May 26, 2026

TrkA-NAM

- A novel None-Opioid Treatment of Severe Pain Conditions

AlzeCure

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Q&A Session

EXPERIENCES

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

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

from GRÜNENTHAL, Karolinska Institutet, AstraZeneca, Lundbeck

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

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

AstraZeneca, MERCK FROSST, orexo, Karolinska Institutet

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

Roche, Lunds Universitet, FERRING PHARMACEUTICALS

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TrkA-NAM – A novel none-opioid treatment of severe pain conditions

- 14:00 **Welcome & brief presentation of AlzeCure Pharma & agenda** – Martin Jönsson, CEO, AlzeCure
- 14:05 **TrkA-NAM in pain – Major unmet medical needs & indication areas -** Märta Segerdahl, CMO
- 14:20 **TrkA-NAM – Next-generation non-opioid analgesics –** Pontus Forsell, Head of Disc. & Res.
- 14:40 **Q&A** – Moderator Martin Westerberg, FinWire
- 14:55 **Concluding remarks** – Martin Jönsson, CEO, AlzeCure and Martin Westerlund, FinWire

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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)

European Innovation Council

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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

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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 & Orphan indication Erythromelalgia					
	ACD137	Negative allosteric modulator (NAM) of TrkA-receptors	Osteoarthritic Pain & other severe pain conditions					

Positive read-out Phase I trial

Safety, Tolerability & Target engagement

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Grant for phase 2

Selected ACD680 as lead going forwards towards clinic

Positive read-out Phase IIa

Safety, Tolerability & Pain

FDA Orphan Designation

Selected new CD

ACD137

EMA EUROPEAN MEDICINES AGENCY

European Innovation Council

Phase completed **Phase ongoing**

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New scientific article on TrkA-NAM ACD137 characterization

DE GRUYTER

Scandinavian Journal of Pain 2026; 26(1): 20260007

Original Experimental

Pontus Forsell*, Maria Backlund, Veronica Lidell, Azita Rasti, Cristina Parrado Fernandez, Märta Segerdahl, Johan Sandin and Gunnar Nordvall

Analgesic, anti-inflammatory and joint protective effects of ACD137, a selective negative allosteric modulator of TrkA, in models of chemotherapy-induced peripheral neuropathy and osteoarthritis

https://doi.org/10.1515/sjpain-2026-0007
Received November 28, 2025; accepted March 17, 2026;
published online April 27, 2026

Abstract

Objectives: The neurotrophin receptor TrkA is a clinically and genetically validated target in pain signaling. Anti-nerve growth factor (NGF) monoclonal antibodies have shown clinical efficacy but with side effects such as rapidly progressing osteoarthritis limiting their use, potentially mediated via inhibition of NGF/p75NTR signaling. Therefore, we sought to identify novel and selective small molecule negative allosteric modulators of tropomyosin receptor kinase A (TrkA) and to verify their analgesic effect *in vivo*.

neuropathy (CIPN) using paclitaxel and in the mono-iodo acetate (MIA)-induced osteoarthritis model in rats.

Results: ACD137 demonstrated an IC_{50}-value on TrkA of 1.2 nM and showed approximately 17,300- and 17,600-fold selectivivity for TrkA over TrkB and TrkC, respectively. After oral administration in rats, ACD137 reduced mechanical allodynia in the CIPN model in a dose-dependent manner with maximal analgesic efficacy similar to the effect of gabapentin. In a comparative arthritis study using the anti-NGF antibody tanezumab as comparator, ACD137 reduced both evoked and non-evoked pain behavior as well as inflammation with similar efficacy as tanezumab. Surprisingly, ACD137 demonstrated a significant protective effect against knee joint deterioration, something that was not observed with tanezumab.

May 26, 2026

TrkA-NAM in pain

– Major unmet medical needs & indication areas

Märta Segerdahl, MD, PhD, Chief Medical Officer

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Osteoarthritis Pain – Still a Large Unmet Medical Need

Pain starts mostly when starting physical activity, and after strainful activities.
Later in disease, also at rest and during the night. Pain at rest is more common in hip OA

Stiffness in the morning or after inactivity is usually does not last more than 30 min.
Swelling and edema around the joint is not uncommon
Joints can also become sore to touch

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Osteoarthritis – a Wellknown but Underserved Pain Disorder

- Osteoarthritis (OA) affects 595 million people worldwide and is one of the most rapidly increasing health conditions globally[1], In the US, >14 million adults are affected[2]
- Symptomatic knee OA occurs in 10% men and 13% in women ≥60 years, >14 million in the US[2]
- Not only the knee can be affected, also other joints – hip, spine (lower back and neck), hands
- The prevalence rises with increasing age
- Joint replacement – many want to wait for as long as possible
- Current therapies – NNT and NNH
- The risk for side effects in older individuals

[1]*Hatzikotoulas et al. Nature 2025;* [2]*Zhang et al, Clin Geriatr Med 2010, 2013*

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Current Standard of Care Treatment in Knee OA

- Exercise is a core treatment, both to reduce stiffness and to reduce pain
- Weight reduction
- Pharmacological treatments should always be combined with exercise

Pharmacological treatment	Recommendation/ evidence level
Oral NSAIDs, including celecoxib	High level
Paracetamol	Weak level
Opioids weak	Weak level
Duloxetin	Weak level
Intraarticular corticosteroid injections	High level
Topical NSAID, strong opioids	Not recommended

- Pharmacological treatments are tailored individually based on effects and side effects

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Side Effects of Current Pharmacological Standard of Care

- NSAIDs
  - Gastrointestinal – gastritis, gastric ulcers, diarrhoea, nausea are quite common – approx 25% of patients
  - Cardiovascular – myocardial infarction, cardiac failure – <0.5% of patients
  - Kidney function – approximately 2% of patients, BUT a large proportion of older patients admitted to hospital due to drug side effects have kidney failure caused by NSAIDs
- Paracetamol
  - Very few side effects, but also very low efficacy
- Opioids
  - Constipation in almost all patients
  - Nausea
  - Dizziness - falling
  - Impaired cognition

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What Happened to the NGF Antibody Story?

- Monoclonal anti-NGF antibodies were developed in the 2010-ies, and in PhIII of clinical development for OA pain, neuropathic pain and cancer related pain
- The effect was stunning and dose related
- During the development of Pfizer's tanezumab and other anti-NGF antibodies, Rapidly Progressing OA (RPOA) appeared as an unexpected AE
- Mostly in combination with NSAID as rescue treatment
- RPOA was dose dependent, when risk was lower, efficacy was very low
- As a result, anti-NGF mABs never reached the market
- NGF antibodies have also now been applied in pain management for cats and dogs*

The NGF antibodies have validated NGF as a relevant treatment target in pain
A TrkA-NAM, such as ACD137, can avoid the adverse effects seen with the ABs by being selective for the TrkA receptor

**della Rocca et al, 2025*

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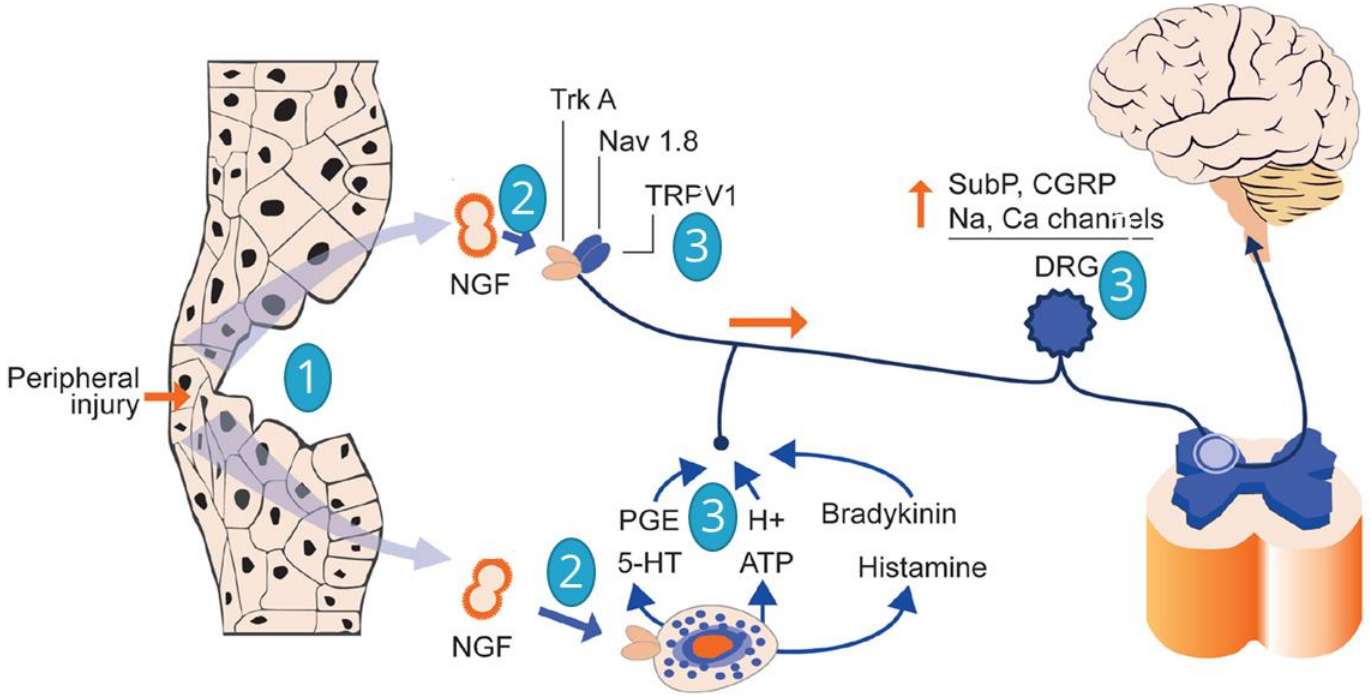
How Does ACD137 Differ from NGF-Antibodies?

Background and target pathway: NGF/TrkA

NGF and its receptor TrkA play an important role in pain sensation and the pathway is both genetically and clinically validated in humans

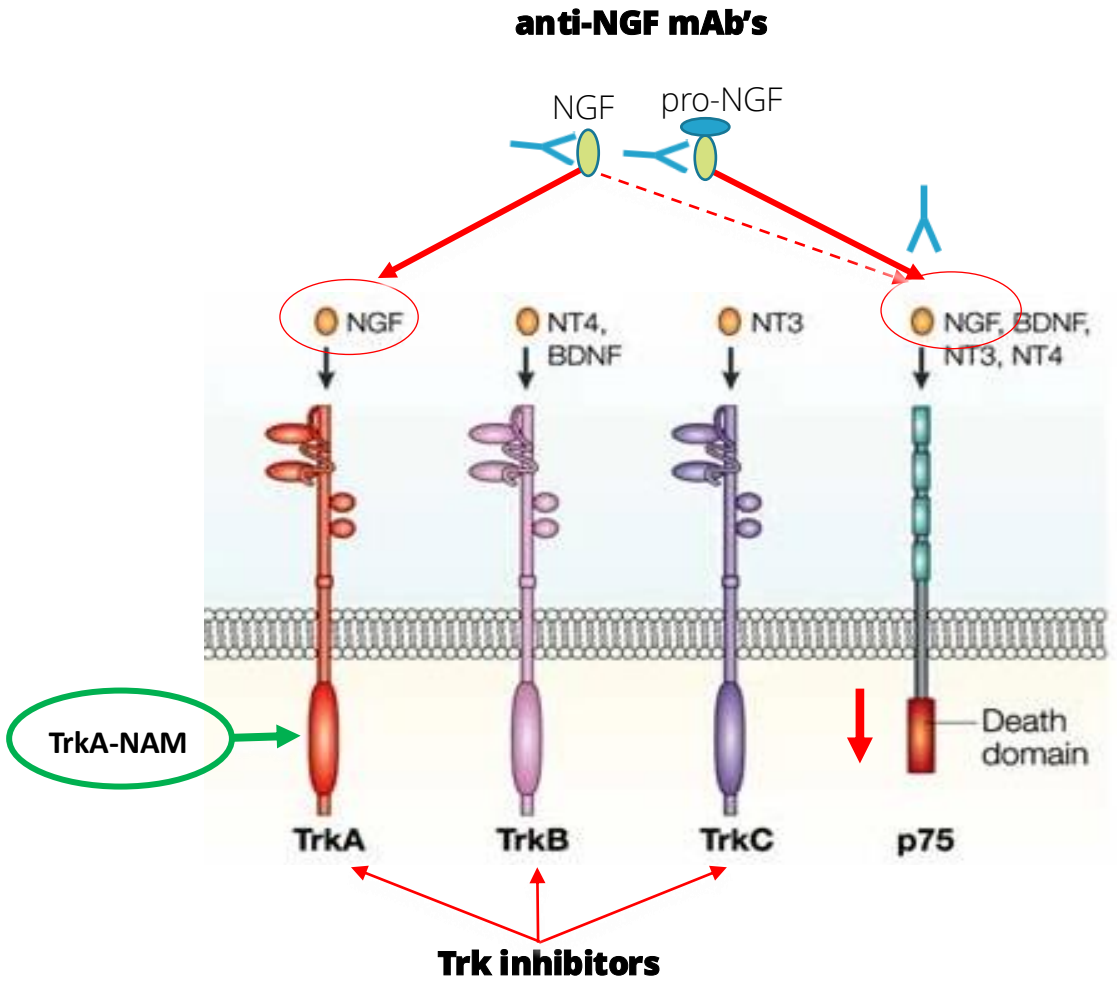
- **1.** NGF is released at the site of an injury.
- **2**. TrkA is the receptor for NGF and it is located on both neuronal and non-neuronal cells.
- **3.** NGF leads to inflammation and increased neuropathic and nociceptive pain.
- **4.** Anti-NGF antibodies, TrkA inhibitors or negative allosteric modulators (NAM) are analgesic in several preclinical models



