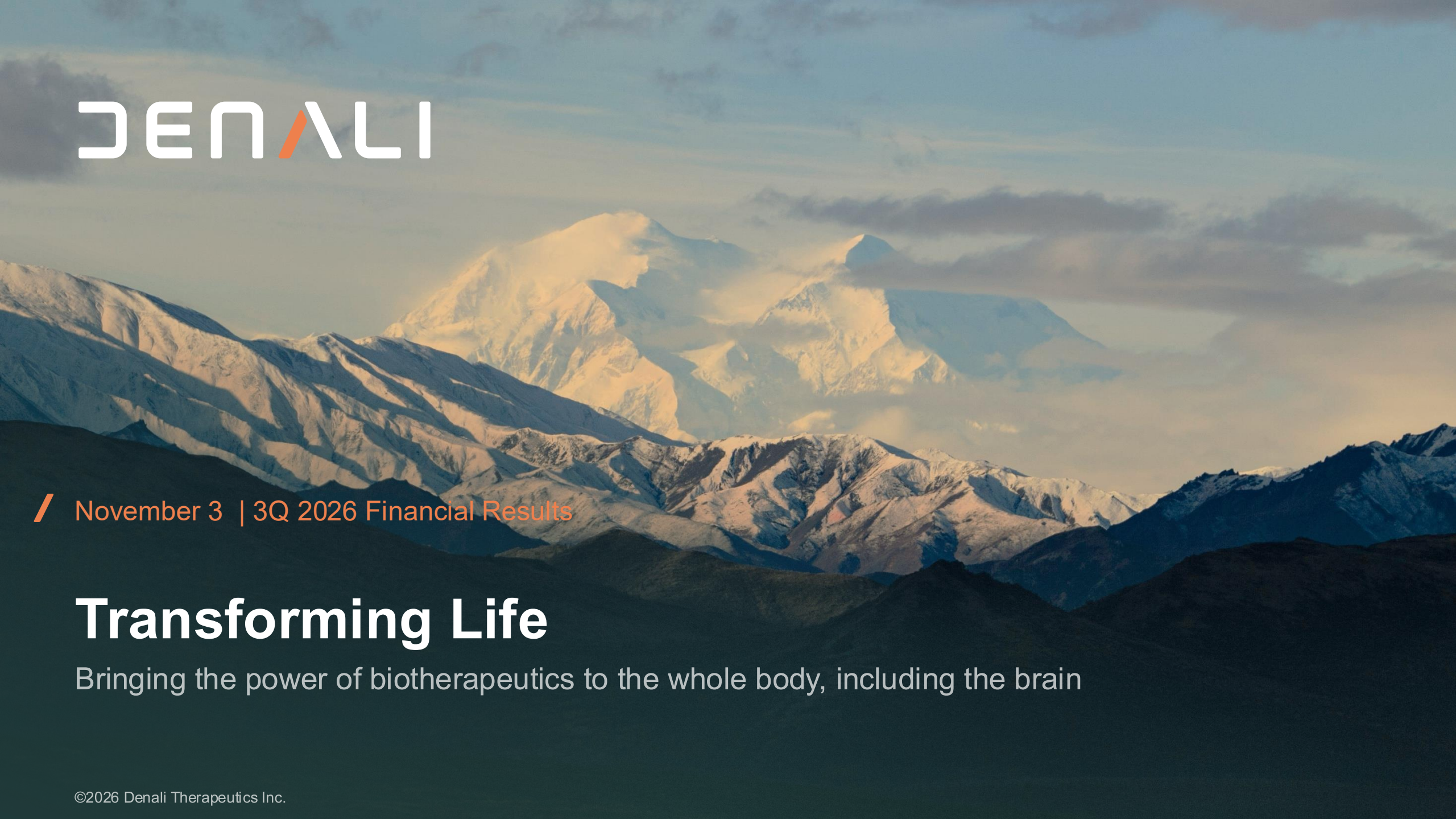


November 3 | 3Q 2026 Financial Results

Transforming Life

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

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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 future results of operations and financial position of Denali Therapeutics Inc. (“Denali” or "Company"); Denali’s business strategy and business plans, forecasts and expectations 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 and its therapeutic and commercial opportunities; plans, timelines, and expectations related to the ETV franchise and ETV-enabled programs, their therapeutic and commercial potential, and potential indication size and market opportunities for each program; plans, timelines, and expectations relating to AVLAYAH®, including forecasted patient and revenue growth, payer coverage and reimbursement, and the pace of patient uptake and time to infusion; 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® and ex-US launches; plans, timelines, and expectations related to DNL126 (ETV:SGSH), including the timing and availability of data and the timing and likelihood of regulatory submissions and approval; plans, timelines, and expectations related to AD treatments, including the potential indication size, market opportunities, and the programs' therapeutic and commercial potential; plans, timelines, and expectations relating to DNL921 (ATV:Abeta), including the Phase 1/1b clinical study, and the timing and availability of data; plans and expectations relating to DNL628 (OTV:MAPT), including the timing and availability of data from the ongoing Phase 1b study; 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

AGENDA

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

Commercial Update – Katie Peng, CCO

Pipeline Highlights – Peter Chin, M.D., CMO

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

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

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

Our Purpose: Transforming Life for People with Serious Diseases



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

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A Powerful Combination: Product, Pipeline, Platform

Leading the field in blood-brain barrier (BBB) therapeutics

AVLAYAH®
(tividenofusp alfa-eknm)

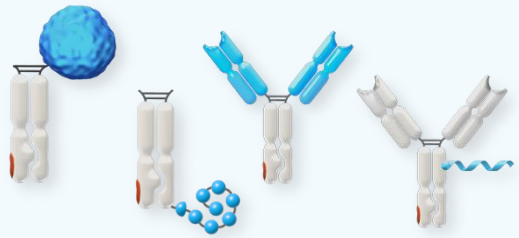
Commercial Product

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



Validated BBB Platform

