

Rights issue presentation  
December 2022



# Developing therapies for Alzheimer's & Pain

Martin Jönsson, CEO

# Disclaimer

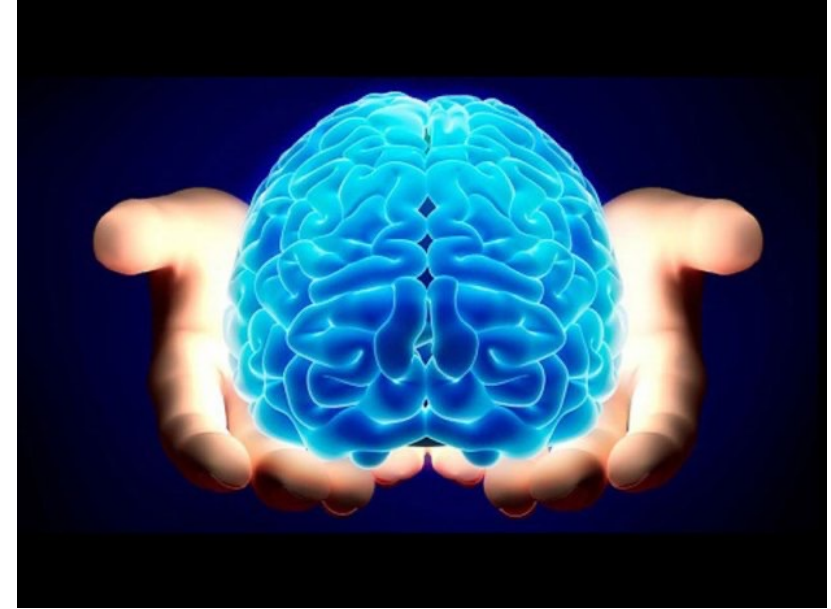
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# Agenda

- Who we are
- Focus areas
- Pipeline & the science
- Progress & goals, incl. Rights Issue



# AlzeCure Pharma – in brief

- Working in **Alzheimer's Disease (AD)** and **Pain** – Hugh unmet medical need & multi-billion sales potential
- Founded in **2016**, out of a research foundation sponsored by **Alzheimerfonden**
- Spin-out from **AstraZeneca** – as a result of them ending their CNS projects 2012
- **Experienced team** with extensive background within pharma industry
- Based at Novum Science Park, **Karolinska Institute**, Stockholm, Sweden
- Three project platforms with multiple **small molecule** candidates
  - **Alzstatin**<sup>®</sup> – An innovative preventive & disease-modifying treatment against Alzheimer's (AD)
  - **NeuroRestore**<sup>®</sup> – A novel first-in-class symptomatic treatment for cognitive disorders, e.g. AD
  - **Painless** – Innovative projects for osteoarthritic & neuropathic pain
- Listed on **Nasdaq First North Premier** Growth Market since Nov. 2018 (Ticker: ALZCUR)





# 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



# Small molecule drugs – AlzeCure’s approach for increased success

## DIFFERENCES BETWEEN SMALL MOLECULES & BIOLOGICS\*

**SMALL MOLECULE  
DRUG**

**LARGE BIOLOGIC**

**AlzeCure focus**



**Small molecule drug**



**Monoclonal antibody**  
c. 25,000 atoms

**Smaller molecules can have increased likelihood of  
penetrating the Blood Brain Barrier**

# A pipeline of small-molecule programs

- Multiple candidates increase chance of success

Platform	Candidate	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
NeuroRestore®	ACD856	Alzheimer's Disease, Sleep disorders, Traumatic brain injuries Parkinson's disease				<b>Positive read-out</b> Phase I trial Safety, Tolerability & Target engagement	
	ACD857	Alzheimer's Disease					
Alzstatin®	ACD679	Alzheimer's Disease					
	ACD680	Alzheimer's Disease					
PainLess	ACD440	Neuropathic Pain				<b>Ongoing phase IIa</b> Planned read-out mid-2023	
	TrkA-NAM	Osteoarthritic Pain & other severe pain conditions					

