March 25, 2026

AVLAYAH™ (tividenofusp alfa-eknm) FDA Approval Conference Call

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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 plans, timelines, expectations related to Denali Therapeutics Inc.'s (“Denali” or the “Company”) 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 AVLAYAH™, including its therapeutic potential, efficacy, safety profile, availability, launch timing, patient access, support services, pricing, reimbursement, coverage, market access, adoption, and revenue growth; plans and expectations regarding the ongoing Phase 2/3 COMPASS study, including the availability and adequacy of data to support global approvals; expectations related to partnerships with AVLAYAH™ distributors and their ability to obtain ex-US approvals; plans, timelines, and expectations related to the ETV franchise and ETV-enabled programs, their therapeutic and commercial potential, and the timing and likelihood of planned regulatory filings; plans and expectations related to DNL126 (ETV:SGSH); plans and expectations regarding Denali's global organization and clinical 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; the potential market opportunities for AVLAYAH™ and other ETV programs; 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 commercial strategies and accelerate commercial launch; future results of operations and Denali's financial position; and statements by physicians, the patient community, and payers 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 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.

Except for AVLAYAH™, the product candidates being developed by Denali are investigational, their safety and efficacy profiles remain unestablished, and they have not been approved by any health authority for any use. AVLAYAH™ was approved by the FDA under the Accelerated Approval Program, and continued approval may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

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.

Introduction & Key Messages

Ryan Watts, Ph.D.
Chief Executive Officer

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Reaching the Summit with the MPS II Community




The biggest challenges in medicine demand unwavering collaboration with the patient community

MPS II – Mucopolysaccharidoses Type II

A New Era for Hunter Syndrome (MPS II) and for Denali

AVLAYAH™
(tividenofusp alfa-eknm)

Now Approved in the U.S.

Historic FDA Approval[1] for the MPS II Community

- First and only FDA-approved therapy for children with MPS II designed to reach the whole body, including the brain

Next-Generation Enzyme Replacement Therapy

- This approval marks the first therapeutic advancement for the MPS II community in 20 years

Validation of the TransportVehicle™ Platform

- First FDA-approved biologic therapeutic in a new class of medicines designed to cross the blood-brain barrier and address a broad range of diseases

Foundation of Our Lysosomal Storage Disorder (LSD) Franchise

- We are fully prepared for commercial launch, establishing the foundation for a strong and growing LSD franchise and leading the way for DNL126 in MPS IIIA

MPS II – Mucopolysaccharidoses Type II; **FDA** – U.S. Food and Drug Administration; **MPS IIIA** – Mucopolysaccharidoses Type IIIA; **1.** AVLAYAH™ [package insert]. March 2026. FDA granted approval under the FDA's Accelerated Approval Program. Continued approval for this indication, which was based on reduction of cerebrospinal fluid heparan sulfate, may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Today's Agenda

Topic	Speaker
Introduction & Key Messages	**Ryan Watts, Ph.D.,** Chief Executive Officer
Hunter Syndrome: Disease Overview & Unmet Need	**Peter Chin, M.D.,** Chief Medical Officer and Head of Development
AVLAYAH™ (tividenofusp alfa-eknm) Clinical Data & Label	
AVLAYAH™ Launch	**Katie Peng,** Chief Commercial Officer
Powering the Broader Denali Portfolio	**Ryan Watts, Ph.D.,** Chief Executive Officer
Q&A	**Ryan Watts, Ph.D.**, Chief Executive Officer **Peter Chin, M.D.**, Chief Medical Officer and Head of Development **Katie Peng**, Chief Commercial Officer **Alexander Schuth, M.D.**, Chief Operating and Financial Officer

Hunter Syndrome: Disease Overview & Unmet Need

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

Mucopolysaccharidosis Type II (Hunter Syndrome)

Underlying Cause and Disease Impact

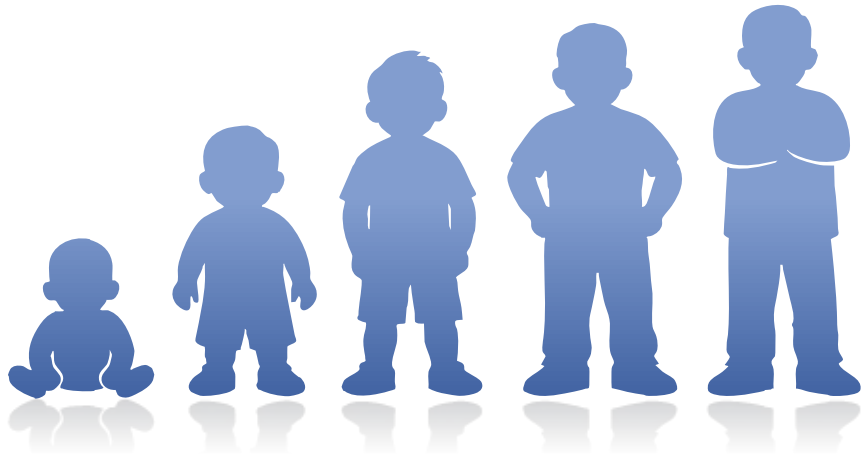
Genetic disorder caused by deficiency in the iduronate 2-sulfatase (IDS) enzyme[1]

Buildup of glycosaminoglycans (GAGs) affects systems throughout the entire body[1]

Gradual loss of function leads to increasing disability as the disease progresses[1]

Cardiac-respiratory failure is the most common cause of death in MPS II[2]