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



Broad Pipeline

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

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

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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, Grand View Research, https://www.grandviewresearch.com/industry-analysis/parkinsons-disease-treatment-market).
MPS – Mucopolysaccharidosis; **PD –** Parkinson's disease; **AD** – Alzheimer's disease

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3Q 2026: Executing Across Our Strategic Priorities



Build on Strong AVLAYAH® Launch

$17.8 million net product revenue in the second full quarter of launch



Advance Zafinofusp Alfa Toward Approval & Launch

Phase 1/2 study completed the prespecified treatment duration for the primary endpoint; on track for a BLA filing in 2027



Establish Proof-of-Concept in Alzheimer's Disease

Initial clinical data from OTV:MAPT and ATV:Abeta programs expected in 2027



Building commercial momentum while advancing pivotal and early clinical programs toward significant 2027 milestones

Commercial Update

Katie Peng, Chief Commercial Officer



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Strong Momentum in First 2 Quarters of AVLAYAH® Launch

2026: Building the foundation across key stakeholders for revenue acceleration

$17.8M

3Q 2026 Net Revenue

PATIENTS

Interest is broad across the eligible MPS II patient population

Patient Demand

PHYSICIANS

High conviction and motivation translating into treatment action

Physician Action

PAYERS

Expanding coverage is accelerating the treatment path

Expanding Access

~$30M to $32M

Projected 4Q 2026 Net Revenue

Our priority remains reaching more eligible patients* and delivering a positive treatment experience with AVLAYAH®

*Pediatric patients, pre-symptomatic or symptomatic neurologic manifestations prior to advanced impairment; All strategies and tactics are subject to Legal review prior to implementation.

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Interest is Broad Across the Eligible MPS II Patient Population



~500 prevalent U.S. patients × **~75%** eligible under the current FDA label

~375
eligible patients

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

"Since my 16-year-old son, Dominic, started AVLAYAH®, I've seen meaningful changes in our everyday life, including more expressive language. As his mom, these changes give me hope for making more memories for our family to treasure."

