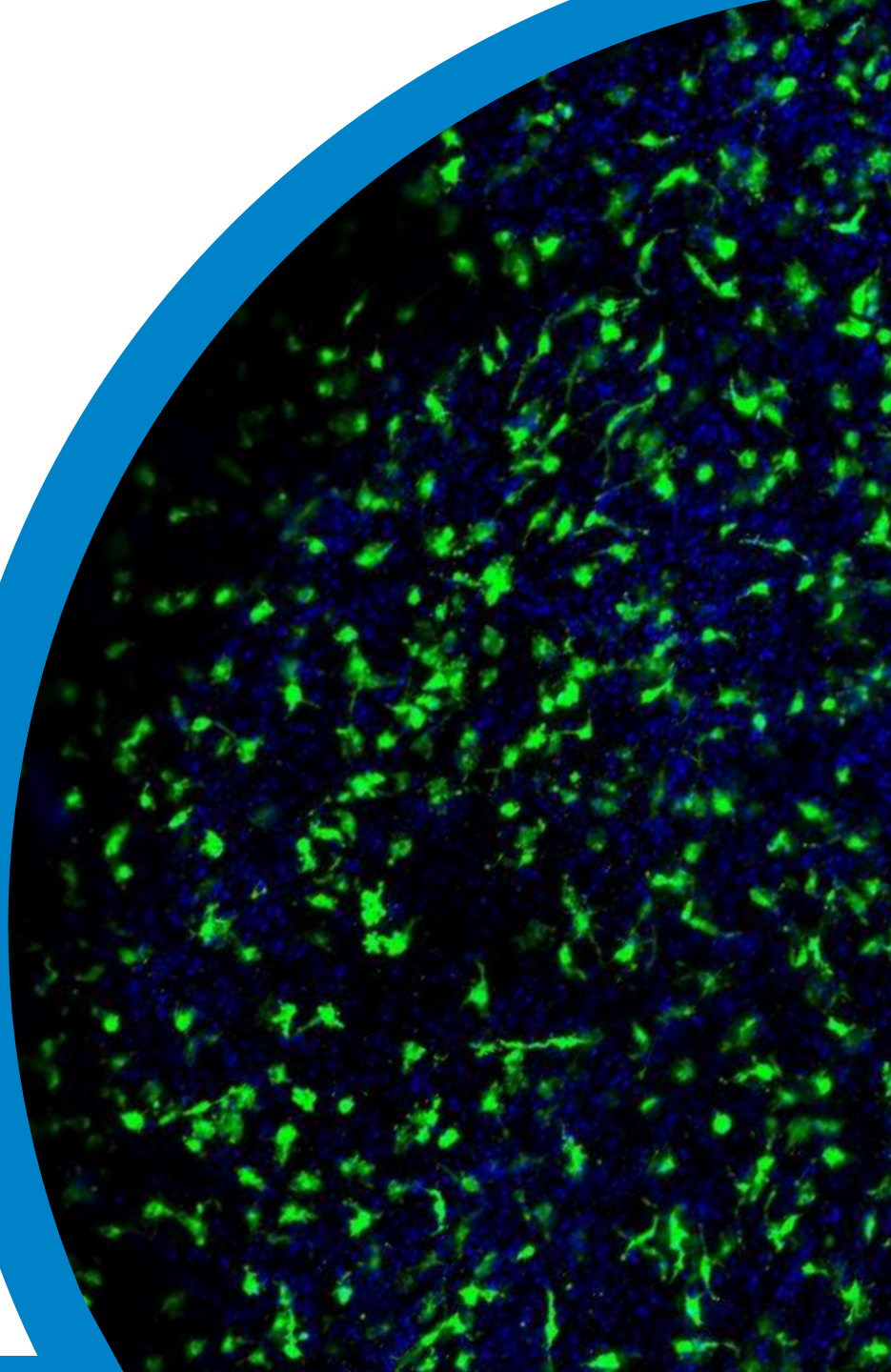
Neuroinflammation-Focused Drug Discovery Using Human Organoids to De-risk Clinical Translation



Steven Visuri, PhD
CEO

Experienced Team Focused on Execution

- Raised $6M in NIH funding to develop Stem Pharm's organoid technology
- 6 Successful startup exits
- 10+ FDA Approvals

