PrimaryPeptides

Developing Breakthrough Neuro Therapeutics using Protein Manipulation

Max S. Cynader, Co-Founder & CEO
Primary Peptides Inc.

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Corporate Overview of Primary Peptides Inc.

- Neuroscience - focused company, spun out of the Centre for Brain Health and the Faculty of Medicine, University of British Columbia, (UBC), Canada
- Unique protein manipulation platform technology to unlock undruggable targets
- Pipeline consists of first-in-class peptide therapeutics, focused on hard-to-drug targets in neuro indications with significant unmet medical need:
  - K13 – Phase 2 ready, neuroprotective agent for acute stroke – partnered with Yabao Pharma for China rights only
  - K13V – Stroke-triggered gene vector for expressing K13 peptide (preclinical)
  - PP-003 - Alpha synuclein for Parkinson's Disease (preclinical)
  - PP-007 - TDP-43 for Amyotrophic Lateral Sclerosis and Frontotemporal Dementia (preclinical)
- Strong patent portfolio and clean cap table
- Highly-experienced management team, Board of Directors and Scientific Advisory Board
- Seeking Series A to advance pipeline and platform

The Problem and Our Solution

The Problem

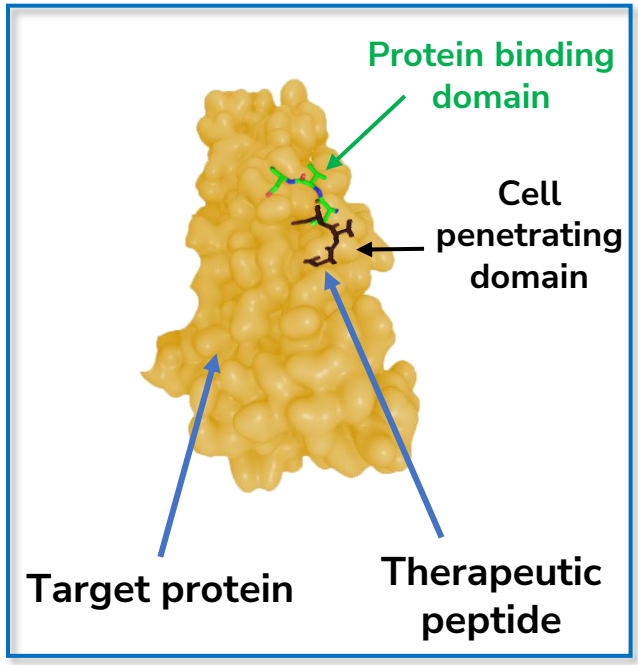
- **Over 85% of the Human Proteome is undruggable using small molecules and antibodies**

Our Solution

- **Differentiated protein manipulation platform using peptides to unlock "undruggable targets" via protein-protein interference and protein degradation**

First in class peptides:

- ✓ Highly selective
- ✓ Target pocket-free zones on specific proteins
- ✓ Non toxic and nonimmunogenic
- ✓ Cell permeable and cross the blood brain barrier (BBB)



- Peptides now widely accepted as a therapeutic modality. Notable examples include multi-billion dollar obesity drugs Semaglutide by Novo Nordisk and Tirzepatide by Eli Lilly, administered by once-weekly subcutaneous injections

GMI Insights, Industry Analysis, Peptide Therapeutics Market, 2023

Robust Pipeline
First-in-Class Peptide Therapeutics in Neurological Disorders

	Assets	Indication	Target	Discovery/ *in vitro* studies	Animal studies	IND enabling studies	IND	Phase 1	Phase 2
1.	K13	Acute Stroke (both ischemic and hemorrhagic)	PTEN & NEDD4	Interference Peptide					yabao Pharmaceutical Greater China rights only
2.	K13V	Automatic Stroke Damage Mitigation (Vascular Dementia)	PTEN & NEDD4	Stroke-triggered gene vector					
3.	PP-003	Parkinson's Disease	α-synuclein	Bi-functional Degrader					
4.	PP-007	ALS/FTD	TDP-43 & CK1δ	Interference Peptide					

Notes:

- K13 Phase 1 study conducted in China (meets standards of Chinese NMPA and US FDA)
- Interference peptides : block protein-protein interactions
- Bi-functional Degraders: block protein signalling pathway & degrade disease causing proteins
- Stroke-triggered gene vector: releases K13 peptide when a stroke occurs
- Amyotrophic Lateral Sclerosis (ALS), Frontotemporal Dementia (FTD)

Large Market Opportunities in Neuroscience

> 15M Patients WW
> $10B market opportunity

Major Neurological Disease

Acute Stroke

FDA fast track possible

> 10M patients WW
> $5B market opportunity

Major Neurodegenerative Disease

Parkinson's Disease

> 500K patients WW
> $1B-5B per indication

Rare Neurodegenerative diseases

ALS, FTD

Orphan Indications

Peptides Cross Blood Brain Barrier and Cell Membrane

Biomarker Driven Development

Strategic Partnering Opportunities

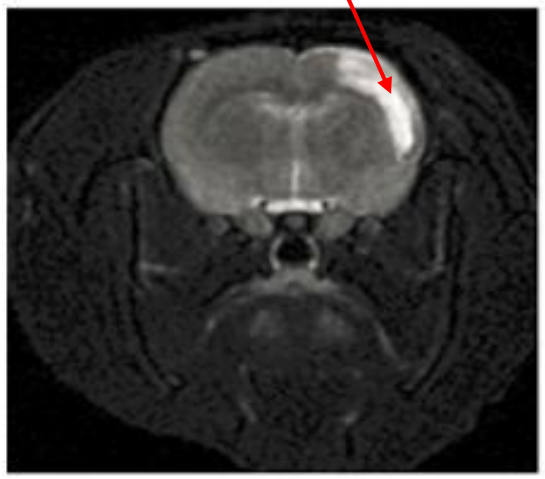
Amyotrophic Lateral Sclerosis (ALS), Frontotemporal Dementia (FTD)

WW estimates based on WHO 2022; NIH 2022, CDC, 2022,; Association for FTD, 2023,, National Institute of Neurological disorders and stroke 2022, World Stroke Organization Global Fact Sheet 2022,

Clinical K13: neuroprotective peptide inhibitor for both Hemorrhagic & Ischemic Stroke
Current standard of care tPA for Acute Ischemic Stroke only

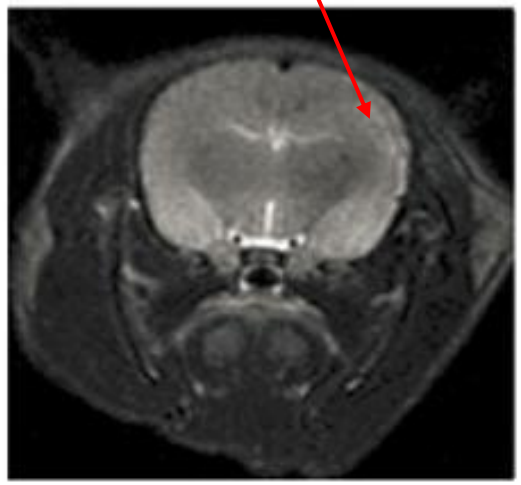
MRI scan of Brain Damage *in vivo* in Stroke Model

Ischemic Infarct Area



Saline

Infarct Area Reduced



K13 injection 6hrs after Stroke

- K13 provides long-lasting morphological & functional protection of neurons against ischemic insults
- Promotes behavioral recovery

K13, Positive Ph 1, good safety and PK data

- Possible delivery up to 6 hrs. after stroke onset, potentially in ambulance setting
  - twice as long as tPA
- No risk of provoking hemorrhages
- Differentiated clinical plan for Phase 2 in surgery induced stroke setting using Aneurysm Coiling Therapy

Global data Acute Ischemic Stroke, Global Drug Forecast and Market Analysis to 2027, July 2018

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K13 : Proposed Phase 2 Trial Plan

