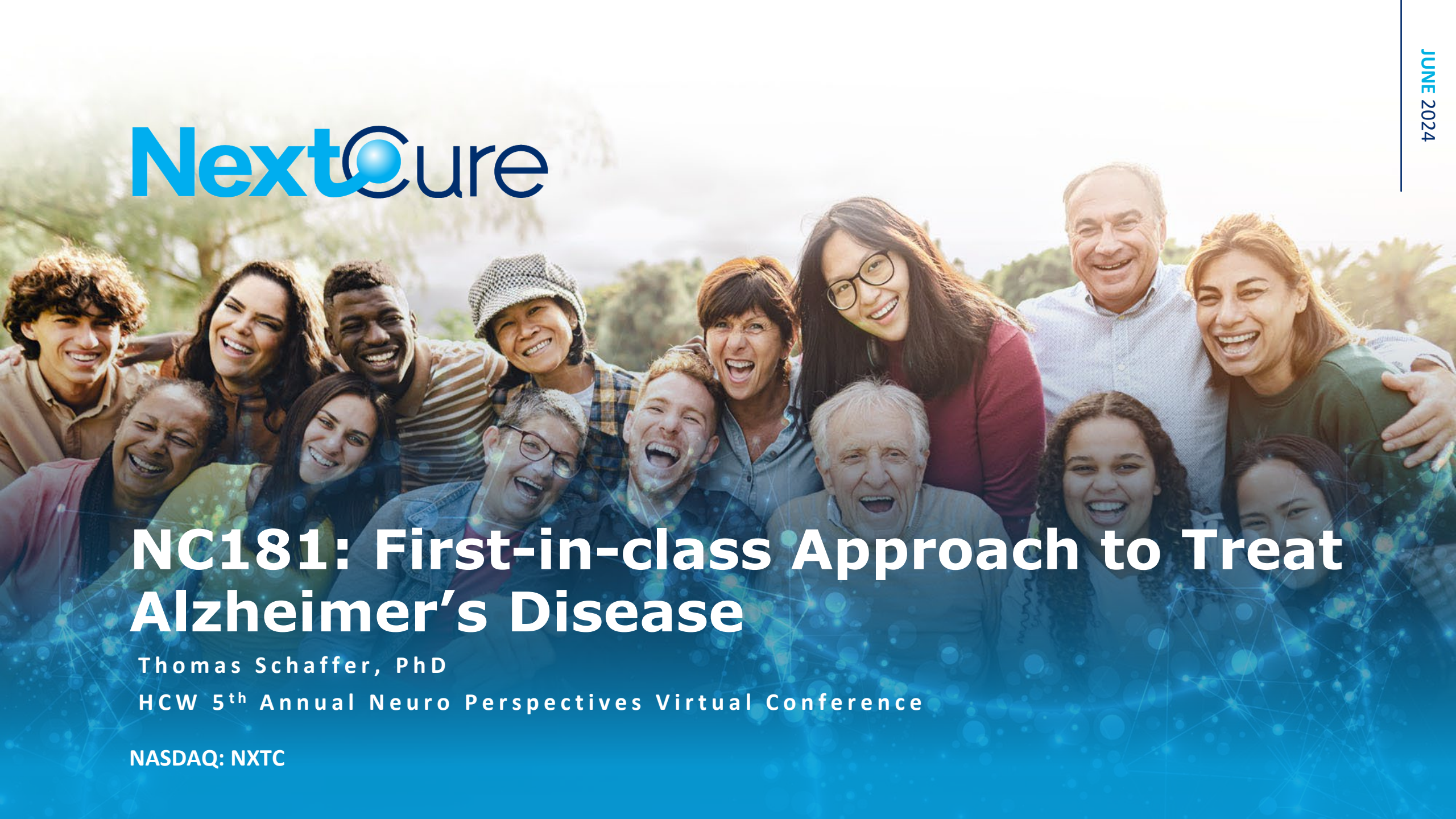
JUNE 2024



NC181: First-in-class Approach to Treat Alzheimer's Disease

Thomas Schaffer, PhD

HCW 5th Annual Neuro Perspectives Virtual Conference

NASDAQ: NXTC

Forward-Looking Statement

To the extent that statements contained in this presentation are not descriptions of historical facts, they may be deemed to be forward-looking statements under the Private Securities Litigation Reform Act of 1995. These statements are based on current expectations, forecasts, assumptions and other information available to NextCure as of the date hereof. Forward-looking statements include statements regarding NextCure's expectations, beliefs, intentions or strategies regarding the future and can be identified by forward-looking words such as "may," "will," "potential," "expects," "believes," "intends," "hope," "towards," "forward," "later" and similar expressions. Examples of forward-looking statements in this presentation include, among others, statements about the development plans for our products, statements about the progress and evaluation and expected timing of results of NextCure's ongoing or planned clinical trials, expectations regarding the potential benefits, activity, effectiveness and safety of our research stage, preclinical stage, and clinical stage therapeutic candidates, NextCure's financial guidance, expected upcoming milestones, and NextCure's plans, objectives and intentions with respect to the discovery and development of therapeutic products. Forward-looking statements involve substantial risks and uncertainties that could cause actual results to differ materially from those projected in any forward-looking statement. Such risks and uncertainties include, among others: the impacts of the COVID-19 pandemic on NextCure's business, including NextCure's clinical trials, third parties on which NextCure relies and NextCure's operations; positive results in preclinical studies may not be predictive of the results of clinical trials; NextCure's limited operating history and no products approved for commercial sale; NextCure's history of significant losses; NextCure's need to obtain additional financing; risks related to clinical development, marketing approval and commercialization; the unproven approach to the discovery and development of product candidates based on NextCure's FIND-IO™ platform; and dependence on key personnel. More detailed information on these and additional factors that could affect NextCure's actual results are described in NextCure's filings with the Securities and Exchange Commission (the "SEC"), including in Item 1A of NextCure's most recent Form 10-K, subsequent Form 10-Q and elsewhere in the Company's filings with the SEC. You should not place undue reliance on any forward-looking statements. Forward-looking statements speak only as of the date of this press release, and NextCure assumes no obligation to update any forward-looking statements, except as required by law, even if expectations change.

