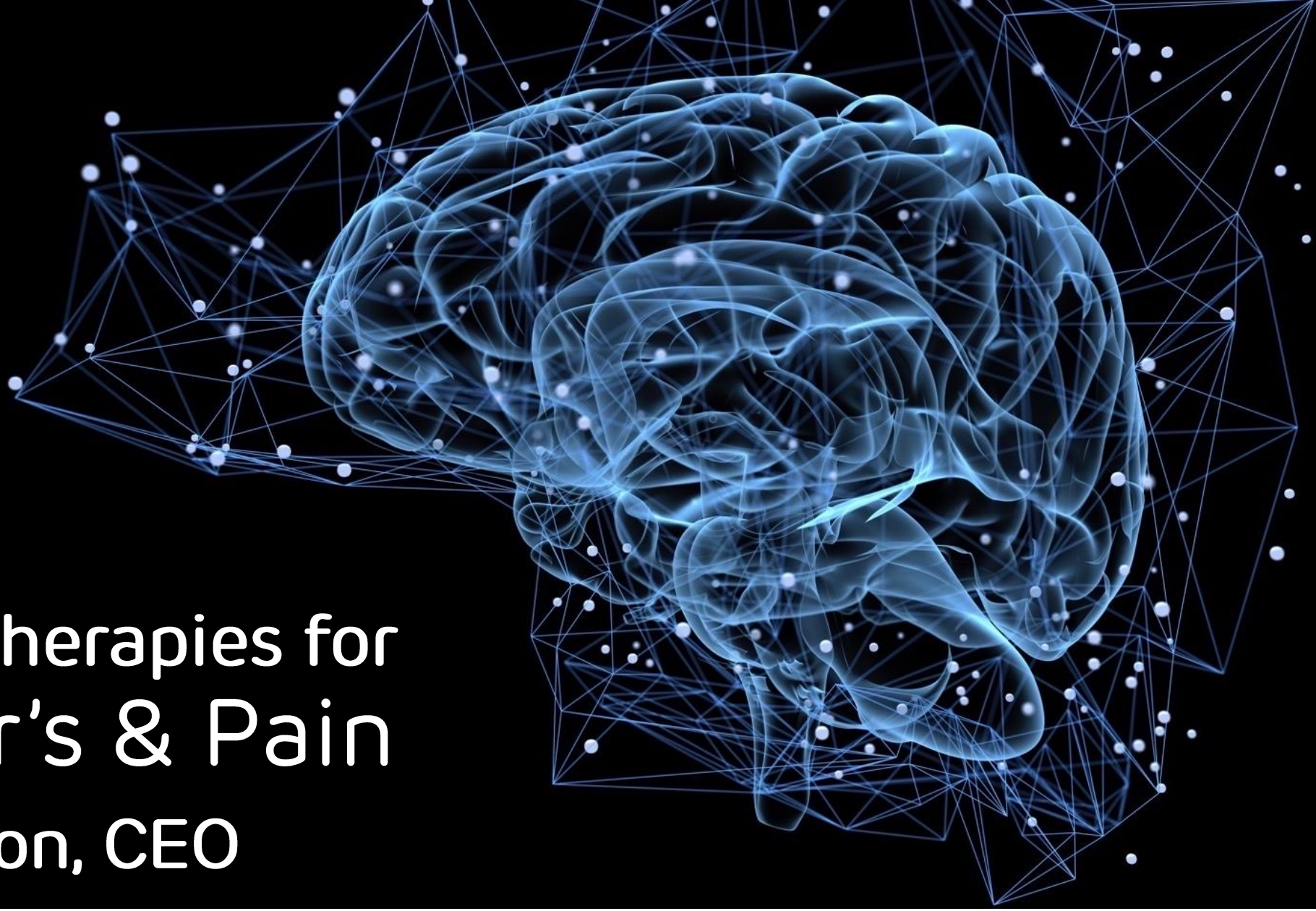
June 11, 2025



Developing therapies for Alzheimer's & Pain

Martin Jönsson, CEO

European Innovation Council

AlzeCure

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AlzeCure

AlzeCure Pharma – in brief

- Working in **Alzheimer's Disease** (AD) and **Pain** – Hugh 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**
  - **Alzstatin®** – An innovative preventive & disease-modifying treatment against Alzheimer's (AD)
  - **NeuroRestore®** – A novel symptomatic treatment for cognitive disorders, e.g. AD with disease modifying potential
  - **Painless** – Innovative projects for osteoarthritic & neuropathic pain

- Listed on **Nasdaq First North Premier** Growth Market, **Sweden**, since Nov. 2018 (Ticker: ALZCUR)
- Market cap: **SEK 300m** (June 9, 2025)
- Cash position: **SEK 20.9m** (Q1 2025 interim report)

European Innovation Council

AlzeCure

Our Business Model

- We 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

AlzeCure

A pipeline of small-molecule programs
– Multiple candidates increase chance of success

Platform	Candidate	Target	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
NeuroRestore®	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	ACD440	TRPV1 antagonist	Neuropathic Pain					
	ACD137	Negative allosteric modulator (NAM) of TrkA-receptors	Osteoarthritic Pain & other severe pain conditions					

Positive read-out Phase I trial
Safety, Tolerability & Target engagement

European Innovation Council
Grant for phase 2

Selected ACD680 as lead going forwards towards clinic

Positive read-out Phase IIa
Safety, Tolerability & Pain

Selected new CD
ACD137

Phase completed **Phase ongoing**

AlzeCure

Close cooperation with leading experts & institutions

Professor Bengt Winblad
Karolinska Institute

Professor Maria Eriksdotter
Karolinska Institute

Professor Henrik Zetterberg
Sahlgrenska and UCL

Karolinska Institutet

GÖTEBORGS UNIVERSITET
SAHLGRENSKA AKADEMIN

UCL

AlzeCure

Professor Jan Lundberg –Board Member

Former global head of R&D at Eli Lilly & global head of research at **AstraZeneca** joined AlzeCure's board of directors

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.

