May 11, 2021

Update on Progress in the Painless Platform

AlzeCure

Today's presenters

Martin Jönsson
CEO

› Extensive experience in various senior management positions with >20 years of international experience in the industry
› Education: MSc in BA from Lund University, Ottawa, Canada & Freiburg, Germany

Märta Segerdahl Storck
CMO
M.D., Ph.D.

› Broad and extensive experience in global development and clinical operations from Pharma industry within CNS and Pain
› Education: M.D., Karolinska Institute, Stockholm, Sweden

Pontus Forsell
Head of Discovery & Research
Ph.D.

› Expert in drug screening with +20 years of experience from industrial research and drug development within CNS and Pain
› Education: Ph.D. in Medical Biochemistry & Biophysics from Karolinska Institute

Johan Sandin
CSO
Ph.D.

› Expert in in vivo Pharmacology with 16 years experience from the drug discovery industry within Neurology
› Education: Ph.D. in Neuropharmacology, Karolinska Institute

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Agenda – May 11, 09:00 – 10:30

Science and Market Update on progress in project platform Painless

- ***09:00*** **- Opening remark**
  - Martin Jönsson – CEO
- **09:03 - Chronic pain – High unmet medical need**
  - Märta Segerdahl - CMO
- ***09:20*** **- AlzeCure's vision and overview**
  - Martin Jönsson - CEO
- ***09:25*** **- Background, progress and plans in Painless**
  - **TrkA-NAM - Project in osteoarthritis and other severe pain conditions**
    - Pontus Forsell - Head of Discovery & Research
  - **ACD440 - A novel VR1 antagonist for neuropathic pain**
    - Johan Sandin - CSO
- ***10:00*** **- Panel discussion and Q&A**
  - Moderator, Anders Hedlund, RedEye
- ***10:25*** **- Concluding remarks**
  - Martin Jönsson

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Märta Segerdahl Storck
M.D., Ph.D., and CMO

May 11, 2021

Chronic pain – a high unmet medical need

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Humanity has experienced pain through history …

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Definition: Pain is an unpleasant sensory and emotional experience

- One out of five individuals worldwide suffer from significant longstanding chronic pain
- 7-8% suffer from neuropathic pain.
- Direct costs equal 0.5-2% of EU GNP costs
- Single most common reason for work disability *(the Work Foundation, OECD)*
- Is associated with higher economic burden, poorer quality of life, worse mental well-being and lower physical functioning
- The chronic pain population is particularly vulnerable – suicide risk as high as in depression.
- The increased risk for suicide is linked to the intensity of pain

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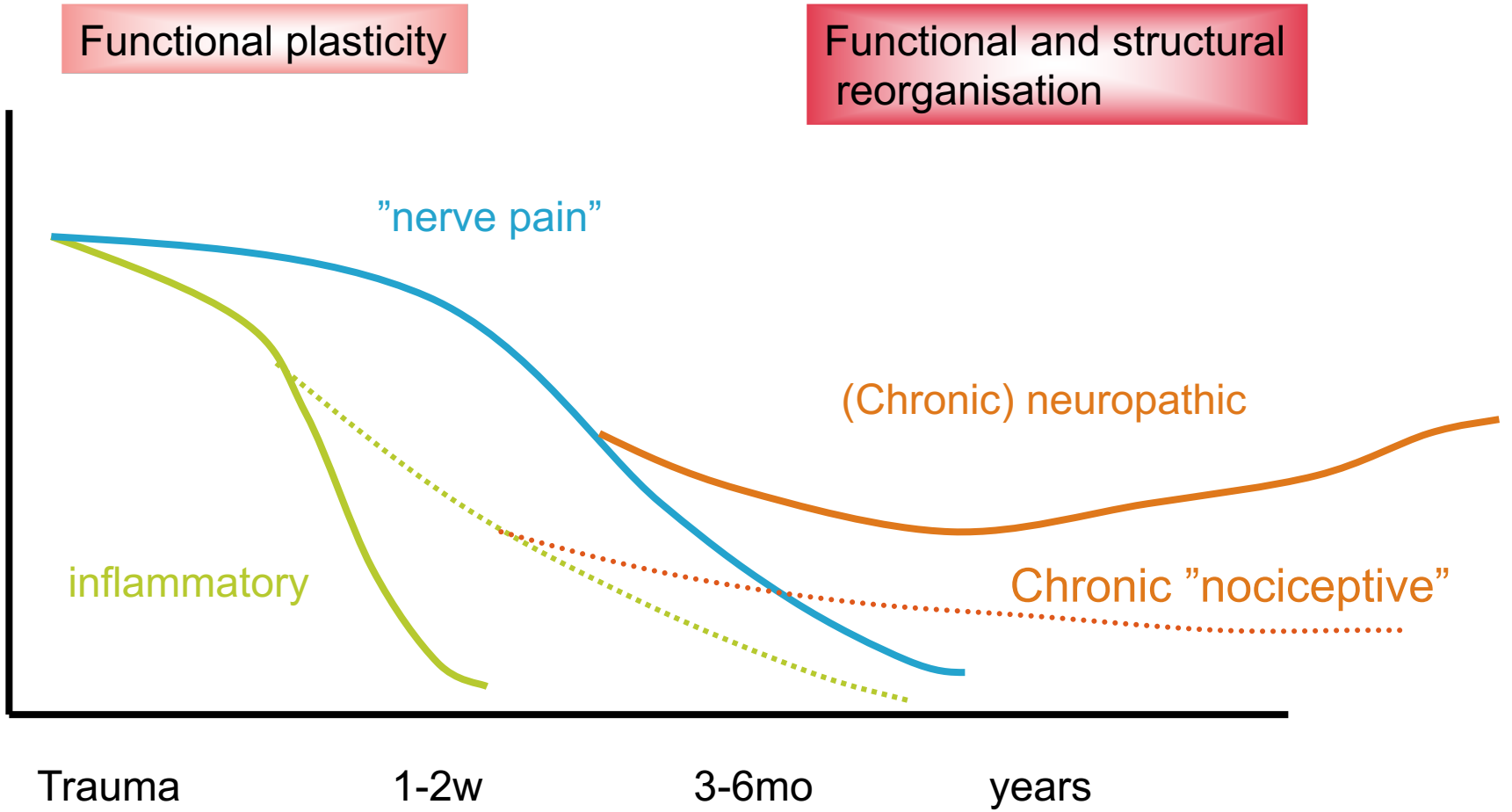
Acute and Chronic pain is not only a question of time



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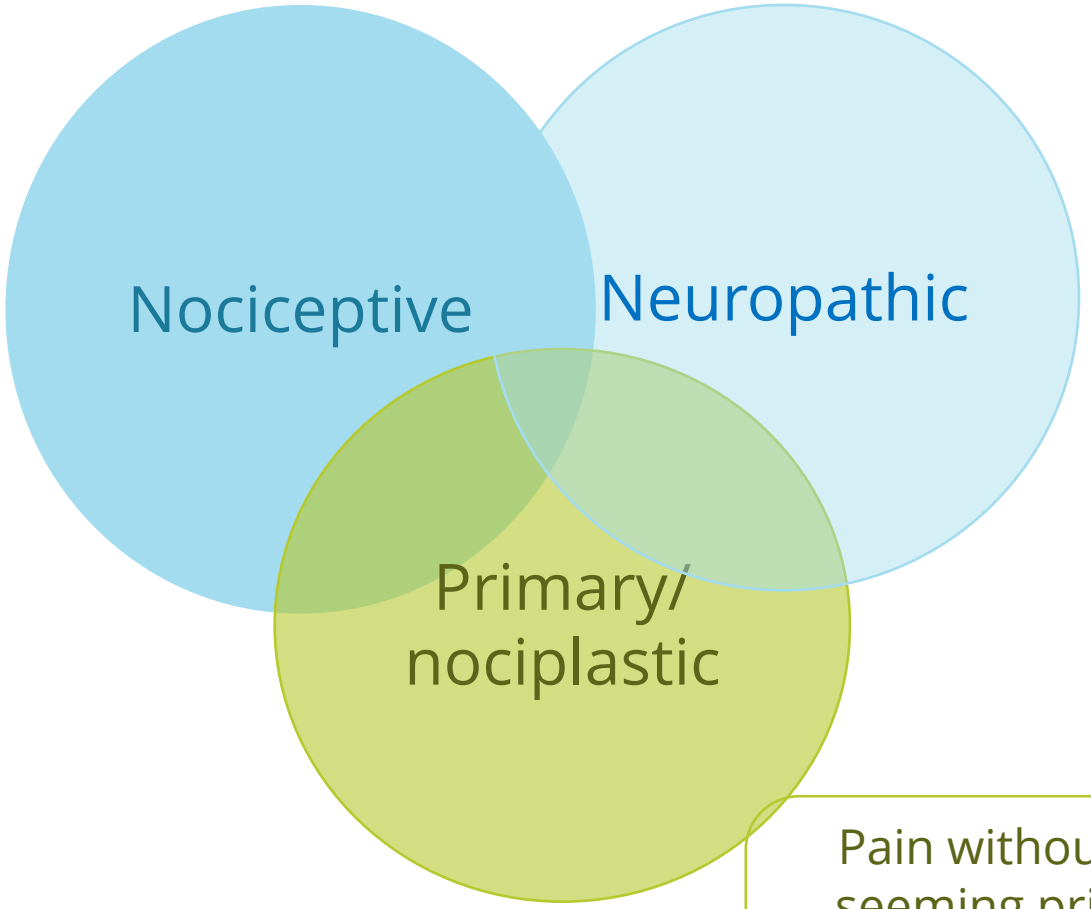
Different types of pain

