New Drug; **GBA-PD** – Parkinson's Disease with GBA mutation; **GD** – Gaucher's Disease;
1. Excluding China and India; **2.** PDUFA target action date of 4/5/26 for accelerated approval

Denali Presentations at the 2026 WORLD*Symposium*™

Date & Time	Title	Format	Poster number	Presenting Author
Tuesday February 03, 2026 15:30-17:30 PST	Persistent Clinical Burden and Unmet Needs in Hunter Syndrome (MPS II) in the United States: A Retrospective Cohort Study	Poster	052	Barbara Burton
Wednesday February 04, 2026 15:30-17:30 PST	Enhanced correction of skeletal muscle and brain pathology in a Pompe mouse model using transferrin receptor-mediated delivery of GAA	Poster	290	Rashi Priya
Thursday February 05, 2026 11:00-12:00 PST	Phase 1/2 Study of Intravenous Tividenofusp Alfa for Mucopolysaccharidosis Type II	Oral presentation	N/A	Joseph Muenzer
Thursday February 05, 2026 11:00-12:00 PST	Preliminary Results from Phase 1/2, First-in-human, Open-label Study of DNL126 in Children with Mucopolysaccharidosis IIIA (MPS IIIA)	Oral presentation	N/A	Elizabeth Jalazo
Thursday February 05, 2026 15:30-17:30 PST	Quality of Life, Unmet Needs, and Treatment Experience of People Living with MPS II and Their Caregivers: A Community Survey	Poster	248	Kristin McKay
Thursday February 05, 2026 15:30-17:30 PST	Tividenofusp alfa treatment in a male sibling pair with non-neuronopathic mucopolysaccharidosis type II	Poster	065	Irene Chang
Thursday February 05, 2026 15:30-17:30 PST	A Phase 1, Multicenter, Open-Label Study Design to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of DNL952 in Adult Participants with Late-Onset Pompe Disease	Poster	204	Amy Berger

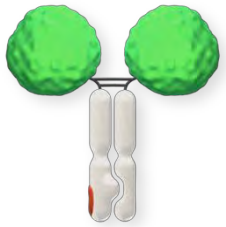
Select presentations being discussed today on Denali's Analyst Call
PDFs of all presentations and posters are available on the Events page of the Investor section of Denali's corporate website at https://investors.denalitherapeutics.com/events

Key Messages for Today



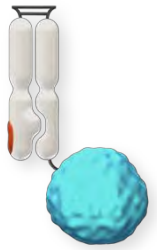
Tividenofusp alfa (ETV:IDS; DNL310)

- Analysis from continued follow-up of Phase 1/2 study in **Hunter syndrome (MPS II)** reinforces the potential for tividenofusp alfa (DNL310) to address the full disease spectrum
- We have established launch readiness in anticipation of April 5, 2026, Prescription Drug User Fee Act (PDUFA) date



ETV:SGSH (DNL126)

- Preliminary Phase 1/2 data in **Sanfilippo syndrome type A (MPS IIIA)** showed 80% mean CSF HS reduction and substantial reduction of disease biomarkers in the CNS and periphery
- Safety profile generally consistent with established ERTs
- Expect BLA filing and accelerated approval in 2027



ETV:GAA (DNL952)

- Design of ongoing DNL952 (ETV:GAA) Phase 1 clinical study presented in addition to preclinical data that shows therapeutic potential to treat both muscle and nervous system manifestations of **Pompe disease**
- Biomarker proof of concept data expected in 2027

Data and plans presented at this year's WORLD*Symposium*™ reflect the strong momentum of our Enzyme TransportVehicle™ franchise

ERTs – enzyme replacement therapies; **BLA –** Biologics License Application

Enzyme TransportVehicle™

MPS II and MPS IIIA

Peter Chin, M.D.
Acting Chief Medical Officer and Head of Development

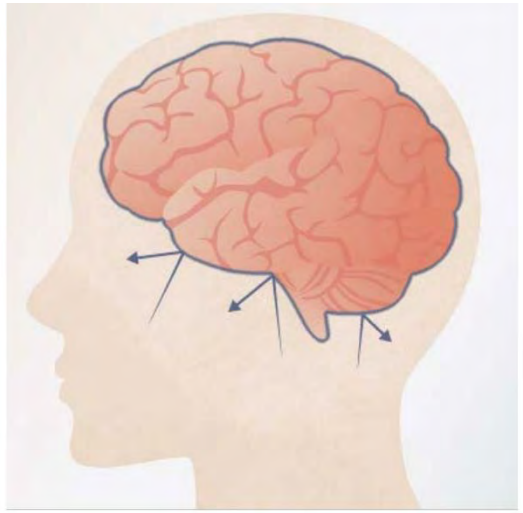
Phase 1/2 Study of Intravenous Tividenofusp Alfa for Mucopolysaccharidosis Type II

Professor Joseph Muenzer, MD, PhD
University of North Carolina School of Medicine, Chapel Hill, NC, USA

DEVELOPING A THERAPY FOR MPS II (HUNTER SYNDROME)

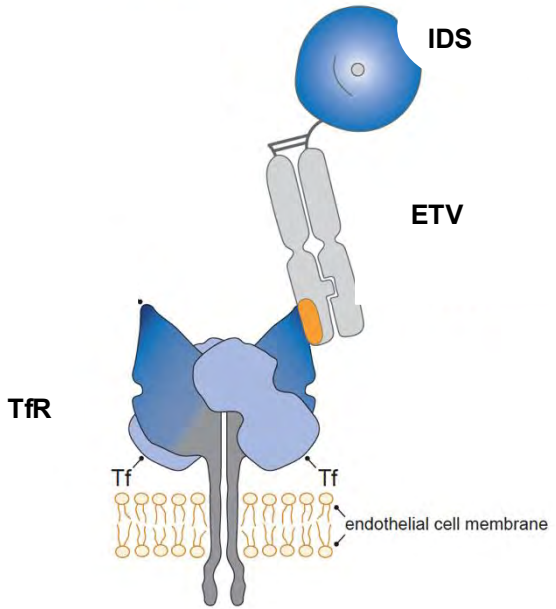
Tividenofusp alfa (DNL310) is an investigational IDS fusion protein engineered for CNS and peripheral delivery to address cognitive, behavioral, and somatic disease control in MPS II with a **weekly IV infusion**[1–3]

THE BBB CHALLENGE



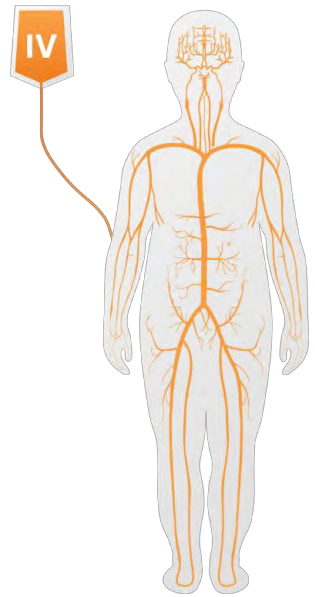
- The BBB is a major obstacle for brain delivery of enzymes

ETV™



- ETV is designed to use the TfR to cross the BBB and enhance delivery of biotherapeutics into the brain
- The TfR is the body's mechanism for iron transport from blood into brain and is highly expressed at the BBB

IV ADMINISTRATION AND BROAD BIODISTRIBUTION



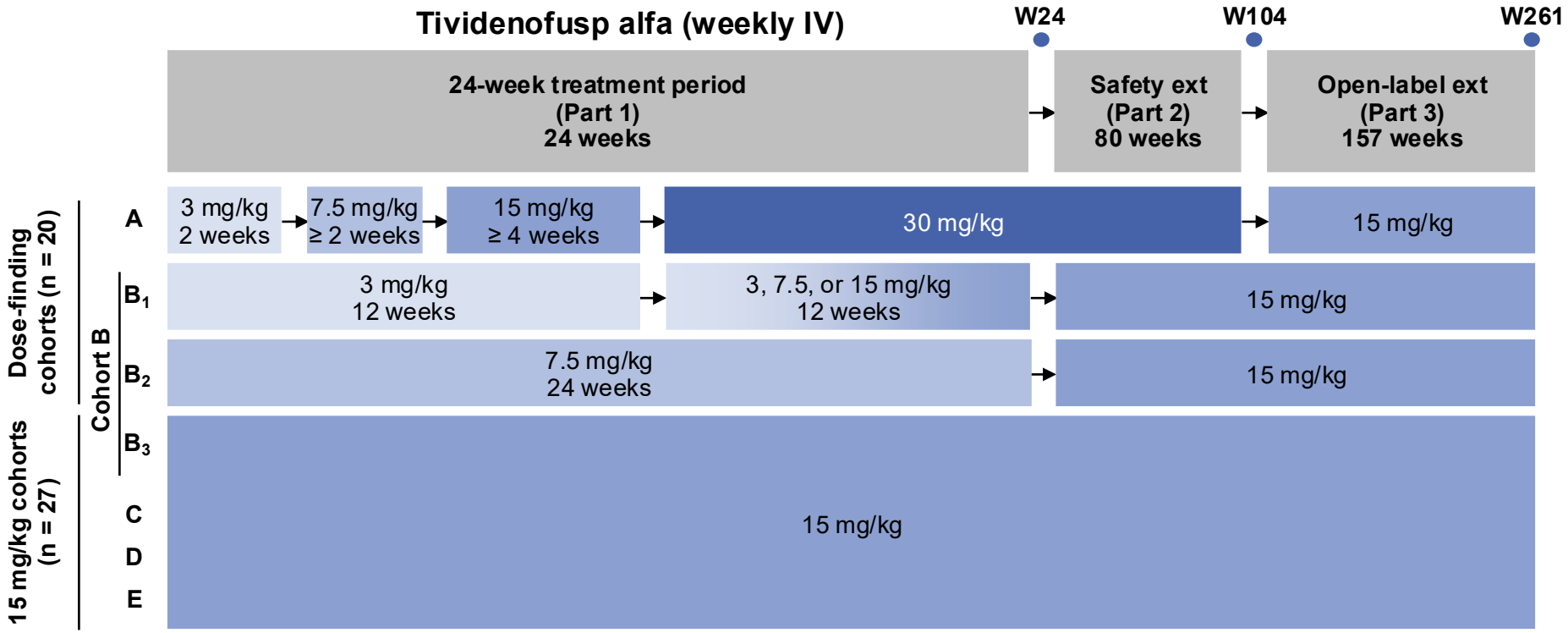
- Design of the ETV is optimized to enable DNL310 to cross the BBB and may also facilitate uptake into peripheral tissues

Tividenofusp alfa has the potential to treat neuronopathic and somatic manifestations of MPS II

1. Muenzer *et al. N Engl J Med* 2026;394:39–50; 2. Bhalla A *et al. Int J Mol Sci* 2020;21:5188; 3. Ullman JC *et al. Sci Transl Med* 2020;12:eaay1163. BBB, blood–brain barrier; CNS, central nervous system; ETV, Enzyme TransportVehicle™; IDS, iduronate-2-sulfatase; IV, intravenous; MPS II, mucopolysaccharidosis type 2; Tf, transferrin; TfR, Tf receptor.

TIVIDENOFUSP ALFA PHASE 1/2 STUDY IN PEDIATRIC PARTICIPANTS WITH MPS II

- Study DNLI-E-0002 is an international, open-label, 24-week study with safety and open-label extension periods (NCT04251026)
  - Data are presented from the clinical cutoff date of March 28, 2025 (when the last participant completed the Week 49 visit)
- 47 male participants with MPS II aged ≤ 18 years (ERT-naive and treatment-experienced) were enrolled into five cohorts (A–E) that differed in inclusion criteria for characteristics such as participant age and MPS II phenotype
- Participants receiving SOC IV ERT at baseline switched to tividenofusp alfa without a washout period



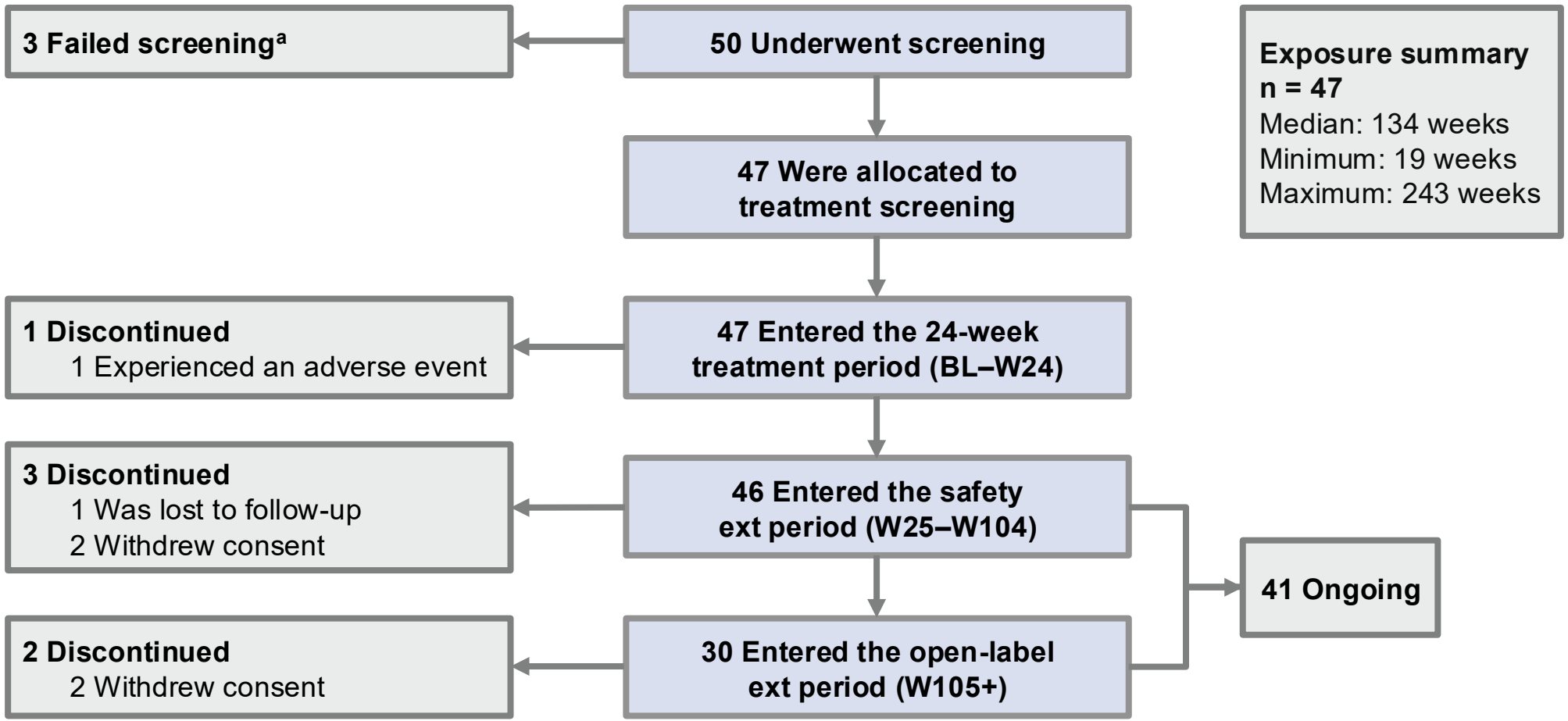
Primary endpoints
- Adverse events
- IRRs
- Other indicators of safety and tolerability

