

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)



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### **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

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## **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 <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





## NADUNOLIMAB (CAN04) OVERVIEW



## IL1RAP overexpressed in most solid tumors

## 100% IL1 RAP- expressing tumors 75%-50% 25% 0% Lisophageal ' INSC oanceatic Colorectal NEOC iver Bladder Breast Cancer cell surface Stroma

**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

ADCC – Antibody-Dependent Cellular Cytotoxicity; NK – Natural Killer; TIR – Toll-Interleukin-1 Receptor



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



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

- $\rightarrow$  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 202 Contargia

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



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

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 OS by IL1RAP subgroup OS by IL1RAP subgroup



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)
- $\rightarrow$  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 – Phase IIb study design

### **Primary endpoint:**

 $\rightarrow$  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
- $\rightarrow$  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:

IL1RAP

IL1RAP



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



# NSCLC – Promising efficacy of nadunolimab combination therapy



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

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

NCG – Nadunolimab/Cisplatin/Gemcitabine; NCP – Nadunolimab/Carboplatin/Pemetrexed

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



 $\rightarrow$  Strongest efficacy in 16 non-squamous patients

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→ 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



## 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)
- $\rightarrow$  Randomized phase II ongoing

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



## Key messages

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



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

![](_page_15_Picture_0.jpeg)

## CAN10 – OPPORTUNITY IN AUTOIMMUNE/INFLAMMATORY DISEASE

![](_page_15_Picture_2.jpeg)

# 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

![](_page_16_Figure_4.jpeg)

UNIQUE OPPORTUNITY FOR CAN10 IDENTIFIED IN LIFE-THREATENING DISEASES

![](_page_16_Picture_6.jpeg)

# Systemic sclerosis – mCAN10 inhibits bleomycininduced skin fibrosis

## Bleomycin (BLM) model

![](_page_17_Figure_2.jpeg)

![](_page_17_Picture_3.jpeg)

## Viral myocarditis – mCAN10 reduces disease severity

![](_page_18_Figure_1.jpeg)

CVB3 – Coxsackievirus B3; IL1RA – IL-1 Receptor Antagonist (blocks IL-1α/IL-β signaling)

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## 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)

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## MILESTONES & INVESTMENT HIGHLIGHTS

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# Upcoming milestones

## Nadunolimab

PDAC	NSCLC	TNBC	CAN10	Additional milestones
<ul> <li>Start of Phase IIb trial in 150-200 patients early 2024</li> <li>Phase IIb top-line data in 2025</li> </ul>	<ul> <li>Efficacy/biomarker data from CANFOUR 2023 and 2024</li> </ul>	<ul> <li>Safety and efficacy data from Phase I at ESMO in Q4 2023</li> <li>Randomized Phase II top-line data in late 2024</li> </ul>	<ul> <li>Phase I recruitment and treatment ongoing</li> <li>Phase I data in 2024</li> </ul>	<ul> <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** 

![](_page_21_Picture_4.jpeg)

# Cantargia – Investment highlights

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