Alector Corporate Overview

February 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," "should," "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, including the sufficiency of cash to fund operations through 2027; 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 collaborations; 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 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, including the anticipated timing and detail regarding PROGRESS-AD; 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, 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 submissions 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 and geopolitical events 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 clinical trials or statements regarding ongoing 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 Programs and Technologies

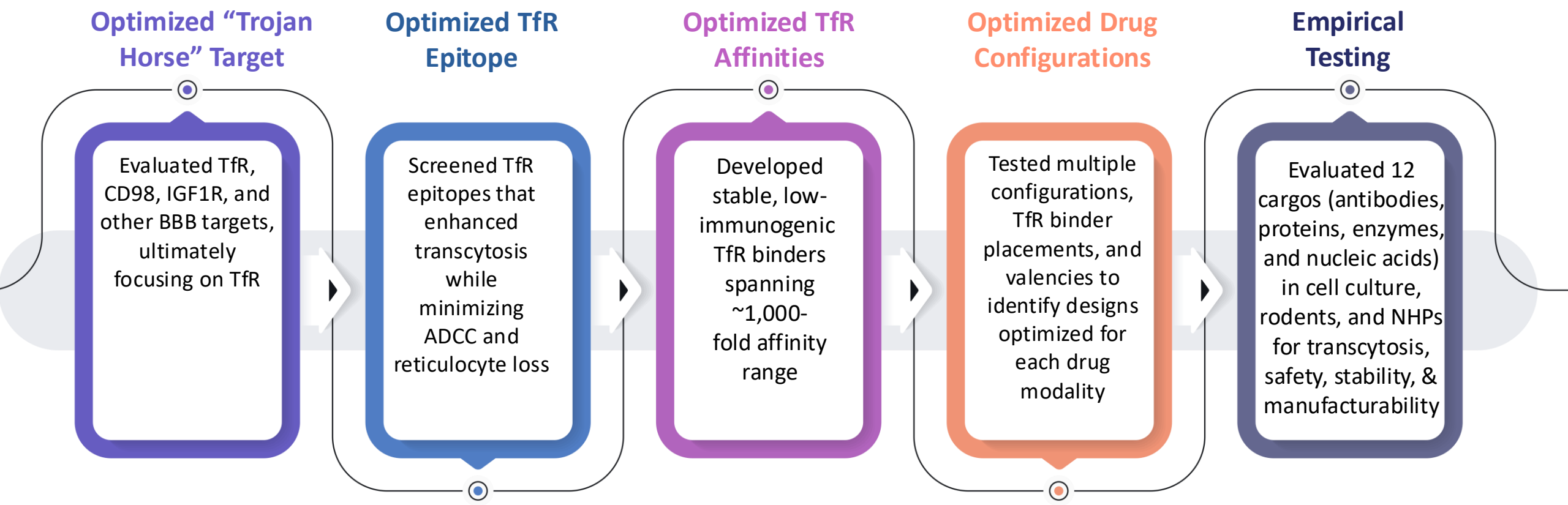
TARGET AND MODALITY	CANDIDATE	THERAPEUTIC AREA	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ALECTOR'S COMMERCIAL OWNERSHIP	RIGHTS
PGRN-Abs	AL101	AD						*U.S. 50/50 profit share and co-promote. Tiered double-digit royalties ex-U.S.*	GSK
Aβ-Abs	AL137-ABC	AD							alector
GCase-ERT	AL050-ABC	PD, GD, LBD							alector
Tau siRNA	AL064-ABC	AD, FTD							alector
α-Syn siRNA	ADP062-ABC	PD							alector
NLRP3-siRNA	ADP065-ABC	Neuro							alector

1. *Cash, cash equivalents, and marketable securities as of December 31, 2025 were $256.0M; ABC = Alector Brain Carrier; AD = Alzheimer's disease,*

PD= Parkinson's disease, GD = Gaucher Disease, LBD = Lewy body dementia, Aβ = amyloid beta, Abs = antibodies, ERT = enzyme replacement therapy, UD = Undisclosed, siRNA = small interference RNA

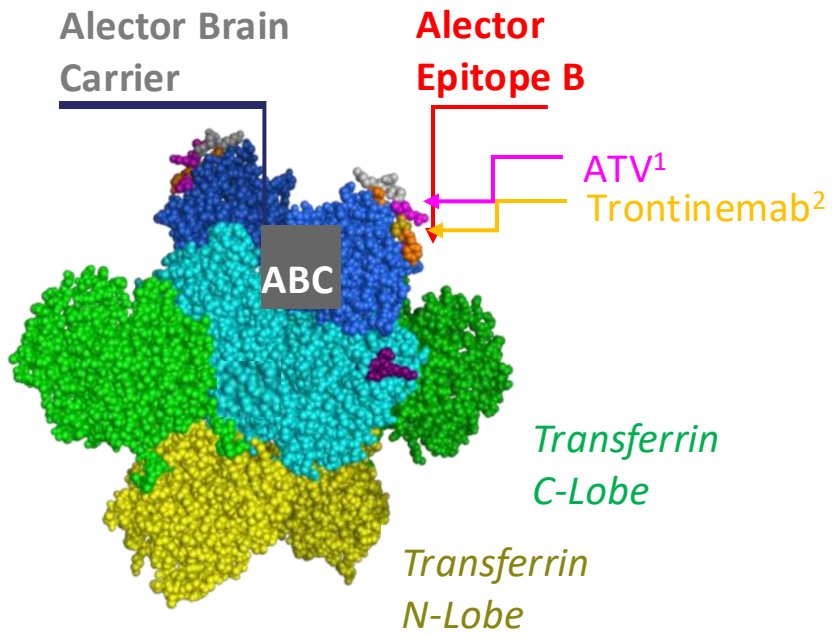
Alector Brain Carrier (ABC) Technology

Development of Alector Brain Carrier (ABC)

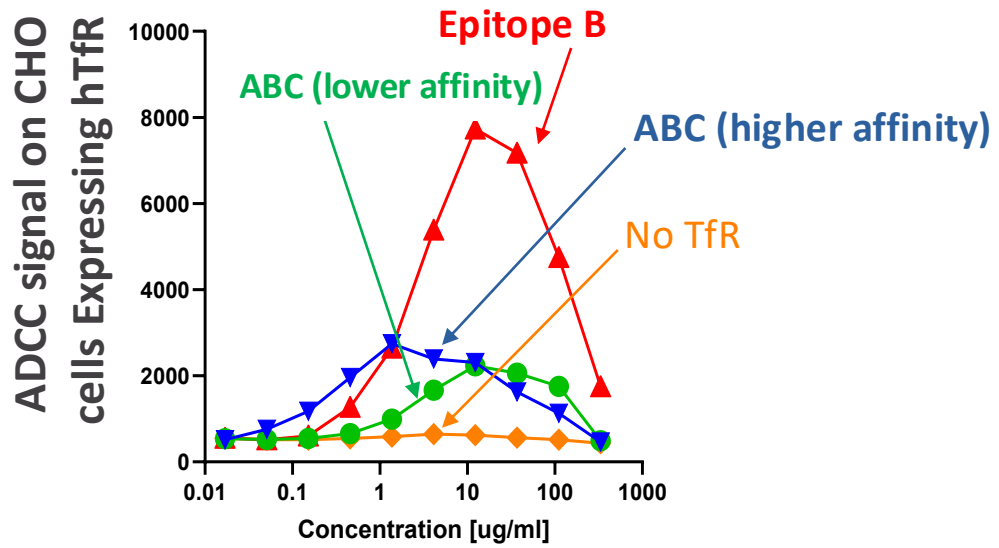


Alector Brain Carrier (ABC) Epitope is Associated with Reduced TfR-Dependent ADCC

Human TfR Bound to Transferrin with Annotated BBB Technology Epitopes



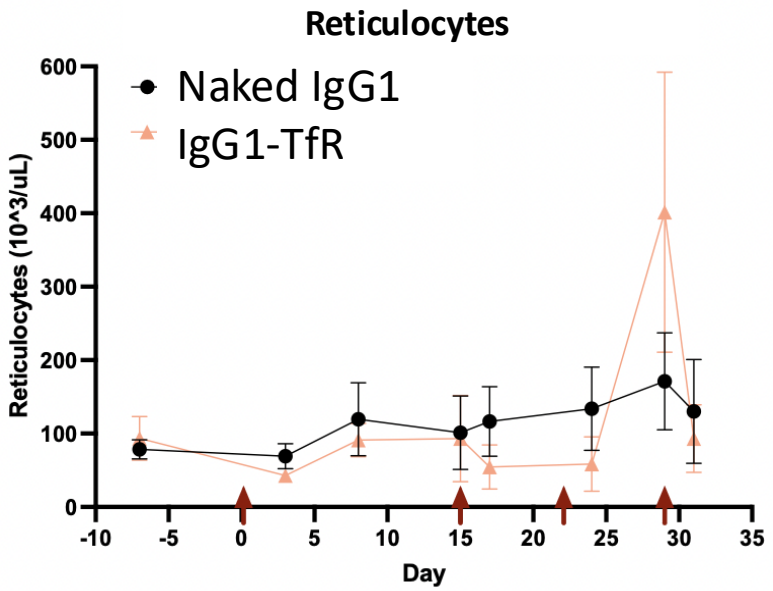
TfR Dependent ADCC is Determined by the TfR Binding Epitope



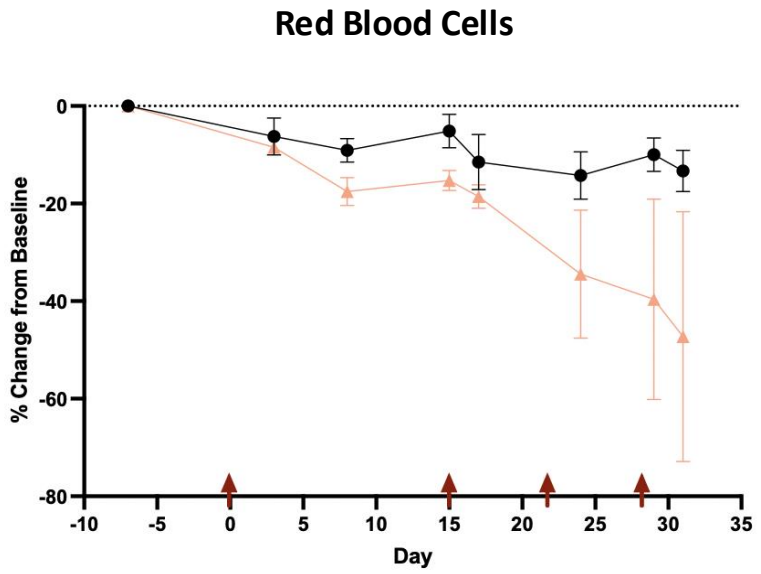
ABC Epitope or Alector Epitope B bind TfR at the same affinity and were formatted and tested on otherwise identical antibodies. Structure of human transferrin receptor-transferrin complex from 1SUV. (1) ATV epitope (Kariolis et al., 2000); (2) Trontinemab epitope (Alector internal data).
Alector Epitope B binds TfR at the same region as Denali's ATV and Roche's trontinemab. ADCC = Antibody-Dependent Cell Cytotoxicity. ADCC activity was used here as a surrogate for TfR-dependent hematologic adverse effects.

Antibody Binding to TfR Epitope B Leads to Reduction in RBCs and HGB in NHP Even With a Cis-LALAPS Mutation that Silences Half of the Effector Function

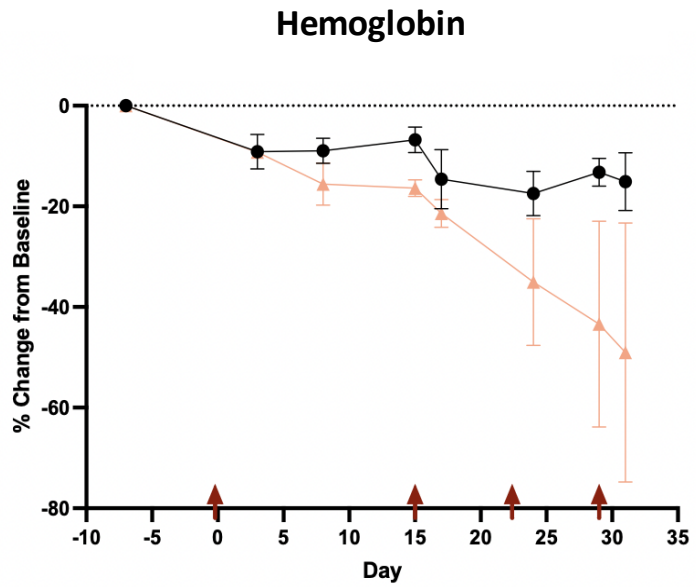
Reticulocyte reduction and recovery following treatment



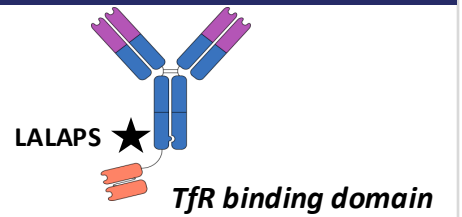
Decreased Red Blood Cell (RBC) counts observed



Sustained decrease in hemoglobin (HGB)



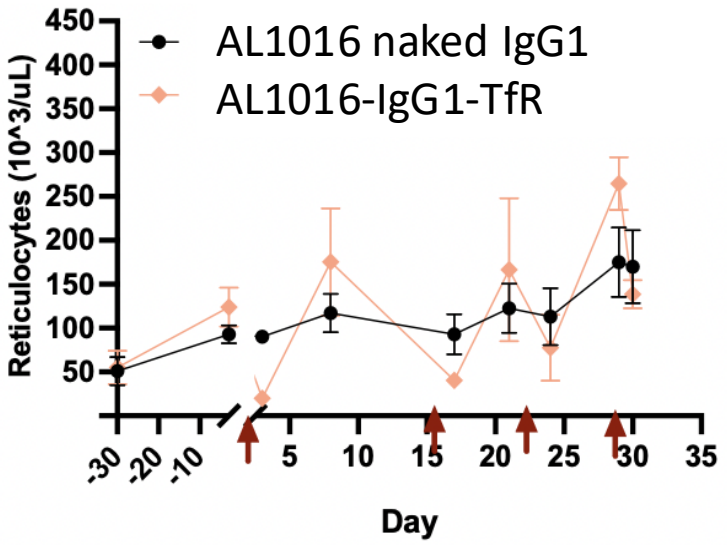
Cis LALAPS



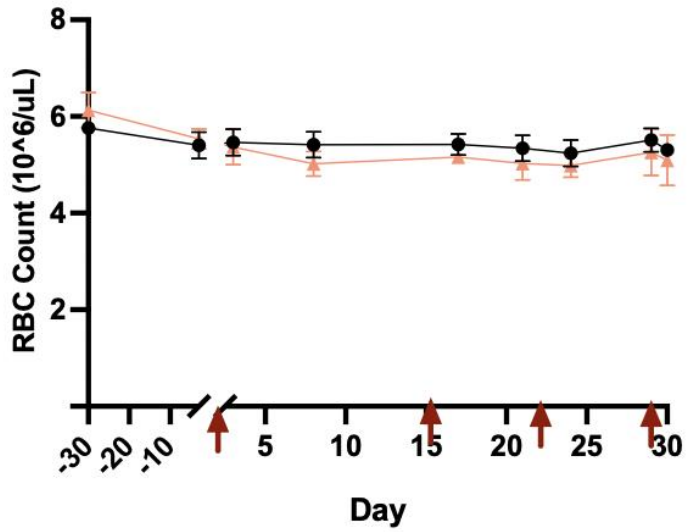
NHP were dosed intravenously on D1, D15, D22, and D29 (indicated by red arrows) at 50 mg/kg. Blood samples for hematology were collected 7 days prior to dosing and on D3, D8, D15, D17, D24, D29, and D31. Reticulocytes, hemoglobin and red blood cell counts are presented.

Antibody Binding to Alector's TfR ABC Epitope with Full Effector Function Does Not Show Reduction in RBCs or HGB in NHP

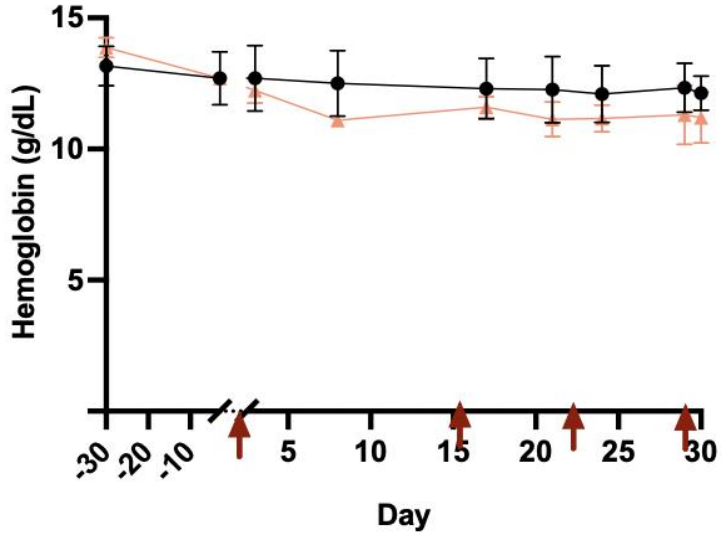
Reticulocyte Recovery Following Treatment



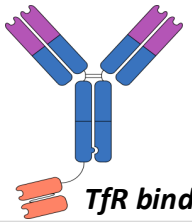
No impact on Red Blood Cells (RBC) Counts



No impact on Hemoglobin (HGB) Levels



Full Effector Function



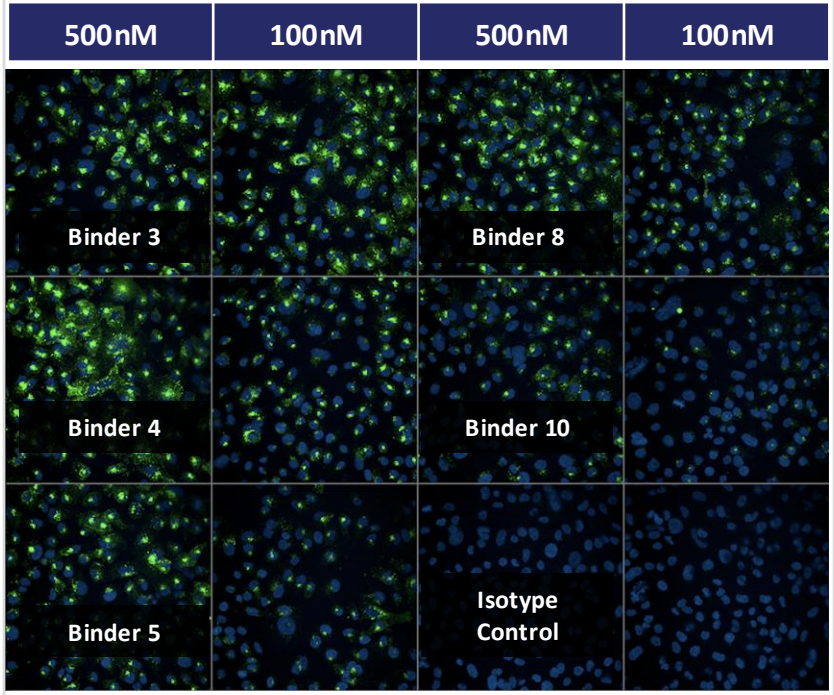
NHP were dosed intravenously on D1, D15, D22, and D29 (indicated by red arrows) at 50 mg/kg with the anti-Aβ antibody AL1016. Blood samples for hematology were collected after each administration. Reticulocytes, hemoglobin and red blood cell counts are presented. AL1016 contains TfR binding domain with the ABC epitope which binds TfR at the same affinity as the antibody presented in the previous slide.

