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Chief Executive Officer

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NewroBusTM

To Shuttle Biologics Across the Blood-Brain Barrier

NN-843

NewroBus-enabled TNF- α Inhibitor for Alzheimer's



NN-843: a TNF- α Inhibitor Crossing the Blood-Brain Barrier Using NewroBus™ Technology to Treat Alzheimer's Disease



NN-843 is a novel therapy to treat Alzheimer's by targeting TNF- α induced neuroinflammation with a TNF- α Inhibitor efficiently crossing the Blood-Brain Barrier (BBB) using our NewroBus™ technology



IND filing of NN-843 expected in 4Q2027, with the program supported and validated by STTR Phase 1 & 2 NIH grants for a total of \$3.0 million awarded in May 2023 and July 2025



NN-843 built on NewroBus™, our versatile, patented technology to carry biologics across the BBB via TfR1, and available for licensing to companies with biologics requiring to cross the BBB



Experienced scientific, clinical, regulatory and business team with successful track record in developing, launching and licensing-out novel pharmaceuticals



NN-843 IND planned in 4Q2027, followed by Phase 1/1b and EOP1 meeting in 4Q2028. NIH grant of \$2.5 million awarded in July 2025, with additional NIH grants for \$4.5M pending

Experienced Scientific, Clinical, and Business Founding Team



- Marco Taglietti, MD, Chief Executive Officer
 - **35+ years of experience with more than 30 different products brought to market**
 - President and Chief Executive Officer of Scynexis (Nasdaq:SCYX) from 2015 to 2022
 - President and Chief Medical Officer at Forest Laboratories (Nasdaq:FRX) from 2007 until 2014
 - Head of Global Research at Stiefel Laboratories from 2004 to 2007
 - Vice President, Clinical Development, Schering-Plough from 1992 to 2004
- Luciano D'Adamio, MD, PhD, Founder and Chief Scientific Officer
 - **30+ years of experience with more than \$26 million in NIH grants since 2004**
 - Distinguished neuroscientist and professor at Rutgers, The State University of New Jersey
 - Herbert C. and Jacqueline Krieger Klein Endowed Chair since 2017
 - Irene Diamond Professor of Immunology at the Albert Einstein College of Medicine
 - Professor of Clear Fame, University of Naples, Federico II
 - Alzheimer's Medal and the Zenith Award from the Alzheimer's Association.
 - On editorial boards of leading journals and recognized for his groundbreaking work in neurodegenerative diseases and translational neuroscience

The Problem: Alzheimer's Disease Remains a Major Unmet Need

- >7 million Alzheimer's patients in the U.S.¹
 - A \$14.5 billion market by 2029... **a large but unsatisfied market**
- Only partial success of **anti-amyloid biologics**²
 - **Strong biological effect** with reduction of amyloid...
 - ... but only **modest** slowdown of cognitive decline
- ... and **Anti-Tau** products have consistently failed, to date

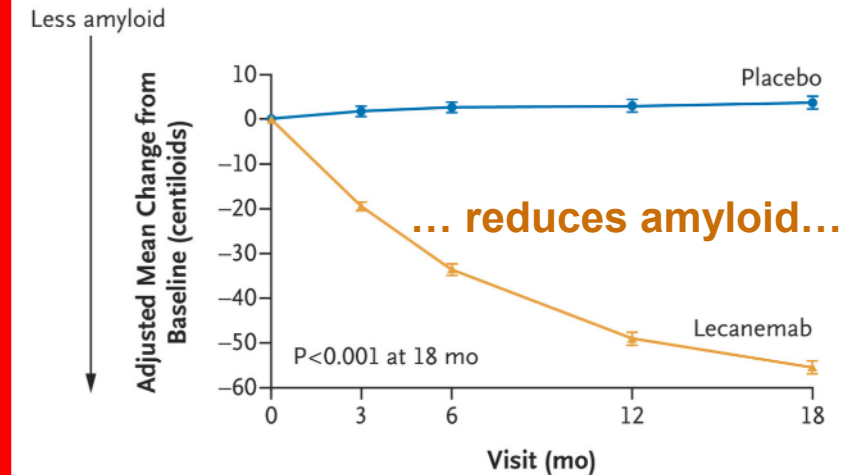
We need to target additional pathogenetic mechanisms!

