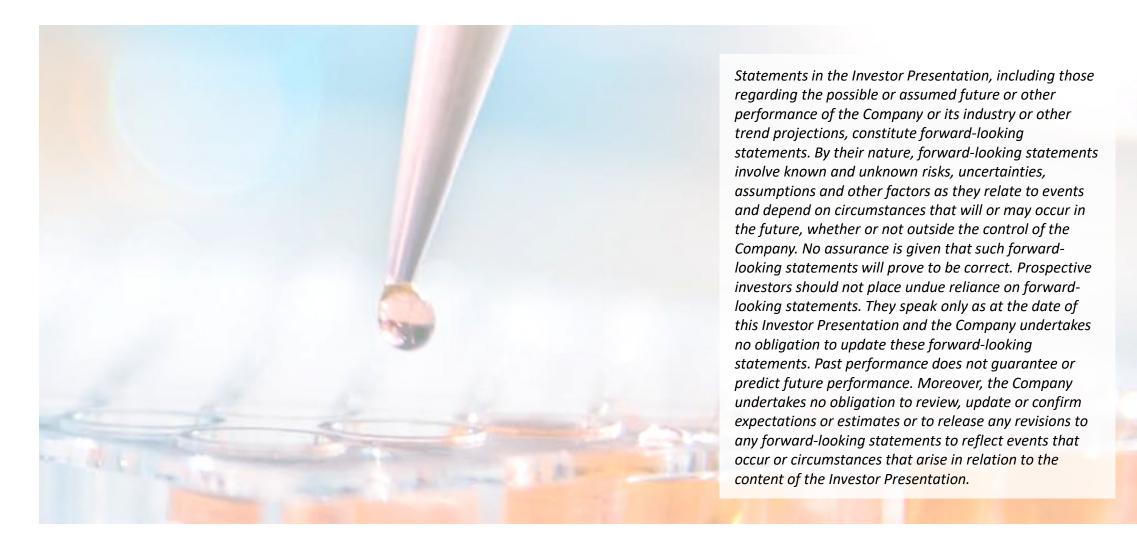


### Safe Harbor Statement





## 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 (initial 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 show good safety and receptor occupancy. New data Q2 2024

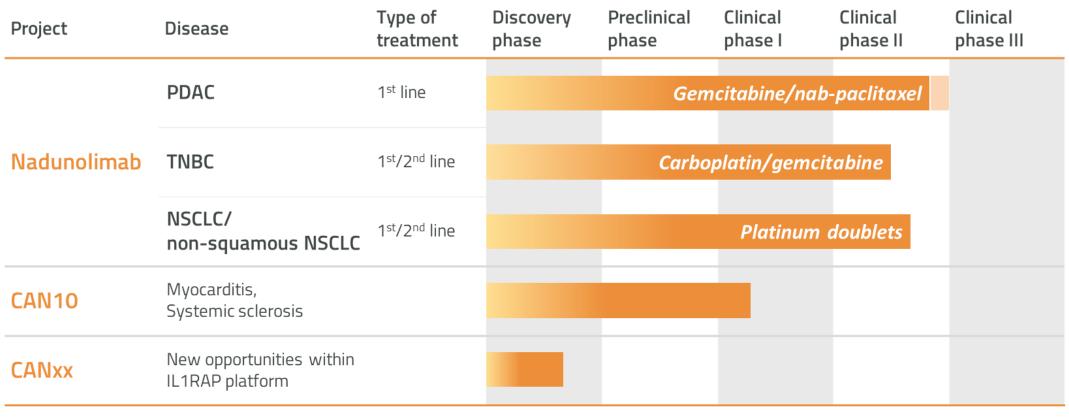


### CORPORATE STRENGTH DRIVING INNOVATION

- Solid cash position with runway into 2025 (195MSEK (19 MUSD) cash & equivalents at Q4 2023)
- Robust patent portfolio: IL1RAP antibody target in oncology (2032), nadunolimab (2035) and CAN10 (2041)



## Current pipeline

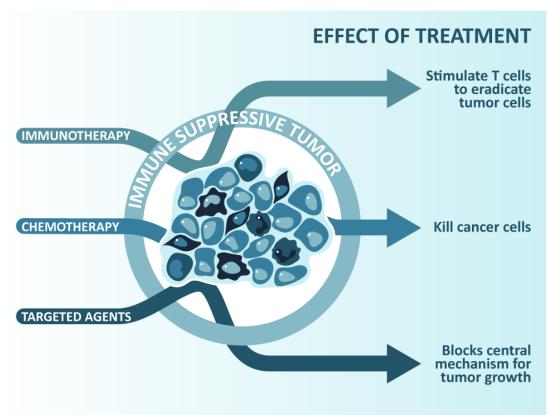


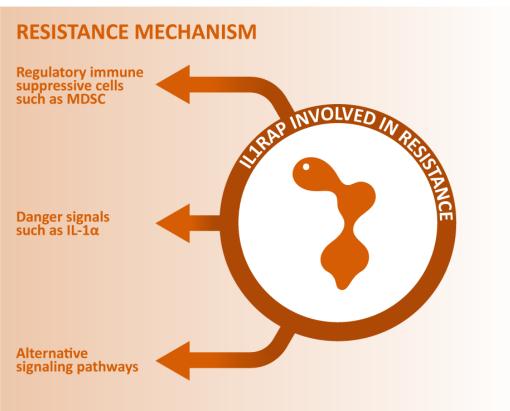
PDAC – pancreatic cancer; TNBC – triple-negative breast cancer; NSCLC – non-small cell lung cancer