Adaptable TfR Binding Affinities and Binding Kinetics for Multiple Drug Modalities

1000-Fold Affinity Range Tailored to Antibodies, Enzymes, and siRNA

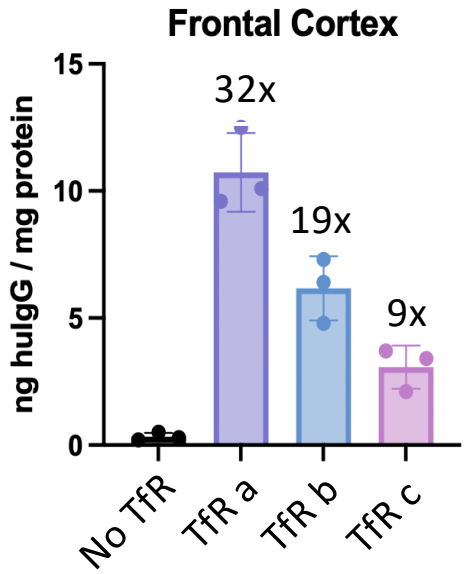
TfR Binder	KD (nM)
Binder 1	5
Binder 2	19
Binder 3	126
Binder 4	127
Binder 5	176
Binder 6	182
Binder 7	274
Binder 8	390
Binder 9	639
Binder 10	1040
Binder 11	1210
Binder 12	4720

ABC Displays Affinity-Dependent Internalization into Human Brain Endothelial Cells



Anti-TfR binders at multiple affinities were incubated on hCMEC/D3 cells for 2 hours. Internalized antibodies were detected with anti-huIgG in green; nuclei were labeled in blue with DAPI

TfR Affinity-Dependent Entry to the Frontal Cortex of NHP



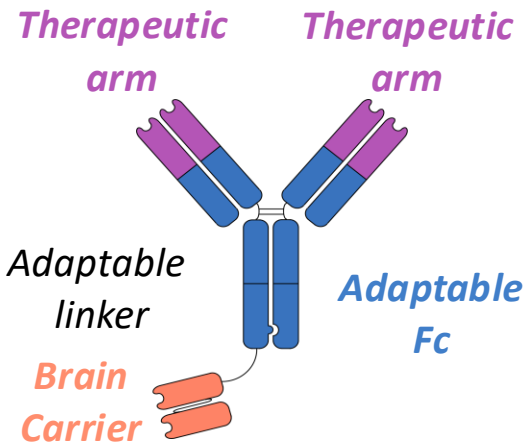
NHP were IV dosed with 2 doses of 3 mg/kg, 8d apart; Vessel depleted lysates from frontal cortex were analyzed by MSD for huIgG concentrations and normalized to protein concentration determined by BCA; fold changes are relative to no TfR control

ABC: Designed for Lower Dosing, Improved Efficacy and Safety, and SubQ Delivery Across Antibody, Enzymes and siRNA Drug Modalities

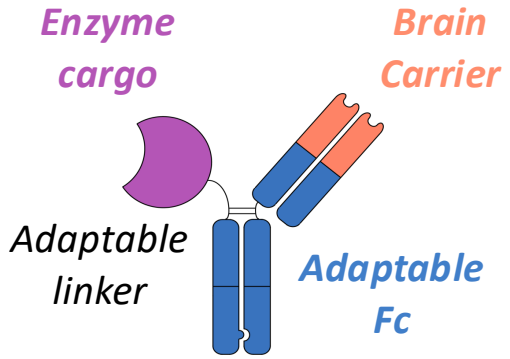
Versatile Features

- **Versatile:** ABCs as Fab and scFv that bind transferrin receptor (TfR) in multi-specific formats
- **Adaptable Fc:** Optimizing effector function and half-life
- **Tailored for Cargo:** Wide range of TfR affinities and drug configurations that are compatible with multiple cargo
- **Tailored for Development:** Designed for testing in non-human primates and manufacturability
- **Validated:** In NHPs for antibodies, enzymes, siRNA

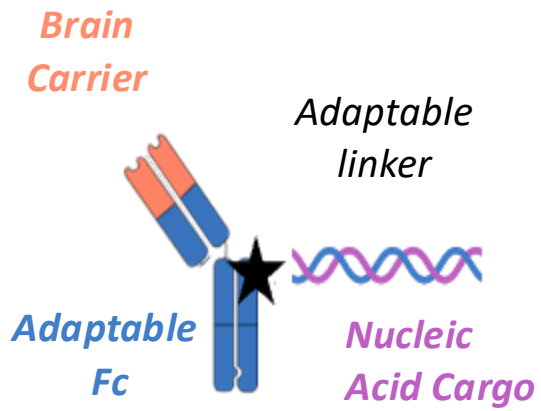
Antibody Cargo



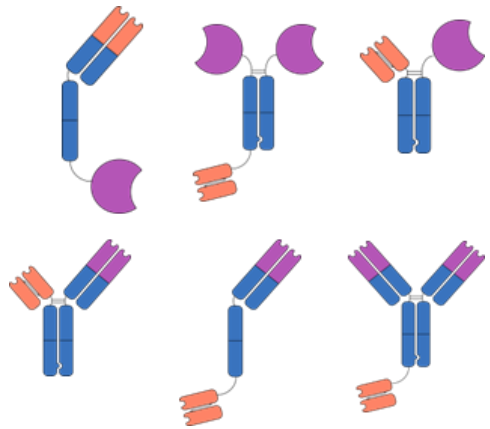
Enzyme Cargo



Nucleic Acid Cargo



Versatile Configurations

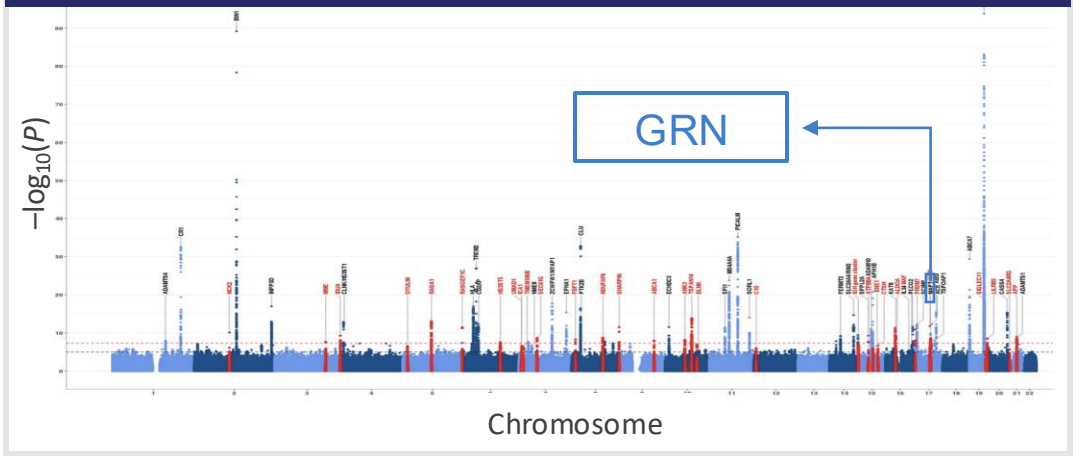


Alector's Progranulin-Elevating Program For Alzheimer's Disease

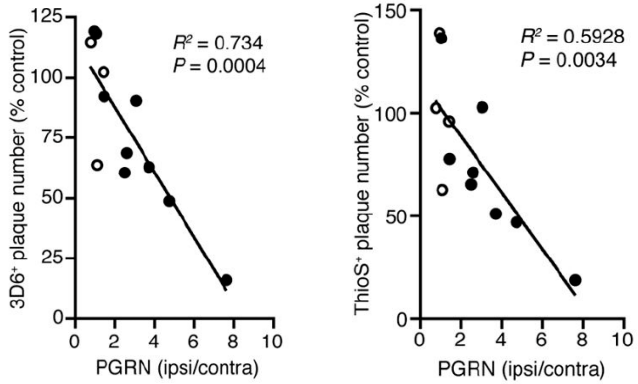
Partnership with GSK

Nivisnebart (AL101): Rationale for Alzheimer's Disease and Mechanism of Action

Progranulin (PGRN) is a Risk Gene for AD[1]

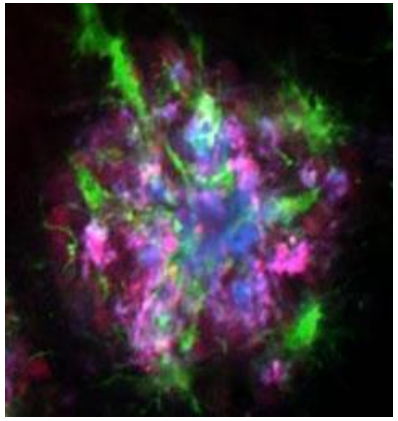


PGRN is Protective in AD Model[2]

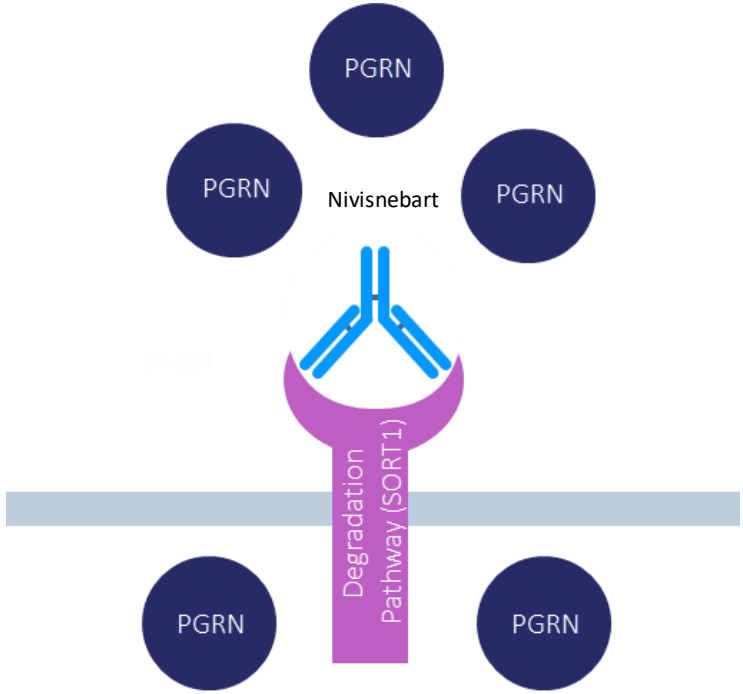


PGRN overexpression decreases Aβ plaque load in the dentate gyrus of AD mice

PGRN in Aβ Plaques[2]



Nivisnebart is a Human Monoclonal Antibody that Increases Levels of PGRN

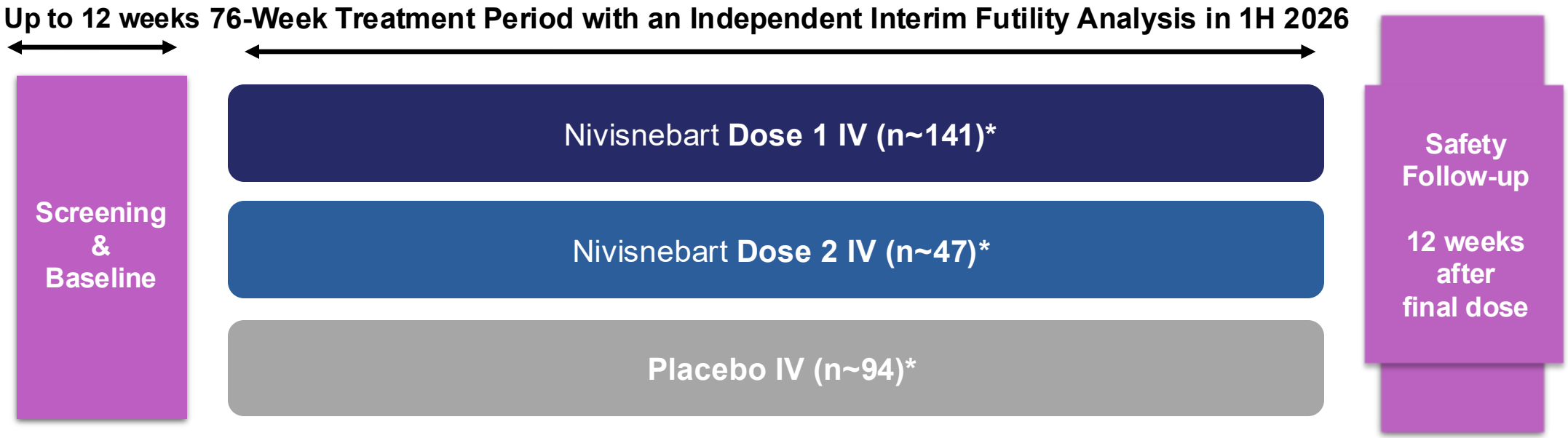


1. https://doi.org/10.1101/2020.10.01.20200659 (Left); ARTFL Diagnoses. The breakdown of clinical diagnoses among ARTFL FTD mutations carriers. [Courtesy of Adam Boxer.] https://www.alzforum.org/print - series/1093496 (Right). 2. Mendsaikhan A, et al. Characterization of lysosomal proteins Progranulin and Prosaposin and their interactions in Alzheimer's disease and aged brains: increased levels correlate with neuropathology. *Acta Neuropathol Commun.* 2019 Dec 21;7(1):215.

Nivisnebart: Phase 2 PROGRESS-AD Study Design

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF NIVISNEBART IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE

Completed Enrollment in April 2025



Key inclusion criteria
- Age 50 - 85 years, inclusive
- Diagnosis of MCI due to AD up to mild AD dementia
- Amyloid positivity (by PET or CSF)

Primary endpoint
Change from Baseline in CDR - SB across Weeks 52, 64 and 76.

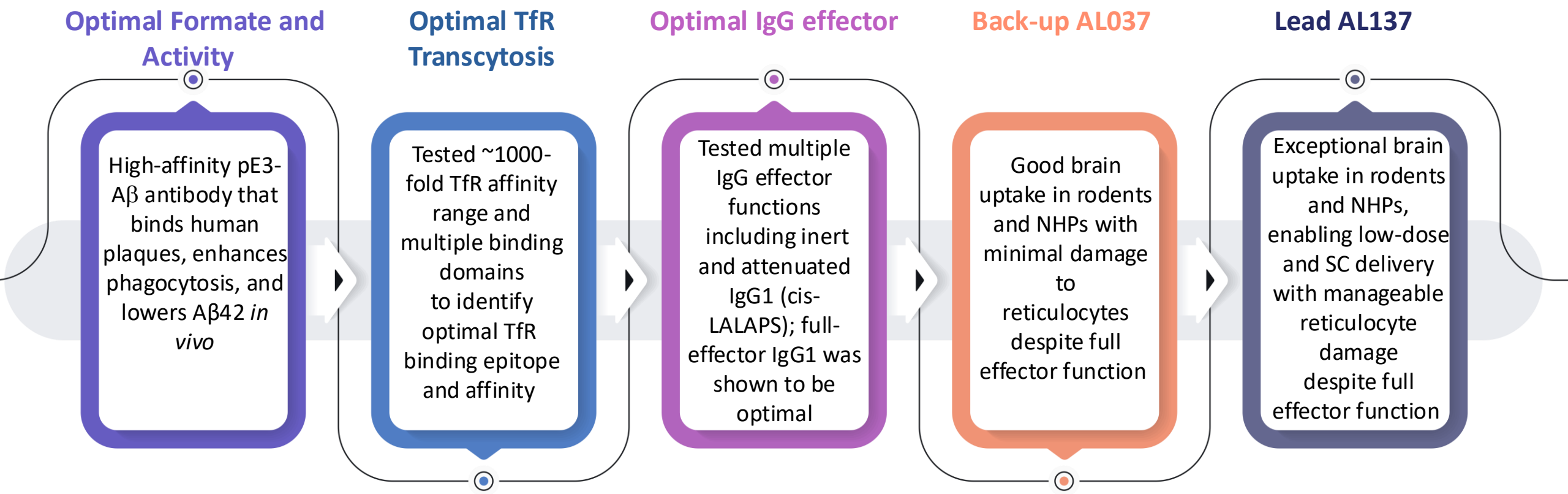
Key secondary endpoints
Change from Baseline across Weeks 52, 64 and 76 for iADRS, ADAS - Cog14, ADCS - iADL, ADCS - ADL - MCI, ADCOMS

