



# NeuraWorx

Enhancing Glymphatic Flow for Brain Health

Chris Minar  
[chris@neuraworx.com](mailto:chris@neuraworx.com)  
952 240 2125

# Company Purpose

To revolutionize brain health by leveraging the glymphatic system to prevent, treat, and potentially reverse neurological disorders

# Problem: The Neurological Treatment Gap

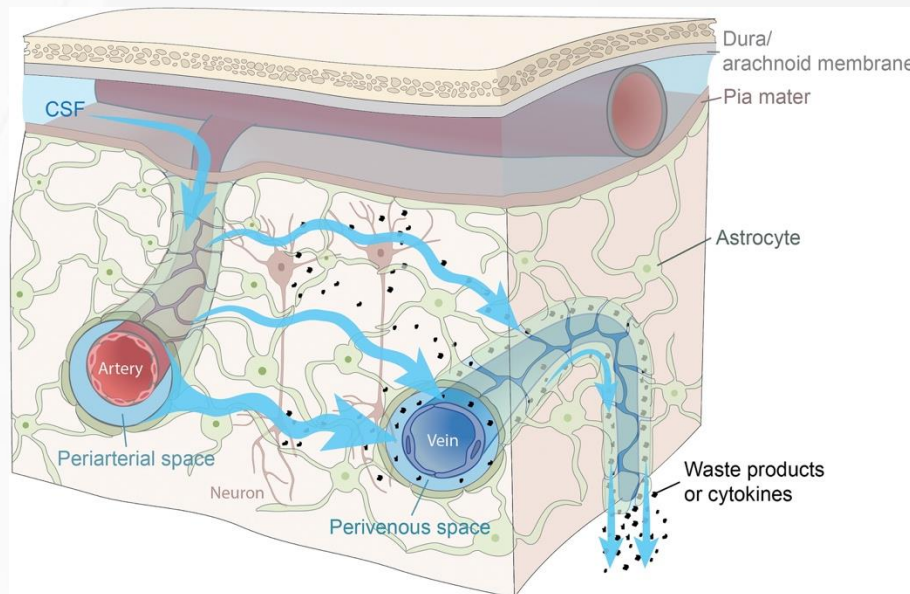
## Many neurological disorders lack effective therapy

- Alzheimer's
- Parkinson's
- Traumatic brain injury
- Multiple sclerosis
- Subacute ischemic stroke
- Cerebral small vessel disease
- Epilepsy
- Autism
- Chronic kidney disease
- Normal pressure hydrocephalus
- Postoperative delirium
- Huntington's disease
- Amyotrophic lateral sclerosis
- Etc...

>185 million people globally

## Glymphatic dysfunction links to neurological disorders

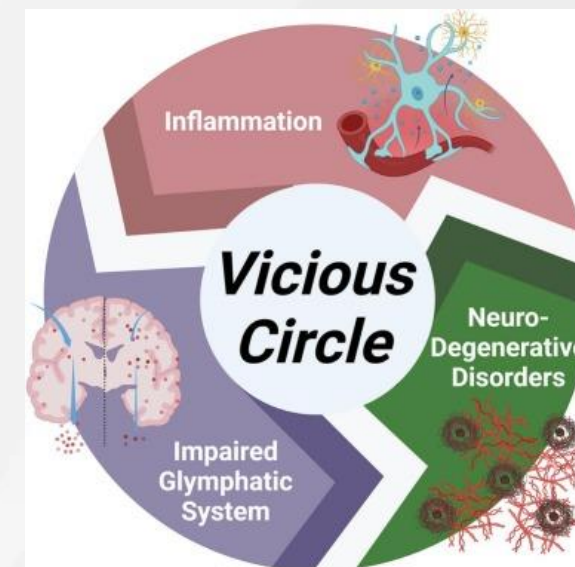
- Glymphatic dysfunction causes reduced cerebral spinal fluid (CSF) flow, **biomolecule imbalance**, **neurodegeneration** and **cognitive decline**



Benveniste H, Nedergaard M. Cerebral small vessel disease: A glymphopathy? Curr Opin Neurobiol. 2022

## Glymphatic dysfunction drives a feedback loop

- Glymphatic dysfunction maintains a self-perpetuating feedback loop
- Restoration of glymphatic function is needed



