STREAM BIOMEDICAL

rhPDV$_{LG3}$: Targeted Human Therapeutic

Novel First-in-Class Recombinant Biologic

Rapid Neurovascular Repair & Regeneration

APRIL 2025

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Forward Looking Statements

Statements made about Stream Biomedical, other than statements of historical fact, reflect the company's beliefs and assumptions founded on currently available data and information. Statements of Stream Biomedical's progress, results, timing of preclinical and clinical trials and projections for product pipelines are examples of forward-looking statements and are based only on current information, assumptions, and expectations that by definition involve risks, uncertainties, and are subject to factors that could cause actual results to differ substantially from statements made, including but not limited to: risks associated with the success of preclinical studies; clinical trials; research and development programs; regulatory approval processes for clinical trials; competitive technologies and products; patents, engagement and/or termination of corporate and other strategic partnerships and the need for additional funding or financing.

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Summary Highlights - Investigational Agent rhPDV$_{LG3}$

Novel biological agent, first-in-class, novel clinical therapeutic category
Potentially transformative therapeutic agent for neurology

Platform therapeutic: Multiple potential CNS indications
Both acute and chronic neurodegenerative diseases

Recombinant biologic: Repairs neurovascular injury to protect the CNS
Repairs BBB, neurogenic, vasculogenic, neuroprotective, anti-inflammatory

Clinical study: Initiate phase 1b in Q3 2025
Safety and confirm initial efficacy in humans

Near-term value inflection point: Clinical study readout Q1 '26
Pursue clinical development across a range of acute and chronic neurodegenerative diseases

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MANAGEMENT TEAM

Bill Schwieterman, M.D. CEO and & Board Member

10 years as former senior supervisor within Center for Biologics of Food and Drug Administration (FDA)

Nazia Kazmi, M.S.

AD, Clinical Trial Operations

>18 years of experience in Clinical Operations and Trial Management

Huston Davis Adkisson, Ph.D.

Chief Scientific Officer

27 years of academic and industrial experience. Co-founder and former Chief Scientific Officer at ISTO Technologies, Inc.

Bryan Clossen, Ph.D.

Director of Translation Programs

15 years of academic and industry experience in translational modeling of neurotrauma for drug discovery.

Seth Fisher

CMC Process Engineer

20+ years of experience in development of biologics from discovery through clinical manufacturing

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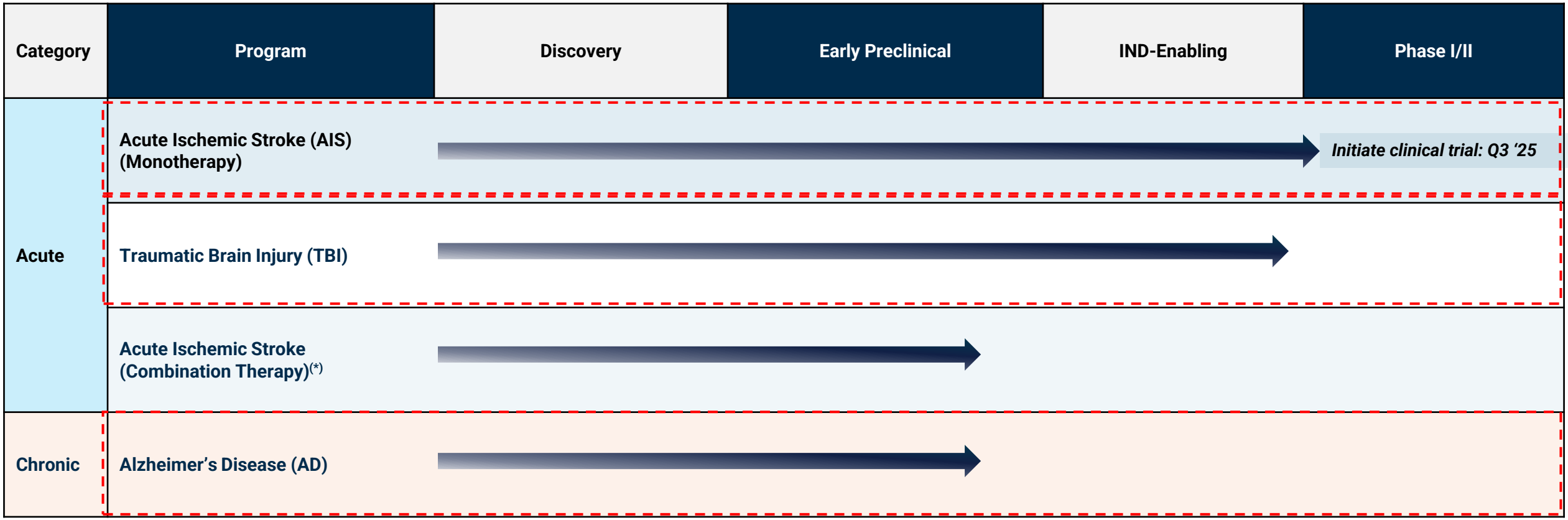
abbvie AMGEN CHELSEA THERAPEUTICS FDA isto BIOLOGICS PERCEPTIVE ADVISORS RUSH UNIVERSITY MEDICAL CENTER TAMU MEDICINE

Addressing Unmet Needs in Multiple CNS Diseases



Lead indications

GMP manufacturing completed

(*) Combination therapy with Tissue Plasminogen Activator (tPA)

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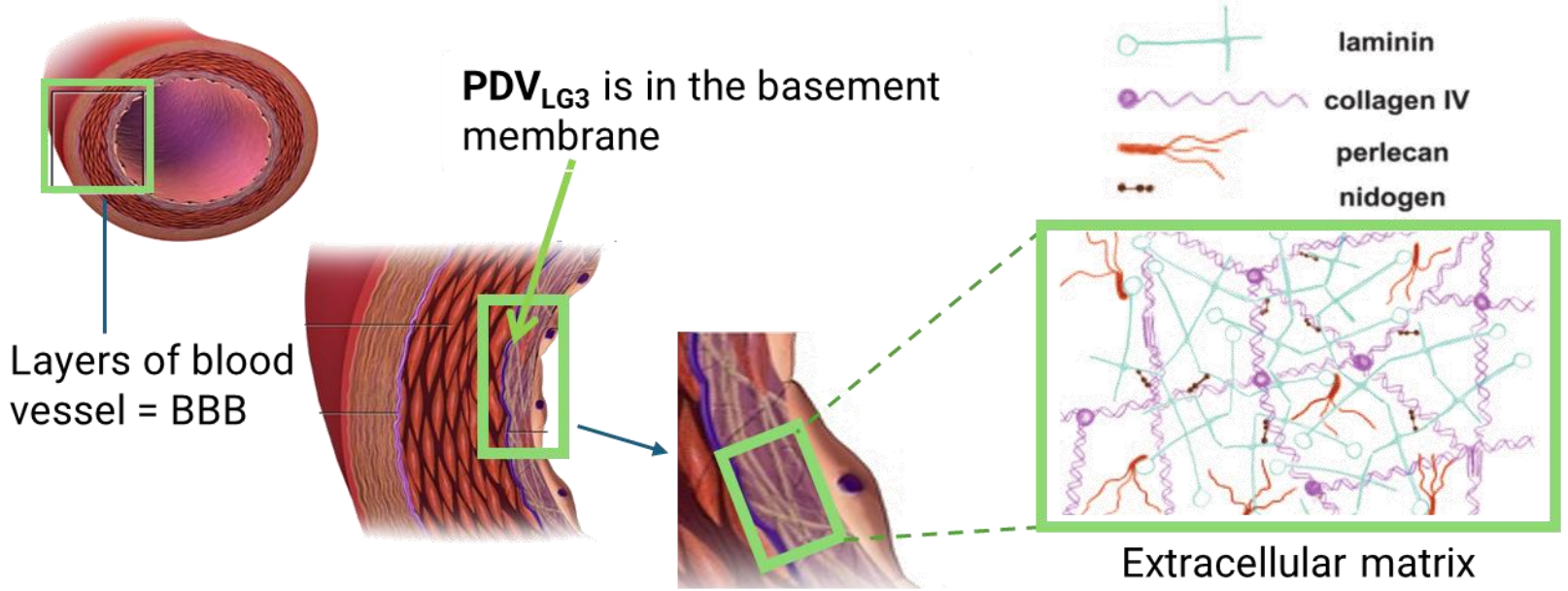
Perlecan, the Parent Molecule of PDV_{LG3} Is Located Within the BBB

RECOMBINANT BIOLOGIC REPAIRS NEUROVASCULAR INJURY TO PROTECT THE CNS

Perlecan Domain V LG3 (PDV_{LG3}) is released from the basement membrane following injury



Bardin, Matthieu. (2022). Lipid mediators of the resolution of inflammation in vascular ageing. Physiol Rev. 2005 Jul;85(3):979-1000. doi: 10.1152/physrev.00014.2004.

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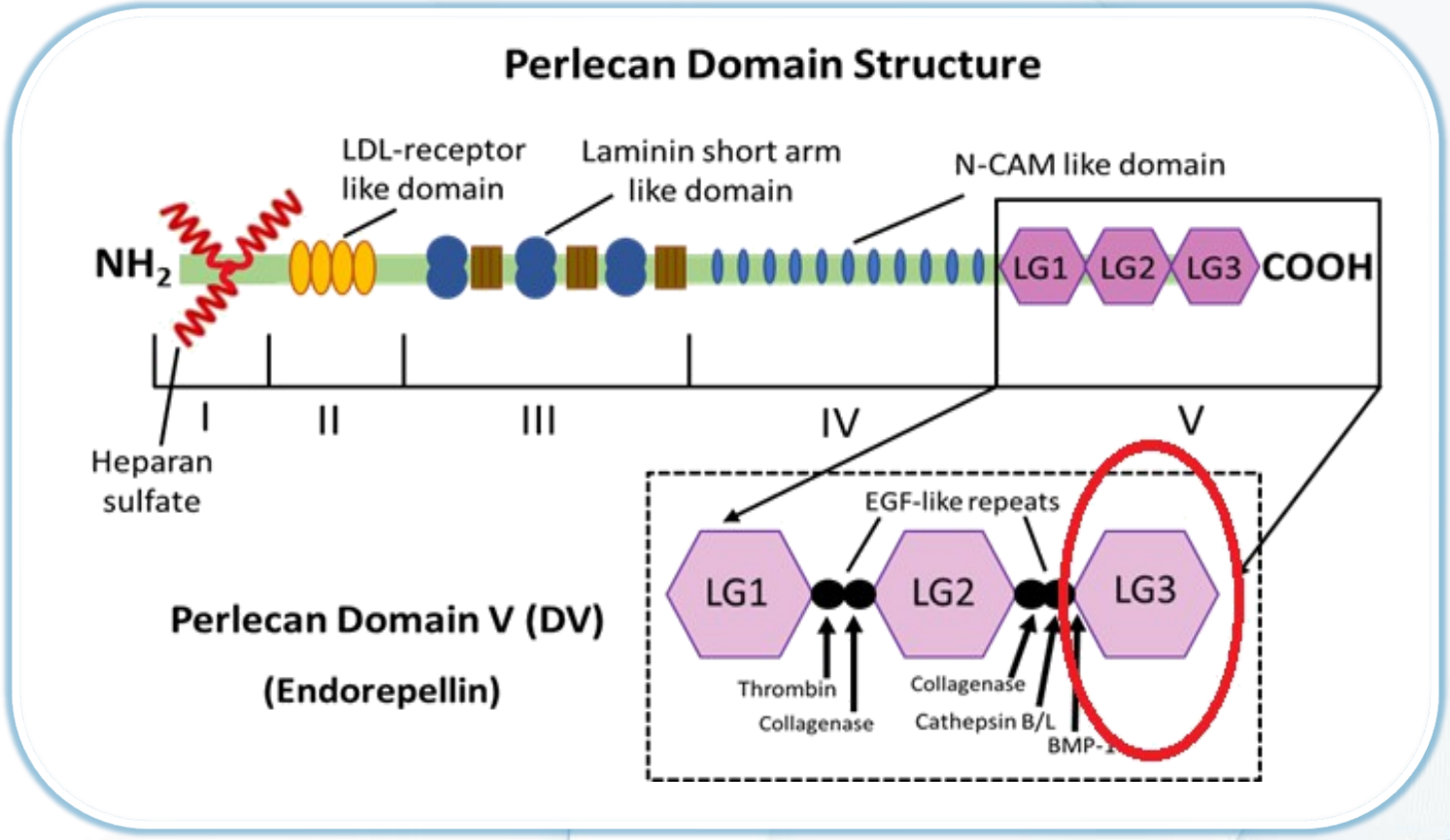
PDV_{LG3} Is a Fragment of Perlecan Released Upon Hypoxia/Injury to BBB

PDV_{LG3} Key Properties

- Rapidly released in response to hypoxia/anoxia
- Homes to site of injury
- Anti-inflammatory effects
- Plays important role in cell signaling and interaction with other proteins
- Supports new blood vessel formation

PDV_{LG3} Biological Effects

- Repairs BBB and CNS
- Neuroprotective
- Neuroregenerative
- Vasculogenic
- Anti-inflammatory



J Cell Biol. 2019 Oct 7;218(10):3506-3525. doi: 10.1083/jcb.201807178. Epub 2019 Sep 20.