Biomarkers: Amyloid PET, Tau PET, CSF and Plasma

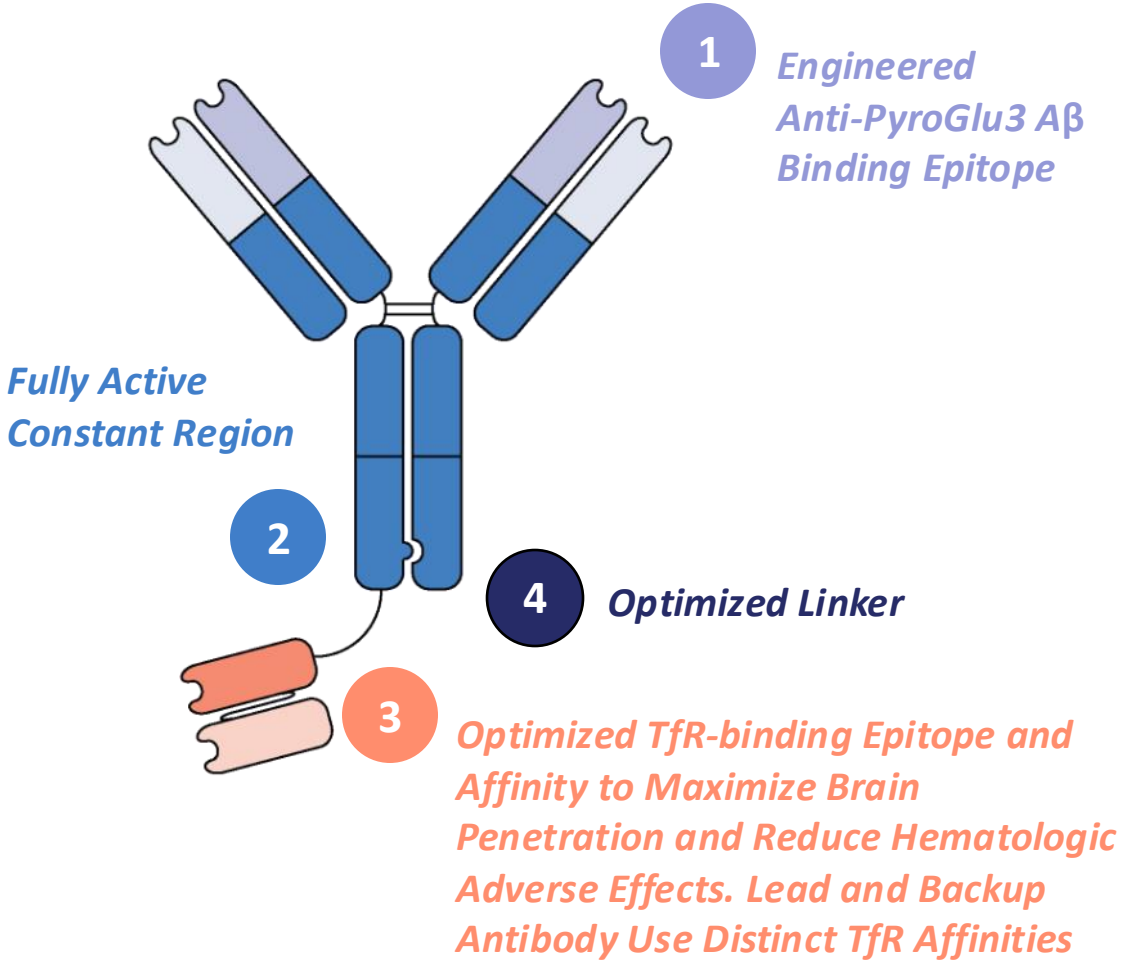
alector *Planned sample size

Alector Brain Carrier (ABC)-Enabled Anti-Aβ Antibodies for Alzheimer's Disease

The Development of AL137: A Brain Penetrant Anti-Aβ Antibody for Alzheimer's Disease



The Optimal Design of ABC-Enabled Anti-Aβ Lead (AL137) and Back-up (AL037) Antibodies



Targeted Design Features:

Selectivity

- Engineered high-affinity, fully human antibody that selectively binds toxic Aβ plaques

Potency

- Fully active effector function enabling robust recruitment of myeloid cells to remove Aβ plaques

Safety

- Proprietary ABC with tuned affinity, binding kinetics, and binding epitope seeks to facilitate effective brain penetration and plaque removal while minimizing hematologic adverse effects

Convenience

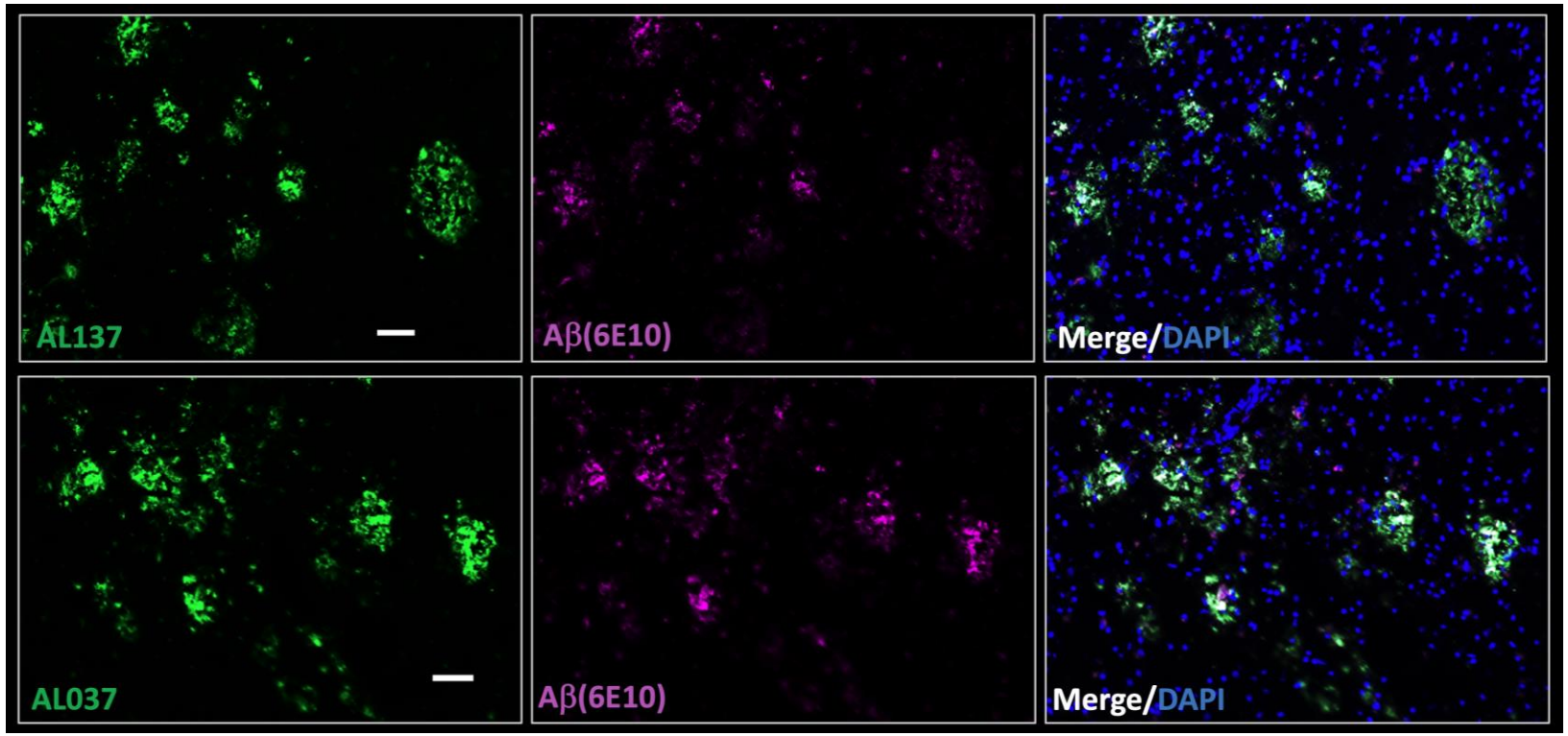
- ABC enables potential for low dosing regimen and subcutaneous delivery

Optimization

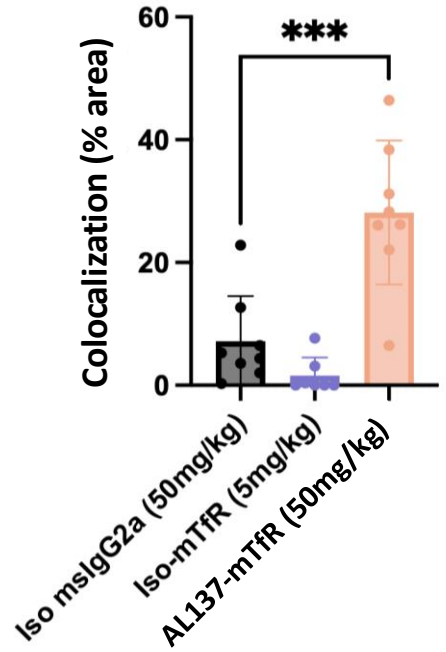
- Screened for TfR epitopes, affinity and linkers for brain transport, stability, immunogenicity, and hematologic adverse effects

Optimal Activity; AL137 and AL037 Bind to Aβ Plaque in Human and Mouse AD Brains

Alector Anti-Aβ Antibodies Colocalize with Aβ Plaques on Human AD Brain Sections



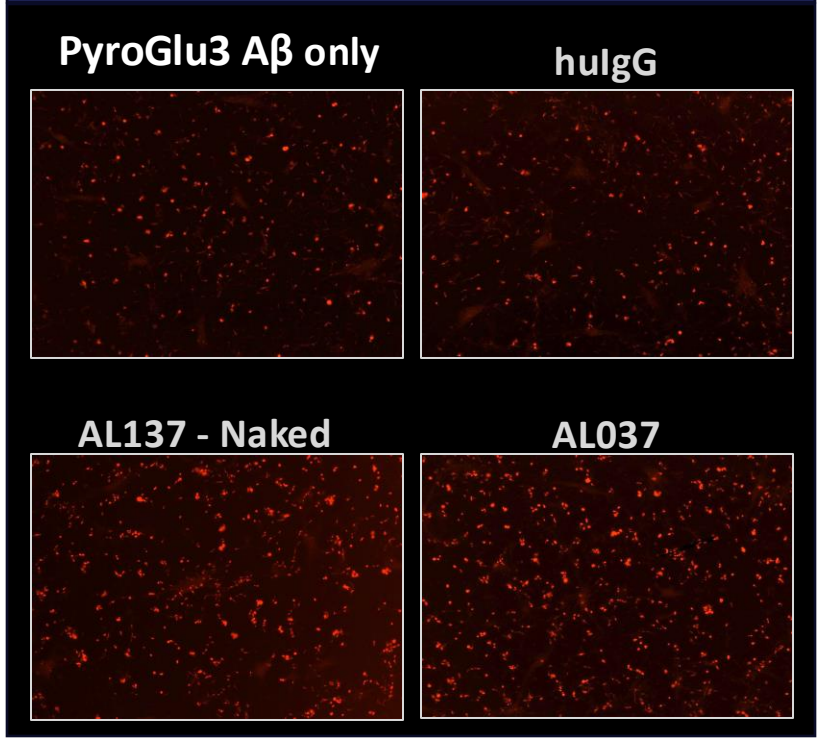
Alector Anti-Aβ Antibodies Colocalize with Aβ Plaques in 5XFAD Mouse



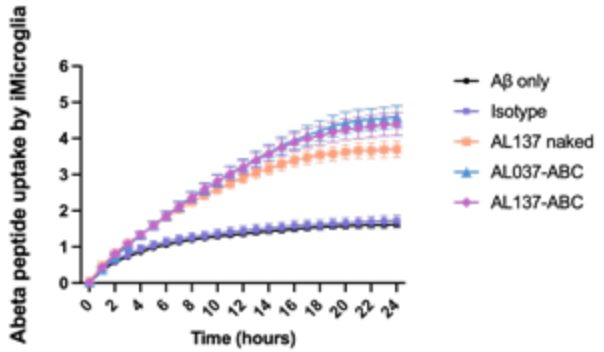
Left: Unfixed, frozen human AD sections (medial temporal gyrus) were obtained from the Banner Institute, AZ; plaques were assessed by IFL with AL137 and AL037 (both in green) and anti-Aβ (6E10, pink); nuclei were counterstained with DAPI (blue); images acquired with a 10x objective; scale bar= 50 µm; Right: 8mo 5XFAD were dosed 4 times weekly with AL137 surrogate (with mTfR) and assessed for plaques by IFL with anti-Aβ (6E10); dosed antibodies detected with anti-msIgG2a; plaque and dosed antibody colocalized area in the hippocampus was quantified using a proprietary brain segmentation app

Optimal Activity TfR Transcytosis and IgG Effector: AL137 and AL037 Facilitate Phagocytosis of Aβ by Human Microglia and Distribute Throughout the Brain

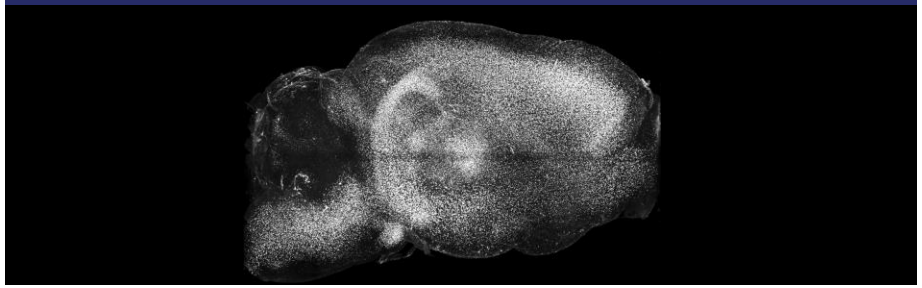
Fluorescent Imaging of PyroGlu3 Aβ Phagocytosed by Microglia in 24h



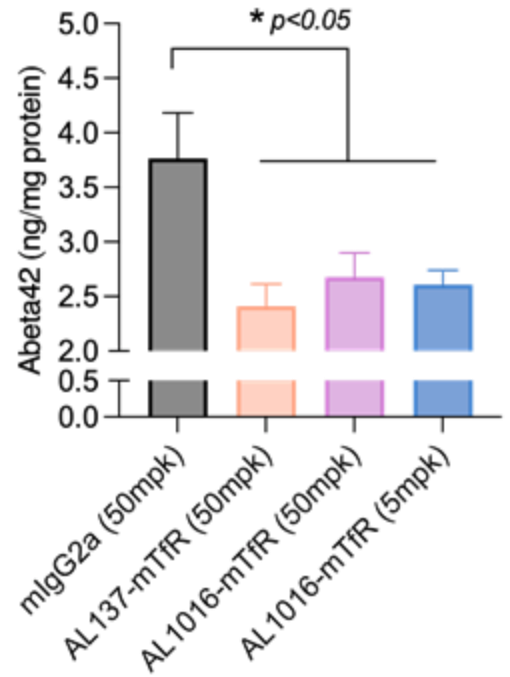
AL137-Dependent Phagocytosis of PyroGlu3 Aβ by Human IPSC Microglia in Culture



AL137 Surrogate Binding to Aβ Plaques



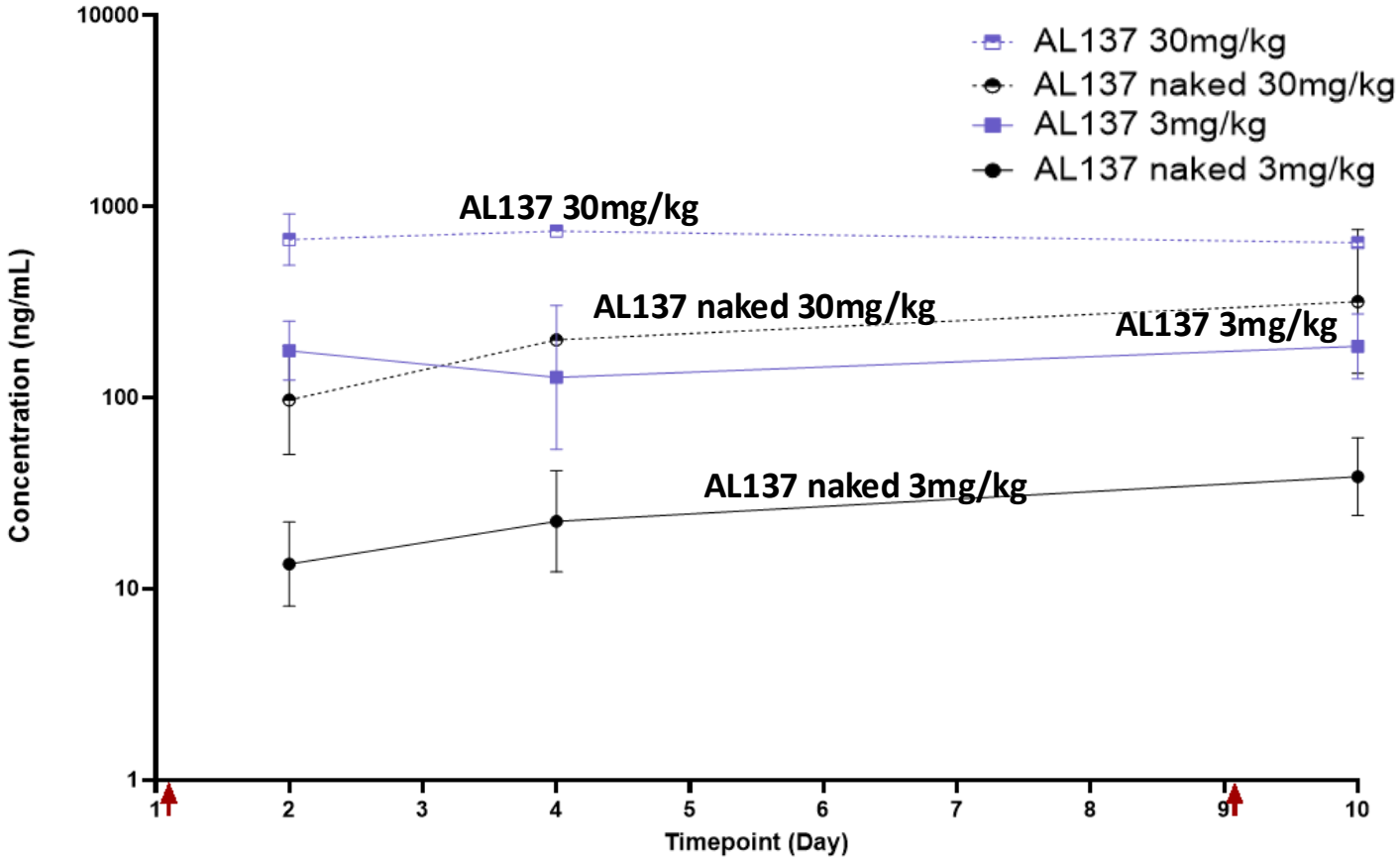
Reduction in Brain Aβ42 in AL137-mTfR dosed Mice