Phase completed

Phase ongoing

# Close cooperation with leading experts & institutions



Professor Bengt Winblad  
Karolinska Institute



Professor Maria Eriksdotter  
Karolinska Institute



Professor Henrik Zetterberg  
Sahlgrenska and UCL





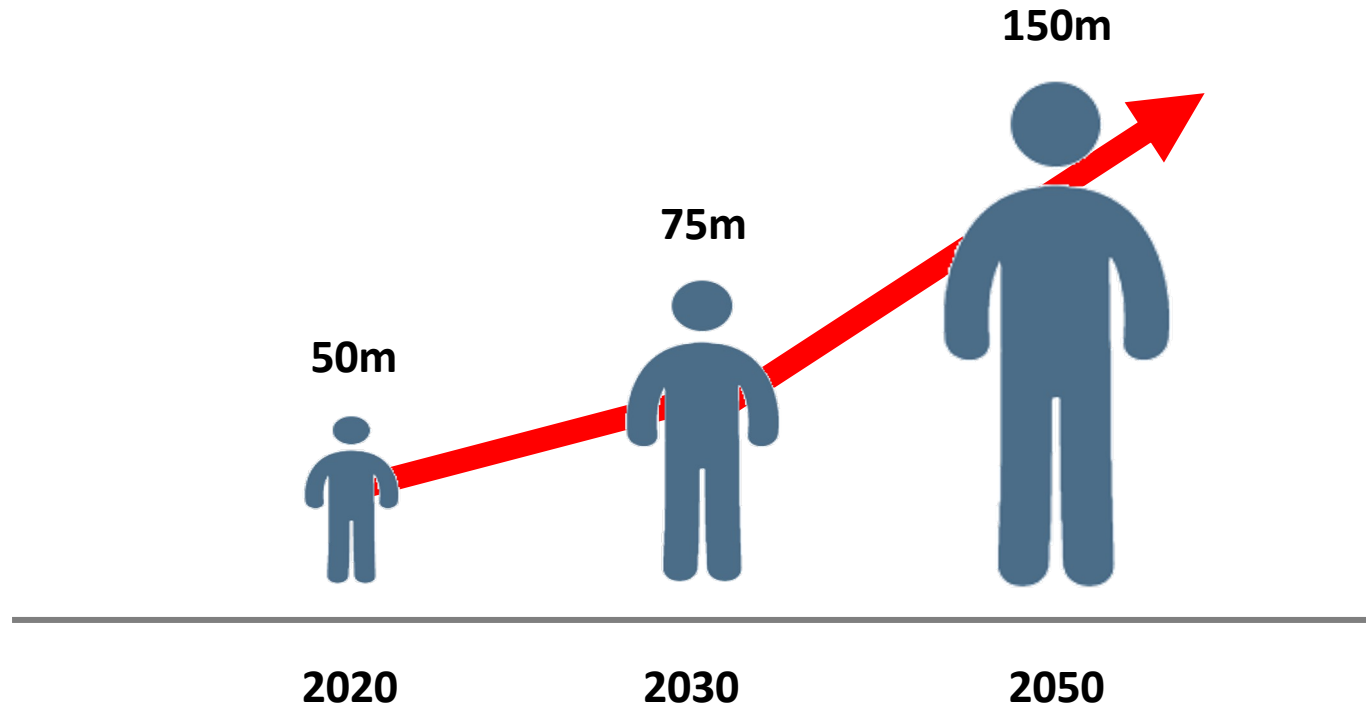
# Our primary Focus area

## Alzheimer's Disease

- Costs the society more than oncology and cardiovascular diseases TOGETHER
- The patient population and costs are expected to TRIPLE in the next 30 years



# Tripling patient population – due to the aging population



- **50 million** people worldwide live with dementia ...
- ... and **doubling every 20 years**
- Alzheimer's accounts for 60 - 80% of all dementia cases

# Alzheimer's Disease – Progressive & lethal disorder with lack of therapies

Pre-symptomatic Alzheimer's  
*10 - 20 years prior to symptoms*

Symptomatic Alzheimer's  
*7 - 10 years life expectancy*



- In Pre-symptomatic Alzheimer's, **A $\beta$  amyloid pathology & plack** is building up in the brain but there are no clinical symptoms
- There are no preventive treatments for this stage of Alzheimer's

- The stage includes **dying neurons in the brain** which leads to **speech problems, memory loss and dementia**, and symptoms start manifesting



