



# Unlocking the Potential of Gene Therapy for All

Mar 2024



# Capsida Biotherapeutics



Foundation in capsid engineering with focus on building a new class of targeted, non-invasive gene therapies















Pipeline of wholly owned and partnered programs in rare and more common Neurological and Ophthalmology diseases



Fully integrated capabilities: capsid engineering, cargo optimization, discovery, preclinical research, process development, manufacturing, and clinical development

# Company History

2019		<b>Founded</b> Based upon breakthrough AAV engineering technology from the laboratory of Viviana Gradinaru
	 	<b>Series A</b> \$50M Series A co-led by Westlake Village BioPartners and Versant Ventures
2021		<b>Partner</b> AbbVie CNS deal <b>\$90M</b> upfront including equity
		<b>Partner</b> CRISPR Research Collaboration
2022		<b>Hire &amp; Partner</b> Hired new CEO to lead experienced management team and initiated second partnering process
2023	 	<b>Partner</b> Prevail / Lilly CNS deal <b>\$55M</b> upfront including equity
		<b>Partner</b> AbbVie Ophthalmology deal <b>\$70M</b> upfront including equity
	 	<b>Data Milestones</b> ASGCT Industry Symposium on <b>Breakthrough Capsids (up to 68% neurons)</b> and ETDD Presentation on <b>genetic epilepsy (STXBP1 preclinical data)</b>
		<b>Partner</b> Kate Therapeutics Manufacturing Collaboration

# Leadership Team and Board of Directors

Decades of Industry Experience and Drug Development Expertise

## Leadership



**Peter Anastasiou**  
Chief Executive Officer



**Susan Catalano, PhD**  
Chief Scientific 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



**Clare Ozawa, PhD**



**Beth Seidenberg, MD**



**Viviana Gradinaru, PhD**  
Founder



**Rita Balice-Gordon, PhD**



**Frank Verwiel, MD**



**Peter Anastasiou**  
Chief Executive Officer





# Recent FDA Approvals Create Significant Momentum

## Gene Therapy Approvals

Growing number of successfully developed and approved gene therapy products transformative for patients:

**Hemgenix™** (Hemophilia B)

**Zolgensma™** (SMA)

**Roctavian™** (Hemophilia A)

**Skysona™** (CALD)

**Vyjuvek™** (Dystrophic epidermolysis bullosa)

**Luxturna™** (RPE65 retinal dystrophy)

**Zynteglo™** (β-thalassemia)

**Elevidys™** (DMD)

**Casgevy™** (Sickle cell disease)

**Lyfgenia™** (Sickle cell disease)



## Breakthrough Neurological Therapies

FDA Approval for disease modifying CNS therapies based on biomarker data:

**Qalsody™** (SOD1 ALS)

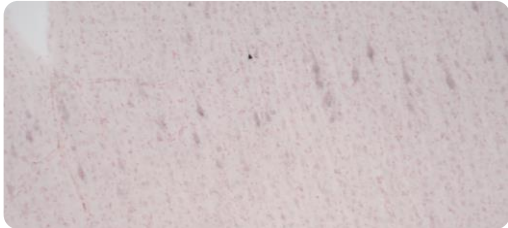
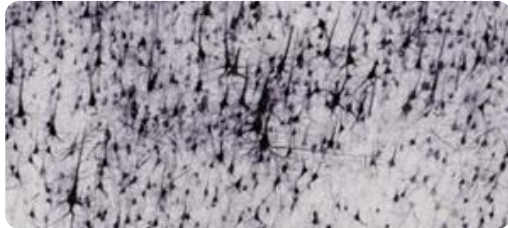
**Leqembi™** (AD)

