Neuronasal

A De-Risked Parkinson's Disease and Concussion Treatment Opportunity

March 2023

Executive Summary

Nose-to-Brain Drug Treatment for Central Nervous System (CNS) Disorders leading with the Parkinson's Disease indication

Company Name
Neuronasal, Inc.

HQ Location
Wexford, PA

Development Stage
Clinical

Seeking
$10M Series A

Use of Proceeds
Advance lead program through Phase 2a

- **The Problem –** Parkinson's Disease, second only to Alzheimer's in prevalence, has no treatment that stops or reverses its otherwise relentless and permanently disabling progression.
- **The Promise: N-acetylcysteine (NAC) –** A published 3-month study combining intravenous (IV) plus oral NAC treatment showed, for the first time, repair of Parkinson's disease brain damage using an FDA-approved validated disease biomarker. However oral NAC alone does not reach the brain thru the blood-brain barrier and chronic IV NAC is impractical for life-long disease treatment.
- **The Solution –** Neuronasal has shown that simple non-invasive direct nose-to-brain dosing delivers the same amount of NAC to the human brain as IV, providing a unique practical proprietary outpatient treatment to halt or reverse disabling Parkinson's disease brain injury.
- **What is NAC –** NAC is a potent antioxidant drug FDA-approved for non-CNS indications via oral, IV or pulmonary delivery with impeccable 30+ year safety record.
- **De-risking –** Seven specific factors work together to greatly reduce the risk of this drug development program.

Seven De-risking factors

Each factor alone is valuable, but taken together they make the certainty of clinical and commercial success very high

Factor #1
Repurposed drug

Factor #2
Patent protected

Factor #3
Safety record

Factor #4
Proof of concept in man

Factor #5
Registered delivery device

Factor #6
Experienced Team

Factor #7
Outside support

- **Repurposed Drug –** NAC's 30+ years of FDA approval provides a simplified 505b2 approval pathway for N2B NAC and multiple sources of commercial GMP manufacturing.
- **Issued Patent –** Covering nose-to-brain NAC delivery to treat CNS disease
- **Safety record –** NAC's impeccable 30+ year safety record is for non-CNS indications via oral, IV and pulmonary delivery greatly reduces the risk of unanticipated adverse effects.
- **Proof of concept –** A published study combining IV+oral NAC reversed Parkinson's disease brain injury as demonstrated with a validated disease biomarker and improved clinical outcomes.
- **Registered device –** Neuronasal's specialized nasal medical device partner has a proprietary easy-to-use disposable N2B delivery device compatible with NAC with an FDA Device Master File.
- **Experienced Team -** Track record of pharmaceutical development success at companies such Merck, Sanofi-Aventis and Ricerca BioSciences,
- **Outside support –** In 2014 the UK-based Cure Parkinson's Trust selected NAC "as the most promising of the 32 compounds evaluated" and has pledged to provide scientific and financial support to Neuronasal for its Parkinson's clinical trials.

