Alector Corporate Overview

November 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 Pipeline is Built on a New Foundation: Alector Brain Carrier (ABC)

Earlier clinical programs pioneered novel targets with standard antibodies; every program in today's pipeline is built on ABC

EARLIER PROGRAMS

Standard antibodies against novel targets without Brain Carrier

- Progranulin and microglia-modulating drugs targeting TREM2, CD33, MS4a pathways
- Five clinical candidates, spanning Ph 1 to Ph 3, in frontotemporal dementia and Alzheimer's disease
- Partnerships with GSK and AbbVie

TODAY

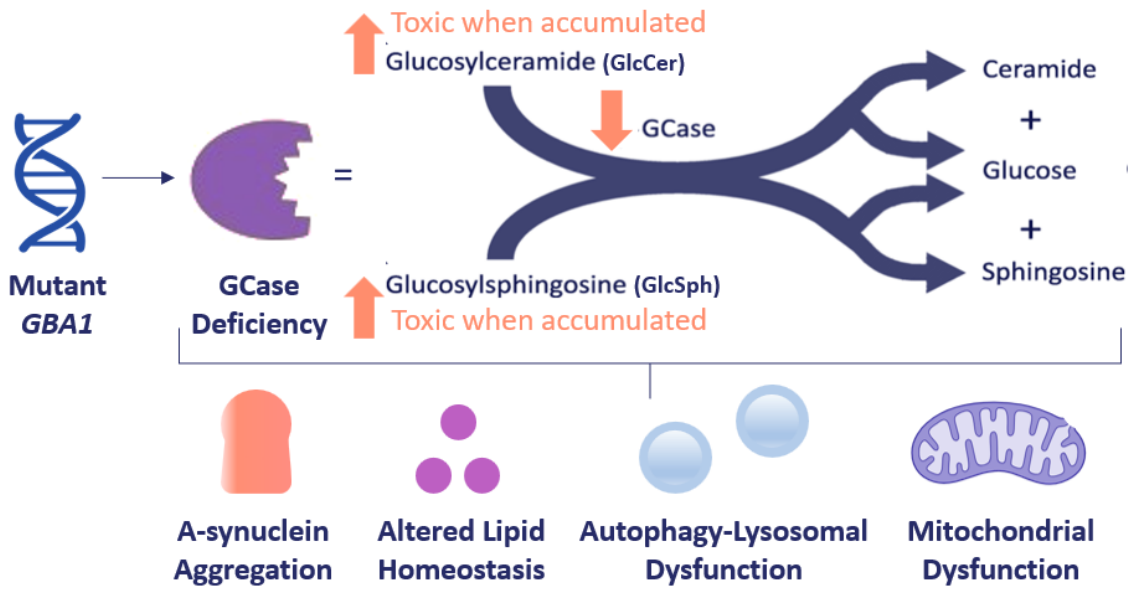
ABC-enabled new drug modalities to validated targets

ANTIBODIES	ENZYMES	siRNA
AL137 anti-Aβ	**AL050** GCase ERT	**AL164** tau **AL062** α-syn **ADP065** NLRP3

Alector has evolved into a differentiated brain-delivery platform spanning three modalities, with validated targets, pharma partnership validation, and extended runway.

AL050: Brain-Penetrant GCase ERT – Licensed to Genentech (2026)

UPFRONT PAYMENT*	MILESTONES*	ROYALTIES*
$100M	**Up to $1.17B**	**Tiered**
	Development, regulatory and commercial	*On net sales*

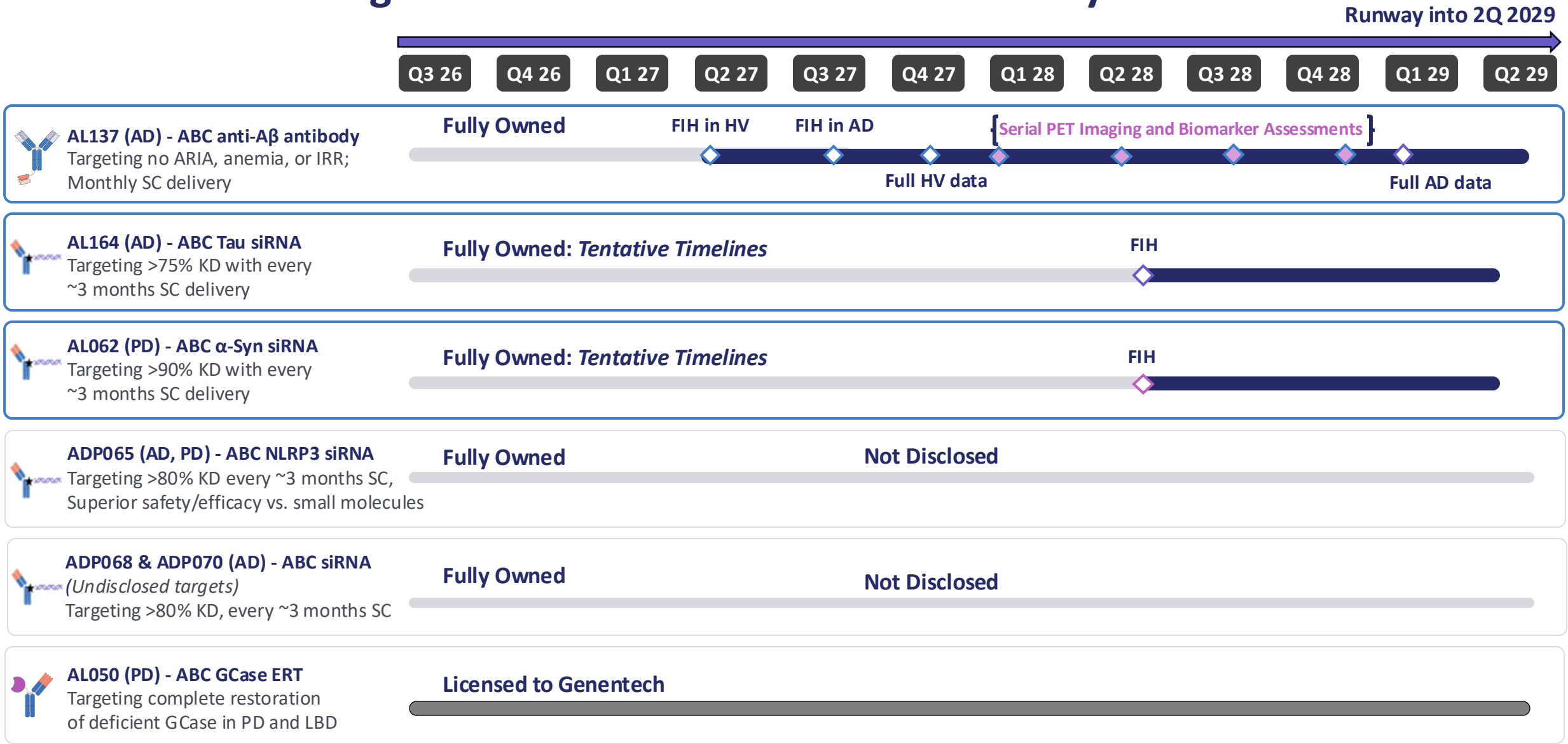


AL050 OVERVIEW

- GCase deficiency affects up to 1.5M PD[1] and 2.4M LBD[2] patients with GBA1 mutations and also contributes to idiopathic disease.
- No approved therapy addresses the underlying deficiency.
- AL050 combines an engineered, longer-lasting GCase with our Alector Brain Carrier (ABC) platform for peripheral dosing.
- AL050 aims to restore cellular function and slow disease progression.

1. Smith L, Schapira AHV. GBA Variants and Parkinson Disease: Mechanisms and Treatments. Cells. 2022 Apr 8;11(8):1261.
2. Nalls MA, et al. A multicenter study of glucocerebrosidase mutations in dementia with Lewy bodies. JAMA Neurol. 2013 Jun;70(6):727 - 35.
**Amounts shown are before any payments due to Spur Therapeutics Limited pursuant to the Option and License Agreement dated August 14, 2026.*

Our Assets and Targeted Milestones Within Our Runway



** Dates and differentiation represent forward-looking statements subject to the risks and uncertainties listed on slide 2. 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=Injection-related reaction; ERT=Enzyme Replacement Therapy; FIH=First-in-Human; HV=Healthy Volunteer. Timelines represent forward looking statements*

AL137

Alector Brain Carrier-enabled

Anti-amyloid beta (Aβ) Antibody Program

The Growing Global Burden of Alzheimer's Disease



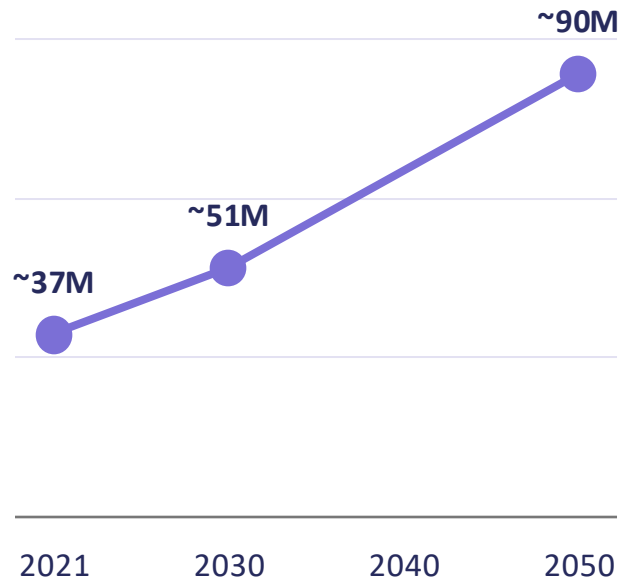
~10M New dementia cases each year, about one every 3 seconds

~2M Estimated dementia deaths in 2021

~$1.3T Annual global dementia burden, projected to reach $2.8T by 2030

~$70B Next generation AD treatment market

Estimated people living with Alzheimer's disease worldwide (millions)

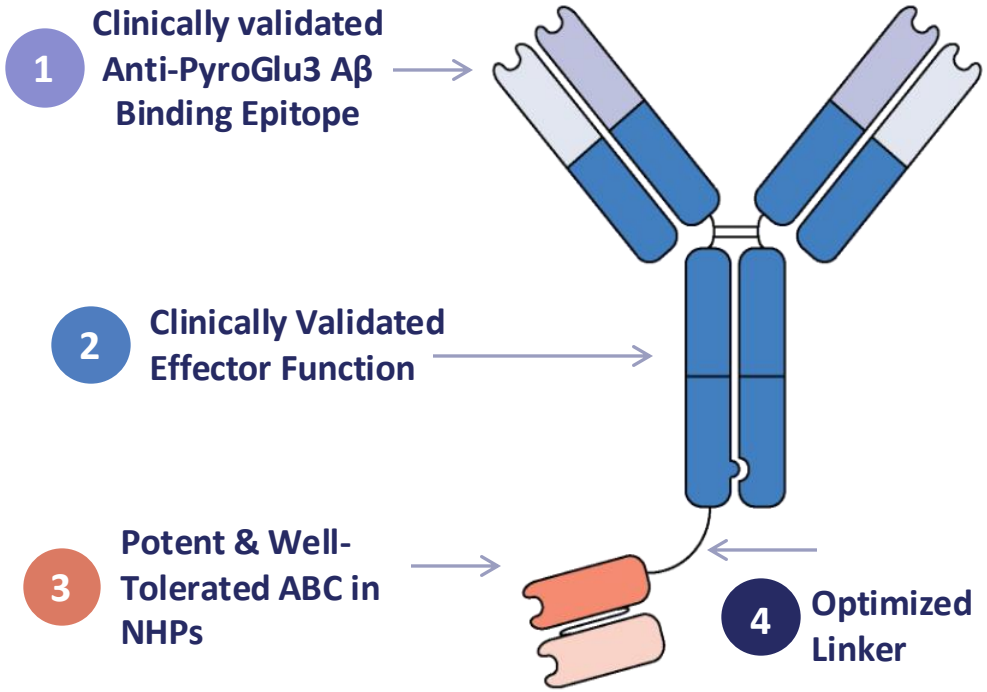


Aβ is an aggregation-prone peptide that forms plaques, a pathological hallmark of Alzheimer's disease

Sources: WHO Dementia Fact Sheet (2026); WHO Global Status Report (2021). AD estimates = 65% of projected dementia prevalence (WHO range: 60–70%); approximate, not independently modeled.

AL137: Targeting Aβ with Best-in-Class Efficacy, Safety and Convenience

Designed for superior brain exposure, reduced ARIA and hematologic risks, and monthly at-home subcutaneous delivery



AL137 Targets a Clinically Derisked Aβ Epitope
PyroGlu3 Aβ clinically validated by donanemab

AL137 Retains Clinically De-Risked, Full IgG1 Effector
Designed for maximal Aβ plaque clearance

AL137 Incorporates ABC with a Favorable Hematologic Safety Profile
Designed for maximal brain exposure, reduced anemia and ARIA risk

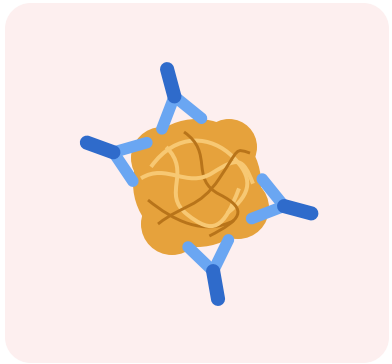
AL137: Low Projected Efficacious Dose and Favorable Tolerability
Designed for SC delivery and low cost of goods with no adverse findings

FIH Q2 2027 | **Clinically Validated PyroGlu3 Aβ and Full Fc Effector Function; Favorable Phase 1a HV Safety Would Further De-Risk AL137.**

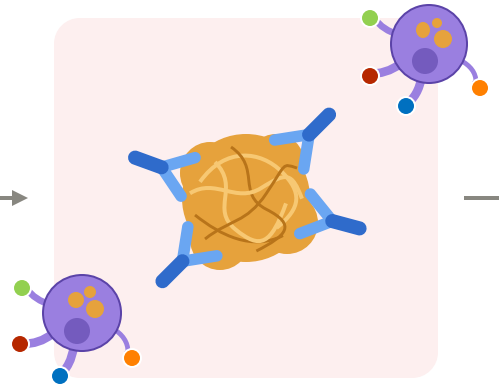
Anti-Aβ Antibodies Require Fc Effector Function to Recruit Microglia and Clear Plaques

Microglia "Excavators" express all three major classes of Fcγ receptors; all can be engaged by IgG1 "Surveyors" antibodies

