Corporate Deck

Alector Brain Carrier Platform & Pipeline

September 2026

Forward-Looking Statement

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially," "predict," "project," "should," "target," "will" or the negative of these terms or other similar expressions. Forward-looking statements contained in this presentation also include, but are not limited to, statements regarding: our future financial condition; results of operations; business strategy and plans; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates and our Alector Brain Carrier (ABC) blood-brain barrier technology platform; our plans, timelines, and expectations related to our product candidates in our clinical and pre-clinical programs and our ABC platform, including with respect to the availability of data, the initiation of future clinical trials and plans and expectations regarding planned regulatory filings with respect to such programs; expectations regarding the timing and financial benefit of our operations; and objectives of management for future operations, as well as statements regarding industry trends.

We, Alector, Inc. ("Alector"), have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: Alector's plans relating to its research programs, preclinical and clinical development programs and the development and manufacturing of its product candidates and its Alector Brain Carrier (ABC) blood-brain barrier technology platform, including its programs and product candidates incorporating the ABC platform; the ability of Alector's preclinical studies and clinical trials to demonstrate safety and efficacy of its product candidates, and other positive results; the timing and focus of Alector's clinical trials, and the reporting of data from those trials, the expected potential benefits of strategic collaborations with third parties and Alector's ability to attract collaborators with development, regulatory, and commercialization expertise; Alector's estimates of the number of patients in the United States, Australia, the European Union, and world-wide who suffer from the diseases it is targeting and the number of patients that will enroll in its clinical trials; the anticipated timing of enrollment in its clinical trials; the size of the market opportunity for Alector's product candidates in each of the diseases it is targeting; Alector's ability to expand its product candidates into additional indications and patient populations; the success of competing therapies that are or may become available; the beneficial characteristics, safety, efficacy, and therapeutic effects of Alector's product candidates; the timing or likelihood of regulatory filings and approvals, including Alector's plans for IND and CTN submissions, timing of clinical data, and any expectation to seek special designations, such as orphan drug or breakthrough designation, for its product candidates for various diseases; Alector's ability to obtain and maintain regulatory approval of its product candidates; Alector's plans relating to the further development and manufacturing of its product candidates, including additional indications that it may pursue; existing and future regulations and regulatory developments in the United States and other jurisdictions; Alector's reliance on third parties to conduct clinical trials of its product candidates, and for the manufacture of its product candidates for preclinical studies and clinical trials; the impact of worldwide economic conditions, including macroeconomic conditions, inflation, supply chain disruptions, trade tariffs, and economic impacts of pandemics or other public health outbreaks, geopolitical events and international conflict on our business; and the other risks, uncertainties and assumptions discussed in the public filings we have made and will make with the Securities and Exchange Commission ("SEC"). These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

This presentation may contain results from our preclinical studies and clinical trials or statements regarding ongoing preclinical studies and clinical trials, and this presentation does not speak to, and you should make no assumptions about, any further information or data relating to those trials. In addition, the information we have chosen to publicly disclose regarding our product candidates has been selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise. If the initial data that we report differ from updated, late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

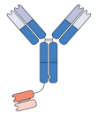
This presentation discusses certain investigational therapeutic agents which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidate for the therapeutic use for which it is being studied.

This presentation may contain statistical data based on independent industry publications or other publicly available information, as well as other information based on our internal sources. We have not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, we make no representations as to the accuracy or completeness of that data.

Except as required by law, we undertake no obligation to update any statements in this presentation for any reason after the date of this presentation. We have filed Current Reports on Form 8-K, Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and other documents with the SEC. You should read these documents for more complete information about us. You may obtain these documents for free by visiting EDGAR on the SEC website at www.sec.gov.

Our Assets

AL137 (AD)*, AL037 backup molecule
ABC Anti-Aβ Antibody



2026: NHP IND-enabling studies
2027: Targeting First-in-Human

- High brain exposure, planning SC delivery
- Full effector function to optimize efficacy
- Targeting no ARIA, anemia, or IRR
- Ph 1b – amyloid PET reduction, safety

AL064/AL164 (AD)*
ABC Tau siRNA

2026: NHP knockdown validation
2027/8: Targeting First-in-Human

- Durable target knockdown
- Targeting SC delivery every 3 months
- Favorable safety
- Ph 1b – Tau reduction & safety

AL062 (PD)*
ABC α–Syn siRNA

2026: NHP safety and efficacy planned
Targeting 2028: First-in-human – Synuclein reduction

- Potentially superior efficacy vs. blocking Abs
- Durable target knockdown
- Targeting SC delivery every 3 months

ADP065 (AD)*
ABC NLRP3 siRNA

2026: NHP safety & efficacy planned
Targeting 2028: First-in-human – functional readouts of NLRP3 reduction in CSF (IL-1β, IL-18)

- Potentially superior brain penetration and knockdown vs. small molecules
- Targeting SC delivery every 3 months

AL050 (PD, LBD)*
ABC GCase ERT

2026: NHP exposure and rescue validation

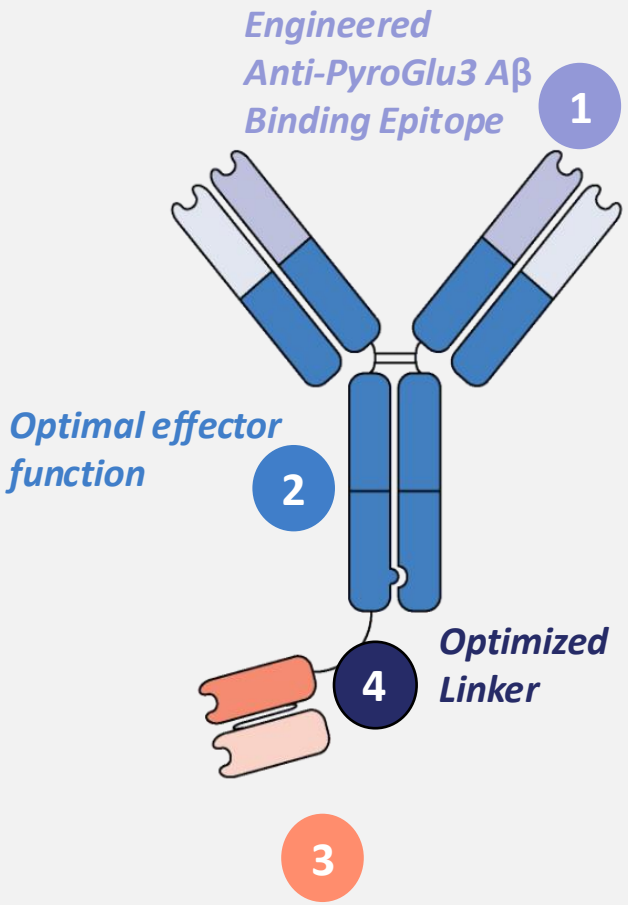
- Targeting First ERT for PD-GBA
- Targeting all GCase LOF mutations
- Enables flexible dosing regimen
- Ph 1b Engagement, GlcSph reduction

** Dates and differentiation represent forward-looking statements subject to the substantial risks and uncertainties listed on slide 2. FIC= first-in-class; AD=Alzheimer's disease; PD=Parkinson's disease; LBD=Lewy Body Dementia; α-Syn=Alpha Synuclein; SC-=subcutaneous; NHP=Non-Human Primates; ABC= Alector Brain Carrier; ARIA=Amyloid-Related Imaging Abnormalities; IRR=Infusion-related reaction; ERT=Enzyme Replacement Therapy*

AL137

ABC-enabled Anti-amyloid beta (Aβ) Antibody Program

AL137: Best-in-Class Molecular Design Combining Eight-Attribute Advantage



Selective Binding to Toxic Aβ
Designed to bind PyroGlu3 Aβ Epitope

Facilitates Phagocytosis of Aβ
Induces Microglia to remove Aβ plaques

High Brain Distribution and Exposure
Double-digit nM 24h after 10 mg/kg IV in NHPs

Low Projected Efficacious Dose
Intended to support low monthly dose

Supports SC Delivery
Superior relative brain exposure vs. IV

Favorable Safety Profile
No adverse effects observed at the SC doses tested

Full Effector Function
Designed to maximally recruit brain immune cells to remove Aβ plaques

High-Productivity Manufacturability
High-expressing cell line designed to support large-scale manufacturing

Targeting Best-in-Class Efficacy, Safety and Ease of Use With Reduced Safety Monitoring

alector

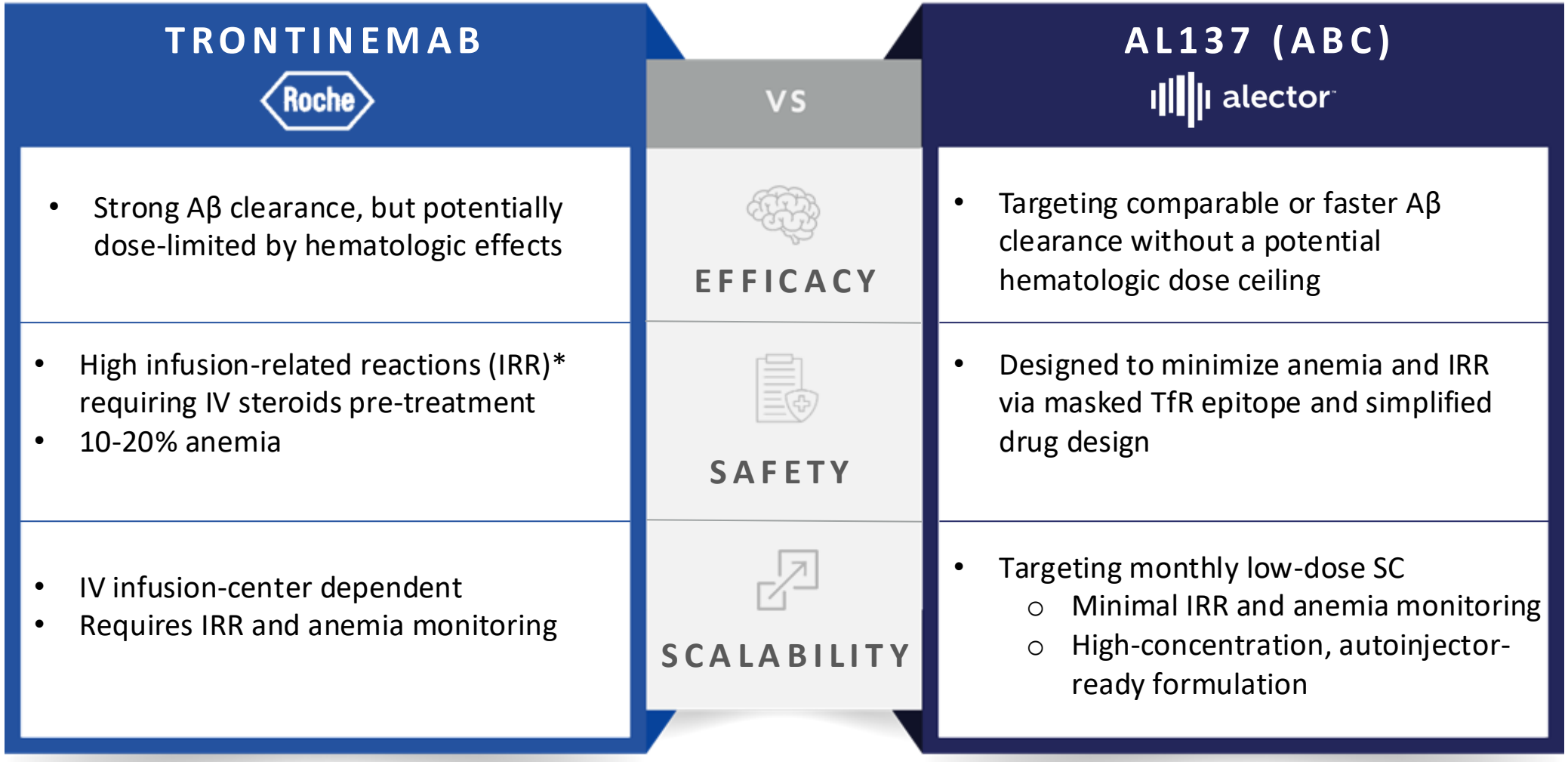
SC = subcutaneous

AL137 Designed to Overcome Efficacy Constraints of Third-Generation Anti-Aβ Antibodies

1st Generation	2nd Generation (e.g. Trontinemab)	3rd Generation (e.g. AbbVie Denali, Korsana)	Next Generation (Alector's ABC)
Approach: No TfR, full effector function	**Approach:** Exposed TfR binding epitope	**Approach:** Exposed TfR binding epitope	**Approach:** TfR epitope blocks reticulocyte-associated FcγR co-binding while preserving plaque-associated FcγR engagement
Safety Risk: ARIA risk	**Safety Risk:** No ARIA, but anemia risk with full effector function	**Safety with Compromised Efficacy:** Anemia control via dampened effector, potentially reducing plaque clearance	**Enhanced Safety Without Loss of Efficacy:** Reduced ARIA risk and controlled anemia

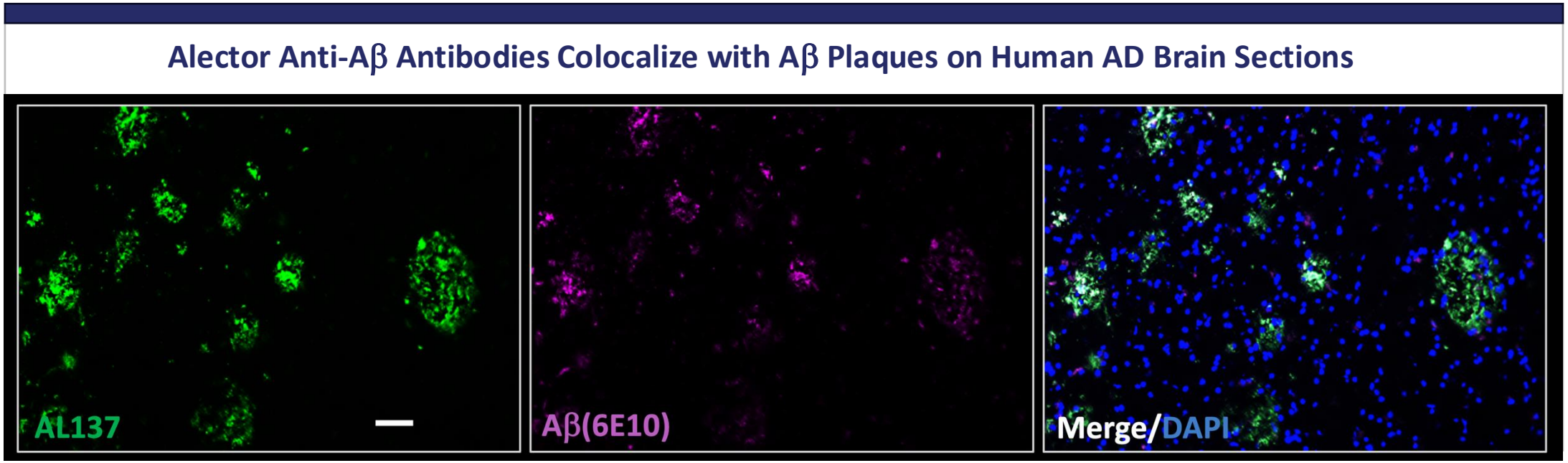
The Alector Advantage: Our 'Masked Epitope' technology targets high brain penetration and full efficacy without the safety trade-offs of previous generations. We do not choose between potency and safety - we aim to capture both in full.

AL137: Next-Generation Brain-Enabled Anti-Aβ Antibody Designed to Overcome Trontinemab's Tolerability and Scalability Constraints



*50% and 45% of patients at 1.8mg/kg and 3.6mg/kg, respectively (AlzForum).