Clinical Course

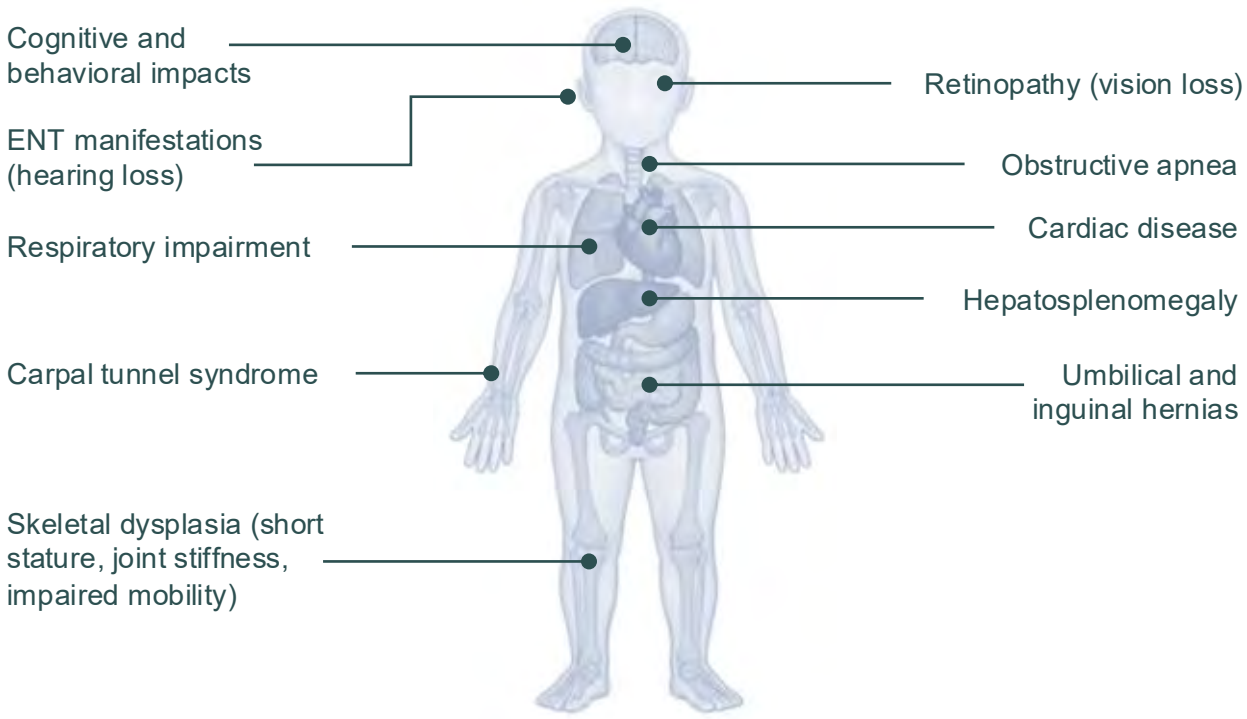


Diagnosis[3]	Birth ↔ 4 years
Progression[4]	Rapid ↔ Slow
Life Expectancy[1]	Teens ↔ Mid-Age

MPS II – Mucopolysaccharidoses Type II; **GAG** – Glycosaminoglycan; **ENT** – Ear, nose, and throat; **1.** Hashmi MS, Gupta V. Mucopolysaccharidosis Type II. [Updated 2023 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Accessed January 21, 2026. https://www.ncbi.nlm.nih.gov/books/NBK560829; **2.** D'Avanzo F, et al. *Int J Mol Sci*. 2020;21(4):1258; **3.** McBride KL, et al. *Genet Med*. 2020;22(11):1735-1742; **4.** Nan H, et al. *Biomed Res Int.* 2020:2408402.

MPS II: Progressive Spectrum Disease Affecting Body and Brain

Patients with MPS II are Affected in Most Organ Systems[1-4]



Neurologic Manifestations

- Cognitive[1,3,4], behavioral[1,3,4], hearing[1] and motor decline[5]
- Experienced by most patients[6,7]; severity spans the clinical spectrum

Peripheral Manifestations

- Multisystem involvement[8]
- Progressive somatic burden[8]

The broad range of systems impacted by MPS II necessitates a whole-body treatment approach

MPS II – Mucopolysaccharidoses Type II; **1.** Hashmi MS, Gupta V. Mucopolysaccharidosis Type II. [Updated 2023 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Accessed January 21, 2026. https://www.ncbi.nlm.nih.gov/books/NBK560829; **2.** D'Avanzo F, et al. *Int J Mol Sci*. 2020;21(4):1258; **3.** Ream MA, et al. *Genet Med*. 2023;25(2):100330; **4.** McBride KL, et al. *Genet Med*. 2020;22(11):1735-1742.; **5.** Phillips D et al, *Medical Research Archives*, 2024;12(11). Accessed March 19, 2026. https://doi.org/10.18103/mra.v12i11.5915; **6.** Lau H et al, *Mol Genet Metab Rep* 2023; 37:101005.; **7.** Wraith JE, Scarpa M, Beck M, et al. *Eur J Pediatr*. 2008;167:267-277; **8.** Nan H, et al. *Biomed Res Int.* 2020:2408402.

Therapeutic Goal: Treat the Whole Body, Including the Brain

Unmet Needs with Current Standard of Care Enzyme Replacement Therapy

Neurologic Manifestations

Current ERT does not cross the BBB and does not reduce CNS GAG accumulation[1-5]

Cognitive and behavioral symptoms and hearing loss are inadequately addressed by current therapy

Peripheral Manifestations

Patients may experience above-normal levels of urine GAGs even after treatment with current IV ERT[5,6]

Cardiac and skeletal symptoms are also often not addressed by current therapy[7]

New therapies are needed to adequately address both the neurologic and peripheral manifestations of MPS II

BBB – Blood-brain barrier; **CNS** – Central nervous system; **ERT** – Enzyme replacement therapy; **GAG** – Glycosaminoglycan; **IV** – Intravenous; **MPS II** – Mucopolysaccharidosis type II; **1.** Al-Hertani W, et al. *Int J Mol Sci.* 2024;25(16):8573; **2.** Giugliani R, et al. *Int J Mol Sci*. 2021;22(20):10938; **3.** Bhalla A, et al. *Int J Mol Sci*. 2020;21(15):5188; **4.** Argueta C, et al. *Mol Genet Metab.* 2025;144(3):109055; **5.** Muenzer J, et al. *Mol Genet Metab*. 2025;146(4):109284; **6.** Muenzer J, et al. *Genet Med*. 2011;13(2):95-101; **7.** Muenzer J. *Mol Genet Metab*. 2014;111(2):63-72.