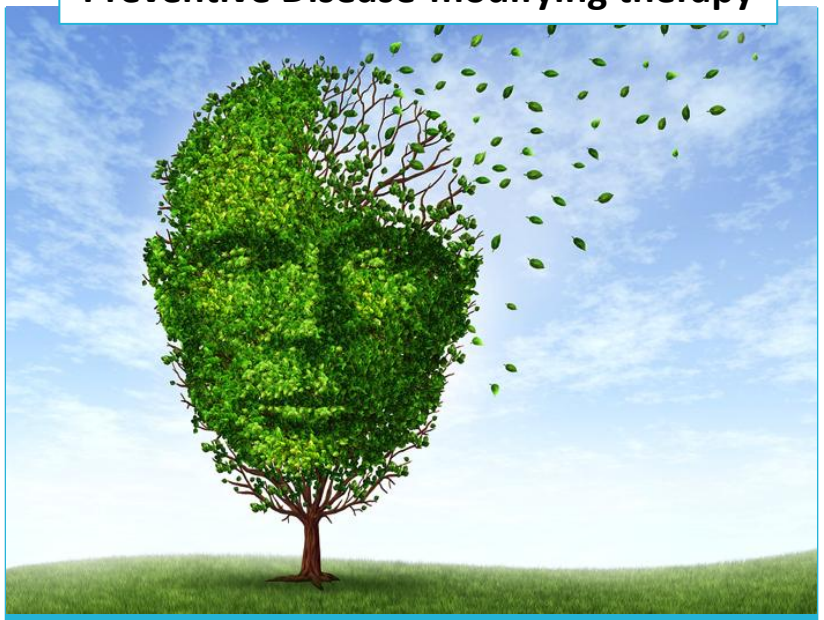
Professor Jan Lundberg

https://www.alzecurepharma.se/en/eli-lillys-and-astrazenecas-former-head-of-research-dr-jan-lundberg-invests-in-alzecure-and-is-proposed-for-election-to-its-board/

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

Preventing or delaying Alzheimer's

Alzstatin®

MoA: Gamma-Secretes-Modulator

Targeting Toxic Amyloid Production

- *Novel Oral Small Molecule*

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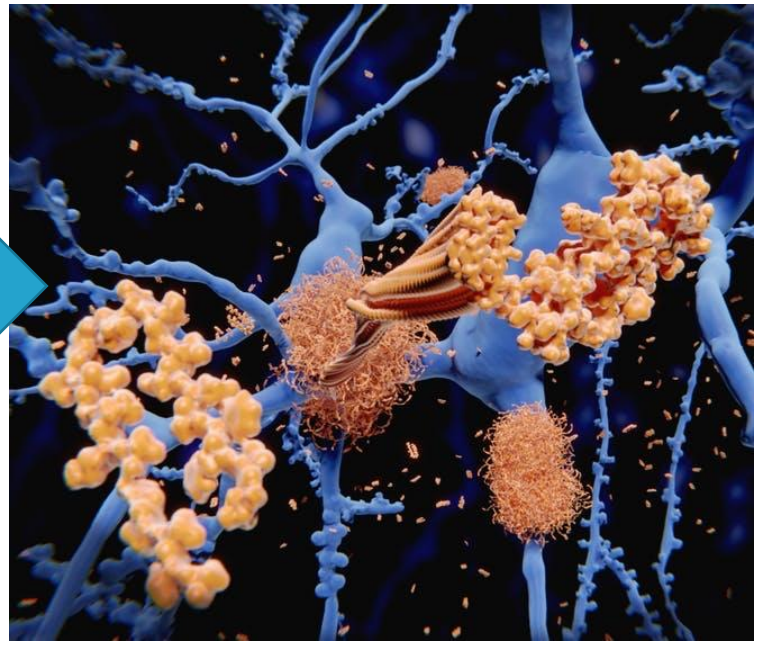
The Alzheimer's brain and its destruction

Toxic protein formations – **Aβ42** amyloid pathology & plaque – are harming and destroying the brain. The formation process is called the **Amyloid Cascade**



Toxic protein formations, built up of Aβ-42, are harming and destroying the brain structures.