Pain due to damage to non-neural tissue and is due to the activation of nociceptor:

Osteoarthritis, gout, trauma, tumours, rheumatoid diseases, visceral pain



Pain due to an injury or disease affecting the peripheral or central nervous system, e.g.:

Peripheral neuropathy, chemotherapy induced, post surgical after expected healing

Pain without any seeming primary cause, e.g.:

Fibromyalgia, migraine

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Nociceptive Pain – Typical conditions

- E.g. Osteoarthritis (OA), chronic low back pain, includes both joints and adjacent tissues
- Over 240 million people worldwide suffer OA pain, 12% of adults have chronic low back pain
- Standard of Care NSAIDs have poor efficacy
  - As do second line analgesics: opioids, intra articular steroids
- Treatment gaps
  - 5 out of 6 do not get sufficient pain relief with existing therapies
  - Due to non-response, side effects or high risk for worsening of other common conditions
  - Anti-NGF antibodies not approved based on risk-benefit
- Currently this is substantial research to identify disease mechanisms to then develop disease modifiers, but nothing there yet

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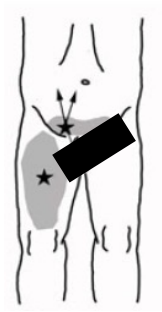
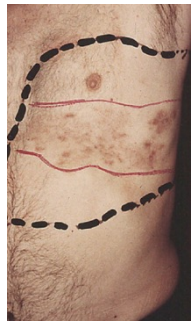
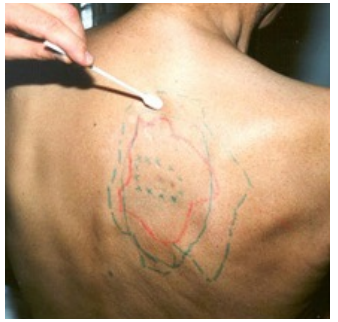
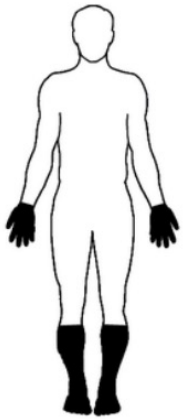
Peripheral Neuropathic Pain

- In the great majority of patients, this is a life-long condition
- The population includes patients with painful diabetic polyneuropathy, chemotherapy induced pain, post nerve injury pain, post herpetic neuralgia, as well as several other backgrounds
- Patients often have an increased pain response than normal or even feel pain on normally not painful stimuli, as well as ongoing pain
- Pain provoking stimuli add substantially to ongoing pain

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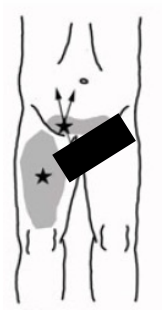

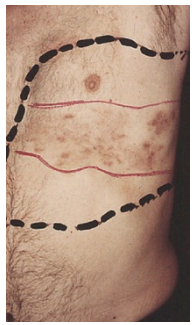

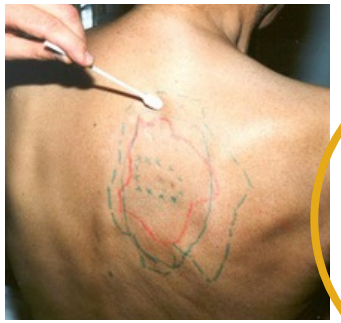

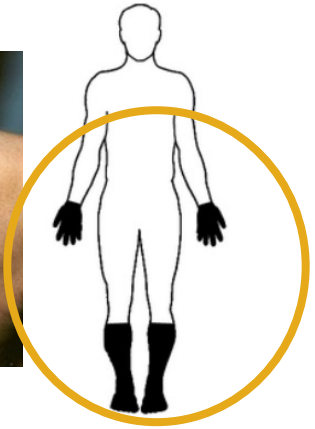

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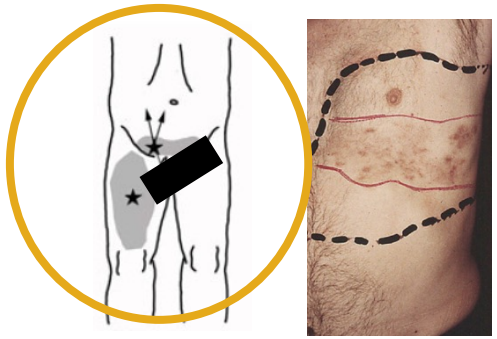

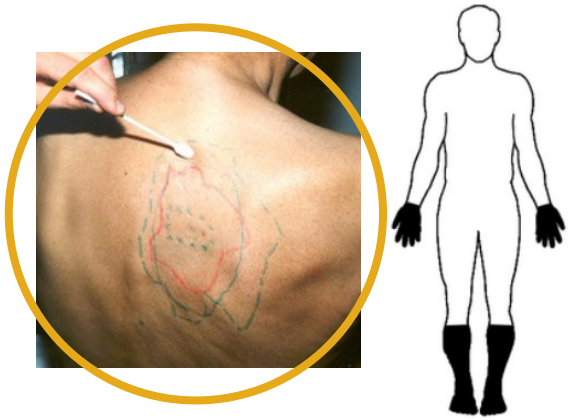

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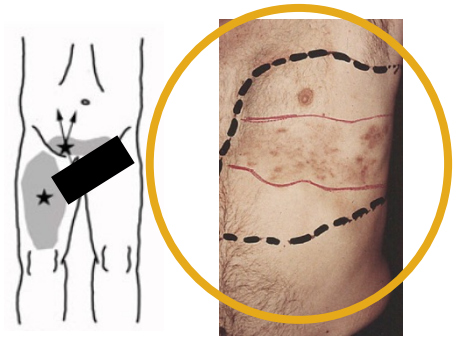

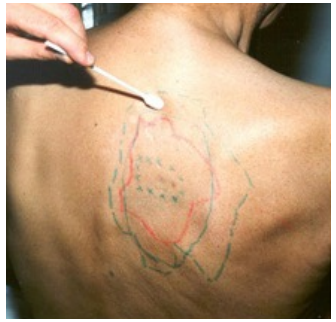

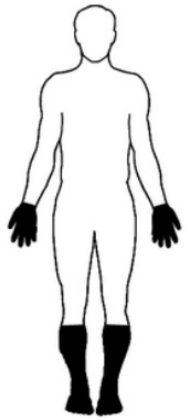

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Neuropathic pain – Common but ”invisible”

- After surgery, 8-10% of patients suffer pain lasting for more than 3-6 months
- One out of five of people with cancer have cancer-related neuropathic pain, as a result of the disease or its treatment
- Worldwide, 47 million individuals suffer from painful diabetic neuropathy, increasing with increasing rate of diabetes
- One out of 4 people will experience shingles, 10% of them will develop chronic postherpetic neuralgia
- Worldwide, 33 million people have HIV, 35% suffer neuropathic pain, unresponsive to treatment

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The impact of chronic pain

- Health-related quality of life for individuals with chronic pain is rated as low as for those with depression, heart disease or poorly controlled diabetes
- Chronic pain also affects family and friends
- Quality of life is more dependent on the severity of the chronic pain than on its underlying cause
- Neuropathic pain is generally more severe, and is associated with worse health, compared to non-neuropathic pain
- Seventeen percent of those who had pain with neuropathic characteristics had health-related quality of life scores equivalent to “worse than death” in a U.K. study

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One tool does not fit all…

… instead we need to have a tool kit enabling us to give the right treatment to the right patient

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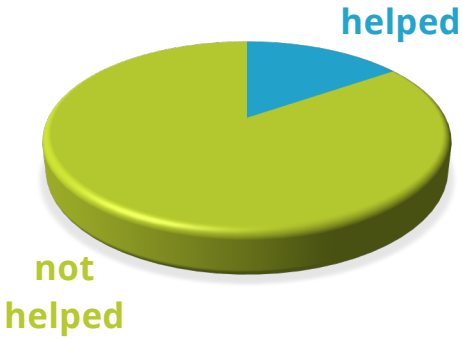
There is a high unmet need in treatment options for neuropathic pain

- The standard of care first line treatments have poor efficacy

DULOXETINE

GABAPENTIN/ LYRICA



LIDOCAINE PATCH

- Other less common treatments, second or third line treatments include capsaicin patches, other antidepressants and antiepileptics, botulinum toxin
- Opioids are third-line treatments
- In all, less than one in three respond in clinical trials, in real life data, it is in the range of one in 7 individuals

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There is a high unmet need also in chronic nociceptive pain

- In acute and chronic low back pain, nonsteroidal anti-inflammatory drugs (NSAIDs), like naproxen, ibuprofen, celecoxib, are used, but they help less than one in 10 or more
- These should also not be taken regularly by people with cardiovascular disease, asthma, gastritis, inflammatory bowel disease, renal failure…
- Topical NSAIDs are good for sprains and strains but have limited efficacy over time
- Opioids are used in severe acute pain, but are also used in chronic pain, without evidence and with troublesome effects

- In summary, available options give limited effect in one of 6-7 patients, and carry troublesome side effects

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The opioid epidemic in the US has put a focus on side effects of strong pain medications highlighting the need for non-opioid approaches.