Key secondary endpoints
- CSF HS
- Urine HS
- Adaptive behavior (Vineland)
- Liver volume

Key exploratory endpoints
- Serum NfL
- CSF biomarkers
- Hearing threshold
- Cognition (BSID-III, KABC-II)

Figure adapted from *New Engl J Med*, Muenzer J *et al.*, An Intravenous Brain-Penetrant Enzyme Therapy for Mucopolysaccharidosis II, Vol. 394, pp. 39–50. Copyright © 2026 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. BSID-III, Bayley Scales of Infant Development, Third edition; CSF, cerebrospinal fluid; ERT, enzyme replacement therapy; ext, extension; HS, heparan sulfate; IRR, infusion-related reaction; KABC-II, Kaufman Assessment Battery for Children, Second Edition; NfL, neurofilament light chain; SOC, standard of care; W, week.

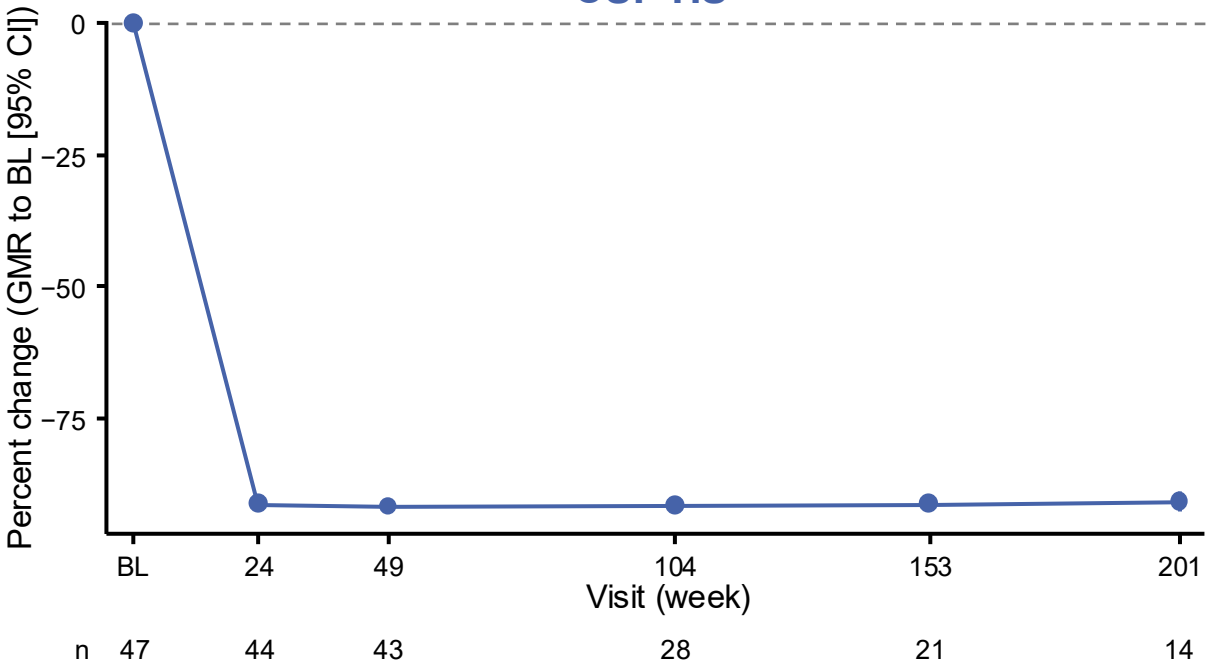
PARTICIPANT ENROLLMENT AND DISPOSITION



[a]Three participants were excluded due to withdrawal of consent, missing/not available DQ at screening, and lack of preexisting liver enlargement. BL, baseline; DQ, developmental quotient.

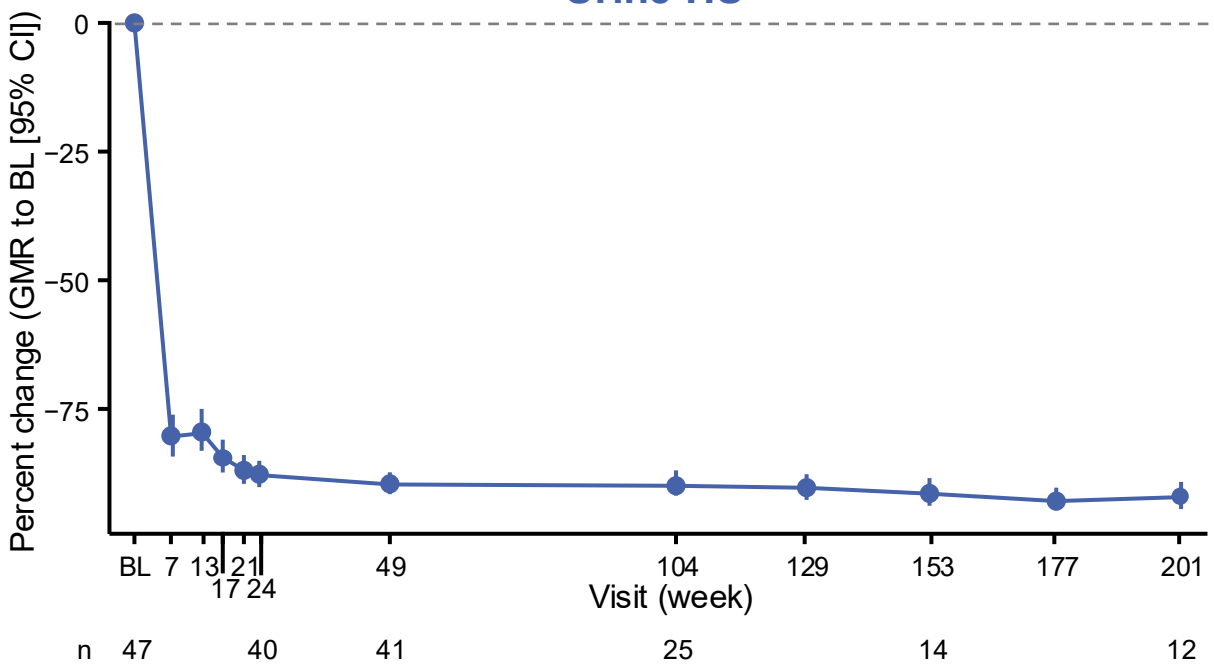
CNS AND PERIPHERAL BIOMARKERS: CSF AND URINE HS

CSF HS



Participants below ULN (n/N), %					
0	93.2	97.7	96.4	95.2	92.9

Urine HS



Participants below ULN (n/N), %					
0	57.5	61.0	68.0	78.6	83.3

Substantial reductions and normalization of CSF and urine HS were achieved with tividenofusp alfa treatment, and these reductions were maintained long-term

Full methodologies for biomarker assays and statistical analyses are published in Muenzer *et al. N Engl J Med* 2026;394:39–50. ULN ranges were determined as the 97.5th percentile using CSF samples from 67 pediatric individuals without MPS II (median [min, max] age: 8.88 [0.06, 25.3] years) or urine samples from 149 pediatric individuals without MPS II (median [min, max] age: 4.93 [0.05, 17.2] years). CI, confidence interval; GMR, geometric mean ratio; ULN, upper limit of normal.

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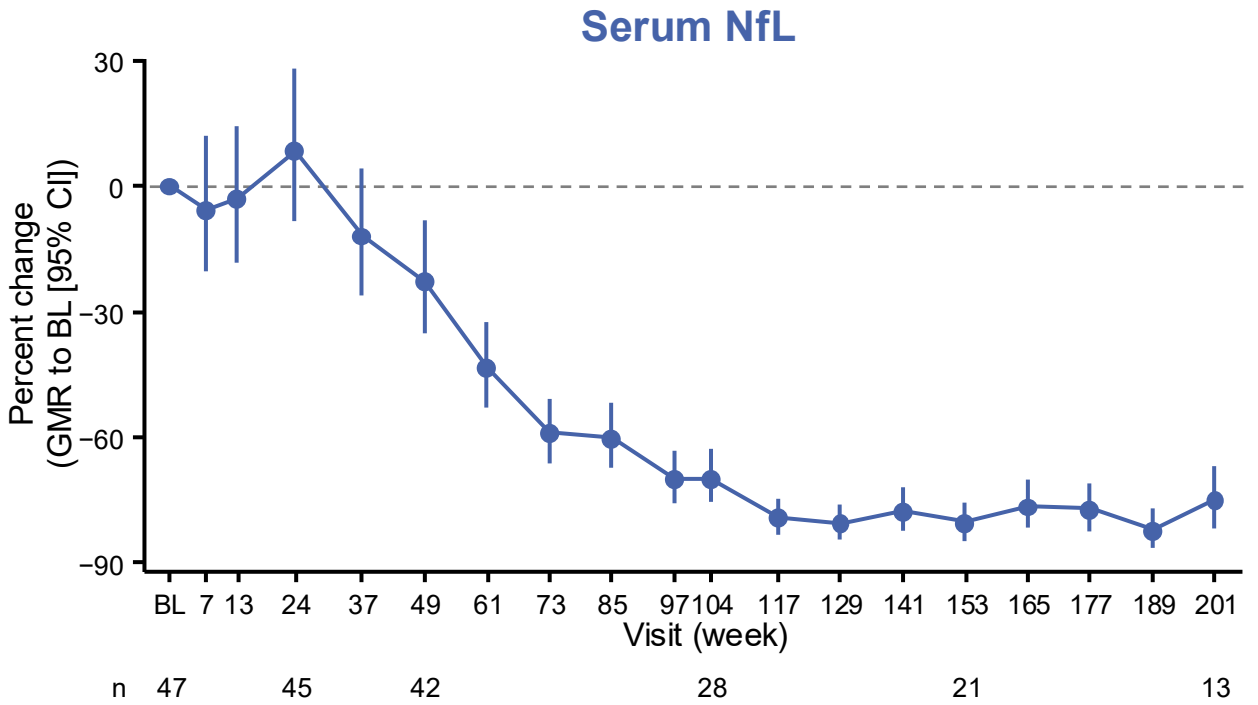
CNS BIOMARKERS: SERUM NfL



Participants below ULN (n/N), %					
19.1	24.4	26.2	75.0	85.7	61.5

Substantial reduction in serum NfL, a marker of neuronal damage, was achieved with tividenofusp alfa treatment, with normalization in most participants by Week 104

Full methodologies for biomarker assays and statistical analyses are published in Muenzer *et al. N Engl J Med* 2026;394:39–50. ULN ranges from Schjørring *et al.* 2023 were used for serum NfL;[1] if the participant was aged < 3 years at that visit, an upper limit of 16.6 ng/L was used, else an upper limit of 13.9 ng/L was used. 1. Schjørring ME *et al. Scand J Clin Lab Invest* 2023;83:403–7.