1) 2023 Alzheimer's Disease Facts and Figures, *Alzheimers Dement* 2023, 19(4) 1598-1695

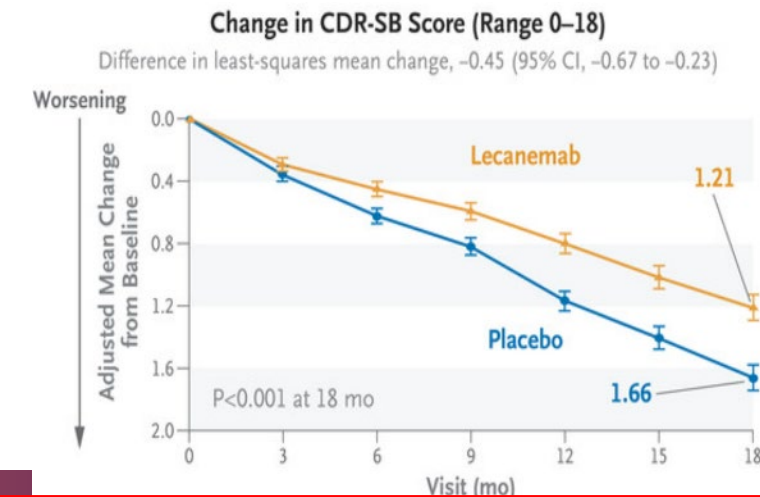
2) <https://www.nejm.org/doi/full/10.1056/NEJMoa2212948>

Leqembi's biological effect...

B Amyloid Burden on PET



... but with modest clinical effect!



Solution: a TNF- α Inhibitor Crossing the Blood-Brain Barrier

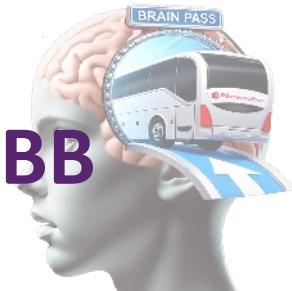


- Growing evidence that TNF- α drives brain inflammation playing a role in Alzheimer's
- **A TNF- α inhibitor (TNFI) crossing the BBB could transform the treatment of Alzheimer's** as TNFIs Remicade and Humira did with Crohn's Disease or Rheumatoid Arthritis
- **But current TNFIs don't cross Blood-Brain Barrier (BBB)!**

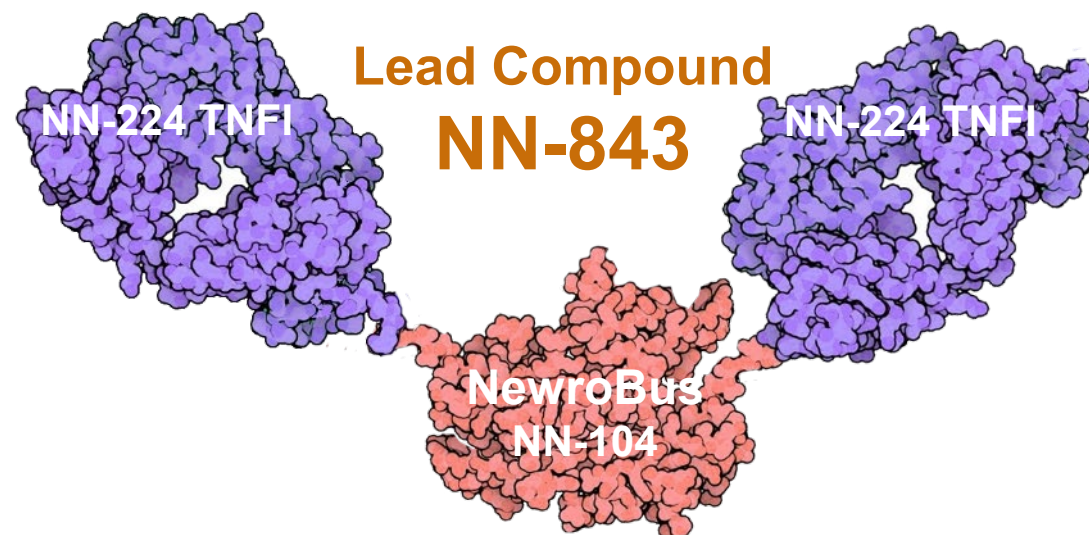
- **NanoNewron's Solution: NN-843 and NewroBus™**
 - **NN-843:** a potent TNF- α inhibitor crossing the BBB using NewroBus
 - **NewroBus:** nanobody designed to shuttle biologics across the BBB

NN-843: Lead Compound in Alzheimer Disease

A Potent TNF- α Inhibitor Engineered to Efficiently Cross the BBB



- **Lead compound NN-843 for the treatment of Alzheimer's Disease**
 - NN-843 crosses the BBB via TfR1 in rats **after S.C. administration**
 - Excellent **CSF/Serum ratio (~1:2)**
 - **High inhibition of brain TNF- α in rats**
 - **Favorable safety profile**
 - NN-843 does not cause hematotoxicity
 - Low immunogenicity potential