*Sales: > US\$ 2bn/year*

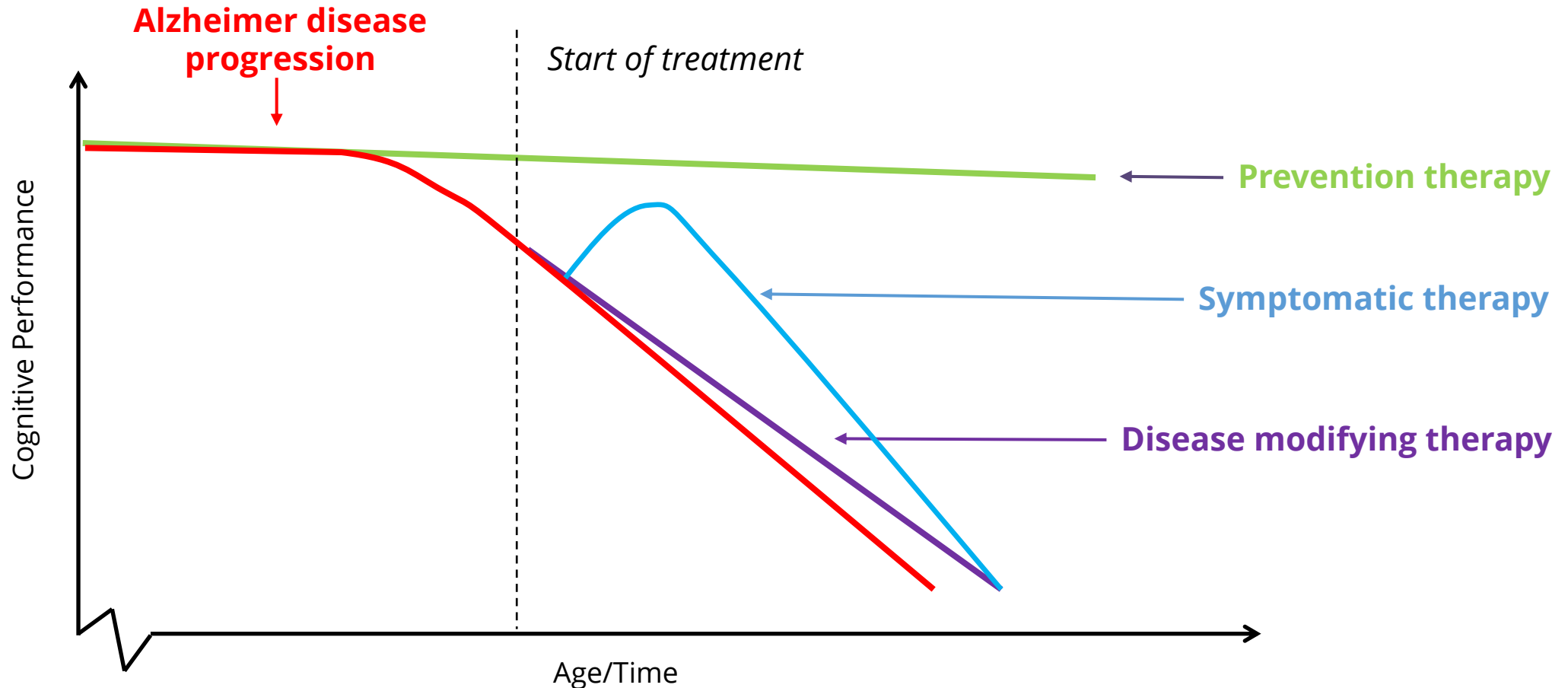
No drugs available

Very few drugs available - *associated with low efficacy and severe side effects*

