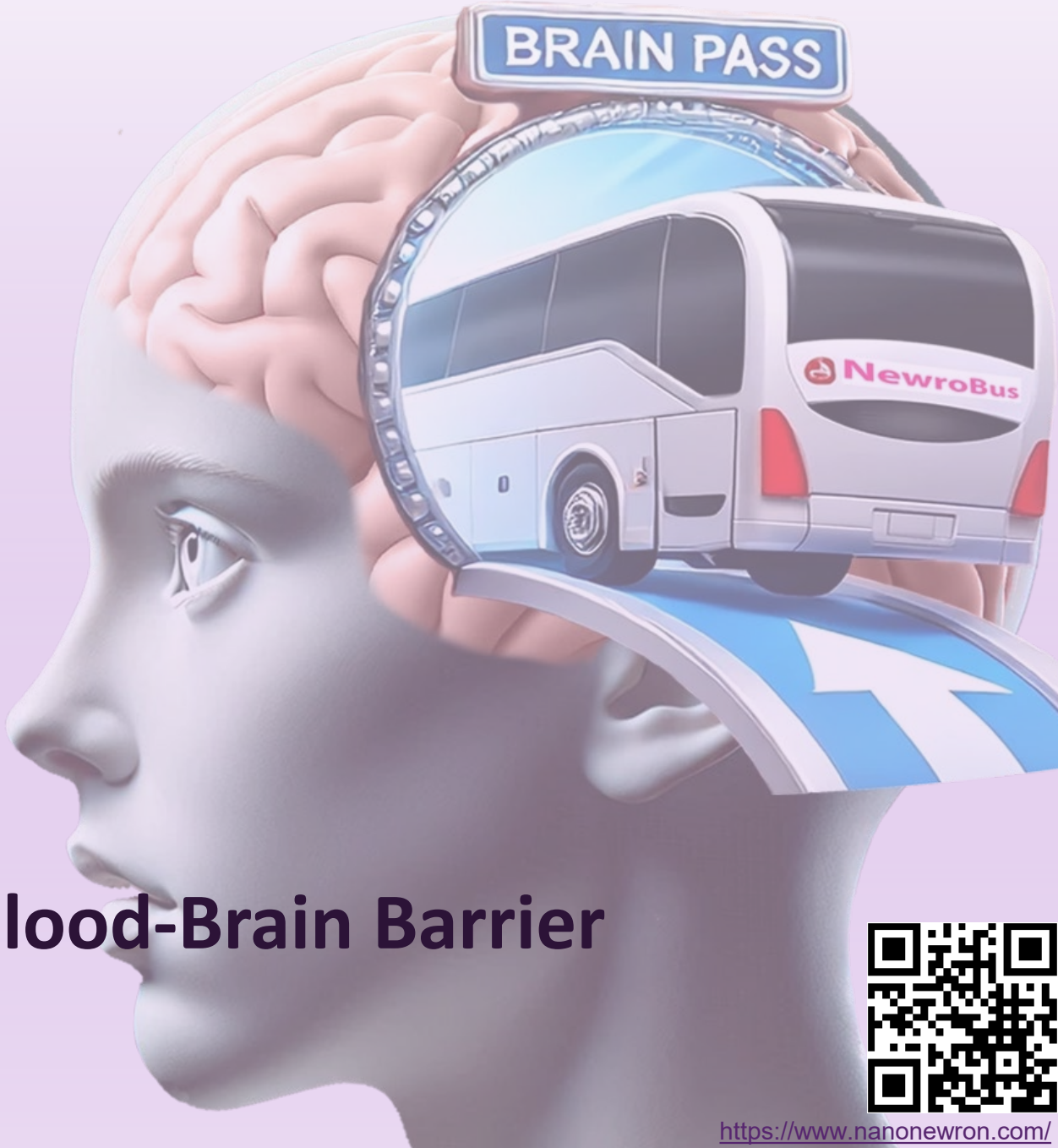
NanoNewron™

New Treatments for CNS Diseases



NewroBus™

Carrying Biologics Across the Blood-Brain Barrier

https://www.nanonewron.com/

Forward-Looking Statements

This presentation contains “Forward-Looking Statements” Forward-Looking Statements reflect our current view about future events. When used in this presentation, the words “anticipate,” “believe,” “estimate,” “expect,” “future,” “intend,” “plan,” or the negative of these terms and similar expressions, as they relate to us or our management, identify forward-looking statements. Such statements, include, but are not limited to, statements contained in this presentation relating to our business strategy, our future operating results and liquidity and capital resources outlook. Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. Because forward–looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. Our actual results may differ materially from those contemplated by the forward-looking statements. They are neither statements of historical fact nor guarantees of assurance of future performance. We caution you therefore against relying on any of these forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include, without limitation, our ability to raise capital to fund continuing operations; our ability to protect our intellectual property rights; the impact of any infringement actions or other litigation brought against us; competition from other providers and products; our ability to develop and commercialize products and services; changes in government regulation; our ability to complete capital