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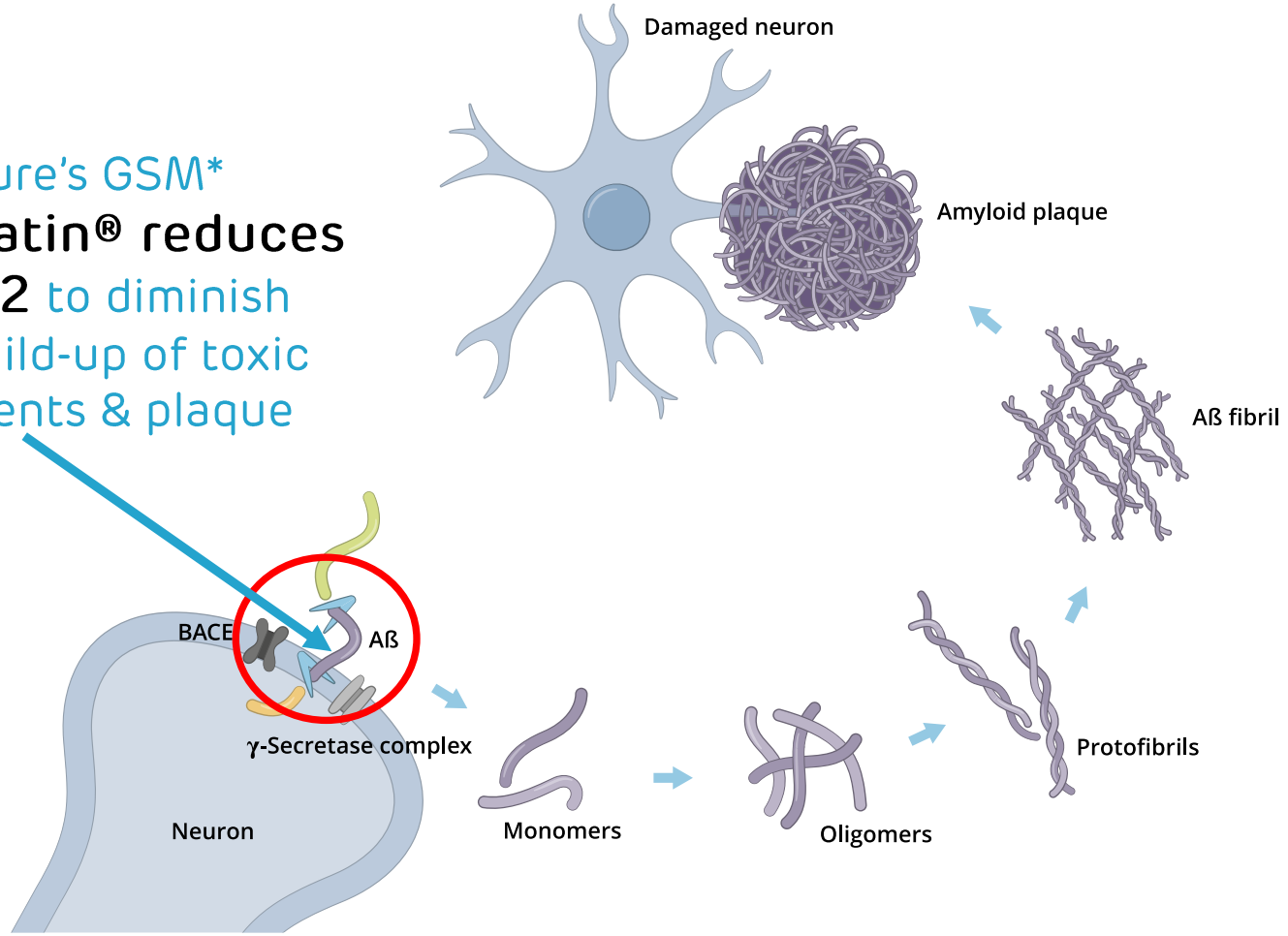
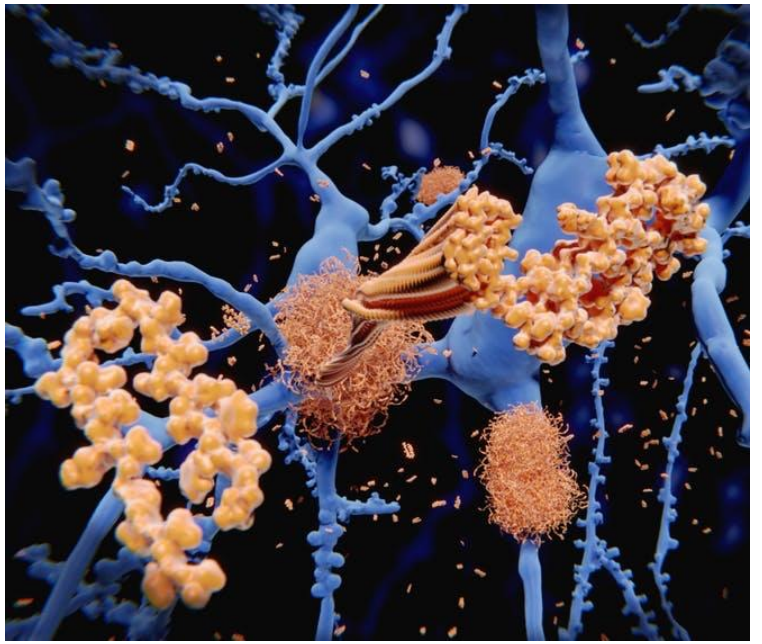
The Amyloid Cascade -Generates toxic & damaging fragments, including plaques, destroying neurons & brain structures

AlzeCure's GSM*
Alzstatin® reduces Aβ -42 to diminish the build-up of toxic fragments & plaque





Toxic protein formations, built up of Aβ-42, are harming and destroying the brain structures.