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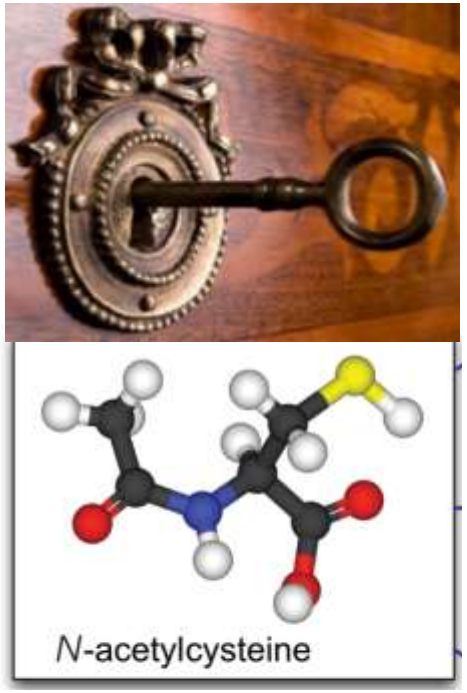
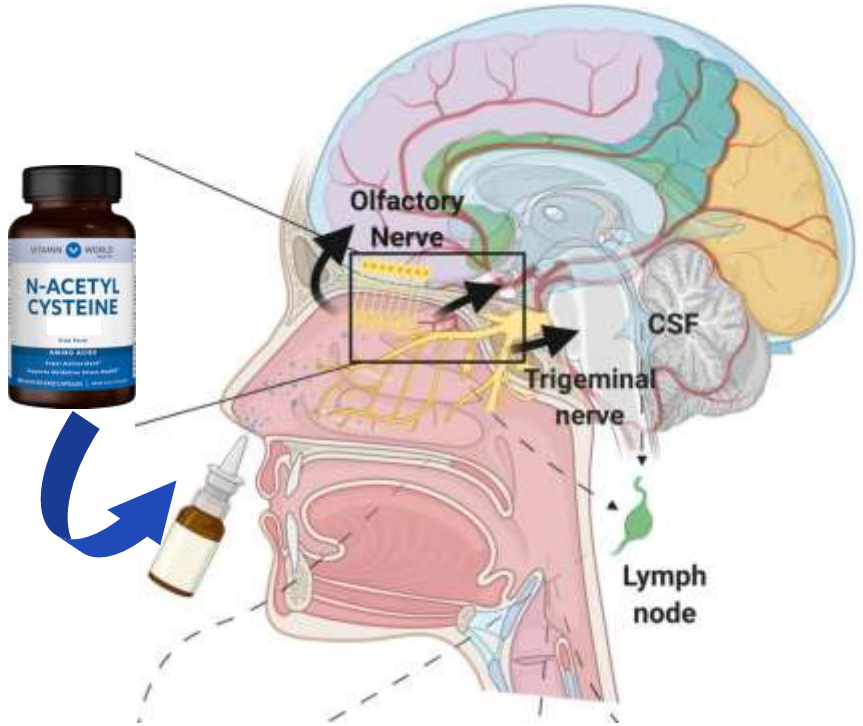
High Probability of Clinical Success
When Sufficient Brain Delivery is Achieved

Clinical benefit of Intravenous (I.V.) NAC demonstrated in Parkinson's disease. But I.V. dosing is impractical for life-long out-patient drug therapy.

Clinical benefit of Oral NAC shown in military post-blast concussion where extreme blast pressure breaks opens the blood-brain barrier enabling oral drug entry.

Nose to Brain Delivery:
The Key to Unlocking NAC's CNS Potential





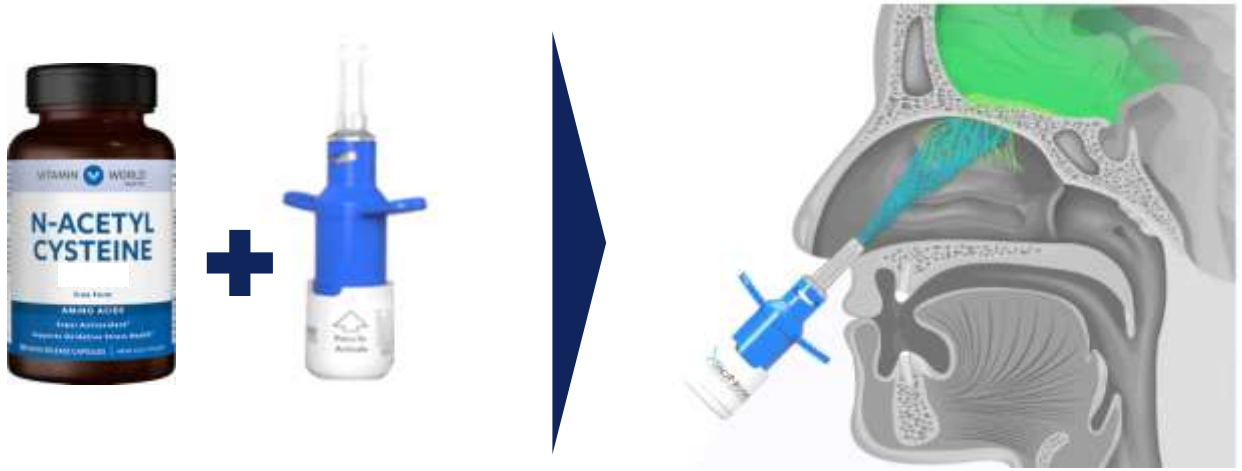
*Dean O et al.

*Central nervous system

NAC Nose-to-Brain (N2B) Delivery is Highly Efficient and Proprietary to Neuronasal

Bypassing the blood-brain barrier, N2B delivers equal brain level of NAC versus to i.v. using 50-fold less drug. Direct N2B delivery via olfactory and trigeminal nerves avoids GI and systemic side effects. Pilot clinical data proves NAC N2B delivery in humans.

Broad patent portfolio for N2B delivery and specialized formulations & intranasal devices for treatment of brain disease.



