INmuneBio
INNATE IMMUNITY

Inflammation and Immunology Repair

Two Platforms in the Clinic: XPro™ and INKmune™

INMB
Nasdaq

November 2024 v4b

FORWARD LOOKING STATEMENTS

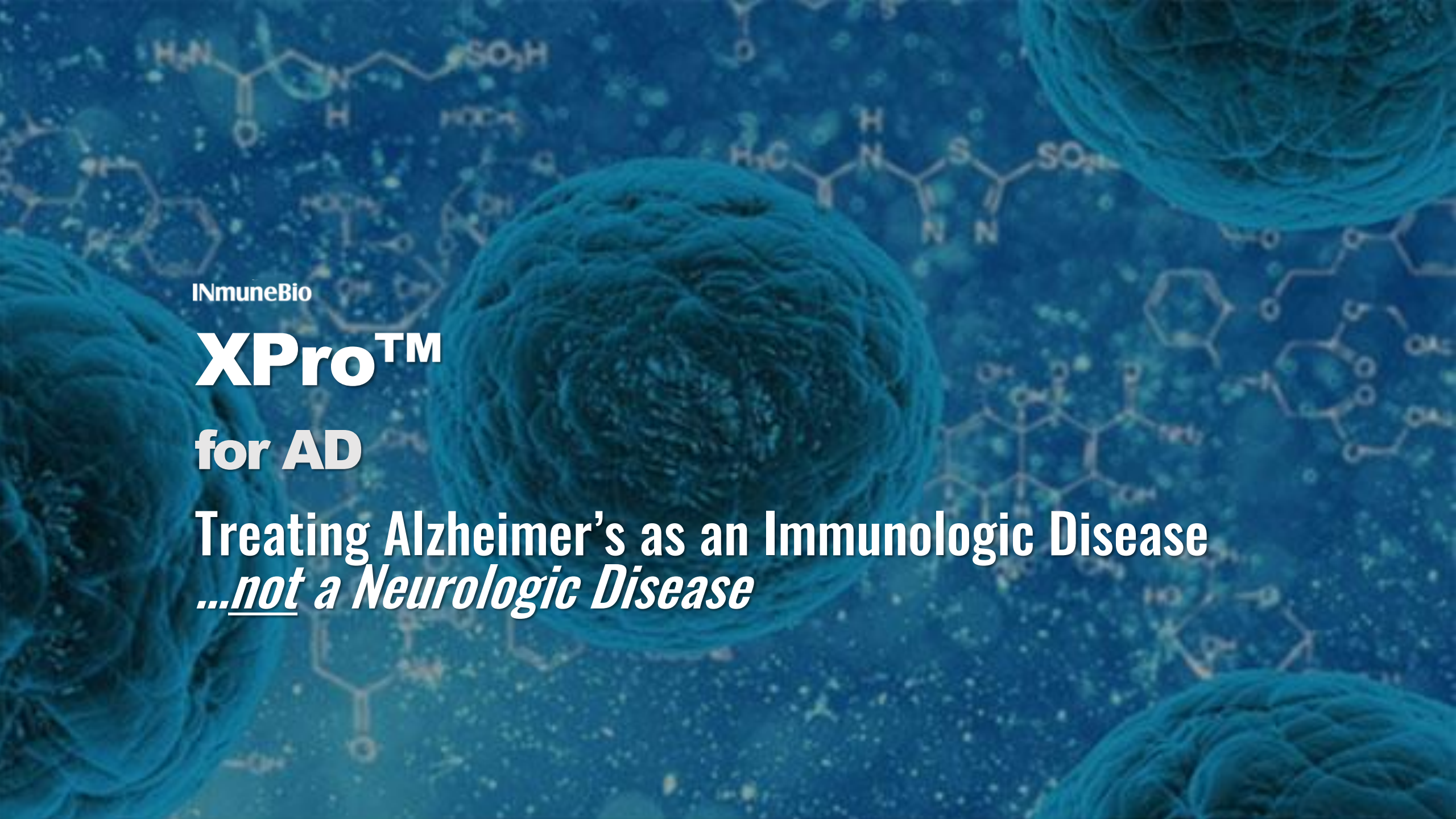
This presentation contains “forward-looking statements” Forward-looking statements reflect our current view about future events. When used in this presentation, the words “anticipate,” “believe,” “estimate,” “expect,” “future,” “intend,” “plan,” or the negative of these terms and similar expressions, 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.

Two Novel Platforms with Near Term Data

- XPro™: Treating Alzheimer's as an Immunologic disease, not a neurologic disease
  - Phase 2 Alzheimer's top-line expected in Q2 2025
  - Treatment Resistance Depression program open by year-end 2024
- INKmune™: Creates memory-like NK Cells to kill cancer
  - Open label Phase 1/2 metastatic castrate resistant prostate cancer with ongoing data readouts
- Clean balance sheet with strong insider participation and ownership

Development Timeline

DN-TNF PLATFORM	DESEASE FIELD	PRE-CLINICAL	PHASE 1	PHASE II (POC)	PIVOTAL	EST.NEXT MILESTONE
XPro™	Early Alzheimer's Disease	→				Full Enrollment Q3-2024 Topline Data ~ 6m Later
XPro™	Treatment Resistant Depression	→				Phase 2 open year-end 2024
NK PRIMING PLATFORM						
INKmune™	Metastatic Castrate Resistant Prostate Cancer	→				Open Label Phase 2 Trial



INmuneBio

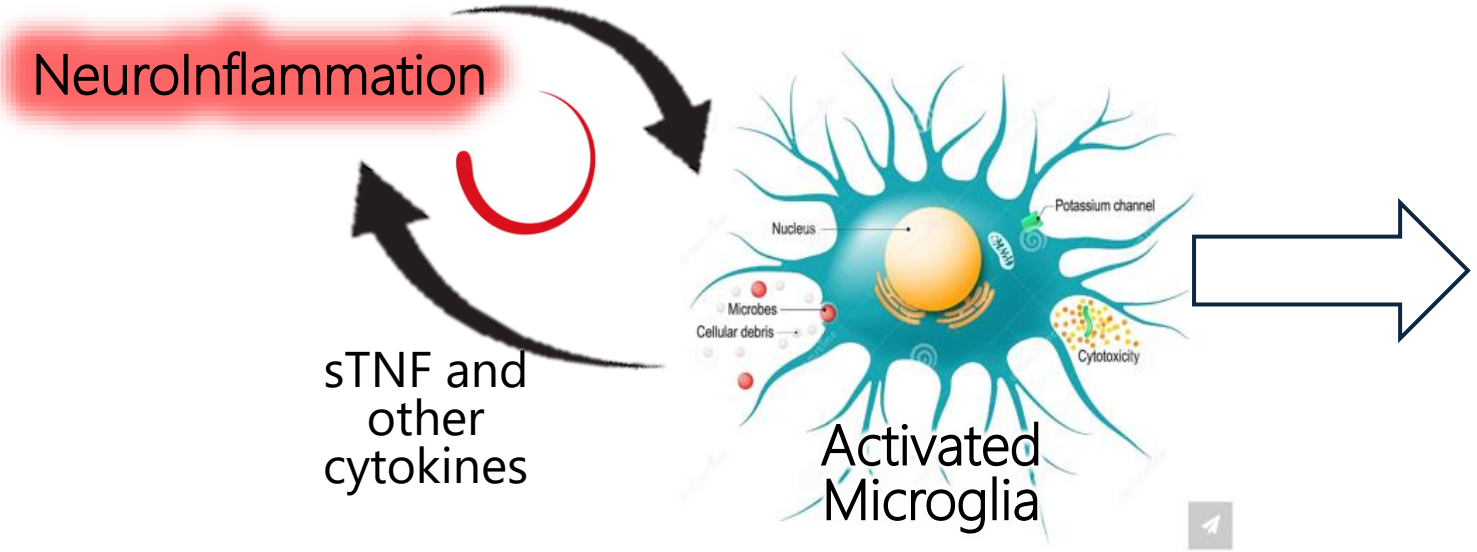
XPro™

for AD

Treating Alzheimer's as an Immunologic Disease

...not a Neurologic Disease

The *"Doom Loop"* of Neuroinflammation and Cognitive Decline



Essential Pathologies of Cognitive Decline

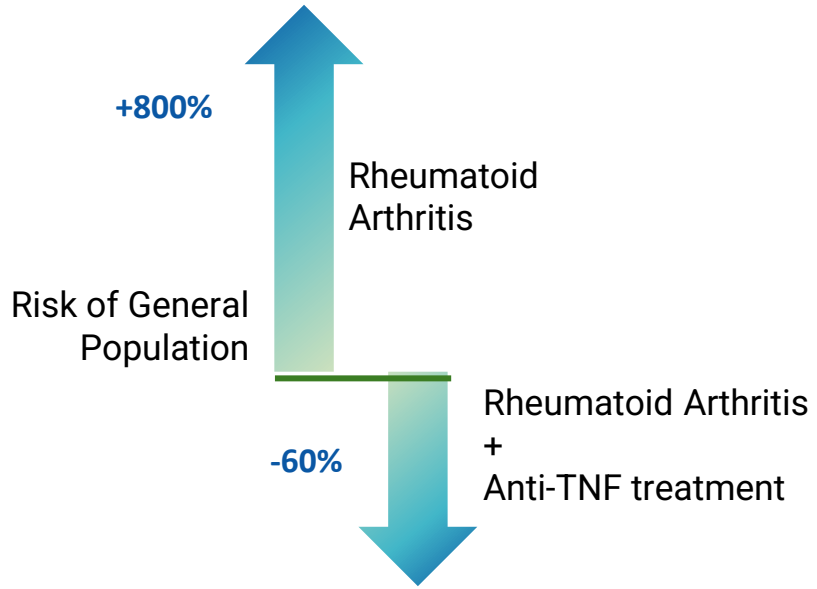
- Synaptic Dysfunction
- Demyelination
- Nerve Cell Death