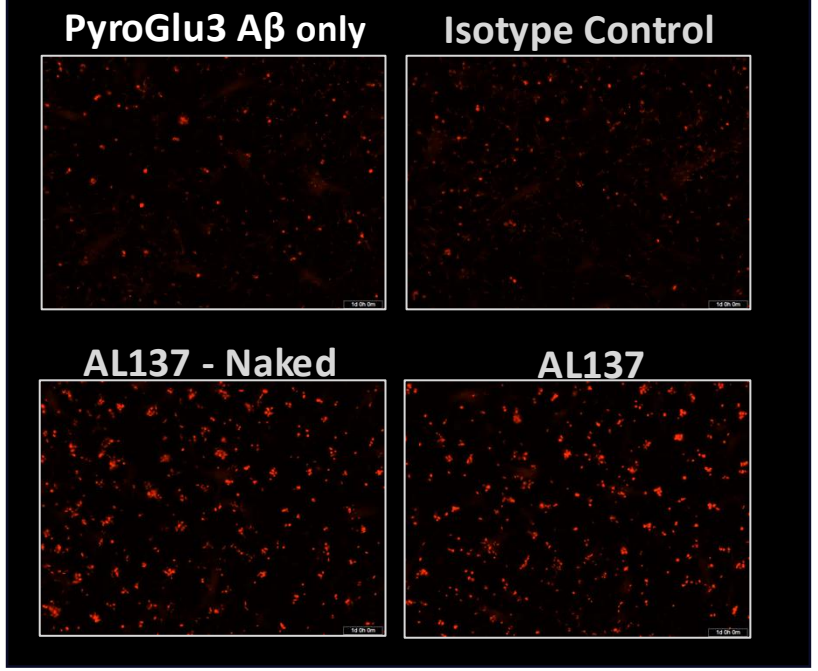
AL137 Binds Aβ Plaques in Human AD Brain Sections



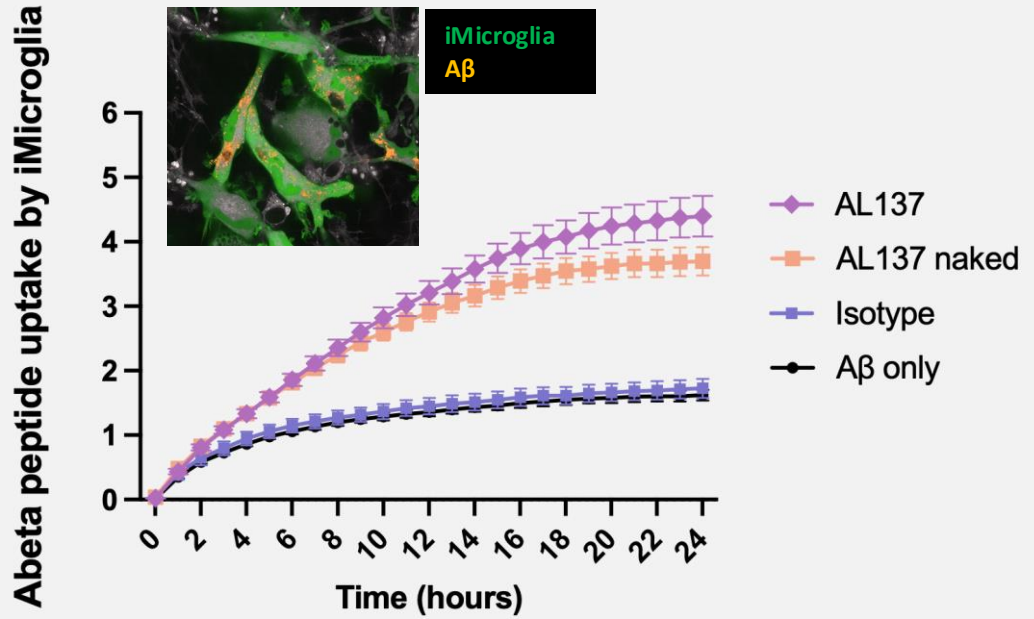
Unfixed, frozen human AD sections (medial temporal gyrus) were obtained from the Banner Institute, AZ; plaques were assessed by IFL with AL137 (green) and anti-Aβ (6E10, pink); nuclei were counterstained with DAPI (blue); images acquired with a 10x objective; scale bar= 50 µm.

AL137 Facilitates Phagocytosis of PyroGlu3 Aβ by Human Microglia

Fluorescent Imaging (red) of PyroGlu3 Aβ Phagocytosed by Microglia in 24h



AL137-Dependent Phagocytosis of PyroGlu3 Aβ by Human IPSC Microglia in Culture



AL137, AL137 - Naked (without the ABC platform), or Isotype huIgG, were incubated with pHrodo-pyroGlu3-Aβ on IPSC-derived CNS triple cultures (containing iMicroglia, iNeurons, human fetal astrocytes) for 24h and imaged hourly for uptake into GFP-iMicroglia. (inset, iMicroglia in green, Aβ in orange)

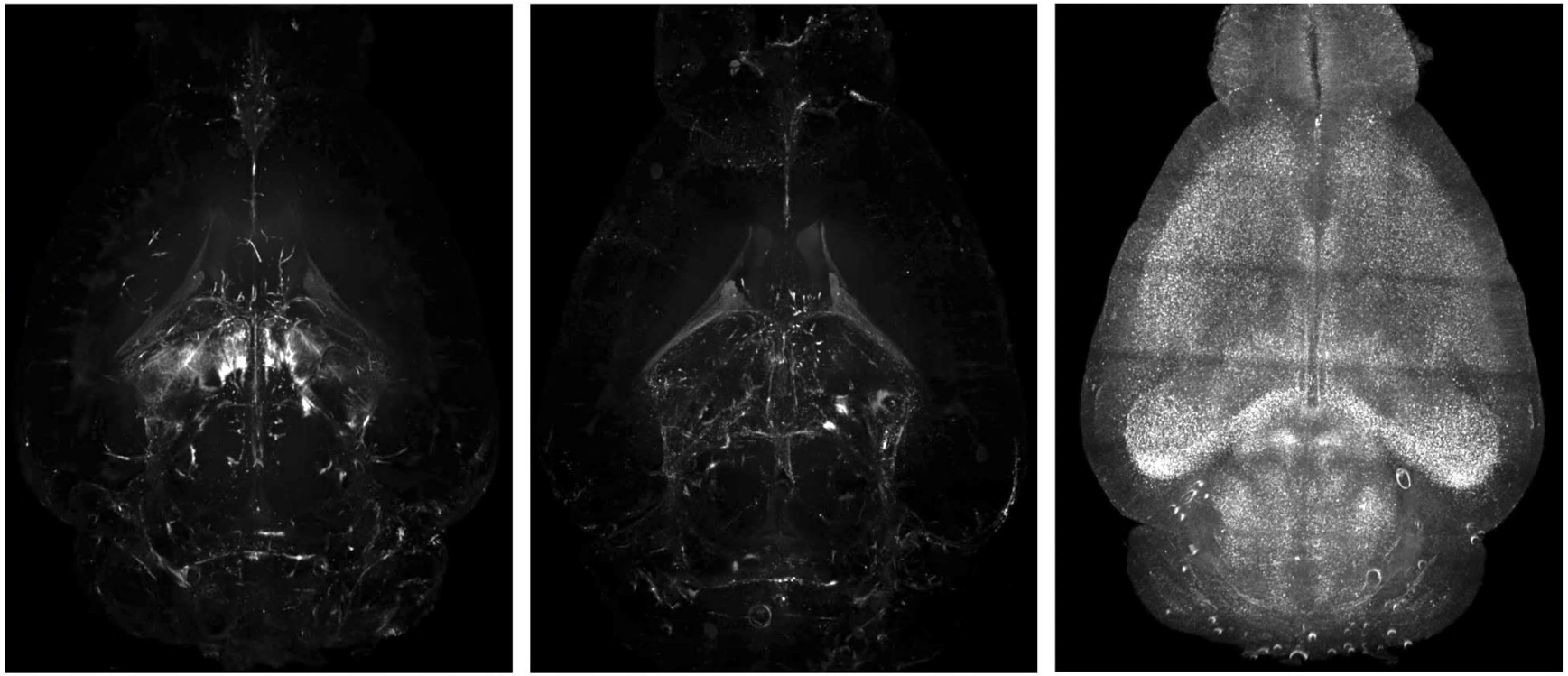
AL137 Surrogate Binds to Aβ Plaques in Mouse AD Brains and Reduces Aβ42

Isotype Control

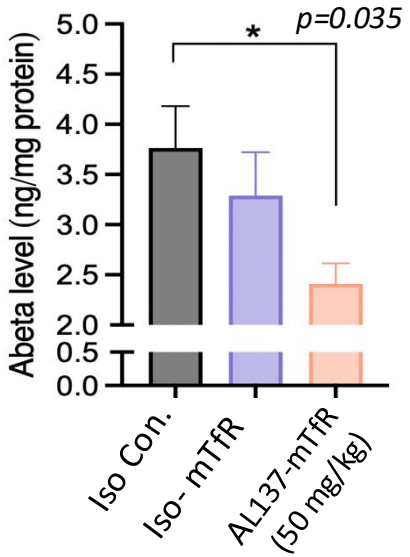
Anti-pE3-Abeta hIgG- No Shuttle

Anti-pE3-Abeta-Alector Brain Shuttle

Human IgG



Reduction in Brain Aβ42 in AL137 mTfR-Dosed Mice

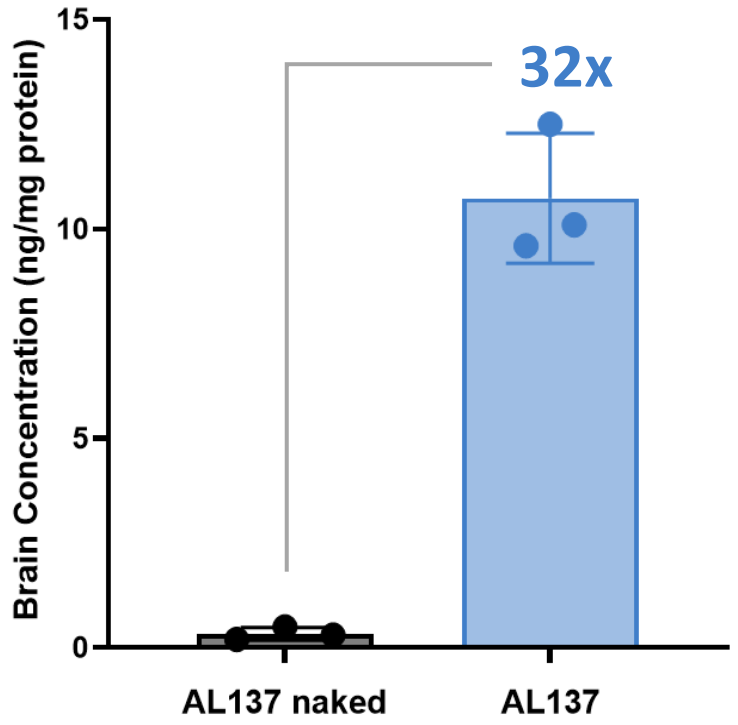


Left) Light sheet microscopy on 9-month-old 5xFAD mice dosed 3 times weekly. Naked antibody labels the vasculature and ventricles while AL137 Surrogate (AL137-mTfR) is bound to amyloid plaques throughout the brain. ((Right) 8-month-old 5XFAD mice were dosed 4 times weekly and Abeta levels in guanidine-solubilized whole brain lysates were assessed by ELISA.

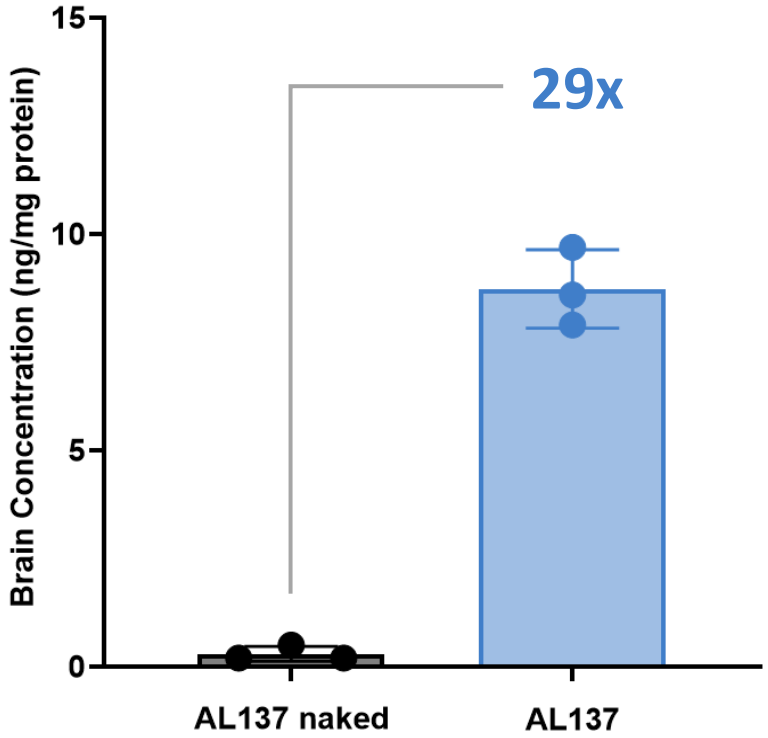
Enhanced Brain Uptake with AL137

AL137 at 3mg/kg reaches 8.4nM in frontal cortex, representing significantly higher brain levels than clinical competitors*

Frontal Cortex



Hippocampus



*Three NHPs per group were dosed on days 1 and 9. Brain tissues were collected 24 hours after the second injection and drug levels were measured in the vessel-depleted fraction. *E.g. to our calculations, trontinemab reaches 2.1nM in the NHP vessel-containing cortex 24h following a single injection of 10mg/kg (Grimm et al., MABS, 2023).*
AL137 naked = AL137 without ABC platform.

