Taking the treatment of neurodegenerative diseases to the next level

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"Next-generation Fc-fusion protein with strong binding for Aß, Tau and α-synuclein aggregates, reduced risk of ARIA, and improved brain delivery"

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CSO

Amyl Tx

AD/PD™ 2026
ADVANCES IN SCIENCE & THERAPY
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Disclaimer

	No, Nothing to disclose
X	Yes, please specify

Company / Name	Honoraria / Expense	Consulting / Advisory Board	Funded Research	Royalties / Patent	Stock Options	Ownership / Equity Position	Employee	Other (Please specify)
Amyl Therapeutics Damien Toulorge		X						

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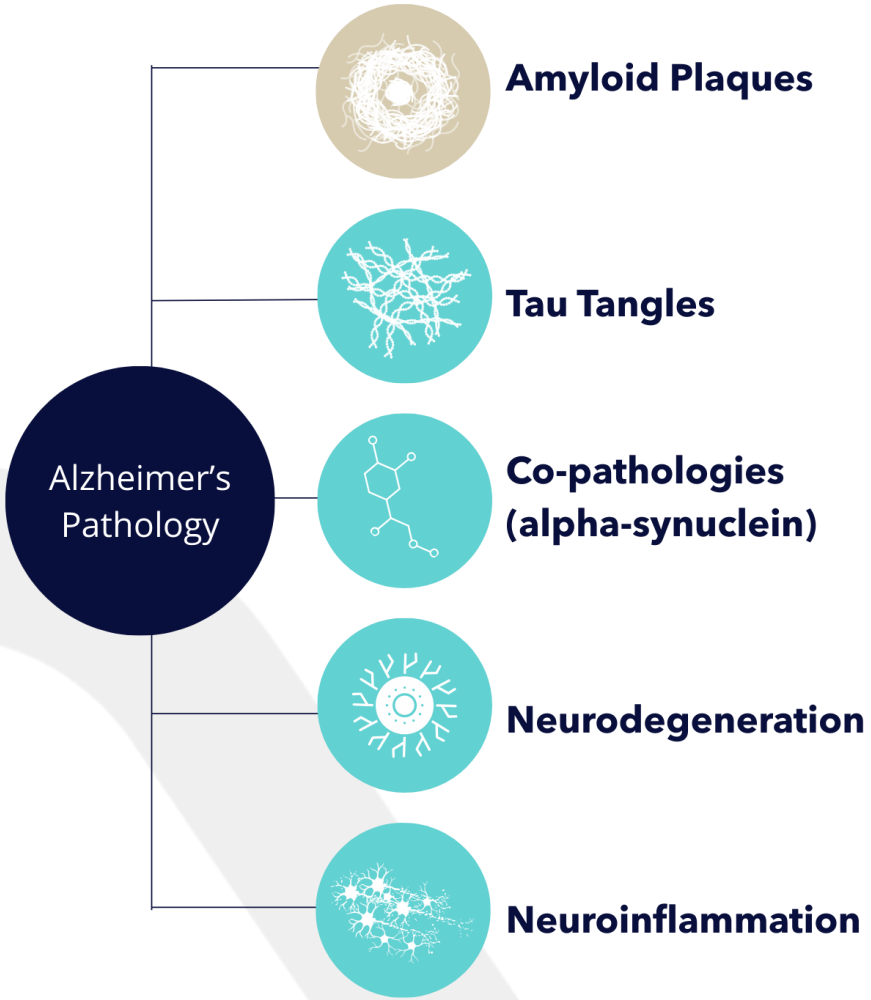
AD is a multifactorial disease



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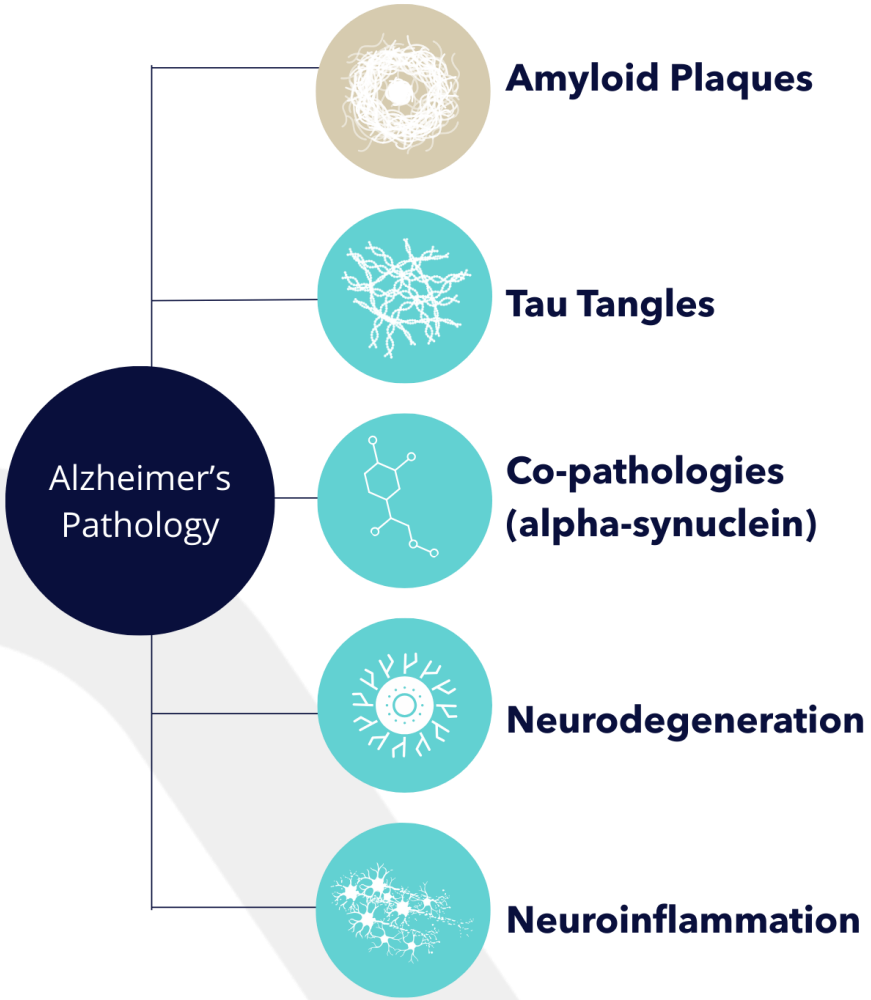
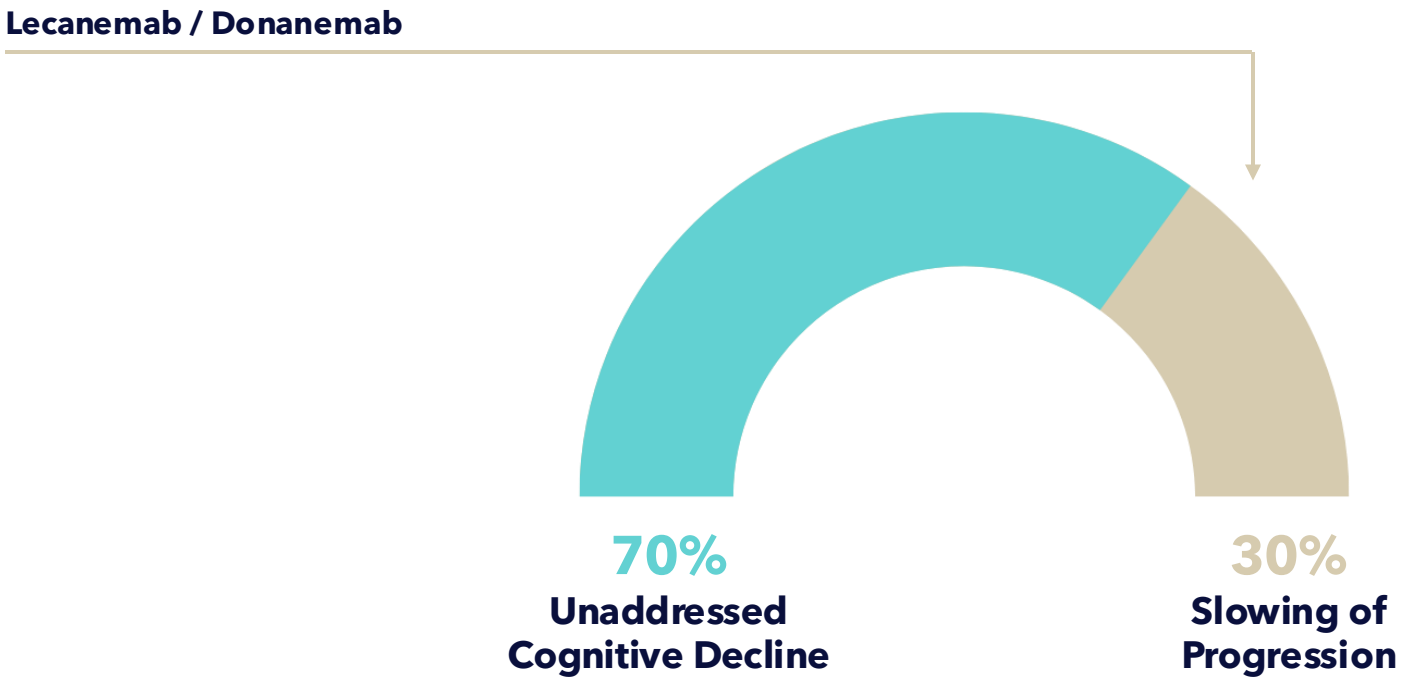
One target is not enough





