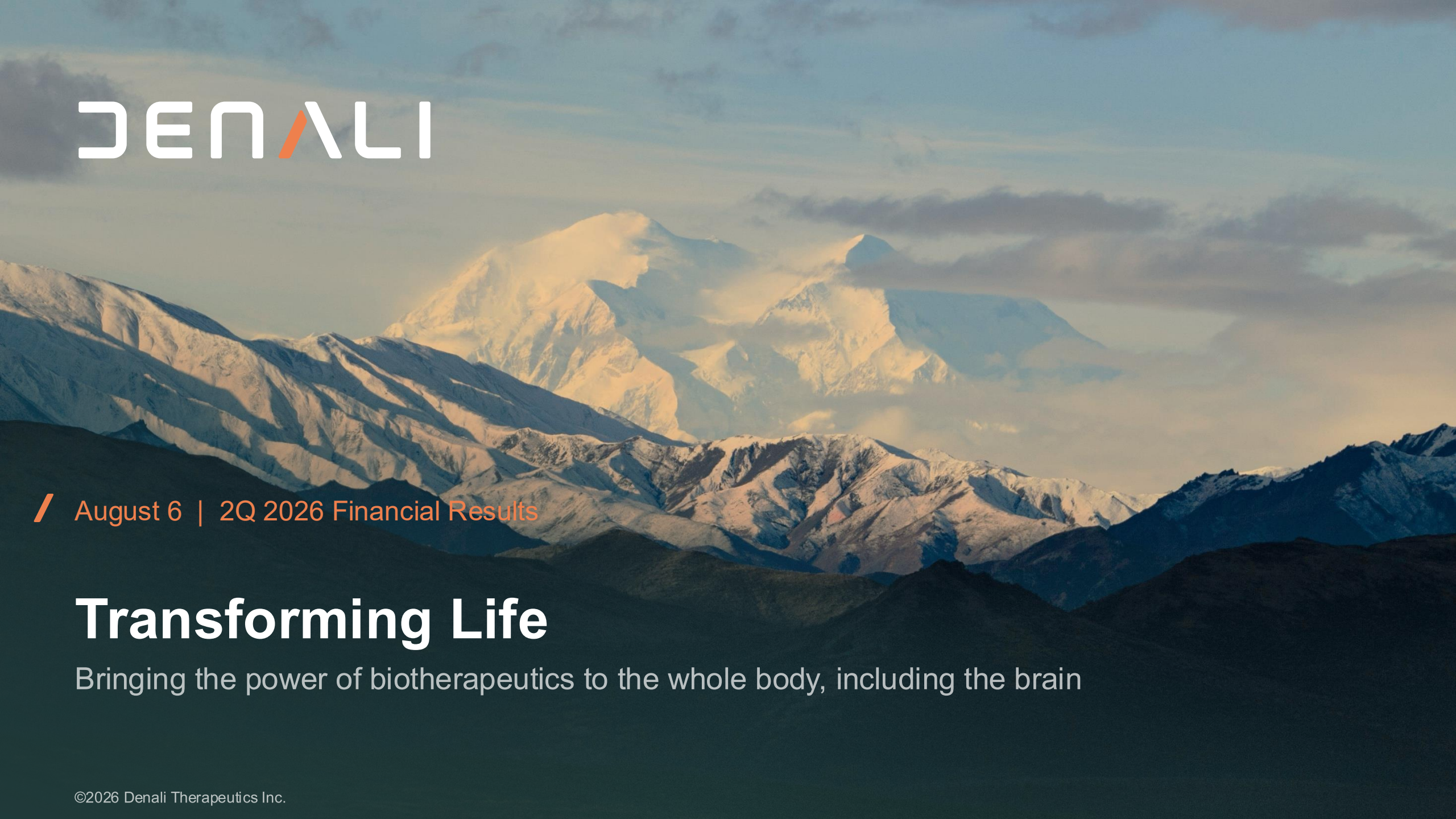


August 6 | 2Q 2026 Financial Results

Transforming Life

Bringing the power of biotherapeutics to the whole body, including the brain

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 "Company"); Denali’s business strategy and business plans, forecasts for revenue and operating expenses, expected progress and expansion, and expected key milestones for Denali's therapeutic portfolio in 2026, 2027, and beyond; plans, timelines, and 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 and first-in-class; plans, timelines, and expectations related to the ETV franchise and ETV-enabled programs, including ETV:SGSH, PTV:PGRN, ETV:GAA, ETV:GCase, and ETV:IDUA, their therapeutic and commercial potential, and the number of patients worldwide for each program; plans, timelines, and expectations relating to AVLAYAH™, including planned launch dynamics, estimated patient and revenue growth, and the likelihood of becoming standard of care for Hunter syndrome; expectations relating to DNL310 and the ongoing Phase 2/3 COMPASS study, including the timing, likelihood, and scope of regulatory approvals and the potential to support a broader indication for AVLAYAH™; plans, timelines, and expectations related to DNL126 (ETV:SGSH), including the timing and likelihood of regulatory approval; plans, timelines, and expectations related to AD treatments and their therapeutic and commercial potential; plans, timelines, and expectations relating to DNL921 (ATV:Abeta), including its best-in-class potential, the Phase 1/1b clinical study, and the timing and availability of data; plans and expectations relating to DNL628 (OTV:MAPT), including its first-in-class potential and the timing and availability of data from the ongoing Phase 1b study; plans and expectations regarding DNL593 (PTV:PGRN), the ongoing Phase 1/2 study, the timing and availability of data, and the potential for accelerated approval; 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; 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.

Except for AVLAYAH™, the product candidates being developed by Denali are investigational and their safety and efficacy profiles remain unestablished. Except for AVLAYAH™, 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.

Agenda and Speakers

A G E N D A

Opening Remarks – Ryan Watts, Ph.D., CEO

Commercial Update – Katie Peng, CCO

Pipeline Highlights – Ryan Watts, Ph.D., CEO

Financials – Alexander Schuth, M.D., COO/CFO

Q&A

Ryan Watts, Ph.D.
Chief Executive Officer

Alexander Schuth, M.D.
Chief Operating and Financial Officer

Katie Peng
Chief Commercial Officer

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

CEO Opening Remarks

Ryan Watts, Ph.D., CEO

Our Purpose: Transforming Life for People with Serious Diseases

We bring the power of biotherapeutics to the whole body, including the brain.