## Cantargia – Strategy to improve current cancer therapies



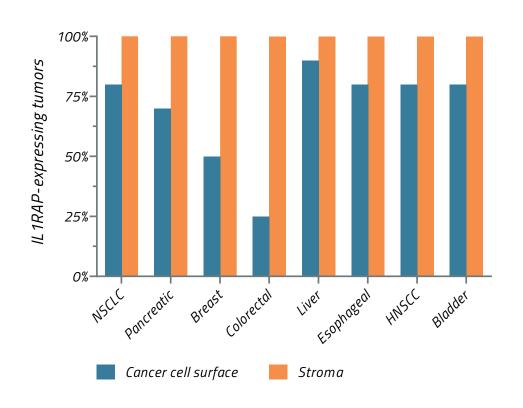


IL1RAP – A NOVEL TARGET WITH SEVERAL OPPORTUNITIES; CURRENT FOCUS ON SYNERGISTIC COMBINATIONS

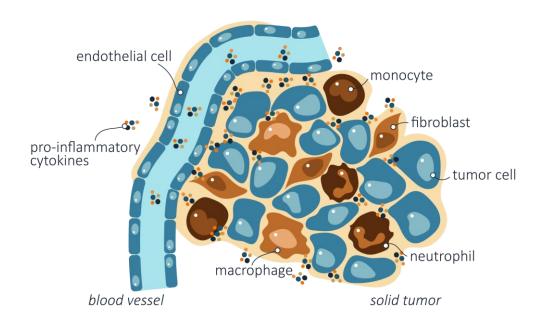


## IL1RAP overexpressed in most solid tumors

#### **IL1RAP EXPRESSION IN SOLID TUMOR TYPES**



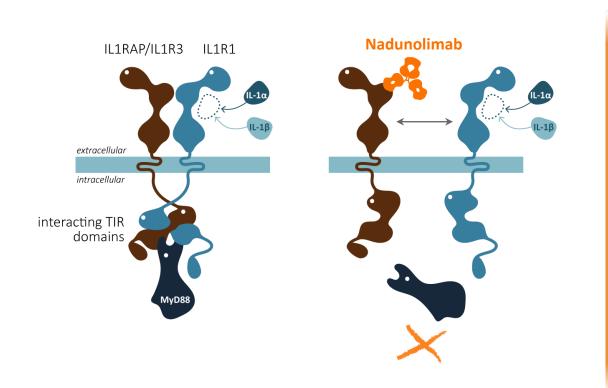
### SEVERAL TUMOR-PROMOTING CELLS EXPRESSING IL1RAP IN THE TUMOR MICROENVIRONMENT

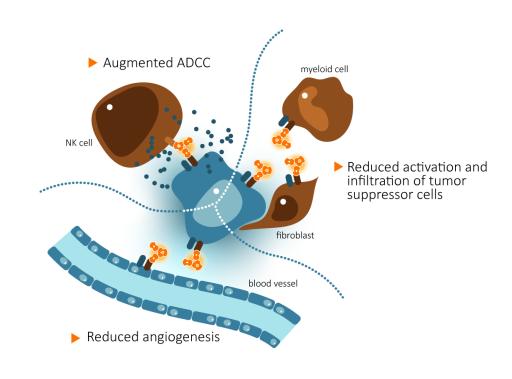


IL1RAP – DISTINCTLY OVEREXPRESSED IN TUMORS; LOW EXPRESSION IN NORMAL TISSUE



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

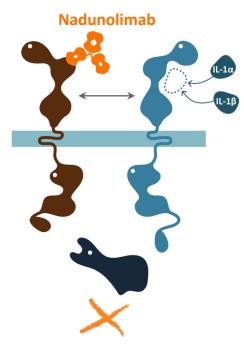




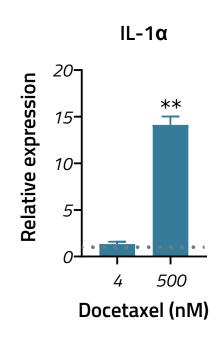
NADUNOLIMAB COUNTERACTS IMMUNE SUPPRESSION AND POTENTIATES THERAPY



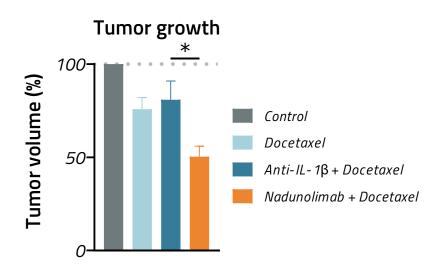
## Nadunolimab potentiates antitumor activity of chemotherapy







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

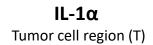


 Nadunolimab + docetaxel reduces in vivo tumor growth more potently than anti-IL-1β + docetaxel

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

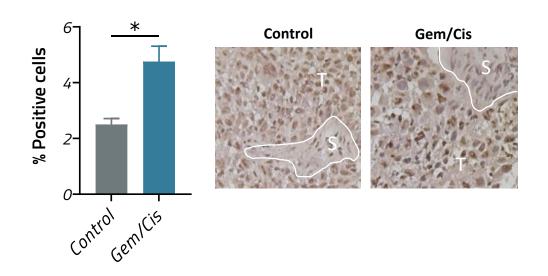


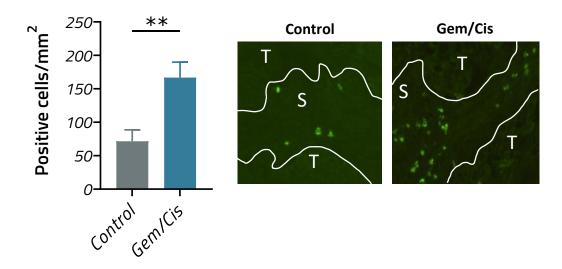
## Chemotherapy induces IL-1 $\alpha$ and IL-1 $\beta$ in the tumor



### IL-1β-converting enzyme

Stromal cell region (S)





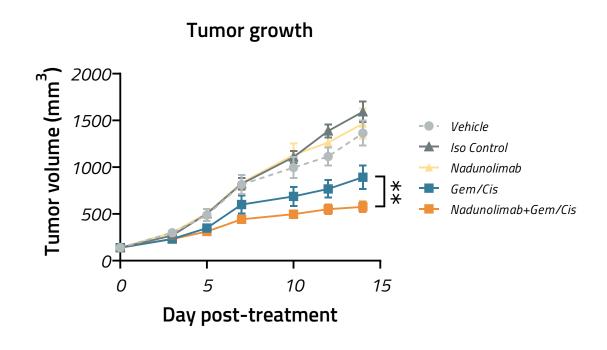
 $\rightarrow$  Gem/Cis induces release of IL-1 $\alpha$  by tumor cells in tumors grown in vivo