Alzheimer's	Cerebral Amyloid Angiopathy	Dementia

NC181

APOE4 mAb for Neurogenerative Diseases

IND mid 2025*

*Pending availability of financing and/or partnering

NextCure

NC181 Treatment for Alzheimer's Disease

Alzheimer's disease is the most common dementia, afflicting nearly 7M Americans

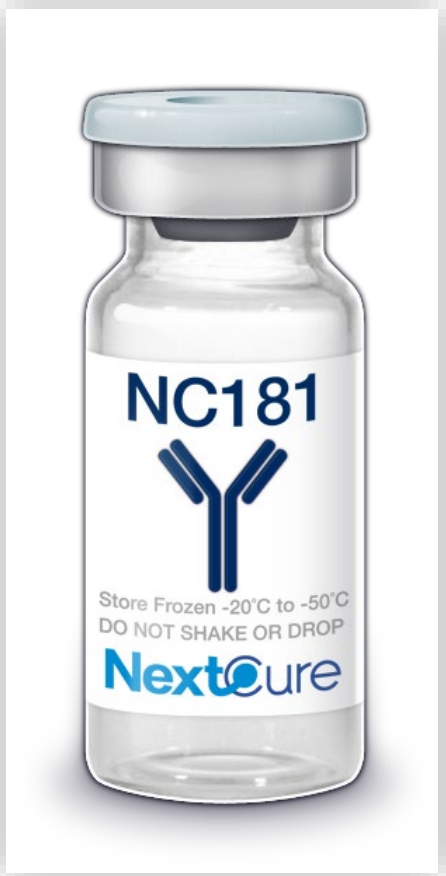
APOE4 is major genetic risk factor for Alzheimer's disease

NC181 is a humanized APOE4 mAb

Top-tier collaboration with Dr. Holtzman, who established the proof of mechanism of APOE4 targeting

NC181

On Track for an IND in mid 2025



COMPLETED

- ✓ Demonstrated activity in disease models
- ✓ Improves brain vasculature
- ✓ Master cell bank available

ONGOING

- Tox studies
- Pre-IND meeting preparation
- Manufacturing of clinical supplies
- Clinical development planning

FIRST-IN-CLASS

Targets APOE4,
a major genetic risk factor
for neurodegeneration

LARGE OPPORTUNITY

Nearly 7 million patients in the US in 2023, expected to hit 13.8 million by 2060

NextCure

NC181

Opportunity for Patients not Benefiting from Amyloid Products

EFFICACY AND SAFETY

Removes plaques
with reduced ARIA susceptibility
compared to anti-Aβ
immunotherapy

FUNCTIONAL CAPABILITIES

Functional screens, mAb production, and biomarkers

Next Wave in Alzheimer's Disease is APOE4

SOLUTION FOR APOE4 AD PATIENTS — **NC181**

Benefits
- Plaque reduction
- Reducing cognitive decline

Limitation
- Safety issues (ARIA toxicities)

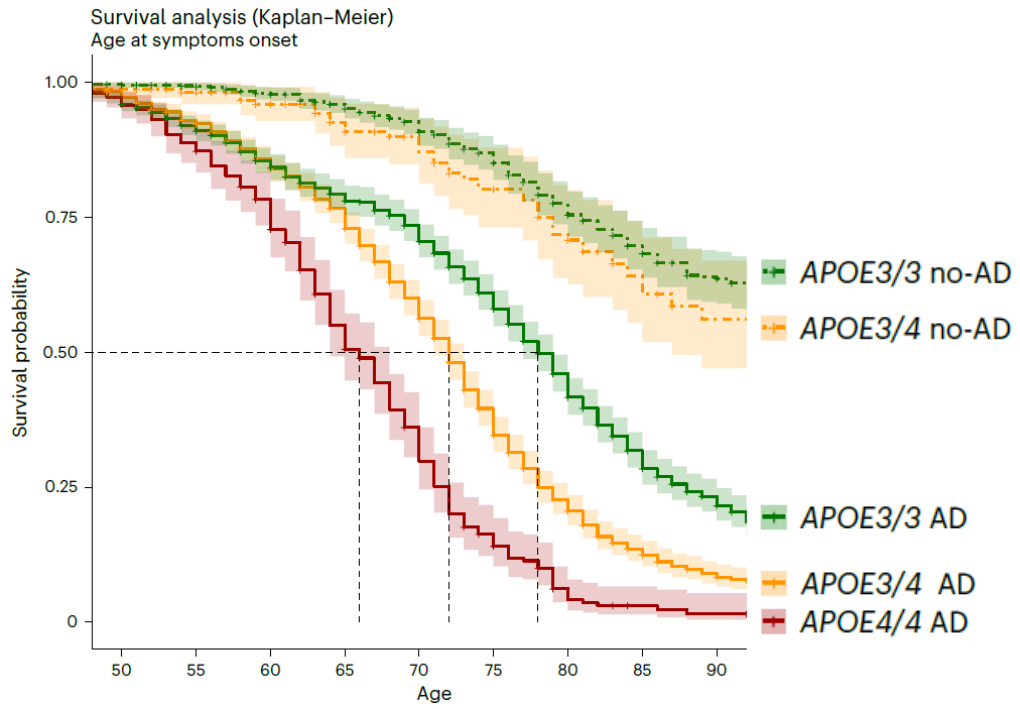
APOE4 carriers
- Lack of benefit from amyloid products
- Increase ARIA toxicities
- Accelerated disease development

