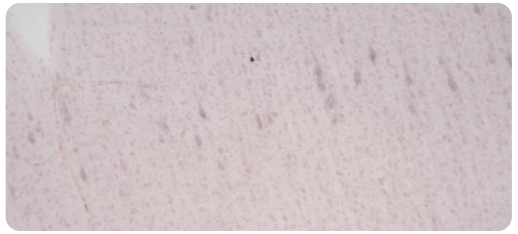
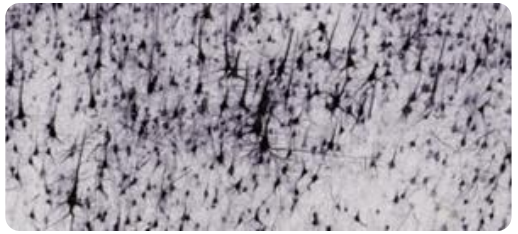
CAPSIDA BIOTHERAPEUTICS

Unlocking the Potential of Gene Therapy for All

December 2024

Capsida is Solving the Challenges of Gen-1 Gene Therapies

Starting in CNS and Ophthalmology, but with IP rights and applicability to all TAs

	CNS Challenges	Capsida Solutions
	Wild Type AAV9	**Capsida Engineered Capsids**
	NHP Cortex 	NHP Cortex 
Crossing the BBB	Limited ability to cross BBB; < 1% neuronal transduction	>70% of neurons transduced in NHPs
Safety Concerns	Liver and dorsal root ganglia (DRG) toxicity	>16x liver and >50x DRG detargeting
Patient Populations	Narrow therapeutic index limits to ultra-rare/rare diseases	Broader TI enables more common diseases across all ages
Route of Administration	Direct injection to brain or CSF causes significant risks and inconsistent expression IV delivery increases risk of off-target effects (especially liver) and triggering immune response	IV limits risks and allows consistent expression No clinical pathology, adverse histopathology, or immune-related AEs

Wholly-owned Programs Approaching the Clinic and Strong Pharma Validation

3 Wholly Owned Programs Approaching Clinical Stage

IV Administered

IND 1H 2025 - Parkinson's caused by GBA mutations (best in class potential)

IND 1H 2025 – STXBP1 Developmental and Epileptic Encephalopathy (first in class)

IND enabling studies– Friedreich's ataxia (best in class potential)

Leadership Team

Decades of industry experience, including drug development and manufacturing expertise

World class investors and scientific advisory teams including co-founder Viviana Gradinaru, PhD

Manufacturing Capabilities

In-house capabilities reduce turn-around times and expedite internal process transfer to support clinical studies

Quickly assess manufacturability

Control the process and associated costs

Partnerships

Key partnerships focused on CNS and Ophthalmology provide validation for the platform

Leadership Team and Board of Directors

Decades of Industry Experience and Drug Development Expertise

Leadership

Peter Anastasiou
Chief Executive Officer

Nicholas Flytzanis, PhD
Founder, Chief Research and Innovation Officer

Nick Goeden, PhD
Founder, Chief Technology Officer

Julie Hakim
Chief Financial Officer

Bethany Mancilla
Chief Business Officer

Rob Murphy
Chief Manufacturing and Quality Officer

Swati Tole, MD
Chief Medical Officer

Board Members

Clare Ozawa, PhD

Beth Seidenberg, MD

Viviana Gradinaru, PhD
Founder

Rita Balice-Gordon, PhD
CEO, Muna Tx

Frank Verwiel, MD
Chairman, Intellia

Peter Anastasiou
Chief Executive Officer

Capsida History and Milestones Achieved

2019

Founded upon breakthrough AAV engineering from laboratory of **Viviana Gradinaru, Ph.D.**

$50M Series A co-led by Westlake Village BioPartners and Versant Ventures

2021

AbbVie CNS deal **$90M** upfront including convertible note (CN); future milestones & royalties

2023

Lilly/Prevail CNS deal **$55M** including upfront & equity commitment; future milestones & royalties

AbbVie Ophthalmology deal **$70M** upfront including CN; future milestones, & royalties

Cost sharing manufacturing collaboration

Lead capsids up to 70% neuronal transduction in NHPs; DC for STXBP1

2024

DC for PD-GBA and Friedreich's ataxia; Excellent manufacturing yields & quality at/above FDA standards

IND-enabling studies initiated for STXBP1, PD-GBA, and Friedreich's ataxia

Novel Human receptor identified derisking clinical translation

FDA grants Orphan Drug Designation for STXBP1 Developmental and Epileptic Encephalopathy program

Pipeline for Rare and Common Diseases Across All Ages

Capsida Wholly Owned Programs

Disease / Target		Cargo	Preclinical	IND-Enabling	Phase 1/2	Status
CNS	STXBP1 Developmental and Epileptic Encephalopathy	Gene Supplementation	CAP-002			• IND Submission 1H 2025 • FDA Orphan Drug Designation (ODD)
CNS	Parkinson's disease associated with GBA mutations	Gene Supplementation	CAP-003			• IND Submission 1H 2025
CNS/Cardiac/ Sensory	Friedreich's ataxia	Gene Supplementation	CAP-004			• IND-Enabling Studies

Partnered Programs

Partner	Disease Area	Co-Development/Co-Commercialization (Co/Co) Option
abbvie	Neurological & Ophthalmology Diseases	One Program, U.S. Profit Share (Neurological)
Prevail THERAPEUTICS A Wholly Owned Subsidiary of Eli Lilly and Company Lilly	Neurological Diseases	One Program, U.S. Margin Share
CRISPR THERAPEUTICS	Neurological Disease	CRISPR owned, Capsida Co/Co Option

Capsida Platform

Capsida – Uniquely Positioned to Lead Gene Therapy

Capsid Engineering Scale

Fully industrialized and roboticized platform

Screening capabilities across cell types in NHPs and human cells

CNS Tropism

>99% specific to neurons

>70% neurons transduced

Broad IP capsids and capsid/cargo

Peripheral Detargeting

>16x liver & >50x DRG detargeted

Superior off-target safety profile

Broad IP protecting detargeting

Therapeutic Expression

Expression in NHPs with potential for full disease correction

Industry leading expression levels across pipeline programs

Clinical Translatability

Identified/patented novel human receptor with complete homology in NHPs and humans

Validated expression in NHPs including primates >20 years old

Manufacturability

In-house process development and GMP manufacturing

Productivity surpassing AAV9

Quality specifications > FDA requirements

Only Capsida has created all the capabilities and results needed to deliver on the promise of gene therapy

Capsida Has Developed Best-In-Class Platform

Leverages rigorous drug development principles and high-throughput automation to identify capsids that meet Target Capsid Profile (TCP) for each indication

Engineered Capsids that Meet or Exceed TCP

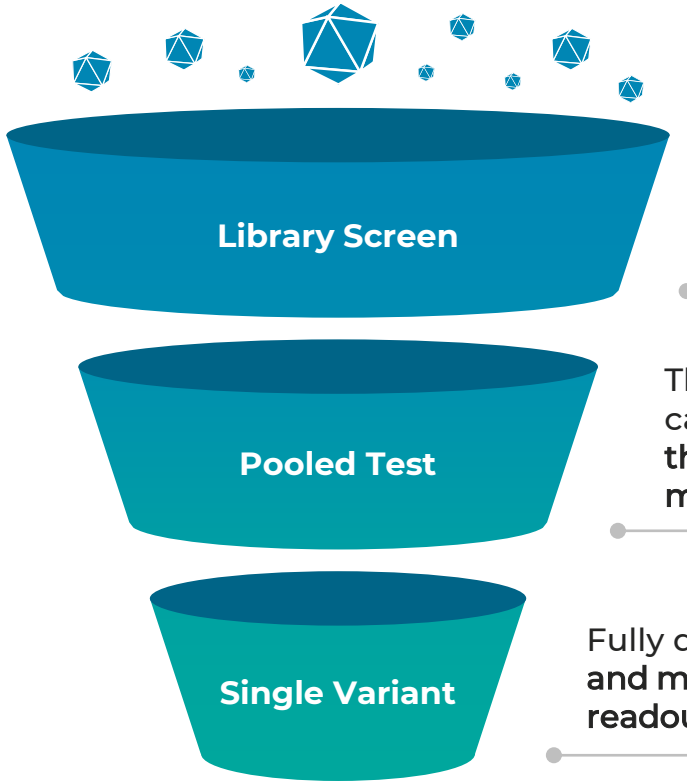
Evolved from engineering in mice to NHPs and screening in human cells to improve human translatability

Industrialized process built around customized robotics platform

Engineer capsids to meet TCP criteria including:

- Targeted tissues and cell type specificity
- High expression levels
- >10x off-target tissue detargeting
- Superior immunogenicity profile
- Superior manufacturability profile

Industrialized Capsid Development



Use directed evolution to create billions of variants screened **directly in NHPs and human cells**

Thousands of Candidate capsids are assessed for **therapeutic expression and manufacturability**