**Skyclarys™** (FA)

**Aduhelm™** (AD)

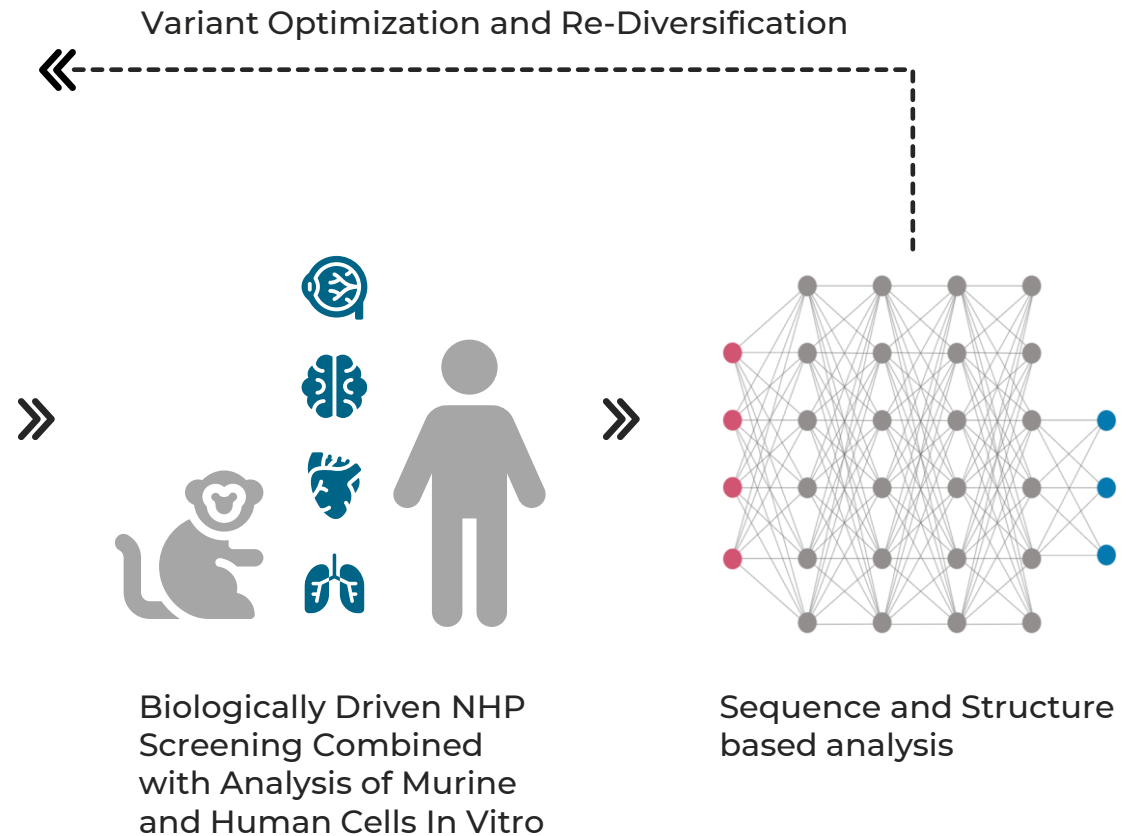
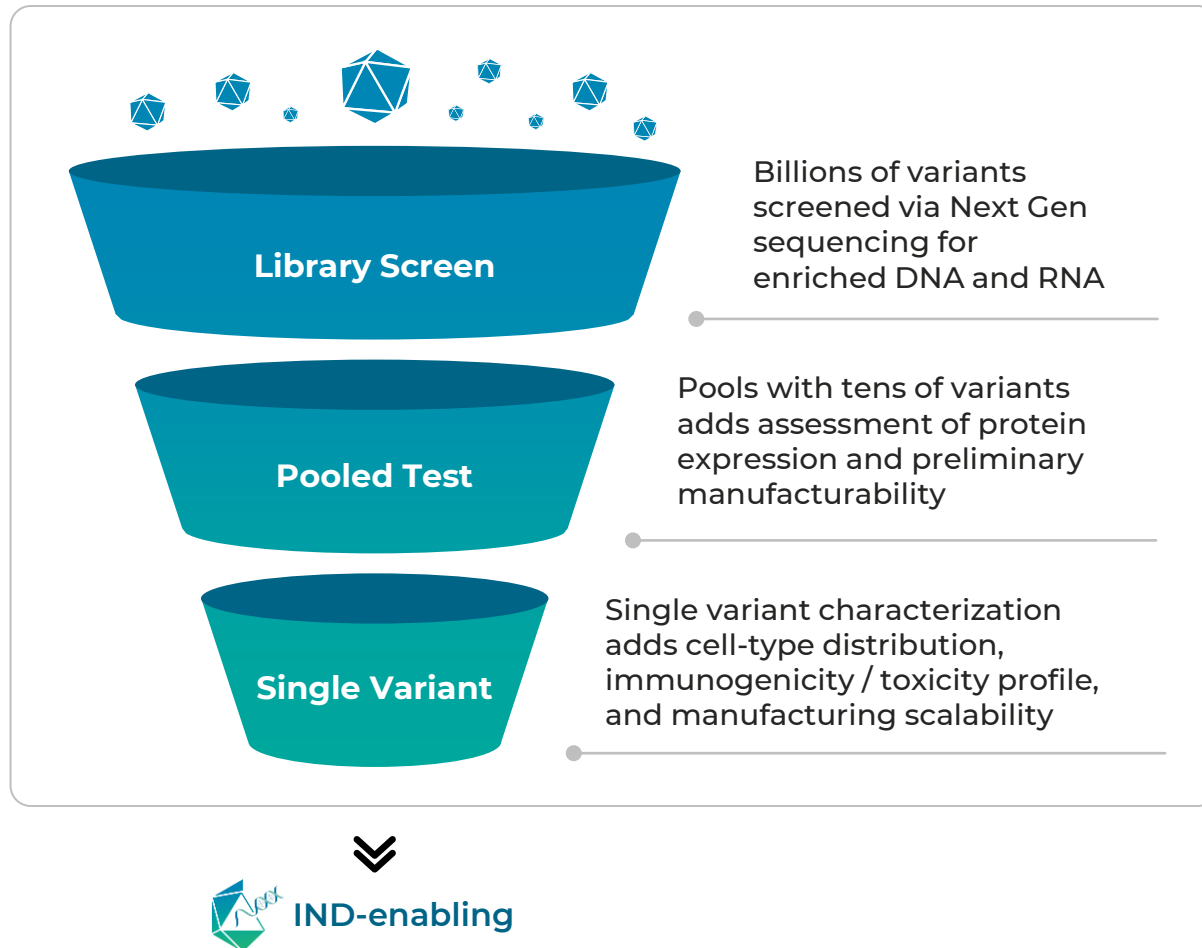


