March 11, 2026

Developing therapies for Alzheimer's & pain

European Innovation Council

AlzeCure

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AlzeCure

AlzeCure Pharma in brief

AlzeCure

AlzeCure Pharma – In brief

- Working in **Alzheimer's Disease** (AD) & **Pain** – high unmet medical need & multi-billion sales potential
- Spin-out from **AstraZeneca** – as a result of their exit from the CNS area
- Founded in 2016, out of a research foundation sponsored by **Alzheimerfonden**
- Based at Novum Science Park, **Karolinska Institute**, Stockholm, Sweden
- Three project platforms with multiple **small molecule** candidates with **first-in-class properties**
  - **NeuroRestore®** – A novel symptomatic treatment for cognitive disorders, e.g. AD with disease modifying potential
  - **Alzstatin®** – An innovative preventive & disease-modifying treatment against AD
  - **PainLess** – Innovative projects for osteoarthritic & neuropathic pain
- Listed on **Nasdaq First North Premier** Growth Market, Sweden, (Ticker: ALZCUR)
- Market cap: **214 MSEK** (260310)
- **Cash position: 50.3 MSEK** (Q4 2025)
- **European Innovation Council** (EIC) **grant** of **27.5 MSEK** (€ 2.5M) for phase IIa Alzheimer's trial

Professor Jan Lundberg – Board member

Former global head of R&D at Eli Lilly & global head of research at AstraZeneca joining & investing

Professor Jan Lundberg

Jan Lundberg, Professor in neurotransmission

Professor Jan Lundberg has more than 25 years of experience from leading positions in global pharmaceutical companies, including as global head of research at Astra and then AstraZeneca (1996 – 2009) and **global head of research & development** at Eli Lilly (2010 – 2018). He has led the development of more than 200 drug candidates, including Alzheimer's & pain, with 30 approved products in several therapeutic areas.

Before joining Astra, Dr. Lundberg was professor of pharmacology at the Karolinska Institute, where he also received his PhD. His research has resulted in over 500 publications in peer-reviewed scientific journals.

Lilly AstraZeneca

European Innovation Council

AlzeCure

Our Business Model

Are a **Research & Development** company

Research & **develop through early clinical phase** and then to **out-license** or **partner** on our projects

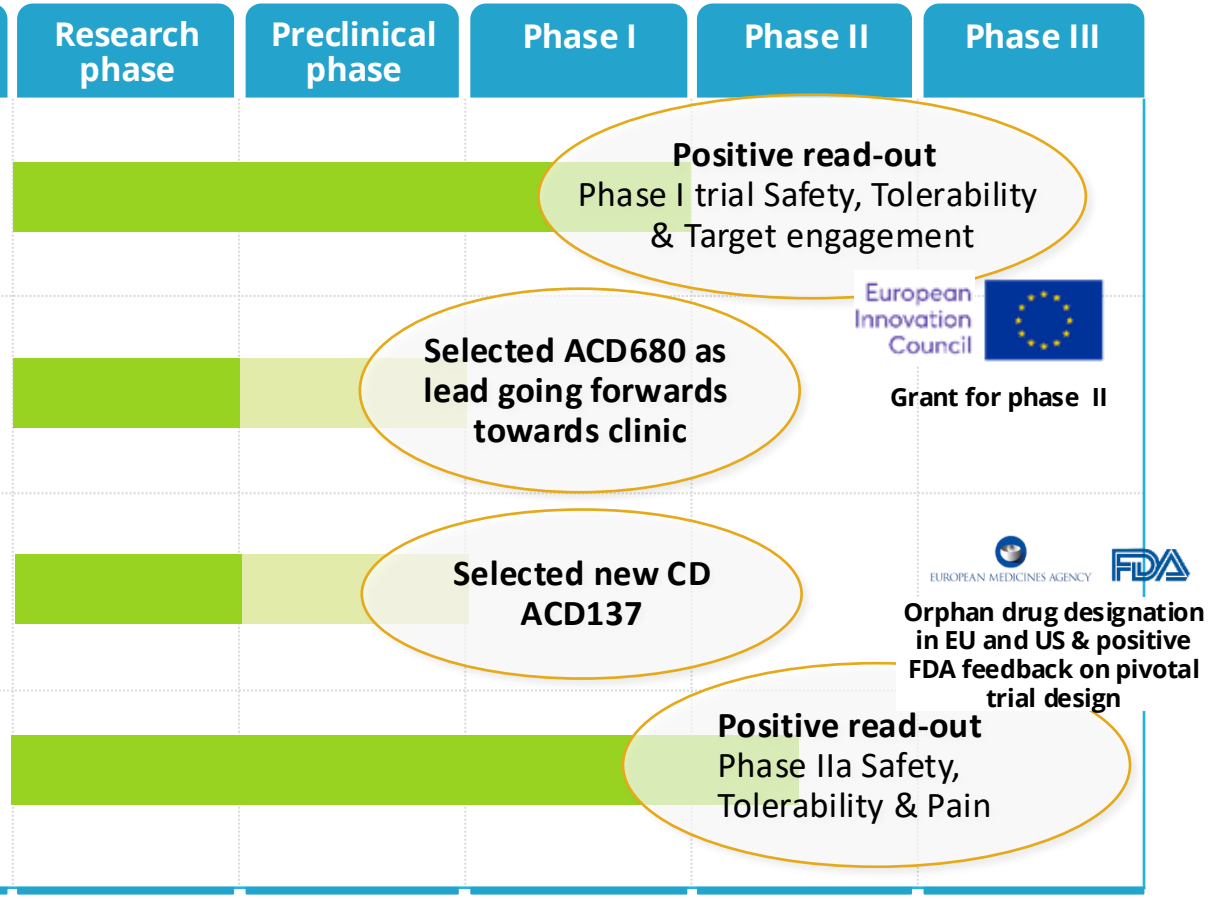
Gain incomes through:

- Upfront payments
- Milestone payments
- Royalties on sold products

A pipeline of Small-Molecule Programs

Multiple candidates increase chance of success

Platform	Candidate	Target	Indication
Neuro Restore®	ACD856	Positive allosteric modulator (PAM) of Trk-receptors)	Alzheimer's Disease, TBI - Traumatic brain injuries Parkinson's disease, Sleep disorders, Depression
Alzstatin®	ACD680	Gamma secretase modulator (GSM)	Alzheimer's Disease
PainLess	ACD137	Negative allosteric modulator (NAM) of TrkA-receptors	Osteoarthritic Pain & other severe pain conditions
	ACD440	TRPV1 antagonist	Neuropathic Pain & Orphan indication Erythromelalgia



Phase completed **Phase ongoing**

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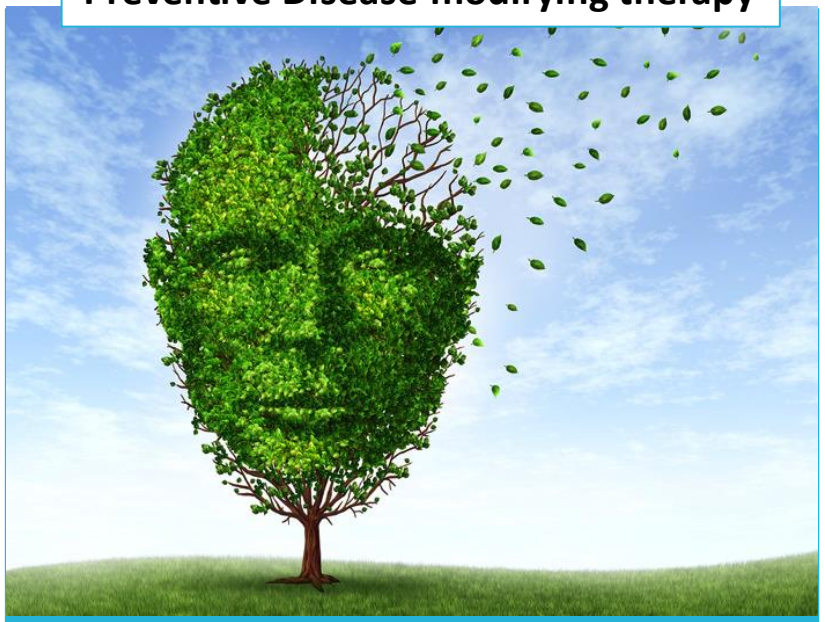
Two Alzheimer's platforms - 1st-in-class properties & potential game-changers

