



Targeting IL1RAP to address unmet needs in severe cancer and autoimmune diseases

Corporate Presentation
Oct 2023

NASDAQ STOCKHOLM MAIN LIST (CANTA.ST)

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Cantargia – Investment highlights



NOVEL IL1RAP ANTIBODIES, POTENTIAL TO TREAT CANCER & INFLAMMATORY DISEASE

- IL1RAP elevated in most solid and liquid tumors
- IL1RAP signaling drives several autoimmune and inflammatory diseases



NADUNOLIMAB: CLEAR ACTIVITY SIGNALS IN CANCER THERAPY WITH UPCOMING CATALYSTS

- Strong clinical interim results in PDAC and NSCLC, and promising initial results in TNBC; >250 patients treated
- Randomized Phase II trial ongoing in TNBC (top-line data late 2024); Phase IIb trial in preparation in PDAC (top-line data 2025)



CAN10: OPPORTUNITY IN AUTOIMMUNITY/INFLAMMATION

- Pronounced activity in models of systemic sclerosis, myocarditis, psoriasis, atherosclerosis and inflammation
- Phase I clinical trial ongoing, initial results in 2024



CORPORATE STRENGTH DRIVING INNOVATION

- Solid cash position with runway to mid/end 2024 (287M SEK cash & equivalents at Q2 2023)
- Robust patent portfolio: IL1RAP antibody target in oncology (2032), nadunolimab (2035) and CAN10 (2041)

Current pipeline

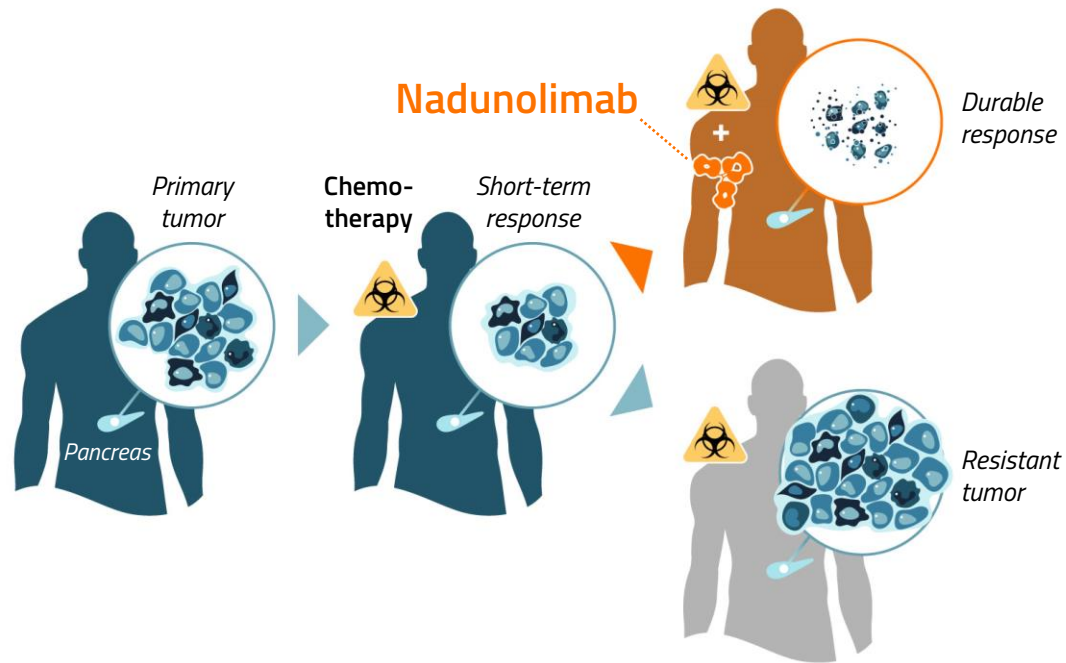
Project	Disease	Type of treatment	Discovery phase	Preclinical phase	Clinical phase I	Clinical phase II	Clinical phase III
Nadunolimab	PDAC	1 st line	Gemcitabine/nab-paclitaxel				
	TNBC	1 st /2 nd line	Carboplatin/gemcitabine				
	NSCLC/ non-squamous NSCLC	1 st /2 nd line	Platinum doublets				
CAN10	Myocarditis, Systemic sclerosis						
CANxx	New opportunities within IL1RAP platform						

PDAC – pancreatic cancer; TNBC – triple-negative breast cancer; NSCLC – non-small cell lung cancer

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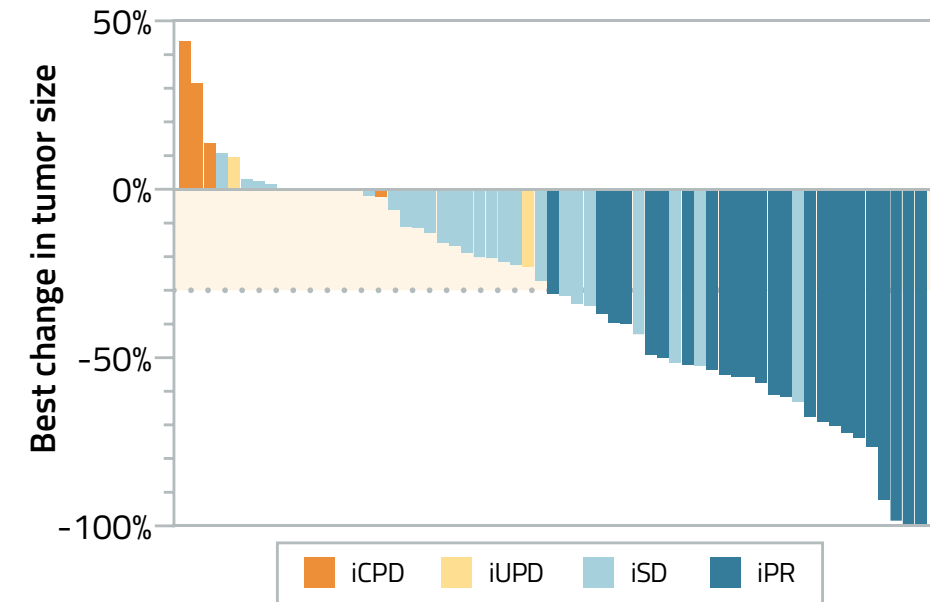
NADUNOLIMAB (CAN04) OVERVIEW

New strategy to treat cancer supported by clinical results



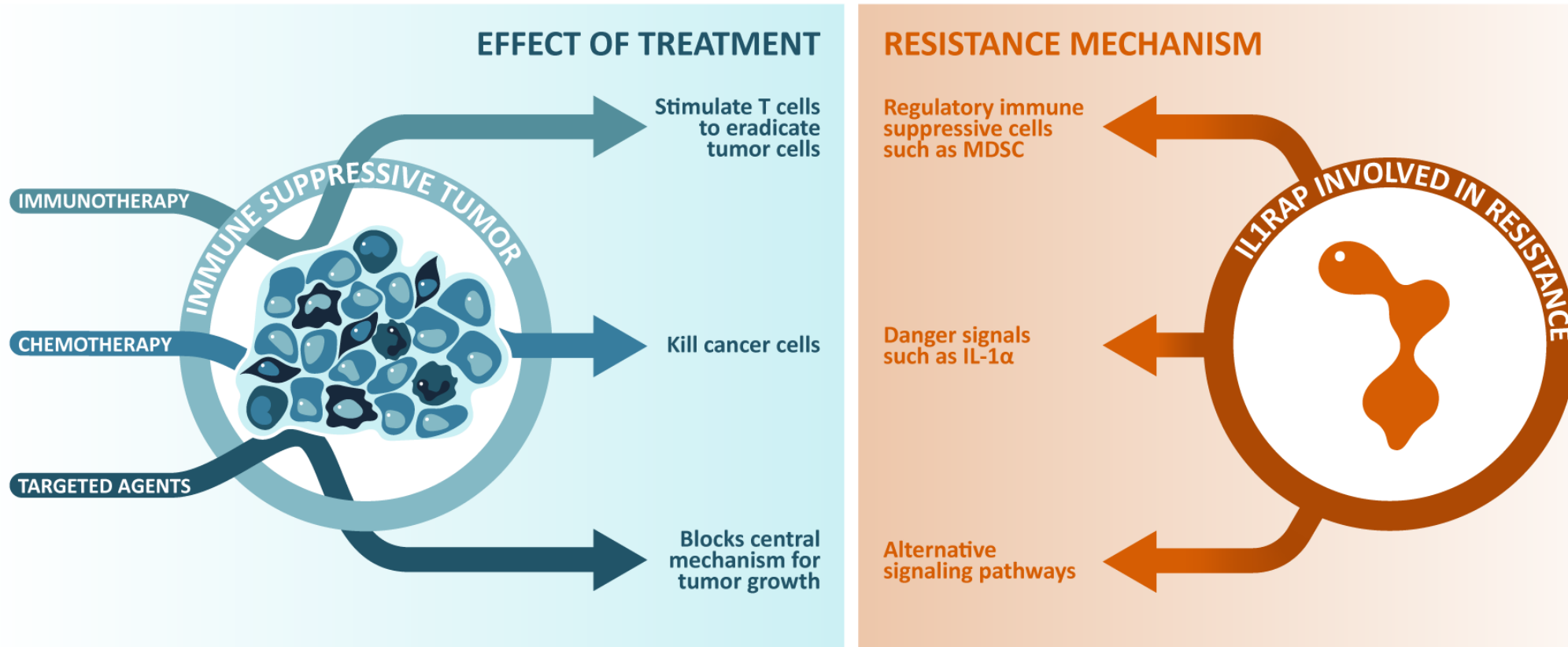
PROMISING DATA IN PANCREATIC CANCER

- Stronger efficacy than expected from chemotherapy alone
- Patients with higher IL1RAP level benefit more



SEVERAL LINES OF EVIDENCE SUGGEST NADUNOLIMAB COUNTERACTS CHEMORESISTANCE

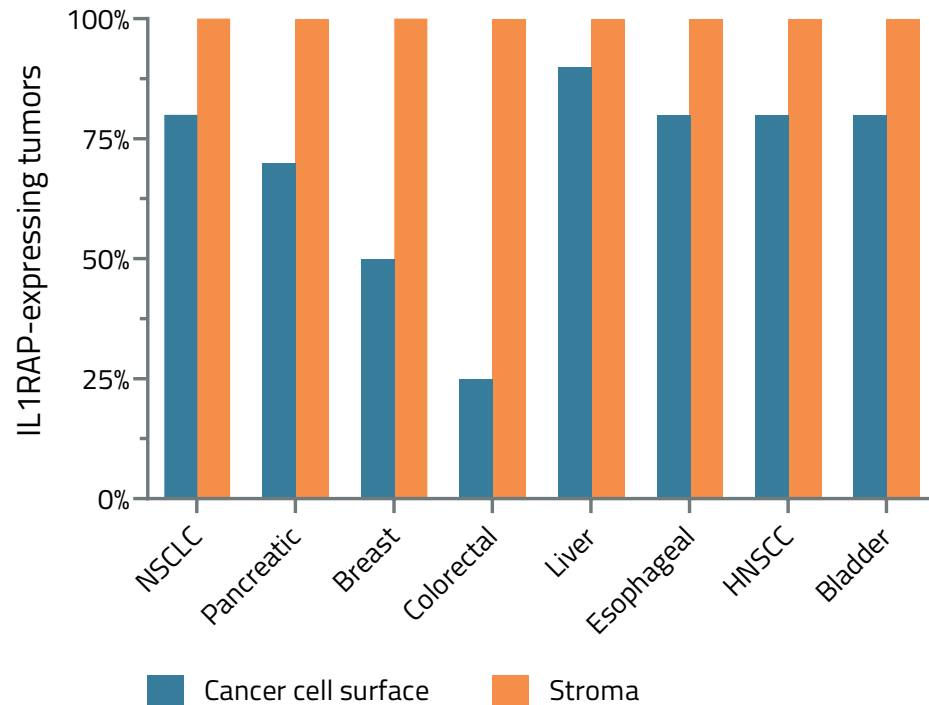
Cantargia – Strategy to improve current cancer therapies