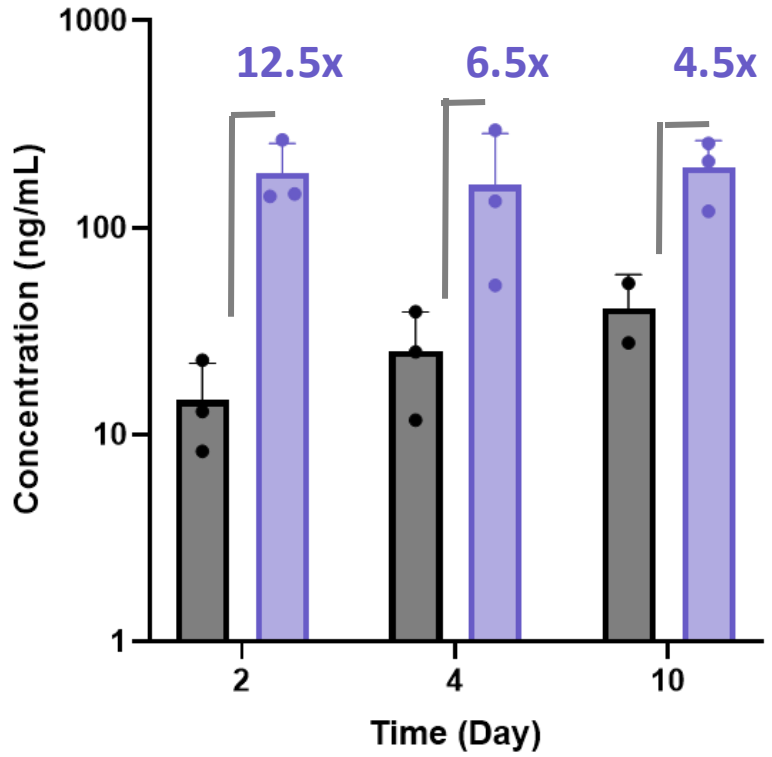
Left and middle top: AL137-Naked (without the ABC platform), Isotype huIgG, AL137, or AL037 were incubated with pHrodo-pyroGlu3 Aβ on IPSC-derived CNS triple cultures (containing iMicroglia, iNeurons, human fetal astrocytes) for 24h and imaged hourly for uptake of pHrodo-labeled pyroGlu3 Aβ into iMicroglia. Middle bottom: Light sheet microscopy on 9-month-old 5xFAD mice dosed 3 times weekly at 5mg/kg. Right: Aβ42 levels were assessed in total brain lysates by ELISA; means +/-SEM, n=16-17 per group; 24-168h post last dose. AL137 = pE3-Aβ Fab2 with mTfR, AL1016 = pE3-Aβ Fab1 with mTfR

Optimal TfR Transcytosis; ABC Enhances CSF Uptake of AL137

CSF Concentration Following Intravenous *Administration of AL137 on D1 and D9*



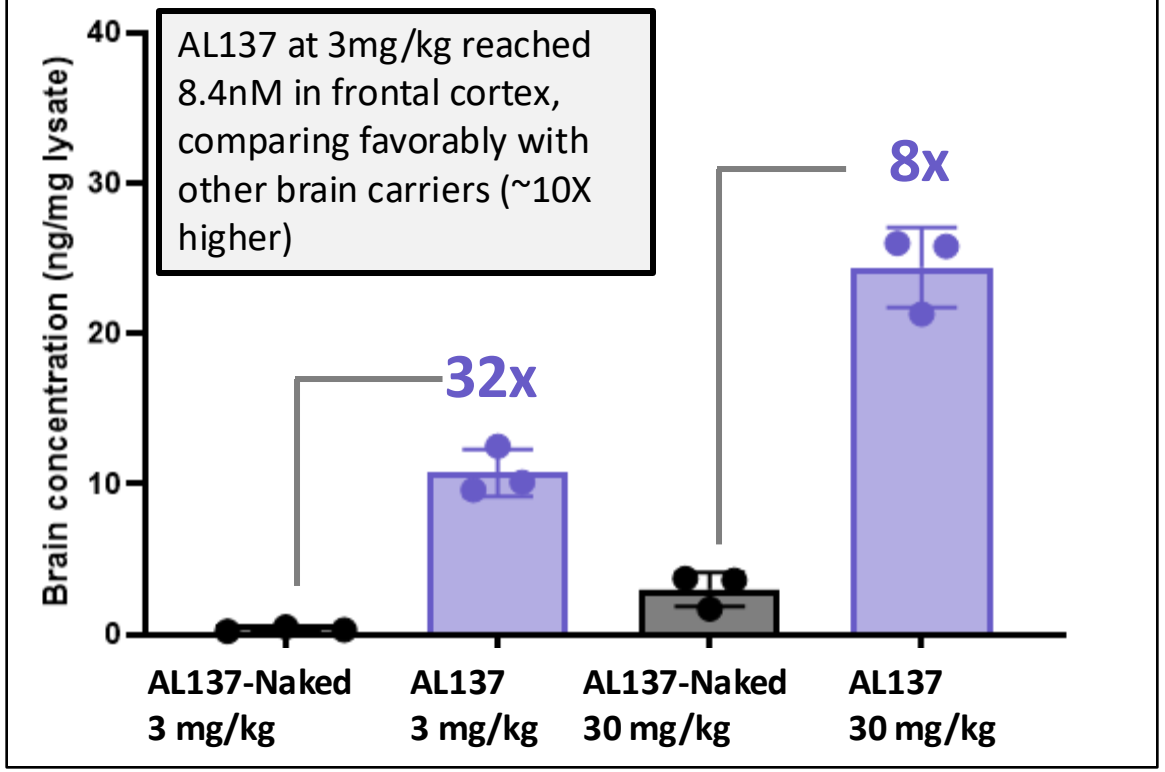
CSF AL137 naked vs AL137 3mg/kg



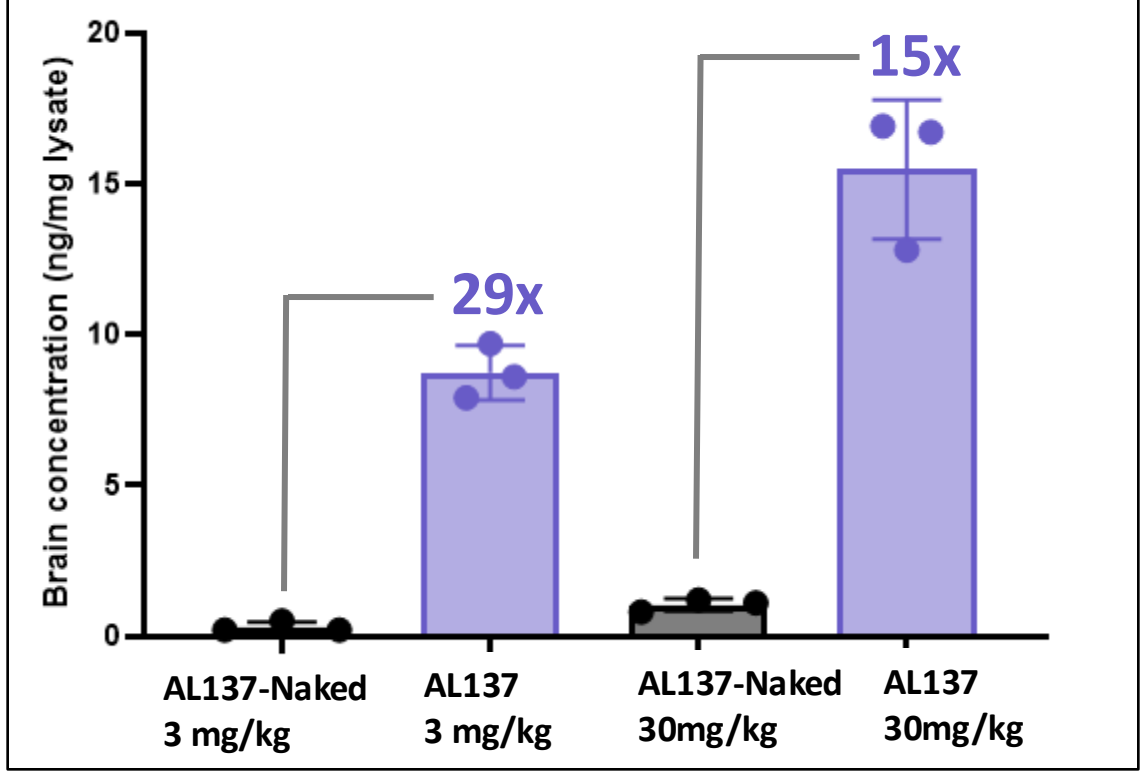
Three female cynomolgus monkeys per group were dosed intravenously on D1 and D9 with 3 or 30 mg/kg of either AL137-Naked (without the ABC platform) or AL137. CSF samples were analyzed for the levels of AL137-Naked (without the ABC platform) and AL137 at 24hrs and 72hrs post 1st administration and 24hrs after the 2nd administration on Day 9.

Optimal TfR Transcytosis; Enhanced Brain Uptake with AL137

Frontal Cortex



Hippocampus



Three female cynomolgus monkeys per group were dosed intravenously on D1 and D9 with 3 or 30 mg/kg of either AL137-Naked (without the ABC platform) or AL137. Brain tissues were collected 24 hours after the second injection and drug levels were measured in the vessel-depleted fraction. AL137-Naked = AL137 without ABC platform.

AL137 Was Well-Tolerated in NHPs at Doses Up to 30 mg/kg

Toxicological Parameters Evaluated:

- Mortality/Morbidity
- Clinical observations
- Body weight
- Food consumption
- Hematology
- Gross necropsy observations
- Organ Weight
- Tissues collected for histopathology evaluation

Summary:

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

AL137 Phase 1 Clinical Plan

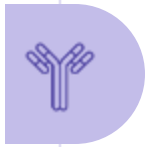
PHASE 1 OBJECTIVES	• Evaluate safety, tolerability, and pharmacokinetics (PK) following single and multiple ascending doses. • Characterize dose-response relationships and target engagement. • Assess pharmacodynamic (PD) markers of amyloid reduction.
STUDY DESIGN	• Phase 1a: Single Dose study in healthy volunteers, including a subcutaneous (SC) dosing arm. • Phase 1b: Multiple Ascending Dose study in early AD patients (including a SC cohort), with potential seamless transition to Phase 2. • Biomarker and imaging assessments (i.e., Aβ PET, pTau217, Aβ, MTBR).

STUDY GOALS	• **Inform drug efficacy, safety, dose finding and delivery mode**, & enable transition to Phase 2.
	  ○ Achieve PET Aβ reduction ≥ trontinemab (~96 centiloids at 3.6 mg/kg, 28 weeks).
	  ○ Keep ARIA-E < 5%.
	  ○ Show no or only mild, fully resolving anemia.
	  ○ Demonstrate amyloid clearance with SC dosing (one SAD and one MAD cohort).
	  ○ Maintain manageable infusion reactions without requiring pre-medication.

Summary and Conclusion

Alzheimer's Disease Impact:

- Approximately 24 million people worldwide affected by Alzheimer's disease[1]
- Aβ pathology remains a key driver of disease progression
- Significant unmet need for safe, effective, and convenient anti-amyloid therapies enabled by BBB technology



Design:

- Designed to treat Alzheimer's disease by delivering an ABC-enabled anti-Aβ antibody targeting PyroGlu3 Aβ with a full effector function, optimized for brain penetration safety and efficacy

Demonstrated:

- Robust brain penetration (~32-fold over a naked antibody representing ~8.4 nM with 3 mg/kg IV administration in NHP)
- Plaque engagement, microglial activation, and reduction of amyloid burden in preclinical models
- Adequate PK, transient effect on reticulocytes and no apparent findings on RBC to date

Clinic Target:

- Targeting IND submission in Q4 2026/Q1 2027
- Simulations support intravenous or subcutaneous delivery at competitive doses

Flexibility:

- Available lead (AL137) and back-up (AL037) drug candidates
  - AL137: Exceptional brain delivery (~10× competitors) with expected manageable reticulocyte impact
  - AL037: Good brain delivery (~5× better than competitors) with expected minimal reticulocyte impact

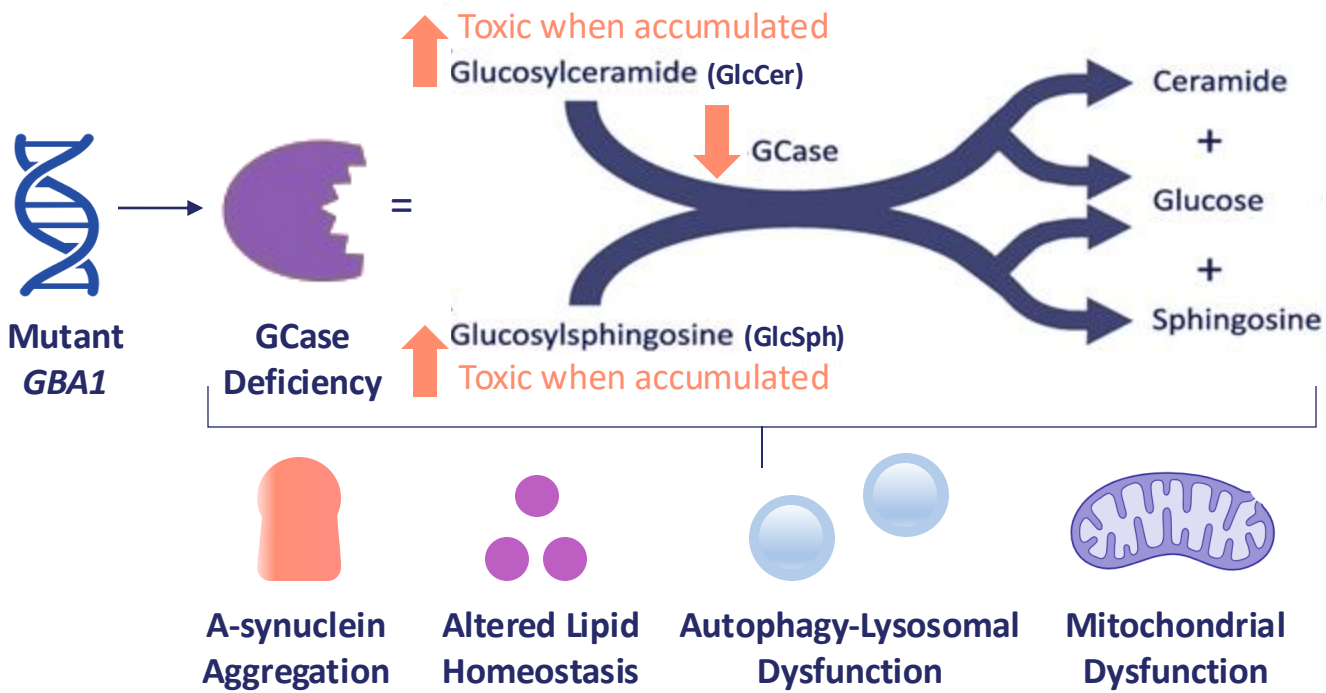
1. Mayeux R, Stern Y. Epidemiology of Alzheimer disease. Cold Spring Harb Perspect Med. 2012 Aug 1;2(8):a006239.

Alector Brain Carrier (ABC)-Enabled GCase ERT for Parkinson's Disease

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

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

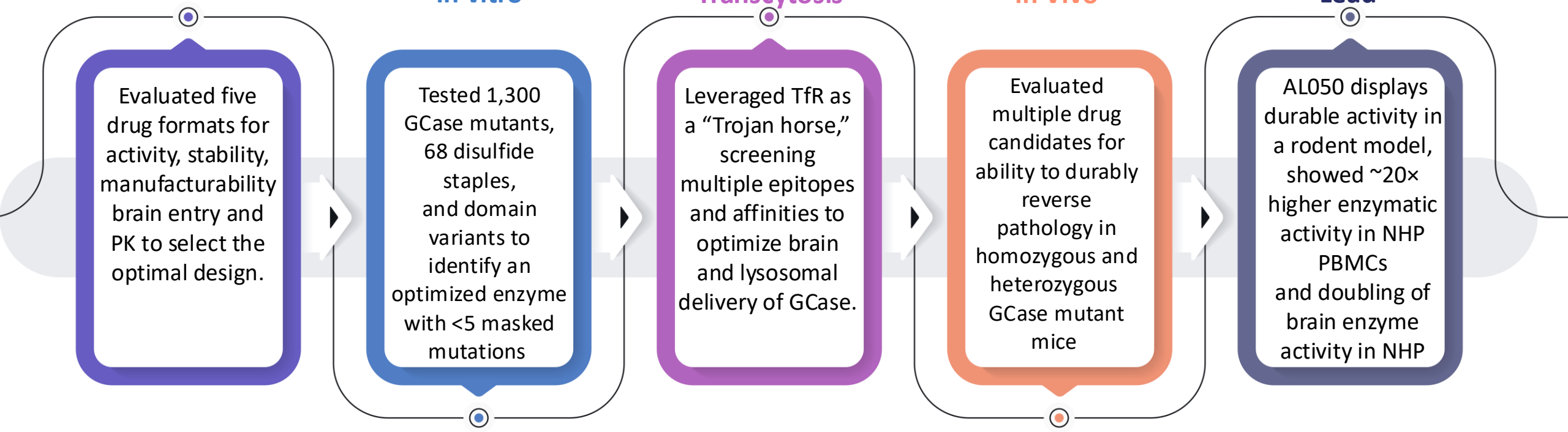
No therapy has effectively restored GCase activity in the brain: Current GCase enzyme replacement therapy does not enter the brain



- **Parkinson's Disease (PD)**
  - ~10 million patients worldwide[1]
  - 0.5-1.5 millions are GBA1 mutation carriers[2]
  - Activity is reduced in non-carriers[2]
- **Gaucher's 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]

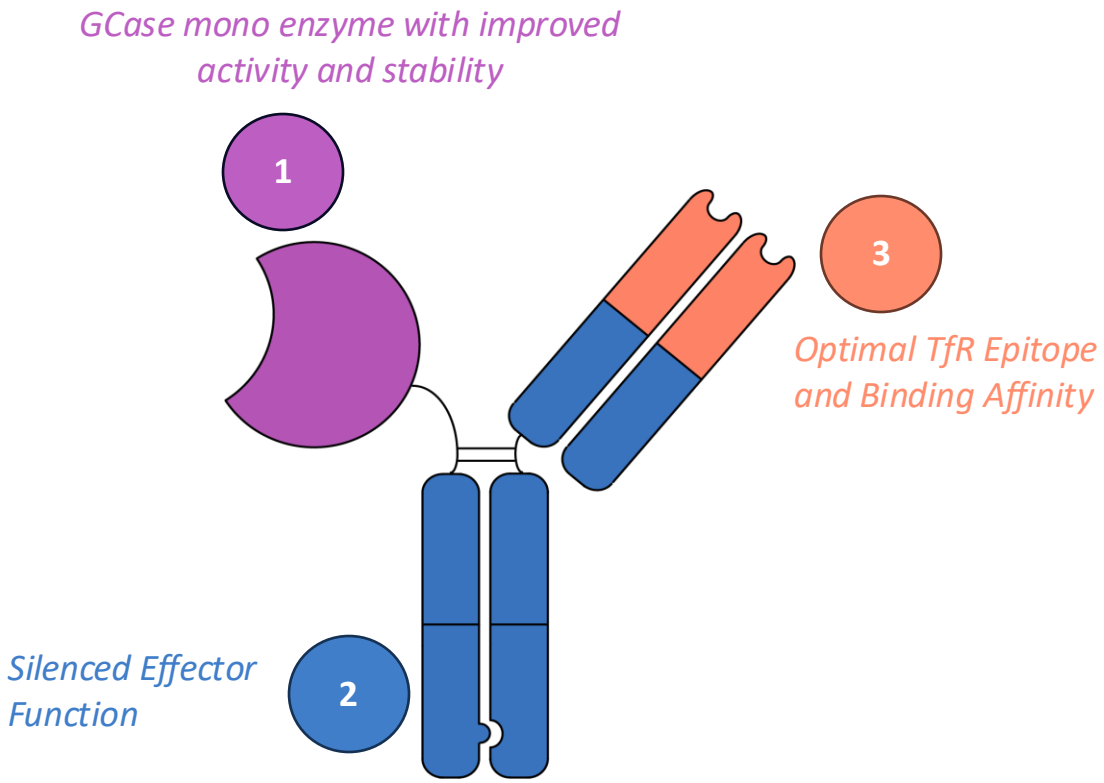
1. Parkinson's Foundation Statistics
2. Smith L, Schapira AHV. GBA Variants and Parkinson Disease: Mechanisms and Treatments. *Cells*. 2022 Apr 8;11(8):1261.
3. Alzheimer's Disease International, Dementia with Lewy Bodies
4. Nalls MA, et al. A multicenter study of glucocerebrosidase mutations in dementia 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