AVLAYAH™ (tividenofusp alfa-eknm) Clinical Data & Label

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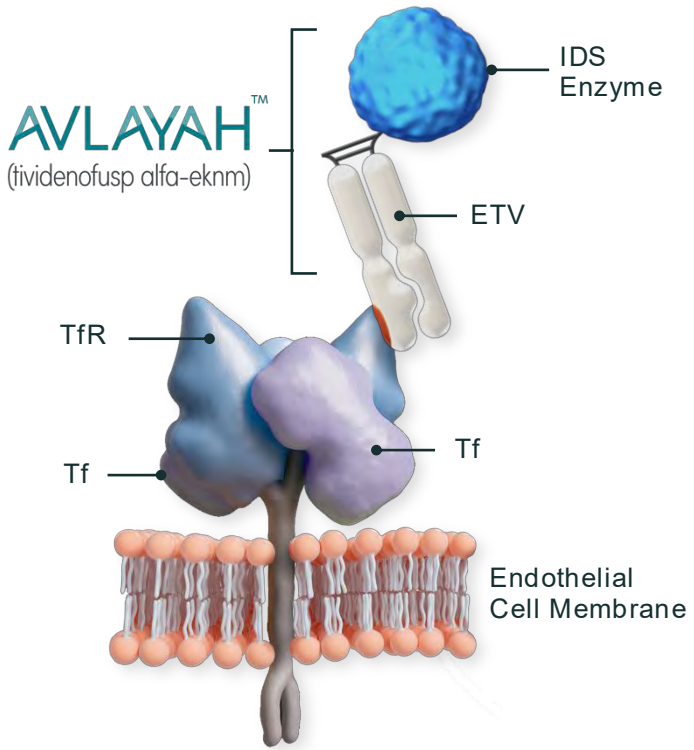
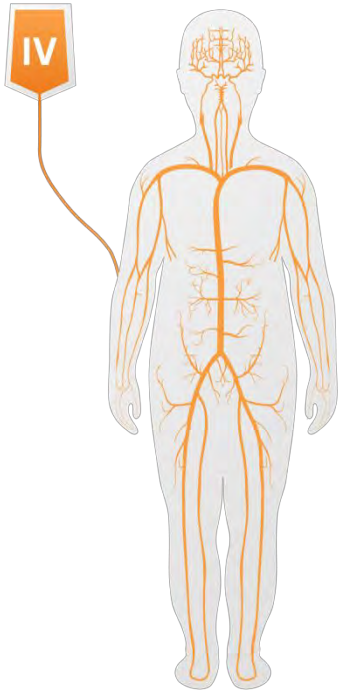
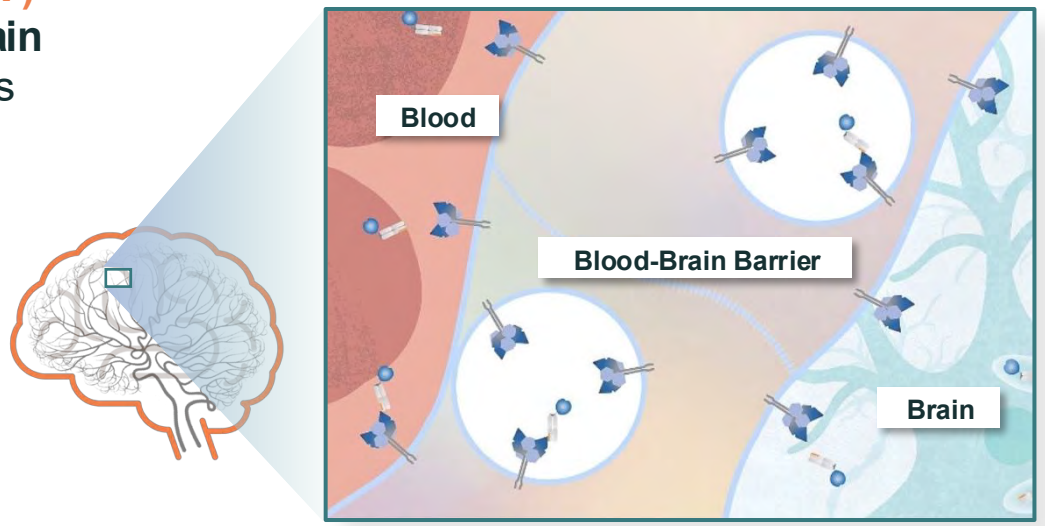
AVLAYAH™ Utilizes the Enzyme TransportVehicle™ (ETV) to Enable Delivery to the Brain and Periphery

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



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





Design of the TV is optimized to enable AVLAYAH™ to cross the blood-brain barrier

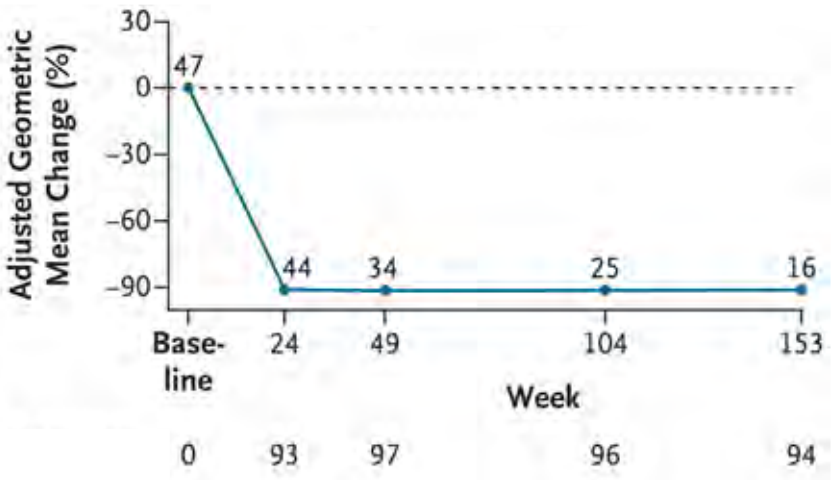
TfR binding may also facilitate delivery into other tissues

IDS – **I**duronate 2-sulfatase; **Tf** – Transferrin

Tividenofusp alfa-eknm Phase 1/2 Results in MPS II: Biomarkers

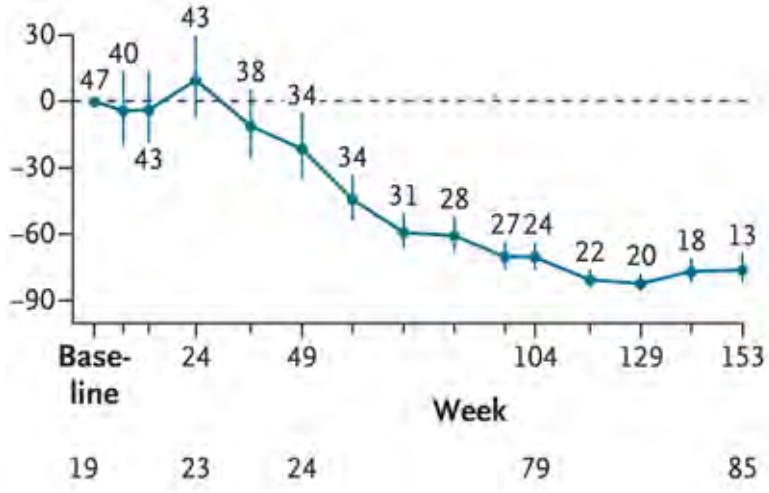
Normalization of CSF HS

Biomarker of CNS disease



Normalization of NfL

Biomarker of neuronal damage



Normalization of Urine HS

Biomarker of peripheral disease

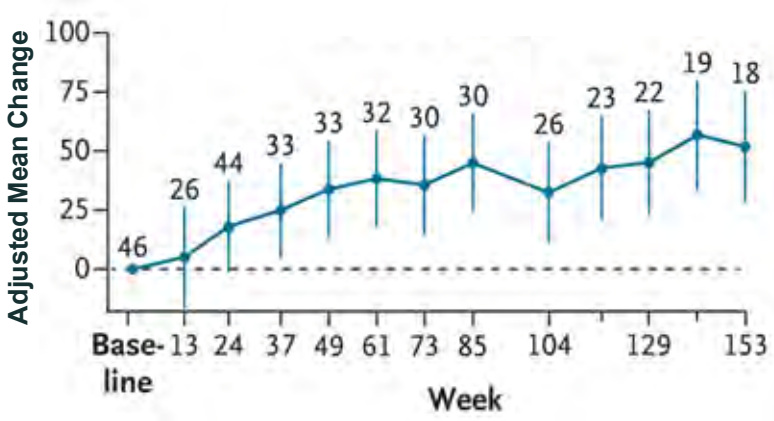
Treatment with tividenofusp alfa-eknm over a median duration of 2 years was associated with reductions in CNS and peripheral biomarkers of substrate accumulation and neuronal injury to levels within the range of unaffected children