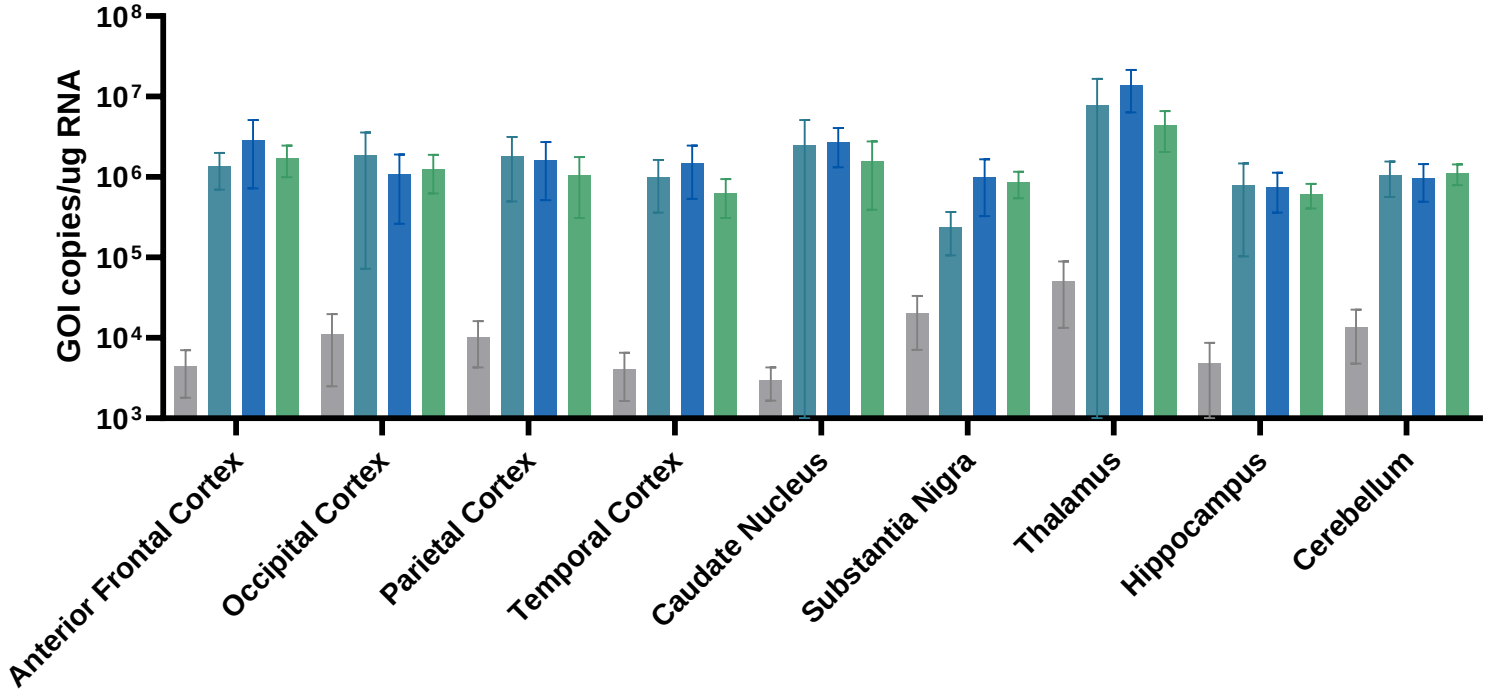
Fully quantitative **efficacy, safety, and manufacturing scalability readouts** for each single variant

Advance development candidates that meet or exceed TCP for each indication

Lead Capsids Demonstrate High Expression Across the CNS and Significant Liver Detargeting with IV-dosing

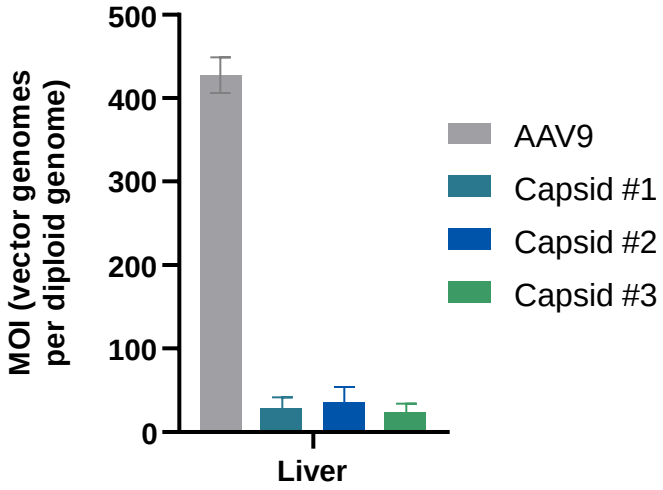
Broad CNS Transduction

Up to ~300x increase in CNS Expression



Liver Detargeting

≥16x decrease in Liver Detargeting

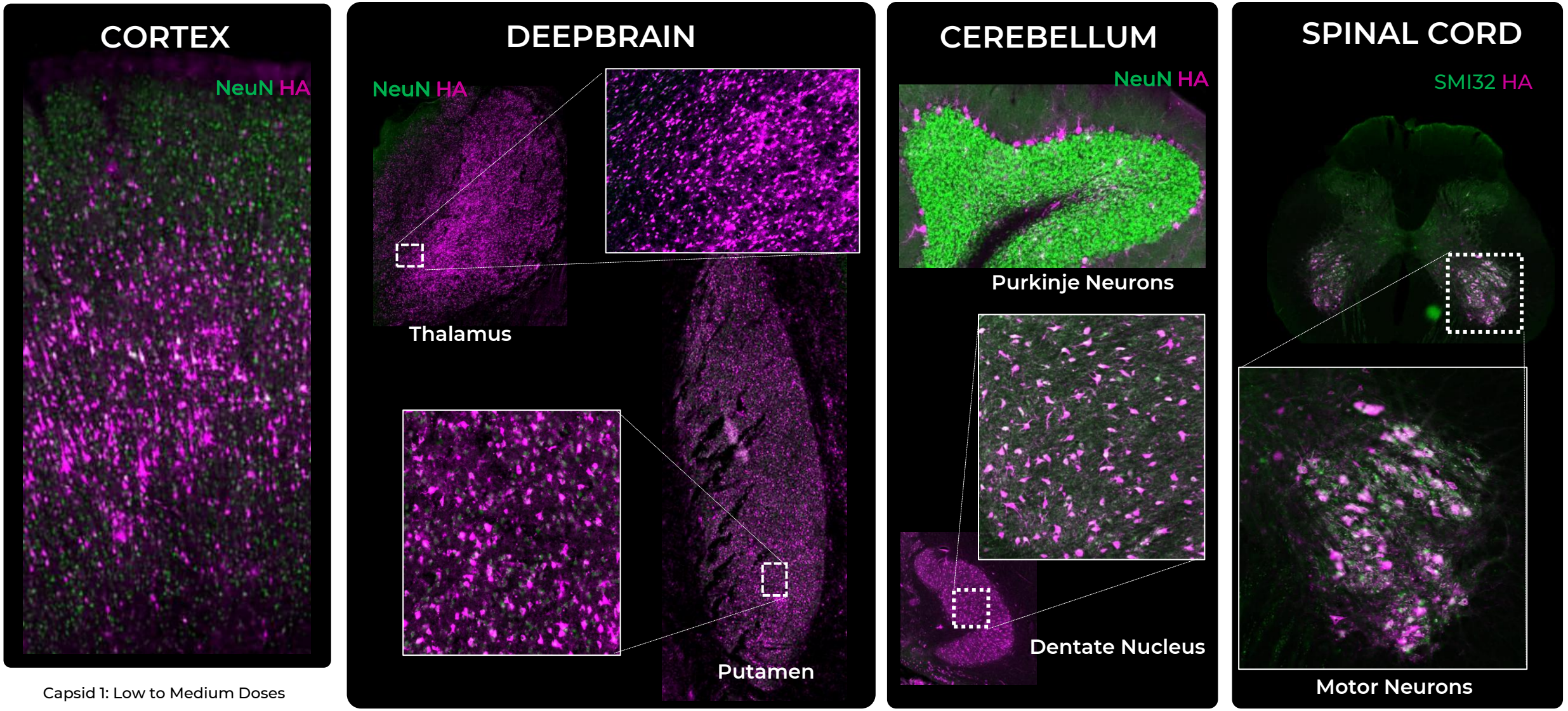


Cargo: HA-GOI | **Dose:** 2.5E13 vg/kg

Species/Age: N = 3 cynomolgus macaques/group, 36-42mo

Capsid selected for CAP-002, CAP-003, and CAP-004 exceeds rigorous criteria for all programs

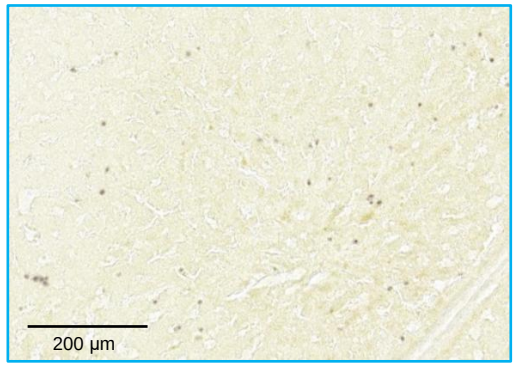
Lead Capsid Results In Widespread Protein Expression Throughout the CNS Following IV Delivery



Capsid 1: Low to Medium Doses

Significant Detargeting of the Liver and No Histopath Findings, Including in DRGs, After IV Dosing in NHPs

Liver



Dose: 2.5E13 vg/kg
In-life: 6 weeks
Species/Age: N = 3 cynomolgus macaques, ~42mo

≥16X detargeted to liver compared to AAV9

Lead capsid is **well tolerated** with no clinical pathology or immunogenicity findings

Unremarkable histopathology across the body, including liver and DRGs

Pipeline Programs

Parkinson's Disease Associated with GBA Mutations

CAP-003 potential to be best-in-class disease modifying therapy

PD-GBA

Mutations in GBA result in decreased GCase activity (25-30% in symptomatic PD-GBA patients) and lysosomal dysfunction

Up to **15%** of PD patients have mutations in the GBA gene[1]

	Limitations of Investigational Therapies	CAP-003 Differentiators
Transduction	— Low neuronal transduction, especially in substantia nigra	+ Up to 70% of neurons transduced (57% in substantia nigra)
Expression	— Don't report GCase activity or haven't seen significant elevations	+ GCase activity > levels needed to treat PD-GBA; reach 172% in cortex and 249% in putamen
Delivery	— Invasive delivery	+ Non-Invasive IV delivery
Safety	— DRG toxicity risks	+ No adverse histopathology across the body, including liver and DRGs

Disease Manifestations

PD is second most common neurodegenerative disease

Motor Symptoms (e.g., resting tremor, rigidity, slowness of movement) and non-motor symptoms (e.g., cognitive decline, psychiatric)

Unmet Need

No approved disease-modifying therapies

Potential for earlier age of onset, more frequent cognitive impairment, more rapid progression vs idiopathic PD[1]