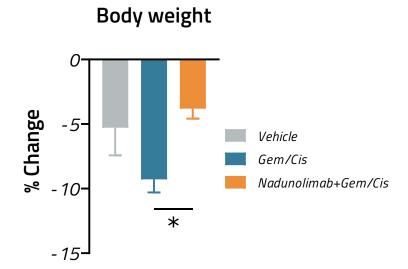
 Gem/Cis also induces release of IL-1β-converting enzyme (ICE) by stromal cells

INCREASED LEVELS OF IL-1 $\alpha$  AND IL-1 $\beta$  RESULTS IN CHEMORESISTANCE



## Targeting IL1RAP uniquely synergizes with chemotherapy



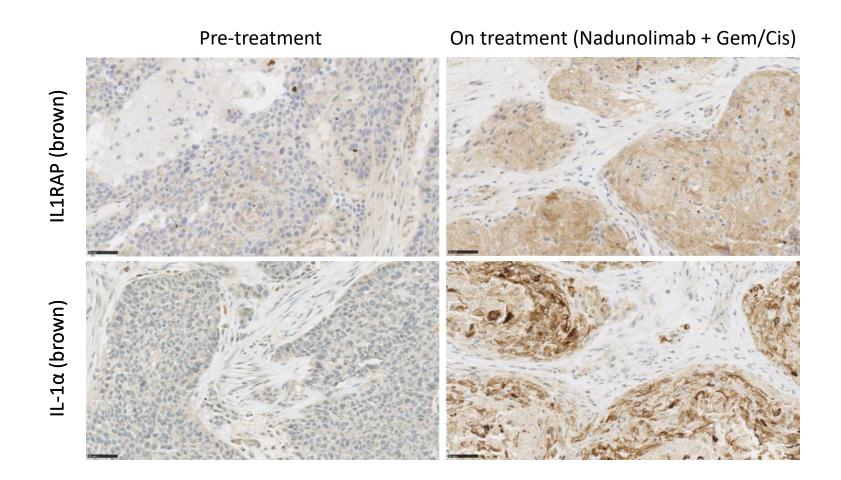


 Nadunolimab increases efficacy of platinum-based chemotherapy in vivo  Nadunolimab also counteracts weight loss after chemotherapy

NADUNOLIMAB HAS POTENTIAL TO IMPROVE CHEMOTHERAPY EFFICACY AND TOLERABILITY



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



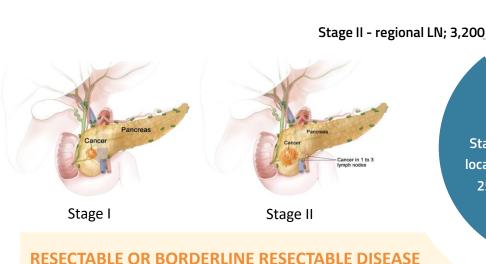
IL-1 $\alpha$  INDUCED BY CHEMOTHERAPY IN LINE WITH PRECLINICAL FINDINGS; WELL ESTABLISHED DANGER SIGNAL – ACTIVITY BLOCKED BY NADUNOLIMAB



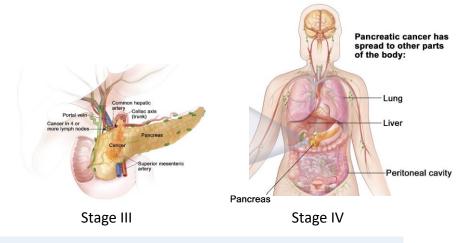
## PDAC – Staging and treatment

### Expected number of cases US 2023: 64,000

Stage I - local: 3,200



Stage IV Stage IV metastatic:
32,000



#### LOCALLY ADVANCED OR METASTATIC DISEASE

#### Survival:

 $\rightarrow$  15.7 – 28.0 mo

#### Treatment:

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

### Survival:

 $\rightarrow$  8.5 – 11.1 mo

#### Treatment:

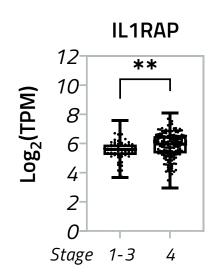
- → FOLFIRINOX if good performance status
- → Gemcitabine/nab-paclitaxel
- → Gemcitabine if poorer performance
- Jan 2023: 1<sup>st</sup> line NALIRIFOX (OS 11.1 mo)

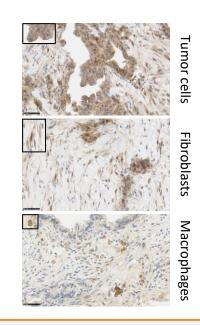
CURRENT DEVELOPMENT FOCUSES ON FIRST-LINE METASTATIC DISEASE WITH POTENTIAL TO MOVE TO EARLIER TREATMENT SETTINGS



### PDAC – IL1RAP linked to poor prognosis

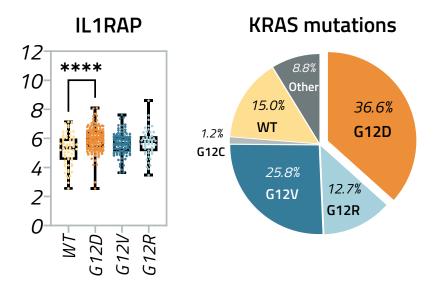
#### **IL1RAP IN PDAC**





- → 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**



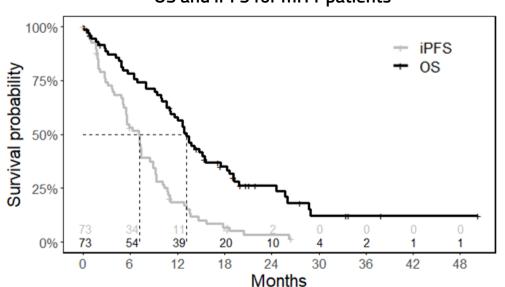
- Over 80 % of PDAC patients have a KRAS mutation; G12D is the most common
- → KRAS G12D has a worse prognosis with HR 1.47 (Bournet et al, 2016)
- → IL1RAP is overexpressed in patients with KRAS G12D