**HUGE UNMET MEDICAL NEED IN BOTH CATEGORIES**



# Therapy Definitions - Symptomatic, Disease modifying & Prevention therapies



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

TARGET TWO KEY AREAS WITH A HIGH UNMET MEDICAL NEED

**Preventive &  
Disease-modifying therapy**



**Alzstatin<sup>®</sup>**

*Targeting Amyloid Production*

- Novel Oral Small Molecule

**Symptomatic & pot.  
Disease-modifying therapy**



**NeuroRestore<sup>®</sup>**

*Improving Neuronal Function*

- Novel Oral Small Molecule

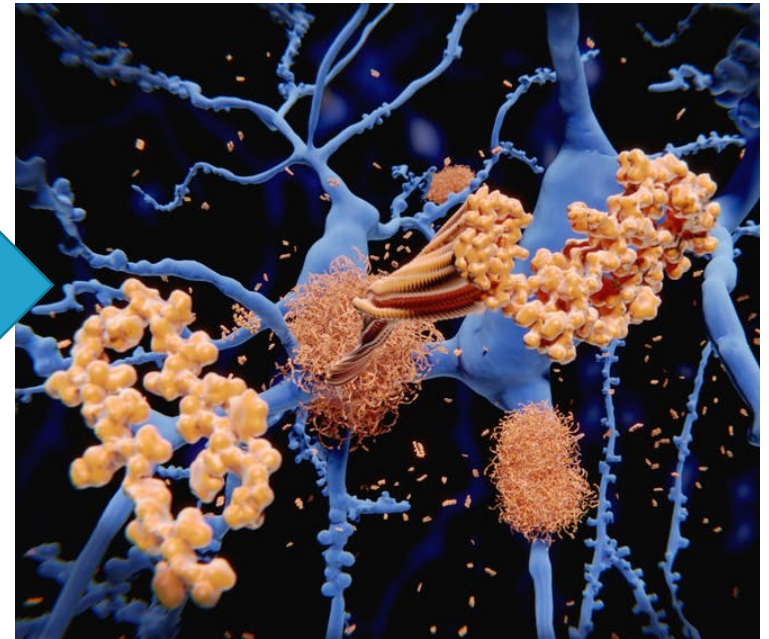


## Alzstatin®

- Preventive & Disease Modifying  
against Alzheimer's

# The Alzheimer's brain and its destruction

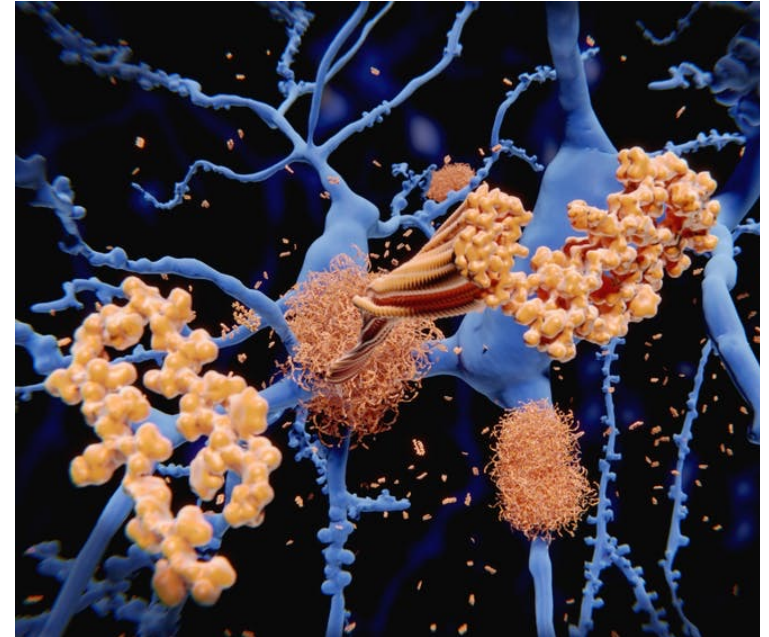
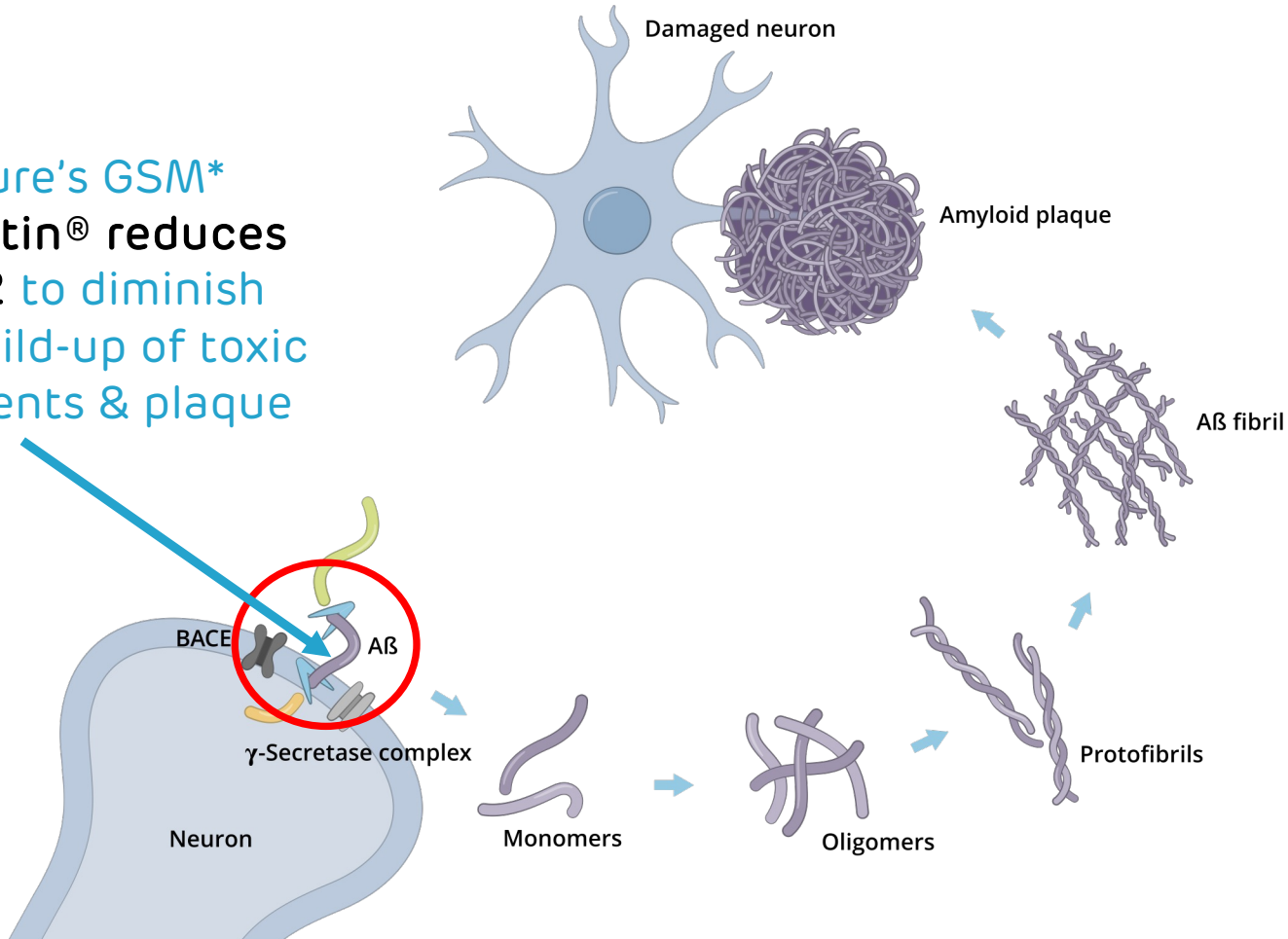
Toxic protein formations – **A $\beta$ -42** amyloid pathology & plaque – are harming and destroying the brain. The formation process is called the **Amyloid Cascade**



Toxic protein formations, built up of A $\beta$ -42, are harming and destroying the brain structures.