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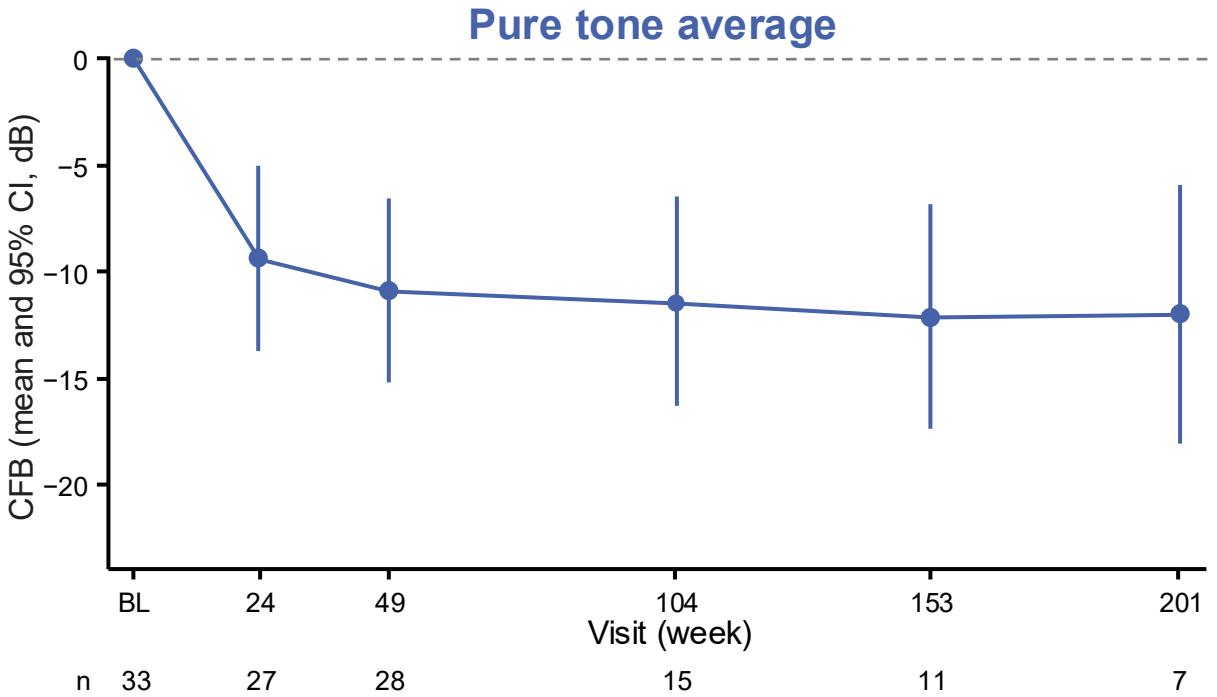
HEARING THRESHOLD

Mean CFB in pure tone average by ABR (eHL) and audiometry (HL)

Visit	n	CFB in dB, adjusted mean (95% CI)	*P* value
W24	27	−9.4 (−13.7, −5.0)	< 0.0001
W49	28	−10.9 (−15.2, −6.6)	< 0.0001
W104	15	−11.4 (−16.3, −6.5)	< 0.0001
W153	11	−12.1 (−17.4, −6.8)	< 0.0001
W201	7	−12.0 (−18.0, −5.9)	0.0002



Hearing threshold as assessed by pure tone average (across 500, 1000, 2000, and 4000 Hz) decreased, reflecting improved hearing from baseline

Full methodologies for hearing assessments and statistical analyses are published in Muenzer *et al. N Engl J Med* 2026;394:39–50. Pure tone average is defined as the average across the four tested frequencies (500, 1000, 2000, and 4000 Hz) and was calculated only if numeric values for all individual frequencies were available. ABR, auditory brainstem response; CFB, change from baseline; dB, decibels; eHL, estimated hearing level; HL, hearing level; Hz, Hertz.

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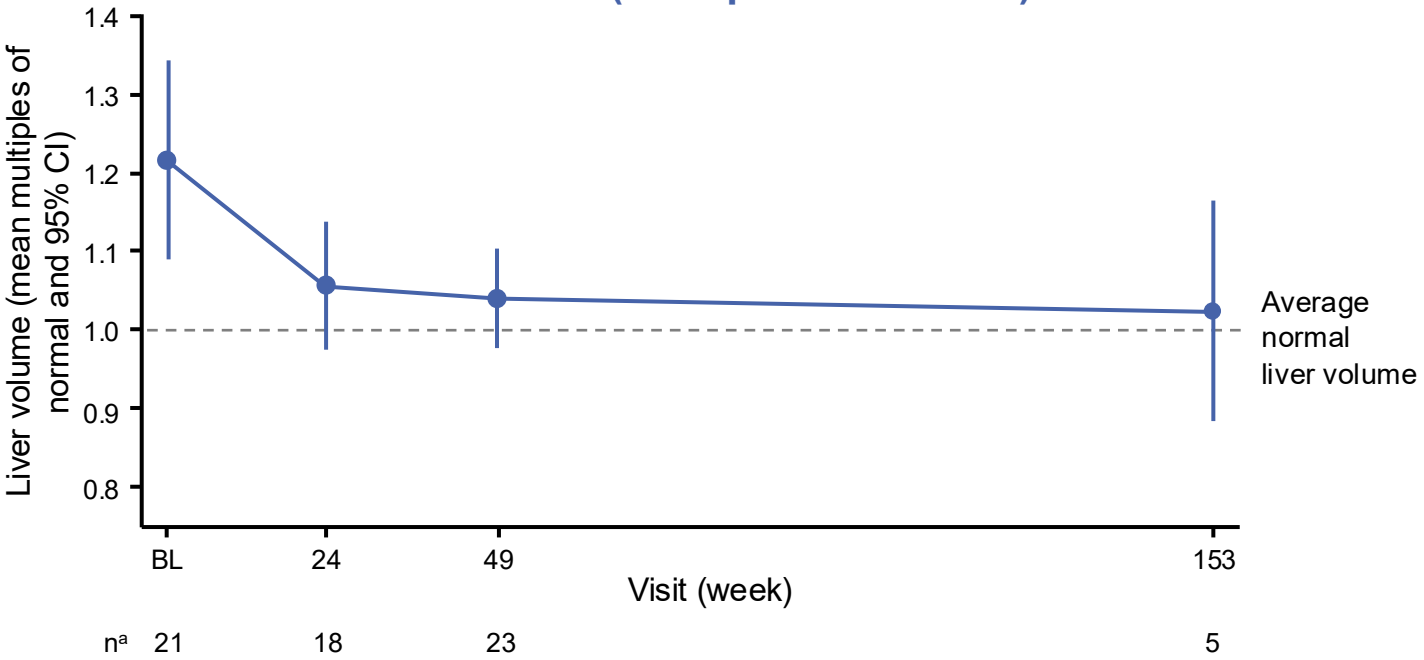
LIVER VOLUME: MRI (COHORTS C, D, AND E)

Liver volume (multiples of normal)



Liver volume (proportion below ULN)[b]

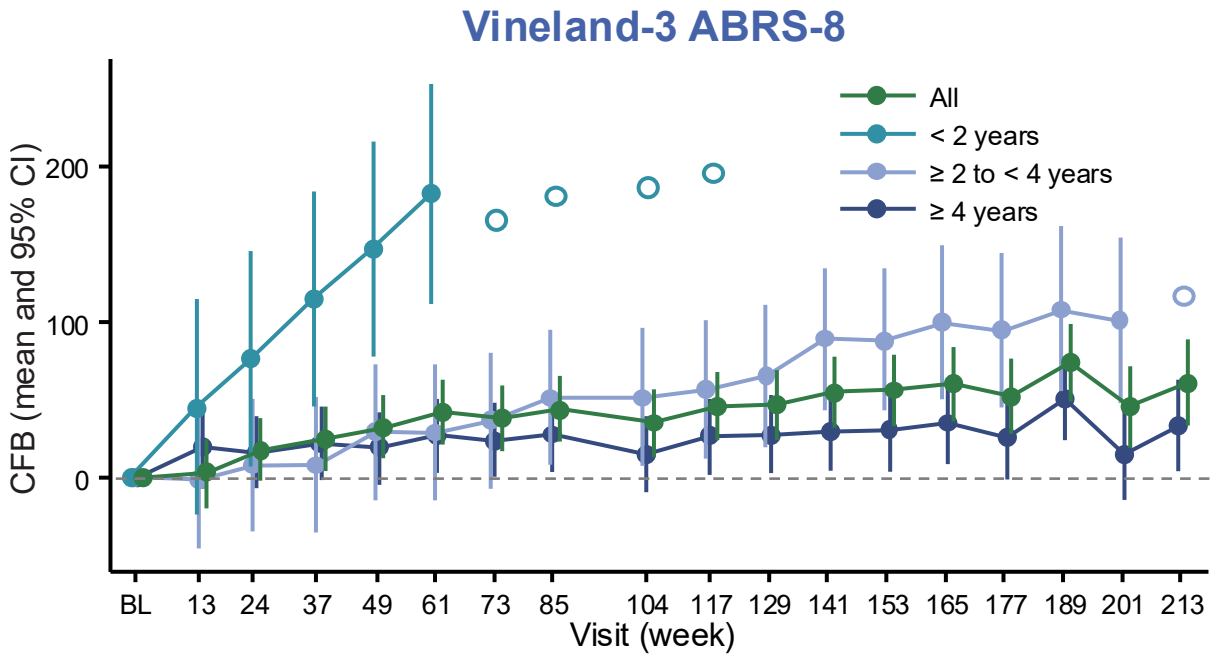
Population	Percent [proportion (n/N)][c] below the ULN[b]			
	BL	W24	W49	W153
All	76.2 (16/21)	100 (18/18)	100 (23/23)	100 (5/5)

All participants had normal liver volume at Weeks 24, 49, and 153

[a]Participants recruited early for whom ultrasound was used at baseline were switched to MRI at later visits; as a result, n at baseline does not match the n at later time points. [b]Values less than the upper bound of the 95% prediction interval for liver volume based on weight and height are defined as normal.[1] [c]n is the number of participants with normal liver volume at that visit; N is the number of participants with available liver MRI volume value at that visit; proportion = n/N. 1. Herden U *et al. Transpl Int* 2013;26:1217–24. MRI, magnetic resonance imaging.

18

ADAPTIVE BEHAVIOR

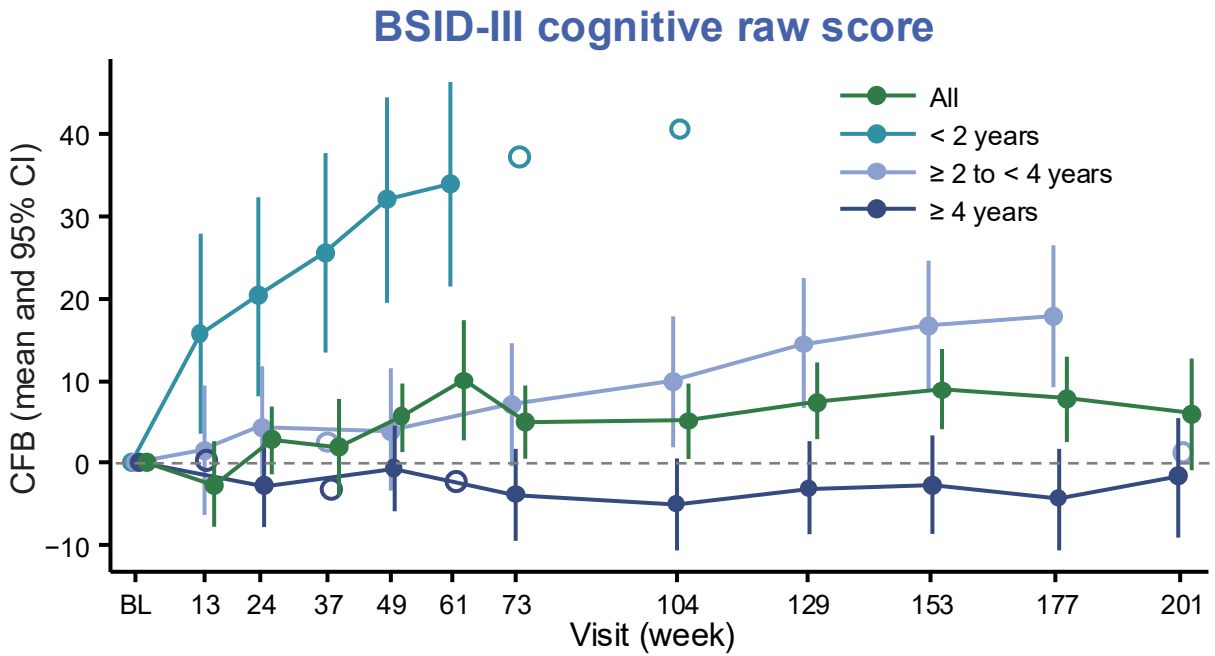


Improvement from baseline in adaptive behavior scores was observed in the younger age groups; stabilization was observed in the ≥ 4 years age group

Full methodologies for assessments of cognitive outcomes and adaptive behavior and statistical analyses are published in Muenzer *et al. N Engl J Med* 2026;394:39–50. ABRS-8 is derived sum of raw scores of eight subdomains (receptive, expressive, personal, interpersonal relationships, play and leisure, coping skills, fine motor, and gross motor). Hollow points indicate visits for which data for less than three participants are available.
ABRS-8, eight-subdomain Adaptive Behavior Raw Score composite; Vineland-3, Vineland Adaptive Behavior Scales, Third Edition.

19

COGNITION



n	39	13	33	9	31	5	23	20	19	16	13	6
< 2 years	5	5	5	5	4	4	2	1				
≥ 2 to < 4 years	9	6	8	2	8		8	6	6	6	4	1
≥ 4 years	25	2	20	2	19	1	13	13	13	10	9	5

Improvement from baseline in cognitive scores was observed in the younger age groups; stabilization was observed in the ≥ 4 years age group

Full methodologies for assessments of cognitive outcomes and adaptive behavior and statistical analyses are published in Muenzer *et al. N Engl J Med* 2026;394:39–50. Hollow points indicate visits for which data for less than three participants are available.