raising transactions; and other factors relating to our industry, our operations and results of operations. There is no guarantee that any specific outcome will be achieved. Investment results are speculative and there is a risk of loss, potentially all loss of investments. Actual results may differ significantly from those anticipated, believed, estimated, expected, intended or planned. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We cannot guarantee future results, levels of activity, performance or achievements. Except as required by applicable law, including the securities laws of the United States, we do not intend to update any of the forward-looking statements to conform these statements to actual results.

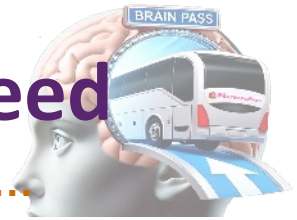
NN-843: a TNF-α Inhibitor Crossing the Blood-Brain Barrier Using NewroBus™ Technology to Treat Alzheimer's Disease

- **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 4Q2026**, 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 expected in 4Q2026 ($7.8M), followed by Phase 1/1b ($17.9M) and End-of-Phase-1 meeting in 4Q2028.** Non-dilutive NIH grant of $2.5 million awarded in July 2025.

Experienced Scientific, Clinical, and Business Funding Team

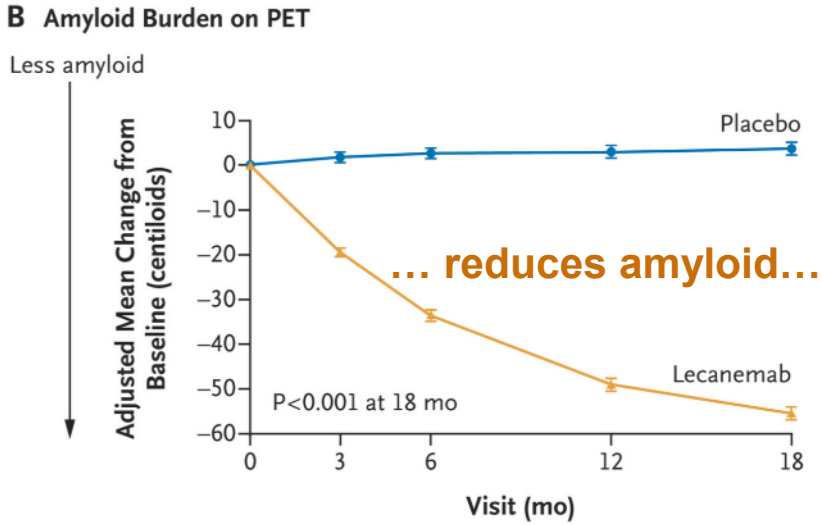
- Marco Taglietti, MD, Chief Executive Officer
  - **35+ years of experience with more than 30 different products brought to market**
  - President and Chief Executive Officer of Scynexis (Nasdaq:SCYX) from 2015 to 2022
  - President and Chief Medical Officer at Forest Laboratories (Nasdaq:FRX) from 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