NGF and TrkA are involved in inflammation as well as in nociceptive and neuropathic pain signaling

Anti-NGF-antibodies are unselective and block all NGF targets

- RPOA seems to be due to an inhibition of the p75 receptor
- This is avoided by ACD137, being selective for the TrkA receptor



Inhibition of p75NTR signaling by anti-NGF mABs might increase inflammation in the knee joint and reduce the natural tissue remodeling/repair of joints, especially when in combination with NSAIDs

ACD137 and its Role in Reducing Pain in Knee Osteoarthritis

Pain and stiffness are present in osteoarthritis

Knee OA causes pain and stiffness, having a great impact of level of daily activity and quality of life

Modulators reduce pain signalling

Negative allosteric modulators of TrkA, such as ACD137 can block the pain induction caused by NGF and thereby reduce OA pain

Improved mobility and wellness

The treatment will lead to less pain and inflammation as well as improved bility for people with knee OA, improving their quality of life

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Chemotherapy Induced Neuropathic Pain

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CINP – a Growing Patient Group

- In 2023, 5-year survival was 85% or more in 25 countries in Europe, North America and Oceania[1]
- In the US, the 5-year relative survival in the US rose from 75% in 1970s to 90% in 2017[1]
- The American Cancer Society today states that common cancer types such as breast cancer and prostate cancer, as well as aggressive forms as testicular cancer, thyroid cancer, and skin melanoma have survival rates of 99-100%.
- An important reason for this is screening programmes, as well as improved treatment regimens.

- Considering the increasing yearly incidence of not the least breast, prostate, colon and lung cancers, the number of individuals is steadily increasing

[1] *Amato et al, Curr Opin Oncol, 2023*

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How Common is Cancer Treatment Related Pain Overall?

- Pain after Irradiation Treatment is high, 38% after ENT-cancers, in general 30-40% (colon and breast cancer)
- Chemotherapy Induced Neuropathic Pain overall is not as well studied epidemiologically, and differs based on type of chemotherapeutic agent and type of malignancy
- The CINP intensity often sets the dose limit for the chemotherapy – an efficacious treatment could help optimization of the chemotherapy and thereby increase effects
- Thus, CINP is very intense in the acute phase, but often attenuates over time, with remaining provoked symptoms in combination with loss of sensation
  - A typical chronic feature is loss of sensitivity in the feet, requiring steady shoes, in combination with ”pins and needles” provoked by cold even at normal ambient temperature

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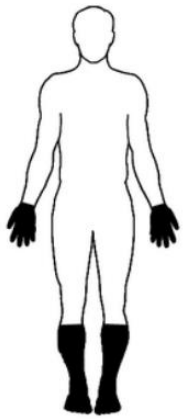
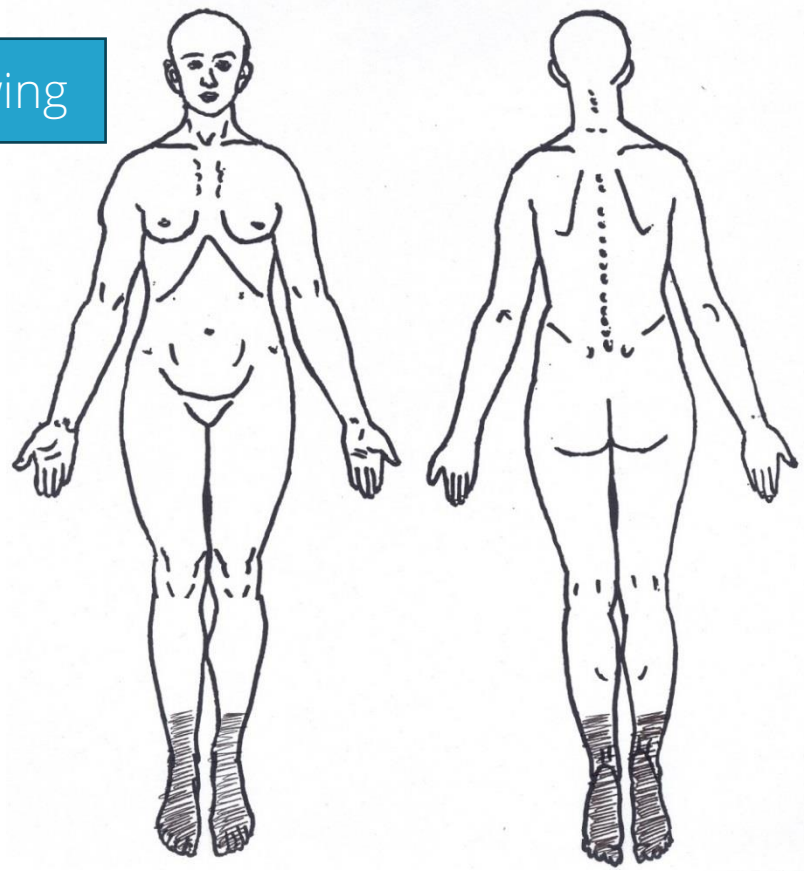
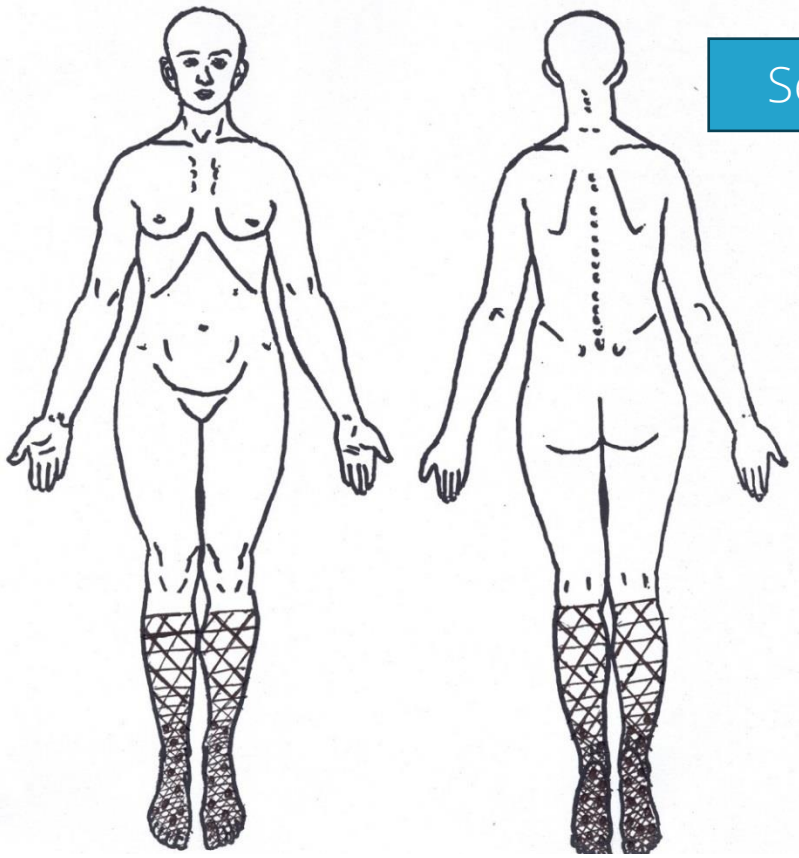
A typical pain drawing of CINP – socks and gloves distribution

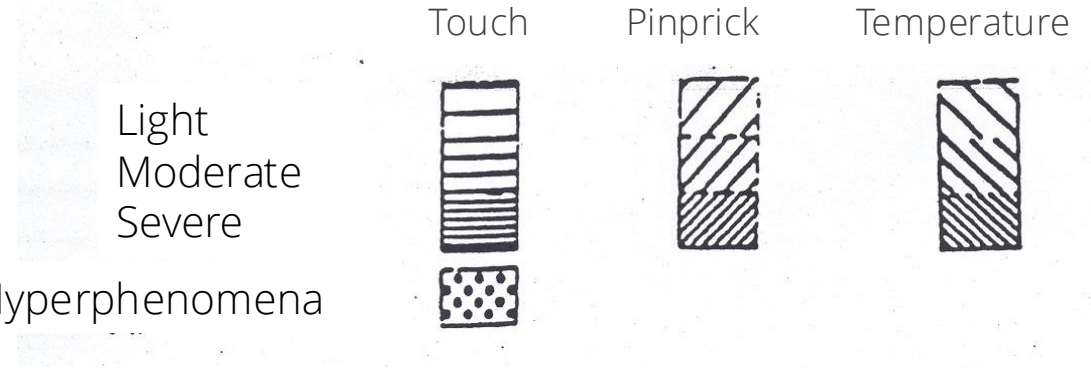
Patient drawing





Sensory testing





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What is the Current Standard of Care for CINP?

- The same treatments as for other peripheral neuropathic pains are used:
  - Serotonin Norepinephrine Reuptake Inhibitors (SNRI)
  - Gabapentinoids
  - Tricyclic antidepressants (TCA)
  - Coping strategies

- There are few studies dedicated in CINP on clinicaltrials.gov
  - One NIH-funded study of duloxetine demonstrated significant reduction of pain vs. placebo*
  - Two ongoing studies (Nav1.7-channel blocker; Ca^{2+}-channel blocker)
  - One completed negative study (pregabalin) **

➢ In clinical experience, the treatment success is lower than for other neuropathic pains, i.e. an NNT of 12-15

**) Smith et al, 2013; **) de Andrade et al, 2017*

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Grading of Treatment Related Adverse Events/ Side Effects

No mention of pain or discomfort

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local, or noninvasive intervention indicated; limiting age appropriate instrumental ADL	Severe or medically significant but not immediately life-threatening; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)	Life-threatening consequences; urgent intervention indicated	Death

Definition: A potentially fatal complication of treatment in certain molecular subgroups of leukemia characterized by fever, rash, dyspnea and/or hypoxia, pulmonary infiltrates, peripheral edema with rapid weight gain, pleuropericardial effusion, acute renal failure, disseminated intravascular coagulation (DIC), bone pain and/or hypotension.

Oncology questionnaires do not assess pain as a treatment related side effects
Information to patients mostly rare or non-existing

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Chemotherapy-induced neuropathy - CINP

Supportive Care in Cancer (2020) 28:5933–5941
https://doi.org/10.1007/s00520-020-05438-5

ORIGINAL ARTICLE

Check for updates

Painful and non-painful chemotherapy-induced peripheral neuropathy and quality of life in colorectal cancer survivors: results from the population-based PROFILES registry

C. S. Bonhof[1,2] · H. R. Trompetter[1] · G. Vreugdenhil[3] · L. V. van de Poll-Franse[1,2,4] · F. Mols[1,2]

- Painful CINP was reported by 9% (n = 45) of survivors and non-painful CINP was reported by 22% (n = 103).
- Time since diagnosis was related to CINP
- Time since diagnosis, a higher disease stage, osteoarthritis, and more anxiety symptoms were related to non-painful CINP
- Survivors with painful CINP reported a worse global quality of life
- No differences were found between survivors with non-painful CINP and those without sensory CINP

Painful CINP must be distinguished from non-painful CINP, as only painful CINP was related to a worse HRQoL.

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Many of the Most Common Chemotherapeutic Agents Cause Neuropathy

Physiol. Res. 73: 333-341, 2024 *https://doi.org/10.33549/physiolres.935162*

REVIEW

Biological Mediators and Partial Regulatory Mechanisms on Neuropathic Pain Associated With Chemotherapeutic Agents

Ziyi LIU[1]*, Sitong LIU[1]*, Yu ZHAO[1]*, Qian WANG[1]
** These authors contributed equally to this work.*

[1]Tumor Center, The First Hospital of Jilin University, Changchun, Jilin, China

Received June 15, 2023
Accepted September 13, 2023

Table 1. Chemotherapeutic agents causing neuropathy.

