DE-RISKED OPPORTUNITY IN MAJOR UNMET MEDICAL NEED

Neuronasal Inc

Parkinson’s Disease-unmet challenge

March 1, 2024

Neuronasal Development

Focus-Chronic Central Nervous System Diseases

Common characteristics

Glutathione deficiency
Oxidative damage
Difficulty in brain delivery of drug
Difficulty of measuring drug effect-long time cycles
Long term treatment required

Selection of Drug Active

Decided on repurposed drugs-known to be safe

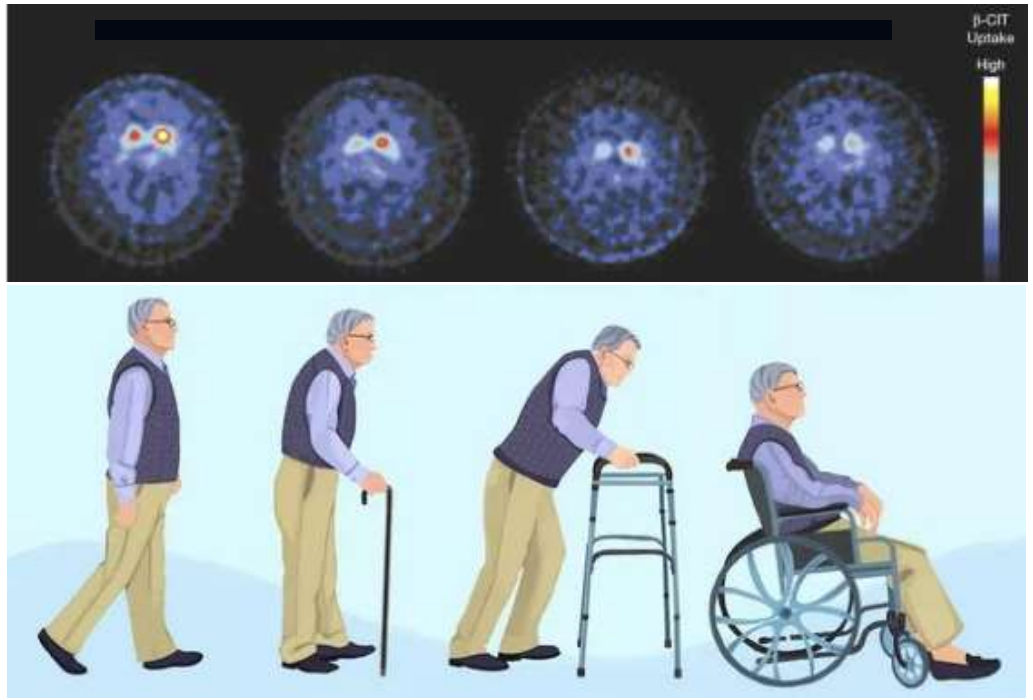
Most early-stage drug candidates fail for two reasons:

- *Toxicity- Phase 1 failure*
- *Lack of efficacy phase 2 and beyond failure*

Selected: n-acetylcysteine (NAC)

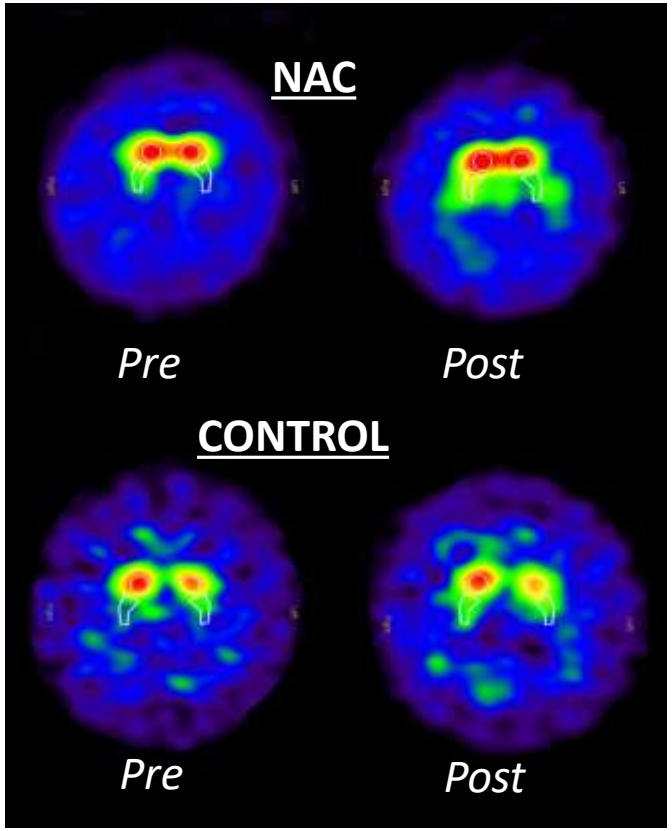
IV + Oral NAC (N-acetylcysteine) **Improves the Dopamine Receptor SPECT (DaTscan) Measure of PD Brain Injury**