# Capsida Addresses CNS Challenges Through our Engineered Gene Therapies

	CNS Challenges	Capsida Solutions
	<p>Wild Type AAV9 (IV Delivery)</p> <p>NHP Cortex</p> 	<p>Capsida Engineered Capsid (IV Delivery)</p> <p>NHP Cortex</p> 
Neuronal Transduction	Limited ability to cross biological barriers, esp. BBB - < 1% <b>transduction</b> with wild type AAV9 IV	Capsida engineered capsids cross BBB with high levels of neuronal transduction – <b>up to 70% neurons</b>
Safety Concerns	Safety concerns / <b>liver toxicity</b>	Enabling lower dosing and <b>~4000x difference</b> in CNS to liver targeting vs wild type AAV9
Patient Populations	Traditional gene therapies <b>primarily for ultra-rare/rare diseases</b>	<b>Access to more</b> common diseases across all ages
Risks	Direct injection into the brain or CSF is invasive with <b>significant risks</b>	Targeted IV admin <b>increases effectiveness</b> and <b>reduces risks</b>

# NHP Driven Targeted Gene Therapy Engineering Platform

High-throughput Process Identifies Capsids that Target Desired Tissues and Cell Types While De-targeting Undesired Tissues



# Automated and High-Throughput NHP Screening Platform Accelerates Identification of Breakthrough Capsids



**Improves data accuracy and reproducibility** – highly consistent process

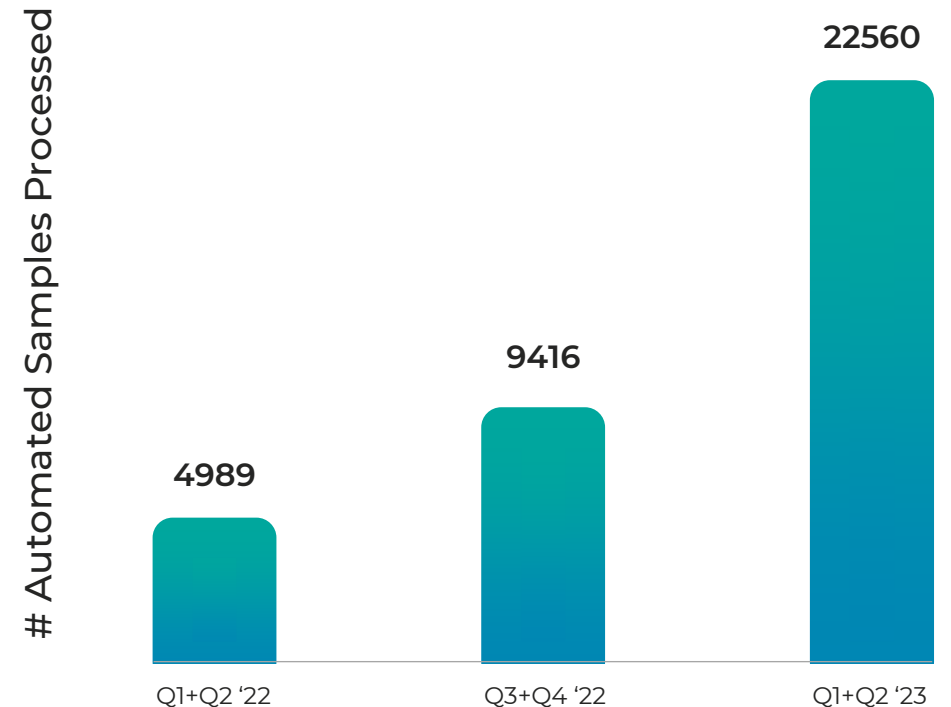


**Increases data quantity** – scale up on animal and tissue utilization



Screening capacity increases **250%**

Sample Processing Scaleup Since 2022

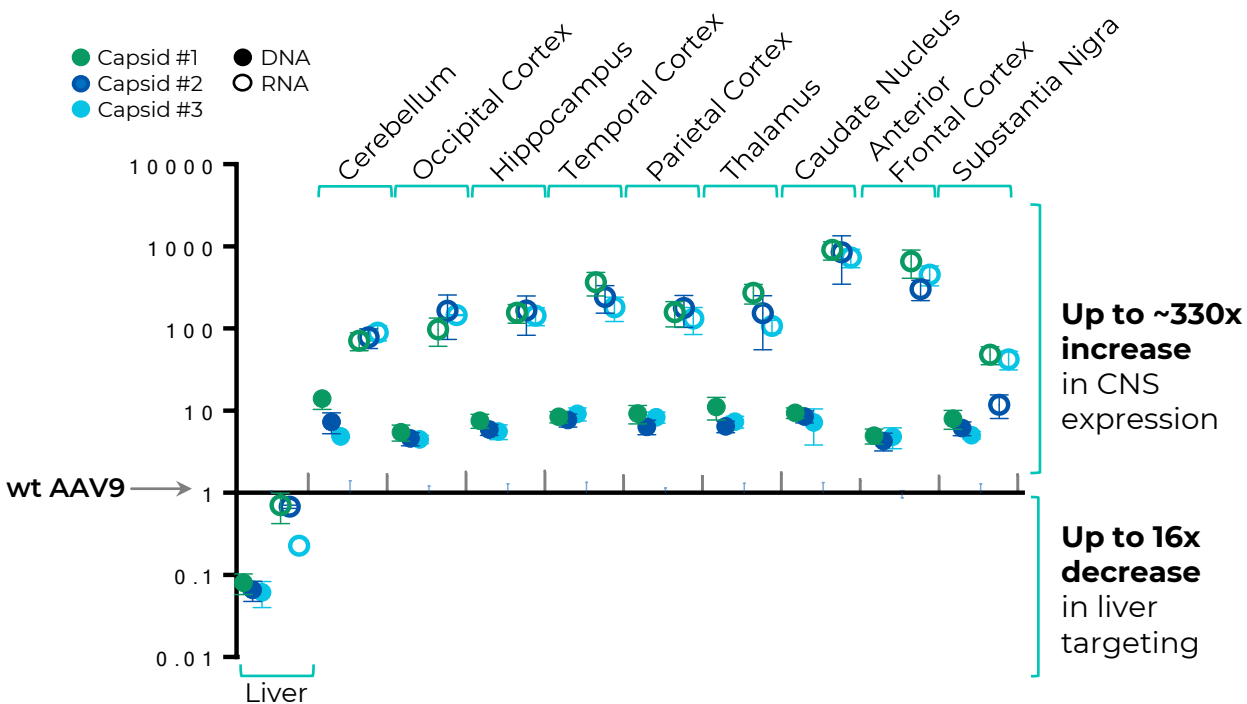




# Gen 5 Capsids Yield Breakthrough Expression Across The CNS And Significant Liver De-Targeting vs WT AAV9

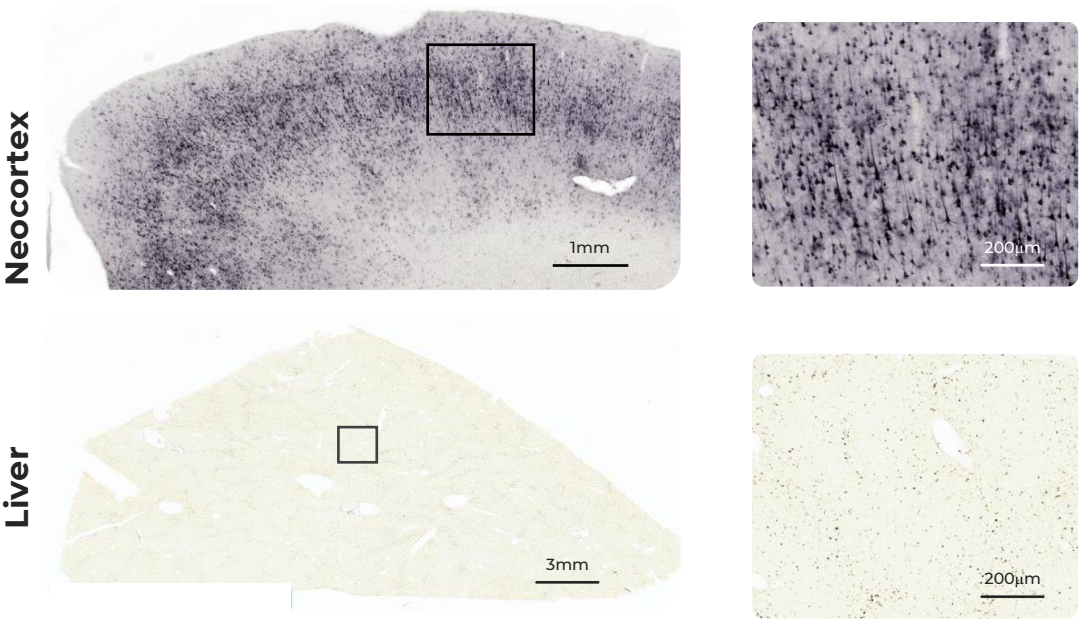
IV Delivery

DNA and RNA Enrichment over AAV9 From Individual Capsid Characterization Studies In Cynos



IV Delivery

Protein localization (HA tagged GOI)

