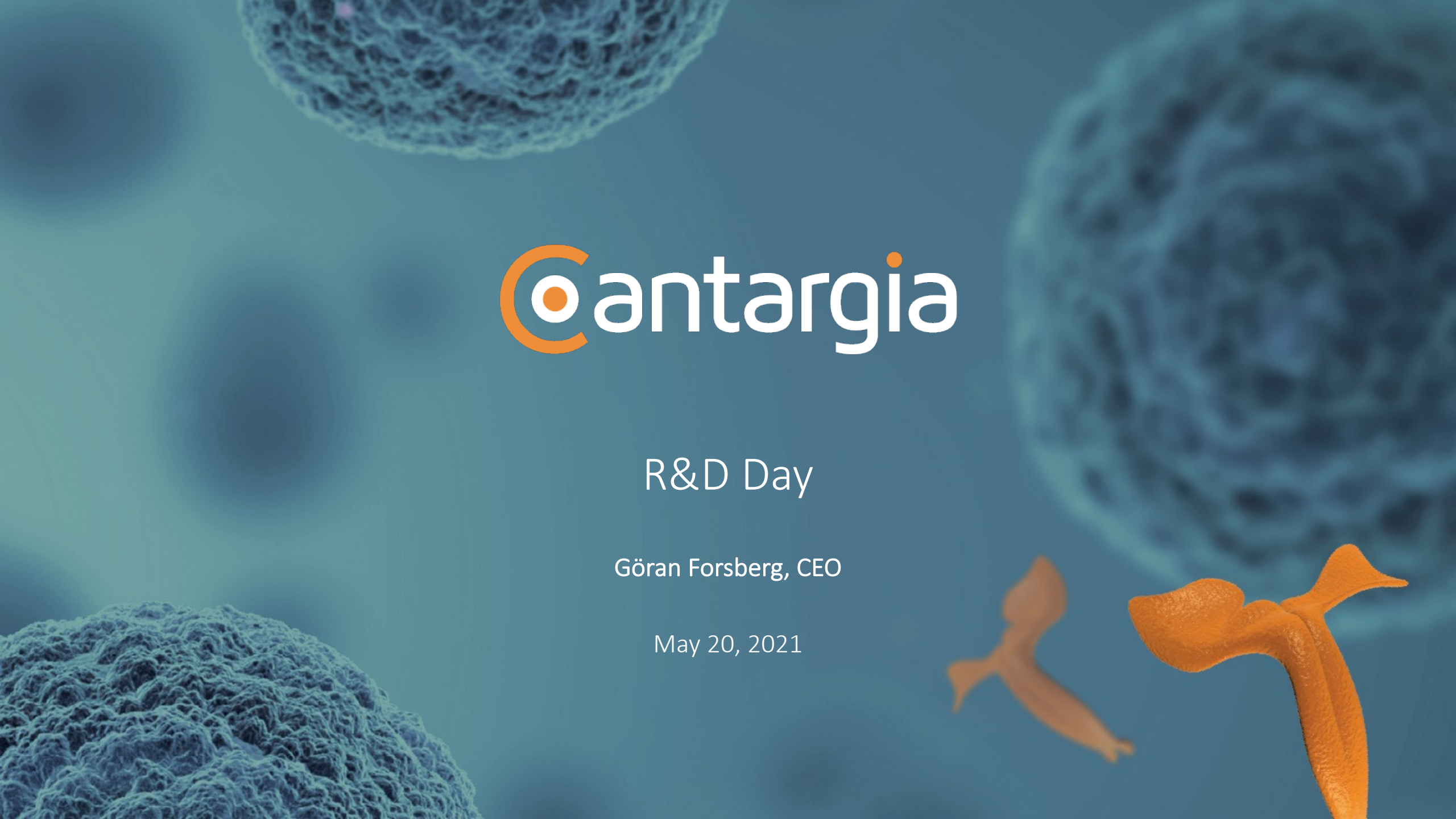



# R&D Day

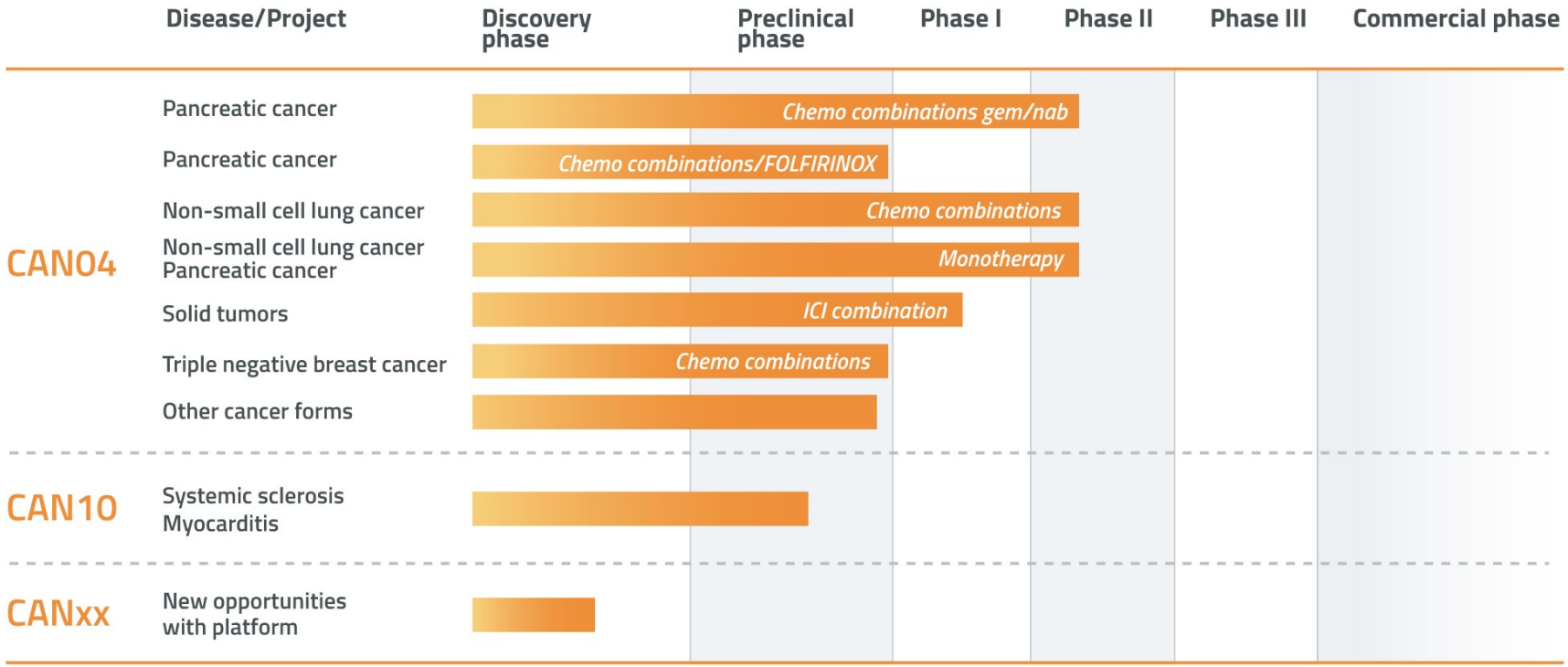
Göran Forsberg, CEO

May 20, 2021

# Safe Harbour Statement

*Statements in the Investor Presentation, including those regarding the possible or assumed future or other performance of the Company or its industry or other trend projections, constitute forward-looking statements. By their nature, forward-looking statements involve known and unknown risks, uncertainties, assumptions and other factors as they relate to events and depend on circumstances that will or may occur in the future, whether or not outside the control of the Company. No assurance is given that such forward-looking statements will prove to be correct. Prospective investors should not place undue reliance on forward-looking statements. They speak only as at the date of this Investor Presentation and the Company undertakes no obligation to update these forward-looking statements. Past performance does not guarantee or predict future performance. Moreover, the Company undertakes no obligation to review, update or confirm expectations or estimates or to release any revisions to any forward-looking statements to reflect events that occur or circumstances that arise in relation to the content of the Investor Presentation.*

# Cantargia – Opportunity to save lives and create value




- Potentially more effective treatment against novel target in clinically validated pathway
- First in class platform technology against novel target
- Well financed to build a broad, diversified pipeline
- Right team and clear plan to position our projects and maximize value

# Cantargia highlights

**UNIQUE IMMUNOTHERAPY ANTIBODY CAN04 IN PHASE IIA CLINICAL DEVELOPMENT**
- Positive interim data set - response rates higher than historical control
- First in class antibody with broader MOA than competitors