MEETING NEEDS OF AD PATIENTS – ADRESSING SHORT TERM NEEDS WITH LONG-TERM BENEFITS

Preventive Disease-modifying therapy



Alzstatin®

Gamma-secretase modulator

Targeting Amyloid Production

- *Novel Oral Small Molecule*

Symptomatic & pot. Disease-modifying therapy

NeuroRestore®

Trk-PAM

Improving Neuronal & Cognitive Function

- *Novel Oral Small Molecule*

Two fast followers to **Roche**, **Eisai** respectively → Provides Concept **Validation**

AlzeCure

NeuroRestore® – *Trk-PAM improving neuronal function & cognition in Alzheimer's disease*

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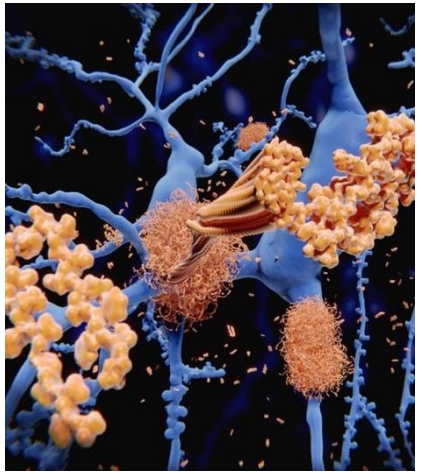
The importance of BDNF & NGF signaling in Alzheimer's

- The neurotrophins Brain-Derived Neurotrophic Factor (BDNF) and Nerve Growth Factor (NGF) bind to their respective receptors, TrkB and TrkA and are **key for brain health and cognition**
- BDNF& NGF signaling are implicated in several key neuronal functions, including **cholinergic function**, hippocampal neurogenesis and **synaptic plasticity**
- **Loss of NGF-dependent cholinergic neurons** in the basal forebrain and hippocampal atrophy are early hallmarks of Alzheimer's disease and **correlates with cognitive decline**
- **Certain genetics** in man, e.g. BDNF-Val66Met polymorphism, leads to **lower levels of BDNF,** and is associated with **more rapid cognitive impairment** and **increased disease progression** in Alzheimer's



Reduced BDNF and/or NGF-levels could limit the brain's ability to withstand pathological conditions

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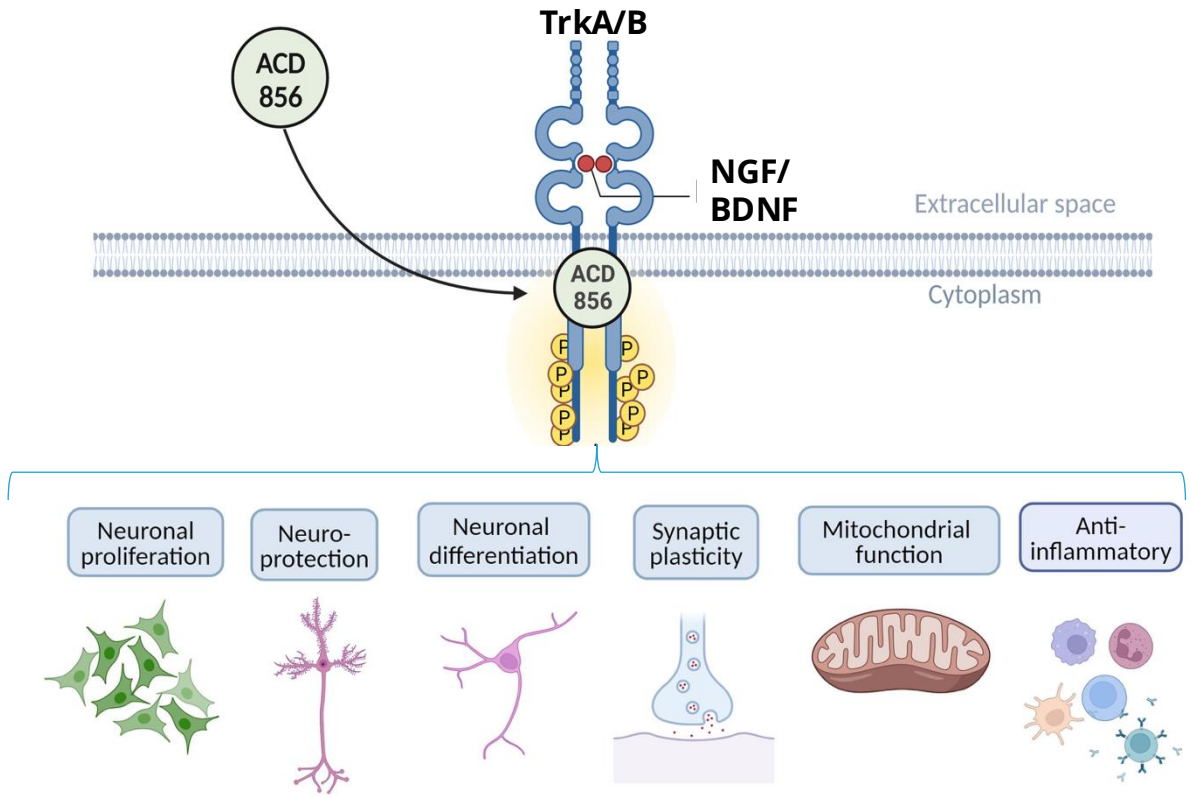
Mechanism of Action of NeuroRestore ACD856

- ACD856 is a novel oral small molecule positive modulator of Trk-receptors **enhancing the signaling** of neurotrophins such as **NGF & BDNF**
- The enhanced signaling leads to immediate **symptomatic effects** & with potential **long-term benefits**
- The long-term effects of ACD856 could include **improved neuronal function, increased mitochondrial function & enhanced cognition**, etc



Potential for **disease modifying effect & improved learning and memory**

Parrado Fernandez C et al. Int J Mol Sci. 2023 Jul 6;24(13):11159. https://doi.org/10.3390/ijms241311159
Dahlström M et al, Cells 2021, Volume 10, Issue 8, 1871. Identification of Novel Positive Allosteric Modulators of Neurotrophin Receptors for the Treatment of Cognitive Dysfunction

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NeuroRestore® – Cognitive Enhancer Improving Learning & Memory Ability

Stages of memory formation

LEARN

Transforming information into a form that can be stored in memory

STORE

Maintaining the encoded information in memory

REMEMBER

Re-accessing the information from the past which has been encoded & stored

NeuroRestore has in pre-clinical models shown that it can improve the ability to learn & remember information, so the information is accurately recollected when needed

Parrado Fernandez C et al. Int J Mol Sci. 2023 Jul 6;24(13):11159. https://doi.org/10.3390/ijms241311159

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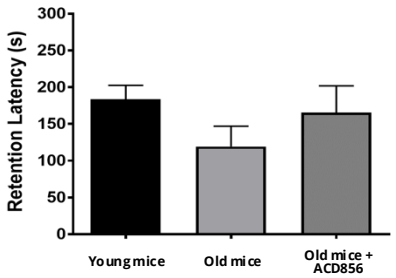
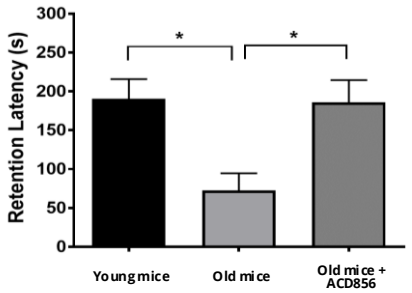
Preclinical data on Pro-cognitive & Disease Modifying Effects

ACD856 improves aged-induced memory impairment

- 18-months old animals were used to study effects on age-induced memory impairment and compared to young animals
- Two memory tests were performed 1 or 11 days after learning

Single dose ACD856	Learning	Test #1 – Day 1	Test #2 – Day 11
-30 min	t=0 min		





ACD856 could fully revert the memory impairment in old animals to the level in young animals

Supporting data

- ✓ **Improves memory impairment**, presumably via increased synaptic function/plasticity
- ✓ **Increases the levels of BDNF** in cortical neurons and in brains of aged mice
- ✓ **Enhances neurite outgrowth** and neuronal proliferation
- ✓ **Protects against amyloid-beta** induced neurotoxicity
- ✓ **Improves mitochondrial function**
- ✓ Displays a **sustained antidepressant-like effect**