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Summary

- Disabling chronic pain affects one in five worldwide
- Patients with chronic pain have a very low quality of life
- Chronic nociceptive and neuropathic has a huge impact on employment, family economy, physical function and mental health
- Direct societal cost are very high
- There is a high unmet need for better, more specific and safer treatments

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AlzeCure Pharma

- Founded in **2016**, out of a research foundation sponsored by Alzheimerfonden
- **Experienced team** with extensive background within Pharma industry
- Based at Novum Science Park, **Karolinska Institute**, Stockholm, Sweden

- Working in **Alzheimer's Disease** (AD) and **Pain** – multi-billion markets / great unmet medical need
- Three project platforms with multiple candidates
  - **NeuroRestore®** - A novel first-in-class symptomatic treatment for cognitive disorders, e.g. AD
  - **Alzstatin®** – An innovative disease-modifying treatment for AD
  - **Painless** – Innovative projects for osteoarthritic and neuropathic pain
- Listed on **Nasdaq's First North Premier Growth Market** since Nov. 2018 (Ticker: ALZCUR)
- Market cap: **SEK 261m** (May 10, 2021)
- Cash position: **SEK 94m** (Q1 2021 report)

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Our Business Model

- We are a **Research & Development** company
- Research & **develop to early clinical phase** and then **out-license** our projects

- Gain incomes through:
  - **Upfront payments**,
  - **Milestone payments** and
  - **Royalties** on sold products

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Our primary Focus area

Alzheimer's Disease

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

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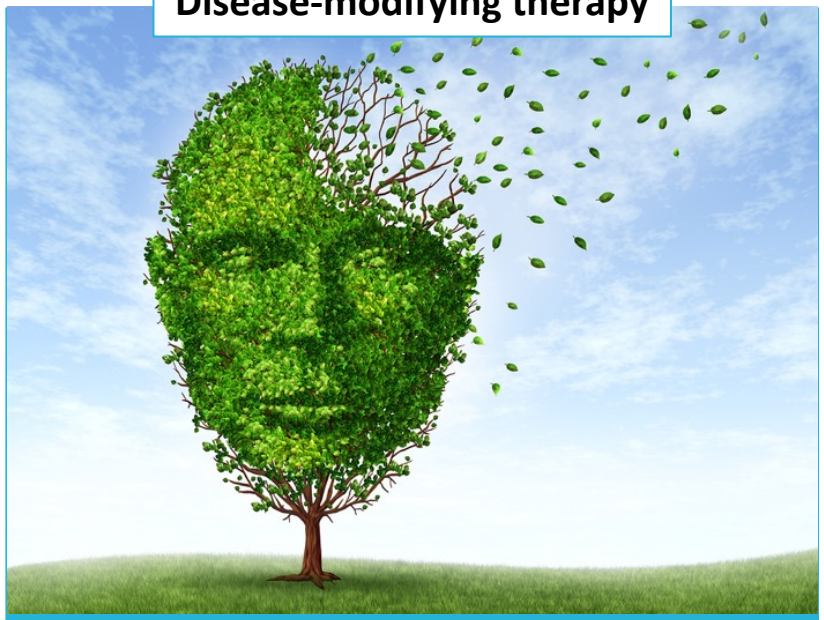
Two Alzheimer's platforms - 1st-in-class properties & potential game- changers

TARGET TWO KEY AREAS WITH A HIGH UNMET MEDICAL NEED

Disease-modifying therapy



Alzstatin®

Targeting Amyloid Production

- *Novel Oral Small Molecule*

Symptomatic therapy

NeuroRestore®

Improving Neuronal Function

- *Novel Oral Small Molecule*

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Our second Focus area

Pain

- Suicide due to chronic pain is as common as due to depression
- Most common cause for sick leaves, creating 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

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Our platform PAINLESS – Targeting unmet medical needs within pain

Neuropathic pain*

25 – 30 million patients

Project: **ACD440**

Osteoarthritis & severe pain conditions

250 – 300 million patients

Project: **TrkA-NAM**

*) Neuropathic pain = Pain initiated or caused by a primary lesion or dysfunction in the somatosensory nervous system

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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					
	ACD857	Alzheimer's Disease					
Alzstatin®	ACD679	Alzheimer's Disease					
	ACD680	Alzheimer's Disease					
Painless	ACD440	Neuropathic Pain					
	TrkA-NAM	Osteoarthritic Pain & other severe pain conditions					

Ongoing

Fully funded Ph I study

Recently ended

Fully funded Ph Ib study

Phase completed **Phase ongoing**

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Key short-term milestones for 2021

- ☑ **Read-out** of clinical 1b study **Painless ACD440** in summer 2021
- ☐ **Read-out** of clinical 1a SAD study **NeuroRestore® ACD856** summer 2021
- ☐ **Start NeuroRestore® ACD856** 1a MAD clinical study in second half 2021
- ☐ **Select CD** for our pain project **TrkA-NAM** in second half 2021
- ☐ **File for 2a clinical study for Painless ACD440** in neuropathic pain second half 2021

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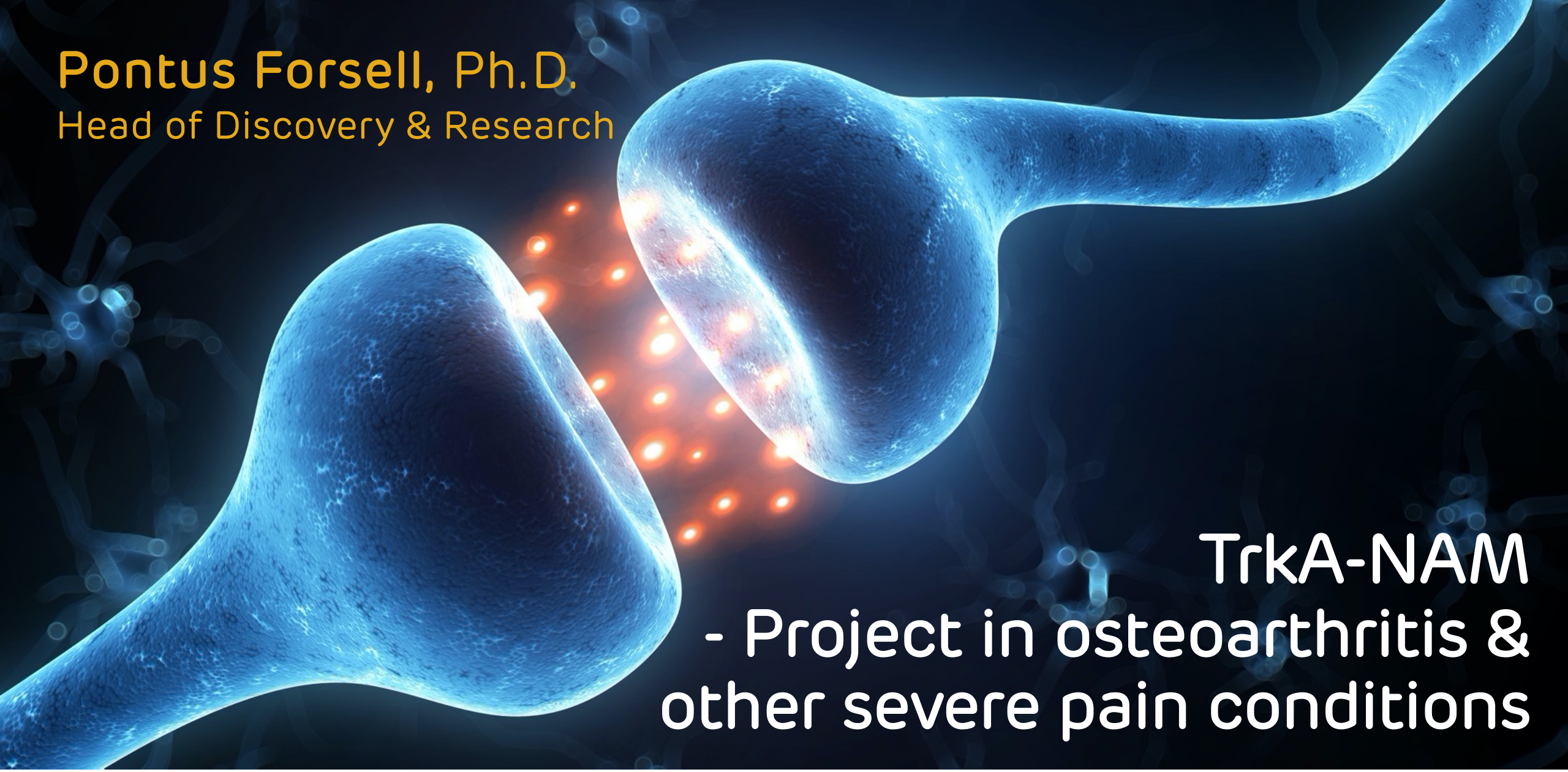