Steven Visuri, PhD
CEO

Prodesse
HOLOGIC
The Science of Sure

Connie Lebakken, PhD
Co-Founder & COO

ThermoFisher SCIENTIFIC
life technologies™

William Murphy, PhD
Co-Founder & CSO

WISCONSIN UNIVERSITY OF WISCONSIN-MADISON
TRS Tissue Regeneration Systems

Ryan Gordon, PhD
CBO

3M Health Care
StemoniX
Stem Pharm

Neurological Diseases Affect 1 in 6

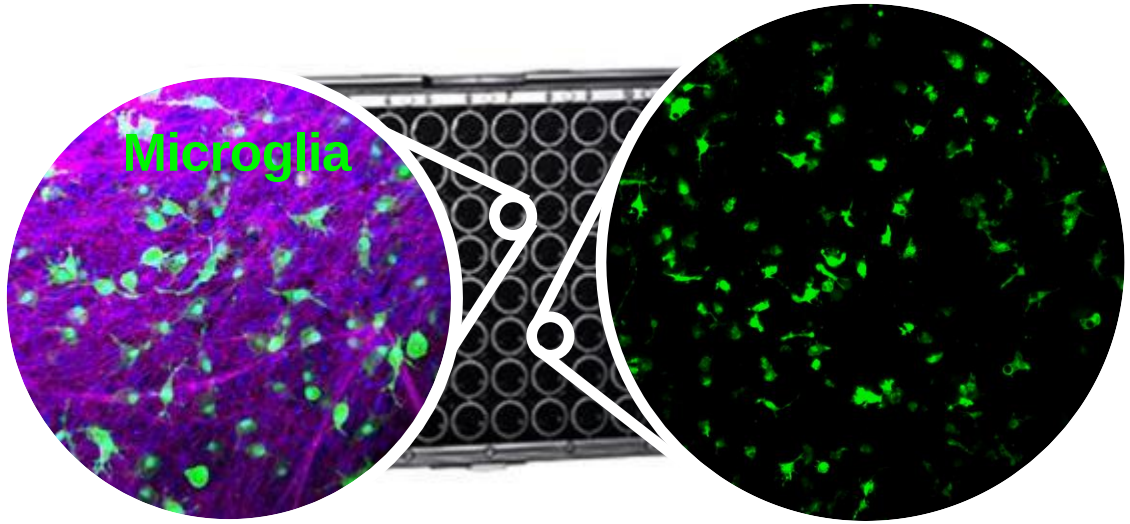
- 10 million deaths annually
- Annual economic cost $800B
- 40M cases of neurodegenerative diseases expected by 2050
- Few effective drugs

Neuroinflammation Drives Many Diseases

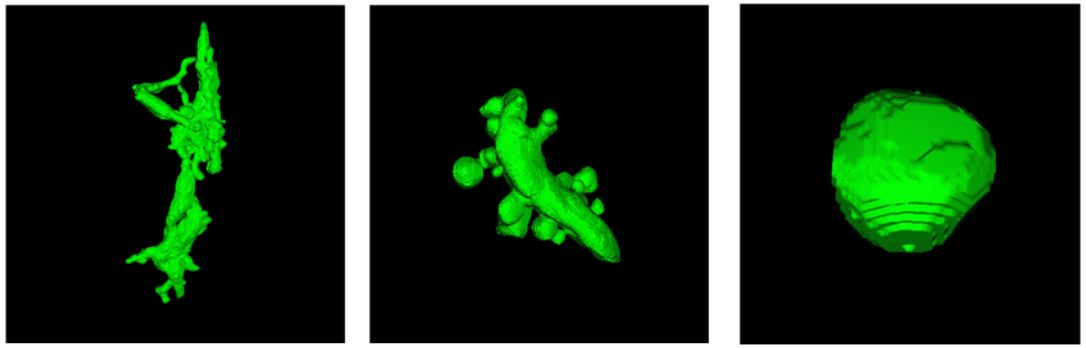
- Major focus for therapeutic intervention
- Tools available to model inflammation are inadequate
- Microglia are the brain's immune cells and drive inflammation
- Microglia are difficult to study in the lab

Neural Organoid Platform Models Neuroinflammation

- Stem Pharm's "planar 3D" organoid enables incorporation of microglia
- Microglia supported with neurons, astrocytes, and vascular cells
- Validated biology - microglia function appropriately