— Jeanette, MPS II Parent & Advocate

Early patient interest in AVLAYAH® treatment is extending into the broader eligible population, supporting continued reach over time

High Physician Conviction is Translating into Treatment Action

PRE-LAUNCH[1]

>80%
Aware of AVLAYAH® before launch

90%
Viewed the data as motivating to prescribe

POST-LAUNCH

~90%
Of targeted HCOs reached with launch messaging

Action
Treatment centers helping families navigate reimbursement and transition

WHY CONVICTION IS HIGH

Meaningful Differentiation
Designed to reach the whole body, including the brain

Motivating Evidence
Data package supports physician confidence

Execution at the Center
Teams support infusion readiness and pursue access while policies evolve

Physician willingness to pursue prior authorizations, appeals and medical exceptions is a visible expression of clinical conviction

Source: Pre-launch physician survey N=35 (Q4 2025).

Expanding Coverage is Accelerating the Treatment Path

Commercial



of Covered Lives[1]

Medicaid

20

State Medicaid Programs list AVLAYAH® as covered

Managed Medicaid coverage growing, with policies consistent with label

- Payer approvals continue across Commercial and Medicaid
- Strong uptake in payer policies at this phase in launch providing HCP confidence that patients can access AVLAYAH®
- Permanent J-Code as of Oct 1

1. Calculated based on the plans that represent 95% of lives within each segment (Commercial and Managed Medicaid).

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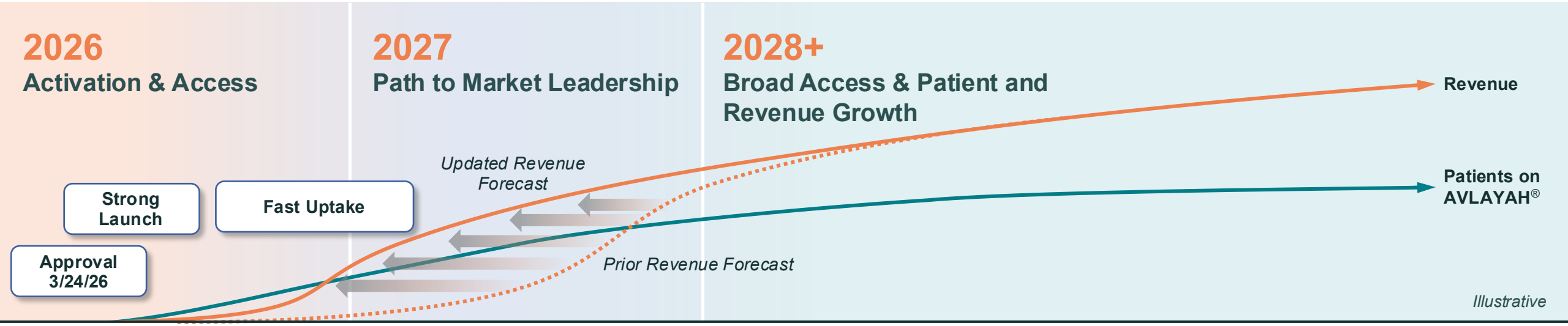
AVLAYAH® U.S. Launch Dynamics

2026: Building the foundation to become the Standard of Care for MPS II pediatric patients*

$17.8M
3Q 2026 Net Revenue

>70%
Commercial Lives Covered

~$30M to $32M
Projected 4Q 2026 Net Revenue



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

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AVLAYAH® U.S. Launch Builds Foundation for Continued Growth

AVLAYAH®
(tividenofusp alfa-eknm)

Strong Launch

Reaching patients and building the commercial foundation for our broader enzyme franchise

Path to Market Leadership

AVLAYAH® is on its way to becoming the U.S. market leader for MPS II

Global Expansion

Label expansion and international launches broaden access to ~2,000 patients worldwide in commercially accessible geographies

U.S. Growth Drivers Market Share Gains • Newly Diagnosed Patients • Rapid Time to Infusion

Pipeline Highlights

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



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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