20

SAFETY OVERVIEW

- Long-term exposure (median ~2.5 years) demonstrated a stable safety profile with no new safety signals since the primary analysis (October 9, 2024)[1]
- All participants experienced at least one TEAE; the maximum severity was moderate in 75% of participants
- In total, 21 participants (45%) had at least one serious TEAE
  - Of these participants, three experienced serious TEAEs considered related to treatment (two had IRRs and one had anemia; previously reported; all continued to receive tividenofusp alfa in the study)
- One participant (2.1%) discontinued treatment due to a TEAE

Most frequently reported TEAEs

Preferred term	All cohorts (n = 47) n (%) of participants
IRR	41 (87%)
Upper respiratory tract infection	32 (68%)
Pyrexia	28 (60%)
Cough	23 (49%)
Anemia	20 (43%)
Diarrhea	20 (43%)
Rash	20 (43%)
Vomiting	20 (43%)
COVID-19	18 (38%)
Rhinorrhea	18 (38%)
Nasal congestion	17 (36%)

Tividenofusp alfa 15 mg/kg had a manageable safety profile in pediatric participants with MPS II

1. Muenzer *et al. N Engl J Med* 2026;394:39–50. TEAE, treatment emergent adverse event.

21

IRRs

Proportion of participants with at least one IRR during each 4-week interval, categorized by severity[a]

- In total, 41 participants (87%) had at least one IRR; among the 47 total participants, the maximum severity was moderate in 55.3% of participants
- IRRs were clinically manageable with standard premedications, slowing the infusion rate, and/or reducing the dose level

IRRs, a known risk of ERTs, were the most common adverse event, decreasing in incidence and severity over time

[a]Proportions were number of participants who had an IRR/number of participants exposed to tividenofusp alfa at any point during that time interval (maximum of one IRR (IRR with highest severity) per participant, per interval.

22

CONCLUSIONS

Treatment with tividenofusp alfa led to substantial reductions from baseline in CNS and peripheral biomarkers of disease

- The majority of participants achieved normalization of CSF and urine HS, and serum NfL
- Reduction and normalization in CNS and peripheral biomarkers was maintained through Week 201

While receiving tividenofusp alfa treatment, CNS and peripheral clinical outcomes showed:

- Improvement from baseline in mean hearing threshold, as assessed by pure tone average
- Normal liver volume at 24, 49, and 153 weeks
- Improvement or stabilization relative to baseline on measures of adaptive behavior and cognition

Tividenofusp alfa demonstrated a stable long-term safety profile with no new safety signals since the primary analysis

- All study participants experienced TEAEs, with IRRs being the most common
- For most participants, the maximum severity for TEAEs was moderate
- Incidence and severity of IRRs decreased, and tolerability improved over time

23

ACKNOWLEDGMENTS

We would like to give a special **thank you to the participants and families** who generously contributed through their participation in this study sponsored by Denali Therapeutics Inc.

We also thank the study principal investigators, collaborators, and the Denali Therapeutics team for the conduct of the study and data collection

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COMPASS, a Phase 2/3, multicenter, double-blind, randomized efficacy and safety study of tividenofusp alfa vs idursulfase in MPS II, is ongoing (NCT05371613)

Thank you for your attention

 Tividenofusp alfa (DNL310) is an investigational drug and has not been approved by any Health Authority 24

TIVIDENOFUSP ALFA TREATMENT IN A MALE SIBLING PAIR WITH NON-NEURONOPATHIC MUCOPOLYSACCHARIDOSIS TYPE II

Irene Chang,[1] Jacqeline Madden,[1] Annie Sako,[1] Jill Dwyer,[1] Daniel Fertek,[2] Adam Scheller,[2] Sharon O'Byrne,[2] Imanol Zubizarreta Arambarri,[2] Peter Chin,[2] Paul Harmatz[1]

[1]UCSF Benioff Children's Hospital, Oakland, CA, USA; [2]Denali Therapeutics Inc., South San Francisco, CA, USA

WORLD*Symposium*™ 2026

Thursday February 5, 2026 from 15:30 to 17:30 PST

Informed consents were obtained to present the information and videos on this poster. We give a special thank you to the participants and families who generously contributed through their participation. We also thank our collaborators and the Denali Therapeutics team for the conduct of the study and data collection.

INTRODUCTION AND CASES

Introduction

- Tividenofusp alfa is an investigational drug designed to cross the blood–brain barrier and treat CNS and somatic manifestations of MPS II (Hunter syndrome)[1]
- We present data for a male sibling pair enrolled in the ongoing open-label Phase 1/2 study of tividenofusp alfa (NCT04251026), including standard-of-care follow-up data beyond the study protocol
- The Phase 1/2 study enrolled 47 male participants with MPS II into five cohorts (A–E), which differed in inclusion criteria
- Both siblings were enrolled in cohort D for individuals with preexisting hepatomegaly and initiated tividenofusp alfa 15 mg/kg weekly intravenously in September 2022
- The younger sibling missed W24 assessments owing to illness not related to the study drug

Table 1. Phase 1/2 study baseline demographics and clinical characteristics

	Older sibling	Younger sibling
Age at diagnosis	6Y0M	3Y10M
Age at tividenofusp alfa initiation	6Y8M	4Y3M
Race and ethnicity	White, not Hispanic or Latino	White, not Hispanic or Latino
Genetic variant	c.1583A>T; p.(Asp528Val)	c.1583A>T; p.(Asp528Val)
Iduronate-2-sulfatase activity	< 1.5 nmol/h/mL	< 1.5 nmol/h/mL
Any prior therapy for MPS II	No	No
Composite cognitive DQ[a]	130.19	102.77
ADA and NAb status	Negative	Negative
Height	120.4 cm	108.7 cm
Weight	23.4 kg	19.8 kg
Physical exam	Orange peel rash on shoulders, mild coarse facial features, mild enlarged tongue, and very mild clawed hands (all clinically nonsignificant)	Very mild clawed hands (clinically nonsignificant)

[a]DQ was calculated as developmental age divided by chronologic age multiplied by 100; a score of 100 indicates age-expected development.

1. Muenzer J *et al. N Engl J Med* 2026;394:39–50.

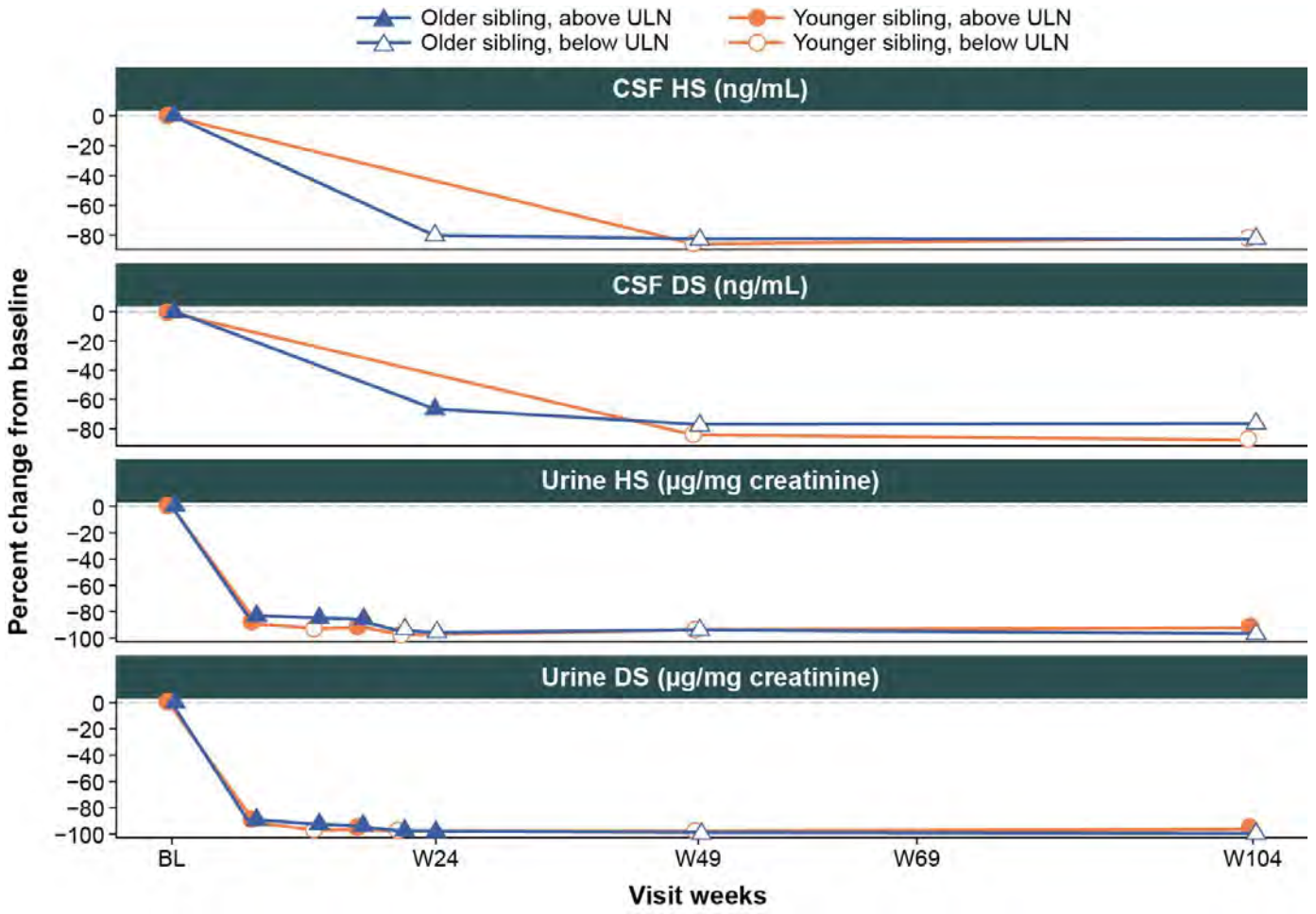
ADA, antidrug antibody; CNS, central nervous system; DQ, developmental quotient; MPS II, mucopolysaccharidosis type II; Nab, neutralizing antibody.

RESULTS

Biomarker assessments from Phase 1/2 study

- In both siblings, levels of CSF HS and DS, and urine HS and DS at study baseline were above the ULN
- **All levels normalized by W49 to within the range for children without MPS II and substantial reductions were maintained through W104**
- For the older sibling (Figure 2):
  - CSF and urine HS were below the ULN at W24 and W21, respectively; CSF and urine DS were below the ULN at W49
  - At W24, CSF HS and DS decreased from baseline by 80.5% and 65.2%, respectively; urine HS and DS decreased by 95.8% and 97.6%, respectively
- At W49 (older sibling), CSF HS and DS decreased from baseline by 83.0% and 76.0%, respectively; urine HS and DS decreased by 93.8% and 98.5%, respectively
- For the younger sibling (Figure 2):
  - W24 data are not available because the visit was missed. Urine HS and DS were below the ULN at W13; CSF HS and DS were below the ULN at W49
  - At W49, CSF HS and DS decreased from baseline by 85.9% and 84.0%, respectively; urine HS and DS decreased by 93.7% and 97.8%, respectively

Figure 2. Change from Phase 1/2 study baseline in CSF HS and DS, and urine HS and DS

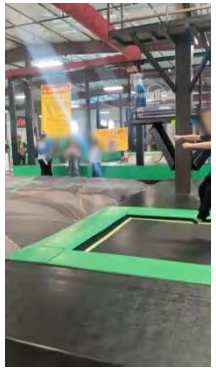


BL, baseline; CSF, cerebrospinal fluid; DS, dermatan sulfate; HS, heparan sulfate; MPS II, mucopolysaccharidosis type II; ULN, upper limit of normal; W, week.

RESULTS

Somatic Manifestations

- Per medical records, mild carpal tunnel syndrome was diagnosed on the older sibling's right side (February 2023) and bilaterally in the younger sibling (August 2023). Follow-up testing in August 2024 showed their carpal tunnel syndrome to be resolved
- In the Phase 1/2 study W24 interview, their parents noted improvements in both children's wrists as they both wanted to play video games now and before they did not because their wrists hurt
- The older sibling had impaired shoulder abduction at Phase 1/2 study baseline, which normalized at W104
- At their most recent 6MWT (August 2025), the older sibling and younger sibling reached 639 and 589 meters, respectively (distances within the typical ranges expected for boys of their age)[1]
- Both siblings followed typical height and weight trajectories expected for their ages, with the most recent height measurements for the older sibling and younger sibling around the 50th and 90th percentiles, respectively



Informed consents were obtained for the sibling pair with MPS II to present the information and videos on this poster.

1. Cacau L *et al. Braz J Cardiovasc Surg* 2016;31:381–8

6MWT, 6-minute walk test; W, week.

RESULTS

CNS Manifestations

Table 2. KABC-II analyses

	Subtest	Screening raw score (age 6Y7M)	W129 raw score (age 9Y1M)	Screening scaled score (age 6Y7M)[a] (Mean = 10, SD = 3)	W129 scaled score (age 9Y1M)[a] (Mean = 10, SD = 3)	Screening scaled score based on age 5 norms[b] (Mean = 10, SD = 3)	W129 scaled score based on age 5 norms[b] (Mean = 10, SD = 3)
Older sibling	Conceptual thinking	21	25	12	N/A	15	17
	Face recognition	15	13	N/A	N/A	13	11
	Expressive vocabulary	29	35	14	16	16	19
	Triangles	25	36	15	17	17	19
	Pattern reasoning	N/A	42	N/A	15	N/A	19
	Hand movements	10	14	12	12	15	19
	NVI (Mean = 100, SD = 15)	–	–	122[c]	143[c]	141[c]	158
	Subtest	**Screening raw score (age 4Y3M)**	**W129 raw score (age 6Y9M)**	**Screening scaled score (age 4Y3M)[a] (Mean = 10, SD = 3)**	**W129 scaled score (age 6Y9M)[a] (Mean = 10, SD = 3)**	**Screening scaled score based on age 5 norms[b] (Mean = 10, SD = 3)**	**W129 scaled score based on age 5 norms[b] (Mean = 10, SD = 3)**
Younger sibling	Conceptual thinking	10	22	10	13	8[b]	15[b]
	Face recognition	11	16	10	N/A	9[b]	13[b]
	Expressive vocabulary	20	31	11	15	10[b]	18[b]
	Triangles	11	26	10	16	8[b]	18[b]
	Pattern reasoning	N/A	13	N/A	11	N/A	16[b]
	Hand movements	5	11	10	12	9[b]	16[b]
	NVI (Mean = 100, SD = 15)	–	–	102	122[c]	89[c]	146[b]

- Select KABC-II subtest scores increased for both siblings from screening to W129 (Table 2)
- By W129, both siblings demonstrated notable KABC-II gains
- At W129, processing and cognitive abilities were in the above average to upper extreme ranges for age
- Standard score gains indicate cognitive development exceeding age-matched KABC-II norms
- Using age-constant norms, the younger sibling showed a faster rate of growth
- KABC-II improvements were consistent with parent-reported academic and functional gains, supporting clinically meaningful cognitive change

KABC-II, Kaufman Assessment Battery for Children, Second Edition; N/A, not administered; NVI, nonverbal index; W, week.
[a]Based on age-appropriate norms; [b]Based on Age 5 norm set; [c]Prorated per manual guidance.