Progressive DaTscan Decline with Parkinson's Disease Severity and Duration



Oral + IV NAC

DaTscan Decline Reversed by Oral+IV NAC



Bu M et al. Dynamic Control of Dopamine Transporter in Neurotransmission and Homeostasis. Npj Parkinson's Disease (2021)7

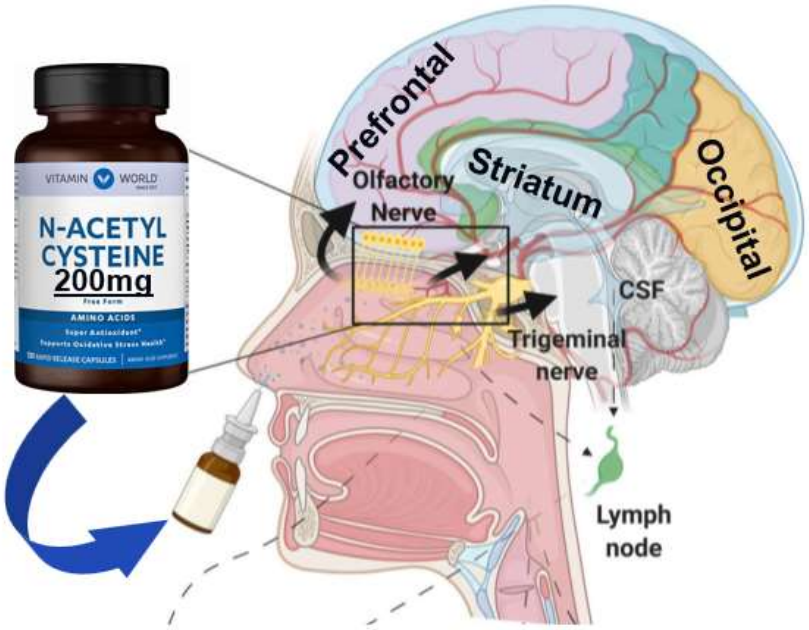
Palermo G et al. Dopamine Transporter Imaging, Current Status of a Potential Biomarker: A Comprehensive Review. Int J Mol Sci 2021;22:11234

Palermo G Ceravolo R. Molecular Imaging of the Dopamine Transporter. Cells 2019;8:972

Monti DA et al 2019. N-Acetyl Cysteine Is Associated With Dopaminergic Improvement in Parkinson's Disease. Clin Pharm Therapeut 104;4:884-890444

IV + Oral N-acetylcysteine (NAC) Improves the Dopamine Receptor SPECT (DaTscan) Measure of PD Brain Injury

- **IV + Oral NAC Regimen Impractical for Lifelong Chronic Treatment.**
- **Neuronasal's Non-invasive Nose-to-Brain NAC Dosing Achieves Brain Levels Equal to or Better than IV**



Monti DA et al 2019. N-Acetyl Cysteine Is Associated With Dopaminergic Improvement in Parkinson's Disease. Clin Pharm Therapeut 104;4:884-890

N-Acetylcysteine (NAC) Addresses the Underlying Cycle of Reactive Oxygen Species Induced Brain Injury in Parkinson's Disease

- NAC regenerates glutathione, the brain's endogenous antioxidant
- NAC repairs oxidized misfolded neurotoxic proteins
- NAC prevents dopamine oxidation and mitochondrial injury and degradation

