INmuneBio
INNATE IMMUNITY

HARNESSING THE POWER OF THE INNATE IMMUNE SYSTEM

Inflammation & Immunology Platforms: XPro™ and INKmune™
To: Repair Innate Immune Dysfunction to Treat Disease

INMB
Nasdaq

Investor Presentation June 2024

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. INB03™, XPro1595, and INKmune™ are still in clinical trials or preparing to start clinical trials and have not been approved by the US Food and Drug Administration (FDA) or any regulatory body and there cannot be any assurance that they will be approved by the FDA or any regulatory body or that any specific results will be achieved. Forward-looking statements are subject to many risks, uncertainties and other factors that could cause our actual results, and the timing of certain events, to differ materially from any future results expressed or implied by these forward-looking statements, including, but not limited to, the risks, uncertainties, and other factors described in our filings with the U.S. Securities and Exchanges Commission, including our most recent reports on Form 10-K, 10-Q, and 8-K, and any amendments thereto.

Anticipated Milestones in 2024 and 2025

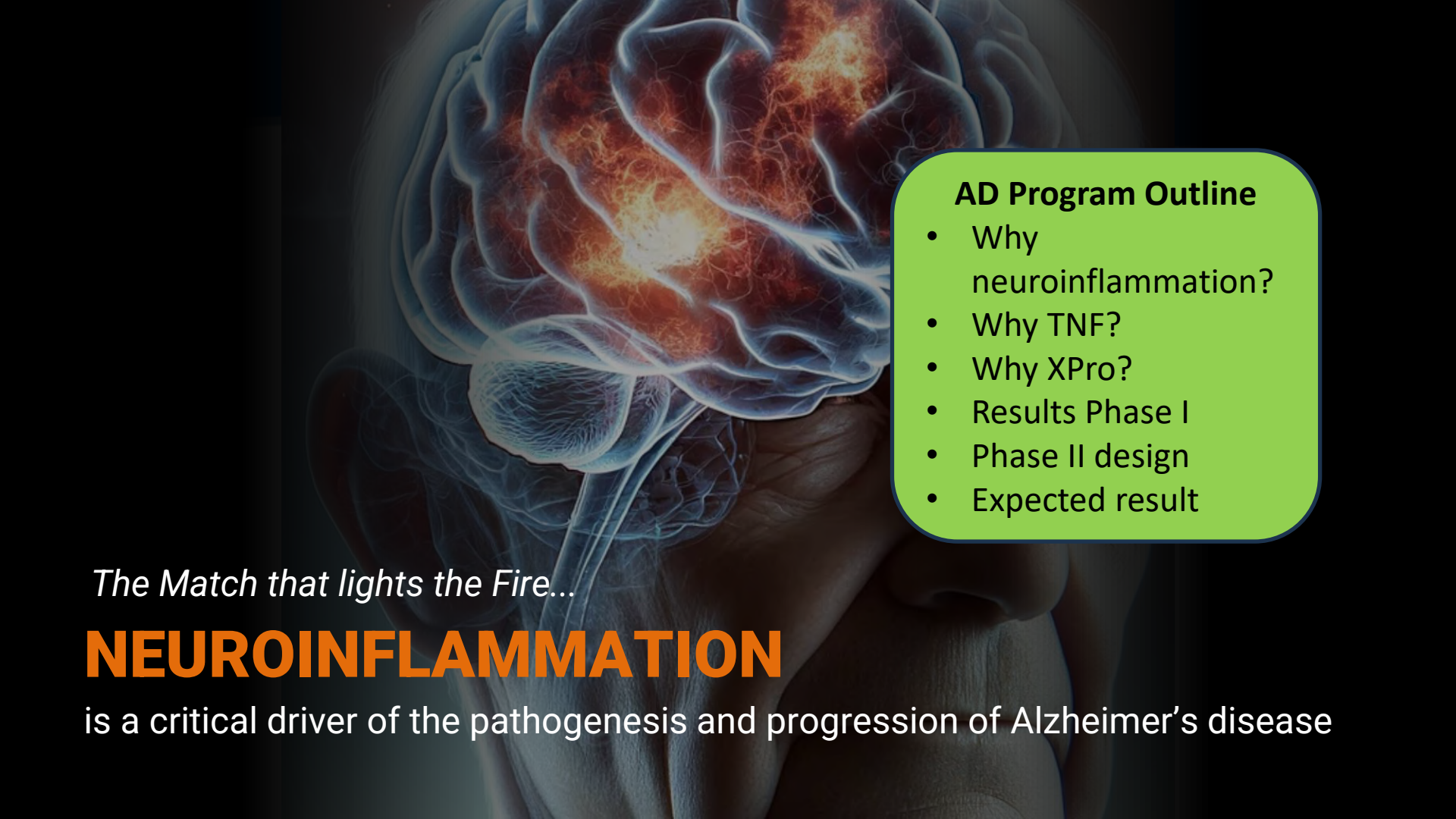
Key Upcoming Clinical & Regulatory Milestones

	EVENT	EXPECTED TIMING
XPro™	Complete Phase 2 AD enrollment	Mid 2024
	Topline Phase 2 AD data	6m from last patient enrolled
	End of Phase 2 FDA Meeting AD	Mid 2025
INKmune™	Pre-clinical Anti-AB and XPro Data	2H 2024
	Initiate Phase 2 TRD trial	2H 2024
	Complete Phase 2 mCRPC enrollment	1H 2025
	Topline Phase 2 mCRPC data	2H 2025
	End of Phase 2 FDA Meeting mCRPC	4Q 2025 or 1Q 2026

INKmune™ Open Label mCRPC Data to be Reported Periodically in 2024 and 2025

DEVELOPMENT PIPELINE

DN-TNF PLATFORM	DESEASE FIELD	PRE-CLINICAL	PHASE 1	PHASE II (POC)	PIVOTAL	EST.NEXT MILESTONE
XPro™	Early Alzheimer's Disease					Full enrollment mid-2024 Topline Data 6m later
XPro™	Treatment Resistant Depression					P2 Start 2024
pSar DN-TNF ("son of XPro")	Ophthalmology Oncology Orphan indications					Future Development
NK PRIMING PLATFORM						
INKmune™	metastatic Castrate Resistant Prostate Cancer					Open label data 2024
INKmune™	Other solid tumors					Open label 2025



AD Program Outline

- Why neuroinflammation?
- Why TNF?
- Why XPro?
- Results Phase I
- Phase II design
- Expected result

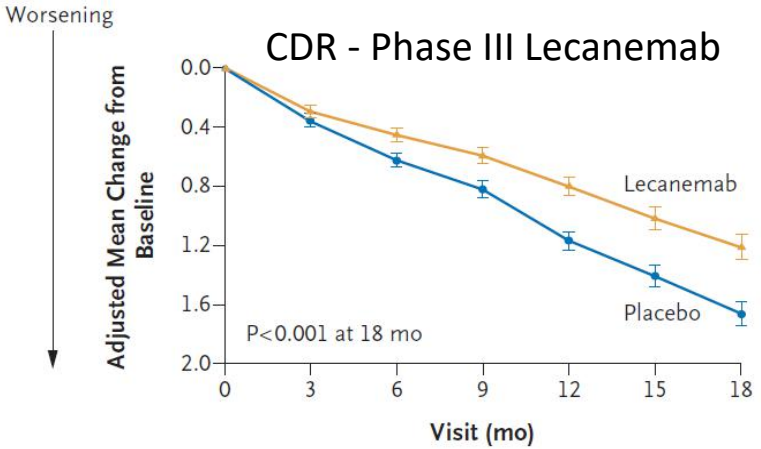
The Match that lights the Fire...

NEUROINFLAMMATION

is a critical driver of the pathogenesis and progression of Alzheimer's disease

What have we learned about treating AD in the last 3 years?

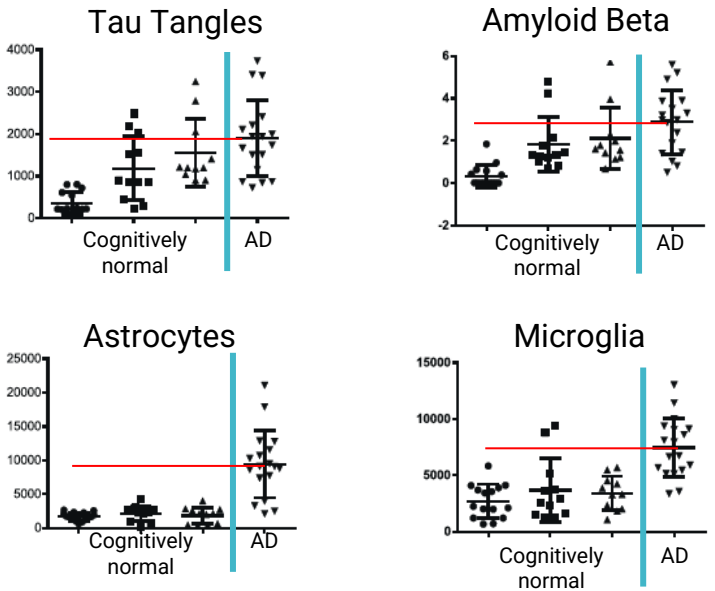
- ***The Good:*** anti-amyloid antibodies removes amyloid from brain
- ***The Surprise:*** removing amyloid plaque has limited effect on progression of cognitive decline
- ***The Bad:*** removing amyloid plaque with anti-amyloid antibodies causes ARIA
- ***The Disappointing:*** targeting tau has no effect
- ***The Conclusion:*** targeting amyloid and tau will not effectively treat cognitive decline of AD!



	% ARIA-E – ApoE4+ve	%ARIA – ApoE4-ve
Lecanemab	11%	5%
Donanemab	23%	16%

From Phase III study publications

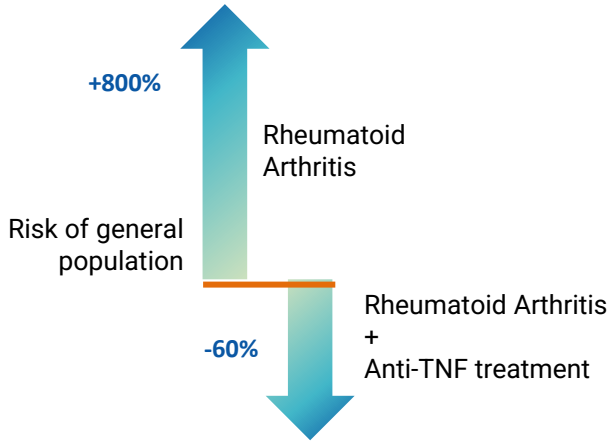
Neuroinflammation causes Cognitive Decline
soluble TNF causes Neuroinflammation



Amyloid and tau is present within the brains of AD patients ***AND*** cognitively normal people. Inflammation is increased in AD brains but ***NOT*** cognitively normal people.

Adapted from: PMID 30336198

TNF inhibitors reduce risk of developing AD

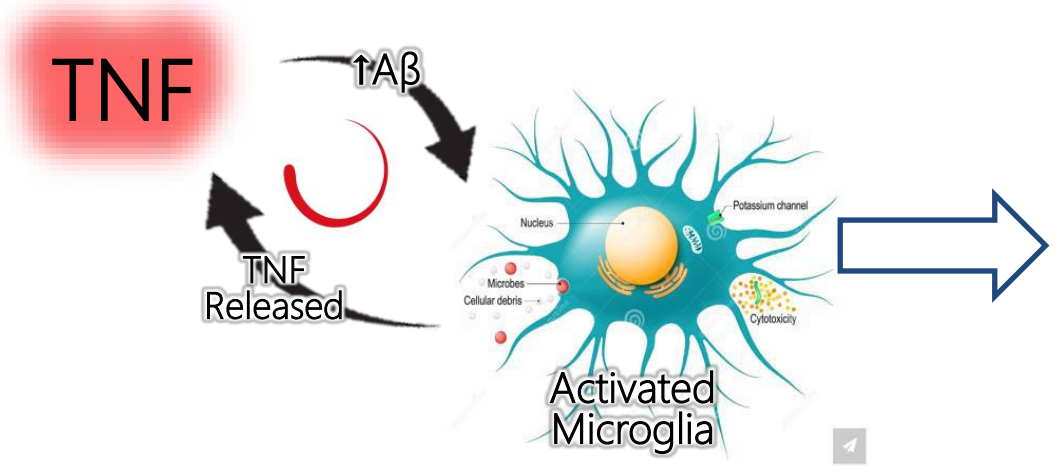


Epidemiological Studies including a meta-analysis of more than 60 Million cases Linking **TNF Blocking Agents** to Reduced Risk of AD

Adapted from PMID: 27470609, 33016914

TNF Plays a Pivotal Role in Neuroinflammation and AD

Pub MED: >1500 papers published on Neuroinflammation and AD



Essential pathologies of cognitive decline

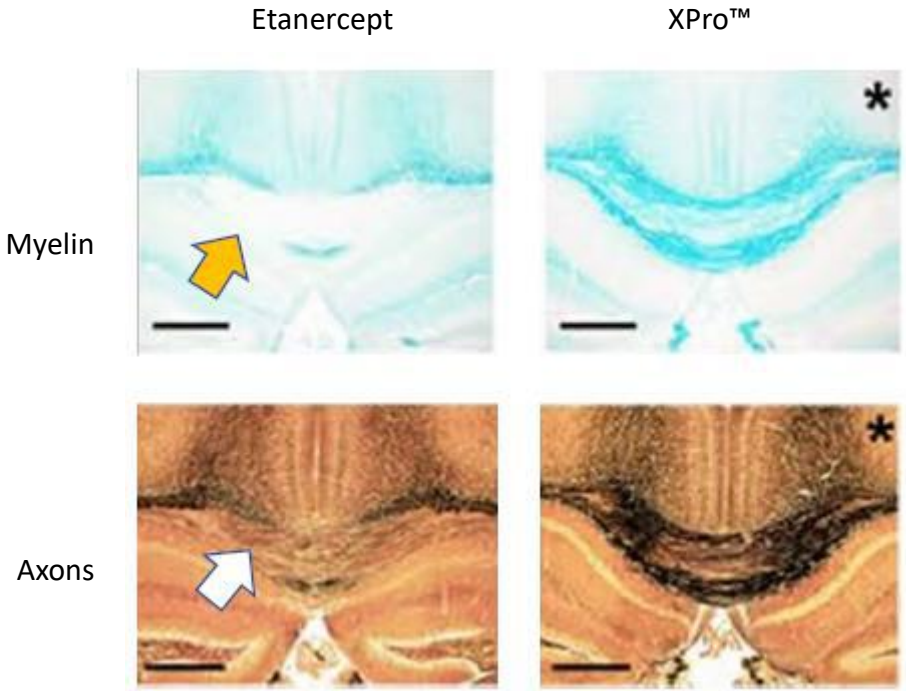
- Nerve cell death
- Synaptic Dysfunction
- Demyelination

1. Chang R, et al. *J Cent Nerv Syst Dis*. 2017;9: 1-5
2. Shamim D, et al. *J Cent Nerv Syst Dis* .2017 ;9:1-10
3. Hulshof LA, et al. *Front Cell Neurosci*. 2022;16:1-17
4. Planas-Fontánez TM, et al. *Brain Res*. 2021;1764:147464
5. Marzan DE, et al. *Glia*. 202;69(6):1583–1604

If drug therapy does not address these problems.
It will not be an effective therapy for AD

XPro™ Safely Prevents Neuroinflammation without Axonal Degeneration and Demyelination

- Currently approve non-selective TNF inhibitors contraindicated in treatment of neurologic diseases like AD
- Currently approved non-selective TNF inhibitors (eg: Etanercept) promote demyelination (yellow arrow) and axonal degeneration (white arrows)
- XPro™ promotes remyelination and axonal regeneration.