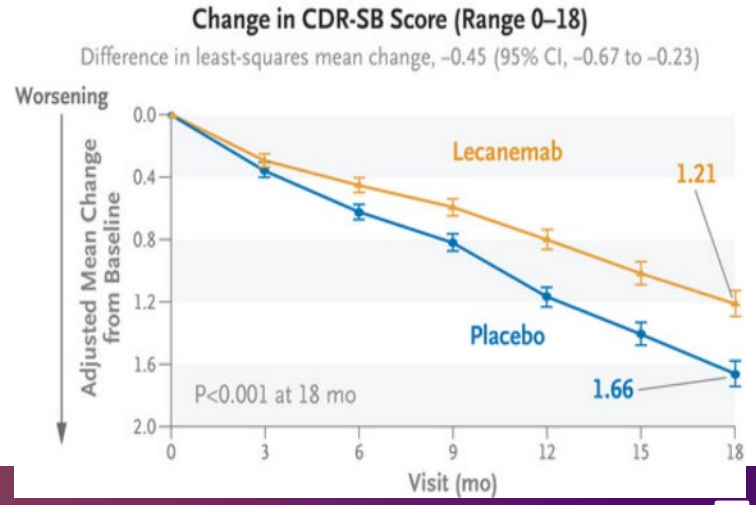


- >7 million Alzheimer's patients in the U.S.[1]
  - A $14.5 billion market by 2029… **a large but unsatisfied market**
- Only partial success of **anti-amyloid biologics** [2]
  - **Strong biological effect** with reduction of amyloid…
  - … but only **temporary** improvements in symptoms
  - **Modest**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

Leqembi's biological effect…



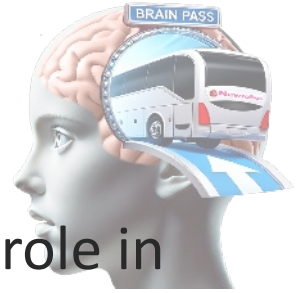
… but with modest clinical effect!



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

Solution: TNF-α Inhibitors Crossing the Blood-Brain Barrier

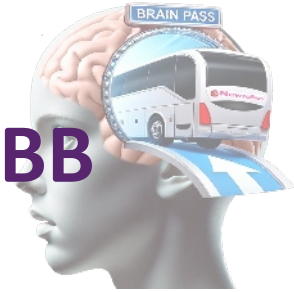


- Growing evidence that dysregulated TNF-α drives brain inflammation and plays a role in Alzheimer's Disease (AD)
- **TNF-α inhibitors (TNFI) could transform the treatment of Alzheimer's** as TNFI Remicade and Humira did with Crohn's Disease or Rheumatoid Arthritis
  - **But TNFI don't cross Blood-Brain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

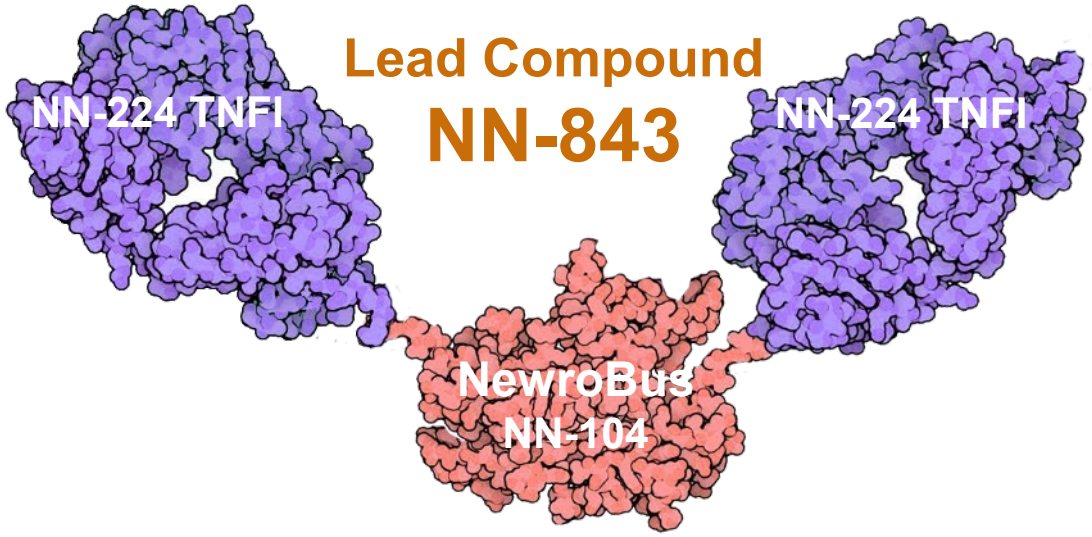
- **NanoNewron's Solution: NN-843 and NewroBus™**
  - **NN-843:** a potent TNF-α inhibitor crossing the BBB using NewroBus
  - **NewroBus:** single-chain nanobody designed to transport biologics across the BBB