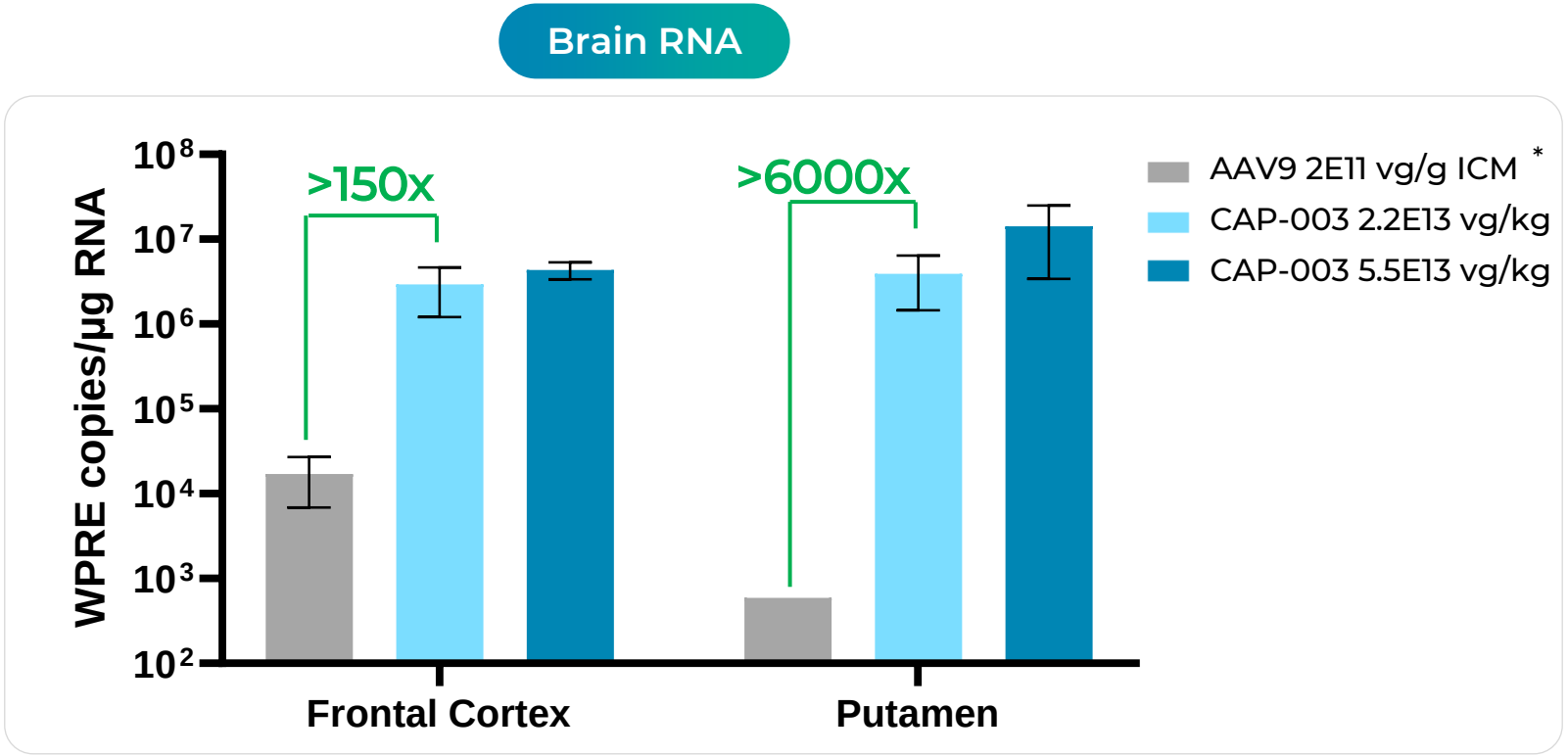
Commercial Opportunity Potential >$1B

Potential to be first IV delivered gene therapy

Up to **150K** prevalent PD-GBA population in US[2] and up to **180K** in the EU[3]

[1]Smith and Schapira 2022; [2]Parkinson's Foundation; [3]Deuschl G The Lancet Public Health 2020

IV-delivered CAP-003 Achieves Superior Expression Compared to ICM-delivered AAV9 in NHPs

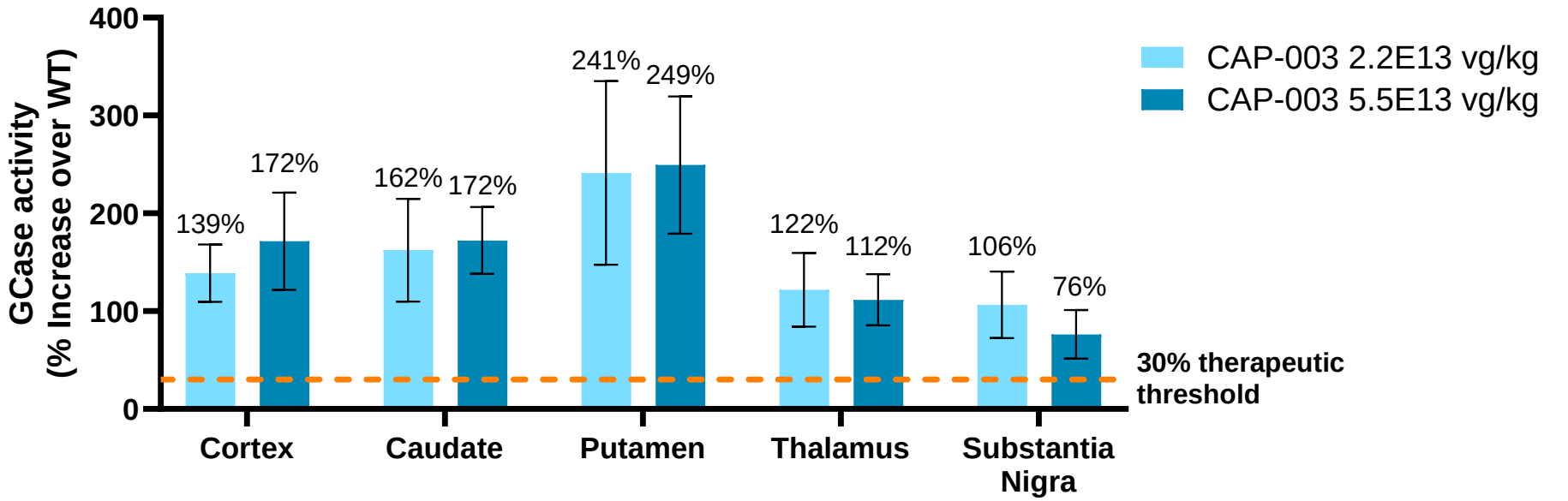


IV-delivered CAP-003 achieves >150-fold higher expression in cortical and >6000-fold in sub-cortical areas compared to ICM-delivered AAV9

*AAV9 ICM data generated from past Capsida study with same expression cassette (promoter, regulatory elements, etc.) but different therapeutic cargo; no protein or %neuron comparison possible

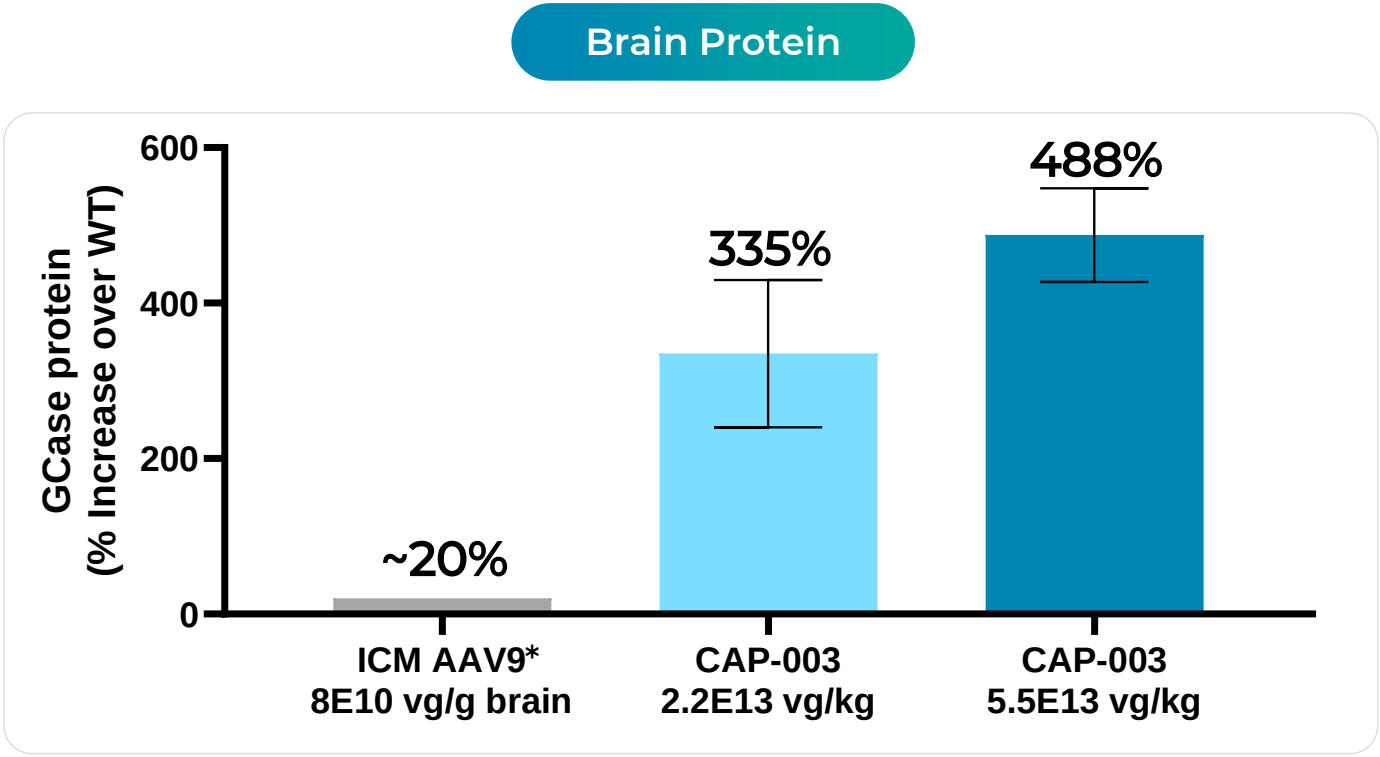
All CAP-003 Doses Exceed 30% Efficacy Threshold for Normalizing GCase Activity in Patients

Brain Activity



GCase activity, including in Substantial Nigra, was 2-8-fold higher than the threshold needed to overcome the expected deficit in patients