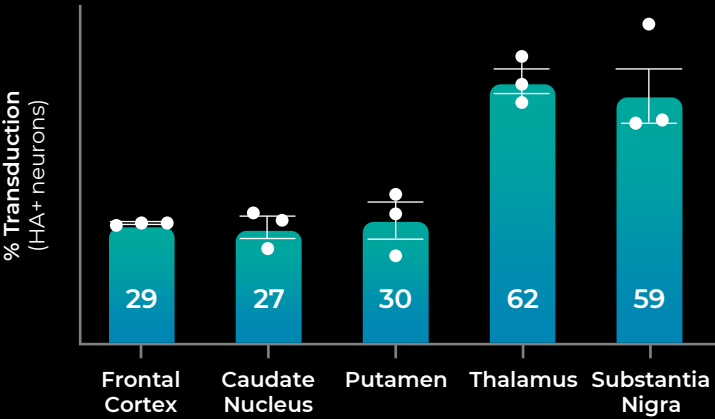
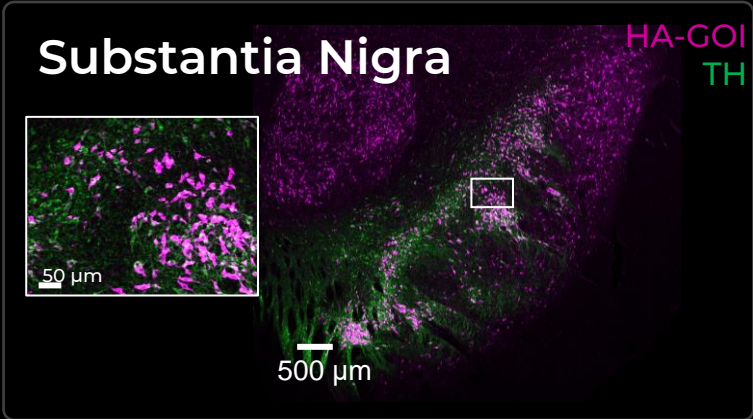
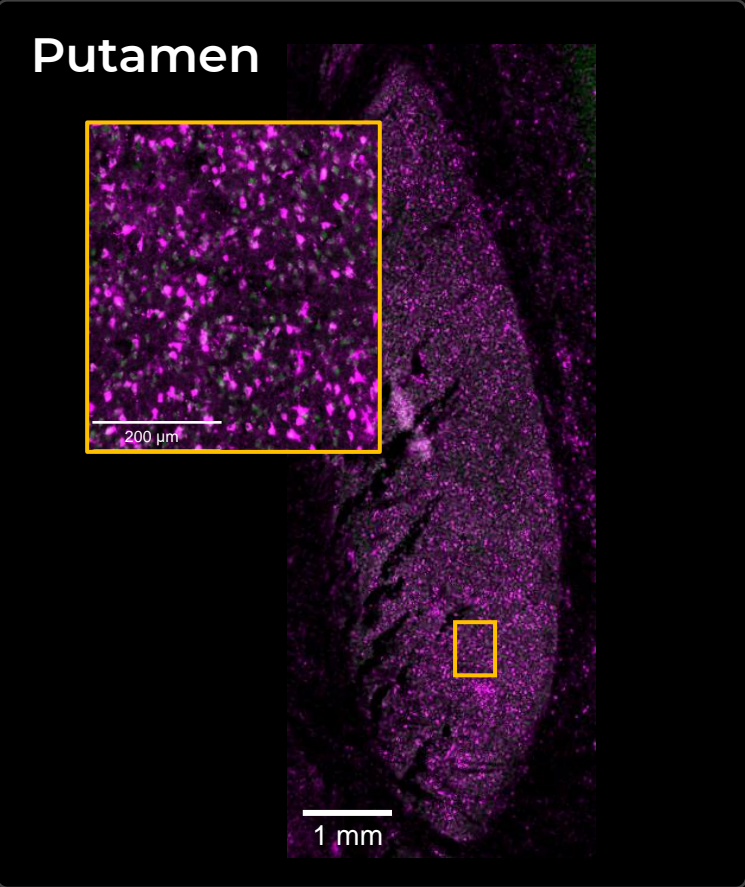
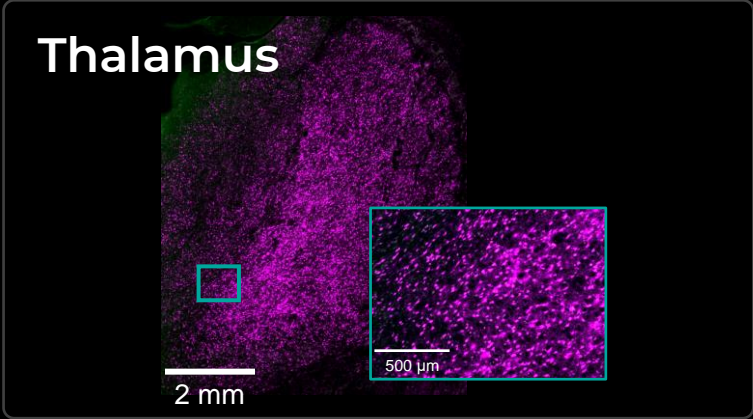
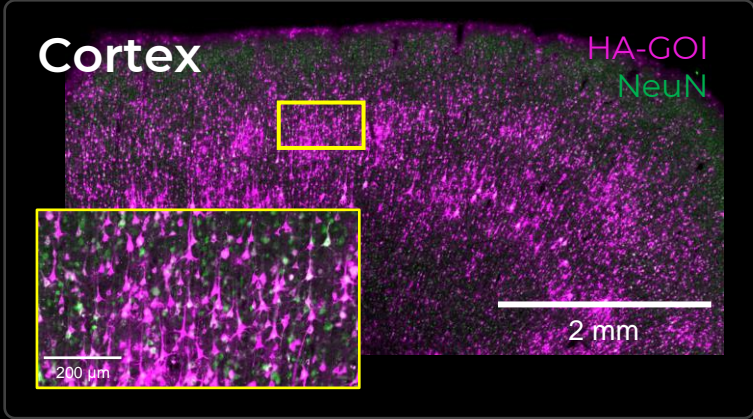