Pontus Forsell, Ph.D.
Head of Discovery & Research

TrkA-NAM
- Project in osteoarthritis & other severe pain conditions

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TrkA-NAM: Goal and background

The goal is to develop selective negative allosteric modulators (NAM) of TrkA for the treatment of osteoarthritis (OA) pain and other severe pain disorders

PROJECT OVERVIEW

Validated pathway	› Mutations in NGF* or TrkA leads to loss of pain perception in man › Anti-NGF antibodies is step changing but demonstrate side-effects
TrkA-NAM Lead optimization	› Potent and selective TrkA-NAMs has been synthesised by AlzeCure › Compounds are active both in a model of arthritic pain and in a model of neuropathic pain
Nociceptive and neuropathic pain	› Large unmet medical need for osteoarthritic pain, neuropathic pain and other severe pain disorders, including need for alternatives to opioids › Blockbuster opportunities for a new analgesic therapy that would avoid adverse events

*) NGF = Nerve Growth Factor

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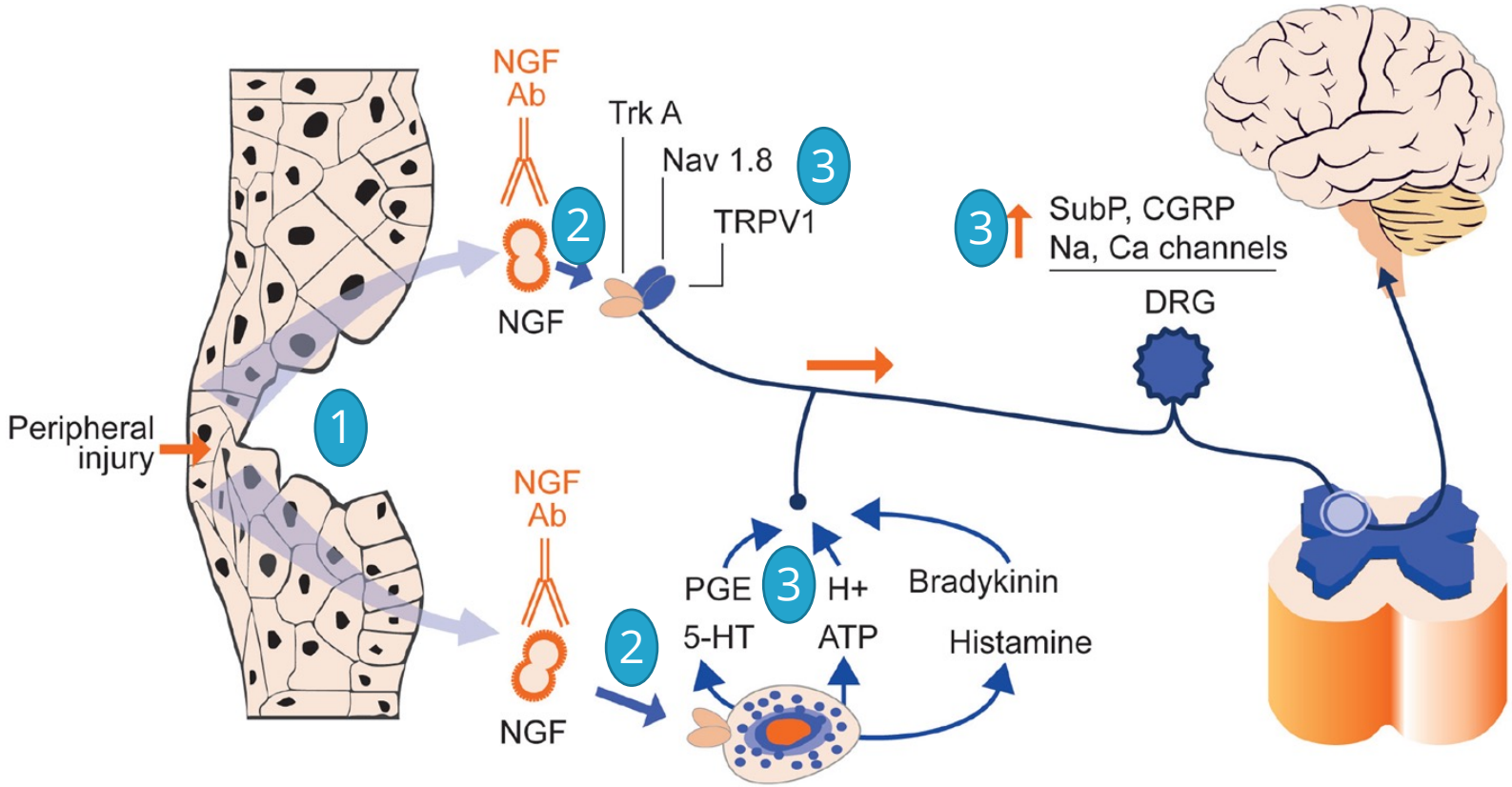
Background: NGF/TrkA and their role in pain sensation

- **1.** NGF is released at the site of an injury.
- **2.** TrkA is the receptor for NGF and it is located on neuronal and on non-neuronal cells.
- **3.** NGF leads to increased pain in several different ways.



NGF and TrkA are involved in pain signaling in both nociceptive and neuropathic pain

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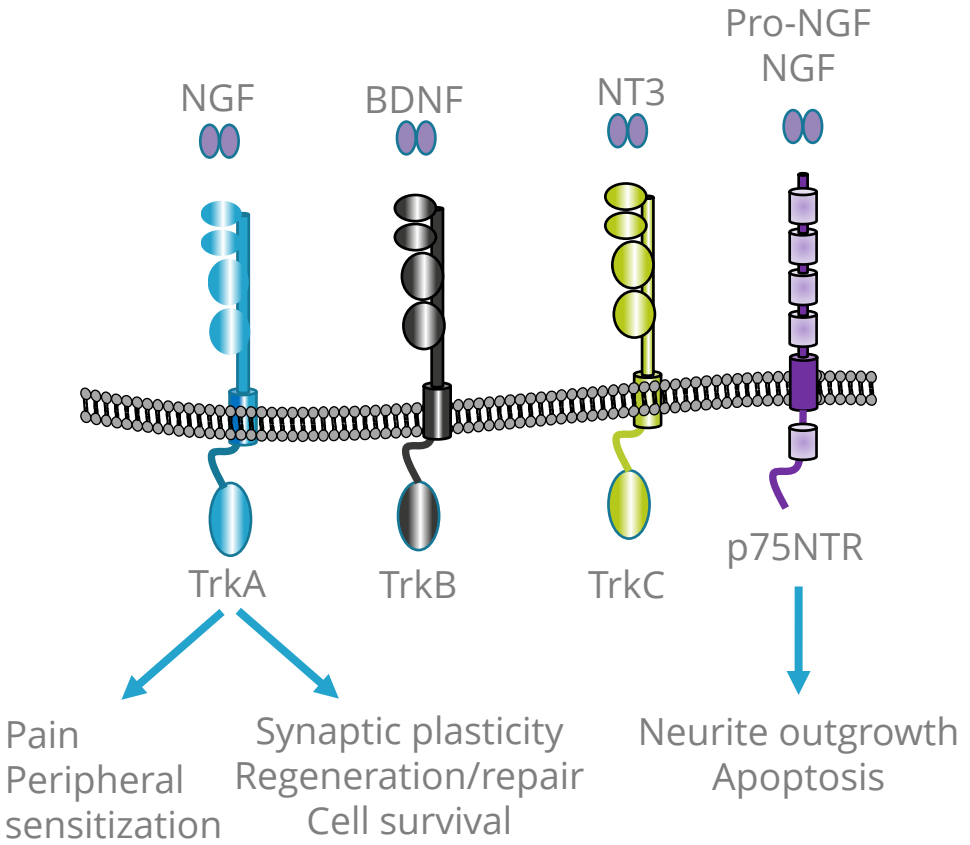
Background: NGF signalling is mediated by its receptors TrkA and p75NTR

- NGF belongs to the neurotrophins, also including BDNF, NT3 and NT4, that are essential for the central and peripheral nervous systems.
- Neurotrophins bind to TrkA, B or C-receptors and to the p75NTR receptor.
- The Trk-receptors are the target for our positive allosteric modulators in NeuroRestore.

- TrkA is the target for TrkA-NAM.
- Small molecules has advantages over antibodies, and they can have complementary roles in pain.



TrkA-NAM is a more selective mechanism than Trk-inhibitors or anti-NGF antibodies.