MPS II – Mucopolysaccharidoses Type II; **CSF** – Cerebrospinal fluid; **HS** – Heparan sulfate; **NfL** – Neurofilament light; Source: Muenzer et al. 2026 *NEJM.*

Tividenofusp alfa-eknm Phase 1/2 Results in MPS II: Clinical

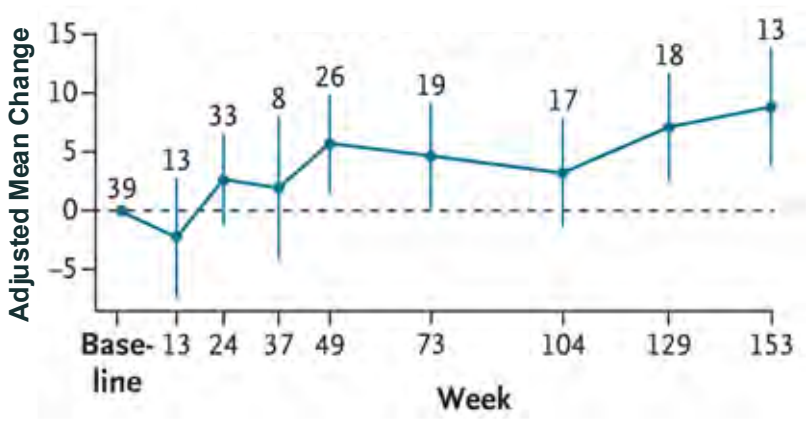
Improvement in Adaptive Behavior

Vineland-3



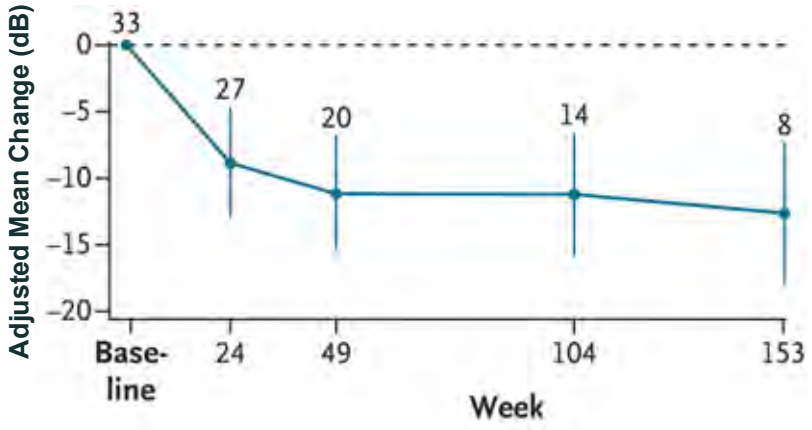
Improvement in Cognition

BSID-III



Improvement in Hearing

Auditory Brainstem Response (PTA)



While on tividenofusp alfa-eknm, clinical outcomes showed skill gains relative to baseline on measures of adaptive behavior, cognition and hearing threshold improvement

MPS II – Mucopolysaccharidoses Type II; **CI** – Confidence interval; **BSID-III** – Bayley Scales of Infant and Toddler Development-Third Edition; **PTA** – Pure tone average. Source: Muenzer et al. 2026 *NEJM*.

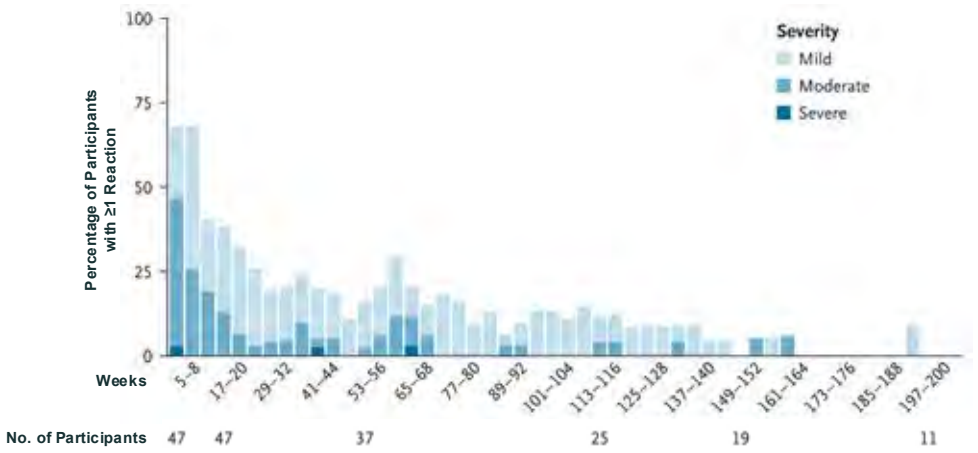
Tividenofusp alfa-eknm Phase 1/2 Results in MPS II: Safety

Summary of Adverse Events

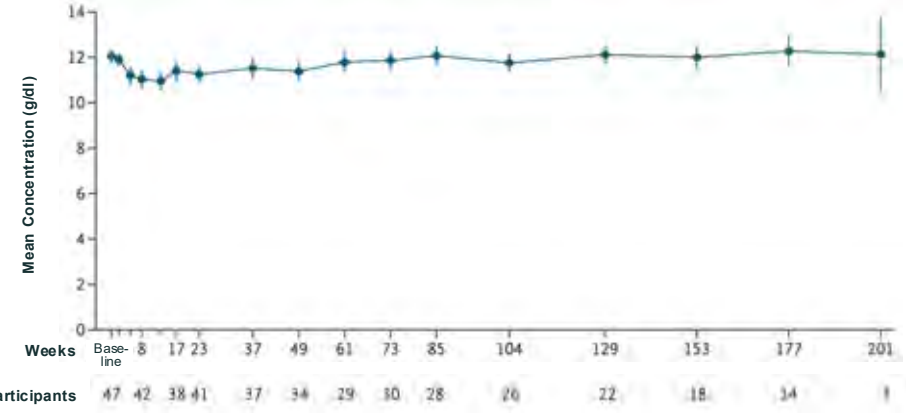
(Safety Analysis Population)