*) GSM = Gamma Secretes Modulator

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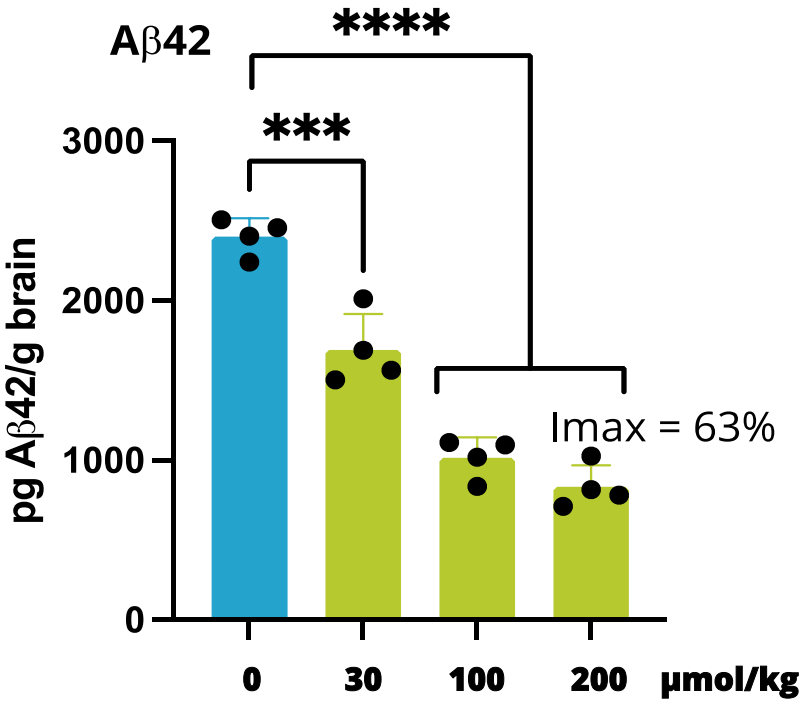
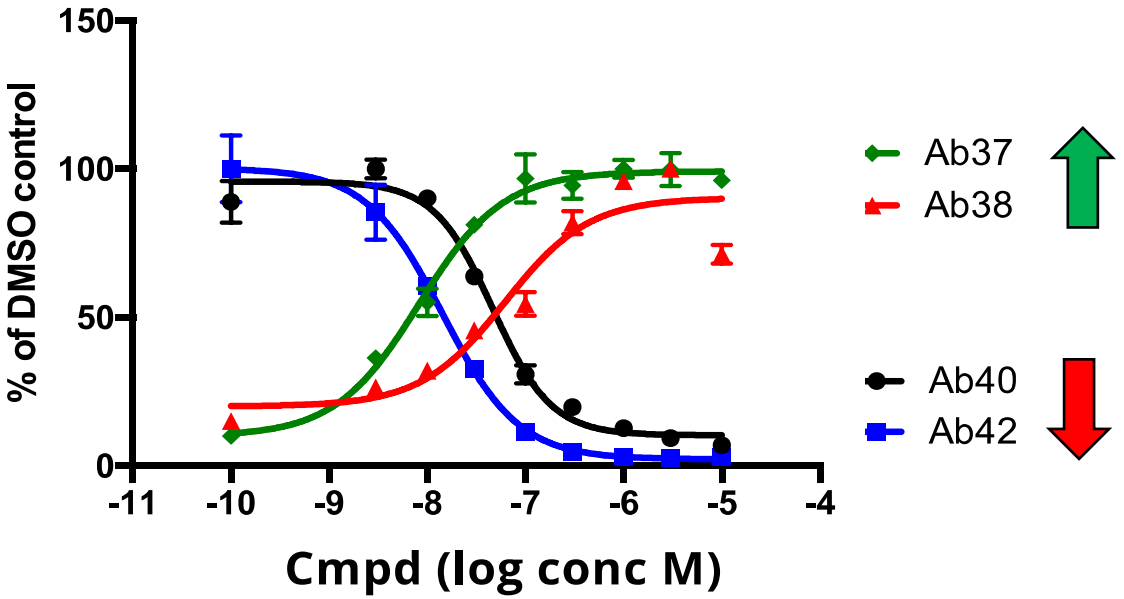
Alzstatin – potent reduction of toxic Aβ42 and increasing protective Aβ37 & 38