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

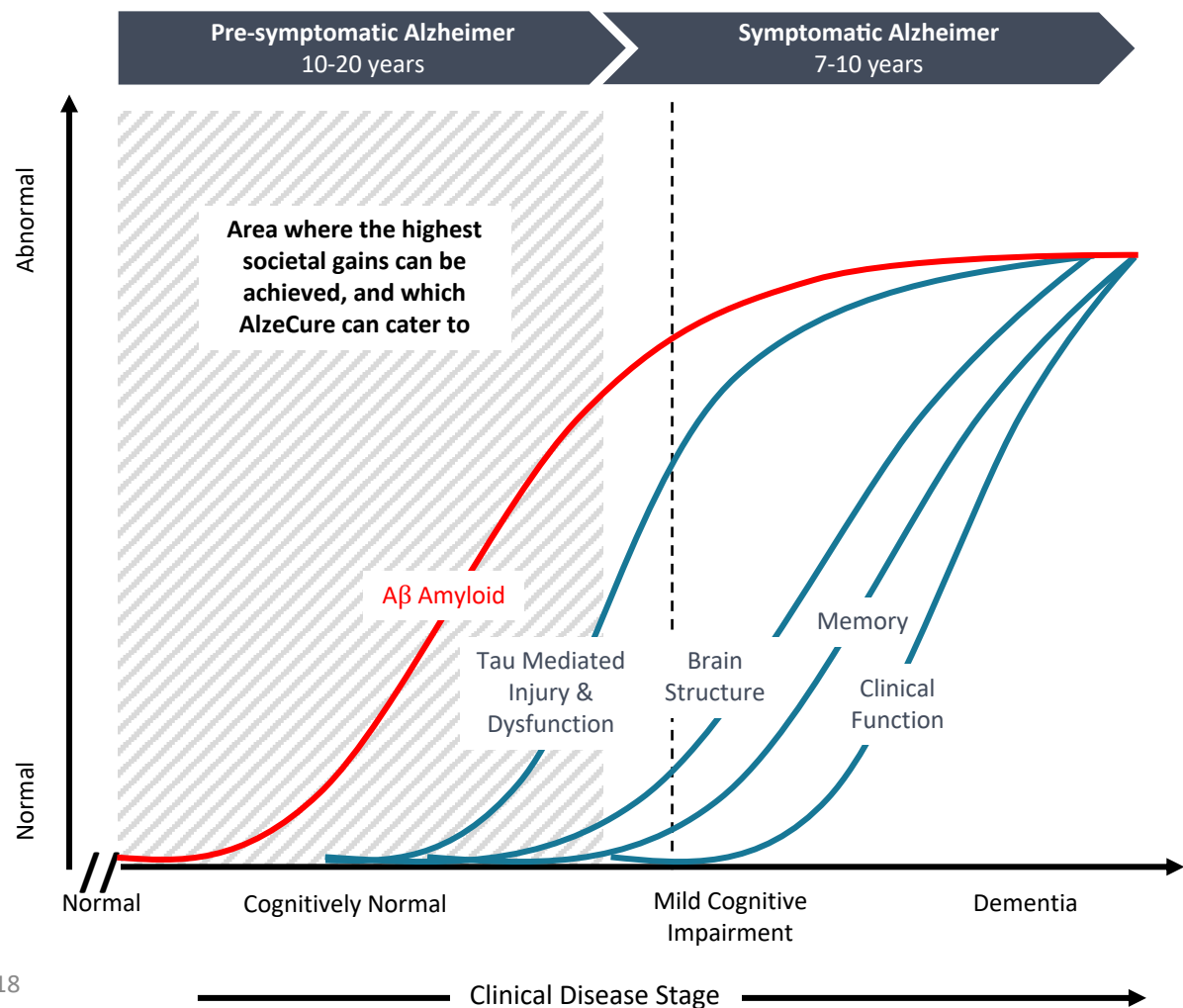
AlzeCure's GSM\*  
Alzstatin® reduces  
A $\beta$ -42 to diminish  
the build-up of toxic  
fragments & plaque