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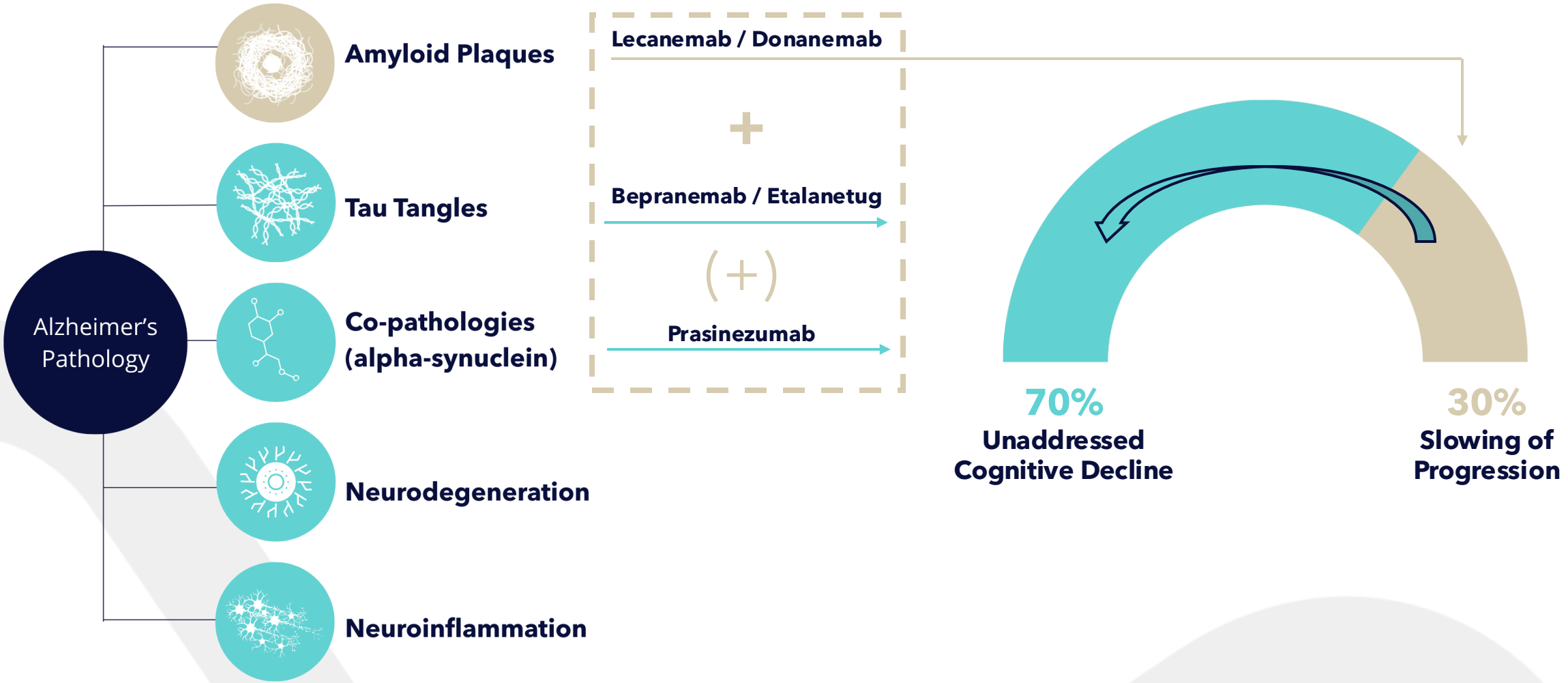
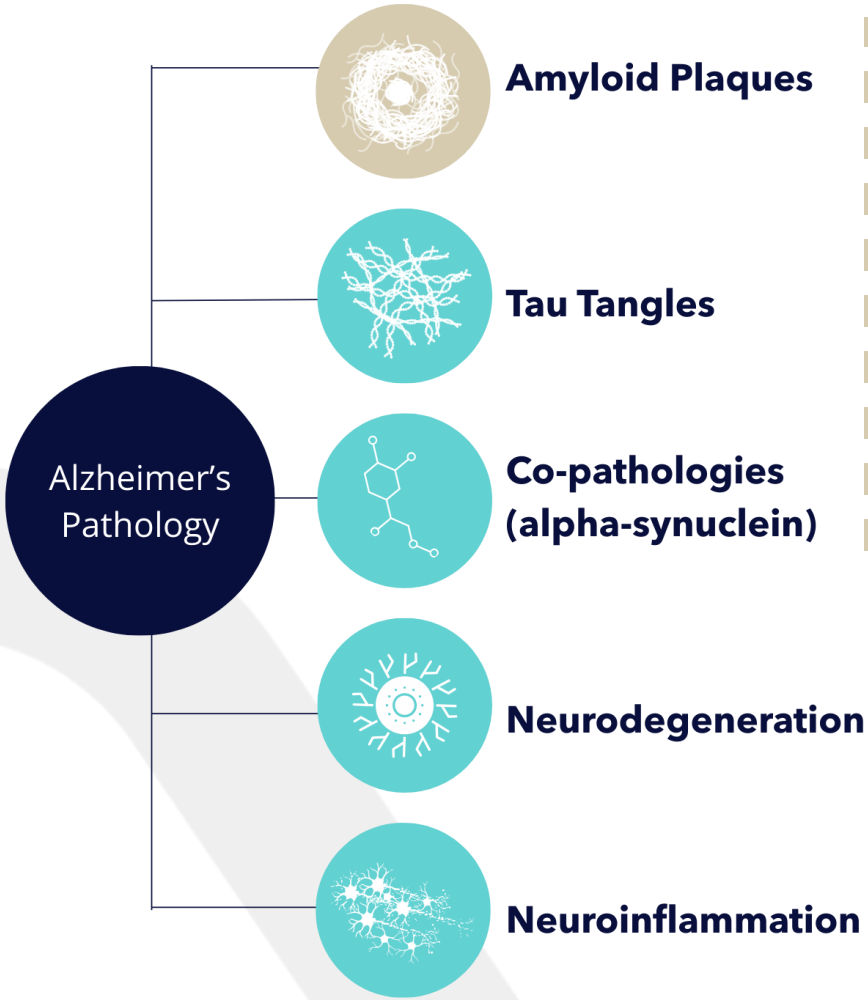
Sims et al., JAMA, 2023
Van Dyck et al., NEJM, 2023

Combining therapies to further reduce cognitive decline



Development of mAb combinations will not be trivial



Lecanemab / Donanemab

+

Bepranemab / Etalanetug

(+)

Prasinezumab

Combination sequence: Co-administration ? Administration after anti-Aβ mAb?

PK/PD interference: if one mAb alters the expression of the target of the other mAb

Safety considerations: toxicological synergies, infusion-related reactions

Immunogenicity: co-administration can activate immunogenic mechanisms that are not observed with each mAb individually