Opportunity
- Need for APOE4 specific therapeutics
- Biomarker driven development

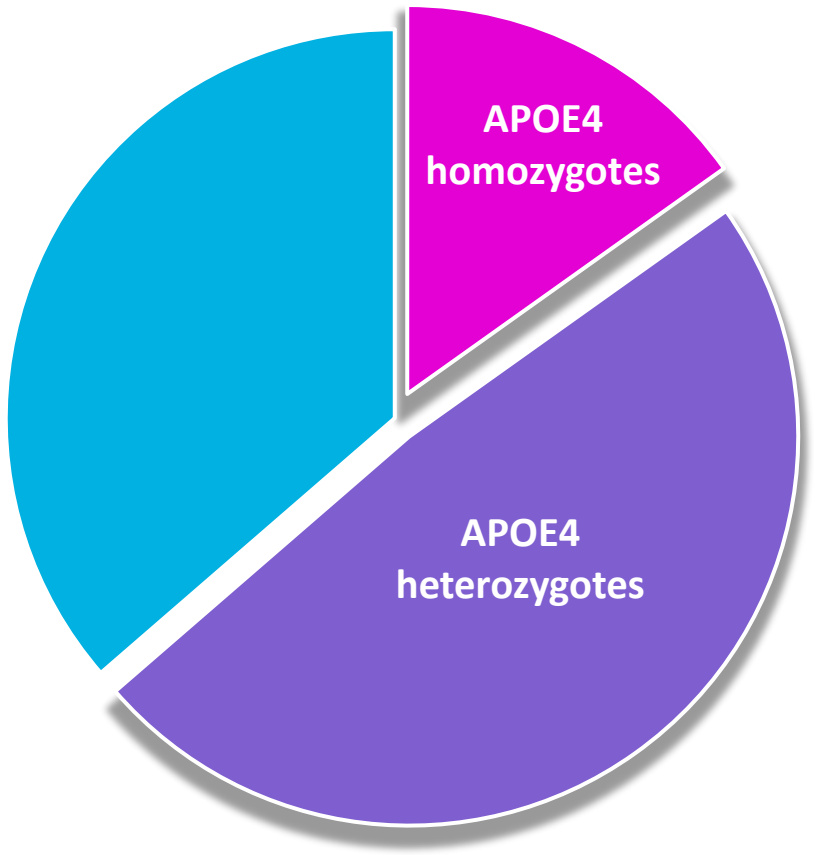
AD Pathology Accelerated in APOE4 Carriers

Opportunity for NC181

Address APOE4-Mediated Decline



>33M People Suffer from Alzheimer's Disease Worldwide



Fortea J, et al. Nat Med 2024

Recent APOE4 Publications Highlight an Area of Unmet Need Not Addressed by Amyloid Products

nature medicine

APOE4 homozygosity represents a distinct genetic form of Alzheimer's disease

Fortea J et al., *Nat Med*, May 2024

Neuron
A Cell Press journal

APOE loss-of-function variants: Compatible with longevity and associated with resistance to Alzheimer's disease pathology

Chemparathy A et al., *Neuron*, Jan 2024

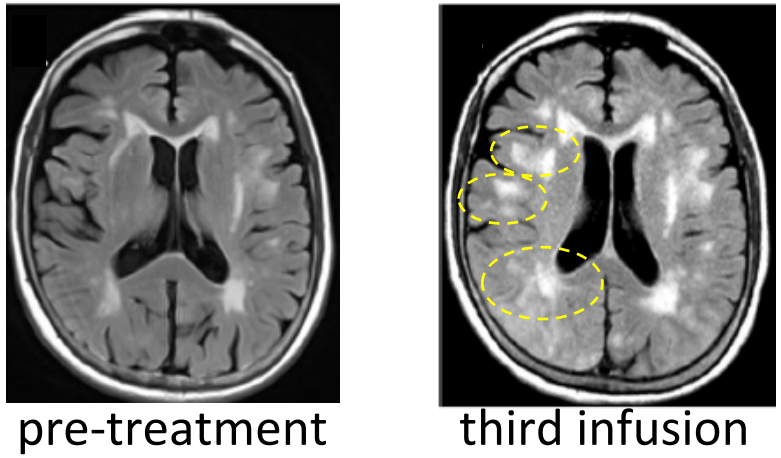
APOE4 Gene Dosage is a Major Risk Factor for Anti-Aβ Immunotherapies

Limitations of Amyloid products in APOE4 Carriers (50-60 % of AD patients)

Lecanemab (Biogen, Eisai)

Donanemab (Lilly)