Rare Genetic Diseases

Hunter (MPS II) / Sanfilippo (MPS IIIA) / FTD-*GRN* / Pompe / Gaucher / Hurler (MPS I)

>30,000
Patients Worldwide[1]

Common Neurodegenerative Diseases

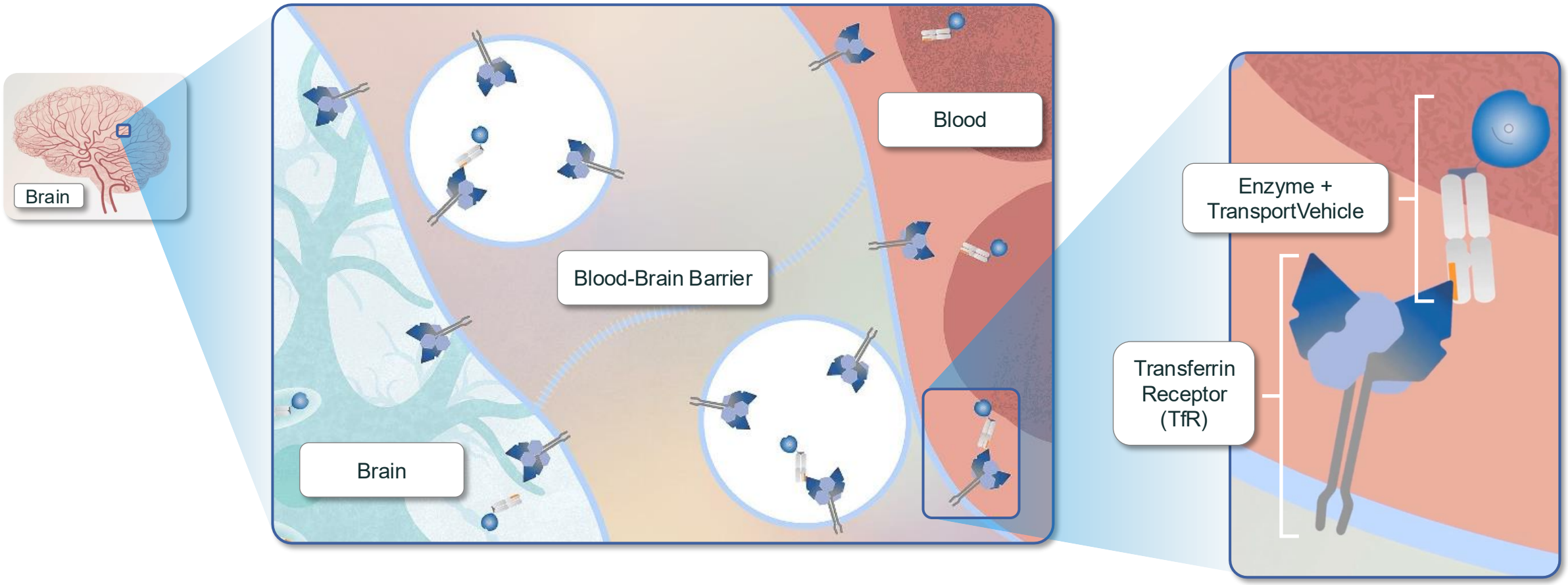
Alzheimer's disease / Parkinson's disease

>40M
Patients Worldwide[1]

1. Denali estimates of worldwide aggregate prevalence, excluding China and India for the lysosomal storage disorders; MPS – Mucopolysaccharidosis

Addressing the Challenge of Delivering Therapy to the Brain

The TransportVehicle™ (TV) is engineered to deliver efficacious concentrations of biotherapeutics across the blood-brain barrier via receptor-mediated transcytosis



Now Approved in the U.S.

AVLAYAH™

(tividenofusp alfa-eknm)

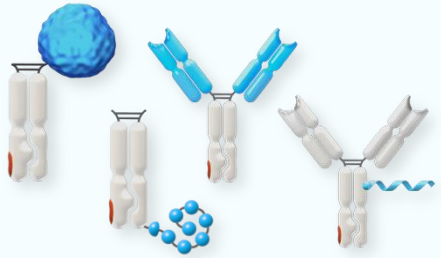
AVLAYAH™ (tividenofusp alfa-eknm), an enzyme replacement therapy, received accelerated approval from the U.S. Food and Drug Administration for the treatment of neurologic manifestations of Hunter syndrome (mucopolysaccharidosis type II) when initiated in presymptomatic or symptomatic pediatric patients weighing at least 5 kg prior to advanced neurologic impairment.

A Powerful Combination: Product, Pipeline, Platform, Capital

AVLAYAH™
(tividenofusp alfa-eknm)

Commercial Product

First FDA-approved product designed to cross the BBB; strong commercial launch and growing brand

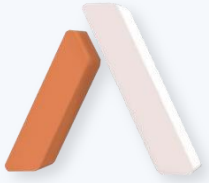


Broad Pipeline

7 clinical programs from rare diseases to Alzheimer's; market opportunity >$10B

Validated TV Platform

Leading BBB technology and team: >350 patents, >20 high-impact publications, >200 patients dosed, >30 dedicated PhD BBB scientists



Operational & Financial Scale

Fully integrated capabilities from discovery to commercial, including own manufacturing; >$1B cash[1]

Denali is built to deliver near-term growth and long-term value

1. Includes cash, cash equivalents and marketable securities of ~$940.0 million as of June 30, 2026, and $195 million in gross proceeds received in July 2026 from the sale of a Priority Review Voucher
FDA – U.S. Food and Drug Administration; TV – TransportVehicle; BBB – blood-brain barrier

2Q 2026 Highlights: A Transformative Quarter for Denali

Commercial

AVLAYAH™
(tividenofusp alfa-eknm)

$3.6 Million
net product revenue in first full commercial quarter

Pipeline

Alzheimer's Disease

DNL628 (OTV:MAPT) & DNL921 (ATV:Abeta)
initiated clinical development with data expected in 2027

Financials

Positioned to Deliver

~$1.1 Billion
pro forma[1] cash, cash equivalents and marketable securities

Strong commercial launch, pipeline expansion into Alzheimer's, and financial strength establish a foundation for near-term growth and long-term value

1. Includes cash, cash equivalents and marketable securities of ~ 940.0 million as of June 30, 2026, and $195 million in gross proceeds received in July 2026 from the sale of a Priority Review Voucher