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**
  - Two molecules of **proprietary TNF-α inhibitor (TNFI) NN-224** linked to NewroBus NN-104
  - NN-843 crosses the BBB via TfR1 in rats **after S.C. administration**
  - **Biological activity tested in rats** with humanized TfR1, Tf, and TNF-α
  - **High inhibition activity against TNF-α**
  - Excellent **CSF/Serum ratio (~1:2)**
  - Broad distribution in the brain tissue
  - High specificity and affinity to human TfR1
  - **NN-843 does not cause hematotoxicity**
  - **Low immunogenicity potential**



Why Targeting Inflammatory Cytokine TNF-α for Alzheimer's?

- **Decreasing the excessive activity of TNF-α reduces the pathophysiologic changes of Alzheimer's Disease (AD)**
- Data in humans
  - Reduced risk of AD in patients treated with TNFI for other conditions[1]
  - Cognitive improvements after peri-spinal administration of TNF-α inhibitors[2]
    - Open-label, small (N=15) study showed 5-point improvement in ADAS-Cog score at 6 months
  - Trend for elevated TNF-α levels in blood and CNS in Alzheimer's patients[3]
- Data in Animal Models
  - TNF-α inhibitor XPro1595 decreases beta-amyloid plaque load in 5xFAD mice[4]
  - TNF-α inhibition in a mouse AD model prevents pre-plaque amyloid-associated neuropathology[5]
  - TNF-α increases excitatory transmission preceding Alzheimer's pathology in young Trem2R47H rats[6]

Odd Ratio[1] of developing AD compared to the general population

TNF Inhibitor	Odd Ratio
etanercept	0.3
etanercept	0.36
etanercept	0.34
adalimumab	0.65
adalimumab	0.28
infliximab	0.73
infliximab	0.64

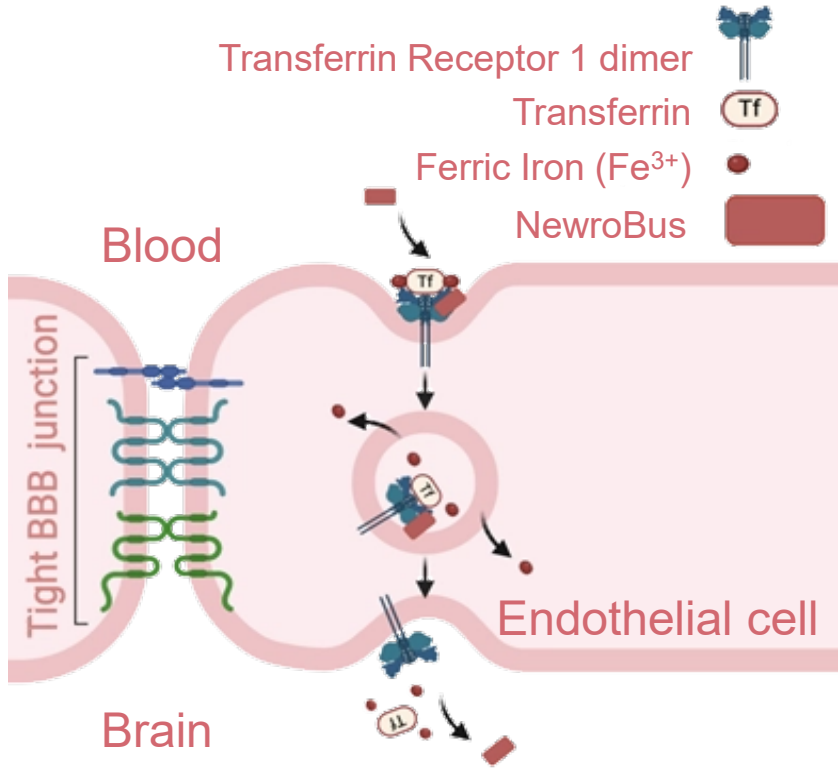
1) Torres-Acosta N. et al (2020) Therapeutic Potential of TNF-α Inhibition for Alzheimer's Disease Prevention. *Journal of Alzheimer's Disease, 78(2)*, 619-626
2) Tobinick E et al (2006) TNF-alpha Modulation for Treatment of Alzheimer's Disease: A 6-Month Pilot Study. *MedGenMed, 8(2)*, 25
3) Plantone D. et al (2023) The Role of TNF-α in Alzheimer's Disease: A Narrative. *Cells, 26;13(1)*, 54
4) MacPherson KM et al (2017) Peripheral administration of the soluble TNF inhibitor XPro1595 modifies brain immune cell profiles, decreases beta-amyloid plaque load, and rescues impaired long-term potentiation in 5xFAD mice. *Neurobiol Dis, 102*, 81-95
5) McAlpine FE et al (2009) Inhibition of soluble TNF signaling in a mouse model of Alzheimer's disease prevents pre-plaque amyloid-associated neuropathology. *Neurobiol Dis 34(1)*, 163-177
6) Ren S et al (2021) TNF-α-mediated reduction in inhibitory neurotransmission precedes sporadic Alzheimer's disease pathology in young Trem2R47H rats, J Biol Chem, 296

