



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

*Corporate Presentation  
Dec 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 into 2025 (200M SEK cash & equivalents at Q3 2023 + 59 MSEK from share issue Oct 23)
- 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 <sup>st</sup> line	Gemcitabine/nab-paclitaxel				
	TNBC	1 <sup>st</sup> /2 <sup>nd</sup> line	Carboplatin/gemcitabine				
	NSCLC/ non-squamous NSCLC	1 <sup>st</sup> /2 <sup>nd</sup> line	Platinum doublets				
CAN10	Myocarditis, Systemic sclerosis						
CANxx	New opportunities within IL1RAP platform						

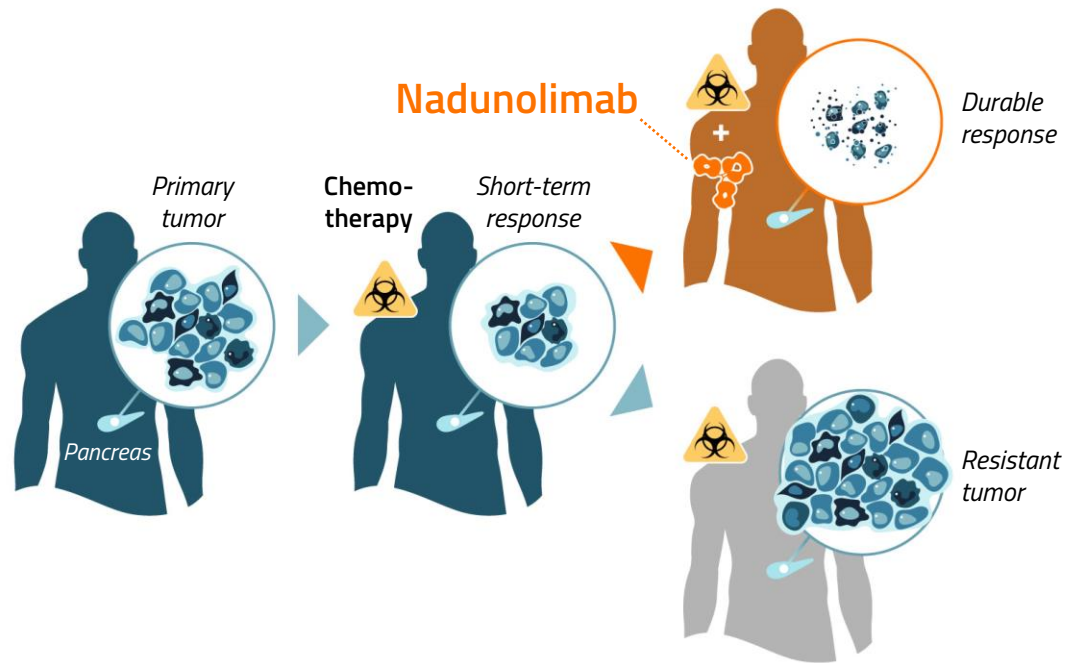
PDAC – pancreatic cancer; TNBC – triple-negative breast cancer; NSCLC – non-small cell lung cancer



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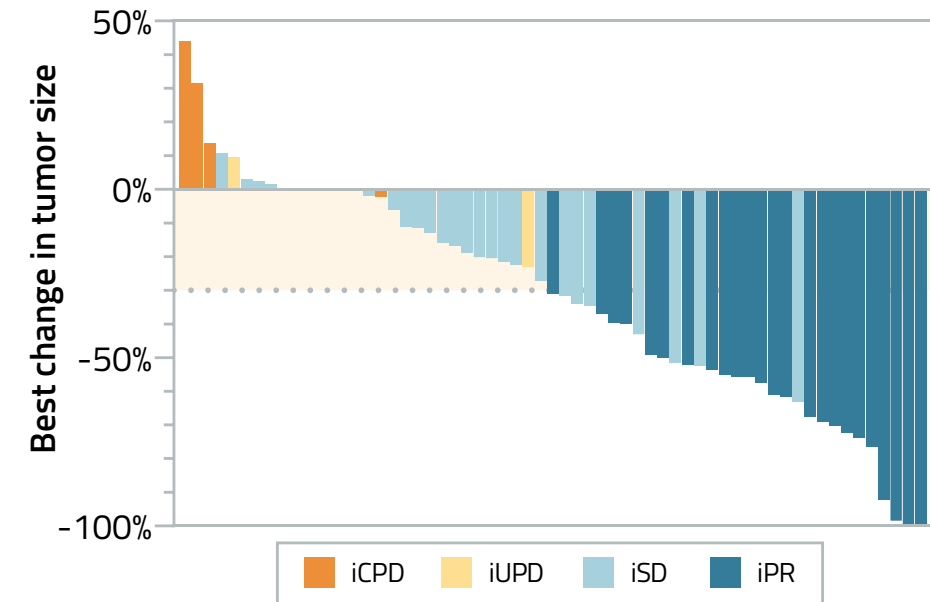
## NADUNOLIMAB (CAN04) OVERVIEW

# New strategy to treat cancer supported by clinical results



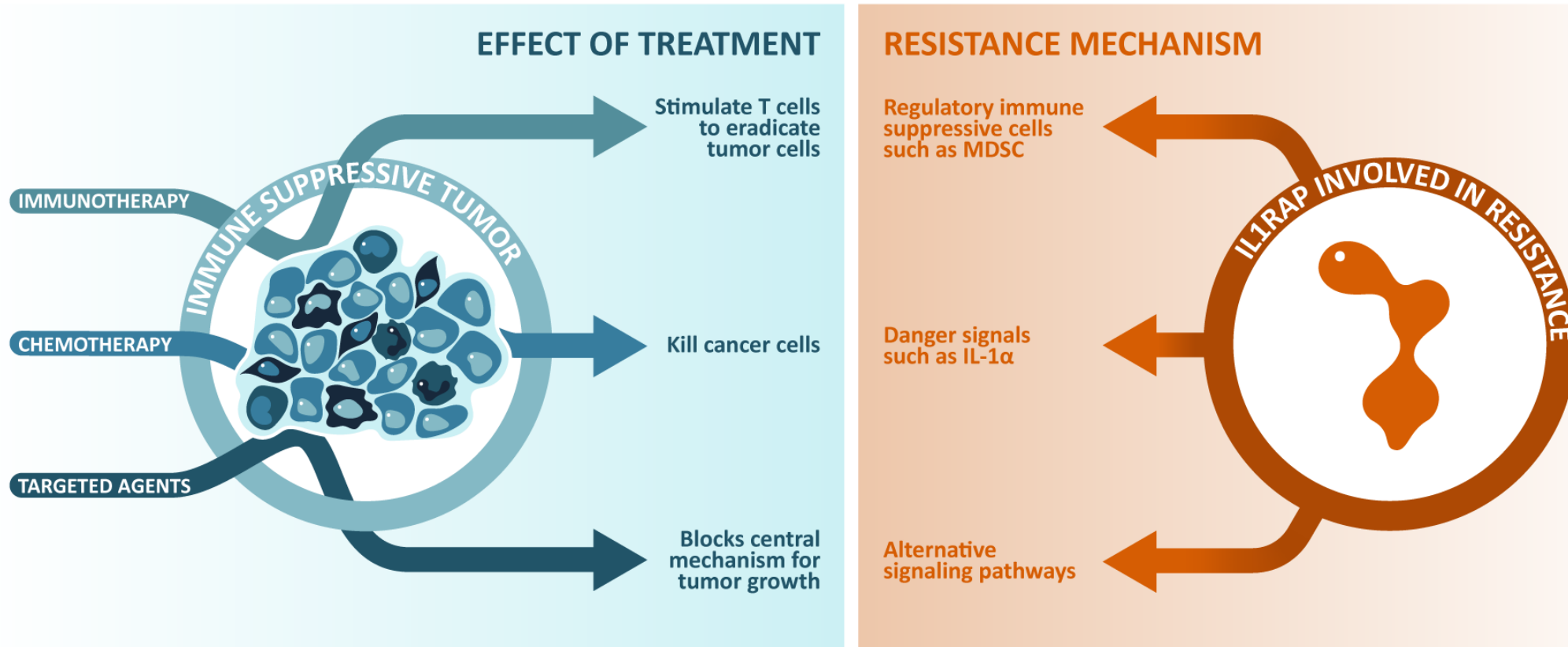
## PROMISING DATA IN PANCREATIC CANCER

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



SEVERAL LINES OF EVIDENCE SUGGEST NADUNOLIMAB COUNTERACTS CHEMORESISTANCE

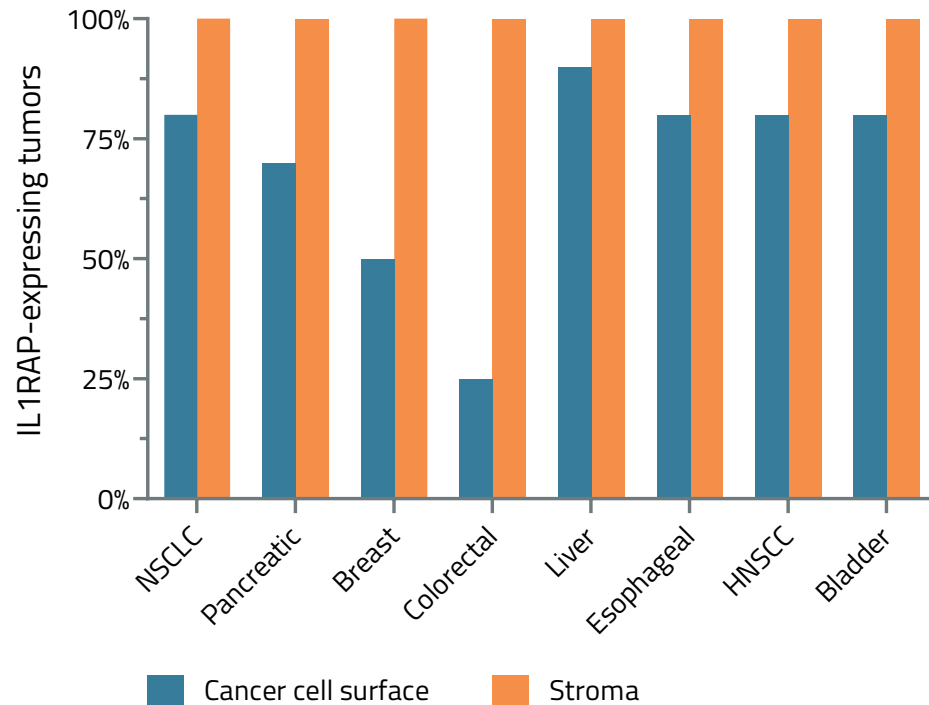
# Cantargia – Strategy to improve current cancer therapies