CONCLUSIONS AND DISCLOSURES

Conclusions

- Tividenofusp alfa treatment substantially reduced and normalized MPS II disease biomarkers and improved somatic manifestations in siblings with non-neuronopathic MPS II
- For cognition, KABC-II findings aligned with parent-reported academic and functional observations, supporting the interpretation of meaningful gains in cognitive abilities and processing
- Given the open-label nature of the study, the results presented here should be interpreted with caution. COMPASS, a Phase 2/3, multicenter, double-blind randomized efficacy and safety study of Tividenofusp alfa vs idursulfase in MPS II is ongoing (NCT05371613)

Scan the QR code to download a PDF of the poster and supplemental file

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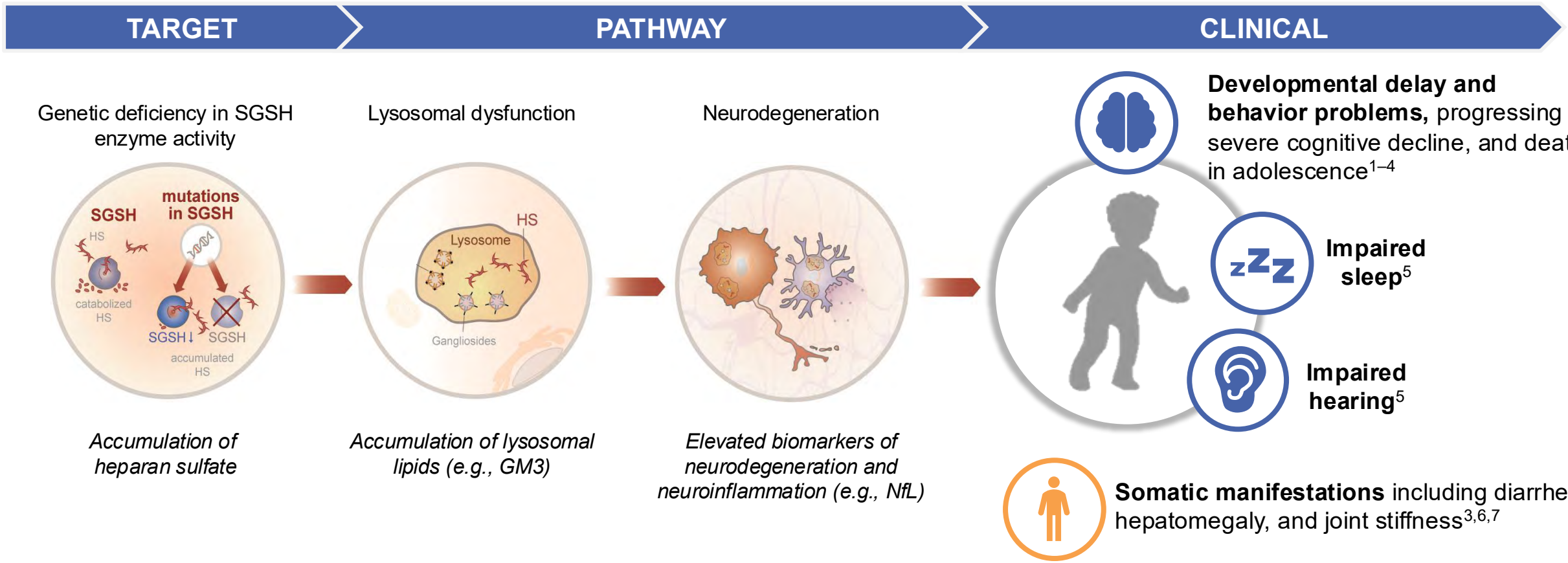
Preliminary Results from Phase 1/2, First-in-Human, Open-Label Study of DNL126 in Children with Mucopolysaccharidosis IIIA (MPS IIIA)

Elizabeth Jalazo, MD
University of North Carolina, Chapel Hill, NC, USA

MPS IIIA Pathogenesis, Biomarkers, and Clinical Manifestations



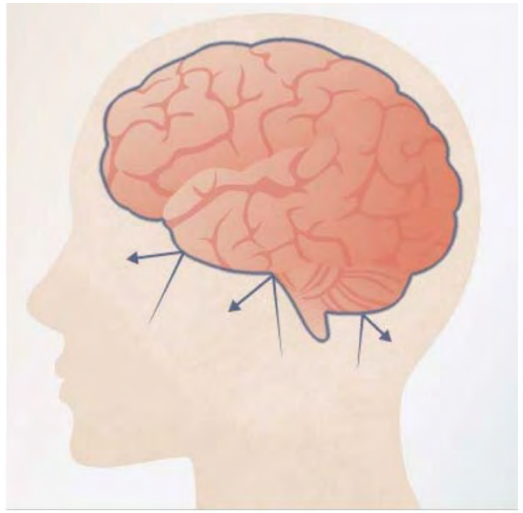
Currently, there are no approved therapies for MPS IIIA, representing a high unmet medical need

GM3, ganglioside monosialic 3; HS, heparan sulfate; MPS IIIA, mucopolysaccharidosis type IIIA; NfL, neurofilament light chain; SGSH, sulfoglucosamine sulfohydrolase.

1. Lavery C *et al. Orphanet J Rare Dis* 2017;12:168; 2. Harmatz P *et al. Mol Genet Metab* 2022;136:249–59; 3. Shapiro EG *et al. Mol Genet Metab* 2017;122S:1–7; 4. Wijburg FA *et al. Acta Paediatr* 2013;102:462–70; 5. Buhrman D *et al. J Inherit Metab Dis* 2014;37:431–7; 6. Heon-Roberts R *et al. J Clin Med* 2020;9:344; 7. Muschol N *et al. Orphanet J Rare Dis* 2022;17:391.

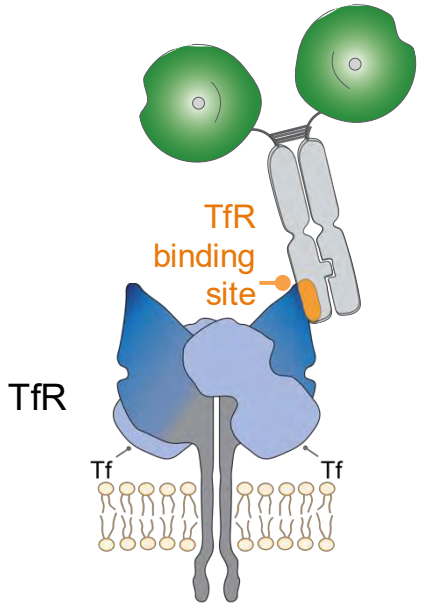
Our Approach to Enzyme Replacement Therapy

THE BBB CHALLENGE



- The BBB is a major obstacle for brain delivery of enzymes

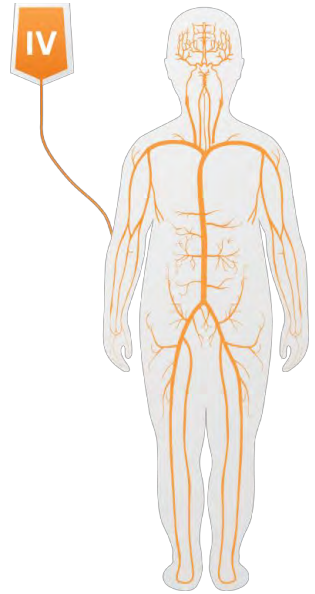
DNL126



DNL126 (ETV:SGSH)

- DNL126 is designed to use the TfR to cross the BBB and enhance delivery of biotherapeutics into the brain
- The TfR is the body's mechanism for iron transport from blood into brain and is highly expressed at the BBB

IV ADMINISTRATION AND BROAD BIODISTRIBUTION



- Design of DNL126 is optimized to enable it to cross the BBB and may also facilitate uptake into peripheral tissues

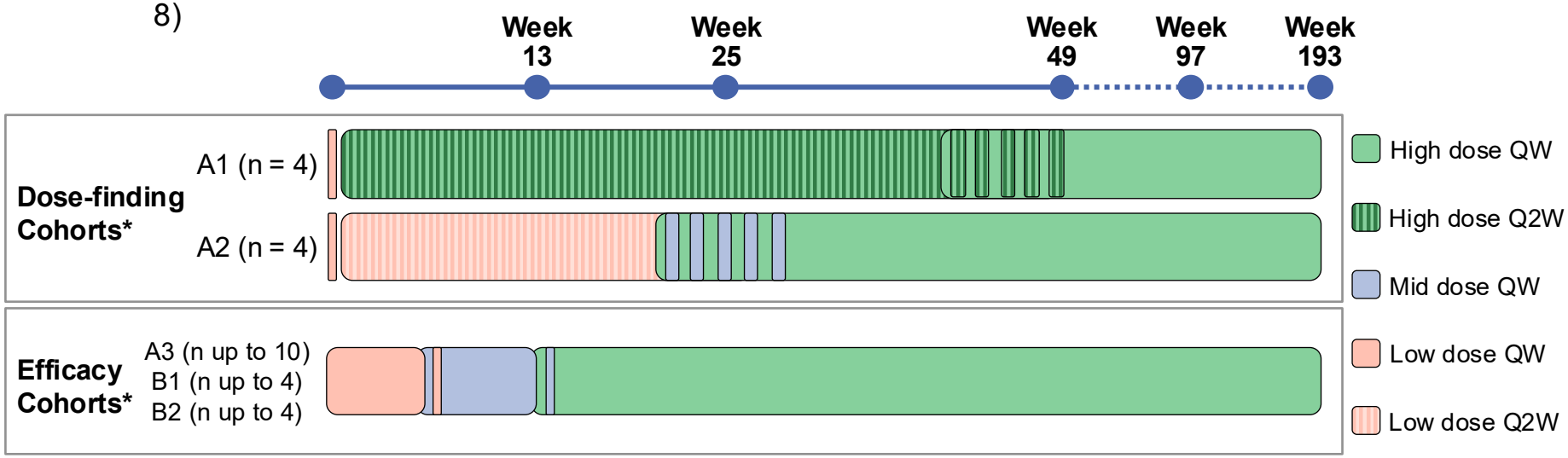
DNL126 is an investigational ERT for MPS IIIA engineered to be brain penetrant and administered by IV infusion

BBB, blood–brain barrier; ERT, enzyme replacement therapy; IV, intravenous; Tf, transferrin; TfR, transferrin receptor.

Jefferies WA *et al.* 1984; Qian ZM *et al.* 2002; Bakardjiev AI, 2021; Arguello A *et al.* 2021; Arguello A, Mahon CS *et al.* 2022; Ullman JC *et al.* 2020; Wang S *et al.* 2020; Gammella E *et al.* 2017; Carlevaro MF, *et al.* 1997.

DNL126 Phase 1/2 Study in Pediatric Participants with MPS IIIA

- Study DNLI-I-0001 is a multicenter, open-label, 25-week study followed by an open-label extension period through 193 weeks (NCT06181136) in up to 26 pediatric participants with MPS IIIA in up to 5 cohorts
- Preliminary data through cut-off date of June 4, 2025
  - **Safety Outcomes:** Dose-finding and efficacy cohorts (n = 14)
  - **Efficacy Outcomes:** Dose-finding cohorts only; at Week 49, dose finding cohorts were receiving the high dose either QW or Q2W (n = 8)



Cohort A1–A3: children with severe and attenuated phenotypes aged ≥ 2 to < 18 years

Cohort B1: children < 28 months of age with a predicted severe phenotype

Cohort B2: siblings of children in Cohort B1

Primary Endpoint

- Percent change from baseline in CSF HS at W49 *(efficacy cohorts only)*

Secondary Endpoints

- Percent change from baseline in urine HS at W49
- Change from baseline in liver volume at W49
- Percent change from baseline in serum NfL at W73
- Participants with CSF HS in normal range at W49 *(efficacy cohorts only)*

Study enrollment (n = 20) completed in September 2025

*Intraparticipant dose escalation occurred at varying times.

CSF, cerebrospinal fluid; QW, once weekly; Q2W, once every 2 weeks; W, week.