AL137 Shows Superior Brain Uptake in NHPs

Company	alector	DENALI	Roche	BIOARCTIC
Calculated Brain Concentration with 10mg/kg dose ***Extrapolated Brain Concentration 24-72h, following 10 mg/kg IV injection in NHP. Linear dose response assumed.***	**12-28 nM (Anti-Aβ antibody)**	**3 nM (Anti-BACE antibody)**	**2.1 nM (Anti-Aβ antibody)**	**5.7 nM (Anti-Aβ antibody)**

	Frontal cortex levels	Fold increase*	Dosing and administration
AL137 Anti-Aβ	0.8 ug/mL, 8.4nM	32x	3 mg/kg, 24hrs. post IV administration

*Kariolis et al, STM 2020; Grimm et al., MABS, 2023; Freskgård, PEGS Europe 2024; *Relative to naked (no shuttle) molecule; Roche had reported 400 ng/g in NHP cortex, which in our calculations is equivalent to 2.1 nM with 10 mg/kg IV injection; BioArctic had reported 0.1 nmol/L/nmol/kg in NHP parietal cortex, equivalent to 5.7 nM with 10 mg/kg IV injection predicted; Denali had reported reaching 9 nM in NHP frontal cortex with 30 mg/kg IV injection, which with the imprecise assumption of a linear dose response would represent ~3 nM with 10mg/kg.*

Full Effector Function is Required for Clinical Efficacy: The Pattern Across a Decade of Anti-Aβ Programs

Reduced Effector – No Benefit

Multiple anti-Aβ antibodies engineered for reduced Fc effector function showed clear efficacy in rodent models, but none demonstrated clinical efficacy in humans*

Full Effector – Clinical Benefit

The two antibodies with reproducible clinical benefit —lecanemab and donanemab —retain full IgG1 Fc effector function*

Partial Plaque Clearance – No Benefit

Gantenerumab shows that partial, slow plaque removal fails clinically — Plaque clearance must be extensively complete to achieve clinical benefit

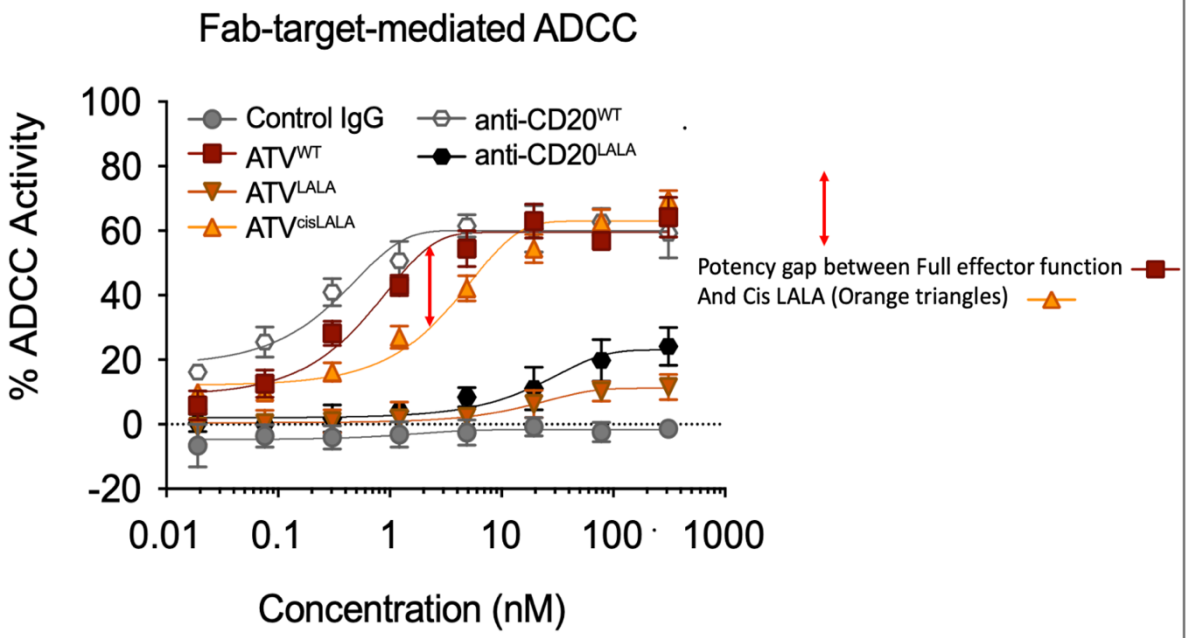
Together, these observations support full and rapid plaque clearance through intact Fc-mediated microglial engagement — the design basis for AL137.

**Meilandt WJ et al. Alzheimers Res Ther. 2019;11:97.; Ostrowitzki S et al. JAMA Neurol. 2022; Alzforum Therapeutics: Ponezumab (program profile); Alzheimer's Res Ther. 2018;10:14 ; Leyhe et al., Alzheimers Res Ther, 2014 Apr 9;6(2):19; acher et al. J Alzheimers Dis. 2012;28:49–69. • JAMA Neurol. (jamanetwork.com/1107996).; van Dyck CH et al. Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine. 2023;388:9-21; Sims JR et al. Donanemab in Early Symptomatic Alzheimer's Disease, New England Journal of Medicine. 2023; Grimm HP et al.Delivery of the Brainshuttle™ amyloid-β antibody fusion trontinemab to non-human primate brain and projected efficacious dose regimens in humans; Kulic L et al. Latest results from the Brainshuttle AD study of trontinemab. AAIC 2025 / Roche Presentation mAbs. 2023.*

Impaired Effector Function Reduces Antibody Potency

The only Aβ antibodies that have shown efficacy in clinical trials for AD are IgG1 with full effector function

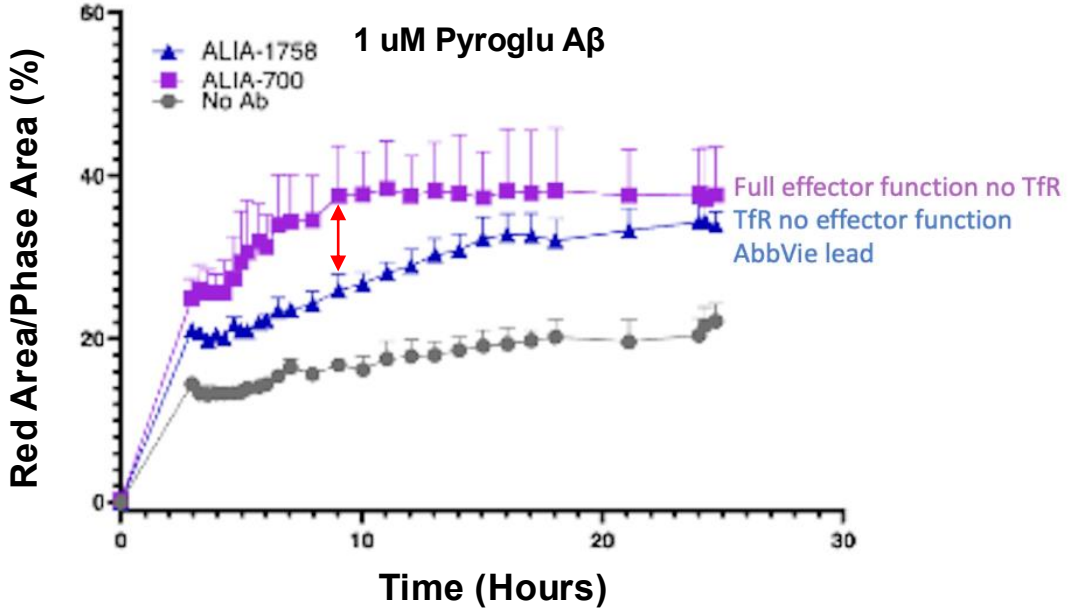
Cis LALAPS Cripples Fc Function, Reduces Potency by 10-Fold at the Expected Brain Concentrations



Compensating for the reduced potency would require injection of ~30mg/kg antibodies, nullifying the brain shuttle advantage

Source: Pizzo ME, Plowey ED, Khoury N, et al. Transferrin receptor–targeted anti-amyloid antibody enhances brain delivery and mitigates ARIA. Science. 2025; https://www.science.org/doi/abs/10.1126/science.ads3204

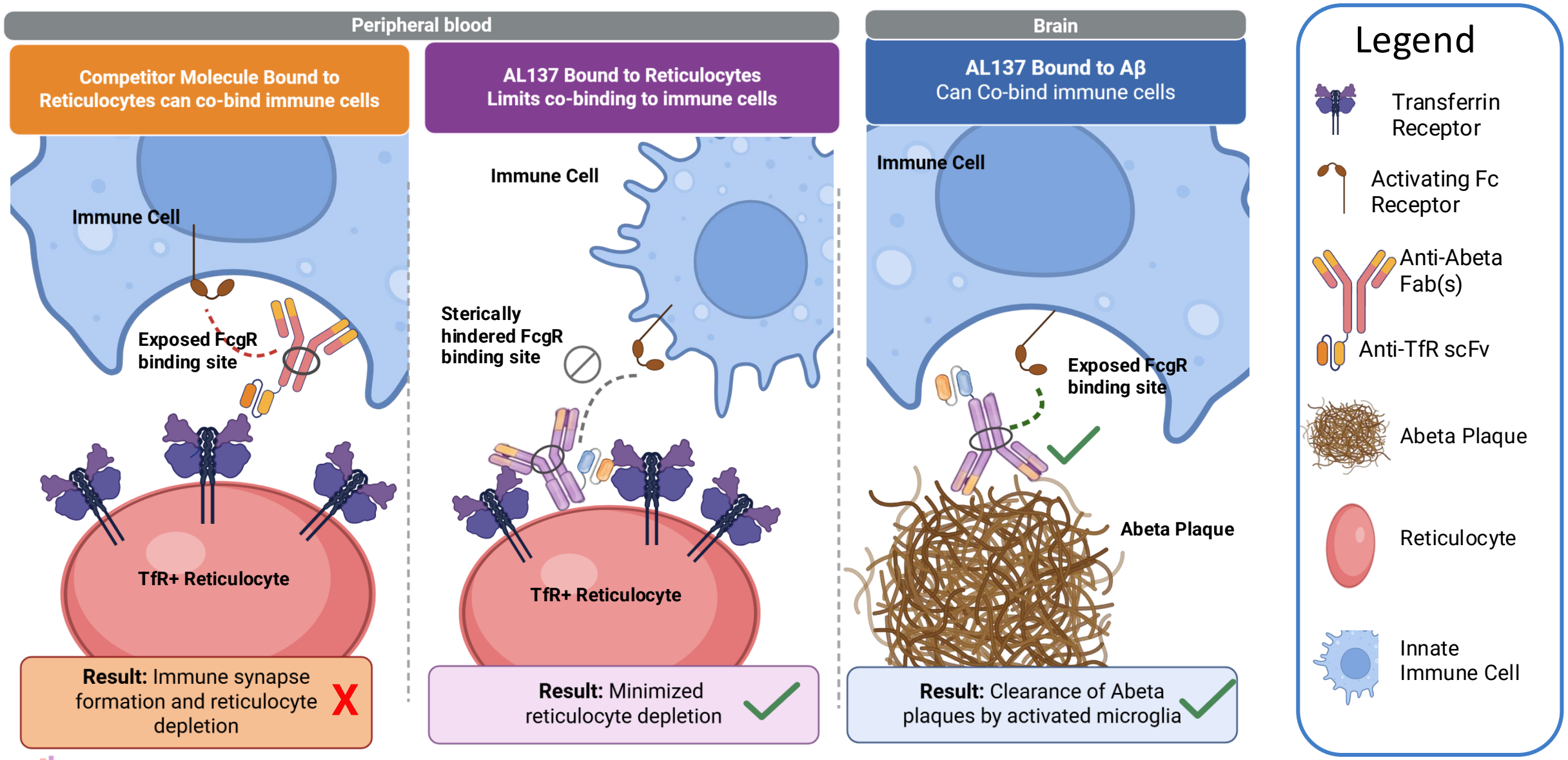
Inactive Fc Slows Down Microglia-Mediated Clearance of Aβ and May Impact Efficacy



Microglia incubated with pHrodo-labeled Aβ and monitored by live cell imaging.

Source: Dukovski D et al. (2025, April 1–5). "Enhanced delivery of anti-pyroglutamate amyloid-beta antibody, ALIA-1758, across the blood–brain barrier via TfR-mediated transcytosis" (Poster no. 853), presented at the AD/PD 2025 International Conference on Alzheimer's and Parkinson's Diseases.

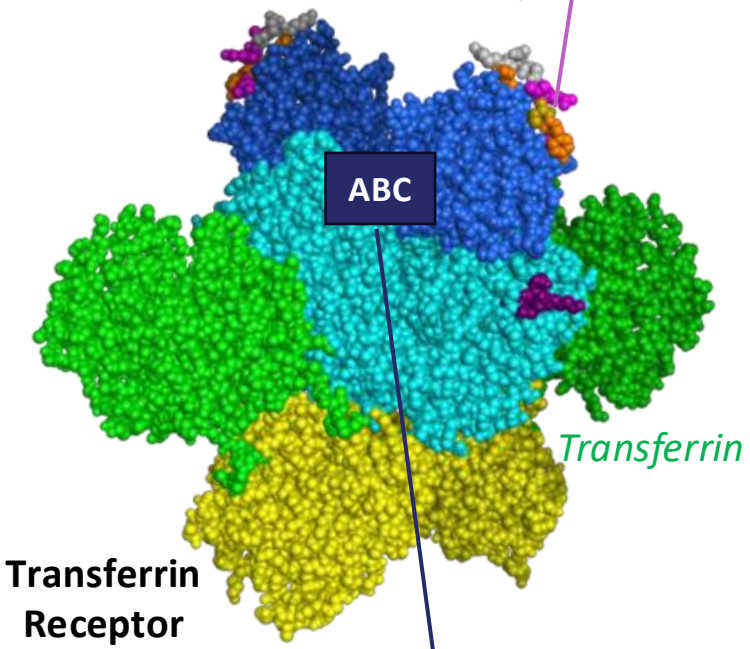
AL137: Unique Brain Shuttle is Designed to Reduce Hematologic Adverse Effects



alector

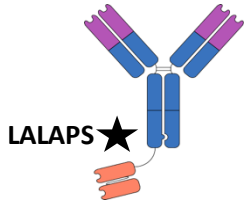
Alector's TfR Binding Epitope Masks FcγR Co-Binding, Driving an Improved Hematologic Profile With Full Effector Function

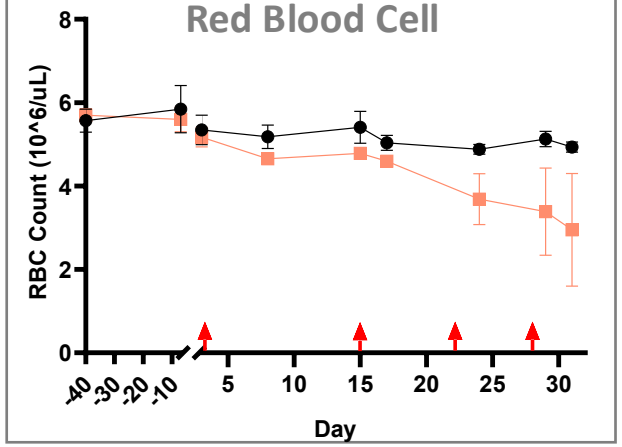
Exposed Epitope
(Does not prevent co-binding to FcγR)
(same epitope as Korsana, Denali, Roche)

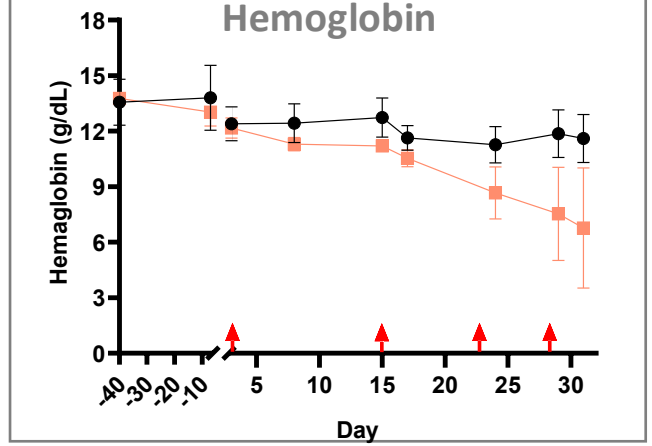


Alector ABC Epitope
(Prevents co-binding to FcγR)