Industry-leading GCase Protein Increases with CAP-003

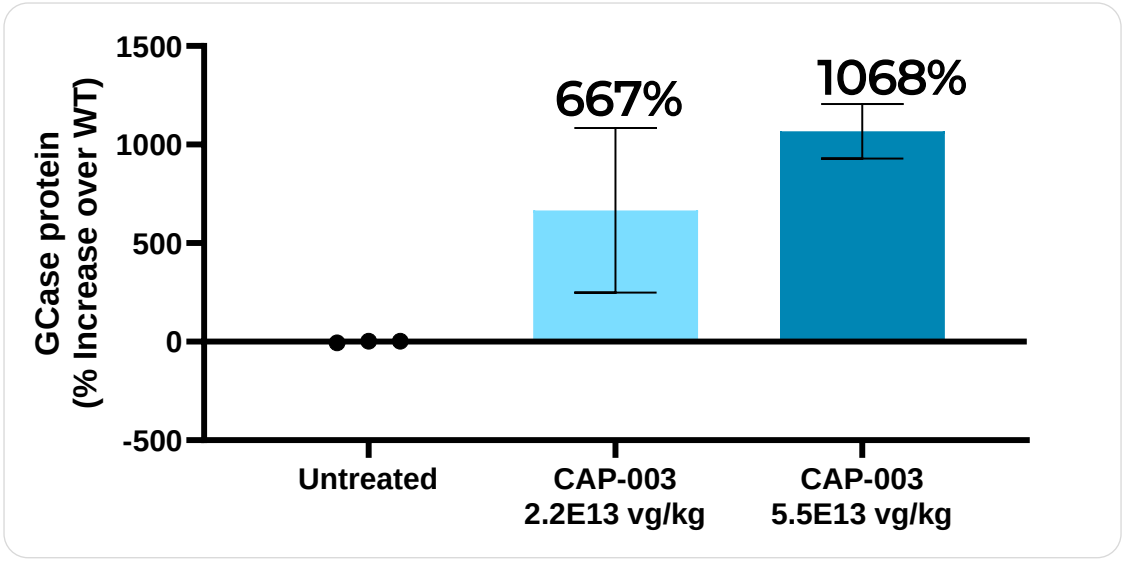


Average GCase protein level increases of IV CAP-003 in NHPs are 8-24x > than ICM AAV9*

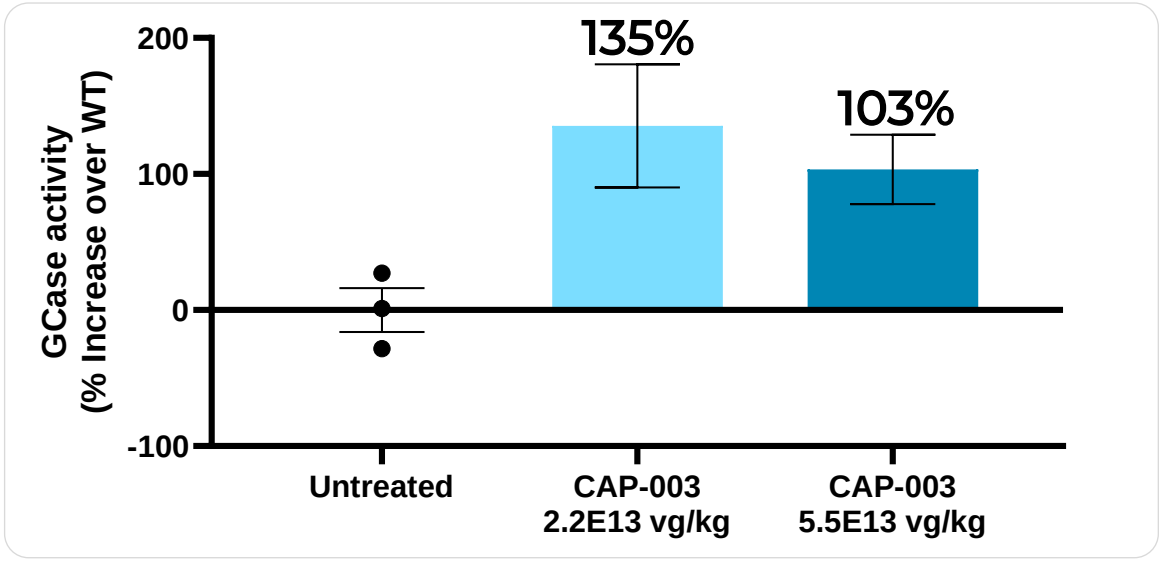
*Reported by Prevail (Source: 2019 S1 filing) in their non-clinical NHP studies (~20% increase across cortex, hippocampus, midbrain)

Marked Increases in GCase Protein and Activity in NHP CSF Support Use as Early Target Engagement Biomarkers

CSF Protein

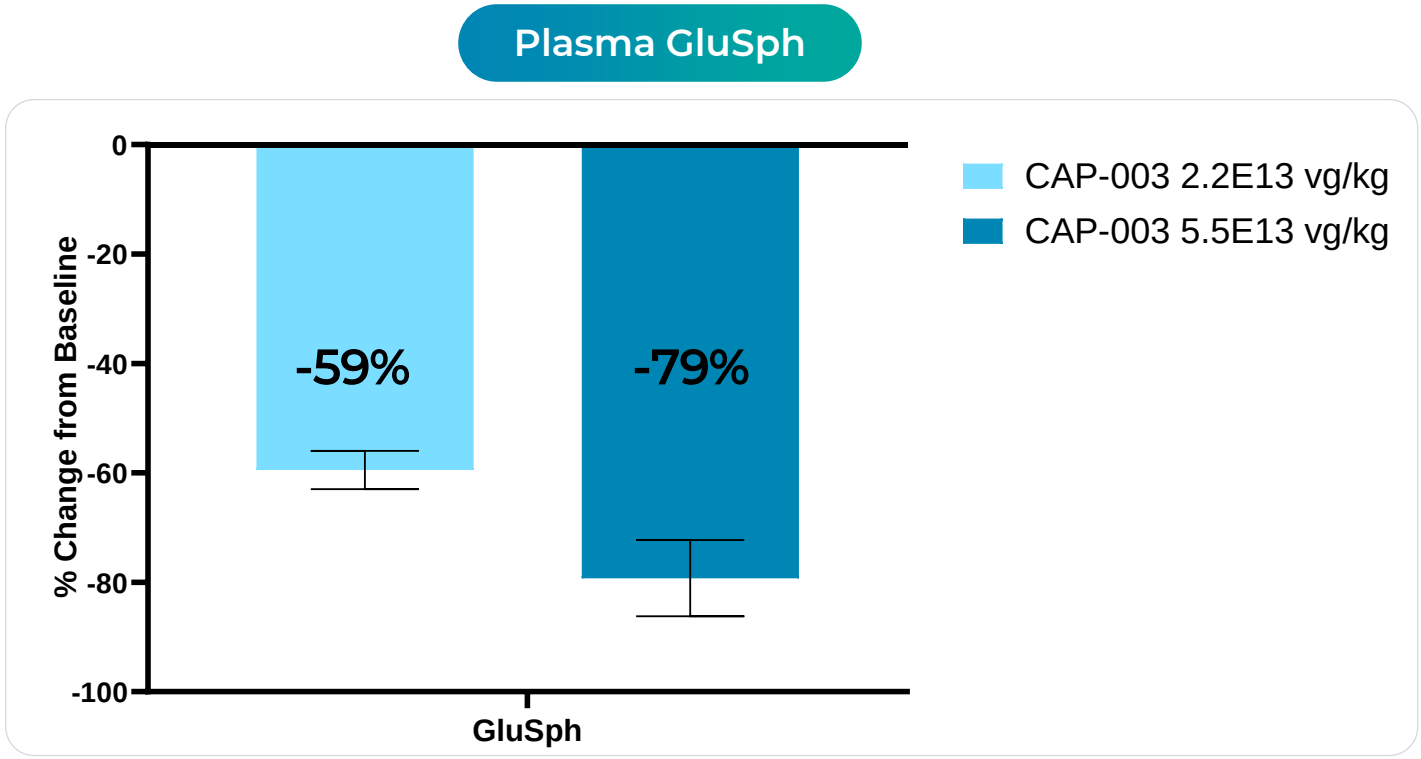


CSF Activity



- Average GCase activity in the brain shows significant positive correlation with GCase protein levels in the CSF and trend of positive correlation with GCase activity in the CSF
- These data raise confidence in the use of CSF GCase biomarkers in the clinic

Strong Target Engagement in the Key Glycolipid Substrate

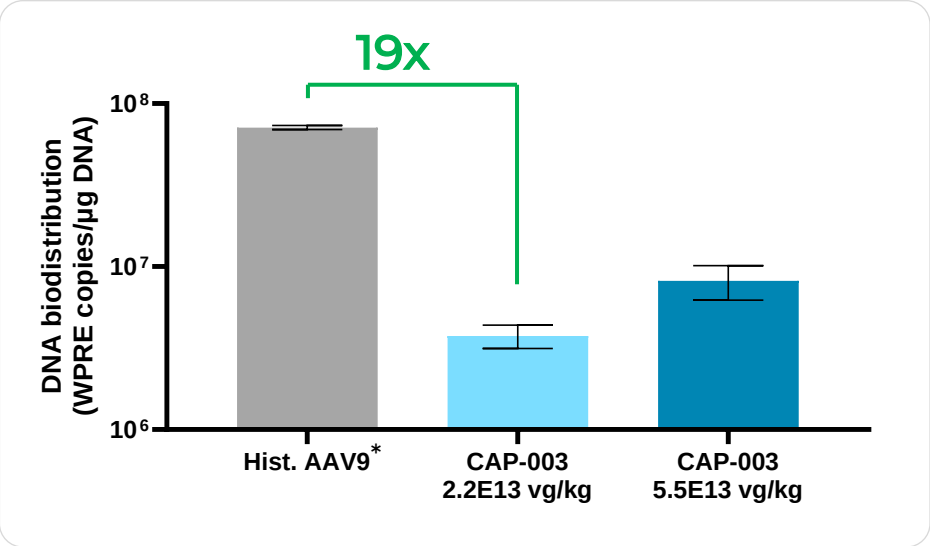


GluSph shows decreased levels in the terminal plasma of CAP-003 treated NHPs, providing evidence of lysosomal activity and target engagement