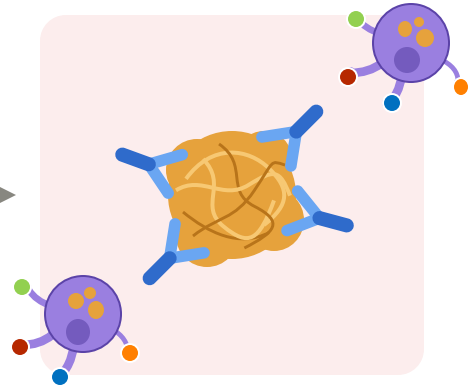
Reduced / No Fc effector Function



Plaque Binding is Effector-Independent

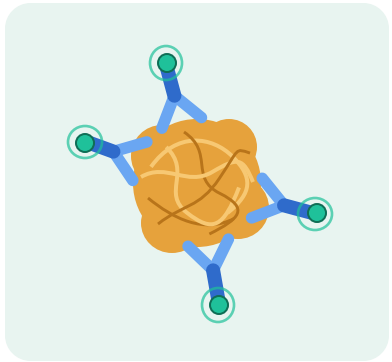


Effectorless Abs. Cannot Recruit Microglia

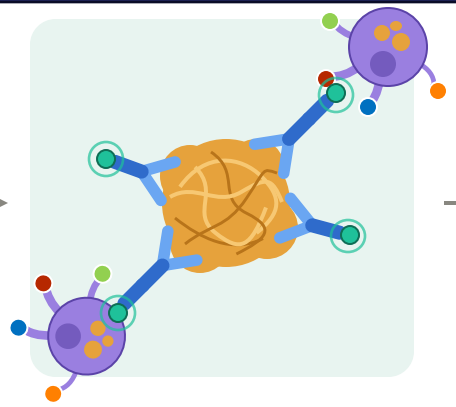


Plaques Persist

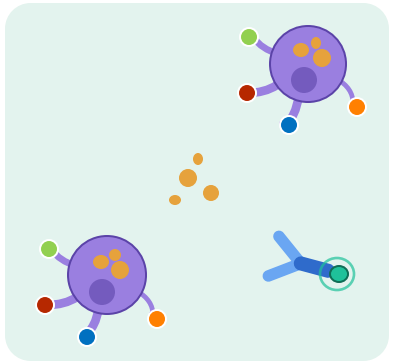
Full Fc effector Function



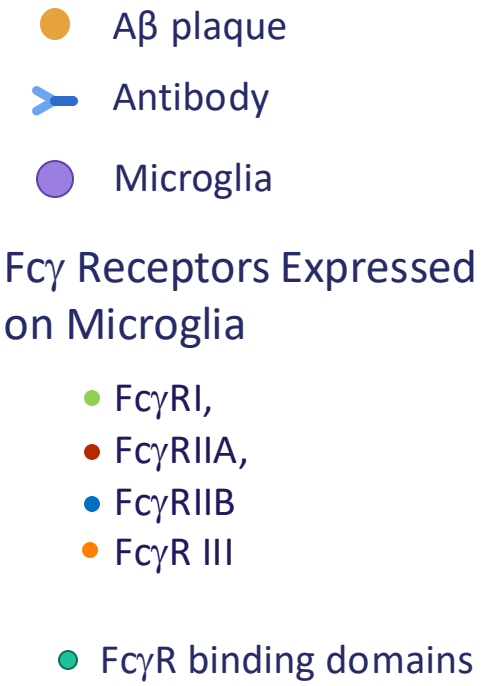
Plaque Binding is Effector-Independent



Effector-Competent Abs Recruit Microglia



Microglia Remove Plaques

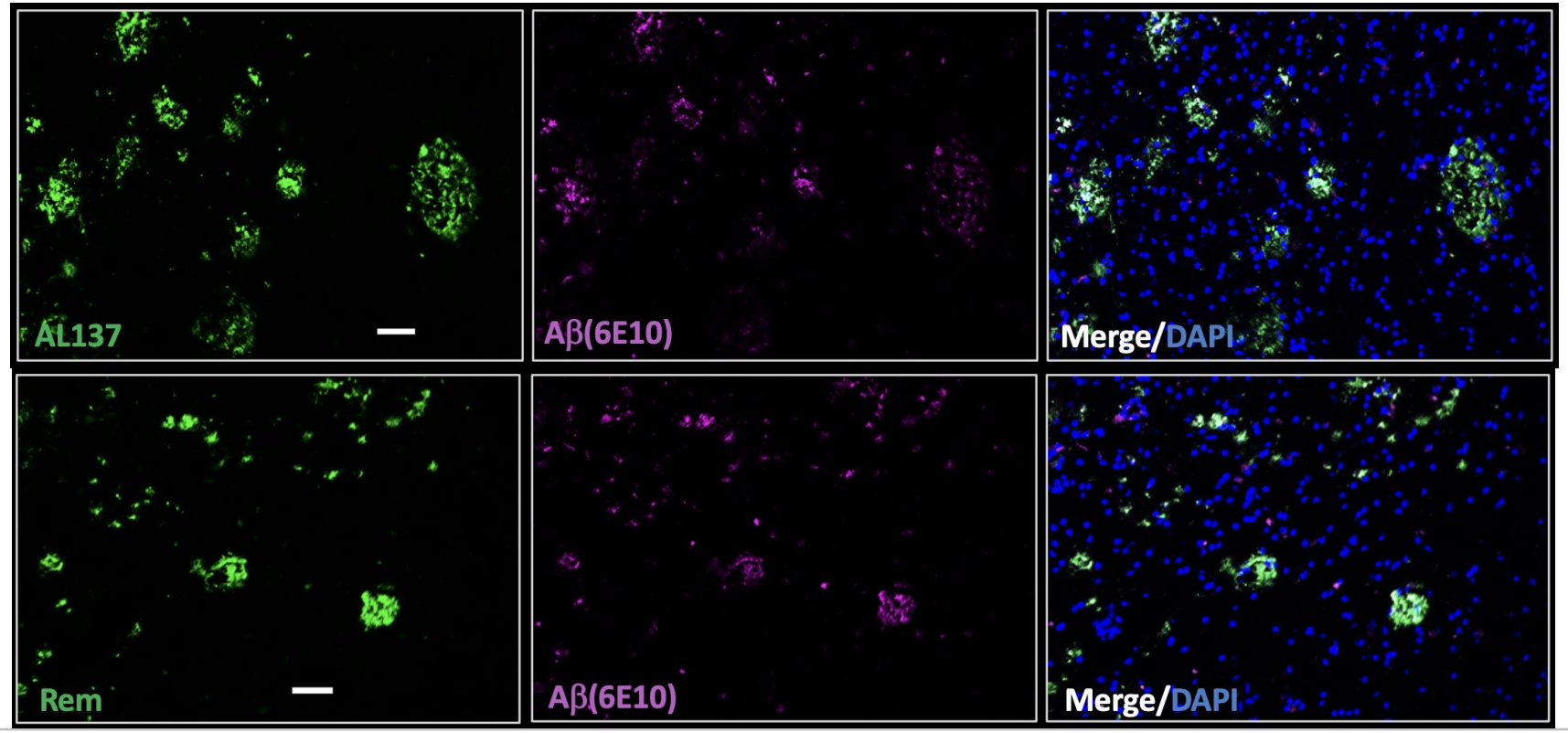


alector

AL137 Binds PyroGlu3 Aβ-Containing Plaques in Human AD Brain Sections

PyroGlu3 Aβ was Clinically Derisked by Lilly's Donanemab and Remternetug (Rem)

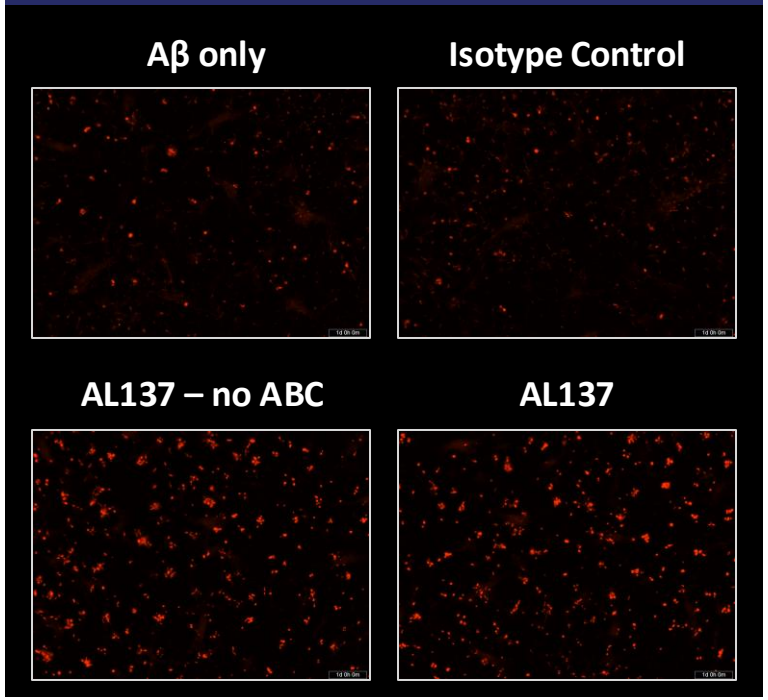
AL137 colocalizes with all identified Aβ plaques on human AD brain sections similar to Rem



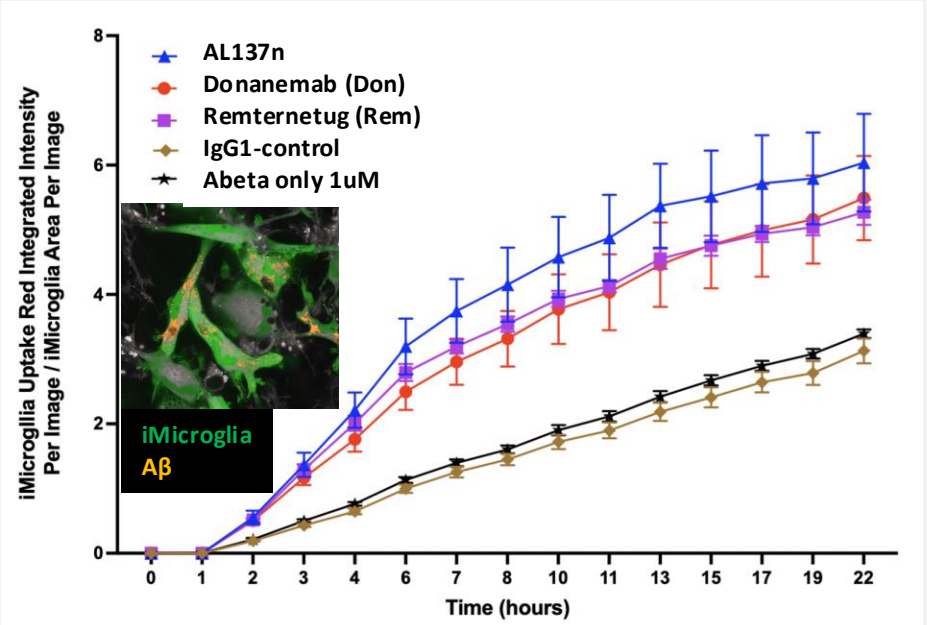
Unfixed, frozen human AD sections (medial temporal gyrus) were obtained from the Banner Institute, AZ; plaques were assessedby IFL with AL137 (green) and anti-Aβ (6E10, pink); nuclei were counterstained with DAPI (blue); images acquired with a 10x objective; scale bar= 500 µm.

AL137 Facilitates Phagocytosis of 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 similar to Don and Rem



Left: AL137, AL137 – no ABC, 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. Right: Quantification of pHrodo-pyroGlu3-Aβ uptake into GFP-iMicroglia (inset, iMicroglia in green, Aβ in orange).

Clinical Evidence Supports Full IgG1 Effector Function in Anti-Aβ Therapy

FULL Effector (IgG1) / Benefit in Human AD

- **Lecanemab** (Biogen/Eisai)**:** positive Phase 3- Approved
- **Donanemab** (Eli Lilly)**:** positive Phase 3- Approved
- **Aducanemab** (Biogen)**:** Extensive plaque removal
- **Remternetug** (Eli Lilly)**:** Extensive plaque removal
- **Trontinemab** (Roche)**:** Extensive plaque removal

All Anti-Aβ Antibodies with Extensive Plaque Clearance (>70%) and/or Clinical Benefit to Date are Wildtype IgG1

REDUCED Effector Function* / No Benefit in Human AD

- **Crenezumab (IgG4)** (Roche)**:** Phase 3 stopped for futility
- **Ponezumab (IgG2)** (Pfizer)**:** no clinical benefit in Phase 2
- **SAR228810 (IgG4)** (Sanofi): clinical trial stopped
- **GSK933776 (Fc-inactivated)** (GSK)****:** clinical trial stopped
- **Sabirnetug (IgG2)** (Acumen)**:** ~25% plaque reduction at 60mg/kg[1]. For reference, Gantenerumab showed no clinical benefit despite ~57% plaque reduction[2]

No Anti-Aβ Antibody with Modified Fc Effector Function Has Demonstrated Sufficient Plaque Clearance or Clinical Efficacy

**IgG4 and IgG2 have reduced effector function compared to IgG1, **no rodent data disclosed;*
[1]https://www.sciencedirect.com/science/article/pii/S2274580724005971?via%3Dihub; [2]https://www.nejm.org/doi/full/10.1056/NEJMoa2304430

Modulating Fc Effector Function in Anti Aβ Antibodies Constitutes An Efficacy Risk

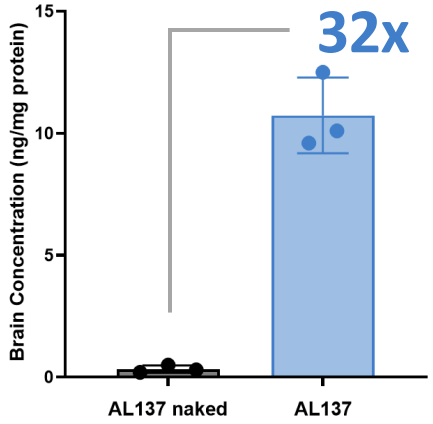
Antibody	Fc Format	Development stage	Potential Liability
Trontinemab[1]	**IgG1, full effector**	Phase 3	**No Fc-Dependent Efficacy Risk**
ABBV-1758[2]	IgG1, no effector	Phase 1/2	**Fc-Dependent Efficacy risk**
DNL921[3]	IgG1, 50% effector	Phase 1/2	**Fc-Dependent Efficacy risk**
KRSA-028[4]	Modified effector	Preclinical	**Fc-Dependent Efficacy risk**
ACU301[5]	IgG2- Reduced effector	Preclinical	**Fc-Dependent Efficacy risk**
AL137	**IgG1, full effector**	**Phase 1, Q2 2027**	**No Fc-Dependent Efficacy Risk**

Despite a Seemingly Crowded Anti-Aβ Field, the Number of High-PTS Candidates May Be Limited, as Several Incorporate Modified Effector Function