Data also suggest a disease-modifying effect by increasing plasticity

Parrado Fernandez C et al. Int J Mol Sci. 2023 Jul 6;24(13):11159. https://doi.org/10.3390/ijms241311159
Märta Dahlström et al. Cells 2021, Volume 10, Issue 8, 1871. *Identification of Novel Positive Allosteric Modulators of Neurotrophin Receptors for the Treatment of Cognitive Dysfunction*

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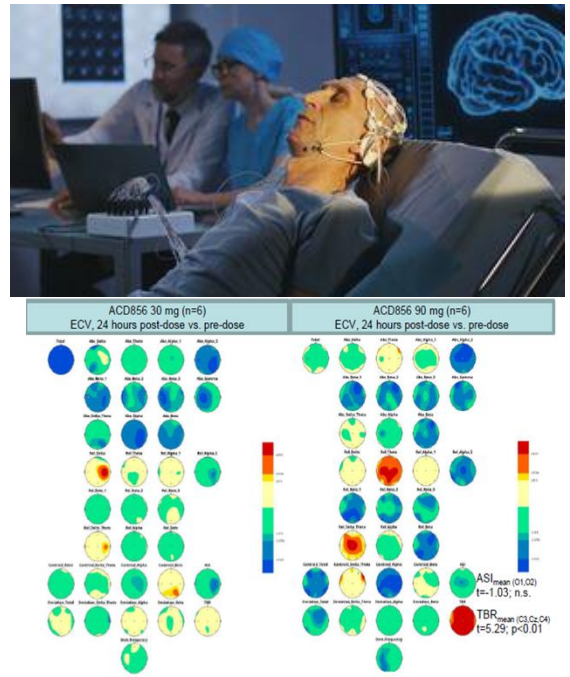
Phase I Demonstrated Safety, Tolerability & Target Engagement

- ACD856 is **safe & well tolerated**
  - Single and repeated dosing with ACD856 did not result in any serious adverse events in healthy volunteers at the tested dose levels
- ACD856 has an **excellent PK profile** suitable for **once daily** oral dosing
  - ACD856 has a rapid absorption, a long half-life of ~ 20 hours, high bioavailability and a linear dose-dependent exposure
- ACD856 **present in CSF** with a ratio of ACD856 in CSF to unbound average ACD856 levels in plasma at **> 37%**
  - **ACD856 pass the BBB** and measured concentrations in CSF confirms a **high exposure** at the level of the brain
- ACD856 MAD qEEG results shows clear **CNS target engagement**
  - EEG pattern supports pro-cognitive as well as antidepressant effects of ACD856



Vigilance control brain maps for 30 and 90 mg cohorts

Now preparing for phase IIa study in Alzheimer's patients

Önnestam, K et al. J Prev Alzheimers Dis (2023): https://link.springer.com/article/10.14283/jpad.2023.89

AlzeCure

Grant financed Phase IIa study to investigate the safety & efficacy of ACD856 in Alzheimer's disease

AlzeCure receives EU grant for Phase 2 clinical trial of NeuroRestore ACD856 for Alzheimer's disease

February 17, 2025

AlzeCure Pharma AB (publ) (FN STO: ALZCUR), a pharmaceutical company that develops candidate drugs for diseases affecting the nervous system, focusing on Alzheimer's disease and pain, today announced that its project NeuroRestore ACD856 has received €2.5m from the EU's European Innovation Council.

This funding will support AlzeCure's planned Phase IIa study of NeuroRestore ACD856 in Alzheimer's patients. In addition, higher doses of ACD856 will be evaluated in humans, as the good safety profile allows for further dosing. ACD856 has the potential to be the first drug in a new category of Alzheimer's drugs – positive allosteric modulators of Trk receptors (Trk-PAMs), which increase BDNF and NGF signaling.

"We are delighted to have been awarded a €2.5m grant from the European Innovation Council (EIC) for our innovative Alzheimer's treatment. The support from the EIC Accelerator program is a recognition of the project and will be crucial in advancing our clinical trials and bringing this much-needed Alzheimer's treatment to patients," said Johan Sandin, Chief Scientific Officer at AlzeCure Pharma

European Innovation Council

https://www.alzecurepharma.se/en/alzecure-receives-eu-grant-for-phase-2-clinical-trial-of-neurorestore-acd856-for-alzheimers-disease/
https://link.springer.com/article/10.1007/s00213-023-06410-x

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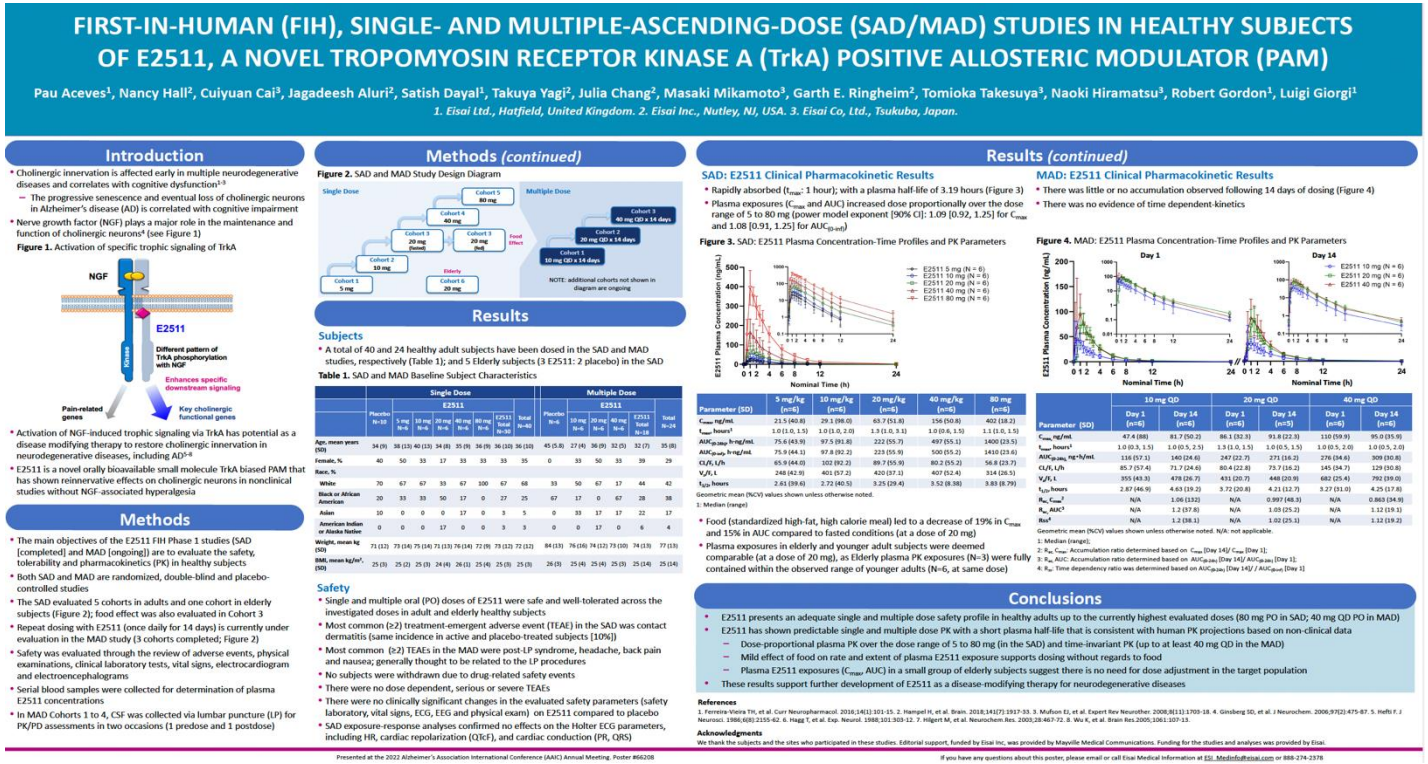
TrkA-PAM by Eisai: Disease-Modifying Therapy for Neurodegenerative Diseases



FIRST-IN-HUMAN (FIH), SINGLE- AND MULTIPLE-ASCENDING-DOSE (SAD/MAD) STUDIES IN HEALTHY SUBJECTS OF E2511, A NOVEL TROPOMYOSIN RECEPTOR KINASE A (TrkA) POSITIVE ALLOSTERIC MODULATOR (PAM)

Pau Aceves[1], Nancy Hall[2], Cuiyuan Cai[3], Jagadeesh Aluri[2], Satish Dayal[1], Takuya Yagi[2], Julia Chang[2], Masaki Mikamoto[3], Garth E. Ringheim[2], Tomioka Takesuya[3], Naoki Hiramatsu[3], Robert Gordon[1], Luigi Giorgi[1]
1. Eisai Ltd., Hatfield, United Kingdom. 2. Eisai Inc., Nutley, NJ, USA. 3. Eisai Co, Ltd., Tsukuba, Japan.