Efficacy reading: the contribution of each mAb must be clearly demonstrated

Patient discomfort: multiple administrations if treatments are not co-formulated

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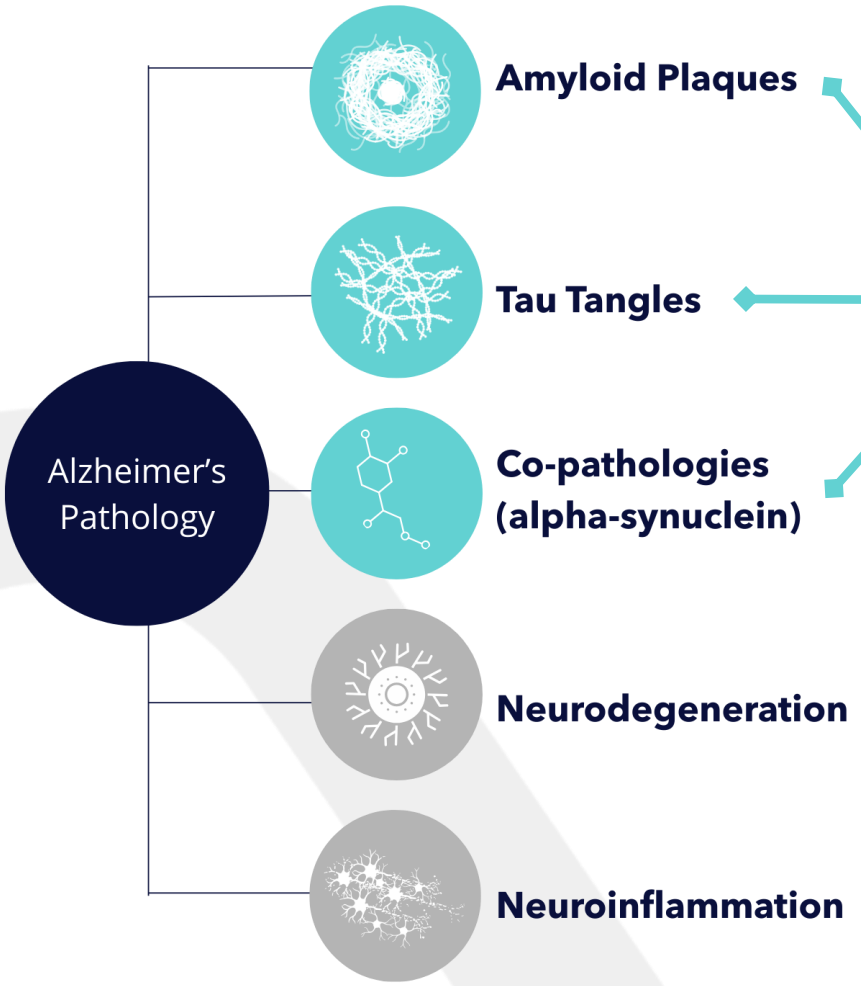
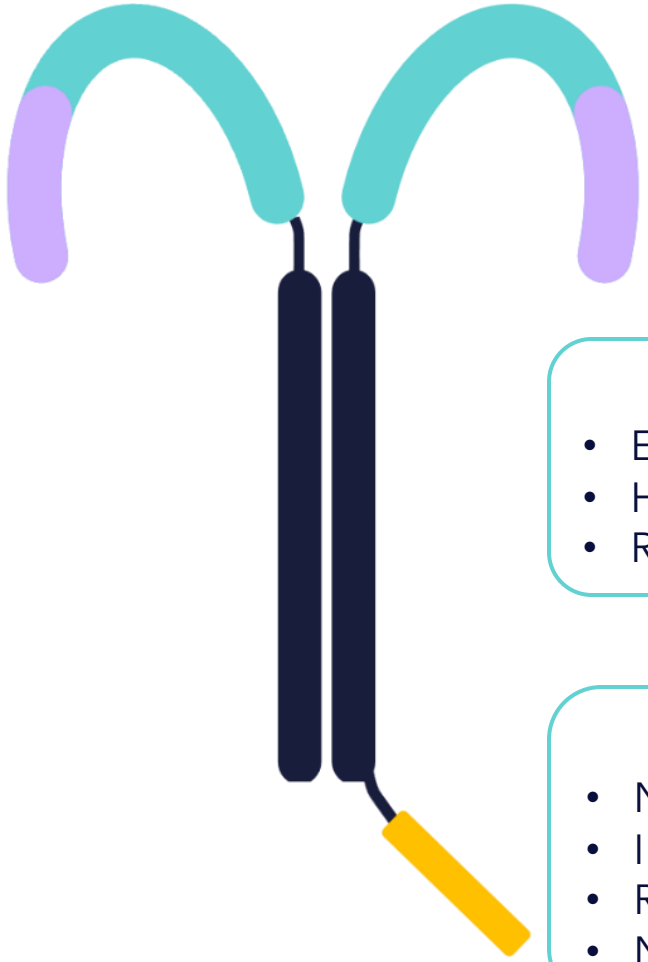
AMX-003: First-in-Class, Shuttled Pan-Amyloid therapy





Selective, high affinity, conformational binder to ALL amyloid aggregates

Proprietary Fc domain

- Enables phagocytosis
- Half-life extension
- Reduced TNF-α release and risk of ARIA

Validated Brain Shuttle

- Novel sequence targeting validated TfR1
- Improved brain penetration
- Reduced ARIA risk
- No TfR1-associated ADCC and anemia

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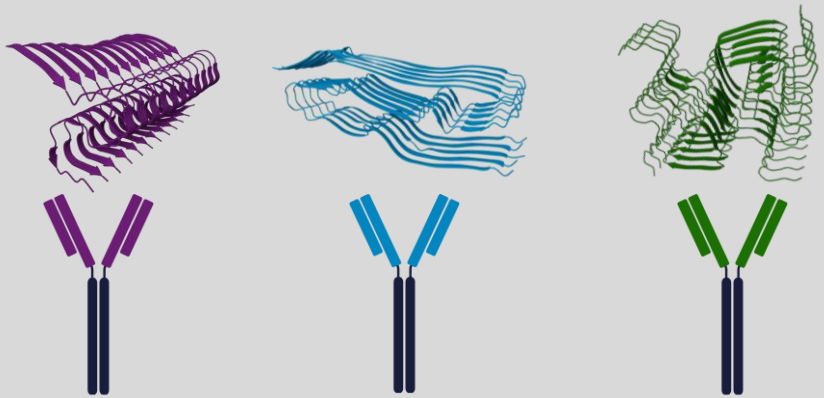
AMX-003 recapitulates the action of three mAbs in a single product

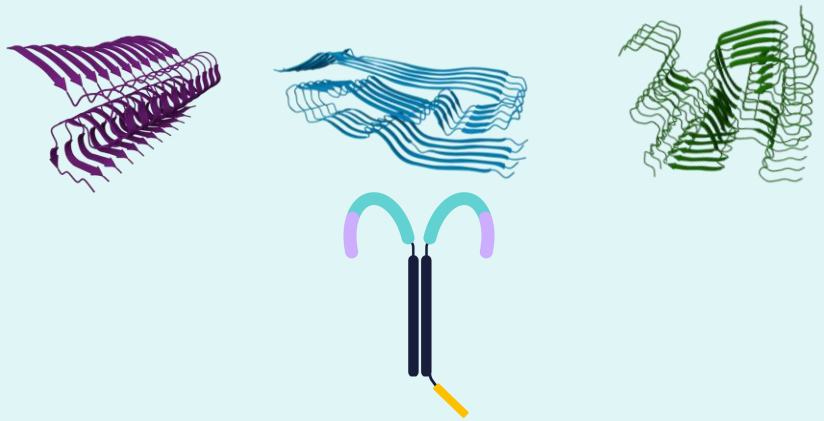
Monoclonal antibodies recognize a specific peptide of a monomer to bind a single type of amyloid

Aβ Tau α-syn



AMX-003 recognizes the conformation common to all fibrils to bind all types of amyloids but not monomers

Aβ Tau α-syn



Test items (same SPR run)	Lecanemab	Etalanetug	Prasinezumab	AMX-003		
	Aβ	Tau	α-syn	Aβ	Tau	α-syn
K_D for fibrils (nM)	0.2	0.2	1.8	0.4	5.6	3.9
Binding to monomers	+	+	-	-	-	-