Category	**Examples**	**Treatment**
Proteasome inhibitors	Bortezomib	Multiple myeloma certain types of lymphoma [47,48]
Platinum-based compounds	Oxaliplatin, cisplatin carboplatin	Solid tumors, i.e., stomach, liver, lung, ovarian, brain, uterine cancers [49]
Taxanes	Paclitaxel, docetaxel cabazitaxel	Ovarian, breast, on-small cell lung, and prostate cancers [48,50]
Vinca alkaloids	Vincristine, vindesine, vinblastine, vinorelbine	Hodgkin lymphoma, testicular cancer, and non-small cell lung cancer [51]
Epothilones	Ixabepilone	Non-small lung, ovarian, and prostate cancers [52]
Immunomodulatory drugs	Thalidomide	multiple myeloma [53]

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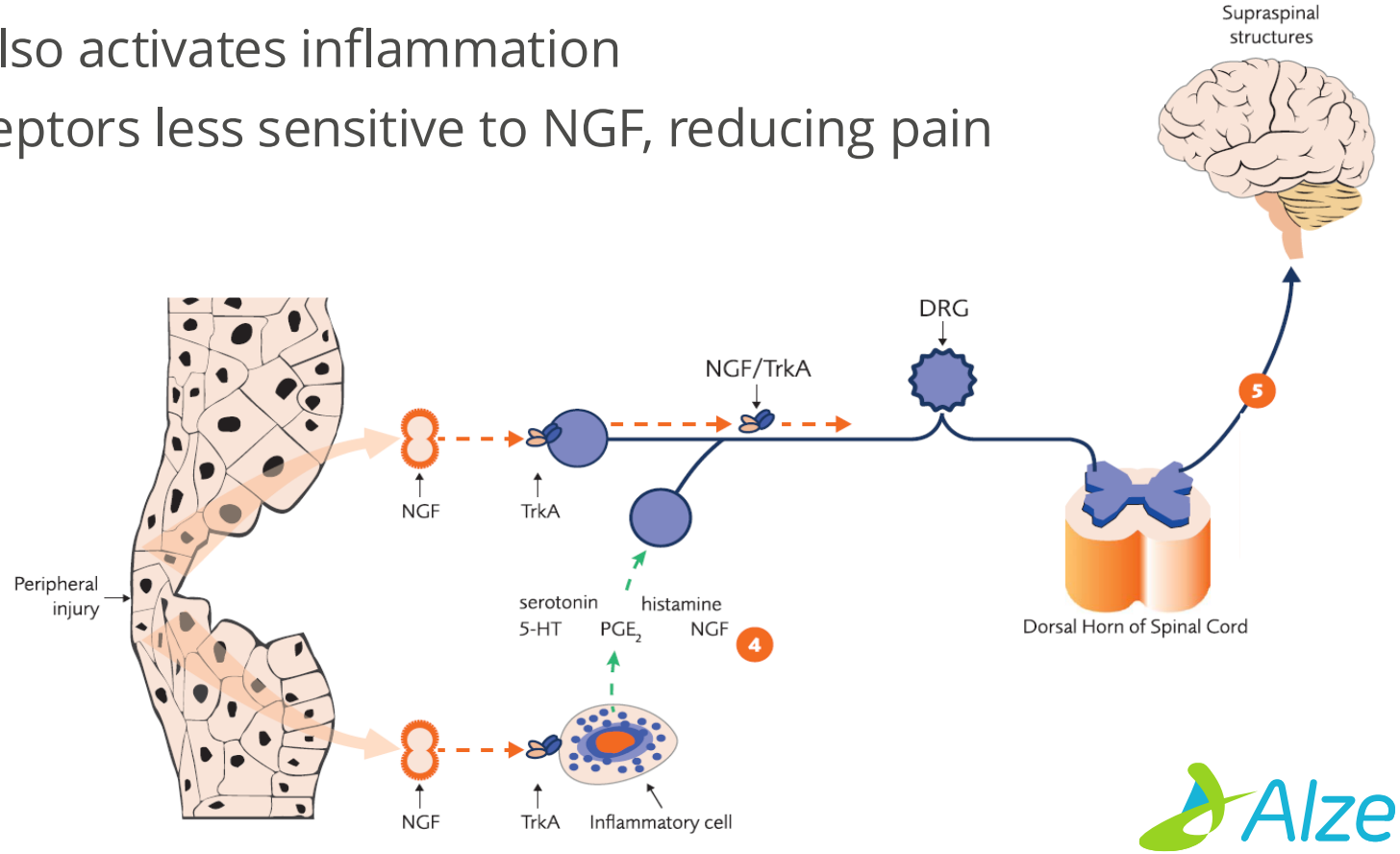
How Does TrkA-NAM Work in Reducing CINP Pain?

- **NGF antibodies have shown promise in alleviating chemotherapy-induced peripheral neuropathy (CIPN) pain, but been halted**
- The TrkA-receptors are present on the sensory nerves, so a stimulation of them, by NGF, gives rise to pain.
- TrkA-receptor stimulation also activates inflammation
- TrkA-NAM makes these receptors less sensitive to NGF, reducing pain and inflammation



Anti-NGF-antibodies are unselective and block all NGF targets

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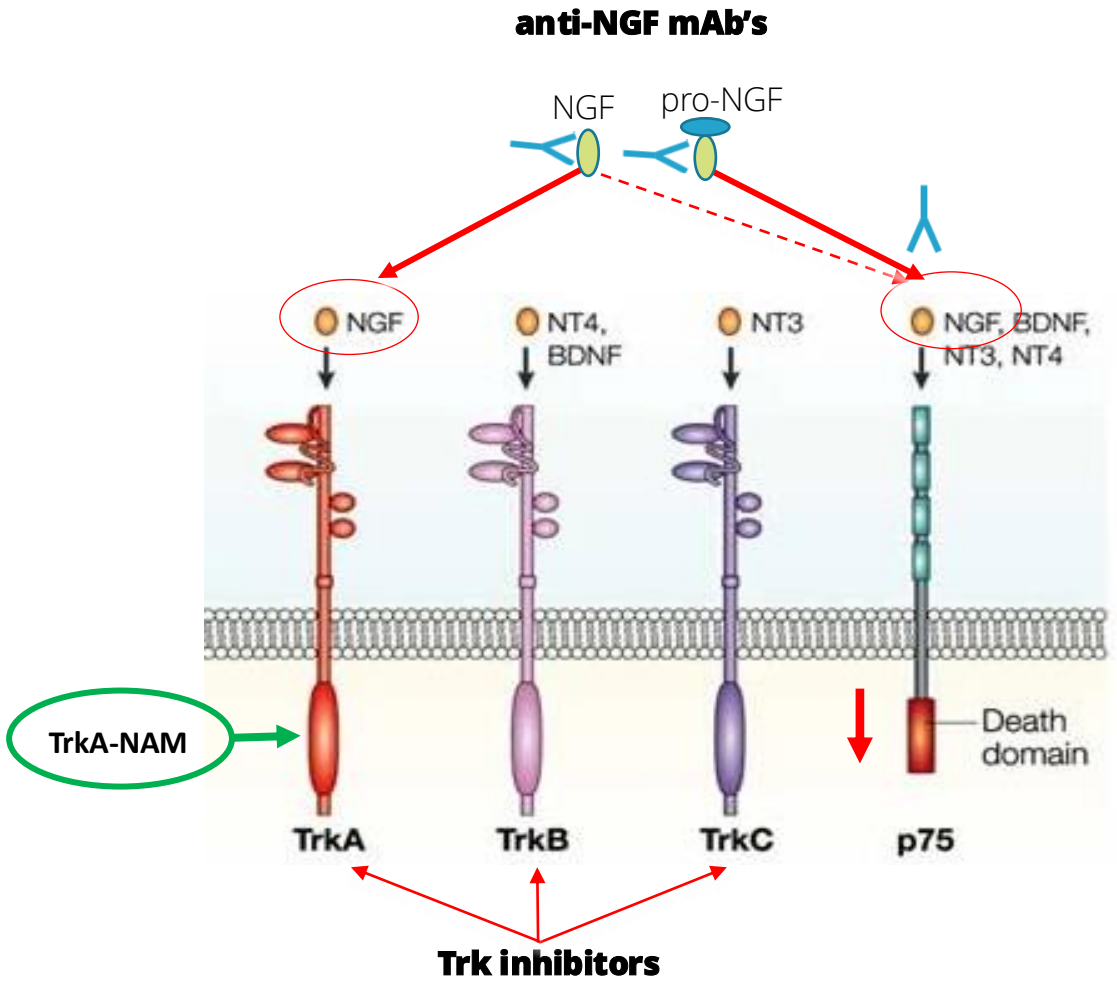
- This is avoided by ACD137, being selective for the TrkA receptor



Inhibition of p75NTR signaling by anti-NGF mABs might increase inflammation in the knee joint and reduce the natural tissue remodeling/repair of joints, especially when in combination with NSAIDs

Summary

- Osteoarthritis pain affects >500 million people worldwide, and increases with age
- Current therapies are not very efficacious and have limited efficacy and tolerability

- Chemotherapy induced neuropathic pain (CINP) is a growing with the increasing successful cancer treatments and increased survival times
- Approximately 9-10% of chemotherapy treated patients develop Chronic CINP
- CINP is a peripheral neuropathic pain, specifically sensitive to thermal stimulation
- Current treatments for neuropathic pain do not work very well

- Based on data with NGF-antibodies, NGF is a validated target for OA pain and relevant also for CINP
- ACD137, not having the side effect profile of the NGF-antibodies, is a very promising candidate for the treatment of acute and chronic CINP

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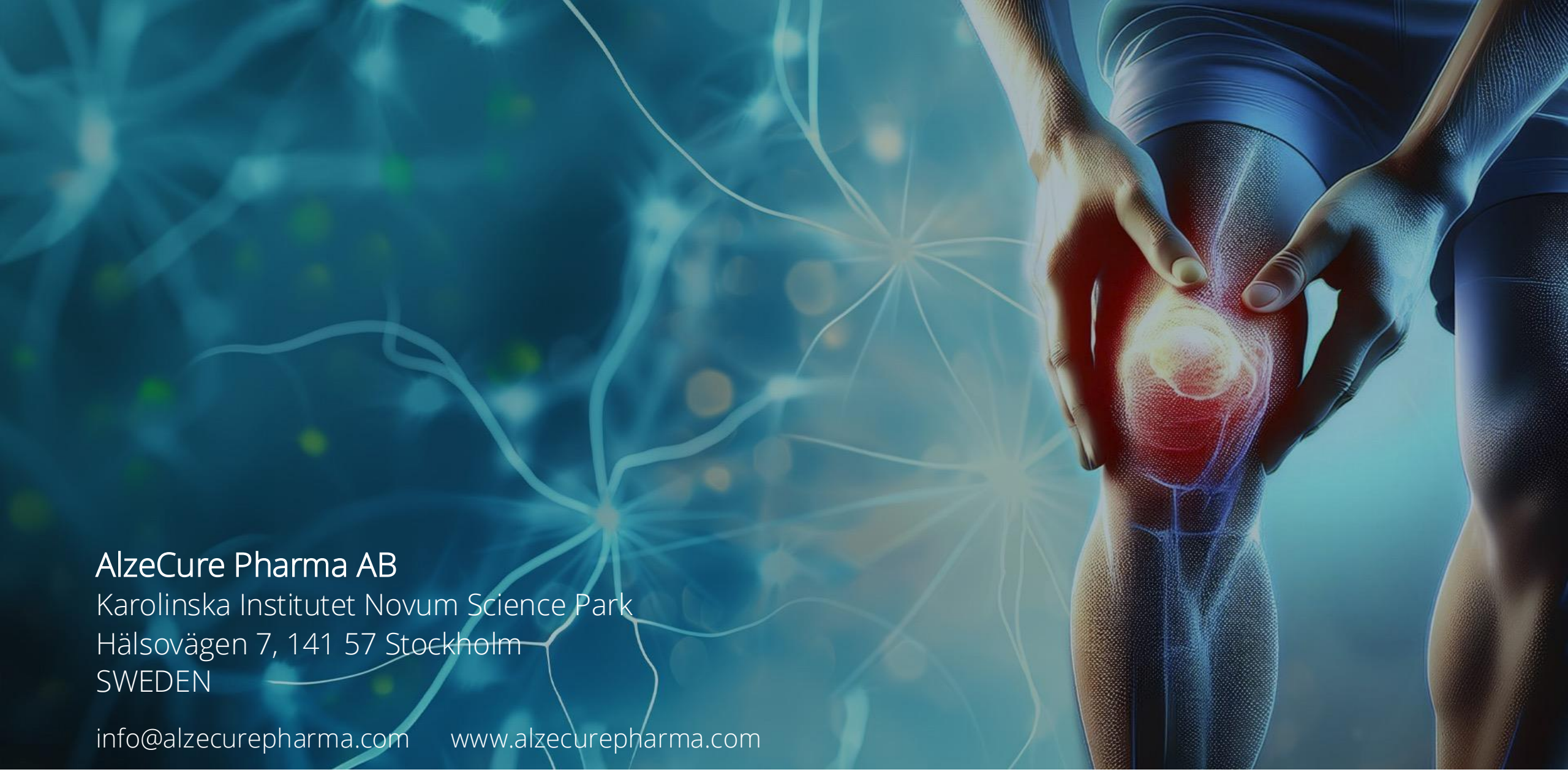