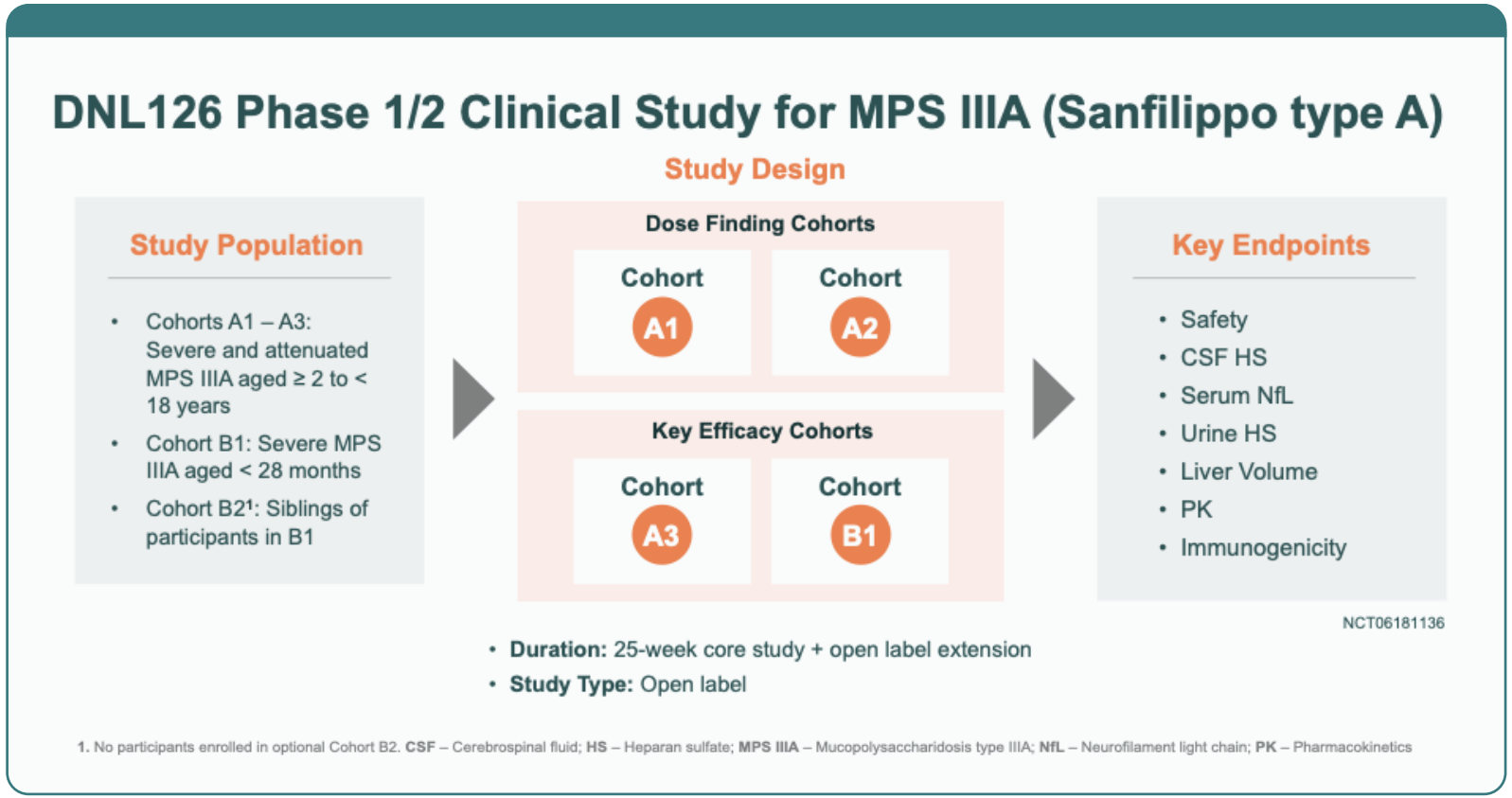
Phase 2/3 Confirmatory Study

65 Participants

COMPASS

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

Zafinofusp Alfa (DNL126): Study Data for Accelerated Approval



Data for BLA Submission

- At least 49 weeks of data for all participants (Cohorts A1-A3, B1; n=20)
- CSF HS reduction from baseline in key efficacy cohorts (n=12) – surrogate endpoint reasonably likely to predict clinical benefit
- Supportive data on central and peripheral biomarkers, clinical endpoints
- Long-term safety up to ~2.5 years