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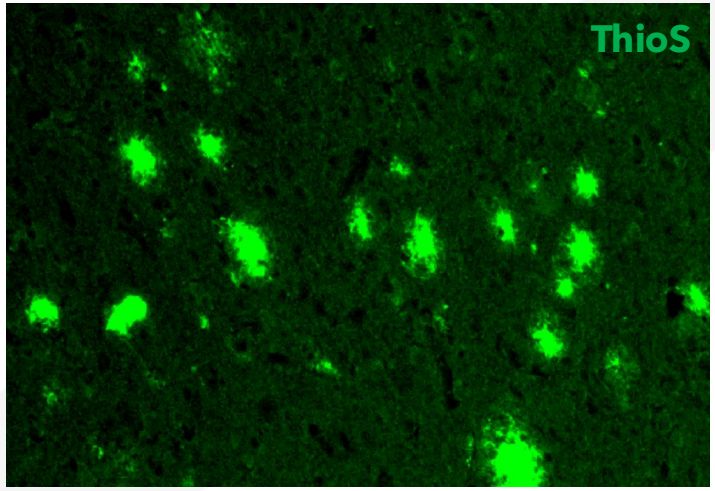
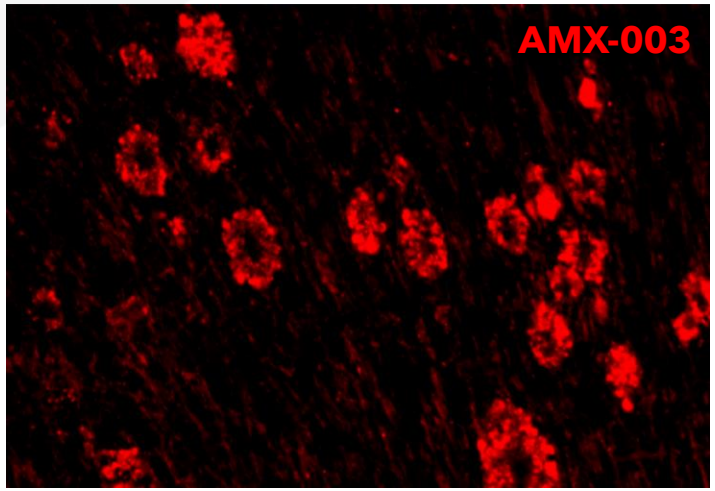
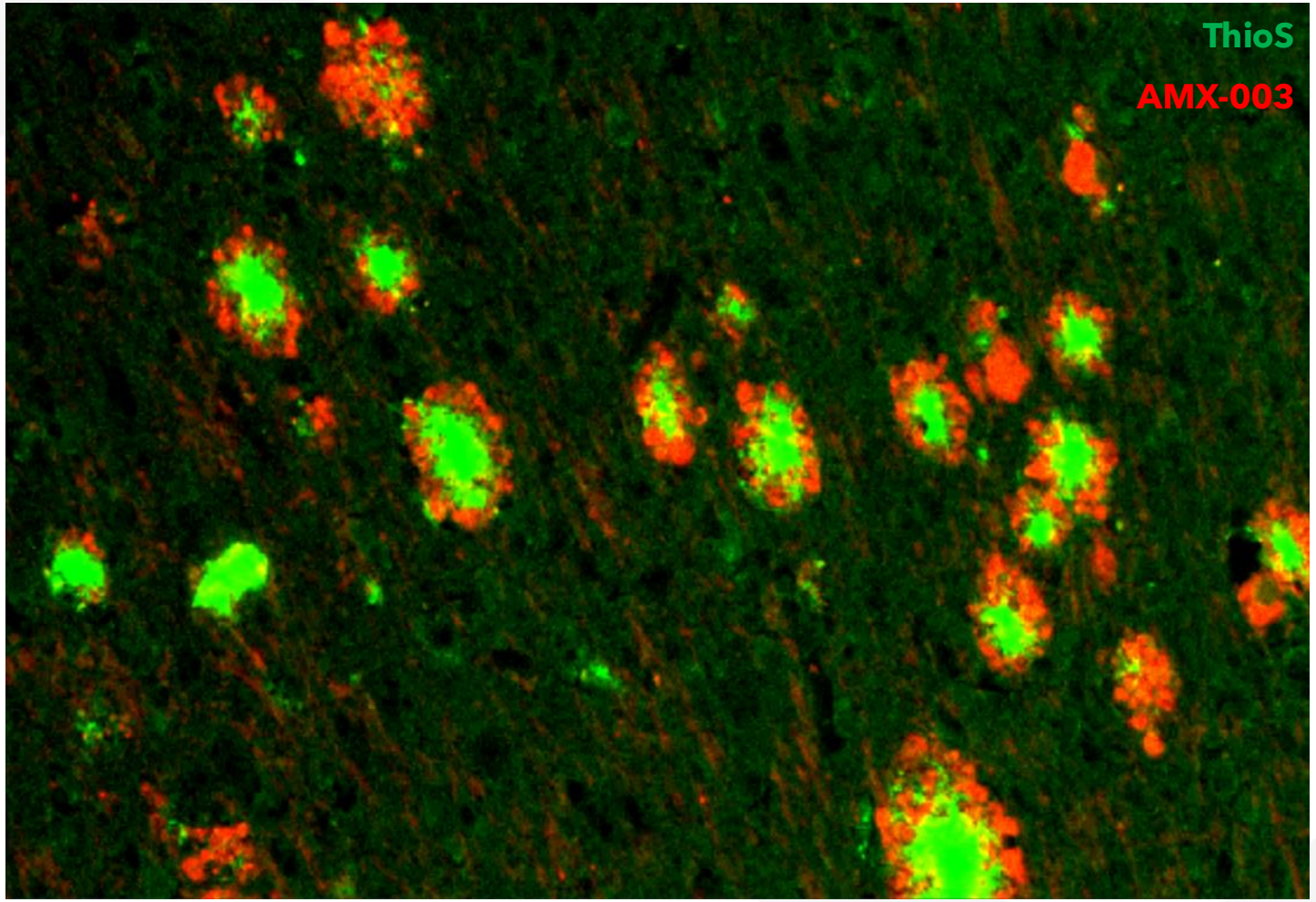
AMX-003 binds to amyloid plaques in 5XFAD mouse brain

Binding to 5XFAD mouse brain (below) and Tg4510 (data not shown)







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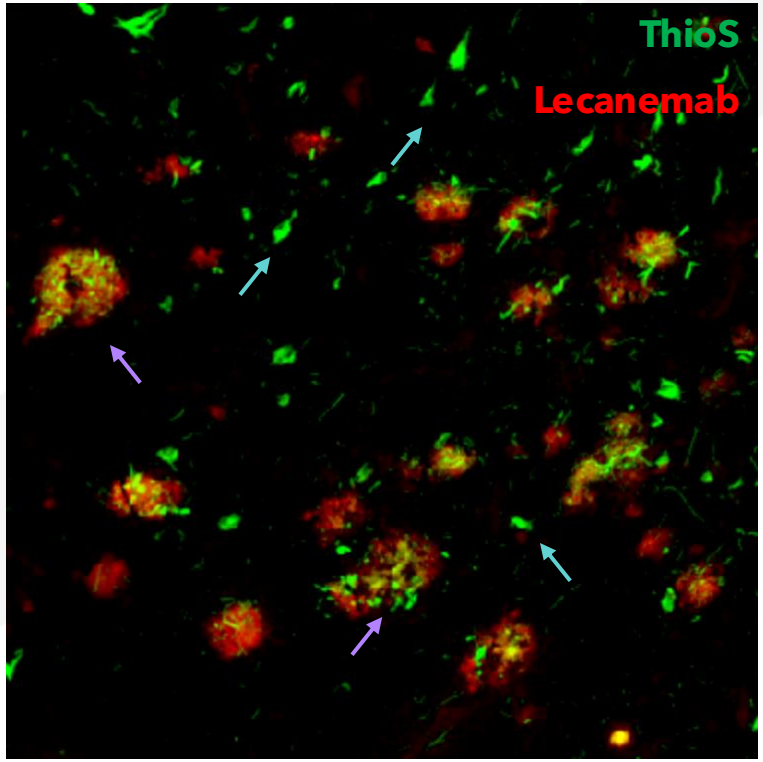
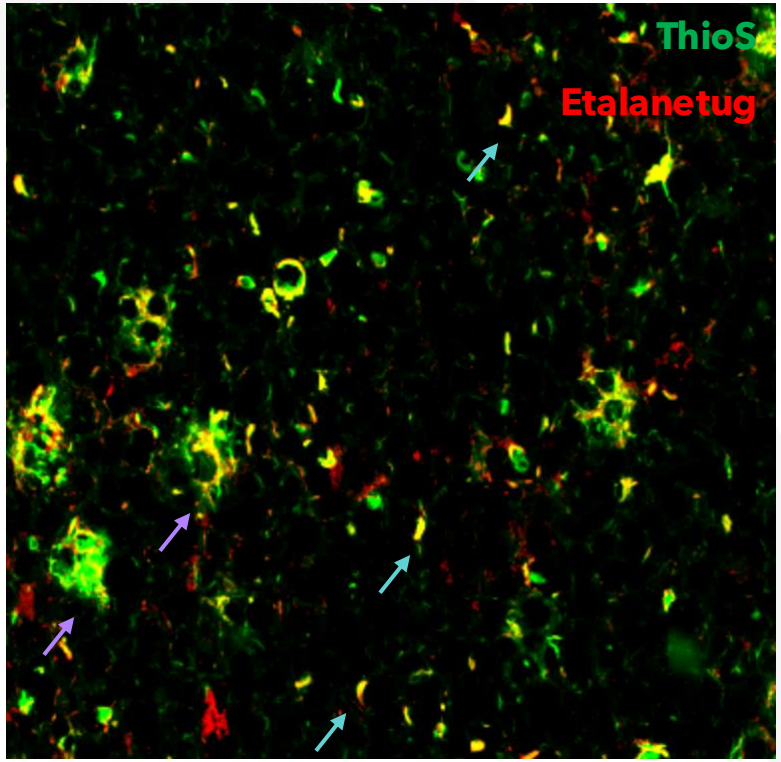
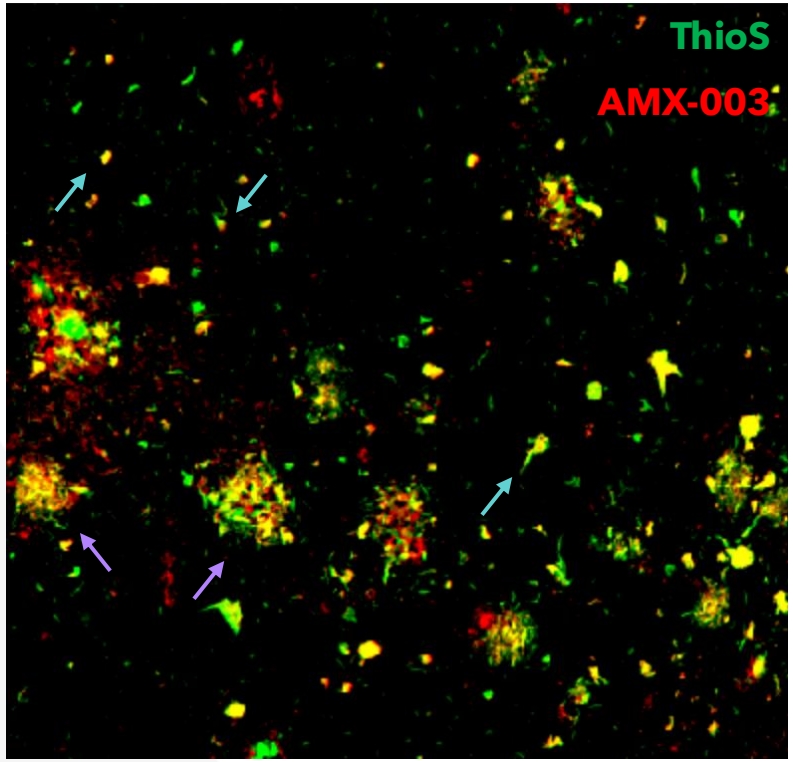
AMX-003 binds to amyloid plaques and Tau NFTs in human AD brain