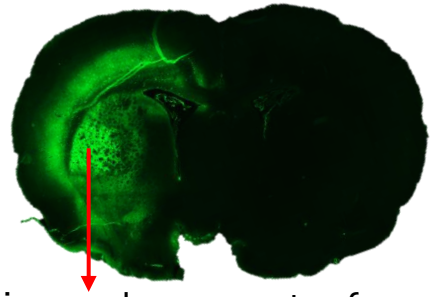
- Adopt a well validated Ph 2 protocol as employed by NoNo Inc., Canada - ClinicalTrials.gov Identifier: NCT00728182, Phase 2 clinical trial, and presented in Hill et al., Lancet Neurol, 2012

- The trial evaluated the neuroprotection of therapeutic NA-1 in a surgery induced stroke setting using Aneurysm Coiling Therapy

- Consulted with Principal Investigator of both Phase 2 and 3 trials. Proposed plan:
  - Dose male and female patients undergoing endovascular repair of brain aneurysm with K13 or placebo as a 10 minute intravenous infusion after completion of the endovascular procedure
  - Proposed efficacy endpoints:
    - Reduction in volume of ischemic embolic strokes
    - Reduction in the number of ischemic embolic strokes
    - Reduction of vascular cognitive impairment, and
    - Reduction of the frequency of large strokes induced by the endovascular procedure.

K13V : Stroke-triggered Gene Vector for K13 Peptide

Specific expression (bright green fluorescence) of a stroke-triggered gene vector in the rat brain



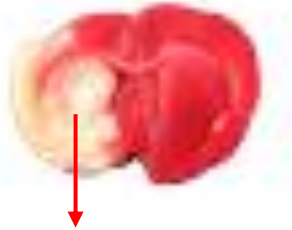
Stroke-triggered gene vector for expressing a therapeutic peptide

The rat brain that was pre-treated with a stroke-triggered gene vector 3 months earlier showed much smaller brain damage after stroke

With a stroke-triggered gene vector

Almost no ischemic infarct area

Without a stroke-triggered gene vector



Big ischemic infarct area

Key Unmet Need in Stroke Damage Mitigation

- There is currently no treatment that can automatically protect the brain from the effects of a stroke
- We have developed a stroke-triggered gene vector method to express therapeutic peptides as a potential approach for automatic stroke damage mitigation
- K13V is a stroke-triggered gene vector. It expresses K13 peptide, saves neurons from death, and can be given to individuals with a high risk of stroke and to those with vascular dementia which is caused by an ongoing series of small strokes
- If K13 has a successful phase 2 trial, we will quickly follow up with the K13V program

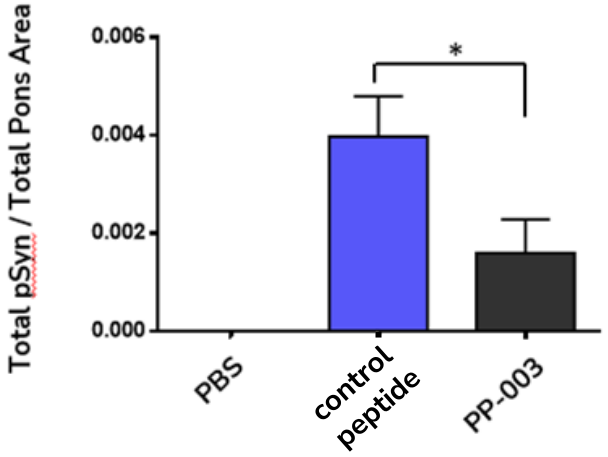
Preclinical PP-003 : targets α-synuclein degradation, a key hallmark of Parkinson's Disease
No approved therapies target α-synuclein

PP-003, First in Class Degradation Peptide for PD

- Evidence supports premise that reducing α-syn levels may be an effective therapy for PD
- Demonstrates efficacy in 4 well characterized PD models
  - ✓ reduces α-synuclein levels
  - ✓ saves neurons, and
  - ✓ rescues behavioral function
- Does not require E3 ligase for degradation
- Peptide crosses the BBB and cell membrane
- Several candidates targeting α-synuclein have failed in clinical studies- unable to cross BBB, or cell membrane