**VISION OF BECOMING AN IMPORTANT PART IN FUTURE CANCER TREATMENTS**
- Combination strategy based on synergies with established therapies

**PLATFORM WITH MANY POTENTIAL THERAPEUTIC AREAS**
- Target IL1RAP found on most solid tumor forms and leukemia
- IL1RAP signalling (IL-1, IL-33 and IL-36) in large number of diseases

**HIGHLY RELEVANT RESEARCH WITHIN CLINICALLY VALIDATED MECHANISMS**
- Focus on opportunities with major unmet medical need

**ROBUST PATENT PORTFOLIO**
- Global patent families on IL1RAP as antibody target in oncology until 2032 and CAN04 until 2035

**NASDAQ STOCKHOLM MAIN LIST ~10,000 SHAREHOLDERS AND LONG TERM INVESTORS**
- Market cap: SEK 3.3bn (USD ~400m) (19 May 2021)
- Cash: SEK 903m (USD 108m) (31 Dec-20)

| Current owners (31 Mar 2021) | |
|---|---|
| Swedbank Robur Funds | 9.7% |
| 4th AP fund | 7.7% |
| Alecta | 6.8% |
| 1st AP fund | 6.3% |
| Six Sis AG | 5.5% |
| Avanza Pension | 3.9% |
| Handelsbanken fonder | 3.1% |
| Sunstone LSV | 3.0% |
| SEB AB, Luxemburg | 2.7% |
| Morgan Stanley | 2.0% |

# Todays program

- 15.00 Welcome and introduction to Cantargia – Göran Forsberg, CEO
- 15.05 Nadunolimab (CAN04) Mechanism of action – David Liberg, VP Research
- 15.25 Nadunolimab updated phase IIa clinical results in pancreatic cancer – Prof Ahmad Awada, Inst. Jules Bordet, Brussels, Belgium
- 15.50 Pancreatic cancer and context for nadunolimab results – Dr Manuel Hidalgo, Weill-Cornell, New York
- 16.10 Nadunolimab current and upcoming clinical trials, Ignacio Garcia-Ribas, CMO
- 16.25 CAN10 project and new preclinical results– David Liberg, VP Research
- 16.45 Q&A
- 17.00 End of presentation