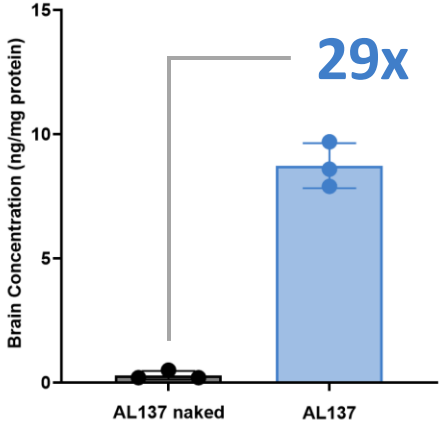
1. Grimm HP et al.Delivery of the Brainshuttle™ amyloid-β antibody fusion trontinemab to non-human primate brain and projected efficacious dose regimens in humans; Kulic L et al. Latest results from the Brainshuttle AD study of trontinemab. AAIC 2025 / Roche Presentation mAbs. 2023.; 2. AlzForum ABBV-1758; 3. Pizzo ME et al. Science. 2025; 4. Korsana Biosciences. Corporate Presentation, February 2026, pp. 18–21;
5. https://investors.acumenpharm.com/news-releases/news-release-details/acumen-pharmaceuticals-announces-nomination-two-enhanced-brain (provisional assessment)

AL137 Displays Potent Brain Exposure

Frontal Cortex (3mg/kg dose)



Hippocampus (3mg/kg dose)



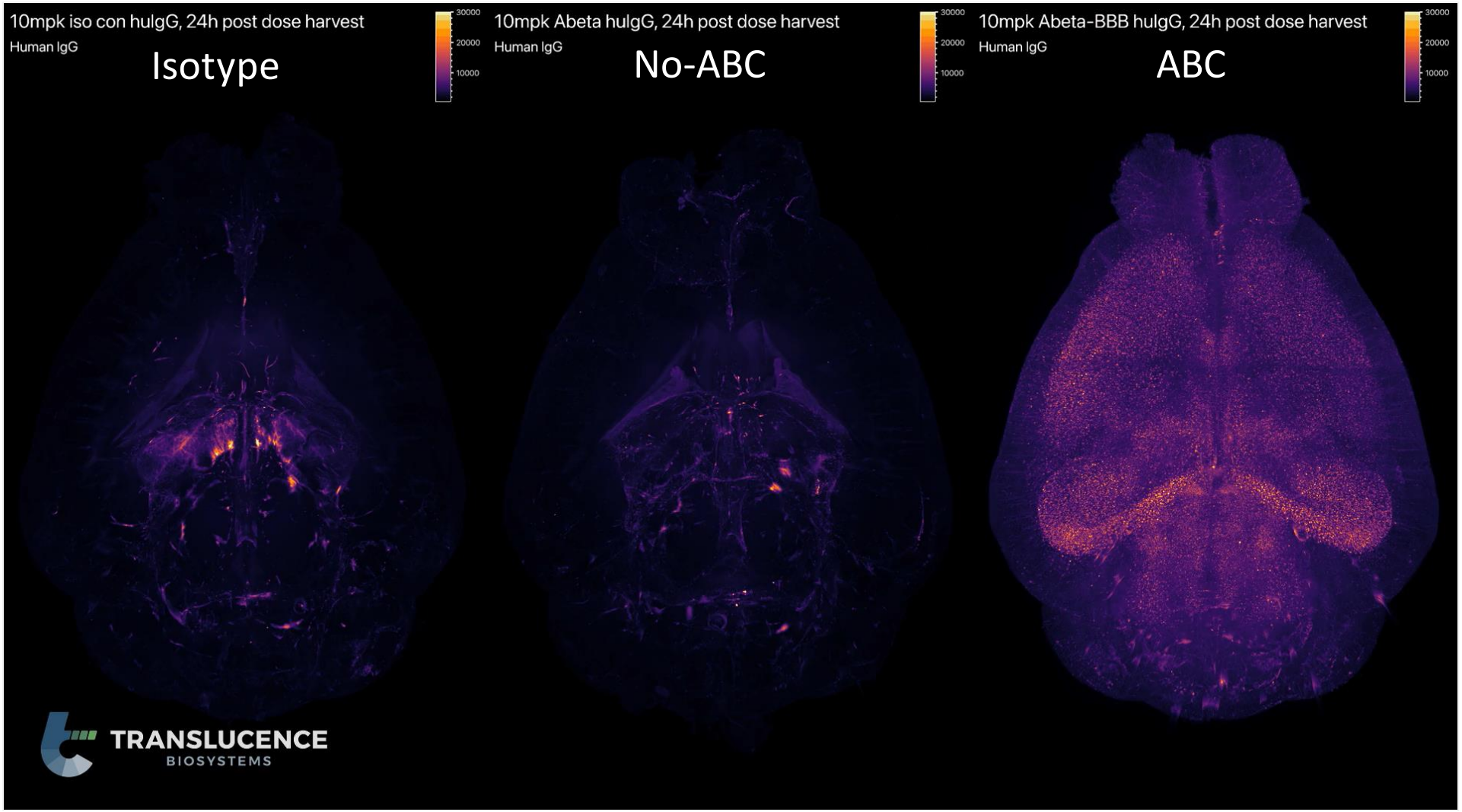
*Three NHPs per group were dosed on days 1 and 9. Brain tissues were collected 24 hours after the second injection and drug levels were measured in the vessel-depleted fraction. *E.g. to our calculations, trontinemab reaches 2.1 nM in the NHP vessel-containing cortex 24h following a single injection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

Estimated NHP Brain Concentrations at 10 mg/kg (Cross-Study Comparison)

Company	alector	DENALI	Roche	BIOARCTIC
AL137 brain concentration was linearly extrapolated from 3mg/kg (8.4 nM brain concentration) to 10 mg/kg to enable comparison with published 10mg/kg competitor data.	28 nM (AL137)	3 nM (Anti-BACE antibody)	2.1 nM (Trontinemab)	5.7 nM (Anti-Aβ antibody)

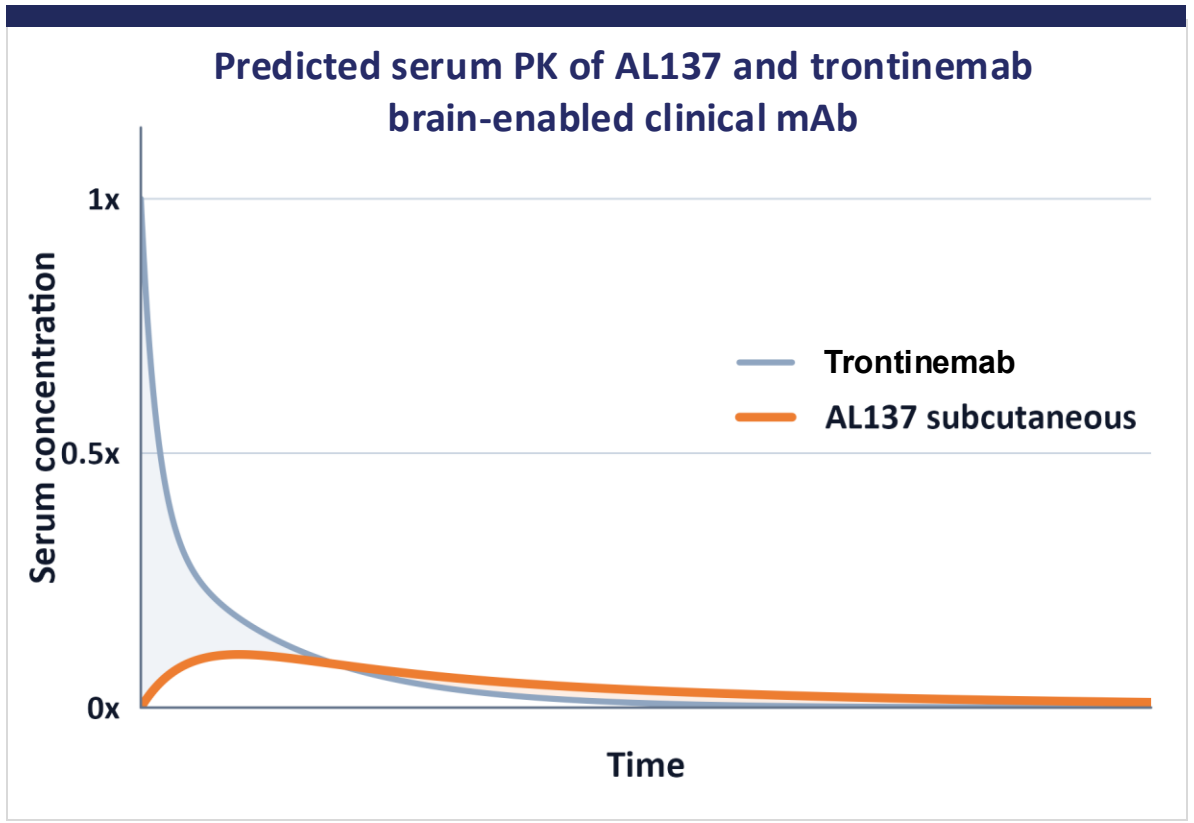
*Kariolis et al, STM 2020; Grimm et al., MABS, 2023; Freskgård, PEGS Europe 2024; *Relative to naked (no shuttle) molecule; Roche had reported 400 ng/g in NHP cortex, which in our calculations is equivalent to 2.1 nM with 10 mg/kg IV injection; BioArctic had reported 0.1 nmol/L/nmol/kg in NHP parietal 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.*

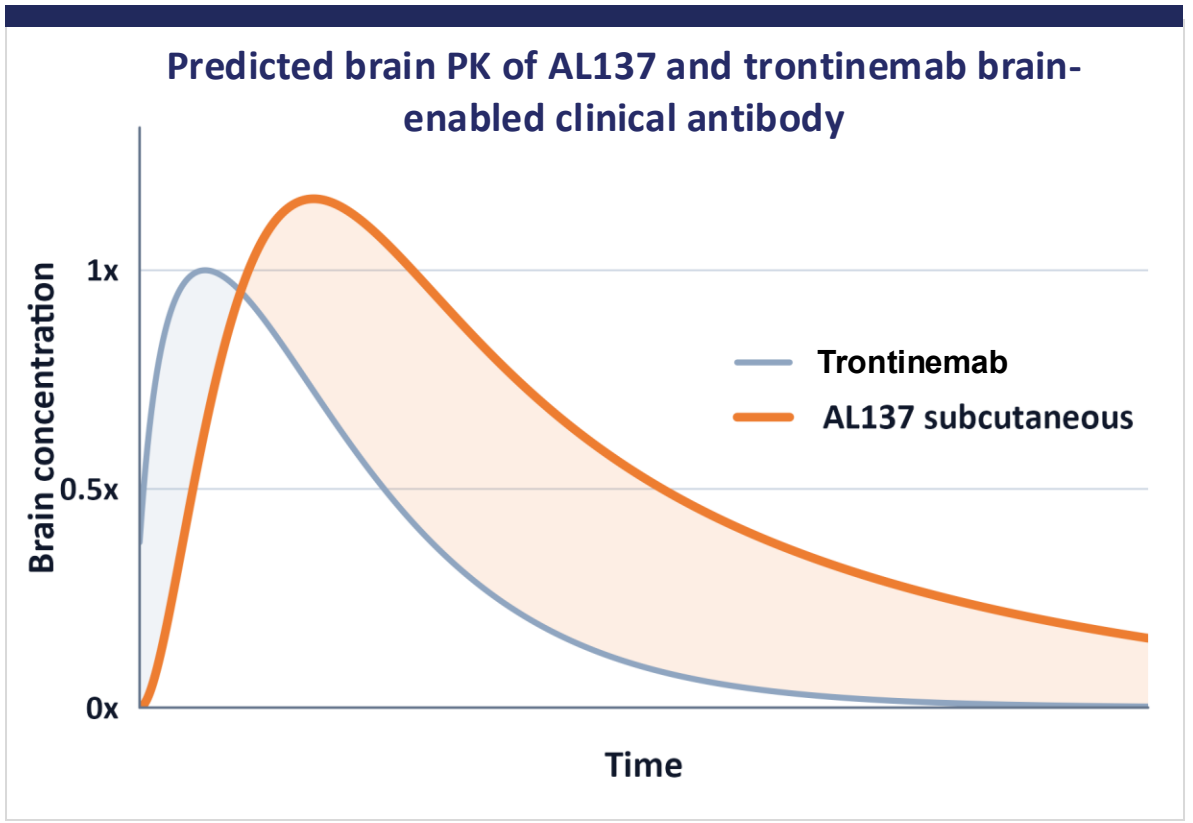
Broad Distribution and Extensive Plaque Labeling in an Alzheimer's Mouse Model



Light sheet microscopy on 7-month-old AD mouse model dosed once at 10 mg/kg and collected after 24h. Naked antibody labels the vasculature and ventricles while AL137 surrogate is bound to amyloid plaques throughout the brain.

AL137 Projected Low, Single-Digit mg/kg Dose with SC Administration





AL137 is projected to achieve ~2× higher brain exposure at a lower dose than trontinemab.
AL137's preferential brain delivery and SC dosing aim to reduce anemia, injection reactions, and ARIA risks.

AL137 Was Well-Tolerated in NHPs at Repeated Subcutaneous (SC) Administration

Delivery

AL137 is delivered SC, the intended clinical route of administration

Safety

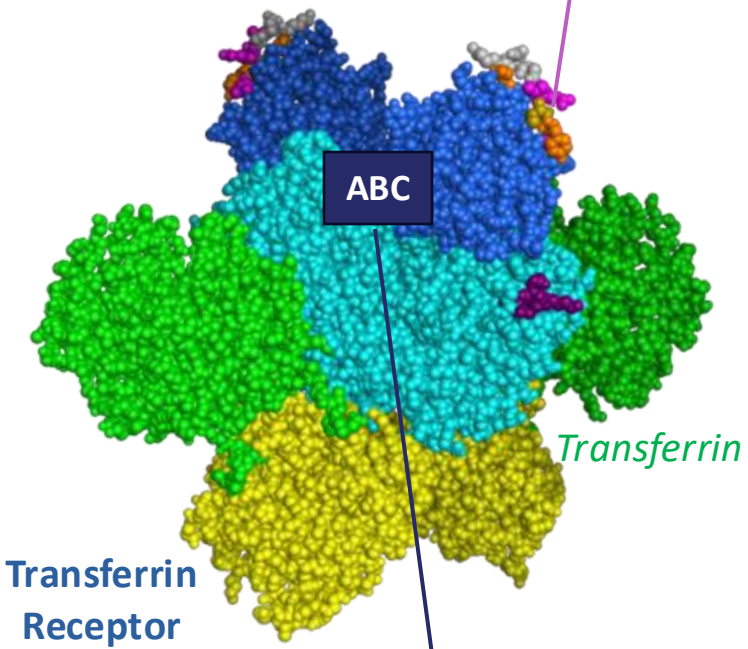
Well-tolerated in IND-enabling studies, with transient reticulocyte reductions but no adverse hematologic or other safety findings.

NOAEL

NOAEL from IND-enabling studies supports planned clinical development.