All Cohorts: Participant Demographics and Characteristics

	Dose-finding cohorts		Efficacy cohorts*		
	Cohort A1 (n = 4)	Cohort A2 (n = 4)	Cohort A3 (n = 4)	Cohort B1 (n = 2)	All cohorts (n = 14)
DNL126 treatment duration					
Completed up to Week 25	4 (100.0%)	4 (100.0%)	4 (100.0%)	1 (50.0%)	13 (92.9%)
Completed up to Week 49	4 (100.0%)	4 (100.0%)	0 (0.0%)	0 (0.0%)	8 (57.1%)
Age at screening (months)					
Median	47.0	57.5	51.5	27.0	49.0
Min – Max	36.0 – 55.0	51.0 – 78.0	33.0 – 87.0	27.0 – 27.0	27.0 – 87.0
Sex					
Female	2 (50%)	4 (100%)	3 (75%)	0	9 (64.3%)
Male	2 (50%)	0	1 (25%)	2 (100%)	5 (35.7%)
Race					
White	4 (100%)	4 (100%)	4 (100%)	2 (100%)	14 (100%)
Ethnicity					
Hispanic or Latino	0	1 (25%)	0	0	1 (7.1%)
p.S298P heterozygous	1 (25%)	1 (25%)	1 (25%)	0	3 (21.4%)

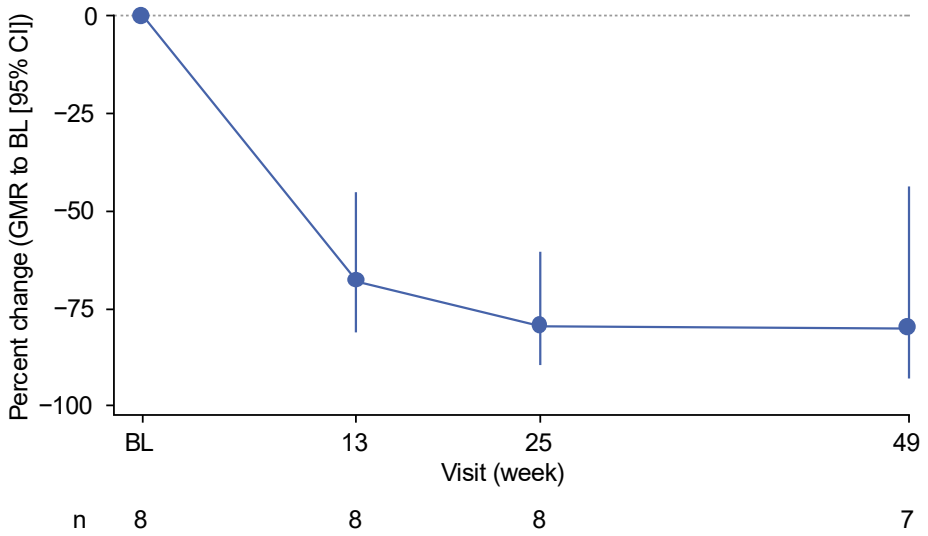
Study population includes a broad spectrum of pediatric ages and genotypes

*No participants were enrolled in Cohort B2.

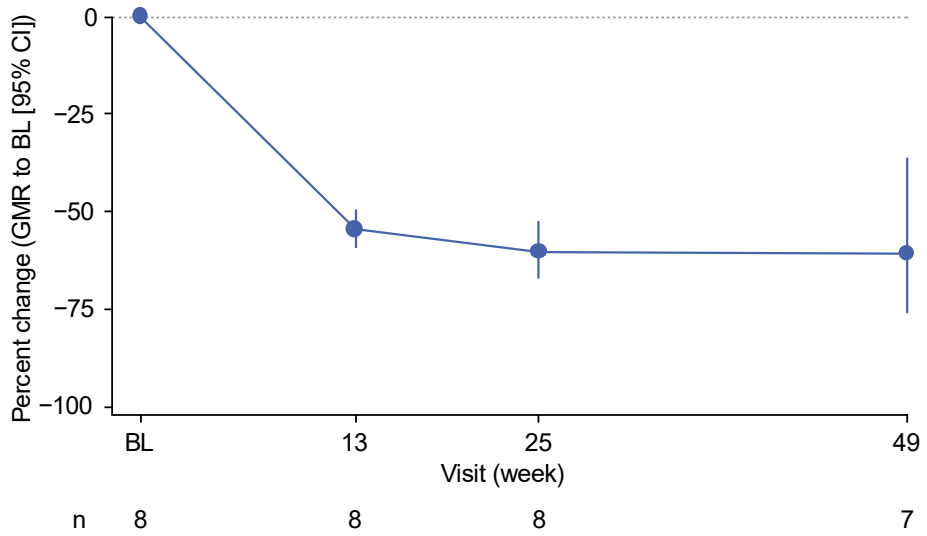
Preliminary Data Phase 1 Dose-finding Cohorts (A1 and A2)

CNS Biomarkers: CSF Heparan Sulfate and GM3

CSF HS



CSF GM3



In Cohorts A1 and A2 at Week 49:

Mean reduction of 80% in CSF HS with 3 of 7* participants within normal range**

Mean reduction of 61% in GM3 with 6 of 7* participants within normal range***

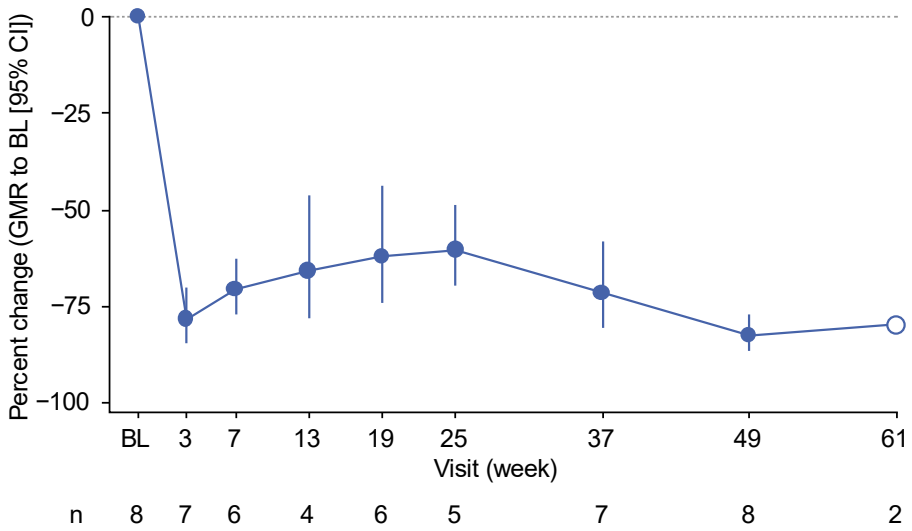
*n = 7 at Week 49 as one participant had lumbar puncture performed early at Week 37. **Age-based biomarker reference ranges were established based on CSF samples from 67 individuals without MPS IIIA (median [min, max] age: 8.88 [0.06, 25.3] years). ***Age-based biomarker reference ranges were established based on GM3 samples from 70 individuals without MPS IIIA (median [min, max] age: 8.77 [0.06, 25.3] years).

BL, baseline; CI, confidence interval; CNS, central nervous system; GMR, geometric mean ratio.

Preliminary Data Phase 1 Dose-finding Cohorts (A1 and A2)

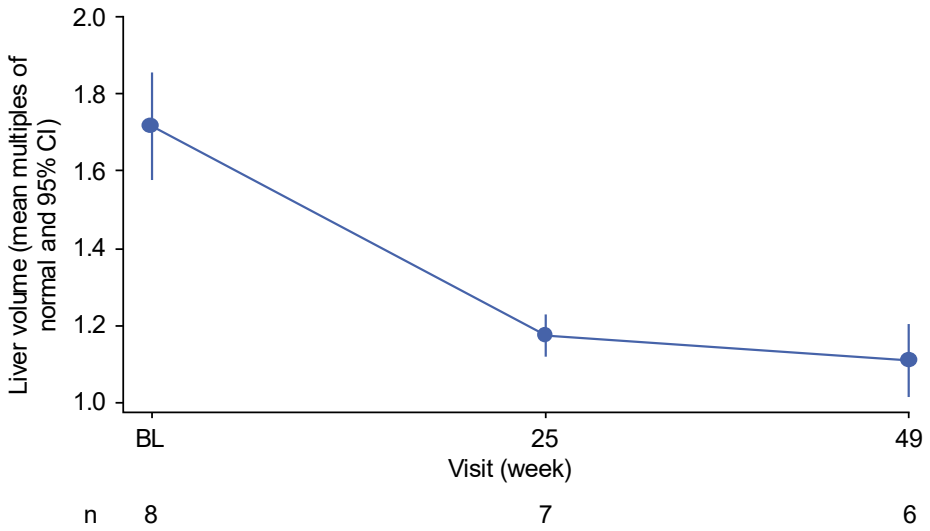
Peripheral Measures: Urine HS and Liver Volume

Urine HS



- Substantial reduction observed by Week 3
  - Variability in response beyond Week 3 due to intra participant differences in dose frequency and dose escalation

Liver volume



- Mean liver volumes 1.72 times normal at baseline
- At Week 49, mean reduction of 0.6 (SD: 0.14) in liver volume multiples of normal

In Cohorts A1 and A2 at Week 49:

Mean reduction of 83% in urine HS, 0 of 8 participants within normal range*

Mild hepatomegaly improved by Week 25; 6 of 6 participants within normal range**

Open circles represent timepoints with less than three samples. MRI, magnetic resonance imaging; SD, standard deviation.

* ULN ranges were determined as the 97.5th percentile using urine samples from 149 pediatric individuals without MPS IIIA (median [min, max] age: 4.93 [0.05, 17.2] years). **One participant had MRI performed outside of Week 49 analysis window, and one did not have data available at time of data cut. Values less than the upper bound of the 95% prediction interval for liver volume based on weight and height are defined as normal (Herden U *et al. Transpl Int* 2013;26:1217–24).

All Cohorts: Safety Overview

- All participants (n = 14) experienced a TEAE assessed by the investigator as related to the study intervention
- The majority of participants experienced TEAEs with a maximum severity of Grade 1 or Grade 2
  - There were no Grade 4 or Grade 5 TEAEs
- Serious TEAEs were reported in 4 (28.6%) participants; none were considered treatment-related
- IRRs were common and reported in all participants
- There were no deaths or TEAEs that led to early discontinuation from the study intervention or the study

TEAEs reported in >30% of participants

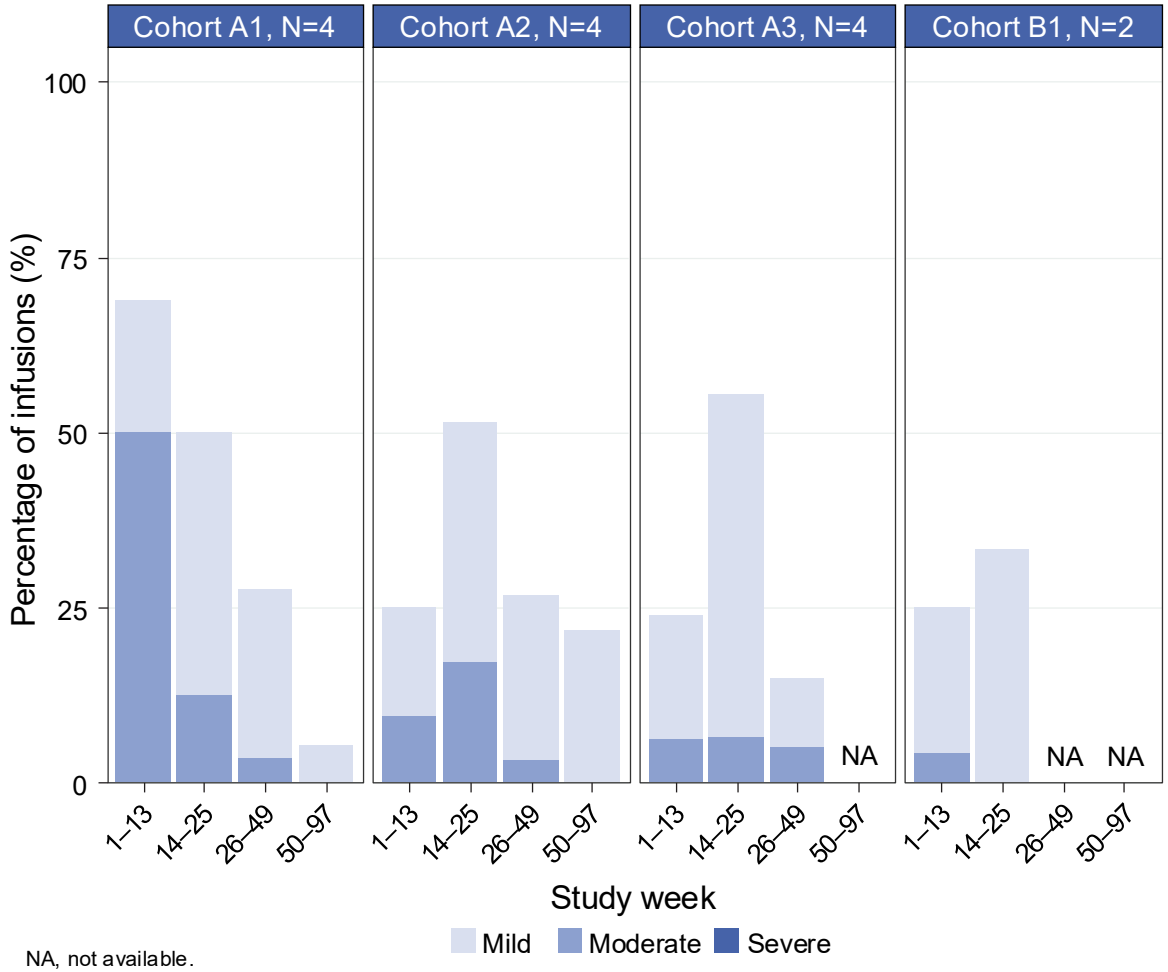
Preferred term	All cohorts (n = 14) [n (%)]
Infusion-related reaction	14 (100)
Upper respiratory infection	9 (64.3)
Vomiting	9 (64.3)
Nasal congestion	7 (50.0)
Cough	6 (42.9)
Diarrhea	5 (35.7)
Ear infection	5 (35.7)
Fall	5 (35.7)
Gastroenteritis	5 (35.7)
Irritability	5 (35.7)

Preliminary data demonstrate that the safety profile of DNL126 in children with MPS IIIA was generally consistent with established enzyme replacement therapies

AESI, adverse event of special interest; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.