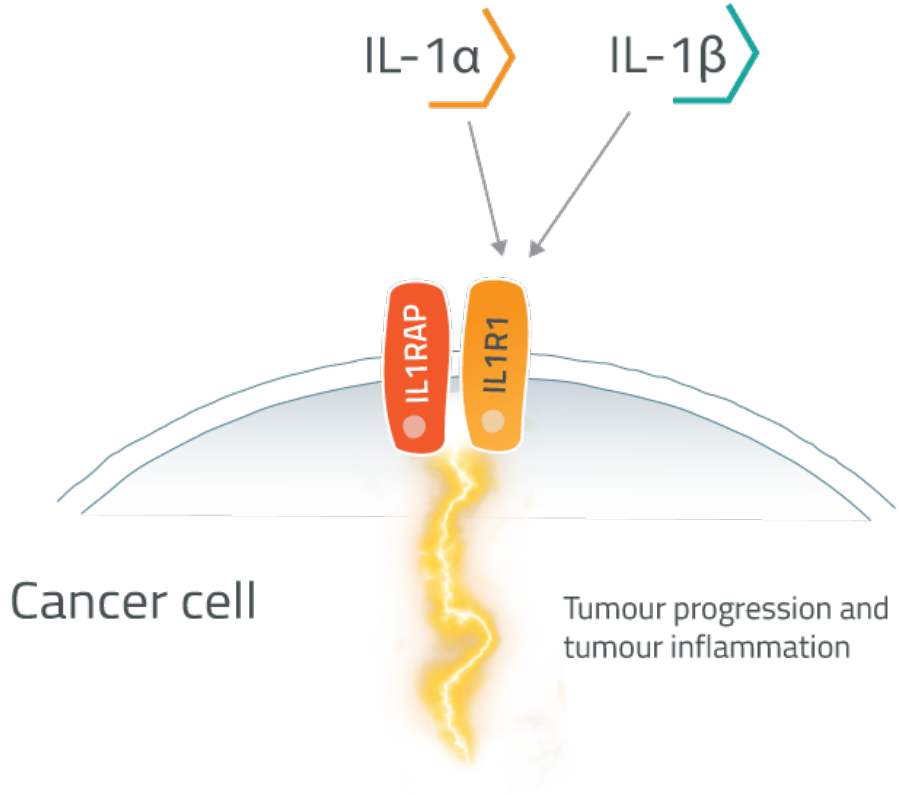
# CAN04 – PRECLINICAL RATIONALE

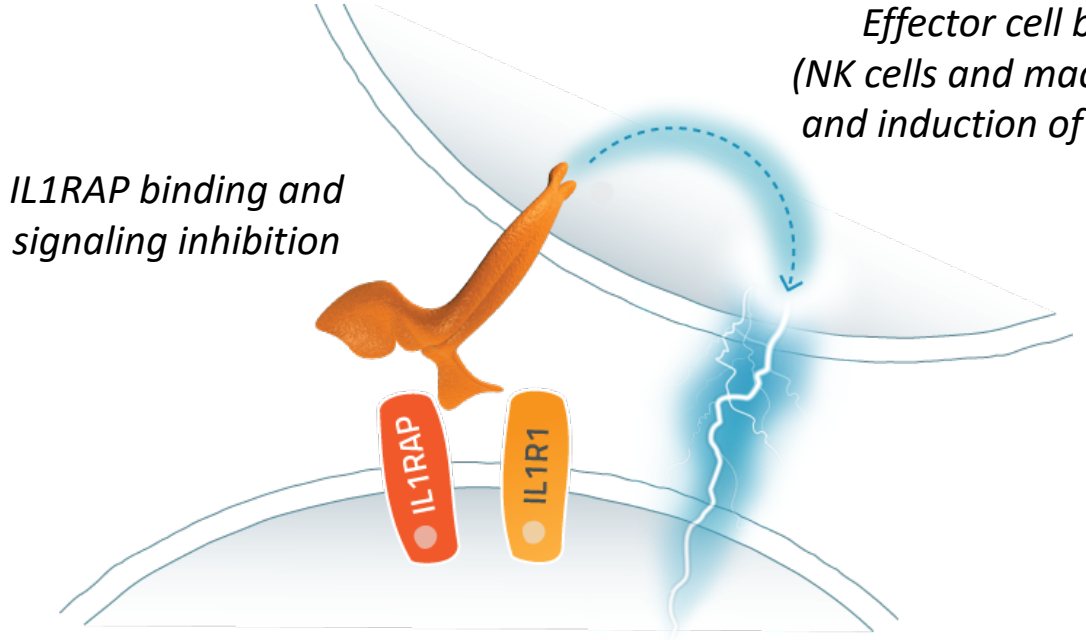
# Targeting IL1RAP in cancer

- IL1RAP is an inflammatory protein expressed by tumor cells and by tumor-supporting cells in the tumor vicinity
- IL1RAP is involved in chronic tumor inflammation and promotes tumor growth and immune suppression – both on tumor cells and on tumor-supporting cells
- IL1RAP is involved in tumor cell survival and resistance to therapeutic interventions