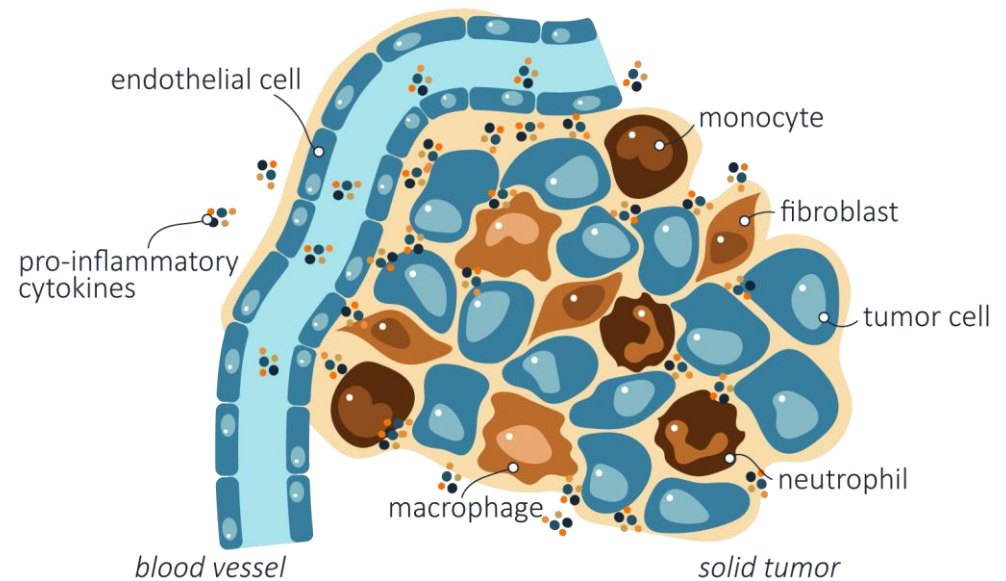
**IL1RAP – A NOVEL TARGET WITH SEVERAL OPPORTUNITIES; CURRENT FOCUS ON SYNERGISTIC COMBINATIONS**

# IL1RAP overexpressed in most solid tumors

IL1RAP EXPRESSION IN SOLID TUMOR TYPES



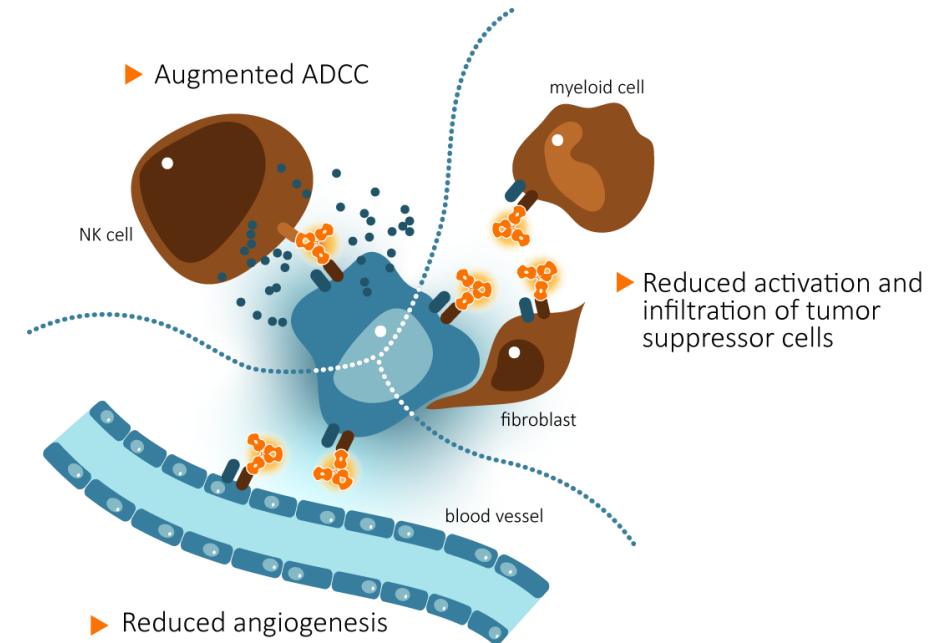
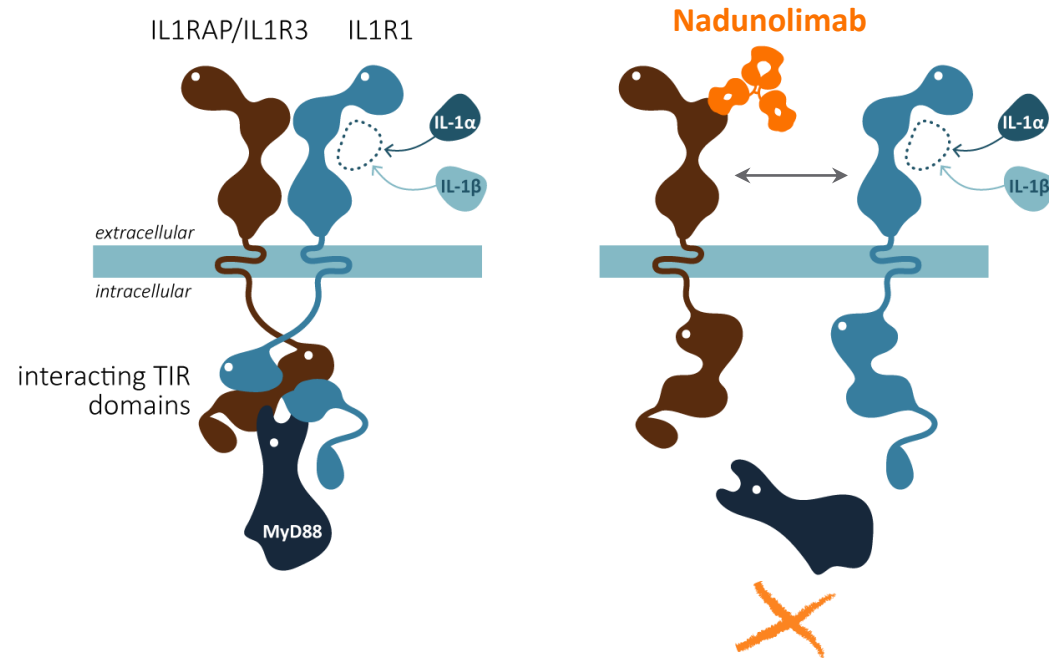
SEVERAL TUMOR-PROMOTING CELLS EXPRESSING IL1RAP IN THE TUMOR MICROENVIRONMENT



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

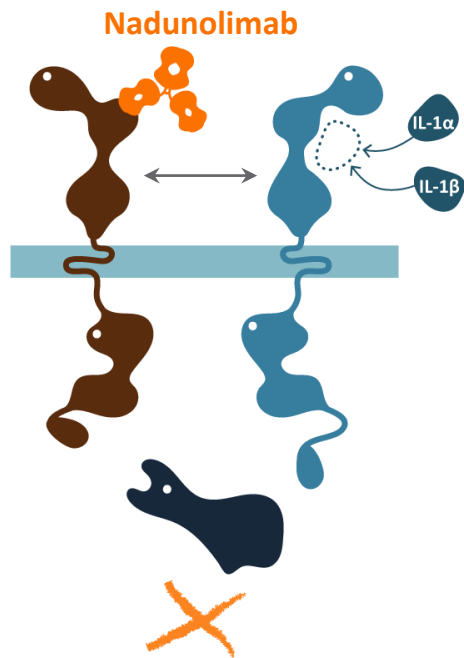


# Targeting IL1RAP provides unique opportunities to treat cancer by IL-1 $\alpha$ / $\beta$ blockade and ADCC

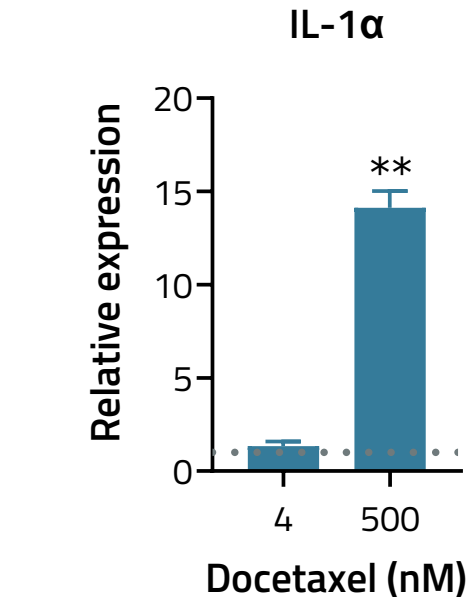


NADUNOLIMAB COUNTERACTS IMMUNE SUPPRESSION AND POTENTIATES THERAPY

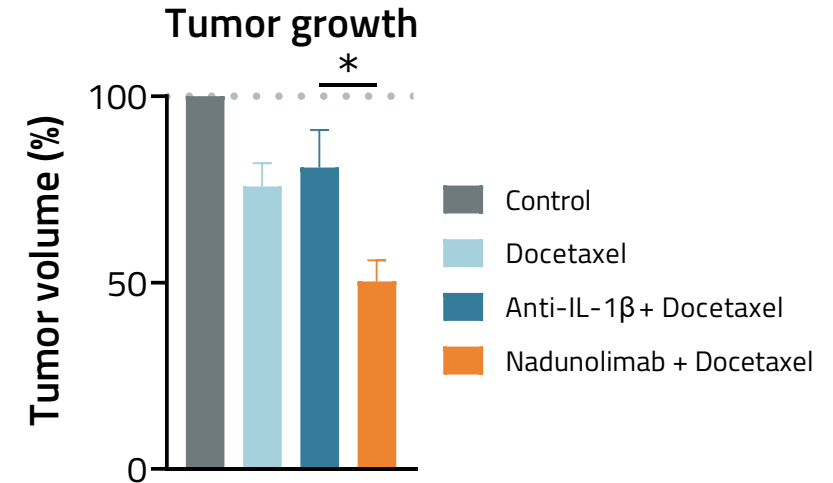
# Nadunolimab potentiates antitumor activity of chemotherapy



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



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



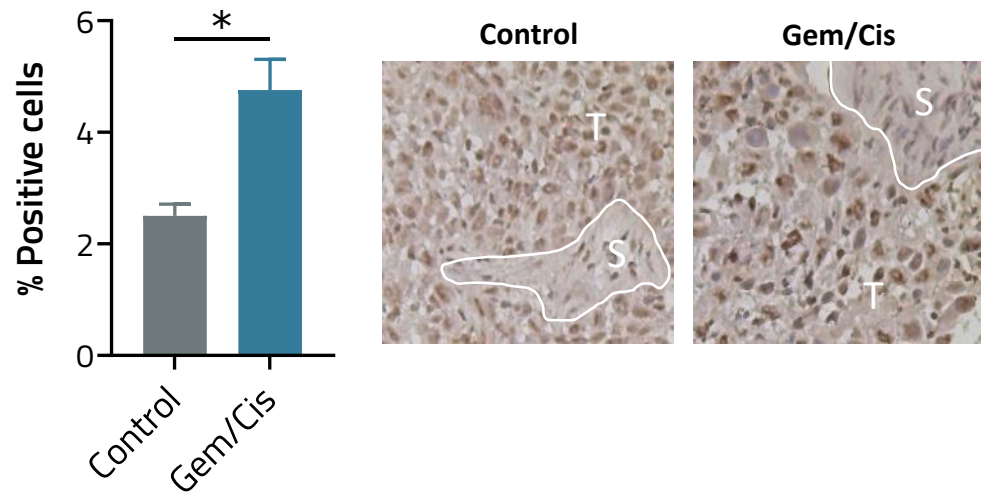
→ Nadunolimab + docetaxel reduces in vivo tumor growth more potently than anti-IL-1β + docetaxel