Introduction

- Cholinergic innervation is affected early in multiple neurodegenerative diseases and correlates with cognitive dysfunction[1-3]
  - The progressive senescence and eventual loss of cholinergic neurons in Alzheimer's disease (AD) is correlated with cognitive impairment
- Nerve growth factor (NGF) plays a major role in the maintenance and function of cholinergic neurons[4] (see Figure 1)

Figure 1. Activation of specific trophic signaling of TrkA

- Activation of NGF-induced trophic signaling via TrkA has potential as a disease modifying therapy to restore cholinergic innervation in neurodegenerative diseases, including AD[5-8]
- E2511 is a novel orally bioavailable small molecule TrkA biased PAM that has shown reinnervative effects on cholinergic neurons in nonclinical studies without NGF-associated hyperalgesia

Methods

- The main objectives of the E2511 FIH Phase 1 studies (SAD [completed] and MAD [ongoing]) are to evaluate the safety, tolerability and pharmacokinetics (PK) in healthy subjects
- Both SAD and MAD are randomized, double-blind and placebo-controlled studies
- The SAD evaluated 5 cohorts in adults and one cohort in elderly subjects (Figure 2); food effect was also evaluated in Cohort 3
- Repeat dosing with E2511 (once daily for 14 days) is currently under evaluation in the MAD study (3 cohorts completed; Figure 2)
- Safety was evaluated through the review of adverse events, physical examinations, clinical laboratory tests, vital signs, electrocardiogram and electroencephalograms
- Serial blood samples were collected for determination of plasma E2511 concentrations
- In MAD Cohorts 1 to 4, CSF was collected via lumbar puncture (LP) for PK/PD assessments in two occasions (1 predose and 1 postdose)

Methods *(continued)*

Figure 2. SAD and MAD Study Design Diagram

Results

Subjects

- A total of 40 and 24 healthy adult subjects have been dosed in the SAD and MAD studies, respectively (Table 1); and 5 Elderly subjects (3 E2511: 2 placebo) in the SAD

Table 1. SAD and MAD Baseline Subject Characteristics

	Single Dose								Multiple Dose							
		E2511								E2511						
	Placebo N=10	5 mg N=6	10 mg N=6	20 mg N=6	40 mg N=6	80 mg N=6	E2511 Total N=30	Total N=40	Placebo N=6	10 mg N=6	20 mg N=6	40 mg N=6	E2511 Total N=18	Total N=24
Age, mean years (SD)	34 (9)	38 (13)	40 (13)	34 (8)	35 (9)	36 (9)	36 (10)	36 (10)	45 (5.8)	27 (4)	36 (9)	32 (5)	32 (7)	35 (8)
Female, %	40	50	33	17	33	33	33	35	0	33	50	33	39	29
Race, %														
White	70	67	67	33	67	100	67	68	33	50	67	17	44	42
Black or African American	20	33	33	50	17	0	27	25	67	17	0	67	28	38
Asian	10	0	0	0	17	0	3	5	0	33	17	17	22	17
American Indian or Alaska Native	0	0	0	17	0	0	3	3	0	0	17	0	6	4
Weight, mean kg (SD)	71 (12)	73 (14)	75 (14)	71 (13)	76 (14)	72 (9)	73 (12)	72 (12)	84 (13)	76 (16)	74 (12)	73 (10)	74 (13)	77 (13)
BMI, mean kg/m², (SD)	25 (3)	25 (2)	25 (3)	24 (4)	26 (1)	25 (4)	25 (3)	25 (3)	26 (3)	25 (4)	25 (4)	25 (3)	25 (14)	25 (14)

Safety

- Single and multiple oral (PO) doses of E2511 were safe and well-tolerated across the investigated doses in adult and elderly healthy subjects
- Most common (≥2) treatment-emergent adverse event (TEAE) in the SAD was contact dermatitis (same incidence in active and placebo-treated subjects [10%])
- Most common (≥2) TEAEs in the MAD were post-LP syndrome, headache, back pain and nausea; generally thought to be related to the LP procedures
- No subjects were withdrawn due to drug-related safety events
- There were no dose dependent, serious or severe TEAEs
- There were no clinically significant changes in the evaluated safety parameters (safety laboratory, vital signs, ECG, EEG and physical exam) on E2511 compared to placebo
- SAD exposure-response analyses confirmed no effects on the Holter ECG parameters, including HR, cardiac repolarization (QTcF), and cardiac conduction (PR, QRS)

Results *(continued)*

SAD: E2511 Clinical Pharmacokinetic Results

- Rapidly absorbed (t_{max}: 1 hour); with a plasma half-life of 3.19 hours (Figure 3)
- Plasma exposures (C_{max} and AUC) increased dose proportionally over the dose range of 5 to 80 mg (power model exponent [90% CI]: 1.09 [0.92, 1.25] for C_{max} and 1.08 [0.91, 1.25] for $AUC_{(0\text{-}inf)}$)

Figure 3. SAD: E2511 Plasma Concentration-Time Profiles and PK Parameters

Parameter (SD)	5 mg/kg (n=6)	10 mg/kg (n=6)	20 mg/kg (n=6)	40 mg/kg (n=6)	80 mg (n=6)
C_{max} ng/mL	21.5 (40.8)	29.1 (98.0)	63.7 (51.8)	156 (50.8)	402 (18.2)
t_{max}, hours[1]	1.0 (1.0, 1.5)	1.0 (1.0, 2.0)	1.3 (1.0, 3.1)	1.0 (0.6, 1.5)	1.1 (1.0, 1.5)
$AUC_{(0\text{-}24h)}$ h·ng/mL	75.6 (43.9)	97.5 (91.8)	222 (55.7)	497 (55.1)	1400 (23.5)
$AUC_{(0\text{-}inf)}$, h·ng/mL	75.9 (44.1)	97.8 (92.2)	223 (55.9)	500 (55.2)	1410 (23.6)
CL/F, L/h	65.9 (44.0)	102 (92.2)	89.7 (55.9)	80.2 (55.2)	56.8 (23.7)
V_z/F, L	248 (42.9)	401 (57.2)	420 (37.1)	407 (52.4)	314 (26.5)
$t_{1/2}$, hours	2.61 (39.6)	2.72 (40.5)	3.25 (29.4)	3.52 (8.38)	3.83 (8.79)

Geometric mean (%CV) values shown unless otherwise noted.
1: Median (range)

- Food (standardized high-fat, high calorie meal) led to a decrease of 19% in C_{max} and 15% in AUC compared to fasted conditions (at a dose of 20 mg)
- Plasma exposures in elderly and younger adult subjects were deemed comparable (at a dose of 20 mg), as Elderly plasma PK exposures (N=3) were fully contained within the observed range of younger adults (N=6, at same dose)

MAD: E2511 Clinical Pharmacokinetic Results

- There was little or no accumulation observed following 14 days of dosing (Figure 4)
- There was no evidence of time dependent-kinetics