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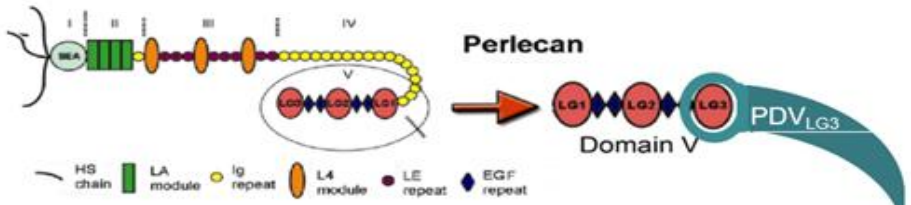
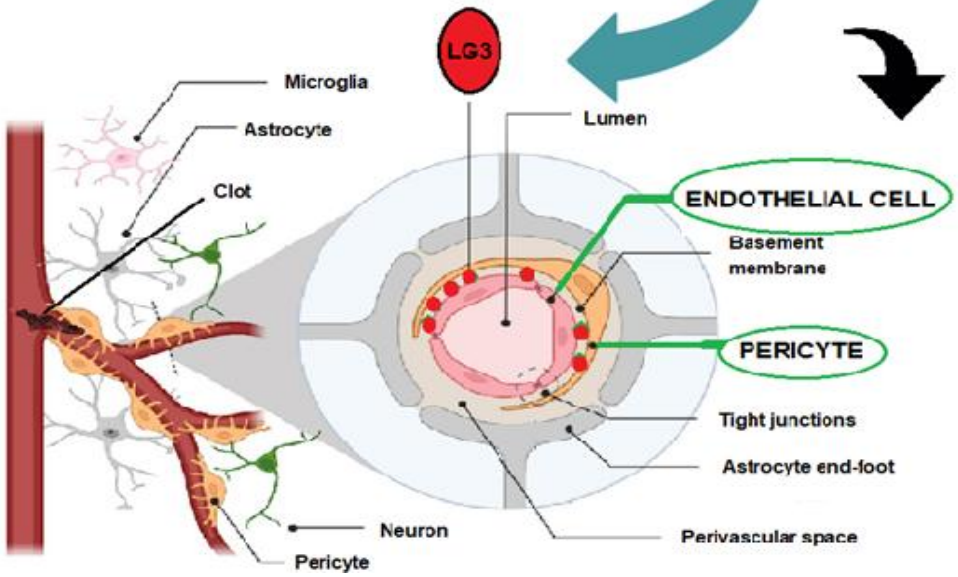
$PDV_{LG3:}$ A Natural Neuroprotective/ Neuroreparative Protein

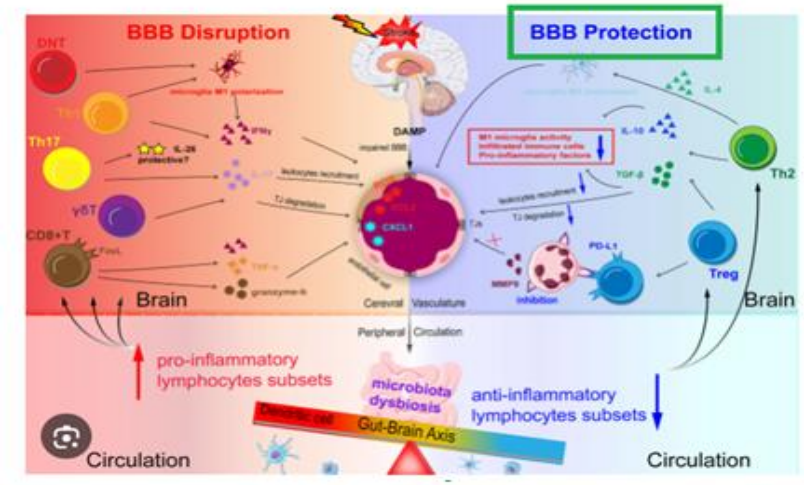
1. LG3 resides naturally in blood vessel wall



2. 21kD LG3 domain released in response to injury



3. LG3 binds to adjacent endothelium and pericytes to seal BBB



4. BBB and neurovascular repair that protects the CNS

Front. Immunol., 22 June 2021 Sec. Multiple Sclerosis and Neuroimmunology Volume 12 - 2021 | https://doi.org/10.3389/fimmu.2021.678744
Image 3 adapted from: Front. Aging Neurosci., 16 April 2023 Sec. Alzheimer's Disease and Related Dementias Volume 15 - 2023 | https://doi.org/10.3389/fnagi.2023.1132077

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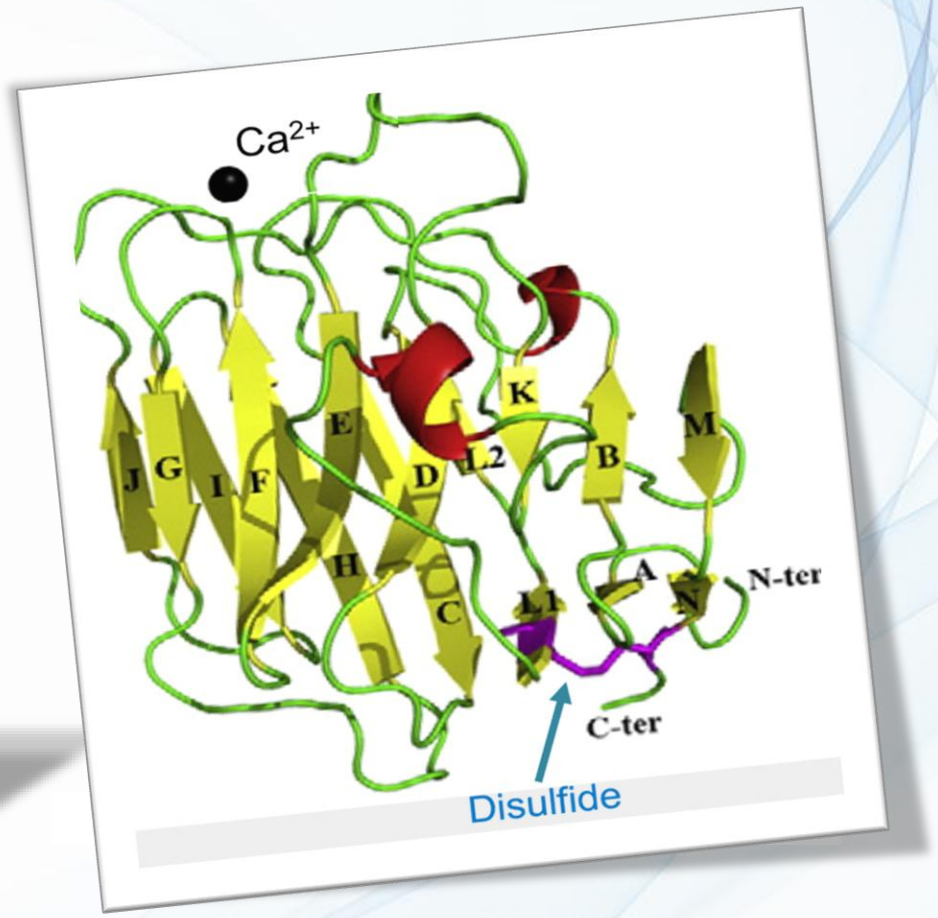
Stream's Product: $rhPDV_{LG3}$

Properties

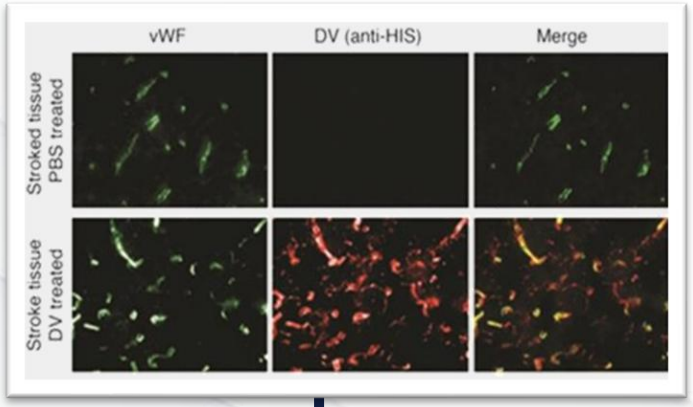
- Produced in *E. coli*
- 21kD non-glycosylated protein
- Administered intravenously
- Readily crosses BBB through active transport
- Homes to site of injury through upregulated integrin receptors
- Durable tissue binding (>48 hours)



J Mol Biol . 2011 Nov 25;414(2):231-42. doi: 10.1016/j.jmb.2011.09.048. Epub 2011 Oct 4.

Summary of Pharmacokinetics/dynamics

A. Crosses the BBB



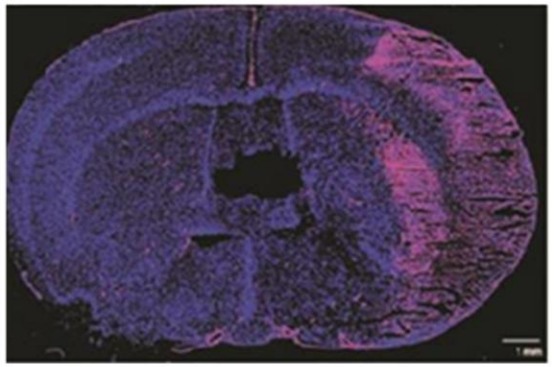
B. By active transport

rhPDV$_{LG3}$ w/out caveolin inhibition

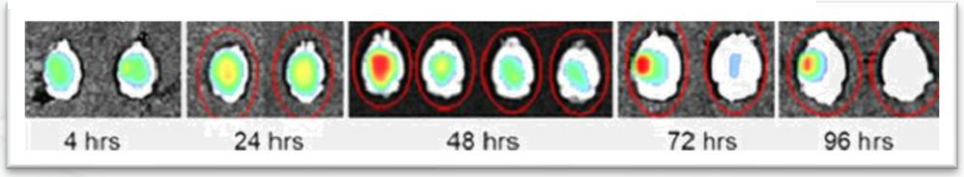
rhPDV$_{LG3}$ w/ caveolin inhibition

A — B — C — D

C. Homes to the site of injury



D. Has persistent receptor binding >48h



Brain persistence CCA-MCA stroke – mice (6 mg/kg, intraperitoneal)