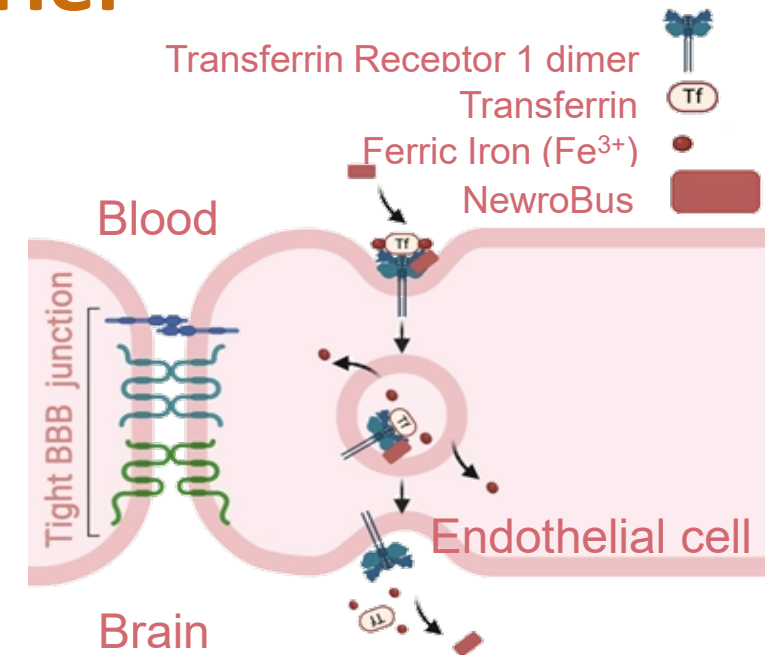


What is the NewroBus™ Technology?



NewroBus is our patented, versatile brain-carrier technology

- NewroBus carries large biologics into the brain across the BBB by exploiting the natural mechanism of **Transferrin Receptor 1 (TfR1)** transcytosis
- **NewroBus: a Best-in-Class TfR1 Brain Carrier**
 - High BBB permeability (**High CSF/Serum ratio >0.7**)
 - High humanness with **low immunogenicity**
 - Excellent safety



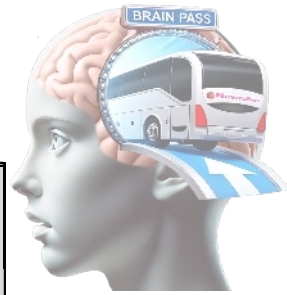
Our Achievements and Accomplishments by the Numbers



- Clinical candidate selection
 - **940** nanobodies cloned, produced, and tested for antigen binding
 - **85** anti-TNF- α nanobodies tested for TNF- α inhibitory activity
 - **106** anti-TfR1 nanobodies tested for binding to human TfR1
- Scale-up of **non-GMP/GMP manufacturing** to meet IND and Phase 1 supply needs
- Rat models development
 - **3 different rat models** generated with humanized TfR1, TF, and TNF- α
 - **40 germline** and humanized TfR1b nanobodies tested in vivo for BBB permeability.
 - **32 heterotrimers and heterodimers** evaluated for TNF α inhibitory activity and BBB permeability
- Additional studies
 - **2 tox studies** in humanized rats to assess hematological side effects
 - **ex-vivo human dendritic cells and T cells immunogenicity** assessment of nanobodies
 - **Crystallography** studies
- **Total costs for work performed before NIH grant awarded in July 2025: \$5,700K**
 - Dr. D'Adamio's NIH Grants at Rutgers: \$ 5,200K
 - NanoNewron's STTR Phase 1 NIH Grant awarded in 2023: \$ 500K