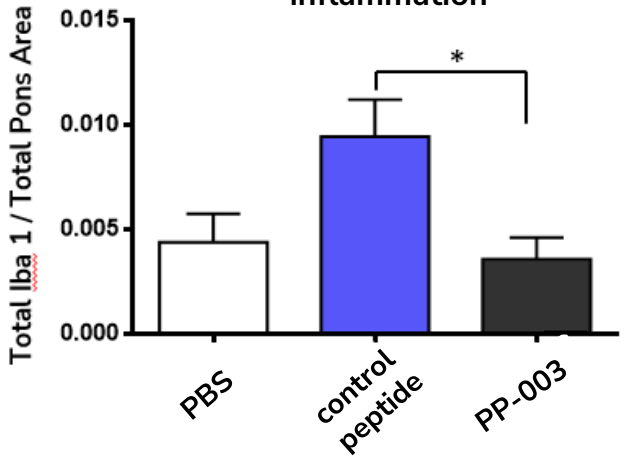
PP-003 reduces α-syn Aggregation & Brain Inflammation *in vivo*

pS129syn staining shows pathogenic α-syn aggregates



Demonstrates effectiveness of PP-003 in reducing preformed α-syn fibril (PFF) induced α-syn aggregation

lba1 staining shows brain inflammation



Demonstrates effectiveness of PP-003 in reducing PFF induced brain inflammation

*P<0.05 comparison between PP-003 and the control peptide

Publ. Jin et al. Development of an α-synuclein knockdown peptide and evaluation of its efficacy in Parkinson's disease models. Commun.. Biol 4, 232 (2021).

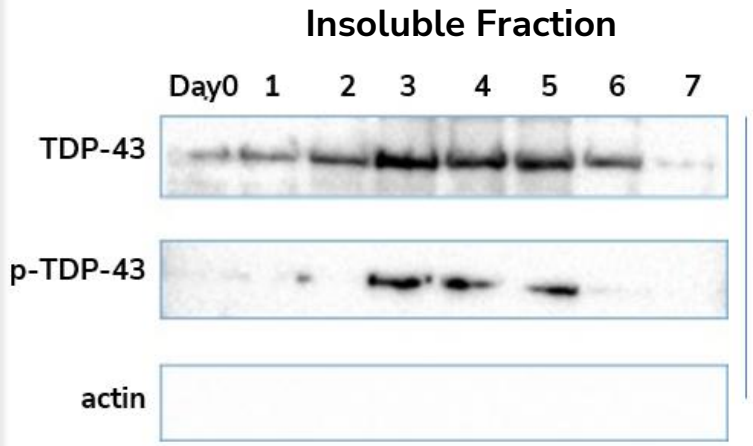
PBS is phosphate buffered saline; pS129syn is Serine 129 phosphorylated α-synuclein; lba1 is Ionized calcium binding adaptor molecule 1

Preclinical PP-007: targets TDP-43 proteinopathies present in 97% of ALS patients
ALS poorly controlled by current therapies with different mechanism of action

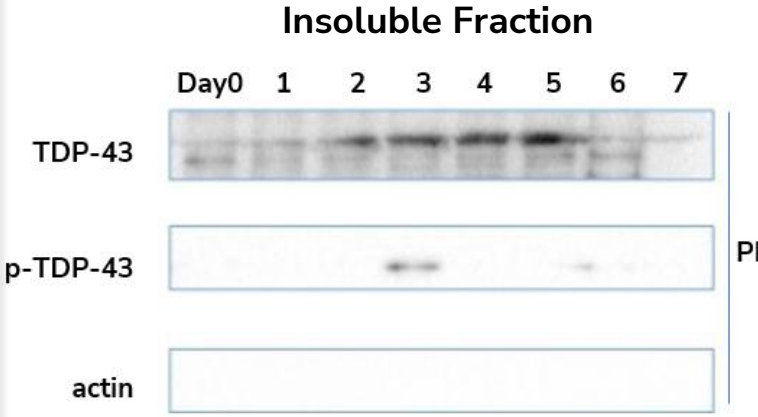
PP-007, First in Class Interference Peptide for ALS