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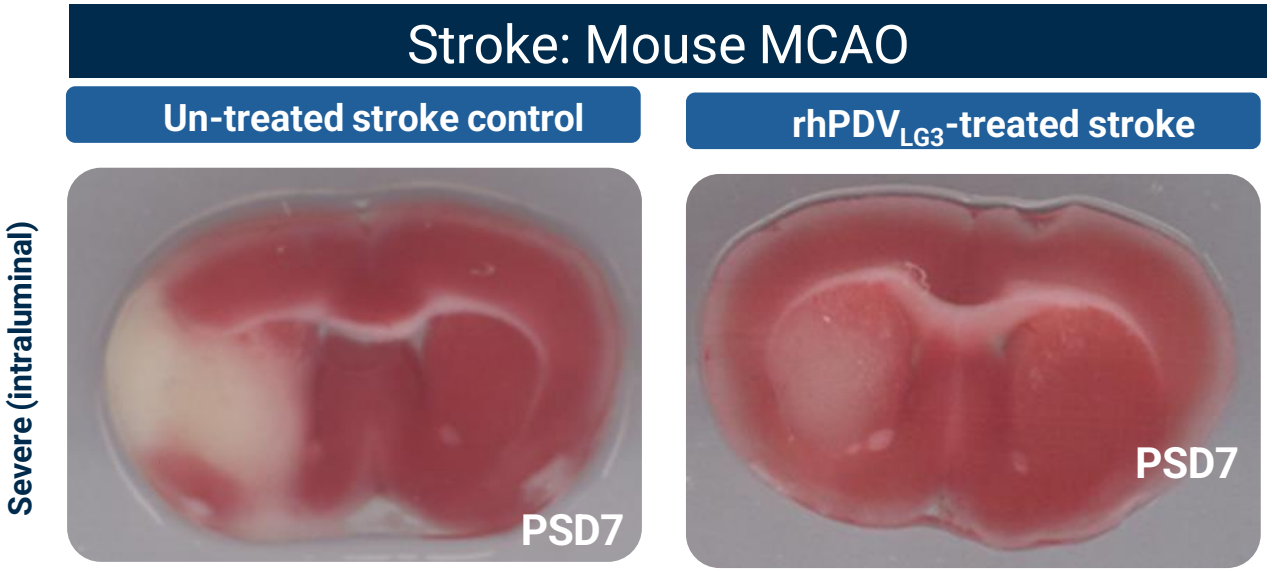
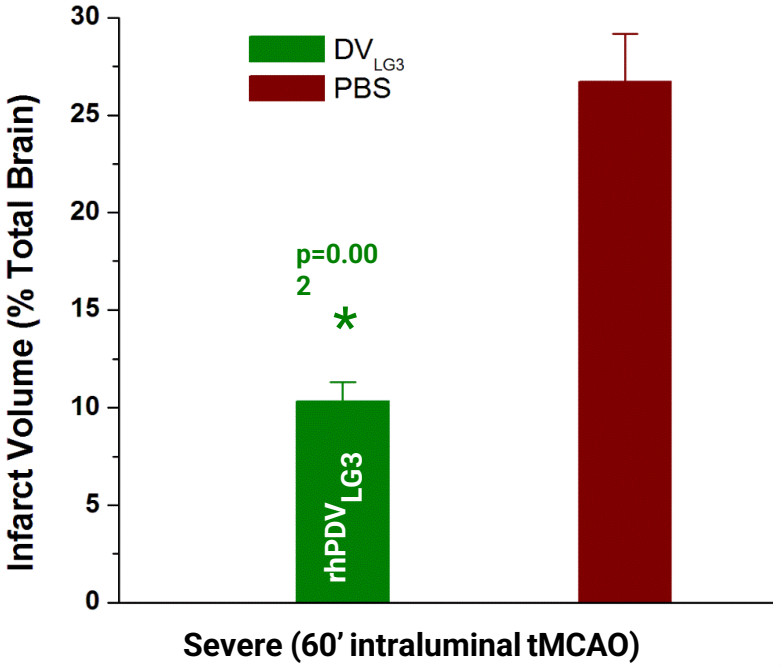
rhPDV$_{LG3}$ Is Significantly Neuroprotective

rhPDV$_{LG3}$ (6 mg/kg) reduces infarct volume by >60% following severe stroke in mice





Drug Selection Study: rhPDV$_{LG3}$ only shown 7 days after 60 min transient MCAO filament stroke in mice.

Stream/Tulane - Biose et al 2021

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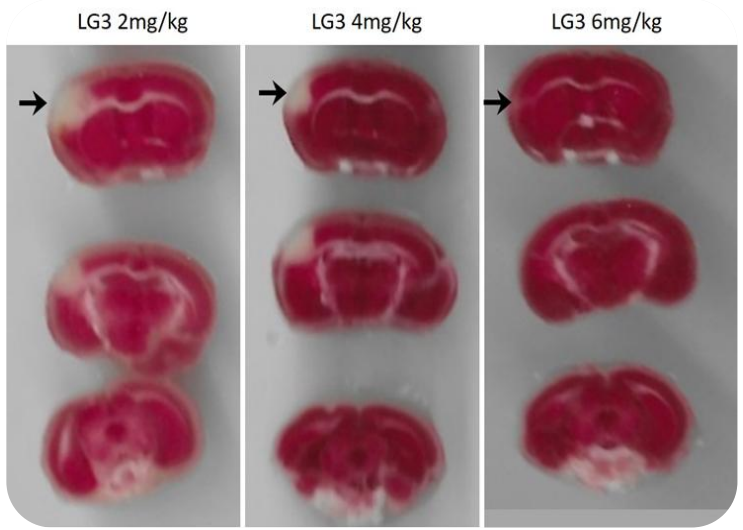
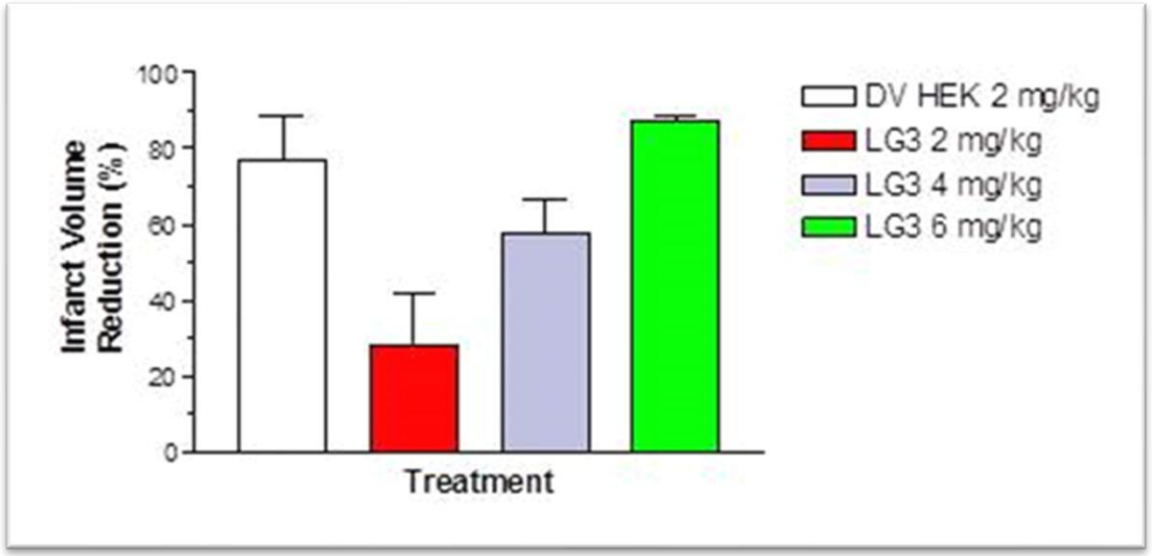
rhPDV$_{LG3}$ Provides Dose-Dependent Increase in Neuroprotection

rhPDV$_{LG3}$ dose-dependently reduces infarct volume (stroke injury) following cortical stroke in mice

Stroke: Mouse CCA-MCA



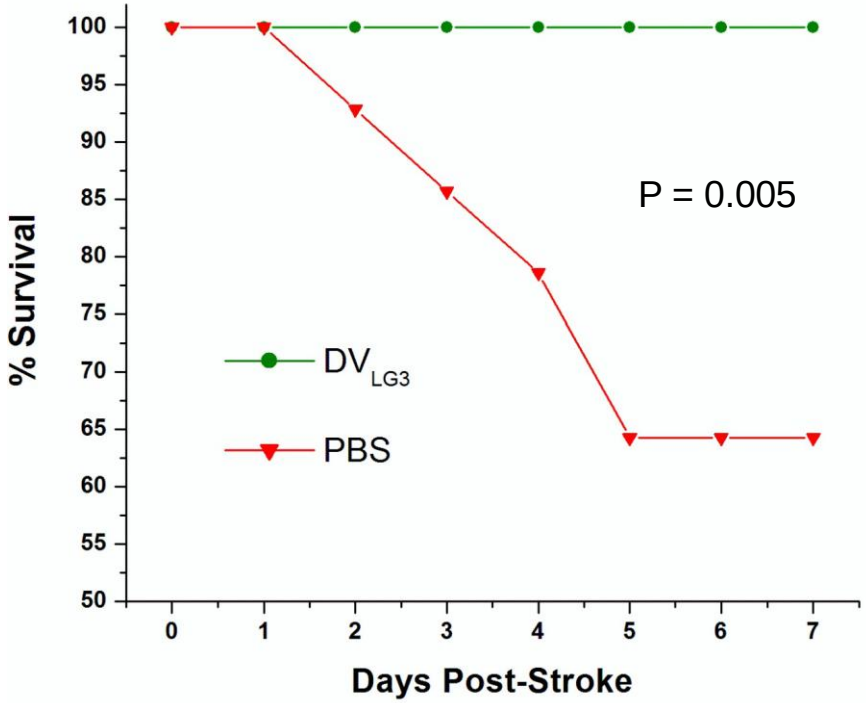


rhPDV$_{LG3}$ Reduces Mortality Following Severe Stroke in Mice

rhPDV$_{LG3}$ reduces 7-day mortality

Stroke: Mouse MCAO

- Control mortality rate: **36%**
- rhPDV$_{LG3}$ mortality rate: **0%**
- Reduction in mortality rate correlated with reduced infarct volume and improved health and functional outcomes *(see next page)*



Drug Selection Study: rhPDV$_{LG3}$ only shown 7 days after 60 minute transient MCAO filament stroke in mice.

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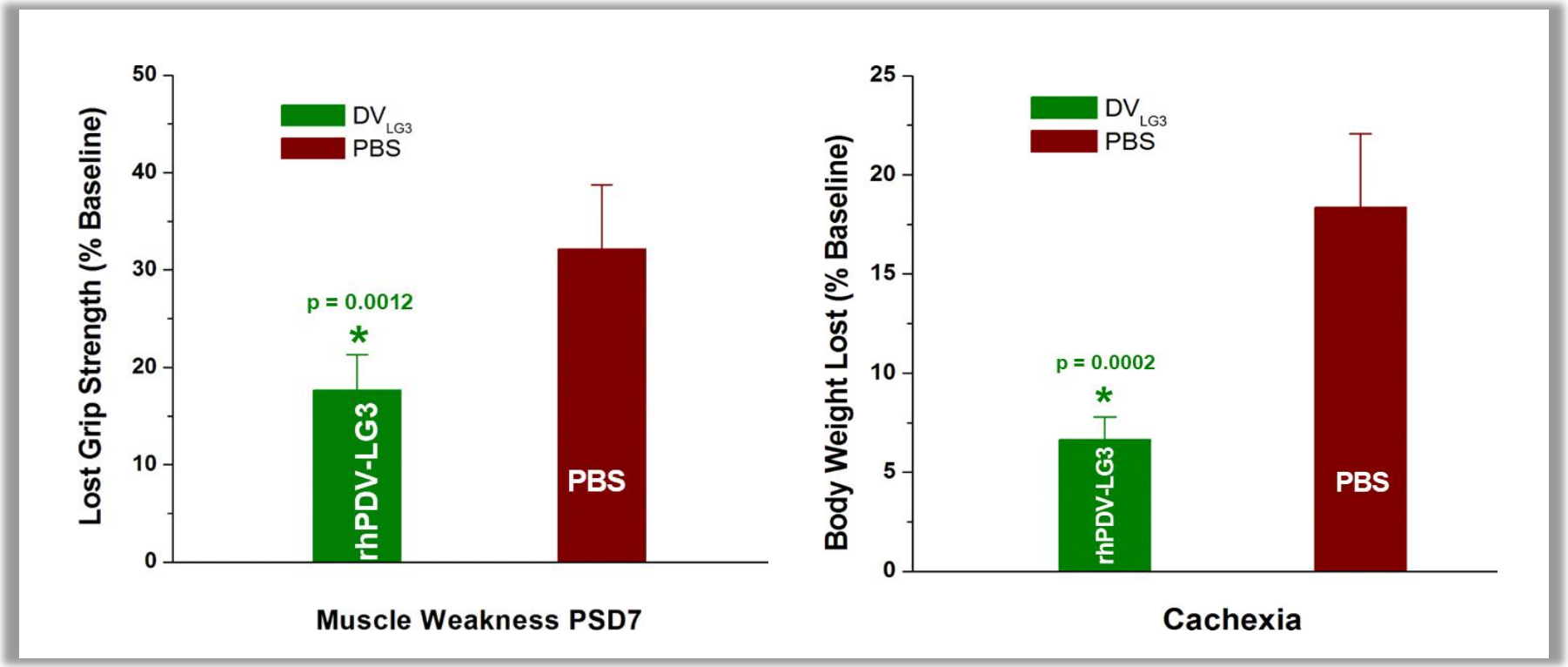
Stream/Tulane: Biose et al 2021

rhPDV$_{LG3}$ Significantly Improves Function and Weight Retention Following Severe Stroke

Stroke: Mouse MCAO

Improves sensory-motor function and body weight retention



Drug Selection Study: rhPDV$_{LG3}$ only shown 7 days after 60 minute transient MCAO filament stroke in mice.