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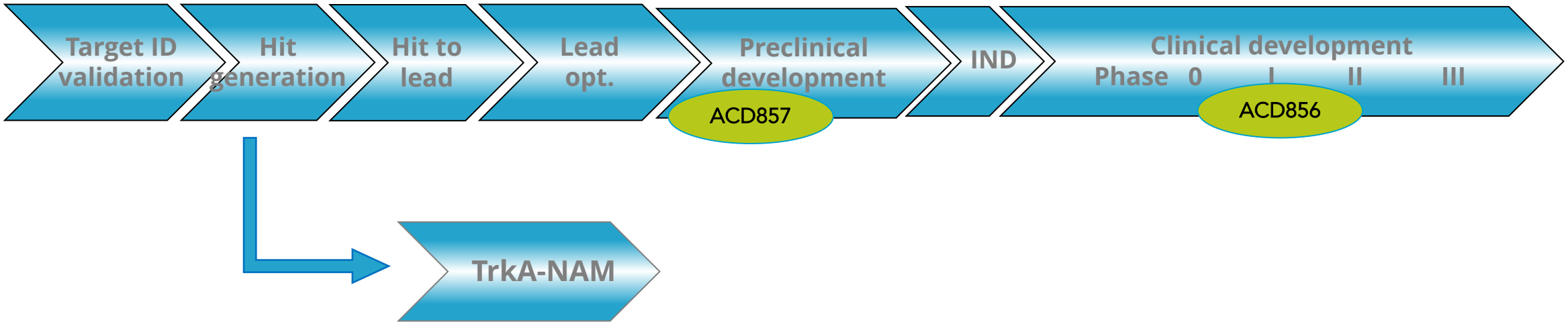
Background: AlzeCure's TrkA-NAM program

AlzeCure's TrkA-NAM program originates from the NeuroRestore platform

NeuroRestore, positive allosteric modulators of Trk-receptors



TrkA-NAM, negative allosteric modulator of TrkA

The identification of TrkA-NAM adds further value to our shareholders in a cost-effective manner

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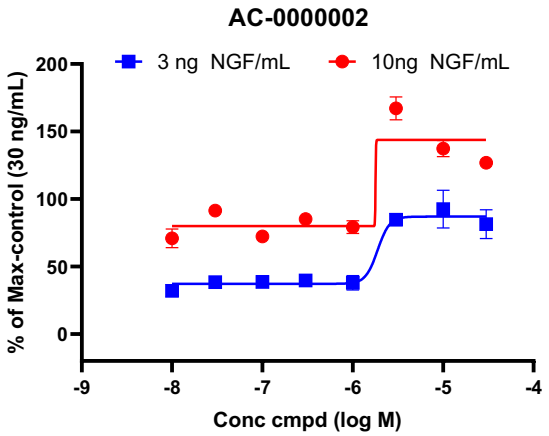
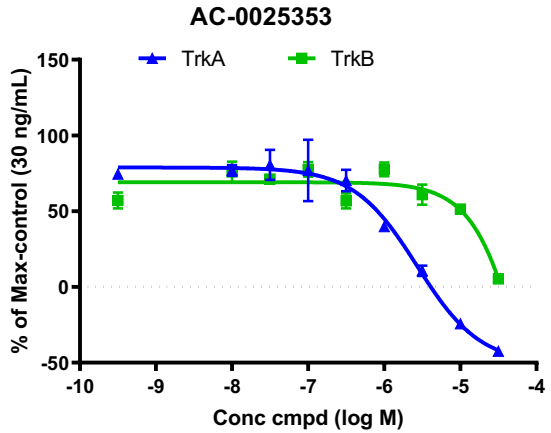
History: AlzeCure's TrkA-NAM program

- **2013**: A positive allosteric modulator of TrkA was identified
- **2015**: The first TrkA-selective negative allosteric modulator was identified
- **2020**: Highly potent and in vivo active TrkA-NAM compounds

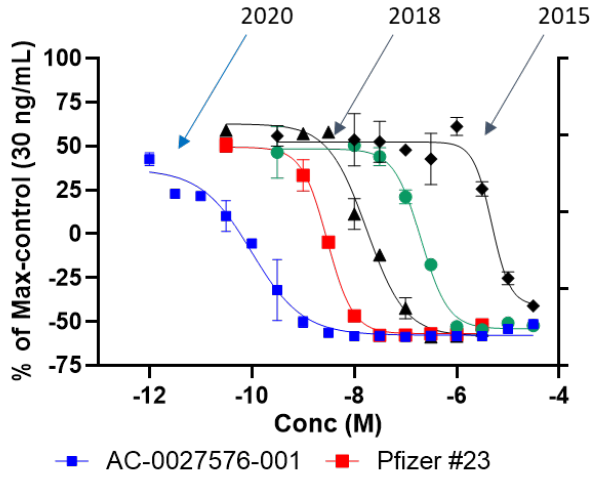
2013
First hit (NeroRestore)



2015
First selective TrkA-NAM



2020
Potent and selective TrkA-NAM's



Many compounds available for selection and development

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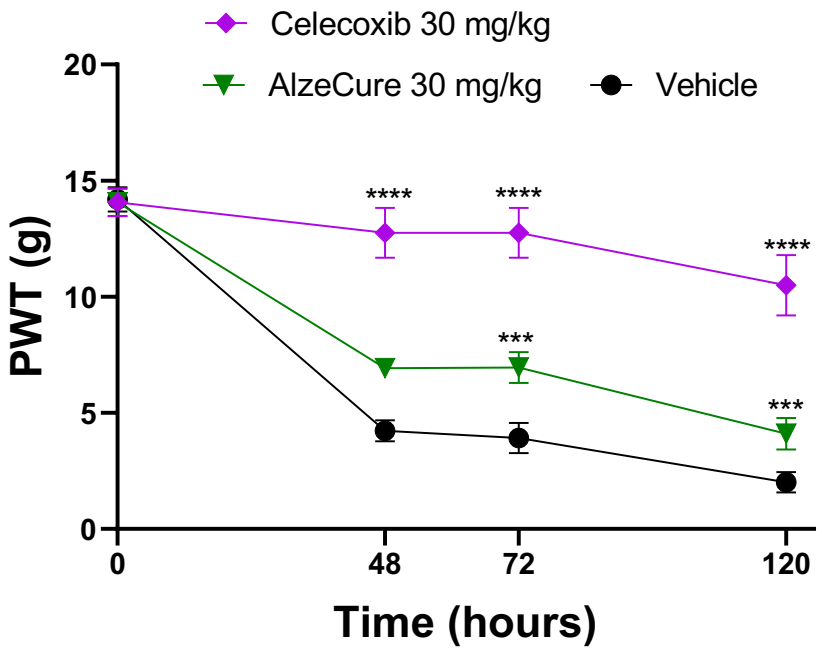
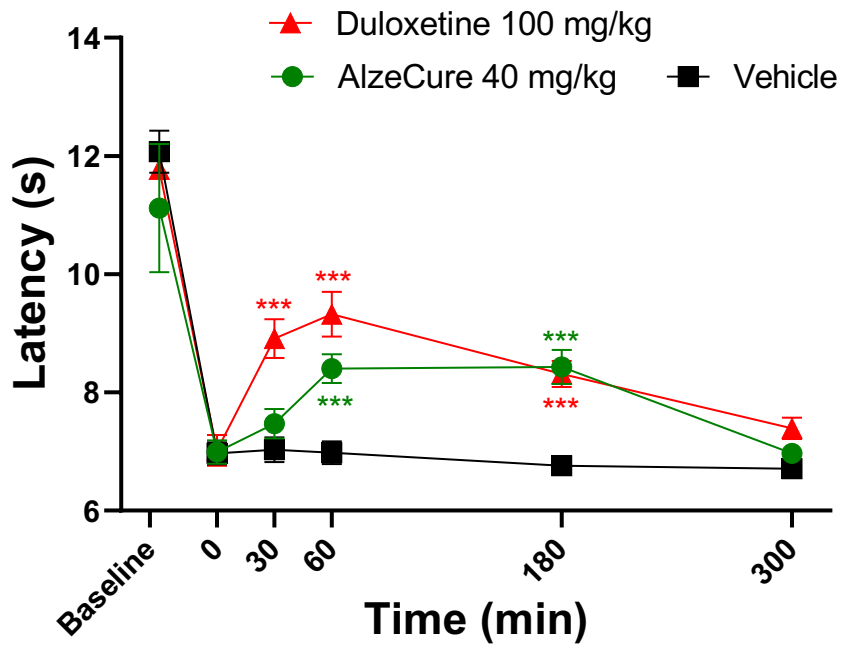
Efficacy: TrkA-NAM's are effective in different pain models

TrkA-NAM's have been demonstrated to have analgesic effects in several acute or chronic pain models

Model of osteoarthritis pain



Model of neuropathic pain



AlzeCure's TrkA-NAM is effective in both osteoarthritis pain and neuropathic pain models

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Competition: Limited competition with small molecule approach

Compound	Company	TrkA (nM)	TrkB (nM)	TrkA vs TrkB	Status	Indication
AC-0027628	**AlzeCure**	**0.004**	**1800**	**450,000**	**Preclin**	**OA* & other pain conditions**
Cmpd #10	Array Bio. Ashai Kasei	0.038	210	5,500	Phase 2	OA LBP^
Cmpd #23	Pfizer	0.64	145	230	inactive	OA
Cmpd #1	Merck	99	>81000	>820	inactive	OA