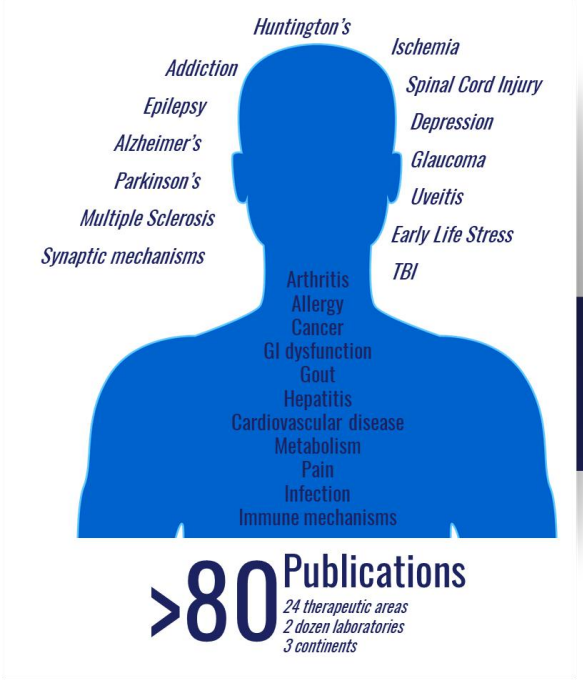


Karamita; Therapeutic inhibition of soluble brain TNF promotes remyelination by increasing myelin phagocytosis by microglia. https://doi.org/10.1172/jci.insight.87455

Traditional TNF Inhibitors Cause Immunosupression and Demyelination

XPro Addresses the Side-effects of Currently Approved TNF Inhibitors

XPro1595 summary



	Non-selective TNF inhibitors	XPro1595
Decreases inflammation	yes	yes
Immunosuppression	yes	No
Demyelination	yes	No
Neuroprotective	no	yes
Enhances neuroplasticity	no	yes

PHASE 1B CLINICAL TRIAL DESIGN AND RESULTS

N=18 : 6 Patients per Cohort

Goals

Study Design

- Open label, three dose, 3-month study
  - 0.3 mg/kg
  - 0.6 mg/kg
  - 1.0 mg/kg
- XPro1595 administered via weekly Subcutaneous injections
- Biomarkers assessed at baseline and 3 months

Key Enrollment criteria

- AD Diagnosis

Plus at least one of the ***following inflammatory biomarkers:***

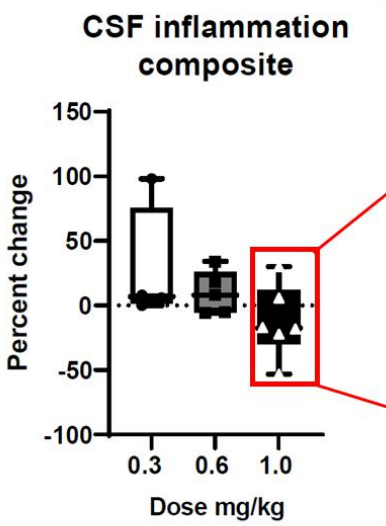
- C-reactive Protein >1.5 mg/mL
- Erythrocyte sedimentation rate > 10 mm/Hr
- Hemoglobin A1c > 6% DSST
- One APOE4 allele

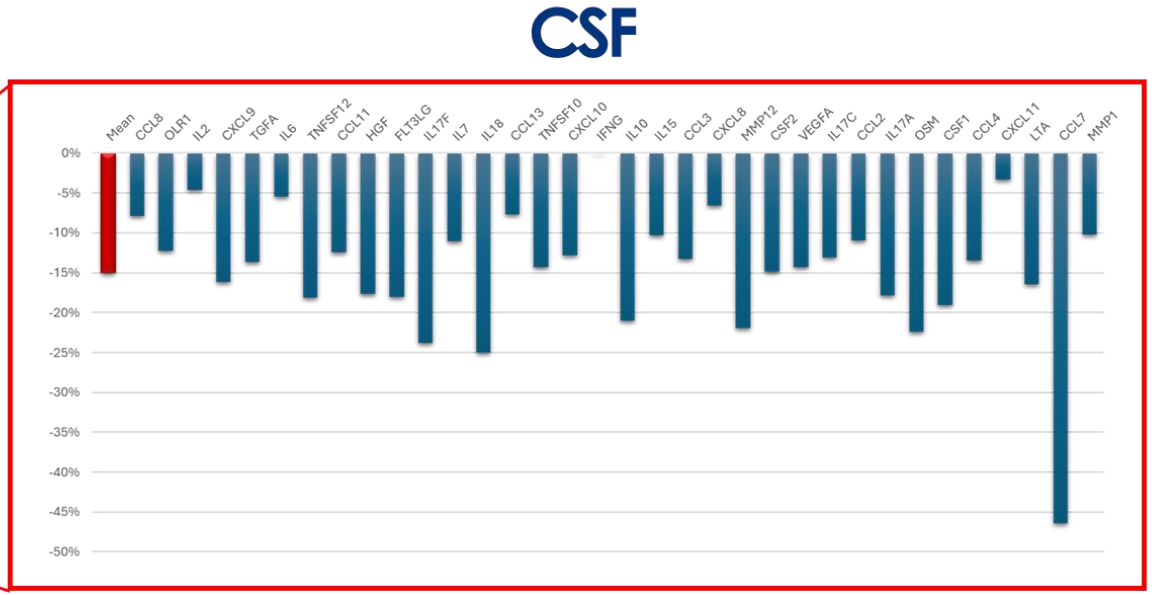
- Safety
- Reduce Biomarkers of Neuroinflammation
- Reduce Biomarkers of Neurodegeneration
- Dose Identification
- Confirm enrichment criteria identify patients with Neuroinflammation

Phase 1b Results: TARGET ENGAGEMENT

XPro™ DECREASES NEUROINFLAMMATION IN AD Patients

Decreased Inflammatory Cytokines in CSF after 3 months at 1mg/kg/QW dose





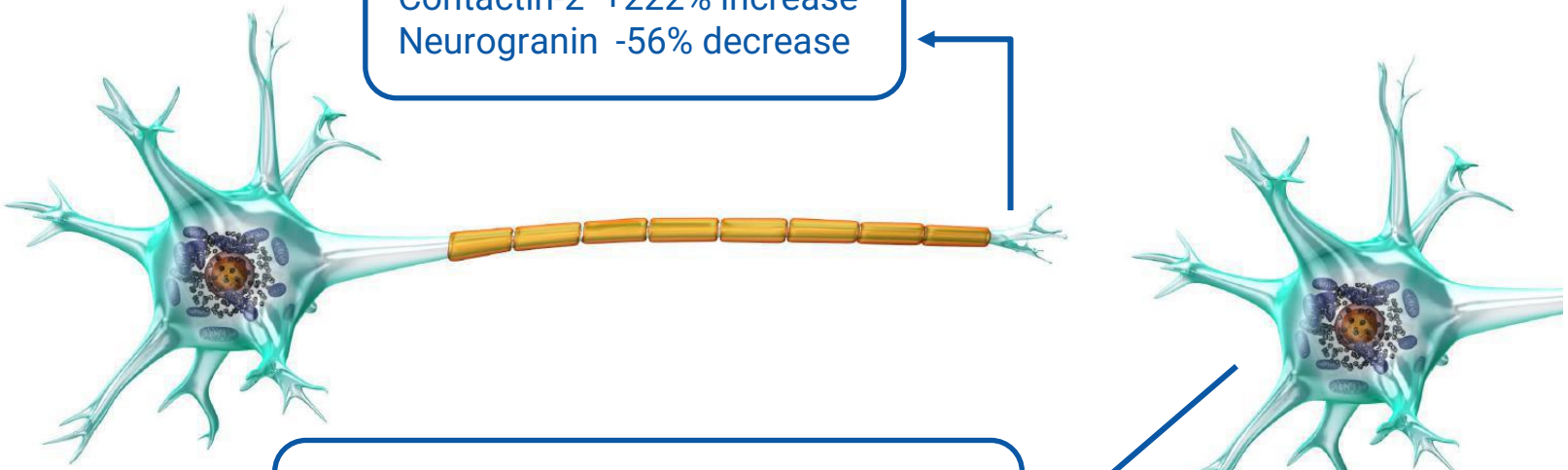
**1 mg/kg group (N=6)*

Phase 1b Results: CSF PROTEOMICS

XPro™ Decreases Neurodegeneration and Improves Synaptic Function

Downstream benefits of decreasing neuroinflammation

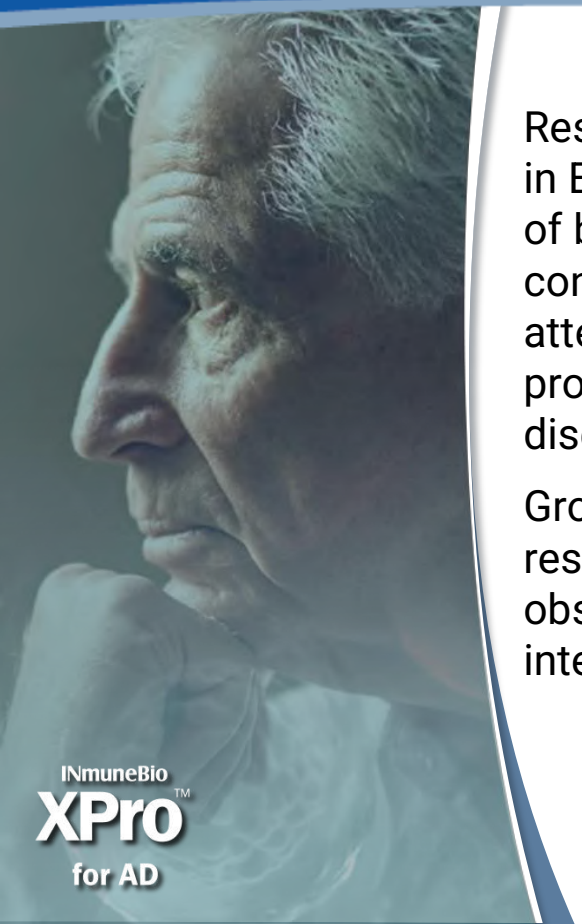
Synaptic Proteins
Contactin-2 +222% increase
Neurogranin -56% decrease



Neuronal Injury
pTau 217 -46% decrease
Visinin-like protein 1 (VILIP-1) -91% decrease

Functional Change in AD Patients after 4 weeks of XPro™

Pilot study of 7 moderate to severe AD Patients; 1 mg/kg once a week subQ

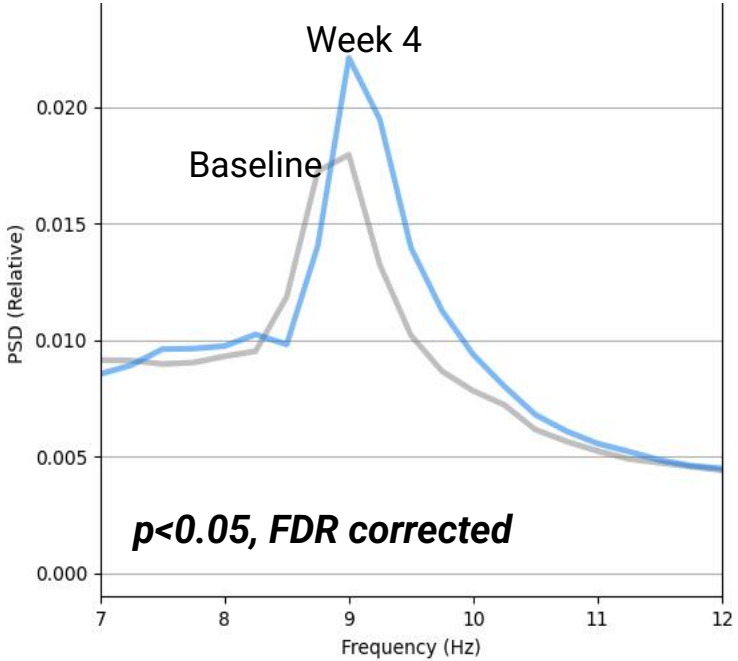


Resting alpha-band power in EEG is a broad measure of brain network connectivity, which is attenuated with the progression of Alzheimer's disease.