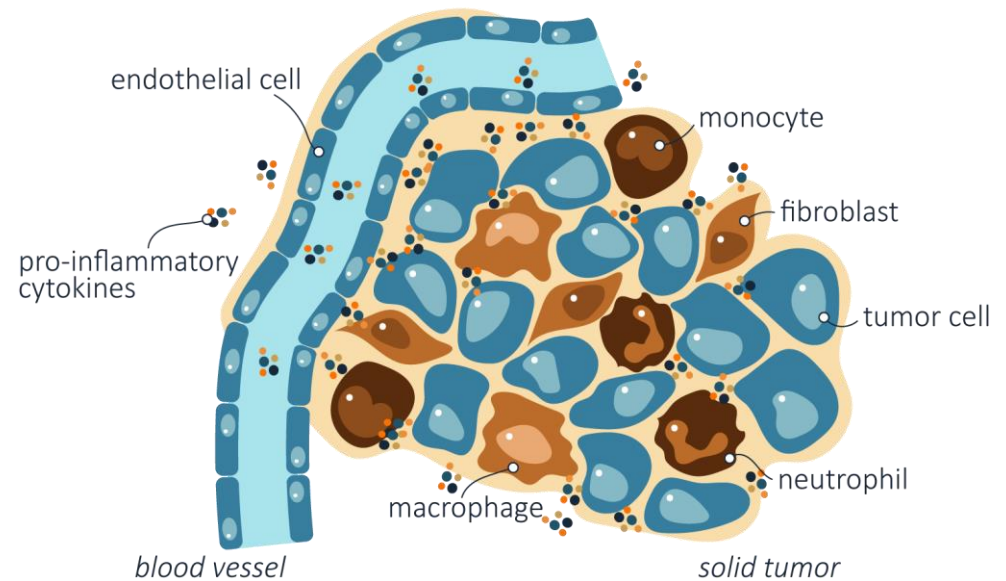
IL1RAP – A NOVEL TARGET WITH SEVERAL OPPORTUNITIES; CURRENT FOCUS ON SYNERGISTIC COMBINATIONS

IL1RAP overexpressed in most solid tumors

IL1RAP EXPRESSION IN SOLID TUMOR TYPES

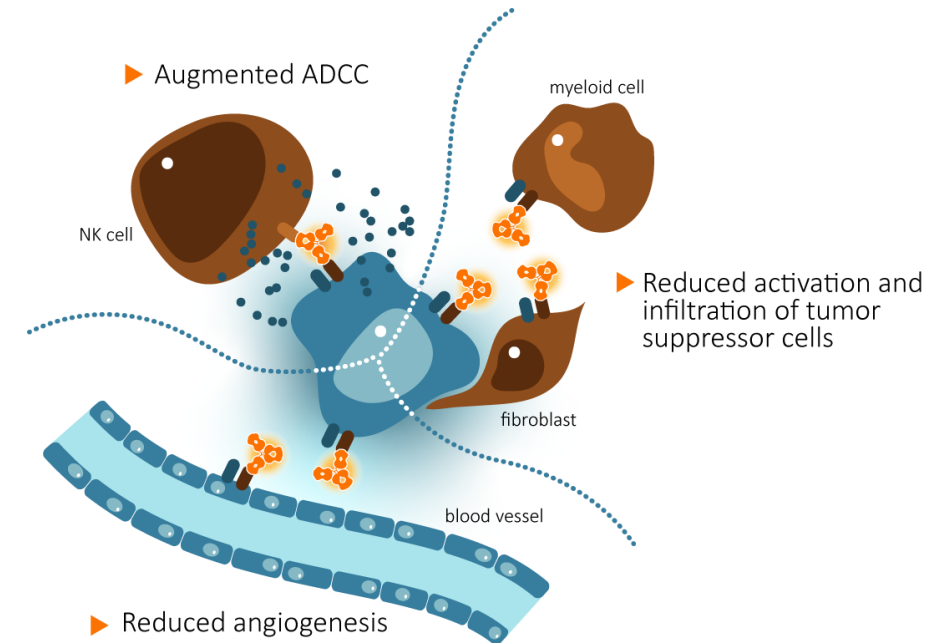
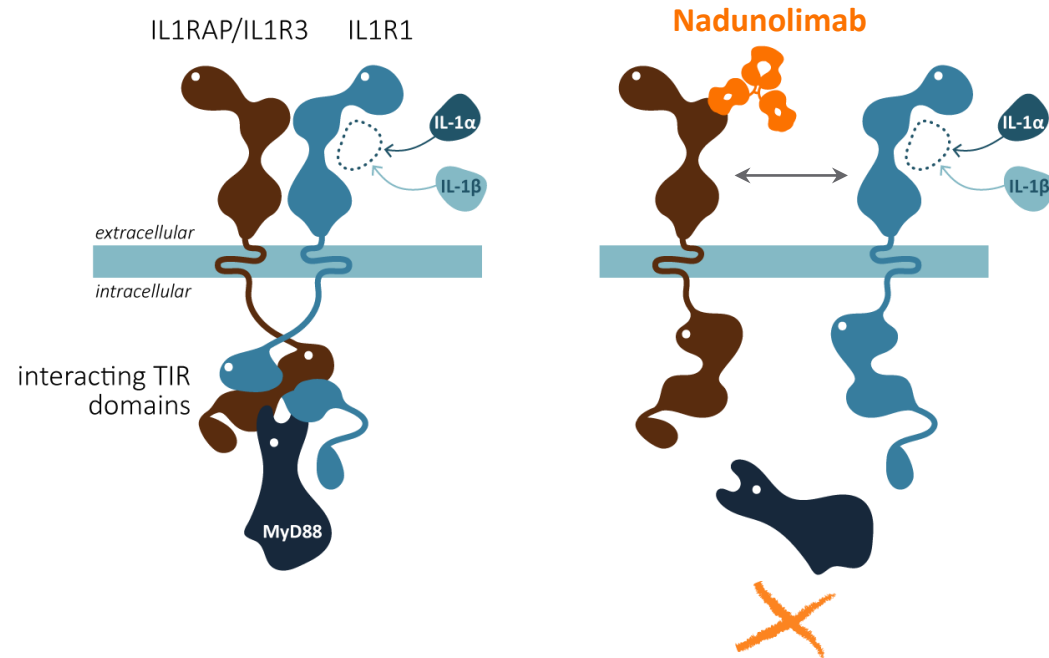


SEVERAL TUMOR-PROMOTING CELLS EXPRESSING IL1RAP IN THE TUMOR MICROENVIRONMENT



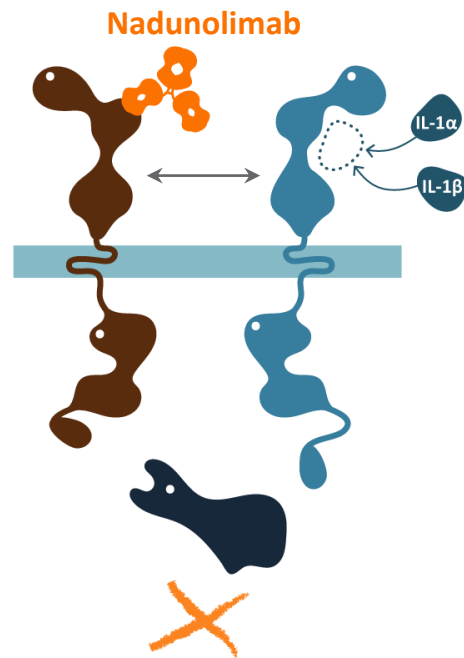
IL1RAP – DISTINCTLY OVEREXPRESSED IN TUMORS; LOW EXPRESSION IN NORMAL TISSUE

Targeting IL1RAP provides unique opportunities to treat cancer by IL-1 α / β blockade and ADCC

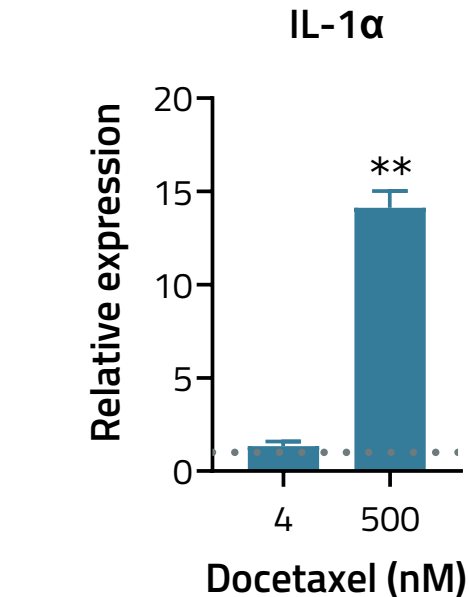


NADUNOLIMAB COUNTERACTS IMMUNE SUPPRESSION AND POTENTIATES THERAPY

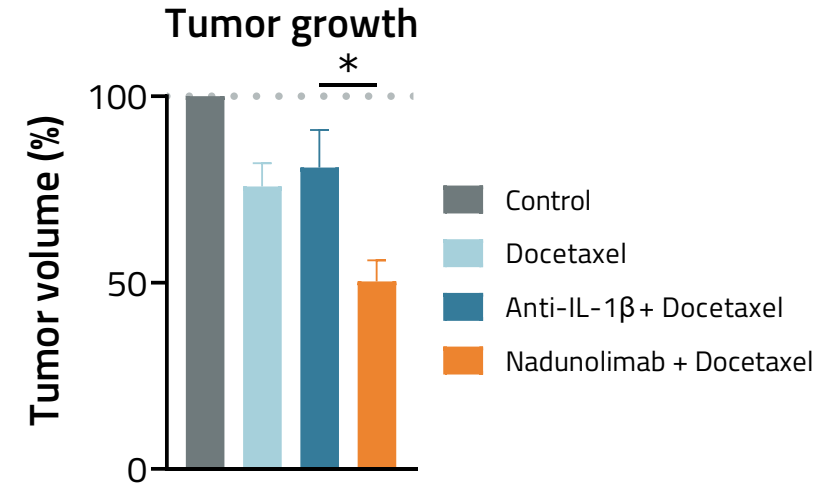
Nadunolimab potentiates antitumor activity of chemotherapy



→ Nadunolimab blocks both IL-1α and IL-1β signaling



→ Docetaxel induces IL-1α release by tumor cells in vitro



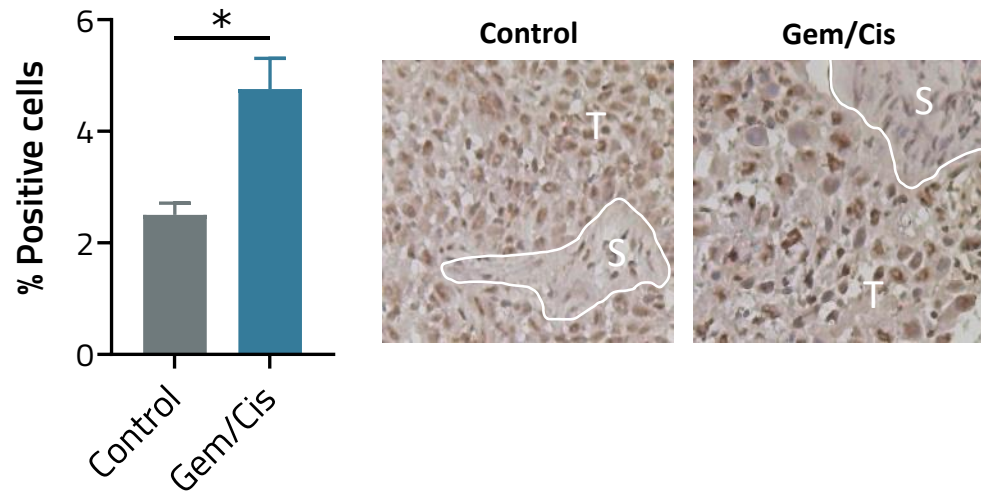
→ Nadunolimab + docetaxel reduces in vivo tumor growth more potently than anti-IL-1β + docetaxel

NADUNOLIMAB INCREASES DOCETAXEL EFFICACY IN CONTRAST TO IL-1β BLOCKADE

Chemotherapy induces IL-1 α and IL-1 β in the tumor

IL-1 α

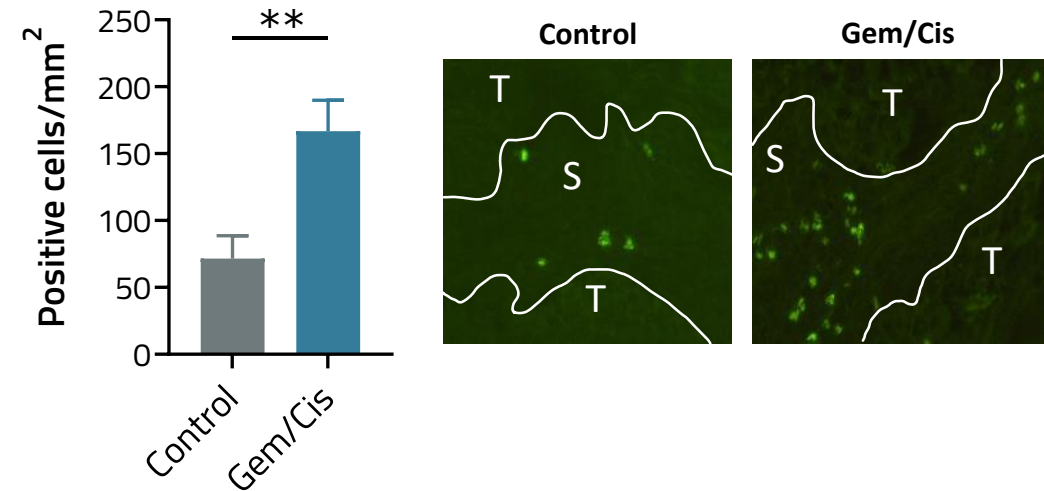
Tumor cell region (T)