Stream/Tulane: Biose et al 2021

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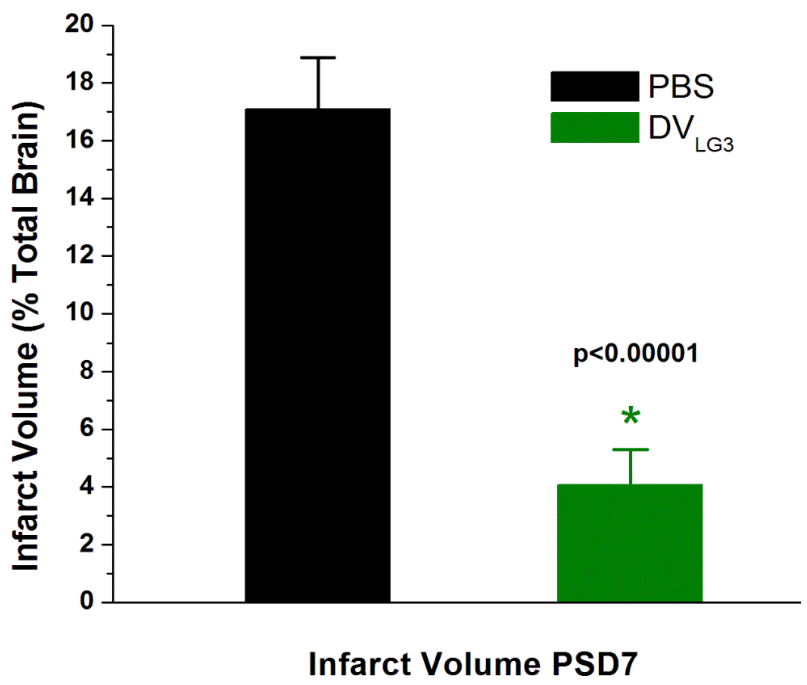
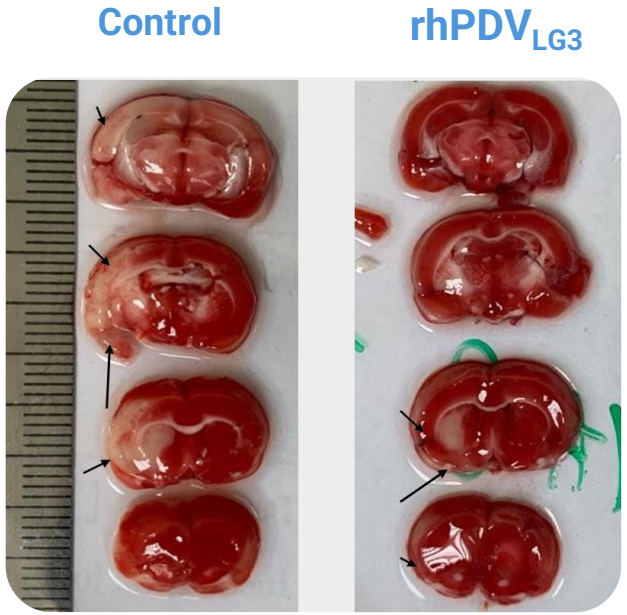
rhPDV$_{LG3}$ Is Neuroprotective Across Species, Stroke Models, and Multiple Routes of Administration

IV administration of rhPDV$_{LG3}$ (3 mg/kg) is significantly neuroprotective in rats following severe stroke

Stroke: RAT MCAO





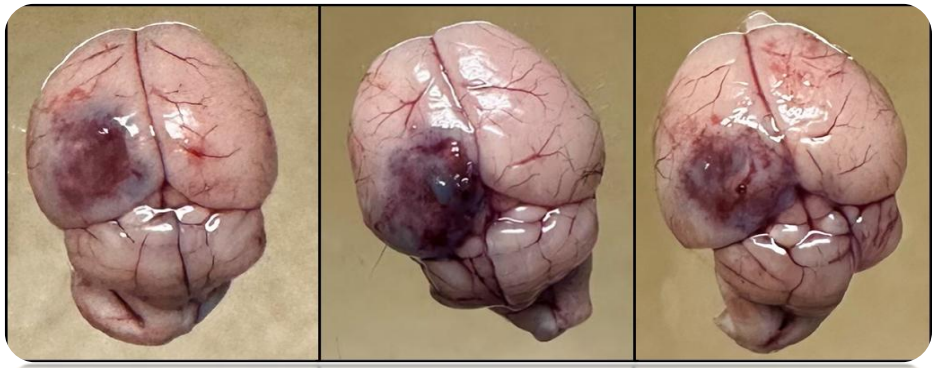
Stream/MDBio: 2020

$rhPDV_{LG3}$ Restores BBB Integrity at 24 Hours Following Severe TBI

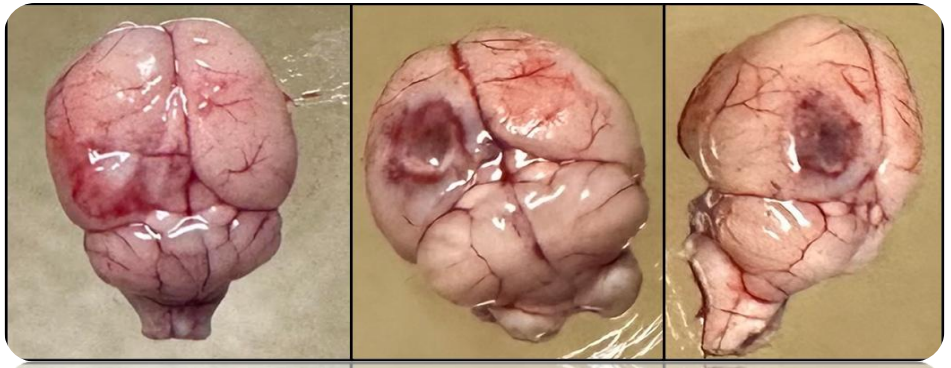
$rhPDV_{LG3}$ (6 mg/kg) significantly reduces Evan's blue permeation following severe impact TBI (2mm) in mice

TBI: Mouse CCI Severe

PBS Treated – 24hr Post-Impact



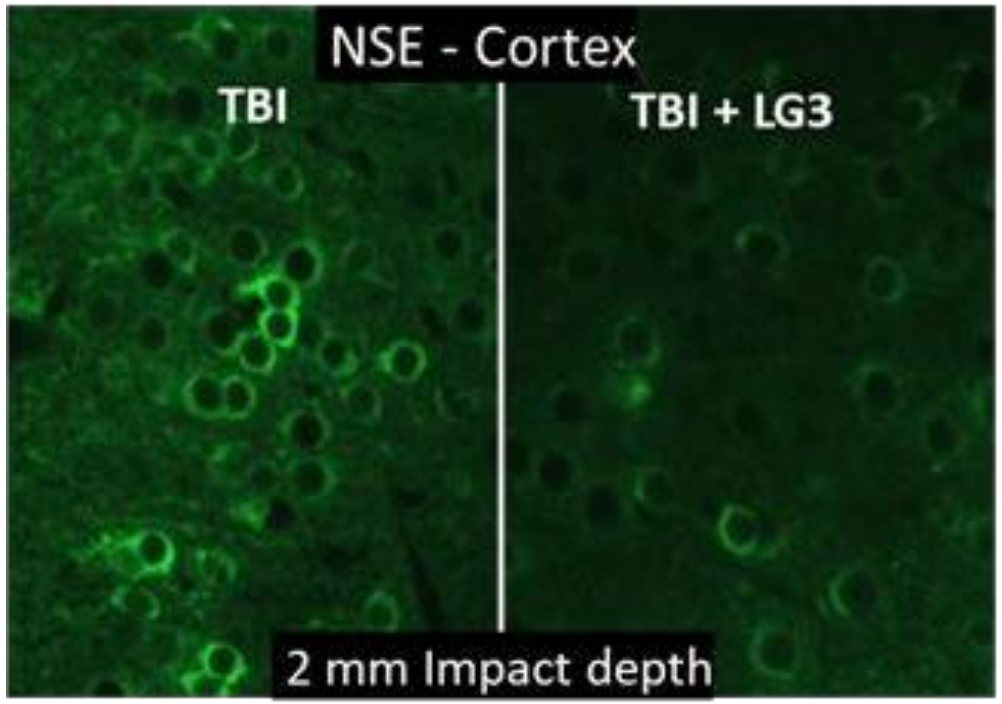
$rhPDV_{LG3}$ Treated – 24hr Post-Impact

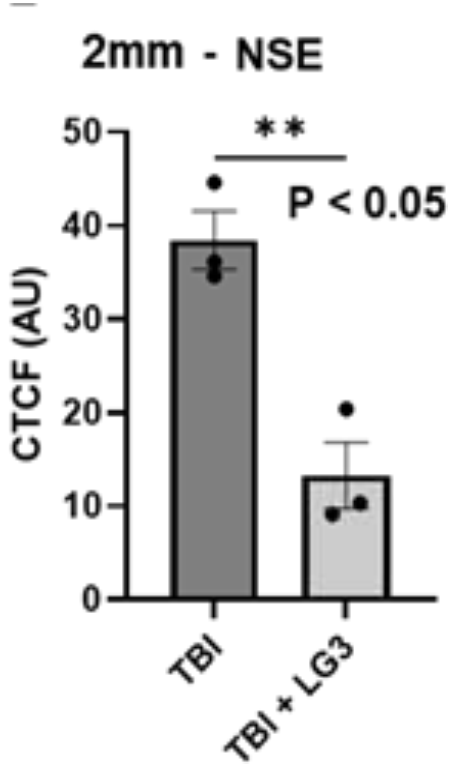


rhPDV$_{LG3}$ Is Neuroprotective After Severe TBI

rhPDV$_{LG3}$ reduces neuron-specific enolase (NSE), a biomarker of neuron injury, > 72% following single dose administration in young male mice subjected to CCI-TBI (2mm); Day 7