Event	Part 1: 24-Week Treatment Period (N=47)	Part 2: 80-Week Safety Extension (N=46)	Part 3: 157-Week Open-Label Extension (N=27)	All Periods (N=47)
	number of participants (percent)			
Adverse event†	47 (100)	41 (89)	25 (93)	47 (100)
Mild	8 (17)	3 (7)	8 (30)	2 (4)
Moderate	35 (74)	30 (65)	15 (56)	32 (68)
Severe	4 (9)	8 (17)	2 (7)	13 (28)
Serious adverse event‡	6 (13)	11 (24)	4 (15)	18 (38)
Treatment-related serious adverse event§	3 (6)	0	0	3 (6)
Adverse events of special interest¶				
Infusion-related reaction	27 (57)	15 (33)	4 (15)	29 (62)
Anemia	11 (23)	2 (4)	1 (4)	11 (23)
Adverse event leading to discontinuation of study participation	1 (2)	0	0	1 (2)
Adverse event leading to dose reduction	22 (47)	11 (24)	4 (15)	27 (57)
Adverse event leading to dose interruption	34 (72)	37 (80)	15 (56)	43 (91)
Most frequent adverse events				
Infusion-related reaction	39 (83)	26 (57)	11 (41)	41 (87)
Upper respiratory tract infection	11 (23)	20 (43)	8 (30)	28 (60)
Pyrexia	11 (23)	17 (37)	6 (22)	26 (55)
Cough	8 (17)	14 (30)	6 (22)	22 (47)
Vomiting	14 (30)	10 (22)	6 (22)	20 (43)
Diarrhea	9 (19)	10 (22)	4 (15)	19 (40)
Rash	10 (21)	8 (17)	6 (22)	19 (40)
Anemia	18 (38)	3 (7)	2 (7)	18 (38)
Covid-19	6 (13)	13 (28)	2 (7)	18 (38)
Rhinorrhea	9 (19)	8 (17)	4 (15)	18 (38)

Infusion-Related Reactions Over Time



Hemoglobin Levels Over Time



Infusion-related reactions, a known risk of ERTs, were the most common adverse event, decreasing in incidence and severity over time

MPS II – Mucopolysaccharidoses Type II; **ERTs** – Enzyme Replacement Therapies; Source: Muenzer et al. 2026 NEJM

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Select Highlights of AVLAYAH™ U.S. Prescribing Information

Indications and Usage	• AVLAYAH™ is indicated for the treatment of neurologic manifestations in patients with Hunter syndrome (MPS II) when initiated in presymptomatic or symptomatic pediatric patients weighing at least 5 kg prior to advanced neurologic impairment • AVLAYAH™ is not recommended for use in combination with other enzyme replacement therapies
Dosage and Administration	• Recommended AVLAYAH™ maintenance dosage is 15 mg/kg administered once weekly as an intravenous infusion over ~4 hours • AVLAYAH™ treatment should be initiated with a dose escalation regimen
Clinical Studies and Pharmacodynamics	• **CSF HS:** Treatment with AVLAYAH™ resulted in a significant 91% mean reduction of CSF HS from baseline with 93% of patients having CSF HS levels below the upper limit of normal (ULN) at Week 24 • **Urine GAGs:** At baseline, 4% of patients had total urine GAG levels below the ULN. After treatment with AVLAYAH™ 68% of patients had total urine GAG levels below the ULN at Week 24
Safety	• Boxed warning regarding hypersensitivity (including anaphylaxis) consistent with other approved ERTs • Infusion-Associated Reactions: Manage with monitoring and infusion rate adjustment; discontinue if severe • Anemia: Typically early onset and manageable with supportive care; monitor hemoglobin • Membranous Nephropathy: one case reported; monitor serum creatinine and urine protein to creatinine ratio

MPS II – Mucopolysaccharidoses Type II; **CSF** – Cerebrospinal fluid; **HS** – Heparan sulfate; **GAG** – Glycosaminoglycan; **ERTs** – Enzyme replacement therapies

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Clear Path from Accelerated to Full Approval

Phase 1/2 Study

47 participants

AVLAYAH™
(tividenofusp alfa-eknm)

U.S. Accelerated Approval Achieved

Supports Select Country Approvals

Phase 2/3 Confirmatory Study

63 participants

COMPASS

Supporting Conversion to U.S. Full Approval, Label Expansion and Global Approvals

AVLAYAH™ Launch

Katie Peng
Chief Commercial Officer

Setting a New Bar for the Treatment of MPS II

AVLAYAH™
(tividenofusp alfa-eknm)

The first FDA-approved enzyme replacement therapy (ERT) to cross the **blood-brain barrier** to reach the brain in addition to the body

9 out of 10

individuals had normal levels* of CSF HS after 6 months and 12 months of treatment

At the start of the study, 0 individuals had normal levels* of CSF HS; the majority had previously received ERT

9 out of 10

individuals had normal levels* of uGAGs after 12 months of treatment

At the start of the study, 2 individuals had normal levels* of uGAGs; the majority had previously received ERT

* "Normal levels" refers to biomarker levels typically seen in people without Hunter syndrome; **MPS II** – Mucopolysaccharidoses Type II; **CSF** – Cerebrospinal fluid; **HS** – Heparan sulfate; **uGAGs** – Urine glycosaminoglycans; **ERT** – Enzyme replacement therapy; All strategies and tactics are subject to Legal review prior to implementation. Source: Muenzer et al. 2026 *NEJM*.

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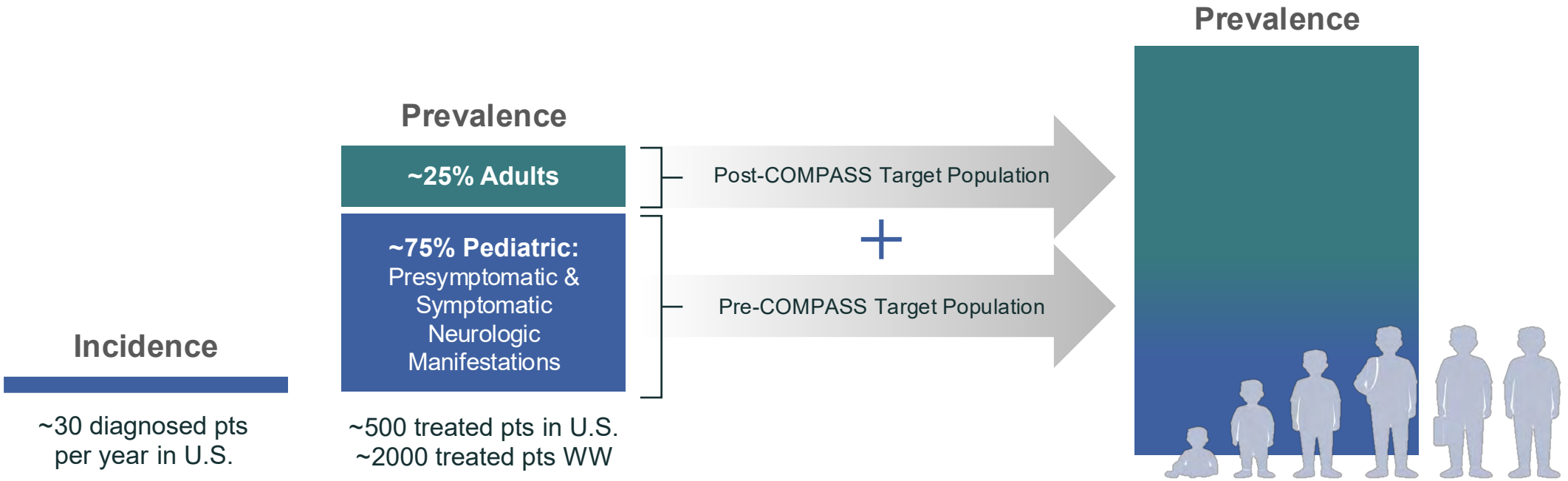
AVLAYAH™ Has the Potential to Reduce Disease Burden, Leading to Growth in the MPS II Population

