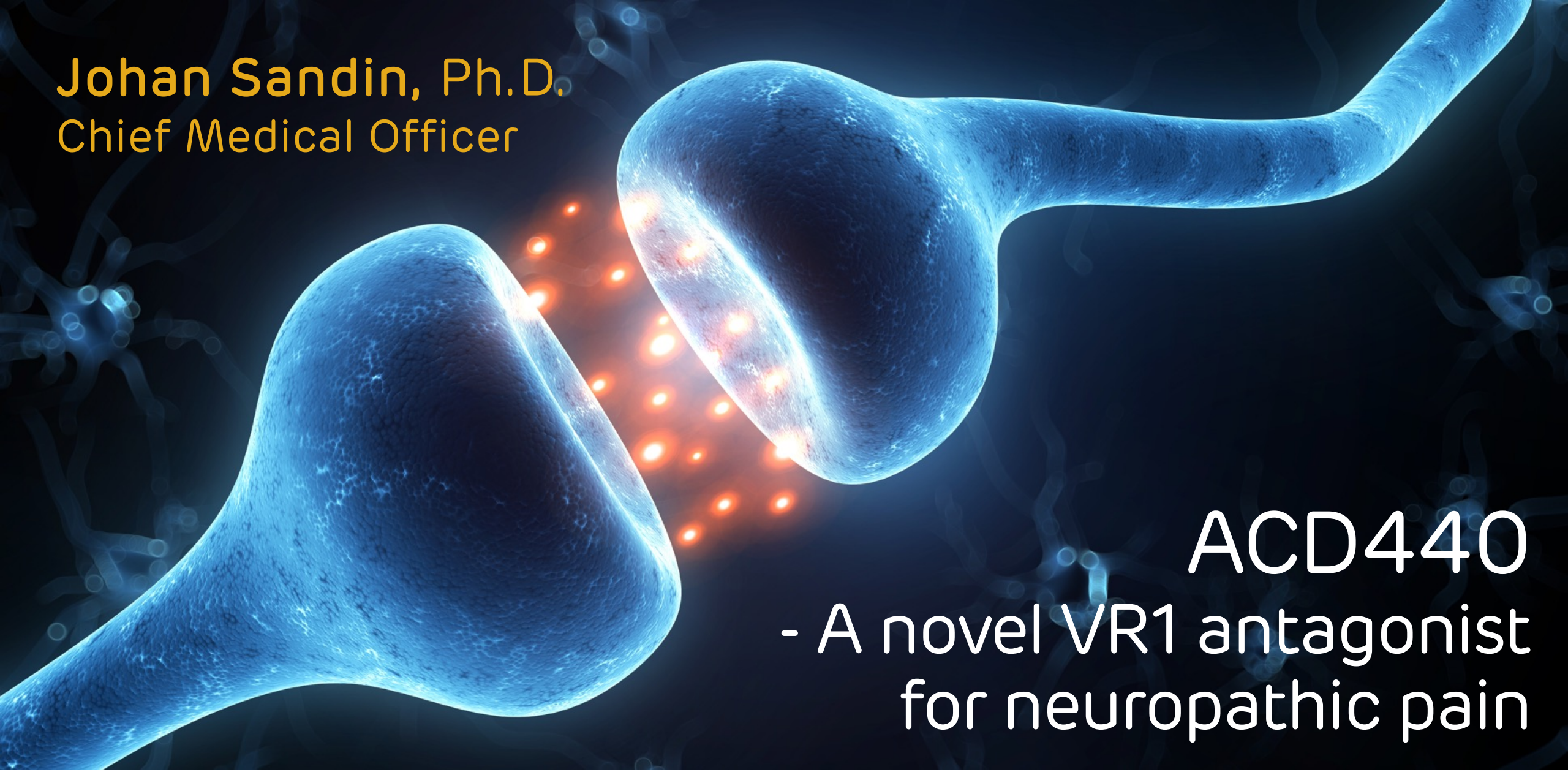

Johan Sandin, Ph.D.
Chief Medical Officer

ACD440
- A novel VR1 antagonist for neuropathic pain

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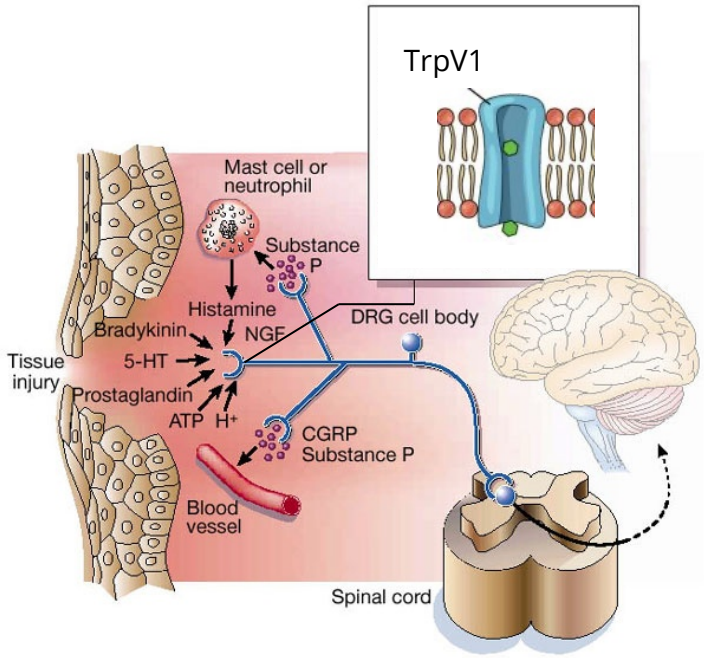