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

# Chemotherapy induces IL-1 $\alpha$ and IL-1 $\beta$ in the tumor

## IL-1 $\alpha$

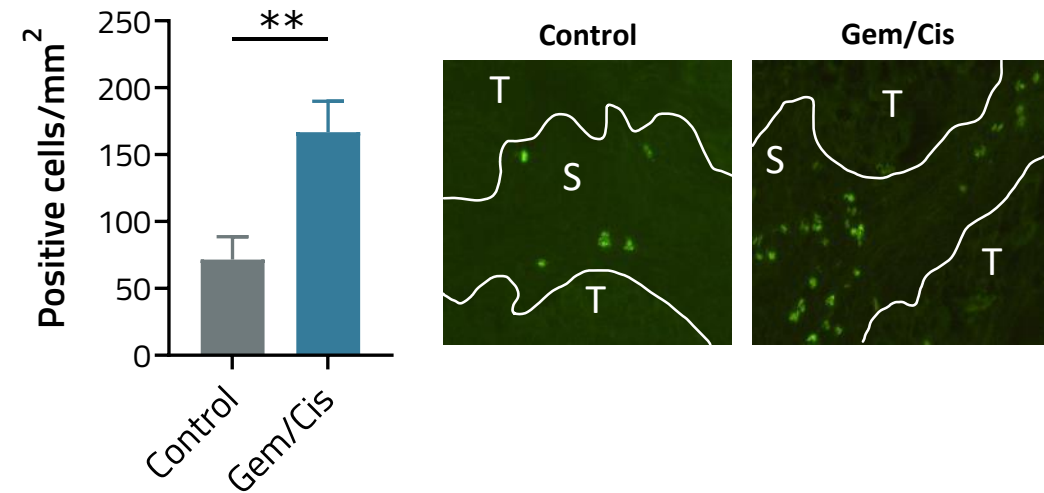
Tumor cell region (T)



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

## IL-1 $\beta$ -converting enzyme

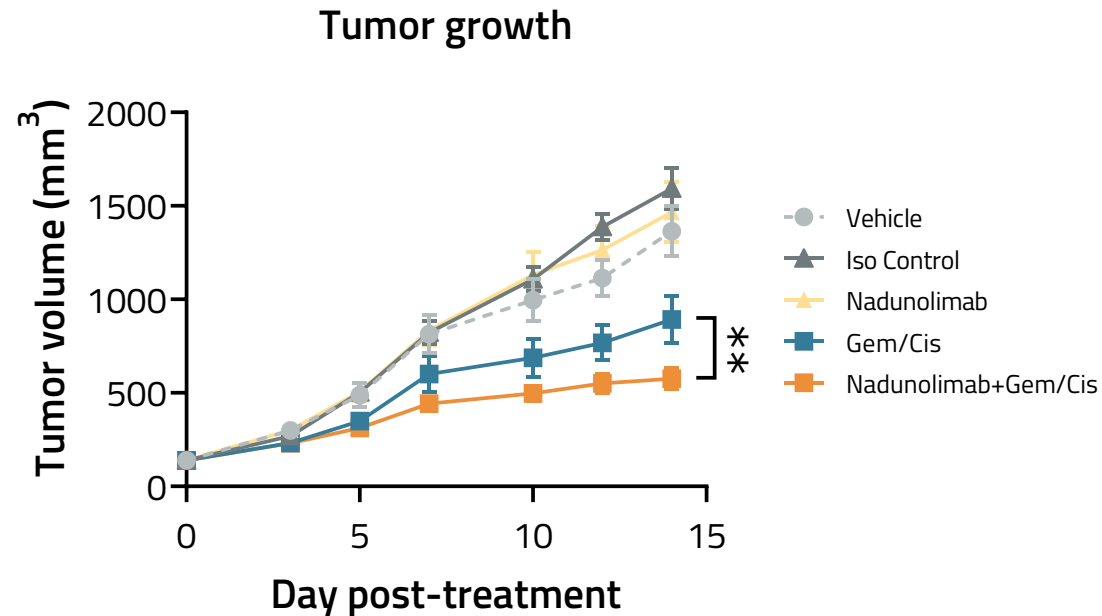
Stromal cell region (S)



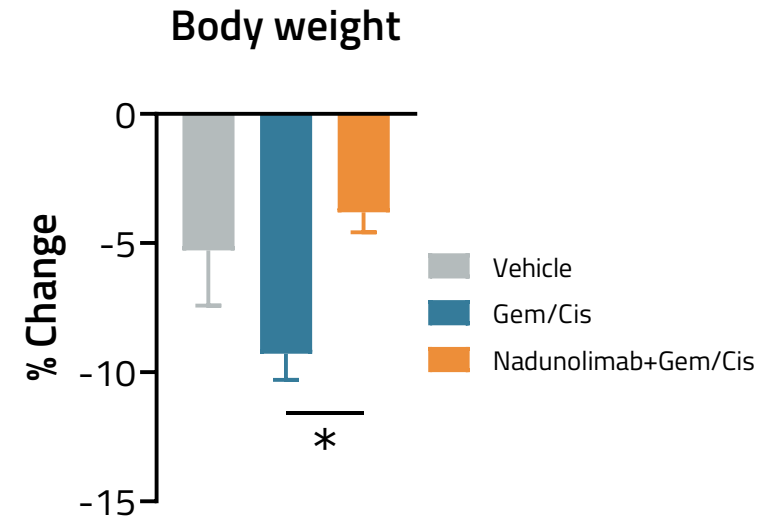
→ Gem/Cis also induces release of IL-1 $\beta$ -converting enzyme (ICE) by stromal cells

INCREASED LEVELS OF IL-1 $\alpha$  AND IL-1 $\beta$  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

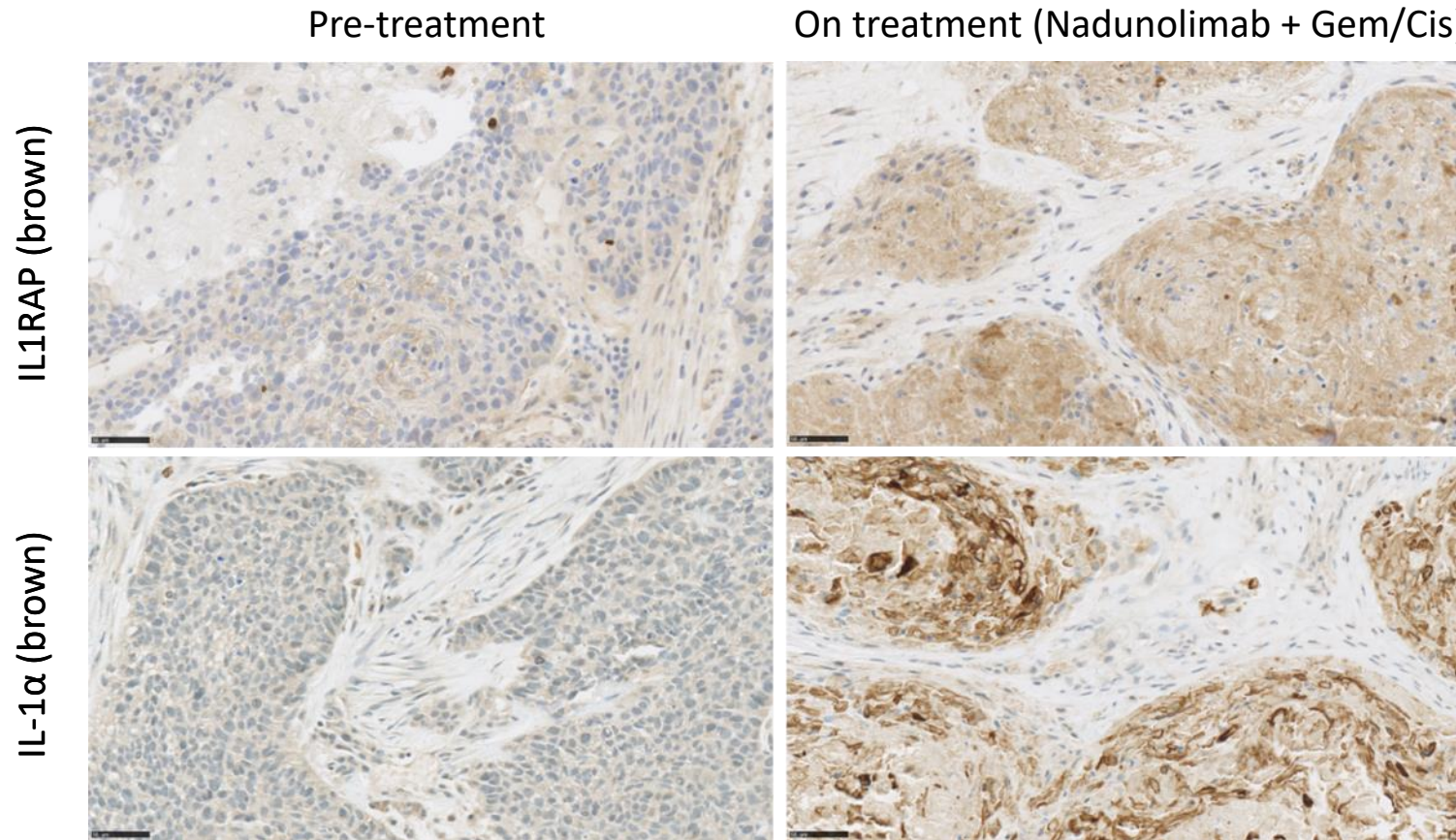
**NADUNOLIMAB HAS POTENTIAL TO IMPROVE CHEMOTHERAPY EFFICACY AND TOLERABILITY**

A microscopic image of cells, likely cancer cells, with a blue overlay. The cells are spherical and have a textured, fibrous surface. The background is a soft, out-of-focus blue.

## NADUNOLIMAB (CAN04) CLINICAL RESULTS



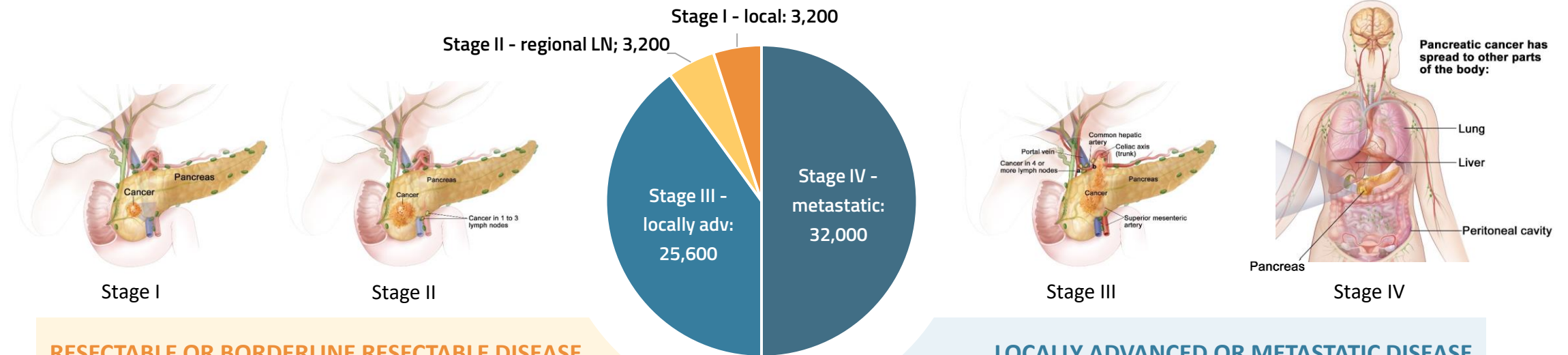
# NSCLC – Induction of IL1RAP and IL-1 $\alpha$ with therapy