ABC Delivers Reduced Anemia Risk with a Full Effector

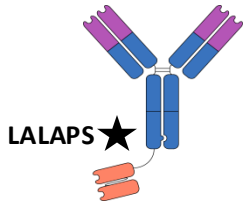
Exposed Epitope
(Co-binding to FcγR)
(same epitope as Korsana, Denali, Roche)



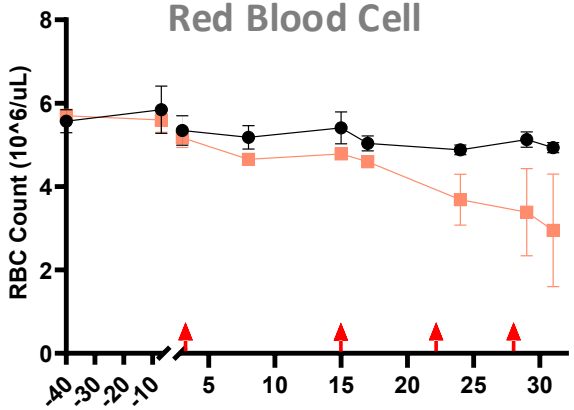
Transferrin Receptor (TfR)

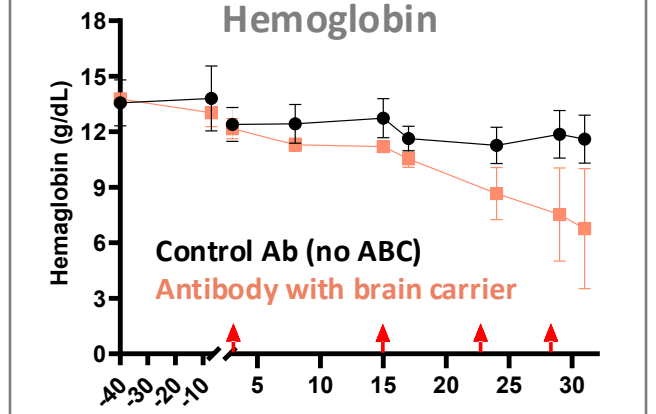
Alector ABC Epitope
(Reduced co-binding to FcγR)

Exposed Epitope + Cis LALAPS

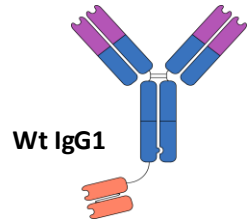


TfR binding domain

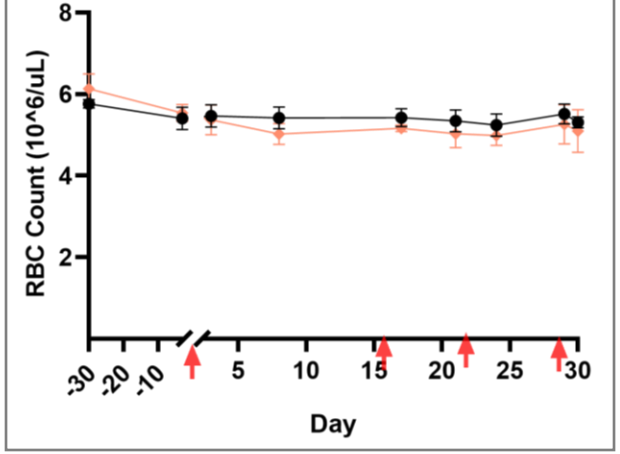


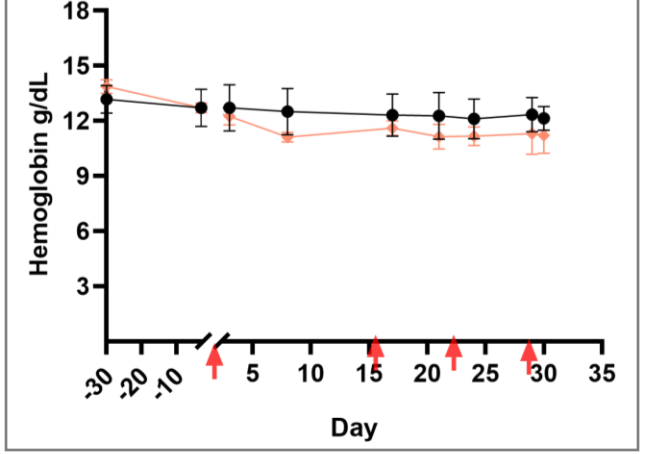


Alector's ABC Epitope + Full Effector Function



TfR binding domain





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.

Anti-Aβ Brain Shuttle Landscape; AL137 Potential Best-in-Class Advantages

Despite a Crowded Field, Few Candidates May Have High PTS Due to Unvalidated Fc Modifications, Brain Shuttles, or Aβ Epitopes

Company	Candidate	Stage	Principal development risk / uncertainty
Roche	Trontinemab	Phase 3	Shuttle Hematologic/IRR Risk; apparent Lower Brain Exposure vs. AL137
AbbVie / Aliada	ALIA-1758	Phase 1/2	Reduced Fc effector- efficacy risk
Korsana	KRSA-028	Preclinical	Modified Fc Effector; Mutation-Dependent Efficacy/Safety Risk
Denali	DNL921	CTA submitted	Reduced Fc effector- efficacy risk
BMS / BioArctic	BAN2803	Preclinical	Potential lower shuttle potency vs. AL137; exposure risk
Eisai / BioArctic	BAN2802	Preclinical	Potential lower shuttle potency vs. AL137; exposure risk
SciNeuro / Novartis	SNP234	Preclinical	Unvalidated shuttle (CD98?); safety/efficacy uncertainty
Acumen / JCR	ACU301	IND-enabling	IgG2-derived Fc; unvalidated Aβ oligomer clinical efficacy
Prothena	PRX012-TfR	Preclinical	N-terminal Aβ target; prior un-shuttled PRX012 ARIA risk
ALECTOR	**AL137**	**FIH Q2/27**	**Validated pyroGlu3 Aβ epitope; full IgG1 Fc; superior brain exposure; favorable NHP safety; low-dose SC potential**

AL137 Phase 1 Clinical Plan

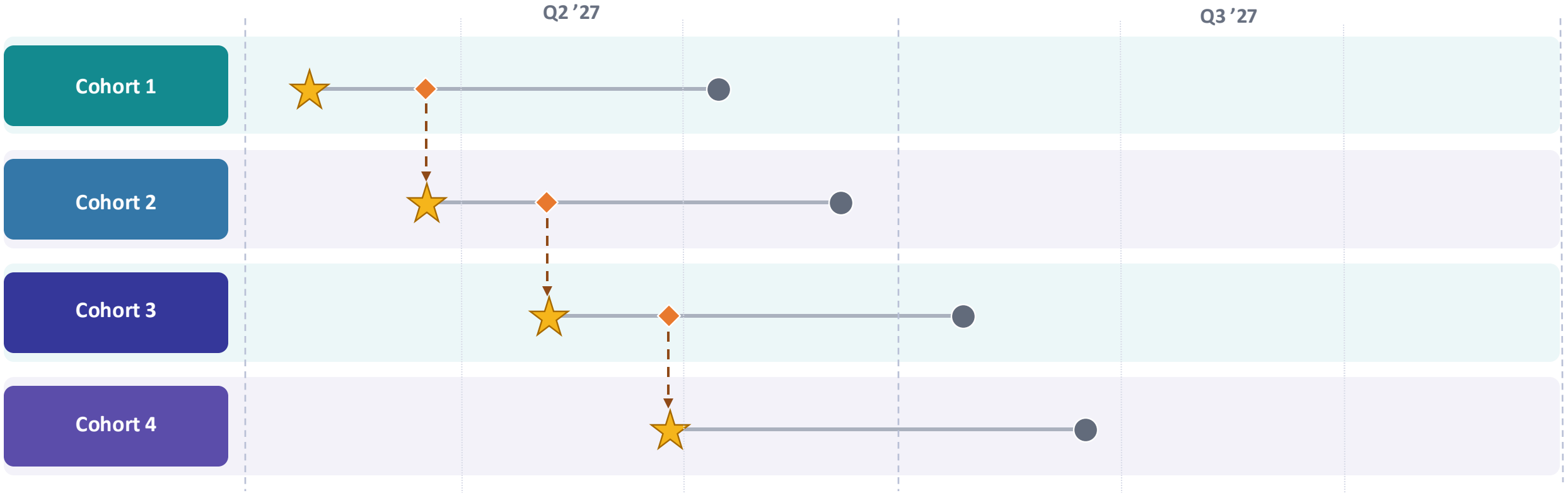
PHASE 1 OBJECTIVES	• **Assess safety, tolerability, and exposure** across ascending doses. • **Characterize dose-response and PD markers** of amyloid reduction.

STUDY DESIGN	• **SAD in Healthy Volunteers (SC)**
	  ○ Assess safety, anemia, and injection-related reactions.
	  ○ Measure serum and CSF exposure over time.
	• **MAD in Early AD Patients (SC)**
	  ○ Assess safety, anemia, injection-related reactions, and ARIA.
	  ○ Measure drug exposure, biomarkers (pTau217, MTBR), and amyloid PET.

STUDY GOALS	• **Target 90% amyloid clearance** by PET with monthly SC dosing. • **Demonstrate favorable serum and CSF biomarker changes** (e.g., pTau217). • **Demonstrate favorable safety**, with low rates of anemia, injection-related reactions, and ARIA.

SAD in Australia — Targeted Cohort Timeline

SC dose escalation in healthy volunteers; monitor safety, hematology, injection reactions, and serum/CSF exposure. Timeline assumes no safety-related delays.



Clinically validated pyroGlu3 Aβ and full Fc effector function reduce AL137's efficacy risk; favorable Phase 1 HV safety data by Q3 2027 could significantly increase its PTS.

alector

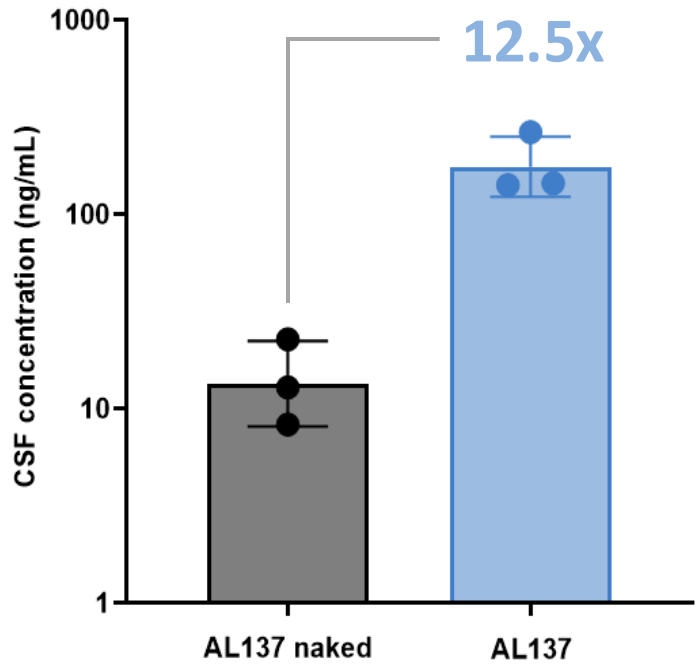
First Participant First Dose

Dose Escalation Review

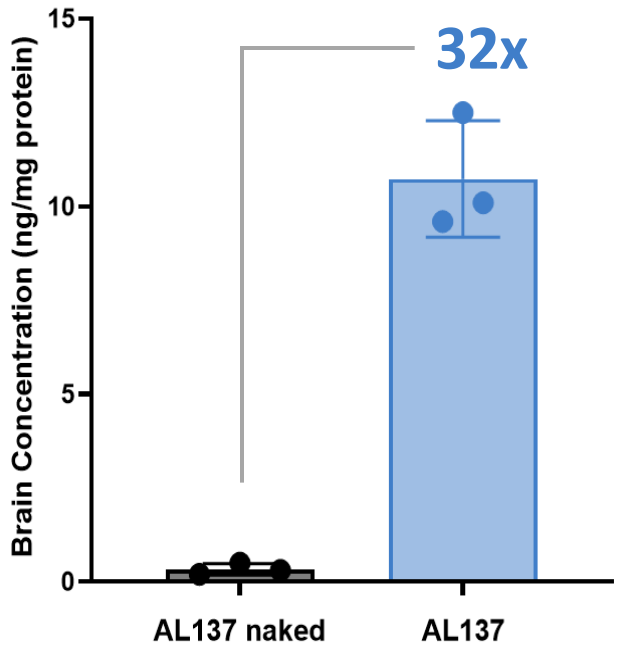
End of Study Visit

CSF Exposure of AL137 Is Expected to Predict Exposure in Brain Tissues

Concentrations of AL137 naked vs AL137 in the CSF



Concentrations of AL137 naked vs AL137 in the Frontal Cortex

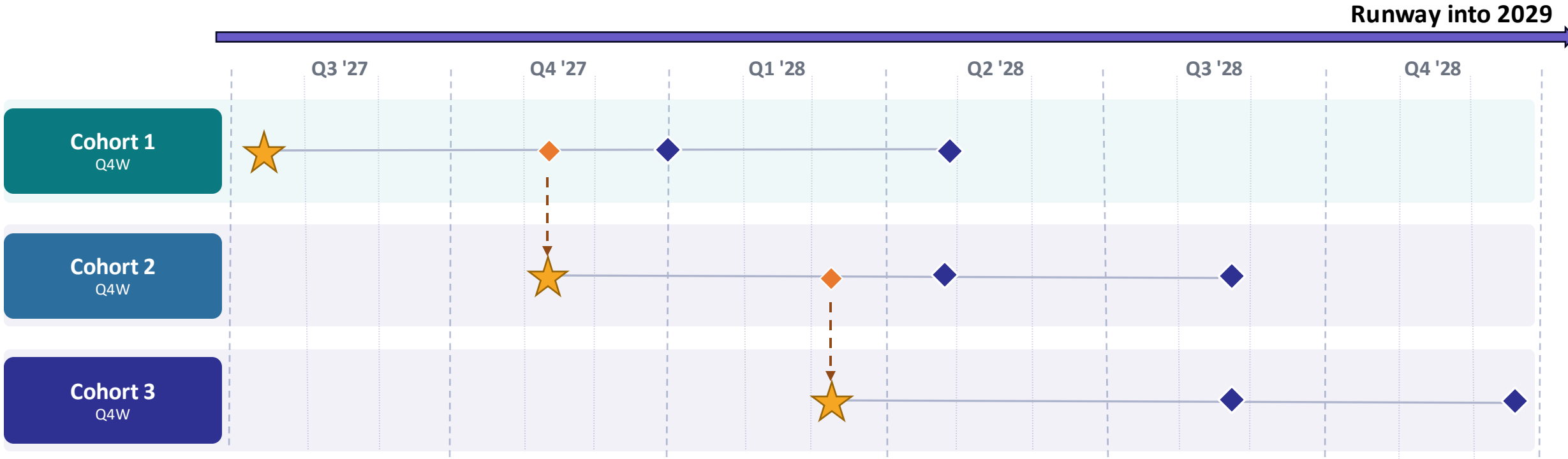


At a clinically relevant dose of 3mg/kg, AL137 reaches mean concentrations of 184 ng/mL on Day 2 in the CSF

Three NHPs per group were dosed on days 1 and 9 with 3mg/kg. CSF samples or brain tissues were collected 24 hours after the first injection (left) or second injection (right) and drug levels were measured in the vessel-depleted fraction.