~4000X difference in CNS expression vs liver targeting with Capsida's breakthrough capsids relative to wtAAV9

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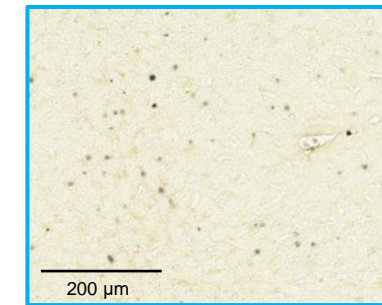
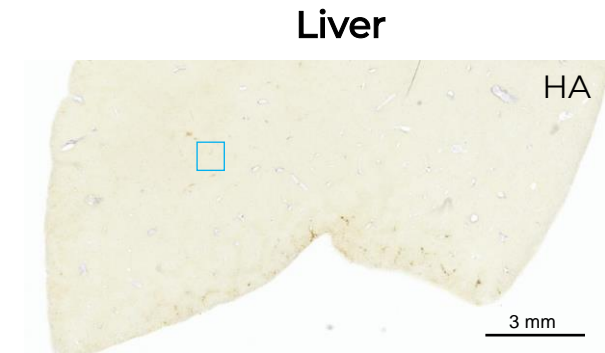
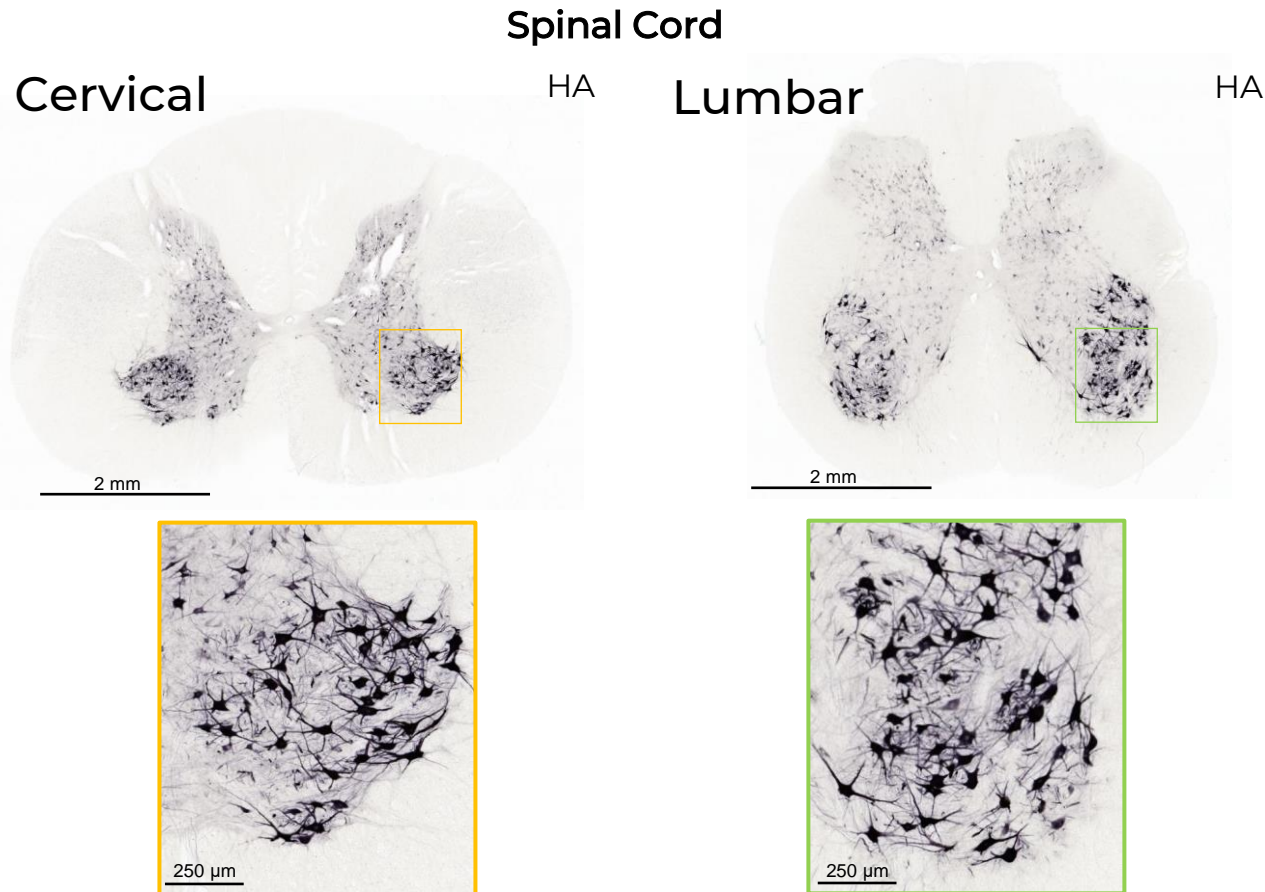
Lower efficacious doses  
Wider Therapeutic Index