Week 49 data will be presented in 1Q 2027 supporting BLA submission in 2027

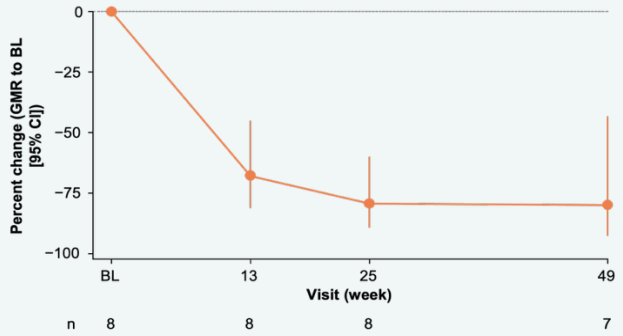
BLA – Biologics License Application; **AA** – Accelerated approval; **CSF** – Cerebrospinal fluid; **HS** – Heparan sulfate

Zafinofusp Alfa: Preliminary Data Phase 1 Dose-Finding Cohorts

CNS Biomarkers

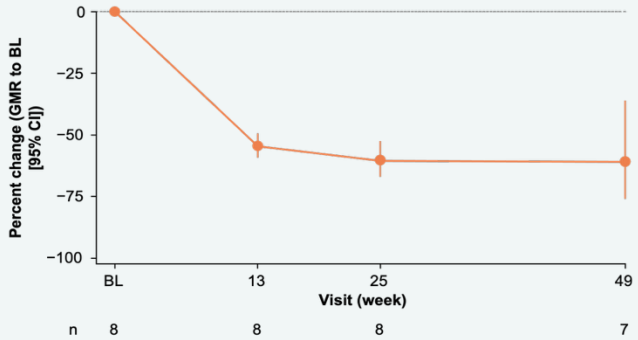
-80% CSF HS

Mean reduction at Week 49; 3 of 7 within normal range



-61% CSF GM3

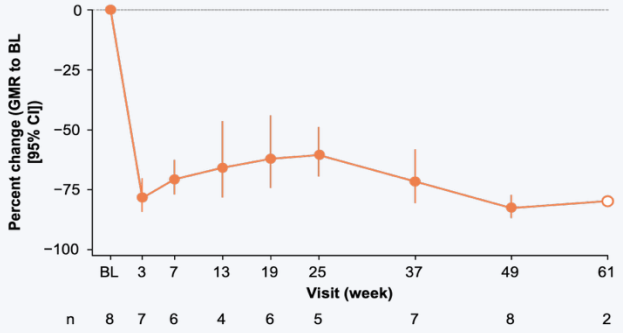
Mean reduction at Week 49; 6 of 7 within normal range



Peripheral Effects

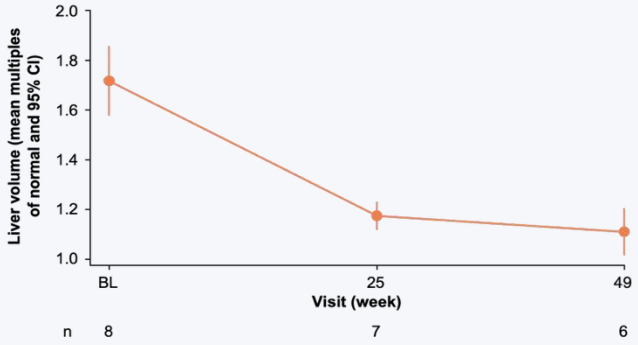
-83% Urine HS

Mean reduction at Week 49



Liver Volume

Normalized in all participants



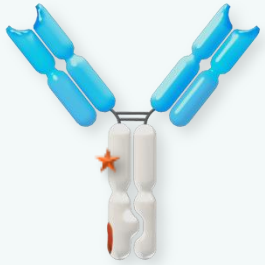
Cohorts A1 and A2 at Week 49

- Substantial reductions in CNS biomarkers, including the ability to normalize
- Substantial reductions in peripheral disease biomarkers with normalized liver volume
- Infusion related reactions were the most common adverse events