→ Gem/Cis induces release of IL-1 α by tumor cells in tumors grown in vivo

IL-1 β -converting enzyme

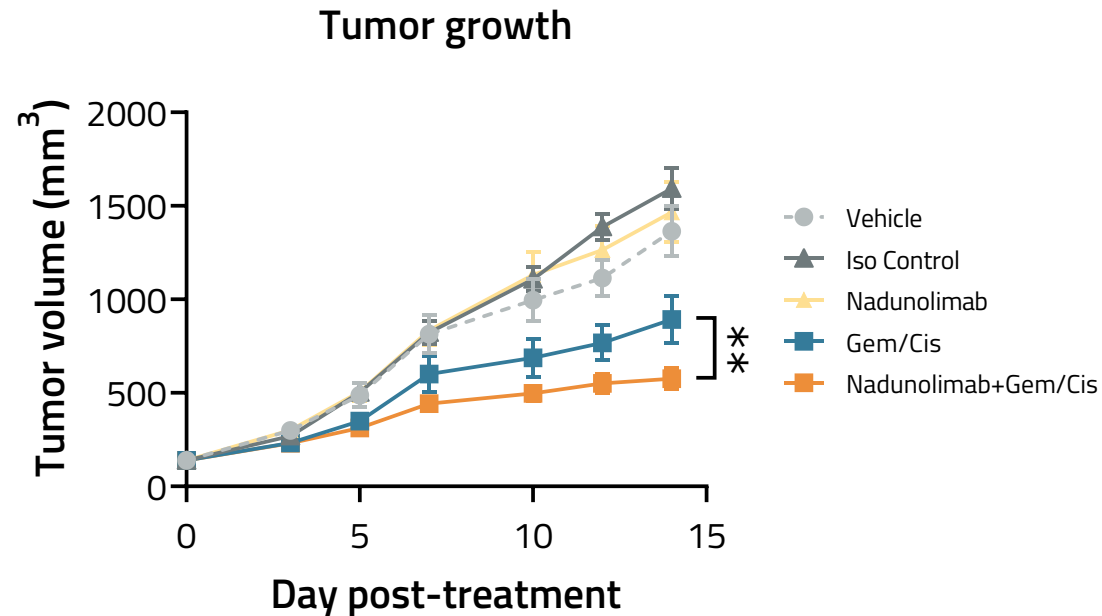
Stromal cell region (S)



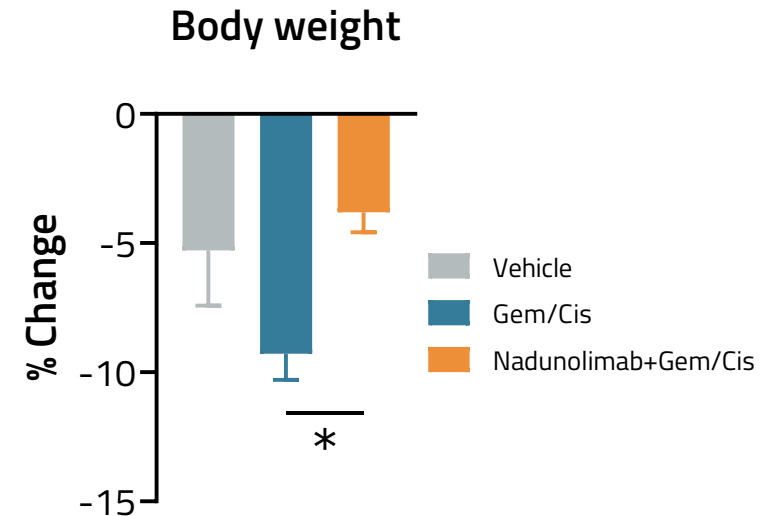
→ Gem/Cis also induces release of IL-1 β -converting enzyme (ICE) by stromal cells

INCREASED LEVELS OF IL-1 α AND IL-1 β RESULTS IN CHEMORESISTANCE

Targeting IL1RAP uniquely synergizes with chemotherapy



→ Nadunolimab increases efficacy of platinum-based chemotherapy in vivo



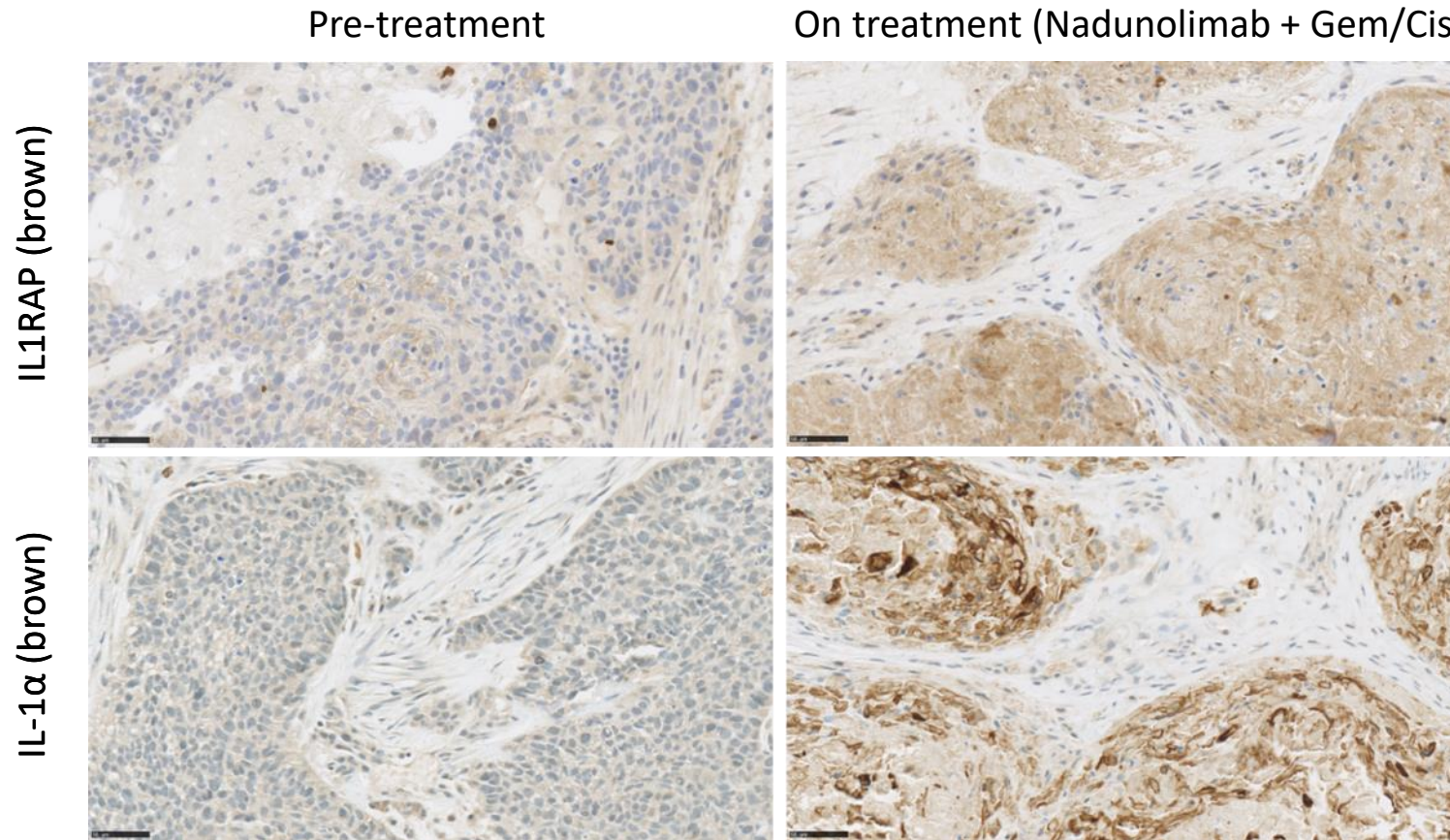
→ Nadunolimab also counteracts weight loss after chemotherapy

NADUNOLIMAB HAS POTENTIAL TO IMPROVE CHEMOTHERAPY EFFICACY AND TOLERABILITY

A microscopic image showing several cells with a complex, textured surface. The image is overlaid with a semi-transparent blue band across the center, which contains the title text. The background is a soft, out-of-focus blue.

NADUNOLIMAB (CAN04) CLINICAL RESULTS

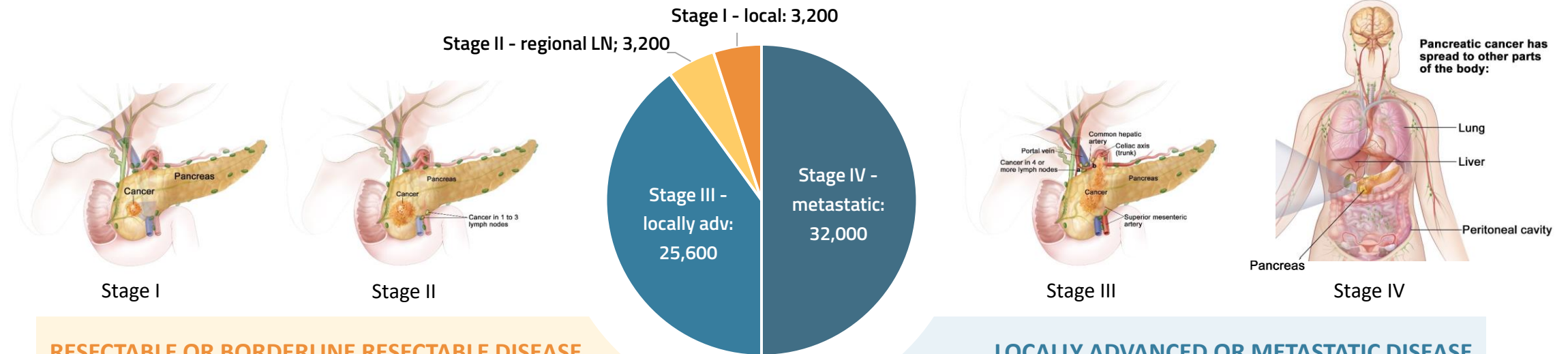
NSCLC – Induction of IL1RAP and IL-1 α with therapy



IL-1 α INDUCED BY CHEMOTHERAPY IN LINE WITH PRECLINICAL FINDINGS;
WELL ESTABLISHED DANGER SIGNAL – ACTIVITY BLOCKED BY NADUNOLIMAB

PDAC – Staging and treatment

Expected number of cases US 2023: 64,000



RESECTABLE OR BORDERLINE RESECTABLE DISEASE

Survival:

→ 15.7 – 28.0 mo

Treatment:

- Neoadjuvant: gemcitabine+radiotherapy or mFOLFIRINOX
- Radical pancreatic resection
- Post-op chemo (gemcitabine+capecitabine or mFOLFIRINOX) or chemo+radiotherapy

LOCALLY ADVANCED OR METASTATIC DISEASE

Survival:

→ 8.5 – 11.1 mo

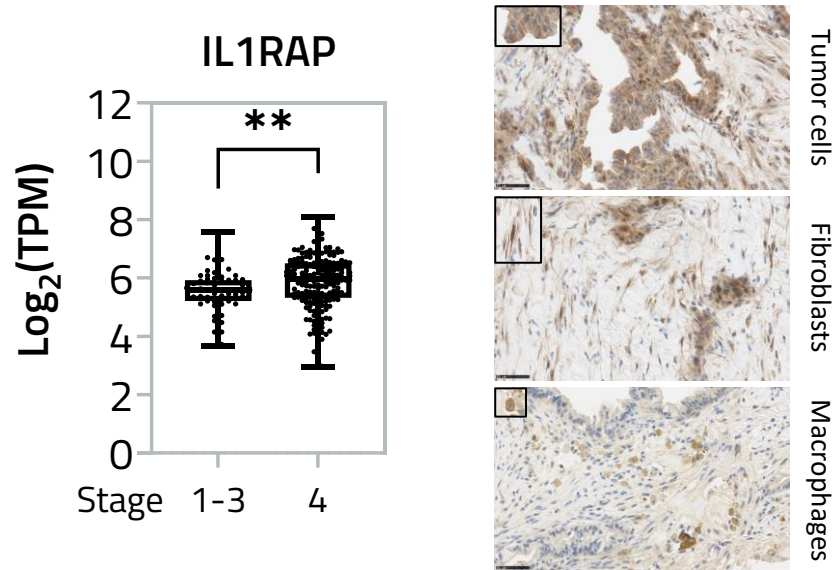
Treatment:

- FOLFIRINOX if good performance status
- Gemcitabine/nab-paclitaxel
- Gemcitabine if poorer performance
- Jan 2023: 1st line NALIRIFOX (OS 11.1 mo)