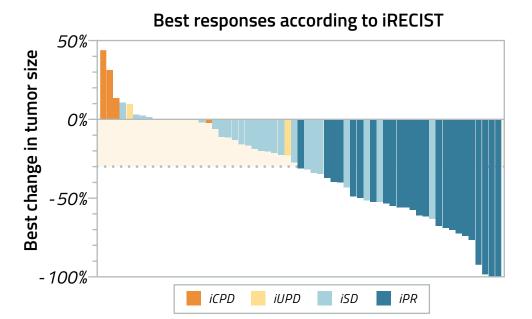
CLEAR LINK BETWEEN IL1RAP, KRAS G12D AND PDAC PROGNOSIS



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





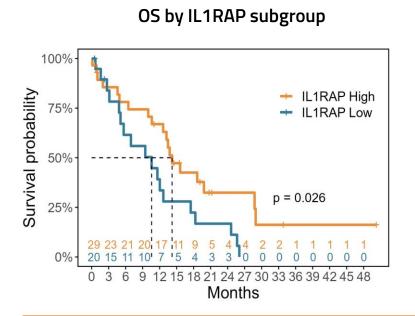


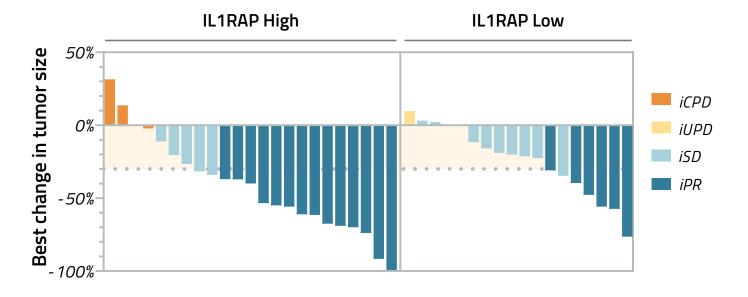
### Nadunolimab combination with Gem/Abraxane in 1st line PDAC (n=73):

- → 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

### PDAC – Strong efficacy in patients with high tumor IL1RAP level





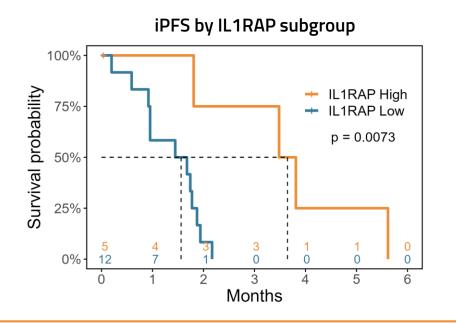
## Efficacy analysis for IL1RAP High (n=29) vs IL1RAP Low (n=20) PDAC patients (1<sup>st</sup> line, combination with Gem/Abraxane):

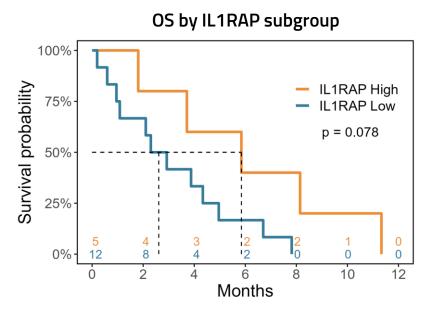
- → Significantly prolonged OS in ILRAP High vs IL1RAP Low patients (14.2 vs 10.6 mo; p=0.026)
- → Deeper and more durable responses in IL1RAP High subgroup: 11 patients had 50% or more tumor size decrease

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

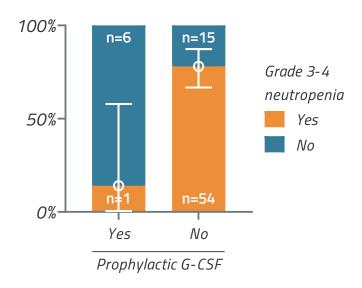


## PDAC – Safety profile is manageable and supports MOA

- → 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%	

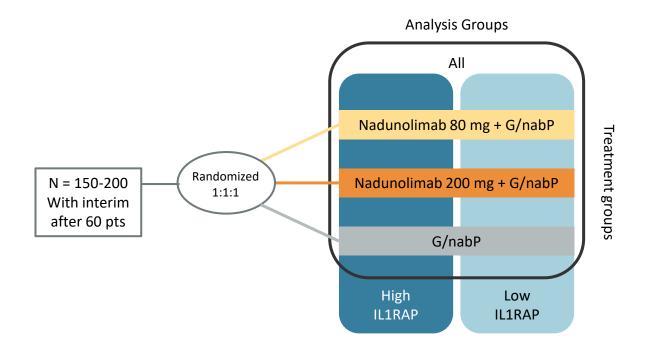
### All Patients in All Cycles



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



### PDAC – Phase IIb study design



### **Primary endpoint:**

→ PFS

### **Pre-planned interim review:**

→ After 60 pts to allow strategic next steps incl. regulatory

### **Timelines:**

→ FPI planned for mid 2024 (US regulatory approval obtained)

### **Geography:**

→ USA and Europe



## Nadunolimab PDAC milestone targets

mid-2024	H1 2025	H2 2025	H1 2026	H1 2027	H1 2028	H2 2028
Start PANFOUR study	PANFOUR enrolment completed	PANFOUR study results				
	FDA meeting	FDA EOP2 meeting				
	Phase III study	preparation	Start Phase III study	Phase III enrolment completed	Phase III study results	
					Potential	Potential US

### Confirm CANFOUR high IL1RAP results and accelerated path to market

- Interim efficacy & subgroup analysis
- Discuss and agree dose and data driven patient selection strategy for Phase III / BLA
  - IL1RAP or KRAS or serum BM patient selection

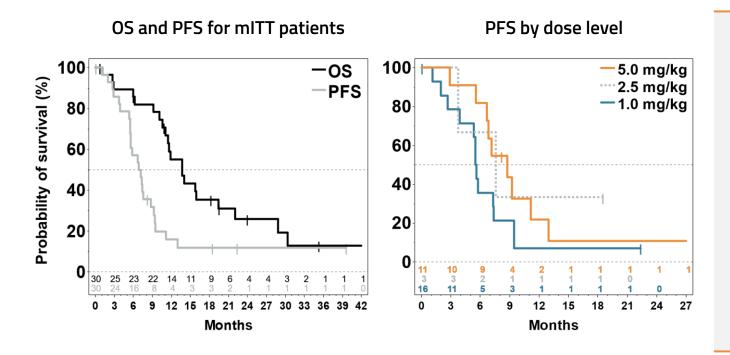
Potential I BLA / MAA m submission

Potential US market launch

PANFOUR study design address FDA Project Optimus and Frontrunner guidelines and de-risks development with interim snapshot to evaluate efficacy, safety and biomarker subgroup analysis