IL-1 $\alpha$  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

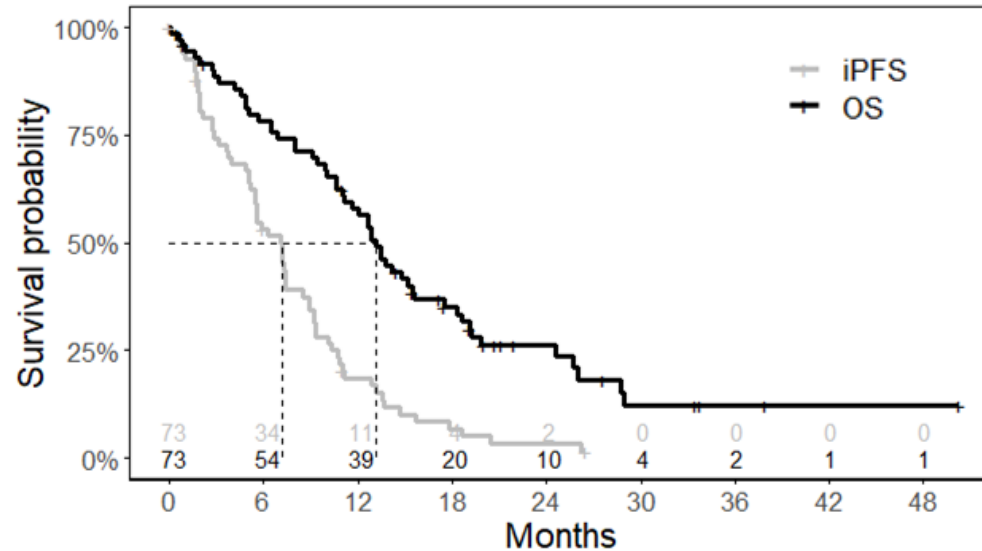
### Treatment:

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

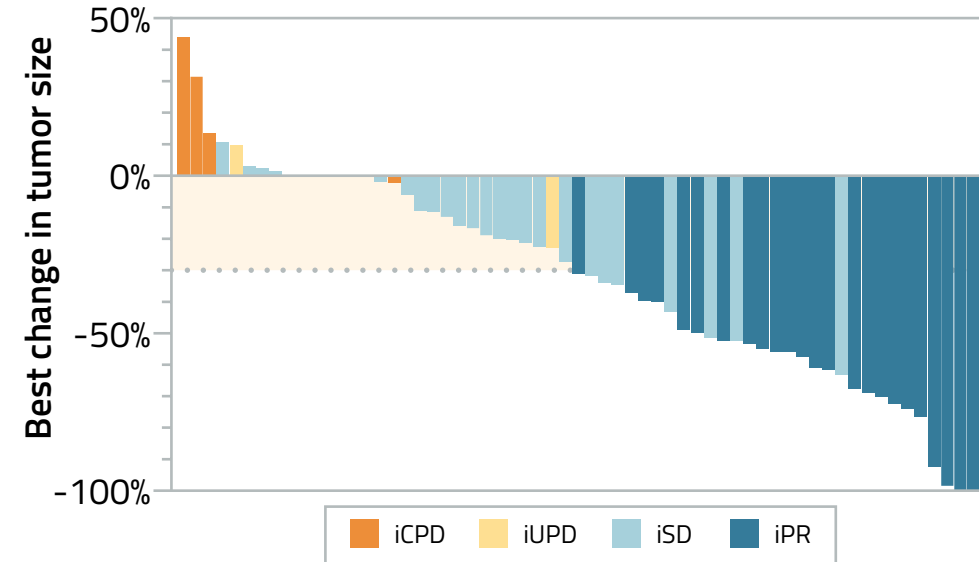
CURRENT DEVELOPMENT FOCUSES ON FIRST-LINE METASTATIC DISEASE WITH POTENTIAL TO MOVE TO EARLIER TREATMENT SETTINGS

# PDAC – Positive interim data in 1<sup>st</sup> line patients

OS and iPFS for mITT patients



Best responses according to iRECIST



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

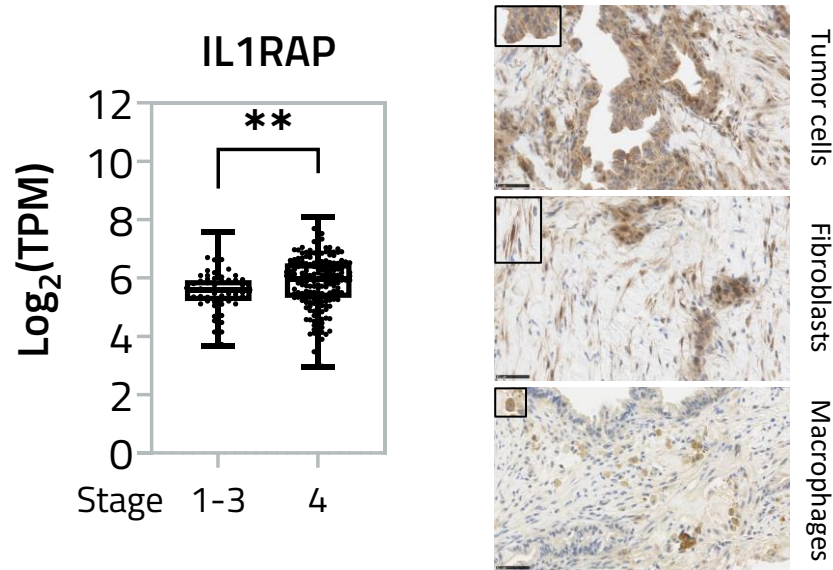
- 33% response rate with long OS and iPFS
  - Additional 5 (7%) patients had on-treatment benefit beyond progression
- Promising OS (13.2 mo), iPFS (7.2 mo) and DCR (71%); 2 patients still on treatment

**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, N Engl J Med 2013); OS 9.2 mo, PFS 5.6 mo, ORR 36%, DCR 62%, (NAPOLI-3, ASCO GI 2023)  
iCPD – Confirmed Progressive Disease; iUPD – Unconfirmed Progressive Disease; iSD – Stable Disease; iPR – Partial Response (all according to iRECIST)

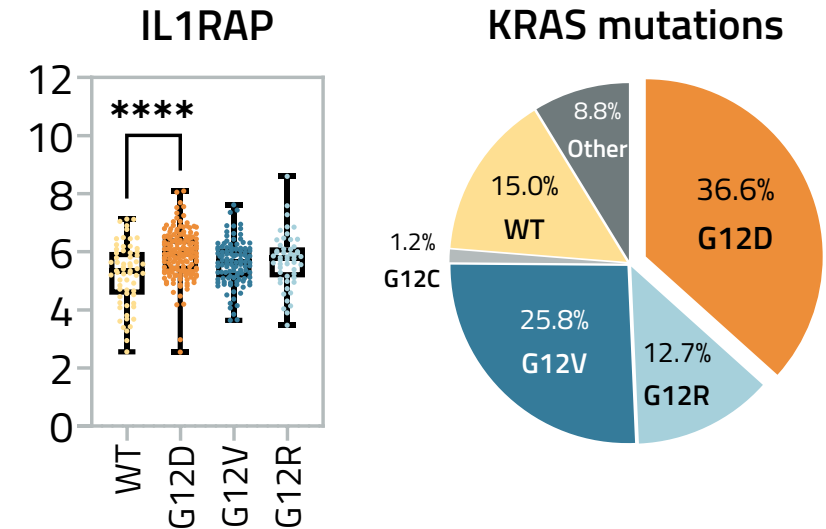
# PDAC – IL1RAP linked to poor prognosis

## 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 1<sup>st</sup> line Gem/Abraxane

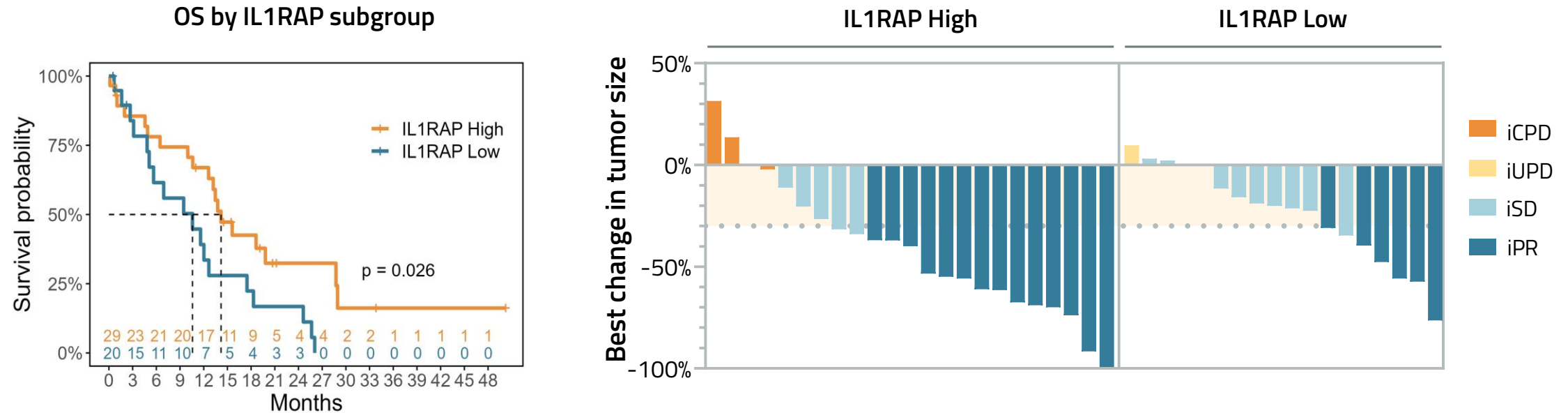
## KRAS MUTATIONS IN PDAC



- 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 – Strong efficacy in patients with high tumor IL1RAP level



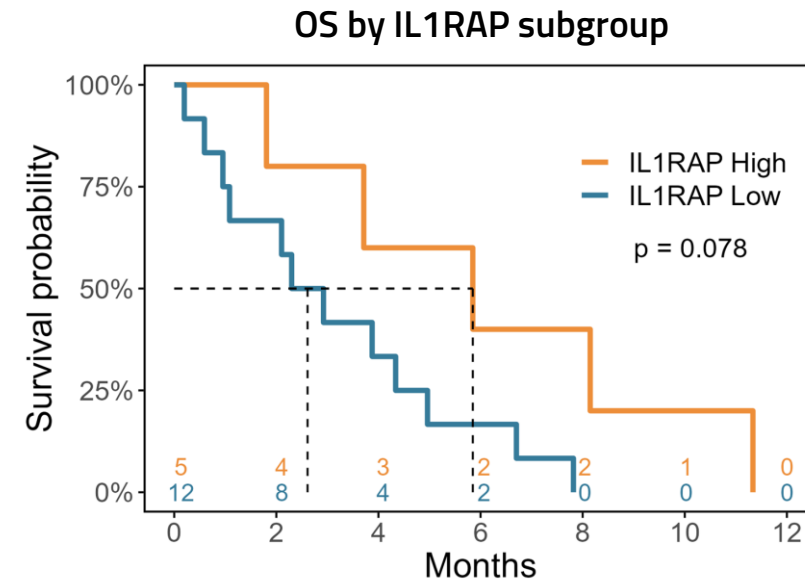
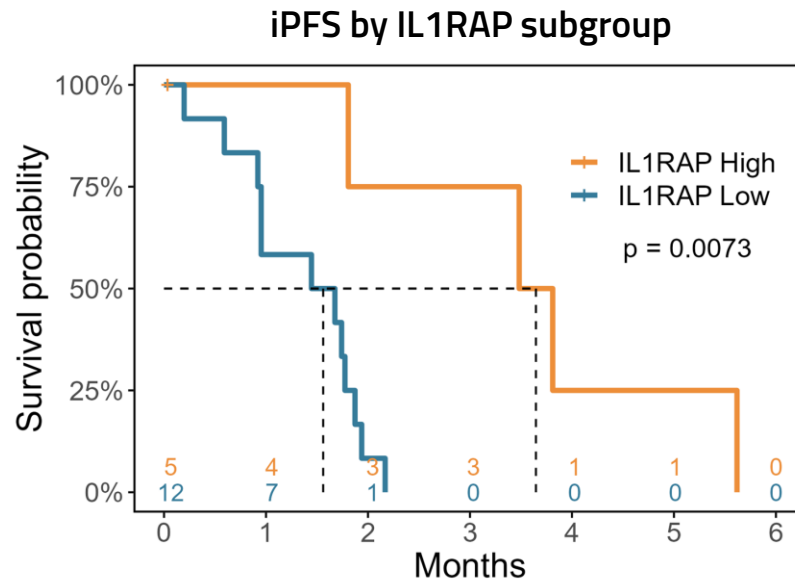
**Efficacy analysis for IL1RAP High (n=29) vs IL1RAP Low (n=20) PDAC patients (1<sup>st</sup> line, combination with Gem/Abraxane):**