Group level increase in resting alpha power was observed over the 4-week intervention with XPro

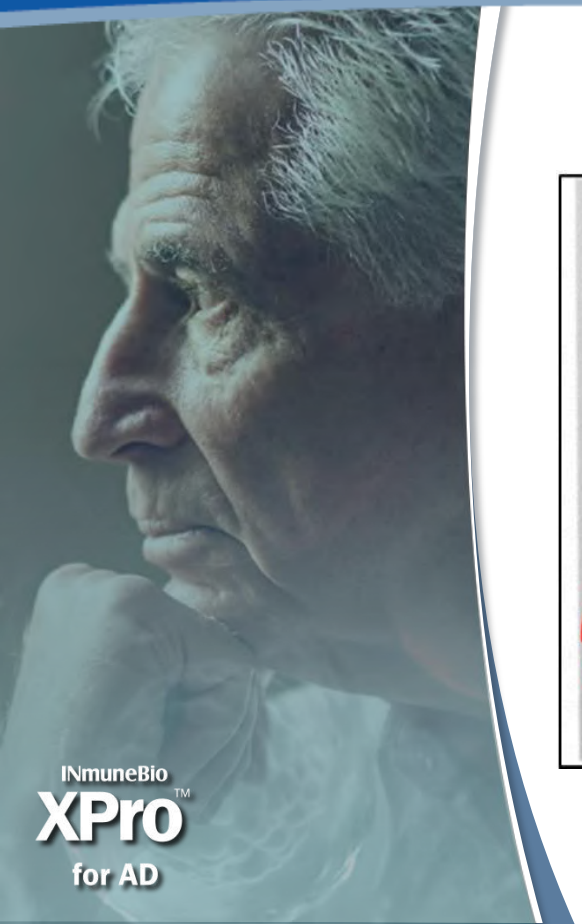
Cumulus

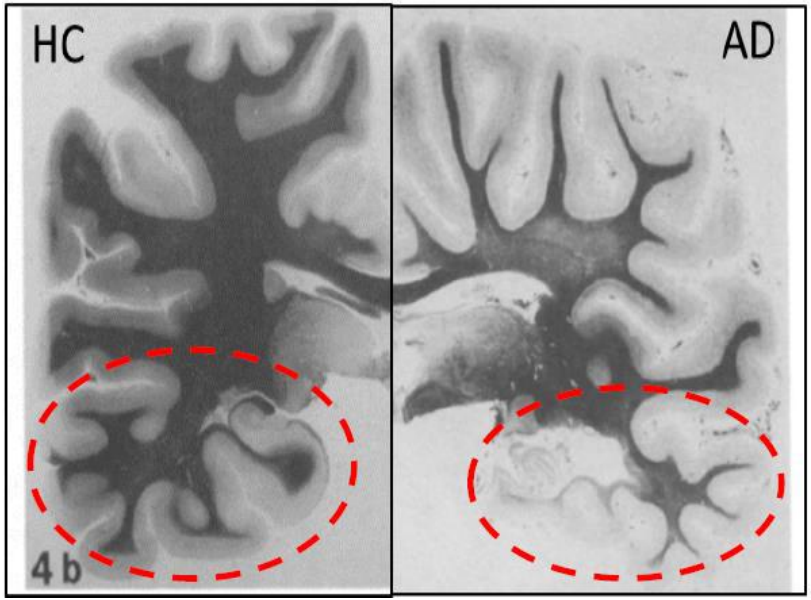
EEG Alpha Power after 4 weeks of XPro1595 treatment

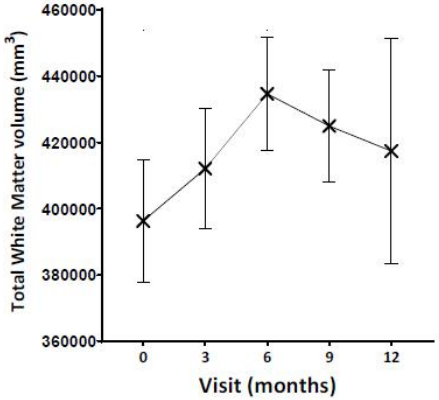


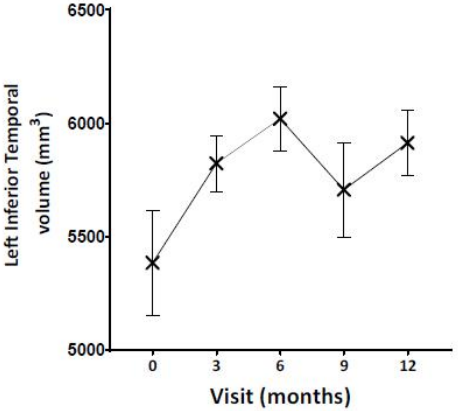
Phase 1b Data

Structural Benefit: XPro™ INCREASED WHITE MATTER VOLUME

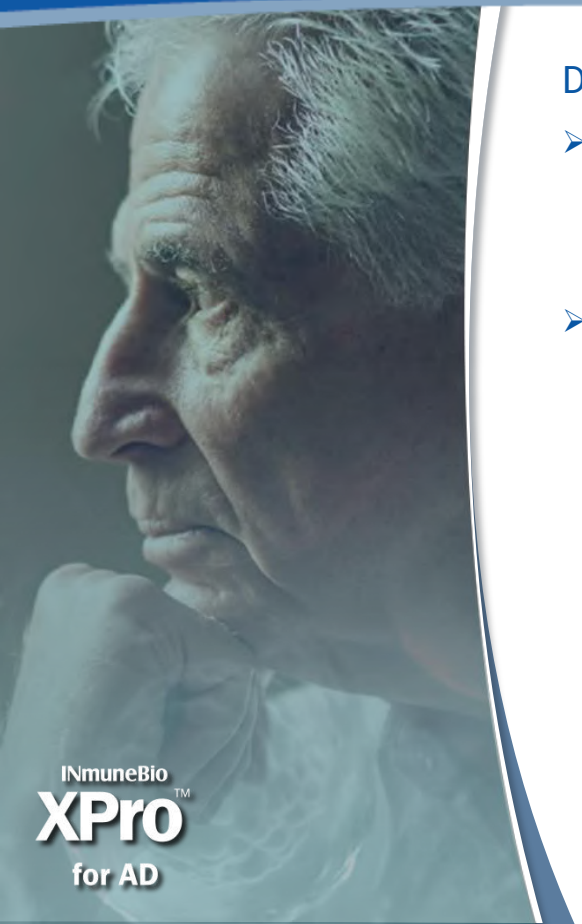








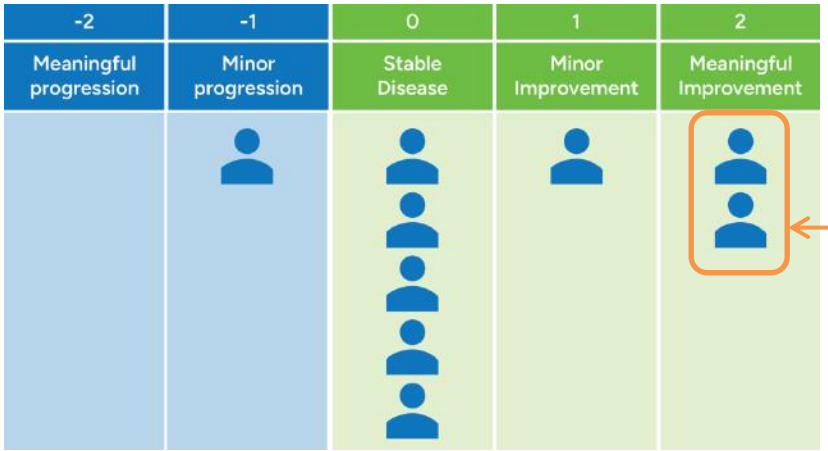
CLINICAL BENEFIT IN PHASE I TRIAL: stable disease



Disclaimer: small N, disease status heterogeneity, short time period

- Assessments administered:
  - Cognitive: MMSE, Verbal Fluency Test, Digit Symbol Coding
  - Neuropsychiatric Inventory
  - Bristol Activities of Daily Living Scale

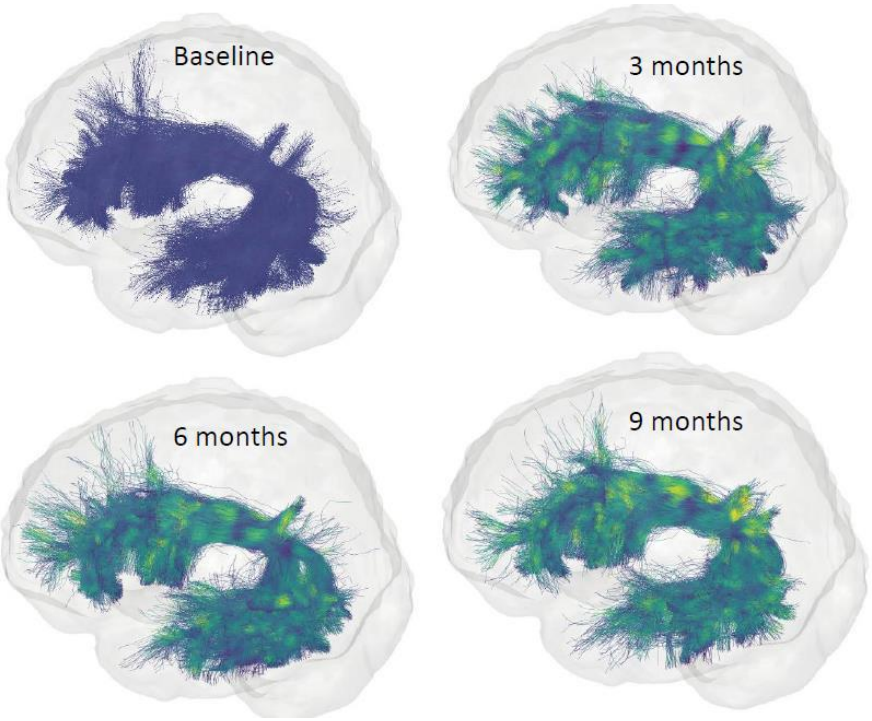
- To compare across patients of different disease states, Dr. Judith Jaeger issued each patient a qualitative score of (-2, -1, 0, 1 ,2) based on her assessment of the overall change over 3 months.



Patients with the greatest improvement in cognition had the largest reduction in neuroinflammation

Phase 1b Results: Changes in Axonal Fiber Density (AFD) in AD White Matter Tracts

REMODELING AND REPAIR OF WHITE MATTER TRACTS AFTER XPro™



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

A 6 MONTH, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF XPro™ IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE WITH BIOMARKERS OF INFLAMMATION

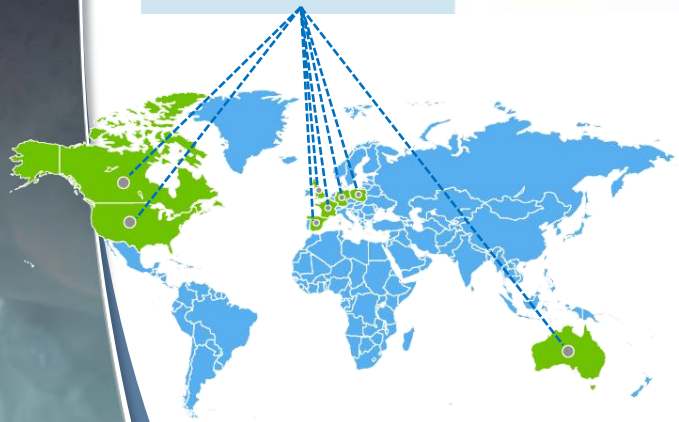
Key enrollment criterion

- 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

Primary Endpoint
- EMACC



Treatment
- 2:1 (XPro1595:Placebo)
- 1 mg/kg XPro1595 weekly subQ injection

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

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

EMACC: Early/ Mild Alzheimer's Cognitive Composite

Why use EMACC as our primary endpoint?

The EMACC provides an accurate cognitive assessment in patients with **Early** Alzheimer's Disease

Measure what matters!

- Traditional endpoints (CDR/ADAS-Cog) optimized for cognitive changes that occur in *moderate to severe* AD patients. These are not the same cognitive changes that occur during early AD.

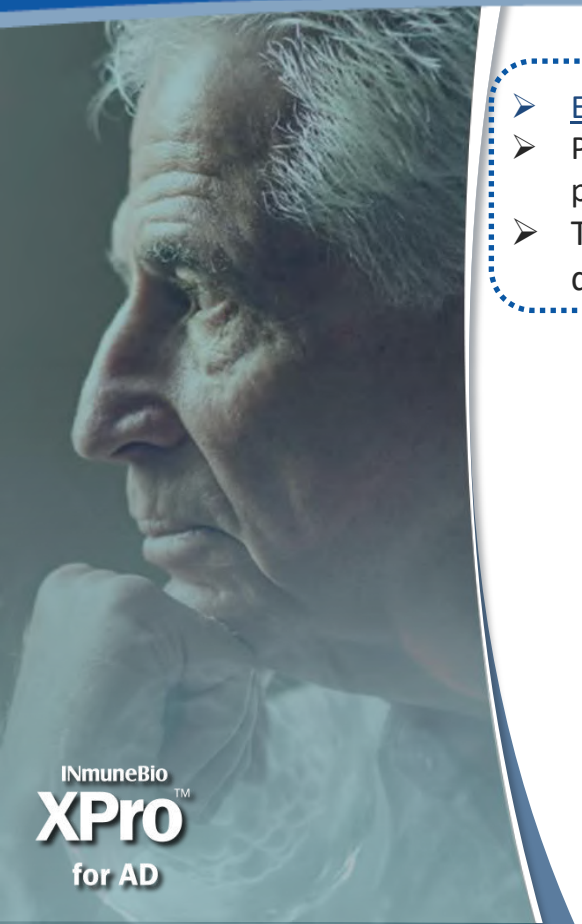
Psychometrically "sound"

- EMACC was empirically derived by pharma to measure change in Early AD
- No floor or ceiling effects
- Lower variance and shorter retest intervals provides smoother measure of cognitive change

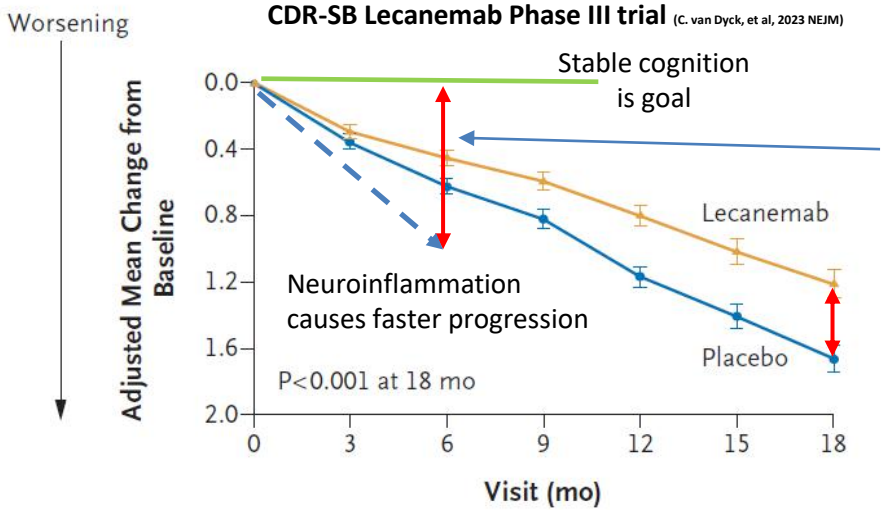
Why is this important?