7

# Nadunolimab (CAN04) – an anti-IL1RAP antibody with dual functions

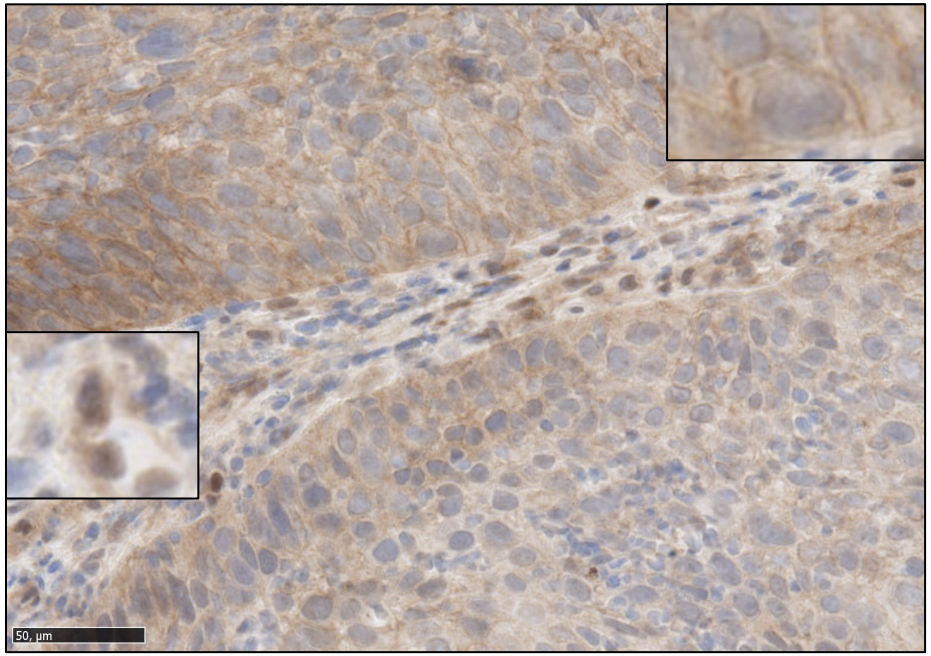


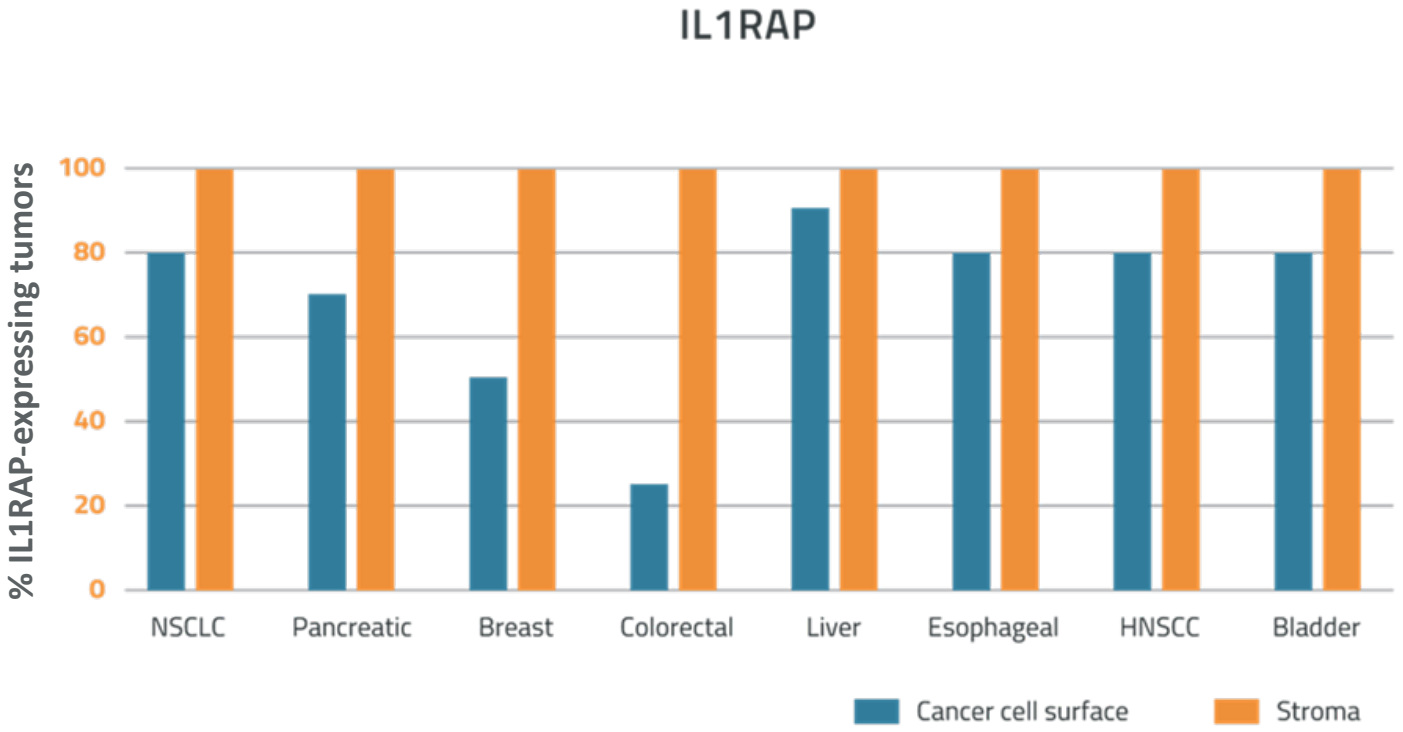

1. CAN04 blocks signalling (stops tumour progression and inflammation)
2. CAN04 stimulates the immune defence (e.g. natural killer cells) to eradicate tumour cells