- 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):**

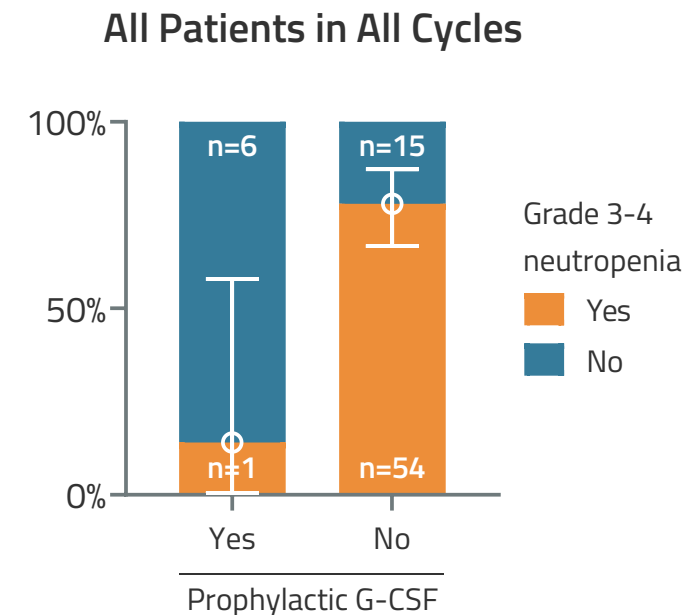
- Significantly prolonged iPFS in IL1RAP High vs IL1RAP Low patients (3.6 vs 1.6 mo;  $p=0.0073$ )
- Trend for OS advantage in IL1RAP High patients (5.8 vs 2.6 mo;  $p=0.078$ )

**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

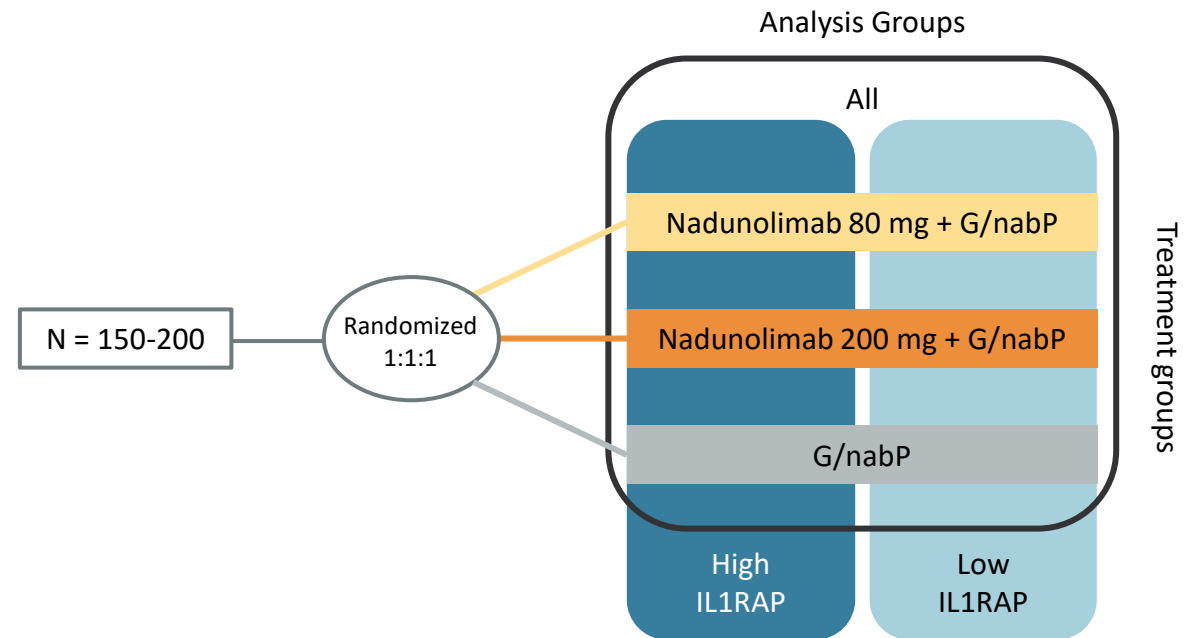
## Timelines:

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

## Geography:

- USA and Europe

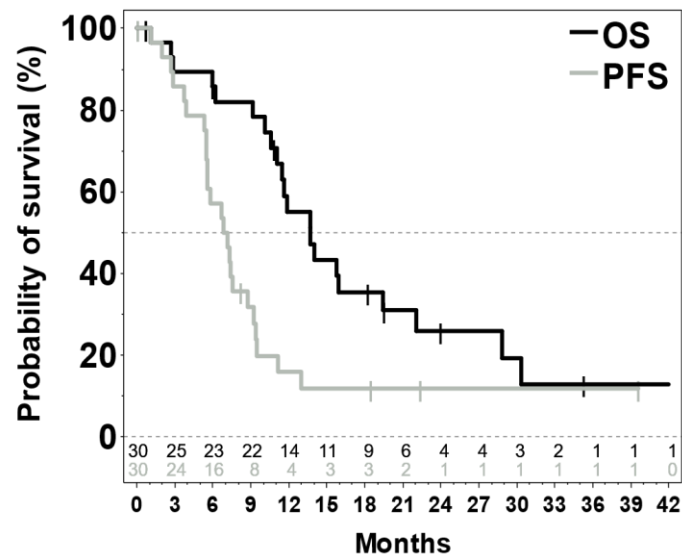
Open-label, randomized, controlled, non-comparative, 3-arm study evaluating 2 dose levels of nadunolimab + gemcitabine/ nab-paclitaxel with gemcitabine/nab-paclitaxel as control:



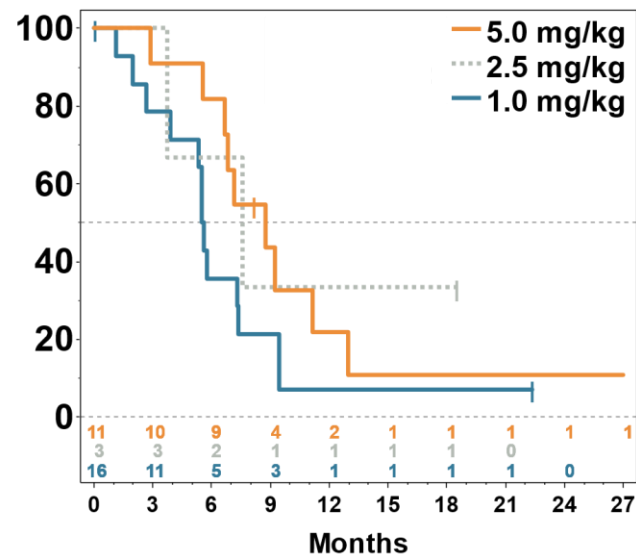
PHASE IIB TRIAL TO VALIDATE STRONG SIGNAL OF ACTIVITY IN IL1RAP HIGH PATIENTS

# NSCLC – Promising efficacy of nadunolimab combination therapy

OS and PFS for mITT patients



PFS by dose level

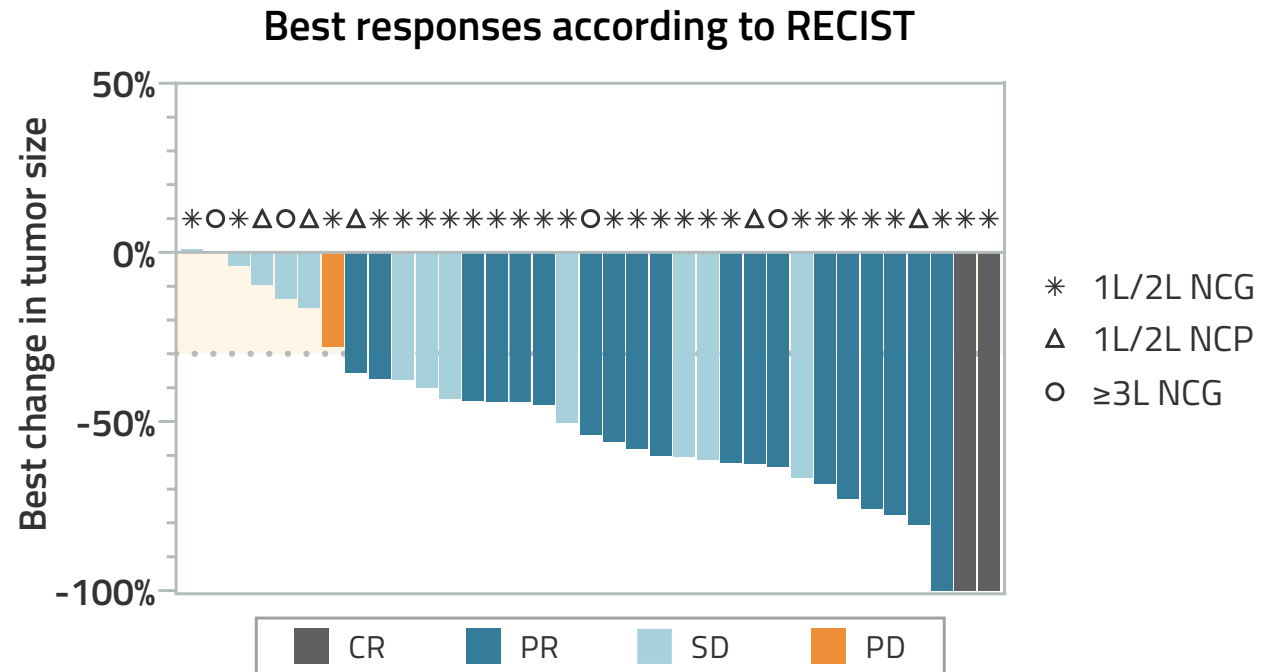


## Nadunolimab combination with Gem/Cis in 1<sup>st</sup>/2<sup>nd</sup> line NSCLC (n=30):

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

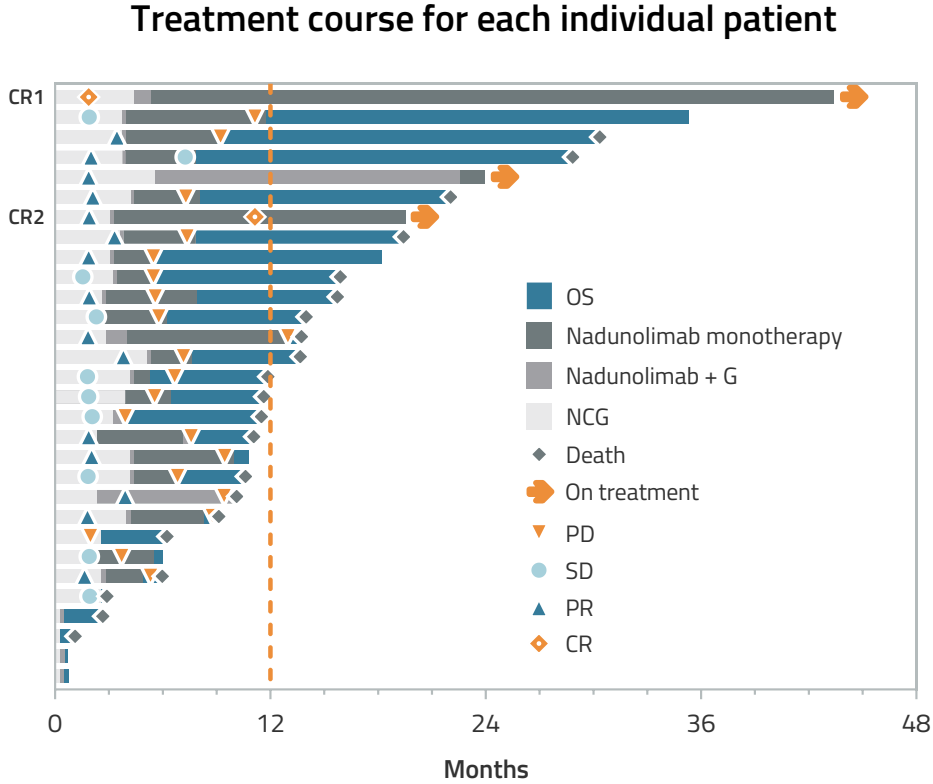
**CONSISTENTLY HIGH RESPONSE RATES WITH NADUNOLIMAB AND PLATINUM DOUBLETS**



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

	All (n=30)	Historical data <sup>1,2</sup>	Non-squamous (n=16)	Non-squamous, historical data <sup>3</sup>
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%

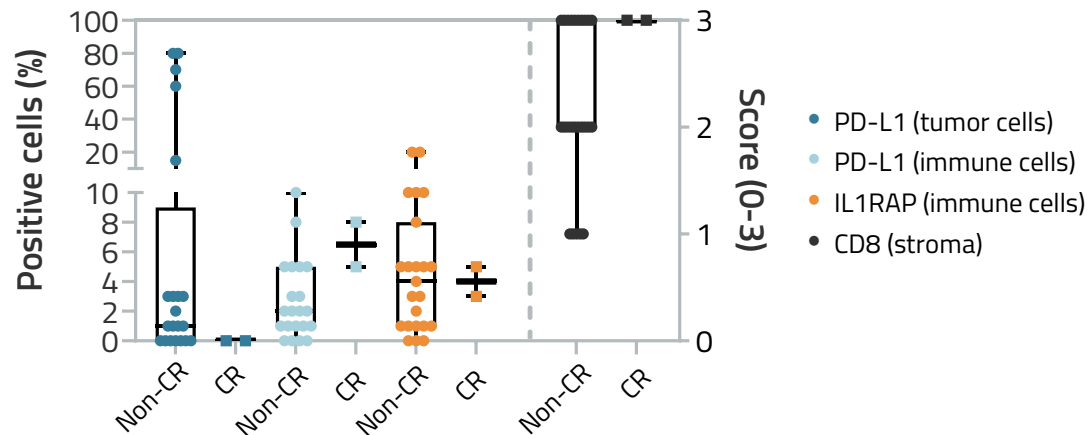
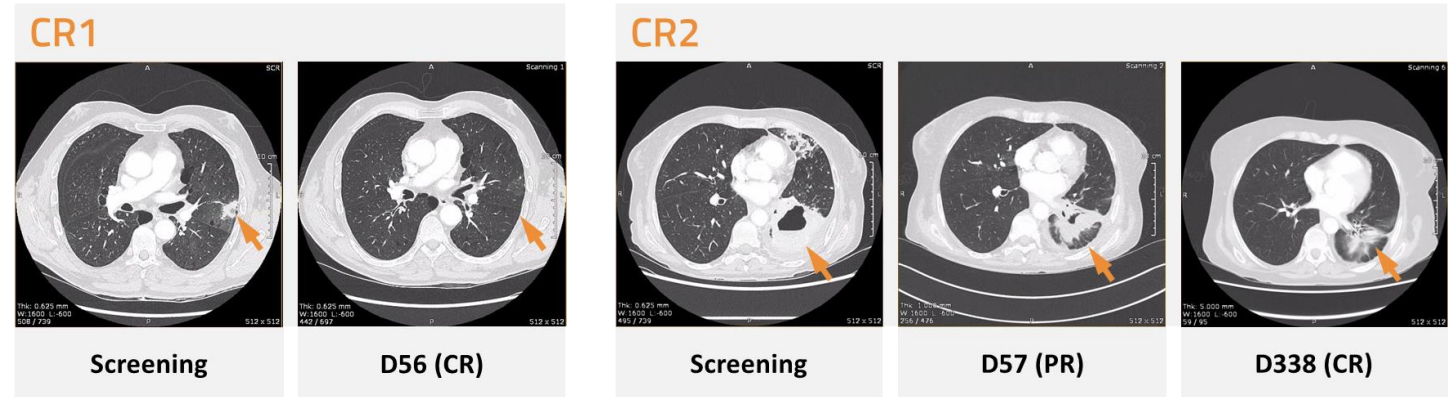
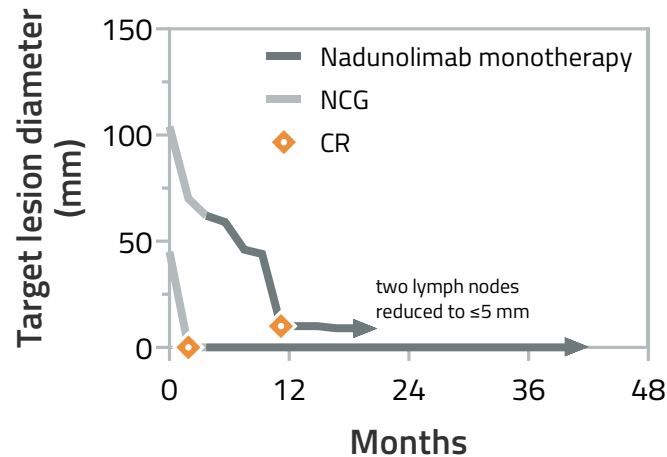
- Strongest efficacy in 16 non-squamous patients
- Long-term benefit of nadunolimab combination therapy, including two complete responses



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

<sup>1</sup> Schiller et al, N Engl J Med 2002; <sup>2</sup> Scagliotti et al, J Clin Oncol 2008; <sup>3</sup> Gandhi et al, N Engl J Med 2018  
 PD – Progressive Disease; SD – Stable Disease; PR – Partial Response; CR – Complete Response; NCG – Nadunolimab/Cisplatin/Gemcitabine

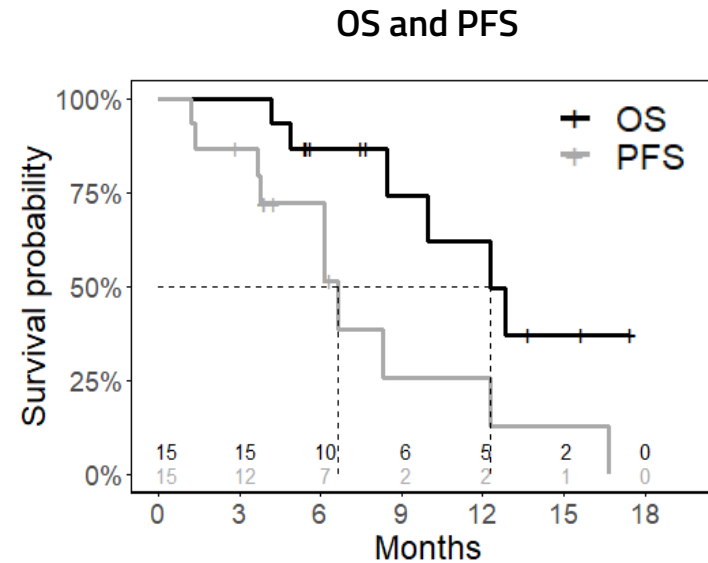
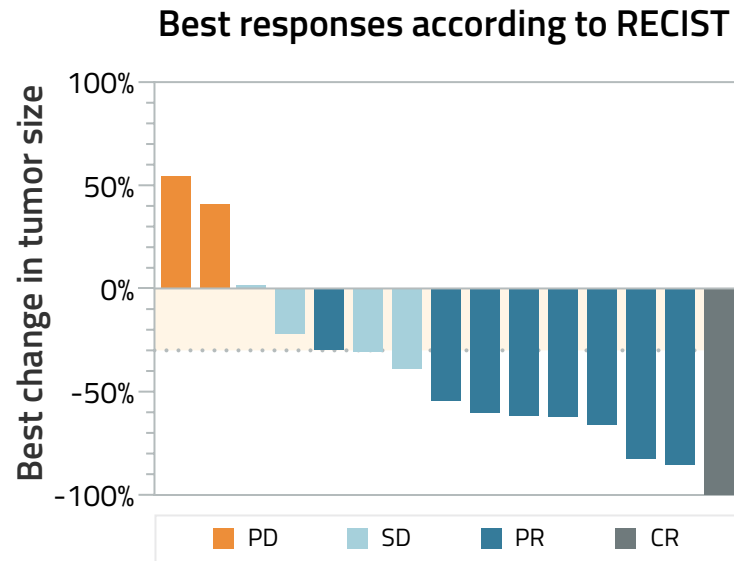
# NSCLC – Complete responders with distinct biomarker profile



- 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<sup>-</sup> tumor cells, PD-L1<sup>+</sup> 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 1<sup>st</sup>/2<sup>nd</sup> line metastatic TNBC:

### 15 patients enrolled in the dose-escalation phase:

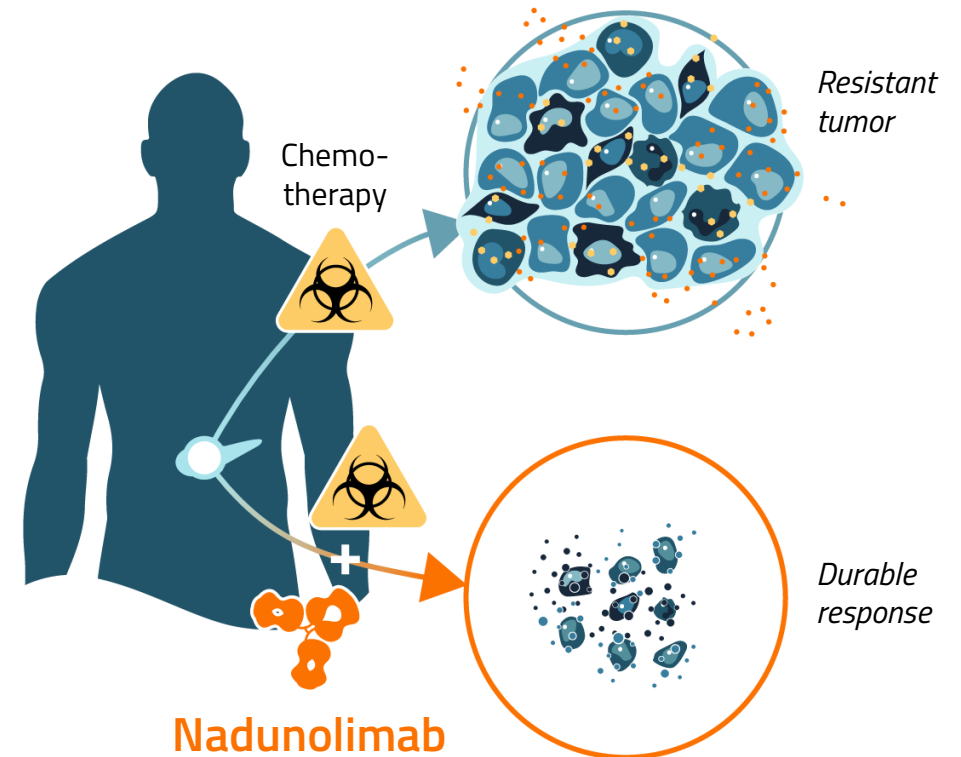
- Preliminary ORR: 60% (1 CR, 8 PR, 4 SD, 2 PD)
- Preliminary median OS 12.3 mo, median PFS 6.6 mo
- Acceptable safety profile (G-CSF given prophylactically to control neutropenia)
- Randomized phase II ongoing

Benchmark Gem/Carbo: OS 11.1 mo, PFS 4.1 mo, ORR 30% (O'Shaughnessy et al, J Clin Oncol 2014)

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

# Key messages

- Nadunolimab, investigated in almost 300 patients, shows efficacy both as monotherapy as well as in combination
- Clinical results strongly support potential unique first-in-class opportunities in PDAC, NSCLC and TNBC; controlled phase 2 trial ongoing in TNBC and in preparation for PDAC
- PDAC patients with high IL1RAP level respond best to nadunolimab combination therapy despite a worse prognosis
- The mechanism includes counteracting chemotherapy resistance through upregulation of both IL-1 $\alpha$  and IL-1 $\beta$ , signaling through IL1RAP; the mechanism is highly relevant for ADC combination strategies



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

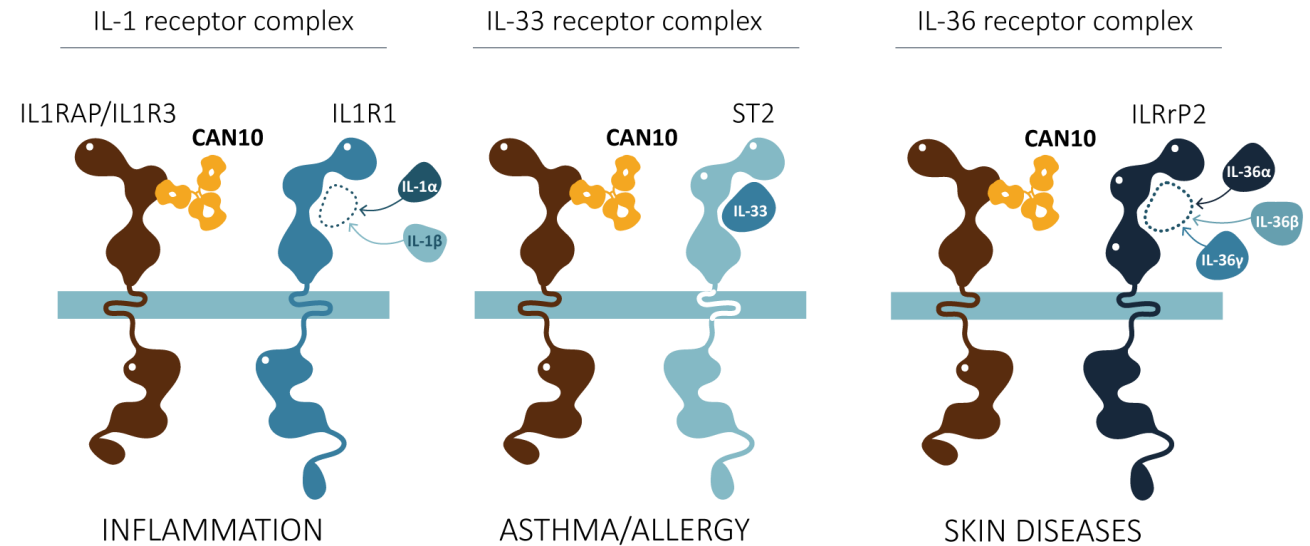
A microscopic image showing several cells with a complex, textured surface. The image is overlaid with a semi-transparent blue layer, which serves as a background for the text. The cells are primarily in the upper half of the frame, with one large cell on the left and another on the right. The blue overlay covers the entire image, creating a uniform background for the text.

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

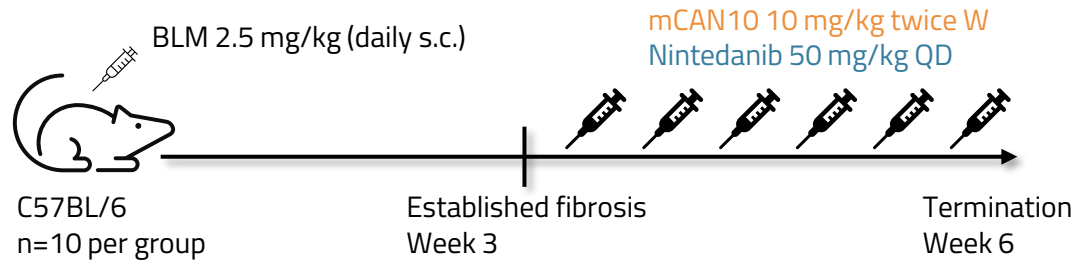


- Inflammation of the myocardium that can lead to fibrosis and loss of contractile function
- Can be both autoimmune and viral
- The estimated incidence of myocarditis is approximately 22 per 100,000 and the disease accounts for approximately 0.6 per 100,000 deaths annually worldwide

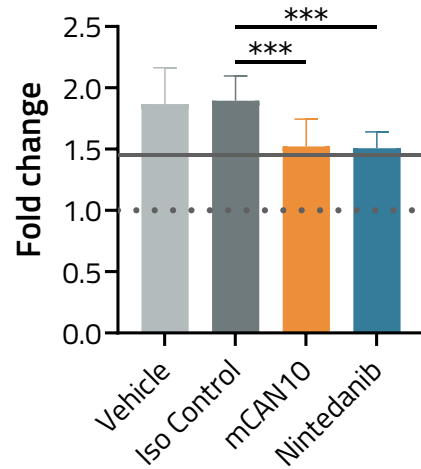
- Chronic, autoimmune connective tissue disorder characterized by inflammation and fibrosis of the skin and internal organs
- The leading cause of death – interstitial lung disease where the unmet need is particularly high
- The estimated annual incidence is about 4.5 per 100,000 in North America and 1.8 per 100,000 in Europe

# Systemic sclerosis – mCAN10 inhibits bleomycin-induced skin fibrosis

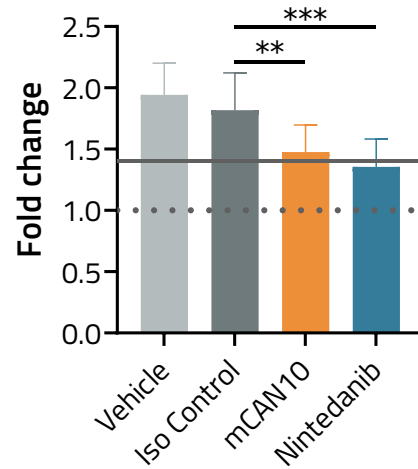
## Bleomycin (BLM) model



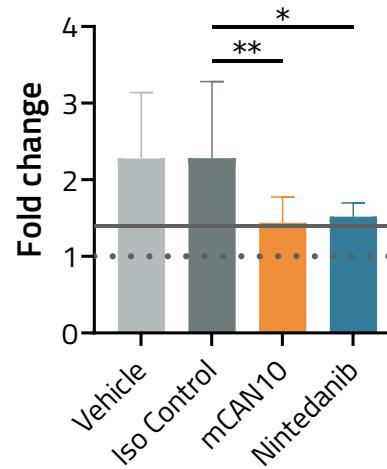
### Dermal thickness



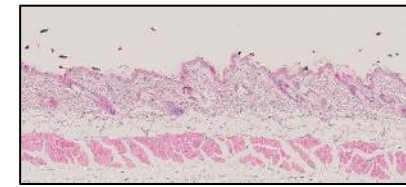
### Myofibroblast count



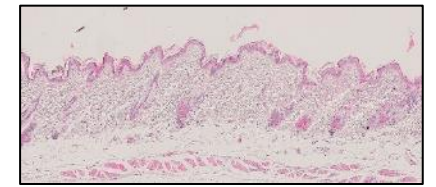
### Hydroxyproline



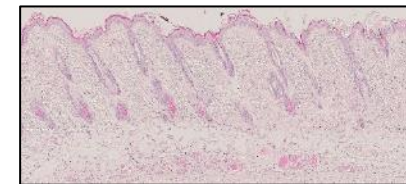
### No BLM (6 wks)



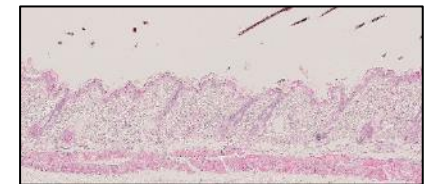
### Baseline BLM (3 wks)



### BLM (6 wks) Iso Control

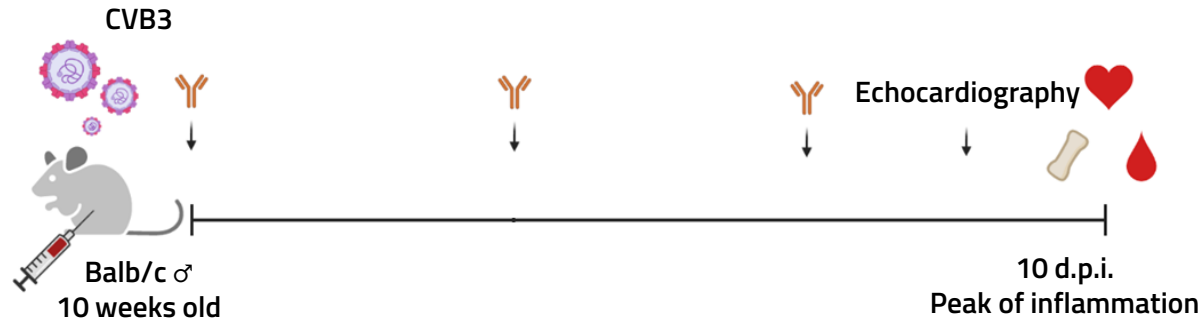


### BLM (6 wks) mCAN10

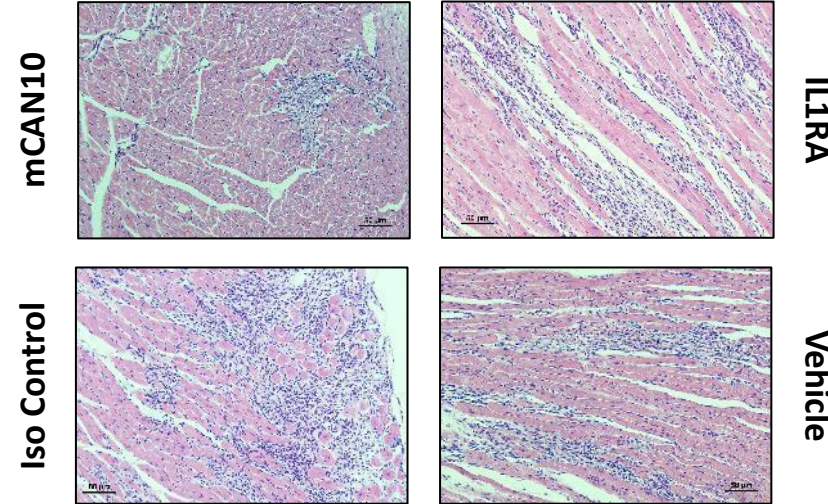
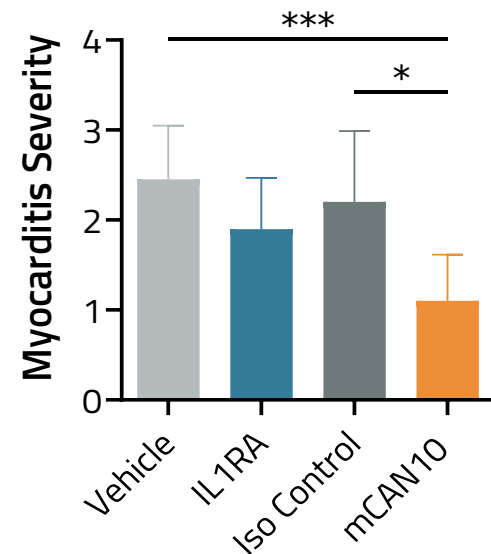