CURRENT DEVELOPMENT FOCUSES ON FIRST-LINE METASTATIC DISEASE WITH POTENTIAL TO MOVE TO EARLIER TREATMENT SETTINGS

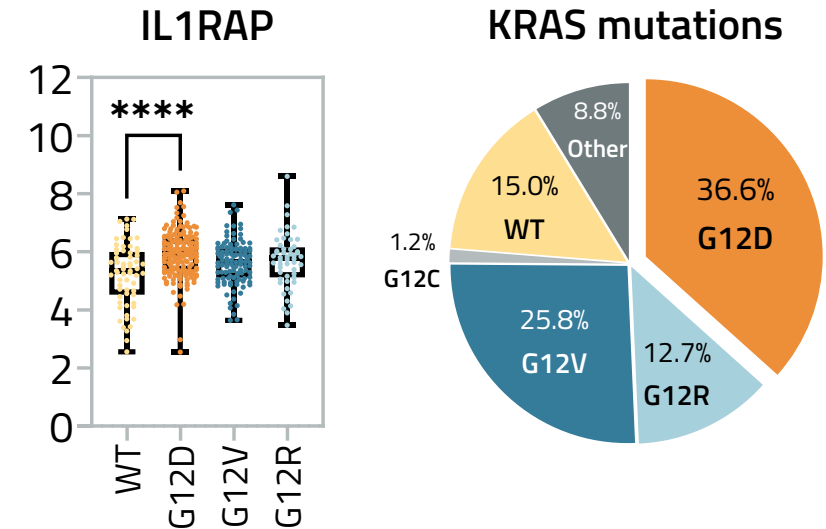
PDAC – IL1RAP linked to poor prognosis

IL1RAP IN PDAC



- IL1RAP levels increase with tumor stage
- IL1RAP expressed on both tumor cells, cancer-associated fibroblasts and macrophages in tumor microenvironment
- High IL1RAP correlates with lower efficacy after 1st line Gem/Abraxane

KRAS MUTATIONS IN PDAC

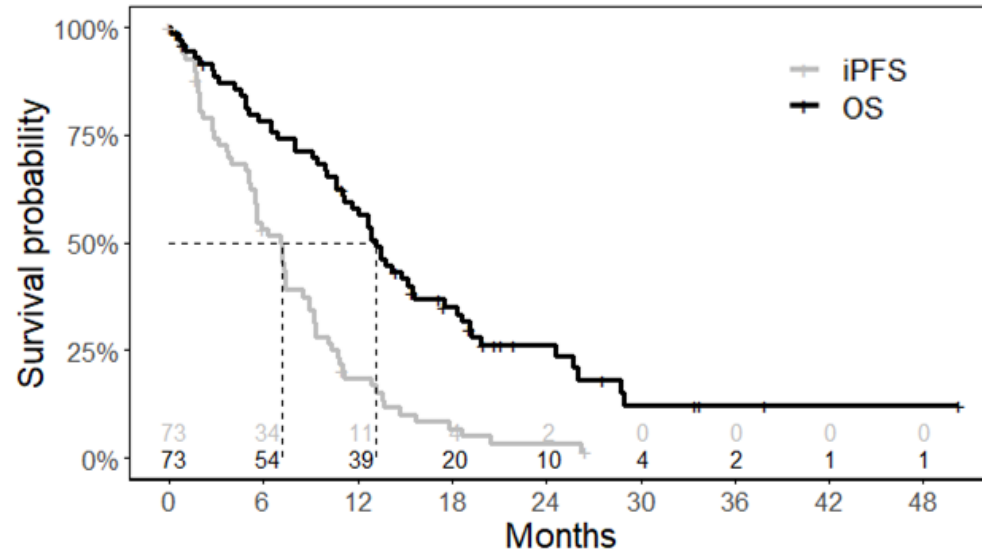


- Over 80 % of PDAC patients have a KRAS mutation; G12D is the most common
- KRAS G12D has a worse prognosis with HR 1.47 (Bournet et al, 2016)
- IL1RAP is overexpressed in patients with KRAS G12D

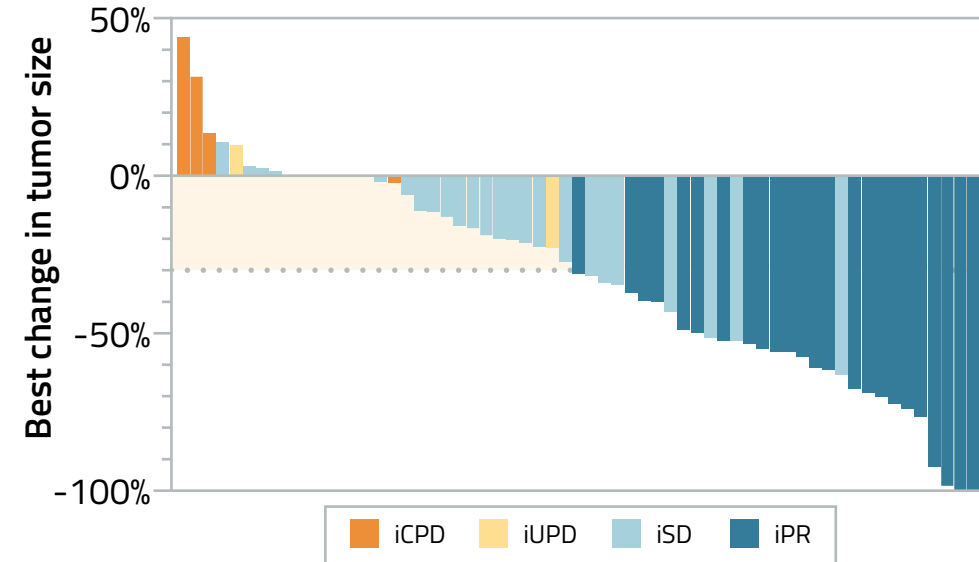
CLEAR LINK BETWEEN IL1RAP, KRAS G12D AND PDAC PROGNOSIS

PDAC – Positive interim data in 1st line patients

OS and iPFS for mITT patients



Best responses according to iRECIST



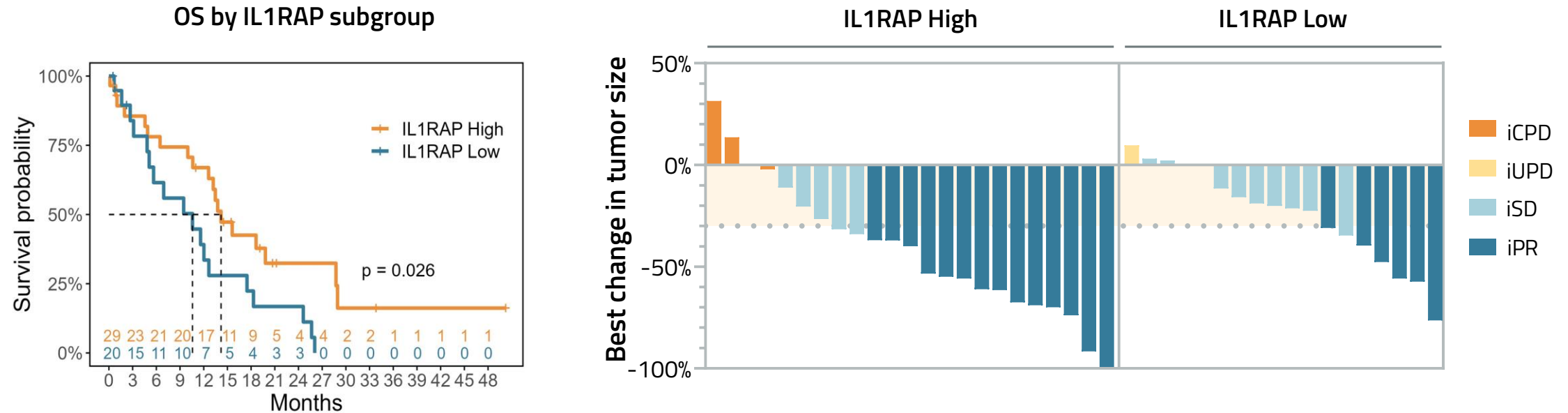
Nadunolimab combination with Gem/Abraxane in 1st line PDAC (n=73):

- 33% response rate with long OS and iPFS
 - Additional 5 (7%) patients had on-treatment benefit beyond progression
- Promising OS (13.2 mo), iPFS (7.2 mo) and DCR (71%); 2 patients still on treatment

PFS AND OS LONGER THAN EXPECTED GIVEN HISTORICAL CONTROL IN PDAC – PHASE IIB TRIAL IN PREPARATION

Benchmark Gem/Abraxane: OS 8.5 mo, PFS 5.3 mo, ORR 23%, DCR 48% (Von Hoff et al, 2013); OS 9.2 mo, PFS 5.6 mo, ORR 36%, DCR 62%, (NAPOLI 3 trial, ASCO GI 2023)
iCPD – Confirmed Progressive Disease; iUPD – Unconfirmed Progressive Disease; iSD – Stable Disease; iPR – Partial Response (all according to iRECIST)

PDAC – Strong efficacy in patients with high tumor IL1RAP level

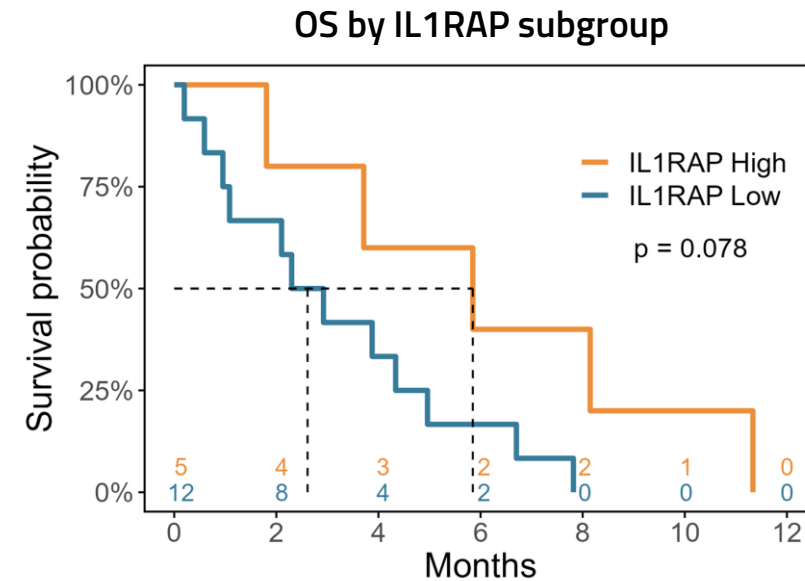
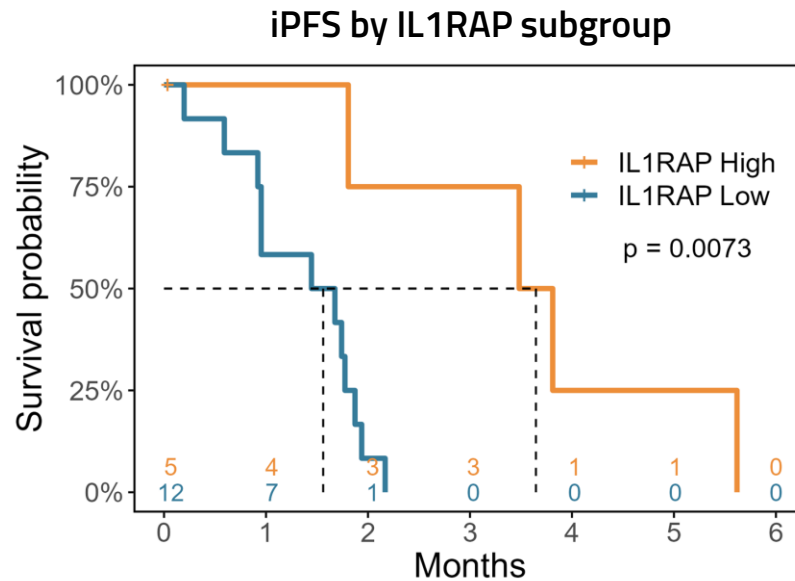


Efficacy analysis for IL1RAP High (n=29) vs IL1RAP Low (n=20) PDAC patients (1st line, combination with Gem/Abraxane):

- Significantly prolonged OS in ILRAP High vs IL1RAP Low patients (14.2 vs 10.6 mo; p=0.026)
- Deeper and more durable responses in IL1RAP High subgroup: 11 patients had 50% or more tumor size decrease

NEW DATA IN IL1RAP HIGH PATIENTS SUPPORT ONGOING DEVELOPMENT AND EXPLORATION OF NEW OPPORTUNITIES

PDAC – Strong efficacy in patients with high tumor IL1RAP level



Monotherapy efficacy analysis for IL1RAP High (n=5) vs IL1RAP Low (n=12) PDAC patients (late-stage, typically progressed after two lines of chemotherapy):