Current Standard of Care Paradigm

The prevalent MPS II population reflects a higher early death rate for individuals born with severe disease

Potential Future Treatment Paradigm

Potential for a larger MPS II population over time as disease burden is reduced



MPS II – Mucopolysaccharidosis type II; **Pts** – Patients; **WW** – Worldwide; All strategies and tactics are subject to Legal review prior to implementation.

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Our Stakeholders Are Ready and Waiting for AVLAYAH™

Physicians[1]

90% **view AVLAYAH™'s data as highly motivating to prescribe**

- Recognize significant **unmet needs** across **brain and body**
- **No overall concerns** with safety profile

"This novel treatment should have a profound impact on individuals and families living with this devastating disease."

— MPS II HCP

Patients & Caregivers[2]

80% **are aware of new treatments coming and excited to try AVLAYAH™**

- Perceive significant **unmet needs**, across **brain and body**
- **Advocacy orgs** and **peer-to-peer** communications **most influential**

"We are hopeful a new treatment will be approved by the FDA that will benefit him neurologically, as well as his overall quality of life."

— Recently diagnosed Hunter family

Payers[3]

90% **of commercial lives represented in conversations with payers**

- **Perceive therapeutic benefit** due to ability to cross the BBB
- View AVLAYAH™'s **benefit/risk profile favorably**

"We recognize the clinical need for the MPS II patients and will likely manage to FDA approved label."

— US Commercial Payer

1. HCP Insights from HCP Survey (N=68) conducted in Q1 2025 and from KOL Adboard conducted March 2025; **2.** Caregiver Insights from Caregiver Survey (N=47) Conducted Q4 2024;
3. Payer Insights from AdBoard conducted April 2025 and Payer Engagements; All strategies and tactics are subject to Legal review prior to implementation.

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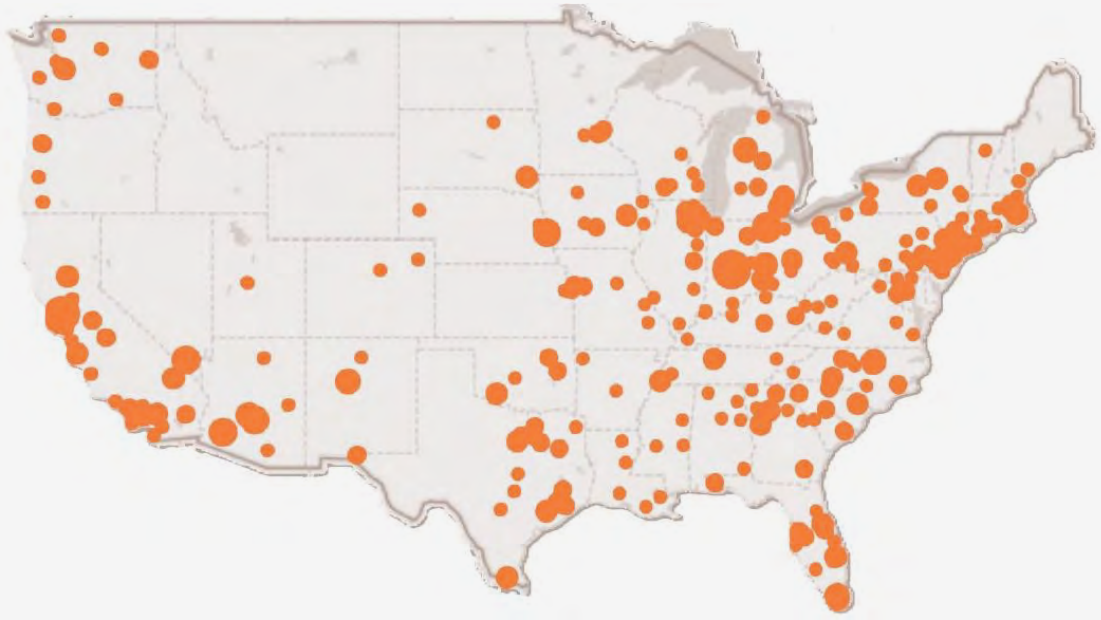
Concentrated Stakeholders Enable Us to Reach All Treaters Across the 80 to 100 Centers of Excellence in the U.S.

MPS II Patient Distribution



~500 patients in the U.S. on SoC ERT

Most MPS II patients treated by **clinical geneticists at ~80-100 genetic centers**

Denali has **established relationships** with **all major** MPS II treatment centers

Sales force **has profiled and segmented** all accounts with MPS II patients **to optimize execution**

MPS II – Mucopolysaccharidosis type II; **ERTs** – Enzyme replacement therapies; All strategies and tactics are subject to Legal review prior to implementation.

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Built a Winning Team Ready for Launch

Launch Leadership Team

Significant Experience Across Functions

- Product Strategy
- U.S. and Global Marketing
- U.S. / Ex-U.S. Market Access
- Market Planning and Analytics
- Medical Affairs & Med Info
- Field Sales
- Field Medical
- Patient Advocacy

19 Product/Indication Launches for Global Blockbusters

- Including Rare Diseases

US Field Team

Deep Industry and Disease Expertise

- 25 Years Average Biopharma Industry Experience
- 96% LSD / Rare Disease Experience
- Average Rare Disease Experience: 12 Years

Multiple Successful Product Launches

- All Rare Diseases

LSD – Lysosomal storage disorders; All strategies and tactics are subject to Legal review prior to implementation.

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Our Pricing Principles

Access

Enable broad, equitable, and sustainable access for patients, the healthcare system, and society

Affordability

Address affordability by providing comprehensive support to patients and families

Fuel R&D

Ensure our ability to fuel R&D in the pursuit of meaningful and impactful treatments

Value of Our Medicines

Reflect the clinical, economic, and societal value delivered by our medicines

AVLAYAH™'s price reflects its therapeutic value and commitment to broad access

All strategies and tactics are subject to Legal review prior to implementation.