AlzeCure has synthesized novel and highly potent and selective TrkA-NAM's

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

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Summary

- NGF and TrkA is involved in pain sensation and validated targets
- Selective TrkA-NAM's could be a safer approach than anti-NGF antibodies
- AlzeCure have identified potent, selective and in vivo active TrkA-NAM's
- Preclinical characterization of compounds are ongoing
- Limited competition with respect to small molecule approach

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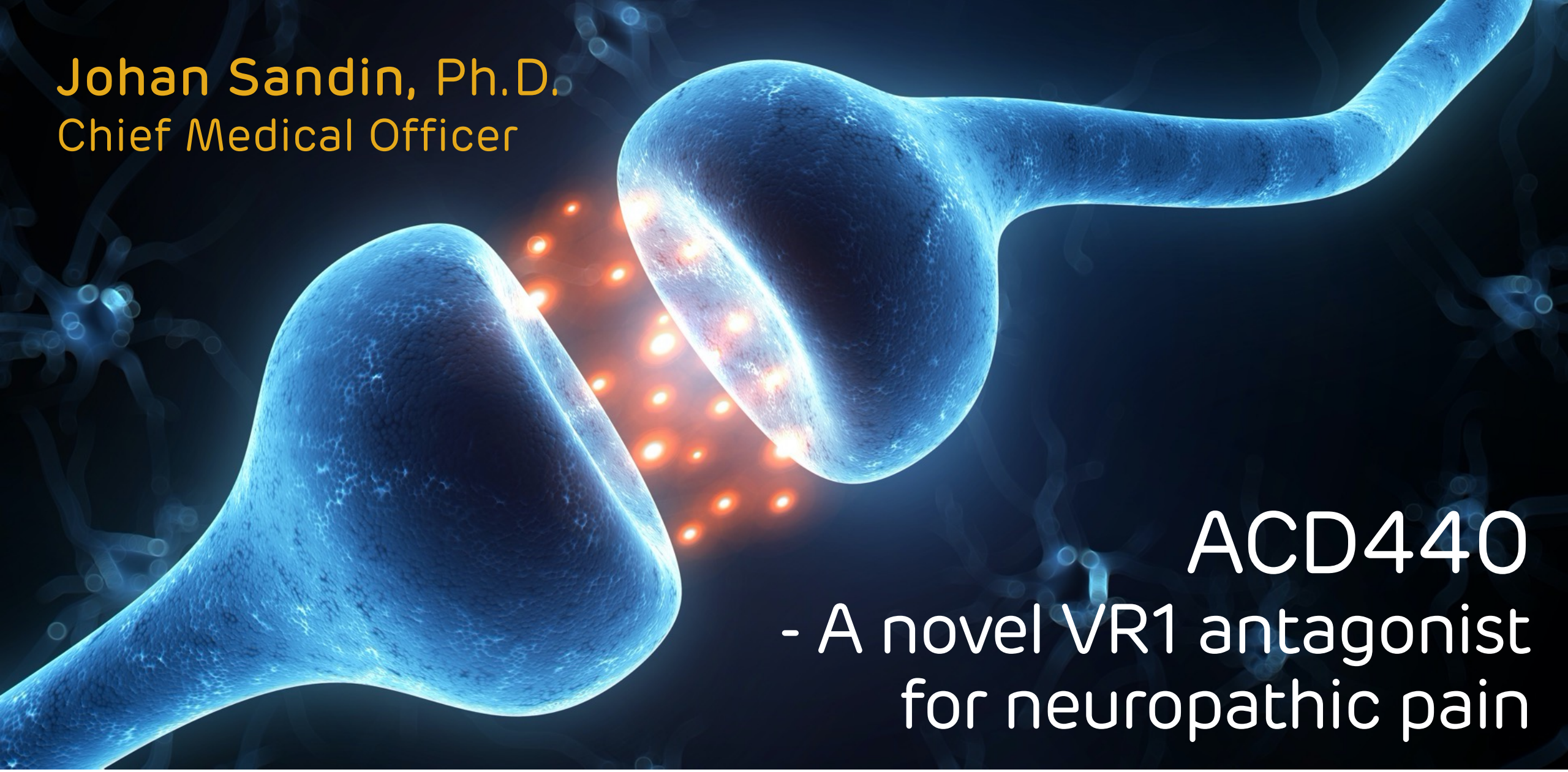

Johan Sandin, Ph.D.
Chief Medical Officer

ACD440
- A novel VR1 antagonist for neuropathic pain

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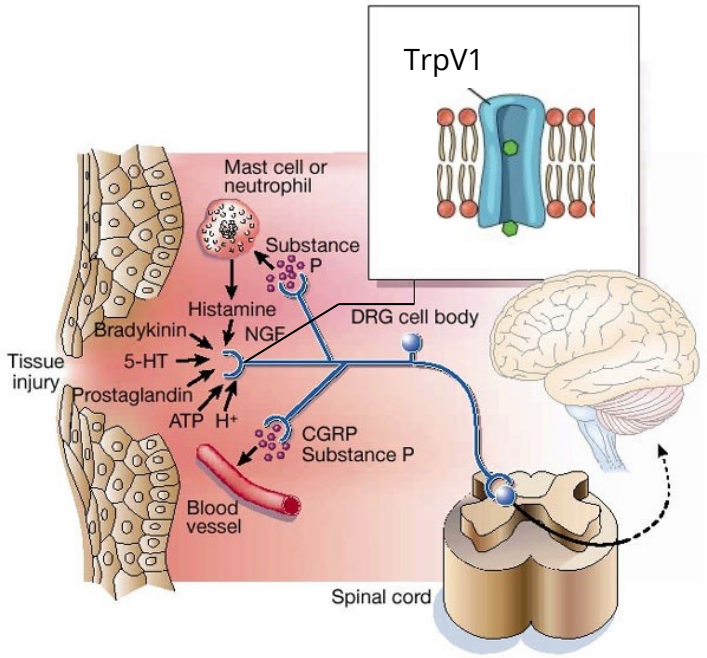
ACD440 – Target mechanism central to pain signaling

- The transient receptor potential cation channel subfamily V member 1 (TrpV1), also known as the vanilloid receptor 1 (VR1), is a protein that plays a central role in the transduction of pain.

- VR1 is activated/sensitized by e.g.:
  - Temperature (heat)
  - Low pH
  - Endogenous agents (eg, NGF, bradykinin, prostaglandins, etc)
  - Exogenous agents (eg. capsaicin)



Modified from Julius and Basbaum Nature 2001:413

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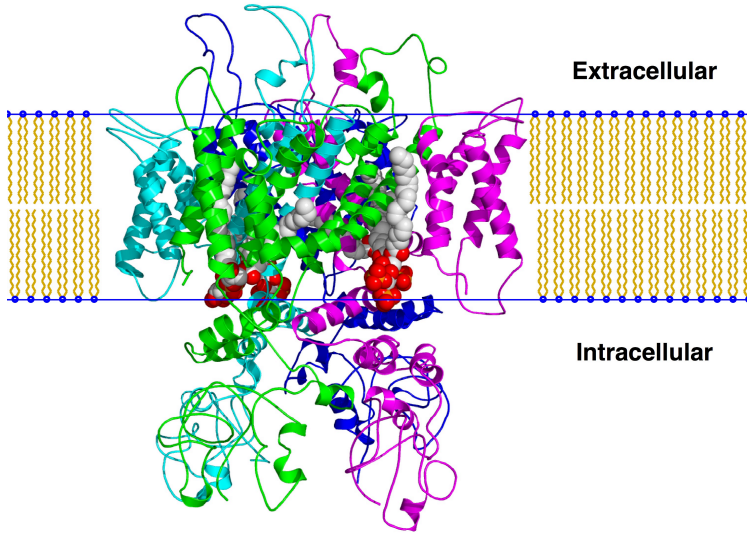
ACD440 – Target also located in peripheral tissues

- VR1 is widely distributed in the body including:
  - Skin
  - Eye
  - Mucosa
  - Sensory nerve fibers
  - Mast cells and epidermal keratinocytes
  - Blood vessels and epithelial cells of hair follicles



VR1 located in the cell membrane

- VR1 receptors are also upregulated in the skin of a subset of neuropathic pain patients

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ACD440 – Clinical asset suitable for topical use

- ✓ VR1 antagonist originally in development as an oral drug for nociceptive pain (osteoarthritis)
- ✓ Mode of action confirmed in previous clinical model studies
- ✓ Preclinical studies showed analgesic effects of ACD440 in neuropathic pain
- ✓ Physico-chemical properties of compound suitable for a topical formulation
- ✓ Synthesized compound for clinical studies available in larger quantities
- ✓ A topical gel was developed for the Phase 1b proof-of-mechanism study