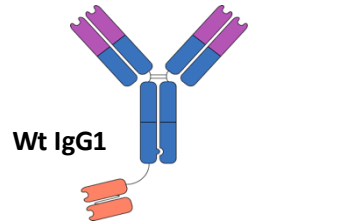
Exposed Epitope + Cis LALAPS

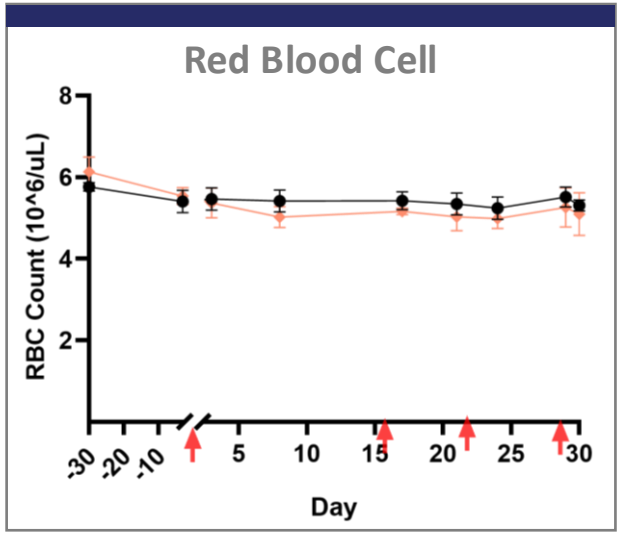


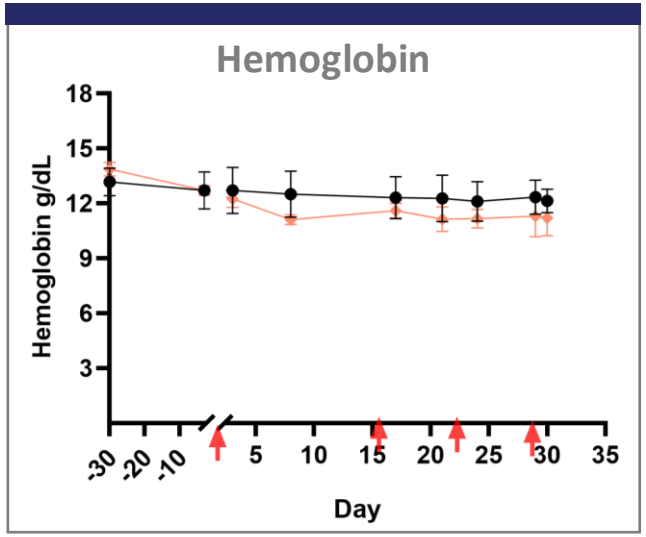




Alector's Masked ABC Epitope + Full Effector Function



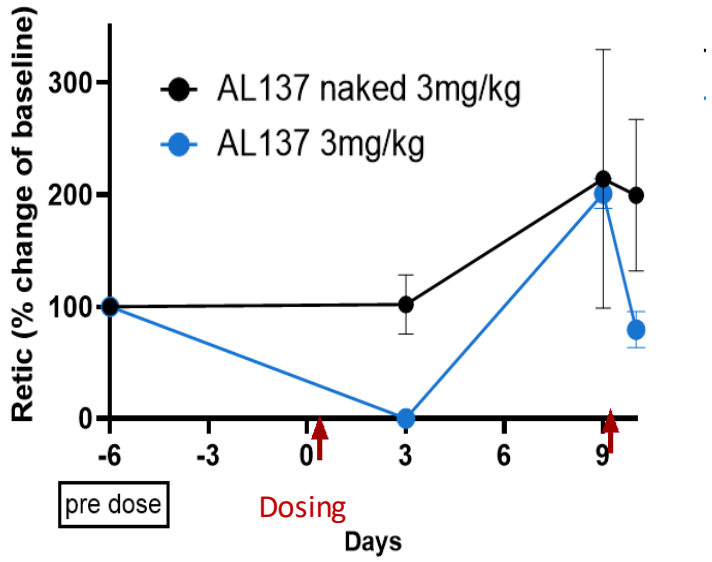




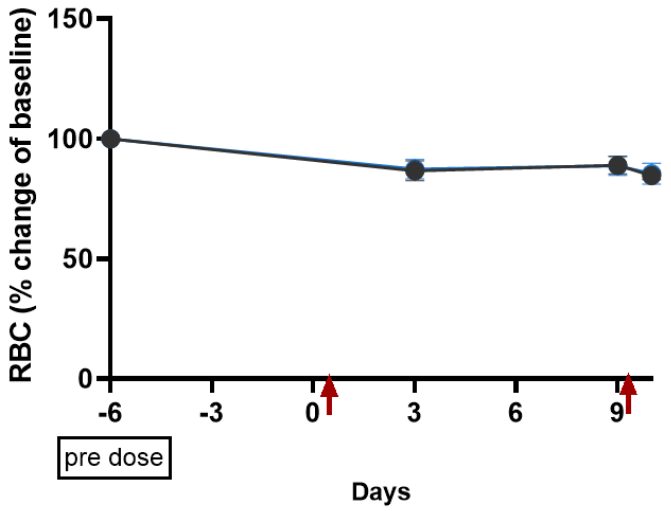
Left: Structure of human transferrin receptor-transferrin complex from 1SUV. Middle left: ABC and exposed epitope Abs bind TfR with similar affinity. The exposed epitope targets the same TfR region as Roche (Alector internal data), Denali (Kariolis et al., 2020), and Korsana (February 2026 corporate deck).
NHP IV dosing (50 mg/kg, D1, 15, 22, 29) showed stable hematology (hemoglobin, RBCs) only for the ABC epitope binder.

AL137 Displays an Improved Hematologic Profile With A Full Effector Function

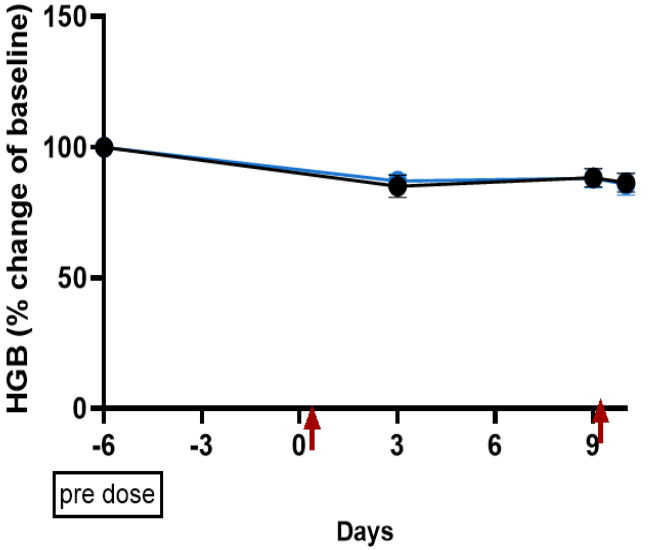
Reticulocyte



Red Blood Cell



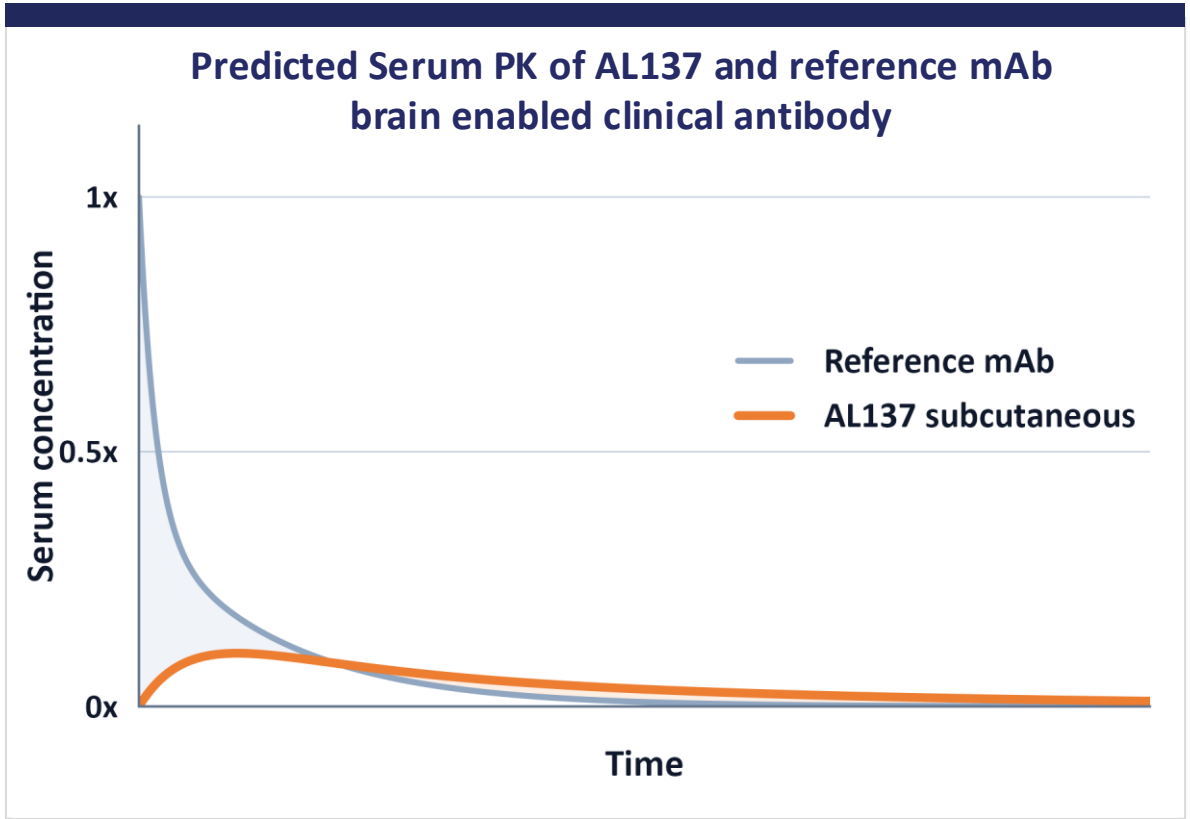
Hemoglobin

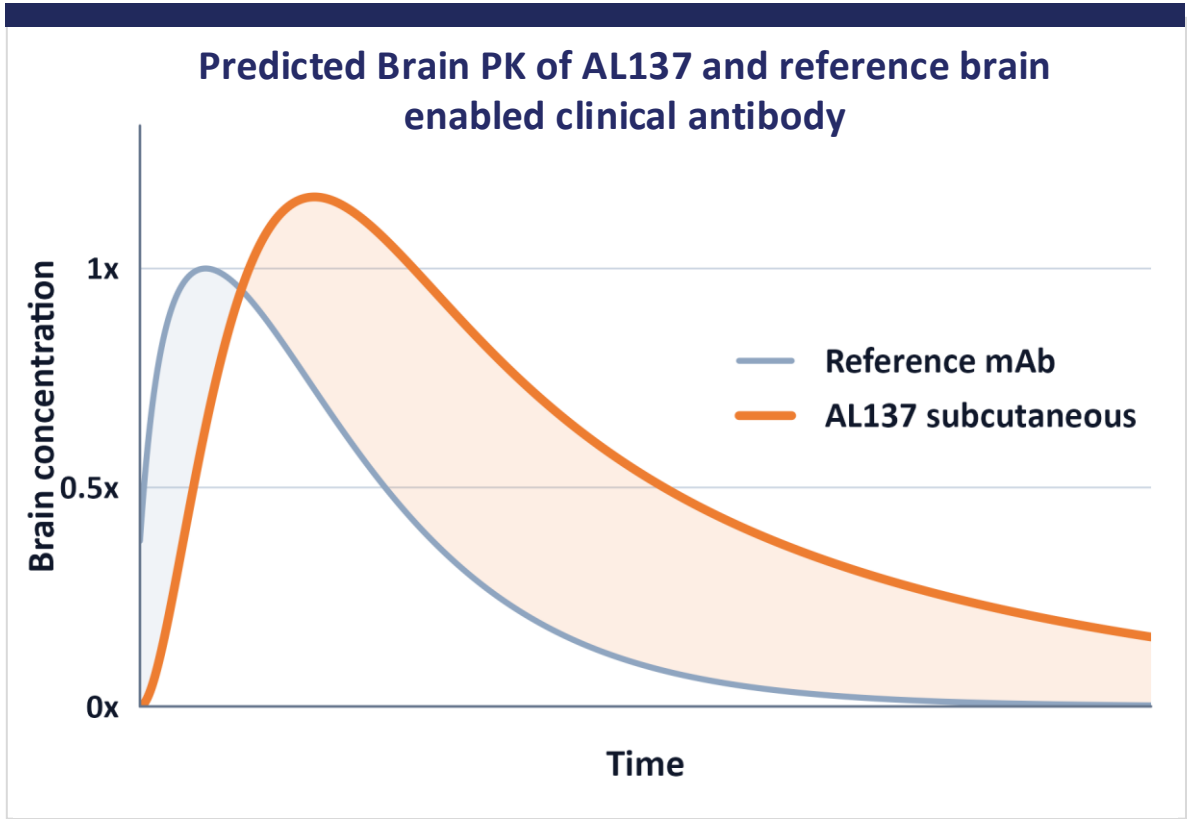


Three NHPs per group were injected on days 1 and 9 (red arrows). Blood samples were analyzed for reticulocytes, red blood cell counts and hemoglobin levels at the indicated times. AL137 caused a transient decrease in reticulocytes but did not negatively impact red blood cell count. AL137-Naked = AL137 without ABC platform.

AL137 Projected to Display Superior Brain Exposure with Subcutaneous Administration

Suitable for traditional subcutaneous formulation without additive technology





AL137 predicted to have higher brain exposure at a lower dose relative to a clinical reference antibody. AL137 brain whole-lysate AUC is projected to be approximately 2x the reference. The preferential brain distribution and SC delivery targets lower Cmax related hematologic, ARIA, and infusion reaction adverse effects

AL137 was Well-Tolerated in NHPs at Doses Up to 30 mg/kg IV in a 9-Day, Two-Dose Study

Toxicological Parameters Evaluated:

- Mortality/Morbidity
- Clinical observations
- Body weight
- Food consumption
- Hematology
- Anatomic pathology

Summary:

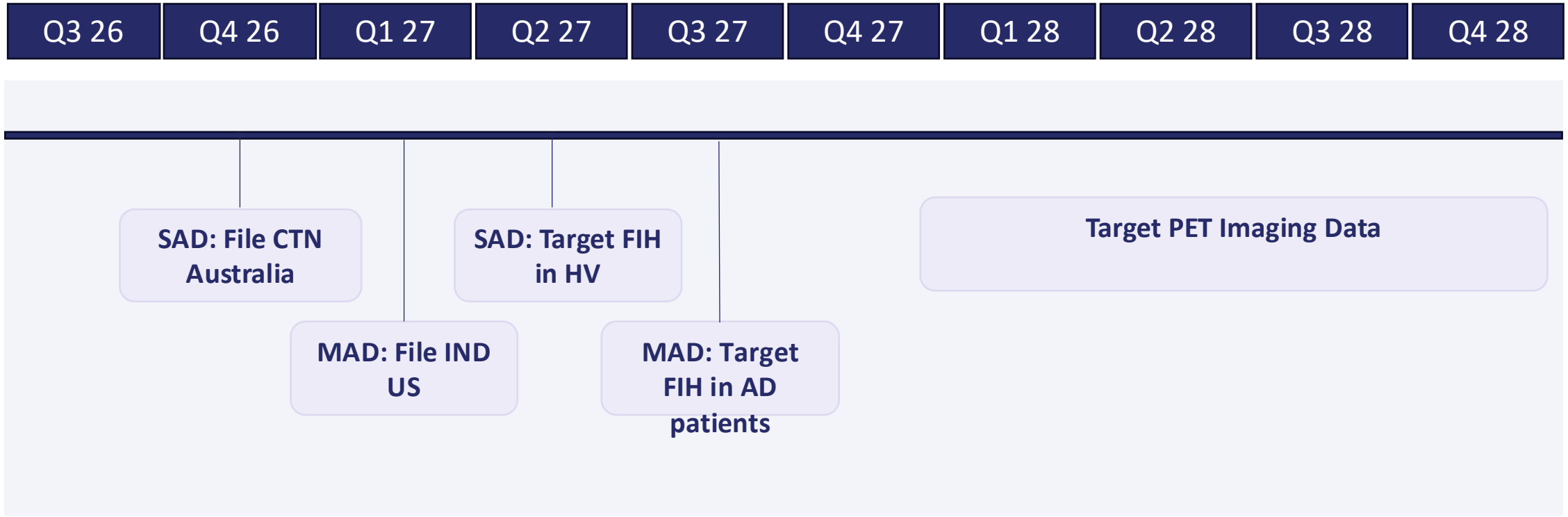
- Administration of AL137 was well tolerated at doses up to 30mg/kg
- As expected, transient reduction in reticulocytes was observed
- No test-article related adverse findings were identified throughout the conduct of this study

Three NHPs per group were dosed on days 1 and 9 with 3 mg/kg and 30mg/kg . Animals were sacrificed 24 hours after the second injection and toxicological parameters were evaluated.
Note: This data is separate from our IND-enabling tox study, which has not been reported.