- Greater dynamic range allows measure of stable, worsening or improved cognition
- Allows for shorter and smaller clinical trials

STATISTICAL POWER: WHY XPro CLINICAL TRIALS ARE SHORT AND SMALL



- Enrichment strategy selects patients with neuroinflammation
- Patients with neuroinflammation have faster cognitive decline with lower variance than patients without neuroinflammation resulting in steeper decline of placebo group
- The goal of XPro therapy in AD is to PREVENT cognitive decline not SLOW cognitive decline



Large delta between treatment placebo increases statistical power

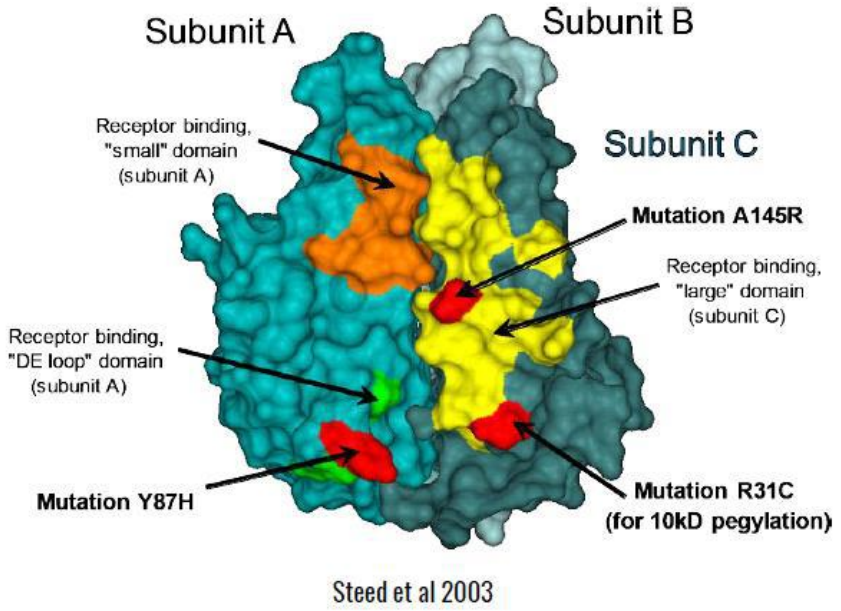
SUMMARY: PHASE 2 XPro FOR AD

ENROLLMENT TO COMPLETE MID 2024 WITH TOP LINE DATA APPROXIMATELY 6 MONTHS FROM LAST ENROLLMENT

- **Enriching for patients that have AD with inflammation (ADi) derisks Phase II clinical trial**
  - ADi patients have faster progressing disease with less variance derisks clinical trial design
- **Primary end-point is cognitive and functional measures that are meaningful and relevant for Early AD patients**
  - EMACC has greater dynamic range to detect change in the appropriate cognitive symptoms
  - GAS allows us to assess cognitive functional change important to each patient.
  - EMACC will detect cognitive improvement
- **Statistical plan equivalent to industry standard using CDR**
  - 6-month CDR end-point identical to lecanemab and donanemab Phase III trials

XPro: A TNF INHIBITOR DESIGNED TO TREAT NEUROLOGIC DISEASE

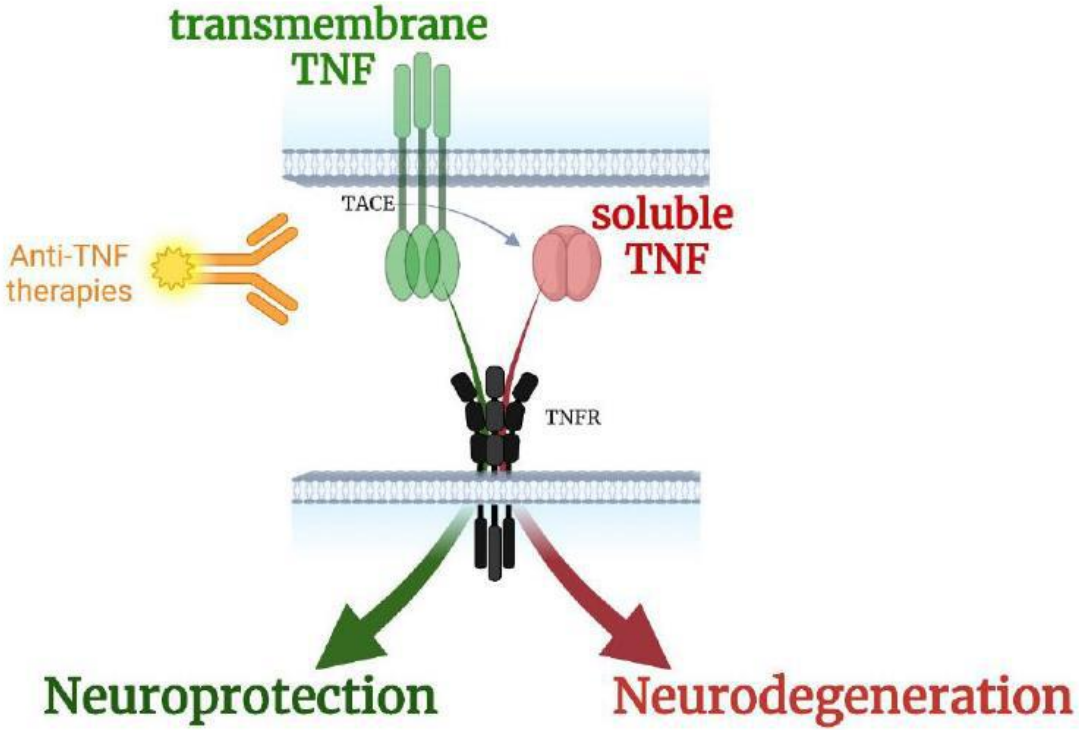
XPro1595: a selective inhibitor of ONLY soluble TNF



Steed et al 2003

XPro1595 is identical to the human soluble TNF monomer with the exception of mutations in the receptor binding domain and another for pegylation.

TNF BIOLOGY IS COMPLICATED: TWO CYTOKINES WITH OPPOSITE EFFECTS

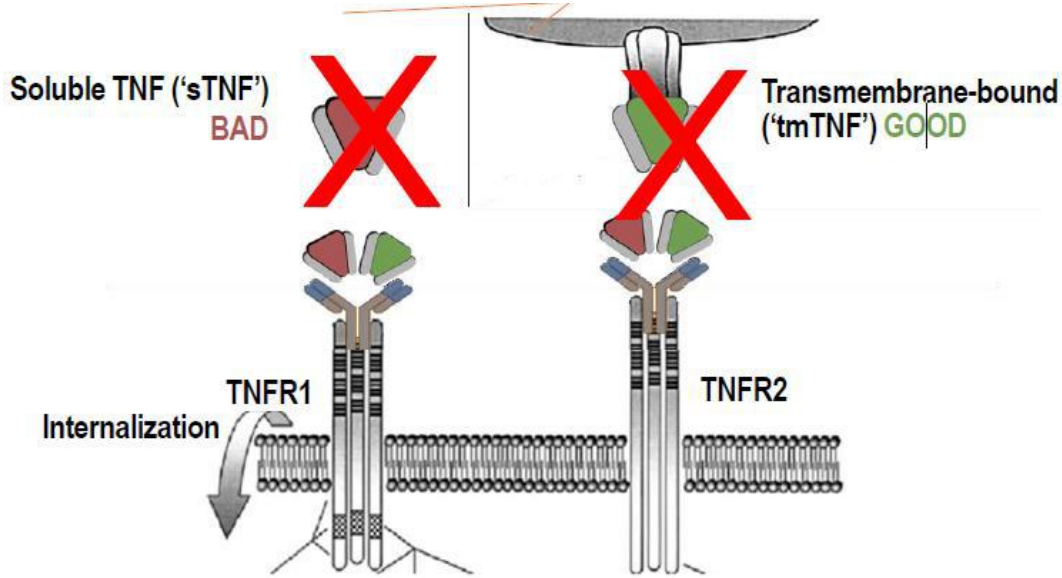


XPro IS VERY DIFFERENT FROM CURRENTLY APPROVED TNF DRUGS

Precise neutralization of the TNF ligand that drives disease

- **Soluble TNF (sTNF):** "bad" TNF that is known to cause acute and chronic inflammation and cell death
- **Transmembrane TNF** (tmTNF): "good" TNF improves the immune response, is neuroprotective and promotes remyelination

Approved TNF inhibitors block both cytokines



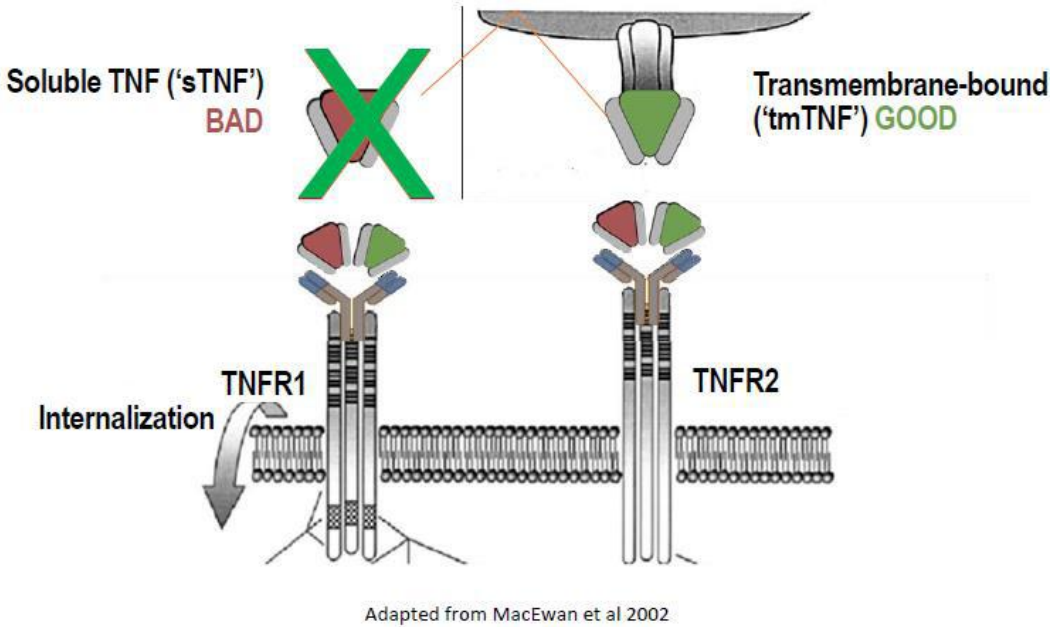
D. MacEwan et al, Cellular Signaling, 2002

XPro IS VERY DIFFERENT FROM CURRENTLY AVAILABLE DRUGS

Precise neutralization of the TNF ligand that drives disease

- **Soluble TNF (sTNF):** "bad" TNF that is known to cause acute and chronic inflammation and cell death
- **Transmembrane TNF** (tmTNF): "good" TNF improves the immune response, is neuroprotective and promotes remyelination
- **Safety:** Preserving tmTNF function prevents immunosuppression and demyelination

XPro blocks soluble TNF



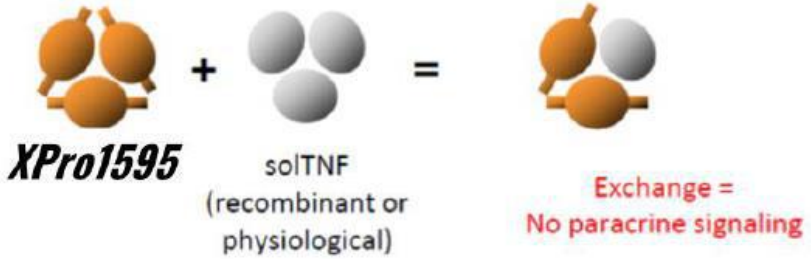
Adapted from MacEwan et al 2002

XPro UNIQUE MECHANISM OF ACTION

Precise neutralization of the soluble TNF using Dominant-Negative technology

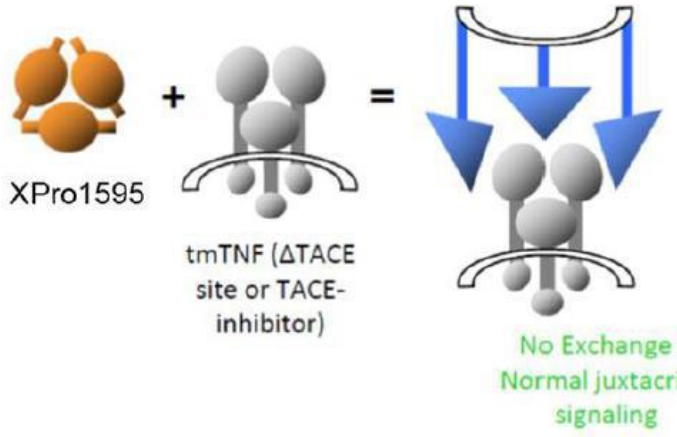
Xpro1595 freely exchanges with soluble TNF monomers to form inactive heterotrimers

Inflammatory soluble TNF eliminated:
No paracrine signaling through receptors



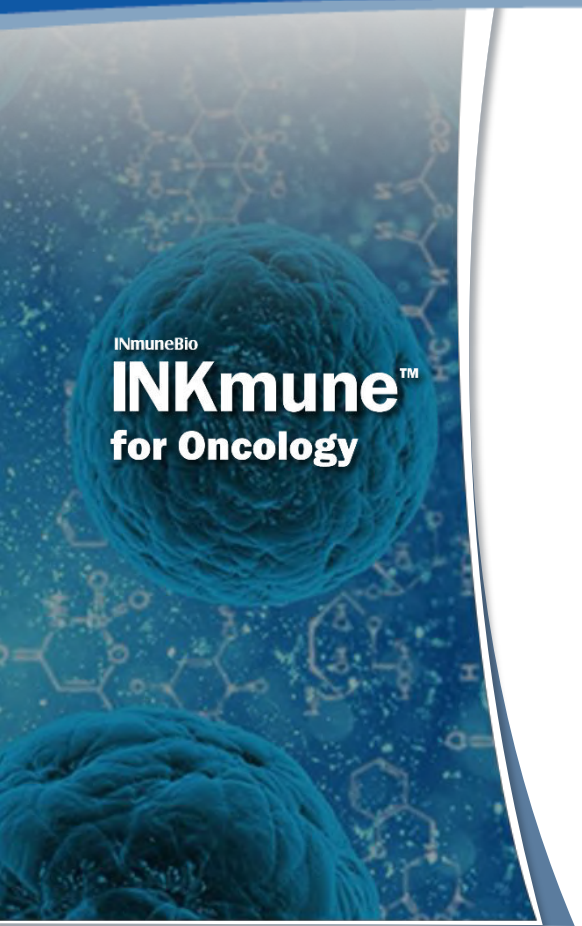
tmTNF homotrimers are anchored to the cell membrane, XPro1595 cannot exchange