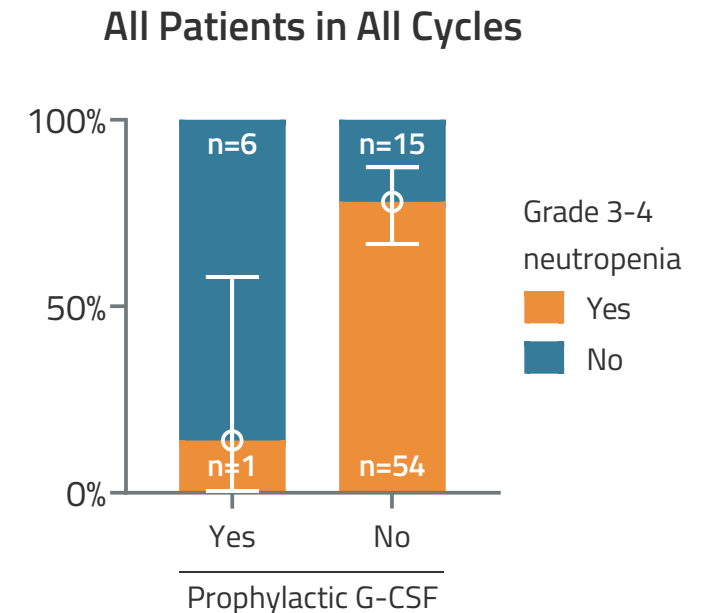
- Significantly prolonged iPFS in IL1RAP High vs IL1RAP Low patients (3.6 vs 1.6 mo; $p=0.0073$)
- Trend for OS advantage in IL1RAP High patients (5.8 vs 2.6 mo; $p=0.078$)

NADUNOLIMAB MONOTHERAPY RESULTS SUPPORT EFFECTS IN IL1RAP HIGH PATIENTS

PDAC – Safety profile is manageable and supports MOA

- Neutropenia manageable through G-CSF prophylaxis
 - In 7 patients given G-CSF prophylaxis, only 1 developed grade 3-4 neutropenia
- Only 1 % peripheral neuropathy grade 3-4 observed (17% in historical controls)

Grade 3 or higher AEs	Gem/Abraxane Von Hoff, 2013 (n=421)	Nadunolimab+Gem/Abraxane CANFOUR (n=76)
Neutropenia	38%	65%
Leukopenia	31%	24%
Thrombocytopenia	13%	15%
Febrile neutropenia	3%	13%
Anemia	13%	13%
Fatigue	17%	8%
Diarrhea	6%	3%
Peripheral neuropathy	17%	1%



**G-CSF PROPHYLAXIS IMPLEMENTED IN FUTURE TRIALS;
POTENTIAL REDUCTIONS OF SOME SIDE EFFECTS TO BE DOCUMENTED IN RANDOMIZED TRIALS**

Median duration of treatment 5.5 mo (ref 3.9 mo); most common reasons for termination: gastrointestinal events or general health deterioration.
No patients discontinued due to neutropenia.

PDAC – Phase IIb study design

Primary endpoint:

- PFS

Pre-planned subgroup analysis based on baseline IL1RAP expression on tumor cells/stromal cells:

- Screening biopsy or availability of archival tissue will be required to allow IHC determination for IL1RAP expression

Correlative biomarkers to be investigated:

- Serum IL-6, IL-8, CRP, cytokine panel
- Serum ctDNA
- Tumor tissue RNA sequencing

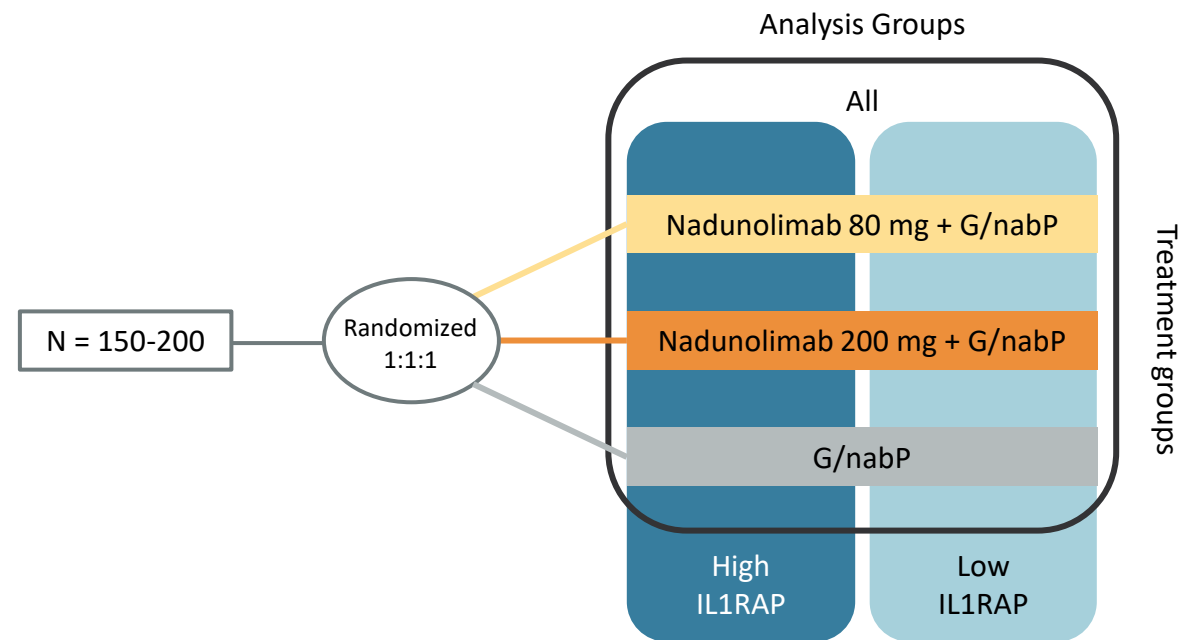
Timelines:

- Regulatory submission H2 2023
- FPI early 2024; top-line results 2025

Geography:

- USA and Europe

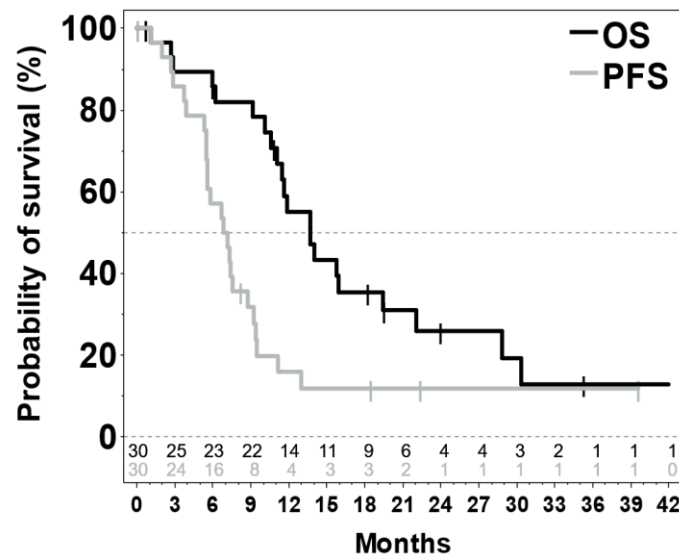
Open-label, randomized, controlled, non-comparative, 3-arm study evaluating 2 dose levels of nadunolimab + gemcitabine/ nab-paclitaxel with gemcitabine/nab-paclitaxel as control:



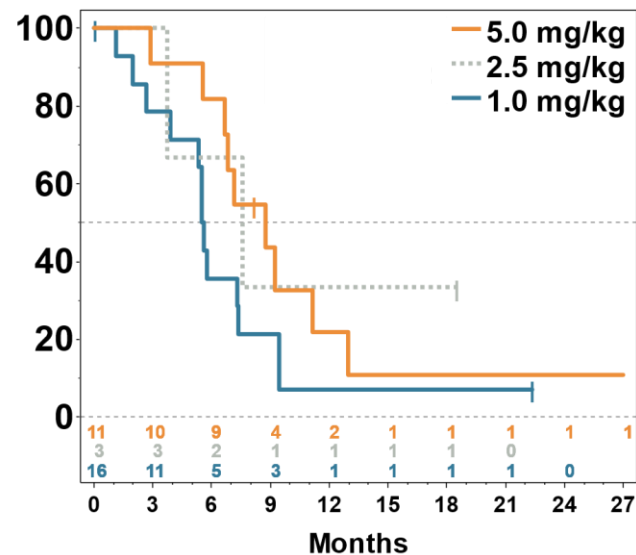
PHASE IIB TRIAL TO VALIDATE STRONG SIGNAL OF ACTIVITY IN IL1RAP HIGH PATIENTS

NSCLC – Promising efficacy of nadunolimab combination therapy

OS and PFS for mITT patients



PFS by dose level

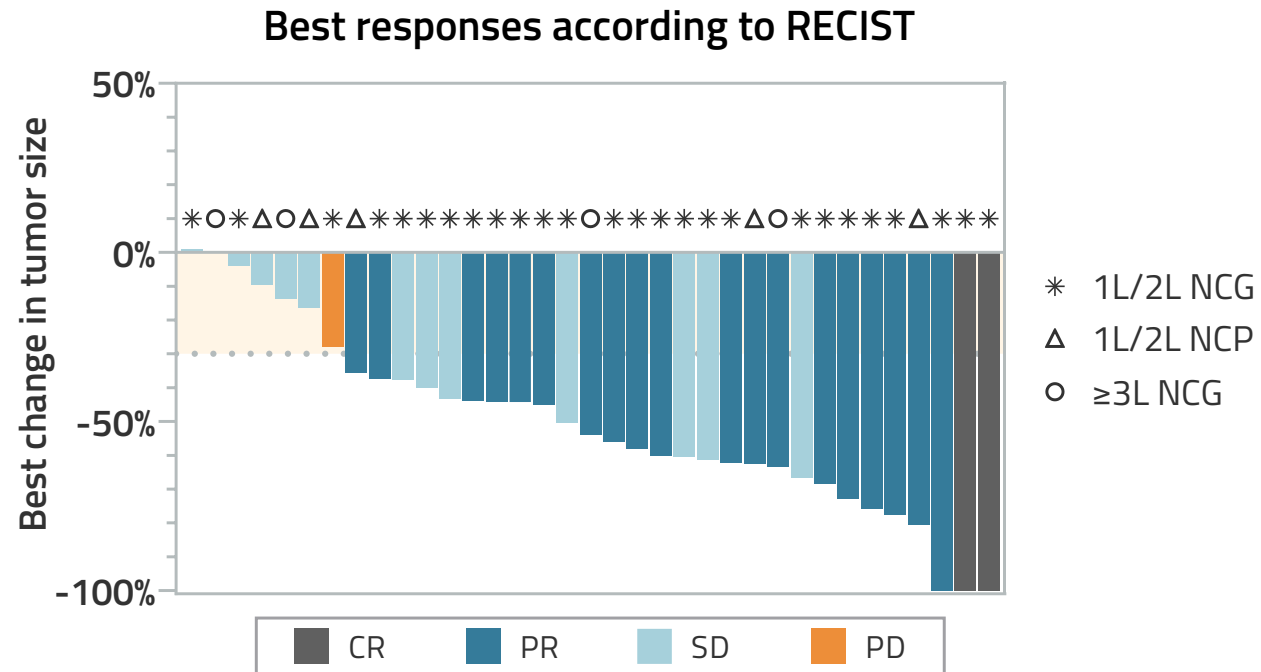


Nadunolimab combination with Gem/Cis in 1st/2nd line NSCLC (n=30):

- ORR 53%, 13.7 mo median OS, 7.0 mo median PFS (dose-response trend for PFS)
- Generally well tolerated; neutropenia frequency higher than expected for chemo (managed by dose reductions or G-CSF)

STRONG EFFICACY OF NADUNOLIMAB IN COMBINATION WITH GEM/CIS IN 1L/2L NSCLC

NSCLC – Promising efficacy of nadunolimab combination therapy



High ORR to nadunolimab and platinum doublets in different lines of therapy:

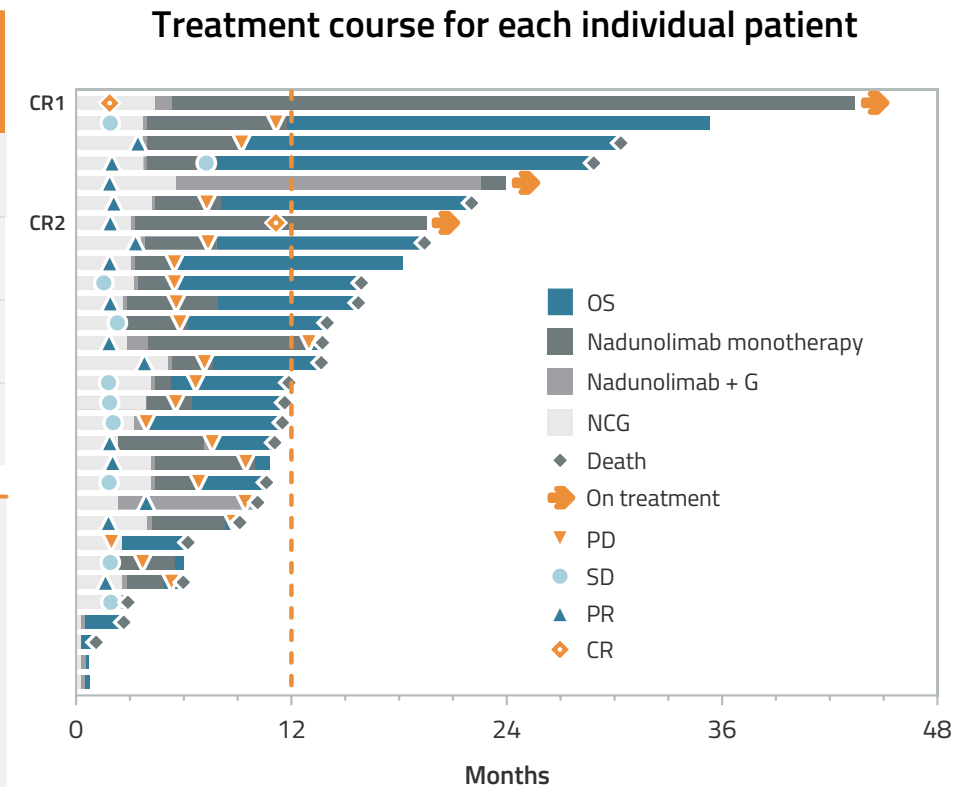
- Gem/Cis 1st/2nd line: ORR 53% (n=30)
- Carbo/Pemtrex 1st/2nd line: ORR 60% (n=5)
- Gem/Cis ≥3rd line: ORR 50% (n=4)

CONSISTENTLY HIGH RESPONSE RATES WITH NADUNOLIMAB AND PLATINUM DOUBLETS

NSCLC – Long-term benefit with strong signal in non-squamous subtype

	All (n=30)	Historical data ^{1,2}	Non-squamous (n=16)	Non-squamous, historical data ³
Median OS	13.7 mo	10.3 mo	15.9 mo	11.3 mo
Median PFS	7.0 mo	5.1 mo	7.3 mo	4.9 mo
ORR	53%	22-28 %	56%	19%
Complete response	6.7% (n=2)	<1%	12.5% (n=2)	<1%

- Strongest efficacy in 16 non-squamous patients
- Long-term benefit of nadunolimab combination therapy, including two complete responses

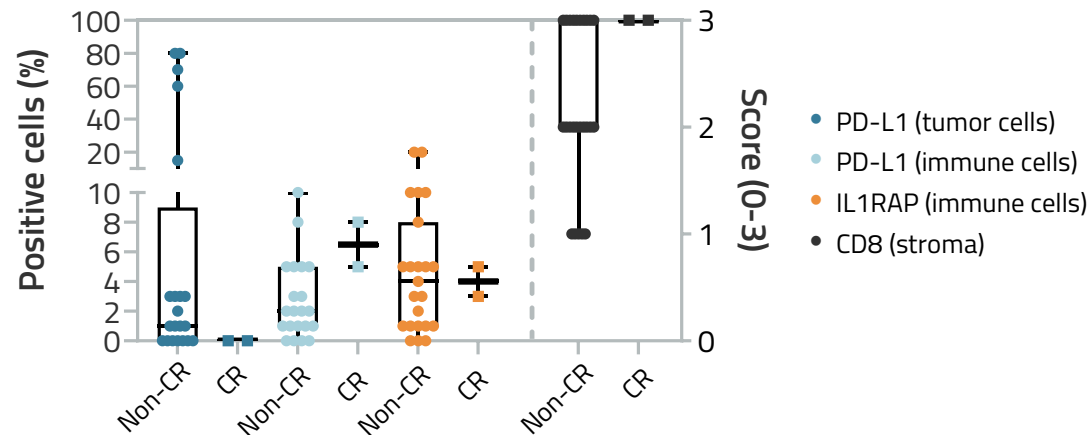
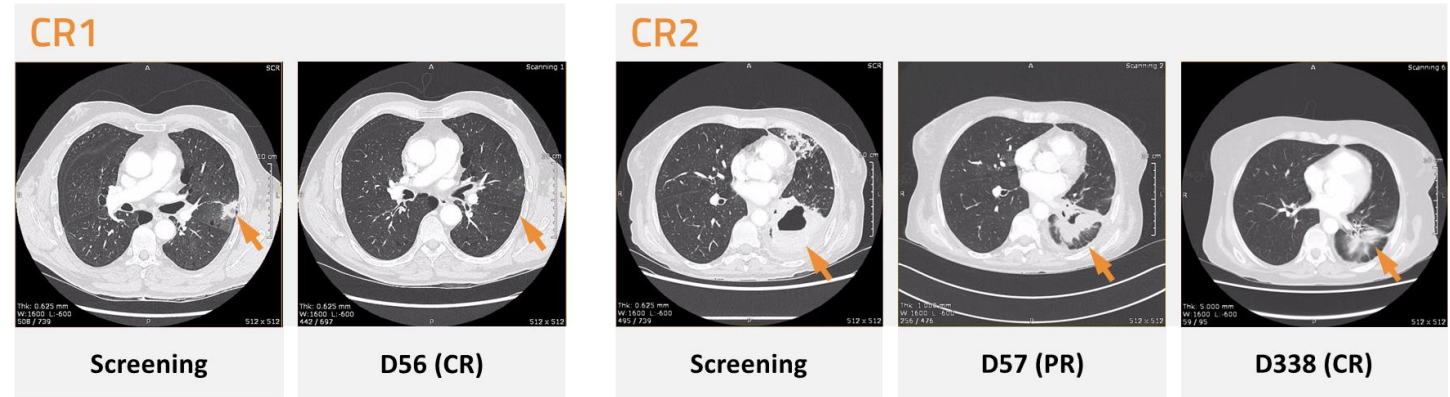
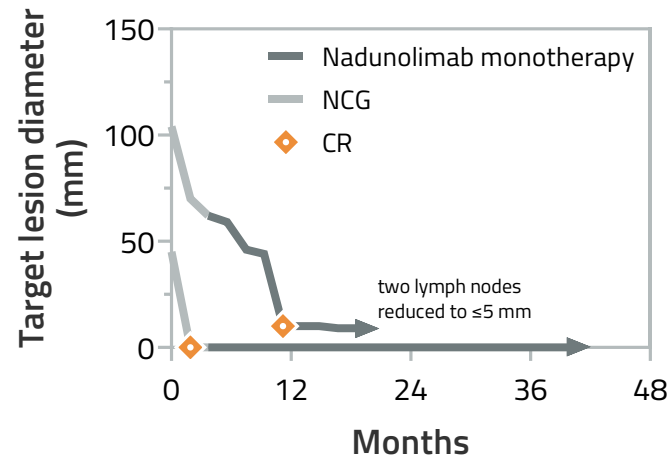


NADUNOLIMAB COMBINATION THERAPY COMPARES VERY FAVORABLY TO HISTORICAL DATA FOR CHEMOTHERAPY ALONE

¹ Schiller et al, N Engl J Med 2002; ² Scagliotti et al, J Clin Oncol 2008; ³ Gandhi et al, N Engl J Med 2018

PD – Progressive Disease; SD – Stable Disease; PR – Partial Response; CR – Complete Response; NCG – Nadunolimab/Cisplatin/Gemcitabine

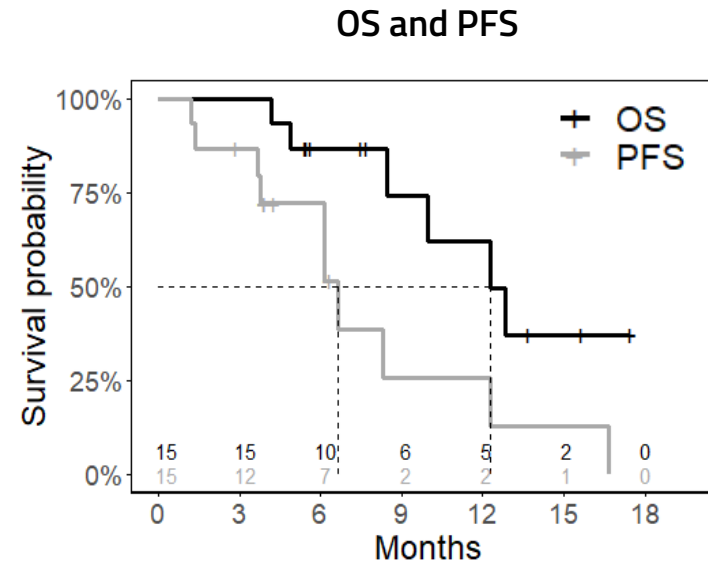
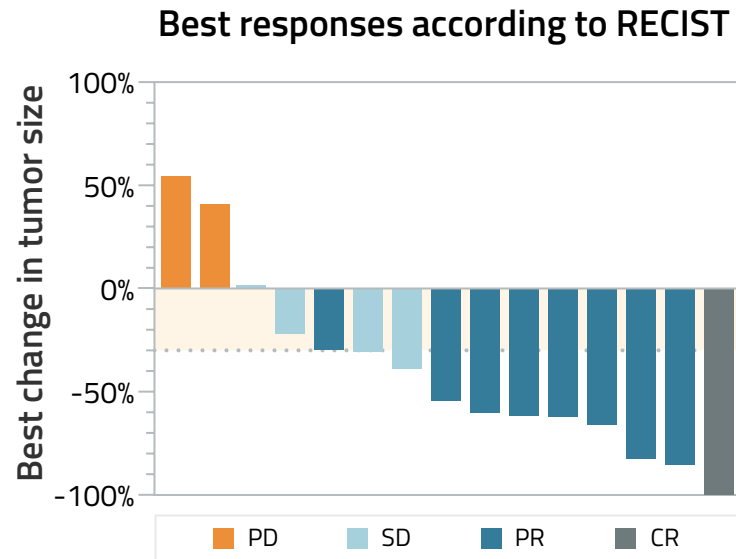
NSCLC – Complete responders with distinct biomarker profile



- One CR maintained over 3 yrs (CR1), second CR achieved on nadunolimab monotherapy approx. 9 mo post-chemo (CR2)
- Both non-squamous, progressed on pembro, with PD-L1⁻ tumor cells, PD-L1⁺ immune cells in tumor

SIGNAL OF NADUNOLIMAB MONOTHERAPY ACTIVITY RESULTING IN COMPLETE RESPONSE

TNBC – Promising early safety and efficacy



Nadunolimab combination with Gem/Carbo in 1st/2nd line metastatic TNBC:

15 patients enrolled in the dose-escalation phase:

- Preliminary ORR: 60% (1 CR, 8 PR, 4 SD, 2 PD)
- Preliminary median OS 12.3 mo, median PFS 6.6 mo
- Acceptable safety profile (G-CSF given prophylactically to control neutropenia)
- Randomized phase II ongoing

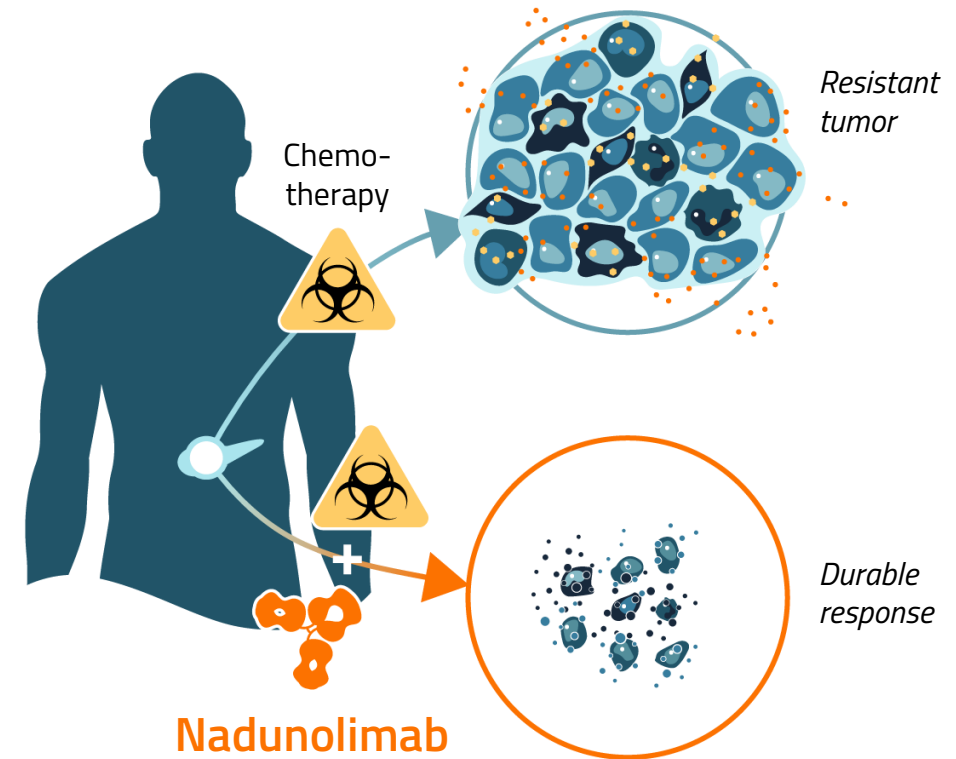
RESPONSE RATE OF NADUNOLIMAB COMBINATION THERAPY WELL ABOVE HISTORICAL DATA FOR CHEMOTHERAPY ONLY¹

¹ O'Shaughnessy et al, J Clin Oncol 2014

PD – Progressive Disease; SD – Stable Disease; PR – Partial Response; CR – Complete Response

Key messages

- Most chemotherapies induce chemoresistance already after a few months of therapy. Chemotherapy can upregulate both IL-1 α and IL-1 β , signaling through IL1RAP.
- Clinical results strongly support potential unique first-in-class opportunities in PDAC, NSCLC and TNBC.
- PDAC patients with high IL1RAP level respond best to nadunolimab combination therapy despite having a worse prognosis.