What is the NewroBus™ Technology?

NewroBus is a versatile brain-carrier technology platform exploting TfR1

- The blood-brain barrier (BBB) keeps out from the brain large molecules, e.g. biologics
- NewroBus transports large molecules into the brain by exploiting the natural mechanism of **Transferrin Receptor 1 (TfR1)** to carry Transferrin (Tf) across the BBB

- **NewroBus: a Best-in-Class TfR1 Brain Carrier**
  - Four different NewroBus molecules are available
    - Selected from a large pool of >450 humanized nanoantibodies
    - No interference with Tf binding and uptake
  - High humanness with **low immunogenicity potential**
  - High specificity: binds exclusively to human TfR1, not rodent TfR1
  - High BBB permeability (**High CSF/Serum ratio >0.7**) tested in rat models with the human TfR1 gene
  - High tolerability, with **low risk for anemia** in humans, as tested in rats with humanized TfR1/Tf complex



Business Plan Based on Two Strategies

1) Continue aggressive development of NN-843 for Alzheimer's
   - Novel approach targeting TNF-α inflammation with high brain penetration, TNF-α inhibition and excellent tolerability
   - Animal models in humanized TfR1 rats available 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
   - **Multiple short-(18-24 months), medium- and long-term inflection points**

2) License NewroBus™ Technology to other companies for non-dilutive funds
   - **Four different NewroBus molecules currently available for licensing**
   - Potential life-cycle management of commercial products
   - Enhancing brain penetration of other novel biologics
   - Potential for other therapeutic areas and combination therapy
   - **Additional source of non-dilutive funding in the short term**

Our Achievements to Date 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 TNFα 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 to date** **$5,700K**
  - Dr. D'Adamio's NIH Grants at Rutgers: $ 5,200K
  - NanoNewron's STTR Phase 1 NIH Grant (2023): $ 500K

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

IND Filing in 4Q2026 and End-of-Phase-1 Meeting in 4Q2028

Activities	2025		2026				Costs to IND	2027				2028				Costs IND→EOP1
	Q3	Q4	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
	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	J F M	A M J	J A S	O N D	
1. CMC/Manufacturing Scale-Up							**$ 1,750K**									**$ 1,350K**
Qualification, Formulation, Stability		Assays	Formulation		Stability		$ 1,150K				Stability Studies					$ 600K
Non-GMP and GMP Production		nGMP	GMP				$ 600K				GMP					$ 750K
2. Preclinical Mechanistic Studies							**$ 1,500K**									
Cognition and behavior studies			*in vivo* Models				$ 950K									
In vitro Pathology/Organoid Studies			*in vitro* Models				$ 550K									
3. IND Program and Safety Studies							**$ 2,600K**									**$ 1,500K**
Toxicology program*			PK	IND Tox			$ 2,600K		Long-Term Tox Studies							$ 1,500K
4. Regulatory/Operations							**$ 1,500K**									**$ 1,800K**
IND and EOP1 Activities			Pre-IND	IND Prep		IND	$ 600K					EOP1 Preparation			EOP1	$ 400K
Operations/Aministrative Costs	Operations/Administration						$ 900K	Operations/Administration								$ 1,400K
5. Clinical Program							**$ 450K**									**$ 13,250K**
Clinical Phase 1 Preparation					Phase 1 Prep		$ 450K									$ 250K
Phase 1 SAD/MAD Study									SAD	MAD						$ 5,500K
Extended Treatment Phase 1b												Phase 1b				$ 7,500K
Total Cost by Phase							**to IND Filing: $ 7,800K**									**From IND to End-of-Phase-1 Meeting: $ 17,900K**