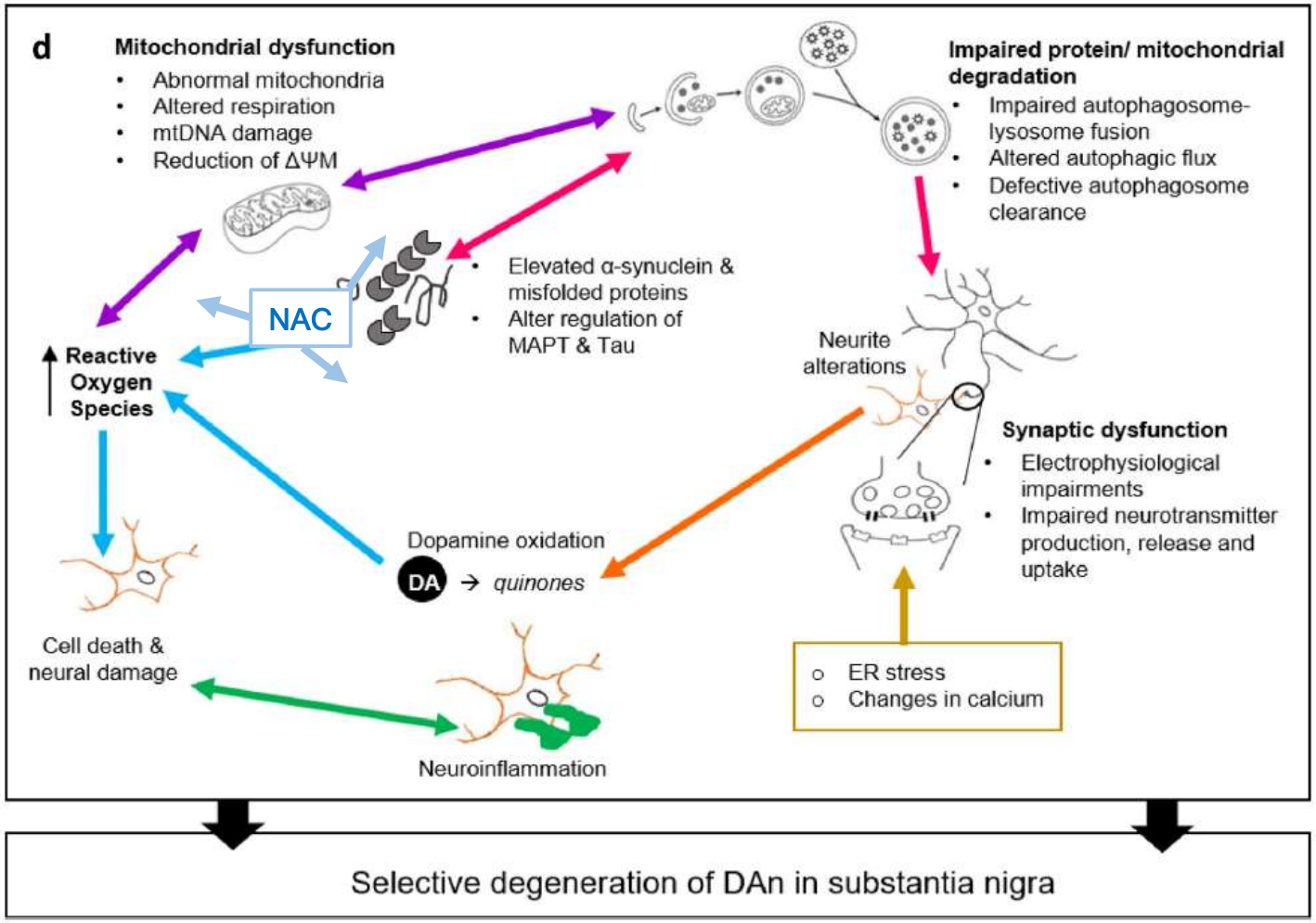


Figure 1. Modified from Tran J et al. Genetic predisposition of Parkinson's disease revealed in patient-derived brain cells. Njp|Parkinson's Disease (2020)6:8 https://doi.org/10.38/s41531-020-0110-8. "DAn in substantia nigra" refers to degeneration of dopaminergic neurons in the region of the brain most severely affected by Parkinson's disease.