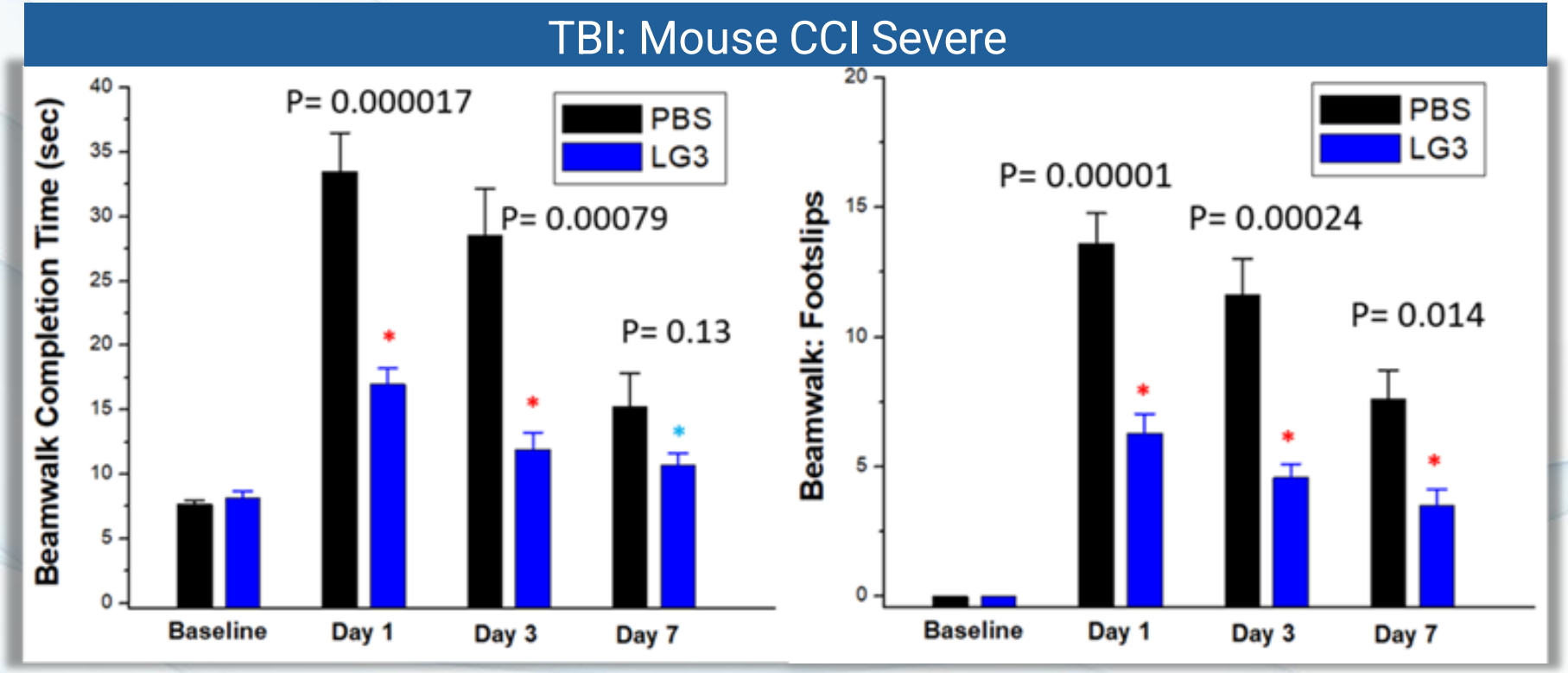
TBI: Mouse CCI Severe





rhPDV$_{LG3}$ Restores Motor Function After Severe TBI

rhPDV$_{LG3}$ (6 mg/kg) significantly improves acute beam-walk performance following CCI (2mm) in mice

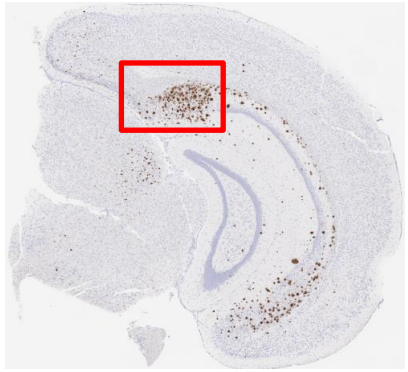


- rhPDV$_{LG3}$ results in profound improvements 24 hours after CCI-TBI
- Functional improvements persist through Day 7
- Footslip performance exhibits high resolution for detection of motor deficits

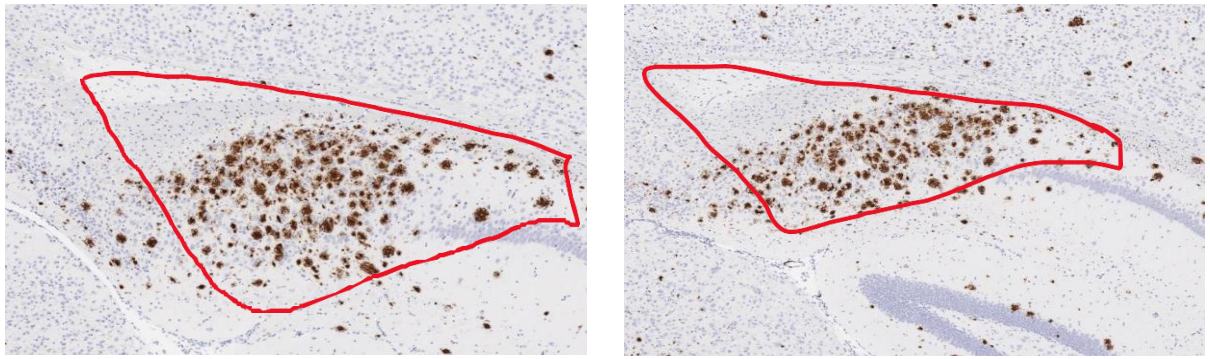
rhPDV$_{LG3}$ Reduces Amyloid Burden in the Hippocampus
Dorsal subiculum = hippocampal tissue most sensitive and prognostic for AD in animals/humans

- ✓ rhPDV$_{LG3}$ treated (30 days) 3-month-old female 5xFAD mice displayed significantly less amyloid deposition in the hippocampus (dorsal subiculum)
- ✓ Reduction in volume of dorsal subiculum is prognostic of AD in humans

PBS

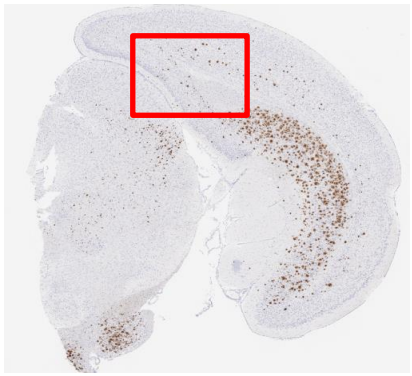


Hippocampus

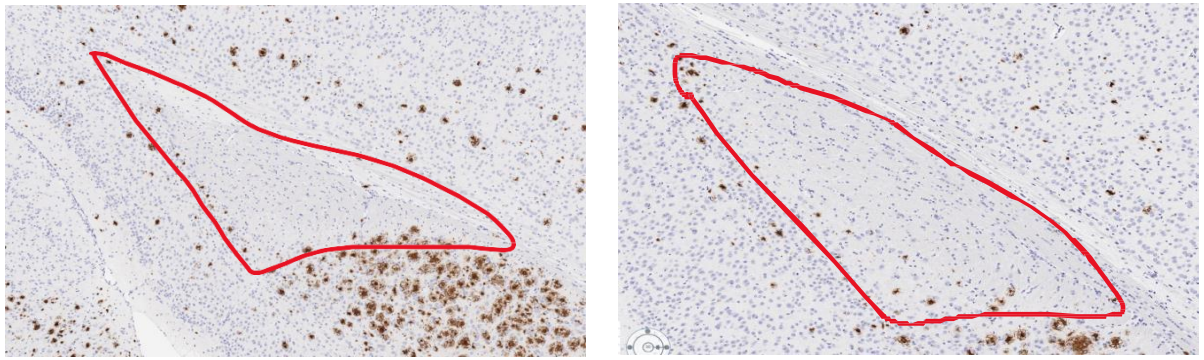


Dorsal subiculum

rhPDV$_{LG3}$



Hippocampus



Dorsal subiculum

Aim 2 Report: In Vivo Assessment of rhPDV$_{LG3}$ for Disease Modification in Alzheimer's Mice, Stream/UTHSC/Premier: 2023

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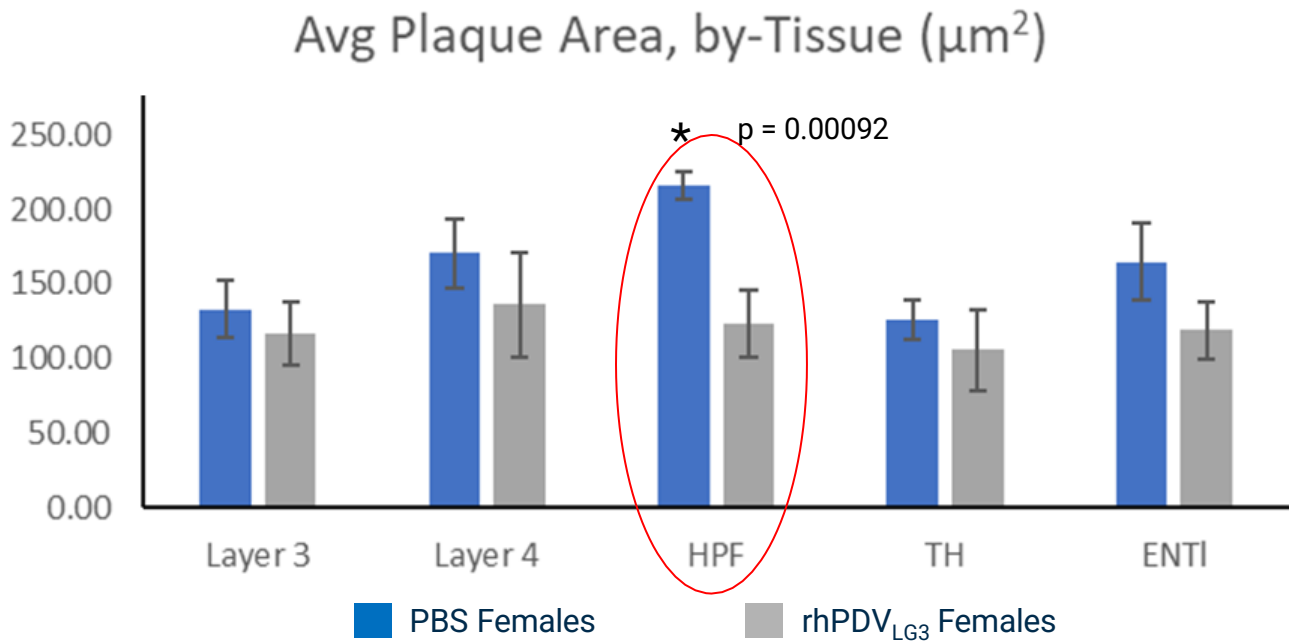
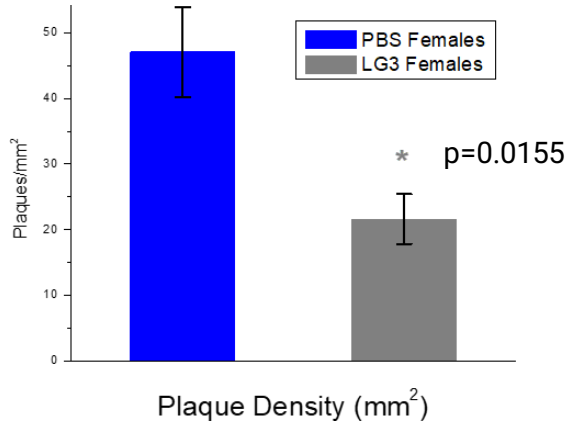
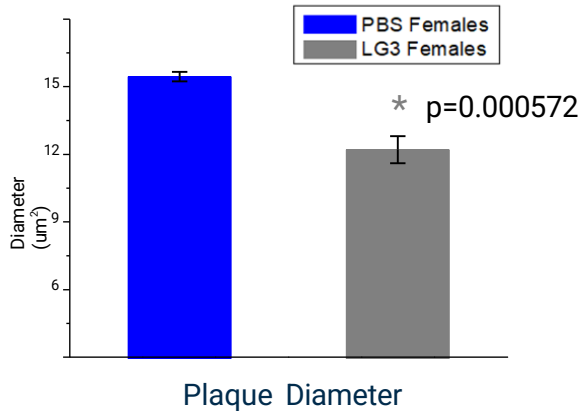
rhPDV$_{LG3}$ Reduces Amyloid in Brain Tissues, Most Prominently in the Hippocampus

rhPDV$_{LG3}$ reduces hippocampal amyloid plaque area, density, and average diameter in 3-month-old female 5xFAD mice