All Cohorts: Infusion-related Reactions

Infusion-related reactions by cohort and study week



- IRR frequency and/or severity decreased after Week 25 in all cohorts (limited data available for Cohorts A3 and B1)
- Reduced IRR severity and/or frequency through Week 25 were observed in cohorts utilizing gradual dose escalation (Cohorts A2, A3 and B1)
- IRRs were manageable with premedications, infusion-rate adjustments, and/or infusion interruptions
  - Slow graduated rates adapted from Castells (2008) were utilized to prevent further IRRs in one participant

NA, not available.

The denominator for the interval is based on the total number of infusions administered during the interval, and the numerator represents the total number of infusions with an IRR during the interval, in which only the most severe one per dosing visit, per participant is counted. As of the data cut date, no Cohort A3 participants had reached Week 50 and no Cohort B1 participants had reached Week 26.

Castells MC et.al. *J Allergy Clin Immunol* 2008;122:574-80.

Conclusions

Preliminary results from dose-finding cohorts demonstrate that 49 weeks of DNL126 treatment resulted in substantial reductions in CSF and peripheral biomarkers, with some participants achieving normalization

- CSF HS: 80% mean reduction at Week 49, with normalization in 3 of 7 participants
- CSF GM3: 61% mean reduction at Week 49, with normalization in 6 of 7 participants
- Urine HS: 83% mean reduction at Week 49, no participants within normal range
- Improvement in mild hepatomegaly observed as early as Week 25, with normalization in 6 of 6 participants at Week 49

Preliminary safety data in pediatric participants with MPS IIIA treated with DNL126 were generally consistent with established ERTs

- All participants experienced TEAEs; the majority of TEAEs were mild or moderate in severity
- No treatment-related serious TEAEs, treatment discontinuations or study discontinuations were reported
- Frequently reported TEAEs included IRRs, upper respiratory infection, vomiting, nasal congestion, and cough
- IRRs were manageable and decreased in frequency and severity over time
  - Reduced IRR severity and/or frequency was observed in cohorts utilizing gradual dose escalation

Preliminary results support continued evaluation of DNL126 in the ongoing efficacy cohorts

Acknowledgements

We give a special **thank you to the participants and families** who generously contributed through their participation

We also thank our collaborators and the Denali Therapeutics team for the conduct of the study and data collection

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Thank you for your attention

DNL126 is an investigational drug and has not been approved by any health authority

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Enzyme TransportVehicle™

Pompe Disease

Joe Lewcock, Ph.D.
Chief Scientific Officer

ENHANCED CORRECTION OF SKELETAL MUSCLE AND BRAIN PATHOLOGY IN A POMPE MOUSE MODEL USING TRANSFERRIN RECEPTOR-MEDIATED DELIVERY OF GAA

Rashi Priya, Cinthia V Pastuskovas, Hoang Nguyen, Isabel Becerra, Manuel Montalban, Rajarshi Ghosh, Chau Tran, Jamal Alkabsh, Sonnet Davis, Audrey Reeves, Romeo Maciuca, Tianao Yuan, Jung H Suh, Meng Fang, Neal Gould, Anastasia Henry, Sarah Huntwork-Rodriguez, Stephanie Coffin, Annie Arguello, Cathal Mahon

Denali Therapeutics Inc., South San Francisco, CA, USA

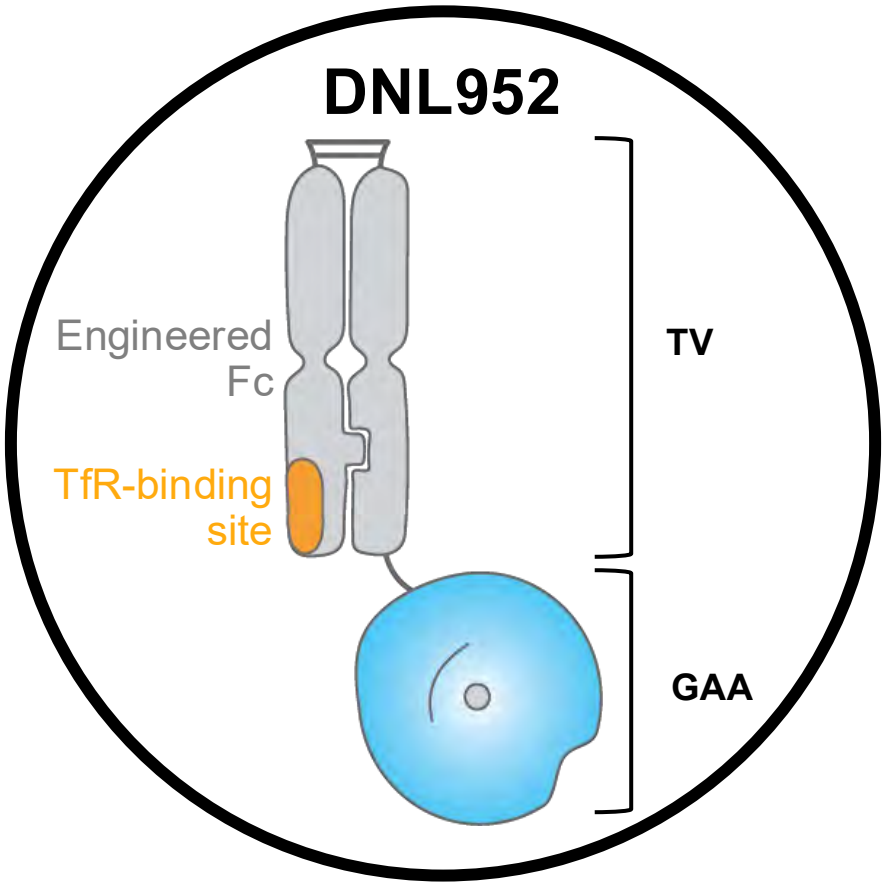
WORLD*Symposium*™ 2026

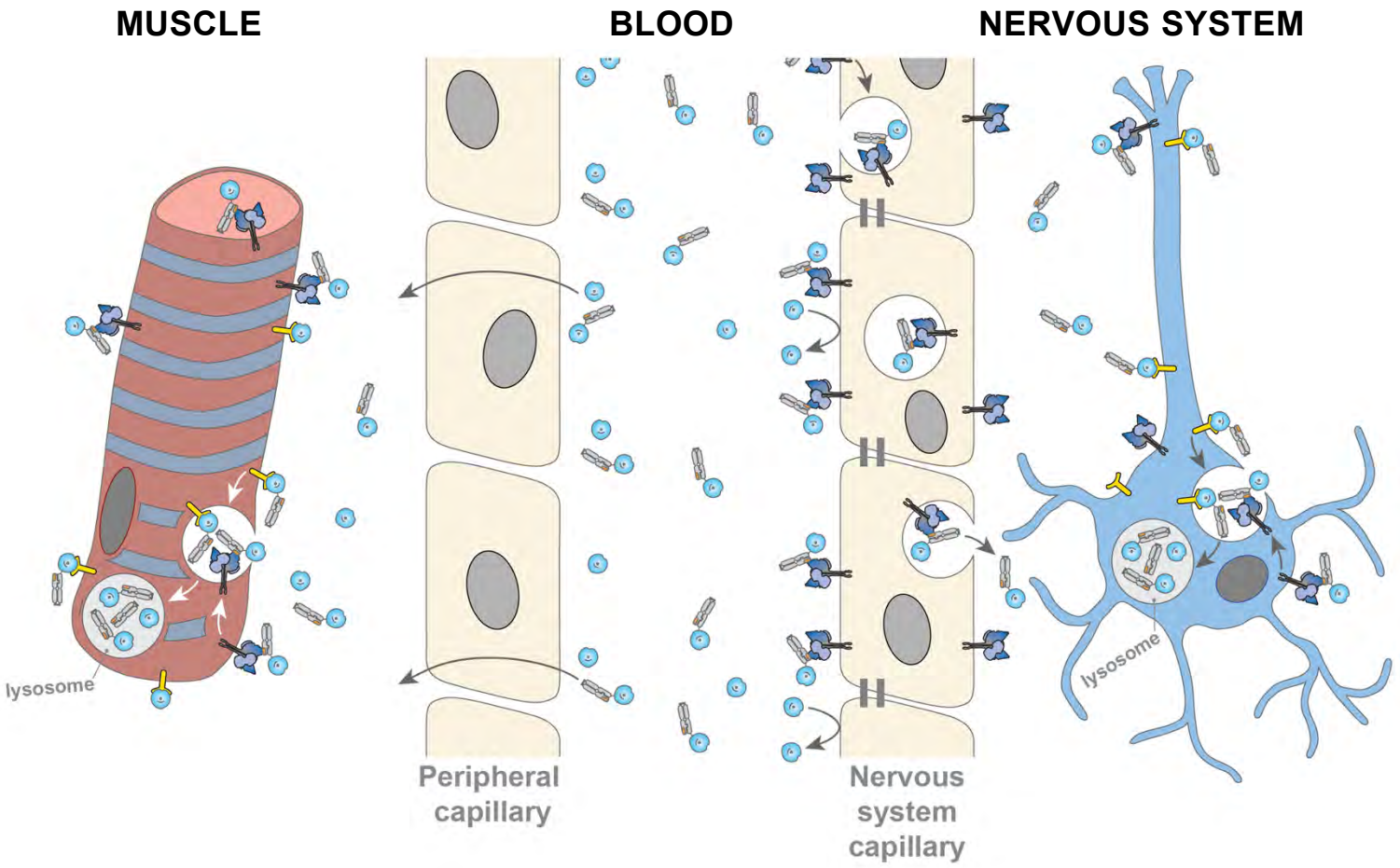
Wednesday February 4, 2026 from 15:30 to 17:30 PST

We thank the Denali Therapeutics team for their contributions to the study design.

DNL952 IS A NOVEL, INVESTIGATIONAL ERT FOR POMPE DISEASE DESIGNED TO IMPROVE GAA DELIVERY TO MUSCLE AND THE NERVOUS SYSTEM

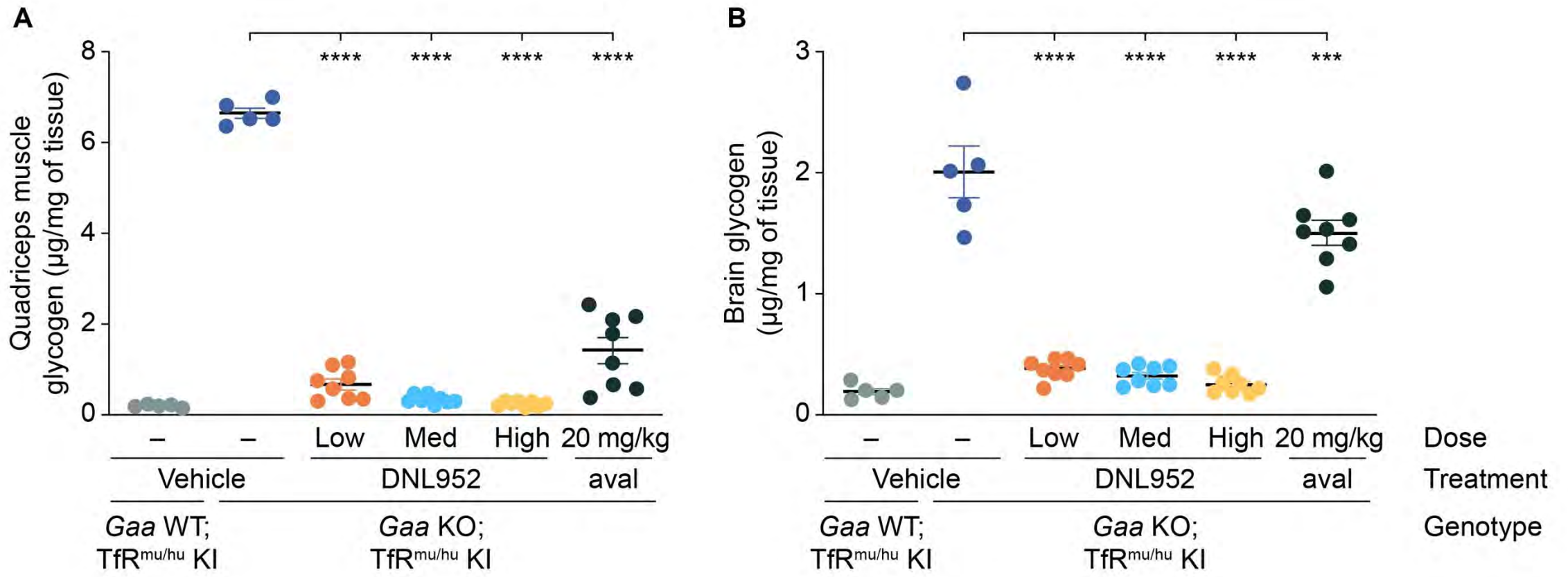
Denali's TransportVehicle™ (TV) platform harnesses the transferrin receptor (TfR) to enhance distribution via receptor-mediated cellular uptake and transcytosis