MAD in US and Australia: Targeted Cohort Timeline & Amyloid PET Readouts

Ascending SC doses in early AD; monitor amyloid PET, serum/CSF biomarkers, safety, ARIA, anemia, and injection-related reactions.



Dose escalation and expansion cohorts will include timepoints W7, W12, W16 and W24 for amyloid PET.

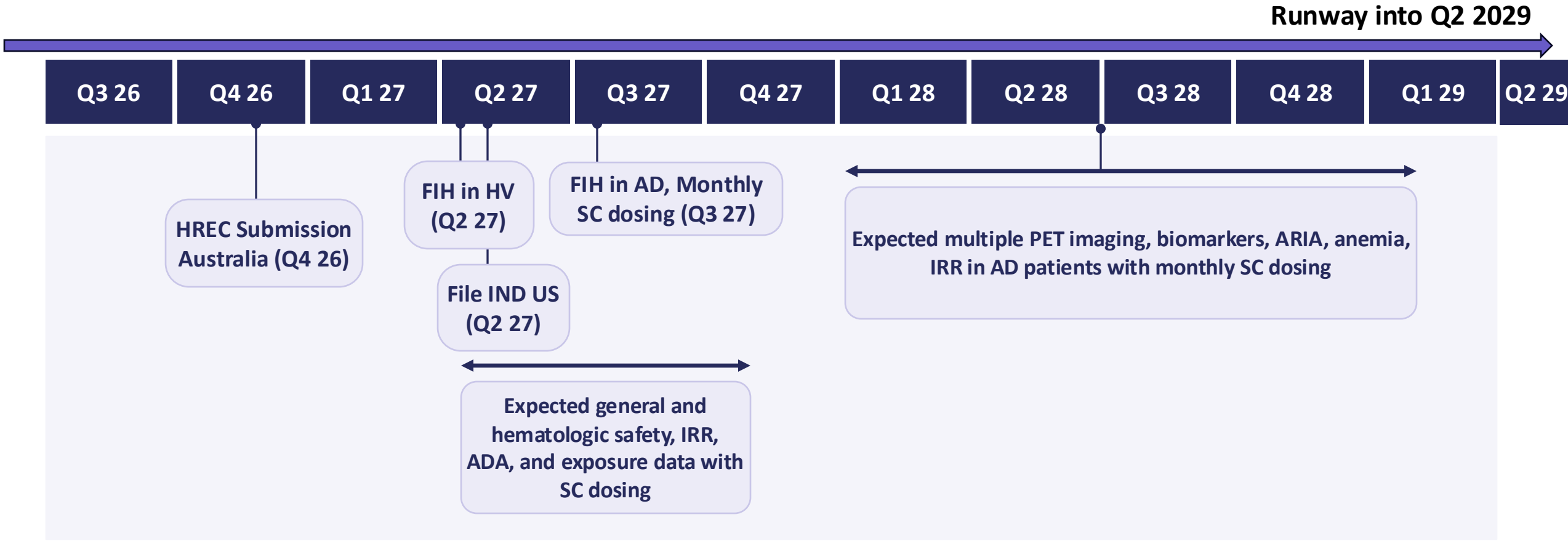
First Participant First Dose

Dose Escalation Review

Amyloid PET Readout (W7 / W24)

Multiple Safety, Biomarker, and Imaging Readouts in AD Patients Throughout 2028, Well Within Our Runway

Summary of AL137 Timeline; Clinical Validation Starting April 2027



AL137: Potential Best-in-Class, De-Risked Anti-Aβ with a Validated Epitope, Full IgG1 Effector, Superior Brain Exposure, Favorable Safety, Low-Dose SC Delivery, and Low COGs.

*AD = Alzheimer's disease; ADA = Anti Drug Antibodies; ARIA = amyloid-related imaging abnormalities; FIH = First in Human; HREC = human research ethics committee; HV = Healthy Volunteers; IRR = Injection-related reaction; PET = positron emission tomography imaging; SC = Subcutaneous dosing. * Dates and statements represent Forward-Looking Statements associated with substantial risks and uncertainties listed in slide 2.*

Alector Brain Carrier Platform for siRNA Cargo

ABC-siRNA Creates Substantial Platform Value Through a Versatile, Plug-and-Play Brain Carrier for Multiple siRNA Cargos and CNS Targets

ABC-Enabled siRNA Platform: Demonstrated Capabilities

Targeting a differentiated profile for peripheral delivery of siRNA therapeutics to the brain

1 Optimized Shuttle

Optimized Affinity, Kinetics, and Format Maximize Brain siRNA Delivery

2 Subcutaneous Delivery

Demonstrated High Brain siRNA Exposure and Potency with SC Dosing in NHPs

3 Infrequent Treatment

Targeting Durable Effects with Dosing Every ~3 Months

4 Broad Brain Distribution

Demonstrated Homogeneous NHP Brain Distribution with Multiple siRNA Cargos

5 Favorable Tolerability

No Platform-Related Adverse Effects or Hematologic Changes in NHPs

6 Potent Target Reduction

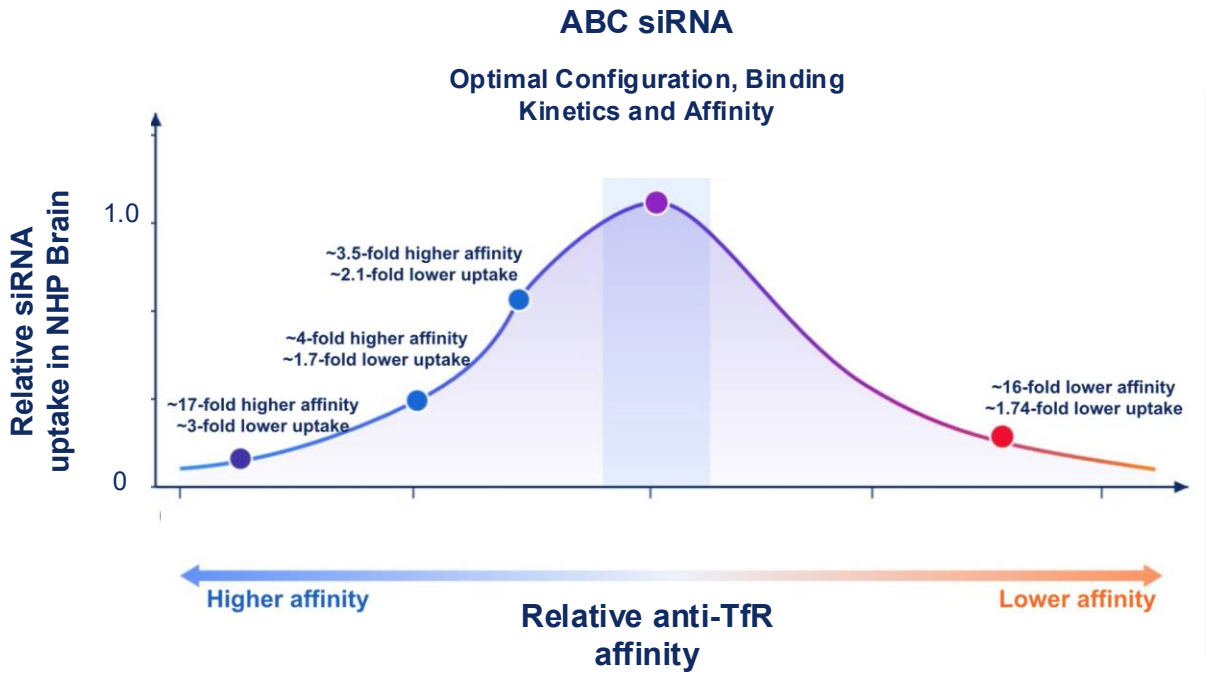
Demonstrated >75% Brain-Wide Target Knockdown with Multiple siRNAs

Targeting convenient, scalable and infrequent treatment of intracellular CNS targets with convenient SC delivery

alector

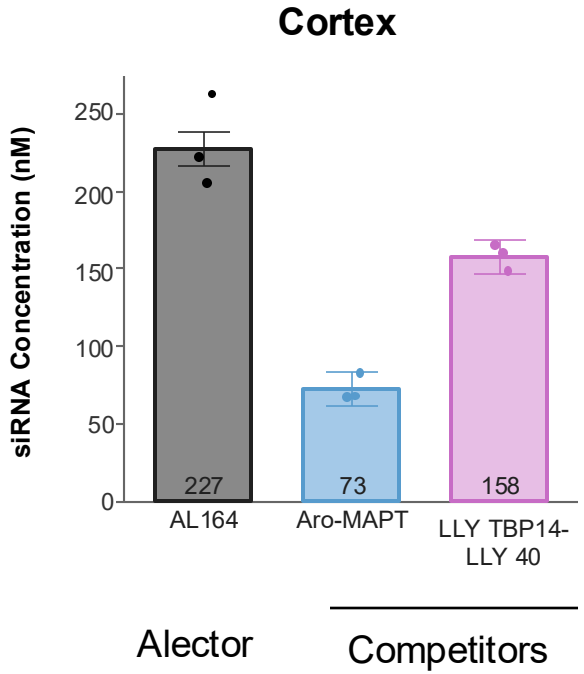
Alector Brain Carrier: Optimized Affinity Drives Superior Brain siRNA Delivery

Optimized anti-TfR affinity, binding kinetics and drug configuration



Graph represents data from 2 different NHP studies with multiple siRNA Cargos

AL164 delivers more siRNA into rodent brain than Arrowhead and Eli Lilly competitor AOCs



HuTfR x hMAPT double KI mice were injected subcutaneously with 3x7.5 mg/kg siRNA dose-equivalent and the level of antisense siRNA in brain tissues was measured at day 29 via MSD assay. n=3/group.

Affinity–uptake relationship is schematic; NHP comparisons are from separate studies.

AL164

ABC-enabled Tau siRNA Program

Tauopathies: A Large and Diverse Disease Burden



~34–40M Estimated people living with AD worldwide

~7/100K Pooled prevalence of PSP; likely underrecognized

~6 Years Median survival after PSP symptom onset

No Tau DMT No approved therapy directly targets tau pathology

Tauopathies include common and rare diseases

Alzheimer's disease

Largest tauopathy population
Amyloid and tau pathology

Progressive supranuclear palsy

Rare primary 4R tauopathy
Rapid clinical progression

Shared need: durable Tau lowering throughout the brain

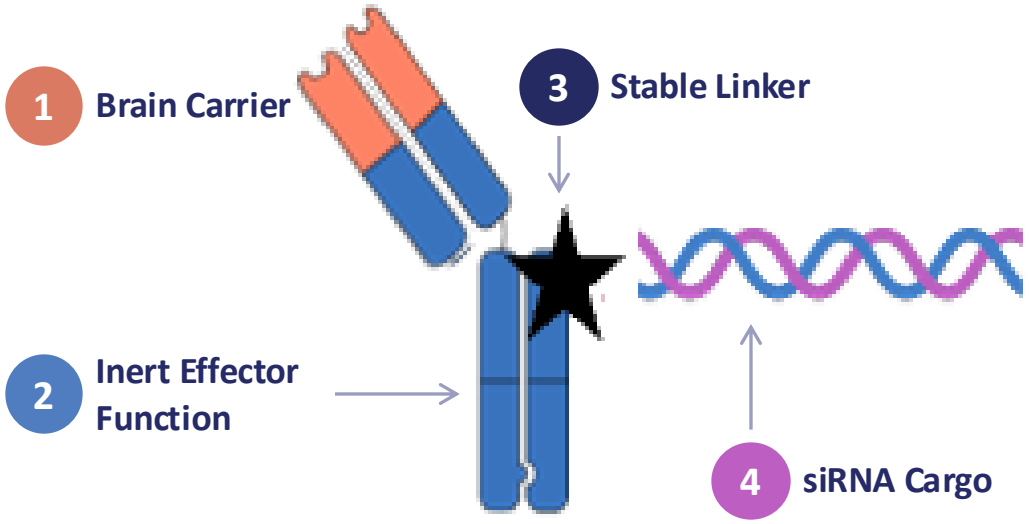
Tau is an aggregation-prone protein that forms neurofibrillary tangles, a pathological hallmark of Alzheimer's disease and primary tauopathies.

alector

Sources: WHO Dementia Fact Sheet, 2026; Lyons S et al. J Neurol. 2023; Litvan I et al. JNNP. 1996; Cummings J et al. Alz ResTher. 2025.

AL164: Aiming for Brain-Wide Tau Reduction Without Invasive Spinal Injections

Designed for intracellular Tau reduction with subcutaneous delivery and broad brain distribution



TARGET VALIDATION

Phase 2 Diranersen reduced Tau pathology and showed encouraging clinical trends, supporting Tau lowering in AD.

THE CHALLENGE:

Antibodies cannot target intracellular Tau; ASOs require invasive IT delivery with uneven distribution and safety risks.

THE AL164 SOLUTION:

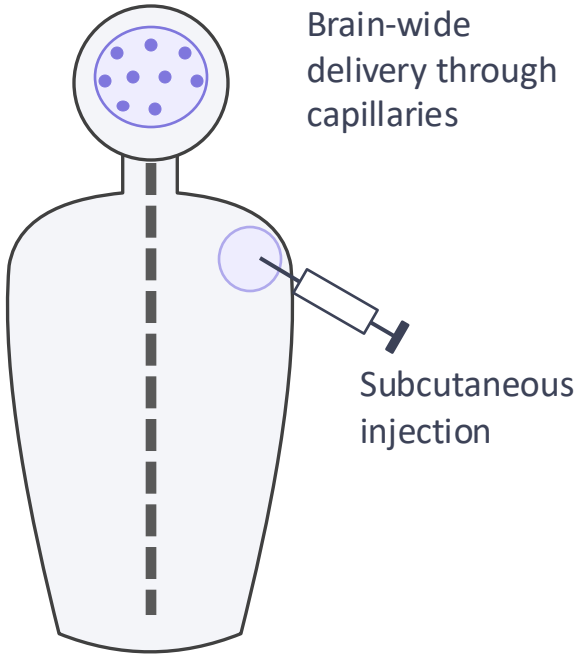
SC-delivered siRNA targeting intracellular Tau with broad brain distribution, improved safety, scalability, and access.

AL164 Combines High Potency, Low Single-Digit mg/kg siRNA-Equivalent SC Dosing, Favorable Safety, and Strong Manufacturability and Developability, with Targeted Dosing Every ~3 Months.