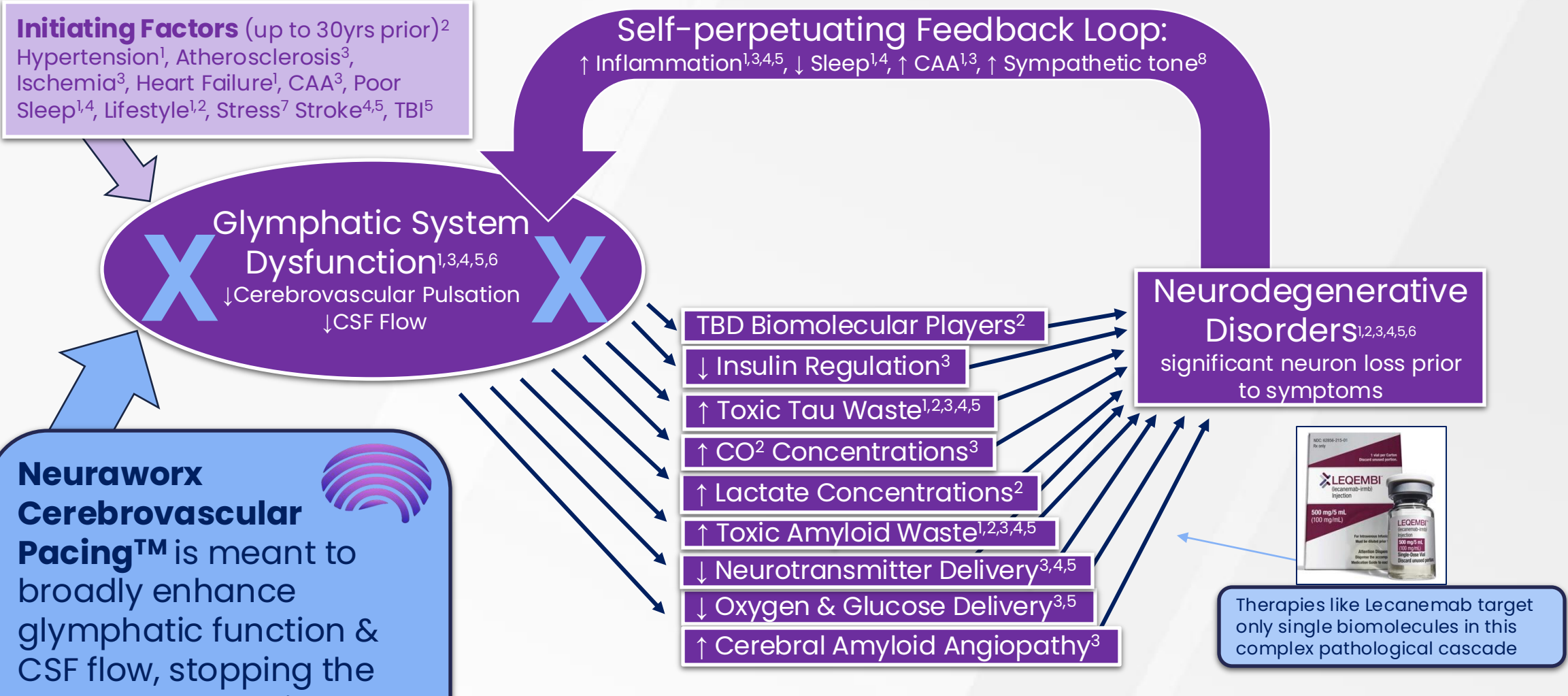
Beschorner N, Nedergaard M. Glymphatic system dysfunction in neurodegenerative diseases. Curr Opin Neurol. 2024 Apr



**Our solution: directly enhances glymphatic function, stopping the feedback loop!**



# Solution: Optimize Brain Fluid Dynamics



1) Nedergaard M, Goldman SA. Glymphatic failure as a final common pathway to dementia. *Science*. 2020 Oct  
 2) Johnson ECB, et al. Cerebrospinal fluid proteomics define the natural history of autosomal dominant Alzheimer's disease. *Nat Med*. 2023 Aug  
 3) Cerasuolo, M, et al. Al Alzheimer's Disease from the Amyloidogenic Theory to the Puzzling Crossroads between Vascular, Metabolic and Energetic Maladaptive Plasticity. *Biomedicines* **2023**, *11*, 861.  
 4) Voumvourakis KI, et. al. The Dynamic Relationship between the Glymphatic System, Aging, Memory, and Sleep. *Biomedicines*. 2023 Jul  
 5) Peters, M.E., Lyketsos, C.G. The glymphatic system's role in traumatic brain injury-related neurodegeneration. *Mol Psychiatry* (2023).  
 6) Zu, Kailu; Deng, Qingwei; Zhang, Hong; Huang, Changsheng,1,3\*. Glymphatic system: a gateway for neuroinflammation. *Neural Regeneration Research* 19(12),p 2661-2672, December 2024.  
 7) Ivanovska M, Naimova M, Murdjeva M. Effects of Stress on the Brain's Glymphatic System. *SEE J Immunol* [Internet]. 2023 Aug. 17  
 8) Ildiaquez JF, Ildiaquez J, Casar JC, Biaggioni I. Neurogenic Orthostatic Hypotension. Lessons From Synucleinopathies. *Am J Hypertens*. 2021 Mar