Figure 4. MAD: E2511 Plasma Concentration-Time Profiles and PK Parameters

Parameter (SD)	10 mg QD		20 mg QD		40 mg QD	
	Day 1 (n=6)	Day 14 (n=6)	Day 1 (n=6)	Day 14 (n=5)	Day 1 (n=6)	Day 14 (n=6)
C_{max} ng/mL	47.4 (88)	81.7 (50.2)	86.1 (32.3)	91.8 (22.3)	110 (59.9)	95.0 (35.9)
t_{max}, hours[1]	1.0 (0.3, 1.5)	1.0 (0.5, 2.5)	1.3 (1.0, 1.5)	1.0 (0.5, 1.5)	1.0 (0.5, 2.0)	1.0 (0.5, 2.0)
$AUC_{(0\text{-}24h)}$, ng·h/mL	116 (57.1)	140 (24.6)	247 (22.7)	271 (16.2)	276 (34.6)	309 (30.8)
CL/F, L/h	85.7 (57.4)	71.7 (24.6)	80.4 (22.8)	73.7 (16.2)	145 (34.7)	129 (30.8)
V_z/F, L	355 (43.3)	478 (26.7)	431 (20.7)	448 (20.9)	682 (25.4)	792 (39.0)
$t_{1/2}$, hours	2.87 (46.9)	4.63 (19.2)	3.72 (20.8)	4.21 (12.7)	3.27 (31.0)	4.25 (17.8)
R_{ac}, C_{max}[2]	N/A	1.06 (132)	N/A	0.997 (48.3)	N/A	0.863 (34.9)
R_{ac}, AUC[3]	N/A	1.2 (57.8)	N/A	1.03 (25.2)	N/A	1.12 (19.1)
Ros^4	N/A	1.2 (38.1)	N/A	1.02 (25.1)	N/A	1.12 (19.2)

Geometric mean (%CV) values shown unless otherwise noted. N/A: not applicable.
1: Median (range);
2: R_{ac} C_{max}: Accumulation ratio determined based on C_{max} [Day 14]/ C_{max} [Day 1];
3: R_{ac} AUC: Accumulation ratio determined based on $AUC_{(0\text{-}24h)}$ [Day 14]/ $AUC_{(0\text{-}24h)}$ [Day 1];
4: R_{os}: Time dependency ratio was determined based on $AUC_{(0\text{-}24h)}$ [Day 14]/ $AUC_{(0\text{-}inf)}$ [Day 1]

Conclusions

- E2511 presents an adequate single and multiple dose safety profile in healthy adults up to the currently highest evaluated doses (80 mg PO in SAD; 40 mg QD PO in MAD)
- E2511 has shown predictable single and multiple dose PK with a short plasma half-life that is consistent with human PK projections based on non-clinical data
  - Dose-proportional plasma PK over the dose range of 5 to 80 mg (in the SAD) and time-invariant PK (up to at least 40 mg QD in the MAD)
  - Mild effect of food on rate and extent of plasma E2511 exposure supports dosing without regards to food
  - Plasma E2511 exposures (C_{max}, AUC) in a small group of elderly subjects suggest there is no need for dose adjustment in the target population
- These results support further development of E2511 as a disease-modifying therapy for neurodegenerative diseases

References
1. Ferreira-Vieira TH, et al. Curr Neuropharmacol. 2016;14(1):101-15. 2. Hampel H, et al. Brain. 2018;141(7):1917-33. 3. Mufson EJ, et al. Expert Rev Neurother. 2008;8(11):1703-18. 4. Ginsberg SD, et al. J Neurochem. 2006;97(2):475-87. 5. Hefti F. J Neurosci. 1986;6(8):2155-62. 6. Hagg T, et al. Exp. Neurol. 1988;101:303-12. 7. Hilgert M, et al. Neurochem Res. 2003;28:467-72. 8. Wu K, et al. Brain Res.2005;1061:107-13.

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If you have any questions about this poster, please email or call Eisai Medical Information at Esi_MedInfo@eisai.com or 888-274-2378

*" These results support further development of E2511 as a **disease-modifying therapy for neurodegenerative diseases"***

The data is **validating & increasing interest in NeuroRestore** ACD856

https://www.alzecurepharma.se/en/alzecure-receives-eu-grant-for-phase-2-clinical-trial-of-neurorestore-acd856-for-alzheimers-disease/
https://link.springer.com/article/10.1007/s00213-023-06410-x

AlzeCure's ACD856 in Comparison to Eisai's E2511

	Eisai E2511	AlzeCure ACD856
Mechanism of Action	Positive allosteric modulator	Positive allosteric modulator
Target	TrkA	TrkA, TrkB and TrkC
Type	Novel small molecule (<400 Da)	Novel small molecule (<400 Da)
IP	Patent granted	Patent granted in US, Japan, EU and China, several territories are processing applications
Stage of dev.	Phase I: SAD/MAD, half-life = 3.2 h	**Phase I: SAD/MAD, half-life = 20 h**
Effect on neurotransmitters	Yes ACh	Yes Serotonin, noradrenaline and dopamine
Effect on neurite outgrowth	No, not reported	**Yes, *in two different in vitro models***
Neuroprotective	Yes, in two in vivo models	Yes, in two in vitro models
Effect on cognition	Not reported	**Yes, *cognitive enhancement in several models***
Effect on depression	Not reported	**Yes, *and long-term effects + additive to SSRI***
Anti-inflammatory effects	Not reported	**Yes, *both in vivo & in vitro***

AlzeCure: Cells. 2021; Drug Discov Today 2022; Psychopharmacology, 2023, International J. Mol. Sciences 2023
Eisai: AAIC, P51985, 2021; ADPD, P186, 2022; AAIC, P62590 and P66208, 2022

Eisai AlzeCure

Alzstatin® – *gamma-secretase modulator targeting amyloid production for prevention and treatment of Alzheimer's disease*

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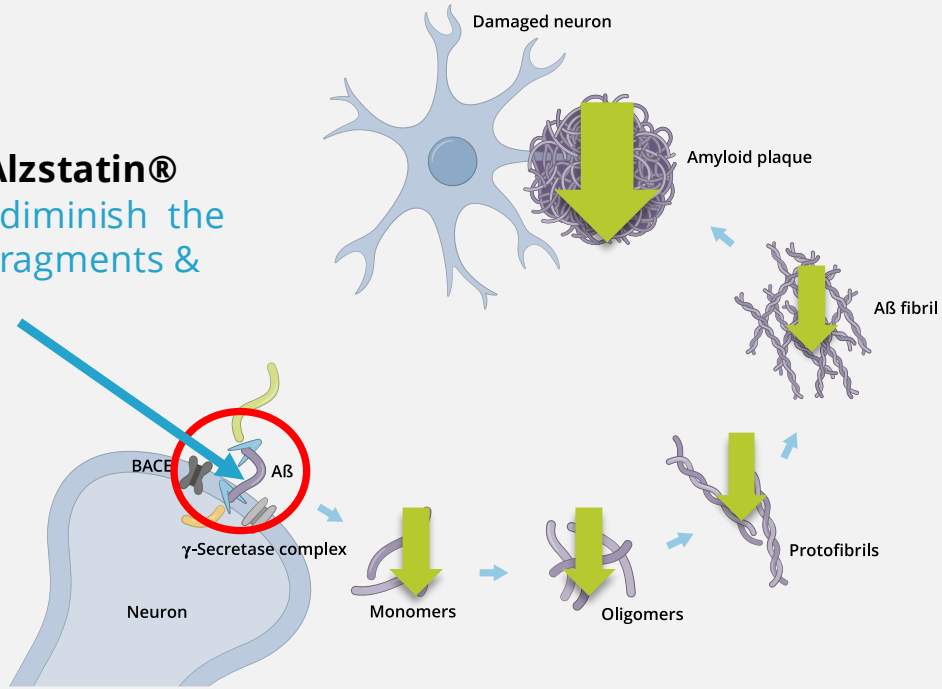
The Alzheimer's Brain and its Destruction by Toxic Protein

The Amyloid Cascade

Toxic protein formations, built up of Aβ42, are harming and destroying brain structures

AlzeCure's GSM[1] **Alzstatin® reduces Aβ42** to diminish the build-up of toxic fragments & plaque