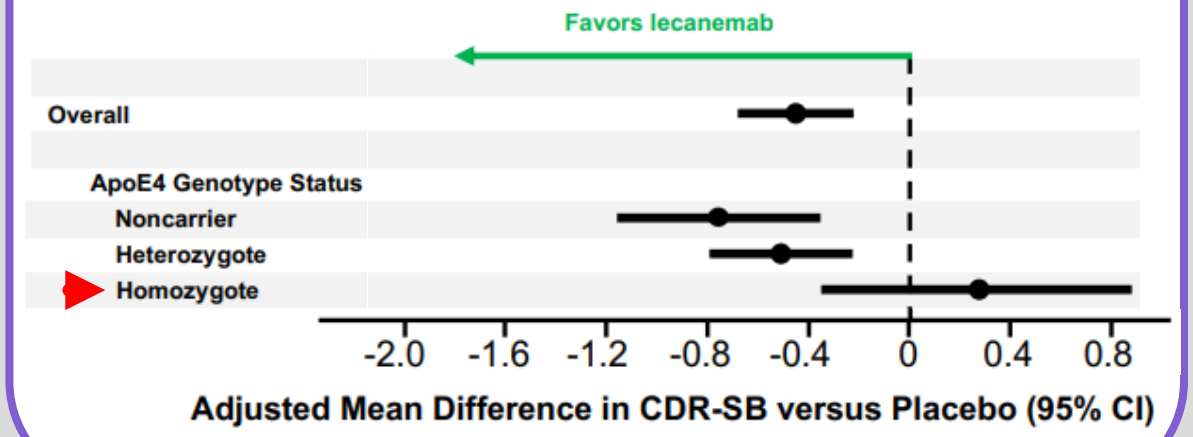
Increased ARIA-E as Observed with Lecanemab



pre-treatment third infusion

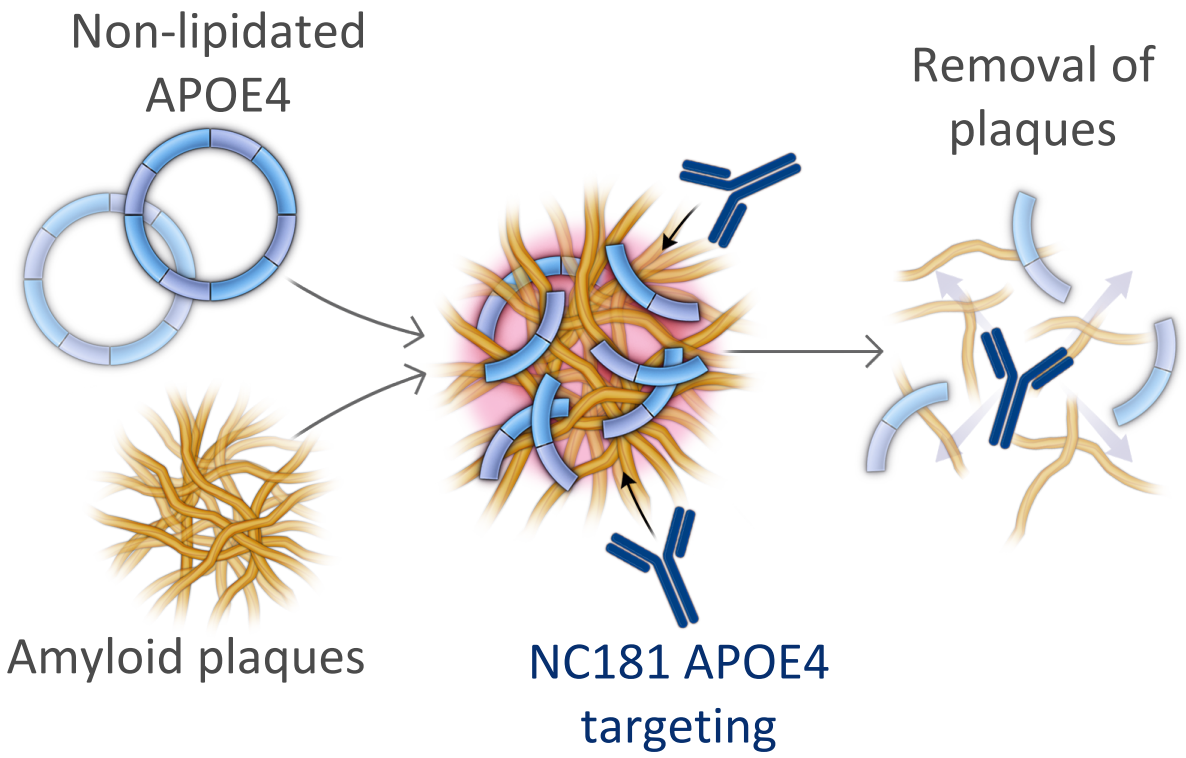
Adapted from Solopova E, et al. Nat Commun (2023)

Limited Clinical Benefits



Adapted from van Dyck, et al. NEJM 2022 (supplemental)