# Why Now: The Imperative for Cerebrovascular Pacing™

## 1) New evidence: cerebrovascular pulsation is key player in glymphatic system function

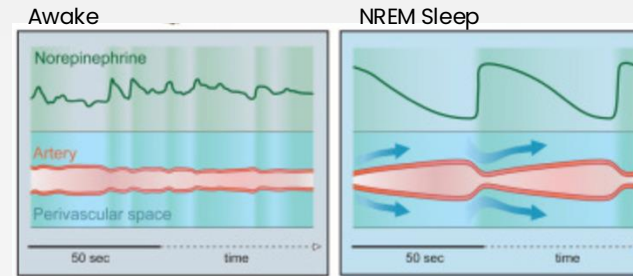
- Natalie L. Hauglund, et al, **Norepinephrine-mediated slow vasomotion drives glymphatic clearance during sleep**, *Cell*, 2025

## 2) New evidence: glymphatic dysfunction strongly correlates and is potentially causal

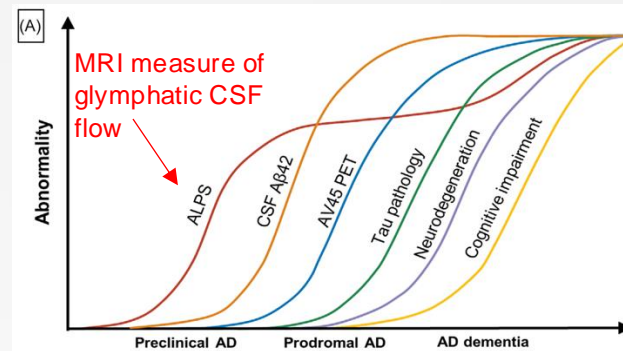
- Huang SY, et al. **Glymphatic system dysfunction predicts amyloid deposition, neurodegeneration, and clinical progression in Alzheimer's disease 2024**
- Hazzard I, et al. **Impaired glymphatic clearance is an important cause of Alzheimer's disease**. *Exploration of Neuroprotective Therapy 2024*
- Liu X, et al. **MRI free water mediates the association between diffusion tensor image analysis along the perivascular space and executive function in four independent middle to aged cohorts**. *Alzheimer's Dement. 2024*

## 3) New NeuroWorx human data

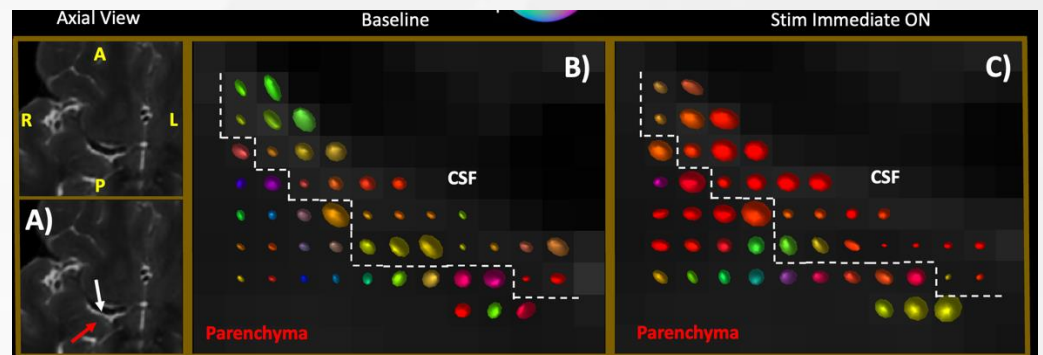
- Cerebrovascular Pacing™ uniquely shows robust glymphatic system enhancement.



Hauglund – Enhanced vasomotion during NREM sleep increases CSF flow in rodent brain.