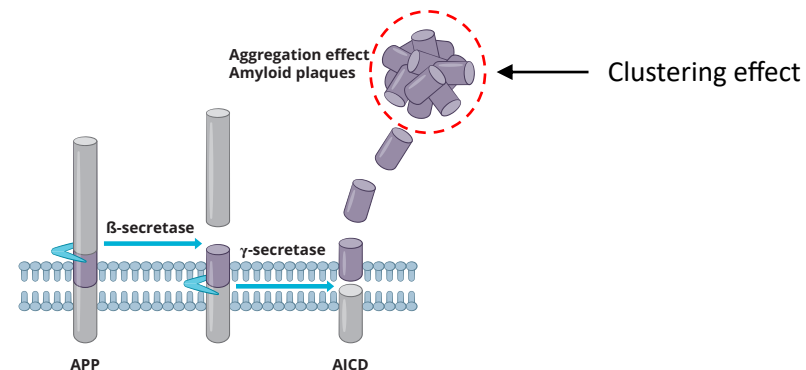


# Alzheimer's Disease Modifier – Preventing or delaying Disease Progression

## ALZHEIMER'S DISEASE PROGRESSION

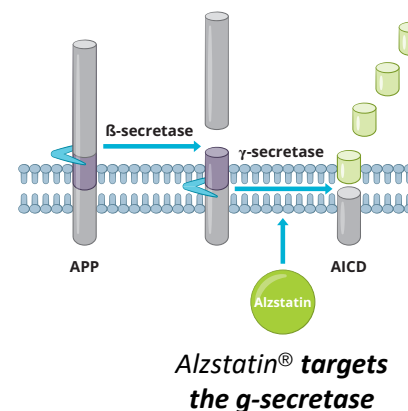


Aβ-42 - main culprit in Alzheimer progression



Found a way to limit Aβ-42 clustering

**Alzstatin®** modulates the enzyme and thereby **limits the clustering effect**



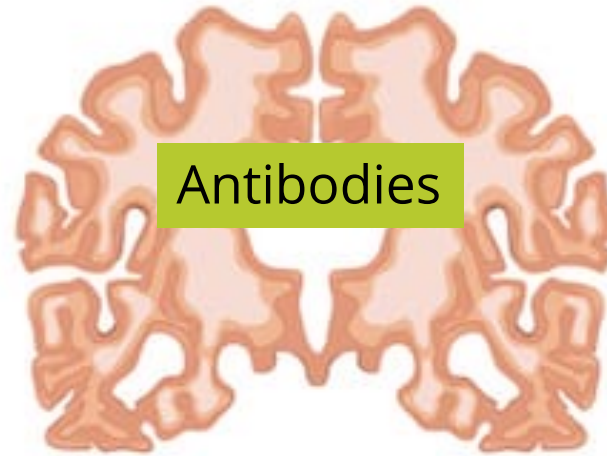


# Brain status at intended treatment initiation

Target patient population - *Alzstatin*® vs *Antibodies*



Healthy brain at risk  
of Alzheimer's



Mild Alzheimer's

- The antibody Aduhelm has the indication, "Mild Alzheimer's disease"\* , where the brain is already heavily damaged and the patient has cognitive symptoms.
- Alzstatin® is targeting an earlier disease stage, identified by biomarkers and risk factors, with the intention to prevent or minimize brain damage.

\*) Indication of Aduhelm® (aducanumab)

# How Alzstatin is expected to differ from the Antibodies\*

## - Key advantages

- **Small molecule therapy**

- Small molecules generally pass much more readily across the BBB to its target site - the brain
- Provides a more cost-effective treatment for chronic use than biologics

- **Oral formulation** => Home treatment

- Don't need to go to the hospital once or twice a month for an infusion of the drug

- **Preventive treatment**

- Taken before the brain is heavily damaged and the patient is diagnosed with cognitive decline and Alzheimer's disease, which is the case for the antibody

- **Fewer side effects**

- Not expected to have the side effects of brain oedema and brain microbleedings (ARIA)  
=> Is not expected to demand regular brain scans, => minimizing hospital visits and costs

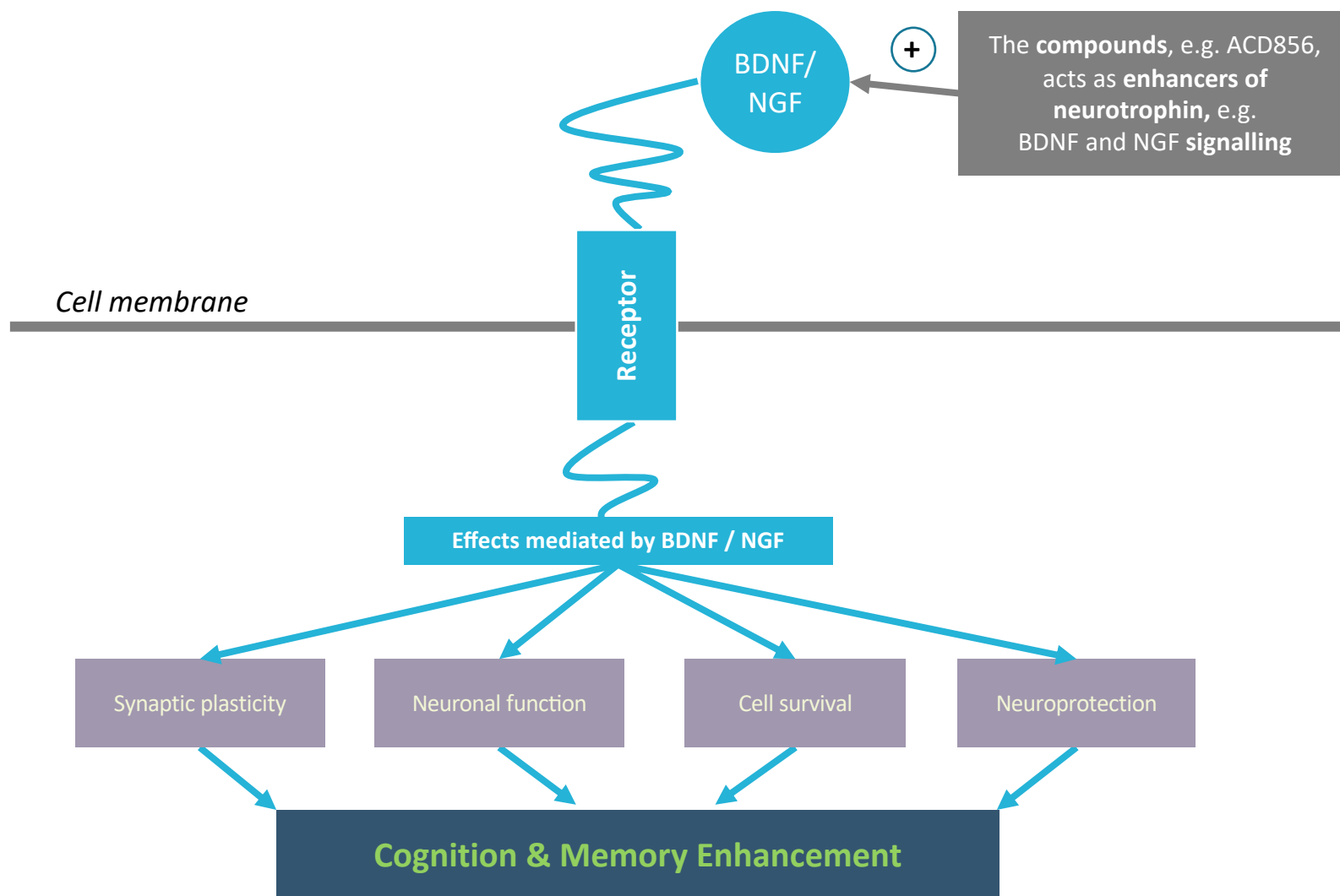
\*) E.g. Aduhelm (aducanumab)