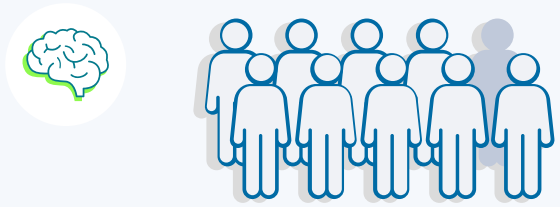
Commercial Update

Katie Peng, Chief Commercial Officer

Setting a New Bar for the Treatment of MPS II

AVLAYAH™
(tividenofusp alfa-eknm)

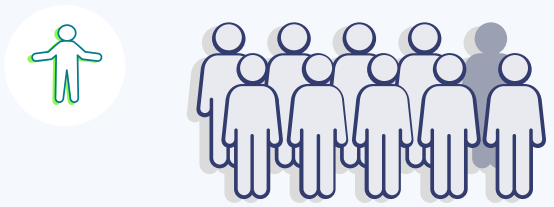
The first FDA-approved enzyme replacement therapy (ERT) to cross the **blood-brain barrier** to reach the brain in addition to the body



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

The most common adverse reaction was infusion-related reactions

* "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*.

AVLAYAH™ is Approved in the U.S. for ~375 Eligible Patients

Global MPS II Population

~2,000

Patients Worldwide Currently Receiving ERT Treatment for Hunter Syndrome in Addressable Markets[1]

~25%

Located in U.S.

U.S. MPS II Population

~500

Prevalent Patients

~30

Incident Patients per Year

~75%

Eligible per FDA Label

Current Eligible MPS II Population[2]

~375

Eligible Patients

Long term goal is to serve all patients with Hunter Syndrome globally, supported by the ongoing Phase 2/3 COMPASS Study

1. Source: EvaluatePharma (excluding China, India and Russia); 2. AVLAYAH is indicated for the treatment of neurologic manifestations of MPS II when initiated in presymptomatic or symptomatic pediatric patients weighing at least 5 kg prior to advanced neurologic impairment.

Strong Momentum with AVLAYAH ™ Launch

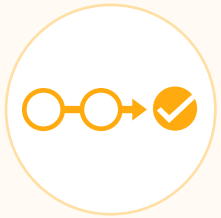
2026: Building the Foundation Across Key Stakeholders for Revenue Acceleration

Reach

Achieve broad patient reach through community-centered, high-touch engagement model

Switch

Activate and maintain switch to AVLAYAH



Access

Support seamless access for patients

Coverage

Drive fast coverage aligned to label

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

Healthcare Organization (HCO) Engagement

High awareness and motivating data translated into broad launch engagement across targeted treating HCOs

PRE-LAUNCH

HCP Awareness Prior to Launch

>80%

Physicians[1] aware of AVLAYAH™

AWARE

PRE-LAUNCH

Data Motivation

90%

View data as motivating to prescribe[1]

MOTIVATED

LAUNCH

Launch Reach

~80%

of HCOs* reached with launch messaging

ENGAGED

Pre-Launch Awareness[2] Helped Drive Strong Launch Engagement

> *I consider AVLAYAH™ mandatory for patients with MPS II because it crosses the BBB. Now all patients should be on AVLAYAH™.*
>
> — MPS II HCP

- HCPs recognize significant **unmet needs** across **brain and body**
- **No overall concerns** with safety profile
- Recognize the breadth and depth of neurologic manifestations

1. HCP insights from HCP Survey (N=35) conducted in Q4 2025
*Defined as HCOs with a valid MPS II pediatric patient claim in last 12 months and/or submitted an AVLAYAH™ Start Form since launch; 2. Based on scientific exchange

Patients and Caregivers are Aware of AVLAYAH™

Patient & Family Webinars

3 Launch Webinars

Focused on Clinical Data and Patient Access

REACHING

100+ Families

>25% of Eligible Patient Pool

Media Coverage

> *"This treatment is important to us — they have a chance now."*
>
> — Marie, MPS II Parent

> *"...the chance to start treatment feels like 'extra time' with her son."*
>
> — FOX6, Wisconsin

Positive Experience with Denali and AVLAYAH™

For the first time, it felt like Adam's world was opening up. We began to see changes in his speech and mobility that meant so much to our family. While his previous treatment helped his body, we always hoped for something that could address what was happening in his brain.

— Miriam, *MPS II Parent & Advocate*

When Cole started AVLAYAH™, all I hoped for was stability — a few more years with my son. But seeing him come alive, so aware of his environment, more active, trying to communicate, I have thrown away all my assumptions. I am allowing myself to look forward and dream of a better future for him.

— Kim, *MPS II Parent & Advocate*

The Denali team is doing a fantastic job navigating the access landscape.

— Terri Klein
CEO, National MPS Society

Today, [our son] is finally receiving a groundbreaking medication that we pray will help improve his quality of life and give him more time to be a kid. Happier, more comfortable, and more himself.

— AVLAYAH™ Caregiver
Facebook Post, Accessed on July 17, 2026

Exceptional Progress on Payer Coverage in the First Quarter After Launch, Exceeding Rare Disease Launch Analogs[1]

Commercial

of Covered Lives[2]

Medicaid

14

State Medicaid Programs list AVLAYAH™ as covered

Managed Medicaid coverage growing, with policies consistent with label

- Motivated and committed HCPs pushing through payer appeals
- Payer approvals across Commercial and Medicaid
- Strong uptake in payer policies at this phase in launch providing HCP confidence that patients can access AVLAYAH™

1. Analogs reflect selected rare disease launches from the five years preceding AVLAYAH's launch: olipudase alfa-rpcp, cipaglucosidase alfa-atga, and pegunigalsidase alfa-iwxj (ERTs); tofersen and delandistrogene moxeparvovec-rokl (rare disease non ERTs). Coverage is compared at the equivalent point post-launch. Data provided by MMIT; 2. Calculated based on the plans that represent 95% of lives within each segment (Commercial and Managed Medicaid).