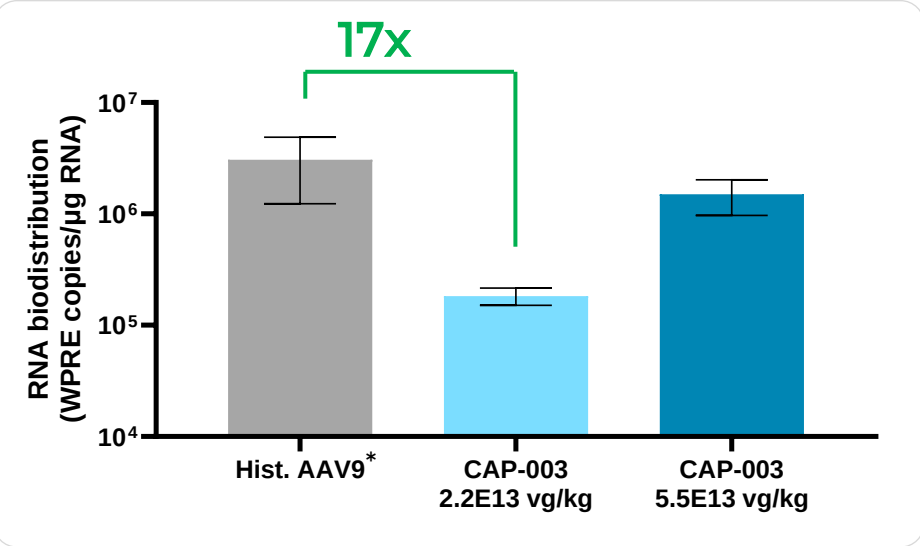
GluSph = Glucosylsphingosine

DNA & RNA Biodistribution to the Liver and DRGs is Significantly Reduced in NHPs Compared to AAV9

Liver DNA



DRG RNA



- Liver biodistribution is 19-fold lower than AAV9 and results in no adverse histopathology
- Expression in DRGs is 17-fold lower than AAV9 and results in no adverse histopathology

*Historical IV-delivered AAV9 comparison (4-week in-life, non-GBA cargo)

Syntaxin-binding Protein 1 (STXBP1) Developmental and Epileptic Encephalopathy

CAP-002 is first-in-disease and best-in-class disease modifying therapy

STXBP1 Genetic Mutation
Autosomal dominant

STXBP1 is expressed in every neuron and is essential for neurotransmitter release

Reduction in STXBP1 levels results in impaired neurotransmission

	Limitations of Investigational Therapies	CAP-002 Differentiators
Transduction	– Inability to achieve brain wide neuronal transduction	+ Widespread transduction through the brain
Expression	– Insufficient	+ Dose-dependent STXBP1 protein expression throughout the cortex
Delivery	– Invasive delivery	+ Non-Invasive IV delivery
Safety	– DRG toxicity risks	+ Unremarkable histopathology across the body, including liver and DRGs

Disease Manifestations

- Refractory seizures
- Developmental delay, cognitive dysfunction, and intellectual disability
- Motor abnormalities
- Early mortality

Unmet Need

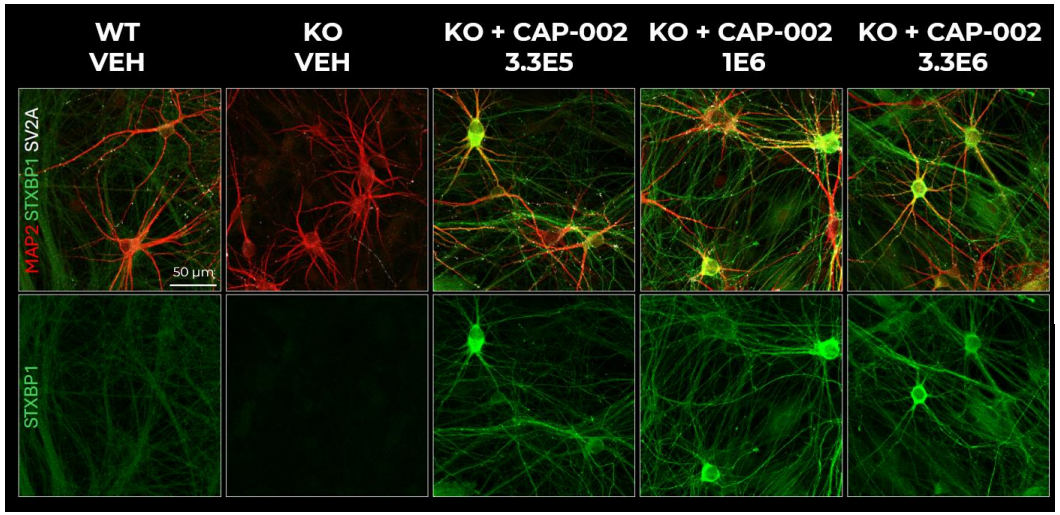
- No approved therapies
- Anti-seizure medications only partially effective

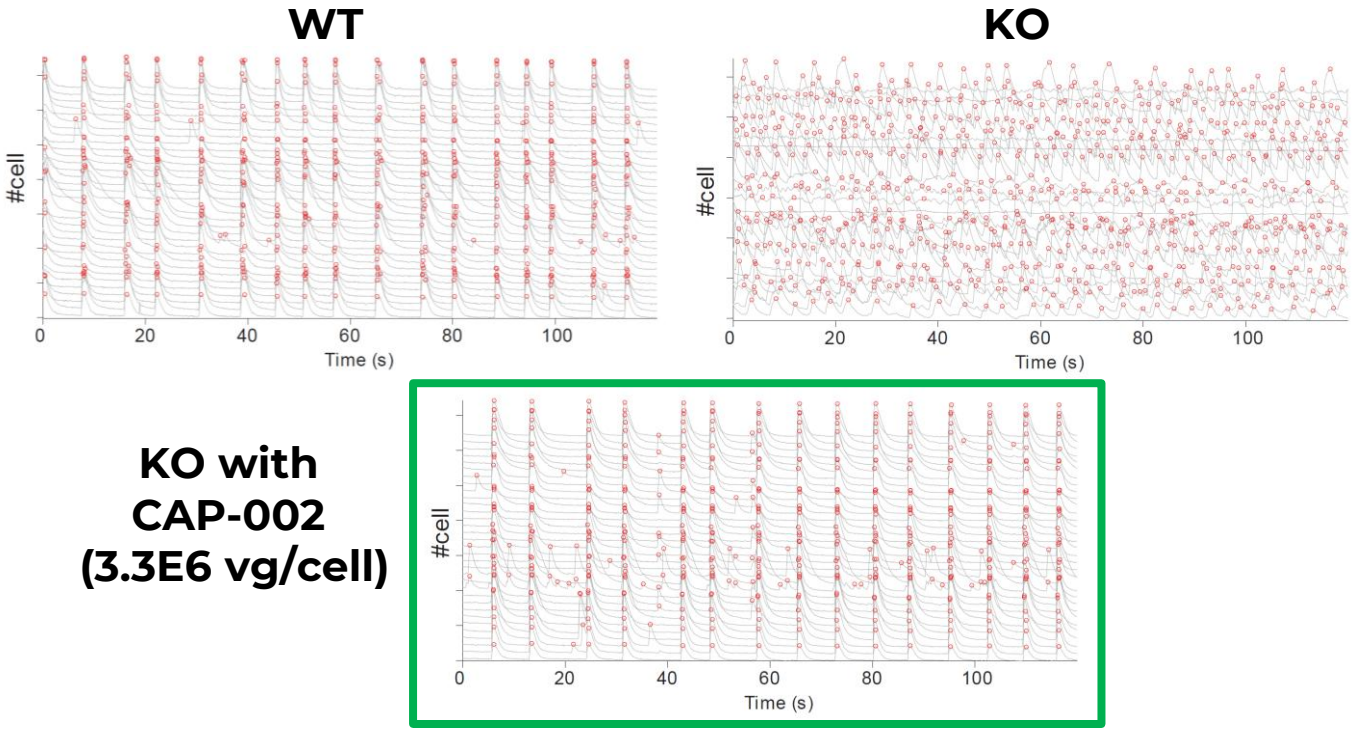
Commercial Opportunity Potential >$1B

- No disease modifying programs in clinical development
- Potential to be first-in-class and first-in-disease
- 1:30,000 live births[1] (up to 4500 in US and EU) and growing

[1]Lopez-Rivera et al., Brain, 2020

CAP-002 Expression in Human iPSC-derived, STXBP1 KO Neurons Restores Protein and Neuronal Network Activity





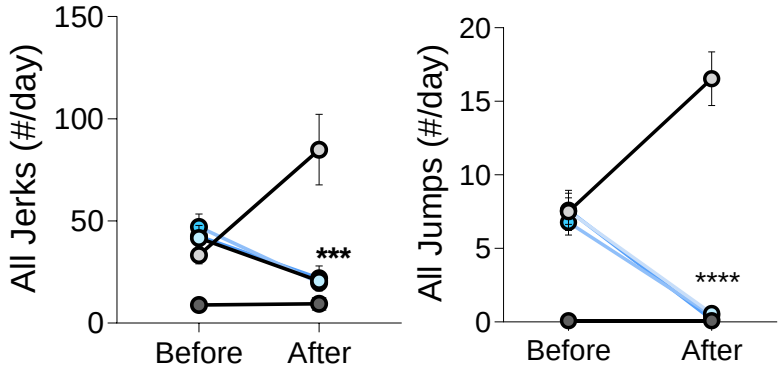
- CAP-002 restores STXBP1 expression to WT levels and achieves a WT cellular distribution pattern in human iPSC-derived STXBP1 KO neurons
- CAP-002 restores synchronous neuronal firing in STXBP1 KO neurons
- These data demonstrate that CAP-002 restores normal network activity in human disease neurons

Generated in collaboration with Neurospector, a CRO established by Matthijs Verhage's laboratory