Alzstatin potently reduces the amount of toxic brain Aβ42 in mice



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

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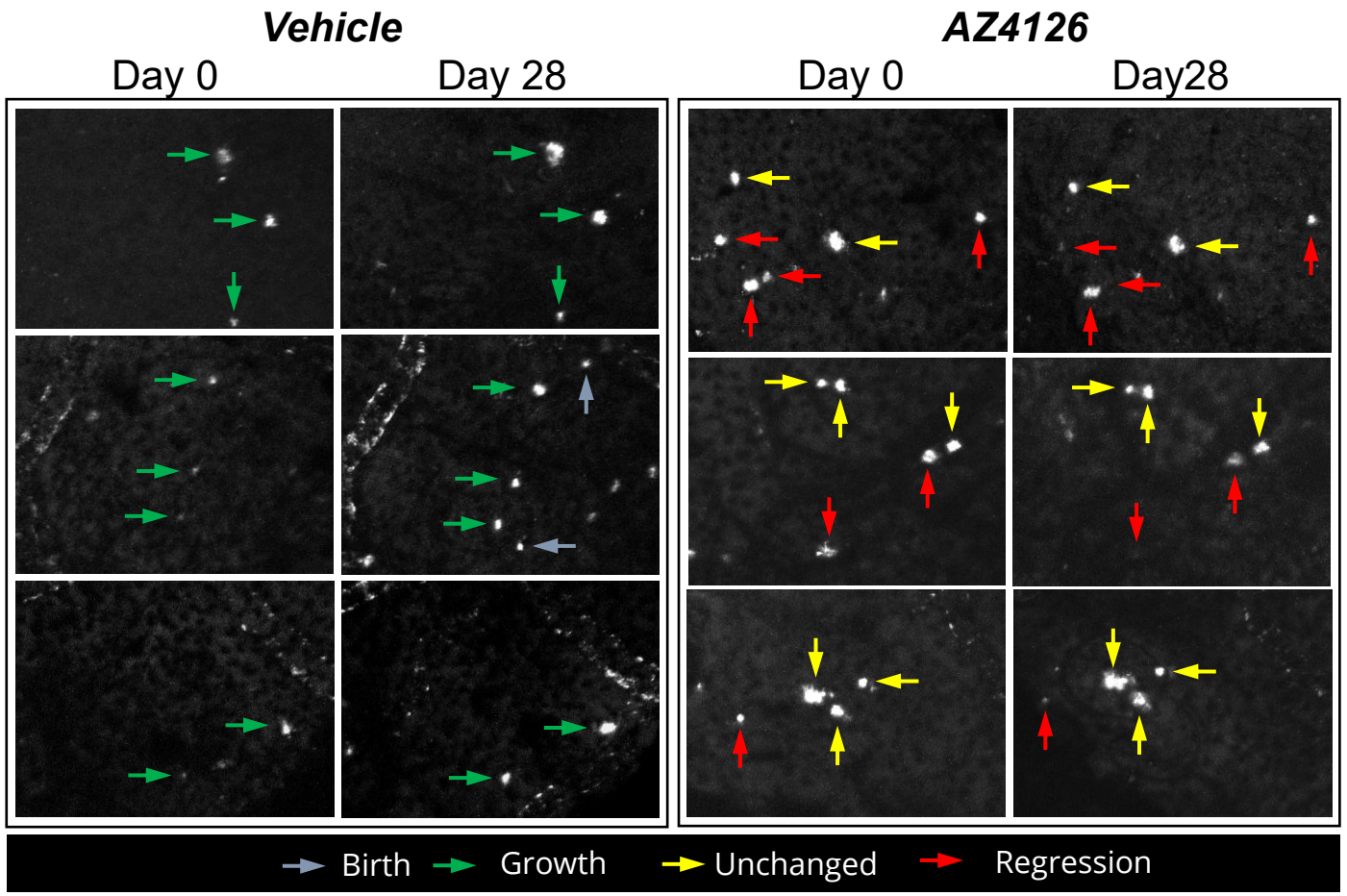
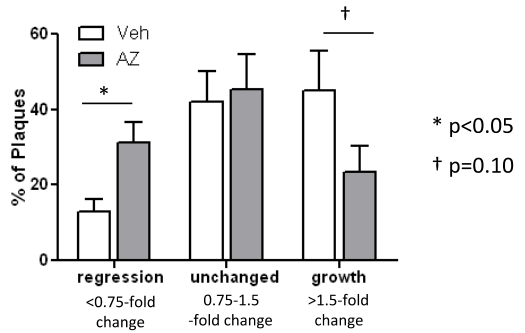
GSM induces plaque regression – New data

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



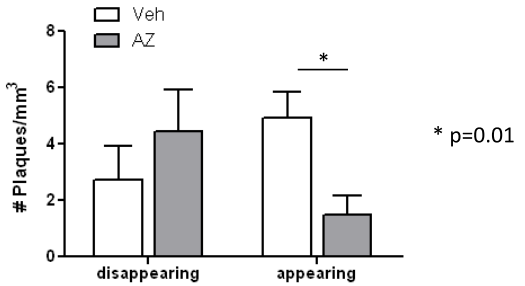
Distribution of Plaque Growth and Regression



* p<0.05

† p=0.10

Plaque appearance or disappearance



* p=0.01

28-day GSM treatment:

- **Reduces** amyloid **plaque growth**
- **Decreases new plaque** appearance
- **Induces plaque regression***

**Plaque regression not reported for Gamma- or Beta-secretase inhibitors suggest that increase in Aβ37 could be responsible*

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/S0022-3565(25)39613-8/fulltext

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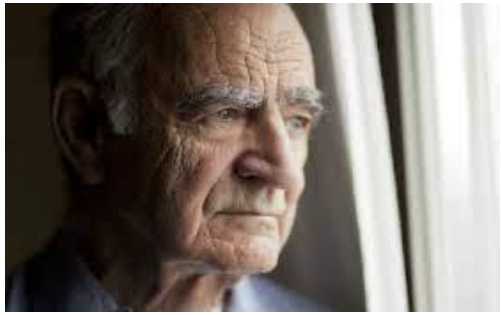
Multiple Target Populations - maintenance & preventive therapy

Maintenance therapy - in patients with established Alzheimer's

- 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* 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

*) E.g. ApoE4

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Attractive Profile
- Early Clinical Proof-of-Mechanism in Phase I/II

- Phase I will demonstrate PoM **and** central target engagement
  - **SAD/MAD studies conducted in healthy volunteers + AD patients**
  - Evaluation of safety and tolerability after single and repeated administration
  - Possibility to explore biomarker effects **showing central target engagement** already in Phase I
    - Aβ42/40 – show **reduction of toxic Aβ-species**
    - Aβ37/38 – show **increase of shorter protective Aβ-species**, establishing gamma-secretase involvement and MoA
    - Measurements done both in CSF and plasma – **biomarker kits available**