Immuno protective transmembrane TNF
unaffected: Allow juxtracrine cell-cell signaling




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

INKMUNE NK CELL PRIMING PROGRAM IN CANCER

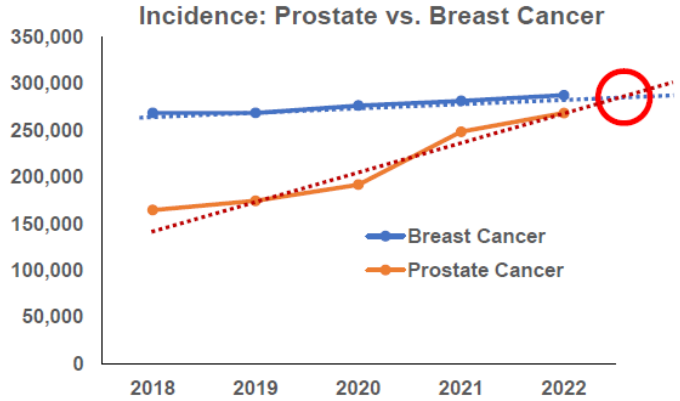


- Novel technology with strong patent protection
- Off-the-shelf program with scalable manufacturing
- Focus on solid tumors
- Timeline:
  - Select patient level data 2H24
  - Phase II data 2H25

PROSTATE CANCER INCIDENCE AND MORTALITY

INmuneBio
INKmune™
for Oncology

Prostate Cancer	2018	2019	2020	2021	2022
Incidence	164,690	174,650	191,930	248,530	268,490
Mortality	29,430	31,620	33,330	34,130	34,500



Rettig 2024

MONTHLY MEDIAN OS BENEFIT OF DRUGS APPROVED FOR mCRPC

INmuneBio
INKmune™
for Oncology

Agent	Sipuleucel-T	Abiraterone	Enzalutamide
Median OS benefit (Months)	4.1	Post-doc: 4.6 Pre-doc: 4.0	Post-doc: 4.8 Pre-doc: 4.0

Docetaxel	Cabazitaxel	Radium-223	PSMA RLT	Olaparib
2.4	2.4	3.6	5.3	2.3

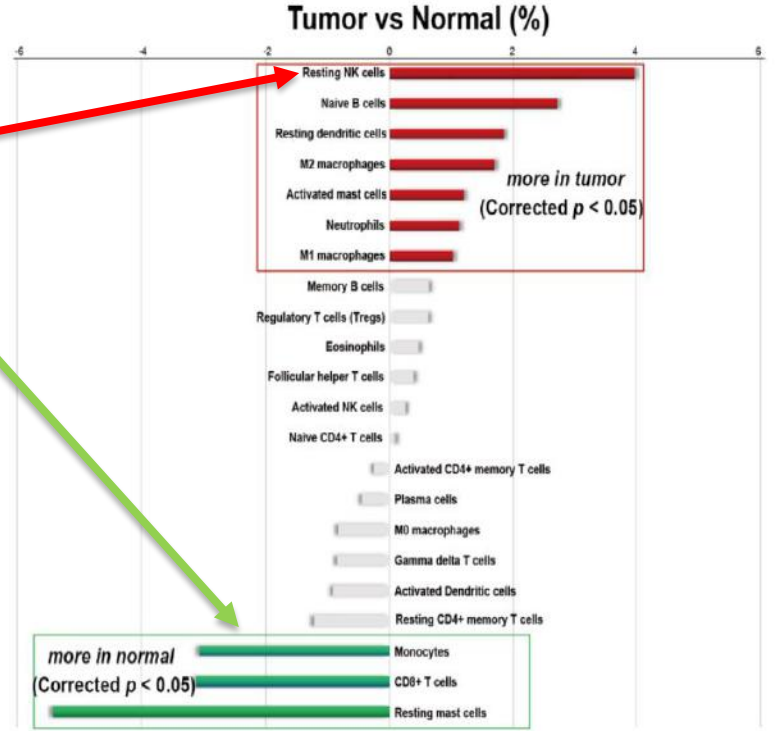
Rettig 2024

INKmune™ Activates Resting NK Cells in mCRPC

Targeting the cells in the TME is critical for control of cancer

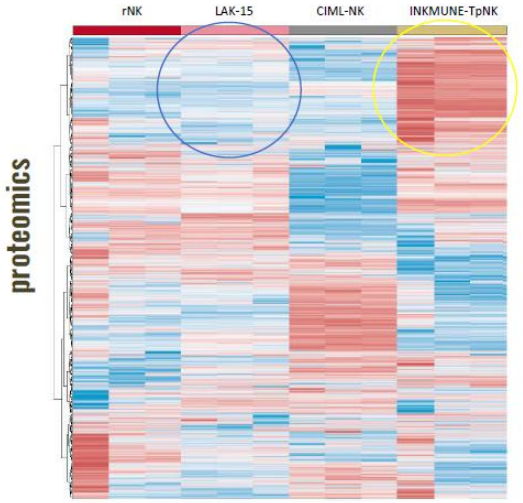
INmuneBio
INKmune™
for Oncology

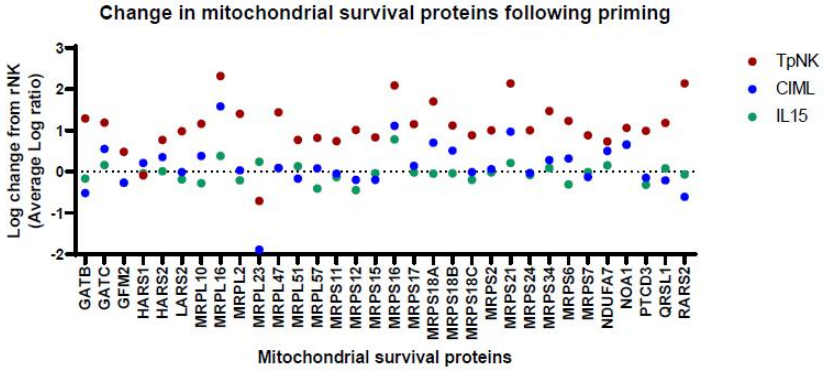
- Prostate cancer immune infiltrate cells are resting NK cells *not* T cells
- Is lack of T cell infiltrate why PDL1 and TIGIT fail in mCRPC?
- NK cells in mCRPC are resting NK cells that do not kill tumor
- INKmune goal: convert resting NK cells to cancer killing memory like NK cells

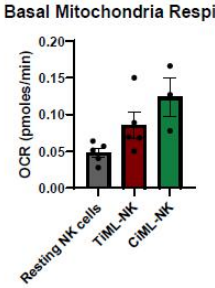


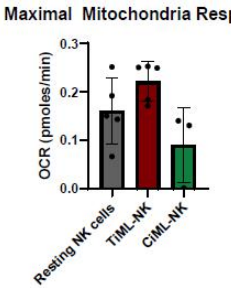
INKMUNE PRIMED NK CELLS PRODUCE CANCER KILLING MEMORY LIKE NK CELLS

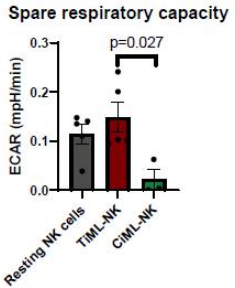
INKmune induces a unique NK cell that survives in a hostile TME to kill tumor cells





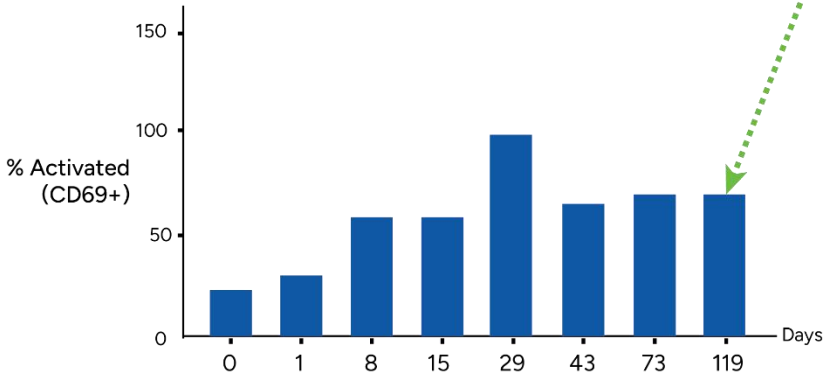




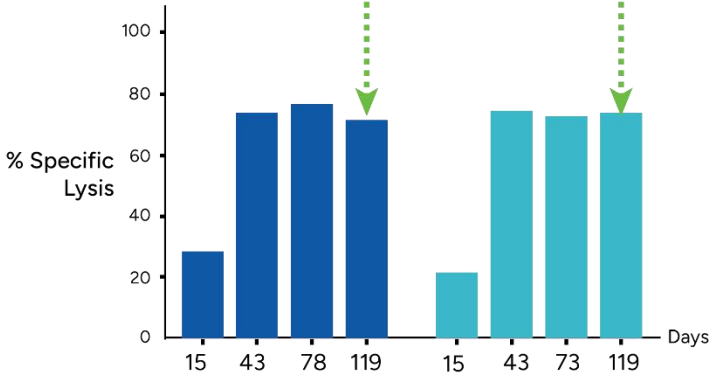


PERSISTENCE MAY BE THE KEY: INKMUNE™ PHASE 1 HUMAN RESULTS

Persistence of activatedtumor-killing memory-like NK cells in blood at 119 days



INKMUNE activated tumor- killing NKG2D+ NK Cells



PB NK + K562
NK - sensitive

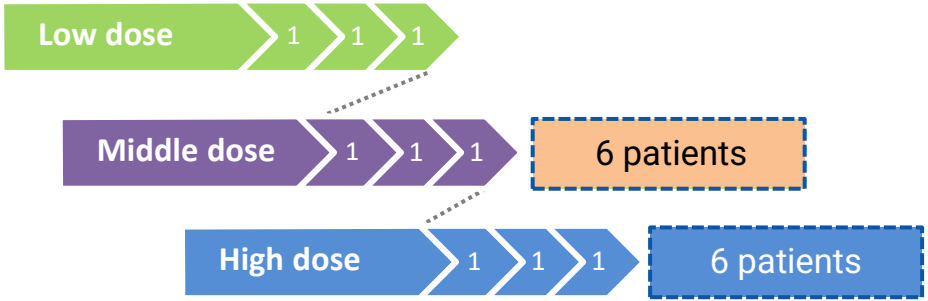
PB NK + Raji
NK - resitant

Safe and well-tolerated as an out-patient
Controls disease with excellent QOL

INKmune mBION12 mCRPC

Currently enrolling middle dose of Phase I portion of trial

Step 1	Step 2	Optional Step 3



6 patient confirmatory group

6 patients

27-30 patients treated at 8 US sites

- ✓ Inclusion criteria: mCRPC without contraindications or recent chemo or immunotherapy
- ✓ Inclusion criteria: mCRPC without contraindications or recent chemo or immunotherapy
- ✓ Definition of effective dose
  - •Safe
  - •Evidence of anti-tumor effects
  - •Manufacturing efficiency

Definitions:

•Short and long-term safety – no drug related SAE
•Short-term immunologic efficacy – converts patient's NK cells to mINK cells that kill tumor cells (ex vivo assay)
•Long-term immunologic efficacy – persistence of mINK cells in patient's circulation
•Anti-tumor effects – evidence of control of tumor burden by PSA, PSMA and/or ctDNA

INTELLECTUAL PROPERTY SUITE

Patent Exclusivity + Ref. Biologic Exclusivity

DN-TNF PLATFORM

10 issued patents
21 pending apps

31 global patent properties

- Compositions
- Formulations
- Treatment Methods

Patent Coverage thru 2033*

Exclusive Patent Licenses
- Xencor
- Pitt

**# years from Marketing Authorization, varies by jurisdiction:

US	12 years**
EP	10 years**
AU	5 years**
CA	8 years**
CN	8 years**
JP	6 years**
KR	6 years**