IP Foundation

Intranasal NAC to treat CNS disorders Notice of Allowance: Nov 2022	**Nose-to-brain Device Exclusivity** Effective: Sep 2021
Use of MRS to Calibrate to and Select Doses of Intranasal NAC Priority: Nov 2019	**Extended Release formulations** Priority: Aug 2019

Strong Clinical Evidence of Therapeutic Potential:
N2B NAC Reaches the Brain; I.V.+Oral NAC Reverses PD Brain Damage

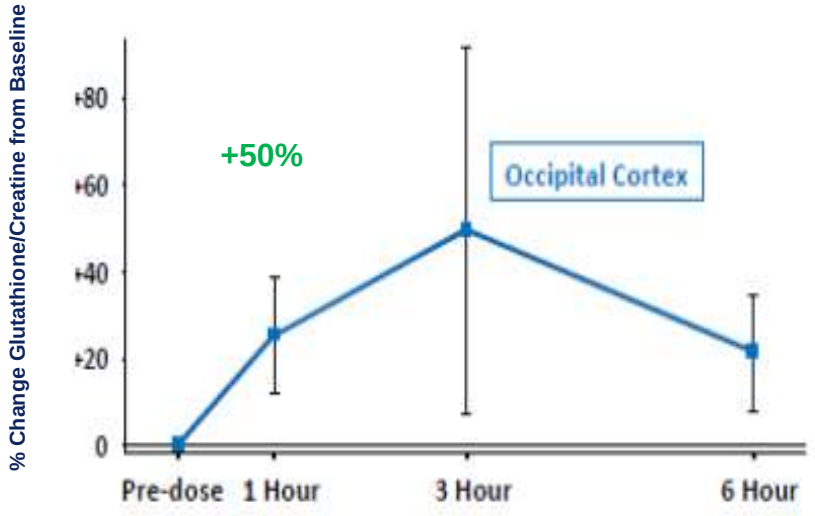
N2B NAC delivery demonstrated in healthy subjects in pilot study

IV+Oral NAC reverses Parkinson's brain injury in patients (shown by both Brain DatScan Imaging and clinical Disease Rating Scale) [1]

Open IND with high probability of Phase I success.

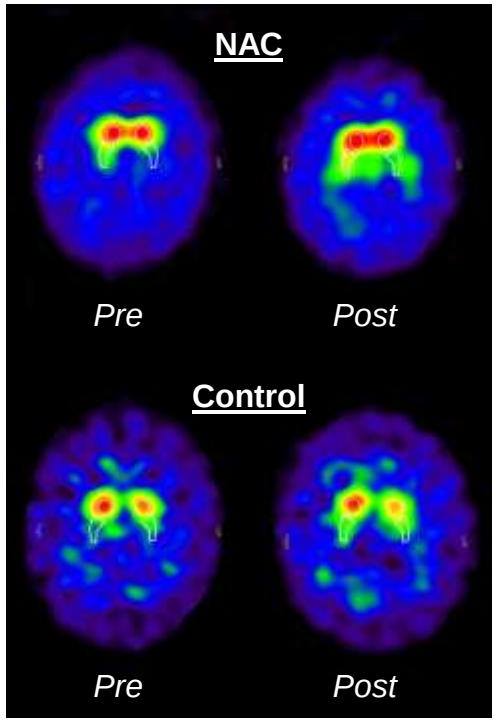
Clinical Demonstration of Safe and Efficient (50x IV) N2B NAC Delivery in Healthy Subjects

N2B NAC 200 mg*



Three-Month Combined I.V.+Oral NAC Treatment Improved DaTscan and UPDRS in Parkinson's Disease Patients[1]

Illustrative DaTscans



[1]Monti DA et al 2019. N-Acetyl Cysteine Is Associated With Dopaminergic Improvement in Parkinson's Disease. Clinical Pharmacology & Therapeutics. 106 (4); 884-890, October 2019..