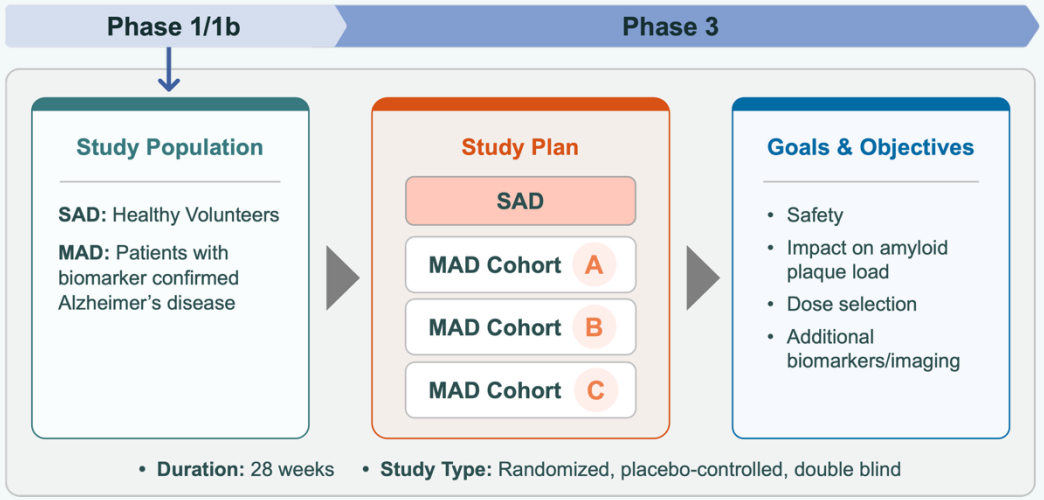
BL – baseline; **CI** – confidence interval; **CNS** – central nervous system; **GMR** – geometric mean ratio. Source: Jalazo et al. WORLD*Symposium*™ 2026

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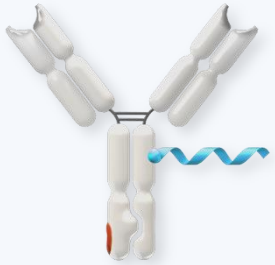
Initial Clinical Data from Both AD Programs Expected in 2027