Targeting neuroinflammation with XPRO™ should stop cognitive decline to allow remodeling and repair

Targeting sTNF in Man Makes a Difference

Prevention of chronic inflammation with anti-TNF therapy lowers risk of AD

TNF Inhibitors Reduce Risk of Developing AD

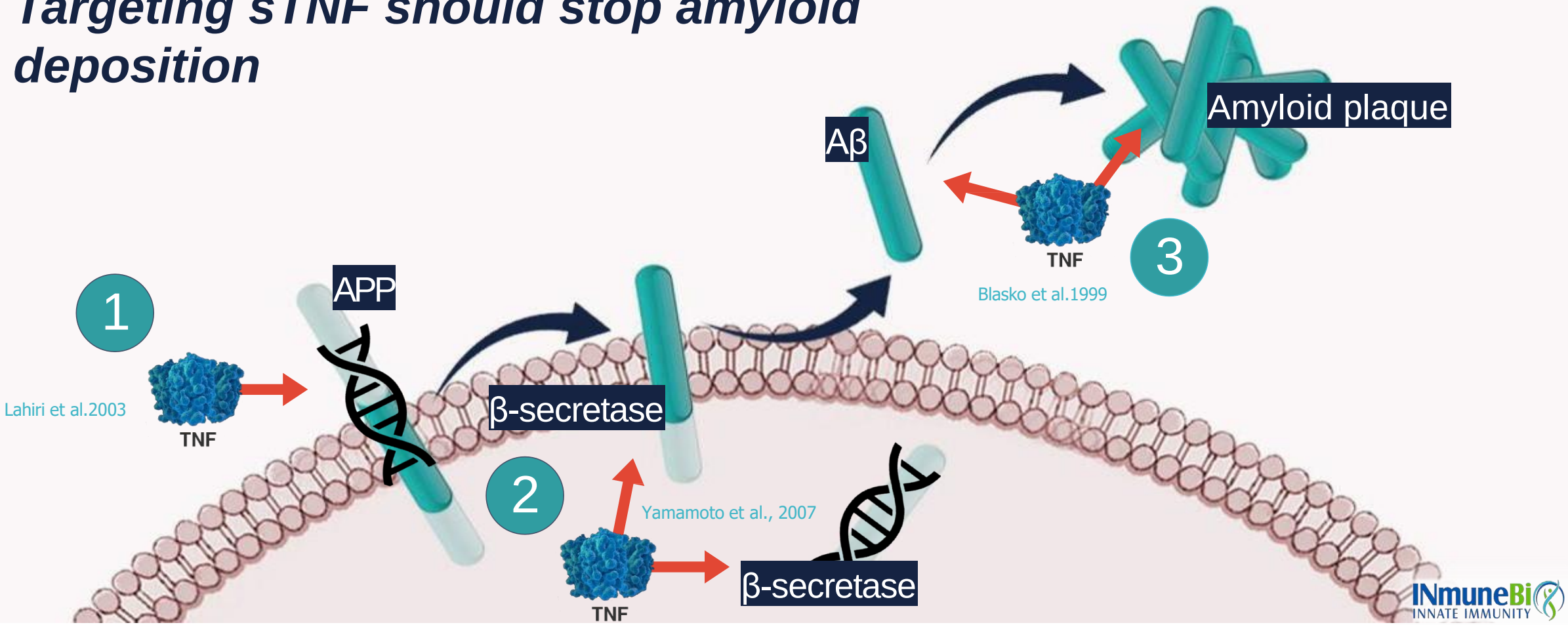


Epidemiological studies including a meta-analysis of more than 60 million cases linking **TNF Blocking Agents** to reduced risk of AD

Soluble TNF Drives Pathology of Alzheimer's

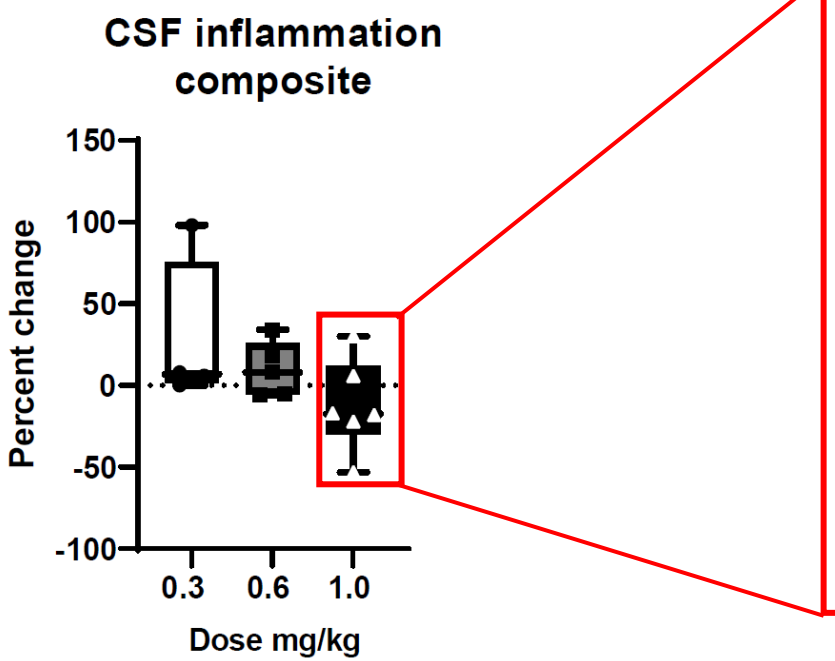
sTNF drives neuroinflammation that promotes amyloid plaque deposition

- ***sTNF drives expression and accumulation of amyloid***
- ***Targeting sTNF should stop amyloid deposition***