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May 26, 2026

TrkA-NAM
– Next-generation non-opioid analgesics

Pontus Forsell, PhD, Head of Discovery & Research

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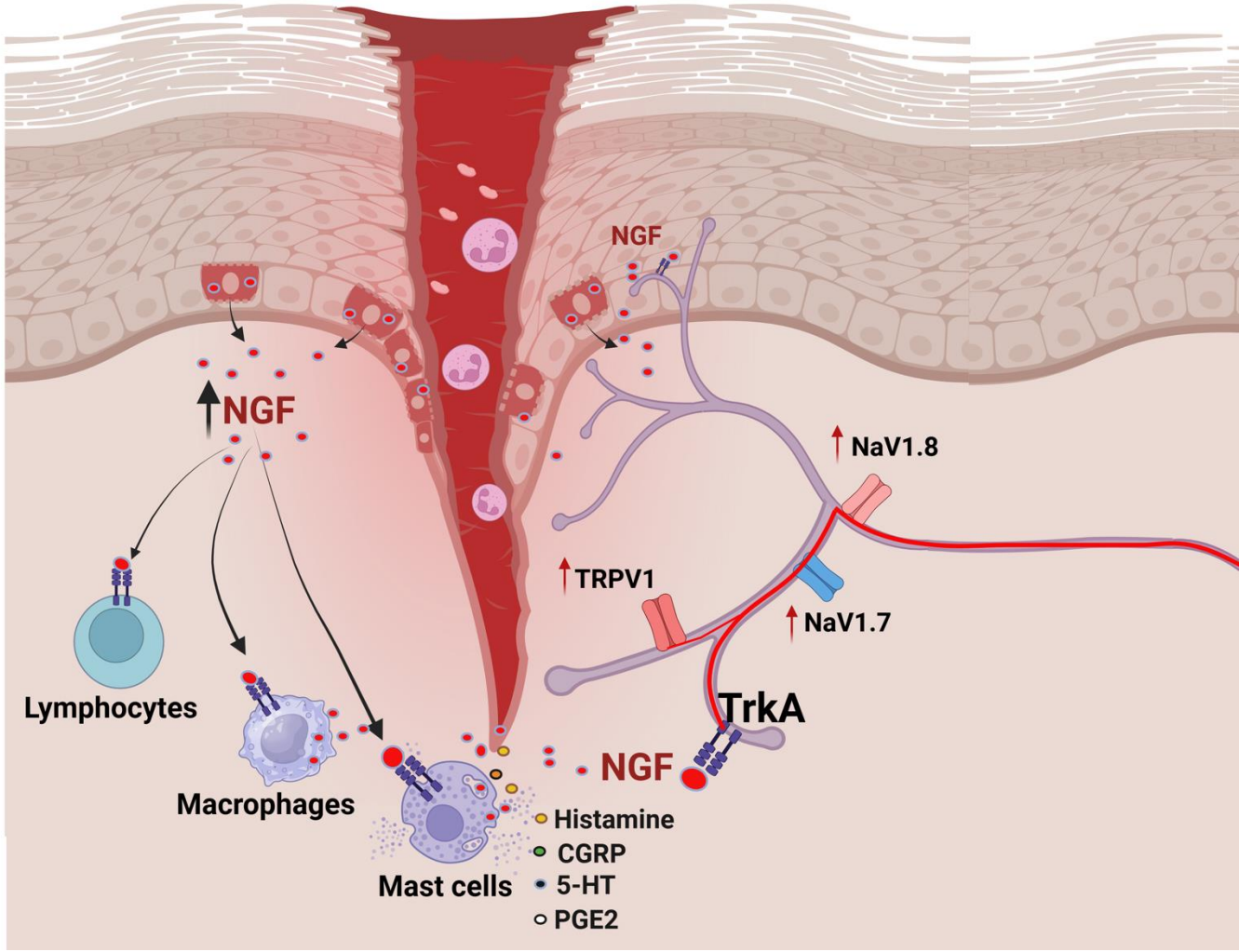
Background and target pathway: NGF/TrkA

Nerve growth factor (NGF) and its receptor TrkA plays an important role in pain sensation and is genetically and clinically validated in humans

- **1. NGF** is released at the site of an injury.
- **2**. **TrkA** is the receptor for NGF and it is located on both neuronal and non-neuronal cells.
- **3.** NGF leads to **inflammation** and **increased neuropathic and nociceptive pain.**
- **4**. Deletion of NGF or TrkA in humans leads to a painless phenotype
- **5. Anti-NGF antibodies** demonstrated a step change in efficacy in several late-stage clinical trials, but side effects limited the clinical usefulness



NGF and TrkA are involved in nociceptive and neuropathic pain signaling

Neurotrophins and mechanisms for targeting NGF/TrkA signaling

- **Neurotrophins binds to Trk-receptors and P75NTR**

NGF regulates multiple pathways such as neuronal survival in the CNS and pain sensation in the PNS.

Multiple attempts has been made to intervene with NGF-signalling:

- **Generation 1 (2000-2008)**

Non-selective Trk-inhibitors (Larotrectinib)

Inhibits TrkA, TrkB and TrkC

- **Generation 2 (2005-2015)**

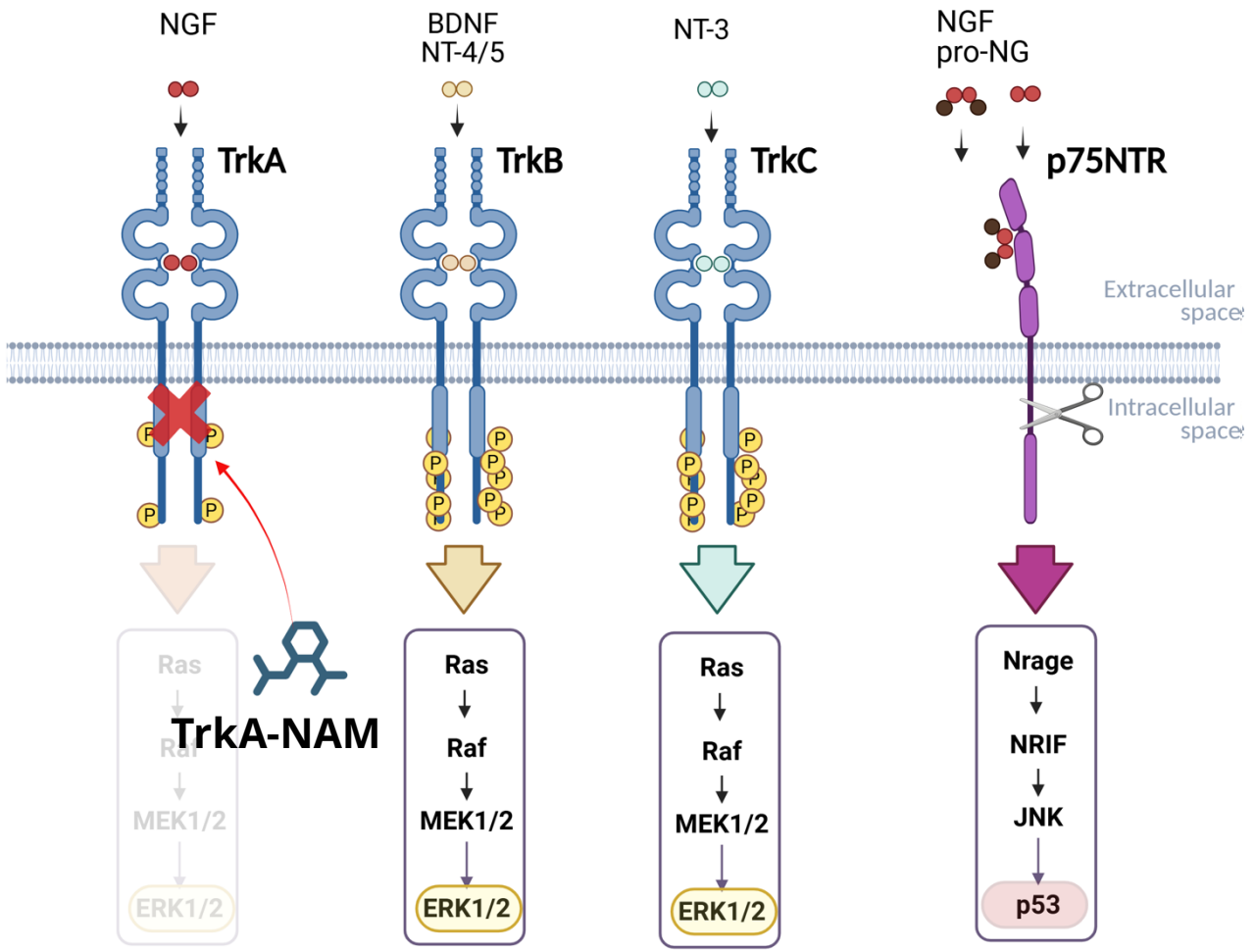
Anti-NGF monoclonal antibodies (Tanezumab)

Inhibits NGF and pro-NGF signalling via TrkA and p75NTR

- **Generation 3 (2015-2026)**

Negative allosteric modulators (NAM) of TrkA (ACD137 and AK1830).

Selective inhibition of TrkA



TrkA is a validated pathway for the treatment of pain
Allosteric modulators might give opportunity for biased signalling

Anti-NGF mAbs are effective in different types of pain

Clinical validation by anti-NGF monoclonal antibodies

Company	Drug name	Phase	Indication
Pfizer/Lilly	Tanezumab PF-04383119 RN624	3 3 3 2 3 3 2 2	OA-pain Low back pain Post herpetic neuralgia Diabetic Peripheral Neuropathy Painful bladder Cancer pain Schwannomatosis Chronic pancreatitis
J&J	Fulranumab	3	OA-pain
Regeneron	Fasinumab SAR164877 REGN475	3 3 2 2 2	OA-pain Low back pain Sciatic pain Pancreatitis pain Vertebral fracture pain

Inhibition of NGF/TrkA signaling is an effective analgesic treatment in several pain indications
Anti-NGF mAbs suffer from some adverse events (RPOA) that was dose-limiting

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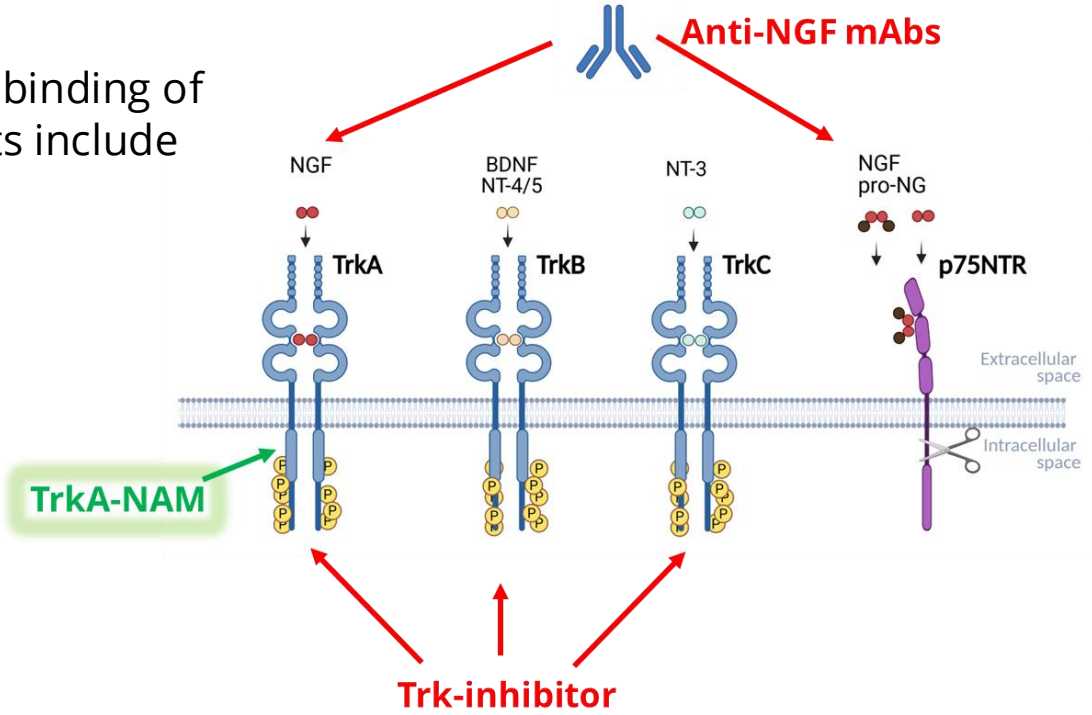
Safety: TrkA-NAM's, a safer mechanism than anti-NGF mAb's?