ACD440 – Target mechanism central to pain signaling

- 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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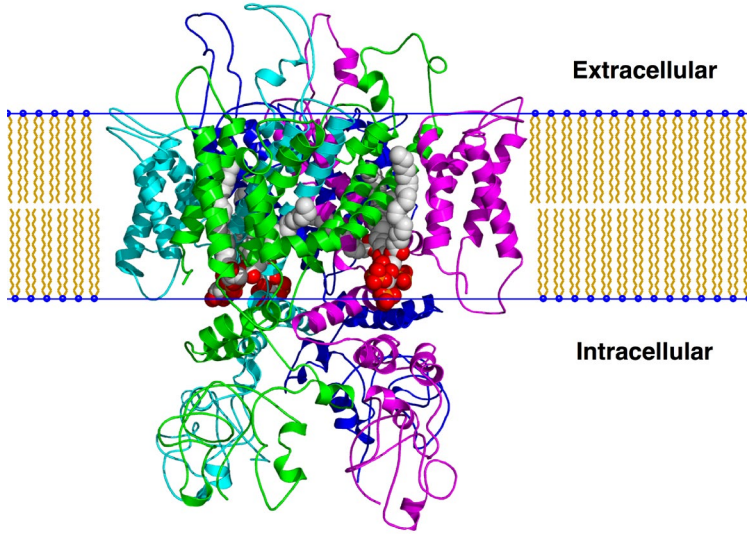
ACD440 – Target also located in peripheral tissues