Microglia phenotype changes in response to stimuli



↑ Sphericity = ↑ Activation

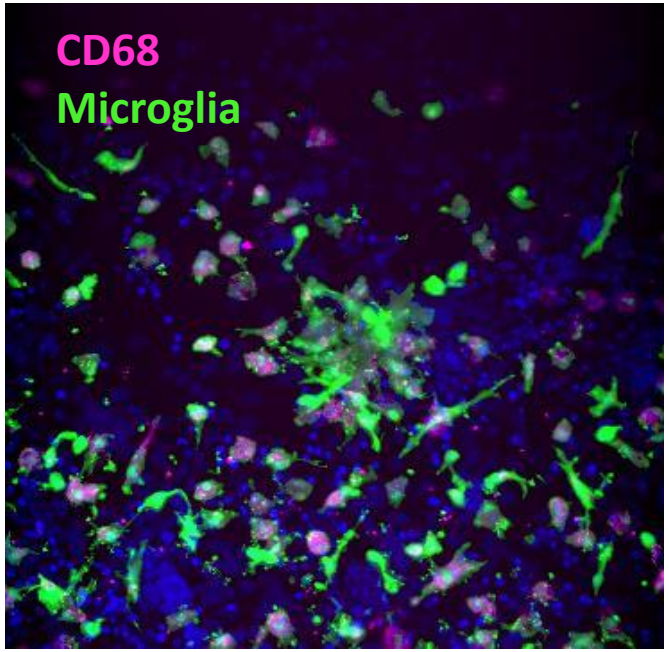
Differentiation: Neuroinflammation in 'Complex' 3D Human Environment

Value Prop: Better Clinical Translation!

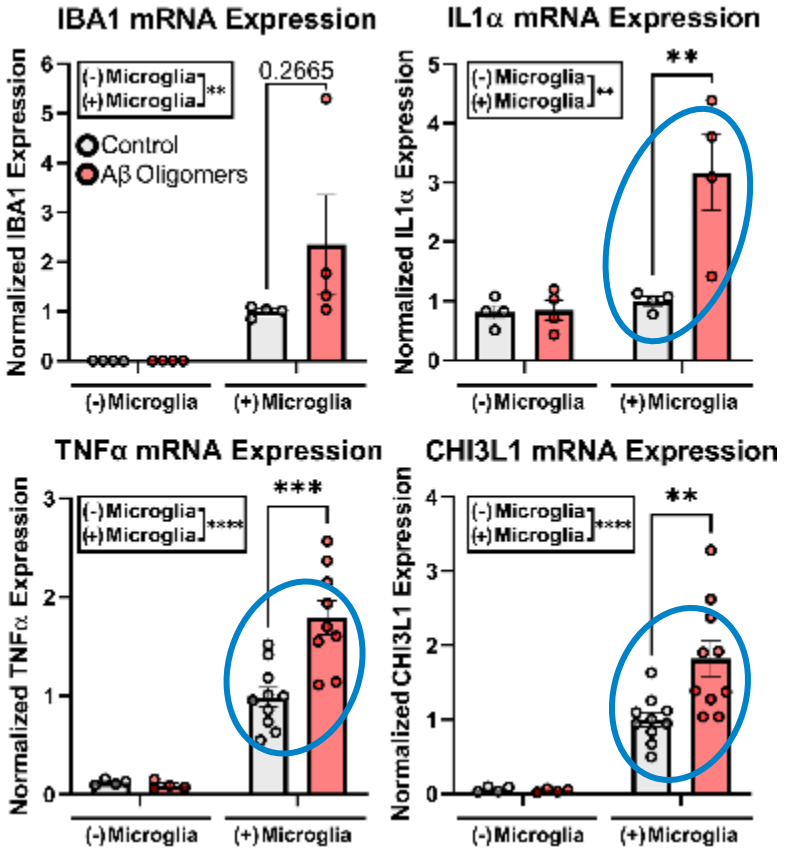
Organoids are the Engine of a Drug Discovery Platform

Case Study: Alzheimer's Disease Model via spiking of amyloid beta

High levels of CD68 expression seen - common marker of microglia phagocytosis



Response to Ab oligomers is microglia specific with elevated expression of immune markers



<u>Rich toolbox of multi-modal readouts:</u>

Transcriptional

Protein

Morphology

Cell health

Function

Strong IP Protection and Clear Competitive Advantage

- Intellectual Property: Licensed patents on organoid and hydrogel technology from University of Wisconsin (WARF)

- Competitive Advantage:
  - Superior biology
  - Only company with *in vivo*-like human microglia in robust screenable format
  - Best-in-class disease models leading to first-in-class/best-in-class drugs