Product Therapeutic Pipeline

Targeting Multiple, Large Unmet CNS Needs

Indication	Research	Preclinical	IND-Enabling	Phase I	Phase 2A
Parkinson's Disease (Symptoms)	→	→	→	→	
Parkinson's Disease (Disease Modification)	→	→	→	→	
mTBI/Concussion	→	→	→	→	
Multiple Sclerosis (relapsing)	→				
Stroke (hemorrhagic)	→				
Alzheimer's Disease	→				

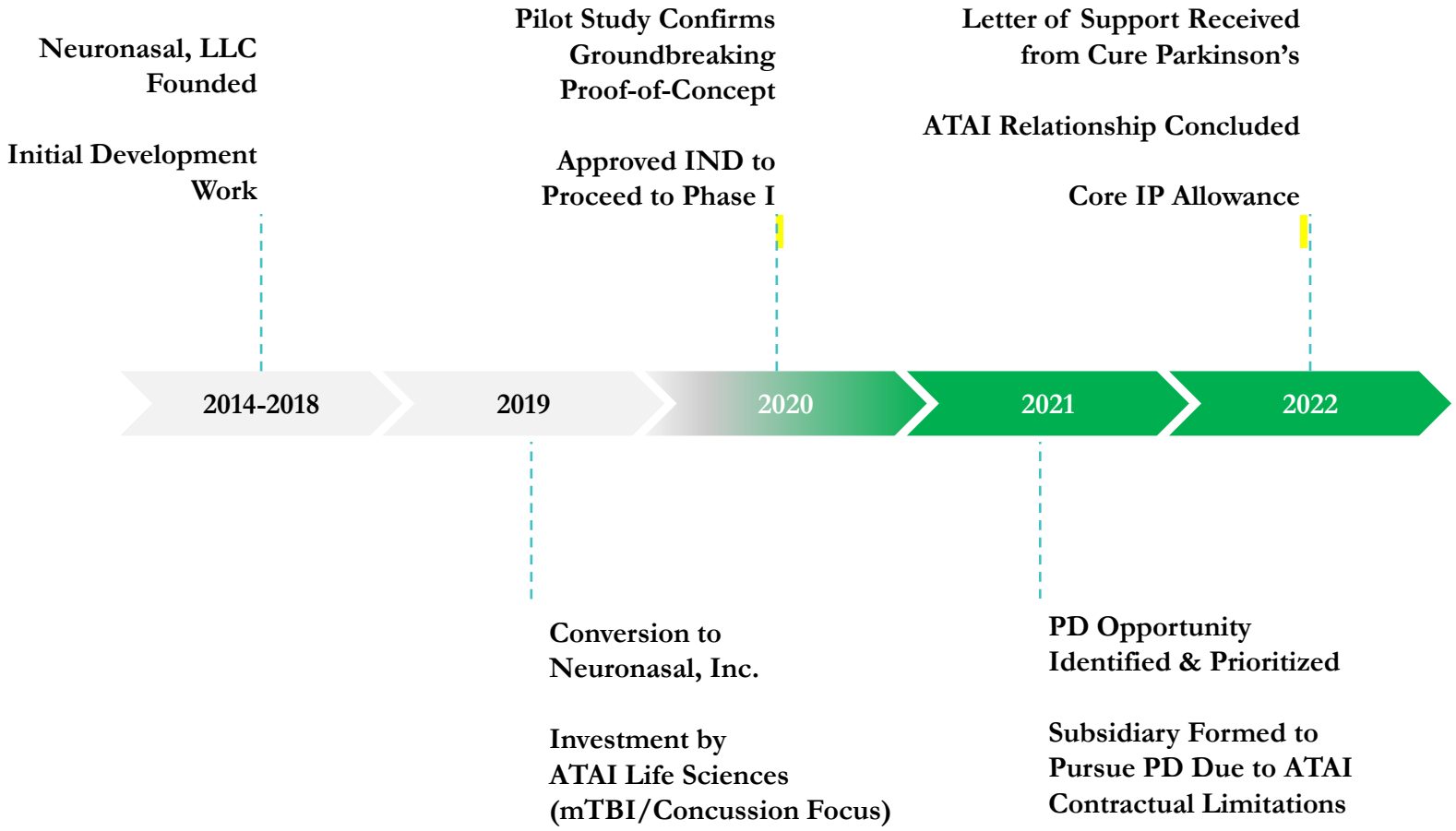
Why Now?

Demonstrated Proof-of-Concept, Key Support, and Clear Path Forward

Successful Pilot Study confirmed groundbreaking N2B delivery throughout the brain

Pledged support received from Cure Parkinson's due to NAC's potential as a Disease Modifying Treatment for Parkinson's.

Company free and clear of past limitations to pursue Parkinson's program. Significant IP milestone recently attained with more expected in the near term. Ready to commence formal Phase I dose-optimization study.