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



VR1 located in the cell membrane

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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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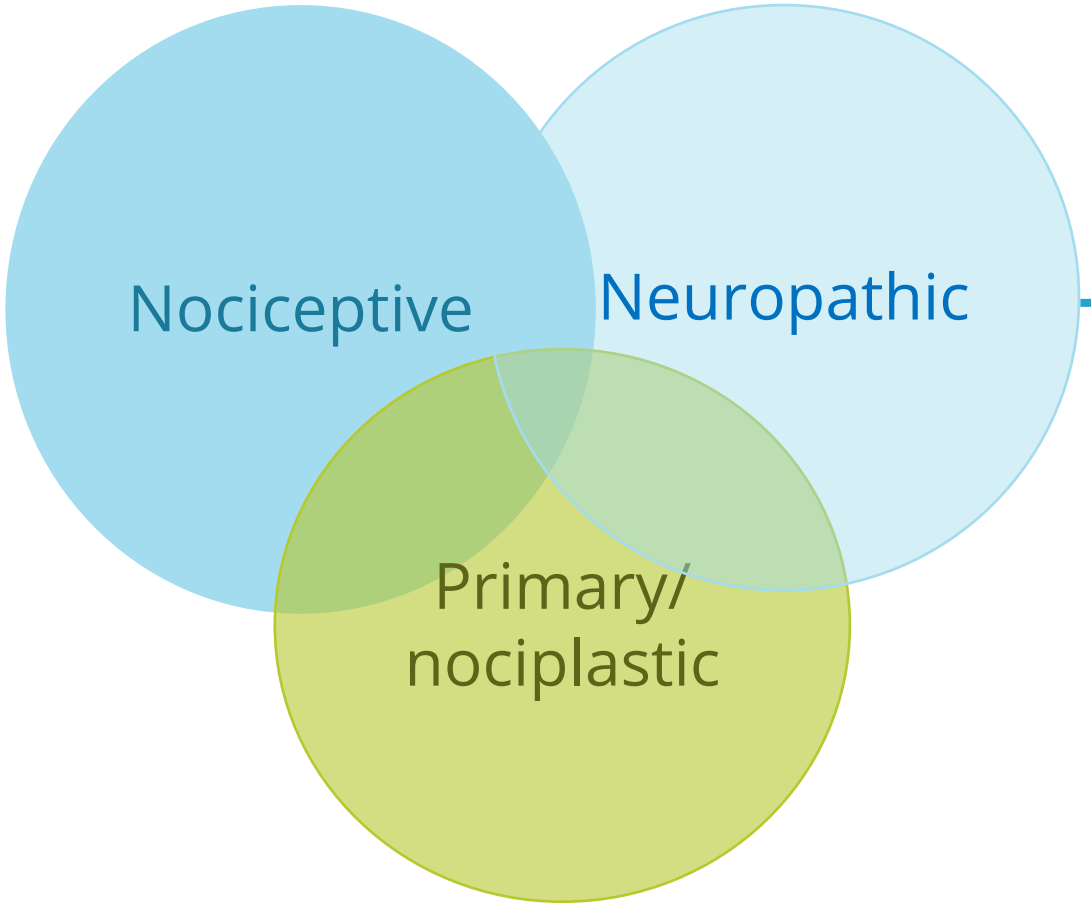
Neuropathic pain – Area of huge unmet need



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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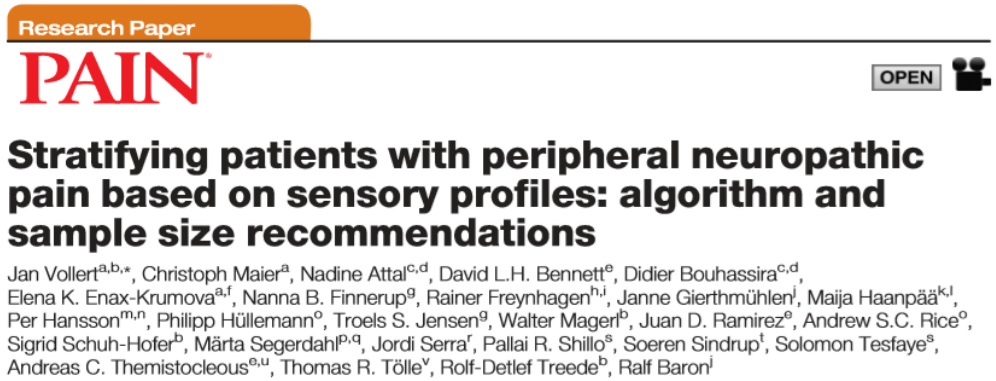
ACD440 – Targeting peripheral neuropathic pain