# Gen 5 Capsid Results In Widespread Protein Expression Across Representative Areas Of The Brain Following IV Delivery



Capsid: Gen 5  
Cargo: HA-GOI  
Species/Age: N = 3 cynomolgus macaques, ~42mo

# Gen 5 Capsid Expression Extends To Spinal Cord And Is Well Tolerated Following IV Delivery



**16X de-targeted**  
compared to  
AAV9

Capsid: Gen 5  
Cargo: HA-GOI  
Species/Age: N = 3 cynomolgus macaques/ ~42mo

Gen 5 capsid is **well tolerated** with no clinical pathology or immunogenicity findings

**Unremarkable histopathology** across the body, including **liver** and **DRGs**



# Pipeline for Rare and Common Diseases Across All Ages

## Capsida Wholly Owned Programs

Disease / Target	Cargo	Discovery	IND-Enabling	Clinical
Genetic Epilepsy due to STXBP1 mutations	Gene Supplementation	CAP-002		
Undisclosed	Gene Supplementation	CAP-003		

## Partnered Programs

Disease / Target	Cargo	Partner	Co/Co Option
Neurological Diseases & Disorders (3)	Undisclosed	abbvie	One Program, U.S. Profit Share
Neurological Diseases & Disorders	Undisclosed	 	One Program, U.S. Margin Share
Ophthalmology Diseases & Disorders (3)	Undisclosed	abbvie	
Friedreich's Ataxia	Editing		CRISPR owned, Capsida Co/Co Option
ALS	Editing		Capsida owned, CRISPR Co/Co Option

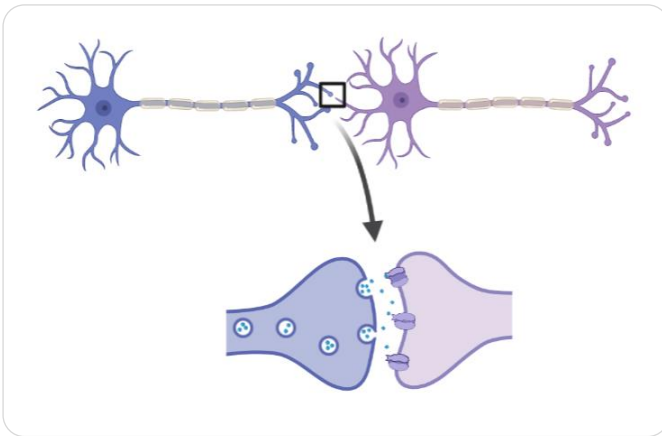
# Syntaxin-binding Protein 1 (STXBP1) Genetic Epilepsy

## 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



## Severe Disease Manifestations

Refractory seizures

Developmental delay, cognitive dysfunction, and intellectual disability

Absent speech

Behavioral issues

Motor abnormalities

Early mortality



## Extreme Unmet Need

No approved therapies

Anti-seizure medications only partially effective



## Robust Translational Evidence

Collaboration & exclusive license with Mingshan Xue, Baylor College of Medicine

Haploinsufficient mouse model shows **dose-dependent correction of seizures, cognitive, and motor deficits** with STXBP1 gene supplementation



## 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<sup>1</sup> (up to 4500 in US and EU) and growing

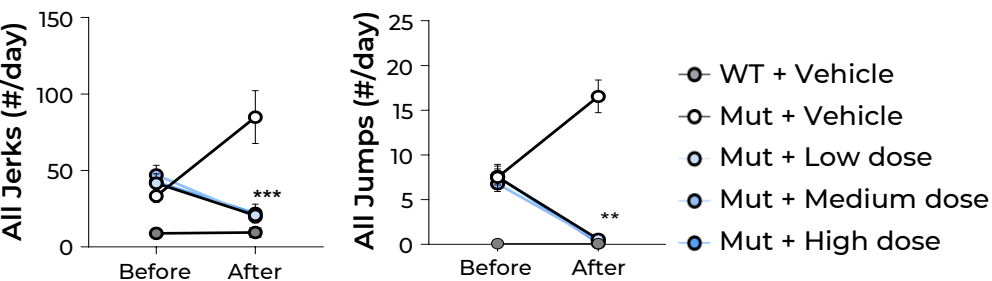
<sup>1</sup>Lopez-Rivera et al., Brain, 2020