NC181
Targeting APOE4 to Remove Plaques



A POTENTIALLY SUPERIOR AND SAFER THERAPY

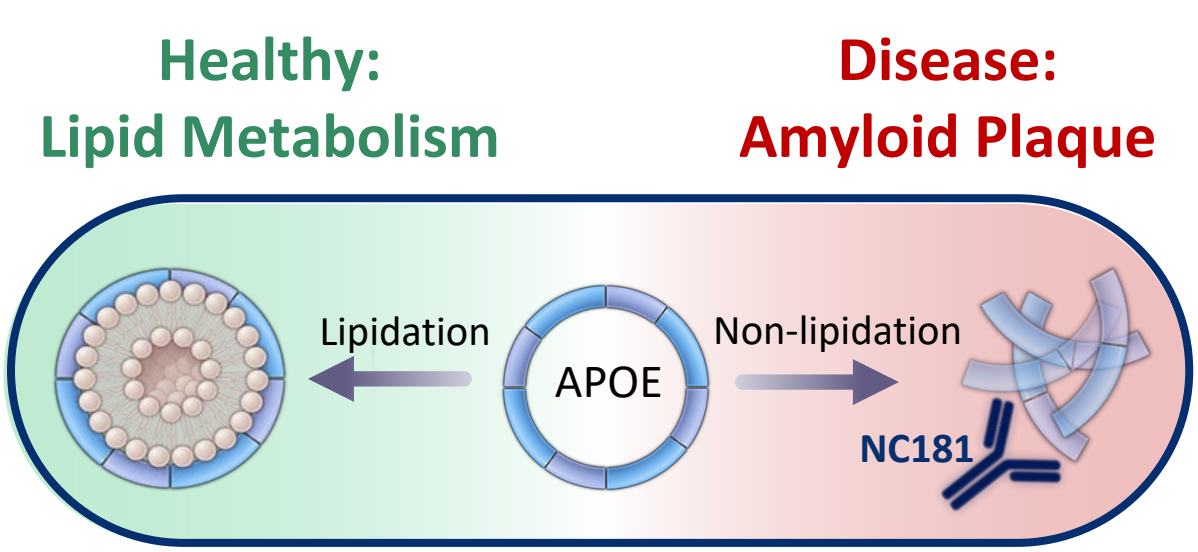
- ✓ Removes amyloid plaques
- ✓ Suppresses neuroinflammation
- ✓ Improves cerebrovascular function
- ✓ Crosses the blood brain barrier (BBB)

POTENTIAL TO EXPAND INTO OTHER INDICATIONS

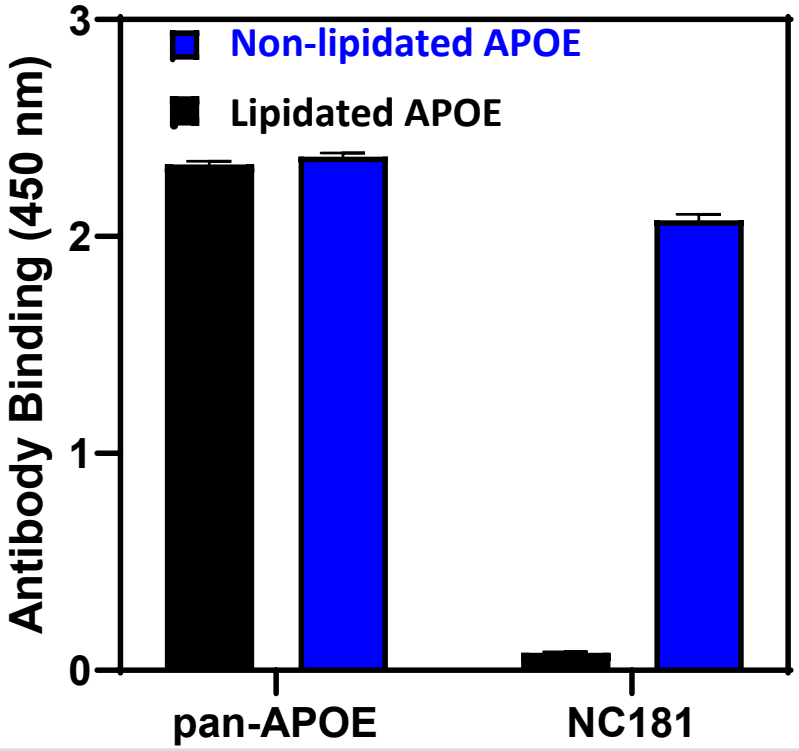
- Cerebral Amyloid Angiopathy (CAA)
- Other dementias