Platform is **validated** and **implemented** into programs

Platform Validated by Peers and Pharma Partners

- Awarded $6M NIH SBIR grants
- Joined StartUp Health Alzheimer's Moonshot
- Graduated from two venture Accelerators
- Broadly validated pharmacological utility through projects with NIH and 10 pharma companies

NIH
National Institutes of Health
SBIR/STTR

Illumina ACCELERATOR

MERCK
Merck Digital Sciences Studio

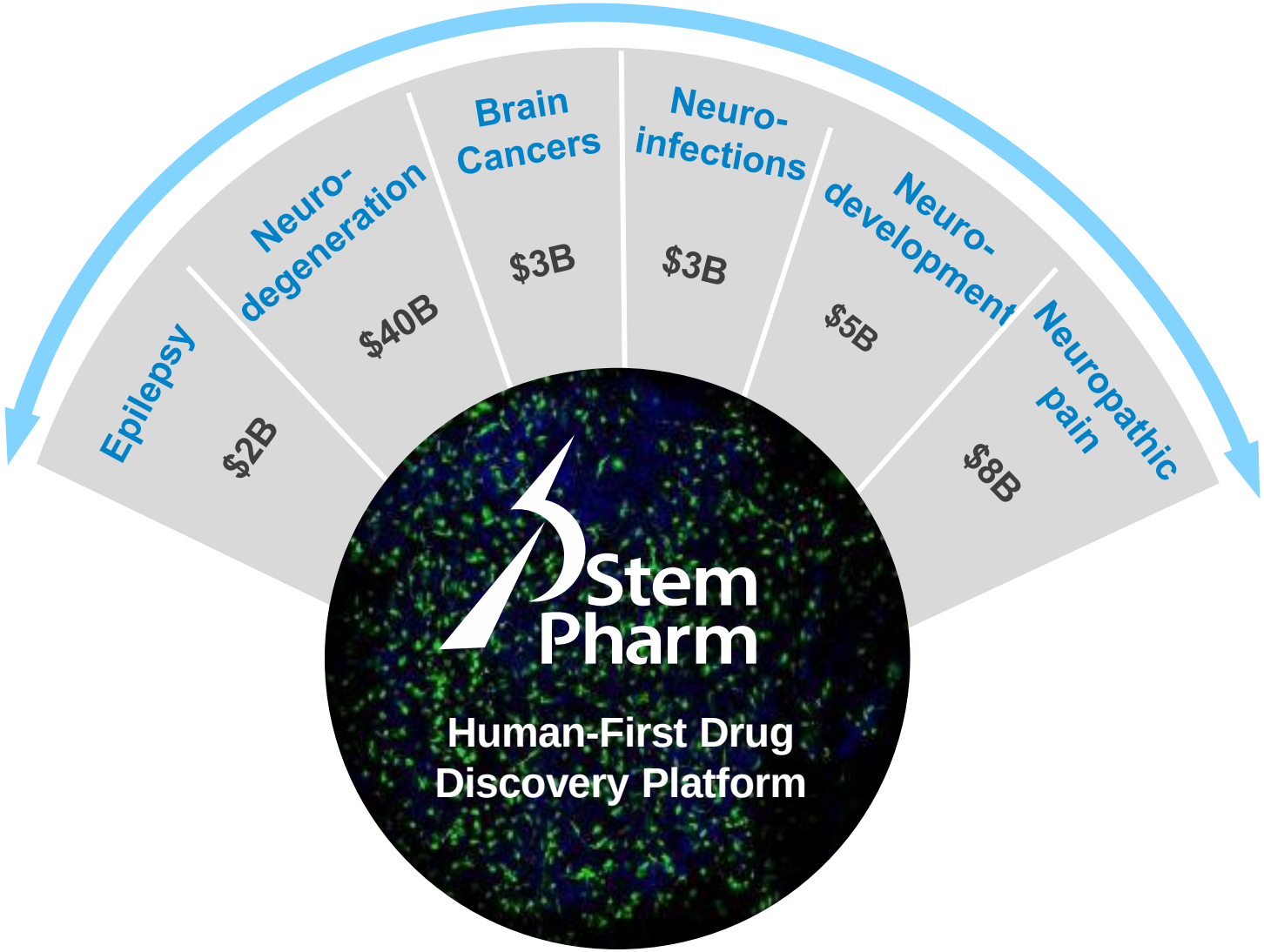
STARTUP +HEALTH®

Stem Pharm

Business Strategy: Develop Internal Pipeline & Out-License

- Identify and advance drugs that modulate microglia/neuroinflammation
- Focus on small molecule
- Generate novel chemistry
- Exit Strategy: Out-license assets or acquisition of platform