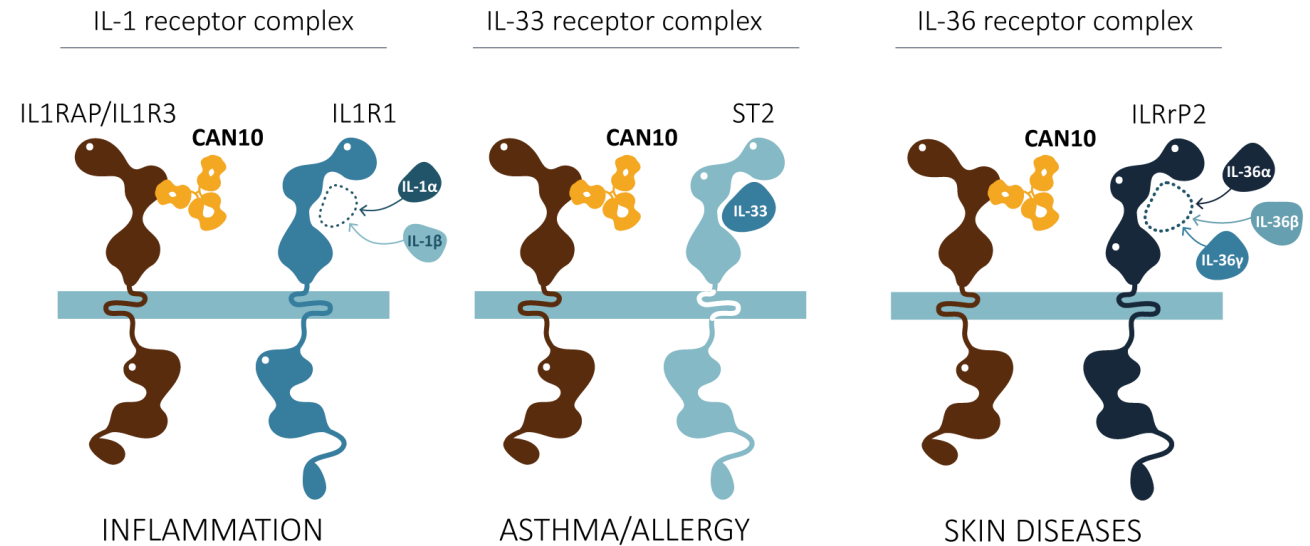
PROMISING EFFICACY OF NADUNOLIMAB WITH CHEMOTHERAPY – CURRENT FOCUS ON RANDOMIZED CLINICAL TRIALS

A microscopic image showing several cells with a complex, textured surface. The image is overlaid with a semi-transparent blue filter. Two cells are in sharp focus in the upper half, while others are blurred in the background and foreground.

CAN10 – OPPORTUNITY IN AUTOIMMUNE/INFLAMMATORY DISEASE

CAN10 – New clinical asset in autoimmunity/inflammation

- IL1RAP-binding antibody potently blocking IL-1, IL-33 and IL-36, without ADCC
- Unique anti-inflammatory activity observed in different mouse models (myocarditis, systemic sclerosis, psoriasis, inflammation)
- Development focusing on systemic sclerosis and myocarditis, diseases involving multiple IL-1 family cytokines



UNIQUE OPPORTUNITY FOR CAN10 IDENTIFIED IN LIFE-THREATENING DISEASES

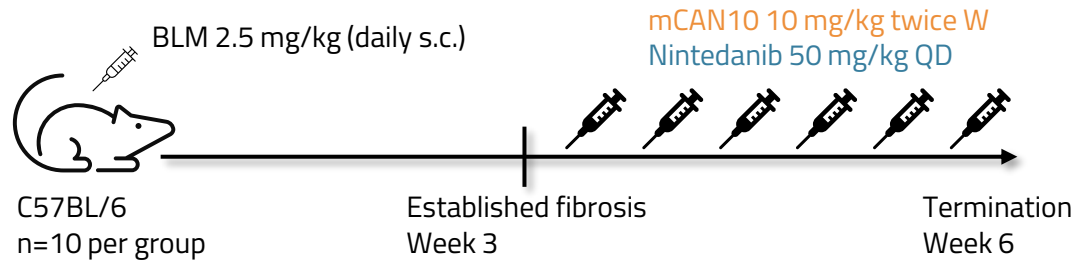
Indications and preclinical development



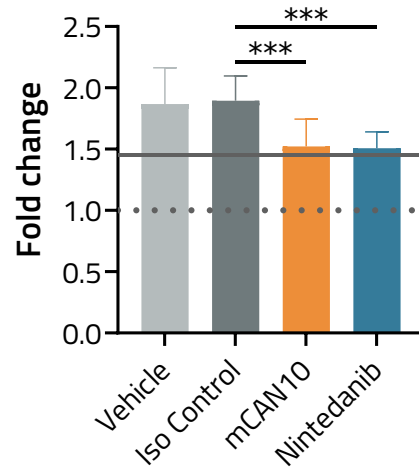
- Inflammation of the myocardium that can lead to fibrosis and loss of contractile function
 - Can be both autoimmune and viral
 - The estimated incidence of myocarditis is approximately 22 per 100,000 and the disease accounts for approximately 0.6 per 100,000 deaths annually worldwide
- Chronic, autoimmune connective tissue disorder characterized by inflammation and fibrosis of the skin and internal organs
 - The leading cause of death – interstitial lung disease where the unmet need is particularly high
 - The estimated annual incidence is about 4.5 per 100,000 in North America and 1.8 per 100,000 in Europe

Systemic sclerosis – mCAN10 inhibits bleomycin-induced skin fibrosis

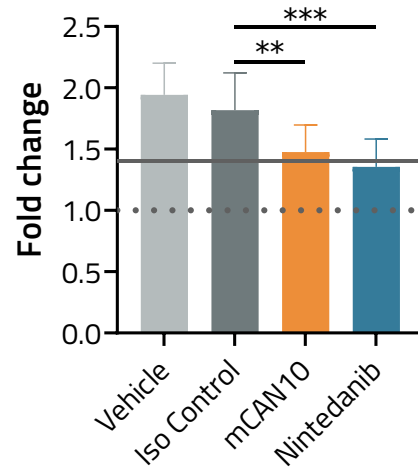
Bleomycin (BLM) model



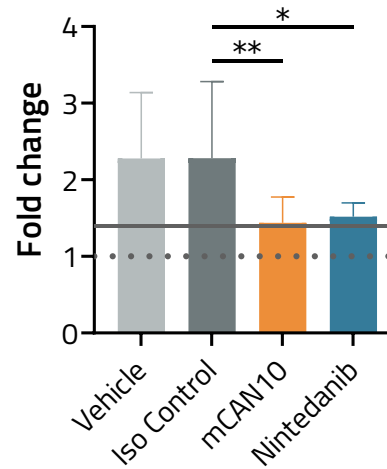
Dermal thickness



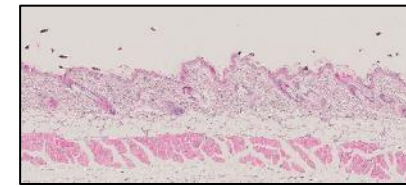
Myofibroblast count



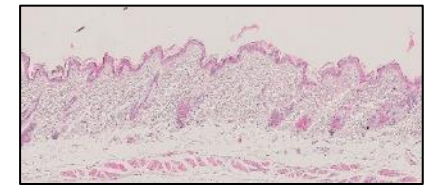
Hydroxyproline



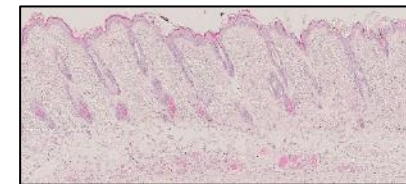
No BLM (6 wks)



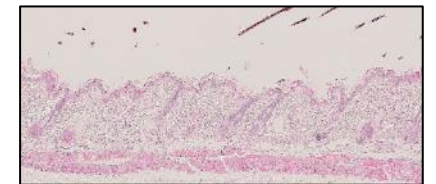
Baseline BLM (3 wks)



BLM (6 wks) Iso Control

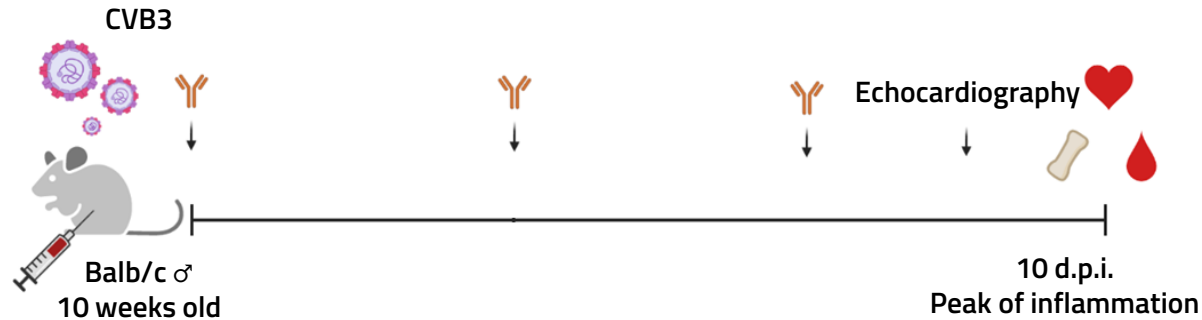


BLM (6 wks) mCAN10

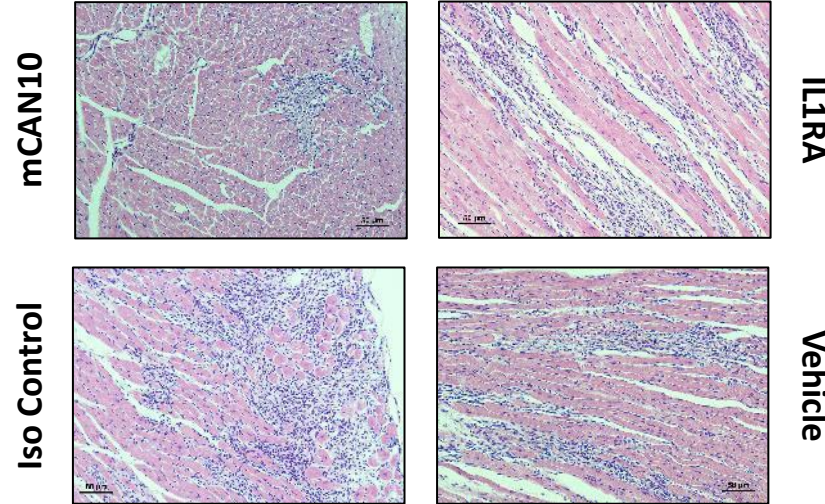
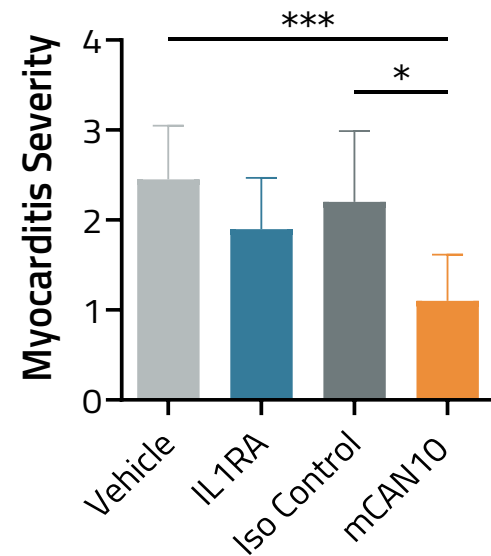