Denali Patient Services Supporting Patients and Caregivers

DENALI
Patient Services

We know every patient's journey is unique. **Denali Patient Services** offers personalized support services to patients, caregivers, and providers navigating therapy with AVLAYAH™

CARE

Compassion, Assistance, Resources, and Education

Your dedicated **Denali CARE Partner** is here for you throughout your treatment journey

Our Denali CARE Team is here to help with:

- **Insurance Coverage**
- **Treatment Coordination**
- **Information and Resources**
- **Financial Assistance**

All strategies and tactics are subject to Legal review prior to implementation.

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AVLAYAH™ Aligned with Rare Disease Launch Dynamics

2026: Building the Foundation Across Key Stakeholders for Revenue Acceleration

Physicians

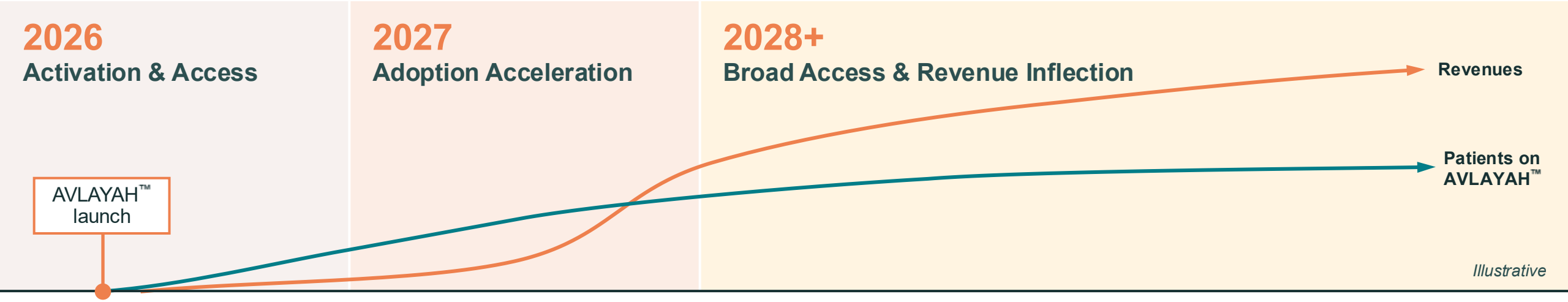
- Support procurement & access challenges
- Instill clinical belief of AVLAYAH™ Activate Centers of Excellence
- In-service & infusion education
- Scientific exchange

Payers

- Secure commercial coverage policies
- Advance Medicaid coverage
- Operationalize prior authorization and medical exception process
- Reduce time from prescription to coverage approval

Patients & Caregivers

- Launch with the advocacy community
- Drive awareness and consideration
- Support patients access to treatment
- Reduce time from prescription to first infusion



All strategies and tactics are subject to Legal review prior to implementation.

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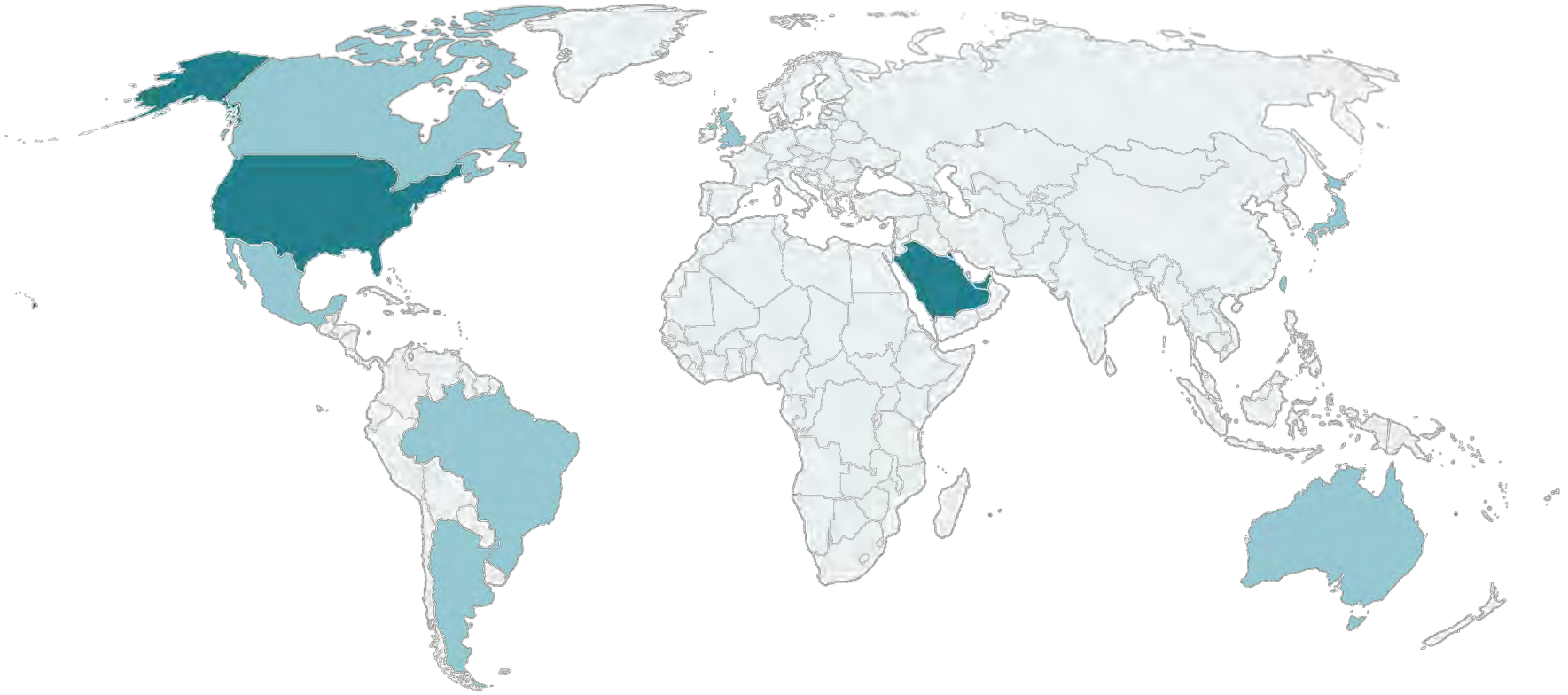
Majority of Global Market Available Based on U.S. Accelerated Approval and/or Phase 1/2 Data



~33% of Market
Short Term[1] (2026-2027)

~33% of Market
Mid-Term[1] (2027-2028)

~33% of Market
Longer Term (2028+)

- We will pursue ex-U.S. approvals via the U.S. Certificate of Pharmaceutical Product (CPP) for marketing authorization or conditional pathways, as available
- We are targeting all ~2,000 patients worldwide in commercially accessible geographies
- Distributor partnerships established across select LATAM and MENA

Note: Based on estimated worldwide split of idursulfase annual revenues of $650M to $700M, assuming we launch in ~90-95% of idursulfase geographies; **1.** COMPASS Phase 2/3 data not needed for regulatory filings; All strategies and tactics are subject to Legal review prior to implementation.