AL164 Aims to Enable Non-Invasive Subcutaneously Administered Delivery of siRNA to the Brain

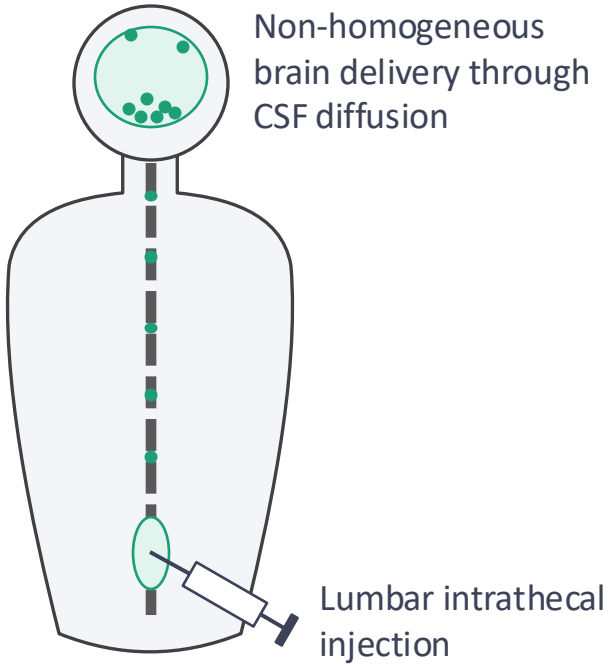
AL164

Systemic route, broad brain exposure



Diranersen

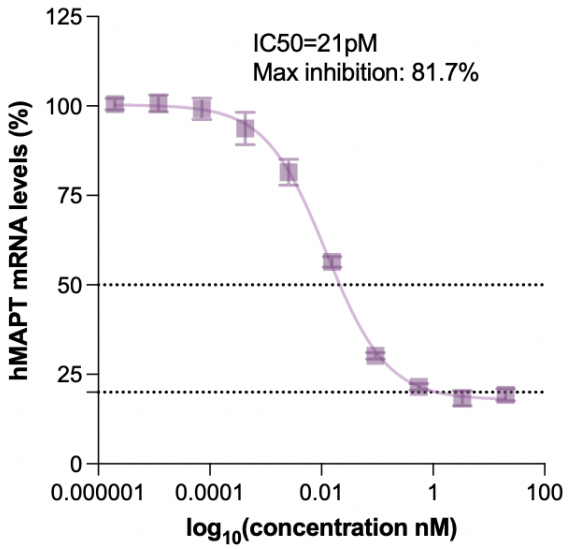
CSF route, regional variability



- **Scalable delivery** for a global AD population approaching 90M by 2050.
- **Broad, homogeneous brain distribution**, avoiding IT-associated variability and spinal accumulation.
- **Favorable tolerability potential**, avoiding IT procedural and ASO-related risks.

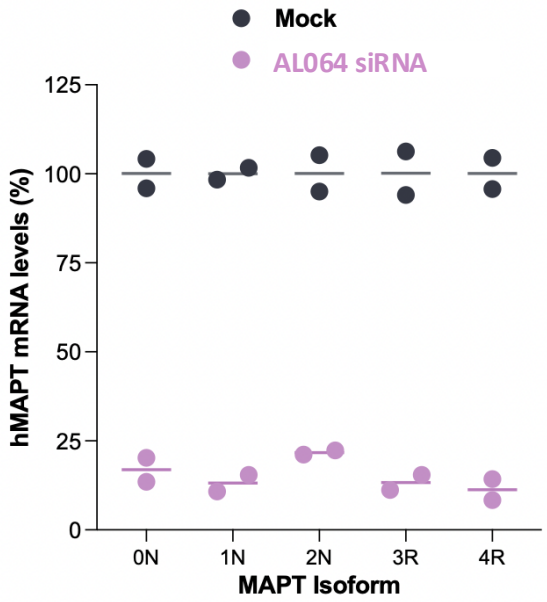
Unmodified AL164 (AL064) Tau siRNA Demonstrates pM Potency in Vitro

Dose-Dependent Knockdown in MAPT Expressing Cell Line



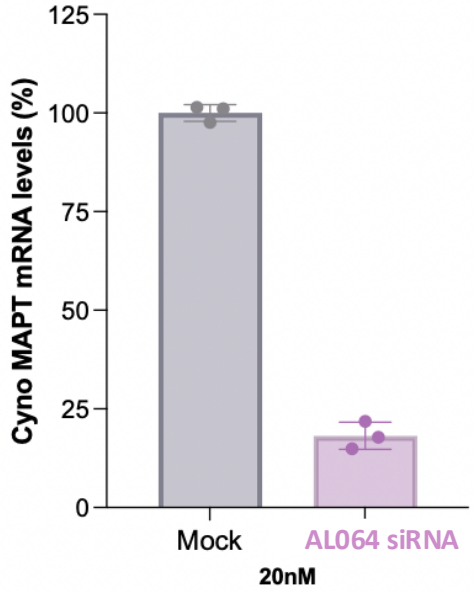
81% inhibition and pM range IC50. AL064 siRNA was transfected into MCF7 cells for 24hr to determine the dose response.

Knockdown all MAPT Isoforms in Human Neuroblastoma Cell Line



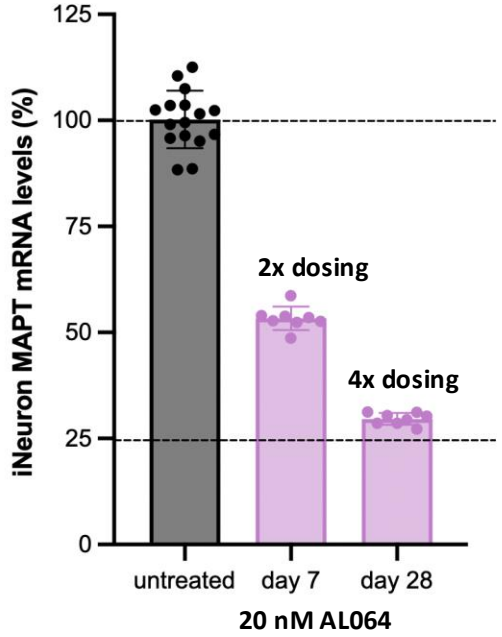
AL064 siRNA was transfected into SH-SY5Y cells for 24hr to determine the knockdown of MAPT isoforms.

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

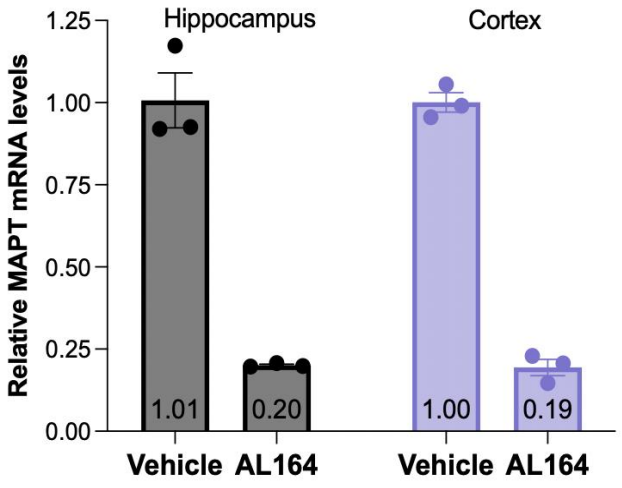


iPSC-derived neurons were treated with AL064 2 or 4 times and Tau mRNA knockdown was determined after 7 or 28 days.

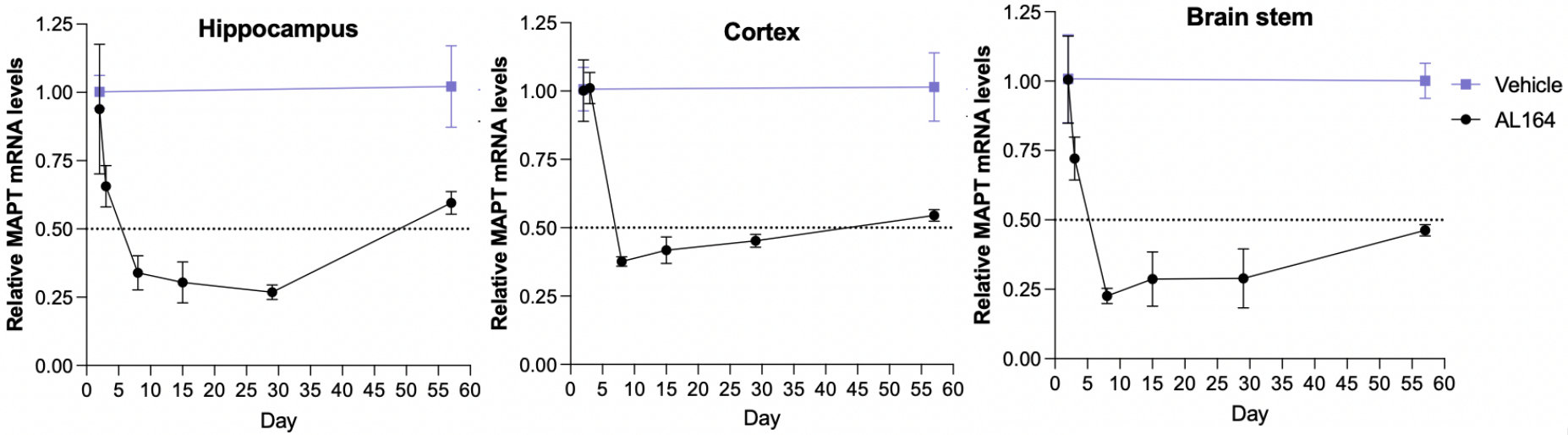
Alector internal data. Leftmost 3 panels were conducted with AL064 siRNA that was not conjugated to ABC, rightmost panel with the siRNA-ABC conjugate molecule. AL064 and AL164 are identical molecules except for a validated modification at the 3' sense strand of AL164

AL164 Induces Up to 81% Durable Tau mRNA Knockdown in Murine Model

Three AL164 Loading Doses Achieve 81% Tau Knockdown in Mouse Brain



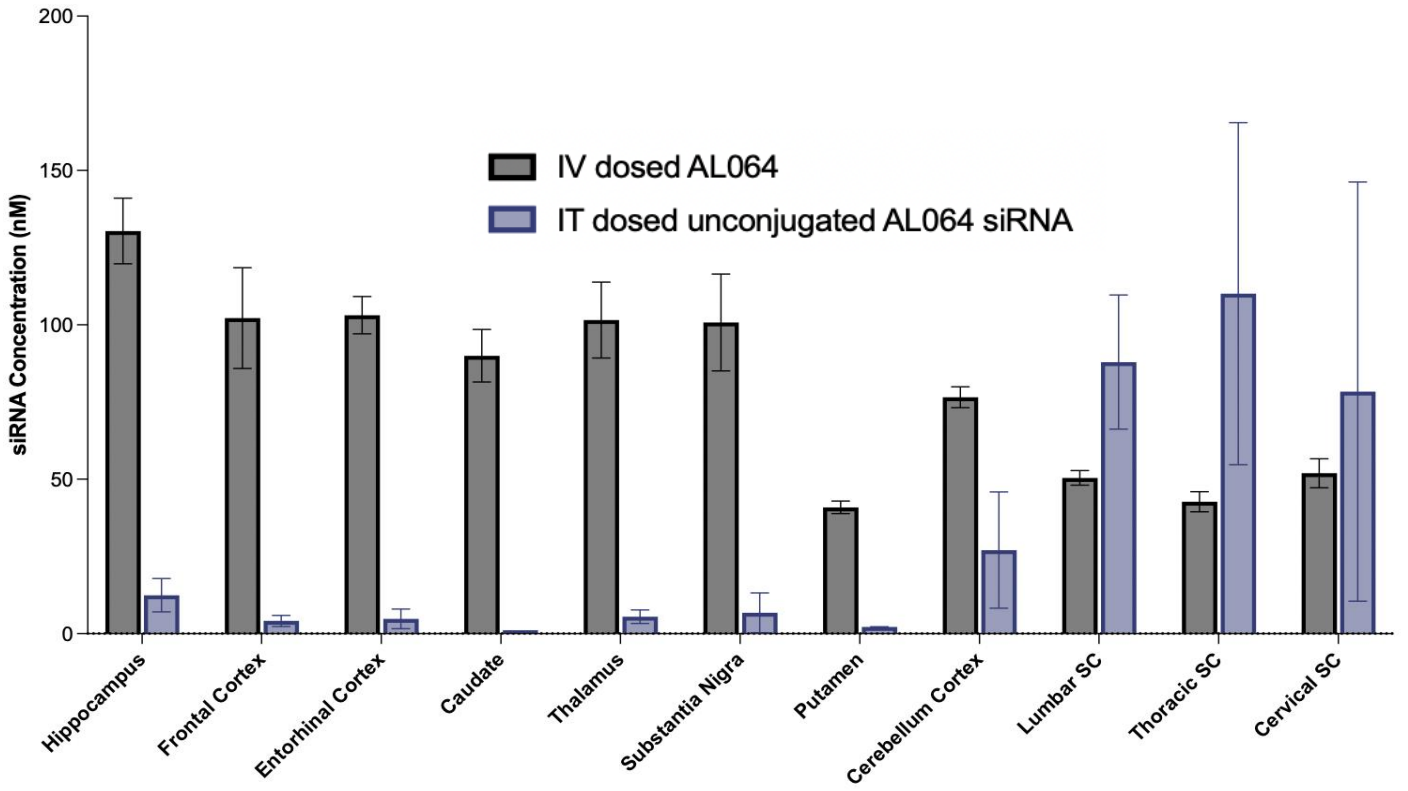
Single-Dose AL164 Maintains >50% Tau mRNA Knockdown for Over 2 Months



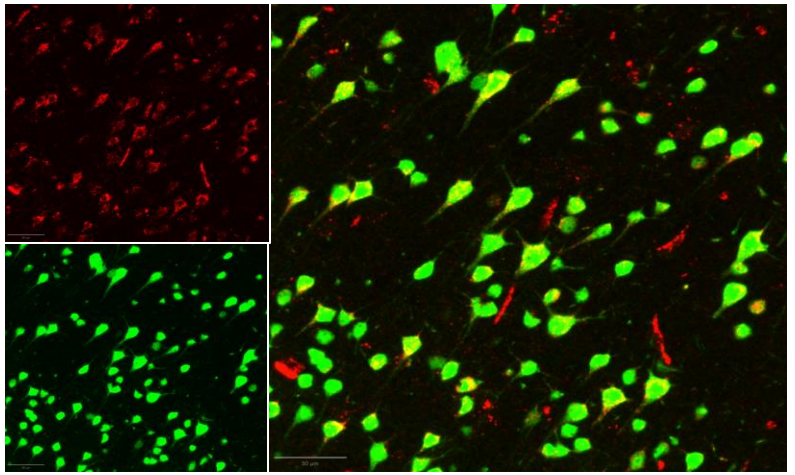
HuTfR x hMAPT double-knockin mice were injected subcutaneously (left) three times with 7.5 mg/kg siRNA-dose-equivalent of AL164 at 1-week intervals and sacrificed two weeks after the last injection or (right) a single dose of 9 mg/kg siRNA-dose-equivalent of AL164 at day 1 and sacrificed at day 2, 3, 8, 15, 29, and 57. hMAPT expression was quantified by qPCR.