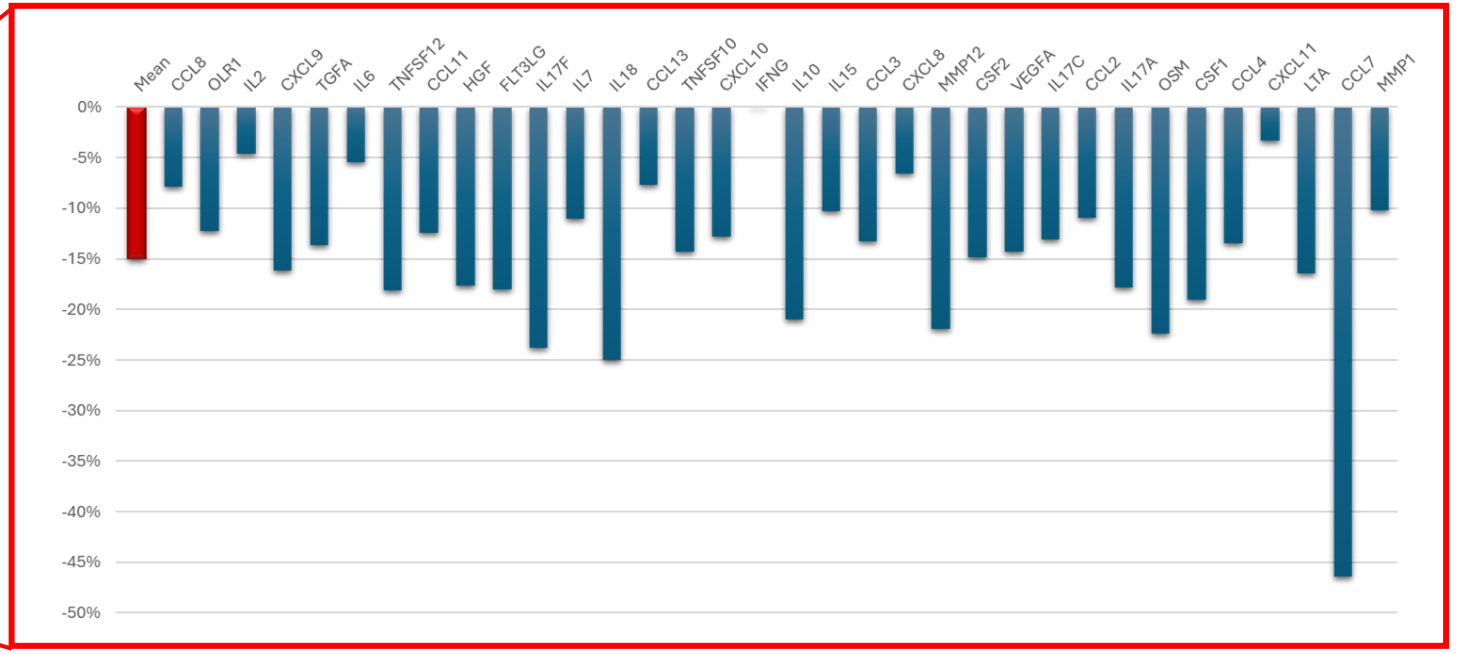


Neutralizing sTNF with XPro™ Decreases Neuroinflammation

Dose-dependent reduction of CSF biomarkers of neuroinflammation in AD patients



CSF



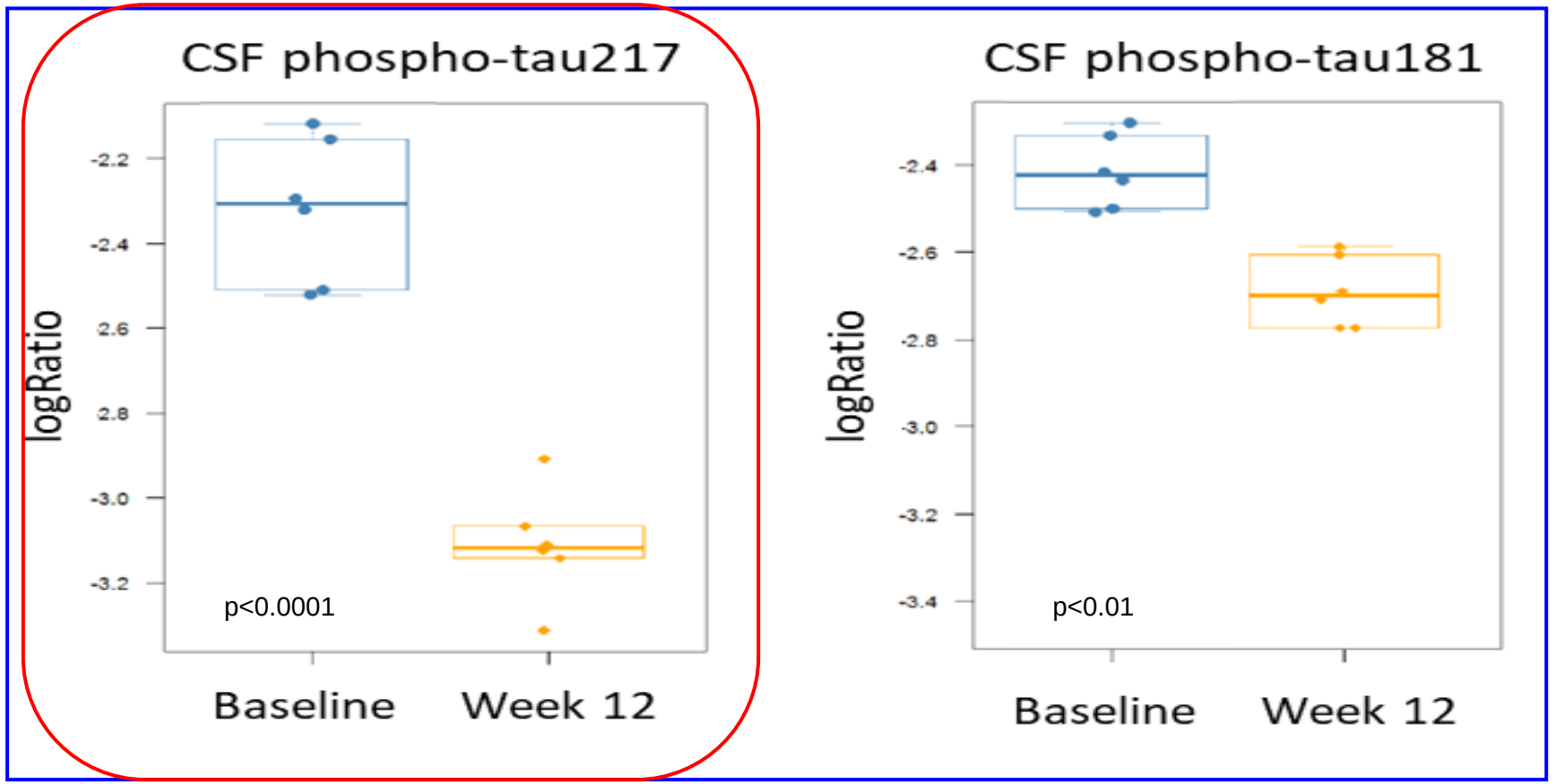
**1 mg/kg group (N=6)*

Phase I results using Olink® Target 48 Cytokine assay in CSF

XPro™ Decreases Neurodegeneration

pTau217 is best biomarker for neurodegeneration in patients with AD*

Phase I data: XPro™ 1mg/kg subQ once a week for 12 weeks decrease pTau in CSF in patients with AD



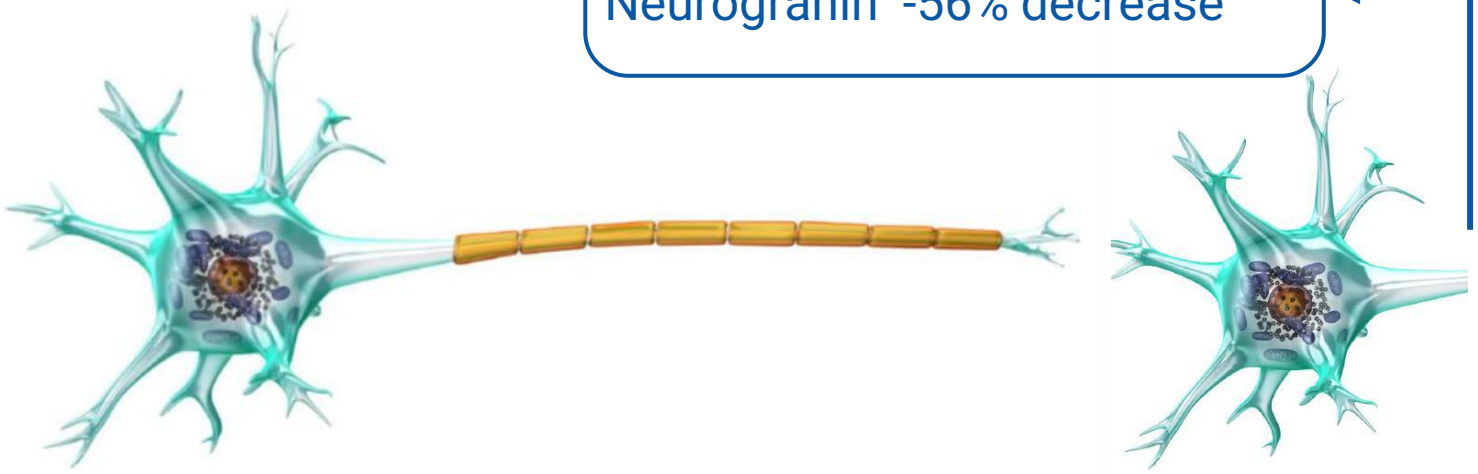
proteome sciences

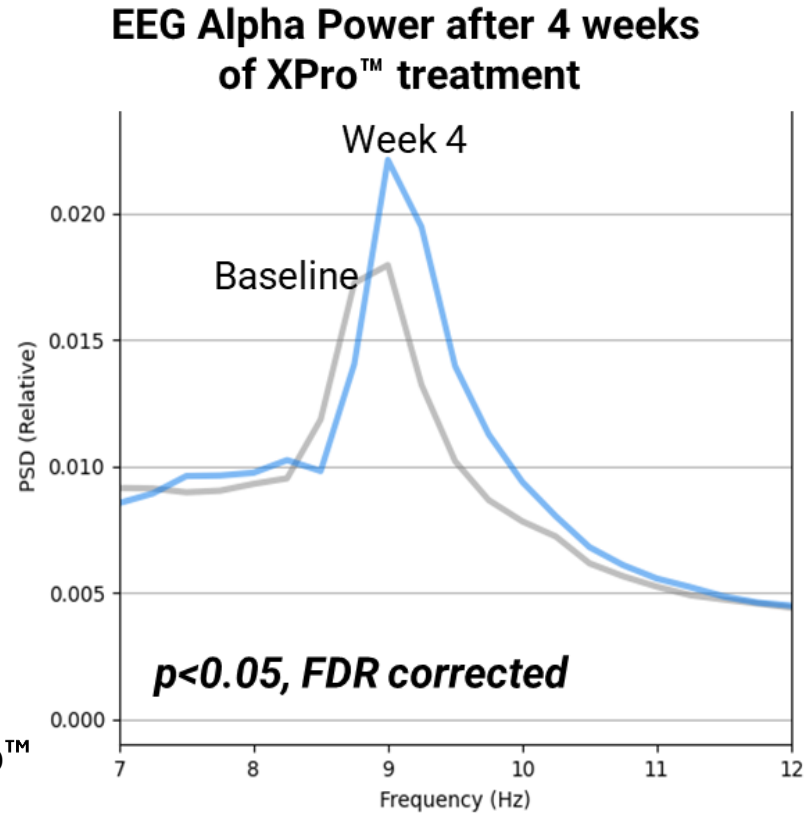
*https://jamanetwork.com/journals/jamaneurology/fullarticle/2813751

XPro™ Improves Synaptic Function

Phase I studies demonstrated changes in synaptic proteins that correspond to improvements in synaptic function as measured by EEG Alpha waves