Huang – ALPS index predicts cognition change through amyloid and neurodegeneration. A, A model integrating the findings in the present study, together with previous studies, depicts an approximative order of ALPS and AD core biomarkers in the AD continuum.



Neuraworx – CSF is driven by arterial motion into surrounding parenchyma. **A)** T2 axial view of PVS **B)** Baseline tensor image with ellipsoids showing general expected alignment with surrounding structures. **C)** Ellipsoids generated from stimulated DTI. Both CSF and parenchyma ellipsoids shows strong expected diffusion preference.

# Market Opportunity

~\$2.5 Billion

Initial Obtainable Market at 1% Penetration

**Dementia: \$1.39 billion/yr**

55 million x 1% = 550,000 patients

**Parkinson's: \$253 million/yr**

10 million x 1% = 100,000 patients

**TBI: \$350 million/yr**

cases w/long-term effects  
20% of 69 million X 1% = 138,000

**Other Disorders: \$506 million/yr**

20 million X 1% = 200,000 patients

# Growth Potential

**Penetration Beyond 1%**

With substantial growth potential as the technology matures, adoption rates increase, and if pricing strategies are optimized.

**CAGR of 7.4%**

we can expect an analogous growth rate for this niche when the product gains traction.

**Increased Awareness**

As awareness of the glymphatic system's role in CNS health grows, the penetration rate could increase, thereby expanding the market, including into other CNS disorders.

**Price Flexibility**

The pricing might decrease with economies of scale or increase with added value or exclusivity, affecting market size.