Peripheral AL064 Delivery Achieves Uniform Brain Exposure and Broad Cortical Neuronal Uptake

AL064 reaches up to 130nM siRNA in NHP brain



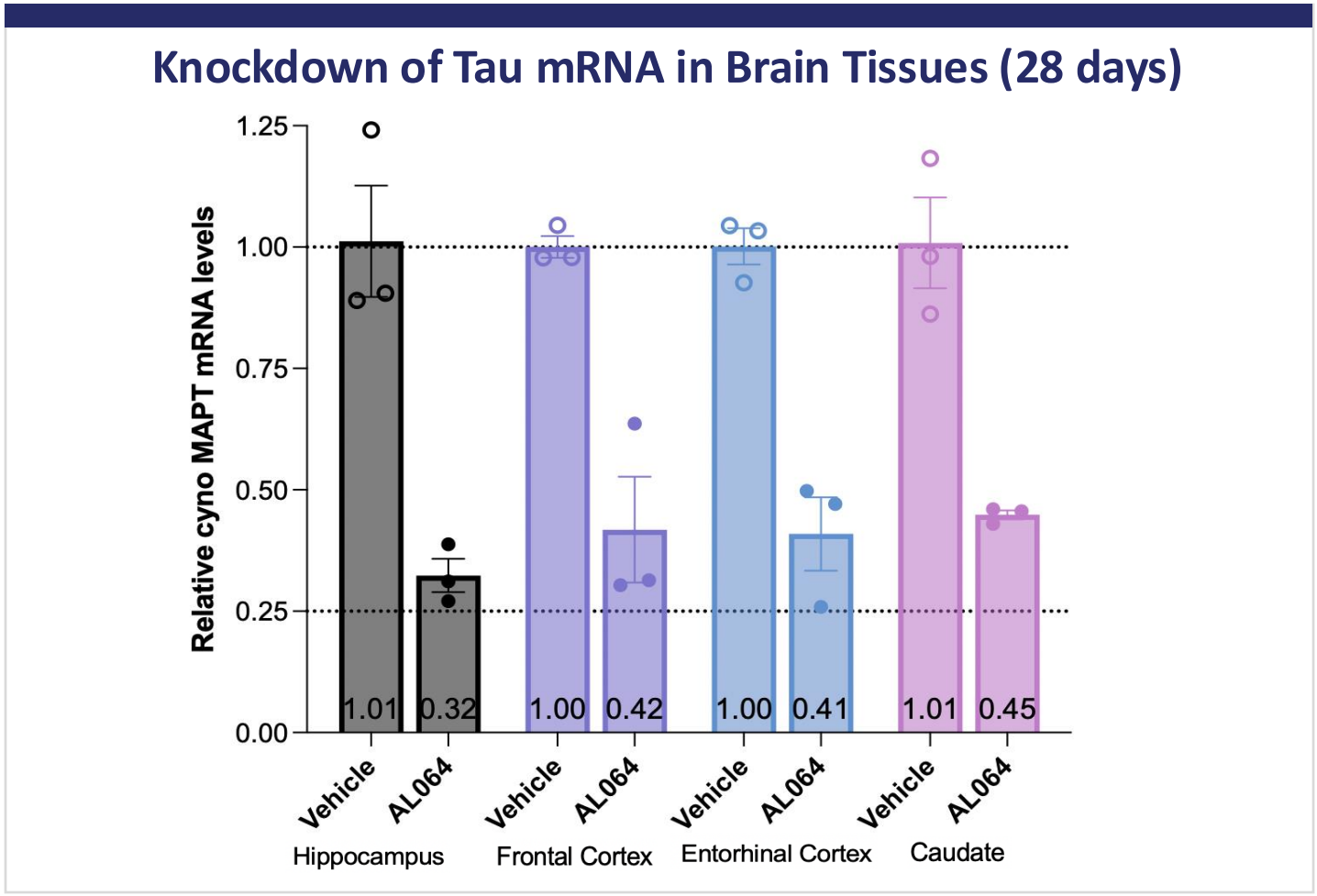
AL064 broadly distributes across cortical neurons



AL064 siRNA (red)
Neuron (Green)
Overlay

Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent, while the IT group received a single dose of 27mg/kg unconjugated AL064 through intrathecal injection at Day 1, and the level of AL064 siRNA antisense strand in different brain regions was measured at day 28 with MSD assay. AL064 siRNA antisense strand in frontal cortex was assessed with RNAscope assay in the IV infusion treated NHPs.

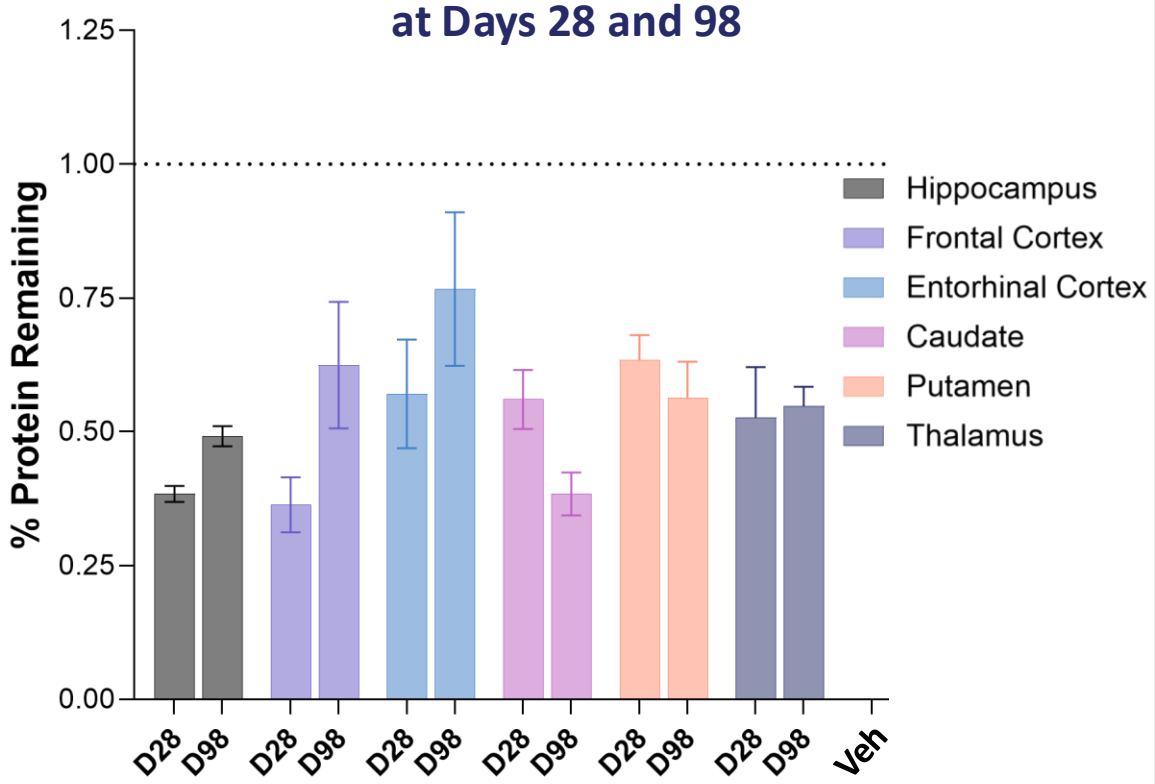
Peripheral AL064 (Unmodified AL164) Achieves Up to 70% Tau mRNA Knockdown in NHPs



Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg and the level of MAPT mRNA in different brain regions was measured at day 28 with qRT-PCR assay.

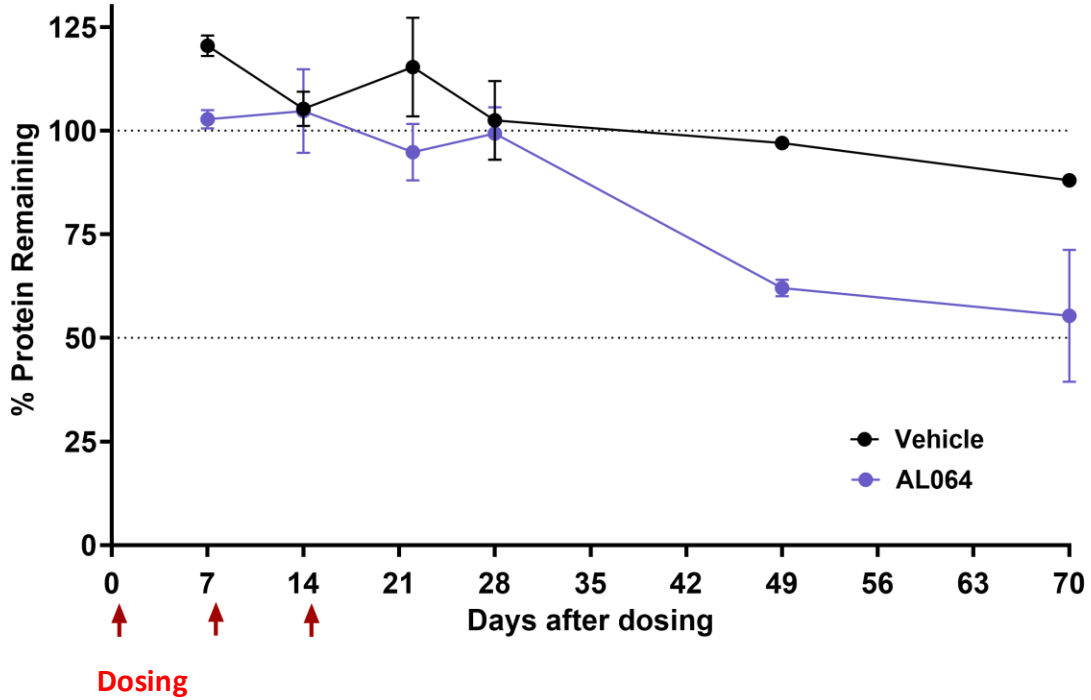
AL064 (Unmodified AL164): Durable pTau217 Reduction in NHP Brain and CSF

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



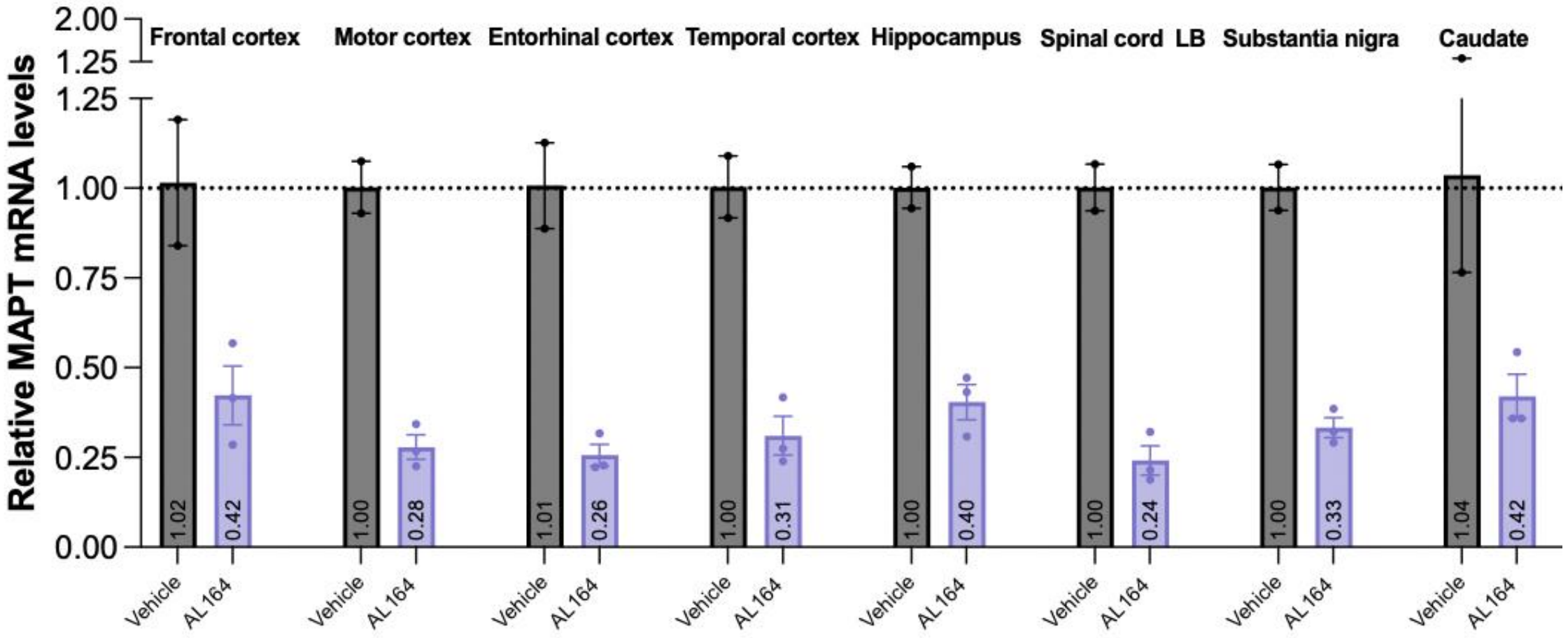
D28 and D98 normalized to experiment-specific vehicle treated cohort.

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 NHP Brain



NHPs (n = 3 per group; n = 2 for vehicle) received subcutaneous (SC) injections of the AL164 at 3 mg/kg siRNA-dose equivalent on days 1, 8, and 15. MAPT mRNA levels in the indicated brain regions were measured by qRT-PCR on day 29.

AL164 Current Status; Targeting FIH in Q2 2028

SAFETY

No AL164/AL064-Related Adverse Findings in NHPs at Doses Up to 30 mg/kg siRNA

- AL164 and AL064 were well tolerated following IV or SC administration in NHPs up to 30 mg/kg siRNA dose
- No test article-related changes in reticulocytes or other hematology parameters were observed
- No test article-related adverse findings were identified across the other safety endpoints, including clinical chemistry and histology

2026 *Fast-tracked manufacturing with a global leader in AOC*

150 mg/mL *Manufacturable for SC delivery*

Q2 2028 *Planned FIH with SC delivery*

AL164 Combines High Potency, Low Single-Digit mg/kg siRNA-Equivalent SC Dosing, Favorable Safety, and Strong Manufacturability and Developability, with Targeted Dosing Every ~3 Months.