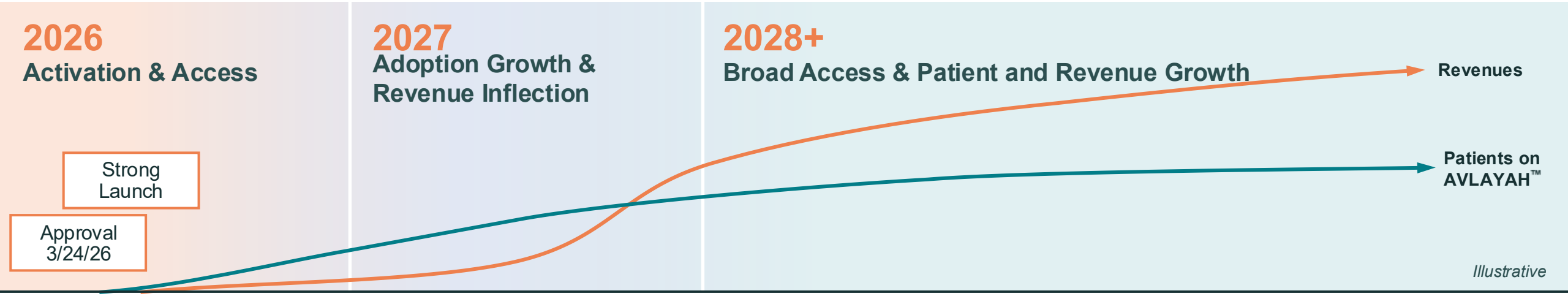
AVLAYAH™ U.S. Launch Dynamics

2026: Building the Foundation To Become the Standard of Care for MPS II Pediatric Patients*

$3.6M 2Q 2026 Net Revenue

>50% Commercial Lives Covered

~$10M to $12M Projected 3Q 2026 Net Revenue

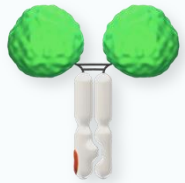
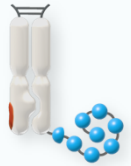


* Pre-symptomatic or symptomatic neurologic manifestations; All strategies and tactics are subject to Legal review prior to implementation.

Building the ETV Franchise Portfolio for Lysosomal Storage Diseases

Delivering the Next-Generation of TransportVehicle-Enabled ERT

- Addressing neurologic and systemic disease
- Scalable commercial infrastructure
- Repeatable rare disease launch model
- Large, validated ~$9B ERT market[2]

	AVLAYAH™ (tividenofusp alfa-eknm)	Zafinofusp alfa (DNL126)	PTV:PGRN (DNL593)	ETV:GAA (DNL952)	ETV:GCase (DNL111)	ETV:IDUA (DNL622)
						
	MPS II Hunter syndrome	**MPS IIIA** Sanfilippo syndrome type IIIA	**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	U.S. accelerated approval Phase 2/3	Phase 1/2	Phase 1/2	Phase 1	IND-enabling	IND-enabling

WW – Worldwide; **IND** – Investigational New Drug; **GBA-PD** – Parkinson's Disease with GBA mutation; **GD** – Gaucher's Disease; **ERT –** enzyme replacement therapy

1. Excluding China and India; **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).

Pipeline Highlights

Ryan Watts, Ph.D., CEO

On Track to Deliver Denali's D3X3 Goals Over 2026-2028

2 Growing Brands

- AVLAYAH™
- **zafinofusp alfa**

4-6 New Clinical Programs

- Continued leadership and invention on BBB technologies

5 Clinical Proofs of Concept

Alzheimer's Disease

- DNL628 (OTV:MAPT)
- DNL921 (ATV:Abeta)

Pompe Disease

- DNL952 (ETV:GAA)

FTD-*GRN*

- DNL593 (PTV:PGRN)

Parkinson's Disease

- DNL151 (LRRK2 inhibitor)

Aiming to deliver near-term value from planned product launches, advancing a robust pipeline, and capturing the full potential of the TransportVehicle™

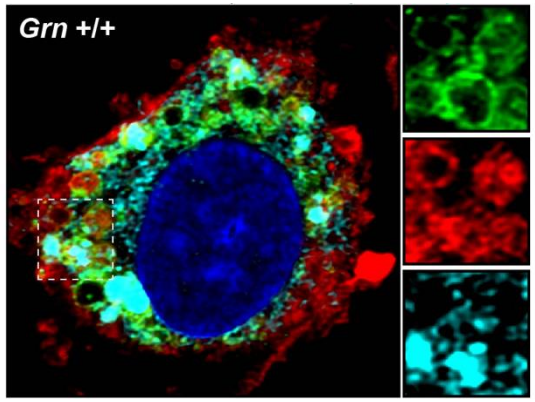
D3 – Deliver, Develop, Discover; **BBB –** Blood-brain barrier

DNL593 (PTV:PGRN) PGRN Replacement for FTD-*GRN*

Rescue of a lysosomal storage disorder caused by *Grn* loss of function with a brain penetrant progranulin biologic

Cell

Todd Logan,[1,6] Matthew J. Simon,[1,6] Anil Rana,[1,7] Gerald M. Cherf,[1,7] Ankita Srivastava,[1,7,8] Sonnet S. Davis,[1] Ray Lieh Yoon Low,[1] Chi-Lu Chiu,[1] Meng Fang,[1] Fen Huang,[1] Akhil Bhalla,[1] Ceyda Llapashtica,[1] Rachel Prorok,[1] Michelle E. Pizzo,[1] Meredith E.K. Calvert,[1] Elizabeth W. Sun,[1] Jennifer Hsiao-Nakamoto,[1] Yashas Rajendra,[1] Katrina W. Lexa,[1] Devendra B. Srivastava,[1] Bettina van Lengerich,[1] Junhua Wang,[1] Yaneth Robles-Colmenares,[1] Do Jin Kim,[1] Joseph Duque,[1] Melina Lenser,[1] Timothy K. Earr,[1] Hoang Nguyen,[1] Roni Chau,[1] Buyankhishig Tsogtbaatar,[1] Ritesh Ravi,[1] Lukas L. Skuja,[1] Hilda Solanoy,[1] Howard J. Rosen,[2,3] Bradley F. Boeve,[3,4] Adam L. Boxer,[2,3]



LAMP2
Lysosome Marker

BMP
Lipid critical for lysosome activity

PGRN
Localized to lysosome

DNL593 Phase 1/2 Clinical Study

Study Population

- **Part A:** Healthy volunteers aged ≥18 to ≤55 years
- **Part B:** *GRN* mutation carriers; symptomatic participants diagnosed with FTD-*GRN*; aged ≥ 8 to ≤80 years
- **Part C:** Participants who complete Part B

Study Plan

Enrollment Completed

- SAD Cohort A
- MAD Cohort B

Optional OLE Ongoing

- MAD Cohort C

Goals & Objectives

- **Part A:** Safety, PK
- **Parts B & C:**
  - Safety, PK, PD biomarkers
  - Clinical, neuropsychology, and imaging outcomes