Binding to human AD brain
Subsequent sections from the temporal gyrus region







Strong binding to plaques No binding to NFTs	Low binding to plaques Strong binding to NFTs	Strong binding to plaques Strong binding to NFTs

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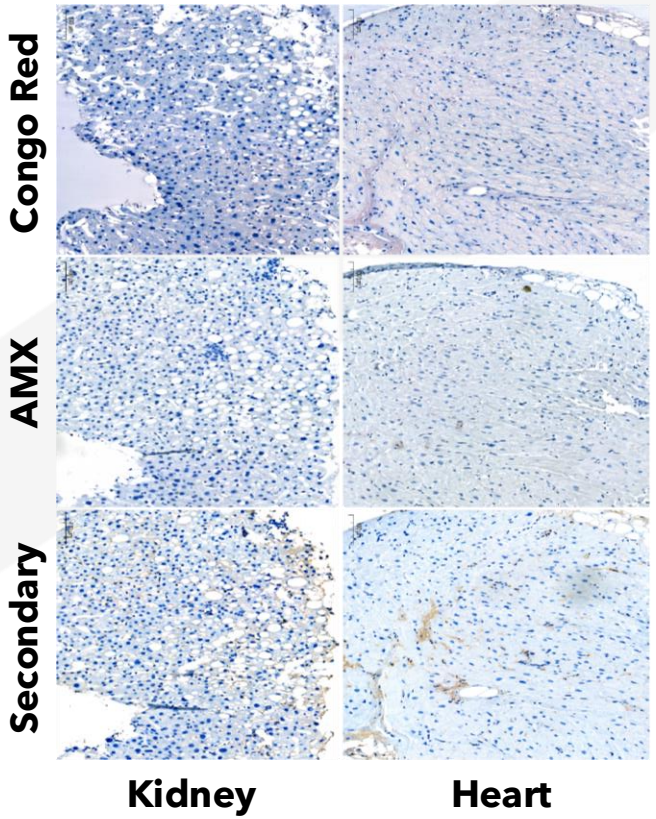
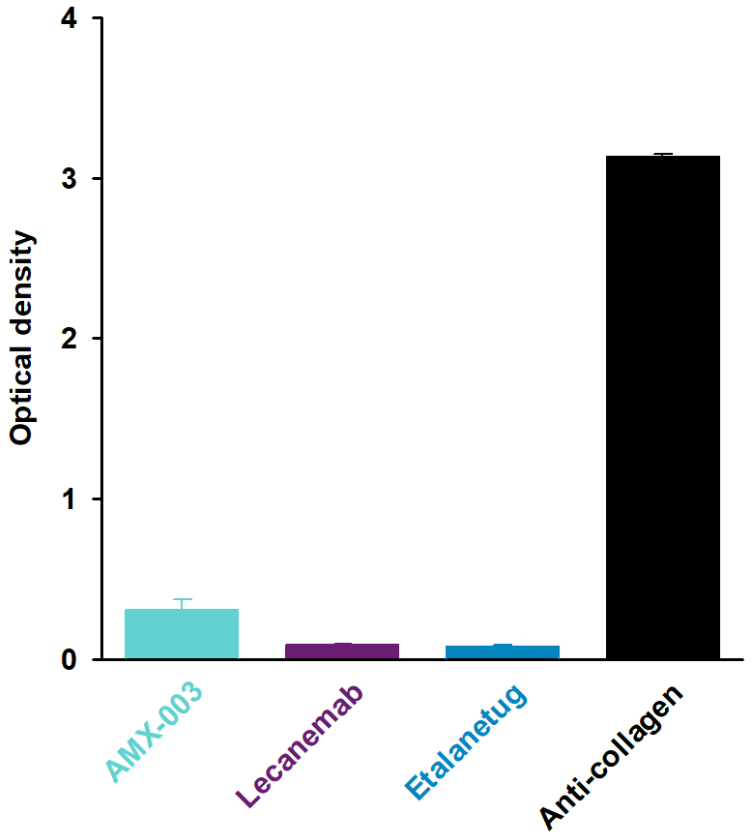
AMX-003 binding to amyloid fold is highly specific

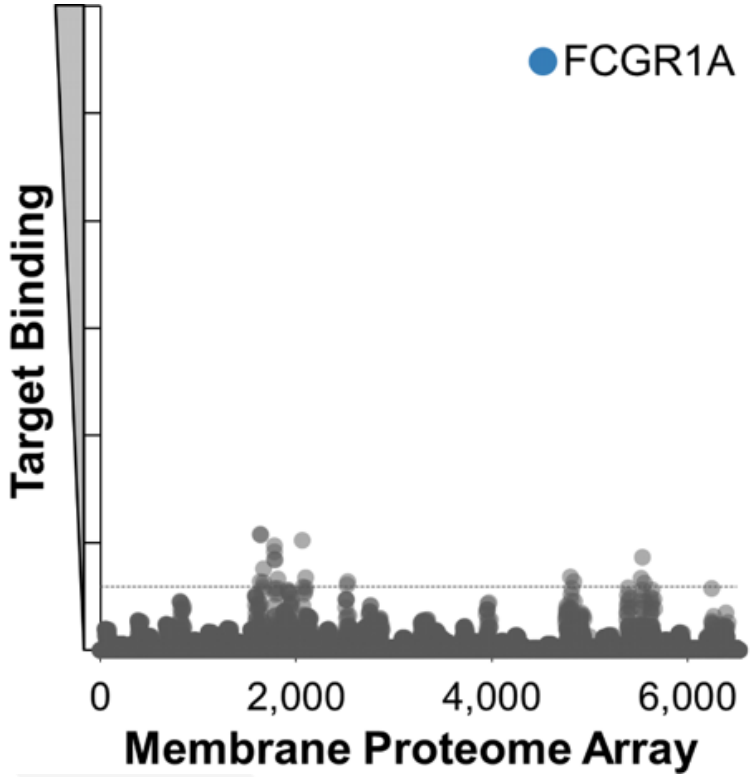
No binding to healthy kidney and heart tissue



No binding to non-amyloid fibrils (Type I human collagen ELISA)