## NSCLC – Promising efficacy of nadunolimab combination therapy



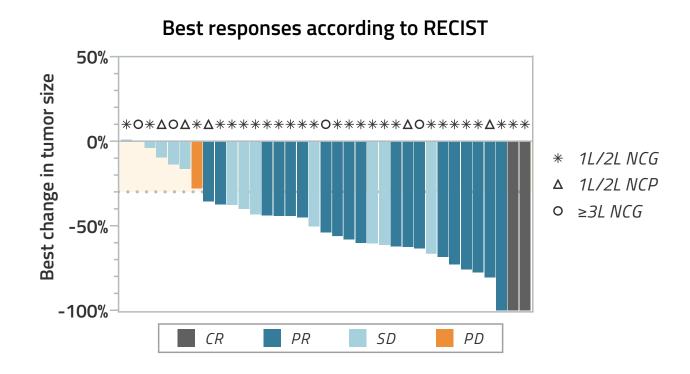
## Nadunolimab combination with Gem/Cis in 1<sup>st</sup>/2<sup>nd</sup> line NSCLC (n=30):

- → 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:

- $\rightarrow$  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)
- $\rightarrow$  Gem/Cis  $\geq$ 3<sup>rd</sup> line: ORR 50% (n=4)

CONSISTENTLY HIGH RESPONSE RATES WITH NADUNOLIMAB AND PLATINUM DOUBLETS

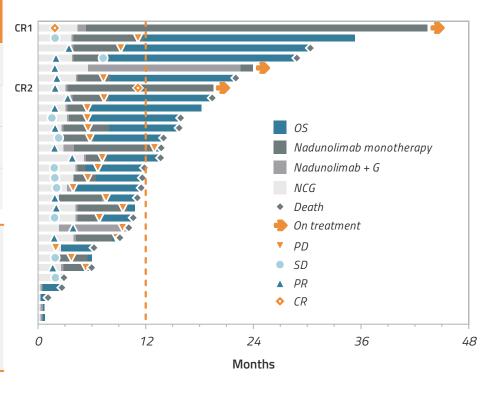


## NSCLC – Long-term benefit with strong signal in non-squamous subtype

	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

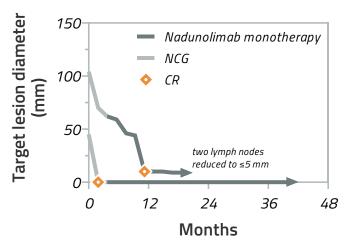
### Treatment course for each individual patient

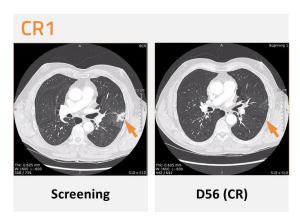


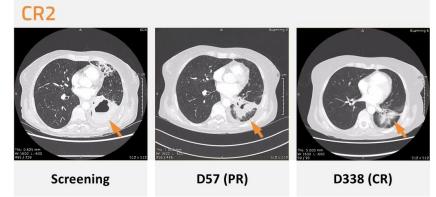
#### NADUNOLIMAB COMBINATION THERAPY COMPARES VERY FAVORABLY TO HISTORICAL DATA FOR CHEMOTHERAPY ALONE

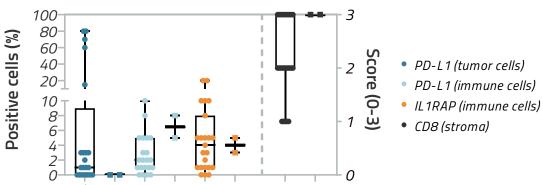


### NSCLC – Complete responders with distinct biomarker profile







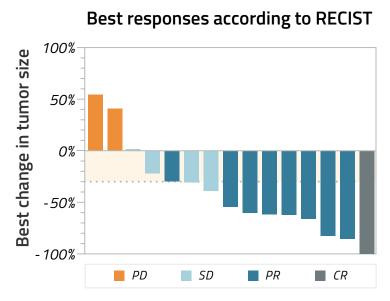


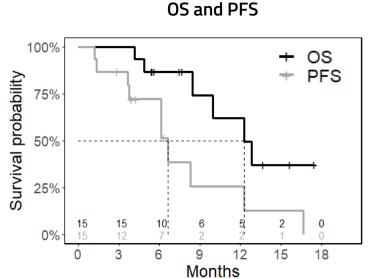
- → One CR maintained over 3 yrs (CR1), second CR achieved on nadunolimab monotherapy approx. 9 mo post-chemo (CR2)
- → Both non-squamous, progressed on pembro, with PD-L1<sup>-</sup> tumor cells, PD-L1<sup>+</sup> immune cells in tumor

SIGNAL OF NADUNOLIMAB MONOTHERAPY ACTIVITY RESULTING IN COMPLETE RESPONSE FURTHER BIOMARKER ANALYSES ONGOING FOR FUTURE DEVELOPMENT STRATEGY



## TNBC – Promising early safety and efficacy





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

## Nadunolimab combination with Gem/Carbo in 1<sup>st</sup>/2<sup>nd</sup> line metastatic TNBC:

### 15 patients enrolled in the doseescalation 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

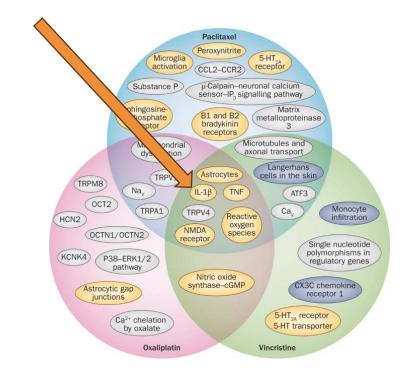
RESPONSE RATE OF NADUNOLIMAB COMBINATION THERAPY WELL ABOVE HISTORICAL DATA FOR CHEMOTHERAPY ONLY