Neuronasal Development

ESTABLISH INTELLECTUAL PROPERTY POSITION

UNEXPECTED RESULTS OF DIRECT NOSE TO BRAIN

DEMONSTRATE DRUG DEVICE COMBINATION DELIVERY:

devices- human pilot trial with positive results-base line formulations

effect-location
duration of effect

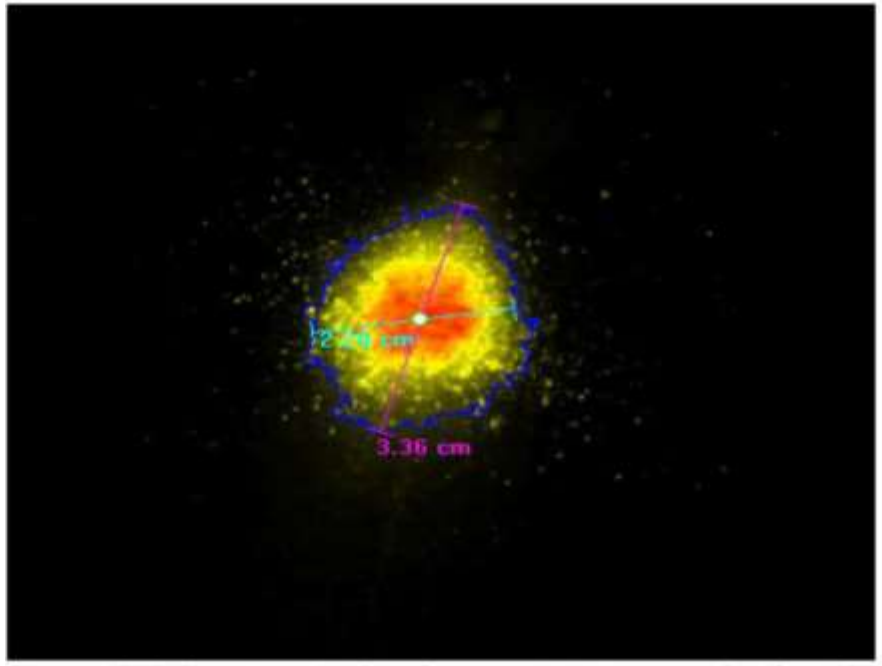
Nose to Brain Drug Delivery- Formulation and Device