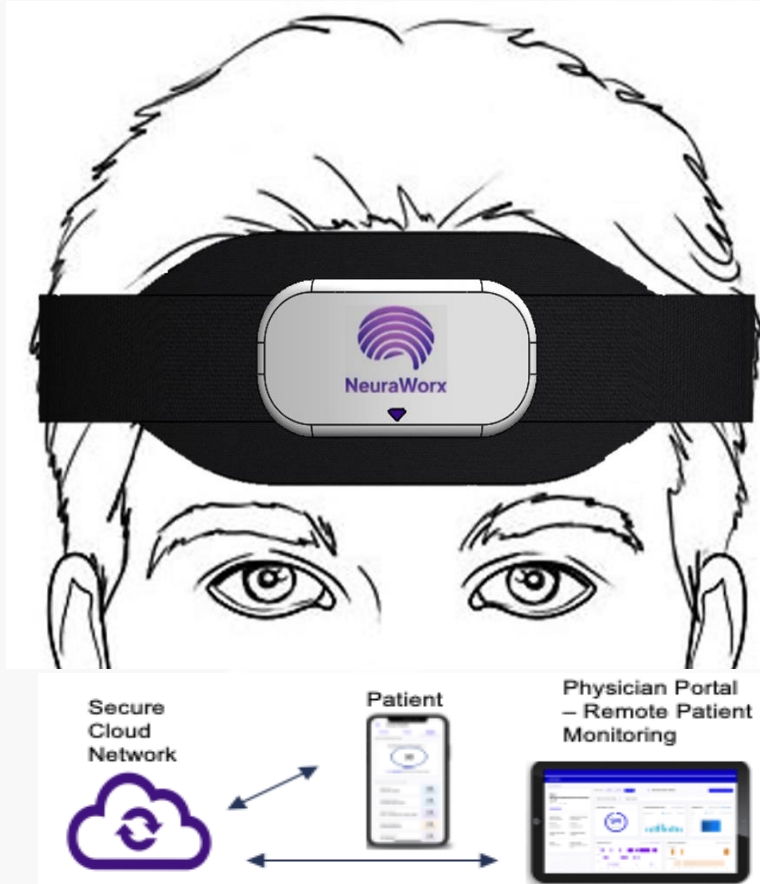
**Other Growth Opportunities : TBA**



# Product: Cerebrovascular Pacing™

## 1<sup>st</sup> Form Factor

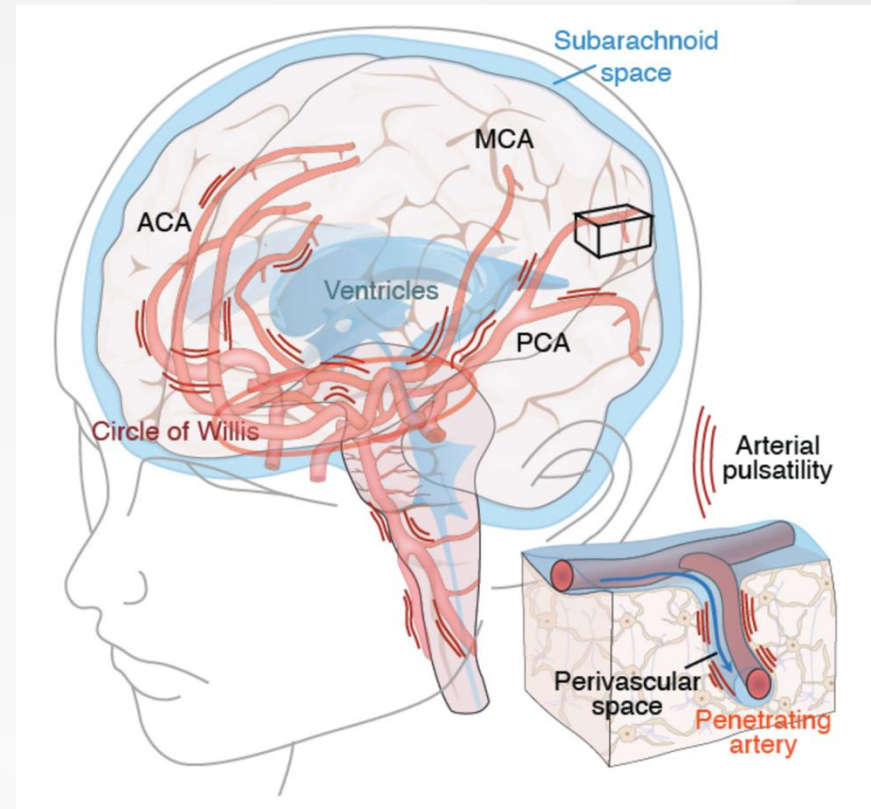
- Directly enhances cerebrospinal fluid flow
- Designed to minimize off-target effects
- Easy to use, with automated personalization



*Design details available upon NDA*

## Prescriptive Mechanism of Action

- Directly enhances cerebrovascular vasomotion
- Whole brain engagement
- Targeting enhanced cerebral homeostasis to modulate glymphatic system dysfunction



Nedergaard M, Goldman SA. Glymphatic failure as a final common pathway to dementia. *Science*. 2020 Oct 2;370(6512):50-56. doi:.



# Chain of Evidence

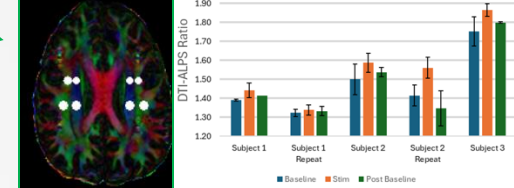
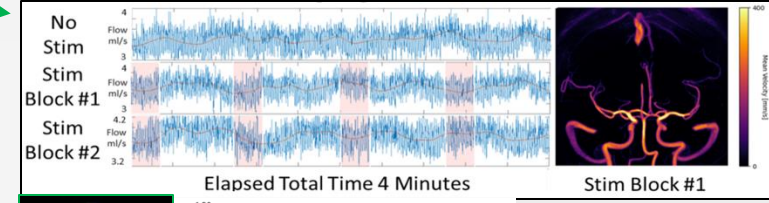
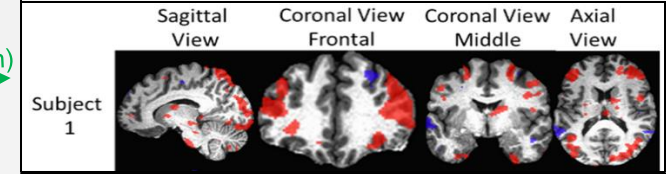
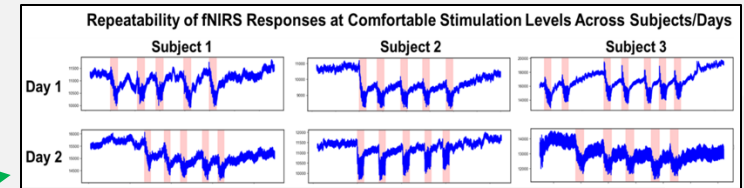
## Cerebrovascular Pacing™ Enhances Pulsatility