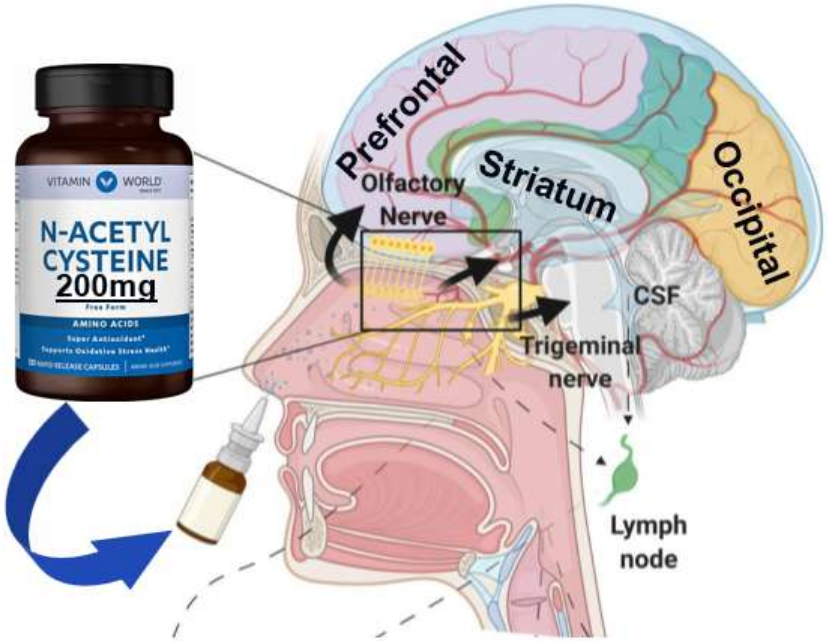
Pilot Study

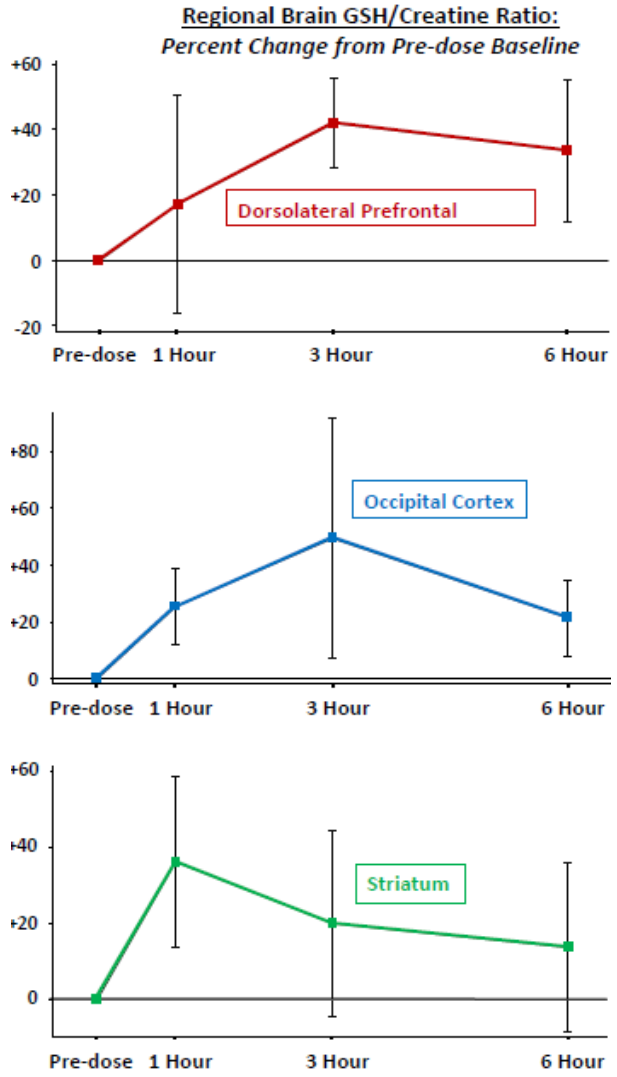
Demonstrated Delivery of NAC to Appropriate Brain Regions

Five healthy subjects given 200 mg NAC intranasally. Magnetic Resonance Spectroscopy (MRS) performed pre-dose and 1-, 3- & 6-hours post-dose to measure NAC-derived glutathione (GSH).

Conclusion: N2B NAC 200 mg effectively raises GSH in multiple brain regions

Data reviewed by FDA and validated by Johns Hopkins University experts.





Planned Phase 1 Study

Dose-finding and Formulation

Leveraging NAC's long established safety profile, Neuronasal's Phase I study will be focused on dose-finding and formulation.

Site selected, team engaged, and contract negotiations with world leading MRS institution underway. IRB submission ready.

Tolerability and MRS bioavailability study planned to be conducted at Johns Hopkins.