NC181 Specifically Recognizes a Disease Associated Form of APOE

APOE Biology

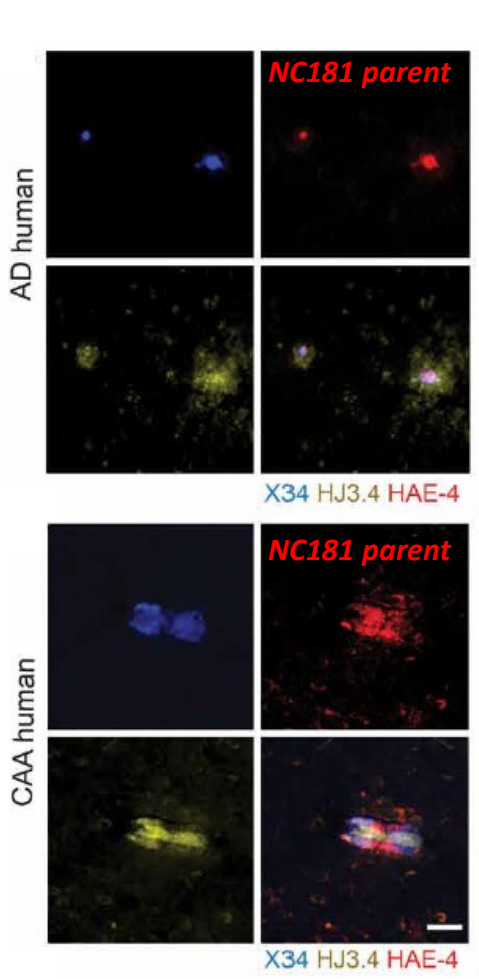


NC181 Recognizes Non-Lipidated APOE



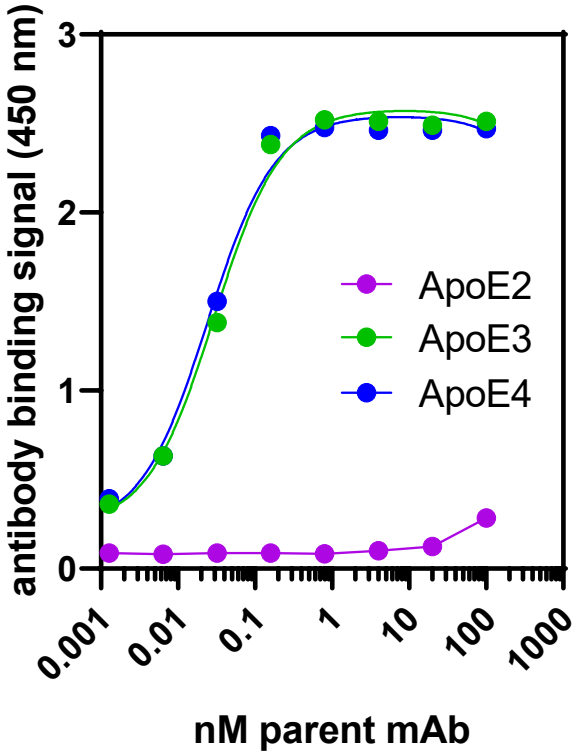
NC181 Binds Amyloid Plaque-associated APOE3 and APOE4

Parent mAb Binds Parenchymal & Vascular Amyloid



Xiong et al. *Sci. Trans. Med*. 2021

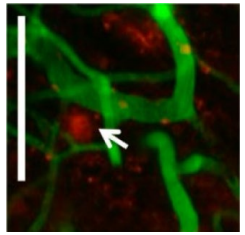
Does not Bind Protective APOE2 Variant



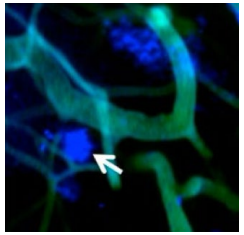
NC181 Targets APOE4 in the CNS and Removes Plaques Safely