Our preclinical data  
Our human feasibility data – 2024

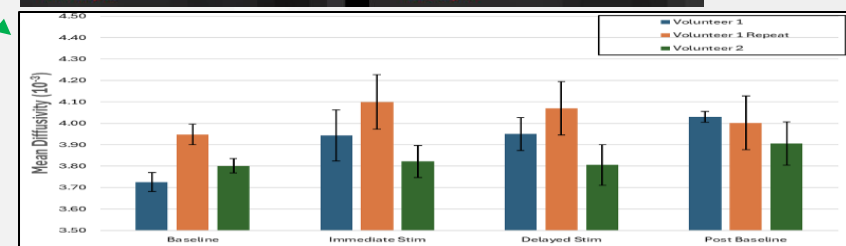
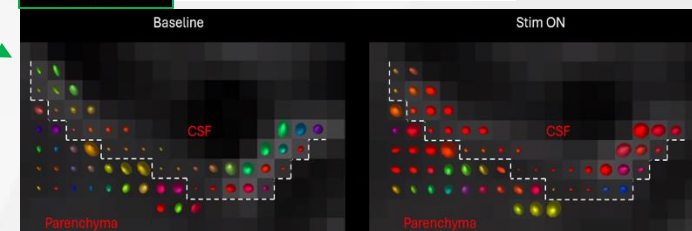
fNIRS (PFC)

fMRI BOLD (whole brain)

4D-flow (whole brain)



Order-of-magnitude enhancement is similar to pathology losses found in several studies (stroke & Alzheimer's related dementia ranged between 0.05 and 0.3)



## Cerebrovascular Pacing™ Enhances CSF flow

Our preclinical data<sup>3</sup>  
Our healthy human data – 2024  
Our human TBI data – 2025

DTI-ALPS (medullary veins)

DTI-PVS (MCA)

DTI-PVS (whole brain)

## Increases Metabolite Regulation

External publications<sup>4,5,6</sup>  
Our pilot study (blood/CSF biomarkers) – 2025-26

## Improves cognition

External publications<sup>7,8</sup>  
Our pivotal study (cognitive measures) – 2026-28

- 1) White TG, Powell K, Shah KA, Woo HH, Narayan RK, Li C. Trigeminal Nerve Control of Cerebral Blood Flow: A Brief Review. *Front Neurosci.* 2021
- 2) Powell, K., Lin, K., Tambo, W. et al. Trigeminal nerve stimulation: a current state-of-the-art review. *Bioelectron Med* 9, 30 (2023).
- 3) Cheng KP, Brodnick SK, Blanz SL, et al. Clinically-derived vagus nerve stimulation enhances cerebrospinal fluid penetration. *Brain Stimulation.* 2020
- 4) Rasmussen MK, Mestre H, Nedergaard M. Fluid transport in the brain. *Physiol Rev.* 2022 Apr 1;102(2):1025-1151. doi: 10.1152/physrev.00031.2020. Epub 2021.
- 5) Iliff, j., et al., The glymphatic system clears amyloid beta and tau from brain to plasma in humans, medRxiv 2024.07.
- 6) Beltran-Ruiz JJ, Reyes-Bello JS, Restrepo-Lugo CM, et al. Pathobiology of the Glymphatic System in the Traumatic Brain Injury: A Narrative Review. *Panam J Trauma Crit Care Emerg Surg* 2022
- 7) Peters ME, Lyketsos CG. The glymphatic system's role in traumatic brain injury-related neurodegeneration. *Mol Psychiatry.* 2023
- 8) Huang SY, et al, Glymphatic system dysfunction predicts amyloid deposition, neurodegeneration, and clinical progression in Alzheimer's disease