Viral myocarditis – mCAN10 reduces disease severity

CVB3 myocarditis experimental design

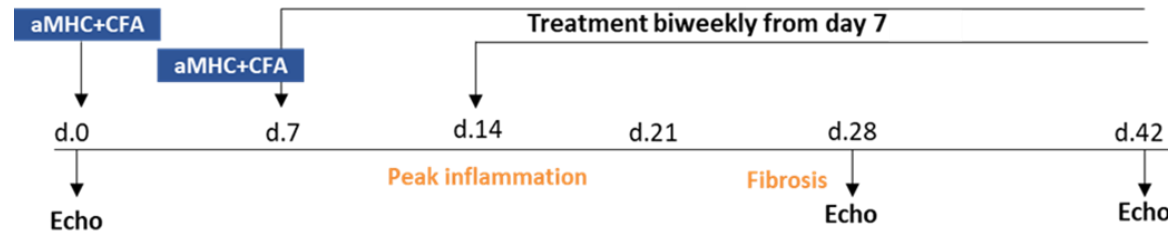


→ mCAN10 reduced disease severity, based on histological scoring of heart sections, and preserved heart function

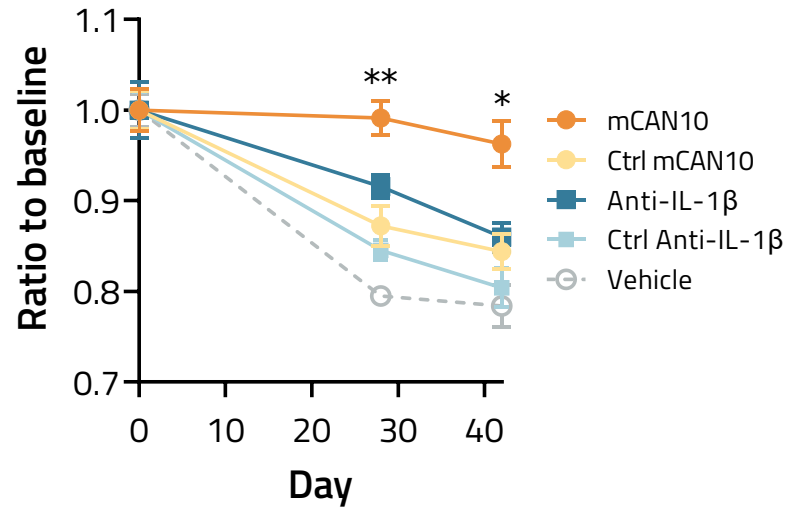


→ mCAN10 also reduced inflammatory leukocyte populations in the heart tissue

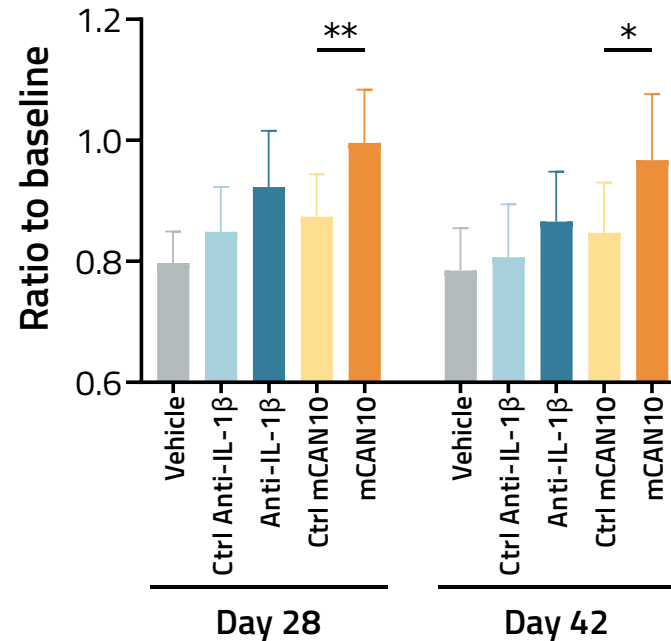
Experimental autoimmune myocarditis – mCAN10 improves heart function



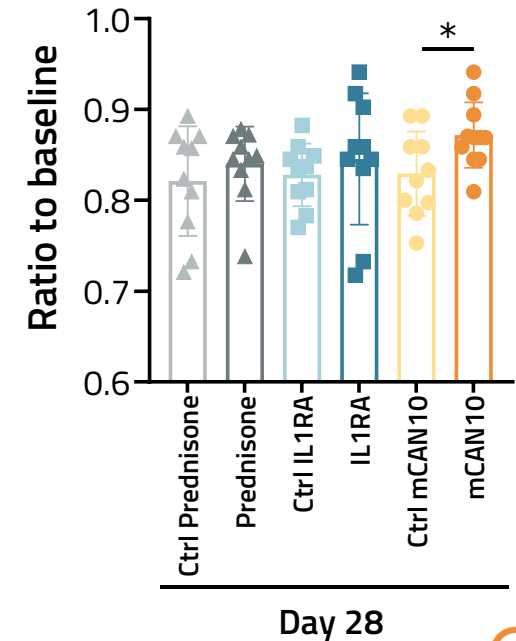
Left Ventricular Ejection Fraction (LVEF)



LVEF (treatment from day 7)

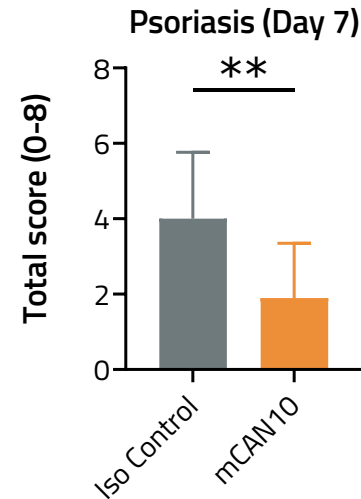
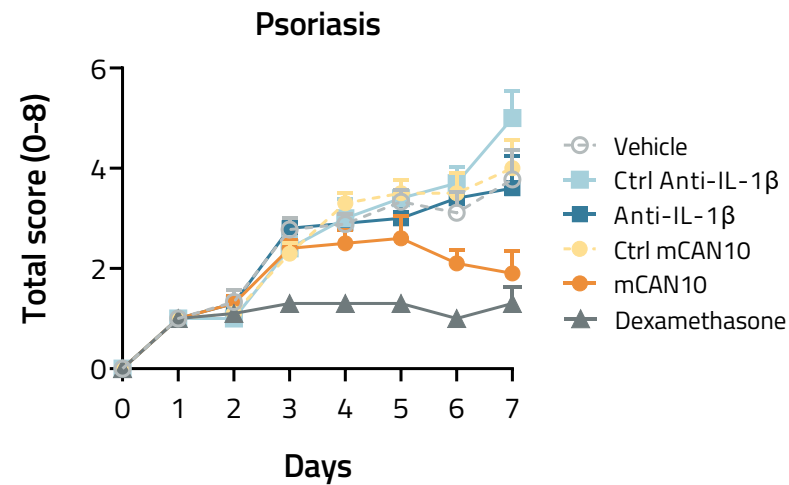


LVEF (treatment from day 7)

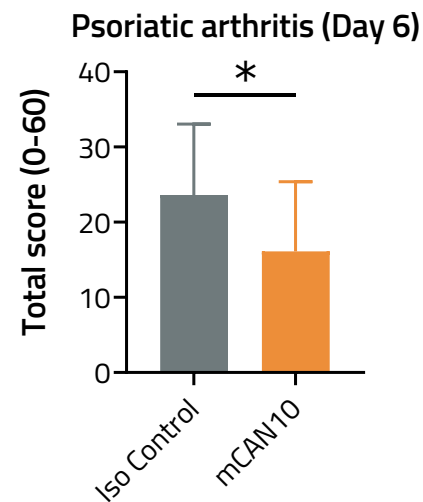
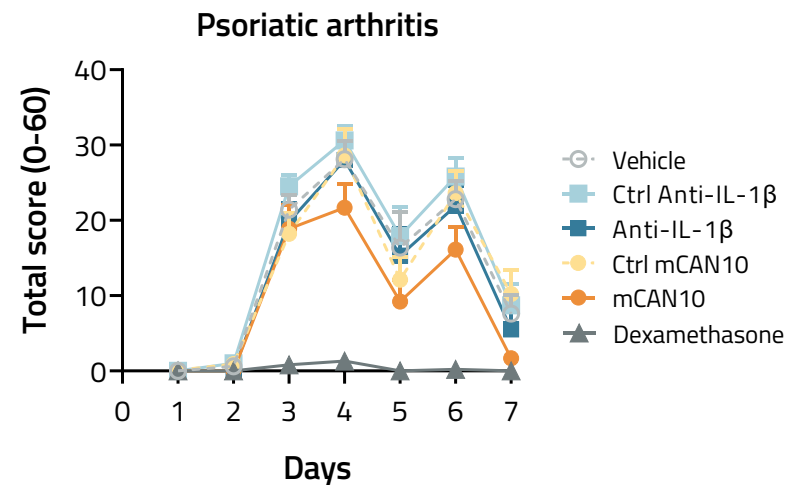


α MHC – α -Myosin Heavy Chain; CFA – Complete Freund's Adjuvant
n=10 per group

Psoriasis and psoriatic arthritis – mCAN10 reduces disease severity



→ mCAN10, but not anti-IL-1 β , reduced the skin inflammation in Imiquimod-induced psoriasis



→ mCAN10, but not anti-IL-1 β , similarly reduced disease severity in mannan-induced psoriatic arthritis

CAN10 – Project status

Status

- CAN10 safe in GLP tox study
- Strong results in several preclinical models, including lead indications myocarditis and systemic sclerosis
- Phase I ongoing, early planning of patient studies (phase IIa)

Clinical phase I study – First data set during 2024

- Phase I in healthy volunteers (SAD) followed by psoriasis patients (MAD); ongoing in Germany
- Up to 80 individuals (safety, pharmacokinetics, biomarkers)

The background of the slide is a microscopic image showing several cells. Two cells in the upper half are in sharp focus, revealing a complex, fibrous internal structure. The rest of the image is blurred, showing other cells in the background. A semi-transparent dark blue horizontal band is positioned across the middle of the slide, containing the text.

MILESTONES & INVESTMENT HIGHLIGHTS

Upcoming milestones

Nadunolimab

PDAC	NSCLC	TNBC	CAN10	Additional milestones
<ul style="list-style-type: none">• Start of Phase IIb trial in 150-200 patients early 2024• Phase IIb top-line data in 2025	<ul style="list-style-type: none">• Efficacy/biomarker data from CANFOUR 2023 and 2024	<ul style="list-style-type: none">• Safety and efficacy data from Phase I at ESMO in Q4 2023• Randomized Phase II top-line data in late 2024	<ul style="list-style-type: none">• Phase I recruitment and treatment ongoing• Phase I data in 2024	<ul style="list-style-type: none">• New clinical data presented from CIRIFOUR, CAPAFour and CESTAFOUR trials• New preclinical and translational results

EXTENSIVE NEWS FLOW EXPECTED DURING 2023-2024

Cantargia – Investment highlights



NOVEL IL1RAP ANTIBODIES, POTENTIAL TO TREAT CANCER & INFLAMMATORY DISEASE

- IL1RAP elevated in most solid and liquid tumors
- IL1RAP signaling drives several autoimmune and inflammatory diseases



NADUNOLIMAB: CLEAR ACTIVITY SIGNALS IN CANCER THERAPY WITH UPCOMING CATALYSTS

- Strong clinical interim results in PDAC and NSCLC, and promising initial results in TNBC; >250 patients treated
- Randomized Phase II trial ongoing in TNBC (top-line data late 2024); Phase IIb trial in preparation in PDAC (top-line data 2025)



CAN10: OPPORTUNITY IN AUTOIMMUNITY/INFLAMMATION

- Pronounced activity in models of systemic sclerosis, myocarditis, psoriasis, atherosclerosis and inflammation
- Phase I clinical trial ongoing, initial results in 2024



CORPORATE STRENGTH DRIVING INNOVATION

- Solid cash position with runway to mid/end 2024 (287M SEK cash & equivalents at Q2 2023)
- Robust patent portfolio: IL1RAP antibody target in oncology (2032), nadunolimab (2035) and CAN10 (2041)

Cantargia IP

→ Lead candidate anti-IL1RAP antibody **CAN04**

Expiry year **2035**

Granted (e.g. Europe, USA, China, Japan)

→ Anti-IL1RAP for treatment of **solid tumors**

Expiry year **2032**

Granted (e.g. Europe, USA, China, Japan)

→ Anti-IL1RAP for treatment of **hematological disorders**

Expiry year **2030**

Granted (e.g. Europe, USA, China, Japan)

→ Anti-IL1RAP for treatment of **myeloproliferative disorders**

Acquired from Cellerant; expiry year **2029**

Granted (USA)

→ Lead candidate anti-IL1RAP antibody **CAN10**

Expiry year **2041**

Granted (USA)

→ Additional patent families covering alternative anti-IL1RAP antibodies

Eg. CAN03, biepitopic anti-IL1RAP etc.