The Development of AL050; An Engineered Brain Enabled GCase Enzyme Replacement Therapy for Parkinson's Disease and Lewy Body Dementia



Alector's Flexible Format Enables Optimal TfR Binding Kinetics and Affinity to Offset the Short Serum Half-life of GCase

The Design of ABC-Enabled GCase Enzyme Replacement Therapy AL050



Targeted Design Features:

Target Population
- 1.1–1.8M GBA-PD/LBD | 14–17M broader PD/LBD (WW)

Potency
- Engineered highly active and stable GCase enzyme
- Optimized TfR affinity/kinetics to enhance blood-brain-barrier transcytosis, cell uptake, and lysosomal delivery

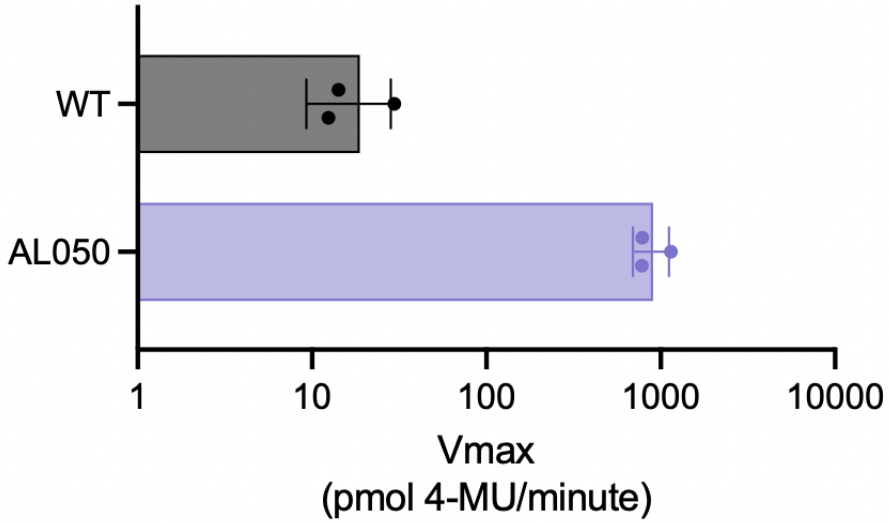
Safety
- Proprietary ABC binding to a unique epitope and a silenced Fc domain to minimize hematological risks

Convenience
- ABC enables potential for low dosing regimen and subcutaneous delivery

Optimization
- Screened for enzyme stability and activity, ABC formats, TfR epitopes and affinity for brain transport, and hematologic adverse effects

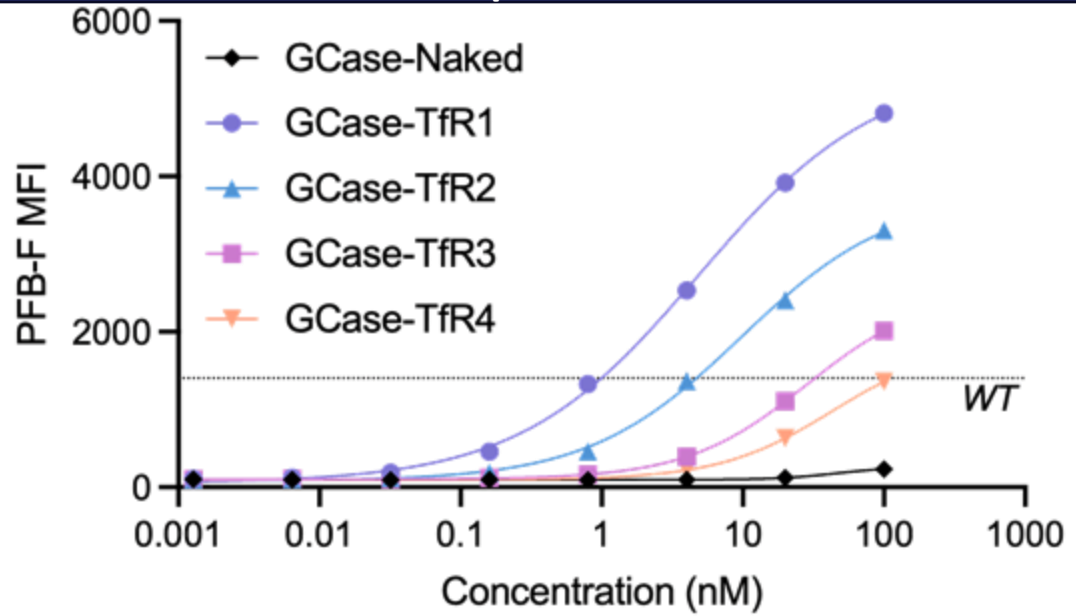
AL050 Optimized for Enzymatic Activity and TfR-mediated Blood Brain Barrier Transcytosis and Lysosomal Delivery

AL050 has up to 48-fold higher activity than WT GCase in vitro



Activity of wild-type and ADP050 GCases was measured as recombinant proteins in a cell-free kinetic enzyme assay using the fluorescent substrate 4-Methylumbelliferyl β-D-glucopyranoside

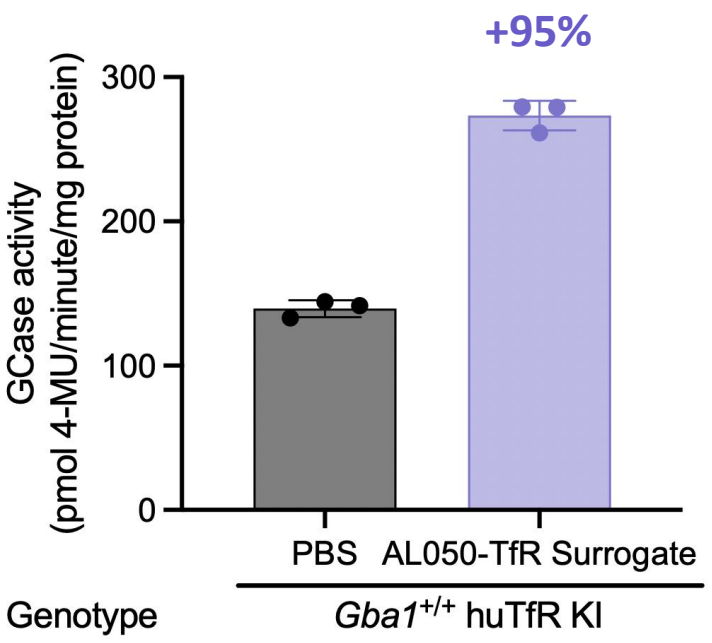
AL050 rescues GCase activity in GBA1 KO neuroblastoma cells in a TfR-dependent fashion



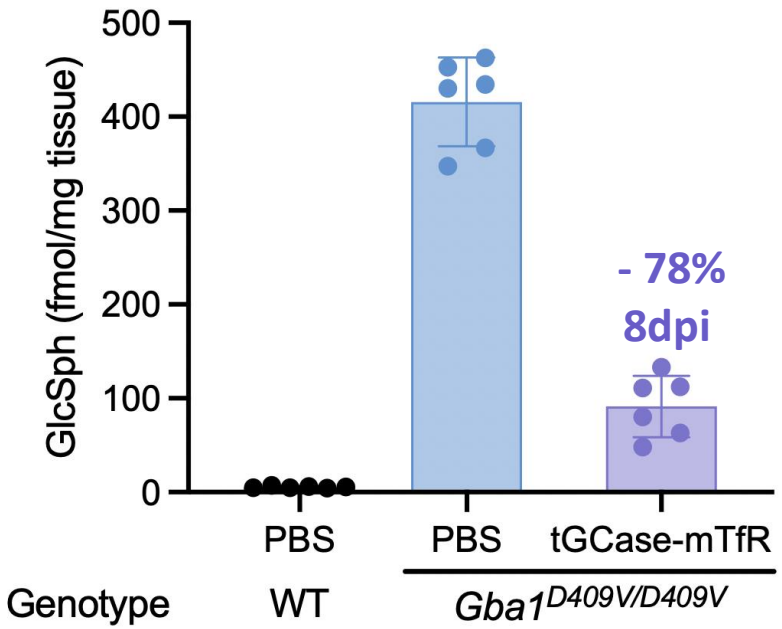
GBA1$^{-/-}$ SH-SY5Y cells were incubated with increasing concentrations of GCase-TfR of increasing affinity for 2 hours. GCase activity was measured by flow cytometry using the GCase fluorescent substrate PFB-FDGlu (1h incubation). GCase-Naked = GCase without ABC platform

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

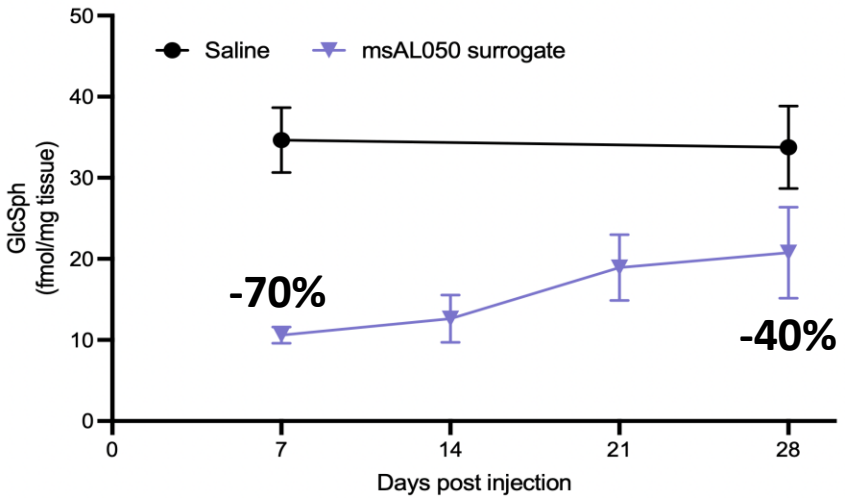
GCase-ABC Increases Brain GCase



GCase-ABC Reduces GlcSph



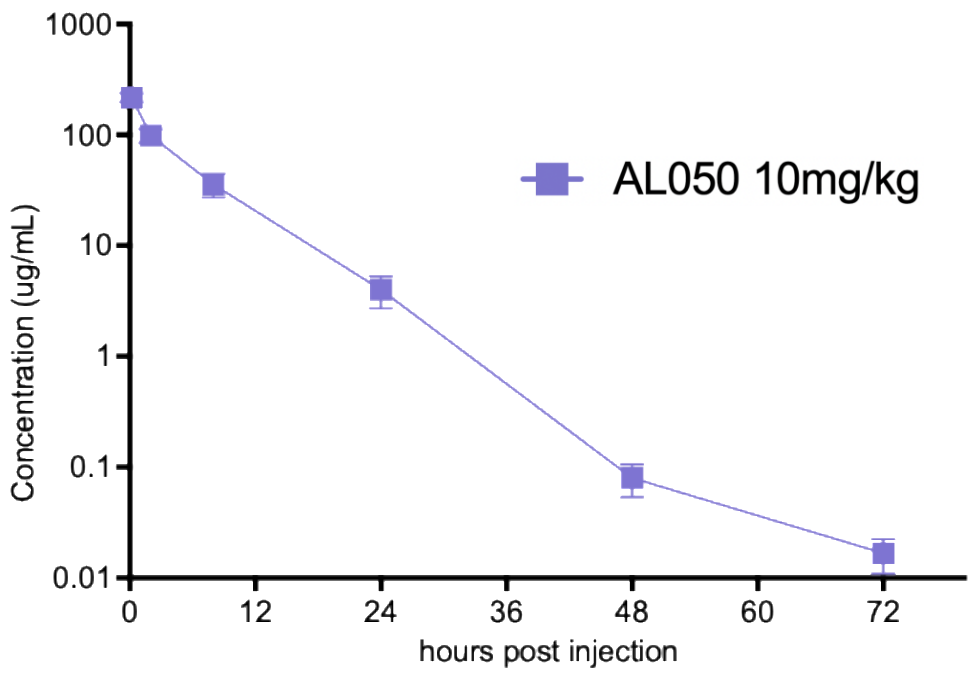
Durable (28d) Reduction in Brain GlcSph



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 Displays ~10 Fold Longer Half-Life in NHP Plasma Compared to Current GCase ERTs

AL050 Displays Plasma Half-Life of ~5 hours in NHPs



Three female cynomolgus monkeys per group were dosed intravenously on D1, D8, with 10mg/kg of AL050 and were sacrificed at D9. Plasma levels were collected at Days -1, (multiple samples post-dose); 2, 3, 4, 8, and 9

Current GCase ERTs Display Protein Half-Life of 5 to 30 Minutes in Plasma

Imiglucerase:

Displays terminal t½ of ~20–30 min **in human patients**

Taliglucerase alfa:

Displays terminal t½ of ~25min **in human patients**

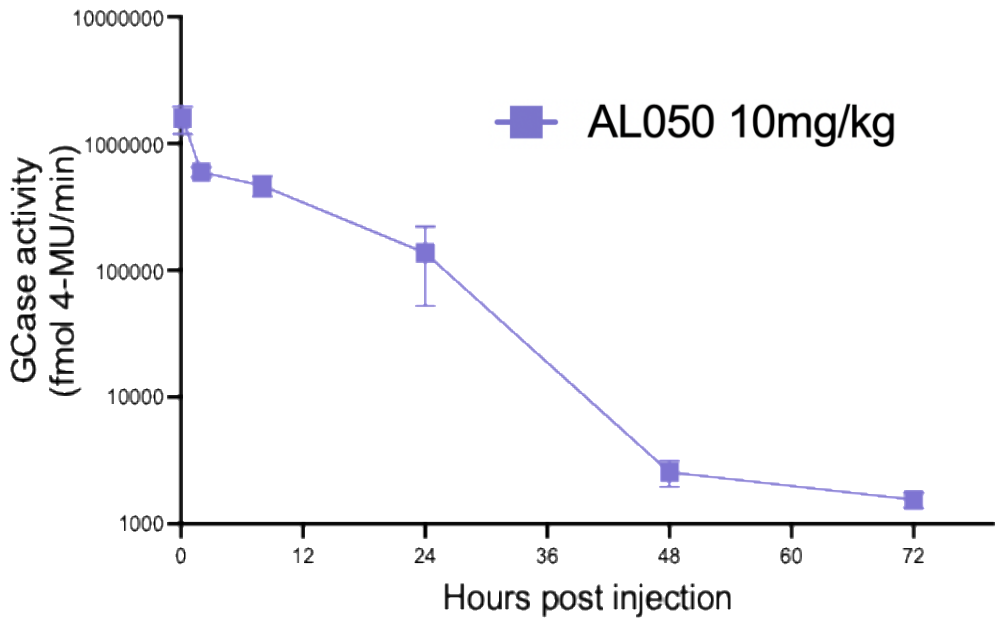
Velaglucerase alfa:

Displays terminal t½ of 5-12 min **in NHP**

- European Medicines Agency (EMA), **Cerezyme EPAR – Scientific discussion**. European Medicines Agency (EMA)
- Therapeutic Goods Administration (TGA, Australia), **AusPAR: Velaglucerase alfa (VPRIV)**. Therapeutic Goods Administration (TGA)
- EMA, **VPRIV EPAR – Public assessment report** European Medicines Agency (EMA)
- TGA, **AusPAR:** Taliglucerase alfa (Elelyso)

AL050 Displays ~40 Fold Longer Enzymatic Activity in NHP Plasma Compared to Current GCase ERTs

AL050 Displays GCase Enzymatic Activity Half-Life of ~6.6 hours in NHP Plasma



Three female cynomolgus monkeys per group were dosed intravenously on D1, D8, with 10mg/kg of AL050 and were sacrificed at D9. Plasma levels were collected at Days -1, (multiple samples post-dose); 2, 3, 4, 8, and 9

Current GCase ERTs Display Enzymatic Activity Half-Life of 4 to 10 Minutes in Plasma

Imiglucerase:

T½ Enzymatic Activity 3.6 – 10.4 min. in **human patients**

Velaglucerase alfa:

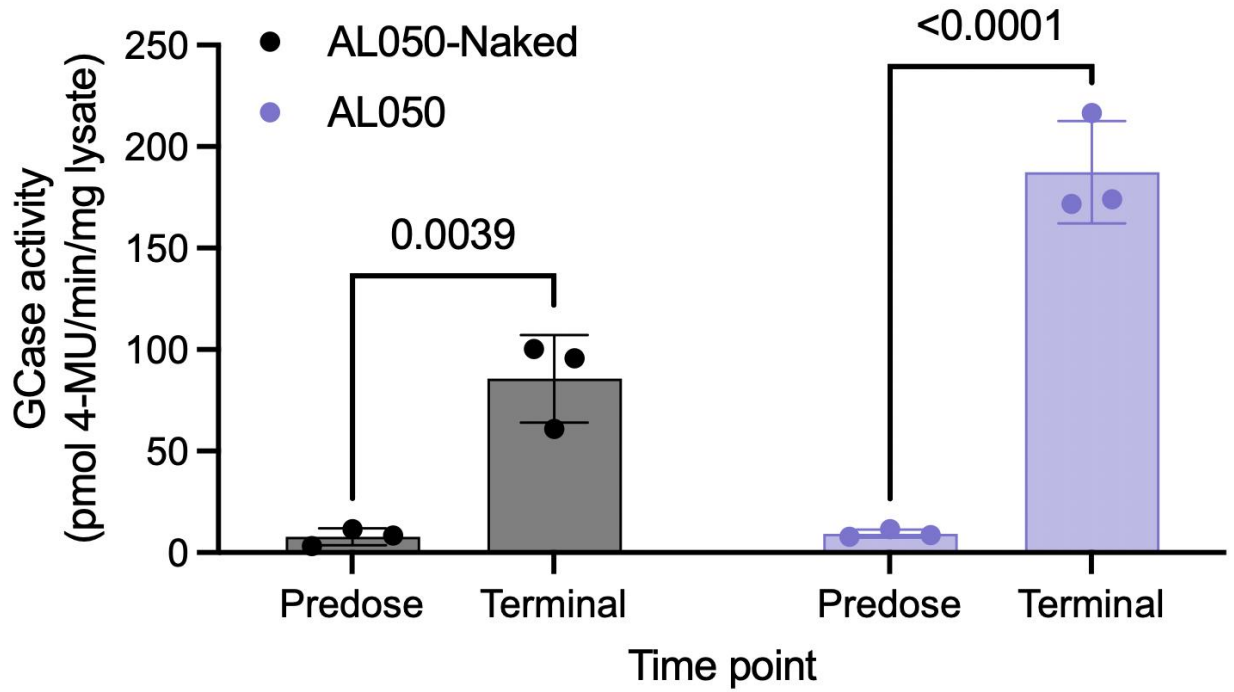
T½ Enzymatic Activity 4.0 – 4.7min. in **NHP**