Next Key Milestones and Costs for NN-843 in Alzheimer's

IND Filing end of 2027 and End-of-Phase-1 Meeting in 4Q2028



Activities	2026				2027				Costs	2028				Costs	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	to IND	Q1	Q2	Q3	Q4	IND→EOP1	
	J F M	A M J	J A S	O N D	J F M	A M J	J A S	O N D	\$	J F M	A M J	J A S	O N D	\$	
1. CMC/Manufacturing Scale-Up									\$ 2,950K					\$ 500K	
Qualification, Formulation, Stability	Methods		Stability Studies						\$ 350K	Stability Studies				\$ 500K	
Non-GMP and GMP Production		non-GMP				GMP			\$ 2,600K						
2. Preclinical Mechanistic Studies									\$ 750K						
Cognition and behavior studies					in vivo Models				\$ 400K						
In vitro Pathology/Organoid Studies			in vitro Organoids Models						\$ 350K						
3. IND Program and Safety Studies									\$ 1,600K					\$ 2,500K	
Toxicology program*				PK	Tox 1	GLP Tox 2			\$ 1,600K	Long Term Tox				\$ 2,500K	
4. Regulatory/Operations									\$ 925K					\$ 1,600K	
IND and EOP1 Activities					Pre IND			★IND	\$ 325K				EOP1	\$ 400K	
Operations/Aministrative Costs	Operations/Administration								\$ 600K	Operations/Administration				\$ 1,200K	
5. Clinical Program									\$ 250K					\$ 8,250K	
Clinical Phase 1 Preparation						Phase 1 Prep			\$ 250K					\$ 250K	
Phase 1 SAD/MAD Study										SAD	MAD			\$ 4,500K	
Extended Treatment Phase 1b												Phase 1b		\$ 3,500K	
Total Costs to Key Milestones	Completed to Date (08/2026): \$									1,750K	To End-of-Phase 1: \$				17,575K
	Remaining to IND: \$									4,725K					

* Assuming no primate studies

NIH \$2.5M Grant in July 2025 is covering current activities up to 1Q2027. Additional NIH grants for \$4.5M are pending

NN-843 – Recent Progress Overview



- **Completed CMC/Manufacturing of NN-843**
 - Generated a stable CHOK1-GenS production cell clone expressing NN-843
 - **10L-scale manufacturing successfully completed**, yielding sufficient API for IND-enabling studies
- **NN-843 Profile Characterization**
 - **Low human immunogenicity** risk demonstrated in ex-vivo DC/CD4+ T cell studies
 - Demonstrated specific binding to human TfR1 and TNF α
 - **High molecular specificity** with binding restricted to its intended targets (human TfR1 and TNF α) and no off-target interactions detected across more than 7,200 human proteins
- **In-vitro study of activity of NN-843 in human CNS-3D inflammatory organoids**
 - **NN-843 reduces A β production** in human CNS-3D inflammatory organoids
 - **NN-843 inhibits TNF α -induced cytotoxicity** without intrinsic toxicity
 - **NN-843 suppresses TNF α -induced inflammatory signaling** and increased network activity
- **PK/Tox IND-enabling Program Preparation**
 - Start of PK/Tox program expected in August 2026
 - Pre-IND meeting expected in October 2026

Business Plan Based on Two Strategic Parallel Paths



- 1) Continue expeditious development of NN-843 for Alzheimer's
 - Novel approach targeting TNF- α inflammation
 - Animal models in humanized TfR1 rats to establish preclinical proof of concept
 - Early Alzheimer's disease as initial target population, an estimated market of 3 to 5 billion dollars
 - Expand use of NN-843 (or a follow-up compound) into additional CNS disorders
 - Parkinson's, Traumatic Brain Injury, Multiple Sclerosis, ALS
- 2) License NewroBus™ Technology to other companies for non-dilutive funds
 - **Four different NewroBus molecules currently available for licensing to potential partners**
 - Potential life-cycle management of commercial products
 - Enhancing brain penetration of other novel biologics
 - Potential for other therapeutic areas and combination therapy
 - **Partnership as additional source of non-dilutive funding in the short term**

For investors multiple short- and medium-term inflection points

NanoNewron as an Investment Opportunity



Company (Partner)	Therapy Target	BBB Carrier	Status	Notes - Out Licensing Deals
Inmune Bio	TNF- α	none	Phase 2	Phase 2 results supportive of TNF- α inhibition as a therapeutic target
Denali (Takeda)	TREM2	TfR1	Terminated due to toxicity	Licensed at pre-IND stage for \$150M upfront and undisclosed milestones and royalties
BioArctic (BMS)	β -amyloid	TfR1	Pre-IND	Licensed for \$100M upfront, \$1.2B milestones and double digit royalties
Roche	β -amyloid	TfR1	Phase 2	Trontinemab in Phase 2 showed clearance of β -amyloid on PET imaging
Manifold (Roche)	Undisclosed	TfR1	Preclinical	Licensed for \$55M upfront, \$2B milestones and royalties
ABL Bio (GSK)	Undisclosed	IGF1R	Pre-IND	Licensed for \$100M upfront, \$2.5B milestones and royalties

Effective and safe brain carriers, like NewroBus, can command highly valued transactions at an early stage of development

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NN-843 is a novel therapy to treat Alzheimer's by targeting TNF- α induced neuroinflammation



IND filing of NN-843 expected in 4Q2027



NN-843 built on NewroBus™, our technology to carry biologics inside the brain via TfR1



Experienced scientific, clinical, regulatory and business team



NIH grant of \$2.5 million awarded in July 2025, with additional NIH grants for \$4.5M pending



Thank you!

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