Synaptic Proteins
Contactin-2 +222% increase
Neurogranin -56% decrease



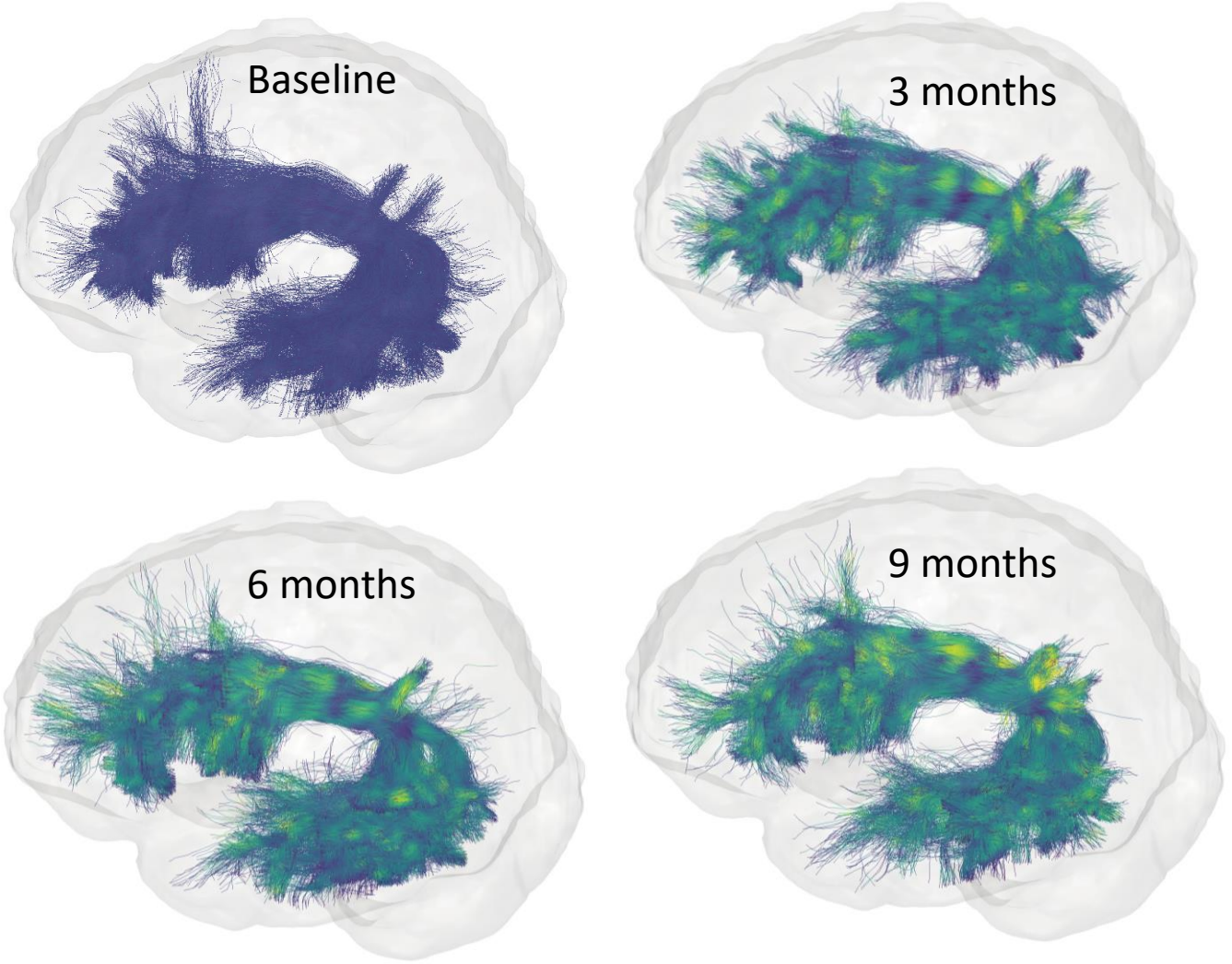


Above: CSF synaptic proteins improved after treatment with 12 weeks of XPro™
Right: Alpha Power EEG improves after 4 weeks of XPro™

Both are data from Phase I trials in AD patients with XPro 1mg/kg once a week by subQ injection

Remodeling and Repair of White Matter Tracts After XPro™

Phase 1b patient: CHANGES IN AFD* IN AD WHITE MATTER TRACTS – CASE STUDY

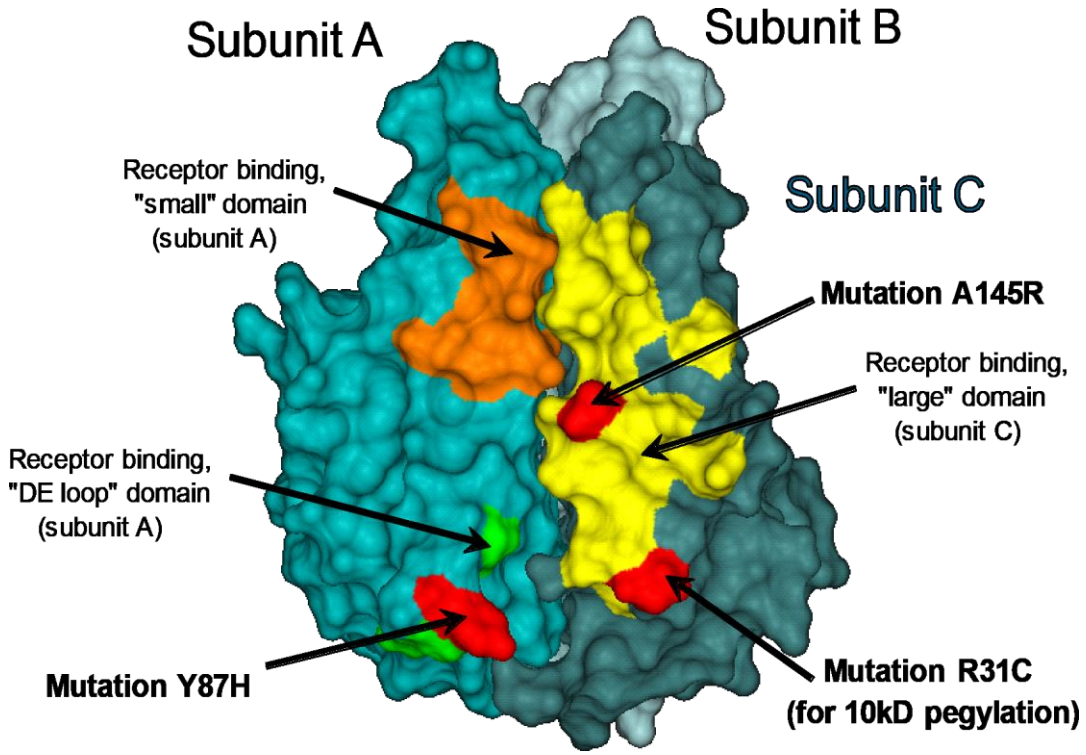


- 65-year-old white male retired due to AD
- Returned to work after 6 months of XPro therapy
- Increasing green/blue shows improvement in axonal quality

*AFD= apparent fiber density – a measure of white matter axonal integrity

XPro™: a TNF Inhibitor Designed to Treat Neurologic Disease

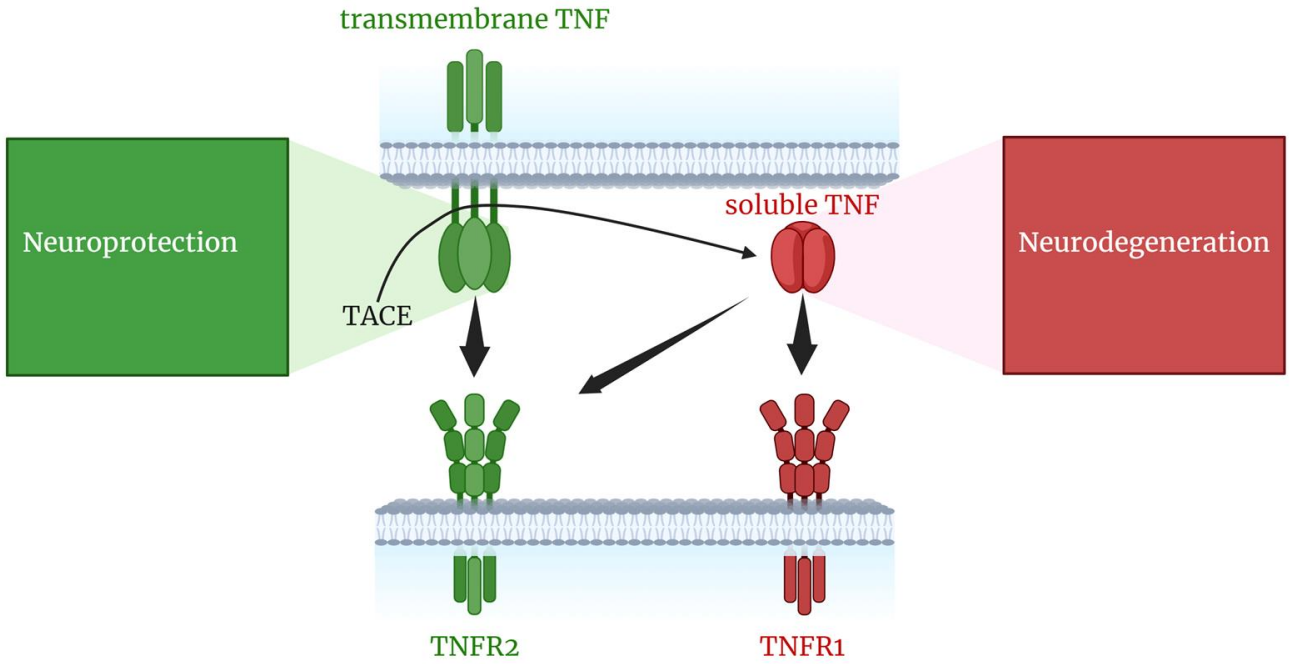
XPro™: a dominant-Negative selective inhibitor of *ONLY* soluble TNF



XPro™ is identical to the human soluble TNF monomer with the exception of mutations in the receptor binding domain and another for pegylation.