NK PRIMING PLATFORM

5 issued patents
5 pending apps

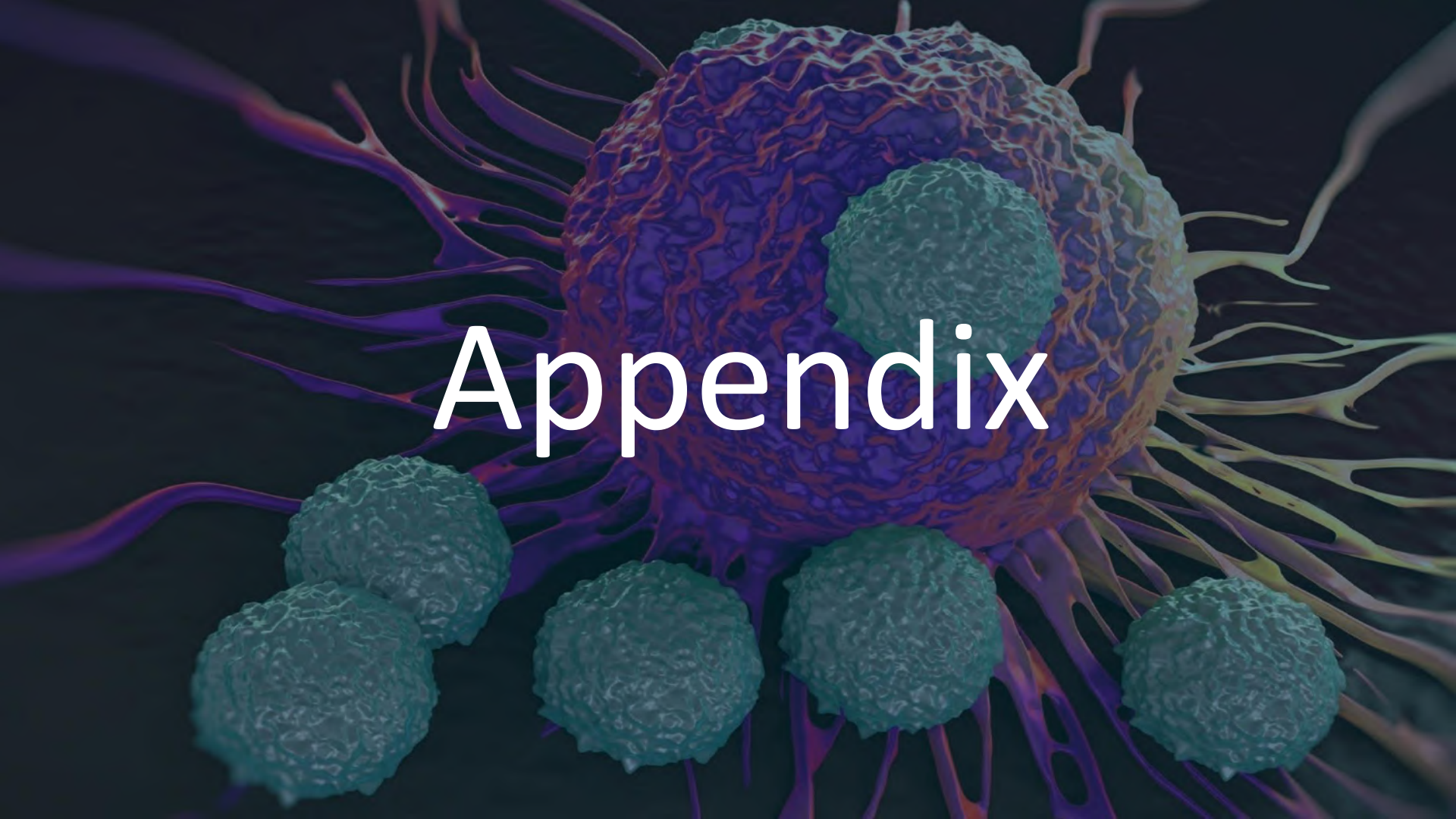
10 global patent properties

- Compositions
- Formulations
- Treatment Methods

Patent Coverage thru 2036*

Exclusive Patent License
- Immune Ventures

*current coverage. Subject to patent term extension up to 5 years and/or issuance of follow on patents


Appendix

Enrichment Criteria used to select patients with AD due to Neuroinflammation

Using simple biomarkers to match patient's disease with XPro's MOA

Peripheral Inflammation cause Central Inflammation

- Patients with elevated biomarkers of peripheral inflammation have increased risk of AD and worsening disease due to neuroinflammation.
- ApoE4 carriers have higher risk of AD

Peripheral Disease	Enrichment Factor	Increased Risk of AD
Genetic	ApoE4	3
Peripheral inflammation	ESR	1.84
Cardiovascular disease	CRP	1.34
T2DM and Metabolic syndrome	HgbA1c	1.8

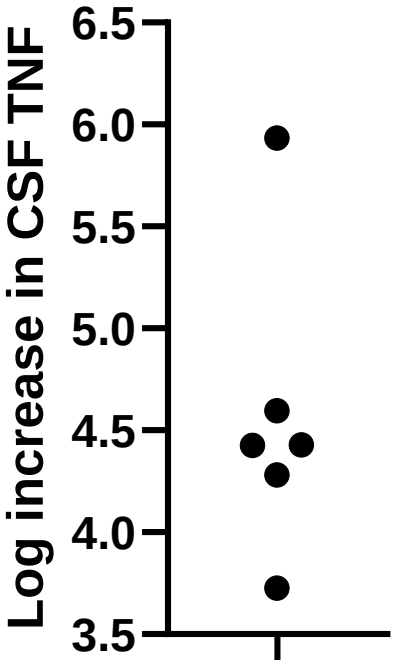
Doi.org/10.1007/s00125-005-0023-4, Jansen 2004
Doi.org/10.3389/fepid.2023.1095236, Cho 2021

*ADNI is a USC publicly available AD database
https://adni.loni.usc.edu/

XPro crosses the BBB to neutralize sTNF in Brain

Phase I CSF from 1mg/kg patients

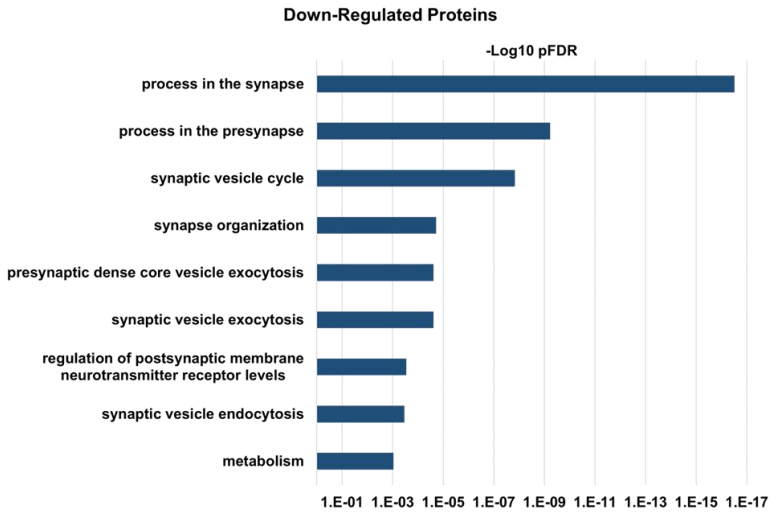
- In OLINK assay, sTNF cross reacts with XPro
- CSF XPro level is a measure of CNS XPro level
- Methodology:
  - Baseline sTNF level at time 0
  - Repeat sTNF level after 12 weeks XPro 1mg/kg/once a week (trough level)
  - Difference between time 0 and 12 weeks presented as log plot
- ***Result:*** XPro trough level after 12 weeks of therapy at least 3.5 logs greater than baseline sTNF level
- ***What does it mean?*** A 2-log excess of XPro is needed to neutralize more then 99.9% of sTNF in the CNS
- ***Conclusion:*** 1mg/kg/QW XPro neutralizes all CNS sTNF in humans



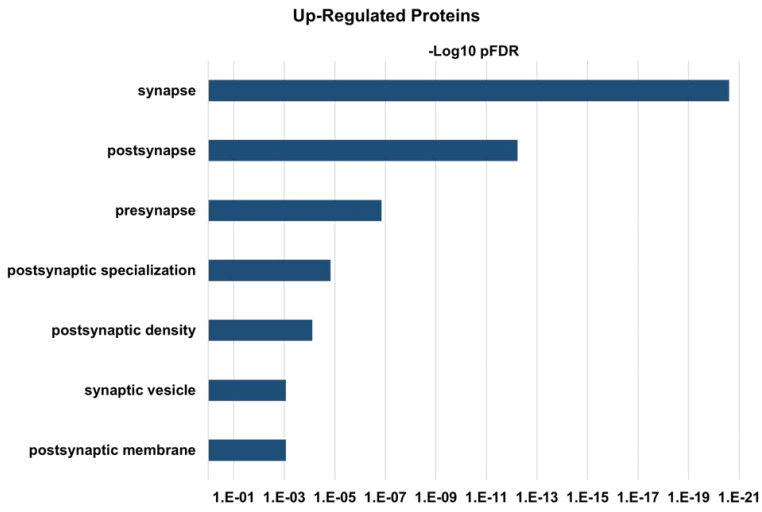
CSF proteome changes after XPro predicts EEG functional response

Phase I patients at 3 months 1mg/kg/QW

A comprehensive analysis of the CSF proteome affected by 3 months of XPro treatment for AD is in progress. Top-level results show a high concentration of synaptic proteins (24%) among the group with significant changes from baseline.

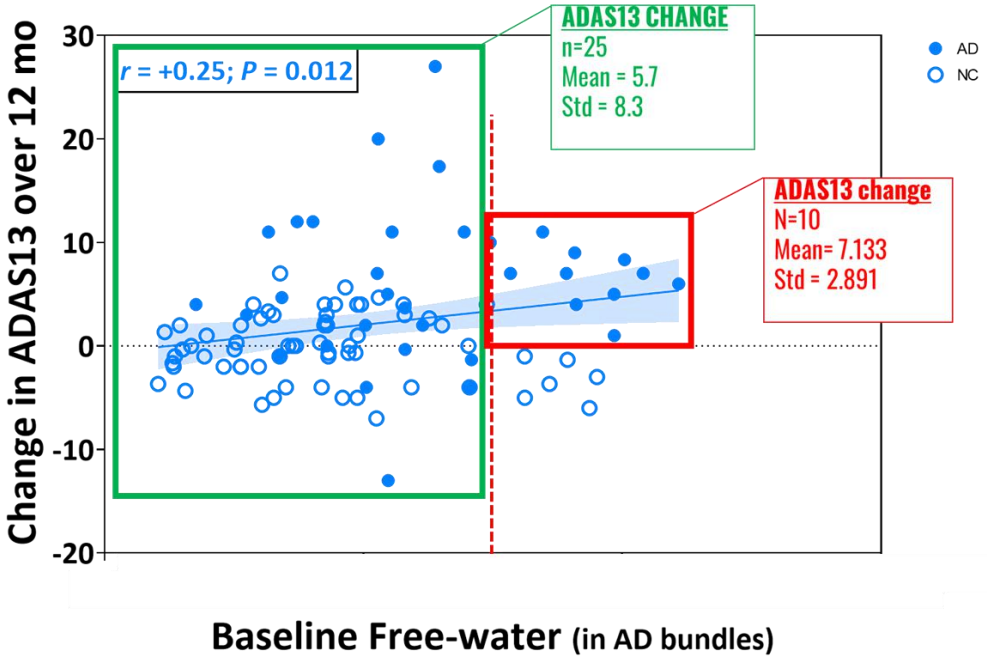


SynGO biological process enrichment for proteins in CSF differentially down-regulated by treatment with XPro1595 1.0 mg/kg/wk for AD

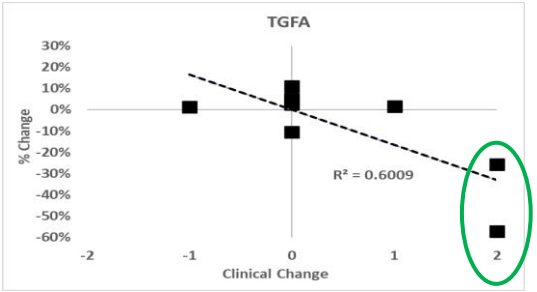


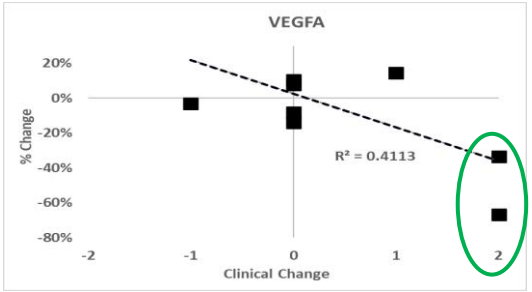
SynGO biological process enrichment for proteins in CSF differentially up-regulated by treatment with XPro1595 1.0 mg/kg/wk for AD

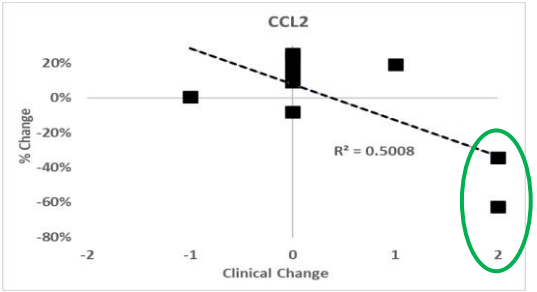
Patients with higher levels of FW have greater cognitive decline (ADAS13) over 12 months in ADNI

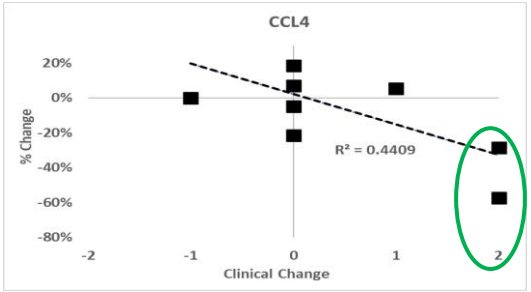


Correlation between decreased neuroinflammation and improved cognition







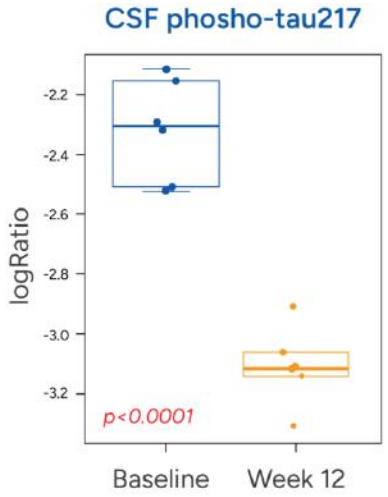


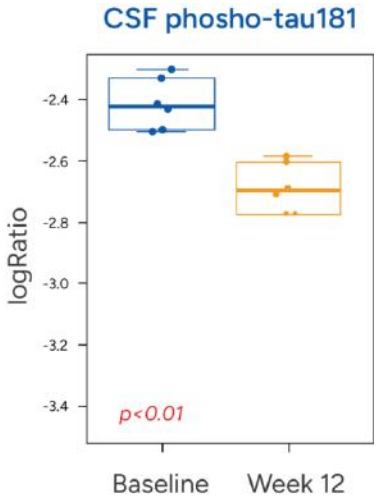
R^2 = 0.4 to 0.6
CSF cytokines by OLINK platform

RESULT OF PHASE I TRIAL – p-tau217 as a sensitive and specific biomarker of AD

BIOMARKER OF NEURODEGENERATION IN AD – pTAU 217/181

CSF following 3 months of therapy with XPro™ (1 mg/kg)