* Assuming no primate studies

Relevant Competition in Alzheimer's Disease

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
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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Version November 06, 2025

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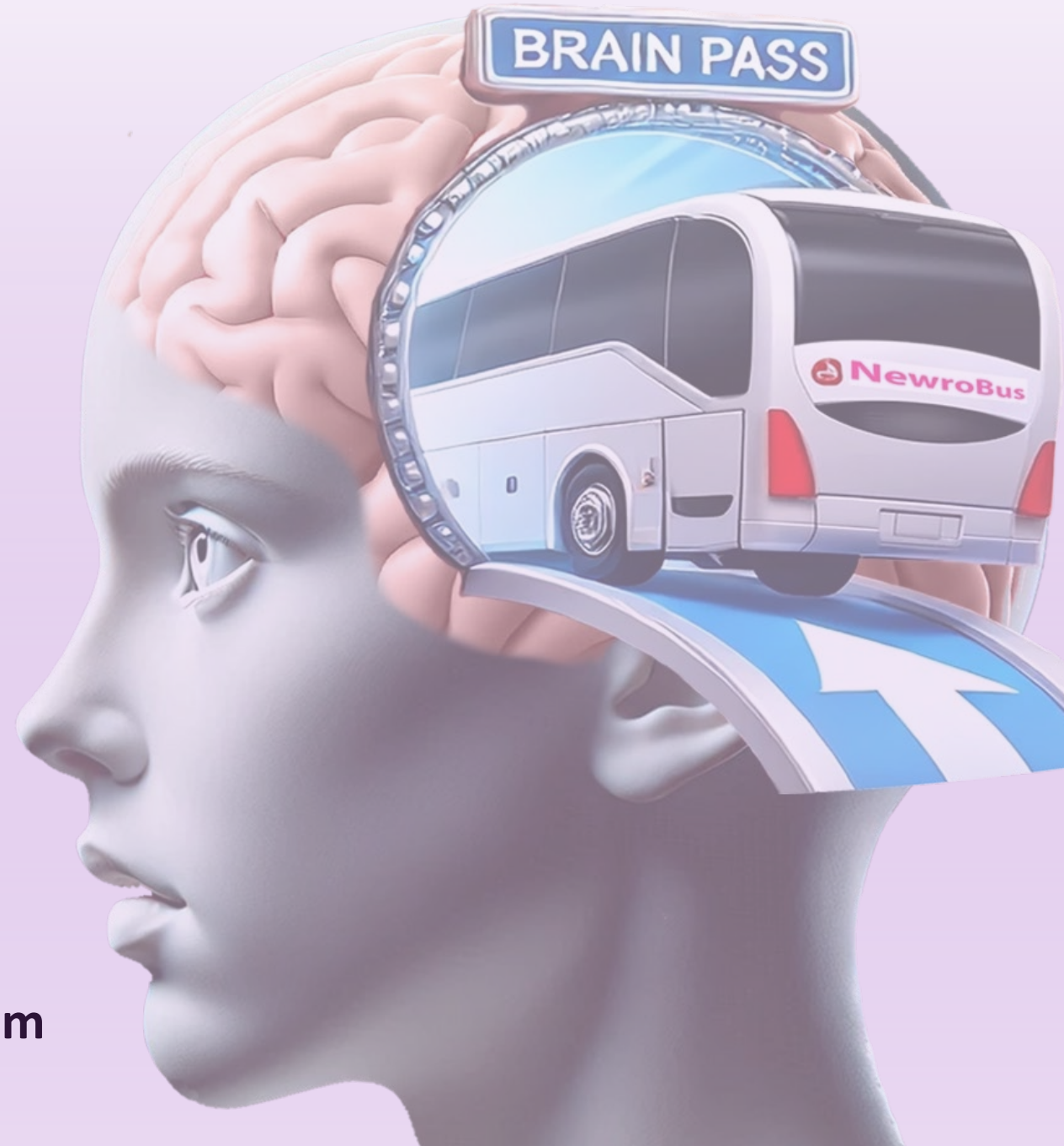

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