No binding to > 6,000 extracellular / transmembrane proteins



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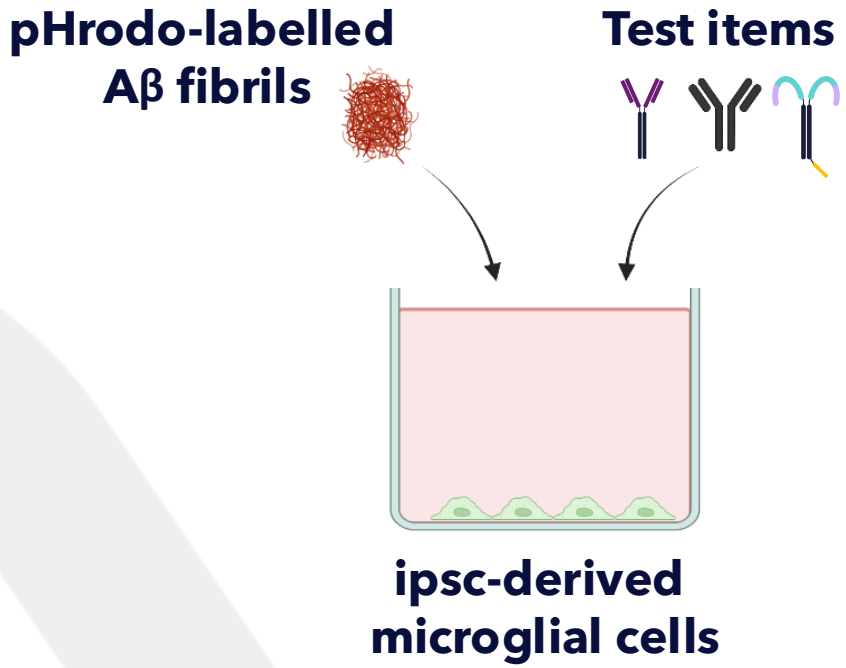
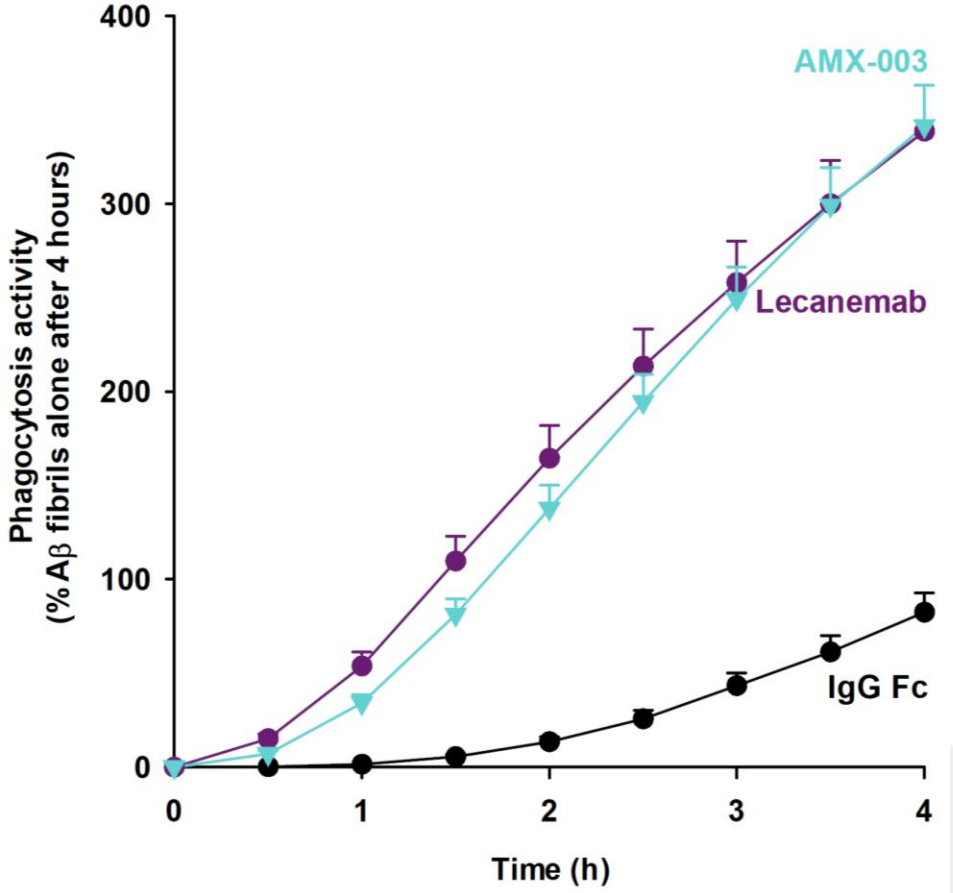
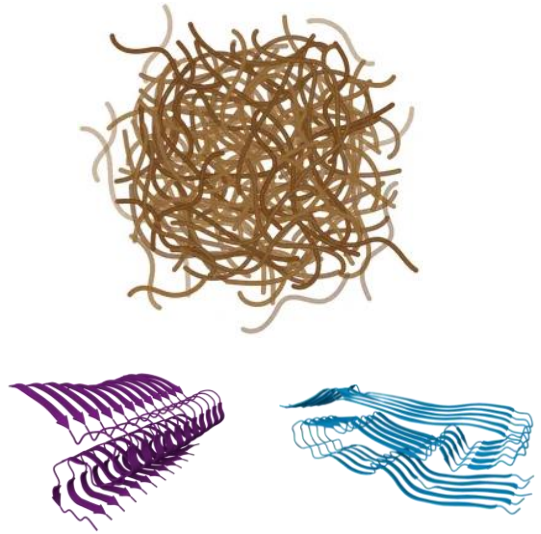
AMX-003 triggers the same increase in Aβ fibrils phagocytosis as Lecanemab using iPSC-derived human microglia

pHrodo-Aβ fibrils incubated with test items (800 nM) iPSC-derived human microglial cells (n=3)