Targets APOE4

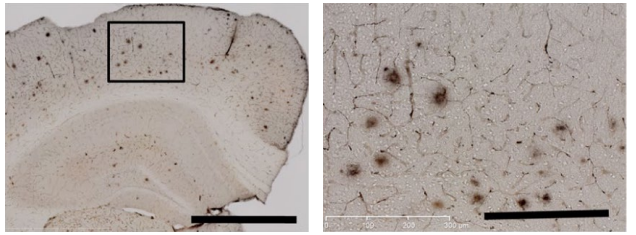
APOE4 STAINING



PLAQUE STAINING



NC181 PARENT STAINING

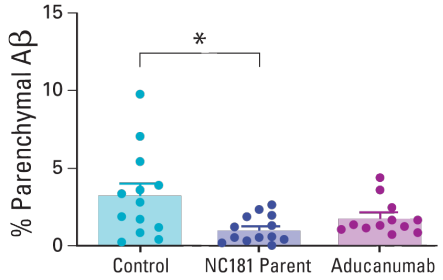


Antibody given systemically and brains harvested for staining

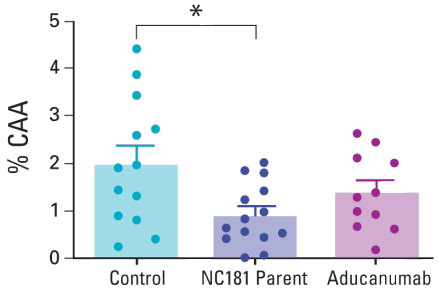
Plaque Localization

Decreases Plaques

PARENCHYMAL PLAQUES

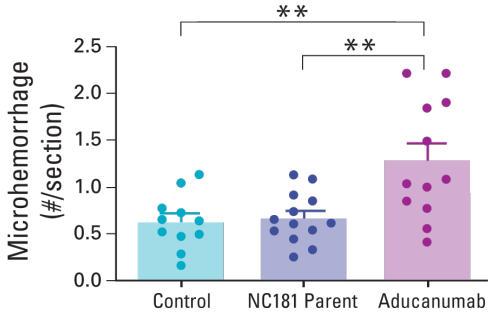


VASCULAR PLAQUES



Plaque Removal

Prevents Microhemorrhages



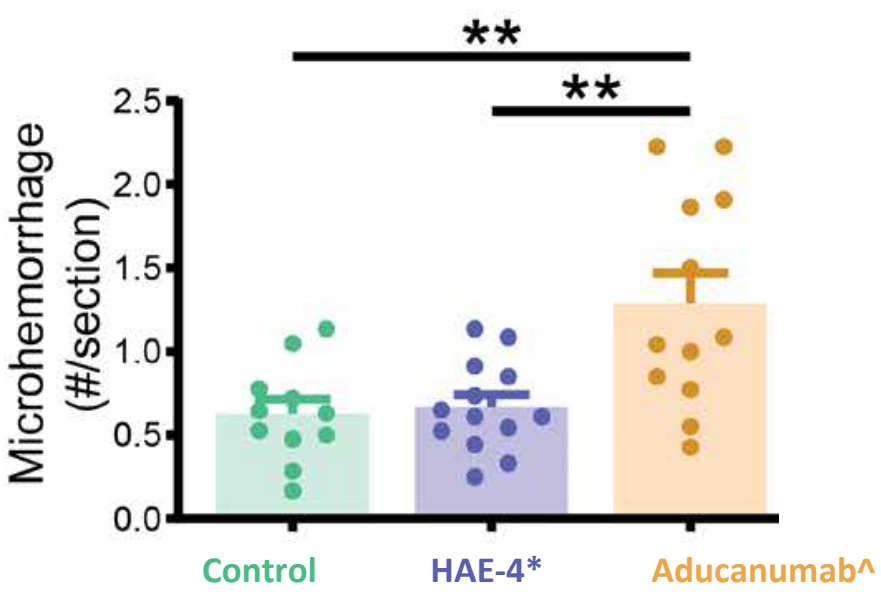
Microhemorrhages Associated with Treatment Induced ARIA* Observed in the Clinic

Lower Side Effects

*ARIA - Amyloid Related Imaging Abnormalities

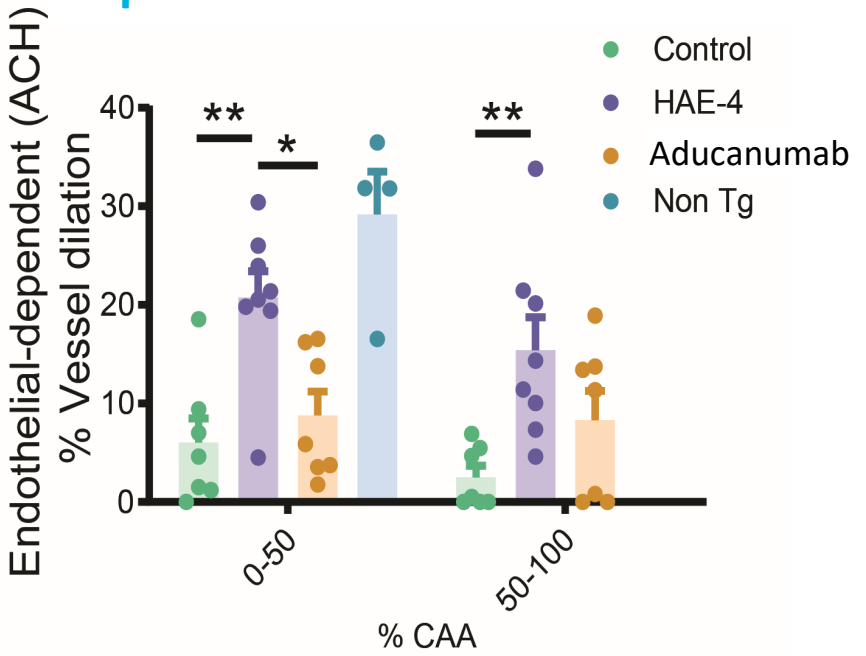
NC181: Reduced Side Effects, Improved Vascular Function, Improved Safety Profile

Reduced Microhemorrhages



Reduced Microhemorrhages by NC181 May Address ARIA toxicities seen with Amyloid products (like Aducanumab)

Improved Neurovascular Function



Increased Dilation of Arteries Following Stimulation with Acetylcholine (ACH)

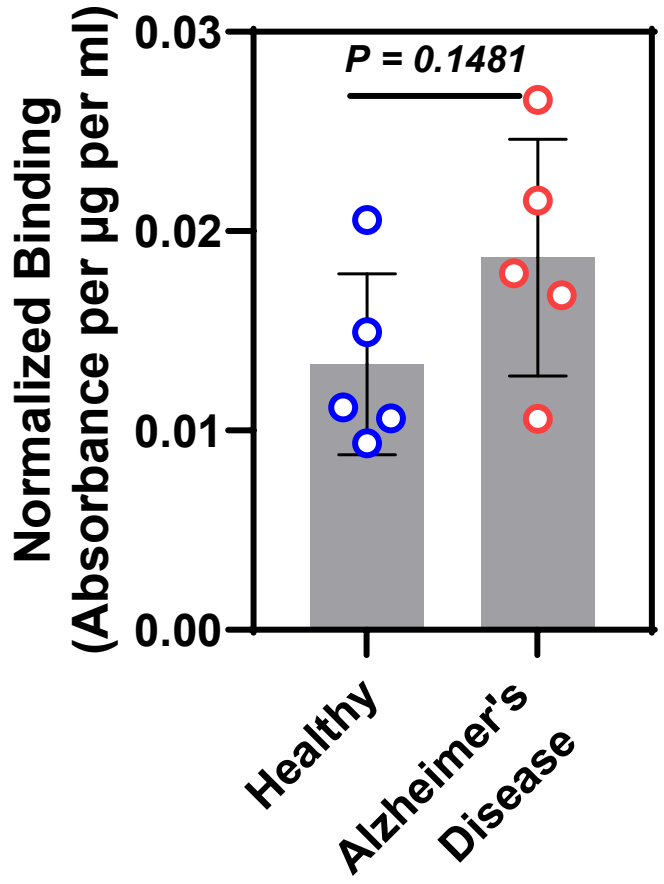
*Murine mAb parent of NC181
^Chimeric version of aducanumab