- **Duration:** 25-week core study + open-label extension (OLE)
- **Study Type:** Randomized, placebo-controlled, double-blind

Strategic Path Forward

- Denali regained full ownership and control of the program from Takeda in 2Q 2026
- Phase 1/2 data now expected in 1H 2027 to allow for longer biomarker observation in OLE, including NfL
- We intend to explore a potential accelerated approval path based on biomarker data

Transformative Time for Alzheimer's Disease

New Opportunities for Success in Neurodegeneration

Biology

New insights into the underlying, multifaceted biology of neurodegeneration

Biomarkers

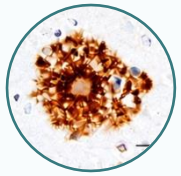
Enabling early diagnosis, monitoring of progression and treatment response

Blood-Brain Barrier

Validated technologies to address key challenge for biologics to reach the brain

Impactful progress in all three historically challenging areas over the past decade has enabled a transformational period for accelerating neurodegeneration medicines

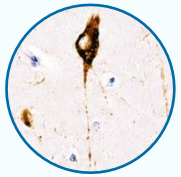
The Next Advances in AD May Depend on Better Brain Delivery



Amyloid-beta

Amyloid plaque

- Plaque clearance clinically validated
- Current limitations
  - Modest efficacy
  - ARIA safety risk

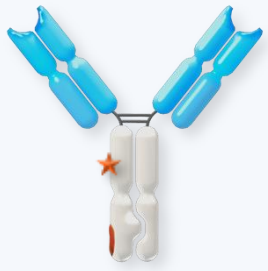


Tau

Neurofibrillary tangle

- Clinical benefit trend from tau reduction
- Current limitations
  - Uneven brain distribution
  - Intrathecal administration burden

TransportVehicle (TV) Opportunity

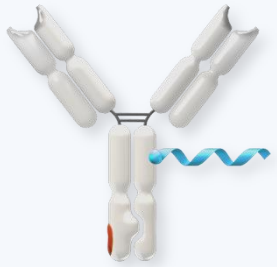


DNL921

(ATV:Abeta)

Potential best-in-class BBB-crossing anti-amyloid

- Improve plaque engagement
- Reduce ARIA potential
- Minimize peripheral immune activation



DNL628

(OTV:MAPT)

Potential first-in-class BBB-crossing tau ASO

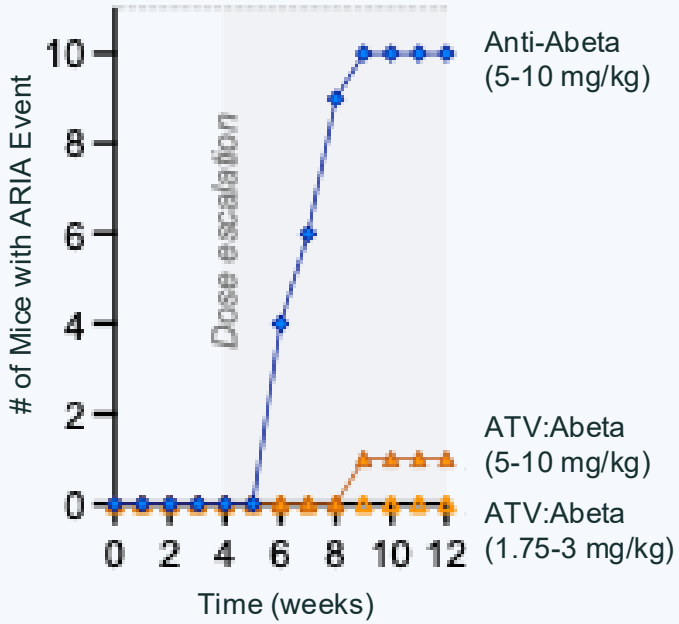
- Broad, uniform brain distribution via the capillary network
- Systemic dosing without intrathecal administration

TV has the potential to transform brain delivery for the next generation of Alzheimer's therapies

ATV:Abeta Reduces ARIA Due to TfR-Mediated Capillary Delivery to Brain in Mouse Model of AD

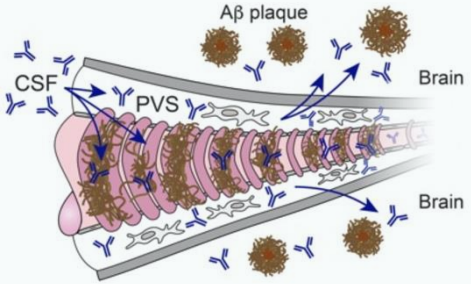
Incidence of MRI Lesions[1]

5xFAD; TfR$^{mu/hu}$ KI; QW IP

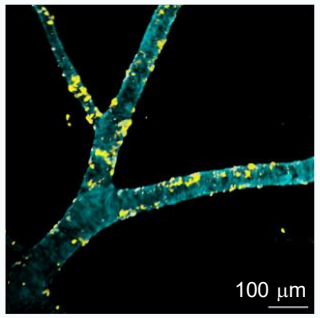


Route of Entry into Brain[2]

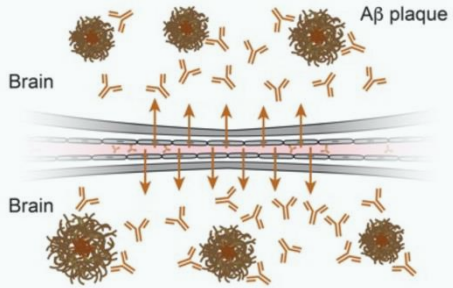
Conventional Anti-Abeta



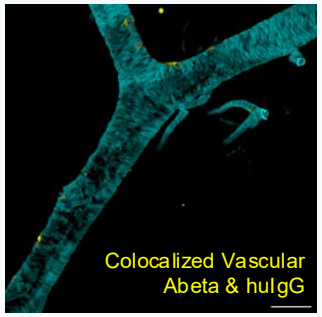
Artery / Arteriole Zone



ATV-Enabled Anti-Abeta



Microvessel (capillary) Zone



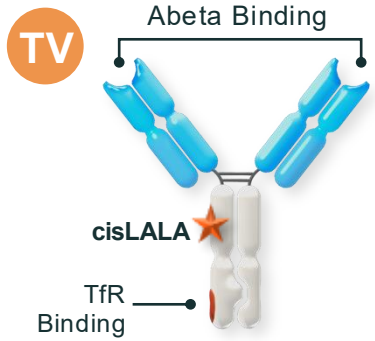
Bypassing arterial vascular plaque via TfR-mediated entry into the brain through capillaries and venules has the potential to improve amyloid-related imaging abnormalities (ARIA)

ATV:Abeta is an investigational compound and has not been approved by any regulatory authority.