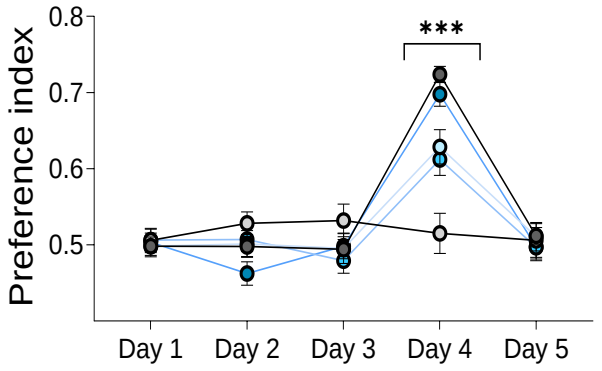
Brain-wide STXBP1 Expression Enables Dose-dependent Correction of Seizures, Cognitive, and Motor Dysfunction in Mouse Model

Epilepsy | **Cognitive Dysfunction** | **Motor Dysfunction**

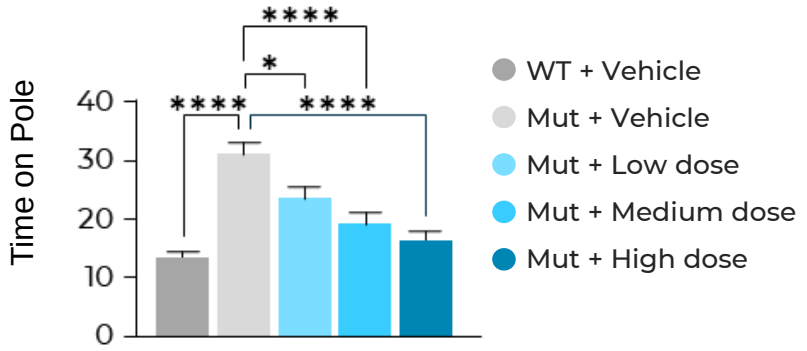
Myoclonic Seizures



Novel Object Recognition



Vertical Pole



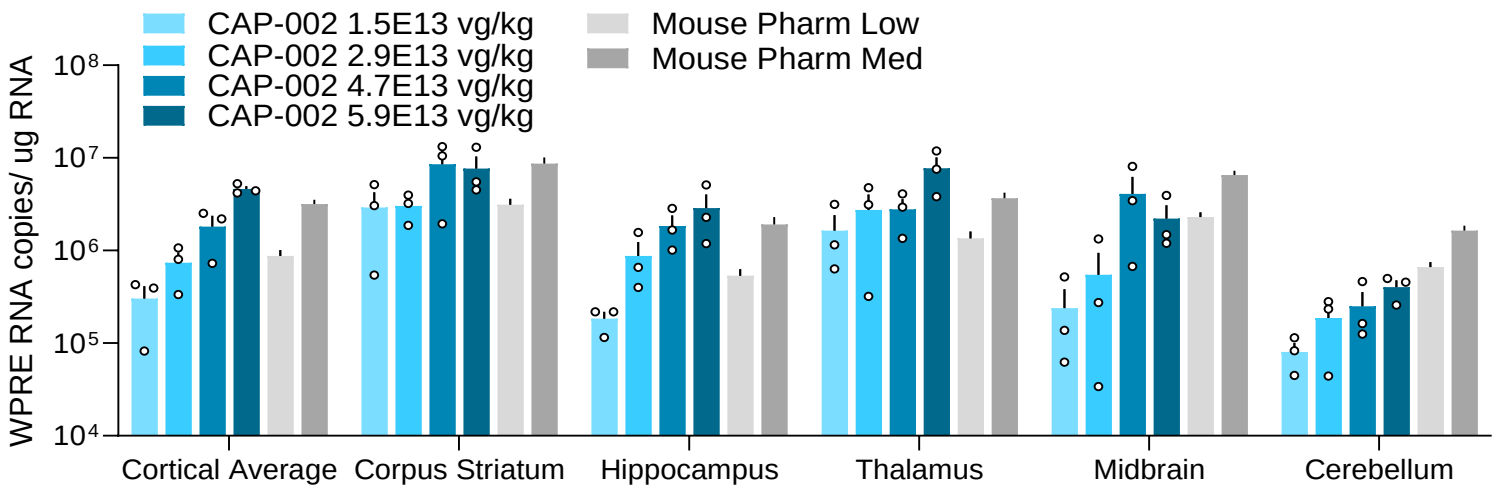
Difference from Mut + VEH: * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$
Seizures: and Vertical Pole: Kruskal-Wallis Test with Dunn's Multiple Comparisons Test; NOR: 2-way ANOVA with Tukey's Multiple Comparisons Test

- A single IV administration of a surrogate capsid expressing the STXBP1 therapeutic cargo achieves significant phenotypic correction at all doses
- Reversal of symptoms in mature mice demonstrates potential for phenotypic correction
- Correction is long-lasting to >1-year post-dosing with no histopathology findings

Murine data generated in collaboration with lab of Mingshan Xue, Baylor College of Medicine

CAP-002 STXBP1 Expression is Expected to Significantly Correct All Disease Phenotypes

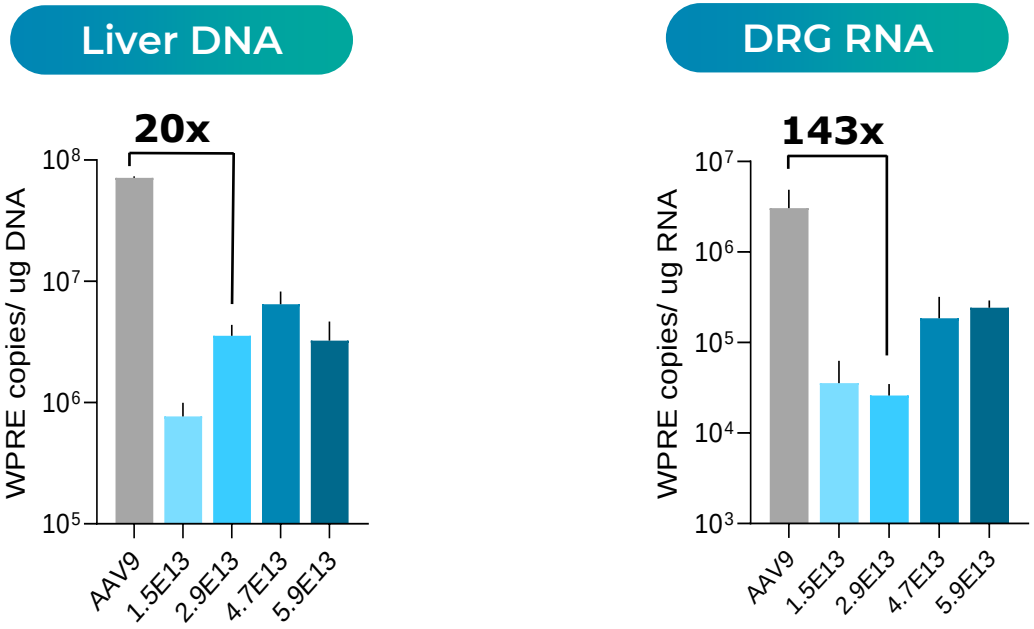
Brain Expression in NHPs Compared to Mouse Pharmacology Study



- RNA expression at 2.9E13 vg/kg is comparable to mouse pharmacology low dose, with prospect for full correction of seizures, and significant, partial correction of cognitive and motor disabilities
- 4.7E13 and 5.9E13 vg/kg doses are expected to achieve further correction across cognitive and motor disabilities

AAV9 is equivalent to the 2.9E13 vg/kg dose

CAP-002 is Substantially Detargeted from Liver and DRGs in NHPs Relative to AAV9



- Detargeting from non-therapeutic areas, including 20x lower liver burden and 143x lower DRG expression
- Well-tolerated safety profile, with no adverse histopathological findings

AAV9 is equivalent to the 2.9E13 vg/kg dose

Friedreich's Ataxia (FA)

CAP-004 potential to be best-in-class disease modifying therapy

Friedreich's Ataxia (FA)
Autosomal recessive

Trinucleotide repeat expansion disorder that results in reduction in frataxin (FXN) protein, leading to death of highly active cells that are dependent on ATP production, mainly cardiomyocytes and neurons

	Limitations of Investigational Therapies	CAP-004 Differentiators
Transduction	— No therapies target CNS, cardiac, and sensory manifestations	+ Substantial transduction across key cell types in CNS, cardiac, and sensory regions
Expression	— Insufficient across key tissues affected by FA	+ Therapeutically meaningful FXN expression expected to achieve full correction
Delivery	— Invasive delivery to CNS	+ Non-Invasive IV delivery
Safety	— Liver toxicity	+ No adverse histopathology across the body, including liver and other non-target tissues

Disease Manifestations

- Instability / Falls
- Hypertrophic Cardiomyopathy
- Ataxia
- Sensory impairment
- Average lifespan is ~37 years old

Unmet Need

- No current treatment that directly address frataxin deficiency
- No therapies address all manifestations
- Several investigational gene therapies only focus on cardiomyopathy

Commercial Opportunity Potential >$1B

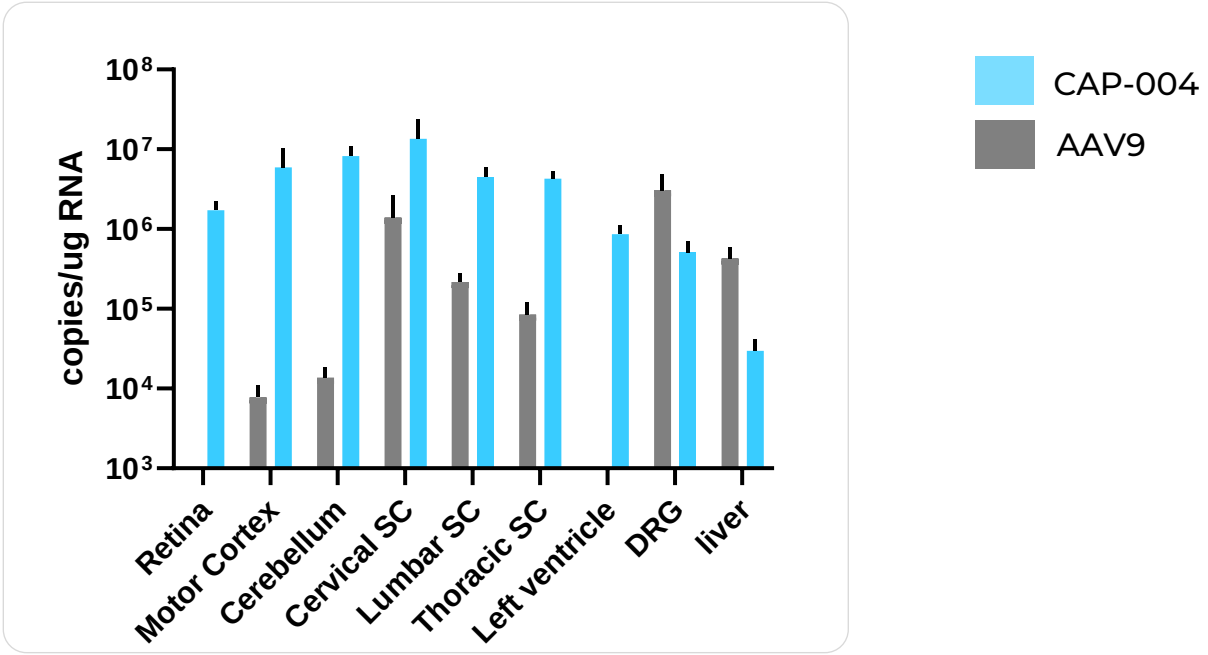
Potential to be first-in-class single IV infusion to treat CNS, cardiac and sensory manifestations