- European Medicines Agency (EMA), **Cerezyme EPAR – Scientific discussion**. European Medicines Agency (EMA)
- Therapeutic Goods Administration (TGA, Australia), **AusPAR: Velaglucerase alfa (VPRIV)**. Therapeutic Goods Administration (TGA)
- EMA, **VPRIV EPAR – Public assessment report** European Medicines Agency (EMA)

AL050 Enhances GCase Activity ~20-fold in Circulating Immune Cells

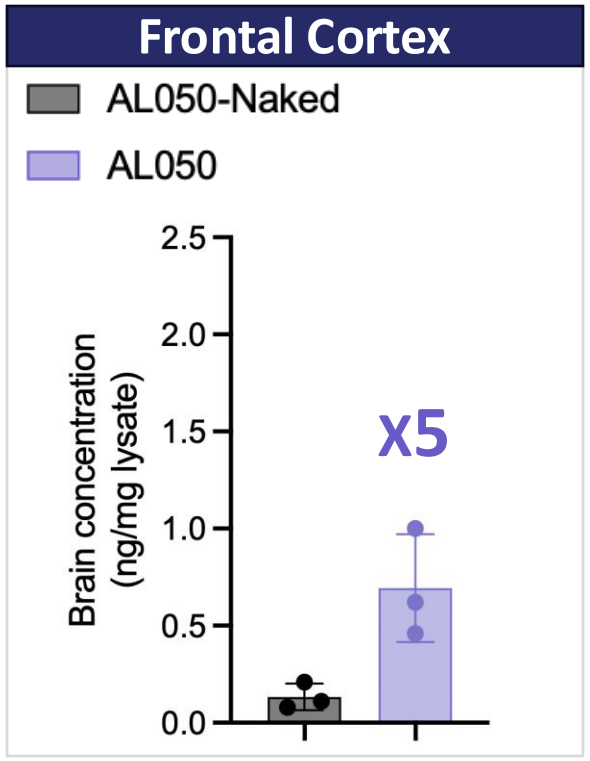
AL050's increase of GCase in peripheral immune cells supports its utility in both non-neuronopathic and neuronopathic Gaucher disease

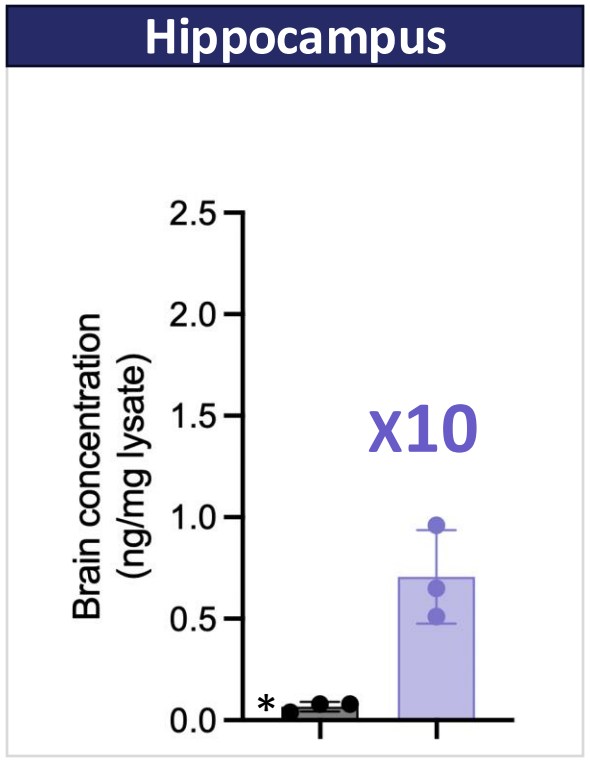
Increased GCase Activity is Measured in PBMCs 24h after Treatment with AL050

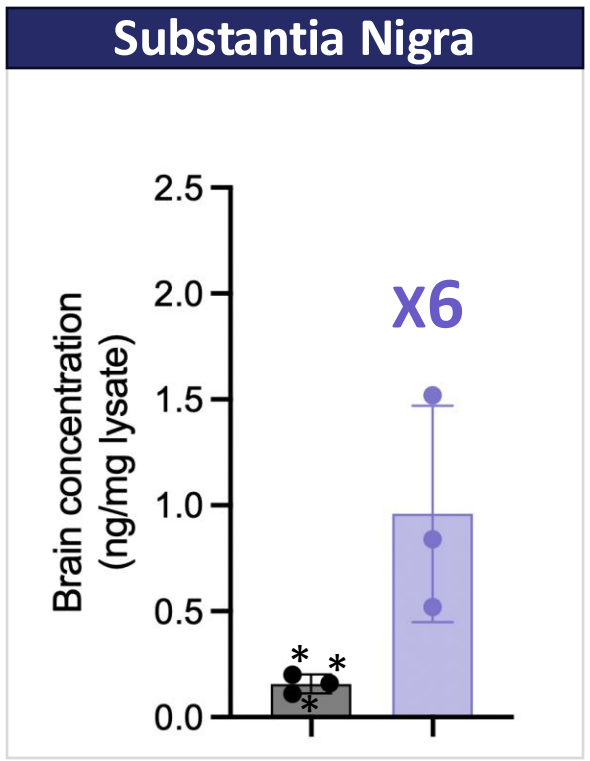


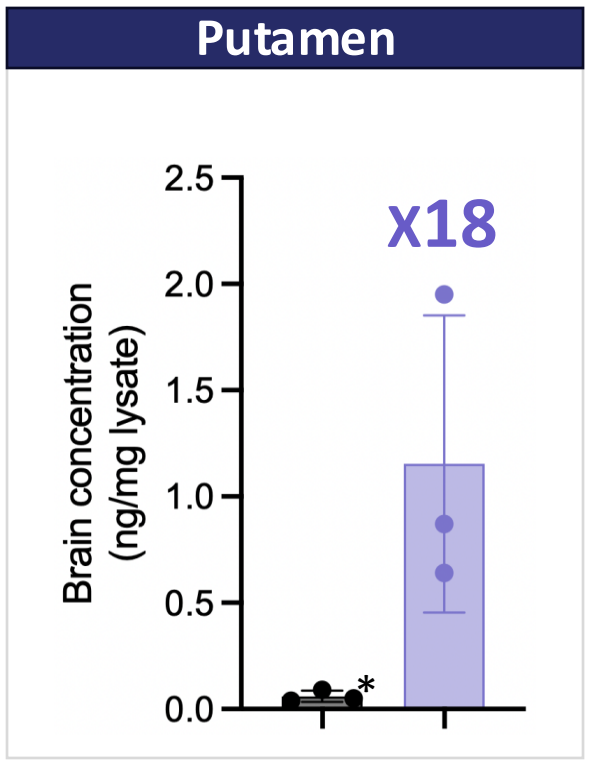
Three female cynomolgus monkeys per group were dosed intravenously on D1, D8, with 10mg/kg of AL050 and were sacrificed at D9. Peripheral blood mononuclear cells were isolated predose or 24h after the last injection. Cells were lysed and GCase activity was determined using a 4-MUG kinetic assay. AL050-Naked = AL050 without ABC platform

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



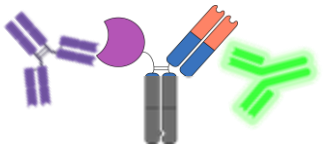






Three female cynomolgus monkeys per group were dosed intravenously on D1, D8, with 10mg/kg of AL050 and were sacrificed at D9. Brain tissues were collected 24 hours after the second injection and drug levels were measured in the vessel-depleted fraction. AL050-Naked = AL050 without ABC platform. Only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

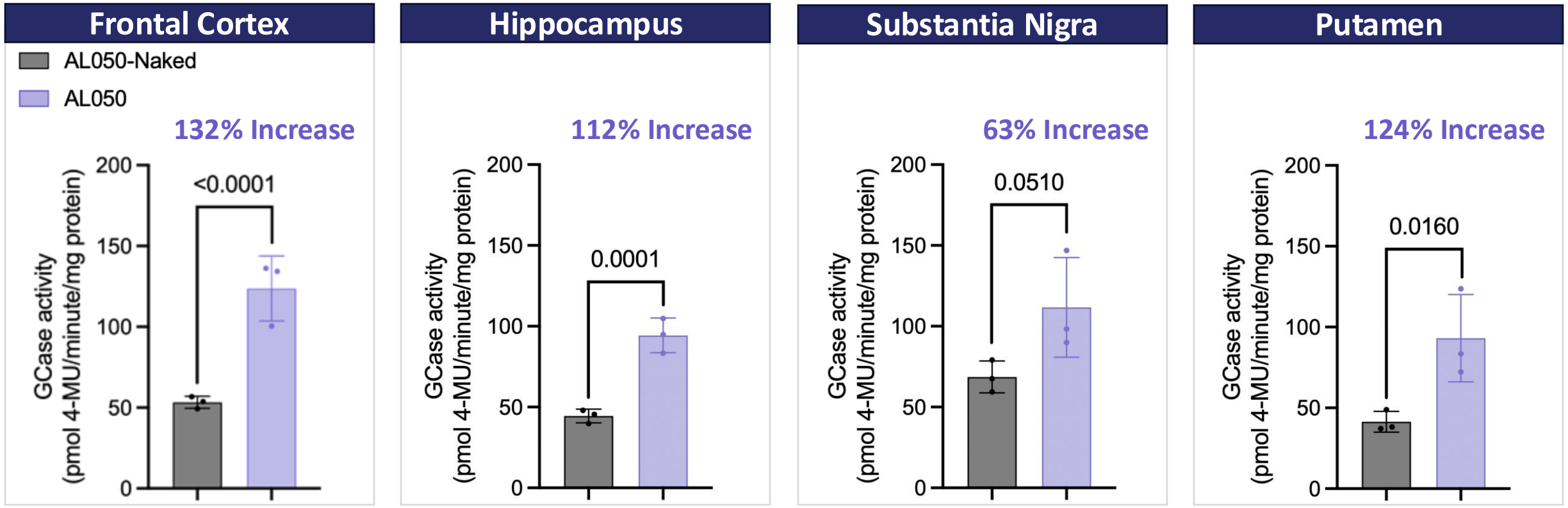
Intact AL050 is Being Detected



*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



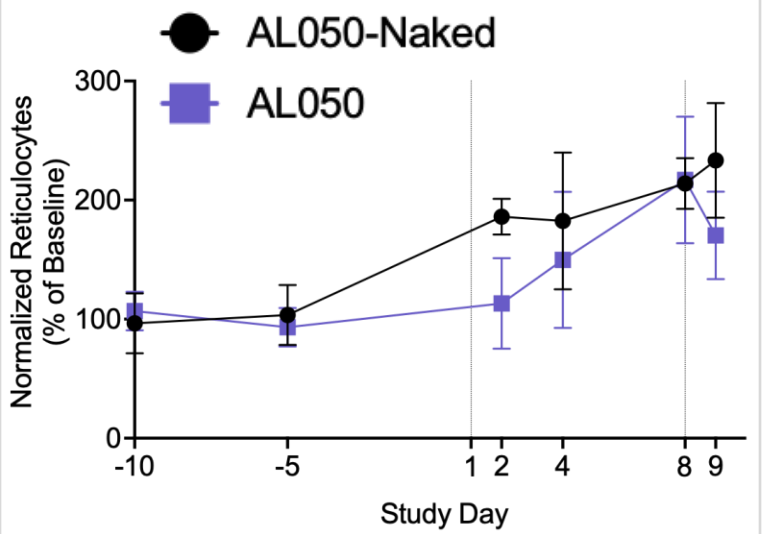
Three female cynomolgus monkeys per group were dosed intravenously on D1, 8, with 10mg/kg of AL050 and were sacrificed at D9. GCase enzymatic activity was determined using a 4-MUG kinetic assay (graphs represent the combination of endogenous NHP GCase and AL050. AL050-Naked = AL050 without ABC platform. 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.

alector

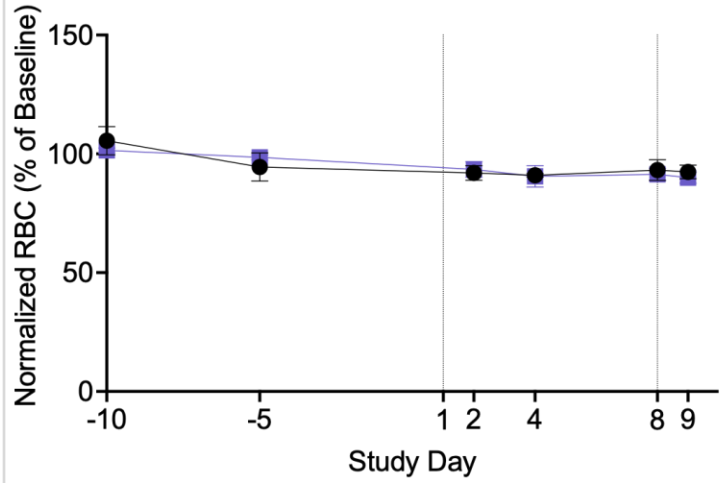
One way ANOVA with Dunnett's multiple comparison test

AL050 Did Not Negatively Impact Reticulocytes, RBC Count or Hemoglobin Levels

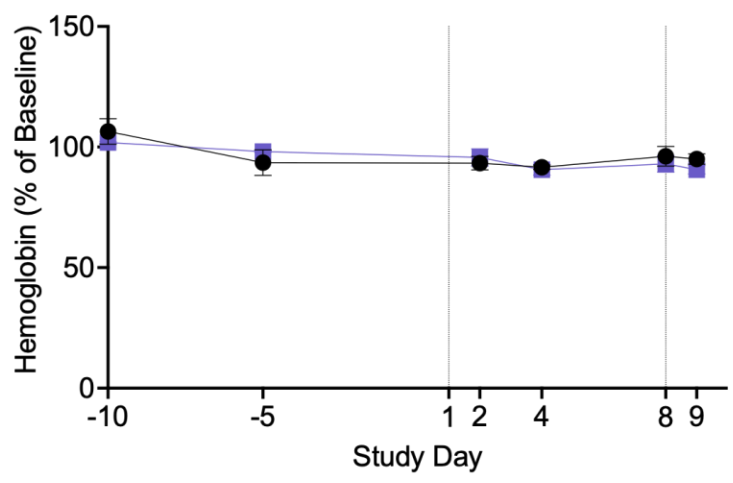
Reticulocyte Counts in Normal Range



Red Blood Cell Counts Were Not Affected



Hemoglobin Levels Were Not Affected



Three female cynomolgus monkeys per group were dosed intravenously on D1, 8, with 10mg/kg of AL050 and were sacrificed at D9 Blood samples were collected at Days -10, -7, 2, 4, 8 (pre-dose), and 9 and were analyzed for reticulocytes, red blood cell counts and hemoglobin levels at the indicated times. Increase in reticulocytes was observed in all groups due to frequent blood collections. AL050-Naked = AL050 without ABC platform; AL050 incorporated the ABC platform.

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, chemistry, coagulation)
- Gross necropsy observations
- Organ Weight
- Histopathology (Anatomic Pathology)
    - Major tissues

Summary:

- There were no AL050-related clinical signs
- No AL050-related impact on body weight, food consumption, hematology, clinical chemistry, and coagulation
- No macroscopic findings associated with AL050 treatment
- No changes in organ weight

AL050 Clinical Plan – Structured Overview

PHASE 1 OBJECTIVES	• Evaluate safety, tolerability, and pharmacokinetics (PK) in healthy volunteers and PD-GBA patients. • Assess systemic and CNS exposure and enzyme activity. • Explore pharmacodynamic (PD) markers of target engagement and substrate reduction.
STUDY DESIGN	• Phase 1a: Single Ascending Dose study in healthy volunteers to assess safety, tolerability, and PK. • Phase 1b: Multiple Ascending Dose study in healthy subjects and PD-GBA patients to assess safety, PK, and PD effects. • Includes exploratory analysis of GCase activity and substrate biomarkers in plasma and CSF.
STUDY GOALS	• Analyze Phase 1 results to inform drug safety, efficacy dosing regimen and delivery mode, to enable design of the Phase 2 proof-of-concept study.