1) GSM = Gamma Secretes Modulator – Reducing build-up of Aβ-42 and plaque

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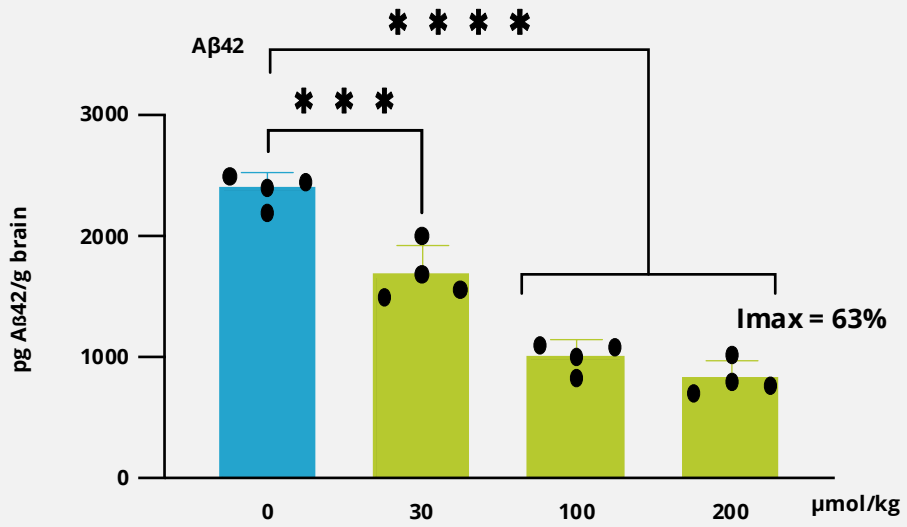
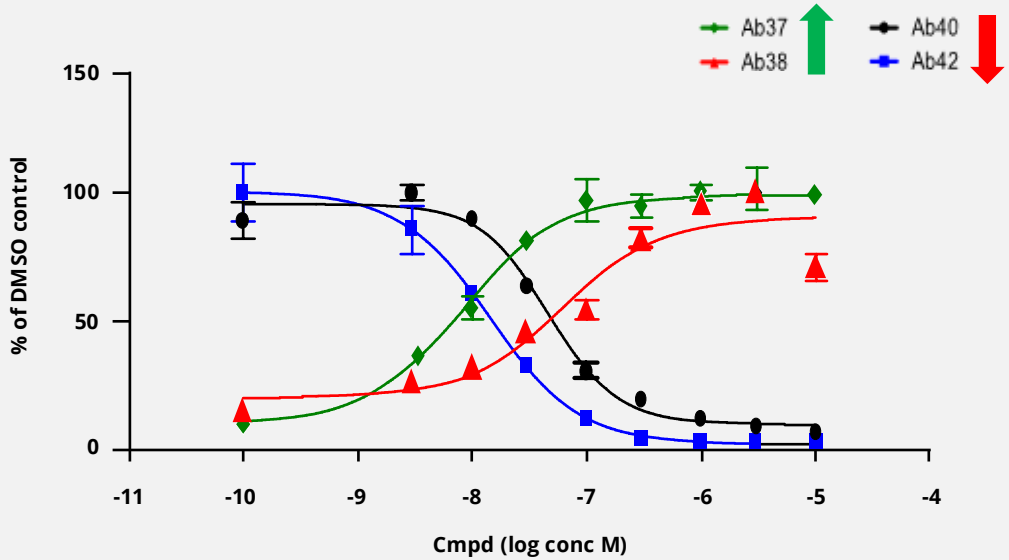
Alzstatin® – Potent Reduction of Toxic Aβ42 & Increasing Protective Aβ37 & Aβ38

Alzstatin® potently reduces the amount of toxic brain Aβ42 in animals



Alzstatin® reduces toxic Aβ42 and Aβ40, while increasing protective Aβ38 and Aβ37 peptides



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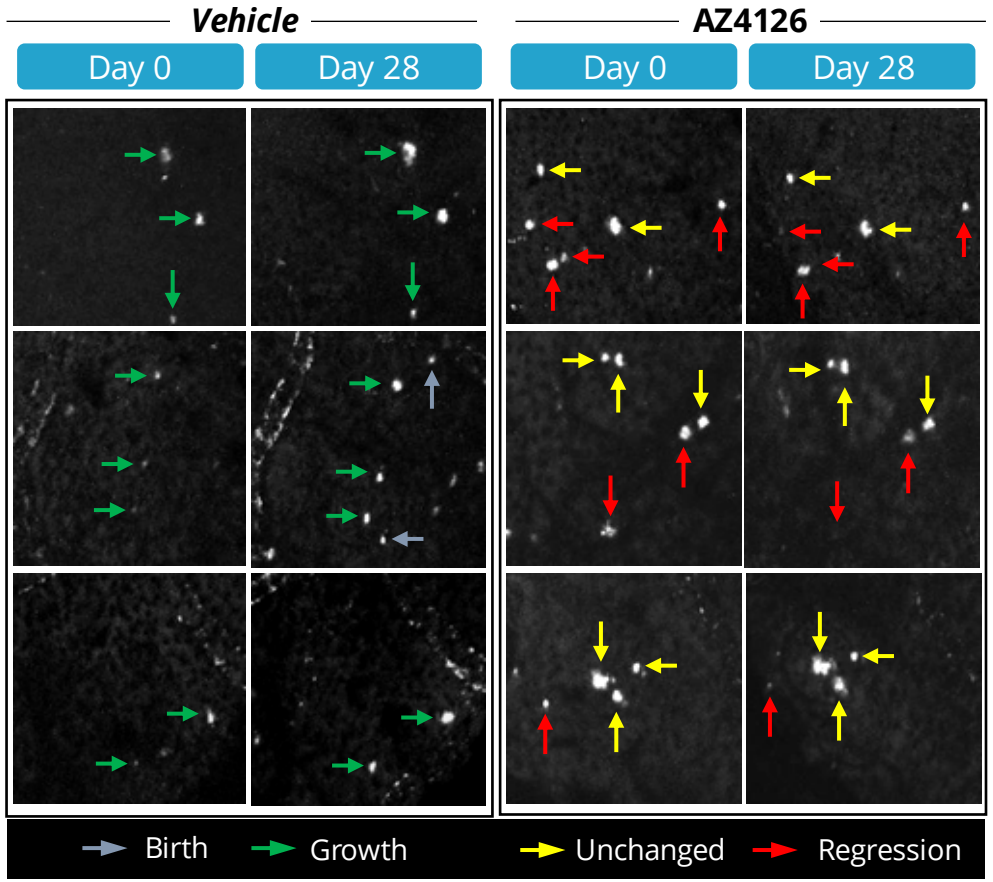
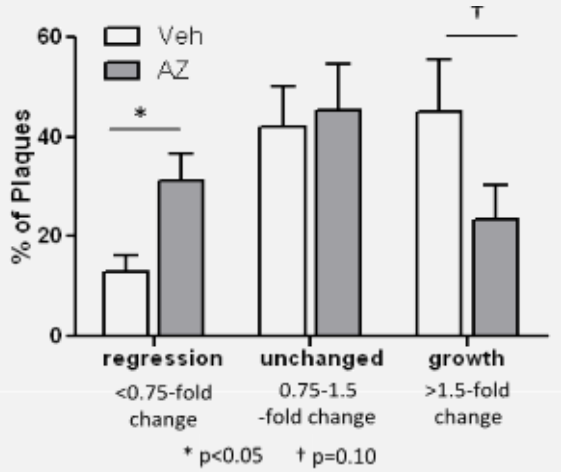
New preclinical data shows Induced Plaque Regression

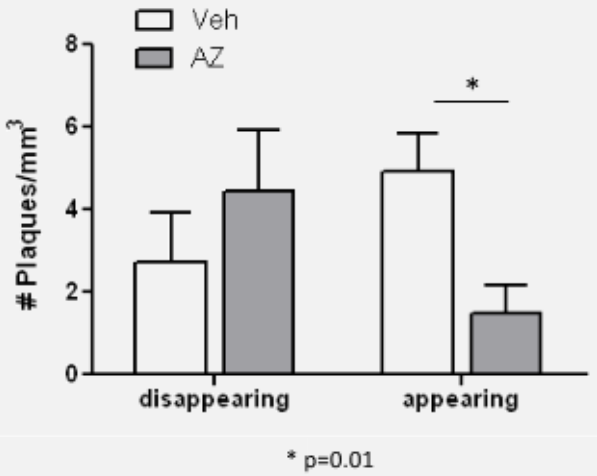
Two-photon-study preclinical study in APP/PS1 mice



Distribution of plaque growth & regression



Plaque appearance or disappearance



28-day GSM treatment

Reduces amyloid **plaque growth**

Decreases new plaque appearance

Induces plaque regression[1]

Nordvall et al, Feb. 12, 2025: γ-Secretase Modulation inhibits Amyloid Plaque Formation and Growth and stimulates Plaque Regression in APP/PS1 Mice, JPET, Feb 12, 2025: https://jpet.aspetjournals.org/article/S0022-