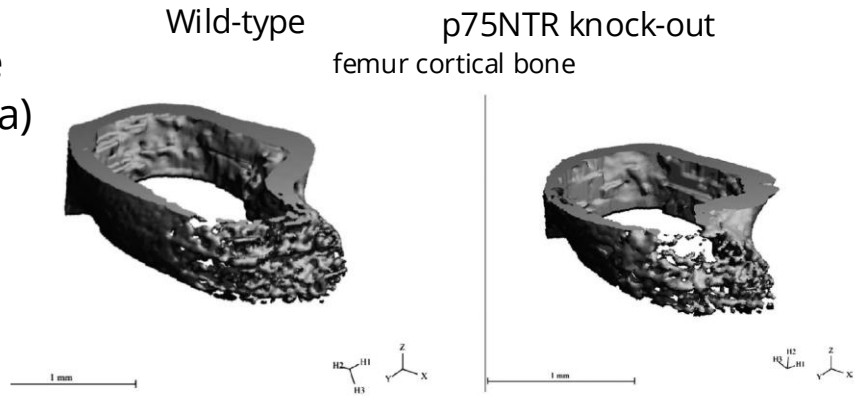
- The anti-NGF antibodies inhibits NGF signaling by blocking binding of NGF and pro-NGF to both TrkA and p75NTR. Adverse events include rapidly progressing OA (RPOA).

- Inhibition of p75NTR might be related to arthropathies:
  - p75NTR is involved in **bone mineralization** and bone homeostasis
  - p75NTR **limits inflammation** in the knee joint

- Trk-inhibitors like Larotrectinib inhibits TrkA, TrkB and TrkC. RPOA has so far not been reported by patients taking Trk-inhibitors.

- TrkA-NAMs have improved CNS safety profile compared to a Trk-inhibitor (Array Biopharma)



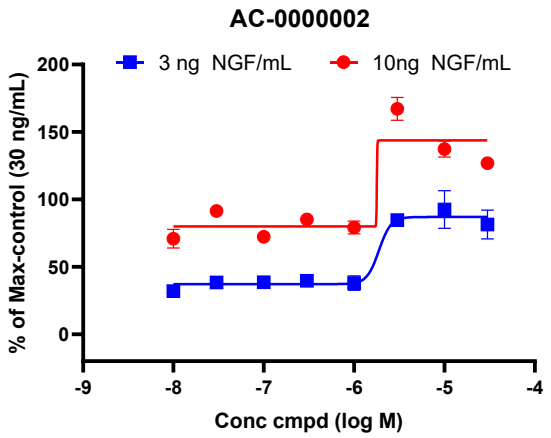


Zhao, Cell Proliferation, 2020

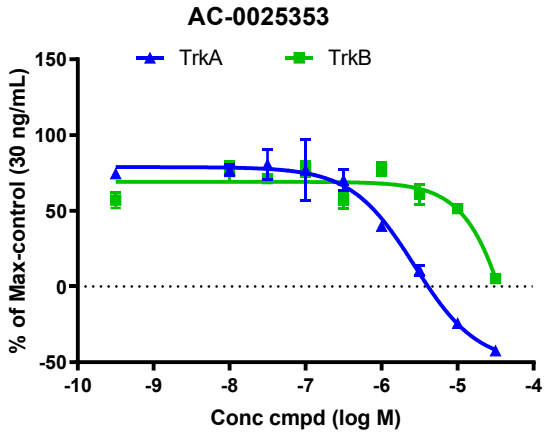
History: AlzeCure's TrkA-NAM program

- **2013**: A compound in series E was identified as a positive allosteric modulator of TrkA
- **2015**: The first TrkA-selective negative allosteric modulator (NAM) in series E was identified
- **2026**: Highly potent, in vivo active and novel TrkA-NAM compounds

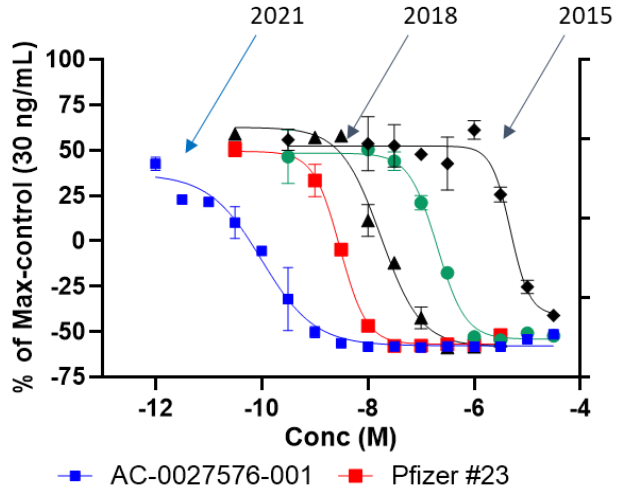
2013
First hit (PAM)



2015
First selective TrkA-NAM



2026
Potent and selective TrkA-NAM's



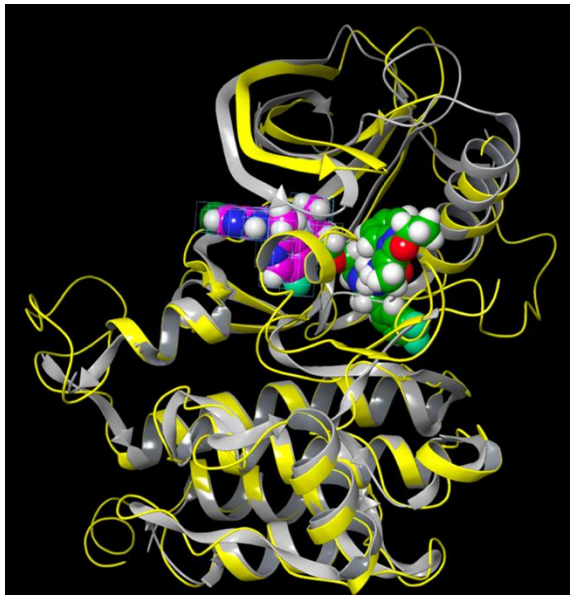
ACD137 selected as a clinical candidate in 2024

TrkA-NAM program in short

860 compounds has been synthesized and tested

- 3 cmpds with IC50 <10 pM
- 11 cmpds with IC50 <50 pM
- 11 cmpds with IC50 <100 pM
- 89 cmpds with IC50 <1 nM

- Selectivity vs TrkB/TrkC is generally very good, usually >10,000-fold selectivity
- Selectivity towards other receptor tyrosine kinases is very high
- X-ray structure has been solved and binding site identified
- Generally low BBB-permeability leading to low brain exposure
- Several TrkA-NAM molecules including ACD137 have a significant analgesic and anti-inflammatory effect in different in vivo models of pain



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Selectivity for TrkA over TrkB and TrkC

Selectivity towards other Trk-receptors is important, especially with respect to safety.

AlzeCure's TrkA-NAM compounds are very selective for TrkA over TrkB and TrkC compared to other TrkA-NAMs, Trk-inhibitors or anti-NGF antibodies.

Compound	MoA	TrkA IC_{50} (nM)	TrkB IC_{50} (nM)	TrkC IC_{50} (nM)
ACD137	TrkA-NAM	1.2 ± 0.15	20,780± 3,530	21,170 ± 6050
Array compound #1 (Ashai Kasei AK1830)	TrkA-NAM	0.20 ± 0.15	524 ± 148	312 ± 8.8
Pfizer compound #23	TrkA-NAM	0.93 ± 0.35	2030 ± 1034	86± 11.6
Zoetis compound #1	TrkA-NAM	0.46 ± 0.21	27.2 ± 13.8	6.9 ± 2.7
Larotrectinib	Trk-inhibitor	9.6 ± 0.87	9.2 ± 2.0	6.0 ± 2.4
GW441756	Trk-inhibitor	374 ± 66	322 ± 71	72.8
Tanezumab (K_d)*	Anti-NGF mAb	0.001	Not reported	1.0

* Results taken from patents or scientific literature

ACD137 is the most selective molecule investigated >17,000-fold selective for TrkA over TrkB and TrkC

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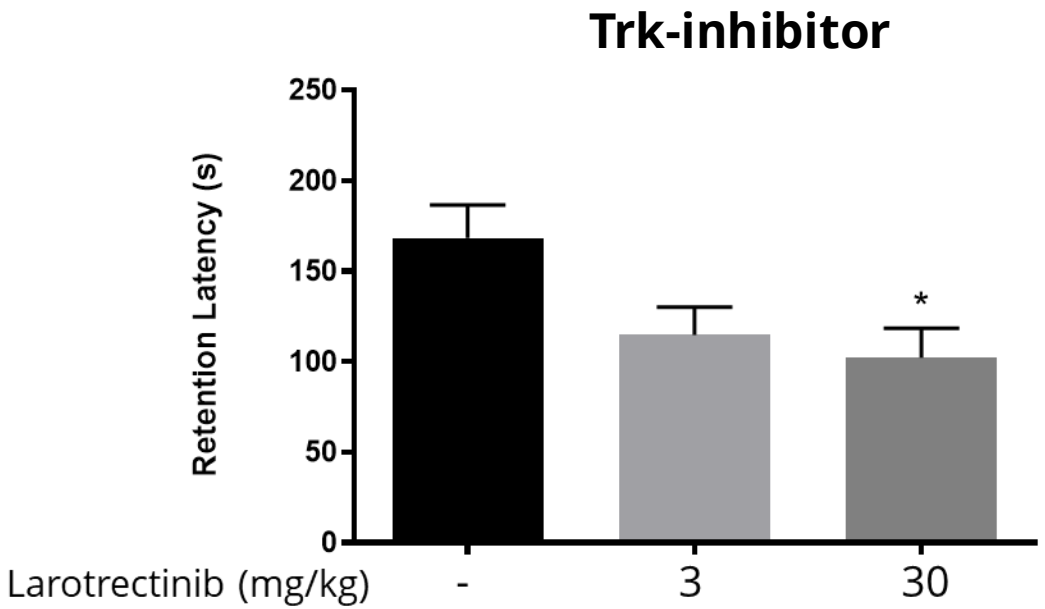
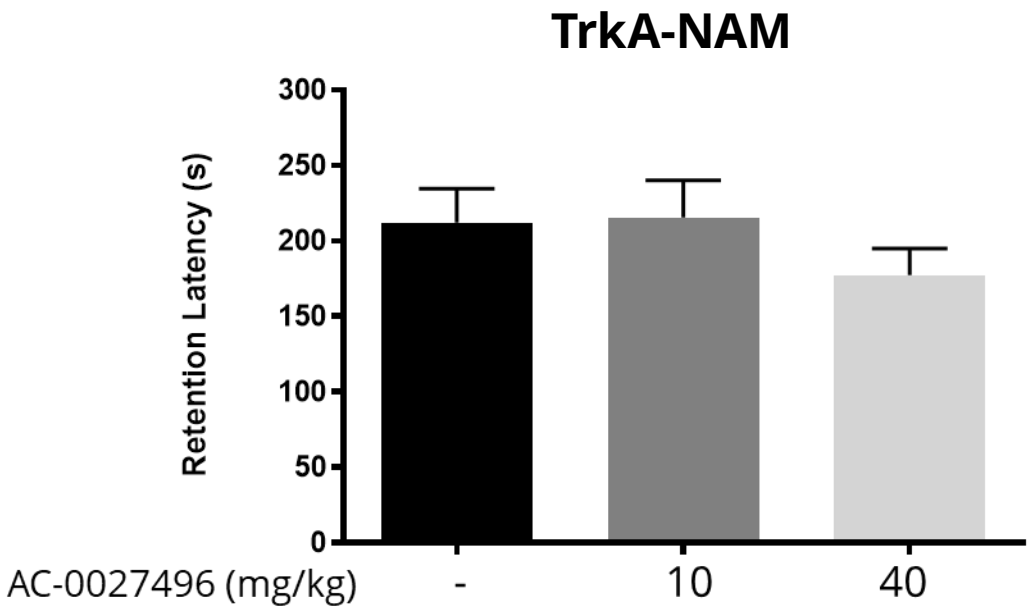
TrkA-NAM does not impair cognition like a Trk-inhibitor does

- Naïve mice were subjected to a memory test to address their cognitive function after a single administration of compound
- Compounds were administered by s.c. injection on day 1 before training session. No compound was administered on day 2, when the memory test was performed





A TrkA-NAM molecule (AC-0027496) does not impair cognitive function in mice

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TrkA-NAM / ACD137

- Selective peripheral targeting of TrkA is a promising pathway for pain relief
- AlzeCure has identified highly potent negative allosteric modulator of TrkA
- ACD137 is one the most selective compound for TrkA over TrkB and TrkC that has been tested
- Selectivity for TrkA over other neurotrophin receptors is probably a key feature to obtain a safe compound

- What about efficacy in different models of pain in animals?