Neuroinflammation is a $60B Market Opportunity



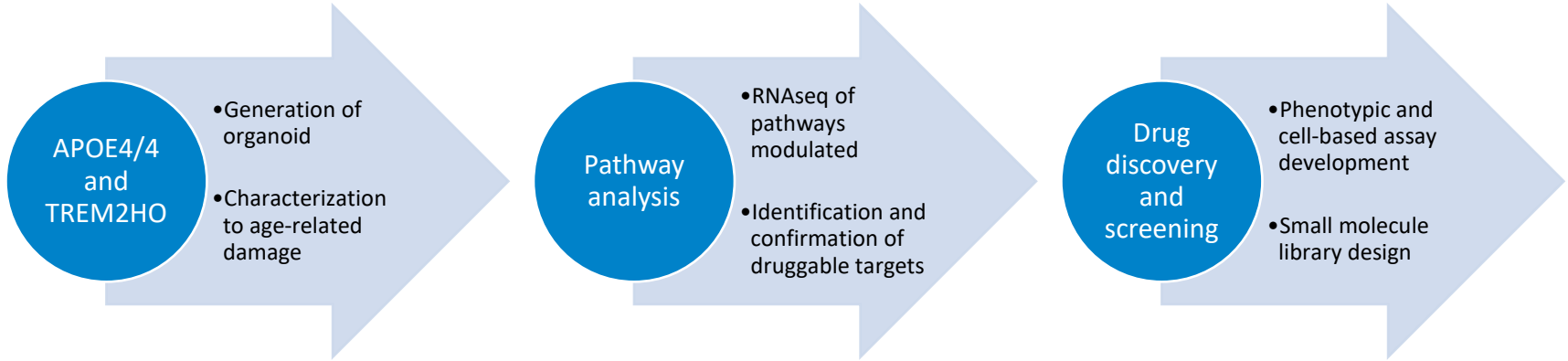
Focused on:

- Temporal Lobe Epilepsy
- Alzheimer's Disease

Alzheimer's Disease Program

Indication	Early-stage Alzheimer's Disease in patients with genetic risk factor(s)
Incidence	1 in 8 over the age of 65 (all AD)
Prevalence	~3M (all AD)
Standard of Care	• Cholinesterase inhibitors • Anti-Amyloid antibody therapies

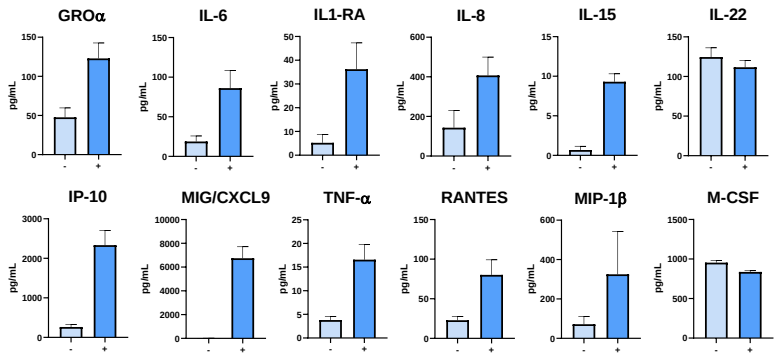
- Therapeutic strategy: reduce AD-related neuroinflammation
- Approach:
  - Model AD with organoids incorporating AD-risk mutations
  - Validate Model by cross referencing transcriptomics vs validated targets and patient data
  - Screen focused libraries to identify lead candidates that impact disease phenotype
- Model validation supported by $0.5M Phase I NIH/NIA SBIR grant
- Screening to be focus of Phase II submission



Temporal Lobe Epilepsy (TLE) Program

Indication	Febrile seizure-induced temporal lobe epilepsy (drug resistant phenotype)
Incidence	68 per 100,000 (in US)
Prevalence	**200,000 patients with drug resistant TLE; 3.4M total prevalence (US)**
Standard of Care	Anti-epileptic drug therapy (often two or more), associated with poor QoL and function (in addition to seizures)