1) Plaque regression not reported for Gamma- or Beta-secretase inhibitors suggest that increase in Ab37 could be responsible

Multiple Potential Treatment Populations for Alzstatin – Maintenance, Combination & Preventive Therapy

Maintenance therapy - in patients with established Alzheimer's disease

- Treatment after initial plaque clearance by monoclonal antibody treatment (as initially proposed by Lilly) e.g., with: Lecanemab (Eisai/Biogen/Bioarctic) & Donanemab (Lilly)

Combination therapy - together with monoclonal antibody treatment - early AD

- Combine plaque clearance by monoclonal antibody treatment and reduction of Aβ42 production by GSM

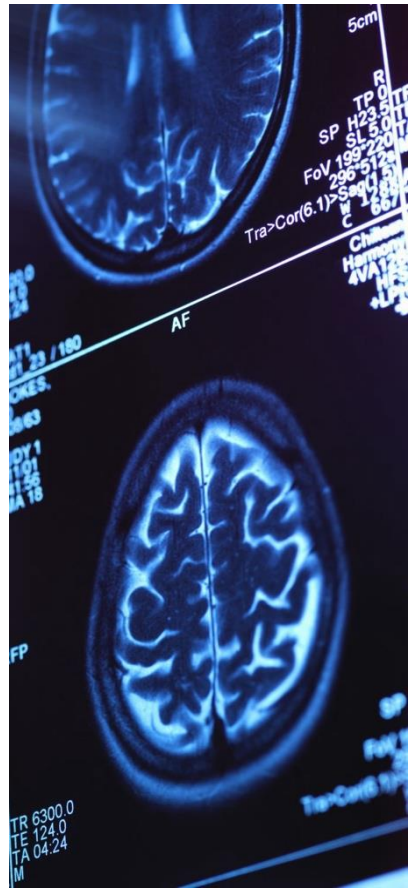
Preventive therapy - based on genetic risk factors[1] and biomarkers

- Early stand-alone treatment before onset of symptoms and any major neurodegeneration occurs (prior to rapid increase in Tau pathology)
- Prevents build-up of amyloid – an early pathological feature of AD
- Familiar forms of the disease (incl. Downs syndrome) suitable for initial proof of concept clinical studies

1) E.g. ApoE4

Early clinical Proof-of-Mechanism – Already in Phase I

- Phase I will demonstrate **proof of mechanism** (PoM) and **central target engagement**
  - SAD/MAD studies conducted in **healthy volunteers + Alzheimer's patients**
  - Evaluation of safety and tolerability after single and repeated administration – SAD/MAD study
  - Possibility to **explore biomarker effects** showing central target engagement already in **Phase I**
    - Show **reduction of toxic Aβ-species** – Aβ42/40
    - Show **increase of shorter protective Aβ-forms** – Aβ37/38
    - Measurements done both in CSF and plasma – using established **biomarker kits**



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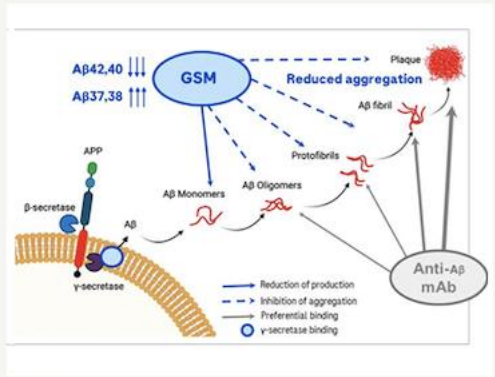
Interim phase II data on a GSM by Roche expected in 2026

RG6289, a FIC oral γ-secretase modulator in Alzheimer's disease

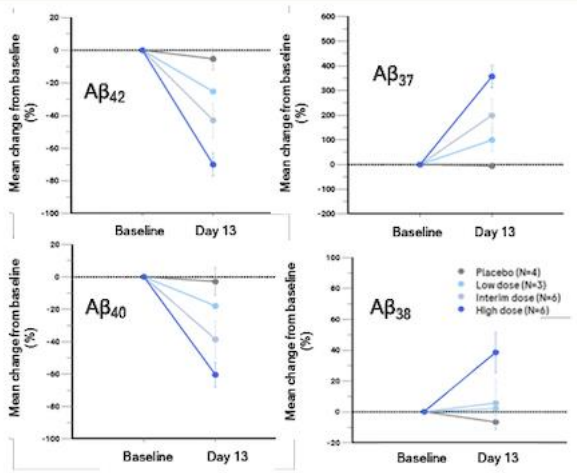
Targeting amyloid precursor protein processing to prevent Aβ-aggregation

GSMs reduce Aβ aggregation[1]



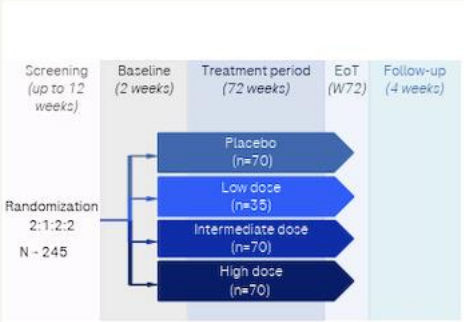
- RG6289 a potentially first-in-class oral GSM with high potency and selectivity
- GSMs alter APP processing: Reduction of Aβ42/40 and elevation of Aβ38/37
- Selective for APP with no effect on Notch
- GSMs prevent amyloid accumulation and halt plaque formation in animal model

Ph I dose escalation results for RG6289[2]



- Daily administrations of RG6289 decreased Aβ42/40 and increased Aβ37/38 concentrations in CSF of healthy volunteers in a dose dependent manner

Ph II (GABriella) study design[3]



- Ph IIa (GABriella) investigates RG6289 in individuals at risk for or at prodromal stage of AD exploring safety, tolerability and effects on AD-related biomarkers
- Interim data expected in 2026

The data is **validating & increasing interest in Alzstatin®**

PainLess – targeting unmet medical needs within pain

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Introduction to our platforms PAINLESS

Osteoarthritis & severe pain conditions

> 300 million patients

Project: **ACD137**

Negative allosteric modulator of TrkA-receptors in research phase

Neuropathic pain

> 600 million patients

Project: **ACD440**

Topical TRPV1 antagonist in clinical Phase II

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ACD137 – Non-Opioid Treatment of Osteoarthritis & Severe Pain

Attractive target population	E.g., **osteoarthritis** in patients who have experienced insufficient pain relief from 1st line standard of care or unacceptable side effects
Clinical validation	Mechanism with **strong validation** – step-changing clinical efficacy with novel anti-NGF mAbs - sets the standard for future therapies
Blockbuster opportunities	**Blockbuster opportunities** for NGF therapies that would avoid adverse events and allow non parenteral routes of administration

Differentiation factors for TrkA-NAM ACD137[1]

- **TrkA ACD137 selective MoA** vs anti-NGF antibodies also effecting p75 signaling
  - Maintain **potent clinical efficacy**
  - **Better safety profile**
- Convenient **oral administration** - small molecule compound
- **No addiction** compared to opioids

1) OA = Osteoarthritis ^) LBP = Lower Back Pain
https://www.alzecurepharma.se/sv/wp-content/uploads/sites/3/2025/09/alzecure-trka-nam-neupsig-2025-poster.pdf
https://www.alzecurepharma.se/en/alzecure-presents-new-positive-data-for-the-trka-nam-pain-project-against-osteoarthritis/

ACD137 positions AlzeCure in next-generation TrkA pain therapies

Compound	Company	TrkA (nM)	TrkB (nM)	TrkA vs TrkB	Status	Indication
ACD137	**AlzeCure**	**0.87**	**26 400**	**30,300**	**Preclin**	**OA[1] & other pain conditions**
Cmpd #10 AK1830	Array Bio. Ashai Kasei	0.038	210	5,500	Phase IIb	OA LBP^
Cmpd #23	Pfizer	0.64	145	230	inactive	OA
Cmpd #1	Merck	99	>81000	>820	inactive	OA

AlzeCure has synthesized novel & highly potent & selective TrkA-NAM's … and is a follower to Asahi Kasei's asset which has entered phase IIb with expected read-out in 2026

ACD137 demonstrates anti-NGF–like efficacy with improved safety profile

TrkA-NAM ACD137 – Efficacy on par with NGF antibody

- We have used the rat **MIA model** to assess the cartilage degeneration, localized inflammation, and pain behaviors after administration of TrkA-NAM compounds, including **ACD137**, as well as **Tanezumab**