Xiong et al. (2021) *Sci Transl Med*

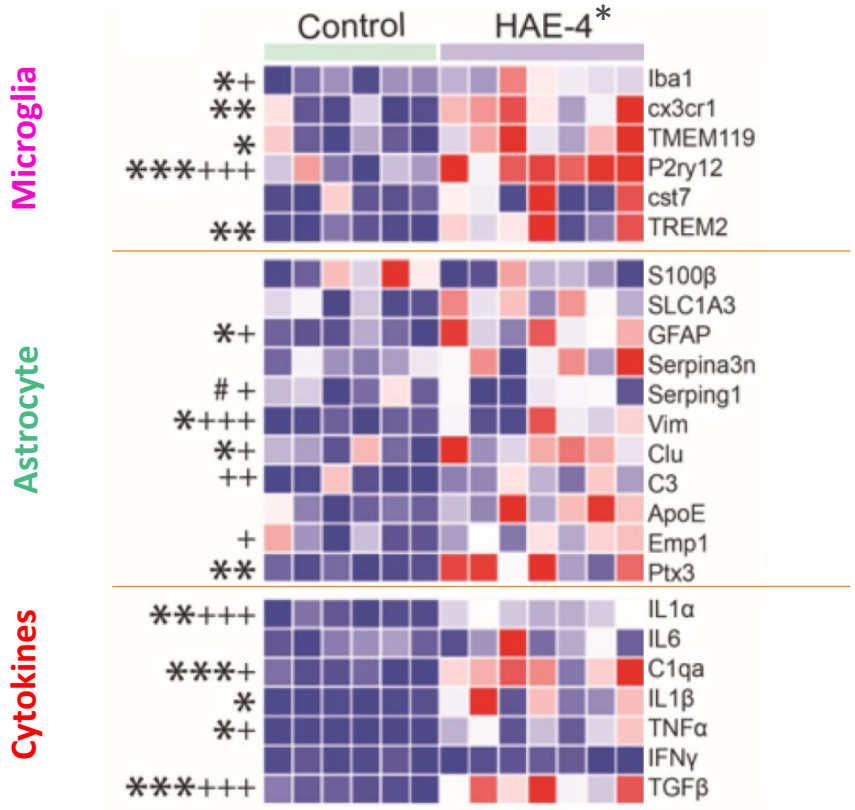
Potential Biomarkers for Clinical Development

Binds Non-Lipidated APOE in AD Patient CSF

NC181



Markers of Acute Neuroimmune Engagement



*Murine mAb parent of NC181

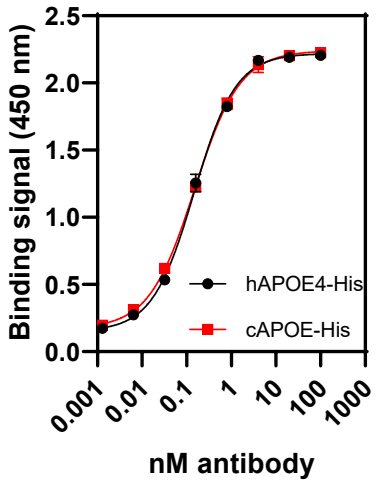
Xiong et al. *Sci. Trans. Med*. 2021

Cyno Safety and PK Study: Well Tolerated and Crosses BBB

Study Design

- Non-naïve cynos dosed i.v.
- 1, 10, 50 mg/kg doses with two cynos per dose level
- Plasma and CSF collected longitudinally for PK & biomarker analysis

NC181 Cross-Reactivity:
Comparable binding to homologus, non-lipidated cyno APOE (cAPOE) and human APOE4 (hAPOE4)



Findings

Clinical

- No significant tox concerns for duration of study
- No statistically-significant changes in clinical chemistry values

PK

Plasma half-life[1]	two compartment model: • α = 2- 3 hrs • β = 6.5 – 11 days
CSF half-life[1]	10.2 – 29 days (non-compartment model)
CSF exposure	~0.02 – 0.03% of plasma concentration (comparable to other therapies)
ADA	In 2 animals (10 m/kg and 50 mg/kg) impacting drug concentration levels for these animals

1.Analysis of 10 mg/kg and 50 mg/kg animals without ADA

NC181 Initial Clinical Development Plan in Alzheimer's Disease

Phase 1 Single and Multiple Ascending Dose Study in AD Patients

Primary Endpoints

- Safety and tolerability
  - -Brain MRI
  - -Vital signs
  - -Physical exam
  - -Clinical chemistry
  - -ECG
  - -C-SSRS

Secondary Endpoints

- Drug PK in plasma and CSF
- Amyloid PET

Exploratory Readouts in Serum and CSF

- Ab42/Ab40 (Plasma)
- P-tau$_{217}$ (Plasma)
- Target engagement (CSF)
- Inflammatory markers:
  - -GFAP (Plasma)
  - -sTREM2 (CSF)
  - -C1qa (CSF)
  - -Ptx3 (CSF)
  - -C3 (CSF)
  - TGFb (CSF)

A First-in-class Approach to Treat Alzheimer's Disease

NC181

SUMMARY

- ✓ Removes amyloid plaques in parenchyma and vasculature
- ✓ Mitigates CAA inflammatory response and improves vascular function
- ✓ Humanization complete with clinical candidate selected
- ✓ Pilot NHP study: competitive PK, well-tolerated and Crosses BBB
- ✓ Biomarker identified to enable early clinical development
- ✓ IND mid 2025 for Phase 1a/1b trials pending availability of financing