8

# IL1RAP expression in solid tumors



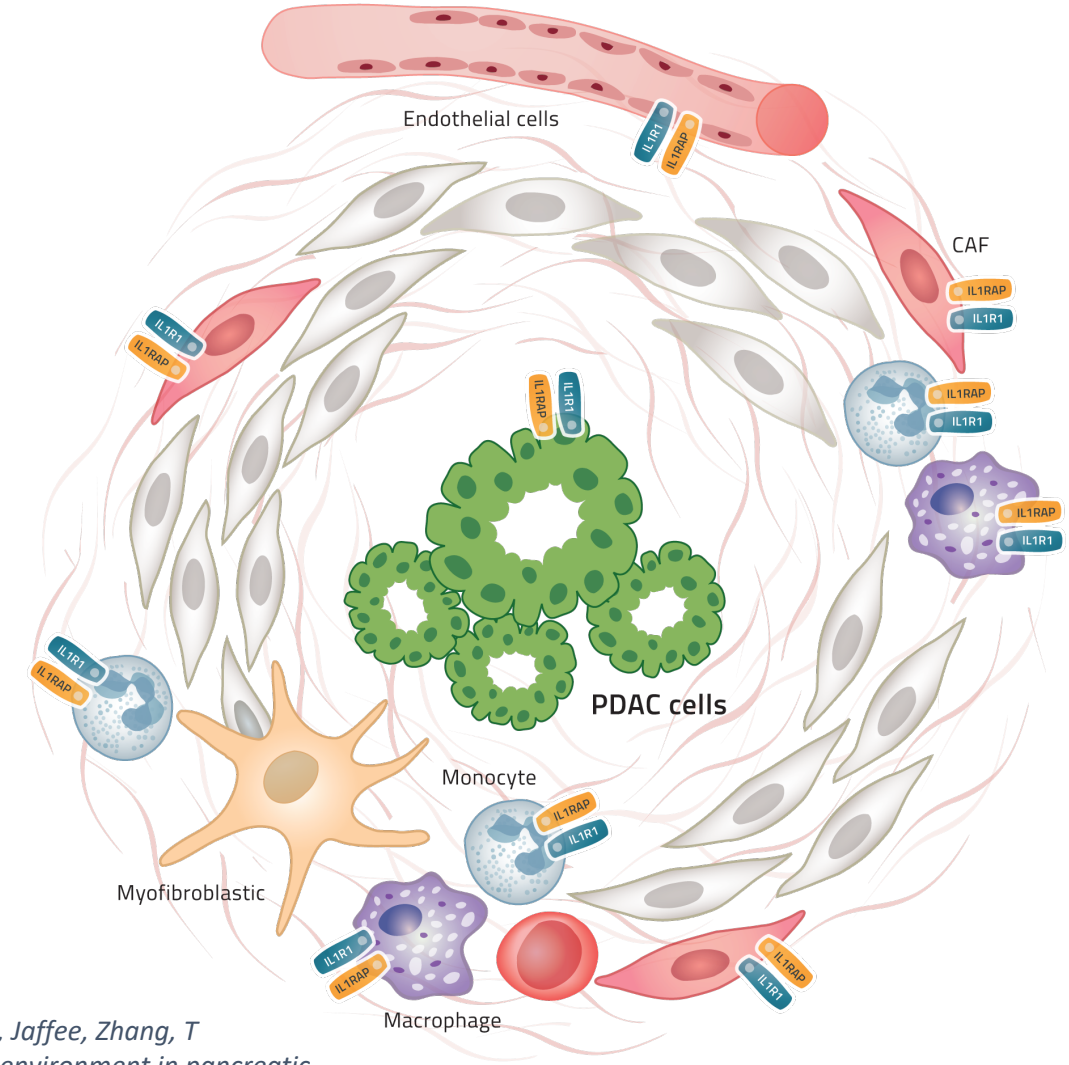

*NSCLC biopsy CANFOUR, IL1RAP staining*




IL1RAP is expressed broadly in solid tumors, both on cancer cells and stromal cells