Summary and Conclusion

GBA1 Gene Mutation Impact:

- Up to 1 million Parkinson's disease (PD) cases are associated with *GBA1* gene mutations[1]
- Up to 2.4 million Lewy body dementia (LBD) cases are associated with *GBA1* gene mutations[2]
- Approximately 125,000 Gaucher disease (GD) cases are caused by *GBA1* gene mutations[3]

AL050 Design:

- AL050 was designed to address GCase deficiencies in PD, LBD, and GD by enhancing GCase, encoded by the *GBA1* gene, delivery to the brain

AL050 Demonstrated:

- Superior activity and stability in vitro and in NHP plasma compared to current GCase ERT
- Good brain penetration and doubling of enzymatic activity over the endogenous enzyme in the NHP
- No hematologic adverse effects

Clinic Target:

- Targeting IND submission in 2027
- Trial design includes SAD and MAD in healthy volunteers and PD subjects, safety, tolerability, serum/CSF PK/PD and exploratory biomarkers

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; 3. Meikle PJ, et al. Prevalence of lysosomal storage disorders. JAMA. 1999 Jan 20;281(3):249 – 54

Alector Brain Carrier (ABC)-Enabled siRNA Programs

SOD-siRNA-ABC:
Proof of Concept Compound

AL064
Tau-siRNA-ABC:
For Alzheimer's Disease and Frontotemporal Dementia

ADP062
αSynuclein-siRNA-ABC:
For Parkinson's Disease and Lewy Body Dementia

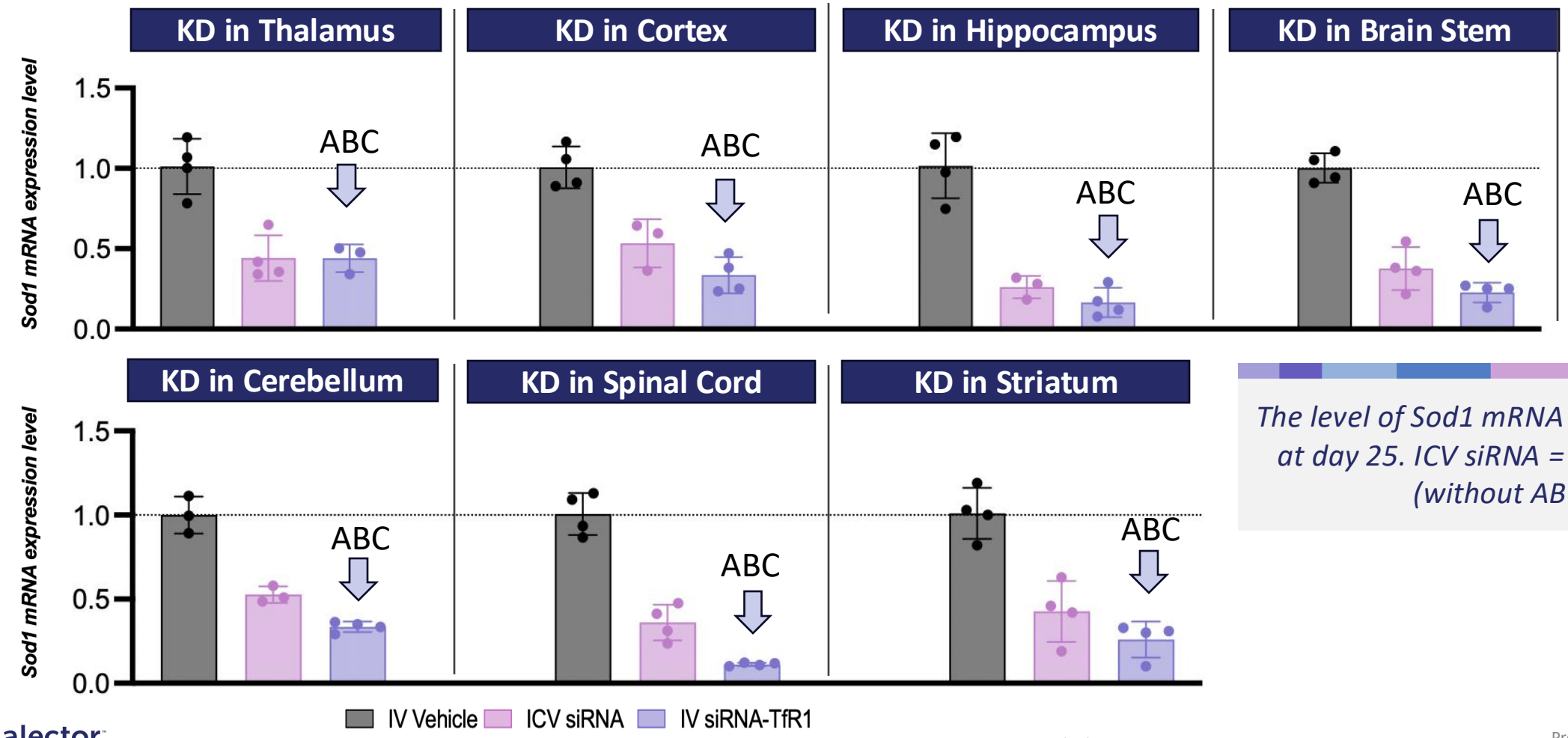
ADP065
NLRP3 siRNA-ABC:
For Multiple Neurodegenerative Diseases

Rationale for Brain Enabled siRNA Therapeutics; Overcoming Limitations of Intrathecal/Intracerebroventricular Delivery

IT/ICV Delivery Challenges	Our Approach
Localized Exposure: High accumulation in the spinal cord, but poor penetration into deep brain regions	**Homogeneous Brain Distribution:** Enables broader, more effective delivery across brain regions
Therapeutic Reach: Suitable for spinal diseases (e.g. SMA), not for deep-brain pathologies	**Applicable to Brain and Peripheral Tissues:** Expands reach to deep-brain and systemic pathologies
Limited Biodistribution: Drug largely confined to CSF-proximal regions	**Better Efficacy:** Broad distribution improves therapeutic potential
Procedural Burden: Invasive, with frequent procedure-related adverse events	**Safe and Easier Delivery:** Minimizes procedure risk and complexity with intravenous or subcutaneous delivery
Cumbersome and Non-scalable: Difficult medical procedure to scale for large patient population	**Convenient and Scalable:** Delivery modality is scalable and easy to distribute

Peripheral SOD1 siRNA-ABC Achieves 50–80% Knockdown (KD) Across Multiple Brain Regions

The magnitude of SOD1 mRNA knockdown mirrors the concentrations of SOD siRNA achieved in the brain

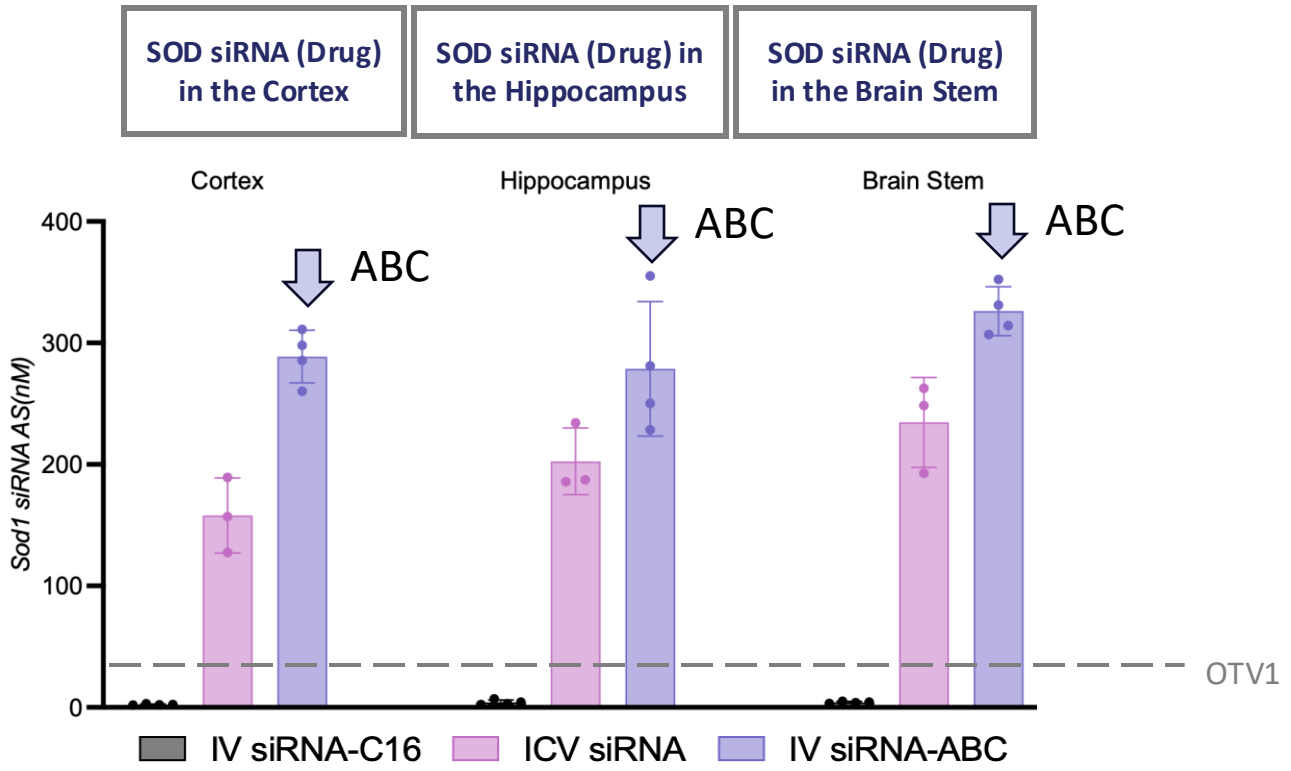


The level of Sod1 mRNA was measured at day 25. ICV siRNA = Naked siRNA (without ABC).

SOD1 - Superoxide dismutase

Comparing the Brain Concentration of ABC-delivered siRNA Vs. Published Competing Technologies

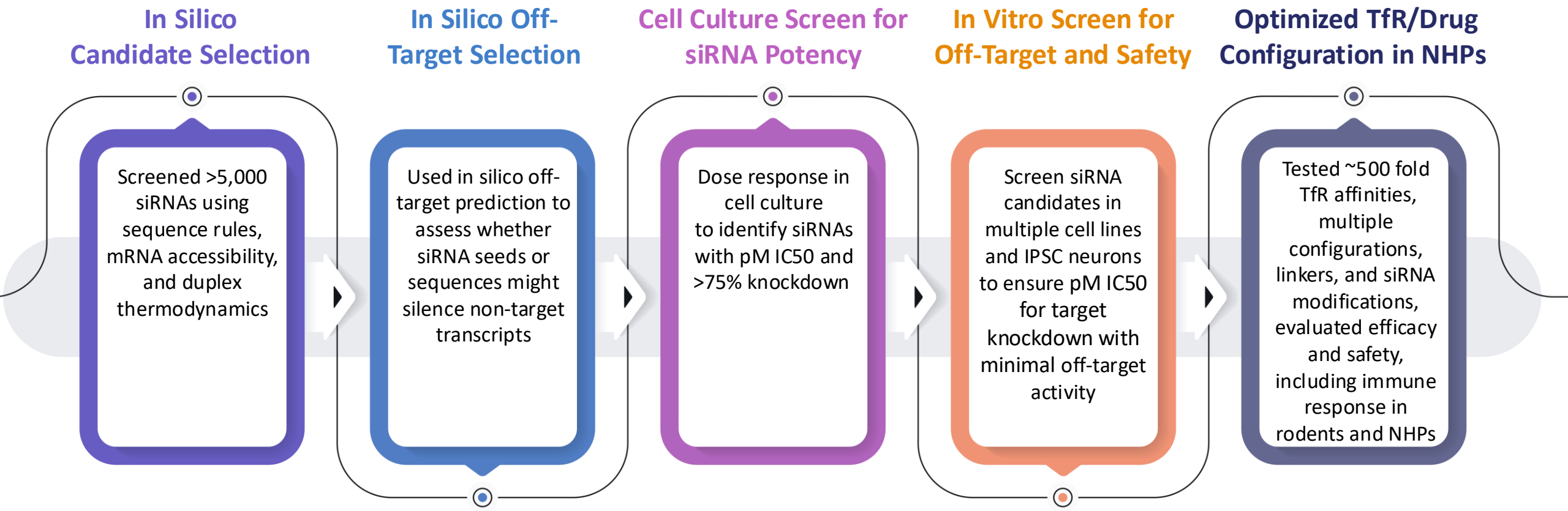
Concentration of siRNA-ABC delivered IV appears superior to the same siRNA delivered ICV



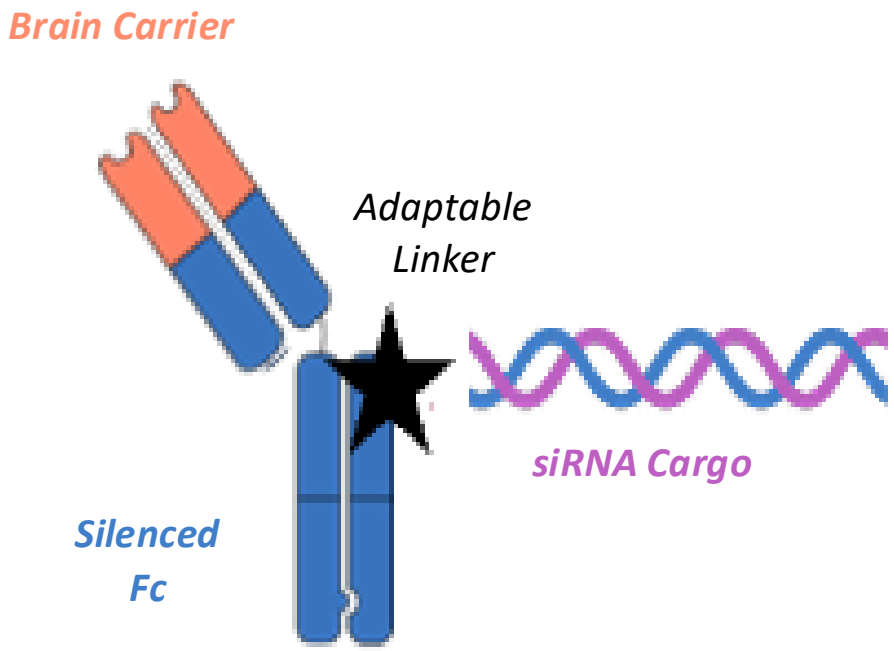
The level of Sod1 siRNA was measured at day 25. Brain tissue lysis was treated with proteinase K to dissociate siRNA from ABC. Sod1 siRNA Antisense strand was measured by LS/MS assay. Denali had reported a peak concentration of ~30nM with their ASO-ATV following 4 IV doses[1].

1. US20240059784A1, 2023. 2. Barker *et al* 2024

The Development of Brain Enabled siRNA for Tau, α–Synuclein and NLRP3



ABC-Enabled Tau siRNA Alzheimer's Disease and Primary Tauopathies



AL064 Drug Features:

Status

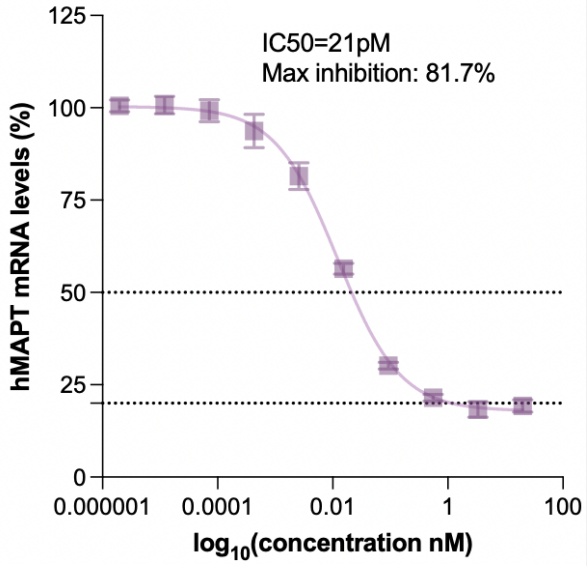
- Would address up to ~24 million AD WW, Fully owned
- Demonstrated robust brain penetration, Tau mRNA knockdown of up to 70%, good safety in NHP
- As part of IND-enabling preparations, a modification to AL064 is planned to improve stability and/or potency.
- Follow-up pipeline includes 2nd generation Tau siRNA (as well as α–Synuclein siRNA and NLRP3 siRNA)

Potency and Safety

- Designed for superior convenience of use and brain distribution compared to siRNA alone
- Engineered for pM potency and minimal off target activity
- Optimized TfR affinity/kinetics to enhance blood-brain-barrier transcytosis, cell uptake, and lysosomal escape
- Proprietary ABC binding to a unique epitope and drug configuration designed to eliminate hematologic risk

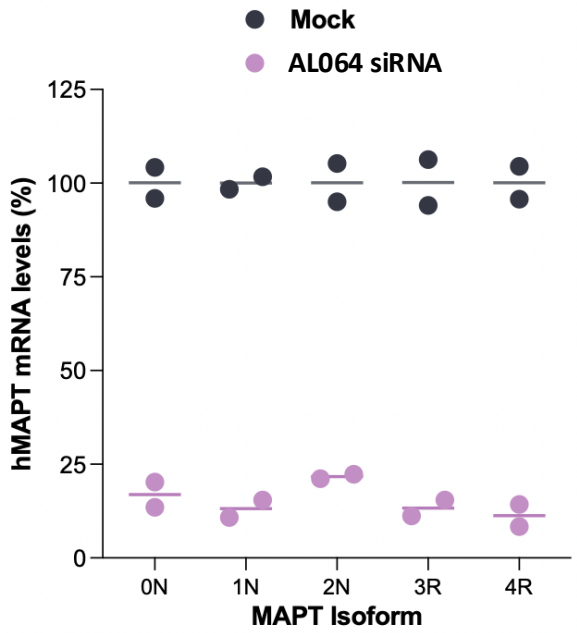
Tau siRNA AL064 Demonstrates High Potency in Vitro

Dose-Dependent Knockdown in MAPT Expressing Cell Line



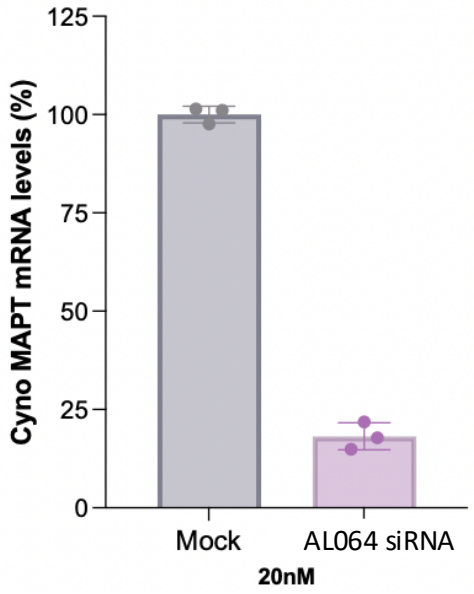
80% inhibition and pM range IC50. AL064 siRNA was transfected into MCF7 cells for 24hr to determine the dose response.

Knockdown all MAPT Isoforms in Human Neuroblastoma Cell Line



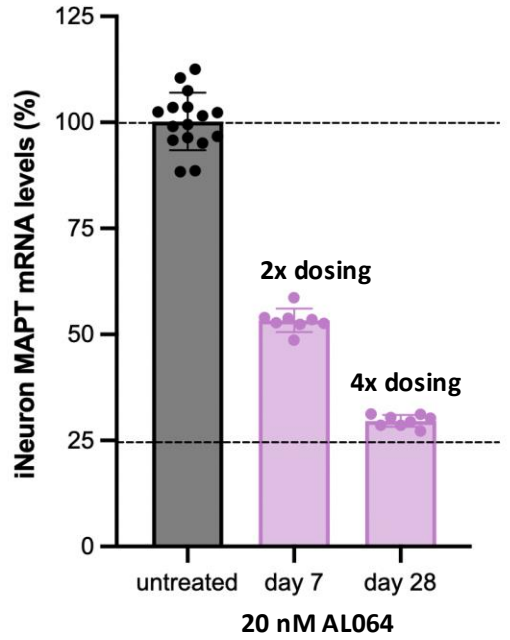
AL064 siRNA was transfected into SH-SY5Y cells for 24hr to determine the knockdown of MAPT isoforms.