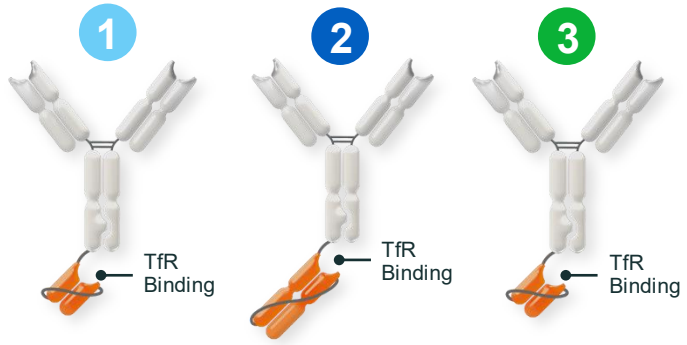
1. Data generated by Biogen; 2. Source: Pizzo et al. Science 2025; ARIA – Amyloid-related imaging abnormalities; TfR – Transferrin receptor

DNL921 Optimized for Robust Brain Delivery, Safety & Stability

DNL921 (ATV:Abeta)

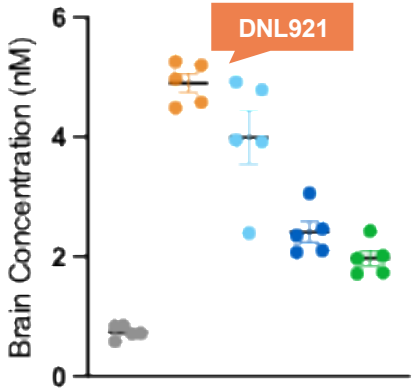


Fusion Molecules[1]

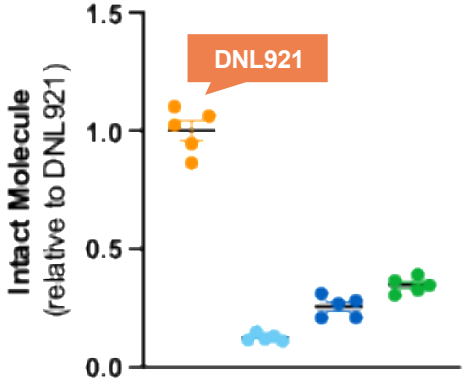


Molecule	Architecture	Epitope	Effector Function
Control	Control IgG	N/A	Full
DNL921	TV- TfR in Fc	Apical	Conditional
Molecule #1	C-term TfR	Protease	Full
Molecule #2	C-term TfR	Apical	Full
Molecule #3	C-term TfR	Apical	None

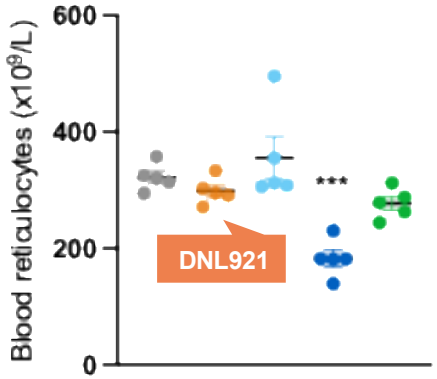
Brain Concentration[2]



Intact Molecule[2,3]



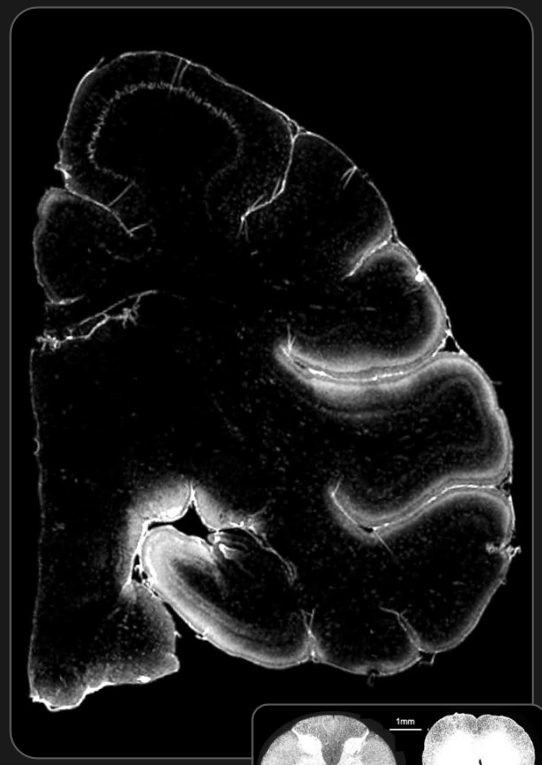
Immature Reticulocytes[2]

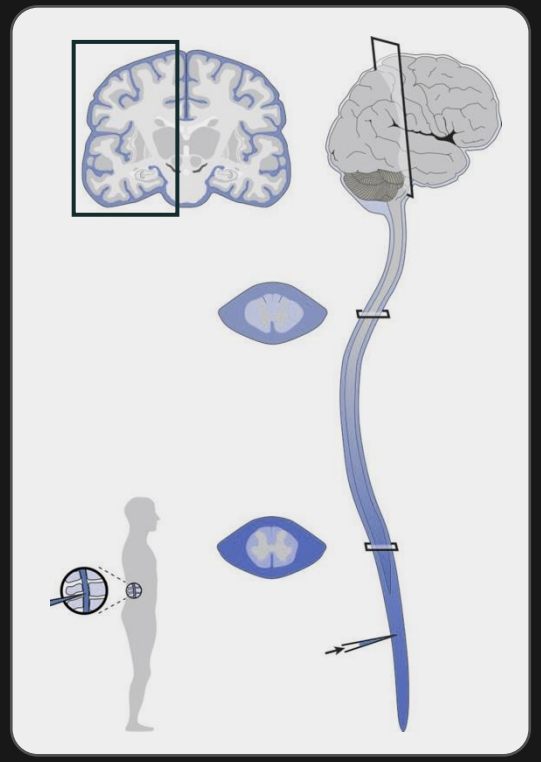


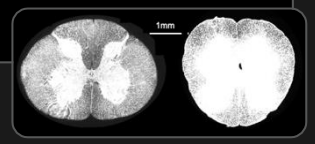
DNL921 (ATV:Abeta) is an investigational compound and has not been approved by any regulatory authority; **1.** Fusion Molecules generated at Denali based on publicly available information on TfR-binding anti-Abeta antibodies currently under development; **2.** Single dose, IV 10 mg/kg (molar-matched), using a mouse model that expressed the full TfR extracellular domain; **3.** hIgG Capture vs. TfR Capture ELISA. Source: Denali Therapeutics data