**AL164 and AL062 incorporate the same ABC shuttle leading to significant manufacturing synergy*

AL062

ABC-enabled α-Synuclein siRNA Program

The Growing Burden of Parkinson's Disease and Lewy Body Dementia

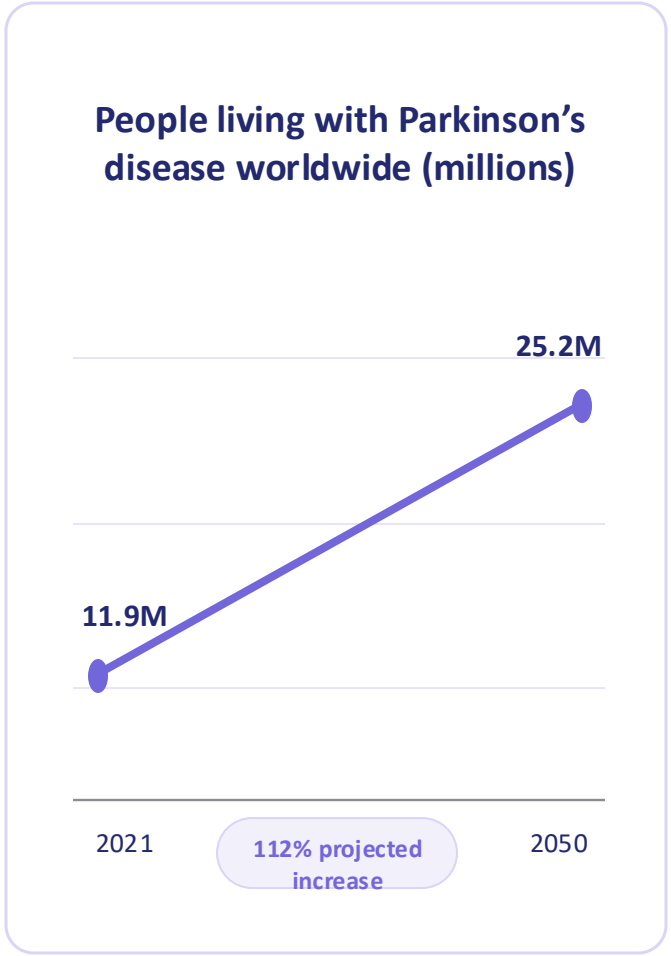


~12M People living with Parkinson's disease worldwide in 2021

~1.4M People living with Lewy body dementia in the U.S.

~$52B Annual U.S. economic burden of Parkinson's disease

No DMT No approved therapy slows progression in PD or LBD

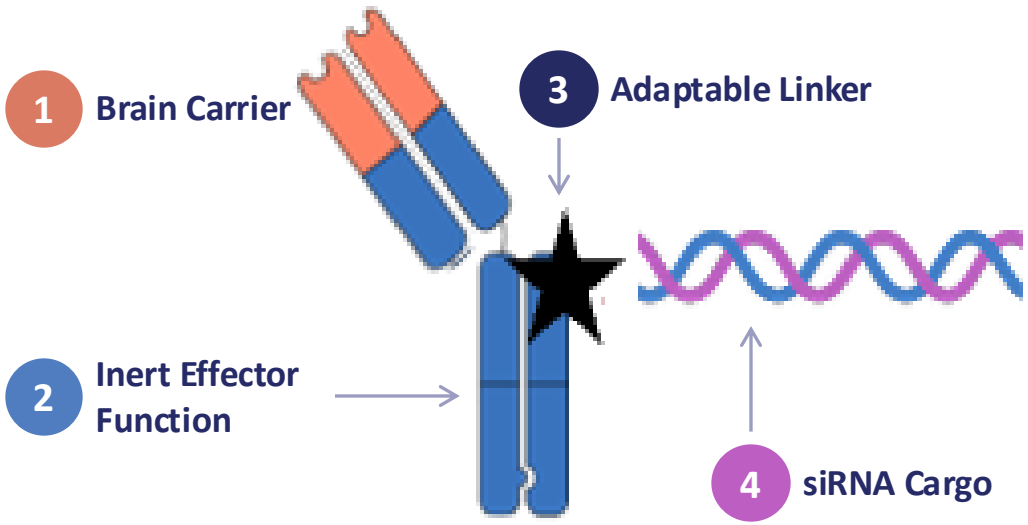


α-Synuclein is an aggregation-prone protein that forms Lewy bodies, a pathological hallmark of Parkinson's disease and Lewy body dementia.

Sources: Su D et al. BMJ. 2025; WHO Parkinson Disease Fact Sheet; NINDS DLB Consortium; Yang W et al. NPJ Parkinsons Dis. 2020.

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

Silencing intracellular α-synuclein production with peripheral delivery and broad brain distribution



THE CHALLENGE:
No approved disease-modifying therapies for PD/LBD; antibodies have limited efficacy against intracellular α-synuclein.

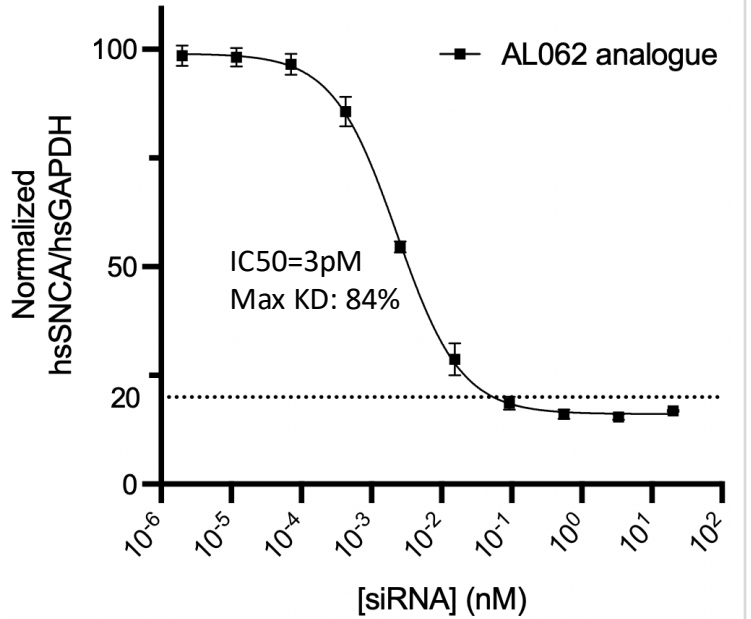
THE AL062 SOLUTION:
Silences intracellular α-synuclein production to target the source of pathology.

PERIPHERAL DELIVERY & BRAIN DISTRIBUTION
Designed for scalable peripheral delivery with broad brain distribution.

AL062 Combines High Potency, Low-Dose SC Delivery, Favorable Safety, and Strong Manufacturability and Developability, Targeting Dosing Every ~3 Months.

AL062 siRNA: High Potency and No Observed Off-Target Activity

Dose-Dependent Knockdown in SNCA Expressing Cell Line



AL062 parental siRNA was 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.

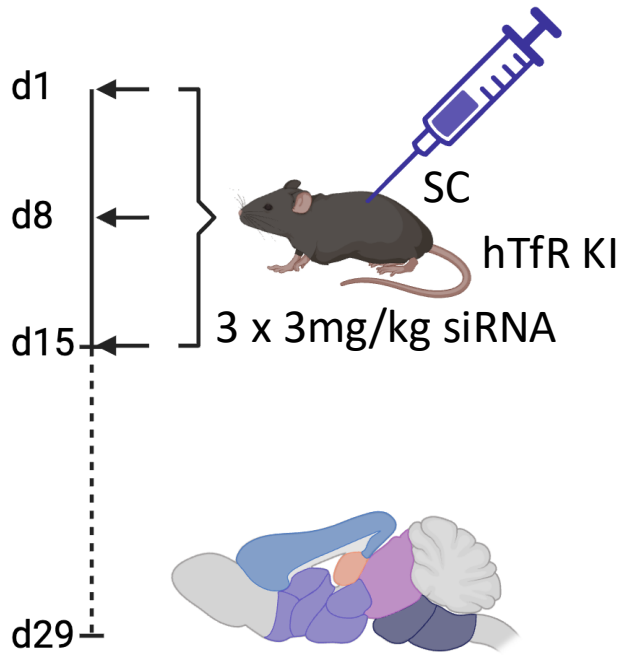
No observed Off-Target in Human Cell Lines at Up to 50nM

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

AL062 parental siRNA was transfected at 50nM into Hep3B or SH-SY5Y cells for 24hr to determine the off-target genes through RNA-sequencing.

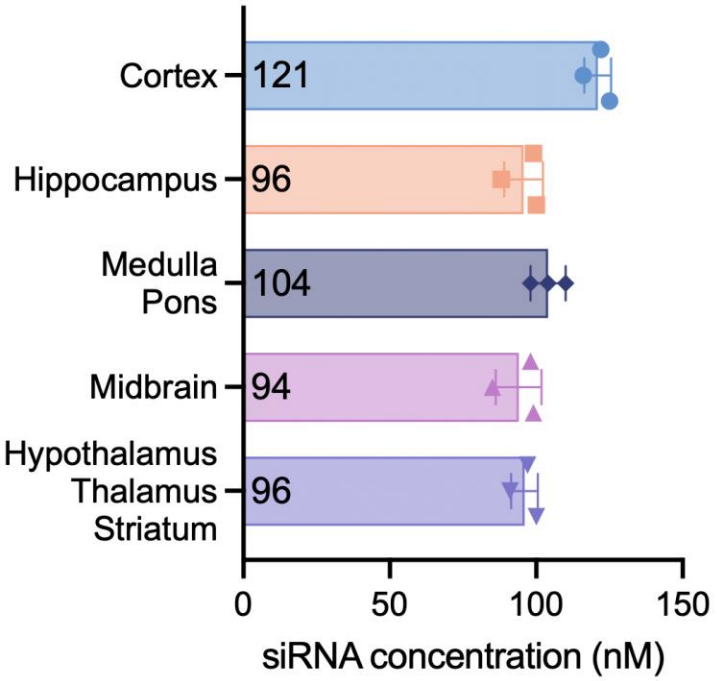
AL062 Significantly Reduces α-Synuclein Expression Throughout the Mouse Brain

Study design



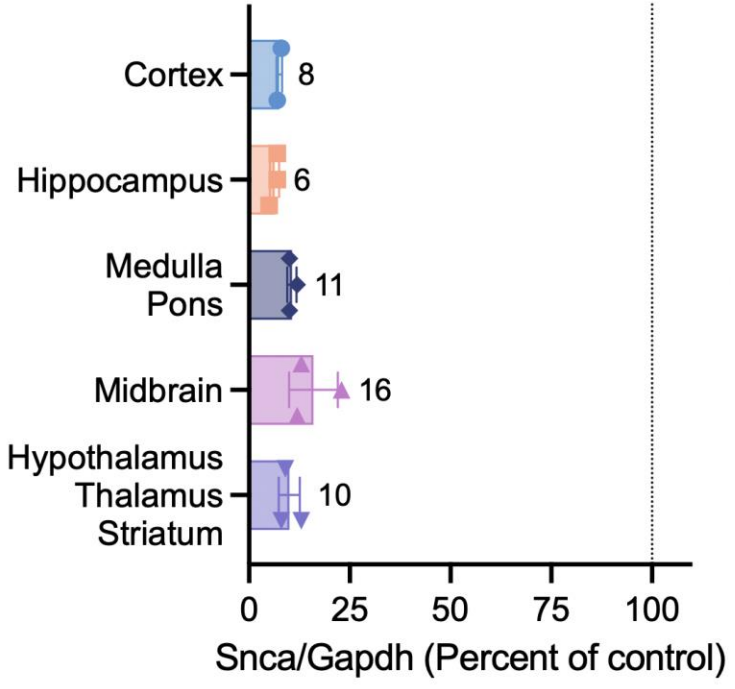
hTfR KI mice were dosed subcutaneously 3 times weekly with 3mg/kg siRNA-equivalent AL062 candidate or diluent. Two weeks post last dose, brains were dissected and evaluated for Snca expression.

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.

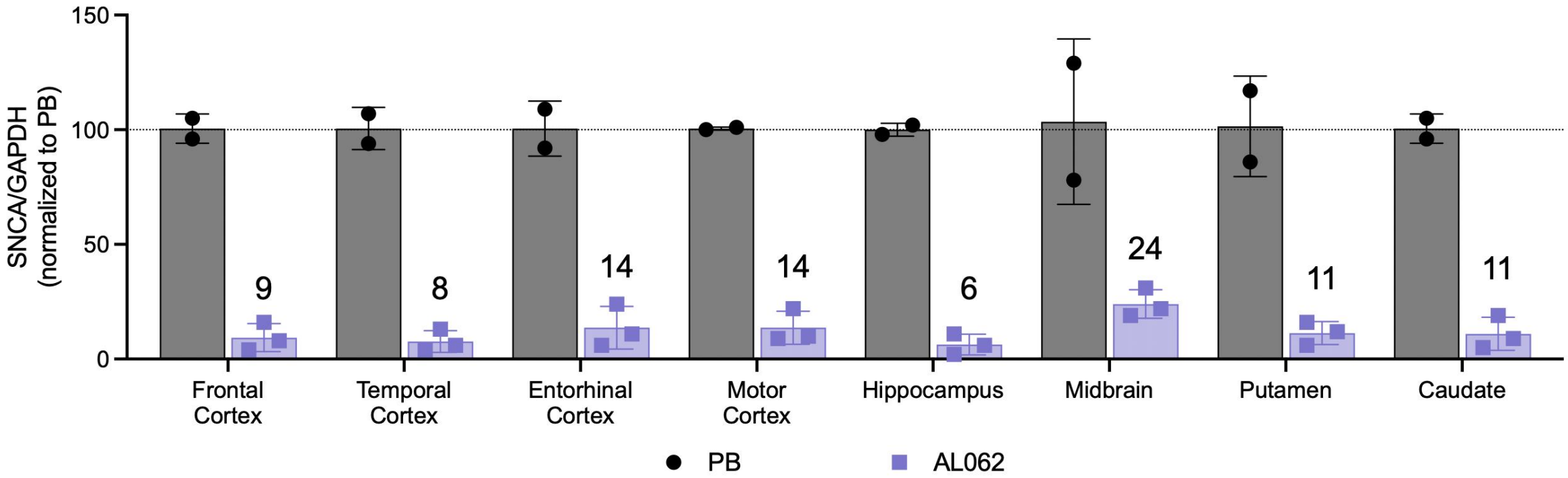
Snca expression was reduced 84-94%



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 knockdown 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 Day 29 and SNCA expression was measured by qPCR. Baseline SNCA expression was lowest in the midbrain and highest in the Hippocampus (not shown). Mean +/- SD

AL062 Current Status; Targeting FIH in Q2 2028

SAFETY

No AL062 related adverse findings in any tissue in NHPs

- AL062 was well tolerated following repeat SC administration in NHPs
- No test article-related changes in reticulocytes or other hematology parameters were observed
- No test article-related adverse findings were identified across the other safety endpoints evaluated, including chemistry and histology

2026 *Fast-tracked manufacturing with a global leader in AOC*

150 mg/mL *Manufacturable for SC delivery*

Q2 2028 *Planned FIH with SC delivery*

AL062 Combines High Potency, Low Single-Digit mg/kg siRNA-Equivalent SC Dosing, Favorable Safety, and Strong Manufacturability and Developability, with Targeted Dosing Every ~3 Months.

**AL164 and AL062 incorporate the same ABC shuttle leading to significant manufacturing synergy*

Alector:

Multiple Paths to Value Creation

One proprietary brain-delivery platform. Multiple therapeutic modalities.

Clinical Milestones Through 2028, Supported by Runway into Q2 2029

01	**Alector Has Evolved**	From conventional antibodies to ABC-enabled therapeutics targeting validated biology.
02	**Partnership Validates the Strategy**	Large Pharma validates ABC technology and extends runway into Q2 2029.
03	**AL137: Near-Term Clinical Opportunity**	Validated Aβ epitope, full IgG1 effector, superior brain exposure, and planned SC dosing.
04	**ABC-siRNA: Broad Platform Potential**	AL164 and AL062: Potent Brain-Wide Knockdown, Favorable NHP Safety, and Targeted SC Dosing.



Thank You