Dose/Device/Formulation MRS Study in Healthy Subjects

- Part 1

  Single ascending 100, 200, placebo, 400mg, 600mg dose for regional brain bioavailability with IV NAC comparator to identify maximally effective dose: 20 subjects.
- Part 2
  - Single-dose 6-part device/formulation comparison and optimization: 20 subjects.
- Part 3
  - Repeat 7-day placebo-controlled dose tolerability & bioavailability: 16 subjects.
- MRS for measurements of GSH in striatum, occipital and prefrontal cortex pre- and 1-, 3-, 6- & 24-hrs post- each dose.
- Tolerability: total nasal symptom score (TNSS) and adverse events.
- Status: Open approved IND. IRB submission ready to file pending final contract negotiations.
- Goal: Identify at least 2 doses and one single- and one multiple-dose device for Phase 2.

Planned Phase 2a Study

Bioavailability/Safety of IN NAC in Parkinson's patients

Objective: to identify a safe N2B dose of NAC with equivalent or better brain bioavailability compared to the 50 mg/kg i.v. NAC dose associated with dopaminergic improvement in Parkinson's disease patients using MRS to measure NAC-derived GSH in disease-relevant regions of the brain.

Randomized, Open-label, Two-cohort, Three-period, Single-dose, Crossover Bioavailability/Safety Study of Intranasal N-acetylcysteine in Parkinson's Disease

- Aim 1
  - Establish the regional (striatum, midbrain and cortex) and temporal (1–6 h and 24 h) single-dose brain bioavailability profile of effective 50 mg/kg i.v. NAC in Parkinson's patients.
- Aim 2
  - Compare the single-dose brain bioavailability and safety profiles of 200 mg and 400 mg IN N2B NAC versus 50 mg/kg i.v. NAC brain bioavailability profile in Parkinson's patients.
- Aim 3
  - Confirm the single-dose safety and tolerability of an equally brain bioavailable IN N2B NAC dose in Parkinson's patients.

Clinical Plan, Timeline, and Bidget

Multipronged and Capital Efficient

Study	2023				2024				2025			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Phase 1												
Part 1												
Part 2												
Part 3												
Phase 2a												
Cost*	**$3.7M**				**$2.7M**				**$2.1M**			

***Includes operating costs**

Management & SAB

The Right Team to Deliver

Partners include two world-renowned scientists in brain damage research.

Assembled Scientific Advisory Board of leading neuroscience and clinical thought leaders.

Management

THOMAS BRADSHAW
CEO/Co-founder Co-inventor IN NAC

DOUGLAS GREENE, MD
Head of R&D / Senior Clinical Advisor, Co-Inventor Nose-to-Brain NAC. Previous Worldwide Head of Clinical Development Merck Pharmaceuticals, Head Regulatory Development Sanofi-Aventis, Head of Research and Development Ikaria Pharmaceuticals.

MICHAEL KAUFMAN, BS, MS
Vice President, Business Development & Commercialization

JOSEPH HULIHAN, MD
Chief Medical Officer

Scientific Advisory Board

RAJIV RATAN, MD, PHD
Chair, Scientific Advisory Board, Co-Inventor IN NAC

RAYMOND SWANSON, MD
Prof and V Chair of UCSF Neuroscience

JOHN LEDDY, MD
President International Concussion Society, Medical Director U of Buffalo Concussion Management

DIETRICH DALTON PHD.
Chair Neurosurgery U of Miami

ADAM FERGUSON, PH.D.
A. Prof Neurological Surgery UCSF PI Brain Injury Center SF GH

AMY KUCEYESKI, PHD.
A. Prof of Math. In Radiology and in Neuroscience

ROLF DRINGEN, PHD
Prof of Neurochemistry U of Tubingen

COL. DALLAS HACK, MD
Dir. Combat Casualty Care Research Program (retired)

Investment Opportunity

Clinical Stage, De-risked Platform for CNS Disorders

- ✓ **Proprietary, Direct N2B NAC Delivery Platform**
- ✓ **De-risked Development Path**
- ✓ **Multiple N2B NAC CNS indications**
- ✓ **The Right Time**
- ✓ **Experienced Team**

Transaction Details

- $10M Series A Preferred Stock
- Favorable pre-money valuation
- Anticipate investors to hold board seats
- Targeted close: Q2 2023

Use of Proceeds

- Advance lead Parkinson’s program through Phase 2a
- Advance mTBI/Concussion program in parallel
- Continued development of pipeline programs
- Company operating costs