OTV Enhances Biodistribution of ASO Evenly Across Brain Regions

Limited biodistribution with intrathecal ASO



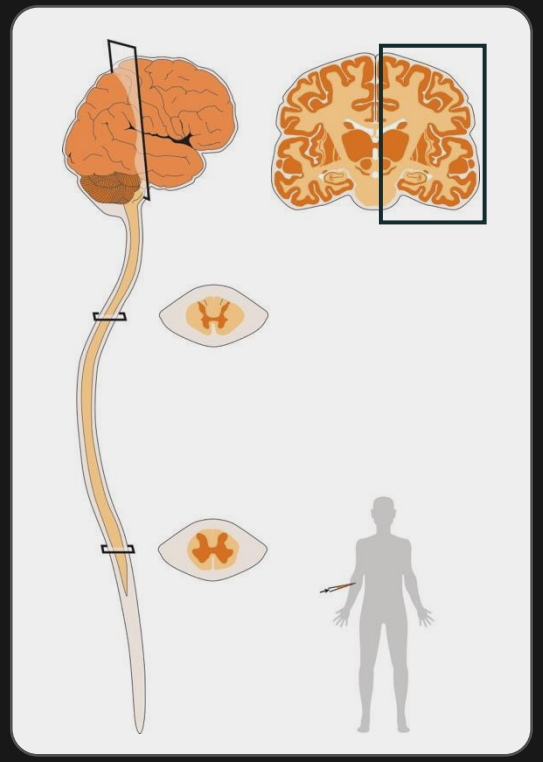


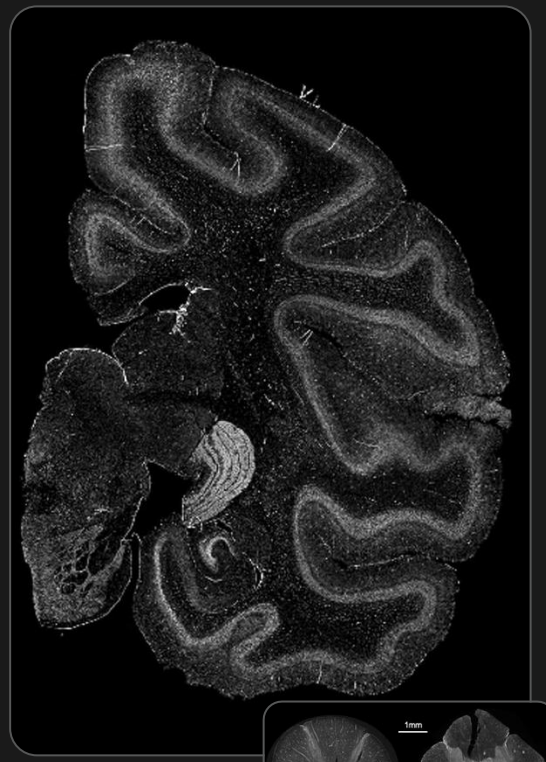


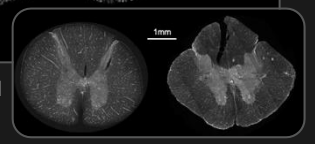
Spinal Cord

Cervical Lumbar

Widespread biodistribution with intravenous OTV:ASO







Spinal Cord

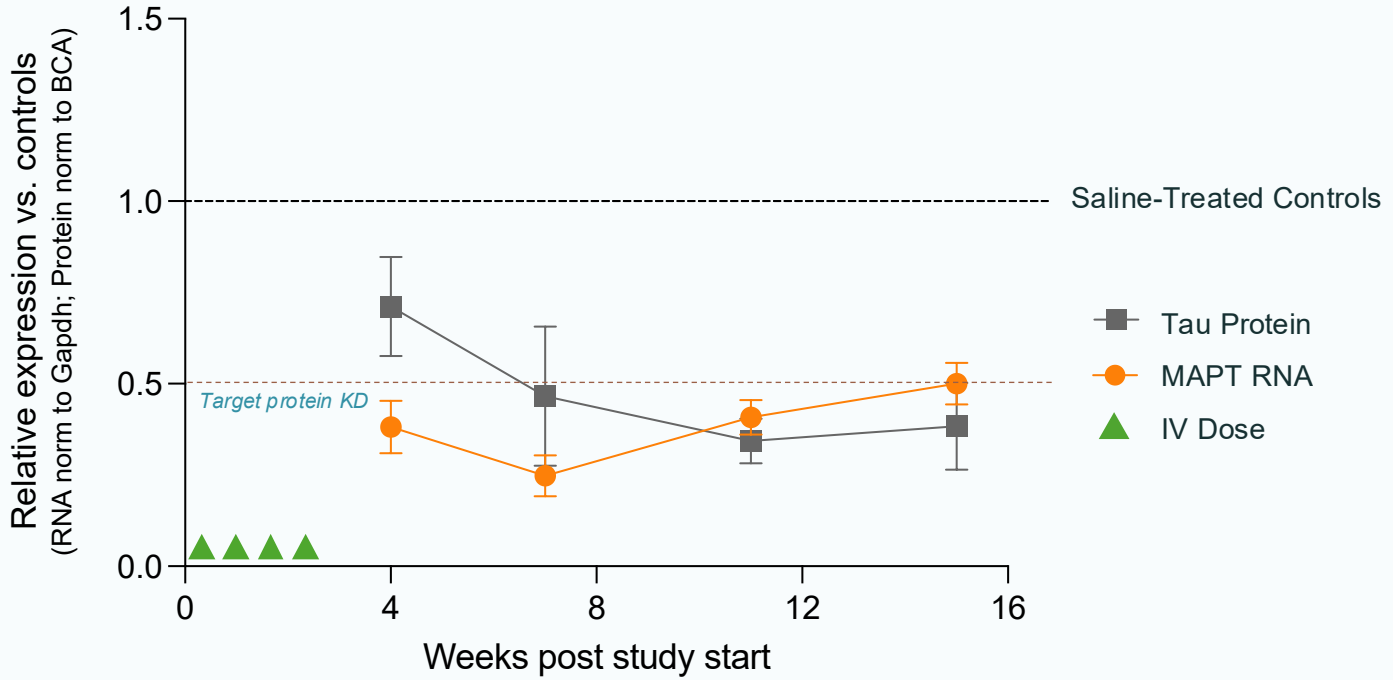
Cervical Lumbar

ASO Immunofluorescence hemibrain coronal section

Adapted from Barker et al. *Science Translational Medicine* 2024

DNL628 Displays Robust and Sustained Knockdown in Mice Expressing Human Tau

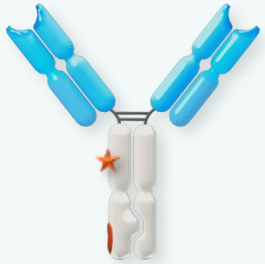
Brain MAPT RNA and Tau Protein Knockdown (KD) Persists for >12 Weeks After Dosing