Aim 2 Report: In Vivo Assessment of rhPDV$_{LG3}$ for Disease Modification in Alzheimer's Mice, Stream/UTHSC/Premier: 2023

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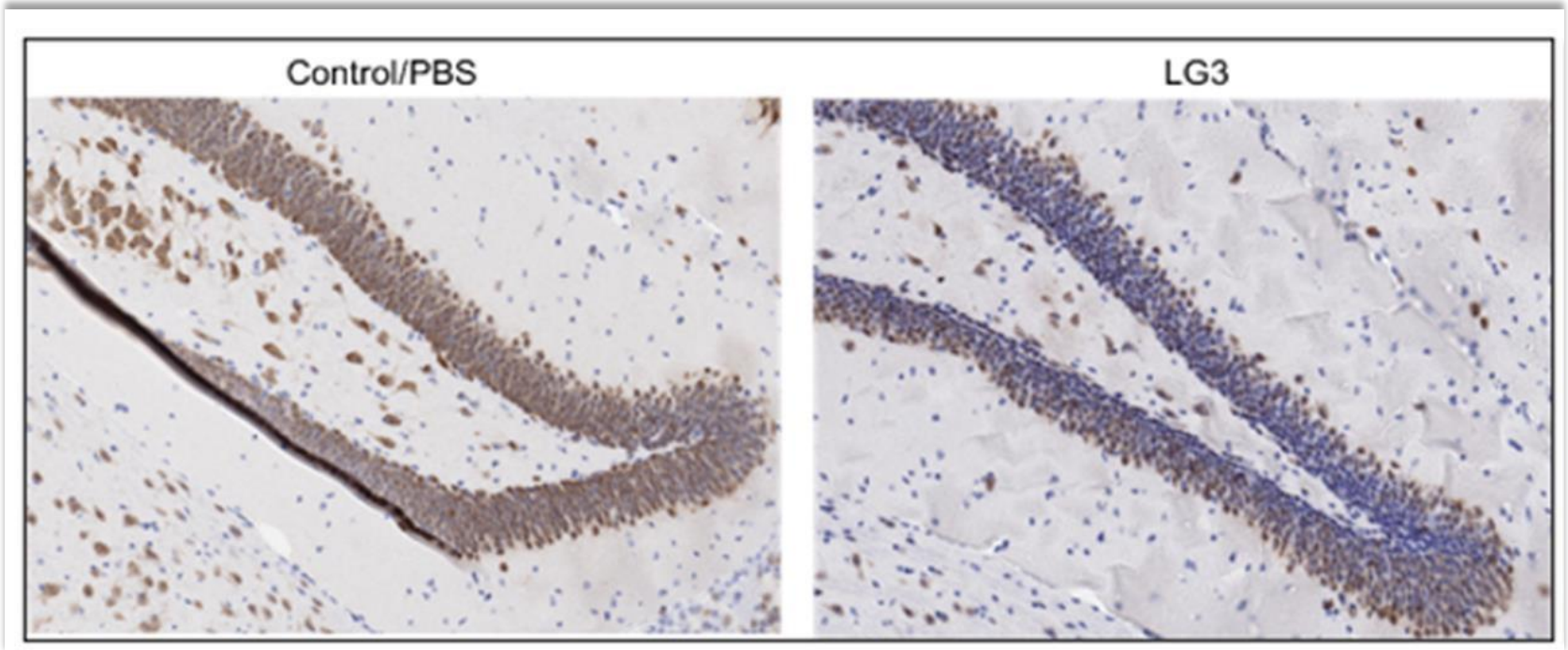
rhPDV$_{LG3}$ Induces Neurogenesis

rhPDV$_{LG3}$ exerts profound effect in the dentate hilus, the center of adult neurogenesis with the potential for restoration of cognitive function

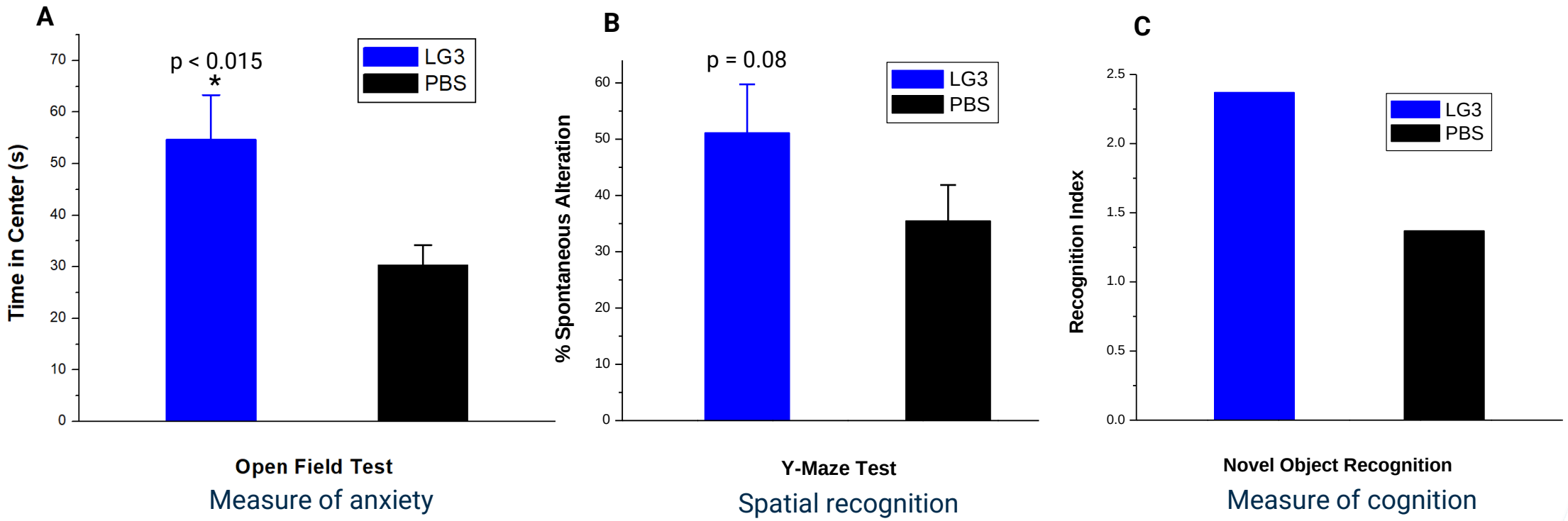


NeuN (mature neurons) x cresyl violet (cell body) in aged male 5xFAD mice reveals significant population of immature neurons in the dentate hilus

Aim 2 Report: In Vivo Assessment of rhPDV$_{LG3}$ for Disease Modification in Alzheimer's Mice, Stream/UTHSC/Premier: 2023

rhPDV$_{LG3}$ Improves Cognitive Functional Measures in a Murine Model of Human AD

Functional improvements in memory and anxiety in aged male 5xFAD mice



Open Field Test
Measure of anxiety

Y-Maze Test
Spatial recognition

Novel Object Recognition
Measure of cognition

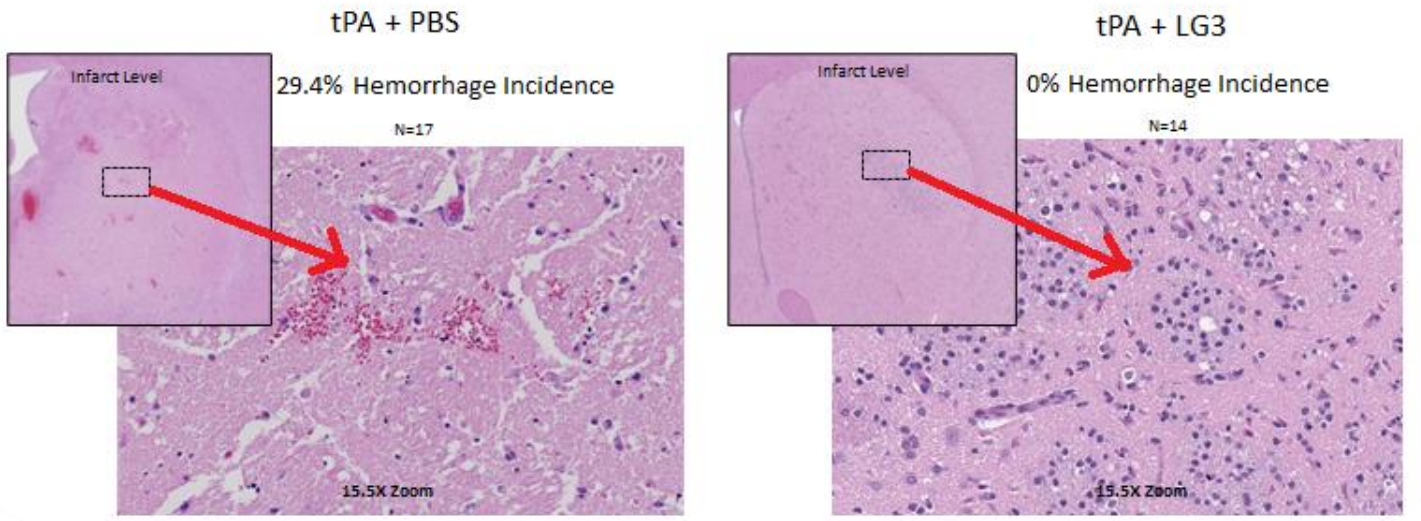
n=7-8/group

rhPDV$_{LG3}$ Stops Hemorrhage Induced by tPA and Neuronal Cell Death

Tissue Plasminogen Activator (tPA) is currently utilized as a first-line option prior to mechanical thrombectomy (MT) for treatment of large vessel occlusion (LVO)

Considerations with tPA:

- Narrow therapeutic window; time of symptom onset < 4.5 hrs
- Rates of clot migration complicating successful retrieval and hemorrhagic transformation may be higher



- Control hemorrhage incidence: **29.4%**
- rhPDV$_{LG3}$ treated hemorrhage incidence: **0%**

Stream/Neurovasc: 2021

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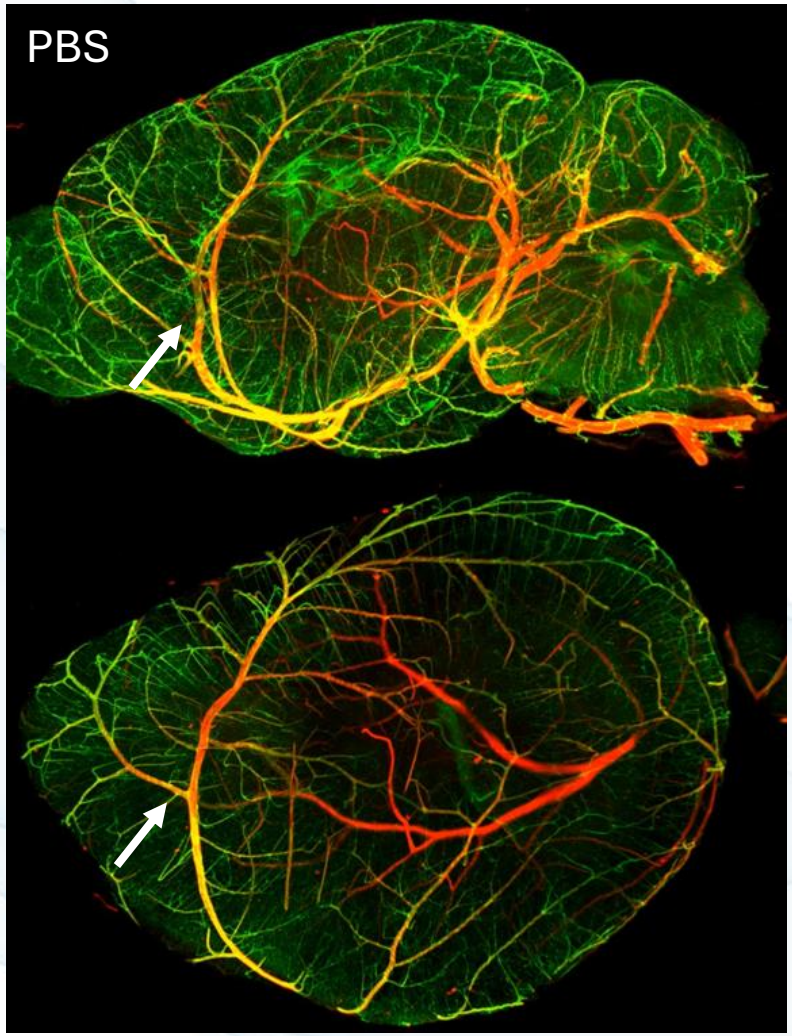
rhPDV$_{LG3}$ Repairs Neurovascular Injury to Protect the CNS