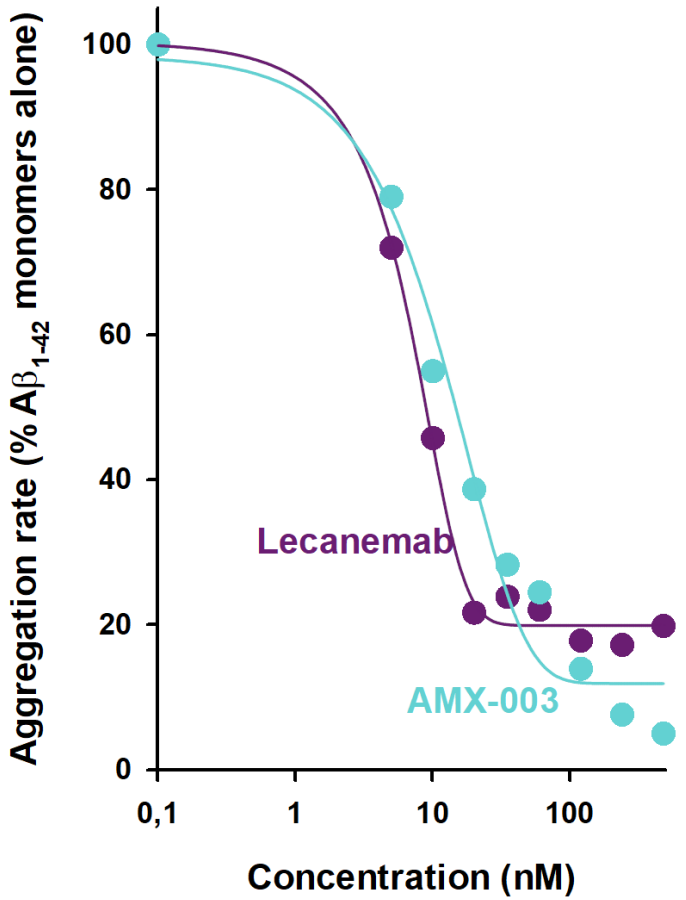


AMX-003 inhibits aggregation of Aβ and Tau monomers *in vitro*

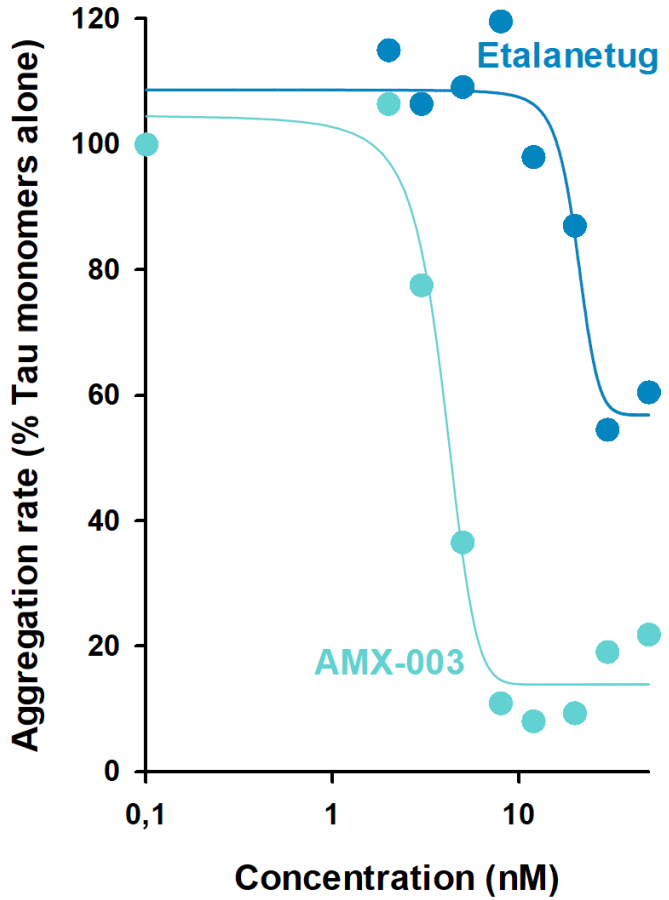


IC_{50} (nM)	Aβ	Tau
Lecanemab	14	NA
Etalanetug	NA	37
AMX-003	9	7

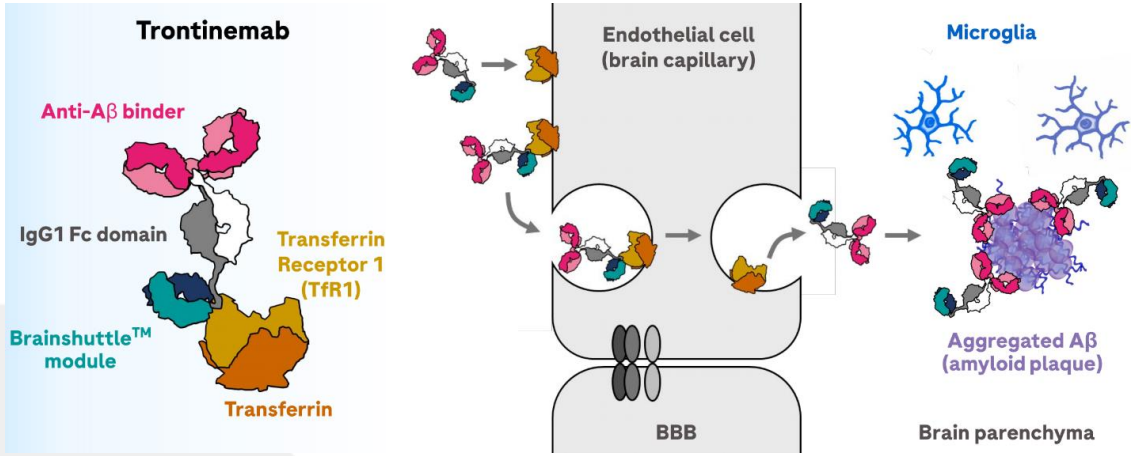
Unseeded aggregation inhibition *in vitro* assay Aβ 1-42 monomers



Unseeded aggregation inhibition *in vitro* assay Tau monomers



TfR1-shuttled AMX-003 shows superior brain penetration than Trontinemab in mouse expressing hTfR1

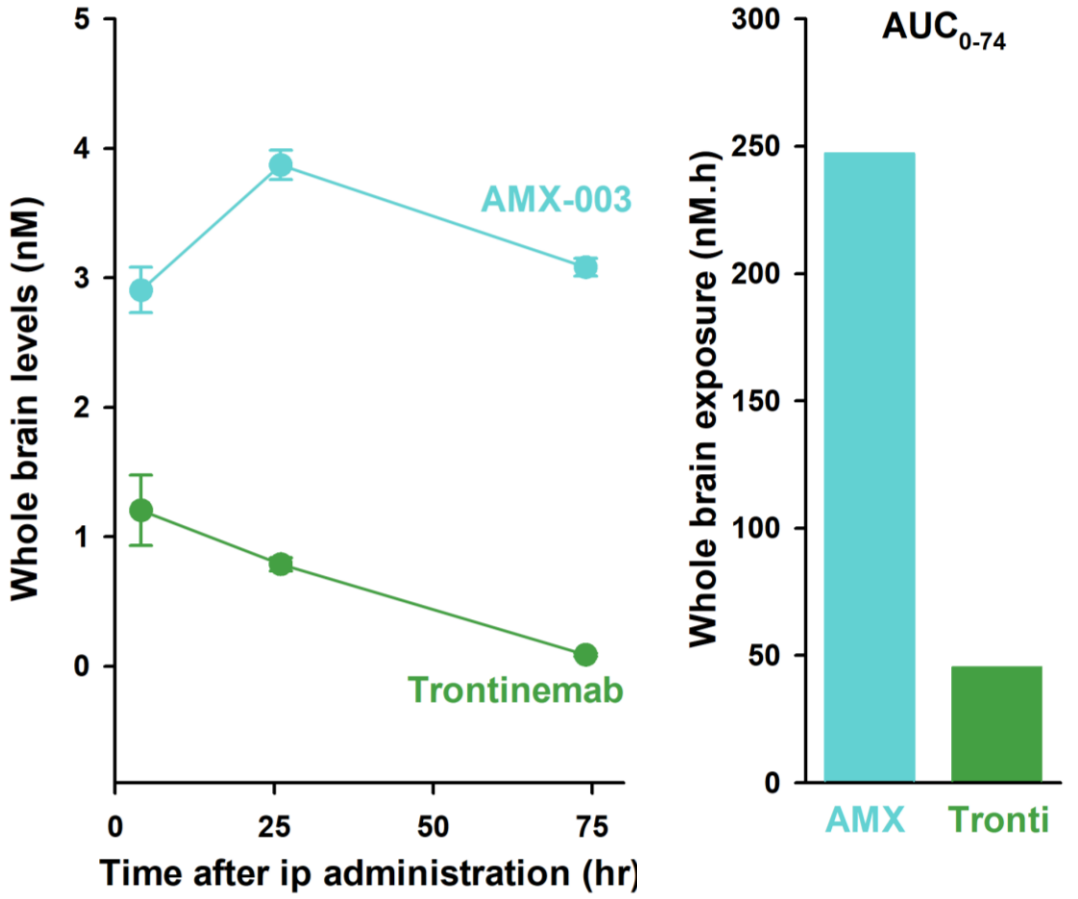


hTfr1 mice

ip 170 nmol/kg

3 mice / group / time point

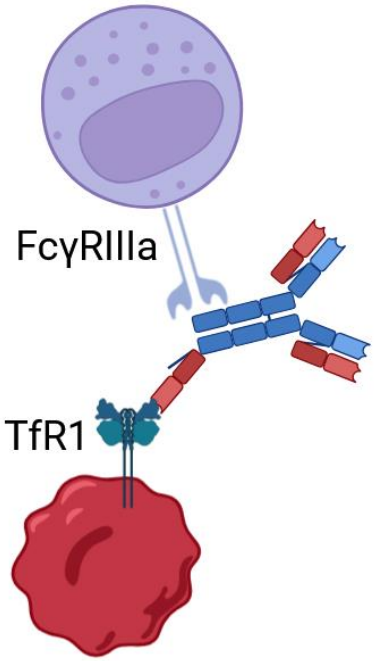
Whole brain levels and AUC



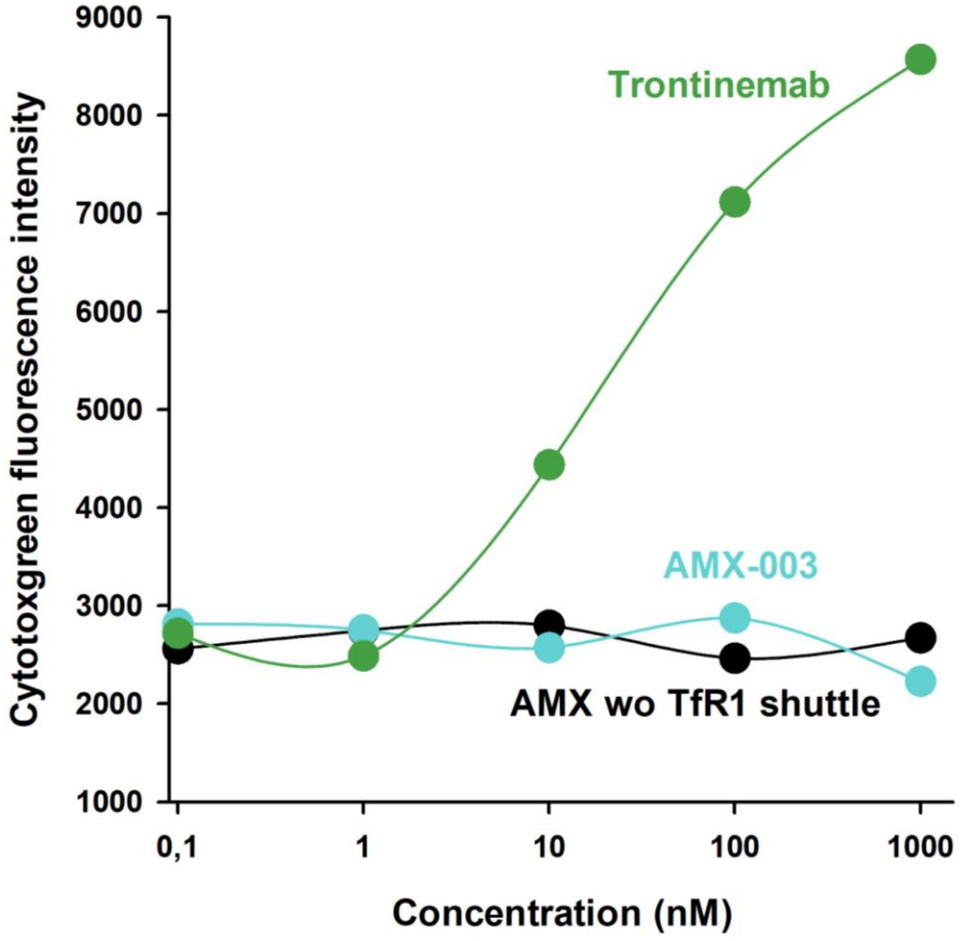
Kulic et al., AD/PD 2025 presentation

AMX-003 does not induce TfR1-associated ADCC

Mild anemia observed in 10-20% of patients treated with Trontinemab through an ADCC mechanism