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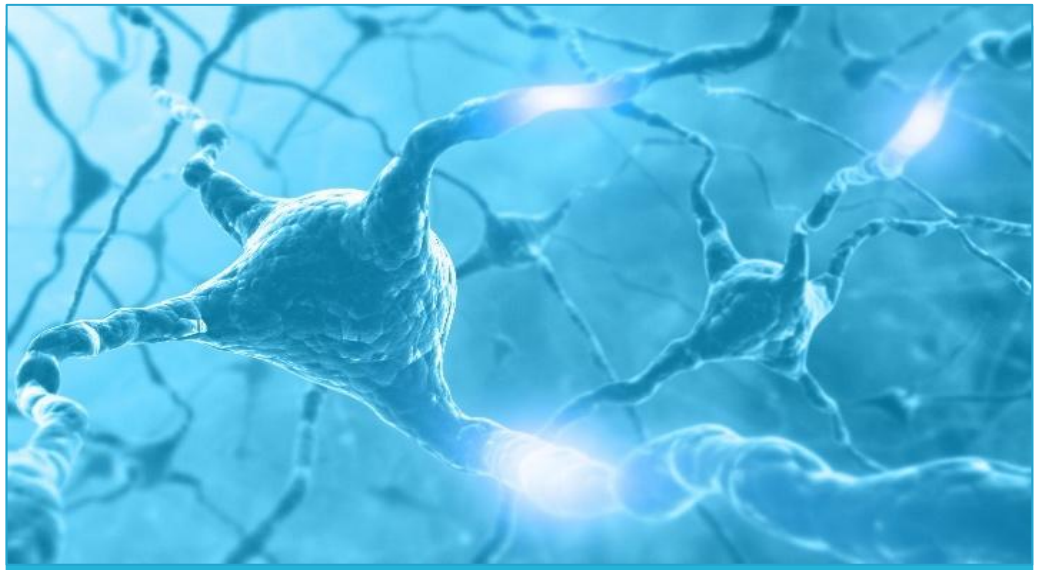
IP position – ACD680

- Recently submitted composition of matter patent application for ACD680
- Patent life expected until **2045**
- Additional 5-year market exclusivity in the USA → **2050**

Improving Learning & Memory Capabilities



NeuroRestore®

Trk-PAM

Improving Neuronal Function & Cognition

- *Novel Oral Small Molecule*

Shown safety, tolerability & target engagement in clinical trial phase 1

=> In preparation for ph 2

European Innovation Council

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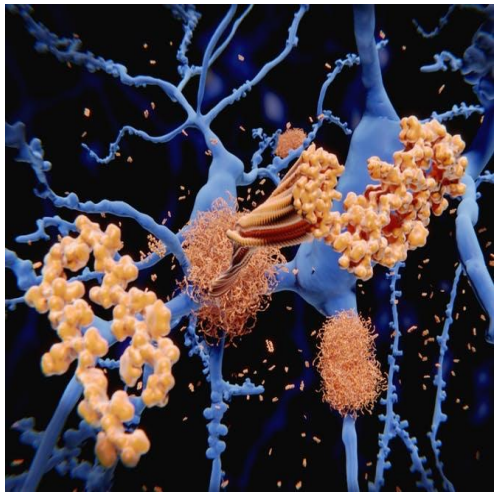
The Relevance of BDNF & NGF Signaling in Alzheimer's

- The neurotrophins Brain-Derived Neurotrophic Factor (BDNF) and Nerve Growth Factor (NGF) are **key for brain health and cognition**
- BDNF& NGF bind to their respective receptors, TrkB and TrkA
- 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, like the 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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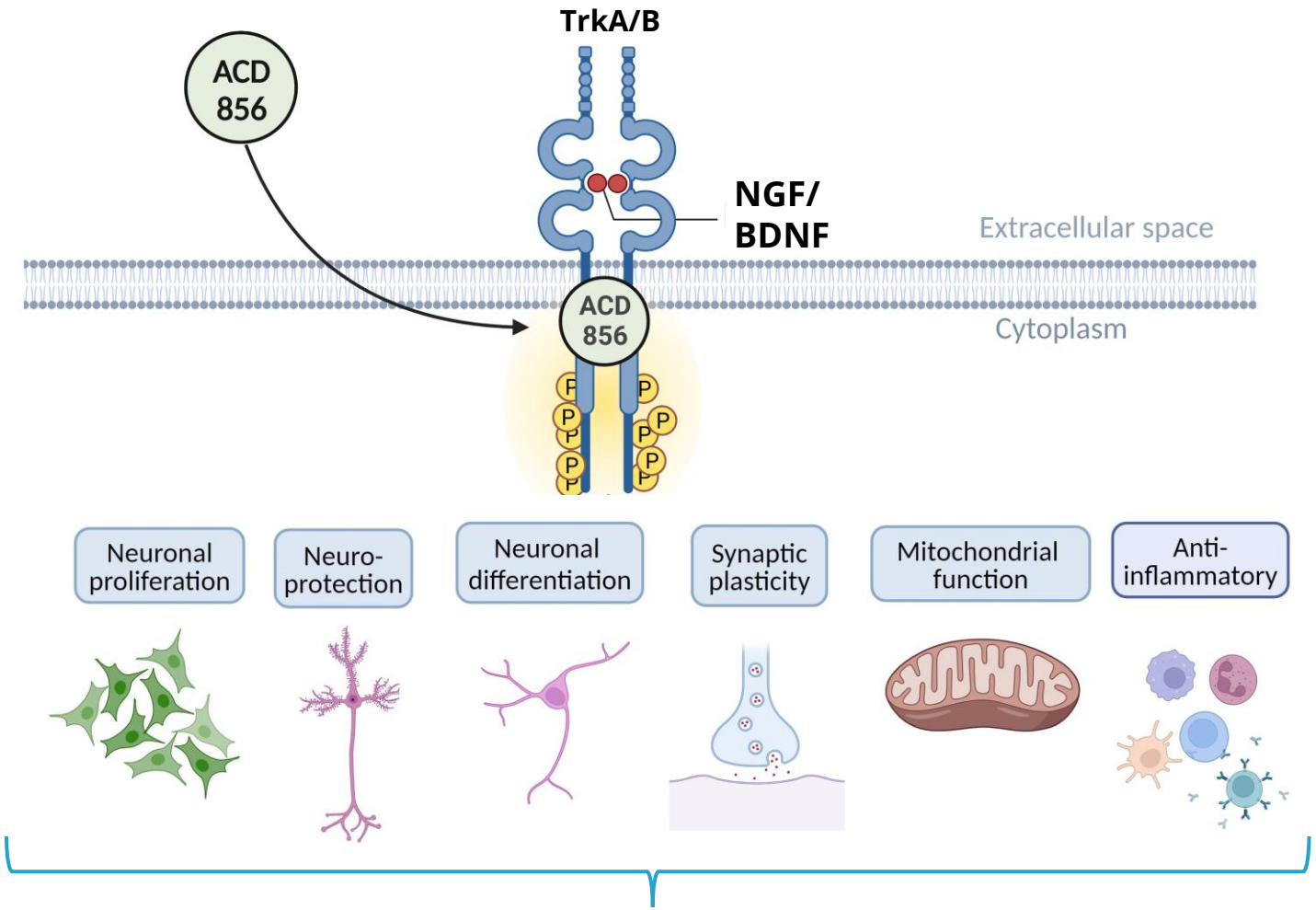
ACD856 - MoA & data supports Disease Modifying Potential