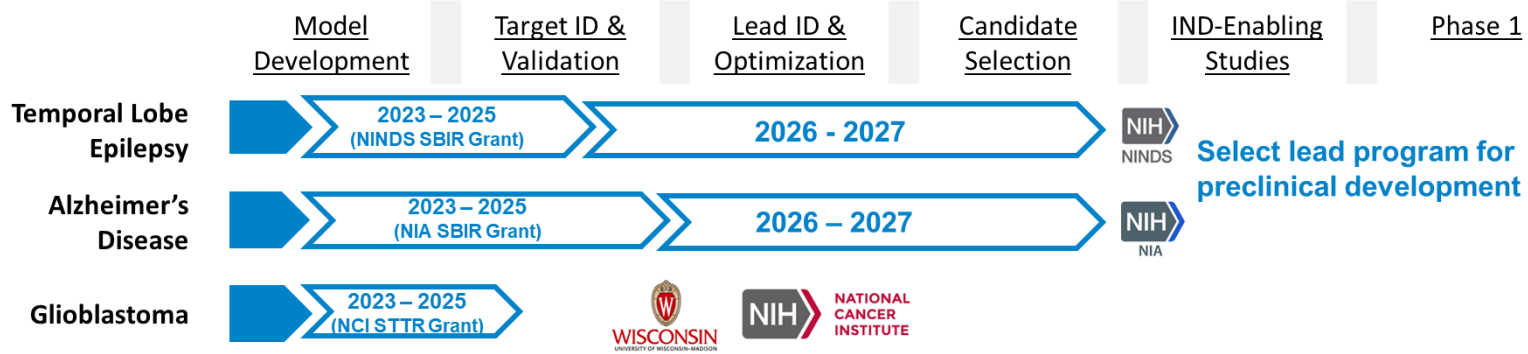
TLE Neuroinflammation Model shows strong response to LPS



- Hippocampus sclerosis forms a nidus for persistent microglia-induced neuroinflammation >> chronic seizures
- Lack of effective therapies – poor models
- Approach:
  - Model TLE neuroinflammation with human organoids using disease-relevant stimuli
  - Validate against patient data and proof set of anti-inflammatory compounds
  - Screen focused libraries to identify lead candidates
  - Model validation supported by $0.5M Phase I NIH/NINDS SBIR grant
  - Screening to be focus of Phase II submission

Stem Pharm Is Raising $3M Seed Round to Advance Its Pipeline

- Built and validated platform on $8M pre-seed (75% non-dilutive)
- 3 active Phase I SBIR grants - **opportunity for $7M in next 18 months**
- **Seed round to be used over ~18 months to get us to lead candidates**:
  - Validate screening assays
  - Perform screens and demonstrate effect on disease relevant pathway
  - Identify most promising hits for lead optimization
  - Expand team



World-Class Advisory Support

Mary Haak-Frendscho, PhD
CEO, Spotlight Therapeutics

- Experienced pharma executive and board member
- Startup and public company experience

Anne Bang, PhD
Director, Sanford-Burnham Prebys

- Expertise in neurological diseases and application of stem cells to disease modeling and drug discovery

Edsel Abud, MD, PhD
Clinical Scholar, Scripps

- Microglia and CNS disease expert
- One of first to develop microglia from human stem cells

Sheila Singh, MD, PhD
Professor & Neurosurgeon,
McMaster University

- Discovered brain tumor initiating stem cells
- Glioblastoma startup and exit

Greg Stewart, PhD
Principal, Alchemy Neuroscience

- VP/Director at several neuroscience pharma companies
- Drug discovery and development program builder

Mahua Dey, MD
Asst Professor & Neurosurgeon,
University of Wisconsin School of Medicine and Public Health

- Investigating immunotherapy and vaccine strategies for malignant brain tumors

Investors and Partners

MERCK
VERGE genomics
illumina
Northpond Ventures
McKESSON
Illumina ACCELERATOR
Microsoft
NIH National Institute of Neurological Disorders and Stroke
WARF Wisconsin Alumni Research Foundation
NIH National Institute on Aging
WISCONSIN UNIVERSITY OF WISCONSIN-MADISON
NIH NATIONAL CANCER INSTITUTE
NA 3RC
Stem Pharm

Stem Pharm

- Forefront of developing therapeutics focused on neuroinflammation
- Validated neural organoid platform with greater clinical translation
- Raising $3M Seed

Thank You!

Steven Visuri, PhD
CEO
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