## Nadunolimab and alleviation of neuropathy

- Themotherapy induce neuropathy by several pathways including IL-1 (neuroinflammation)
- → Nadunolimab, phase 2 data in PDAC with Gem/nabP
  - → lower Grade 3-4 peripheral neuropathy than expected from historical controls (1% vs 17%).
- Further analysis from this trial on grade 1-2 neuropathy strengthens finding
- Counteraction of chemotherapy-induced neuropathy in animal models
- → ADC payloads induce IL-1 system contributing to tumor progression

Detailed data to be presented at upcoming scientific conferences

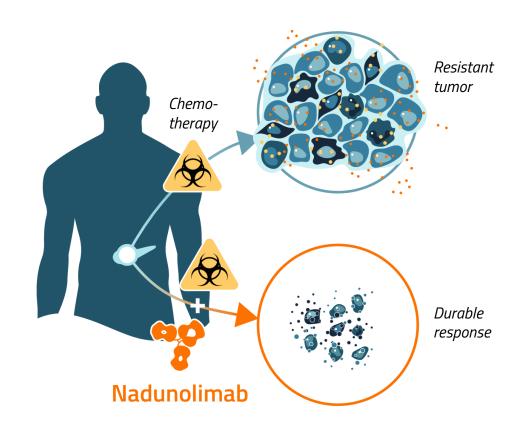


IN ADDITION TO PROMISING EFFICACY NADUNOLIMAB COULD CONTRIBUTE TO SAFER COMBINATION THERAPIES



### Key messages

- → Nadunolimab, investigated in almost 300 pts, 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 having a worse prognosis.
- $\rightarrow$  The mechanism include counteracting chemotherapy resistance through upregulatation of both IL-1 $\alpha$  and IL-1 $\beta$ , signaling through IL1RAP. The mechanism is highly relevant for ADC combination strategies



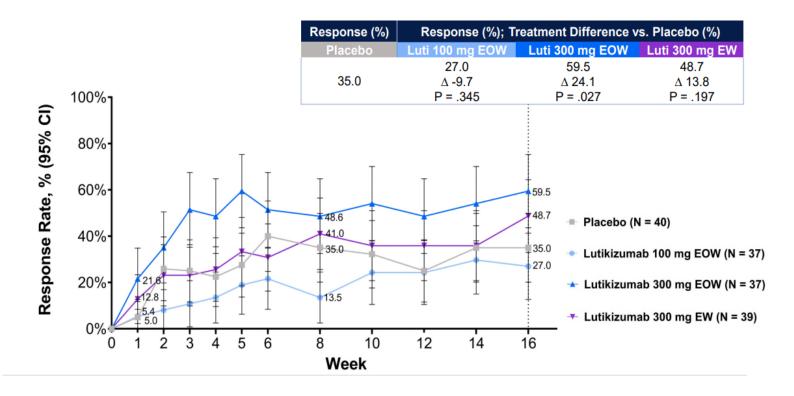
PROMISING EFFICACY OF NADUNOLIMAB-CURRENT FOCUS ON RANDOMIZED CLINICAL TRIALS AGAINST CHEMOTHERAPY





## External validation of IL-1 pathway - lutikizumab in HS

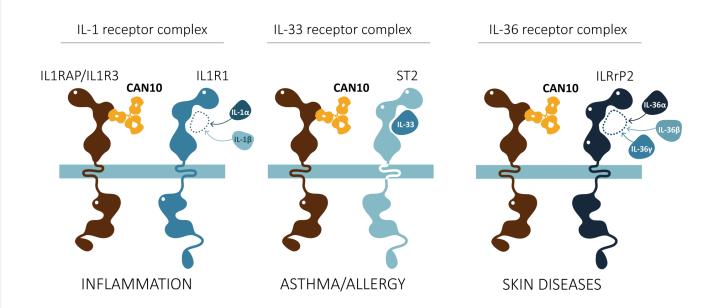
- Lutikizumab is a dual variable domain antibody against IL-1α and IL-β
- Patients treated with lutikizumab experienced higher response rates in the primary endpoint of HiSCR 50 and the secondary endpoint of skin pain NRS30 at week 16 than those treated with placebo
- Patients treated with lutikizumab experienced higher response rates in HiSCR 75 and greater improvement in draining fistula count at week 16 than those treated with placebo
- Lutikizumab entering phase III





## CAN10 – Added value vs IL-1 blockade only

- → 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

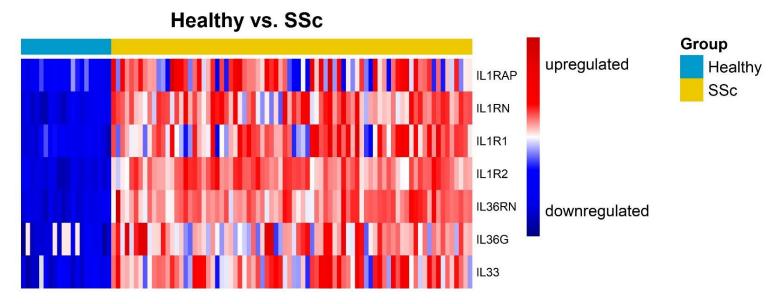


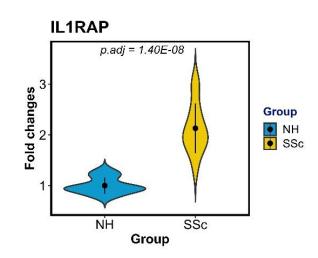
UNIQUE OPPORTUNITY FOR CAN10 IDENTIFIED IN LIFE-THREATENING DISEASES



# IL1RAP and the IL-1/33/36 pathways are upregulated in SSc patient skin

2 publicly available human SSc cohorts show differential expression of IL1RAP and associated genes in SSc skin