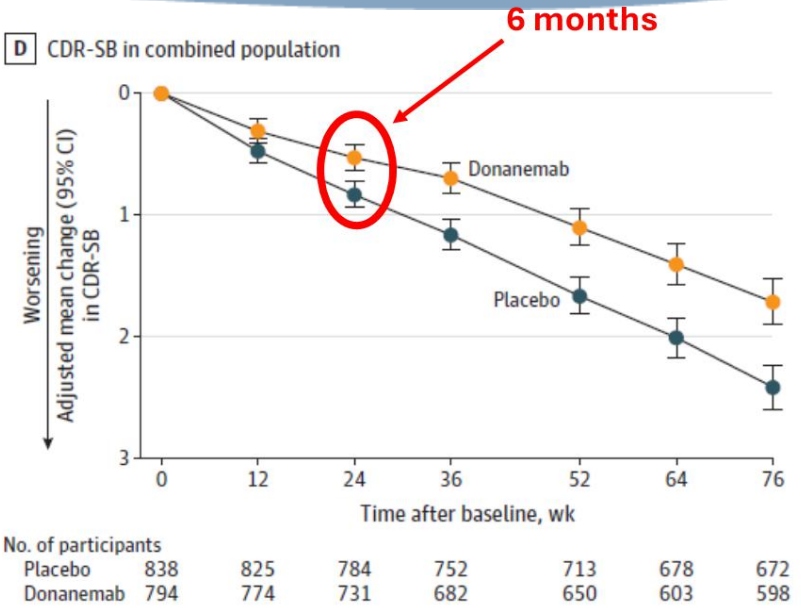


proteome sciences

Phospho-tau is a biomarker of neurodegeneration
Phospho-tau217 correlates best with cognitive dysfunction

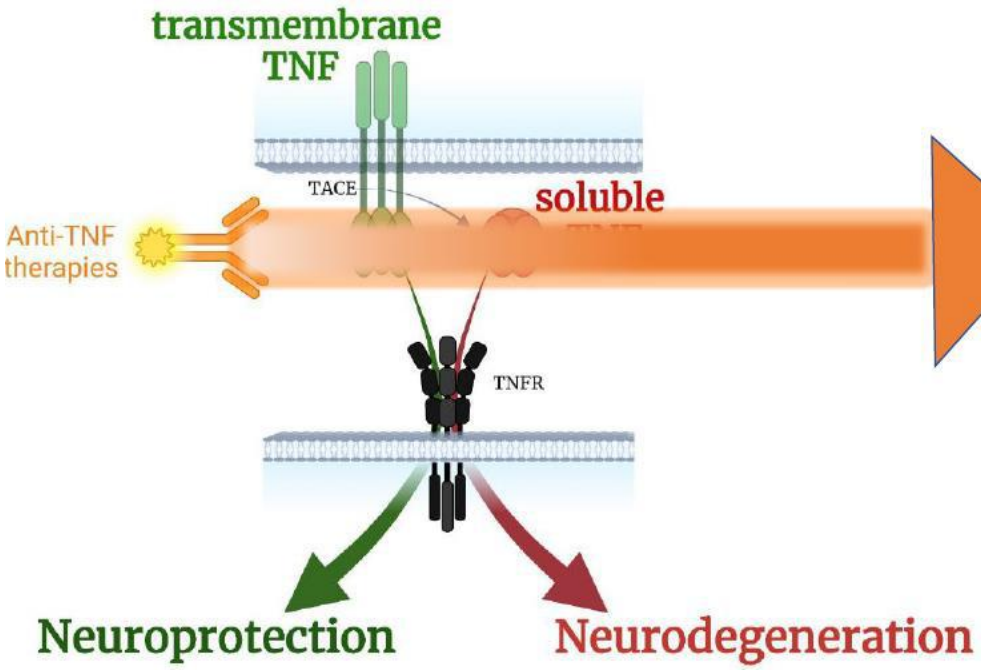
XPro Phase II trial uses conservative statistical plan based on CDR

- Both lecanemab and donanemab Phase III statistically positive at 6 months
- Effects size of XPro at 6 months is “same” as anti-amyloid
- **Conclusion:** XPro needs to be as good as lecanemab for a positive study
- **Expectation:** XPro will be better than lecanemab and donanemab at 6 months



	Placebo/Drug CDR difference	6 m CDR Effect size
Lecanemab	0.24	0.30
Donanemab	0.30	0.30
XPro (est)	0.22	0.28

SAFETY SIDE EFFECTS OF NON-SELECTIVE TNF BLOCKADE ARE ALL FROM BLOCKING TMTNF



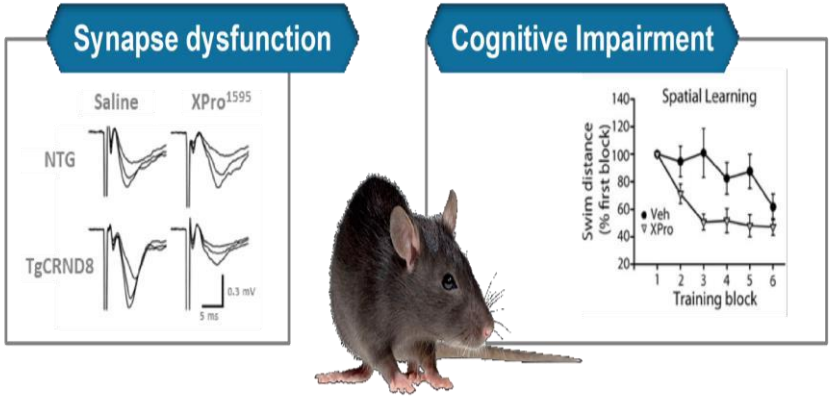
Consequences of blocking tmTNF:

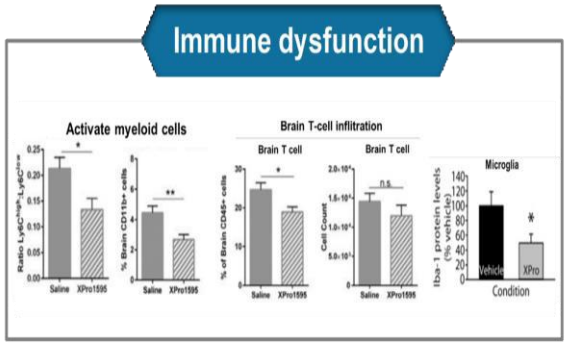
- Infection
- Cancer
- Demyelination

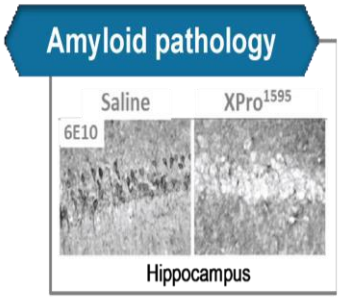
XPro Attenuates AD-like Pathology and Restores Normal Function in Animal Models

Findings in Phase I studies precisely matched findings in animal studies

- Immune Dysfunction
- Amyloid Pathology
- Synaptic Dysfunction
- Nerve Cell Death
- Cognitive Impairment





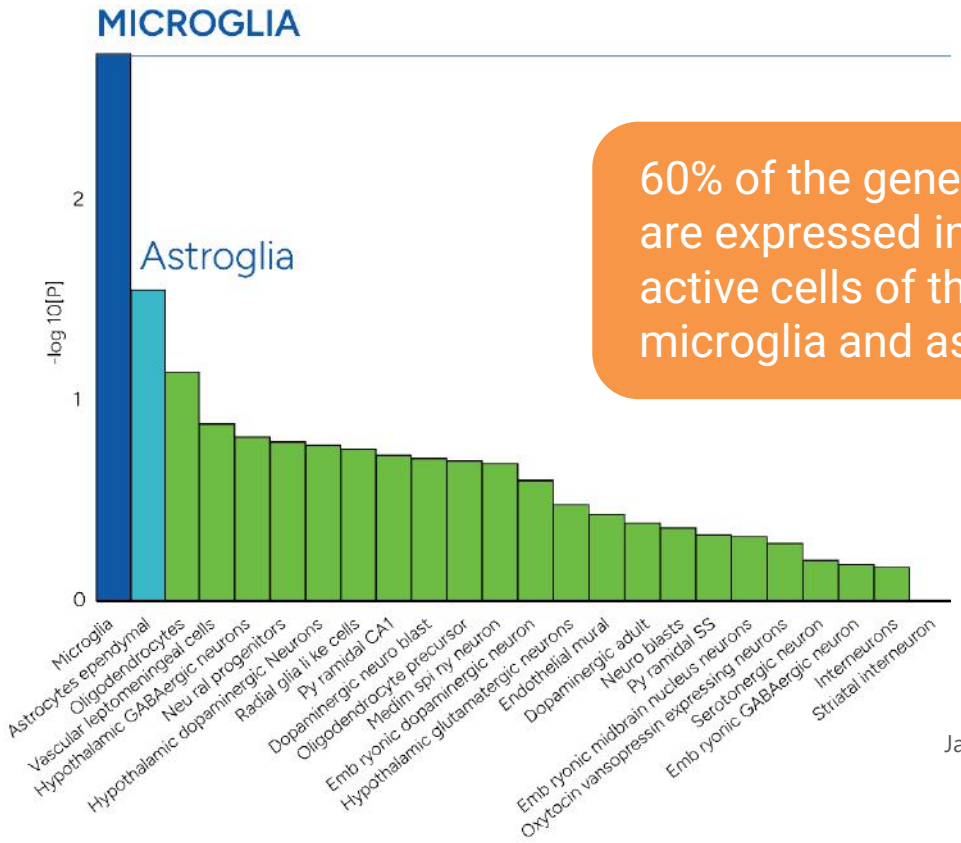


1. Ekert JO, et al. *Int J Geriatr Psychiatry*. 2017;33:688–694
2. Kalovyrna N, et al. *Scientific Reports*. 2018;10;8670
3. Shi JQ, et al. *Brain Research*. 2011;1368:239 -247

INmuneBio XPro™ for AD

Efficacy has been shown in 3xTgAD, 5xFAD, TgCRND8 and aged mice

Large Genetic Profile Study Of AD Patients Demonstrated Strong Association With Immune Dysfunction

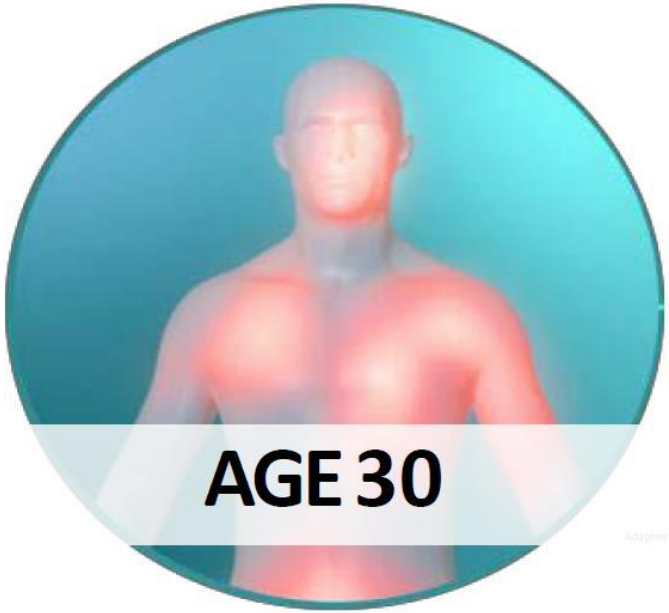


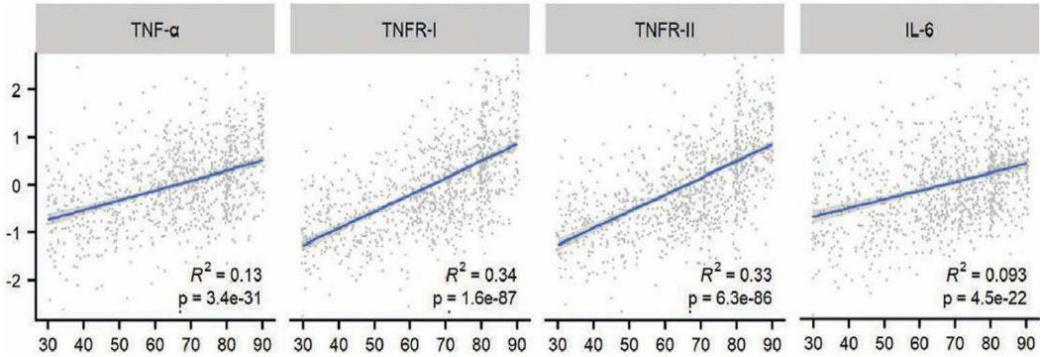
60% of the genes up-regulated in AD are expressed in immunologically active cells of the brain including microglia and astroglia

Genome-wide association study of 71,880 AD cases and 383,378 controls

Jansen IE, et al. *Nature Genetics*. 2019;51:404–413

TNF INCREASES EARLY IN LIFE CONTRIBUTING TO INFLAMMAGING





- Age is the most important risk factor for AD.
- Pro-inflammatory cytokines increase with age
- TNF is the master cytokine driving *age related chronic inflammation* – also known as *inflammaging*.

Parker et al. 2008

Decades of data connects TNF and neuroinflammation with AD

PubMed 2023: >1500 papers on neuroinflammation and AD

"Current evidence suggests that neuroinflammation has a vital role in the pathogenesis and progression of Alzheimer's disease."

— Leng F, Edison P. *Nature Reviews Neurology.* 2020

"In Alzheimer's disease, neuroinflammation, instead of being a mere bystander activated by emerging senile plaques and neurofibrillar tangles, contributes as much or more to the pathogenesis as do the plaques and tangles themselves."