# Dose-dependent Therapeutic Efficacy of Gene Supplementation Enabled by Brain-wide STXBP1 Expression

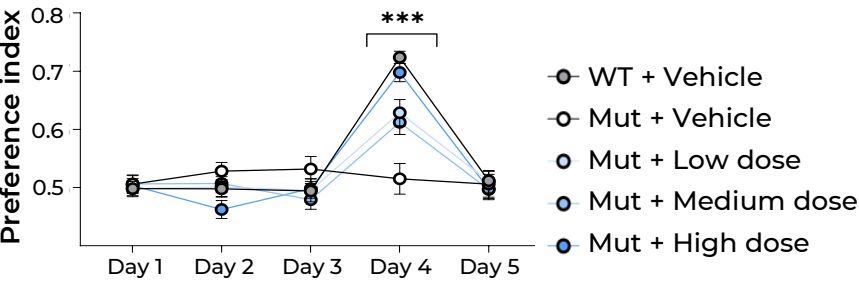
## Epilepsy

### Myoclonic Seizures



## Cognitive Dysfunction

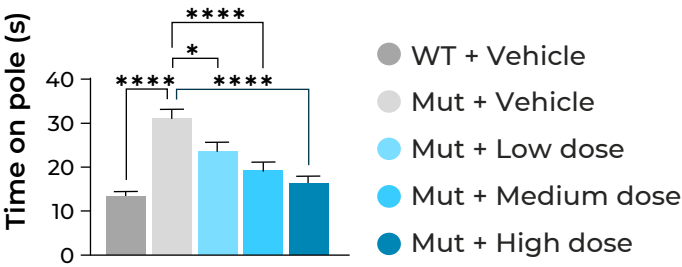
### Novel Object Recognition



Brain-wide Stxbp1 expression achieves significant reduction of myoclonic seizures and novel object recognition in murine model at all doses

## Motor Deficits

### Vertical Pole



### Dystonia

#### Mut + High Dose AAV



#### Dystonia<sup>1</sup> Correction by Gene Supplementation

WT	Mut	Low	Medium	High
0.18	2.50	1.49	0.84	0.62

<sup>1</sup>Medians based on ordinal data

Brain-wide Stxbp1 expression achieves correction of vertical pole motor ability and dystonia (hindlimb clasp) in murine model

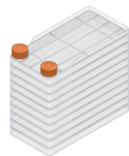
Difference from Mut + VEH: ns, non-significant, \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$

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

Effective treatment of disease manifestations requires brain-wide supplementation of the hSTXBP1 gene **achievable with Capsida's breakthrough capsids** to correct circuits associated with seizure, cognitive and motor phenotypes

# Integrated Process & Analytical Development and cGMP Capabilities Accelerates Capsid Prioritization and Clinical Supply

## Vector Production (VP)



Rapid production of engineered capsids for preclinical studies

## Process & Analytical Development (PAD)



+

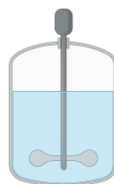


Conduct in-depth manufacturability assessment of lead capsids in suspension process

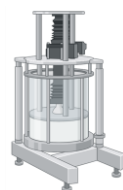
Up to 50 L bioreactor scale

Develop and optimize key analytical assays

## cGMP Manufacturing (MFG)



+



15,000 ft<sup>2</sup> 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



*Experienced MFR and PD staff*



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

# Strong Capital Position Through Venture and Partnerships

**\$265M**  
Funding to Date

**>\$2B**  
In Milestones

**\$50M**  
Series A



**\$90M**  
Upfront & Equity

AbbVie CNS collaboration, up to **\$530M** in development potential milestones, excluding commercial

abbvie

**\$55M**  
Upfront & Equity

Lilly CNS collaboration, up to **\$685M** in potential development and commercial milestones



**\$70M**  
Upfront & Equity

AbbVie Ophthalmology expansion, **\$595M** in potential development milestones, excluding commercial

abbvie

# Looking Ahead

## Advance



Advance differentiated internal development candidates to IND and through clinical proof-of-concept

4000x therapeutic window vs. wt AAV9

Broad and well-tolerated neuronal expression across brain regions and spinal cord with significant liver detargeting

Manufacturability profile inline with wtAAV9

## Collaborate



Collaborate with our partners to achieve milestones and advance potential co-development programs

abbvie



Lilly

Prevail  
THERAPEUTICS

A Wholly Owned Subsidiary of Eli Lilly and Company

## Expand



Expand opportunities to leverage breakthrough capsids for additional high unmet diseases



Neurology



Ophthalmology



Other TA

## Execute



Execute by managing cash and cultivating talent to grow and maximize value creating opportunities for patients and shareholders



# Our Pipeline is Making the Impossible Possible

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