- Precisely blocks CK-1δ phosphorylation of TDP-43
- Offers high specificity compared to kinase inhibitor approaches that often result in off-target effects
- Validated in *in vitro* and *in vivo* models:
  - ✓ blocks TDP-43 phosphorylation & aggregation in neurons
  - ✓ reduces cell death in human neuroblast cells and motor neurons
  - ✓ reduces spinal cord inflammation even when given after disease onset
  - ✓ prevents stress granules formation
- Orphan drug potential

PP-003 blocks TDP-43 Phosphorylation & Aggregation in neurons in Mouse Lumbar Spinal cord after Sciatic Nerve Axotomy



TDP-43 phosphorylation & aggregation upregulated 1-7 days in spinal cord after sciatic nerve axotomy in control mice.



In treated mice with PP-007 (20mg/kg, i.v., once/day for 7 days), TDP-43 phosphorylation & aggregation robustly downregulated.

Actin, cytoplasmic protein marker, confirms purity of insoluble fraction

Neumann, M et al. Ubiquinated TDP-43 in FTD and ALS, Science 314, 130-133 (2006)

The Raise

1) Seeking a $25M USD Series A financing
2) Pre-money valuation of $50M USD
3) One class of common shares
4) Rolling close - accept funds as they are committed

Milestones over the next 3 years with $25M+ raise

Use of Proceeds	Budget (USD)
US IND filed for K13 for Acute Stroke – ready to enter Phase 2 studies	$1M
Phase 2 studies underway for K13	$15M
Continue the development of K13V to IND ready stage	$2M
IND filed for Parkinson's Disease or ALS/Frontotemporal Dementia (FTD). Phase 1 trial underway	$5M
Ongoing operations	$2M

***Note**: K13, neuroprotective stroke asset, is currently partnered with Yabao for Greater China rights only*

Exit Strategy and Rate of Return

1) Three years from the Series A close, one asset in Phase 2 and the second in Phase 1

2) The stroke triggered gene vector, K13V, will be in IND-enabling studies

3) Strategic partnerships with large pharma(s) pursued

4) Achievements will support an IPO, or a buyout in mid 2028

5) Expected pre-money valuation of $300M USD at IPO, yields a 300% return over 3 years

Primary Peptides - An Accomplished Team

Leadership Team

Max S. Cynader, CM, OBC, PhD, FRSC, FCAHS. CEO & Co-Founder
Prof, Medicine, UBC, Canada Research Chair Brain Development & Serial Entrepreneur

Yu Tian Wang, MD, PhD, FRSC
CSO & Co-Founder
Prof. Medicine & Centre for Brain Health, UBC. Chair in Stroke Research & Entrepreneur

David Turner, Chartered Accountant
Chief Financial Officer
30 yrs.+ global experience in Executive Leadership – Life Sciences and Clean Tech

Jack Jin, PhD
Chief Operating Officer
PhD in Neuroscience, UBC. 10 yrs.+ scientific research & company operations

Julie Rezler, MA
VP, Corporate Development
20 yrs.+ Life Sciences – US, Canada & Asia. Former global Management Consultant with PwC

Janice Mallison, MSc
VP, Regulatory & Clinical Affairs
30 yrs.+ Biopharma in Canada, US & Europe

Advisory Board

Ron Petersen PhD, MD
Prof. Neurology & Director of Alzheimer's Disease Research Mayo Clinic. Expert in Parkinson's Disease and lifetime Achievement Award for AD Research

Helen M. Burt, PhD, CAHS, OC
Former Director, Research at Angiotech Pharma. Expert in drug delivery

John Cairns, MD, FRCPC, FRCP (Lond.), FCAHS, FACC
Prof. Medicine, UBC, Cardiology. Steering Committee Chair Cardiovascular clinical trials

Peng Wang, PhD
Discovery and development of 30+new drug candidates including Reslizumab, Cinquil™ and Sanbexin™

William Wei-Guo Jia, MSc, PhD
Company co-founder. Associate Professor, Department of Surgery, UBC. Founder & CSO Virogen Biotech

Seeking Series A

PrimaryPeptides

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