3D vascular imaging: 72 hours post-stroke in adult mice*

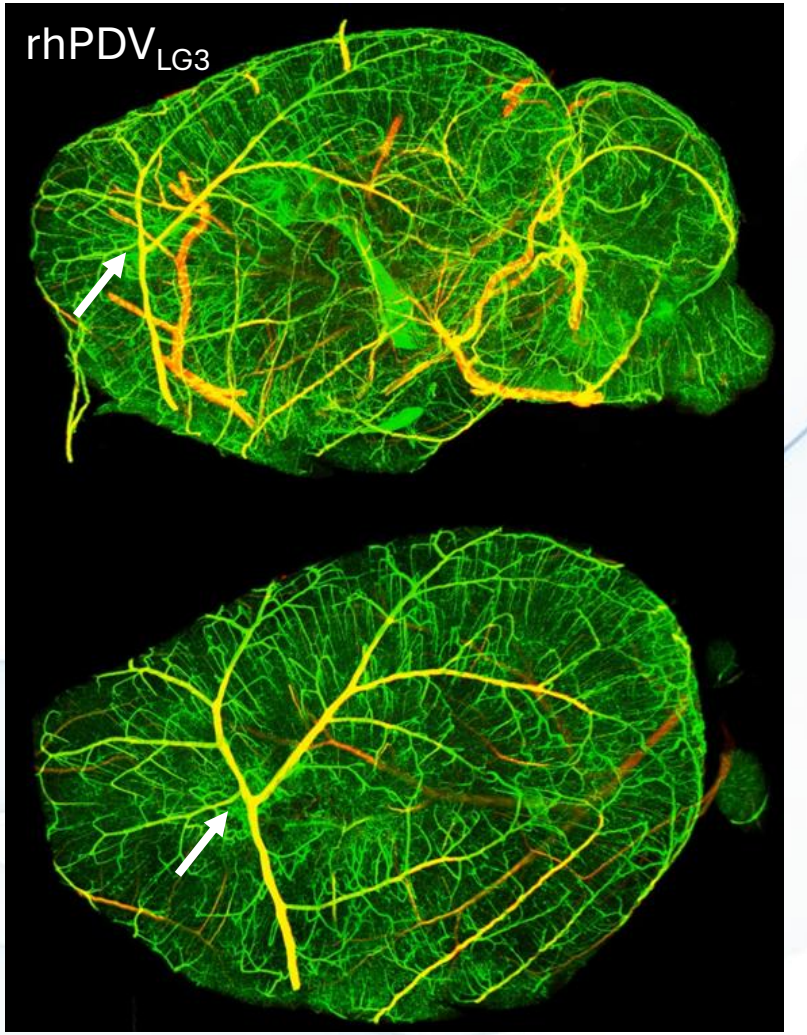
Whole brain

Stroke Area



Whole brain

Stroke Area



*Initial pilot imaging, full data pending. Arrows show point of occlusion (stroke origin)

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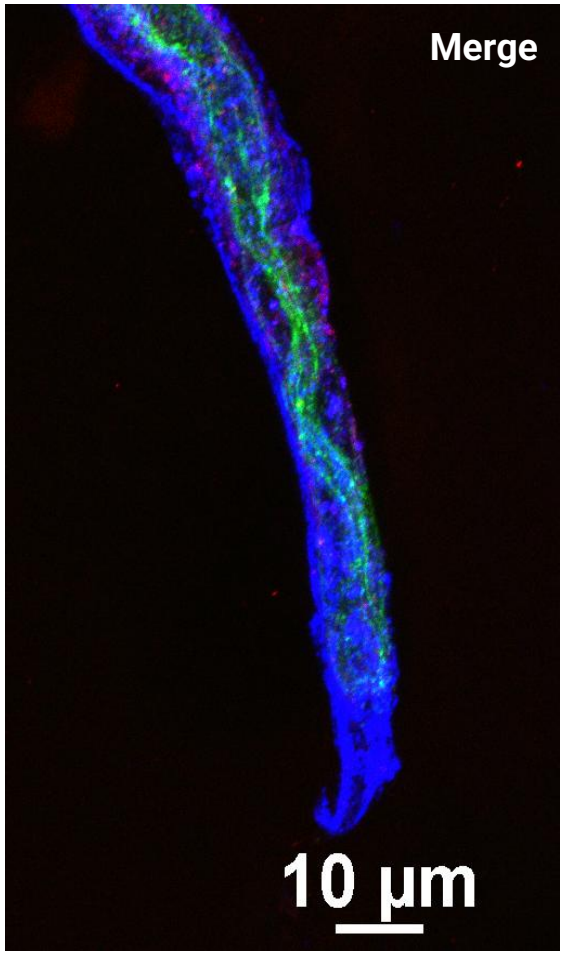
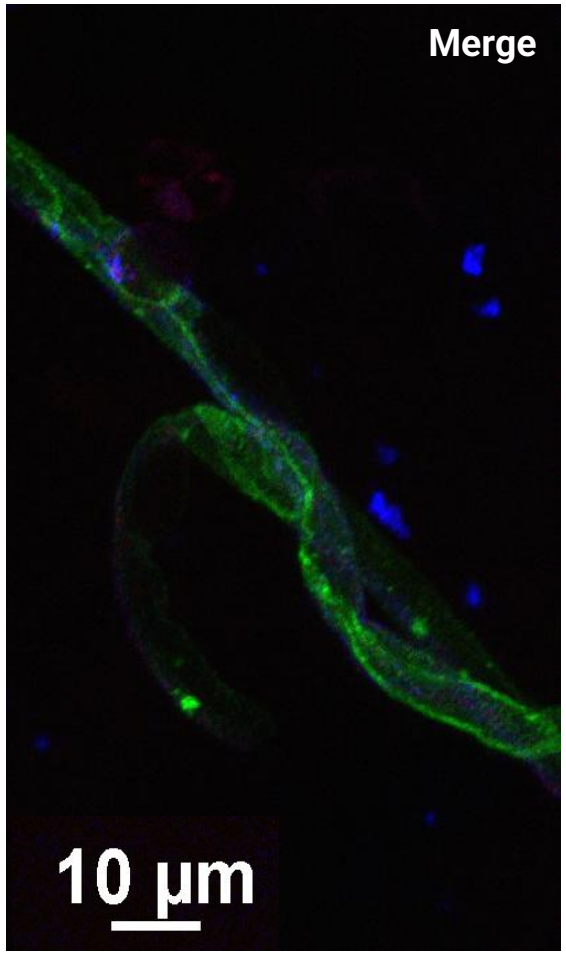
rhPDV$_{LG3}$ Repairs Neurovascular Injury to Protect the CNS
Isolated capillaries 24h post-stroke*

Controls

No Stroke + PBS

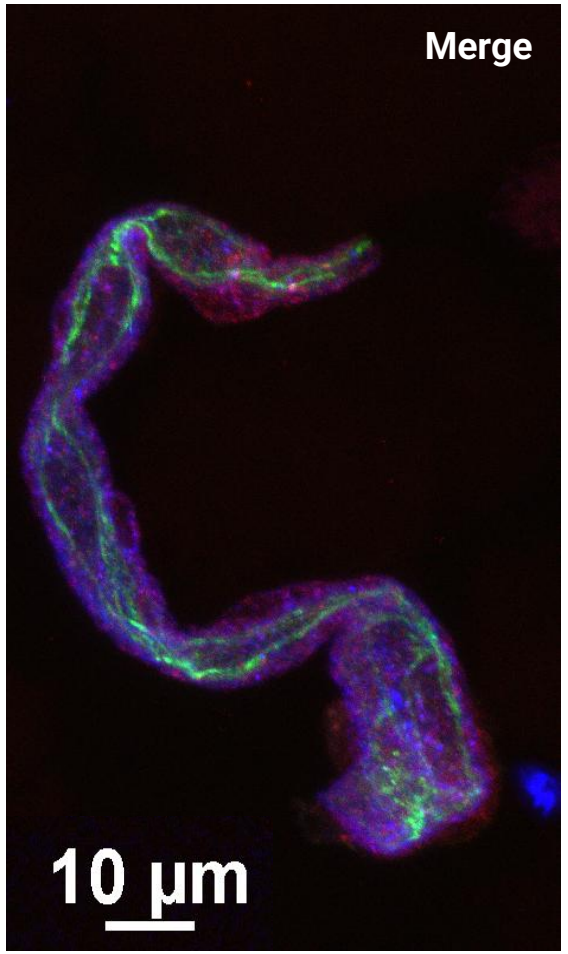


Stroke + PBS



Test

Stroke + rLG3



Evidence of Neuro-vascular Protection and Repair with rLG3

- Increased pericyte coverage
- Upregulated TJ expression
- Preserved vessel integrity

Overlay:
Red = **PDGFRβ** (Pericytes)
Green = **Claudin5** (Tight junction [TJ])
Blue = **Lectin** (BM, reduced in stroke)
Purple = Red + Blue (overlap)

rLG3 = rhPDV$_{LG3}$
PBS = Phosphate Buffered Saline

*Initial pilot imaging, full data pending

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Clinical Development

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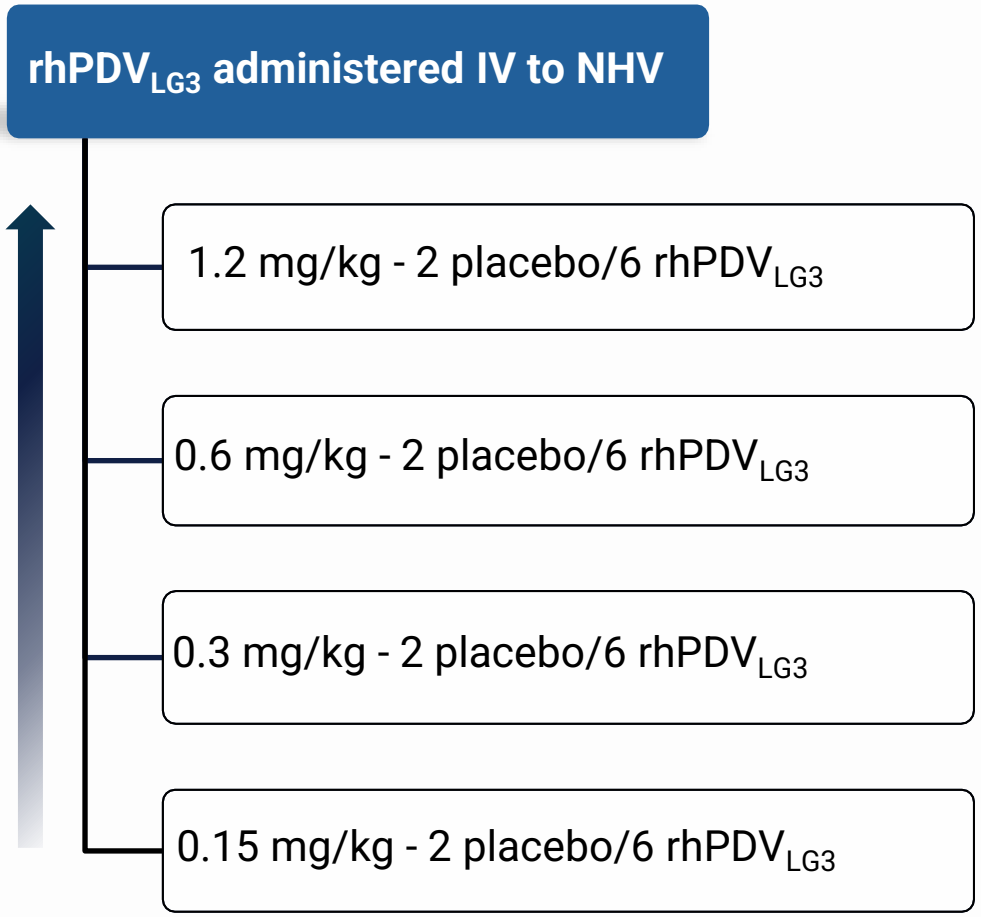
Study 1: Normal Healthy Volunteer (NHV)