~5,000 cases in the US[1] and 15,000 worldwide[1]

1. FARA (Friedrich's Ataxia Research Alliance)

IV CAP-004 Achieves Meaningful Transduction of CNS, Cardiac, and Sensory Tissue with ~10x Liver De-targeting vs. AAV9 in NHPs

RNA expression in FA target regions

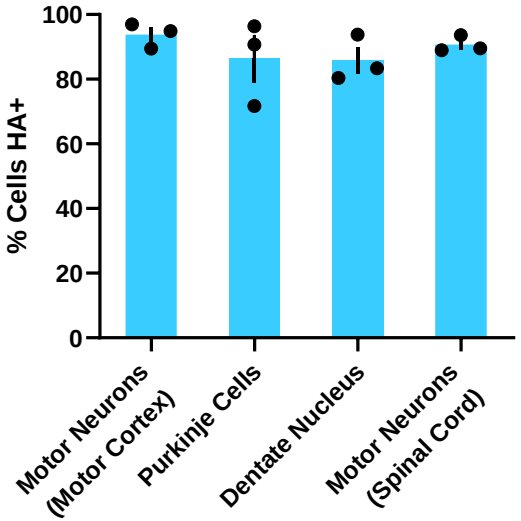


- CAP-004 at a low to moderate dose results in >100-fold higher expression compared to AAV9 across key areas of interest in the CNS
- Meaningful RNA expression in the retina suggests a potential in treating sensory vision loss

DRG = dorsal root ganglia

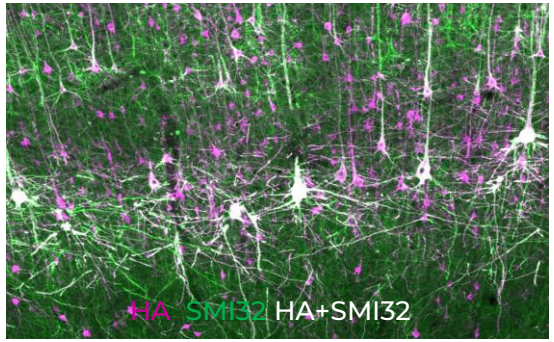
CAP-004 Drives FXN-HA Protein Expression Across Cell Types that are Central to FA Symptoms and Pathology

Percentage of Neurons Expressing HA

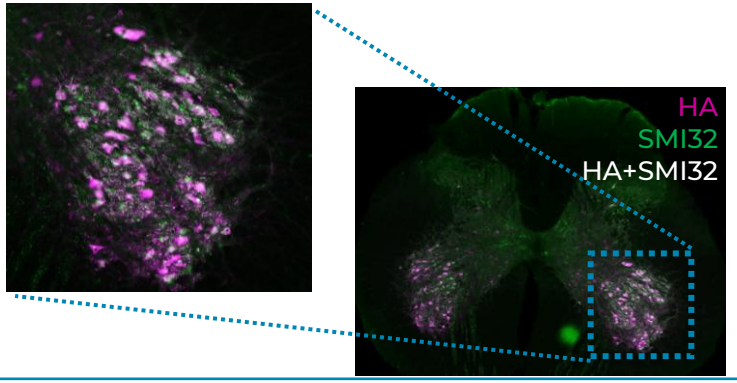


Cargo: hFXN-HA; **In-life:** 4 weeks
Species/Age: N = 3 cynomolgus macaques, ~32mo

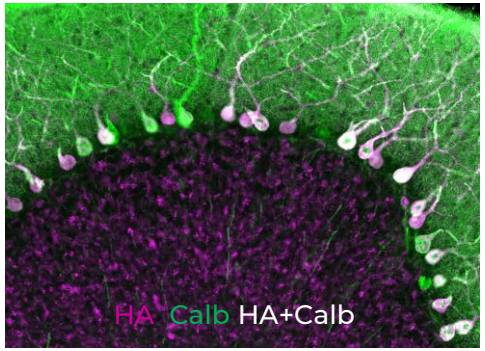
Motor Cortex



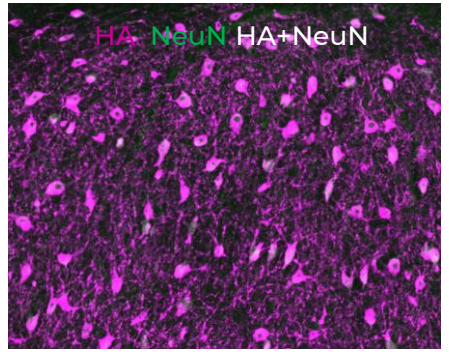
Spinal Cord



Cerebellar Cortex



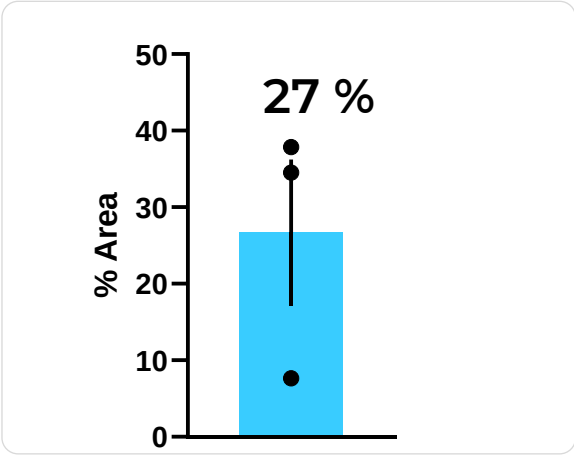
Deep Cerebellar Nuclei



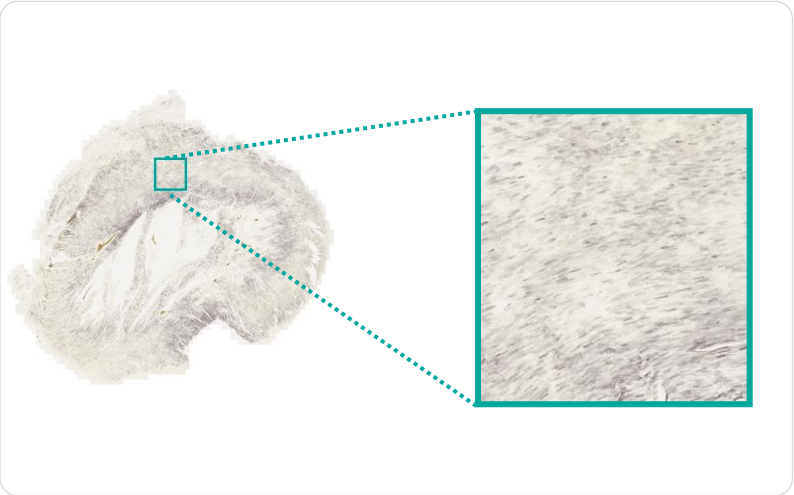
Single IV administration of CAP-004 in NHPs demonstrates potential for complete correction across all CNS target tissues

CAP-004 Cardiac Transduction Reaches ~30% Coverage in the Left Ventricle in NHPs

Cardiac Left Ventricle %HA Positive Area



Cardiac Left Ventricle

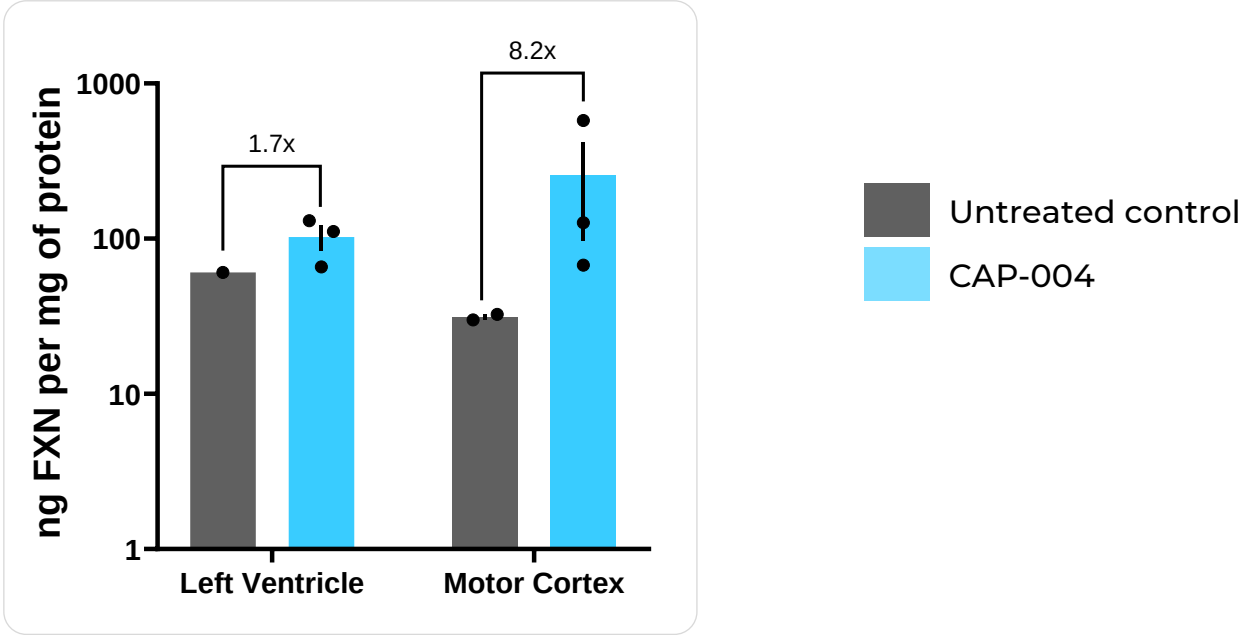


Cargo: hFXN-HA; **In-life:** 4 weeks
Species/Age: N = 3 cynomolgus macaques, ~32mo