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Key Messages for Today

First Meaningful Advancement in 20 Years

Fully Built Rare Disease Commercial Team

AVLAYAH™
(tividenofusp alfa-eknm)

Favorable Competitive Landscape

Community Ready and Waiting

Powering the Broader Denali Portfolio

Ryan Watts, Ph.D.
Chief Executive Officer

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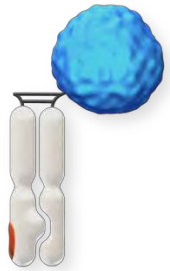
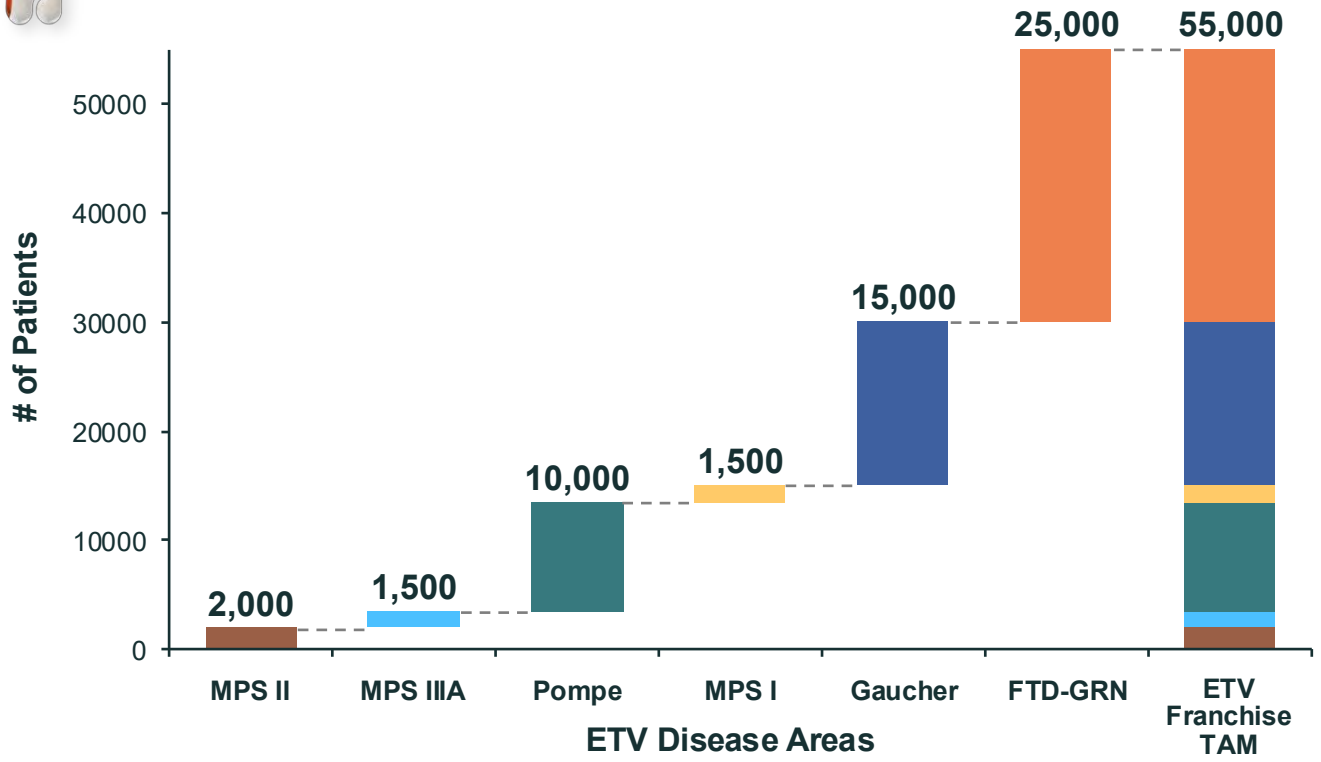
ETV: Foundational Franchise for Lysosomal Storage Disorders



Enzyme TransportVehicle™ (ETV) Franchise

Worldwide Patient Prevalence



Delivering Next-Generation Enzyme Replacement Therapy (ERT)

- ETV platform uniquely addresses neurologic and systemic disease
- Leverage existing infrastructure to drive margins
- Scalable launch model across rare disease franchise
- Large, validated ERT market with 24 approvals[1] (~$9B in sales for marketed therapies[2])

1. Based on systemic ERTs with regulatory approvals in at least one major market (US, EU, Japan), excluding two ERTs that have been discontinued (Adagen and Ceredase), including AVLAYAH™; **2.** Based on Denali internal assessment as of Nov '25 and other syndicated data (Evaluate Pharma, Historic Annual WW Product Sales 2024, downloaded Dec 1 2025, GC Pharma 2024 Investor Day Deck (https://www.gcbiopharma.com/eng/upload/CAO/C55/202510/9e38f129-d9f2-4307-bc4f-ca54f2340512.pdf). Protalix 2024 10-K, GMI Report 2024 (Oct'24, https://www.gminsights.com/industry-analysis/exocrine-pancreatic-insufficiency-treatment-market). USA vs QOL Medical Lawsuit (Filed July'24, https://www.mass.gov/doc/qol-medical-lawsuit/download). **TAM** – Total Addressable Market; **ETV –** Enzyme TransportVehicle™

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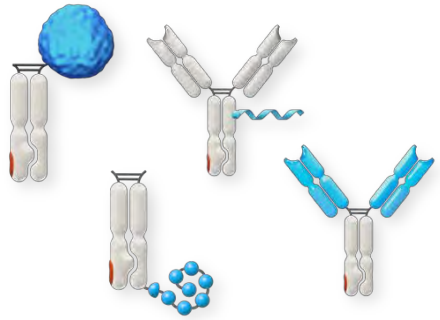
We Have Reached Our First Summit with AVLAYAH™

AVLAYAH™
(tividenofusp alfa-eknm)



Proof

1st FDA-approved biologic designed to cross the blood-brain barrier

Platform

TransportVehicle™ validated in humans, enabling a new class of biologic medicines

Pipeline

ETV franchise foundation fuels expansion into neurodegenerative and other serious diseases

Patients

From rare to common diseases, aiming to transform life for millions worldwide

We remain steadfast in our purpose of transforming life for patients

FDA – U.S. Food and Drug Administration; **ETV** – Enzyme TransportVehicle™

Q&A

DENALI

Thank You