PD RESPONSE OF DNL952 AFTER MULTIPLE DOSES ADMINISTERED EOW SHOWS NEAR NORMALIZATION OF GLYCOGEN LEVELS IN MUSCLE AND BRAIN

Glycogen levels in (A) quadriceps muscle and (B) brain tissue measured at 14 days after the fifth dose

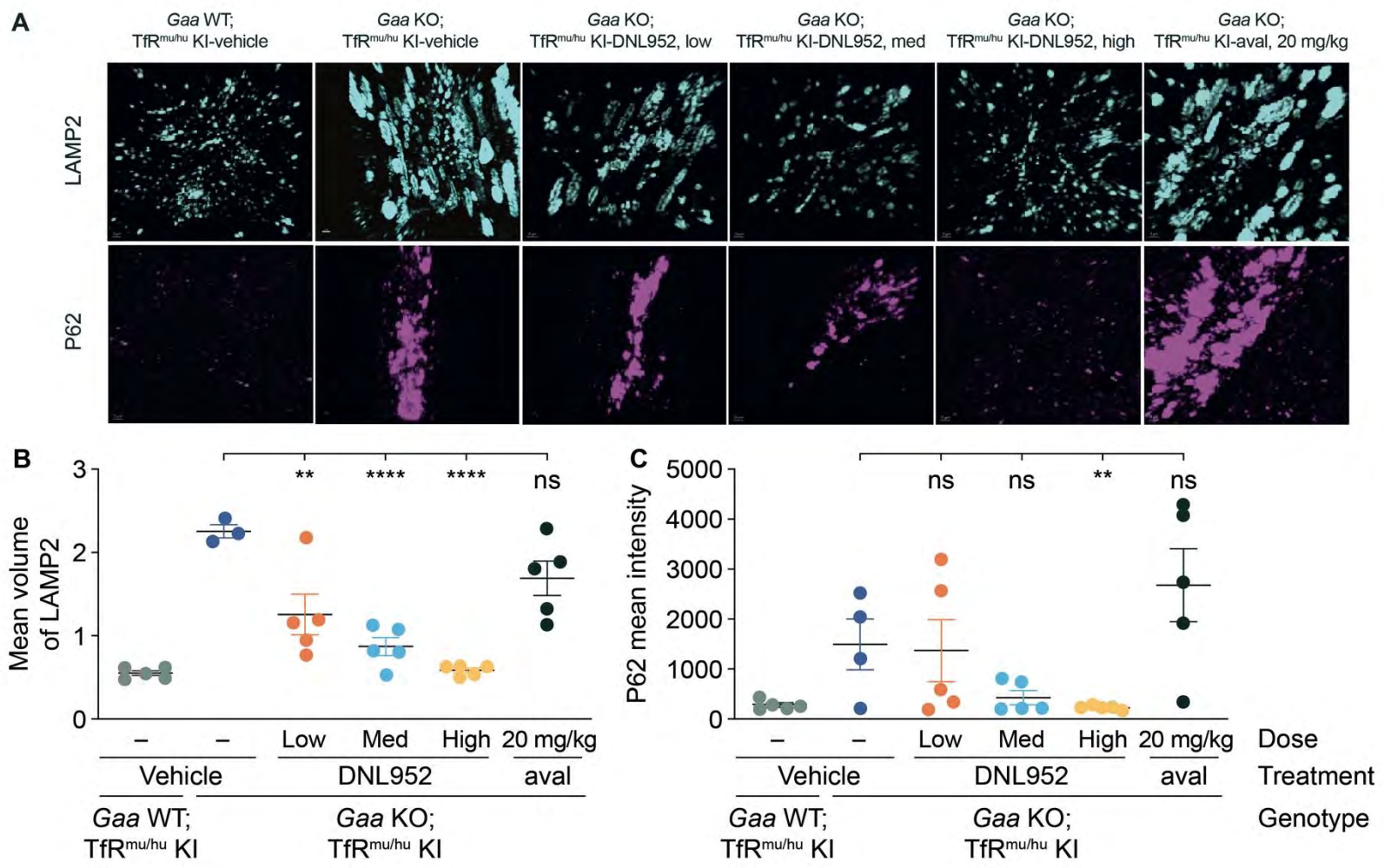


Repeated dosing with DNL952 achieved near-complete glycogen normalization in muscle and brain and demonstrated greater improvement than with avalglucosidase alfa

Gaa KO;TfR$^{mu/hu}$ KI animals (n = 8 per group) received five IV dosings of DNL952 (low, med, or high dose) or aval (20 mg/kg) administered EOW. Vehicle-treated *Gaa* WT;TfR$^{mu/hu}$ KI (n = 5) and *Gaa* KO; TfR$^{mu/hu}$ KI (n = 5) mice served as the nondisease and disease comparator groups, respectively. Levels were assessed using an LC-MS/MS–based method. Data are presented as mean ± SEM. ***P < 0.001; ****P < 0.0001

MULTIPLE DOSES OF DNL952 REDUCES MARKERS OF LYSOSOMAL AND AUTOPHAGIC DYSFUNCTION

Immunofluorescence staining with LAMP2 and P62 in quadriceps muscle after multiple doses



A Next-Generation ERT for Pompe Disease

Differentiated mechanism of action: Engaging the TfR + M6PR to improve cellular uptake & lysosomal delivery

Improved pharmacodynamic response: Enhanced correction of glycogen & downstream pathology, including autophagy

Potential to address nervous system involvement that contributes to deficits in IOPD & possibly weakness in LOPD

(A) Representative images of immunofluorescence of LAMP2 (cyan) and P62 (magenta) of *Gaa* WT;TfRmu/hu KI (n = 5) and *Gaa* KO;TfRmu/hu KI mice treated with vehicle, DNL952 (low, med, or high dose), or aval (20 mg/kg) at 14 days after the final dose are shown; n = 3–5 per group. Scale bar = 2 mm. (B,C) Data are mean ± SEM of quantified (B) LAMP2 and (C) P62 signal.
$^{**}P < 0.01$; $^{****}P < 0.0001$.

CONCLUSIONS AND DISCLOSURES

Conclusions

- Together, the in vitro and in vivo data highlight the differentiated mechanism of action of DNL952 and the speed, depth, and breadth of PD response of DNL952 in muscle and the nervous system, supporting the potential of DNL952 as an innovative new ERT for Pompe disease

Scan the QR code to
download a PDF of the
poster and supplemental file

This poster was sponsored by Denali Therapeutics Inc. **RP**, **CVP**, **HN**, **IB**, **MM**, **RG**, **CT**, **JA**, **SD**, **AR**, **RM**, **TY**, **JHS**, **MF**, **NG**, **AH**, S**H-R**, **SC**, **AA**, and **CM** are employees of Denali Therapeutics Inc., which has filed patent applications related to the subject matter.

A PHASE 1, MULTICENTER, OPEN-LABEL STUDY DESIGN TO EVALUATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF DNL952 IN ADULT PARTICIPANTS WITH LATE-ONSET POMPE DISEASE

Amy C Berger, Isaac V Cohen, Marisa Goo, Sarah Huntwork-Rodriguez, Shyeilla Dhuria, Matthew D Troyer, Carole Ho, Danna Jennings

Denali Therapeutics Inc., South San Francisco, CA, USA

WORLD*Symposium*™ 2026

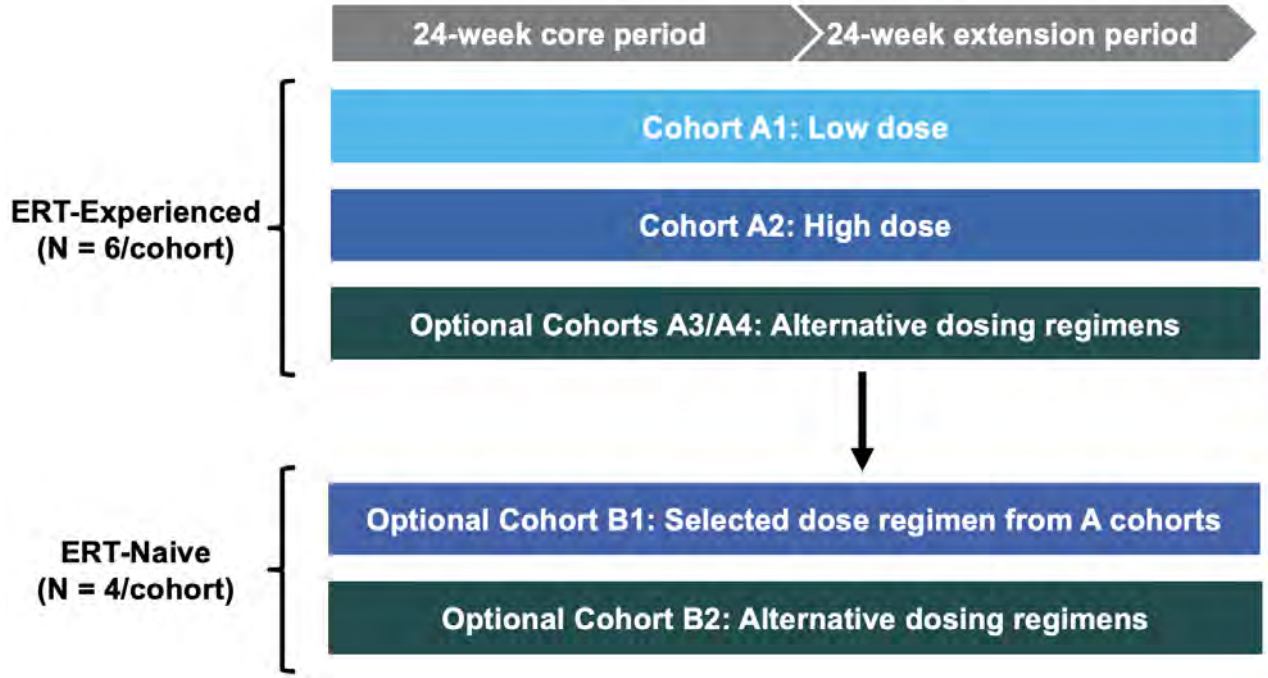
Thursday February 5, 2026 from 15:30 to 17:30 PST

We thank the Denali Therapeutics team for their contributions to the study design.

STUDY DNLI-J-0001: A PHASE 1 OPEN-LABEL STUDY OF DNL952

STUDY OVERVIEW

Key eligibility	All cohorts	• Age ≥ 18 and ≤ 75 years • Confirmed diagnosis of LOPD • Upright FVC ≥ 30% of predicted normal value • Able to ambulate ≥ 40 meters (use of assistive devices is acceptable)
	A cohorts: ERT-experienced	• Have received avalglucosidase alfa or cipaglucosidase alfa at a dose of 20 mg/kg every 2 weeks for at least 12 months
	Optional B cohorts: ERT-naïve	• Have not received any ERT for at least 12 months and have received no more than four total doses at any time
Sample size		• Up to 32 participants
Key endpoints	Primary	• Safety and tolerability
	Secondary	• PK and immunogenicity
	Exploratory	• PD: Urine Glc4, serum CK, and exploratory biomarkers • Efficacy: Motor and respiratory strength and function and patient-reported outcomes



CONCLUSIONS AND DISCLOSURES

- DNL952 is an investigational, next-generation ERT for Pompe disease that leverages the TfR to improve enzyme delivery to muscles and to the nervous system
- Study DNLI-J-0001 is the first-in-human study of DNL952
- Safety, PK, and PD data obtained in this study will support identification of a well tolerated and potentially effective dose for future studies in Pompe disease
- For more information, please visit ClinicalTrials.gov (NCT07354724)

Scan the QR code to download a PDF of this poster

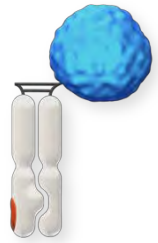
This poster was sponsored by Denali Therapeutics Inc. **ACB**, **IVC**, **MG**, **SH-R**, **SD**, and **DJ** are employees of Denali Therapeutics Inc., which has filed patent applications related to the subject matter. **CH** and **MDT** were employees of Denali Therapeutics Inc. at the time the study was designed.

Leading a New Era of BBB-Crossing Therapeutics

Conclusions

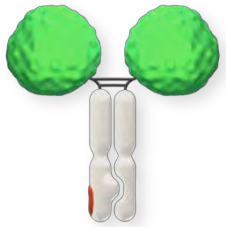
Ryan Watts, Ph.D.
Chief Executive Officer

Key Messages for Today



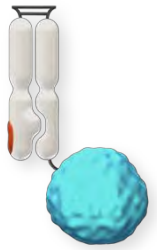
Tividenofusp alfa (ETV:IDS; DNL310)

- Analysis from continued follow-up of Phase 1/2 study in **Hunter syndrome (MPS II)** reinforces the potential for tividenofusp alfa (DNL310) to address the full disease spectrum
- We have established launch readiness in anticipation of April 5, 2026, Prescription Drug User Fee Act (PDUFA) date



ETV:SGSH (DNL126)

- Preliminary Phase 1/2 data in **Sanfilippo syndrome type A (MPS IIIA)** showed 80% mean CSF HS reduction and substantial reduction of disease biomarkers in the CNS and periphery
- Safety profile generally consistent with established ERTs
- Expect BLA filing and accelerated approval in 2027



ETV:GAA (DNL952)

- Design of ongoing DNL952 (ETV:GAA) Phase 1 clinical study presented in addition to preclinical data that shows therapeutic potential to treat both muscle and nervous system manifestations of **Pompe disease**
- Biomarker proof of concept data expected in 2027

Data and plans presented at this year's WORLD*Symposium*™ reflect the strong momentum of our Enzyme TransportVehicle™ franchise

ERTs – enzyme replacement therapies; **BLA –** Biologics License Application

Q&A