Primary human NK cells isolated from PBMCs co-cultured with hTfR1 CHO cells



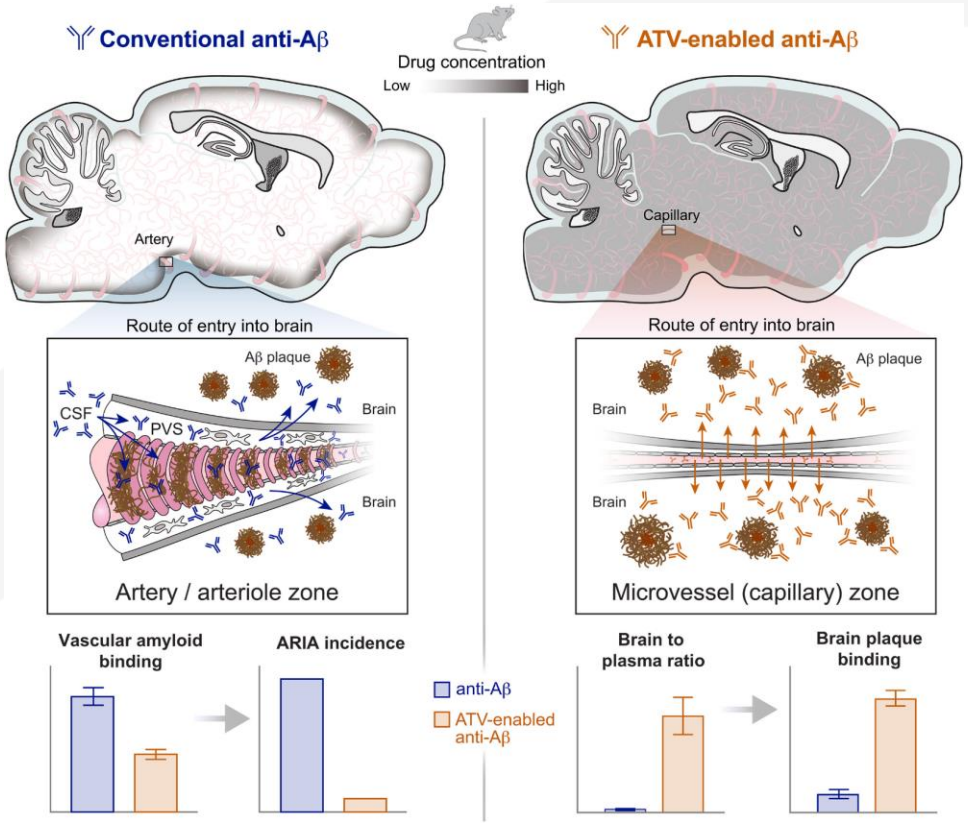
Adapted from 2025 Kulic (CTAD presentation)

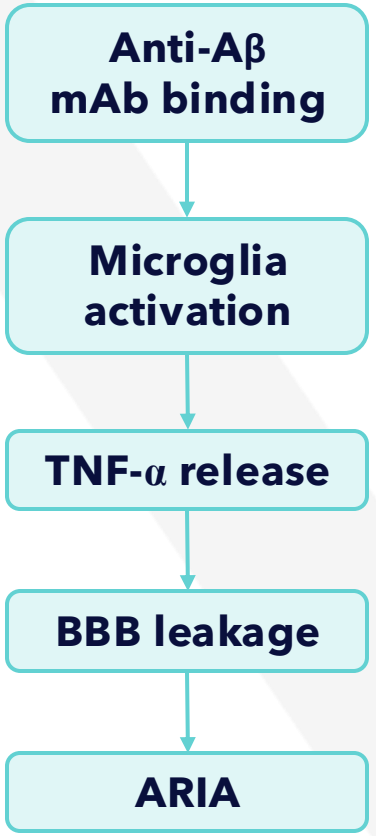
AMX-003 reduces risk of ARIA development via two mechanims

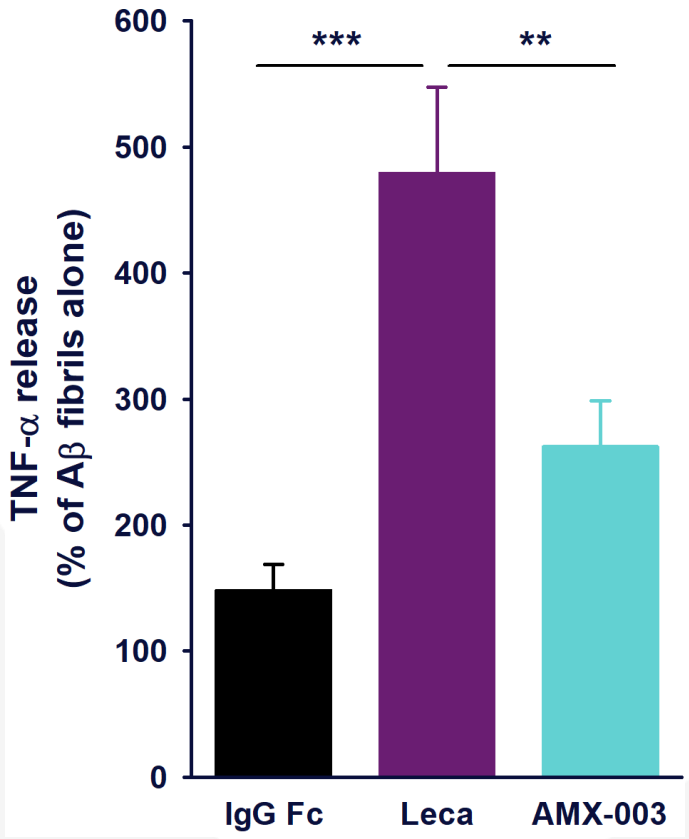
Another route of penetration through shuttling (arteriole vs microvessel)

AND

Reduced TNF-α release vs Lecanemab in iPSC-derived human microglial cells

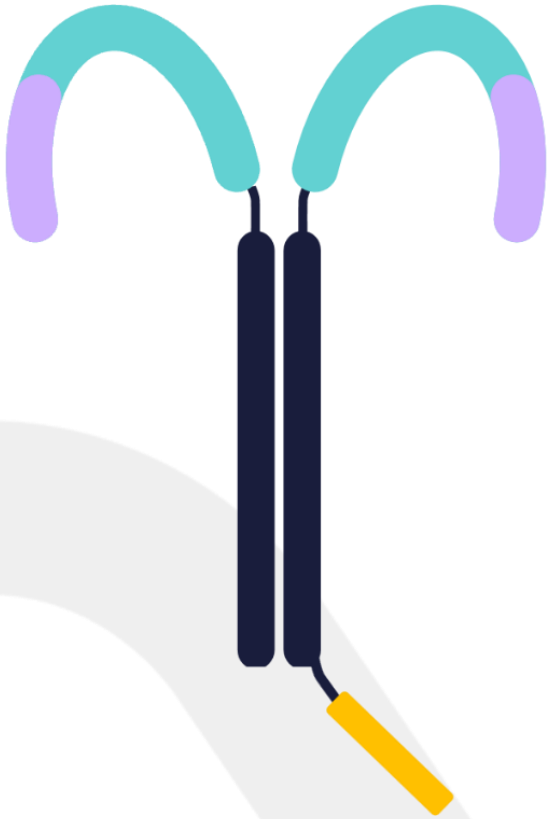






Pizzo et al., Science, 2025
Krick et al., Alzheimers Dement., 2025

Conclusions and future direction



Increased efficacy compared to mAb by binding and clearing all types of amyloid aggregates with a single product

Increased brain penetration through conjugation to a TfR1 shuttle and small size (120 kDa)without the anemia-related adverse events

Increased safety by mitigating ARIA-related risk using two different strategies (TfR1 shuttling + reduced TNF-α release)

Clinical candidate nomination | **In vivo POC** | **Clonal selection**

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Thank you!

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Thank you!

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If you want to see more of our dataset:

Aditya Iyer, Senior Project Manager, Amyl Therapeutics

"Crossing therapeutic boundaries:

An immunotherapeutic simultaneously targeting amyloid-β, Tau, and α-synuclein amyloid aggregates"

21st of March, Hall A3, 18:15