- 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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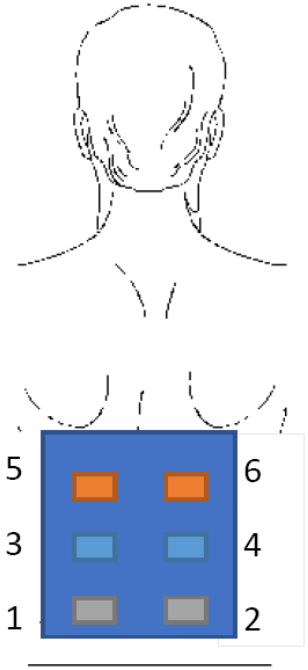
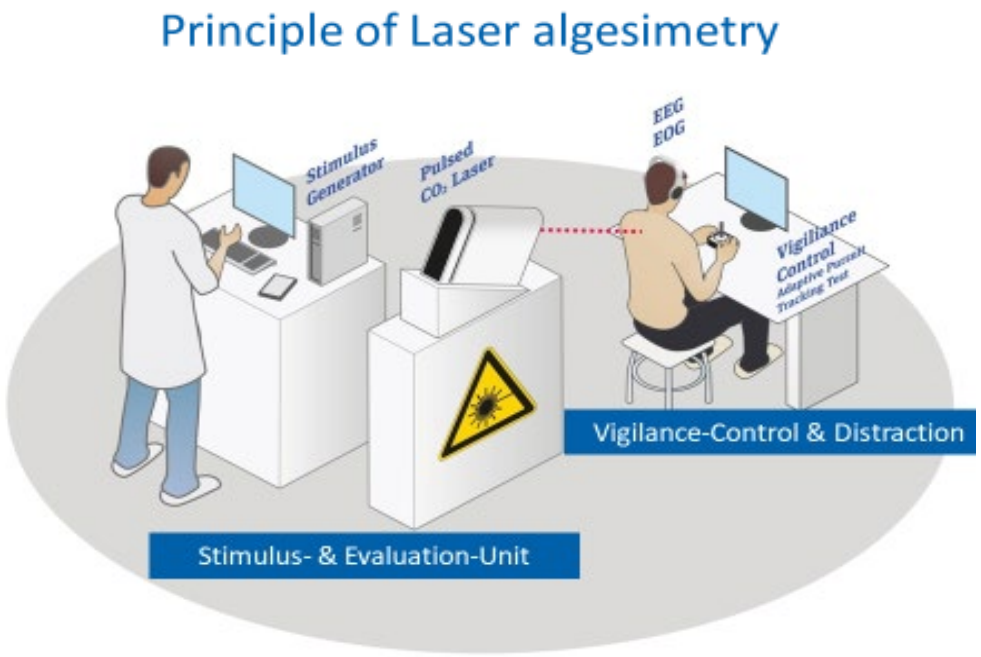
ACD440 – Methodology used in PoM study

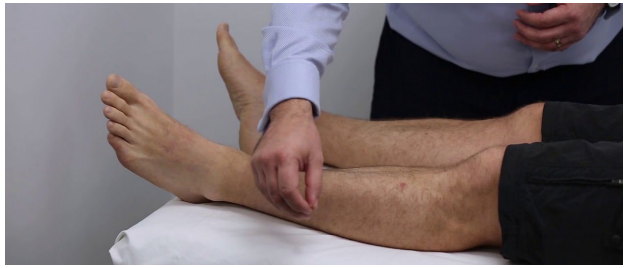


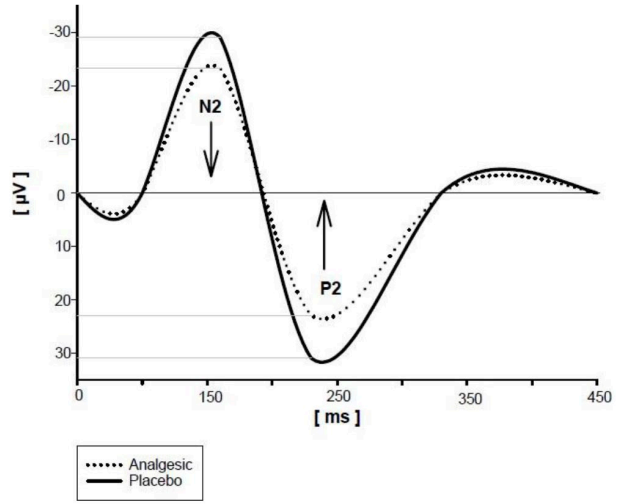
5+6 UVB Level

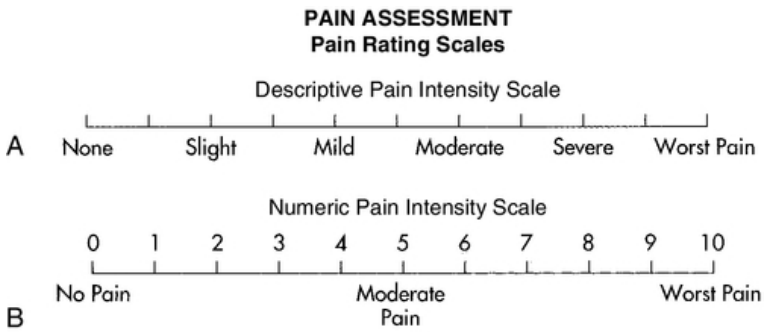
3+4 Strip&Occl.