Dominant-Negative in genetics:
"A mutation producing a rogue protein that interferes with the function of the native protein."

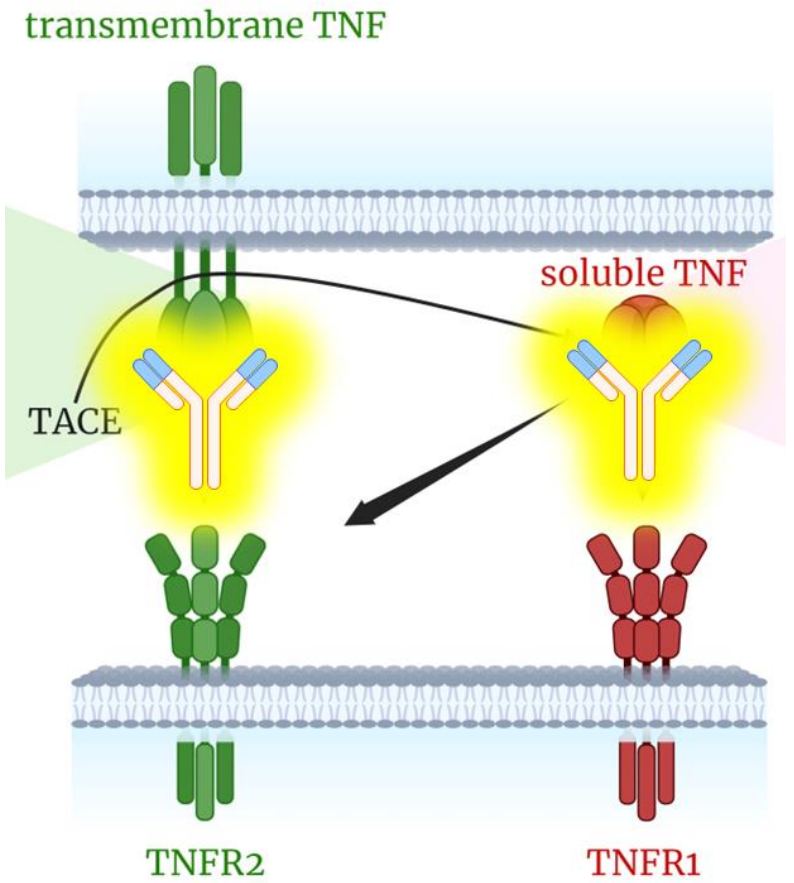
TNF: Two Cytokines, Same Name, Opposite Effects



Soluble TNF cause inflammation, cell death and demyelination

Transmembrane TNF promotes immune function, is neuroprotective and improves synaptic plasticiy

Currently approved TNF inhibitors block both types of TNF causing immunosuppression and demyelination

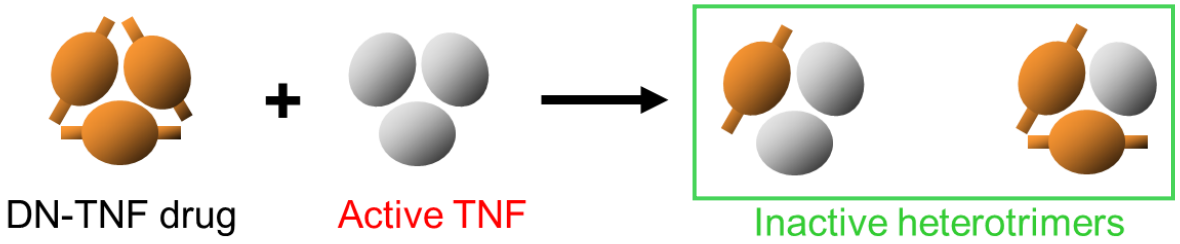


XPro™ unique Mechanism of Action XPro neutralizes sTNF without affecting tmTNF using dominant-negative technology

Targeting sTNF

XPro™ exchanges with sTNF monomers to form inactive heterotrimers

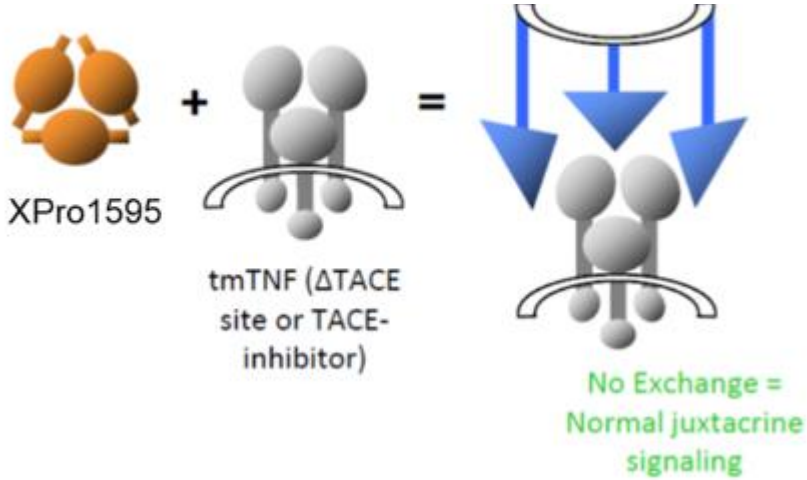
Inflammatory TNF eliminated
No paracrine signaling through receptors



Preserving tmTNF Function

tmTNF homotrimers are anchored to the cell membrane; XPro™ cannot exchange

Beneficial TNF signaling preserved
Improved immune and CNS function



Purpose Built for treating CNS Disease:

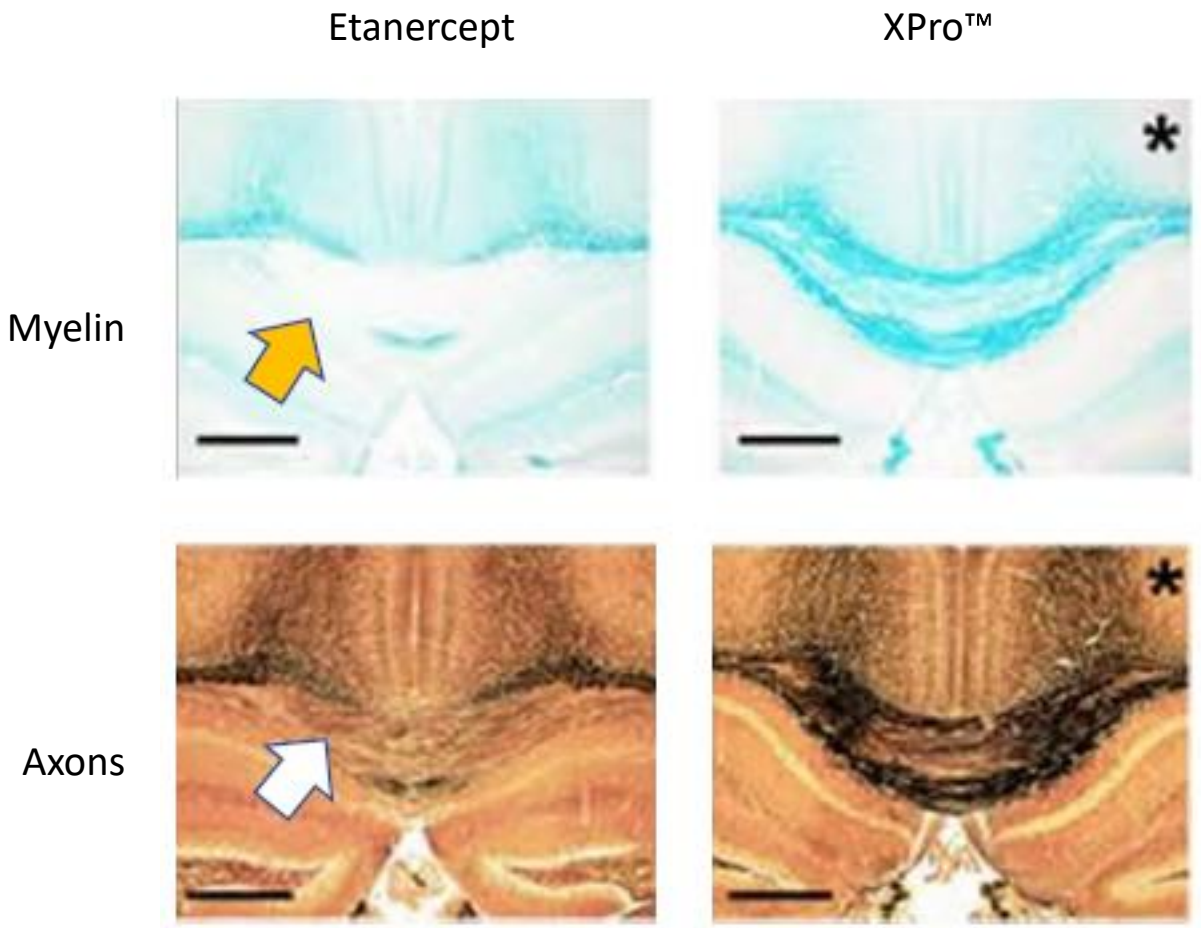
XPro™ neutralizes sTNF without affecting tmTNF