AL137 Phase 1 Clinical Plan

PHASE 1 OBJECTIVES	• Evaluate safety, tolerability, and pharmacokinetics (PK) following single and multiple ascending doses. • Characterize dose-response relationships. • Assess pharmacodynamic (PD) markers of amyloid reduction.
STUDY DESIGN	• Phase 1a: Single Ascending Dose study with subcutaneous administration in healthy volunteers. • Phase 1b: Multiple Ascending Dose study in early AD patients with subcutaneous administration. • Biomarker and imaging assessments (eg Aβ PET, pTau217, MTBR).
STUDY GOALS	• Demonstrate amyloid clearance with SC dosing and achieve PET Aβ reduction comparable to Trontinemab (90% of patients amyloid PET negative at 24 weeks). • Demonstrate low rates of ARIA at efficacious doses, requiring minimal or no MRI monitoring. • Show no or only mild, self-resolving anemia. • Requires no premedication for infusion reactions.

AL137 Clinical Timeline



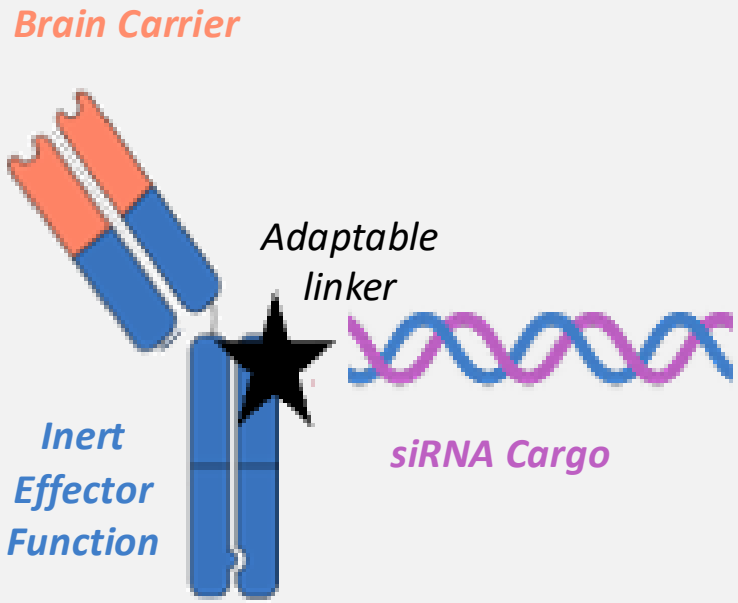
SAD = Single Ascending Dose; MAD = Multiple Ascending Dose; FIH = First in Human; HV = Healthy Volunteers

** Dates and statements represent Forward-Looking Statements associated with substantial risks and uncertainties listed in slide 2.*

AL164/AL064

ABC-enabled Tau siRNA Program

AL064/AL164*: Aiming to Achieve Brain-Wide Tau Reduction Without Invasive Spinal Injections



THE CHALLENGE

Tau drives AD progression, yet antibodies fail against its intracellular pathology, and Tau ASOs require invasive intrathecal delivery with uneven distribution.

THE AL064/AL164 SOLUTION

AL064/AL164 is designed for intracellular Tau reduction, directly targeting a central driver of neurodegeneration. IV/SC systemic delivery and broad homogeneous brain distribution are intended to **improve safety, scalability, and access**.

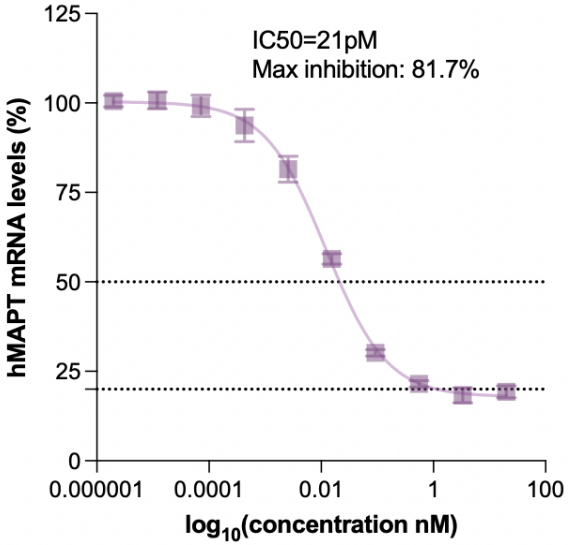
THE DELIVERABLES

2027/8: Targeting first-in-human studies to confirm safety, exposure, and Tau reduction with SC dosing; followed by Phase 1b (AD) to assess Tau reduction (PET and soluble biomarkers) and safety.

**AL064 incorporates a well-validated chemical modification that enhances siRNA stability and is advancing into IND-enabling studies as AL164.*

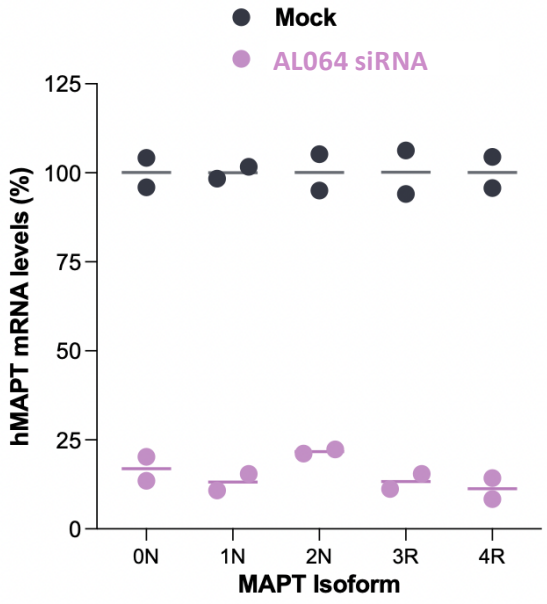
AL064 siRNA Demonstrates High Potency in Vitro

Dose-Dependent Knockdown in MAPT Expressing Cell Line



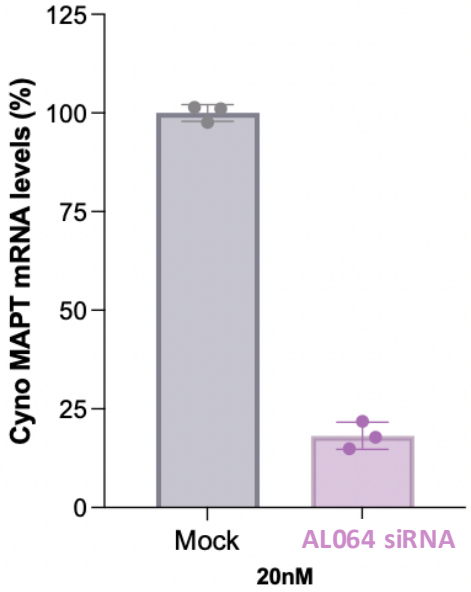
80% inhibition and pM range IC50. AL064 siRNA was transfected into MCF7 cells for 24hr to determine the dose response.

Knockdown all MAPT Isoforms in Human Neuroblastoma Cell Line



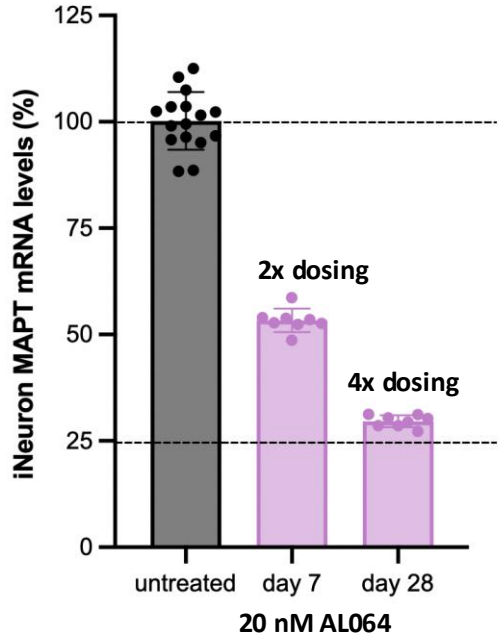
AL064 siRNA was transfected into SH-SY5Y cells for 24hr to determine the knockdown of MAPT isoforms.

Knockdown of MAPT in Cyno Primary Astrocytes



AL064 siRNA was transfected into cyno primary astrocytes cells for 48hr to determine the knockdown of MAPT mRNA.

Knockdown of MAPT in iPSC Neurons by AL064

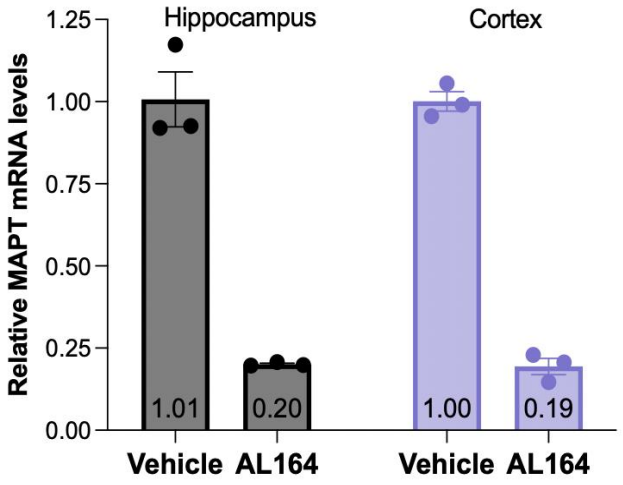


iPSC-derived neurons were treated with AL064 2 or 4 times and Tau mRNA knockdown was determined after 7 or 28 days.

Alector internal data. Leftmost 3 panels were conducted with naked AL064 siRNA (no ABC), rightmost panel with the siRNA-ABC conjugate molecule

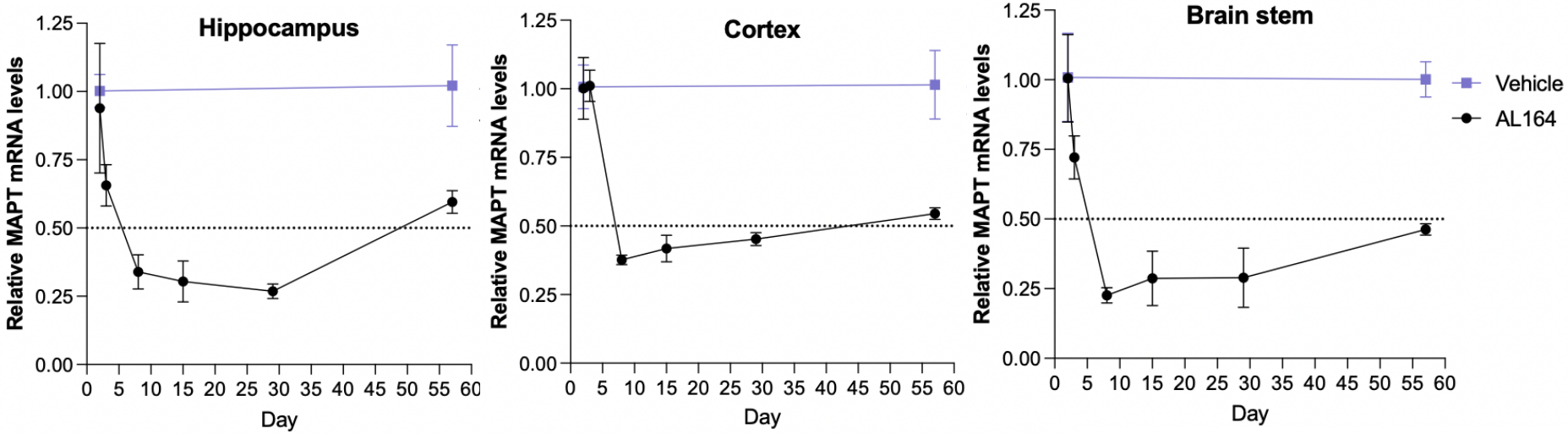
AL164 Induces Up to 81% MAPT Knockdown in Murine Model

3 loading doses of AL164 achieve 81% KD in murine brain



HuTfR x hMAPT double-knockin mice were injected subcutaneously three times with 7.5 mg/kg siRNA-dose-equivalent of AL164 at 1-week intervals. Two weeks after the last injection, animals were sacrificed and hMAPT expression was quantified by qPCR in the Cortex and the Hippocampus.

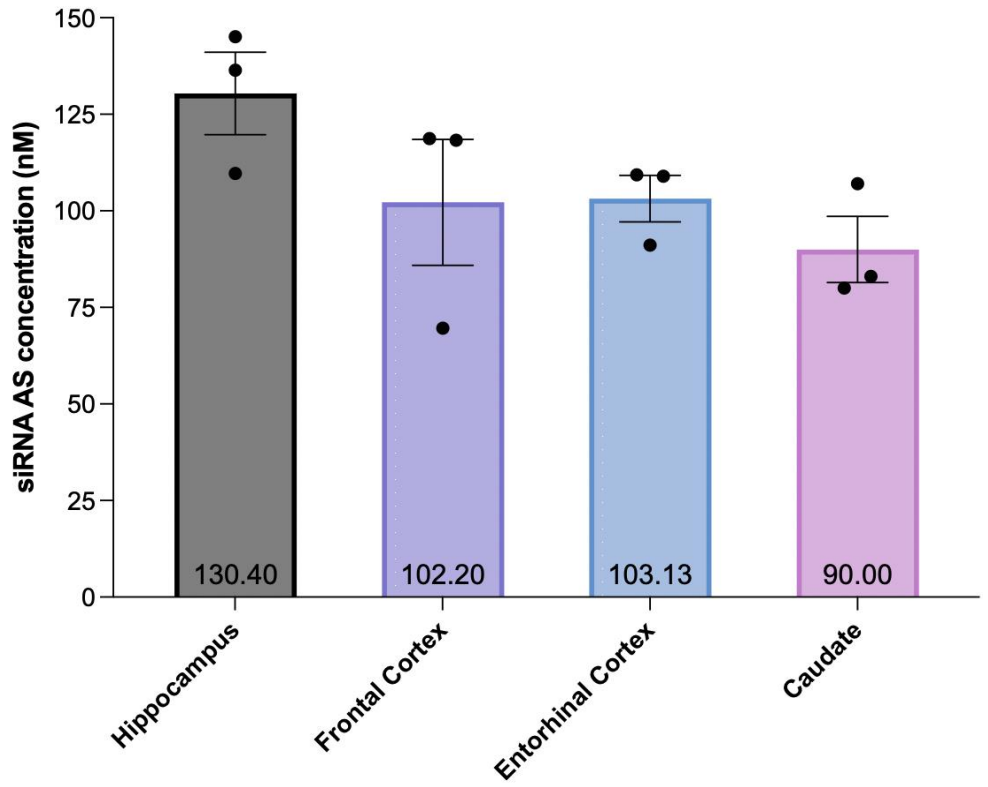
Single dose of AL164 knockdown maintains MAPT mRNA levels below 50% for over 2 months



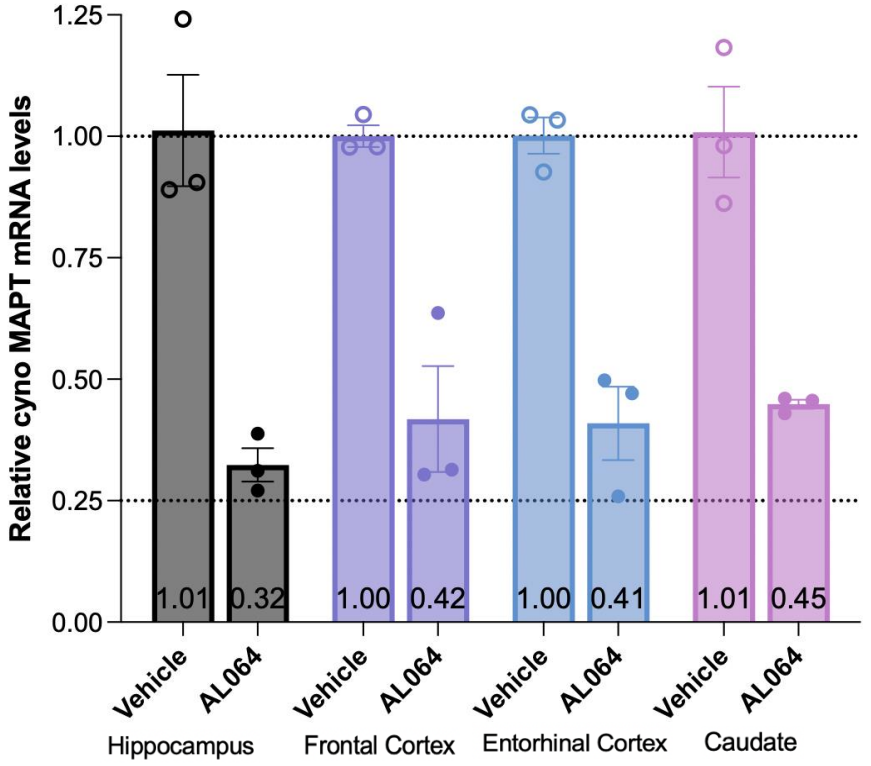
HuTfR x hMAPT double-knockin mice were injected subcutaneously with a single dose of 9 mg/kg siRNA-dose-equivalent of AL164 at day 1. Animals were sacrificed at day 2, 3, 8, 15, 29, and 57 and hMAPT expression was quantified by qPCR in the Cortex and the Hippocampus, and brain stem.