## NeuroRestore®

- A cognitive enhancer  
with neuroprotective potential  
and multiple possible indications



# NeuroRestore® enhances neuronal function & cognitive capabilities



- AlzeCure's compounds act as **enhancers of neurotrophin, e.g. BDNF/NGF signalling**, and the broad effect profile in this specific biological pathway implies **multiple possible indications**, including, e.g.:
  - Alzheimer's disease,
  - Parkinson's disease,
  - Traumatic Brain injury
  - Sleep disorders
  - ...



# 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.

# Positive results in our phase 1 with NeuroRestore ACD856

## AlzeCure's Alzheimer's project NeuroRestore ACD856 shows positive effect on brain activity in clinical trial

September 16, 2022

**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 company has received new data from the clinical phase I study (multiple ascending dose, MAD) with repeated dosing of the drug candidate ACD856, which is being developed against Alzheimer's disease and other indications with cognitive dysfunction.**

New data from a planned exploratory analysis of the MAD study show that ACD856 increases EEG activity in the brain. A clear difference can be seen after vs. prior to administration of the substance. This result combined with previously reported data show that the substance not only crosses the blood-brain barrier, but also reaches and activates neural pathways in the brain, with the potential of having positive effects on cognition.

The MAD phase I study is AlzeCure's third clinical study with ACD856, the company's leading drug candidate within the NeuroRestore platform. The substance is under development as a symptom-relieving treatment for medical conditions where the cognitive ability is impaired, for example in Alzheimer's disease. The primary study objective was to evaluate the drug candidate's tolerability and safety after repeated dosing. As previously reported, ACD856 shows good safety and tolerability in both the SAD and MAD studies.

ACD856 and the other substances in the NeuroRestore platform stimulate several important signaling systems and signaling substances in the brain such as BDNF (Brain Derived Neurotrophic Factor) and NGF (Nerve Growth Factor), which can lead to improved cognition, something that has been demonstrated in previous preclinical studies. 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 traumatic brain injury and depression.



<https://www.alzecurepharma.se/en/alzecure-alzheimers-project-neurorestore-acd856-shows-positive-effect-on-brain-activity-in-clinical-trial/>

# NeuroRestore - Potential Disease Modifying effect

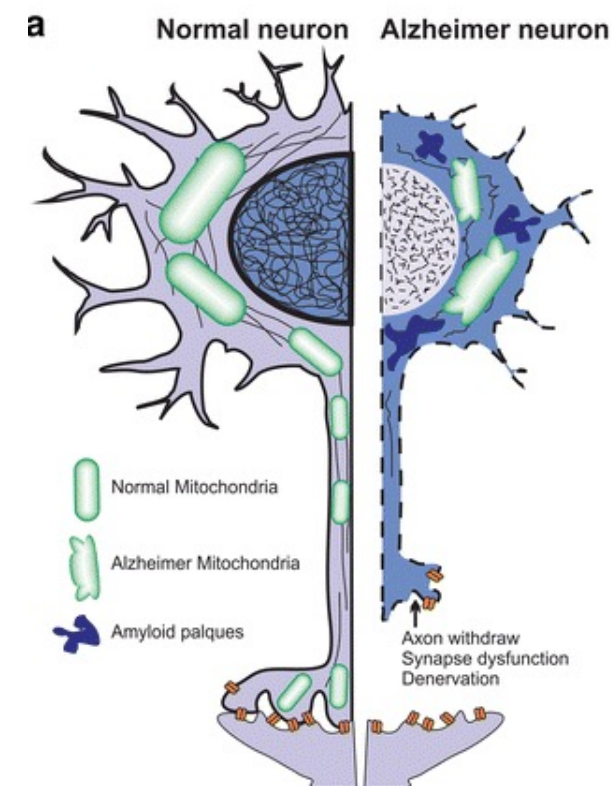
## AlzeCure gets abstract accepted on potential neuroprotective effects of NeuroRestore ACD856

August 30, 2022

**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 an abstract about the research platform **NeuroRestore** and its role in neuroprotection has been accepted for a presentation at ISMND 2022, which this year will be held in Athens, Greece, on October 10-12.