# Competition

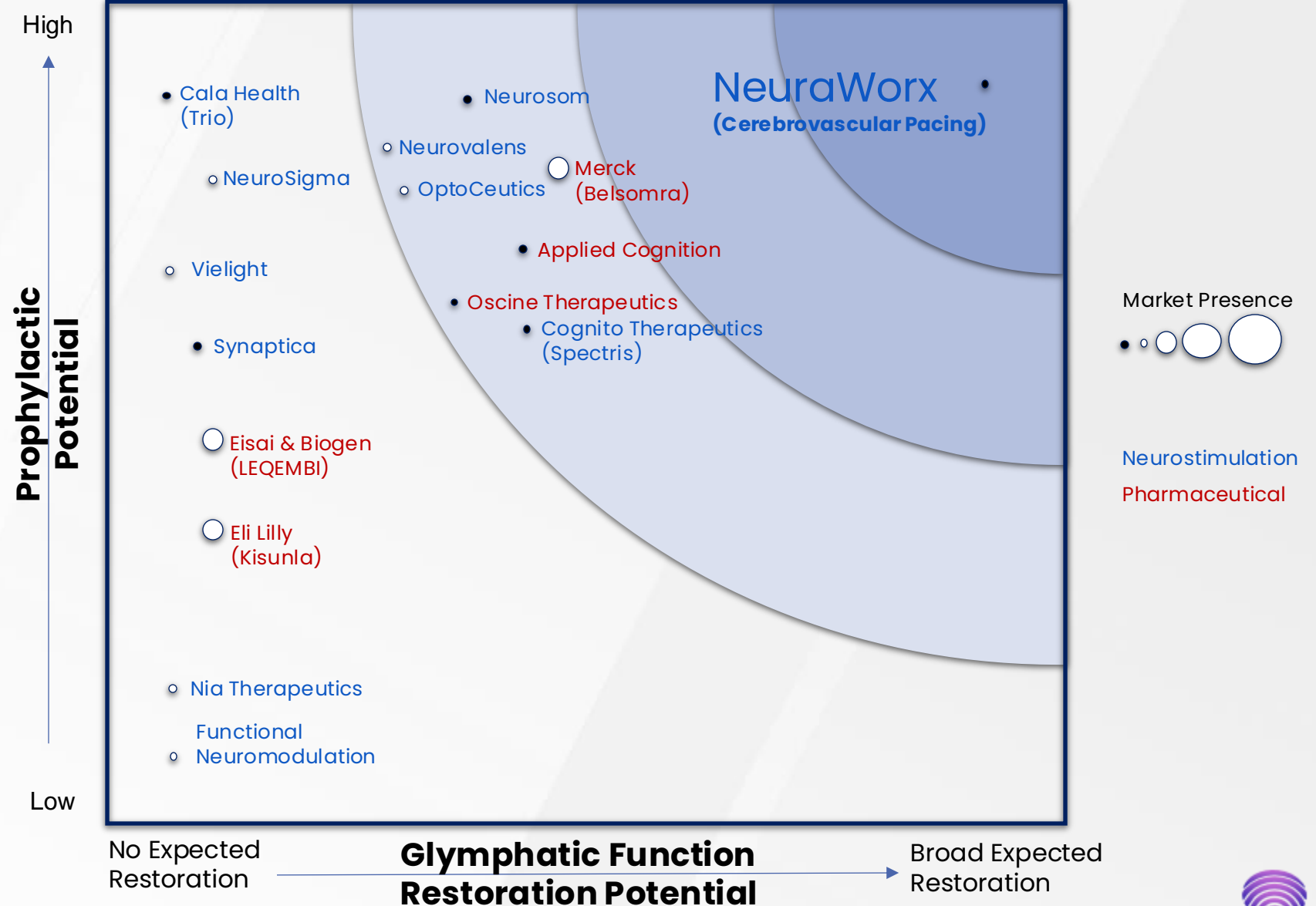
## Critical Success Factors

### 1) Glymphatic Function Restoration

- Competitor therapies target sleep, single biomolecule removal, or non-glymphatic mechanisms
- Only NeuraWorx Cerebrovascular Pacing™ targets direct restoration of glymphatic function

### 2) Prophylactic Potential

- Competitor therapies do not all offer the potential for easy early intervention, necessary for prevention of neurodegeneration
- NeuraWorx Cerebrovascular Pacing™ is intended to be safe and easy to use prophylactically



# Business Model

## Pathway to Revenue



## Product Strategy



**Cerebrovascular Pacing™ System**  
Price TBA\*



**Subscription Fee – software updates & replacement electrodes**

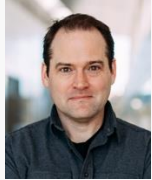
\*Cala Health has new CMS approved codes for the Trio device, and payments of \$3800, plus a \$100/mo subscription fee for additional electrodes and software update  
Spark Biomedical has new CMS approved codes for the Sparrow device, which has a current price of \$4500

# Managing Founders



## **Chris Minar – CEO & Board of Directors**

- Developed/commercialized over 40 medical devices
- Early start-up success in surgical robotics, interatrial shunting, cardiac electrophysiology, structural heart



## **Kip Ludwig, PhD – Research & SAB Member**

- Professor of Biomedical Eng. and Neurosurgery at the University of Wisconsin – Madison
- Multiple neuromodulation roles at CVRx, Mayo Clinic, NIH



## **Justin Williams, PhD – Technology & SAB Member**

- Professor of Biomedical Eng. and Neurosurgery at the University of Wisconsin – Madison
- Co-founder of multiple neuromodulation start-ups