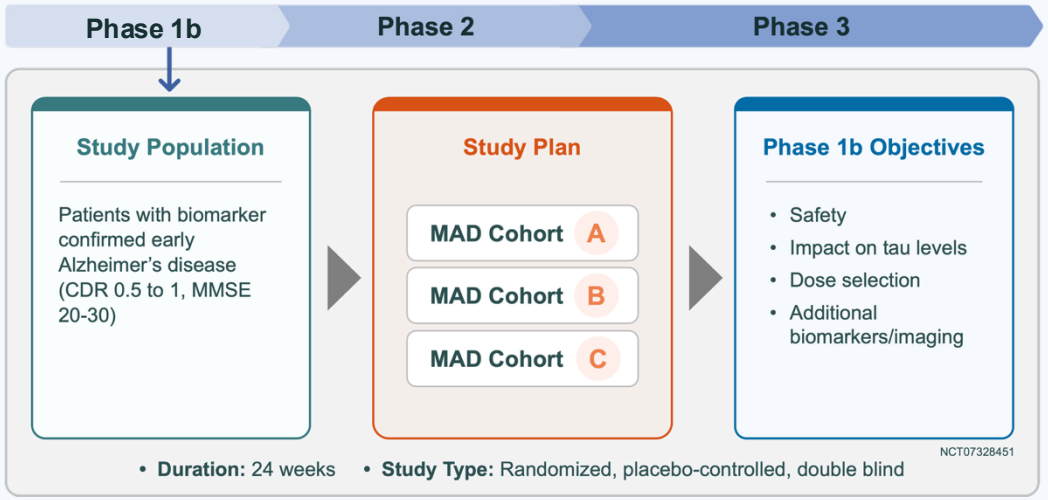
DNL921 Phase 1/1b Clinical Study



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



DNL628 Phase 1b Clinical Study



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

Financial Update

Alexander Schuth, M.D., COO/CFO



A Strong Enzyme Foundation with Broad Pipeline Upside

BBB-Crossing Enzyme Replacement Therapy for Rare Genetic Diseases

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

>30,000 Patients Worldwide

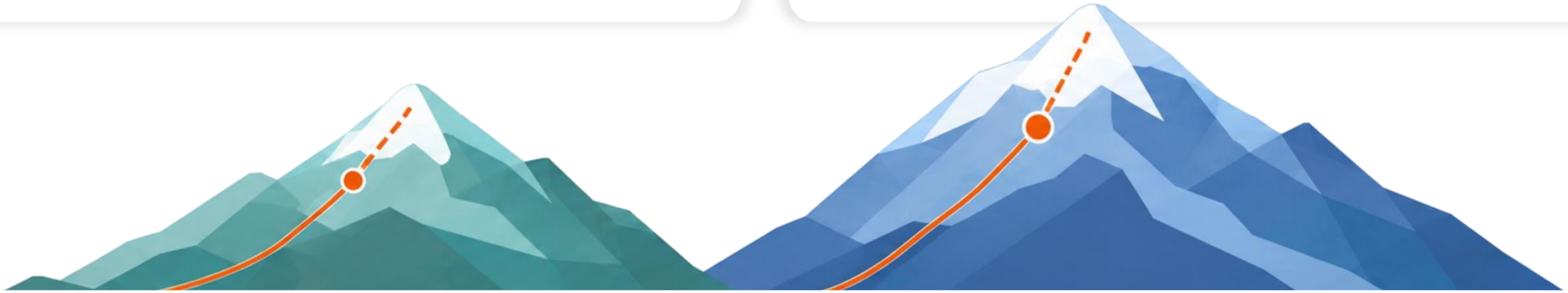
$500M - $1B+ per Indication

BBB-Crossing Biologics for Common Neurodegenerative Diseases

Alzheimer's disease / Parkinson's disease

>40M Patients Worldwide

>$5B per Indication



One TransportVehicle™ platform. Two climbs underway in parallel.

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3Q 2026 Summary: Executing Across Our Strategic Priorities



Build on AVLAYAH®'s Strong Launch → **On track to be U.S. market leader**



Advance Zafinofusp Alfa Toward Approval & Launch → **BLA filing in 2027**



Establish Proof-of-Concept in Alzheimer's Disease → **Initial clinical data in 2027**



Building commercial momentum while advancing pivotal and early clinical programs toward significant 2027 milestones

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

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Q3 2026 Financial Summary

$ in Millions	Three Months Ended September 30, 2026	Three Months Ended September 30, 2025	Nine Months Ended September 30, 2026	Nine Months Ended September 30, 2025
AVLAYAH® Net Product Revenue	$17.8	–	$21.4	–
Total Revenue	**17.8**	–	**21.4**	–
Cost of Goods Sold	0.2	–	0.3	–
R&D Expense	106.1	102.0	307.0	320.9
SG&A	37.5	35.5	107.3	97.1
Amortization of Intangible Asset	0.8	–	1.5	–
Total Operating Expense	**144.5**	**137.4**	**416.0**	**418.0**
Loss from Operations	(126.8)	(137.4)	(394.6)	(418.0)
Gain on Sale of Priority Review Voucher, net	194.0	-	194.0	-
Interest and Other Income, net	2.9	10.5	14.8	34.0
Net Income (loss)	**$70.1**	**($126.9)**	**($185.9)**	**($384.0)**