The abstract, titled *The Trk-PAM ACD856 improves mitochondrial function and increase BDNF levels in primary cortical neurons*, will be presented at the international conference organized by the International Society for Molecular Neurodegeneration (ISMND 2022) by Pontus Forsell, Head of Research and Discovery at AlzeCure. Other Co-authors include Cristina Parrado, Sanja Juric, Märta Dahlström and Johan Sandin, CSO at AlzeCure.

The presentation includes study results showing that the leading drug candidate in the NeuroRestore platform, ACD856, has a potential neuroprotective effect. New preclinical data show that the substance, in addition to strengthening the signaling, also increases the release of Brain Derived Neurotrophic Factor, BDNF, a so-called neurotrophin that has a very central role in memory formation, but also in maintaining normal nerve cell function and protecting them from damage. Moreover, ACD856 has a positive effect both on mitochondrial function and on cell survival, which could indicate potential disease-modifying effects of the substance.



# NeuroRestore ACD856 – Candidate in clinical trials

## - Patent in the US to 2039

## AlzeCure receives US patent for NeuroRestore ACD856

September 8, 2022

**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.

<https://www.alzecurepharma.se/en/alzecure-receives-us-patent-for-neurorestore-acd856/>





# Our second Focus area

## Chronic Pain

- Suicide due to chronic pain is as common as due to depression
- Most common cause for sick leaves, creating misery & high societal costs
- Opioid crisis in the US - is huge & reversing the mean average lifespan of Americans



**Huge need** for more efficacious and safer treatments



# Our platform PAINLESS – Targeting unmet medical needs within pain



## Osteoarthritis & severe pain conditions

> 300 million patients

Project: TrkA-NAM



## Neuropathic pain\*

600 million patients

Project: ACD440





## **Professor David Julius** Nobel prize medicine laureate 2021

University of California, San Francisco, USA



Prize motivation: ... for the discoveries of receptor (TRPV1) for temperature and touch.

The identification of and knowledge about the TRPV1\* receptor is central for the mediation of neuropathic pain, which 7-8% of the adult population is affected by. AlzeCure Pharma is developing a TRPV1 antagonist, which now is in clinical phase, for treatment of this pain condition.

\* ) TRPV1 = Transient Receptor Potential Vanilloid 1  
<https://www.nobelprize.org/prizes/medicine/2021/summary/>

# ACD440 – Novel TRPV1 antagonist in clinical phase for neuropathic pain



## PROJECT OVERVIEW

### Emanates from Big Pharma

- › Approximately **SEK 200m** already **invested** on project development
- › **Mode of action confirmed** in several Phase 1 clinical trials
- › Synthesized compound and formulation developed



### VR1 – 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

- › Developed **topical formulation**
- › **Clinical trial** with topical formulation was initiated and **successfully finalized**
- › Phase 1b study addressed **safety, tolerability & efficacy** – **POSITIVE OUTCOMES**

Received **feedback from FDA**

- **Started phase IIa clinical trial**, June 2022
- **Read-out** planned for **mid-2023**



## Neuropathic pain - Fast growing market

- The most valuable segment within the pain indications
- Poorly served patients
- Huge demand for better drugs

2020  
**\$11 billions**

CAGR to 2027  
12.9% => **\$25 billions**

The Neuropathic Pain market was valued at \$10,8 billion in 2020 globally and is forecast to reach \$25,2 billions by 2027, at a Compound Annual Growth Rate (CAGR) of 12,9%

# TrkA-NAM – Non-Opioid treatment of severe pain conditions

## 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 targeting p75 signaling
  - › *Maintain potent clinical efficacy*
  - › *Better side-effect profile*
- › Convenient **oral administration** - small molecule compound
- › **No addiction** compared to opioids

\*) NAM = Negative Allosteric Modulator

# Successful 2022

... now getting ready for 2023



## Key milestones & activities in 2023

- ❑ **Out-license or partner** on one of AlzeCure's projects in the **Alzheimer's or Pain area**
- ❑ **Pre-IND** meeting on **NeuroRestore<sup>®</sup> ACD856** with **FDA** to prepare next clinical study
- ❑ **Progress Alzstatin<sup>®</sup> ACD680** into the next phase, pre-clinical development
- ❑ **Advance Painless TrkA-NAM** into pre-clinical safety testing towards a clinical candidate
- ❑ **Deliver** clinical **phase 2a study results** from with **Painless ACD440** in neuropathic pain



**Right Issue** – subscription period: **December 6 – 20 2022**

Amount

**SEK 31.7 million** – **>80% guaranteed**

Over-allotment option: up to SEK 15.0 million

Visit our home page to learn more.

[www.alzecurepharma.com](http://www.alzecurepharma.com)



# Key investment highlights in AlzeCure



Targeting areas of **huge unmet medical needs**



**Strong team** with extensive experience and track record



**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 into a **phase II company**

The image is a composite. In the foreground, a pair of hands holds a realistic anatomical model of a human brain, split open to reveal internal structures like the ventricles and cerebellum. The background is a blurred laboratory setting with various glassware and equipment. On the left side, there is a semi-transparent, blue-tinted overlay of a single neuron with its cell body and branching dendrites and axons.

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