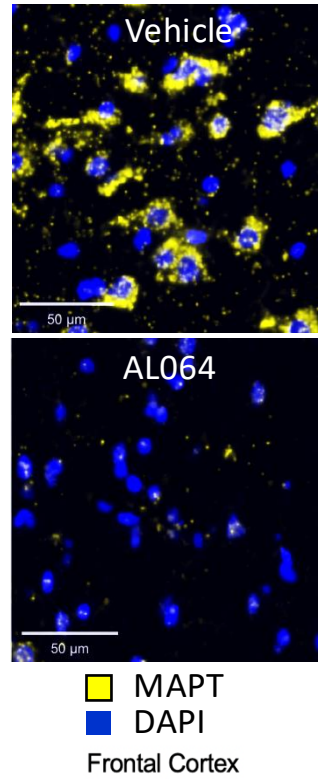
Peripheral AL064: Up to ~130 nM in Brain and ~60-70% mRNA Knockdown in NHPs

Concentrations of AL064 in Brain Tissues (28 days)



Knockdown of Tau mRNA in Brain Tissues (28 days)



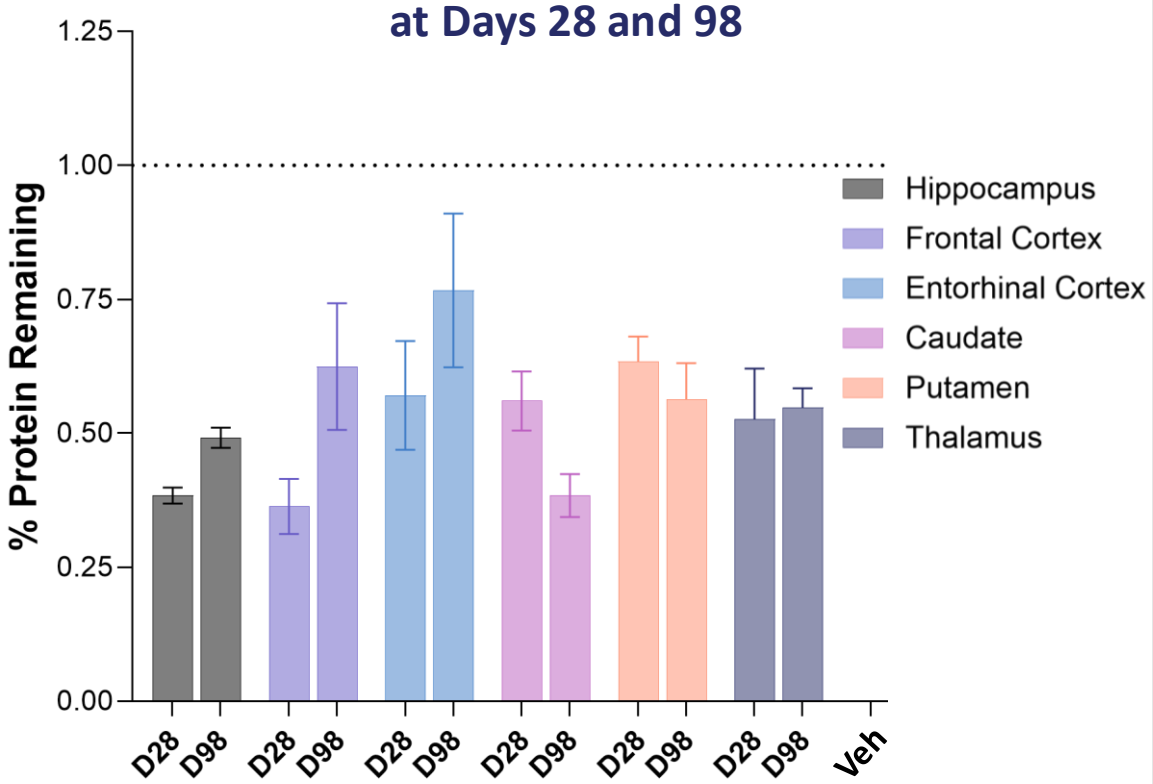


Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent and the level of AL064 siRNA antisense strand in different brain regions was measured at day 28 with MSD assay. Likewise, the level of MAPT mRNA in different brain regions was measured at day 28 with qRT-PCR assay. MAPT mRNA of AL064 siRNA antisense strand in frontal cortex was assessed with RNAscope assay.

AL064: Durable Reduction of Phospho-Tau 217 in NHP Brain and CSF

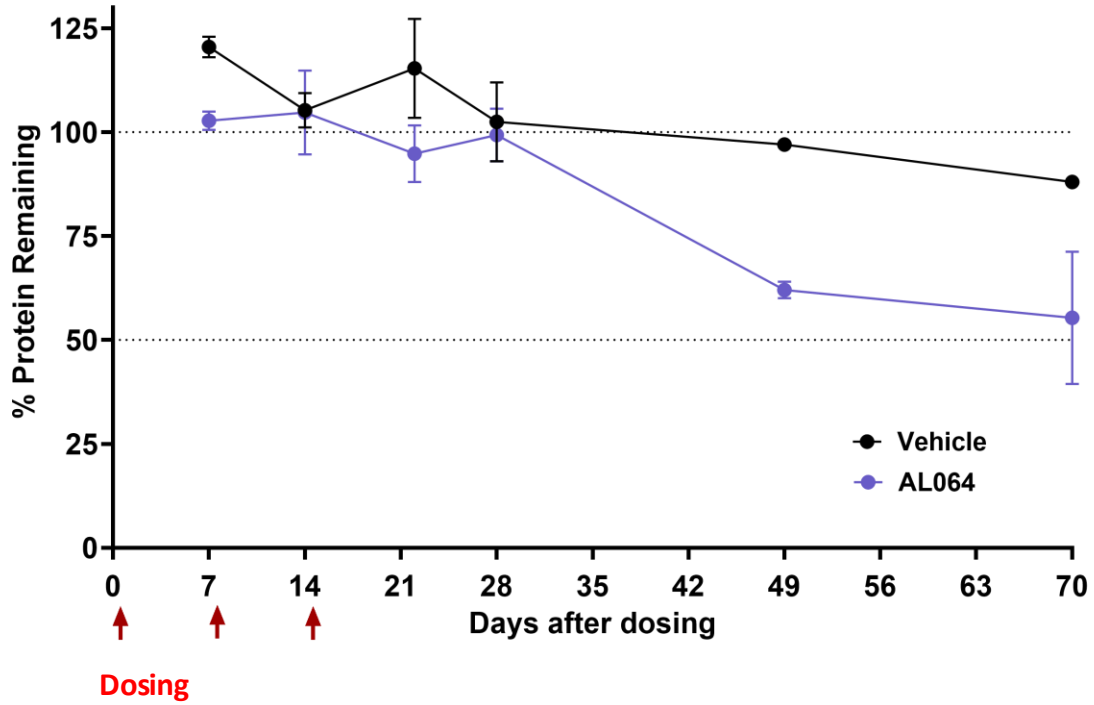
Peripheral IV administration

Up to 60+% Reduction of pTau 217 in NHP Brain at Days 28 and 98



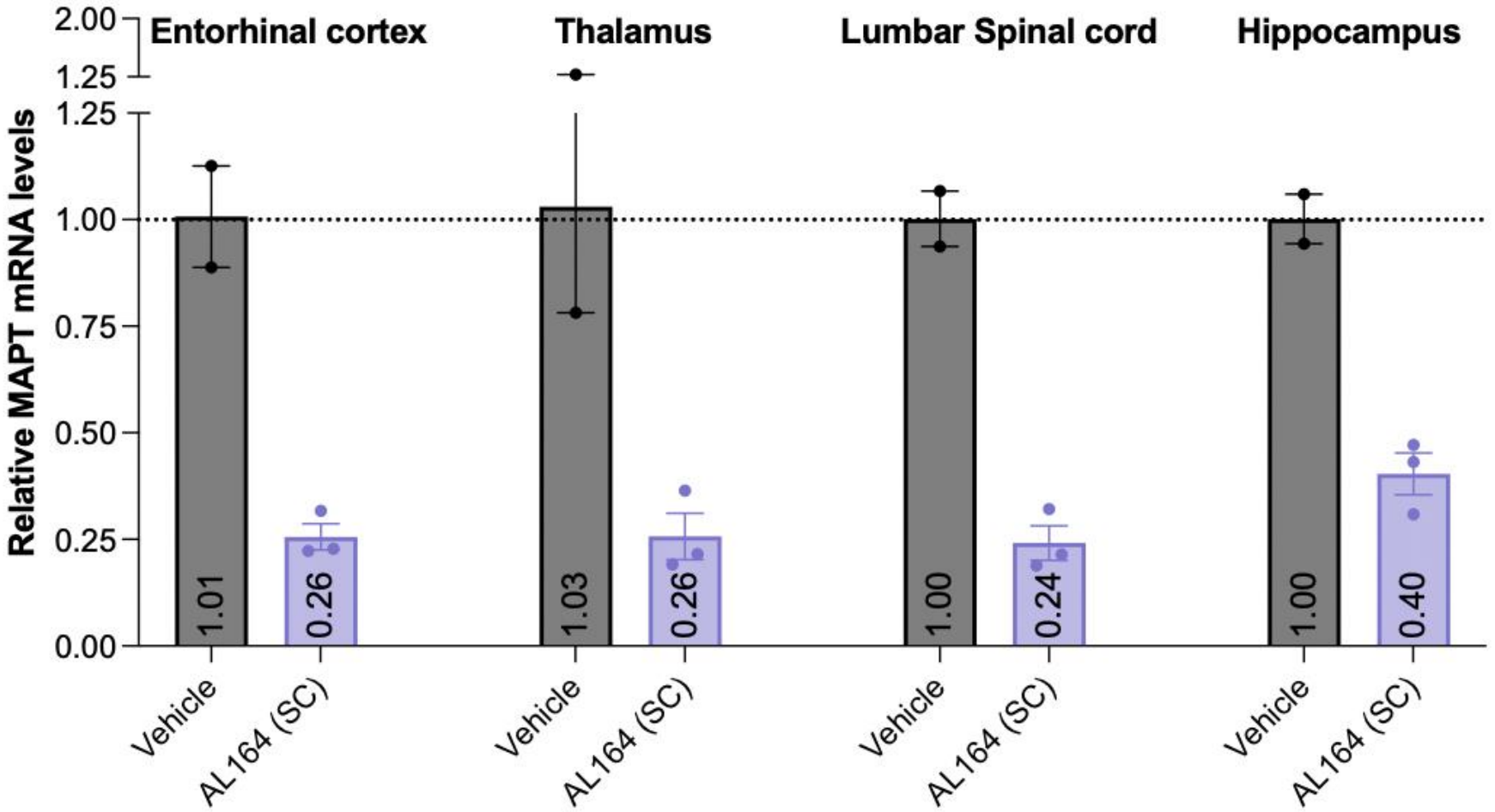
D28 and D98 normalized to experiment-specific vehicle treated cohort.

45% Reduction of pTau 217 in the CSF at Day 70



Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent and the levels of p-Tau217 in different brain regions were measured at day 28 and 98 with MSD assay. pTau217 levels were measured in the CSF at the following timepoints: pre-dose, D7, 14, 22, 28, 49 and 70.

Subcutaneous Delivery of AL164: Up to 76% mRNA Knockdown in NHPs



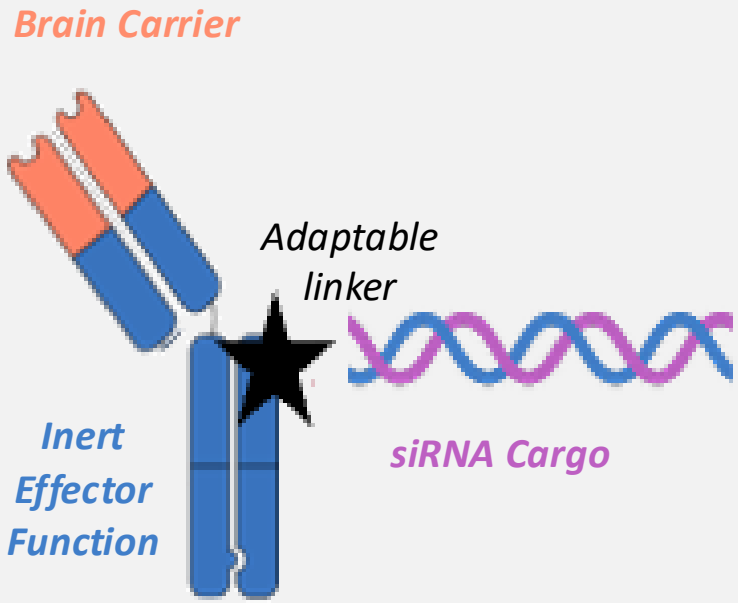
Three NHP per group were injected via SC or IV on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent and the level of MAPT mRNA in different brain regions was measured at day 29 with qRT-PCR assay.