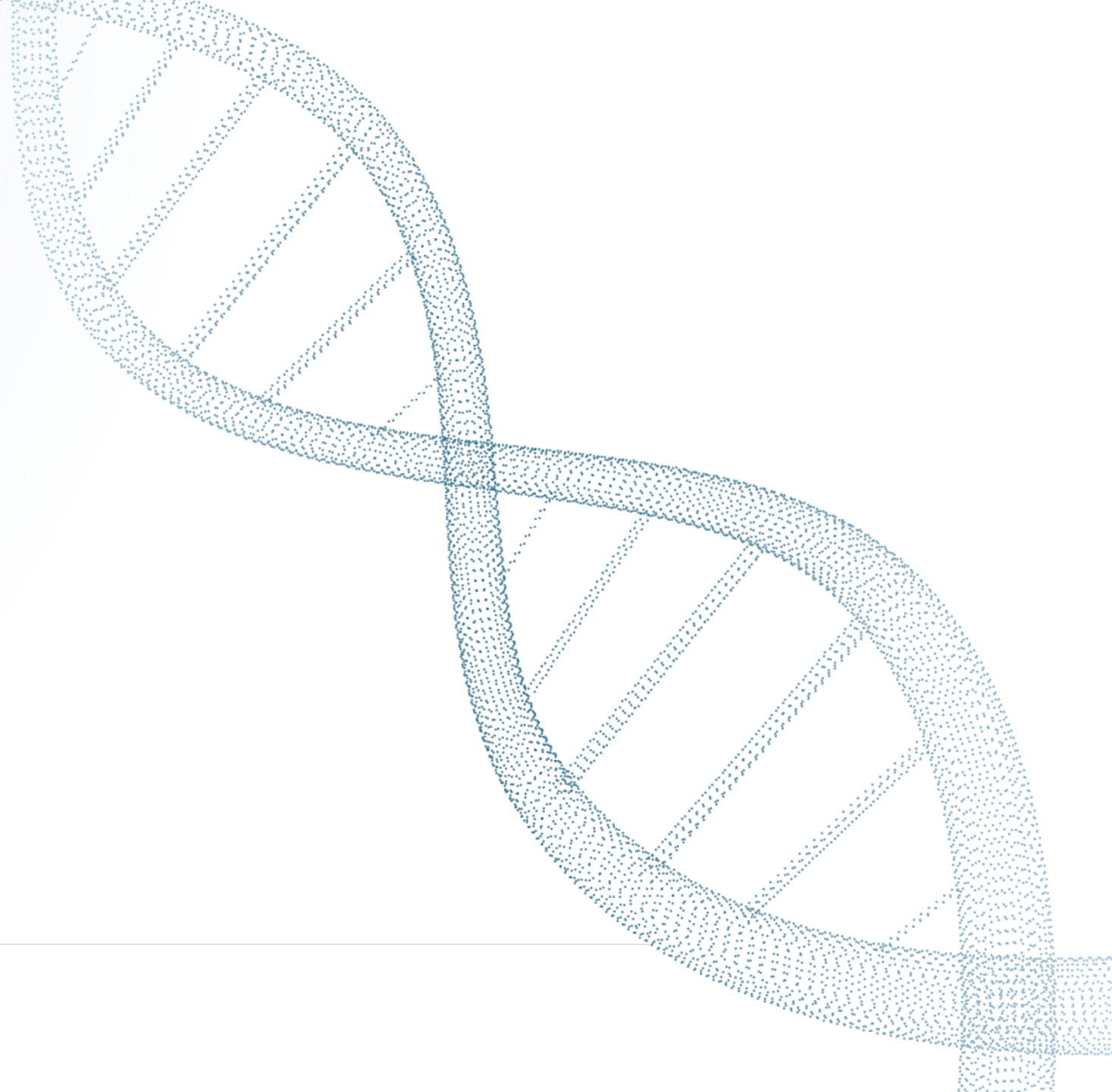
CAP-004 administration results in substantial transduction of cardiac tissue

CAP-004 Treated NHPs Shows Robust FXN Expression in Cerebral Cortex and Cardiac Tissue

hFXN ELISA



IV administered CAP-004 results in 8-fold increase in FXN protein expression in the CNS and 1.7-fold increase in cardiac tissue



Manufacturing

Integrated Process & Analytical Development and cGMP Capabilities

In house capabilities reduce turn-around times and expedite process transfer to support clinical studies

Vector Production		Rapid production of engineered capsids for preclinical studies
Process & Analytical Development		Conduct manufacturability assessment in HEK293 suspension process
		Up to 50 L bioreactor scale
		Develop and optimize key analytical assays
cGMP Manufacturing		15,000 ft^2 cGMP Manufacturing Facility
		Leverages single use systems
		Up to 200L bioreactor scale
		Finish – fill operations
		Unidirectional flow
		In-house QC capabilities for product release
		Modular clean rooms

Excellent yields and quality specifications at or above FDA standards

Capsida Summary

Wholly-owned Programs Approaching the Clinic and Strong Pharma Validation

3 Wholly Owned Programs Approaching Clinical Stage

IV Administered

IND 1H 2025 - Parkinson's caused by GBA mutations (best in class potential)

IND 1H 2025 – STXBP1 Developmental and Epileptic Encephalopathy (first in class)

IND enabling studies – Friedreich's ataxia (best in class potential)

Leadership Team

Decades of industry experience, including drug development and manufacturing expertise

World class investors and scientific advisory teams including co-founder Viviana Gradinaru, PhD

Manufacturing Capabilities

In-house capabilities reduce turn-around times and expedite internal process transfer to support clinical studies

Quickly assess manufacturability

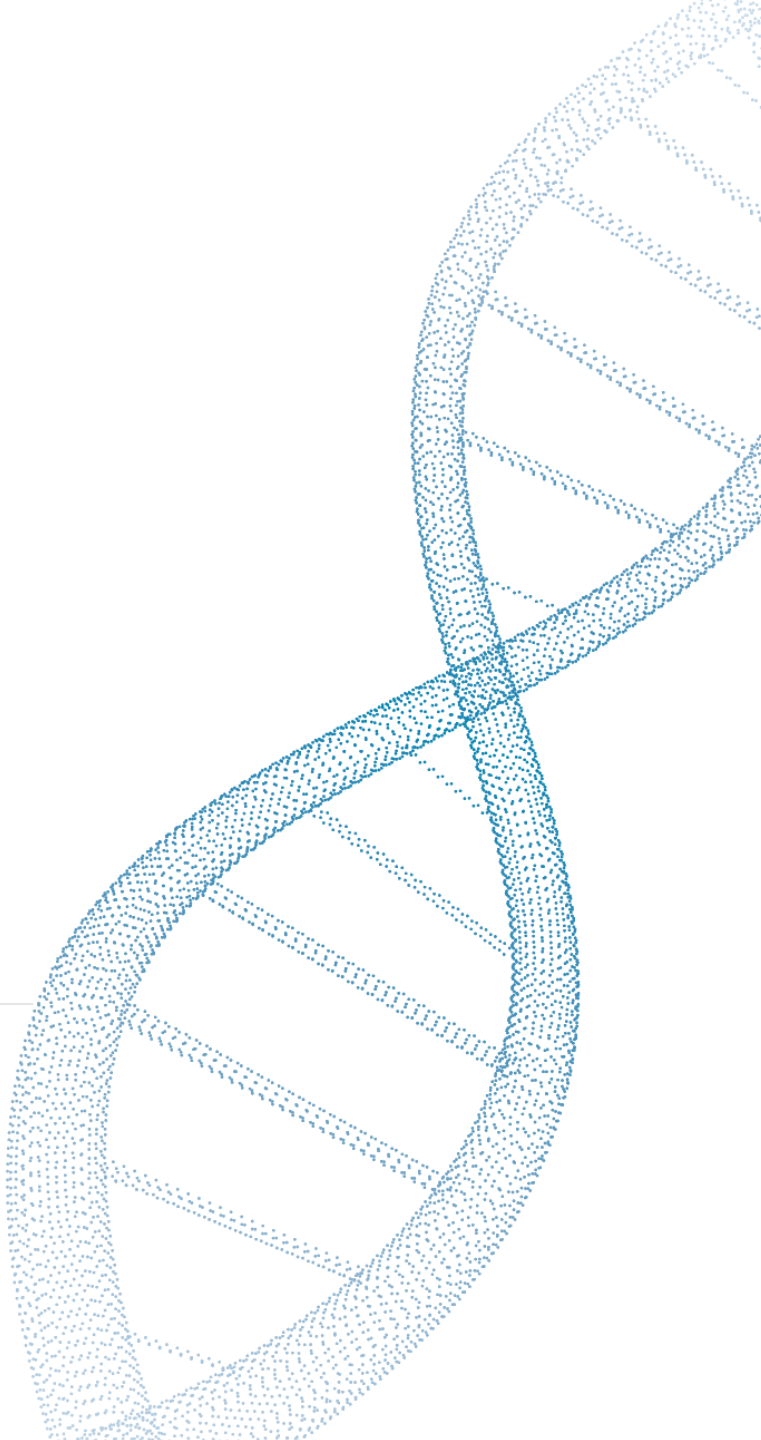
Control the process and associated costs

Partnerships

Key partnerships focused on CNS and Ophthalmology provide validation for the platform

CAPSIDA BIOTHERAPEUTICS

Our Pipeline is Making the Impossible Possible



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