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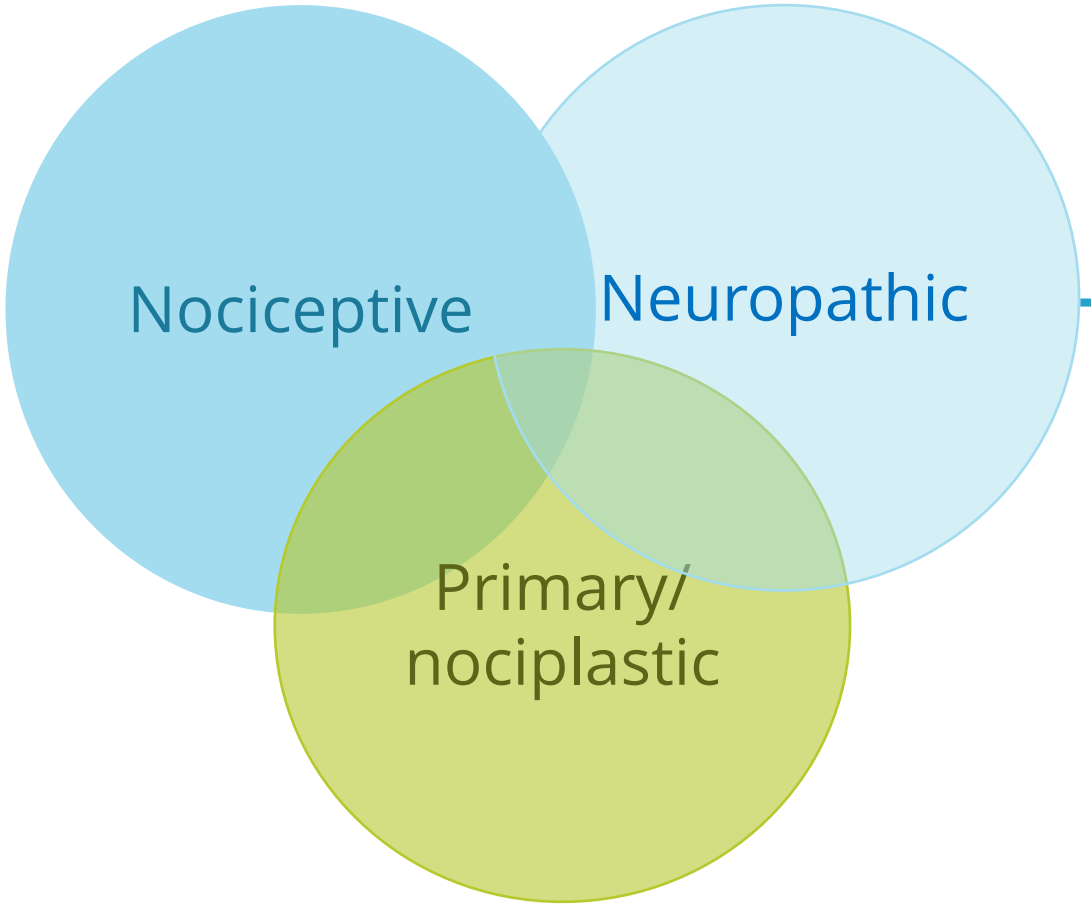
Neuropathic pain – Area of huge unmet need



NEUROPATHIC PAIN

- 7-8 % of adults have pain with neuropathic characteristics, the majority is poorly treated
- The standard of care first line treatments for neuropathic pain have poor efficacy
- Seventeen percent of those who had pain with neuropathic characteristics had health-related quality of life scores equivalent to “worse than death” in a U.K. study
- Patients often show hyperalgesia (increased pain response) or allodynia (normally unpainful stimuli give raise to pain) as well as ongoing pain. Pain provoking stimuli add substantially to ongoing pain, both in intensity and in time

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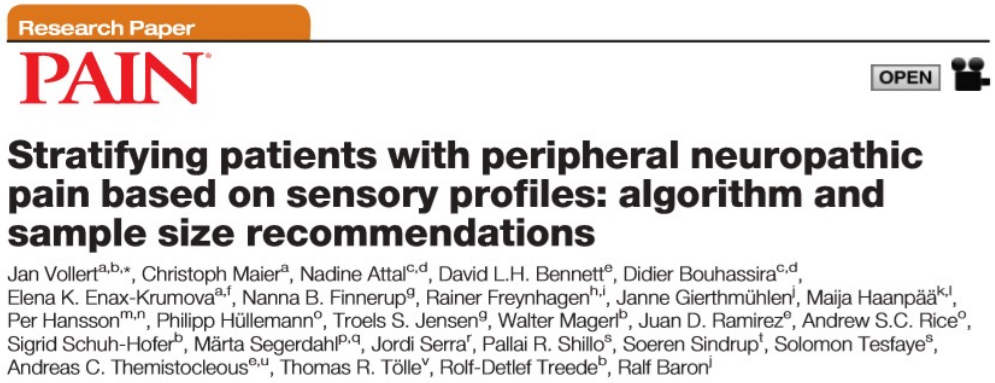
ACD440 – Targeting peripheral neuropathic pain

- Peripheral neuropathic pain
- Target indication based on patients who often have increased sensivitity to sensory stimulation
  - This includes patients with post operative or post traumatic neuropathy, painful polyneuropathy or post herpetic neuralgia
  - Upregulated VR1 receptors can be present in all etiologies

Other indications possible:

- There is evidence that VR1 plays a key role also in nociceptive pain
- Preclinical data generated with ACD440 shows potent effects in several models of nociceptive pain


Research Paper

PAIN

OPEN

Stratifying patients with peripheral neuropathic pain based on sensory profiles: algorithm and sample size recommendations

Jan Vollert[a,b,*], Christoph Maier[a], Nadine Attal[c,d], David L.H. Bennett[e], Didier Bouhassira[c,d], Elena K. Enax-Krumova[a,f], Nanna B. Finnerup[g], Rainer Freynhagen[h,i], Janne Gierthmühlen[j], Maija Haanpää[k,l], Per Hansson[m,n], Philipp Hüllemann[o], Troels S. Jensen[g], Walter Magerl[b], Juan D. Ramirez[e], Andrew S.C. Rice[o], Sigrid Schuh-Hofer[b], Märta Segerdahl[p,q], Jordi Serra[r], Pallai R. Shillo[s], Soeren Sindrup[t], Solomon Tesfaye[s], Andreas C. Themistocleous[e,u], Thomas R. Tölle[v], Rolf-Detlef Treede[b], Ralf Baron[j]

(Vollert et al 2017, PAIN 158 (2017) 1446–1455)

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ACD440 – Outline of Phase Ib Proof-of-Mechanism (PoM) study

- Prospective, double-blind, randomized, placebo-controlled study of safety, efficacy, and pharmacokinetics of ACD440 Gel
- All healthy volunteers (n=24) were subjected to all treatments
- Three different skin conditions were assessed:
  - Normal skin - Tolerability/efficacy on normal skin
  - Stripped skin – Tolerability/efficacy on skin with impaired barrier
  - Skin exposed to ultraviolet B radiation (light sunburn) – Tolerability/efficacy on inflamed skin
- Separate study measuring plasma concentration in 8 subjects with larger areas treated

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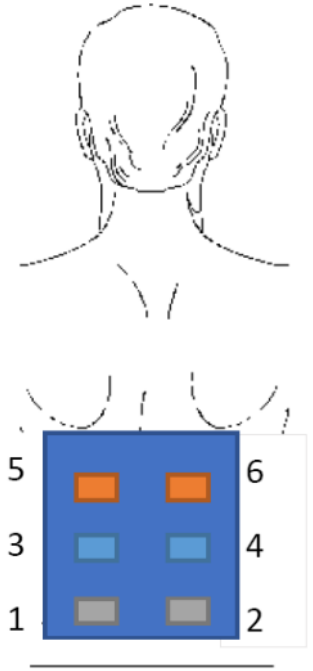
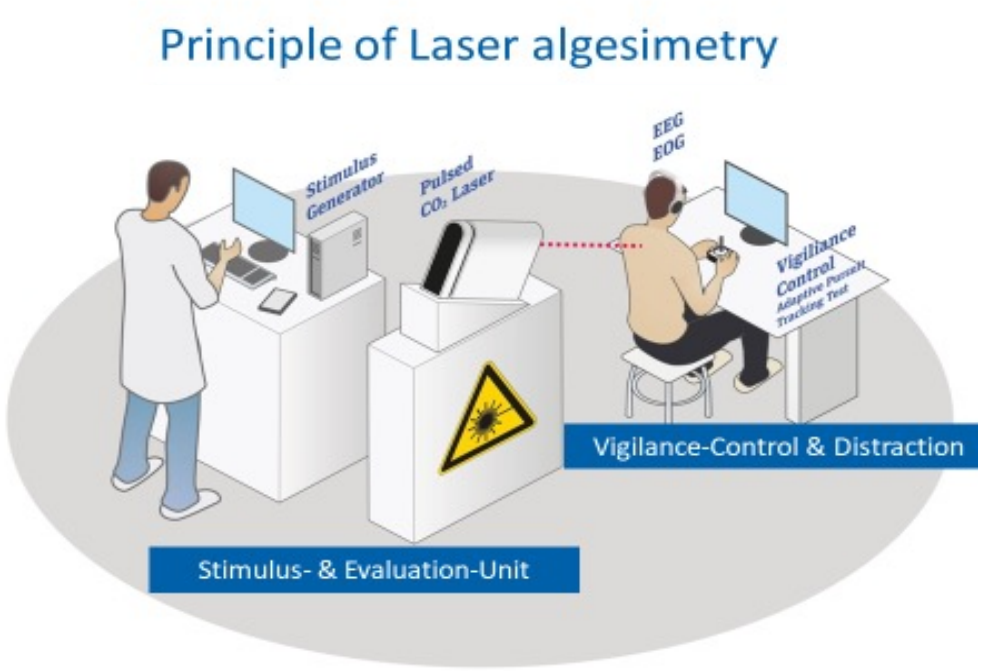
ACD440 – Methodology used in PoM study