XPro™ is the only TNF inhibitor that is safe for the Brain

FDA label on currently approved TNF inhibitors recommend against use for CNS disease

- Currently approved TNF inhibitors are contraindicated in treatment of neurologic disease such as AD
  - promote demyelination (yellow arrow)
  - promote axon degeneration (white arrows)

- XPro™ promotes remyelination and axonal regeneration



Karamita; Therapeutic inhibition of soluble brain TNF promotes remyelination by increasing myelin phagocytosis by microglia. https://doi.org/10.1172/jci.insight.87455

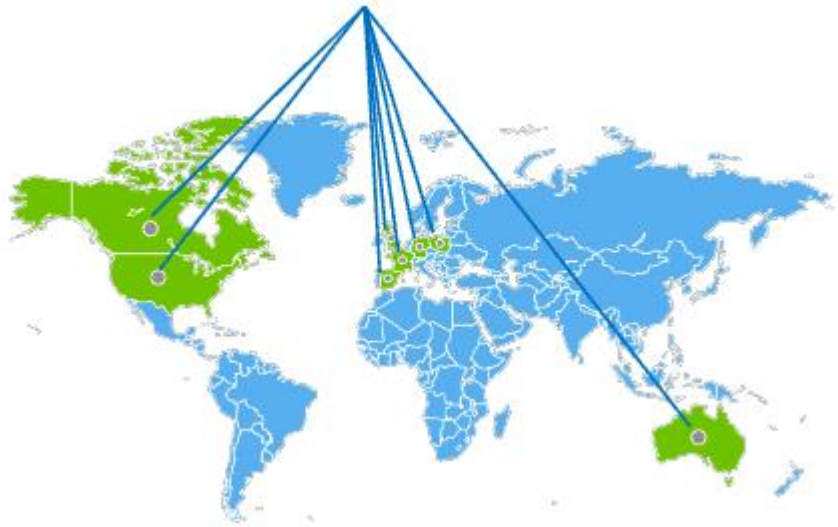
Phase 2 Trial of XPro™ in Patients with Early Alzheimer's Disease

Key enrollment criterion

- Early AD (50-85 yrs) (N=201)
- Amyloid positive
- CDR (0.5 or 1)
- MMSE > 22
- One Inflammatory Biomarker:
- hsCRP (1.5 mg/L)
- ESR (10 mmg/hr)
- HbA1c (6%)
- APOE4+

Baseline	Week 6	Week 12	Week 18	Week 24
Cognition	EMACC	Cognition	EMACC	Cognition
Function		Function		Function
Blood		Blood		Blood
MRI		MRI		MRI

MINDFuL
A study of inflammation in Alzheimer's disease



Treatment

- 2:1 (XPro™:Placebo)
- 1 mg/kg XPro™ weekly subQ injection

Unique design elements
- small and short
- enrichment,
- precise cognitive end-point

Primary Endpoint
- EMACC

Secondary Endpoints
- CDR, ECog
- ADL, NPI
- Blood
- MRI
- Safety

EMACC and CDR: Primary end-point for Early AD clinical trials

	CDR	EMACC
Clinically derived to stage AD	+	
Empirically derived to measure cognitive change in Early AD		+
Clinically validated measurements	+	+
No floor or ceiling effects		+
Lower variance and shorter retest intervals provides smoother measure of cognitive change		+
Greater dynamic range allows measure of stable, worsening or improved cognition		+
Allows for shorter and smaller clinical trials		+

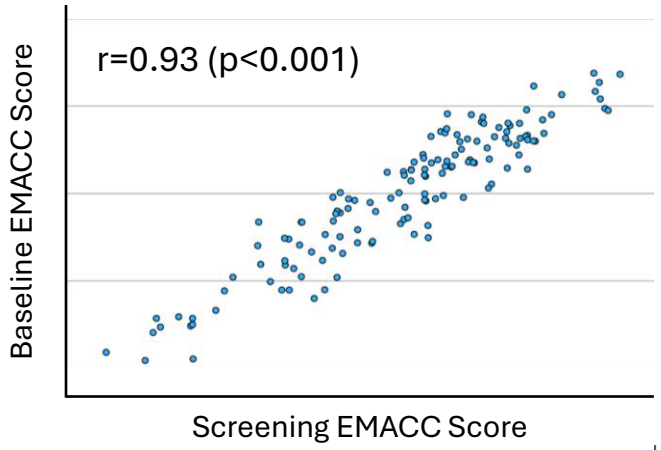
MINDFuL
A study of inflammation in Alzheimer's disease

Webinar: "Why EMACC is the Optimal Tool for Measuring Cognitive Change in Early Alzheimer's Trials"

Phase 2 Trial Summary: Smaller, Shorter, Smarter

Top Line Cognition Results in Q2 2025

- **208 patients enrolled**
  - 56% mild AD, 44% MCI
- **Enrichment for patients with elevated neuroinflammation (ADi) improves precision**
  - AD patients with inflammation progress faster and more reliably allowing for smaller trial size and shorter duration
- **EMACC is purpose built for measuring cognitive decline in patients with early AD**
  - Objective endpoints eliminate caregiver bias
  - Enables measurement of cognitive improvement or decline
- **Three-step process ensures ideal patient selection**
  - High correlation between screening test and baseline measurement




INmuneBio
INKmune™
for Oncology
Off-the-Shelf NK Therapy Converts Patient's Resting NK cells into Cancer Killing memory like NK cells

Problem: Value Proposition (efficacy vs toxicity) of treatments for mCPRC is Poor

- The Facts:
  - Incidence of prostate cancer increasing - >50,000 mCRPC patients in US
  - Current therapies average <6 month survival benefit
  - Safety profile not ideal in patients (avg age: 76 years old)

Toxicity	Total	Severe (grade3 or 4)
Neutropenia	94%	82%
Febrile Neutropenia	8%	n/a
Diarrhea	47%	6%
Nausea	34%	2%
Fatigue	37%	5%

INKmune toxicity – none reported to date

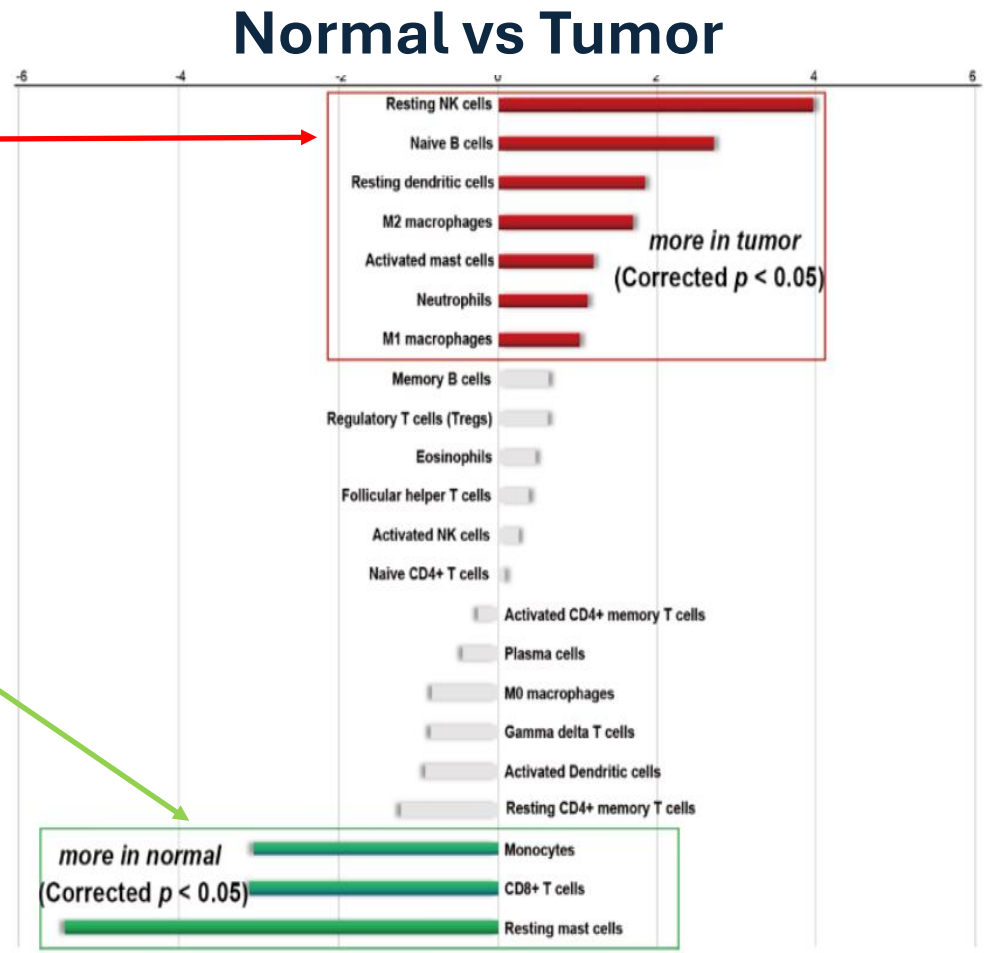
INKmune (treatment of day 1,8, and15)
20min infusion via peripheral vein
Patient goes home after 2 hours