- ACD856 is a novel 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, Memory & Depression

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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NeuroRestore - Cognitive Enhancer Improving Learning and 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 and stored

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

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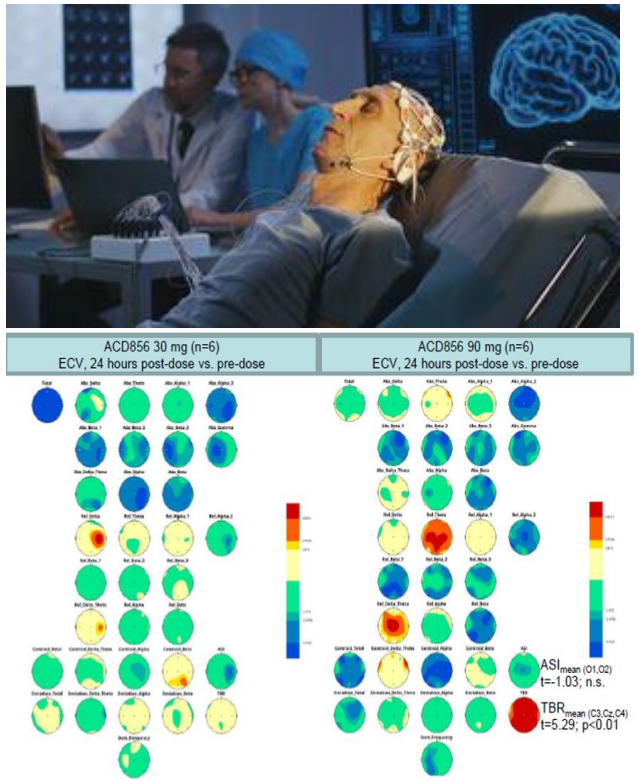
Phase I Study Summary

- 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

=> Now preparing for ph 2



Vigilance control brain maps for 30 and 90 mg cohorts

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

Awarded European Innovation Council Grant

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/

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NeuroRestore ACD856 – Candidate in Clinical Phase

- Patent in the US, China, Japan and Europe to 2039

AlzeCure receives US patent for NeuroRestore ACD856

Long Patent Time

AlzeCure Pharma AB (publ) (FN STO: ALZCUR), a pharmaceutical company that develops a broad portfolio of small molecule candidate drugs for diseases affecting the central nervous system, with projects in both Alzheimer's disease and pain, today announced that the United States Patent Office (USPTO) has issued a patent covering ACD856, which is being developed against Alzheimer's disease and other disorders with cognitive impairment.

USPTO has announced that they have now approved the company's patent application in the US, which refers to ACD856, the leading drug candidate in the NeuroRestore platform, which is being developed against Alzheimer's disease. The patent number is US 11,352,332 and the patent is valid until 2039.

ACD856 and other substances in the NeuroRestore platform stimulate several important signaling systems and signaling molecules in the brain such as BDNF (Brain Derived Neurotrophic Factor) and NGF (Nerve Growth Factor), which can lead to improved cognition. Previous preclinical studies have shown that AlzeCure's drug candidates strengthen communication between nerve cells and improve cognitive ability, including learning and memory functions. New preclinical results also show potential neuroprotective and disease-modifying effects with these substances. The biological mechanism behind NeuroRestore enables several indications, such as Alzheimer's and Parkinson's disease, but also depression.

=> In addition, being a NCE, there is 5 years of expected market exclusivity in the US => 2039 + 5 years = **2044**

https://www.alzecurepharma.se/en/alzecure-receives-us-patent-for-neurorestore-acd856/
https://www.alzecurepharma.se/en/alzecure-is-granted-european-patent-for-neurorestore-acd856/

AlzeCure

Our platform PAINLESS – Targeting Unmet Medical Needs within Pain

Osteoarthritis & severe pain conditions

> 300 million patients

Project: **TrkA-NAM**

Negative allosteric modulator of TrkA-receptors in research phase

Neuropathic pain

> 600 million patients

Project: **ACD440**

Topical TRPV1 antagonist in clinical Phase II

AlzeCure

TrkA-NAM – Non-Opioid Treatment of 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*

- **TrkA 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

*) NAM = Negative Allosteric Modulator

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Competition: Limited Competition with small molecule approach