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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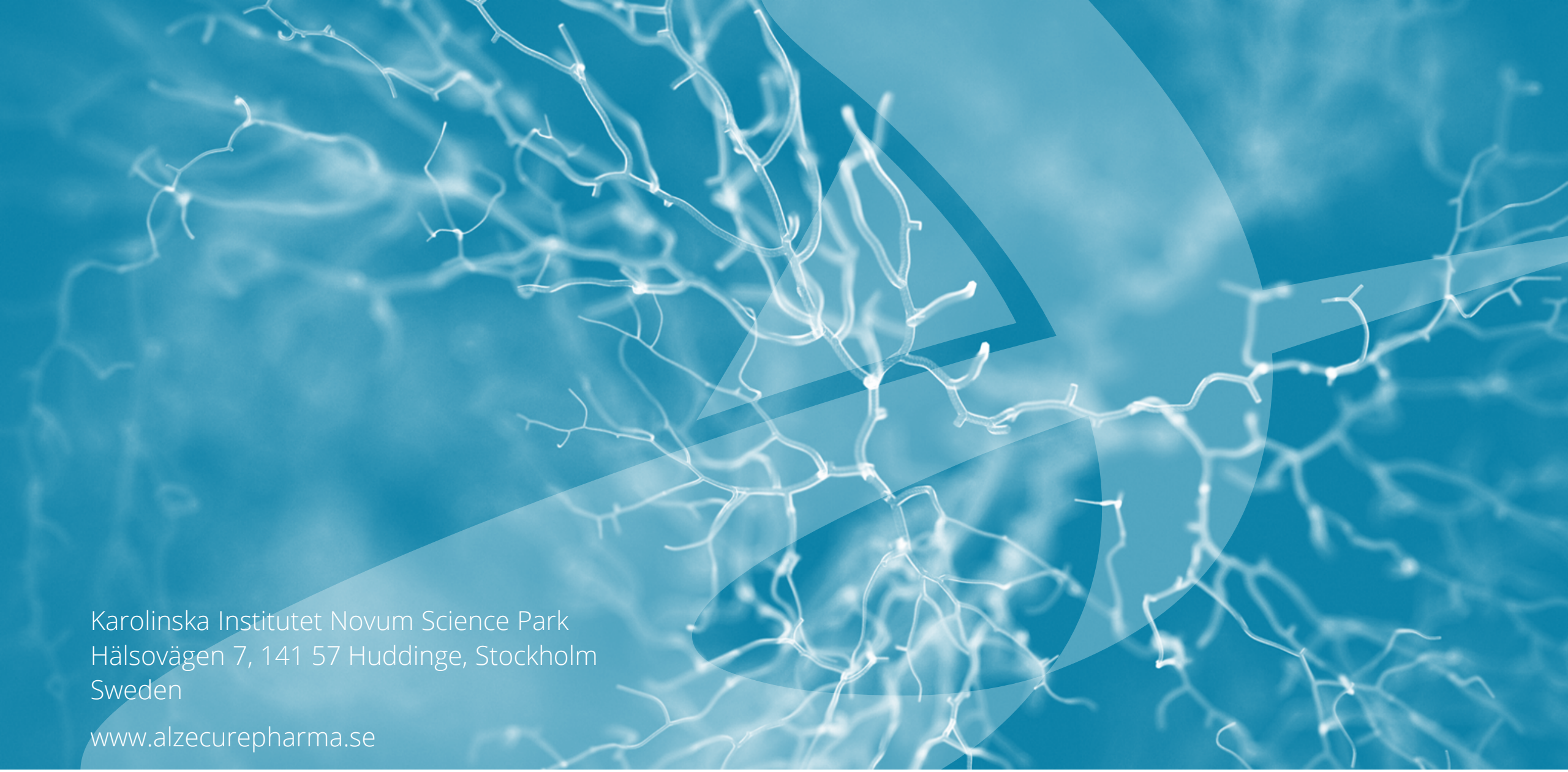

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