# Viral myocarditis – mCAN10 reduces disease severity

## CVB3 myocarditis experimental design

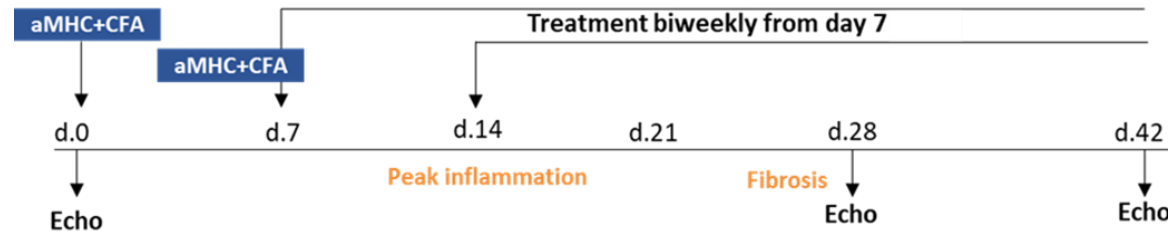


→ mCAN10 reduced disease severity, based on histological scoring of heart sections, and preserved heart function

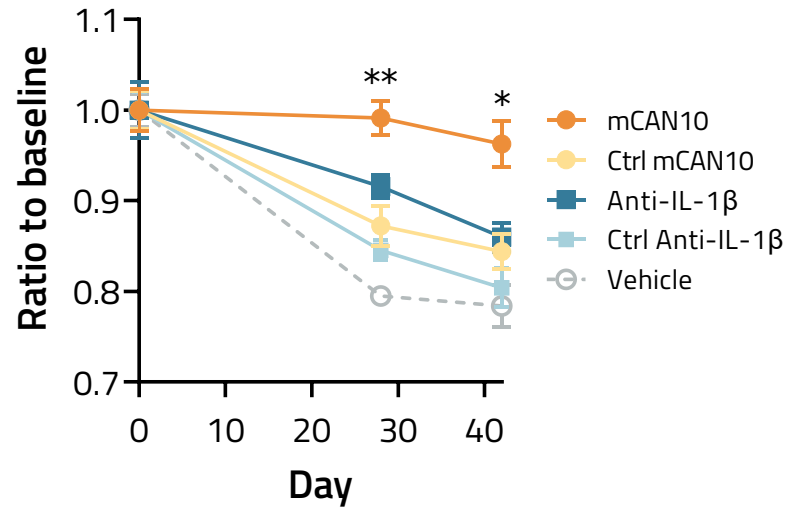


→ mCAN10 also reduced inflammatory leukocyte populations in the heart tissue

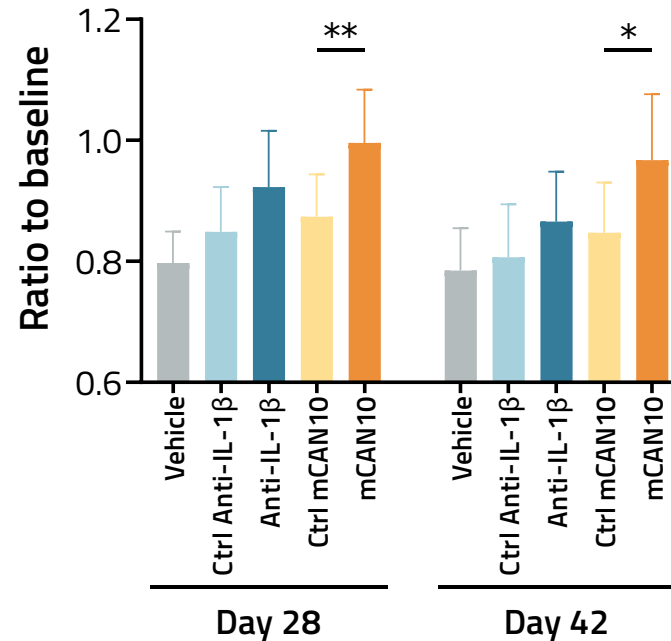
# Experimental autoimmune myocarditis – mCAN10 improves heart function



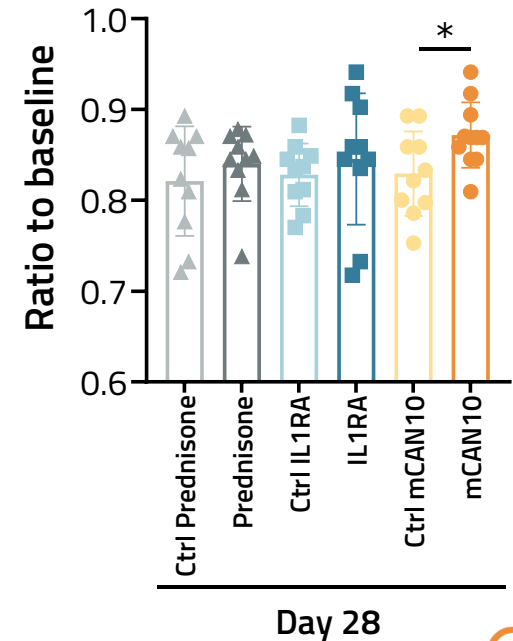
Left Ventricular Ejection Fraction (LVEF)



LVEF (treatment from day 7)

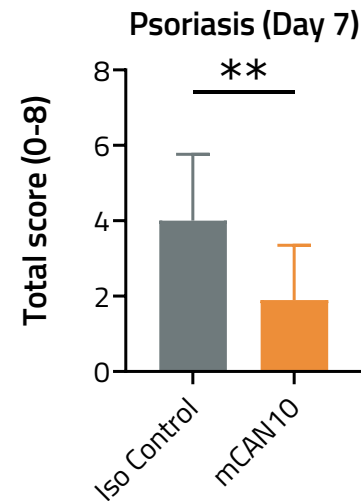
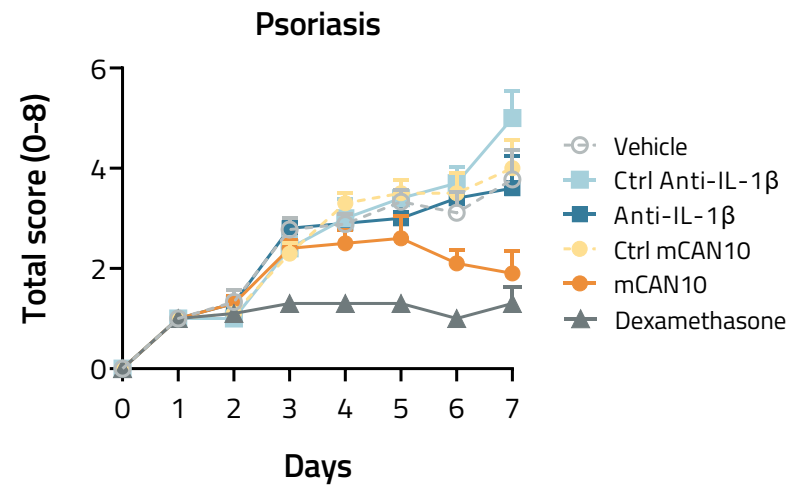


LVEF (treatment from day 7)

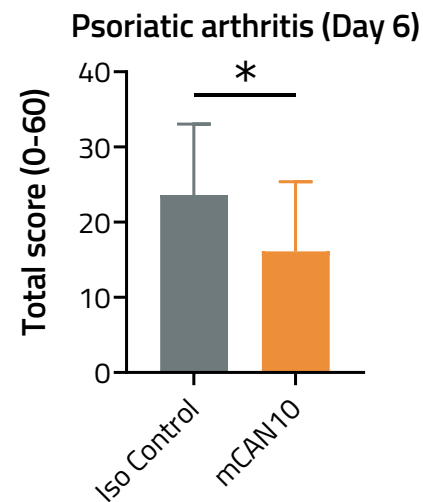
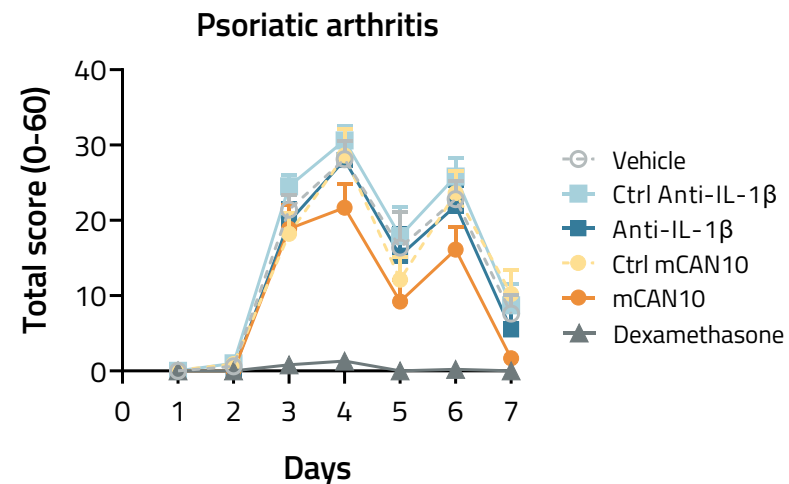


$\alpha$ MHC –  $\alpha$ -Myosin Heavy Chain; CFA – Complete Freund's Adjuvant  
n=10 per group

# Psoriasis and psoriatic arthritis – mCAN10 reduces disease severity



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



→ mCAN10, but not anti-IL-1 $\beta$ , 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)



A microscopic image showing several cells with a textured, mesh-like surface. The cells are set against a blue background. A semi-transparent dark blue horizontal band is positioned across the middle of the image, containing white text.

## MILESTONES & INVESTMENT HIGHLIGHTS

# Upcoming milestones

## Nadunolimab

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

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 into 2025 (200M SEK cash & equivalents at Q3 2023 + 59 MSEK from share issue Oct 23)
- 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.