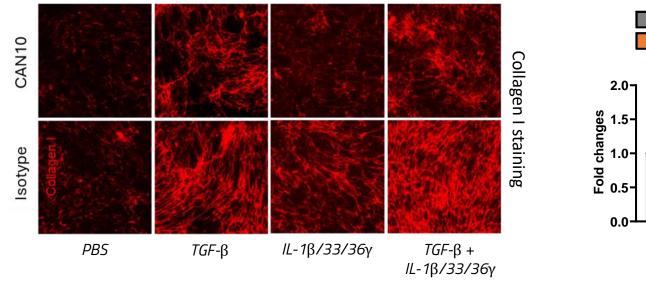
14 SSc vs. 11 healthy

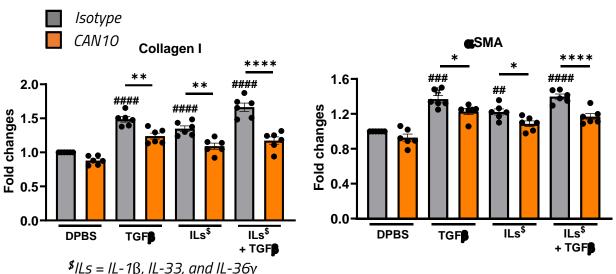
Agilent 2-channel Microarray

Mahoney et al. 2015 GSE59787 Skaug et al. Ann Rheum Dis 2020. GSE130955



# IL-1, IL-33 and IL-36 directly promotes fibrosis in SSc fibroblasts which can be counteracted by CAN10



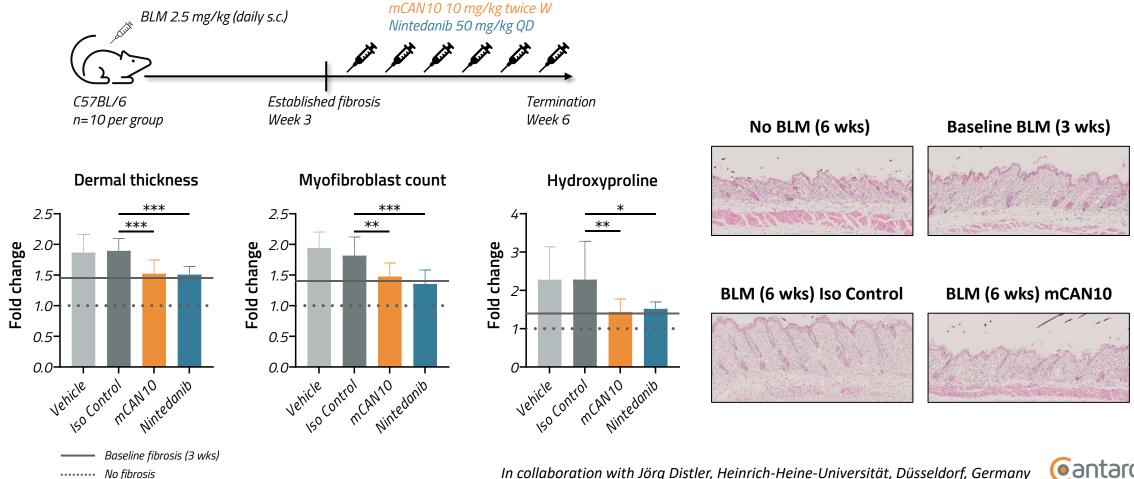


Fibroblasts isolated from SSc patients stimulated with TGF $\beta$  or a combination of IL-1 $\beta$ , IL-33, and IL-36 $\gamma$  (abbreviated as ILs) with or without TGF $\beta$  in vitro. ILs induced deposition of type I collagen and upregulated the protein levels of  $\alpha$ SMA, which could be blocked by CAN10.

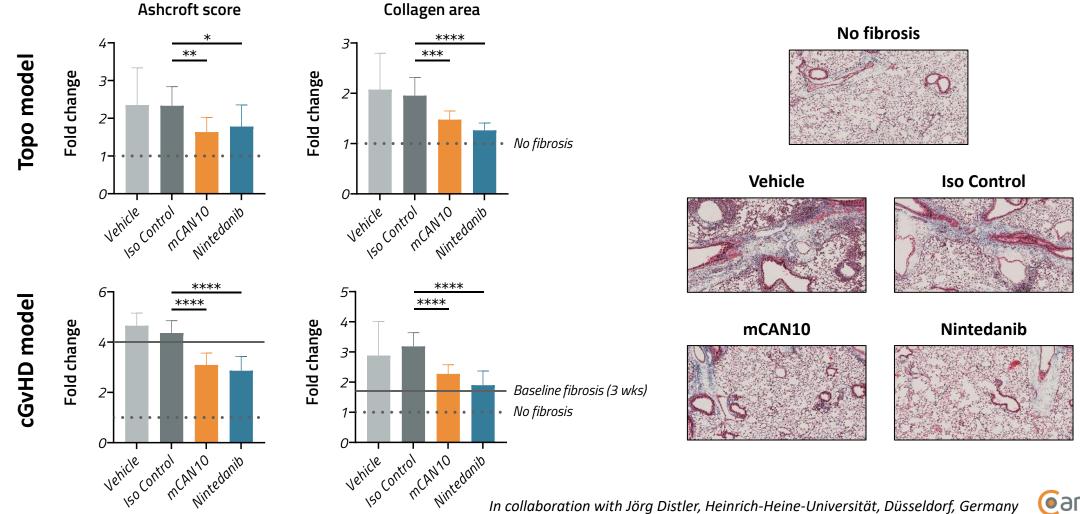


## Systemic sclerosis: mCAN10 inhibits bleomycininduced skin fibrosis

### Bleomycin (BLM) model



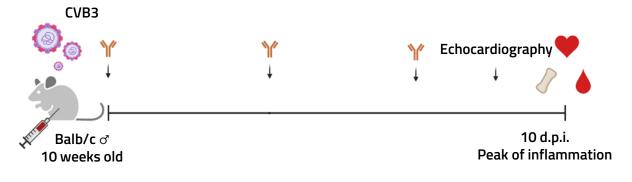
# Systemic sclerosis: Therapeutic mCAN10 treatment reduces lung fibrosis in the Topo and cGvHD models