## **Tamara Bratland – Marketing**

- Senior marketing & product manager roles at Medtronic, Abiomed, Honeywell
- Senior medical device marketing consultant

# Board of Directors



## **Lonny Stormo – Director**

- CEO & cofounder of Pops Diabetes Care
- Previous executive roles at Medtronic



## **Kathryn Dehn – Secretary**

- Associate attorney – Fox Rothschild, LLP
- Expertise in medical device start-ups

# Scientific Advisors



## **Diana R. Kerwin, MD – Clinical Advisor**

- Founder/President of Kerwin Medical Center, focused on research for Alzheimer's and related dementia
- Board Certified in Internal Medicine and Geriatrics



## **Jeffrey L. Cummings, MD – Clinical Advisor**

- Research Professor, Department of Brain Health
- Director, Chambers-Grundy Center for Transformative Neuroscience at UNLV



## **Andrew Grande, MD – Clinical Advisor**

- Professor and Co-director, Stroke, Brain Injury, and Stem Cell Lab at the University of Minnesota
- Asso. Director, Residency Program, Department of Neurosurgery



## **Lisa Shafer, PhD – Scientific Advisor**

- Vice President, Medical Device PD & Reg. at Biogen
- Senior scientific roles at Medtronic, Cerebral Therapeutics, Upsher-Smith, spanning devices, biotech and pharma



## **Angela Bauer, DDS – Dental, Sleep & Cranial Nerve Advisor**

- Founder Cambridge Family Dental
- Residency in Dental Sleep Medicine from Tufts University
- Cranial Nerve/Mandibular anatomy Expert



## **Jeff Tithof, PhD – Glymphatic System Advisor**

- Assistant Professor, Mechanical Engineering, UofM
- Glymphatic System modeling expert



# Financial Opportunity

## Raising \$5.5 million seed round

- \$400,000 secured
- \$5.1 million remaining to be raised

## Use of funds:

- 35% Product development
- 45% Clinical trials
- 20% Operations

## Key milestones:

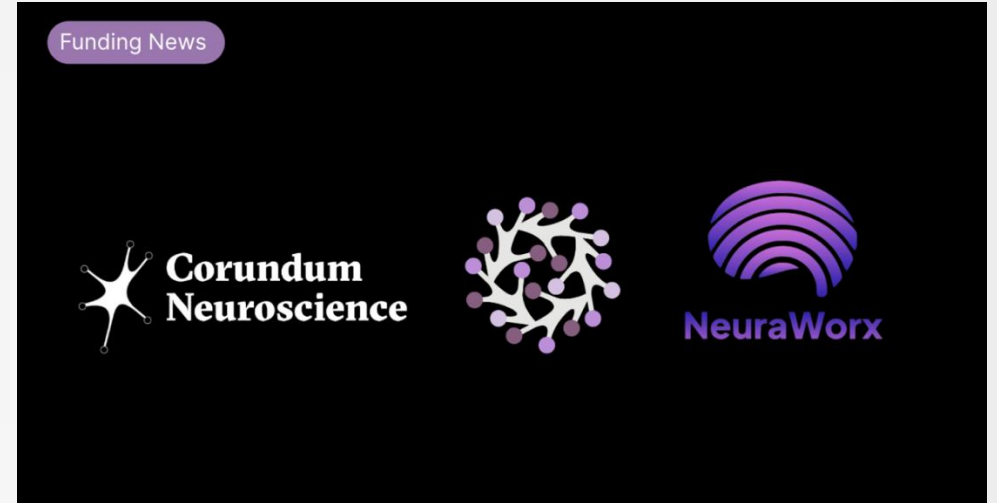
- Complete product development updates
- Complete human feasibility clinical trial
- Complete pilot clinical trial

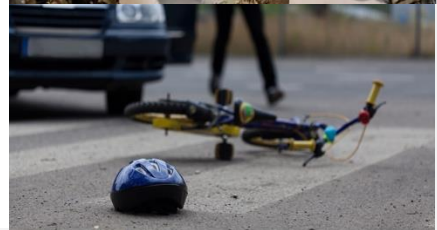
## Investor traction:

- Active due diligence ongoing with multiple investors
- Data room available for serious inquiries

## Timeline:

- Aiming to close round in early Q2 2025
- Multiple paths to exit through strategic acquisition





# NeuraWorx

## Cerebrovascular Pacing™

Unlocking the Healing Potential of the Glymphatic System

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