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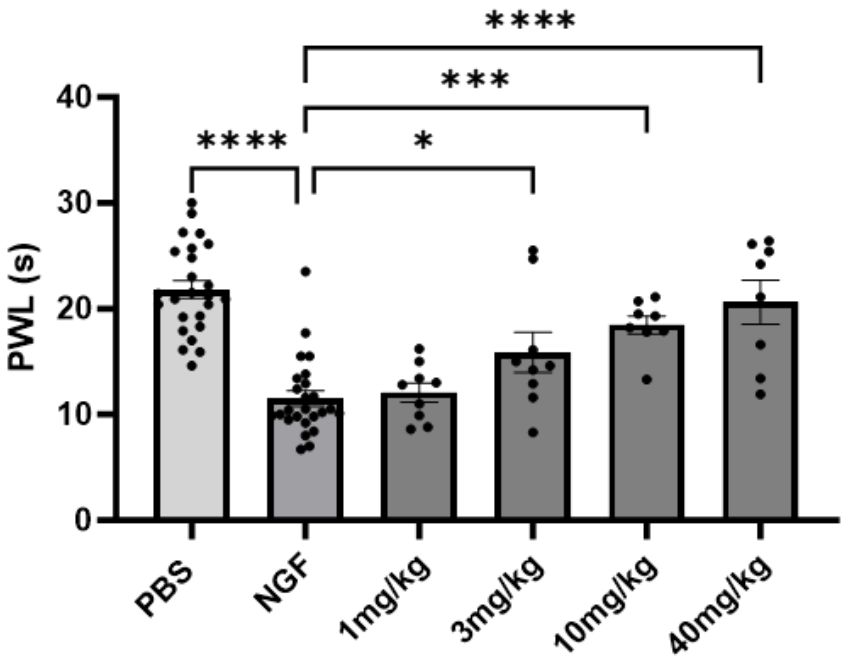
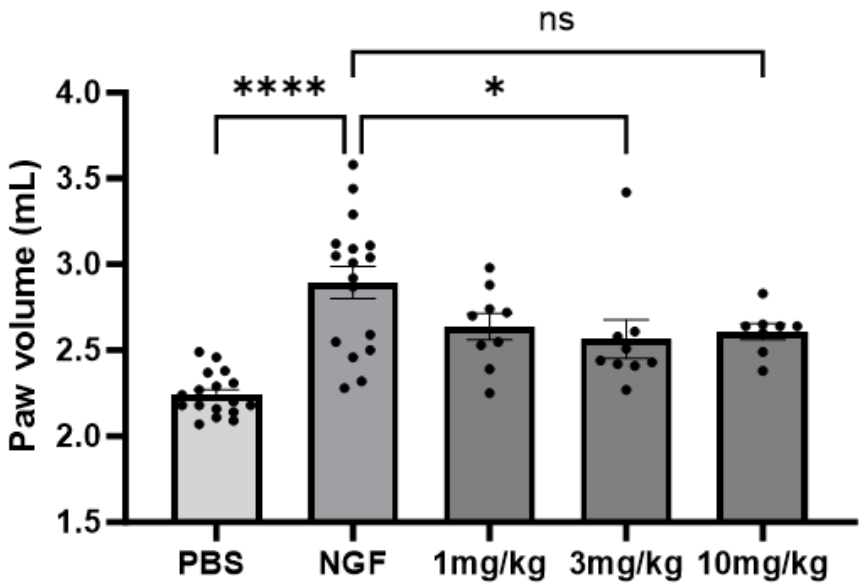
NGF-induced pain and inflammation in rats

Thermal hypersensitivity and inflammation are induced by intradermal injection of 5 μg NGF in the hind paw
ACD137 demonstrates both an analgesic effect and an anti-inflammatory effect.

Analgesic effect



Anti-inflammatory effect



ACD137 shows significant analgesic and anti-inflammatory effects

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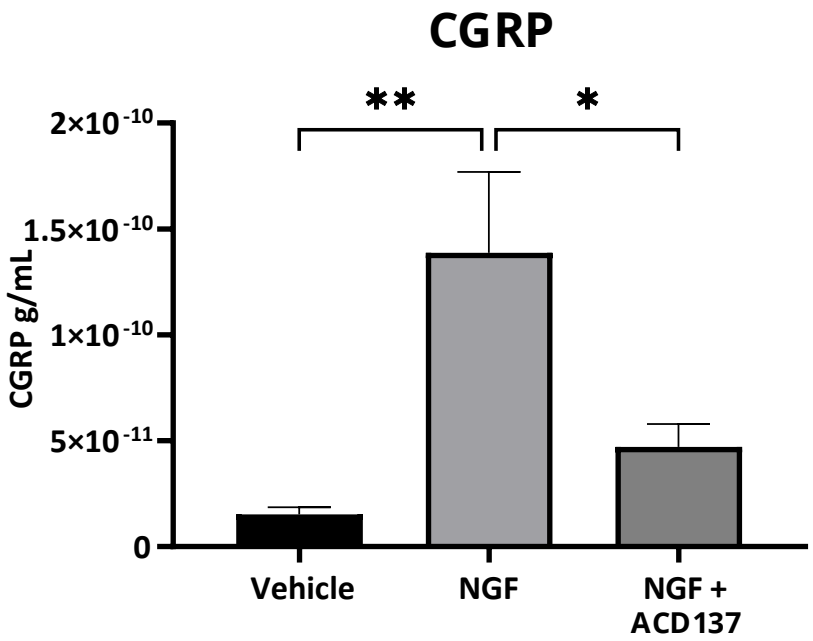
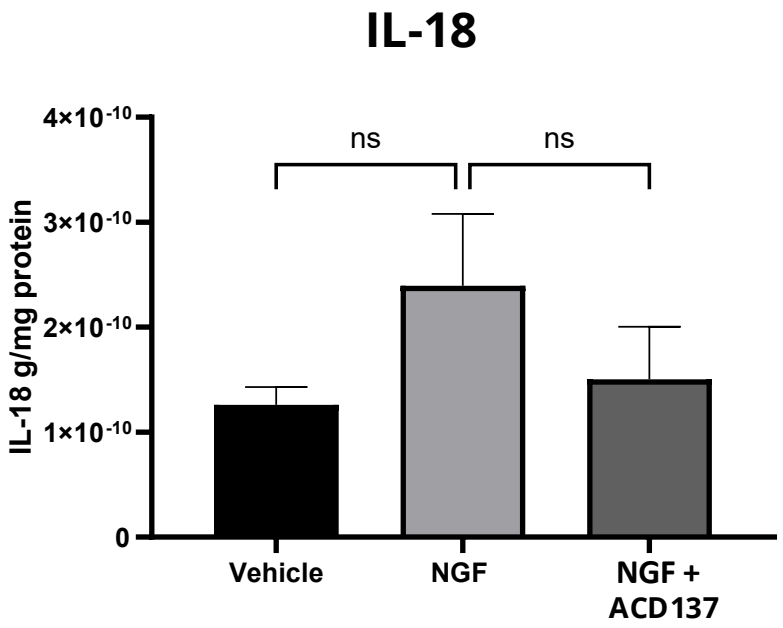
Inflammatory markers in rats

Thermal hypersensitivity and inflammation are induced by intradermal injection of 5 μg NGF.
ACD137 reduces NGF-induced increase in CGRP and IL-18 in skin biopsies from NGF-treated paw.

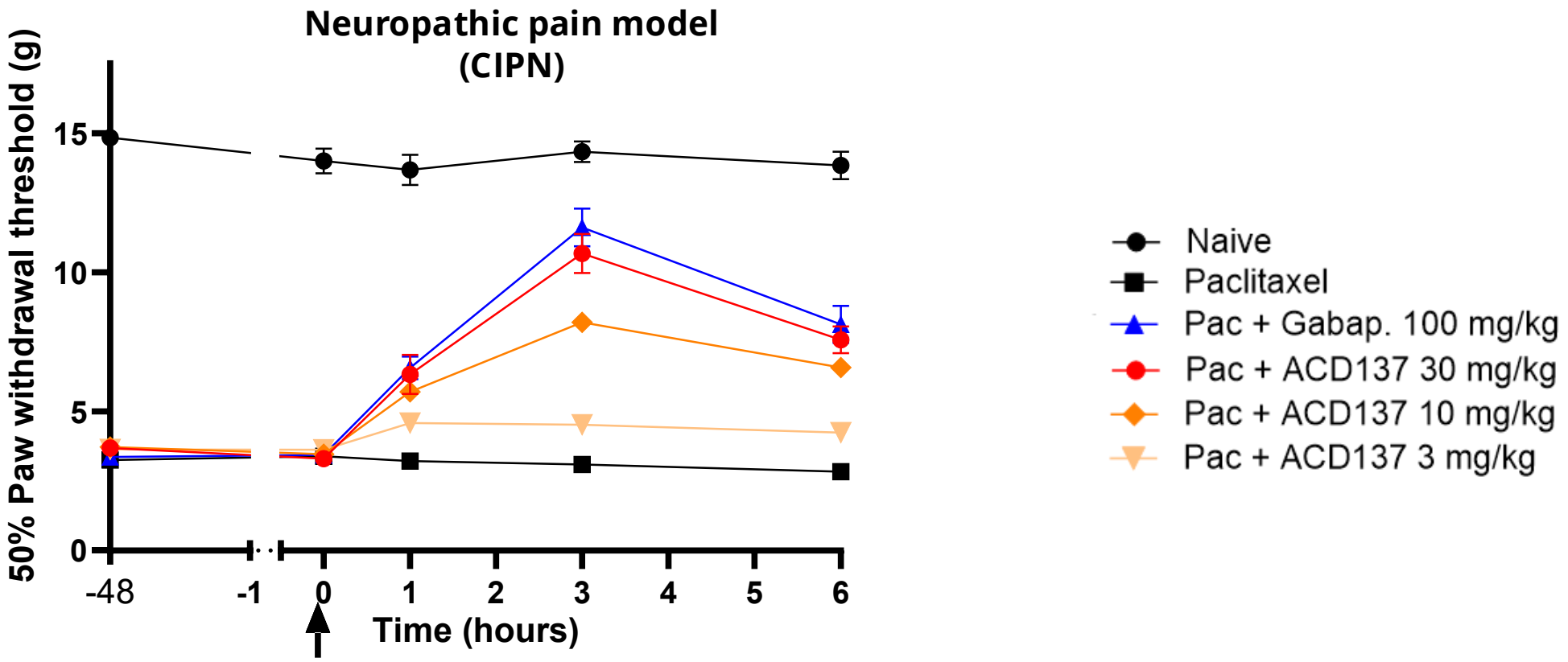




ACD137 significantly reduce levels of CGRP in skin biopsies

Effects of ACD137 in a model of neuropathic pain (chemotherapy-induced peripheral neuropathy (CIPN))

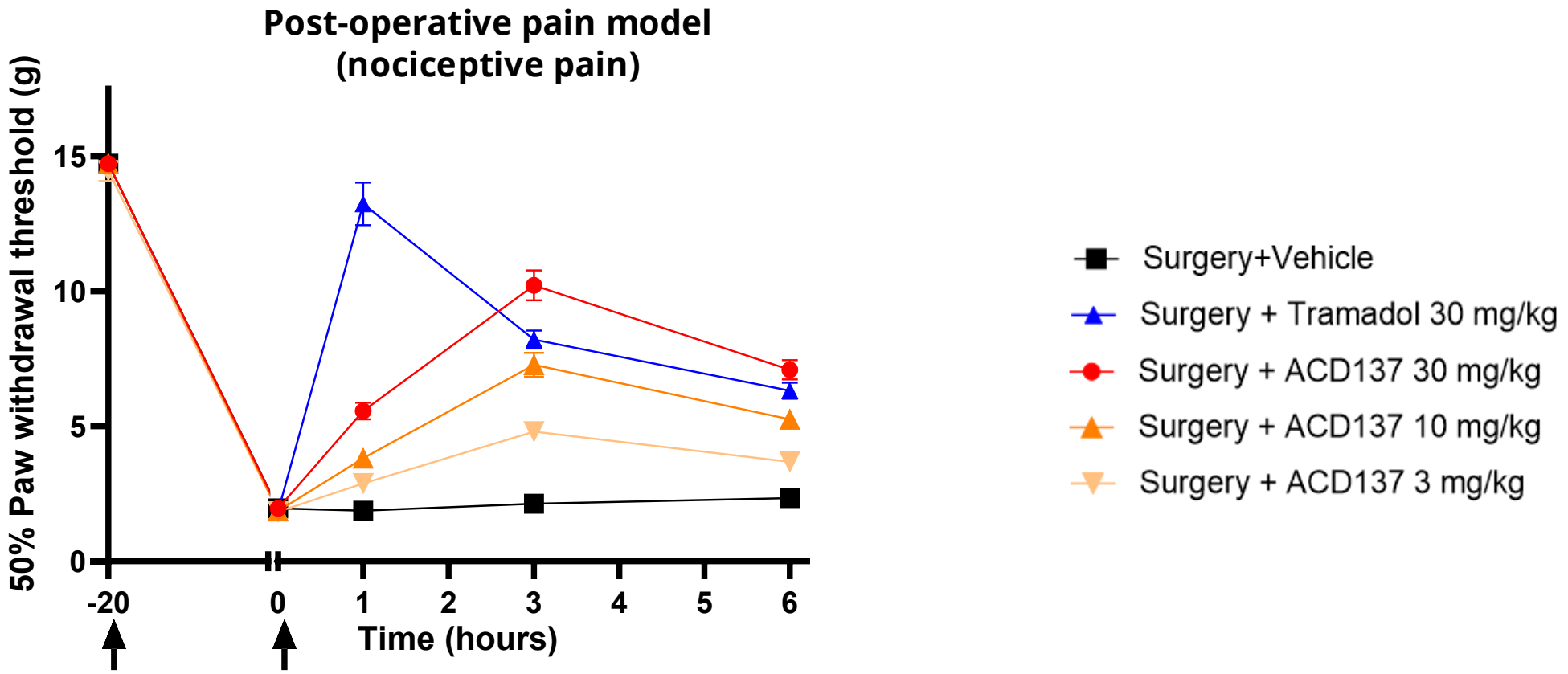
Peripheral neuropathy was induced by repeated injections of Paclitaxel
ACD137 or Gabapentin were administered orally and pain assessment was performed at 1, 3 and 6 hours post-dose