AL062

ABC-enabled α–Synuclein siRNA Program

AL062: Brain-Enabled, Disease-Modifying, Anti-α-Synuclein Therapy for PD/LBD

Monovalent AOC format



THE CHALLENGE

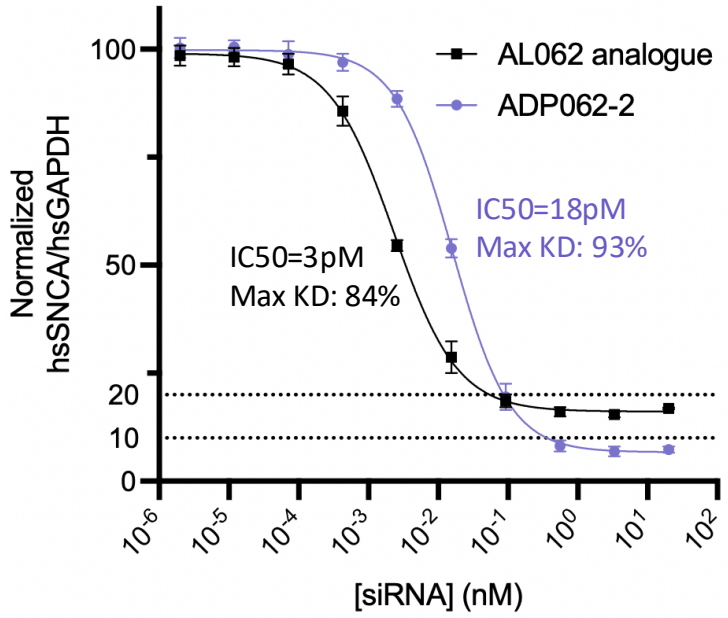
No disease-modifying therapies currently target misfolded intracellular α-synuclein in PD or LBD. Anti-α-synuclein antibodies have largely failed or shown limited benefit, likely due to the intracellular nature of the pathology.

THE AL062 SOLUTION

AL062 targets the source of pathology by silencing intracellular α-synuclein production, designed for peripheral delivery with broad brain distribution as a scalable, disease-modifying approach to PD and LBD.

SNCA (α-Synuclein) siRNA Candidates: High Potency and Low Off-Target Activity

Dose-Dependent Knockdown in SNCA Expressing Cell Line



SNCA siRNA candidates were transfected into C33A cells for 24hr to determine the dose response. SNCA mRNA levels were normalized to GAPDH and reported as percent of mock-treated cells.

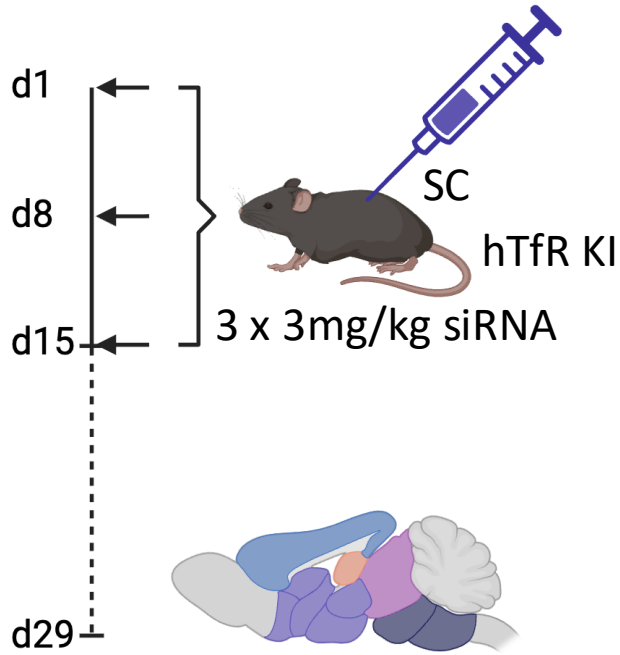
Minimal Off-target in Human Cell Lines

Oligo ID	AL062 analogue	ADP062-2
Hep3B #DEGs 50% KD (FDR < 0.05, log2FC <= -1)	0	1
SH-SY5Y #DEGs 50% KD (FDR < 0.05, log2FC <= -1)	0	0

SNCA siRNA candidates were transfected at 50nM into Hep3B or SH-SY5Y cells for 24hr to determine the off-target genes through RNA-sequencing.

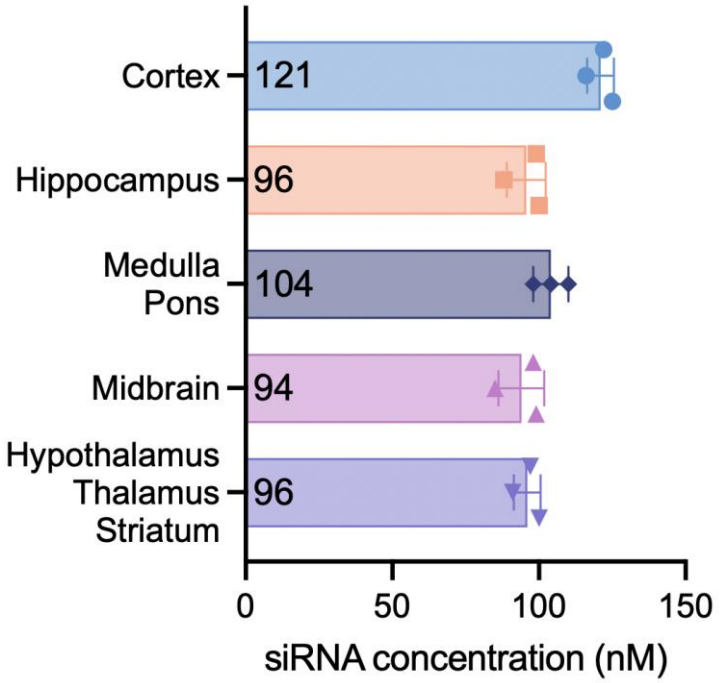
AL062 Significantly Reduces α-Synuclein Expression Throughout the Mouse Brain

Study design



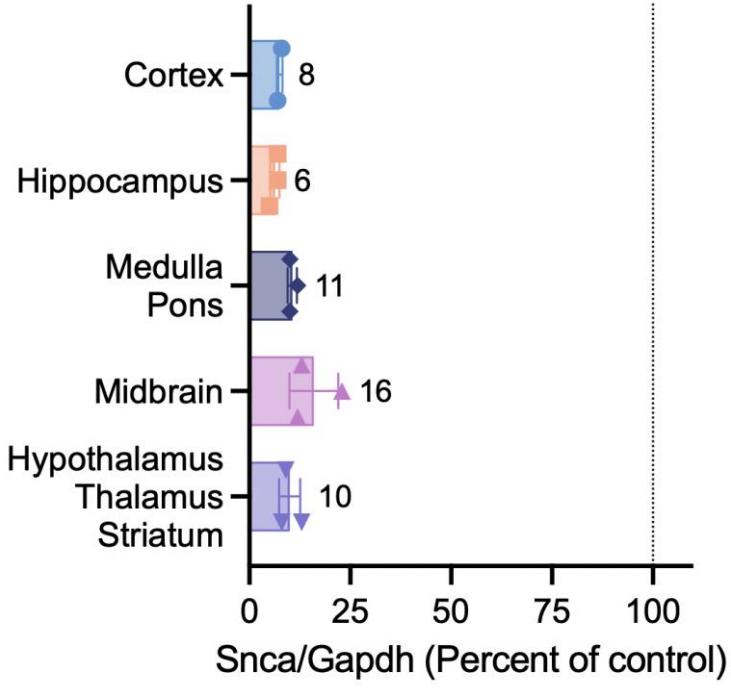
hTfR KI mice were dosed subcutaneously 3 times weekly with 3mg/kg siRNA-equivalent AL062 candidate or diluent. Two weeks post last dose, brains were dissected and evaluated for Snca expression.

AL062 siRNA is delivered throughout the mouse brain



siRNA concentration was determined using an antisense-specific custom assay in brain lysate from multiple dissected brain regions.

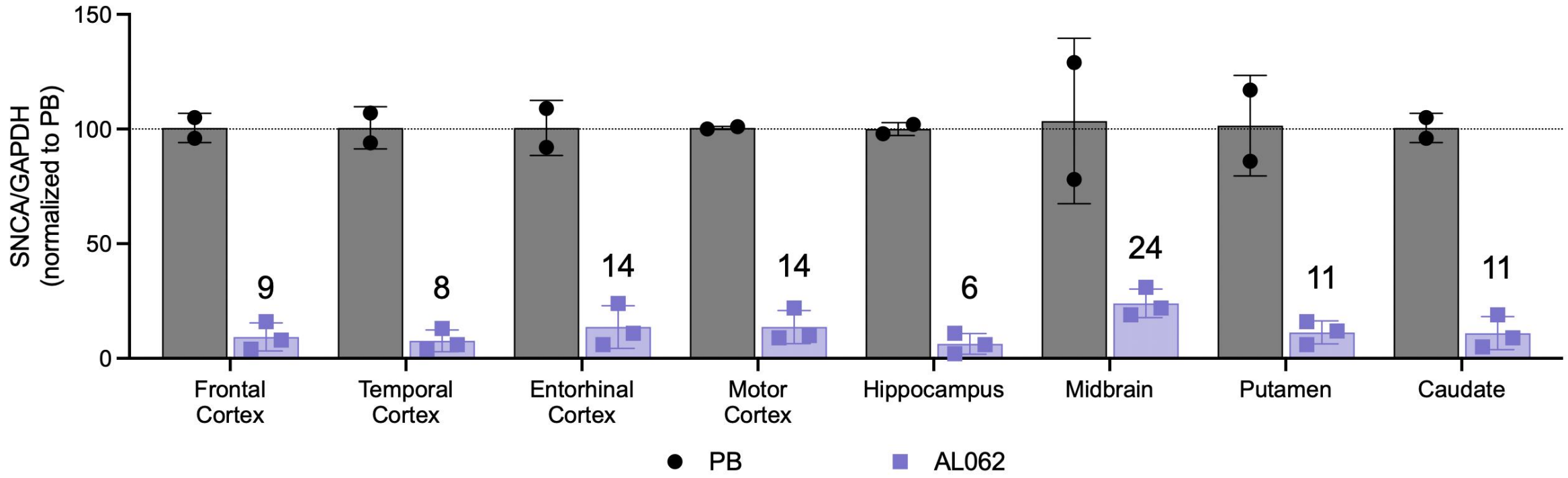
Snca expression was reduced 84-94%



Snca mRNA levels were measured by qPCR and normalized to the housekeeping gene Gapdh. For each brain region, expression level was normalized to its corresponding control.

Subcutaneous Delivery of AL062 Reduced α-Synuclein Expression by up to 94% in NHP Brain

AL062 achieved over 85% SNCA knock down in most brain regions

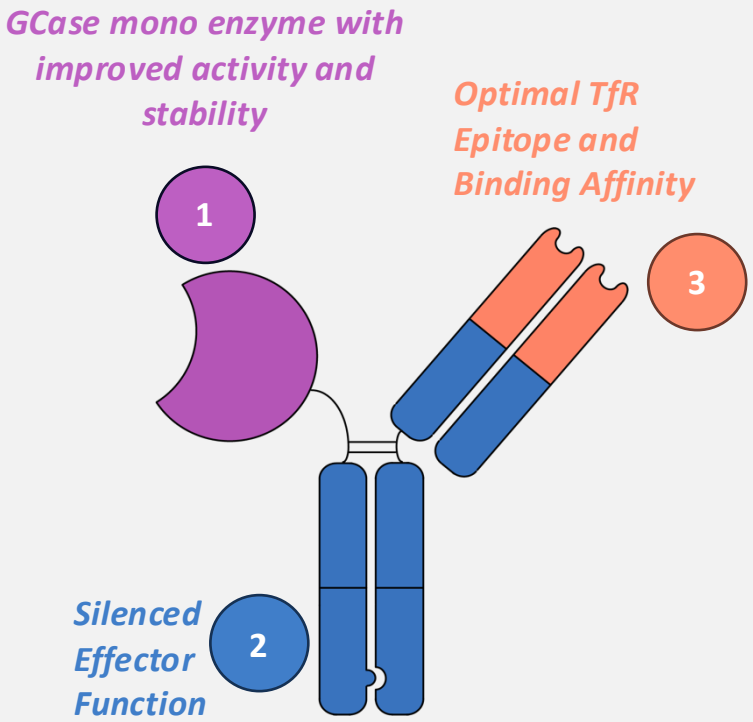


NHPs were injected subcutaneously on days 1, 8, and 15 with 3mg/kg siRNA equivalent dose. Brain samples were collected on d29 and SNCA expression was measured by qPCR. Baseline SNCA expression was lowest in the Midbrain and highest in the Hippocampus (not shown). Mean +/- SD

AL050

ABC-enabled GCase Enzyme Replacement Therapy Program

AL050: First-in-Class, Brain-Enabled, GCase Enzyme Replacement Therapy with Disease-Modifying Potential



THE CHALLENGE

No disease-modifying therapies exist for PD/LBD; Progression is accelerated in GCase LOF and low-activity patients

THE AL050 SOLUTION

AL050: Brain-penetrant GCase enzyme replacement designed to restore activity and reduce toxic substrates, targeting GCase LOF PD/LBD and broader low-activity patients.

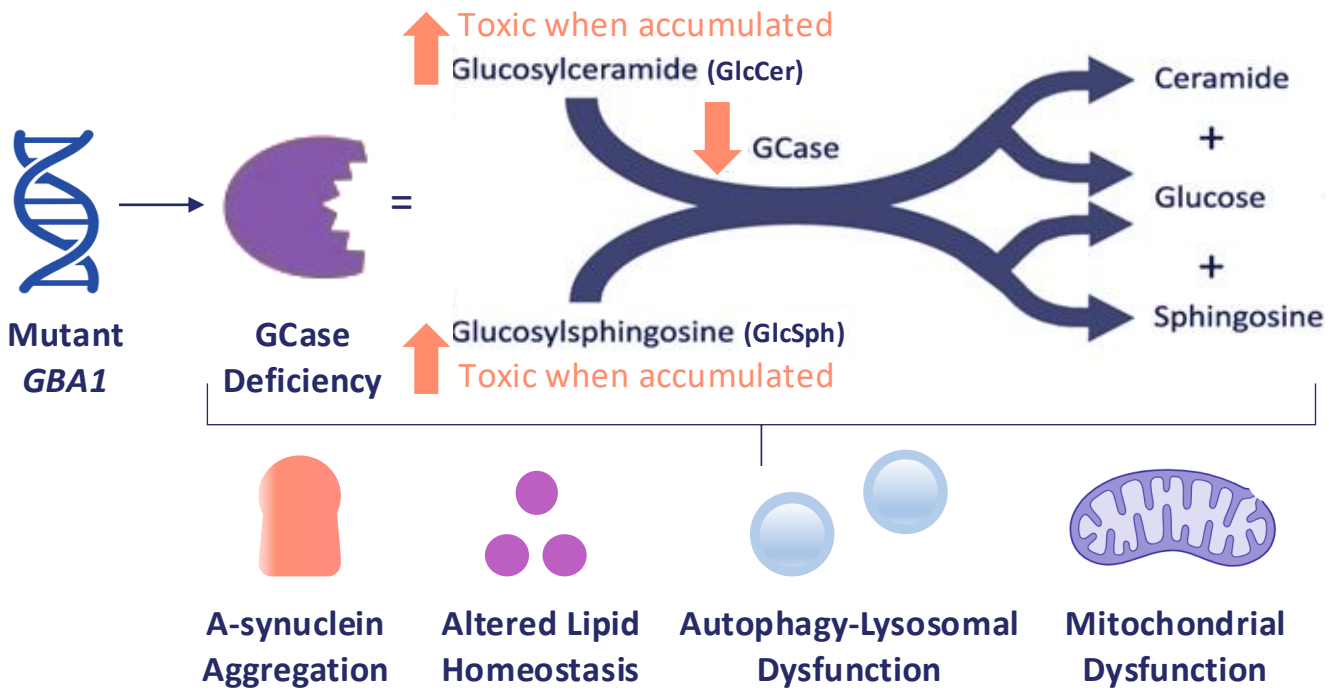
THE DELIVERABLES

2026: NHP validation – Up to 18x increased brain exposure, >2x increase in enzyme activity across multiple brain regions. Well-tolerated in NHPs at 10 mg/kg/week.