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.

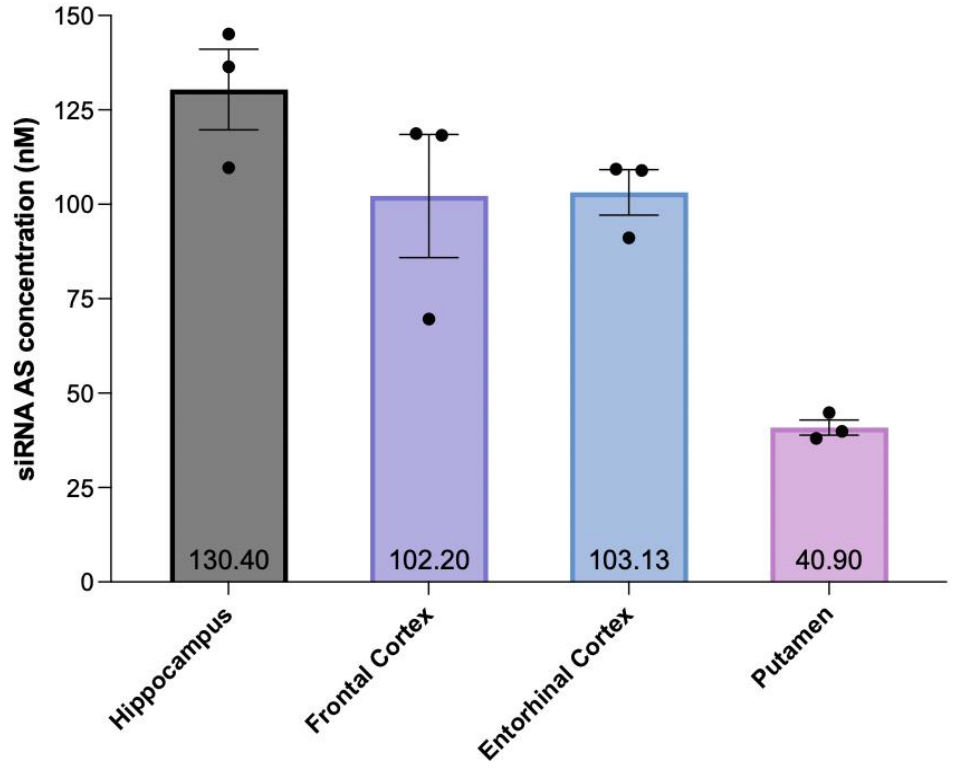
Knockdown of MAPT in iPSC Neurons by AL064



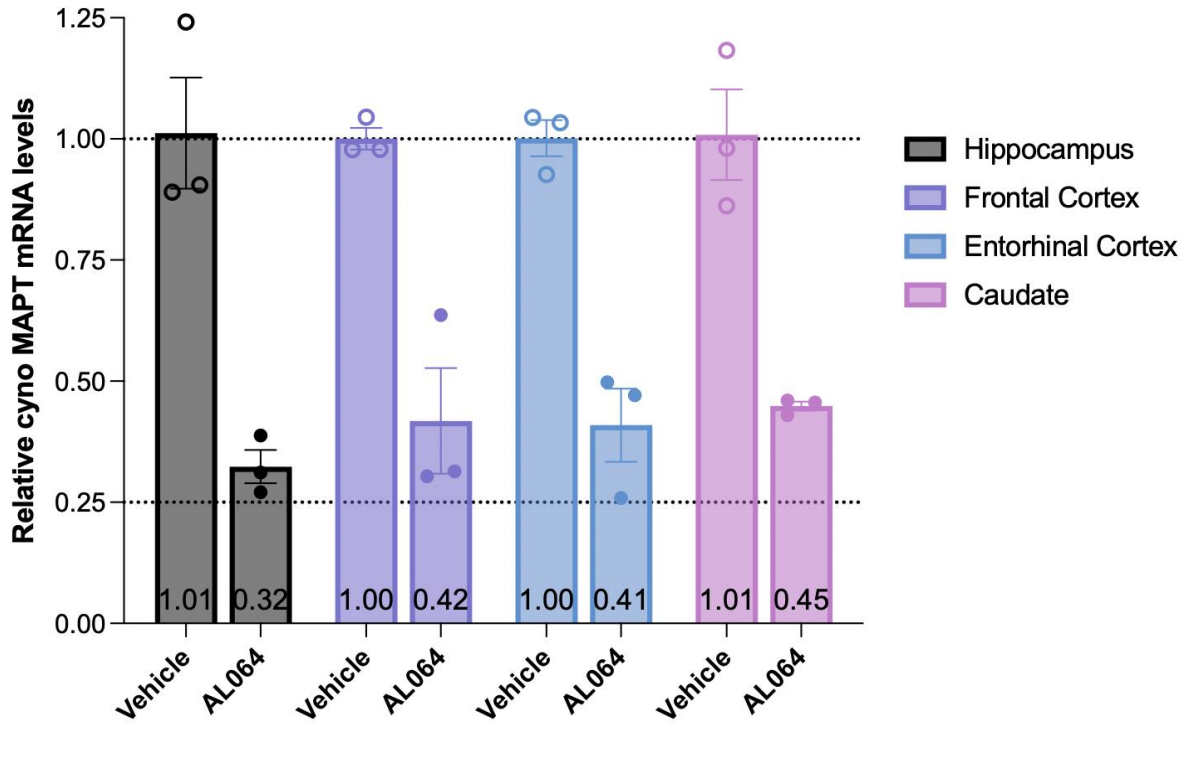
iPSC-derived neurons were treated with AL064 2 or 4 times and Tau mRNA knockdown was determined after 7 or 28 days.

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

Concentrations of AL064 in Brain issues (28 days)



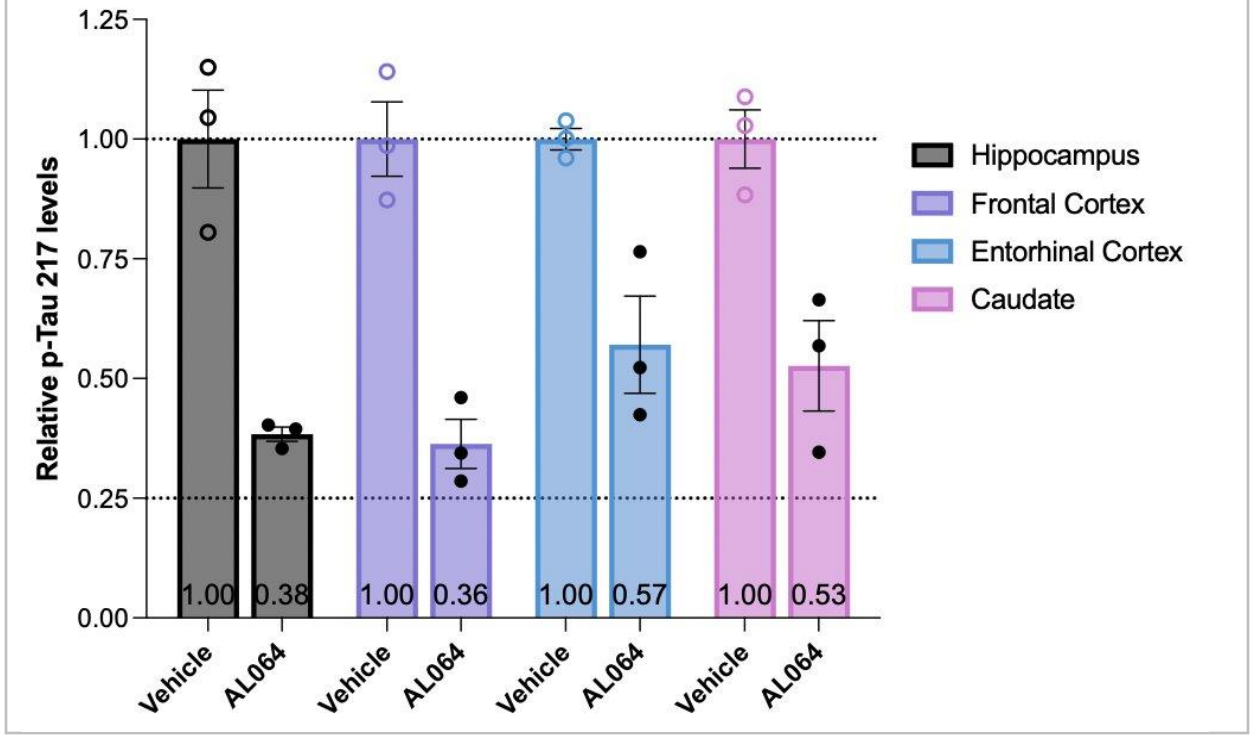
Knockdown of Tau mRNA in Brain Tissues (28 days)



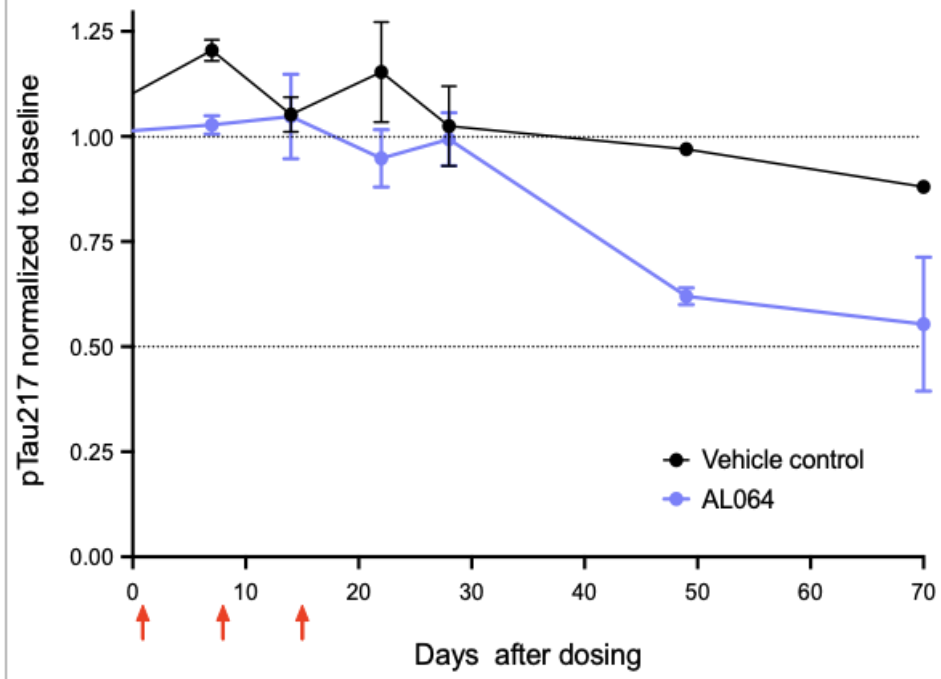
Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent and the level of AL064 siRNA antisense strand in different brain regions was measured at day 28 with MSD assay. Likewise, the level of MAPT mRNA in different brain regions was measured at day 28 with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

Protein Level Knock Down of Phospho-Tau 217 in Brain and CSF of NHP

43-64% Knockdown of p-Tau 217 in Multiple Brain Regions in 28 days



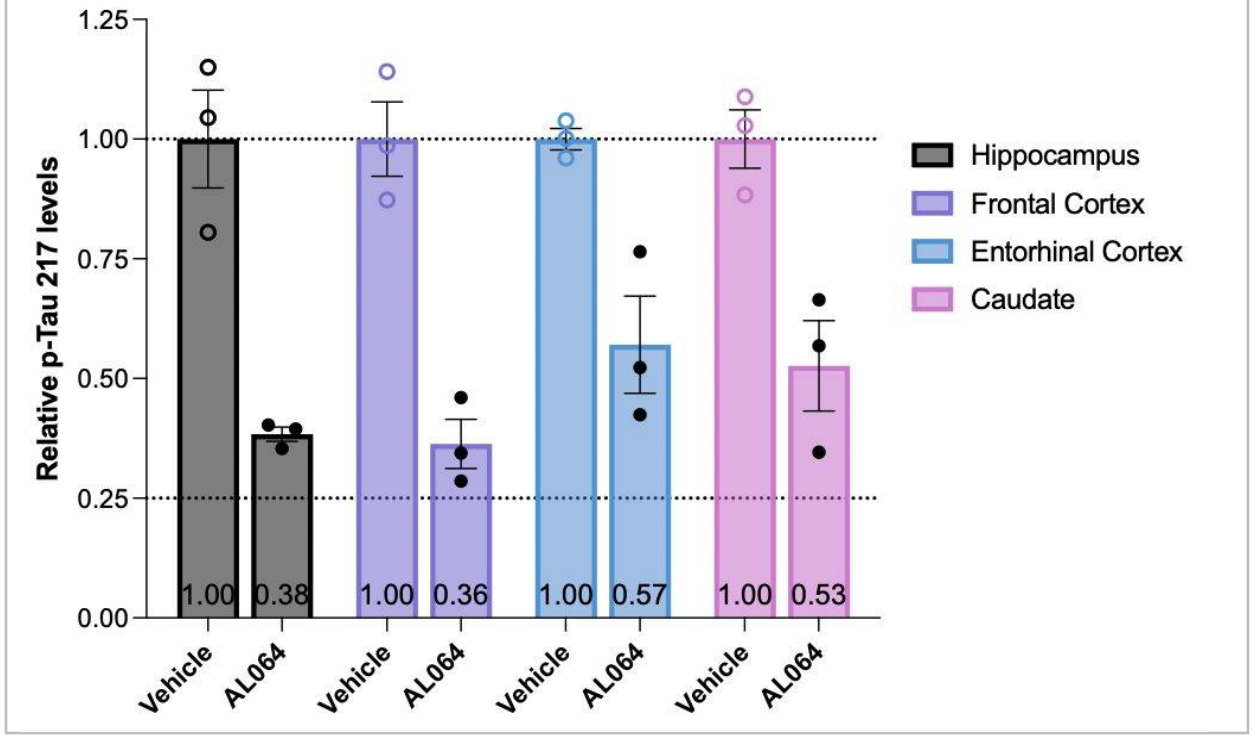
45% Knockdown of p-Tau 217 in the CSF at day 70



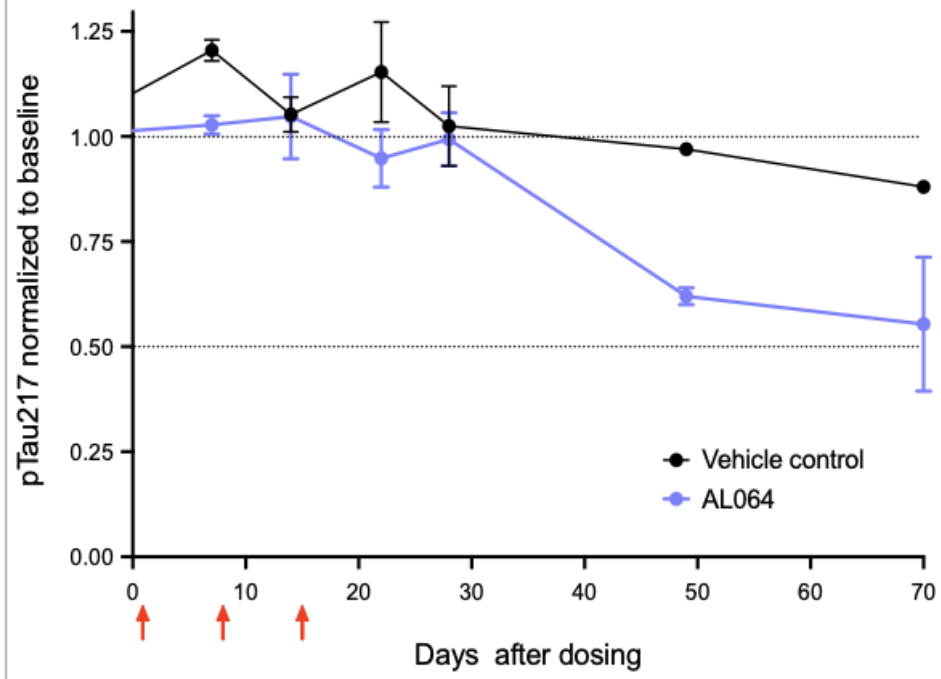
Three NHP per group were injected via IV infusion on days 1, 8, 15 with 3 mg/kg siRNA-dose-equivalent and the levels of p-Tau217 in different brain regions was measured at day 28 with MSD assay. pTau217 levels were measured in the CSF at the following timepoints: pre-dose, D7, 14, 22, 28, 49 and 70.

Peripheral AL064: Knock Down of Phospho-Tau 217 in Brain and CSF of NHP

43-64% Knockdown of p-Tau 217 in Multiple Brain Regions in 28 days



45% Knockdown of p-Tau 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 was measured at day 28 with MSD assay. pTau217 levels were measured in the CSF at the following timepoints: pre-dose, D7, 14, 22, 28, 49 and 70.

AL064 was Well-Tolerated in NHPs at Doses Up to 30 mg/kg siRNA

Toxicological Parameters Evaluated:

- Mortality/Morbidity
- Clinical observations
- Body weight
- Food consumption
- Clinical pathology
- Gross necropsy observations
- Tissues collected for histopathology evaluation

Summary:

- Administration of AL064 was well tolerated at doses up to 30mg/kg (siRNA equivalent dose)
- No test-article related adverse findings were identified throughout the conduct of the study

Summary: Alector's ABC-Enabled Antibodies, Enzymes, and siRNA

Alector Brain Carrier:
TfR "Trojan horse" for brain delivery of multiple drug modality cargo with unique epitope and a ~1,000-fold affinity range to minimize hematologic risk

AL137
Alector Anti-Aβ antibody
Optimized TfR affinity and drug format to achieve high brain antibody levels with manageable hematologic effects. Targeting IND in Q4 2026/Q1 2027.

AL050
Alector GCase ERT
~20× higher enzymatic activity in NHP PBMCs, doubling of brain enzyme activity in NHP, lysosomal delivery, and no hematologic effects. Targeting IND in 2027.

AL064/ADP062/ADP065
Alector siRNA Programs
leverage optimized TfR affinity and format to achieve high brain siRNA levels (~300 nM), lysosomal escape, and effective mRNA knockdown in rodents and NHPs;
IND timing under evaluation.

Validation:
All 3 ABC-enabled drug modalities show favorable PK, validated in NHP and show high manufacturability and good storage stability.

Thank You