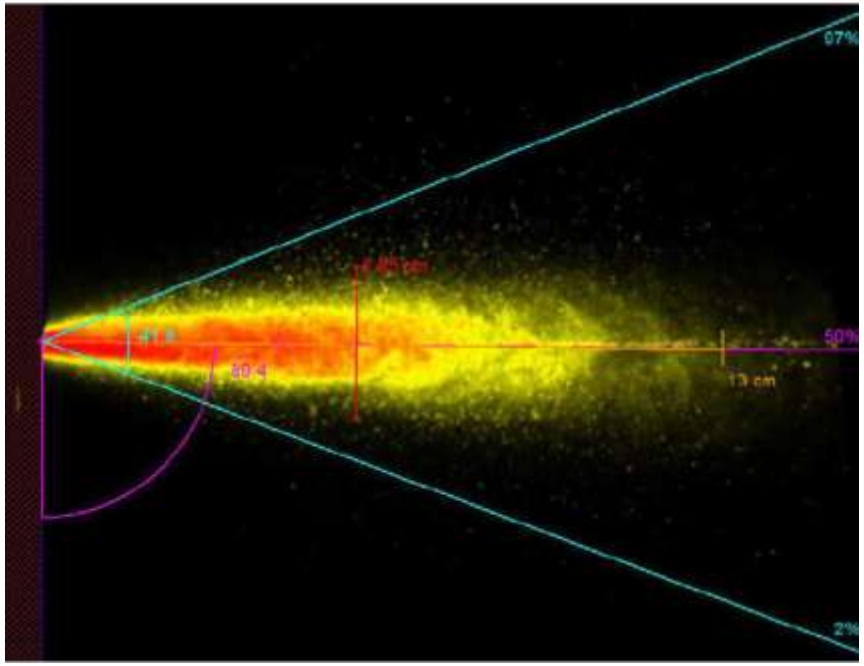
Speed of Particle

Particle size distribution

Spray pattern

Spray Pattern





Phase 1 Trial

Open IND

Phase 1 – dose finding not safety

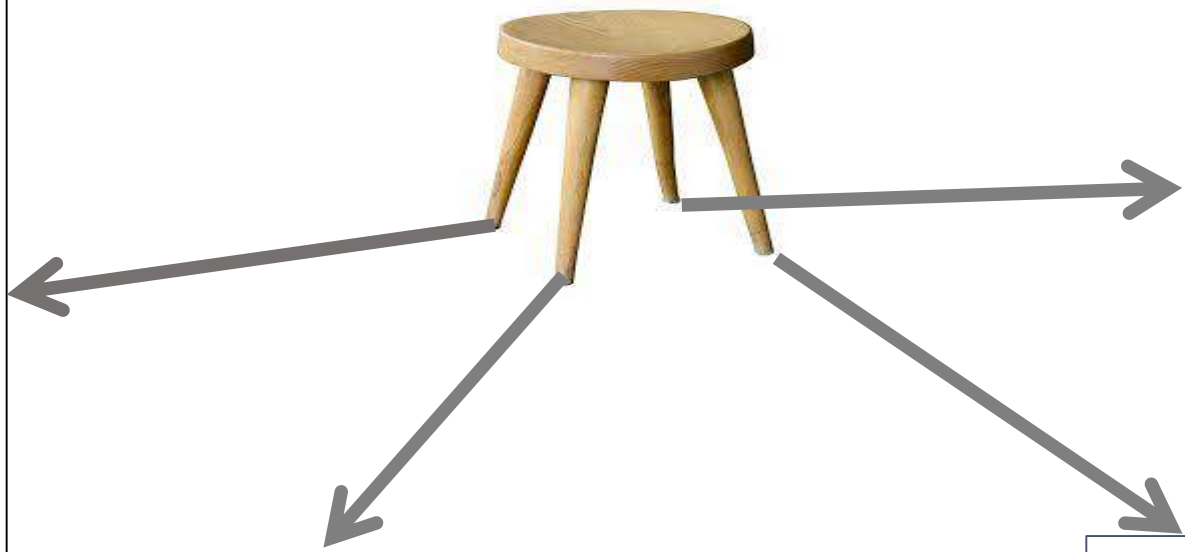
Single escalating dose
Device formulation comparison
Repeat dose

Intellectual Property - Current

Intranasal NAC to treat CNS disorders

- Priority 05/02/2017
- Projected Expiration ~2038
- Publication date November 19, 2020