Synopsis

- SAD study, four cohorts
- N = 32 participants
- Treatment arms: rhPDV$_{LG3}$ or placebo administered intravenously
- Sentinel dosing for first 2 patients of each cohort (1 placebo, 1 rhPDV$_{LG3}$)

Study 2: Patients with Acute Ischemic Stroke
Protocol Design (PAINTS*)

Jeffrey Saver, M.D.
Co-Principal Investigator
Professor and SA Vice-Chair of Neurology at UCLA, and Director of the UCLA Comprehensive Stroke and Vascular Neurology Program

Raul G. Nogueira, M.D.
Co-Principal Investigator
Director of the UPMC Stroke Institute & Professor at the University of Pittsburgh Department of Neurology

Objectives

SAFETY & PRELIMINARY EFFICACY

Synopsis

- A randomized, placebo-controlled, double-blinded, dose escalation, phase 1b
- N = 48 participants, four cohorts
- Inclusion criteria: patients with AIS from large vessel occlusion (LVO) of the anterior cerebral vasculature with successful reperfusion following mechanical thrombectomy
- Treatment arms: rhPDV$_{LG3}$ or placebo administered intravenously following thrombectomy/reperfusion
- Preliminary evidence of efficacy:
  - Clinical outcome measures: mRS, NIHSS, MoCA
  - Neuroimaging: BBB permeability, capillary flow, infarct volume, HARM-sign
  - Serum biomarkers: inflammatory biomarkers, BBB repair biomarkers

**rhPDV$_{LG3}$ Administered Intravenously for Neuroprotection following Thrombectomy in Stroke*

1. *Phase 3 ESCAPE-NA1 Study of the Peptide, Nerinetide in Acute Ischemic Stroke (enrollment completed in Apr 2023) being advanced by NoNO, Inc., a clinical-stage company focused on stroke, based in Ontario, Canada*

Phase 1 Clinical Trial: Initiate Q2 ’26
Proof-of-Concept in Humans

Acute ischemic stroke: optimal patient population for initial study

- Neuroimaging to assess CNS repair
- Homogeneous patient population
- Viable CNS tissue to salvage
- High sensitivity to detect treatment effects
- Biomarker panel to corroborate clinical efficacy

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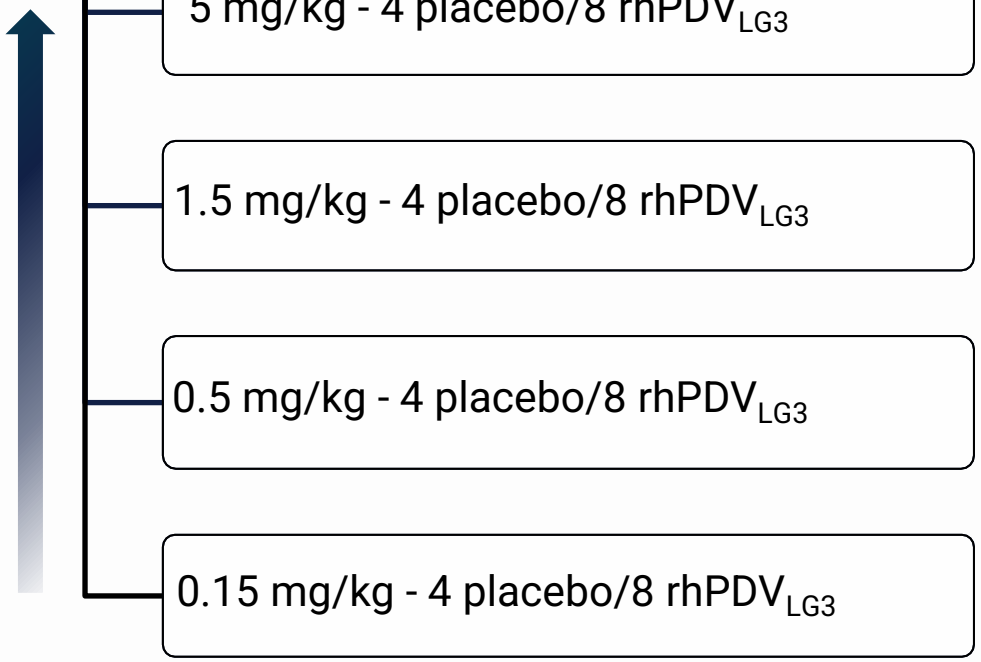
Phase I Protocol Design (PAINTS*): rhPDV$_{LG3}$ Administered IV Post-Thrombectomy

Randomized placebo-controlled four cohort ascending dose trial



Goal = to assess the safety and initial efficacy of rhPDV$_{LG3}$ as a neuroprotective agent

- **Safety:** Starting dose = 30x below NOAEL, sentinel dosing, safety reviews
- **Homogeneity:** All have successful clot removal + successful reperfusion
- **Viable brain tissue** to salvage (meet standard criteria for thrombectomy)
- **High unmet need:** to ensure relatively poor placebo outcomes following reperfusion (≤ 35% near full function); age > 60 years; existing baseline infarction (20 mL); broad time to Rx (0-16 hrs). Maximize effect by administering rhPDV$_{LG3}$ acutely following reperfusion
- **Enhance likelihood of detecting efficacy:** multiple data sources including clinical, radiographic, and serum biomarkers

**rhPDV$_{LG3}$ Administered Intravenously for Neuroprotection following Thrombectomy in Stroke*

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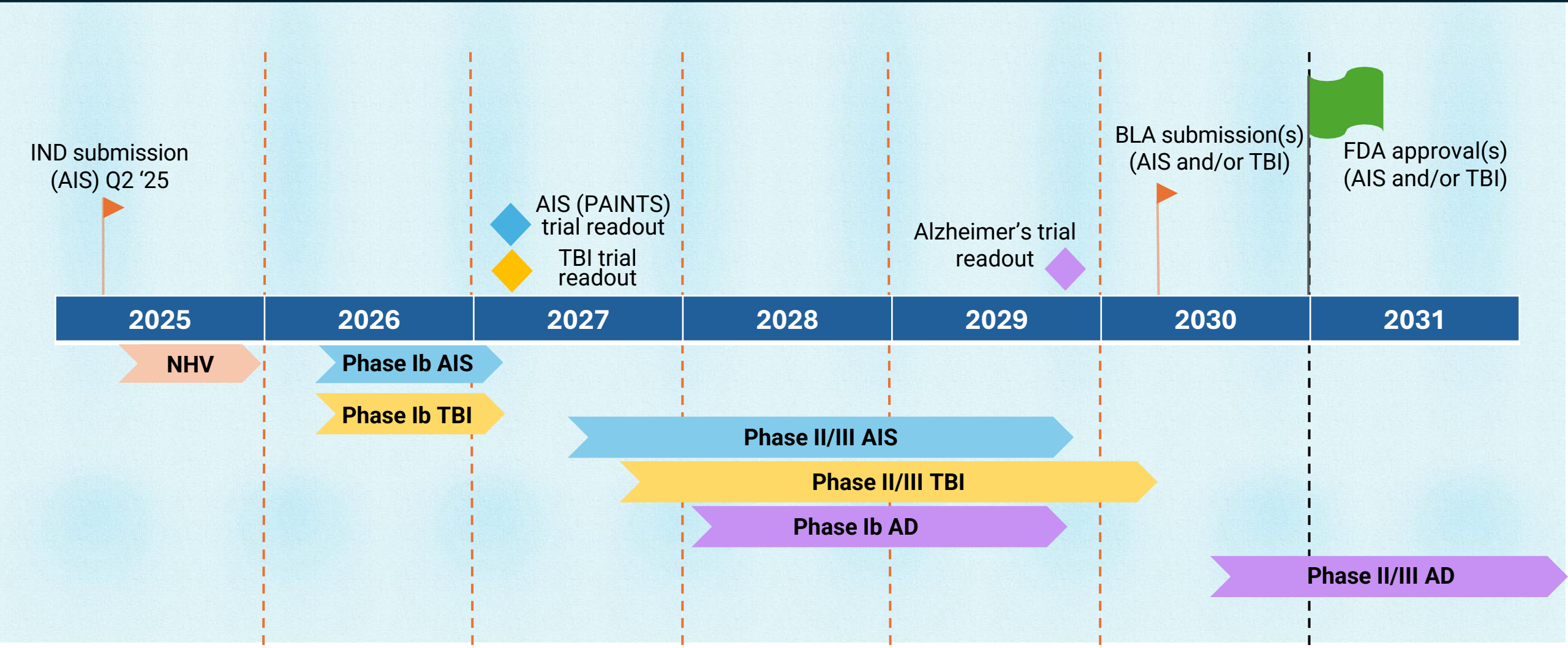
Clinical Milestones for Acute Ischemic Stroke, Traumatic Brain Injury, and Alzheimer's Disease



Key:

Acute Ischemic Stroke (AIS) | Traumatic Brain Injury (TBI) | Alzheimer's Disease (AD) | Normal Healthy Volunteer

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12-Year Data Exclusivity Upon Approval of rhPDV$_{LG3}$ for AIS and/or TBI
Ongoing Data Collection for Generation of New IP Across Indications

Current Patents						
Patent Number	**Title**	**Claims**	**Patent Expiration**	**Patent Term Extension**	**Assumed Patent Life (PTA+PTE)**	**# of WW Jurisdictions**
8,466,105	**Treatment of stroke using domain V of perlecan**	**Stroke/angiogenesis**	**4/9/2031**	5 years	**4/7/2036**	**16**
9,072,713	**Perlecan domain V protects, repairs, and restores ischemic brain stroke injury and motor function**	**Stroke, TBI, SCI**	**4/9/2031**	5 years	**4/7/2036**	**6**
9,358,273	**Use of perlecan domain V in treating amyloidogenic disease**	**Amyloidogenic disease: AD, PD, MCI, Down's, diabetes type 2, prion infection, amyloidosis**	**12/18/2032**	5 years	**12/17/2037**	**1**
PCT/US2021/070948	**Use of perlecan and fragments thereof to reduce the risk of death in stroke patients**	**Stroke mortality, thrombolytic hemorrhage reduction**	**7/26/2041**	5 years	**7/26/2046**	**11+**
PCT/US2023/82138	**Use of perlecan and fragments thereof to treat blood-brain barrier disruption**	**BBB integrity**	**12/1/2043**	5 years	**12/1/2048**	**TBD**

Summary Highlights - Investigational Agent rhPDV$_{LG3}$

Novel biological agent, first-in-class, novel clinical therapeutic category
Potentially transformative therapeutic agent for neurology

Platform therapeutic: Multiple potential CNS indications
Both acute and chronic neurodegenerative diseases

Recombinant biologic: Repairs neurovascular injury to protect the CNS
Repairs BBB, neurogenic, vasculogenic, neuroprotective, anti-inflammatory

Clinical study: Initiate phase 1b in Q3 2025
Safety and confirm initial efficacy in humans

Near-term value inflection point: Clinical study readout Q1 '26
Pursue clinical development across a range of acute and chronic neurodegenerative diseases