Robust and sustained reduction in tau protein with DNL628

DNL628 (OTV:MAPT) is an investigational compound and has not been approved by any regulatory authority.
Triangles indicate individual doses over two-week time period. Source: Denali Therapeutics data

Initial Clinical Data from Both AD Programs Expected in 2027



DNL921 Phase 1/1b Clinical Study

Phase 1/1b → **Phase 3**

Study Population

SAD: Healthy Volunteers

MAD: Patients with biomarker confirmed Alzheimer's disease

Study Plan

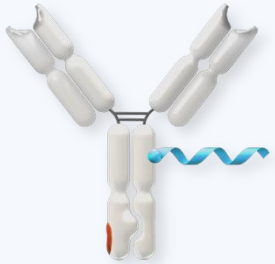
- SAD
- MAD Cohort A
- MAD Cohort B
- MAD Cohort C

Goals & Objectives

- Safety
- Impact on amyloid plaque load
- Dose selection
- Additional biomarkers/imaging

- **Duration:** 28 weeks
- **Study Type:** Randomized, placebo-controlled, double blind

- Phase 1/1b study is ongoing
- Safety and clinical proof-of-concept data in 2027



DNL628 Phase 1b Clinical Study

Phase 1b → **Phase 2** → **Phase 3**

Study Population

Patients with biomarker confirmed early Alzheimer's disease (CDR 0.5 to 1, MMSE 20-30)

Study Plan

- MAD Cohort A
- MAD Cohort B
- MAD Cohort C

Phase 1b Objectives

- Safety
- Impact on tau levels
- Dose selection
- Additional biomarkers/imaging

NCT07328451

- **Duration:** 24 weeks
- **Study Type:** Randomized, placebo-controlled, double blind

- Phase 1b study ongoing
- Clinical biomarker data expected in 1H 2027

Financial Update

Alexander Schuth, M.D., COO/CFO

Our Broad Therapeutic Portfolio

Lysosomal Storage Disorders

Molecule	Indication	Stage
tividenofusp alfa-eknm (ETV:IDS)	MPS II	FDA Approved Phase 2/3
zafinofusp alfa (ETV:SGSH)	MPS IIIA	Phase 1/2
DNL593 (PTV:PGRN)	FTD-*GRN*[1]	Phase 1/2
DNL952 (ETV:GAA)	Pompe	Phase 1
DNL111 (ETV:GCase)	Gaucher	IND-Enabling
DNL622 (ETV:IDUA)	MPS I	IND-Enabling

>30,000 Patients WW[2]

$500M-$1B+ per Indication[3]

Common Neurodegenerative Diseases

Molecule	Indication	Stage
DNL151 LRRK2 Inhibitor	PD	Phase 2a (LRRK2)
DNL628 OTV:MAPT (tau)	AD	Phase 1b
DNL921 ATV:Abeta	AD	Phase 1/1b
DNL111 ETV:GCase	PD	IND-Enabling
DNL422 OTV:SNCA	PD	IND-Enabling

>40M Patients WW[2]

>$5B per AD/PD Indication[4,5]

1. FTD-*GRN* has a lysosomal phenotype and can be considered a rare lysosomal storage disease; **2.** Denali estimates of worldwide aggregate prevalence, excluding China and India for the lysosomal storage disorders; **3.** Lysosomal Storage Disorders Indication market 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); **4.** Alzheimer's disease market opportunity based on Denali internal assessment as of Nov '25 and Evaluate Pharma Analyst Consensus Forecasts 2024 to 2034, Oct '25; **5.** Parkinson's disease market opportunity based on Denali internal assessment as of Nov '25 and other syndicated data (e.g., Herantis Pharma Plc Annual Report 2024; Herantis Pharma PLC (published March 31, 2025), Parkinson's Diseases Treatment Market 2025 to 2030, Gran View Research, https://www.grandviewresearch.com/industry-analysis/parkinsons-disease-treatment-market).
MPS – Mucopolysaccharidosis; **PD –** Parkinson's disease; **AD** – Alzheimer's disease

Capital to Execute

Strong Financial Foundation

$940M

Cash and investments as of Q2 2026

$195M PRV Sale

Gross proceeds from sale of PRV awarded by FDA upon AVLAYAH™ approval

Near-term revenues

Launch of AVLAYAH™ and potential launch of DNL126 in 2027

Key Capital Allocation Priorities

Invest Strategically

- Successful launches of AVLAYAH™ and potentially zafinofusp alfa
- Focused R&D investments to accelerate and expand pipeline

Drive Capital Efficiency

- Apply learnings from AVLAYAH™ to develop next programs faster and at lower cost
- Drive low COGS and high margins from in-house manufacturing and commercial synergies

Maintain Capital Optionality

- Partnerships remain core to strategy
- Diversifying sources of capital

PRV – Priority Review Voucher

Q2 2026 Financial Summary

$ in millions	Three Months Ended June 30, 2026	Three Months Ended June 30, 2025
AVLAYAH Net Product Revenue	$3.6	$–
Total Revenue	**3.6**	–
Cost of Goods Sold	0.1	–
R&D Expense	97.0	102.7
SG&A	36.3	32.3
Amortization of Intangible Asset	0.7	–
Total Operating Expense	**134.1**	**135.0**
Loss from Operations	(130.5)	(135.0)
Interest and other income, net	3.0	10.8
Net Loss	**(127.6)**	**(124.1)**

$940M in cash, cash equivalents and marketable securities as of June 30, 2026, excluding $195M gross proceeds from the PRV sale[1]

1. The transaction closed and proceeds were received in July 2026.

Q&A