ACD137 significantly reduces mechanical allodynia in a model of neuropathic pain

Effects of ACD137 in a model of nociceptive pain

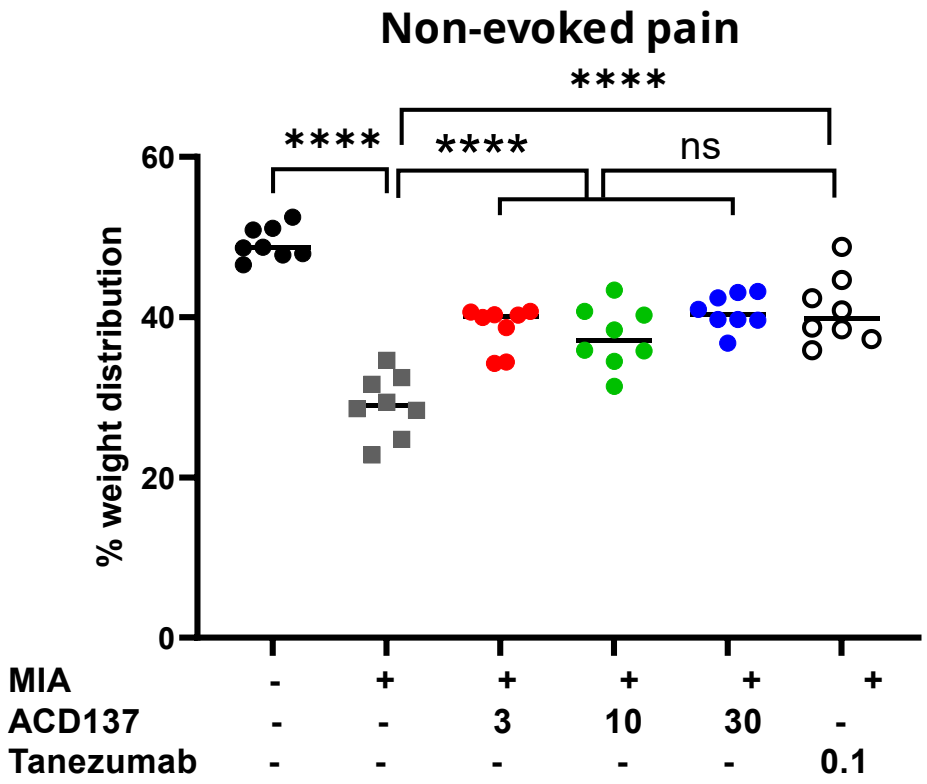
- Post-operative pain was studied in a model of incisional pain (Brennan model)
- ACD137 was administered by oral gavage, and pain assessments were performed at 1-, 3- and 6-hours post-dose

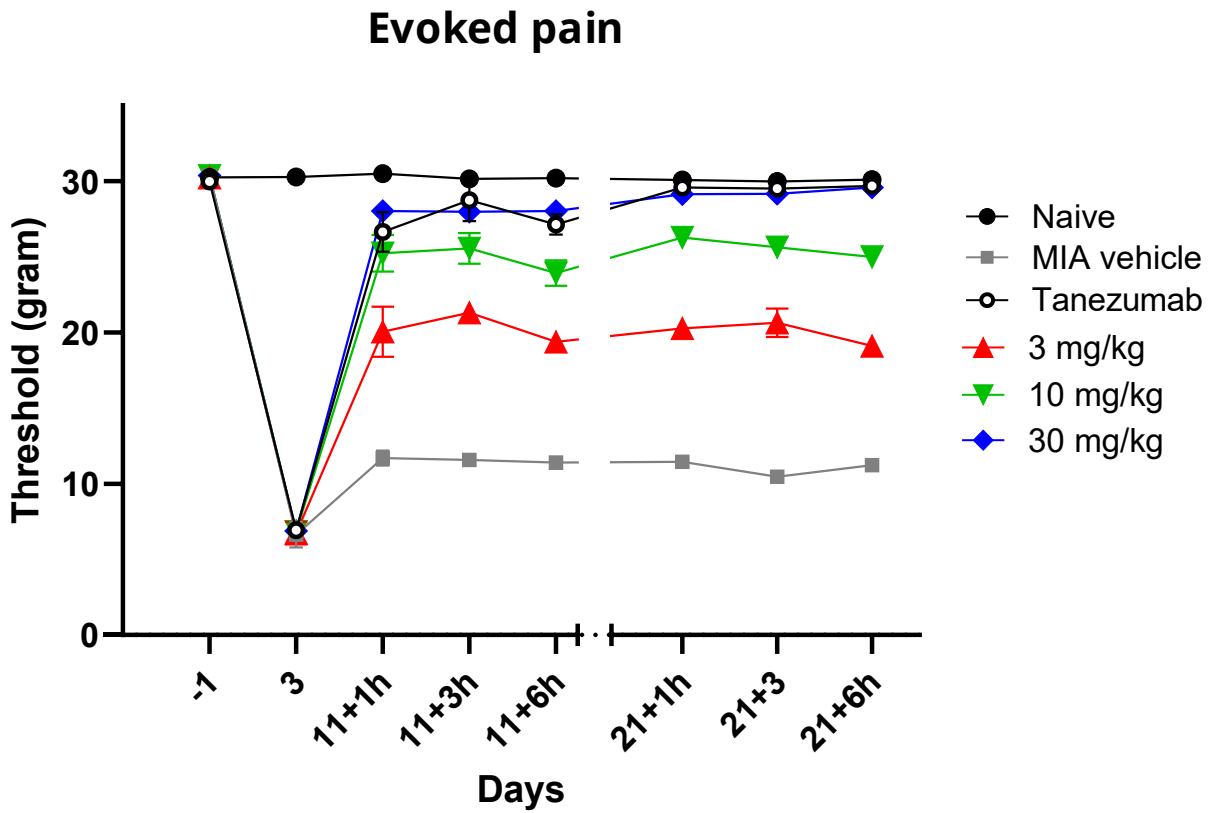


ACD137 significantly reduce mechanical allodynia in a model of nociceptive pain

TrkA-NAM: equivalent pain relief as anti-NGF antibody in a model of OA

Arthritis was induced by injecting mono-iodo acetate (MIA) in the knee joint of the left hind leg
ACD137 was administered twice daily by oral gavage for 18 days from day 3 to 21
Pain was assessed by weight bearing (non evoked pain) and mechanical allodynia (evoked pain)





ACD137 have similar analgesic effect as the anti-NGF antibody Tanezumab

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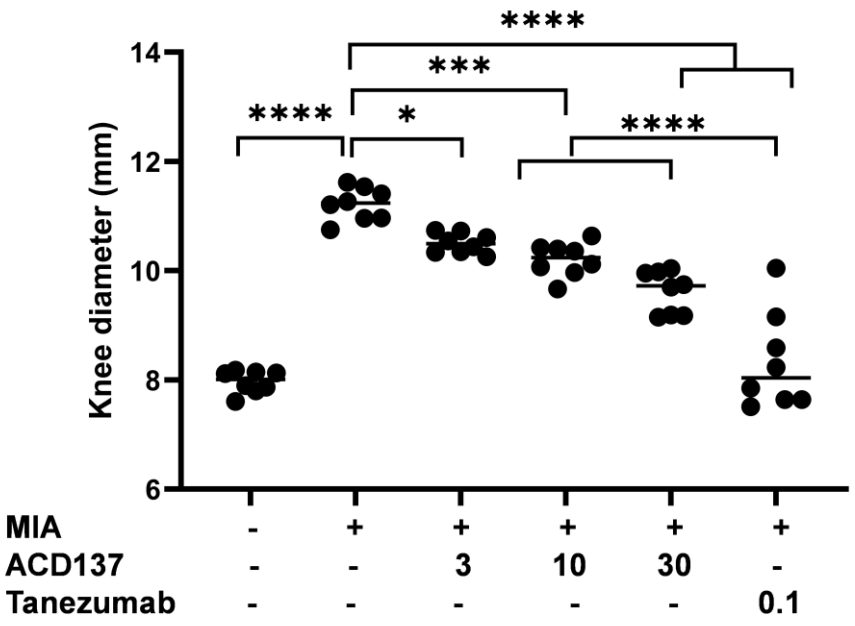
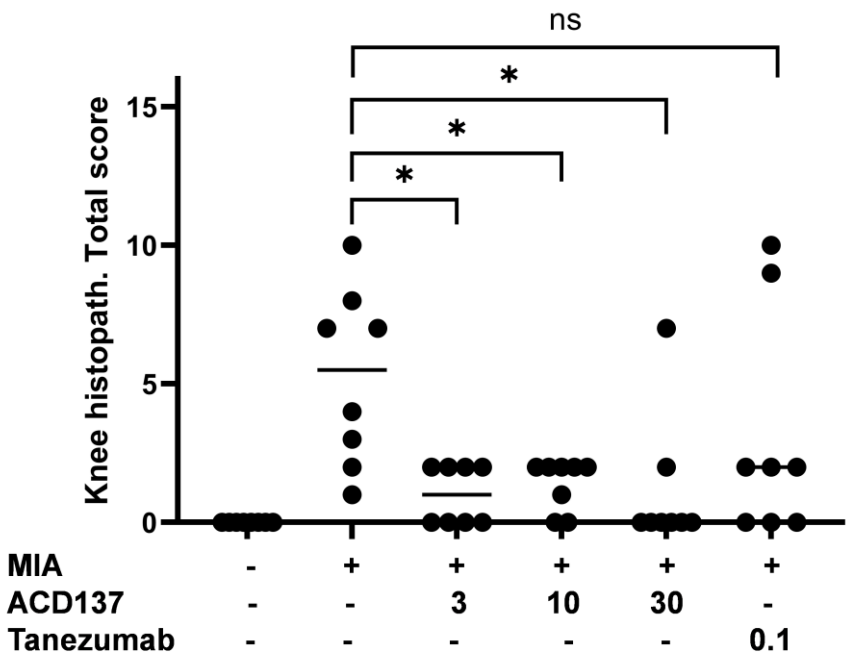
Effects of ACD137 in a rat model of osteoarthritis

Arthritis was induced by injecting mono-iodo acetate (MIA) in the knee joint of the left hind leg
ACD137 was administered twice daily by oral gavage for 18 days from day 3 to 21
Knee joint diameter was used a measure of inflammation and joint pathology was scored by modified Mankin scoring