— Heneka MT, et al. *Lancet Neurol.* 2015

Immune attack: the role of inflammation in Alzheimer disease

Frank L. Heppner[1,2], Richard M. Ransohoff[3] and Burkhard Becher[4]

Review

Neuroinflammation in Alzheimer's Disease

Isaac G. Onyango [1,*], Gretsen V. Jauregui [1], Mária Čarná [1], James P. Bennett Jr. [2] and Gorazd B. Stokin [1,3,4,]

Systemic inflammation and disease progression in Alzheimer disease

C. Holmes, C. Cunningham, E. Zotova, J. Woolford, C. Dean, S. Kerr, D. Culliford, V.H. Perry

Inflammation as a central mechanism in Alzheimer's disease

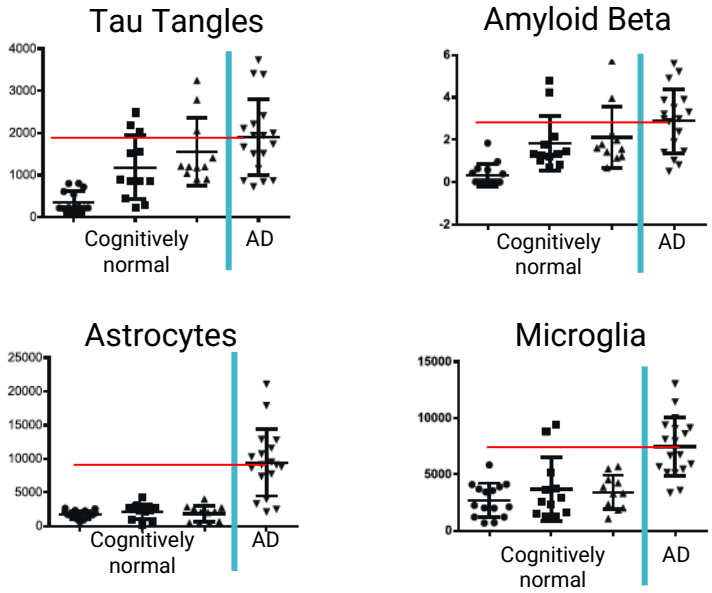
Jefferson W. Kinney[a,*], Shane M. Bemiller[b], Andrew S. Murtishaw[a], Amanda M. Leisgang[a], Arnold M. Salazar[a], Bruce T. Lamb[b]

Neuroinflammation in Alzheimer's Disease

Michael T. Heneka, MD[1,2], Monica J. Carson, PhD[3], Joseph El Khoury, MD[4], Gary E. Landreth, PhD[5], Frederik Brosseron, PhD[2], Douglas L. Feinstein, PhD[6], Andreas H. Jacobs

Neuroinflammation and TNF Causes Alzheimer's Disease

Inflammation, not amyloid or tau, causes AD pathology

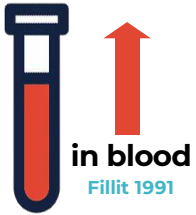


Amyloid and tau is present within the brains of AD patients ***AND*** cognitively normal people. Inflammation is increased in AD brains but ***NOT*** cognitively normal people.

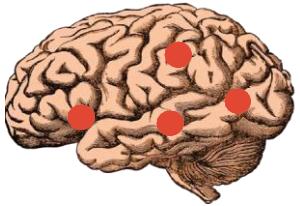
Adapted from: PMID 30336198

TNF long associated with AD and predates deposition of amyloid

in CSF
Tarkowski 2003



in blood
Fillit 1991



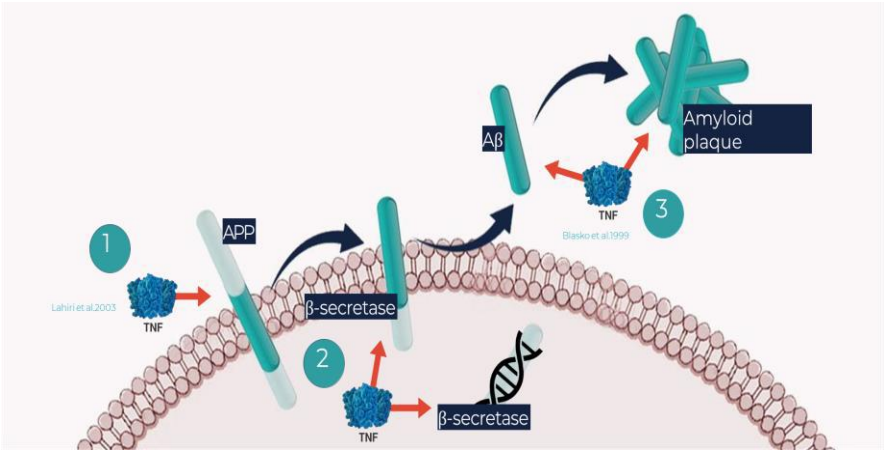
co-localized with plaques
Dickson 1997

corelated with disease progression

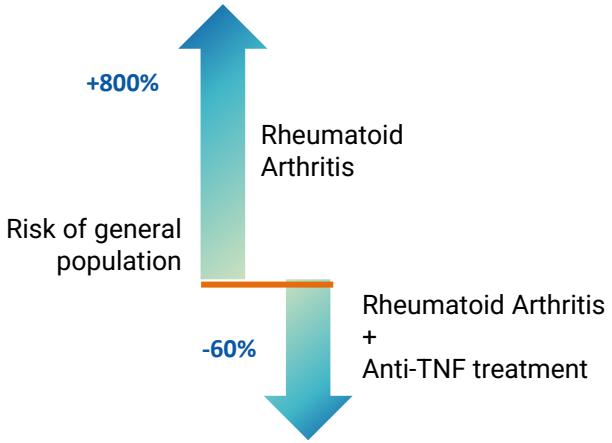
Paganelli 2002

TNF Drives Amyloid Pathology and Risk of AD

- Neuroinflammation predates formation of amyloid
- TNF drives formation of amyloid plaque
- Chronic treatment with TNF inhibitors prevents AD



TNF inhibitors reduce risk of developing AD

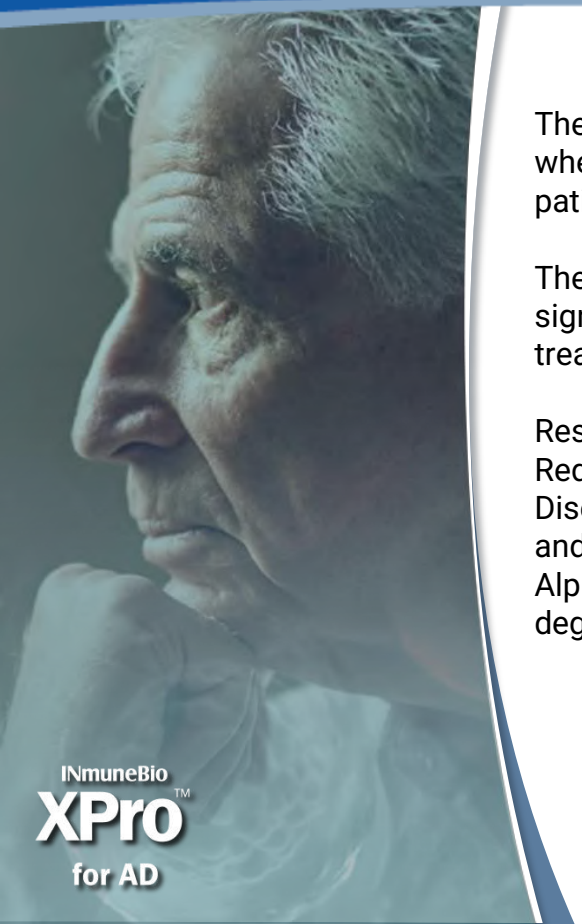


Epidemiological Studies including a meta-analysis of more than 60 Million cases Linking **TNF Blocking Agents** to Reduced Risk of AD

Adapted from PMID: 27470609, 33016914

XPro™ Improves EEG Alpha Power Following 4 Weeks of Treatment

EEG is a biomarker of brain function that can be used as a measure of target engagement



The study evaluated the feasibility of using a portable EEG device to collect quality EEG data when used by the patients at home. EEG was assessed in seven moderate to severe AD patients treated once weekly with 1 mg/kg (sc) of XPro1595 for 4 weeks.

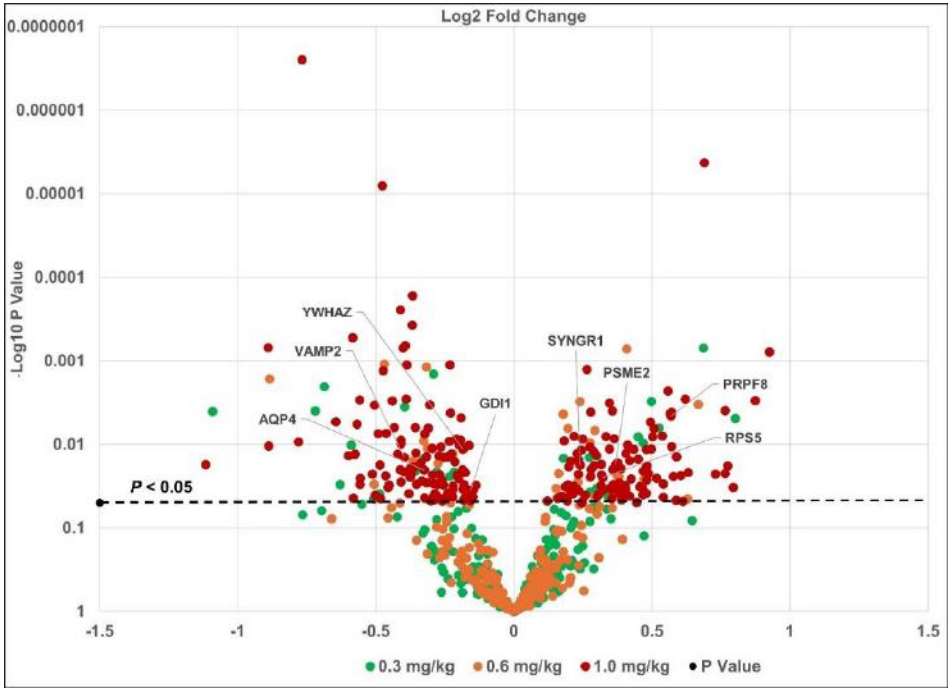
The study demonstrated the feasibility of collecting EEG in advanced AD patients. A significant increase ($p<0.05$) in resting alpha power was observed after 4-weeks of treatment with XPro1595

Resting alpha-band power in EEG is a broad measure of brain network connectivity. Reduced Alpha power is linked with cognitive decline and the progression of Alzheimer's Disease. Alpha waves are essential for internal functions like mental arithmetic, short-term and working memory, and visual-spatial mental imagery exercises. In individuals with AD, Alpha wave power is diminished due to the breakdown of brain networks associated with degeneration.

CSF Proteome dose response Phase I AD

Confirms results of CSF inflammatory cytokine response that 1mg/kg/QW is optimal dose

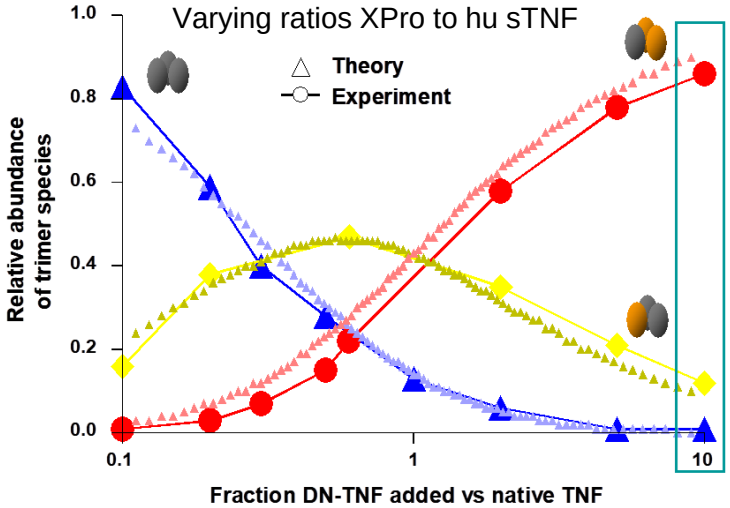
- Unbiased analysis of CSF proteome using Proteome Sciences TMT Calibrator technology
- 35,443 distinct peptide sequences associated with 4,966 protein groups were quantified
- and statistically evaluated
- ***Conclusion:*** Markers of microglial activation, synaptic and axonal dysfunction were
- significantly regulated in CSF from AD patients treated with XPro1595.

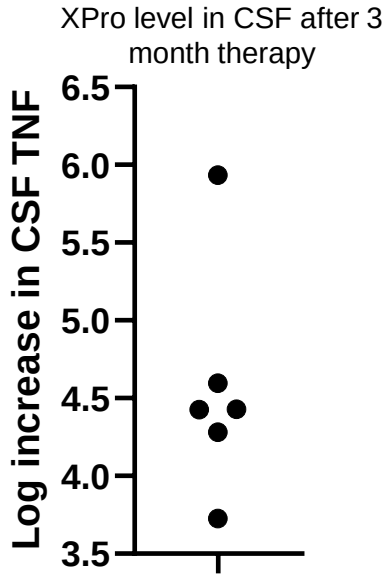


1mg/kg/QW XPro adequate dose to neutralize sTNF in CNS

Phase I CSF from 1mg/kg patients

- Maximum dose determined by drug level at trough
- Trough level must be >2logs higher than CNS TNF level
- XPro 1mg/kg/QW has trough levels that >3 logs CSF basedline sTNF
- **Conclusion:** All CNS sTNF neutralized with 1mg/kg/QW. Increasing dose of XPro will not provide benefit





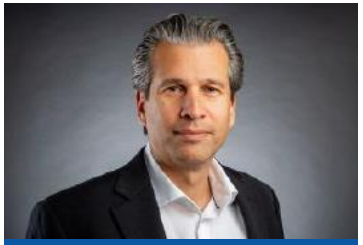
At equilibrium:

DN-TNF = TNF:	Eliminates 75% TNF (1:3:3:1)
2x DN-TNF > TNF:	Eliminates ~88.9% TNF
5x DN-TNF > TNF:	Eliminates ~97.2% TNF
10x DN-TNF > TNF:	Eliminates >99.2% TNF
100x DN-TNF > TNF:	Eliminates >99.99% TNF

MANAGEMENT TEAM

Broad biotechnology background including legal, intellectual property, drug manufacturing, clinical trial management, FDA approval, drug marketing, finance, business development and operations.

Raymond J. Tesi, MD
CEO/CMO & Chairman of the Board



David J. Moss
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General Counsel

Tara Lehner
VP Clinical Operations

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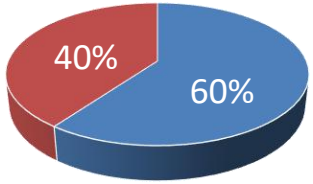
VP CNS Development

Total Addressable Market (TAM): XPro™ in AD

- ✓ Early AD = MCI + mild AD
- ✓ > 40% of Early AD patients have neuroinflammation
- ✓ XPro Total Addressable Market in US = 4.3M
- ✓ XPro estimated market opportunity exceeds $50B

AD patients with neuroinflammation



Nature Aging 2024 https://doi.org/10.1038/s43587-023-00550-7

Total Addressable Market: US XPro for AD

MCI patients -US	7M
Total AD patients – US*	6.7M
mild AD patients -US (50%)	3.8M
Early AD patients -US (3.8+7)	10.8M
XPro eligible - US (40%)	4.3M
TAM value per $10,000	$43B

Sample calculations: $10K annual cost = TAM of $39B
$40K annual cost = TAM of $172B

**https://www.alz.org/alzheimers-dementia/facts-figures*