Compound	Company	TrkA (nM)	TrkB (nM)	TrkA vs TrkB	Status	Indication
ACD137	**AlzeCure**	**0.087**	**26 400**	**30,300**	**Preclin**	**OA* & other pain conditions**
Cmpd #10 AK1830	Array Bio. Ashai Kasei	0.038	210	5,500	Phase 2b	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 ph2b** with expected **read-out summer of 2025**

*) OA = Osteoarthritis ^) LBP = Lower Back Pain

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 OA

https://www.alzecurepharma.se/en/alzecure-presents-new-positive-data-for-the-trka-nam-pain-project-against-osteoarthritis/

AlzeCure

IP position – ACD137

- Recently submitted composition of matter patent application for ACD137
- Patent life expected until **2045**
- Additional 5-year market exclusivity in the USA → **2050**

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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

Positive clinical trial results in 1b & 2a

- Developed **topical formulation to avoid AEs** associated with systemic TRPV1 blockade
- **Clinical trial** with topical formulation was initiated and **successfully finalized**
- Phase 1b study addressed **safety, tolerability & efficacy – POSITIVE OUTCOMES**

Now presented detailed **positive phase 2a data**

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A place in the market for a non-opioid for Peripheral Neuropathic Pain

Current treatment options are insufficient

- Oral treatments used for neuropathic pain have limited efficacy – **Up to 80% aren't experiencing sufficient pain relief**
- Topical treatment, including lidocaine patches and capsaicin patches are used but with limited level of efficacy
- **More than 50% of patients received opioids** despite that not recommended and demonstrated not effective in chronic use
- Recently, a novel non-opioid drug candidate for neuropathic pain received fast track designation by the FDA

=> *Huge potential* *for ACD440 Gel*

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Positive Phase 2a 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 2 trial

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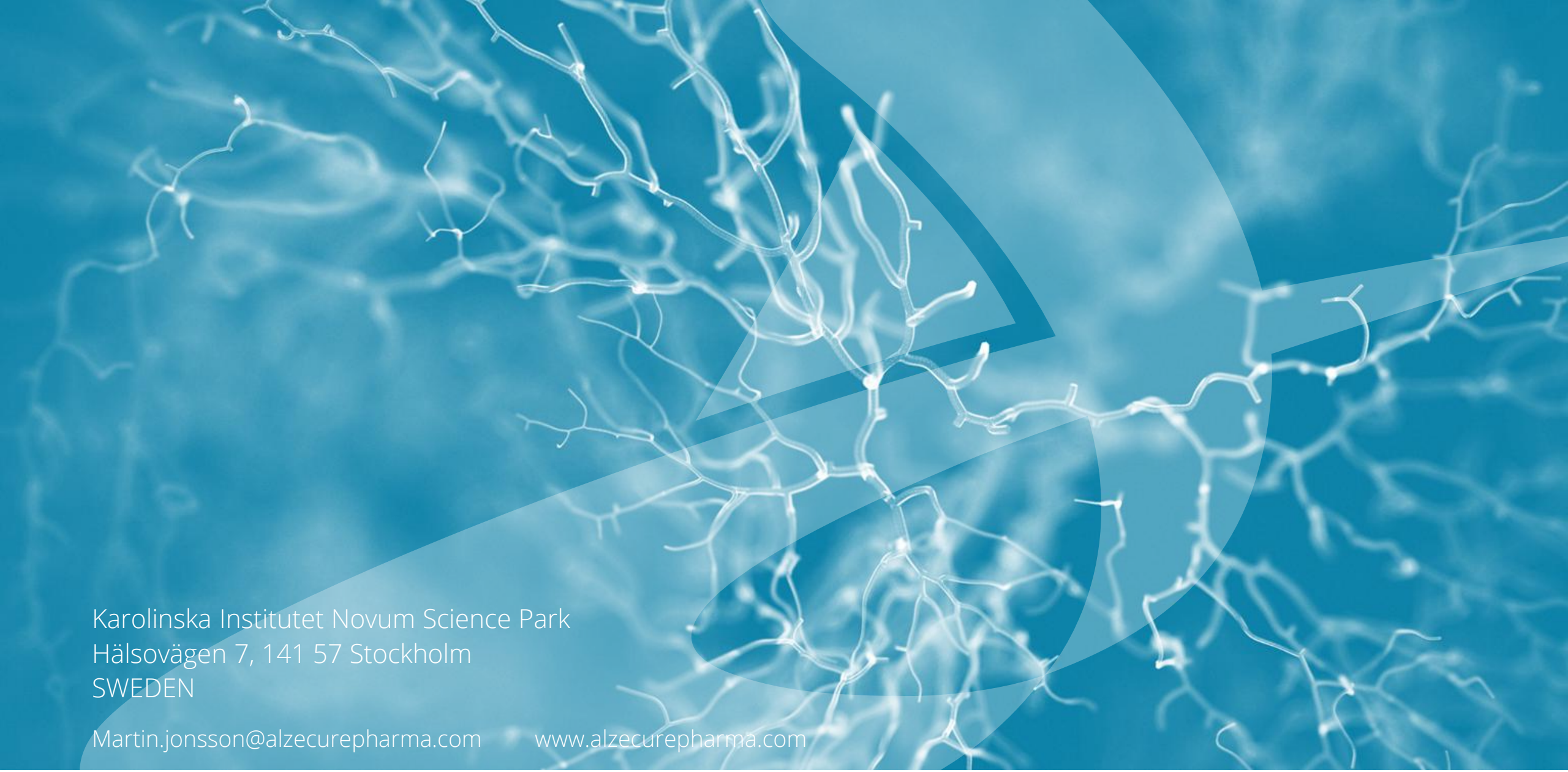
Key Investment Highlights in AlzeCure

- 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

AlzeCure



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