Inflammation

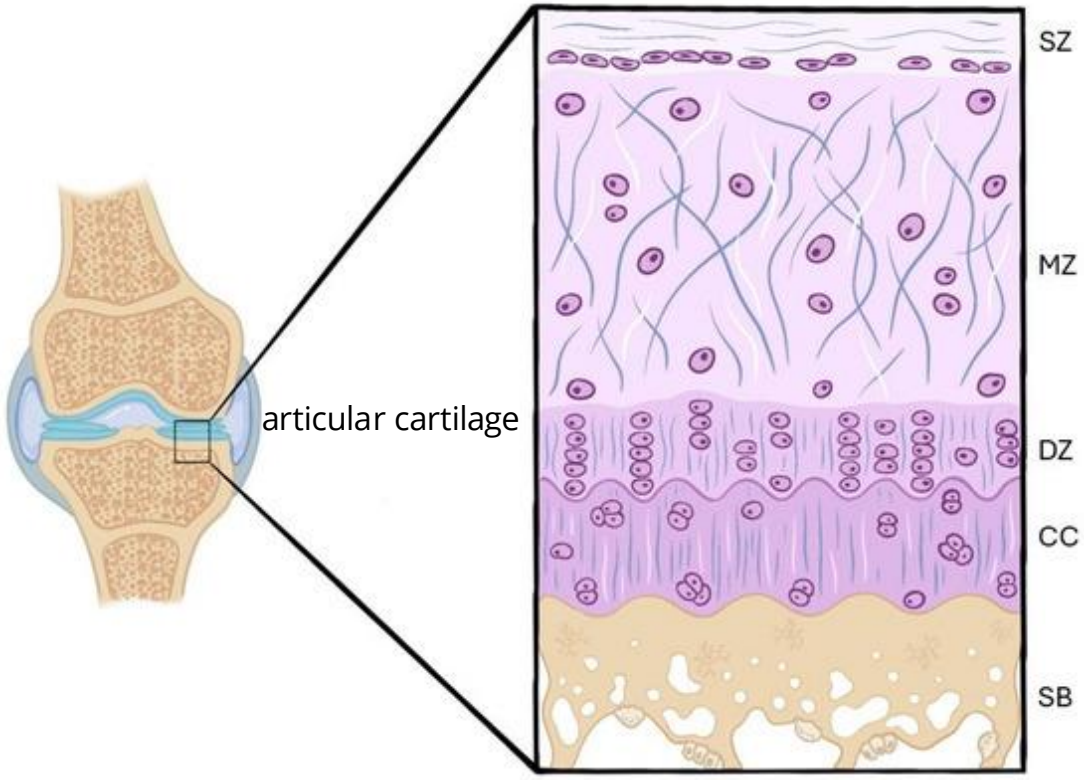


Joint pathology

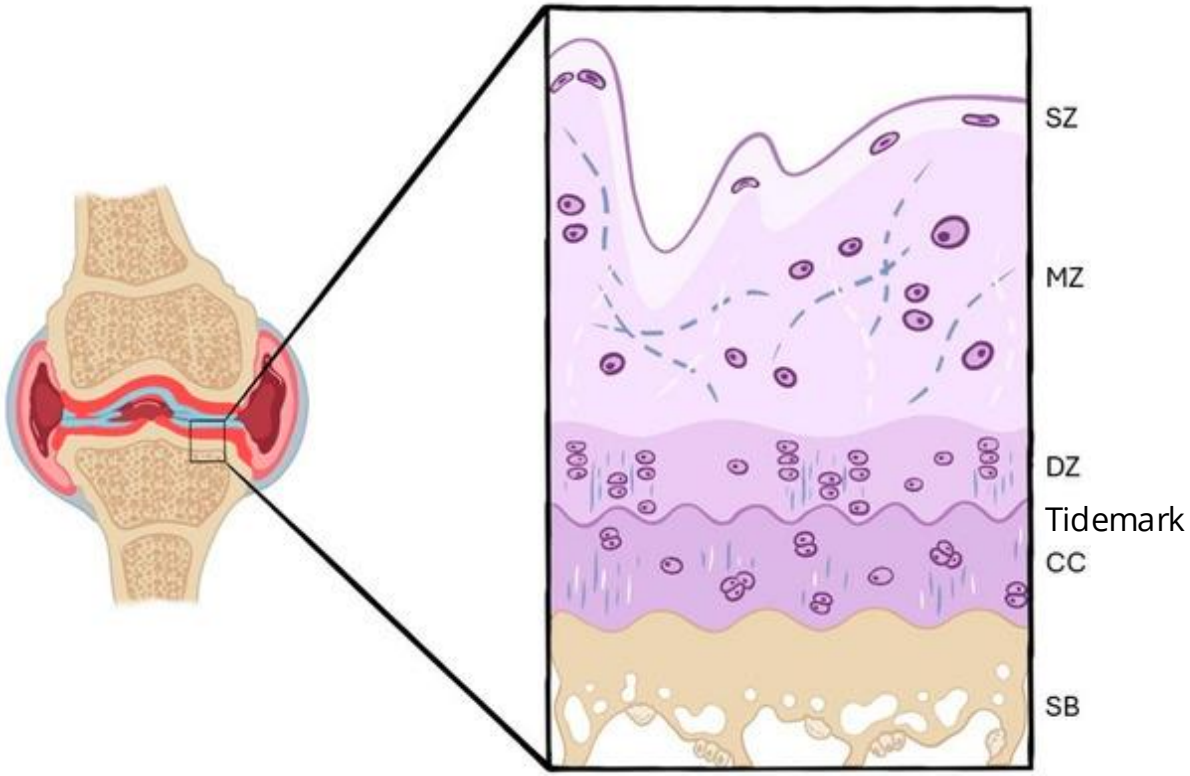


ACD137 have analgesic, anti-inflammatory and joint protective effects in the knee joint
ACD137 have similar analgesic effect as Tanezumab

Changes in the articular cartilage in the presence of OA



SZ—superficial zone
MZ—middle zone
DZ—deep zone
CC—calcified cartilage
SB—subchondral bone



Osteoarthritis: progressive structural disorganization, loss of chondrocytes, cellular abnormalities, and disruption of the collagen fiber network, together with subchondral bone thickening and sclerosis.

Sabucedo-Suárez et al., IJMS, 2025

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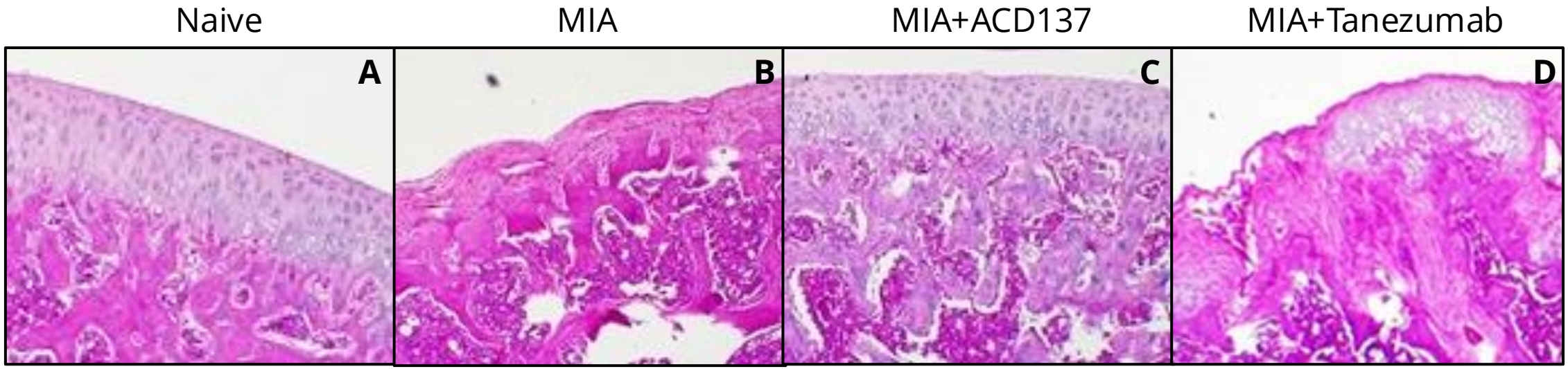
Changes in the articular cartilage in the MIA-model of OA



Representative images of knee joint histopathology.

A. naïve animal showing normal histology with articular cartilage, clear cellular structure and intact tidemark.
B. vehicle-treated MIA animals showing damage in articular cartilage and cellular abnormalities with destroyed tidemark.
C. 30 mg/kg ACD137: normal histology with articular cartilage, clear cellular structure and intact tidemark.
D. 0.1 mg/kg tanezumab: damage in articular cartilage and cellular abnormalities with destroyed tidemark.

All sections were stained with hematoxylin and eosin and pictures were taken using 4X magnification.

ACD137 protects knee joint from degenerative processes

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Summary TrkA-NAM / ACD137

ACD137 :

- Was identified internally by a rigorous medicinal chemistry program
- Is a highly selective and potent negative allosteric modulators of TrkA
- Has analgesic effects in models of both neuropathic and nociceptive pain
- Has anti-inflammatory and protective effects in the knee joint in a rodent model of OA
- Has similar analgesic efficacy as the anti-NGF antibody Tanezumab
- Is currently in preclinical development

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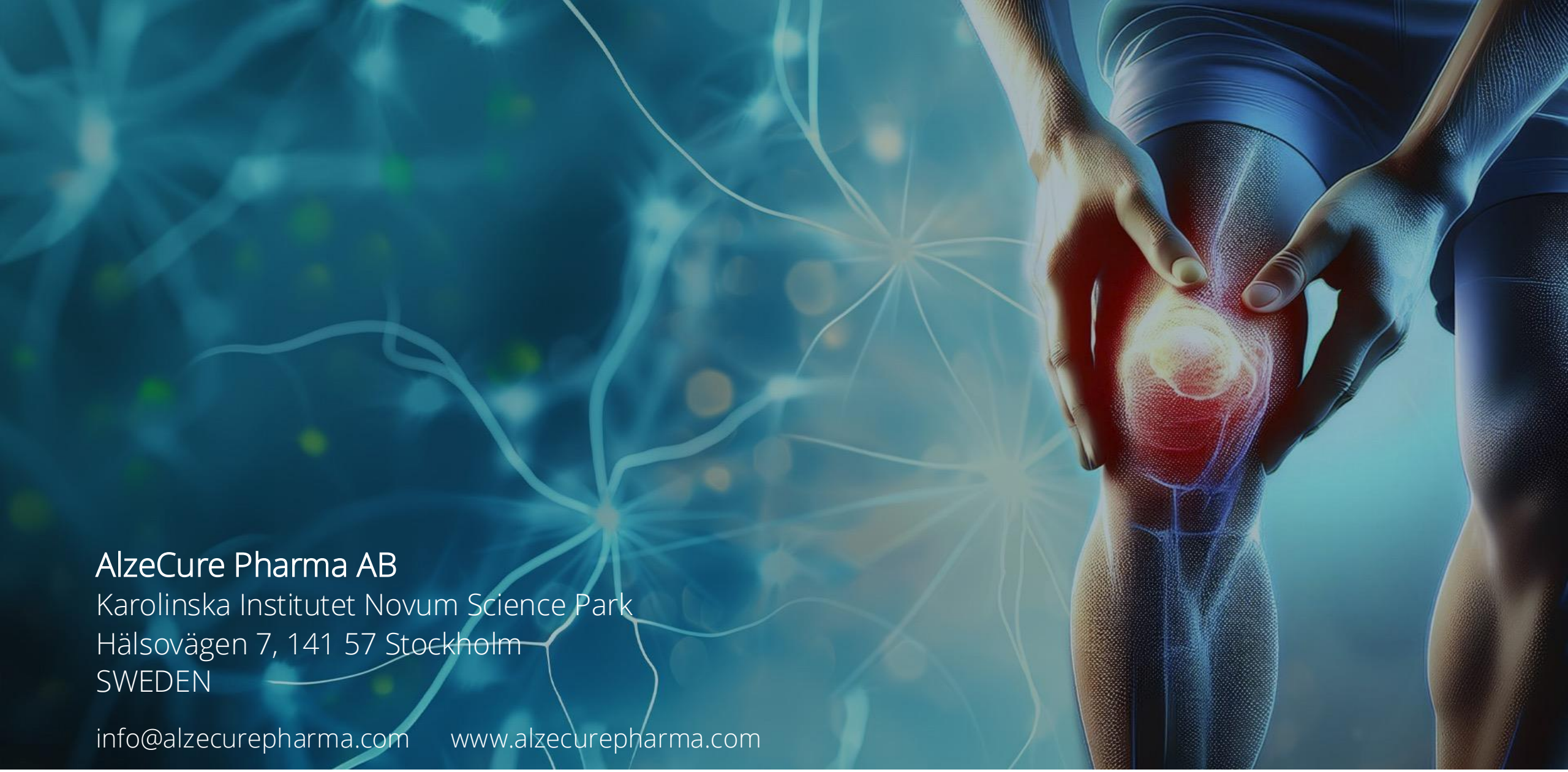

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Q&A session

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Q&A Session

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

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Martin Jönsson
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Roche, Lunds Universitet, FERRING PHARMACEUTICALS

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Take Home Messages

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Key Take Home Messages

- The unmet medical need in osteoarthritis (OA) & Chemotherapy Induced Neuropathic Pain (CINP) is very large and growing, e.g:
  - Today over 500 million are having OA
  - For 2025 the OA market was valued at USD 10B and is projected to annually grow 5 - 8% per year over the coming 10 years
- Strong validation of NGF/TrkA in pain signaling – genetically, preclinically and clinically
- ACD137 is negatively modulating NGF/TrkA signaling
- TrkA-NAM project contains potent and highly selective molecules, including ACD137
- A more selective mechanism - could lead to a safer treatment than anti-NGF antibodies
- TrkA-NAM is under development as an oral medication, and in preparations for clinical trials
- There is a broad potential for TrkA-NAMs in several various pain indications

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Thank You
for attending

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