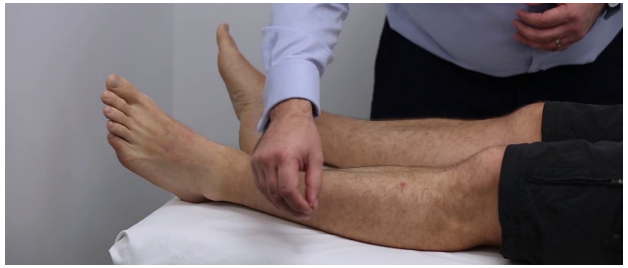


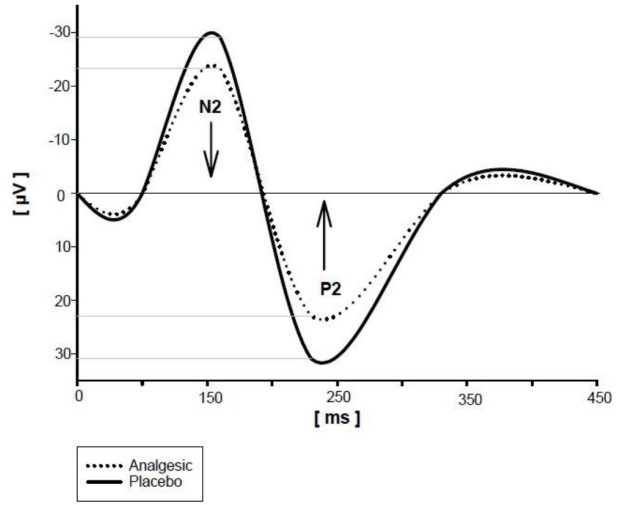
5+6 UVB Level

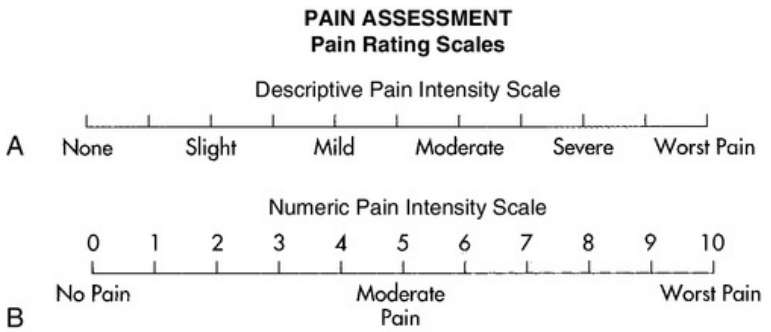
3+4 Strip&Occl.

1+2 Norm open









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ACD440 – Positive PoM study results

- Study execution in full alignment with time plan – no delays due to Covid-19 pandemic
- The study conduct is finished
  - ✓ No drop outs
  - ✓ No systemic or local adverse events
- Topline data presented on April 19
  - ✓ Highly significant analgesic effect of ACD440 on laser evoked pain and mechanical sensitivity
  - ✓ Significant effects seen in all three skin conditions
- Plasma concentration analysis is currently ongoing

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ACD440 – Planning for Phase II and onwards

- Preparations for the Phase IIa study are ongoing
- We have initiated production of study drug for the Phase IIa study
- Apply for a pre-IND meeting with FDA, prior to Phase IIa study
- Submit clinical trial application to regulatory bodies for Phase IIa clinical study by the end of the year
- We are working closely with our scientific advisory board of international experts in neuropathic pain to optimize the clinical program for ACD440
- Development of full Clinical Development Plan for the way to market

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ACD440 – Significant market opportunity

- A high level of unmet need in neuropathic pain management - even small market shares could translate into significant business opportunities
- The opioid epidemic in the US has put a focus on side effects of strong pain medications highlighting the need for non-opioid approaches
- Growing patient base will provide a total market growth
- ACD440 potential for first-in-class and has the potential to be placed as 1st line
- The market as an add-on to orals will be large
- There are not many direct competitors on the market or in pipeline

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ACD440 – Summary

- ACD440 is an antagonist of VR1 - a mechanism central to pain signalling
- Upregulation of VR1 receptors in neuropathic pain patients
- Primary indication is peripheral neuropathic pain – an area of huge unmet need
- PoM Phase Ib study - highly significant analgesic effects with no tolerability issues
- Planning of Phase Iia study ongoing and plan to submit application by end of year

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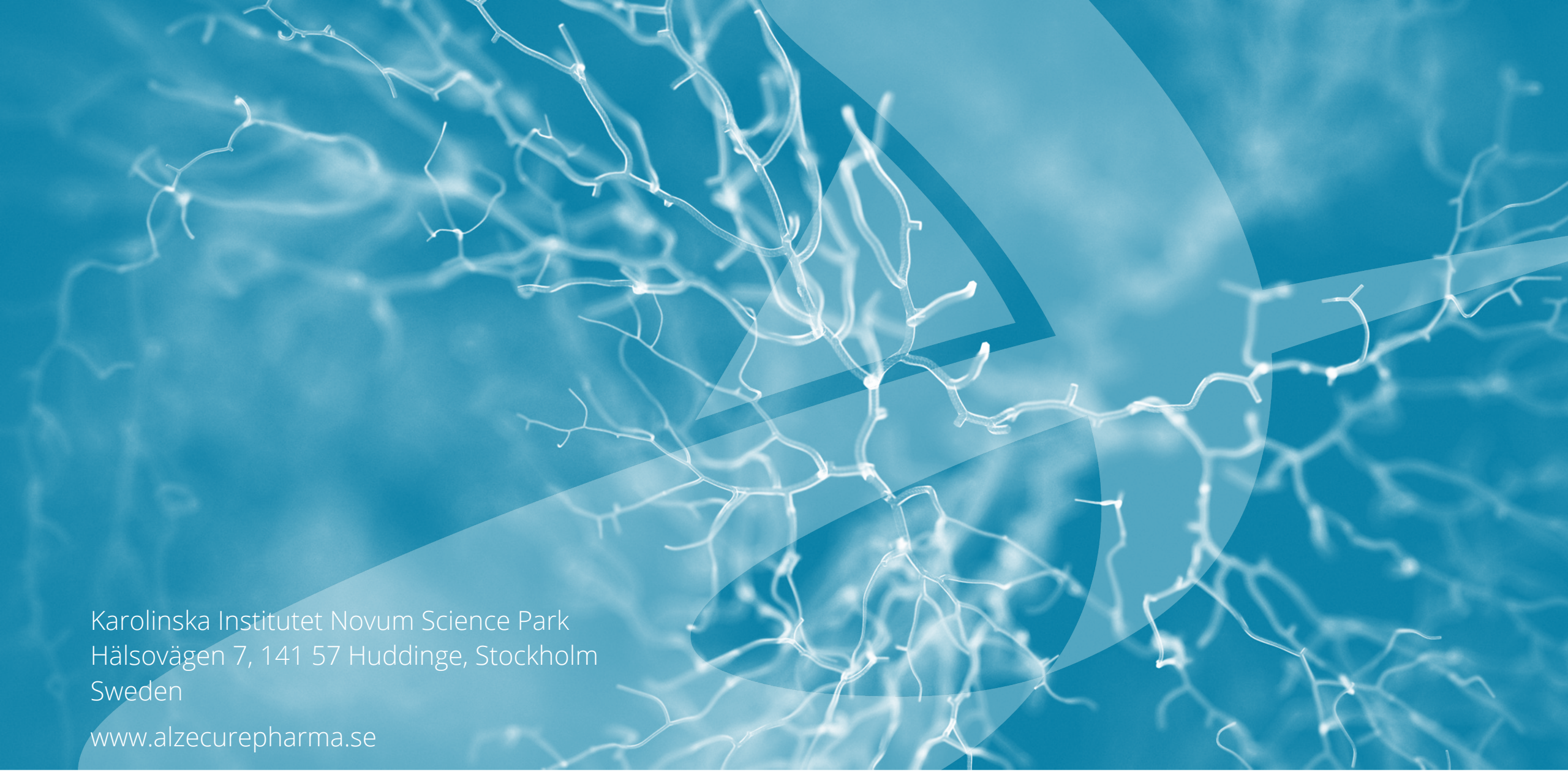

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