Mutations in *GBA1* (the Gene Encoding the GCase Enzyme) are a Major Risk Factor for Parkinson's Disease, Lewy Body Dementia and Gaucher Disease

GBA1 mutations lead to reduced **GCase enzyme activity** and toxic substrate accumulation (GlcCer and GlcSph) in the brain.

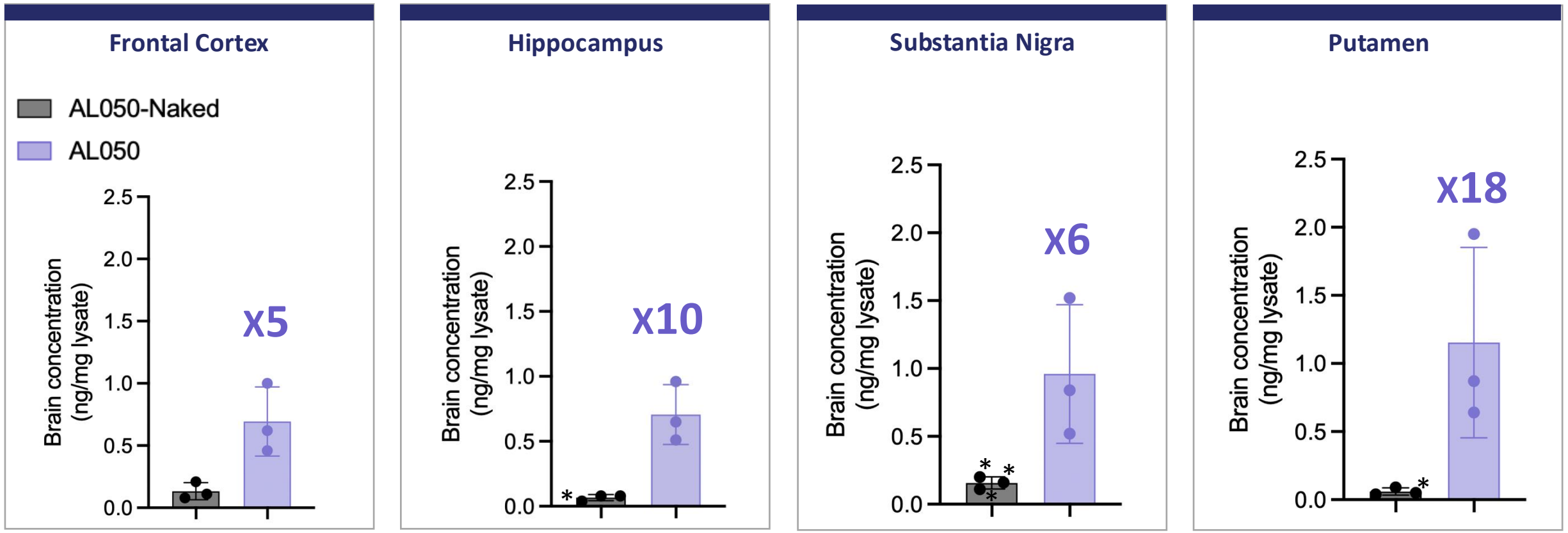
No therapy has effectively restored GCase activity in the brain: Current GCase enzyme replacement therapy does not enter the brain



- **Parkinson's Disease (PD)**
  - ~10 million patients worldwide[1]
  - 0.5-1.5 million are GBA1 mutation carriers[2]
  - Activity is reduced in non-carriers[2]
- **Gaucher Disease (GD)**
  - ~125,000 patients with GBA1 mutation worldwide[5]
  - GD type 1 have increased risk of PD[6]
  - GD type 2 and 3 are neuronopathic[7]
- **Lewy Body Dementia (LBD)**
  - ~5-8 million patients worldwide[3]
  - 0.15-2.4 millions are GBA1 mutation carriers[4]
  - Activity is reduced in non-carriers[4]

1. Parkinson's Foundation Statistics
2. Smith L, Schapira AHV. GBA Variants and Parkinson Disease: Mechanisms and Treatments. *Cells*. 2022 Apr 8;11(8):1261.
3. Alzheimer's Disease International, Dementia with Lewy Bodies
4. Nalls MA, et al. A multicenter study of glucocerebrosidase mutations in dementia with Lewy bodies. *JAMA Neurol*. 2013 Jun;70(6):727 - 35.
5. Meikle PJ, et al. Prevalence of lysosomal storage disorders. JAMA. 1999 Jan 20;281(3):249 - 54.
6. Bultron G, et al. The risk of Parkinson's disease in type 1 Gaucher disease. *J Inherit Metab Dis*. 2010 Apr;33(2):167 - 73.
7. National Gaucher Foundation, Gaucher Disease Types 2 and 3

ABC Enhances Brain Delivery of AL050 by 5- to 18-Fold, Over Naked AL050

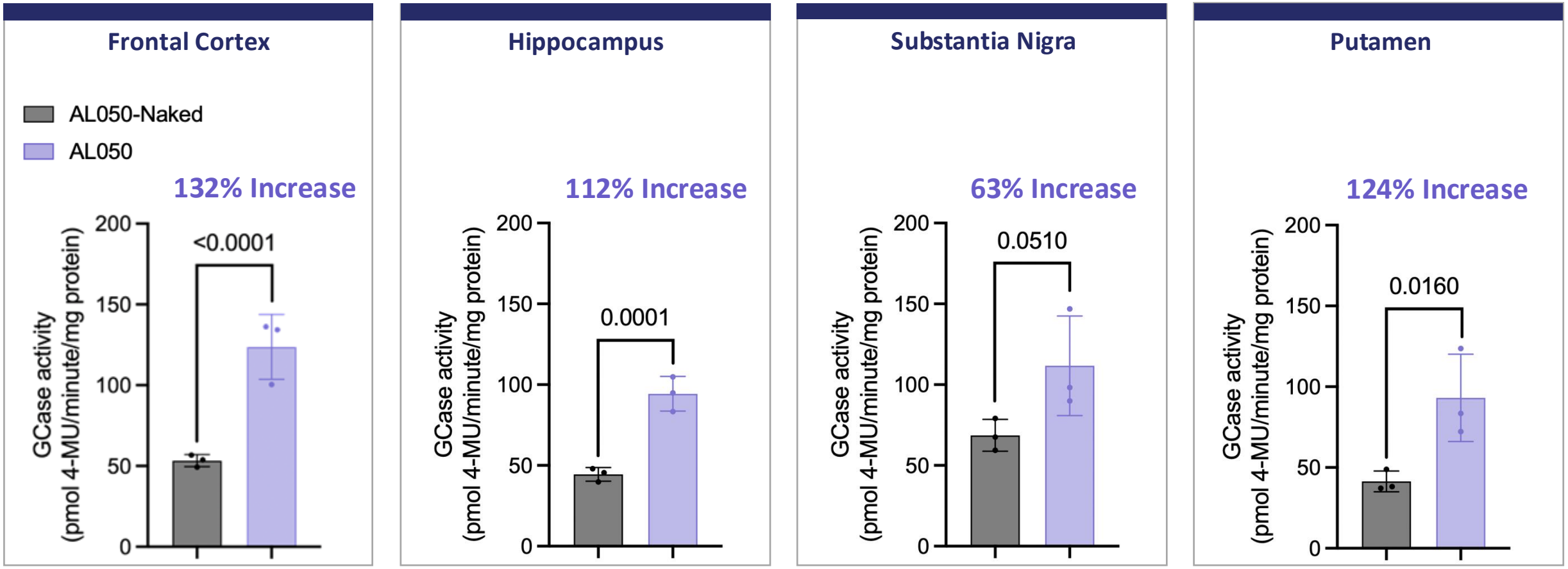


Three female cynomolgus monkeys per group were dosed intravenously on D1, D8, with 10mg/kg of AL050 or AL050-Naked and were sacrificed at D9. Brain tissues were collected 24 hours after the second injection and drug levels were measured in the vessel-depleted fraction. AL050-Naked = AL050 without ABC platform. Only AL050 and not endogenous GCase is being detected with this assay.

*Samples below lower limit of detection graphed at LLOD.

AL050 Increases Brain GCase Activity in NHP by >2 Fold Over Endogenous Levels

Would fully compensate for the less than 50% reduction in GCase activity in PD or LBD

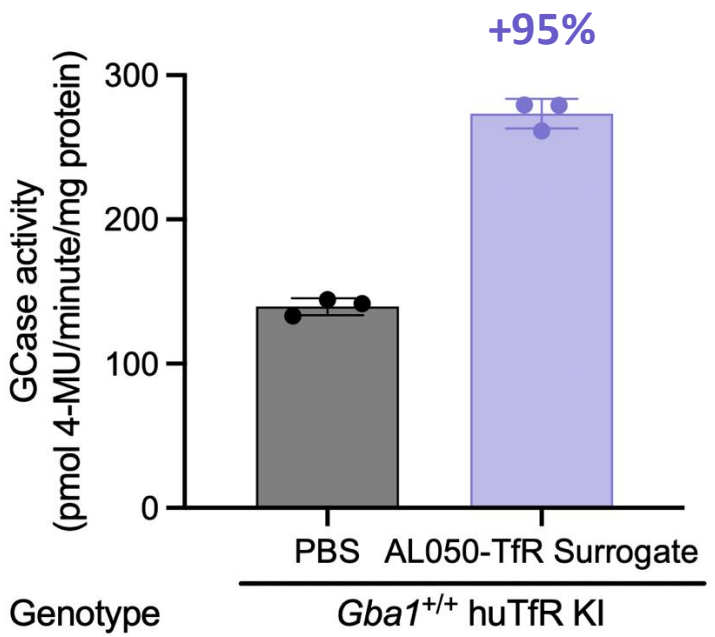


Three NHPs per group were dosed intravenously on D1, 8, with 10mg/kg of AL050 and were sacrificed at D9. GCase enzymatic activity was determined using a 4-MUG kinetic assay (graphs represent the combination of endogenous NHP GCase and AL050 activity). AL050-Naked = AL050 without ABC platform. The enzymatic activity of the Recombinant GCase appears stronger than that of the activity of the endogenous GCase as 27-39% increase in recombinant GCase leads to 63-175% increase in enzymatic activity.

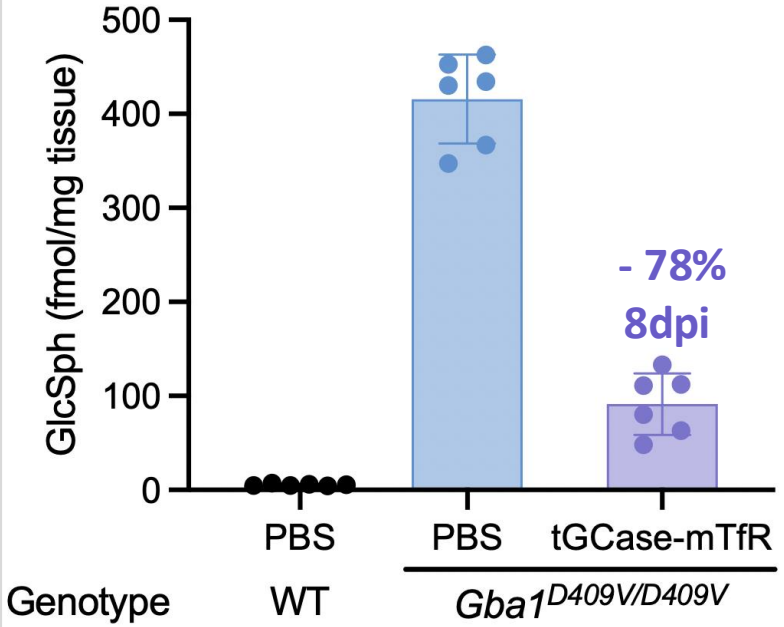
One way ANOVA with Dunnett's multiple comparison test

AL050 Surrogate Rescues Brain GCase Activity and Reduces Toxic Substrate Accumulation in the Brain of *Gba1*-Mutant Mice

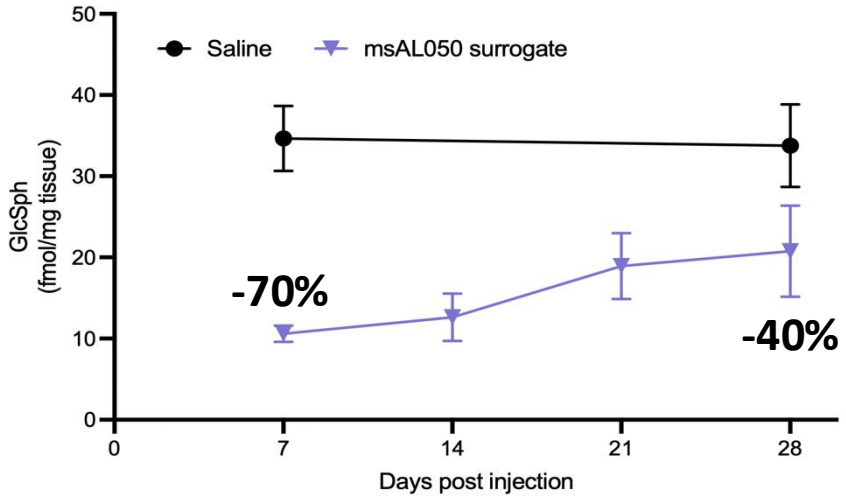
GCase-ABC Increases Brain GCase



GCase-ABC Reduces GlcSph



Durable (28D) Reduction in Brain GlcSph



Wild-type or Gba1-mutant mice were injected once (left, right) or twice (middle) with PBS, or 10mg/kg AL050-huTfR Surrogate (left), tool GCase-msTfR (middle), or AL050-msTfR Surrogate (right). GCase activity (left) was determined by 4-MUG kinetic assay in vessel-depleted brain lysates. Brain GlcSph concentration (middle, right) was determined by LC-MS/MS.

AL050 Was Well-Tolerated in NHPs at 10 mg/kg/week *(Highest dose that was tested)*

Toxicological Parameters Evaluated:

- Mortality/Morbidity
- Clinical observations
- Body weight
- Food consumption
- Clinical pathology (hematology, clinical chemistry, coagulation)
- Gross necropsy observations
- Organ Weight
- Histopathology (Anatomic Pathology)
  - Full tissue list

Summary:

- There were no AL050-related clinical signs
- No AL050-related impact on body weight, food consumption, hematology, clinical chemistry, and coagulation
- No AL050 related macro or microscopic findings

Platform + Multi-Asset Optionality Creates Asymmetric Strategic Value*

Reproducing the ABC platform would require ~5–7 years, creating a strategic moat

Comparable BBB platforms acquired or encumbered — **future access at premium**

Delay **risks competitors defining next-gen** CNS standards

AL137 (ABC Anti-Aβ)
Brain-enabled anti-Aβ; large AD market; differentiated high-value asset.
Targeting FIH 2027

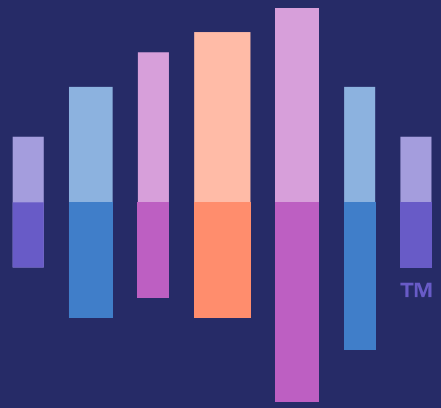
AL050 (ABC GCase ERT)
Brain-penetrant GCase; validated biology; high optionality.
Continue to evaluate timeline to clinic.

ABC siRNA (AL164 + AL062)
Large unmet need; disruptive vs. non-BBB approaches. Targeting FIH 2027/8

Fully Owned Platform and Pipeline;
Rare Opportunity for Transformative Pharma Partnership or Independent Growth

alector

**Dates and statements represent Forward-Looking Statements associated with substantial risks and uncertainties listed in slide 2.*



Thank You