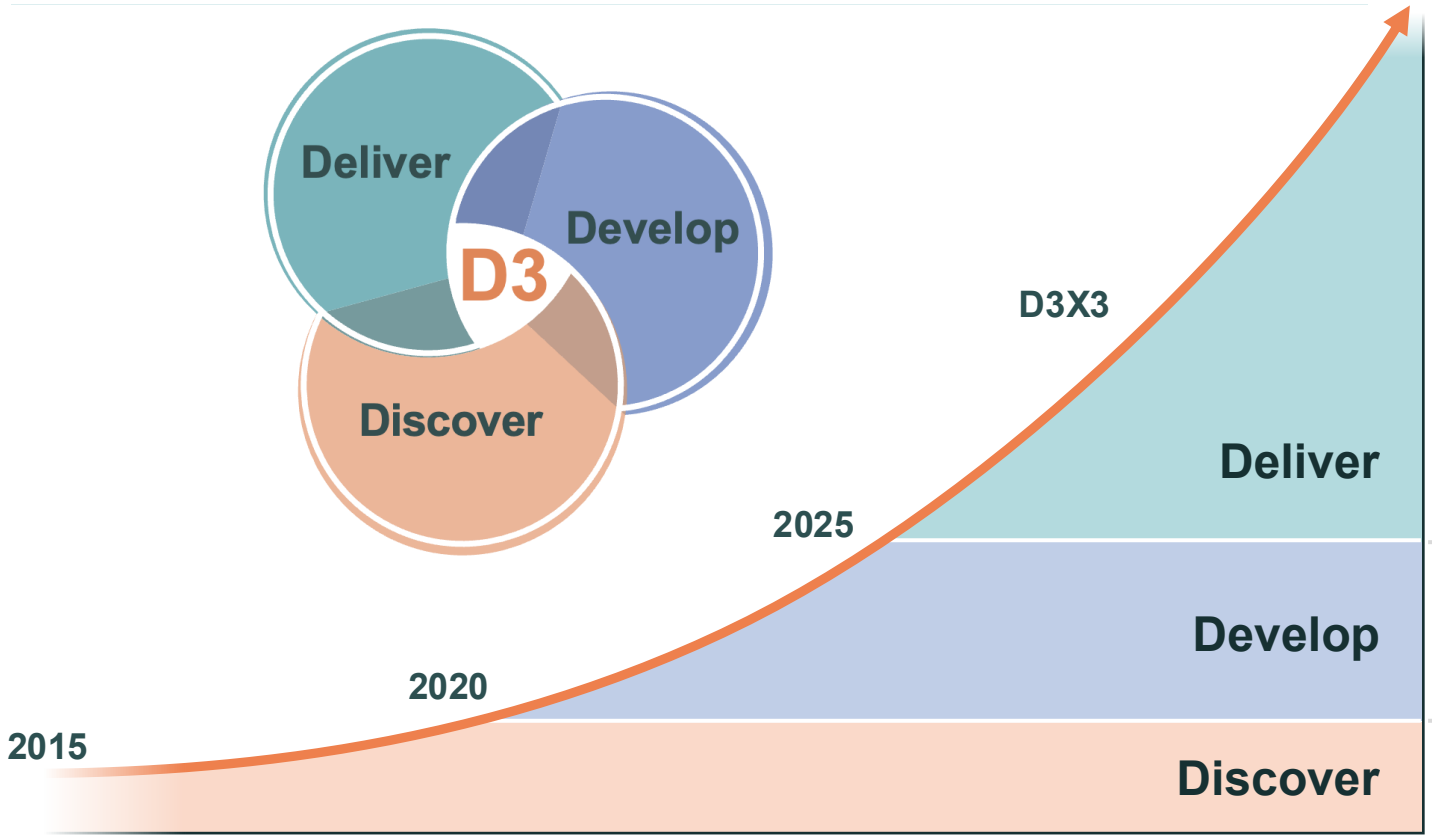
$1.01B in cash, cash equivalents and marketable securities as of September 30, 2026, including $195M gross proceeds from the PRV sale

Closing Remarks

Ryan Watts, Ph.D., CEO



Entering a New Phase on the Path to the Summit



3-Year Goals (D3X3)

2026-2028

2 Growing Brands

5 Clinical Proofs of Concept

4-6 New Clinical Programs

Pioneering a new class of biotherapeutics and capturing the full potential of the TransportVehicle™

Q&A