- Issued May 2023 Concussion
- Issued Feb 2024 Parkinson's Disease

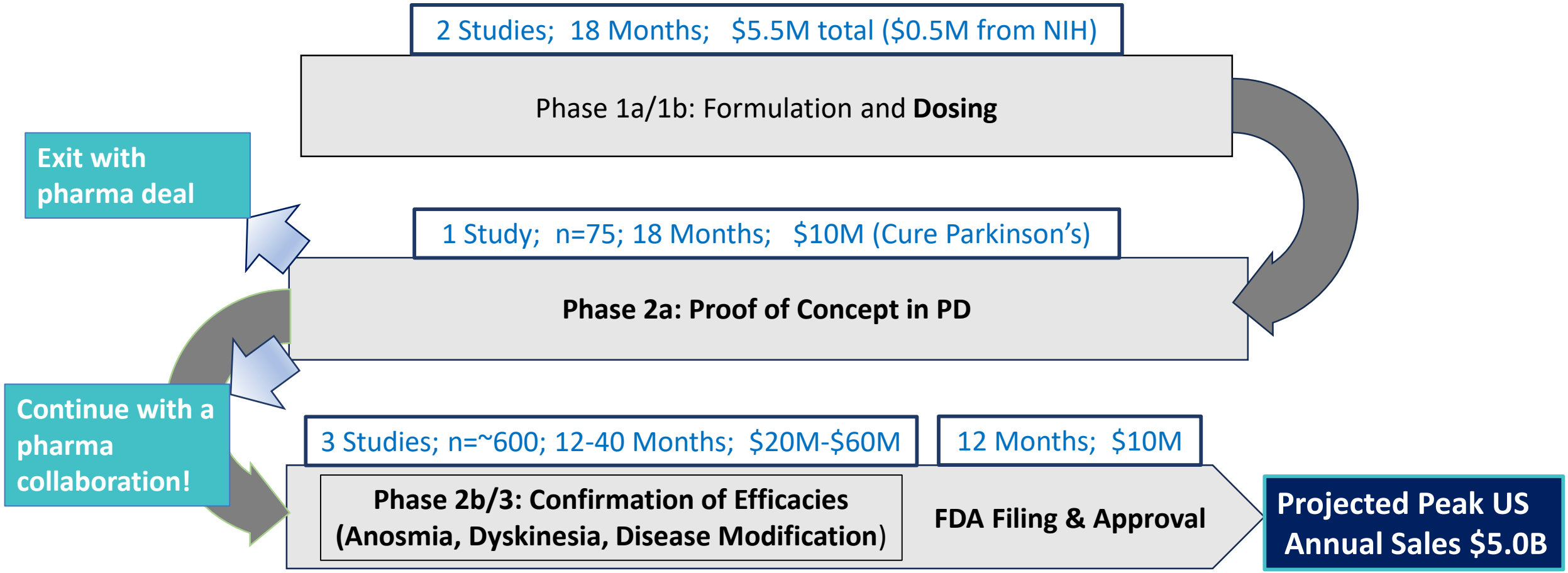


Nose-to-brain device exclusivity
- Device collaboration
- Effective 8/21/2020

Use of MRS to calibrate to and select doses of intranasal NAC
- Priority 11/04/2019
- Projected Expiration ~2040

Formulations
- Extended release
- High Concentration, Preserved solution
- Other
- Priority 08/21/2020
- Projected Expiration ~2041

NAC Development Path to FDA Approval & Launch for Parkinson's Disease(PD)



Future Opportunities

Nose to Brain CNS drug delivery has important potential advantages: targeted delivery; reduced side effects

Other indications:

PSP (progressive Supranuclear Palsy)

Stroke (hemorrhagic)

MS Multiple Sclerosis (relapsing)

Neuronasal's Highly-Experienced Team

Drive Robust Science

- Partners include two world-renowned scientists in brain damage research
- Assembled a Scientific Advisory Board of leading neuroscience and clinical thought leaders

Legal/IP Attorney: Wilson, Sonsini, Goodrich & Rosati

Michael Kaufman, BS
Vice President, Business Development & Commercialization

Joseph Hulihan, MD
Chief Medical Officer

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

Rajiv Ratan, MD, PhD
Chair, Scientific Advisory Board
Co-Inventor IN NAC

Executive Summary

Nose-to-Brain Drug Treatment for CNS Disorders

Company Name
Neuronasal, Inc.

HQ Location
Wexford, PA

Development Stage
Clinical

Seeking
$5M Series A

Use of Proceeds
Advance lead program thru Phase 2a proof-of-concept in Parkinson's

- **Neuronasal** is a clinical stage pharmaceutical company developing a suite of therapeutics targeting large, unmet needs across the Central Nervous System (CNS) space.
- **Proprietary, Direct Nose-to-Brain (N2B) N-Acetylcysteine (NAC) Delivery Platform –** Provides improved, alternative route of administration bypassing the blood-brain barrier (BBB) with pilot human data demonstrating proof-of-concept for direct N2B delivery for CNS indications.
- **De-risked Development Path –** NAC is an FDA-approved drug with 30+ year safety record (via oral and IV delivery). **Established preclinical and clinical molecular proof-of-concept in target patient populations.** Company Pilot human data confirmed safe and effective brain delivery with novel, brain imaging technology. Open IND with high likelihood of Phase I success. Protected by issued patents. Significant IP milestone achieved.
- **Lead Candidate –** N2B NAC focused on Parkinson's Disease (PD) with potential dual path strategy encompassing both disease-modifying and symptom-relief indications. Opportunity to advance mTBI/Concussion program in parallel with several, additional CNS indications identified.
- **The Right Time –** Phase I N2B dose/formulation/device optimization study ready-to-go with FDA letter-to-proceed. *Pledged support from leading PD foundations to fund Phase 2a and follow on*.
- **Experienced Team –** Track record of pharmaceutical development success.