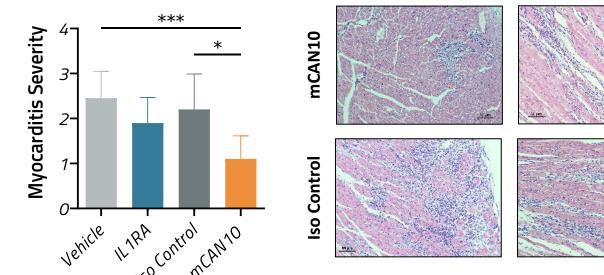


## Viral myocarditis: mCAN10 reduces disease severity

### CVB3 myocarditis experimental design



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

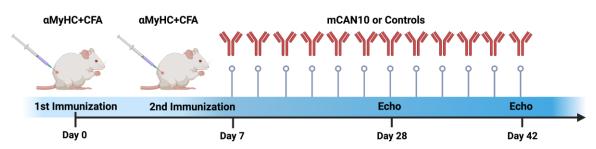


mCAN10 also reduced inflammatory leukocyte populations in the heart tissue

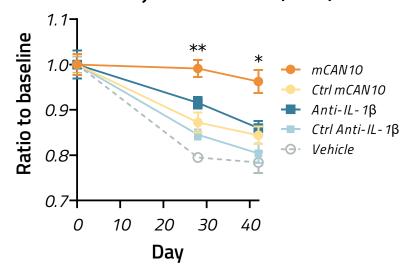
**IL1RA** 

Vehicle

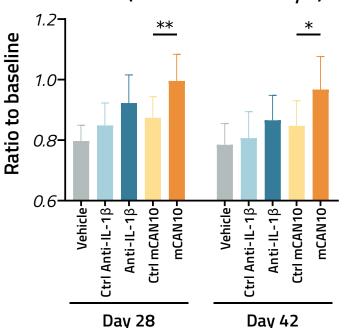
## Experimental autoimmune myocarditis: mCAN10 improves heart function



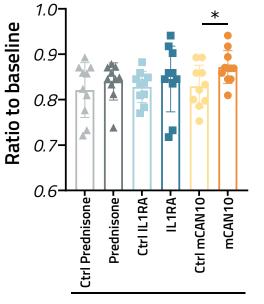
### Left Ventricual Ejection Fraction (LVEF)



### LVEF (treatment from day 7)



### LVEF (treatment from day 7)

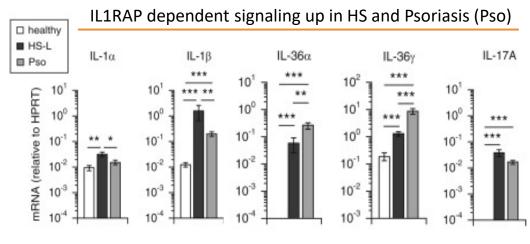


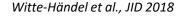
Day 28

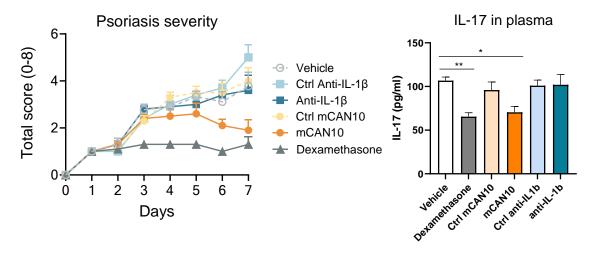


## CAN10 first-in-human study

- → Combined SAD/MAD protocol
- → IV administration in healthy volunteers (SAD)
- → SC administration in subjects with mild to moderate plaque psoriasis (MAD)
- → Safety and PK
- → Building value by adding additional PD analyses
  - Receptor occupancy
  - Ex vivo inhibition assay (proteomics)
  - Psoriasis severity scoring
  - Skin biopsy & skin tape strips (transcriptomics)
- → Phase I SAD ongoing, MAD planned to start Q3 2024
- → Preparations for phase II clinical study ongoing

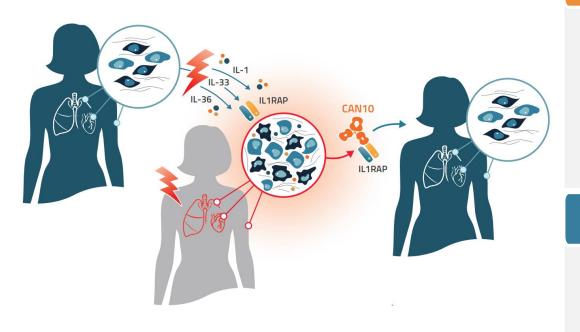








## CAN10 – a potent blocker of IL1RAP function with effects in skin, lung, heart and vasculature



### **Status**

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

### Clinical phase I study – Following plan

- Phase I in healthy volunteers (SAD) followed by psoriasis patients (MAD); ongoing in Germany
- → No safety findings in first 4 SAD groups. Receptor occupancy confirmed to be in line with preclinical model
- → Up to 80 individuals (safety, pharmacokinetics, biomarkers)





## Upcoming milestones

### **Nadunolimab**

### PDAC

- Start of Phase IIb trial in 150-200 patients H1 2024
- Phase IIb top-line data in 2025

### **NSCLC**

Efficacy/biomarker data from CANFOUR during 2024

### TNBC

- Full recruitment H2 2024
- Randomized Phase II top-line data in late 2024

### CAN10

 Phase I data updates during 2024 (including safety and biomarkers)

## Additional milestones

- New clinical data presented from CIRIFOUR, CAPAFOUR and CESTAFOUR trials
- New preclinical and translational results

**EXTENSIVE NEWS FLOW EXPECTED DURING 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 (initial 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 show good safety and receptor occupancy. New data Q2 2024



### CORPORATE STRENGTH DRIVING INNOVATION

- Solid cash position with runway into 2025 (195MSEK (19 MUSD) cash & equivalents at Q4 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)
Mother patent and divisionals

→ Lead candidate anti-IL1RAP antibody CAN10

Expiry year **2041**Granted (USA)
Examination at early stage in remaining territories

→ Anti-IL1RAP for treatment of solid tumors

Expiry year **2032**Granted (e.g. Europe, USA, China, Japan)
Mother patent and divisionals

→ Anti-IL1RAP for treatment of hematological disorders

Expiry year **2030**Granted (e.g. Europe, USA, China, Japan)
Mother patent and divisionals

→ Anti-IL1RAP for treatment of myeloproliferative disorders

Acquired from Cellerant; expiry year **2029** Granted (USA)

→ Additional patent families covering alternative anti-IL1RAP antibodies

Starting point for CANxx project(s)