Solution: Use INKmune™ to Match Therapy with Cancer Biology

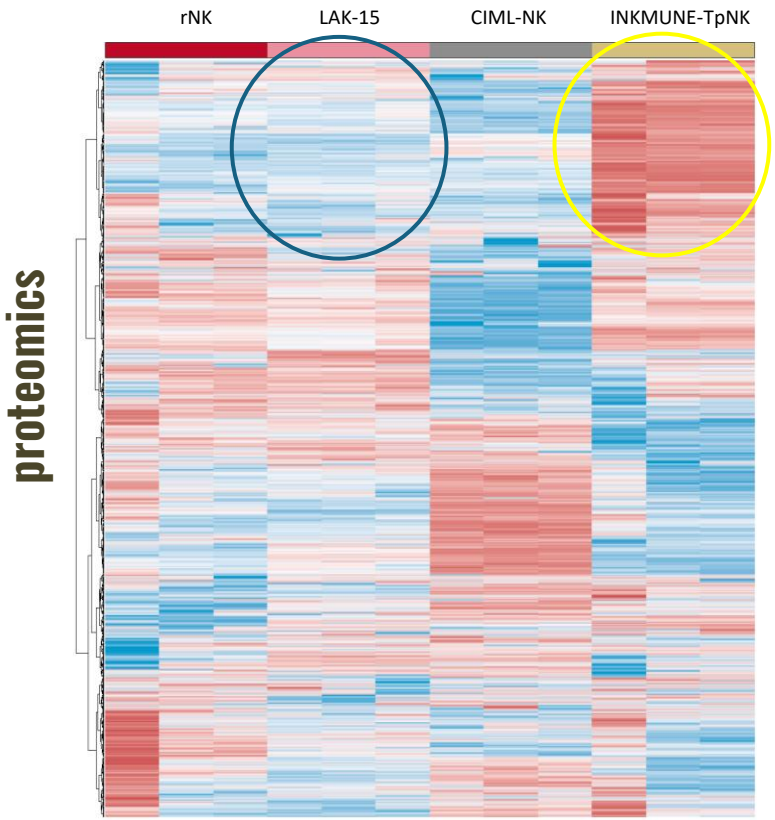
INKmune™ targets the immune cells most prominent in the Tumor MicroEnvironment (TME) of PC

- Prostate cancer immune infiltrate cells are resting NK cells ***NOT*** T cells
- Is lack of T cell infiltrate why immune checkpoint inhibitors fail in mCRPC?
- NK cells in mCRPC are resting NK cells that do not kill tumor

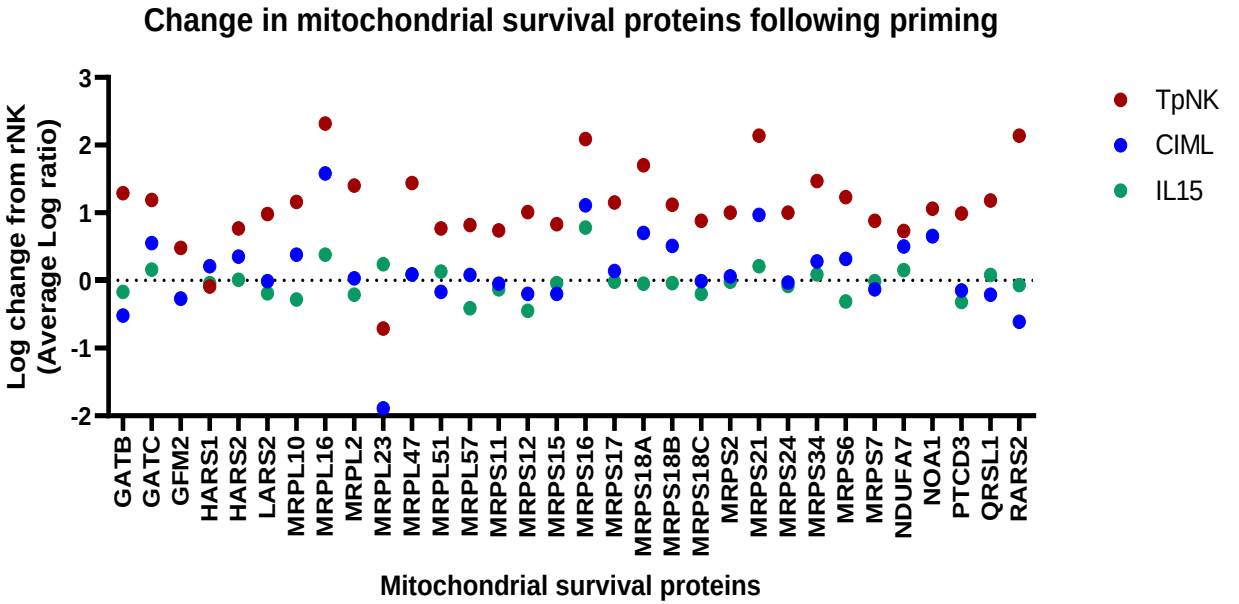
INKmune™ converts resting NK cells to cancer killing memory-like NK cells

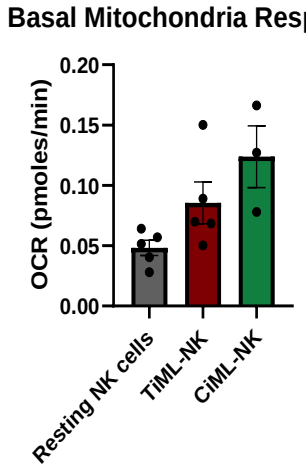


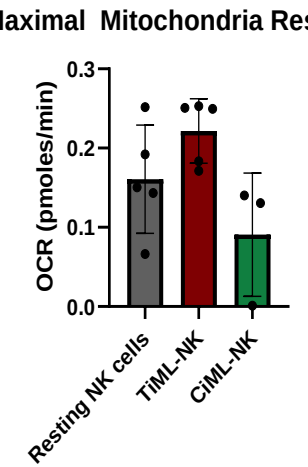
INKmune™ Primed NK Cells "Fitter" Than Cytokine Primed NK Cells