- **Results show:**
  - Potent **pain relief** in both movement-induced and evoked pain
  - Significant **anti-inflammatory effect** was observed following administration of TrkA-NAM compounds

- The **analgesic effect** of ACD137 is **similar to the effect of the anti-NGF antibody Tanezumab**, which have in several clinical trials demonstrated significant and robust pain relief

- ACD137 was also found to display a **protective effect towards articular cartilage damage** and significantly improved a number of cartilage and knee joint structural parameters

- ACD137 was **well tolerated** with **no clinical symptoms or histopathological findings** of rapidly progressing OA, a problematic side effect observed for anti-NGF antibodies, nor were any effects seen on neuronal ganglia

The results emphasizes the broad applicability of our TrkA-NAM ACD137 in various severe pain states, including osteoarthritis

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ACD440 – Novel TRPV1 antagonist in clinical phase for neuropathic pain

Project overview

Emanates from Big Pharma

- Approximately **20M USD** already **invested** in project development
- **Mode of action confirmed** in several Phase 1 clinical trials
- Synthesized compound and formulation developed

TRPV1 – **Optimized for local delivery**

- The vanilloid receptor subtype 1 (TRPV1) is expressed in nociceptive sensory neurons
- TRPV1 is upregulated in the skin of patients with neuropathic pain
- **Strong scientific support** for peripheral/local treatment with TRPV1 antagonists of **both neuropathic & nociceptive pain**

Positive clinical trial results in phase Ib & IIa

- Developed **topical gel formulation to avoid AEs** associated with systemic TRPV1 blockade
- **Clinical trial** with topical formulation was initiated and **successfully finalized**
- Phase Ib study addressed **safety, tolerability & efficacy – POSITIVE OUTCOMES**

Presented detailed positive phase IIa data

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Positive phase IIa results for First-in-Class ACD440

- Demonstrate **Positive Proof-of-Mechanism** (PoM) results **in patients** with chronic **peripheral neuropathic pain** in a placebo cross-over trial
- The patients have had **chronic pain** for many years & were on **concomitant medication**
  - A **significant analgesic effect** on pain induced by cold and heat.
    - The data are **in line with previously** reported phase Ib **results**
  - **Pain reduced** by appr. **50%** - a **clinically significant magnitude**
- The **bedside test identified eligible patients**
- **Well tolerated** as a topical gel on the skin, which shows **suitability for continued clinical development**

Now preparing for next phase II and phase III trial

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Strong regulatory momentum in US and EU

Granted orphan drug designation (US & EU)

- **FDA granted orphan drug designation** for erythromelalgia
- European Medicines Agency (EMA) **granted orphan designation** in the **EU**
- **Positive FDA feedback** supporting **Phase II/III pivotal** trial pathway

EUROPEAN MEDICINES AGENCY

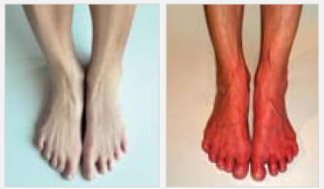
FDA

Reduced regulatory risk across key markets

Erythromelalgia

- Erythromelalgia is a **rare chronic** painful disorder – ”burning feet syndrome” existing in **children & adults**
- Triad of redness, swelling and intense pain
- Pain comes in attacks, flares, **triggered by heat** or exercise
- One **pain** flare **can last** for an hour and **up to days**

Flare on Feet



BEFORE DURING

Flare on Face

BEFORE DURING

Flare on hands

BEFORE DURING

- Divided into Primary erythromelalgia, is mostly hereditary
- **No efficacious medical treatment exists**

https://www.alzecurepharma.se/en/alzecures-pain-project-acd440-granted-orphan-drug-status-in-the-us-by-the-fda/
https://www.alzecurepharma.se/en/alzecure-receives-positive-fda-response-regarding-phase-ii-iii-studies-with-acd440-in-a-rare-disease/

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Summary

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Key Investment Highlights in AlzeCure

- Targeting areas of **significant unmet medical needs**
- **Strong team** with extensive experience and track record – from idea to clinic
- **Platforms** with **first-in-class properties** and potential **game-changers**
- **Parallel investments** in several candidates and potent **follow-up programs**
- **Multi-billion dollar** market **opportunities**
- Evolved from a discovery into a **phase II company** – **supported by EIC***

European Innovation Council

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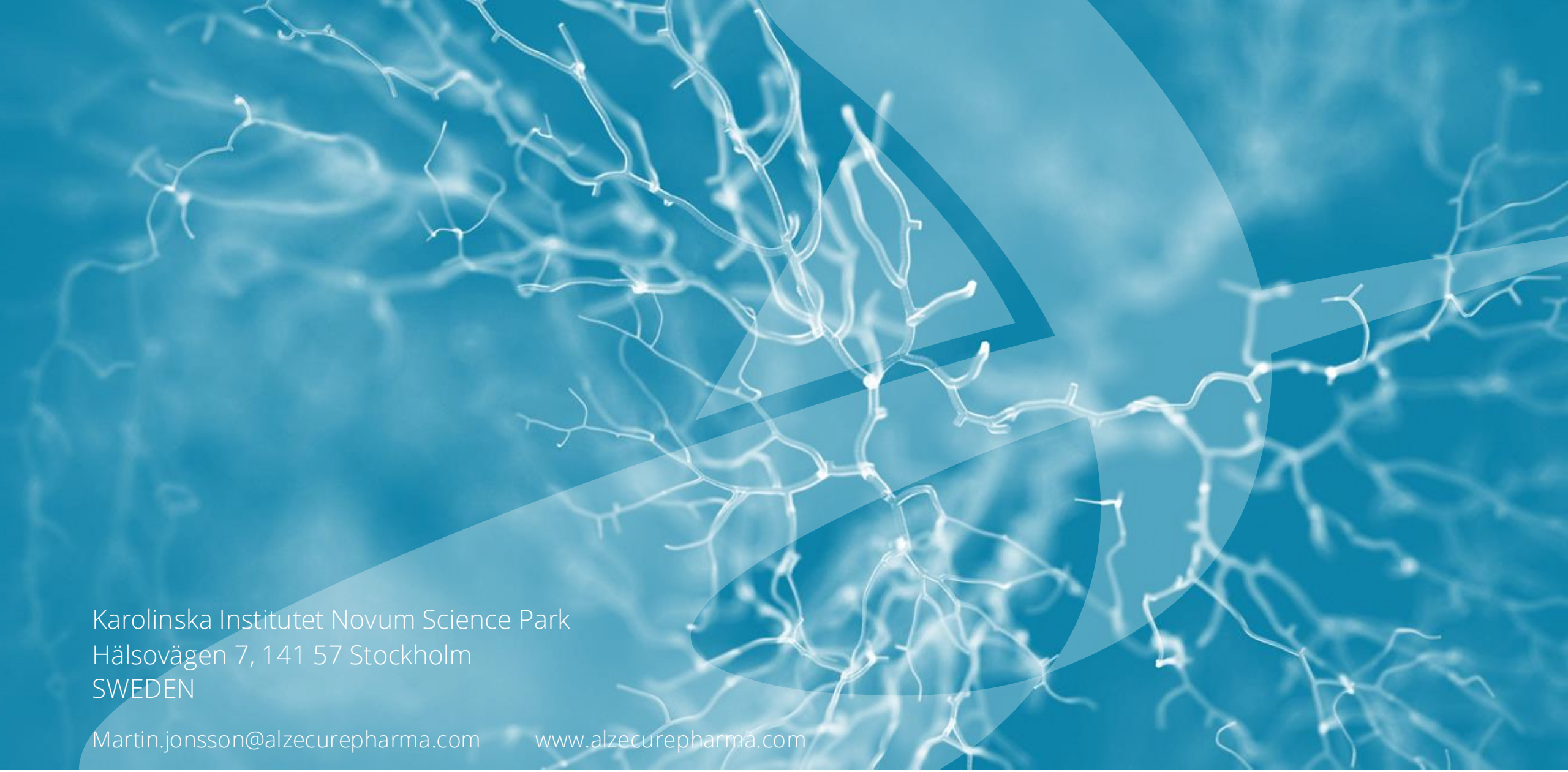

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