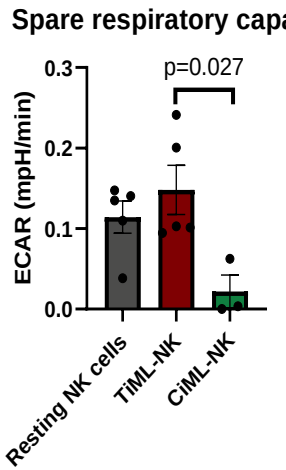


*studies of human NK cells targeting human prostate cancer cells

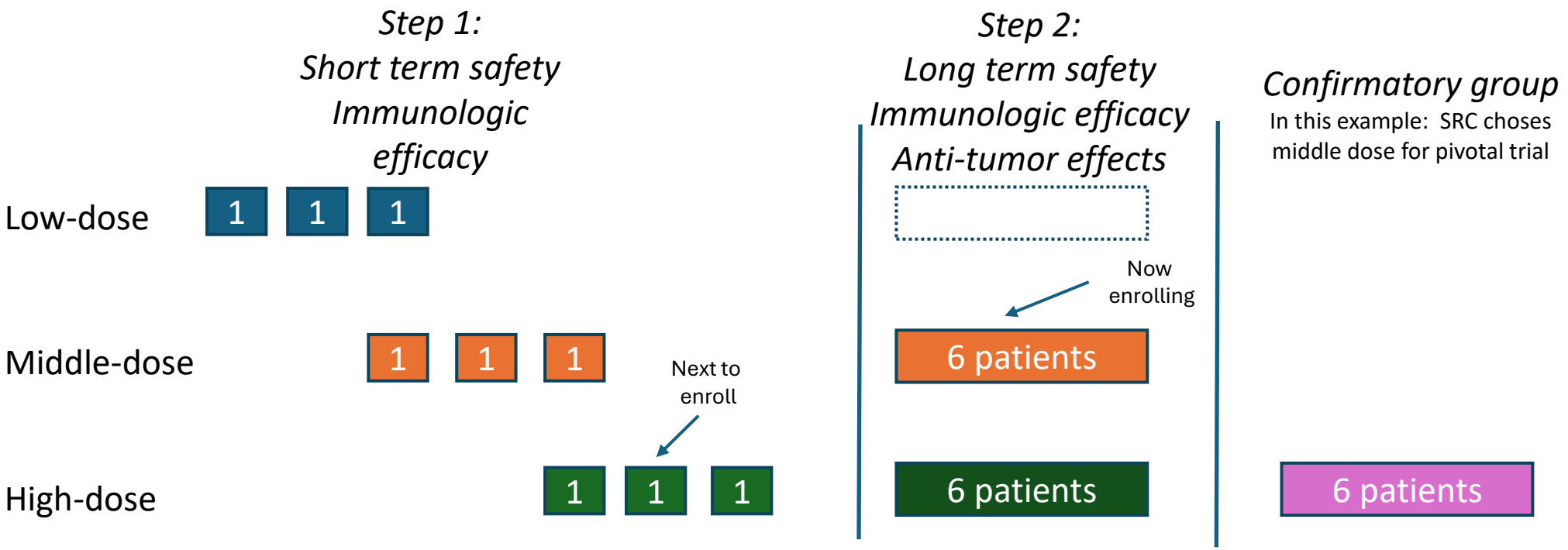








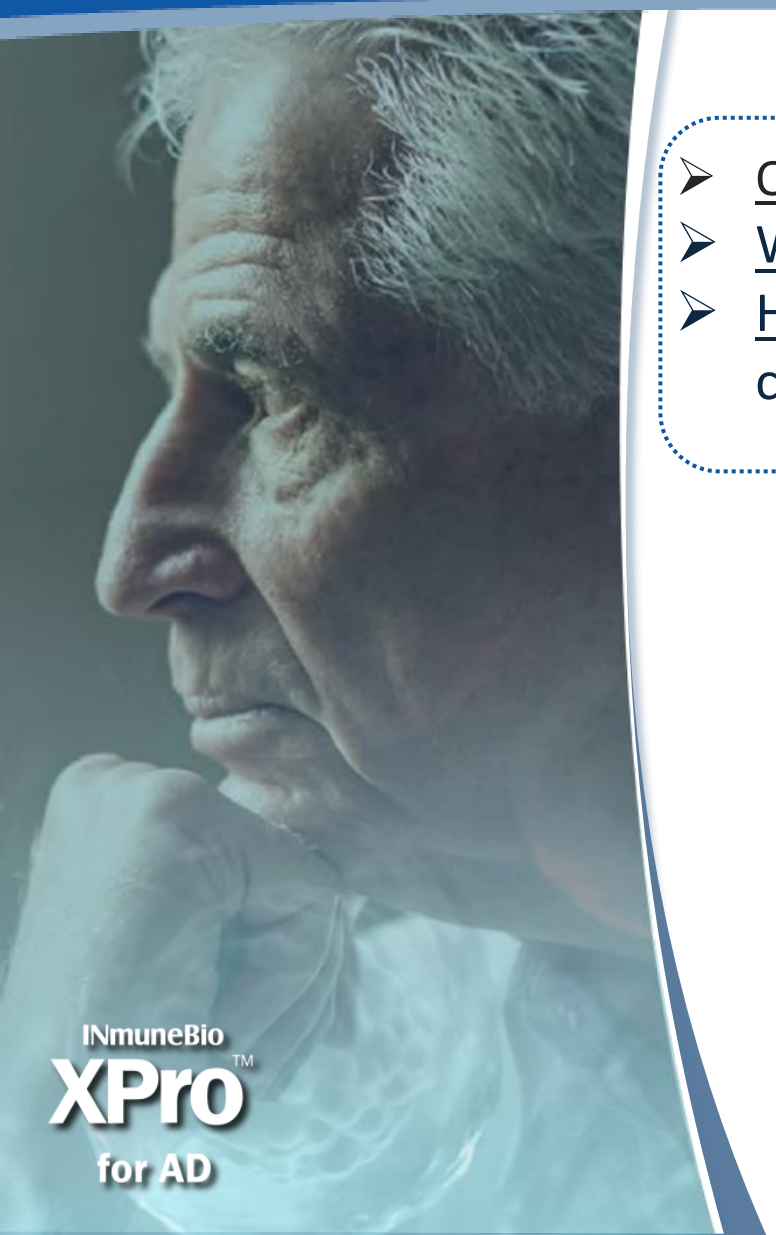
INKmune™ mCRPC Phase I/II Trial Design



Trial will determine:

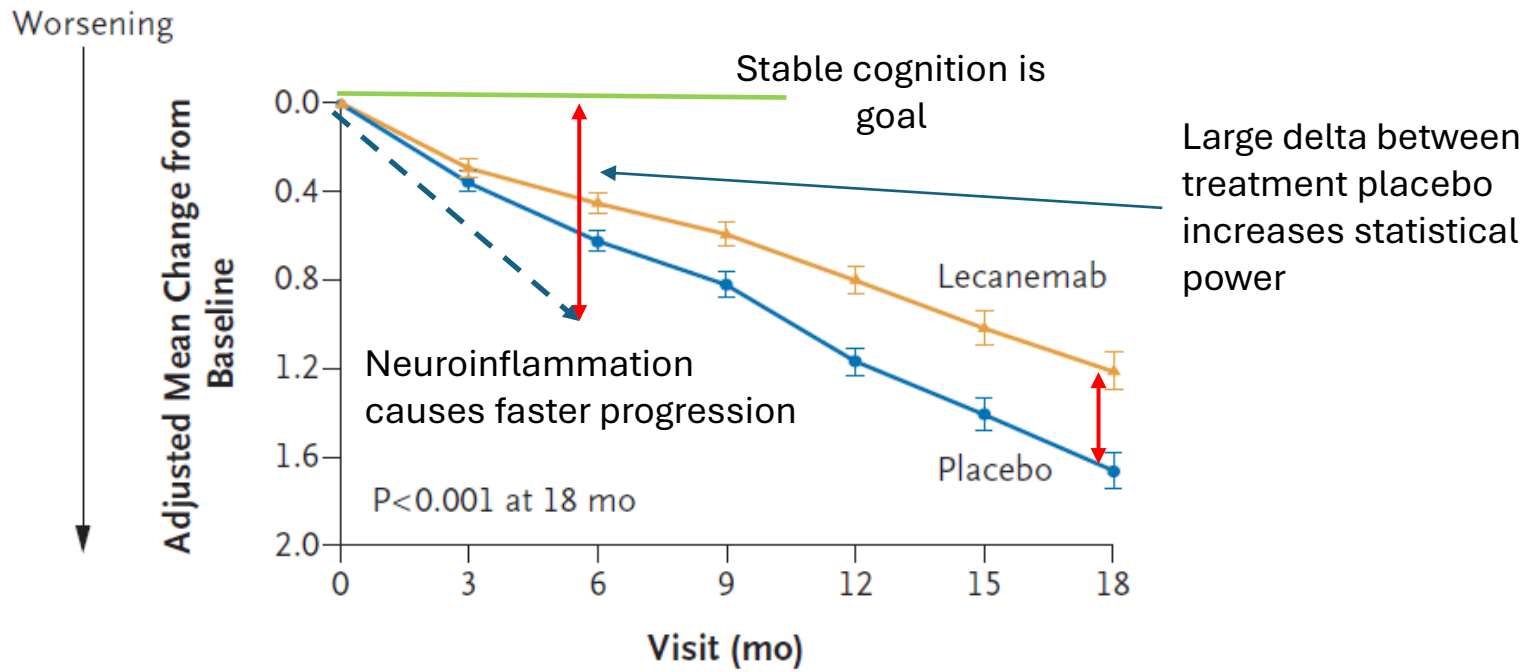
- Effective dose: safe with evidence of tumor effects
- Short and long-term safety – no drug related serious adverse effects
- Immunologic efficacy – converts patient's NK cells to mlNK cells that kill tumor cells (ex vivo assay) with long-term persistence of mlNK cells in patient's circulation
- Anti-tumor effects – evidence of control of tumor burden by PSA, PSMA and/or ctDNA

Ideal Treatment for Early AD should Flatline Cognition!



- Our Goal: Use XPro™ to PREVENT cognitive decline in Early AD
- Why: XPro targets the most important pathology in AD – neuroinflammation
- How: Use a modern precision medicine clinical trial design to derisk the clinical program by matching the XPro MOA with the patient's disease

CDR-SB Lecanemab Phase III trial (C. van Dyck, et al, 2023 NEJM)



Anticipated Milestones in 2024 and 2025

Key Upcoming Clinical & Regulatory Milestones

	EVENT	EXPECTED TIMING
XPro™	Topline Phase 2 AD Data	Q2 2025
	End of Phase 2 FDA Meeting AD	Q3 2025
	Pre-clinical Anti-AB and XPro Data	2H 2024
	Initiate Phase 2 TRD Trial	2H 2024
INKmune™	Complete Phase 2 mCRPC Enrollment	1H 2025
	Open Label Phase 2 mCRPC Data	Ongoing

Contact Us:

Inflammation and Immunology Repair

Symbol: INMB (Nasdaq)

INmune Bio Inc.
225 NE Mizner Blvd.Suite 640
Boca Raton, FL 33432
(858) 964-3720
info@inmunebio.com

Investor Relations:
Daniel Carlson
(415) 509-4590
daniel@inmunebio.com

Mike Moyer
(617) 308-4306
mmoyer@lifesciadvisors.com