*NSCLC – non-small cell lung cancer*
*HNSCC – head and neck squamous carcinoma*

# IL1RAP expression in solid tumors




IL1RAP is expressed by:

- tumor cells
- cells in the tumor microenvironment:
  - cancer-associated fibroblasts (CAF)
  - tumor-associated macrophages (TAM)
  - monocytes
  - neutrophils
  - endothelial cells

IL1RAP-expressing cells react to IL1α or IL1β in the tumor microenvironment

*Adapted from Ho, Jaffee, Zhang, T he tumour micro-environment in pancreatic cancer — clinical challenges and opportunities, Nature Reviews Clinical Oncology 2020*

*PDAC – pancreatic ductal adenocarcinoma*

# IL-1α/β and resistance to therapy

**Interleukin-1 blockade overcomes erlotinib resistance in head and neck squamous cell carcinoma**

Aditya Stanam[1,2], Katherine N. Gibson-Corley[2,5,6], Laurie Love-Homan[2], Nnamdi Ihejirika[3], Andrean L. Simons[1,2,4,5,6]

[CANCER RESEARCH 62, 910–916, February 1, 2002]

**Autocrine Production of Interleukin 1β Confers Constitutive Nuclear Factor κB Activity and Chemoresistance i**

Alexander Arlt,[2] Jens Vorndamm,[2] Susanne Heiner Schäfer[3]

**Serum levels of IL-6 and IL-1β can predict the efficacy of gemcitabine in patients with advanced pancreatic cancer**

S Mitsunaga*[,1,2], M Ikeda[1], S Shimizu[1], I Ohno[1], J Furuse[3], M Inagaki[4], S Higashi[5], H Kato[5], K Terao[6] and A Ochiai[2]

**A Novel Role for the Interleukin-1 Receptor Axis in Resistance to Anti-EGFR Therapy**

Valerio Gelfo [1,2,†], Martina Mazzeschi [1,†], Giada Grilli [1], Moshit Lindze
Gabriele D'Uva [6], Balázs Győrffy [7,8], Andrea Ardizzoni [1], Yosef Yarden
Mattia Lauriola [1,2,*]
Vassilis Georgoulias,[8] Rinat Zaynagetdinov,[2,11,*] and Timothy S. Blackwell[1,2,5,9,10,]

IRAK1 is a therapeutic target that drives breast cancer

Zhen Ning Wee
Puay Leng Lee[1]
Dave S.B. Hoon

Chemotherapy-triggered cathepsin B release in myeloid-derived suppressor cells activates the Nlrp3 inflammasome and promotes tumor growth

Mélanie Bruchard[1,2,8], Grégoire Mignot[1,2,8], Valentin Derangère[1,2], Fanny Chalmin[1,2], Angélique Chevriaux[1–3], an[1,2], Wilfrid Boireau[4], Benoit Simon[4], Bernhard Ryffel[5], Jean Louis Connat[6], los[7], François Martin[1,2], Cédric Rébé[1–3], Lionel Apetoh[1–3,8] & François Ghiringhelli[1–3,8]

**Neutrophil-Derived IL-1β Impairs the Efficacy of NF-κB Inhibitors against Lung Cancer**

Allyson G. McLoed,[1] Taylor P. Sherrill,[2] Dong-Sheng Cheng,[2] Wei Han,[2] Jamie A. Saxon,[1] Linda A. Gleaves,[2] Pingsheng Wu,[3] Vasiliy V. Polosukhin,[2] Michael Karin,[4] Fiona E. Yull,[1,5] Georgios T. Stathopoulos,[2,6,7] Vassilis Georgoulias,[8] Rinat Zaynagetdinov,[2,11,*] and Timothy S. Blackwell[1,2,5,9,10,11]

**ory cytokines defines resistance of inhibitors**

**, Maria Teresa Rodia[1,*], Michela Pucci[1], Massimiliano Dall'Ora[1], ,4], Rossella Solmi[1], Lee Roth[5], Moshit Lindzen[5], Massimiliano a Bertotti[6], Elisabetta Caramelli[1], Pier-Luigi Lollini[1], Livio Trusolino[6], Gabriele D'Uva[7,**], Mattia Lauriola[1,2,**]**

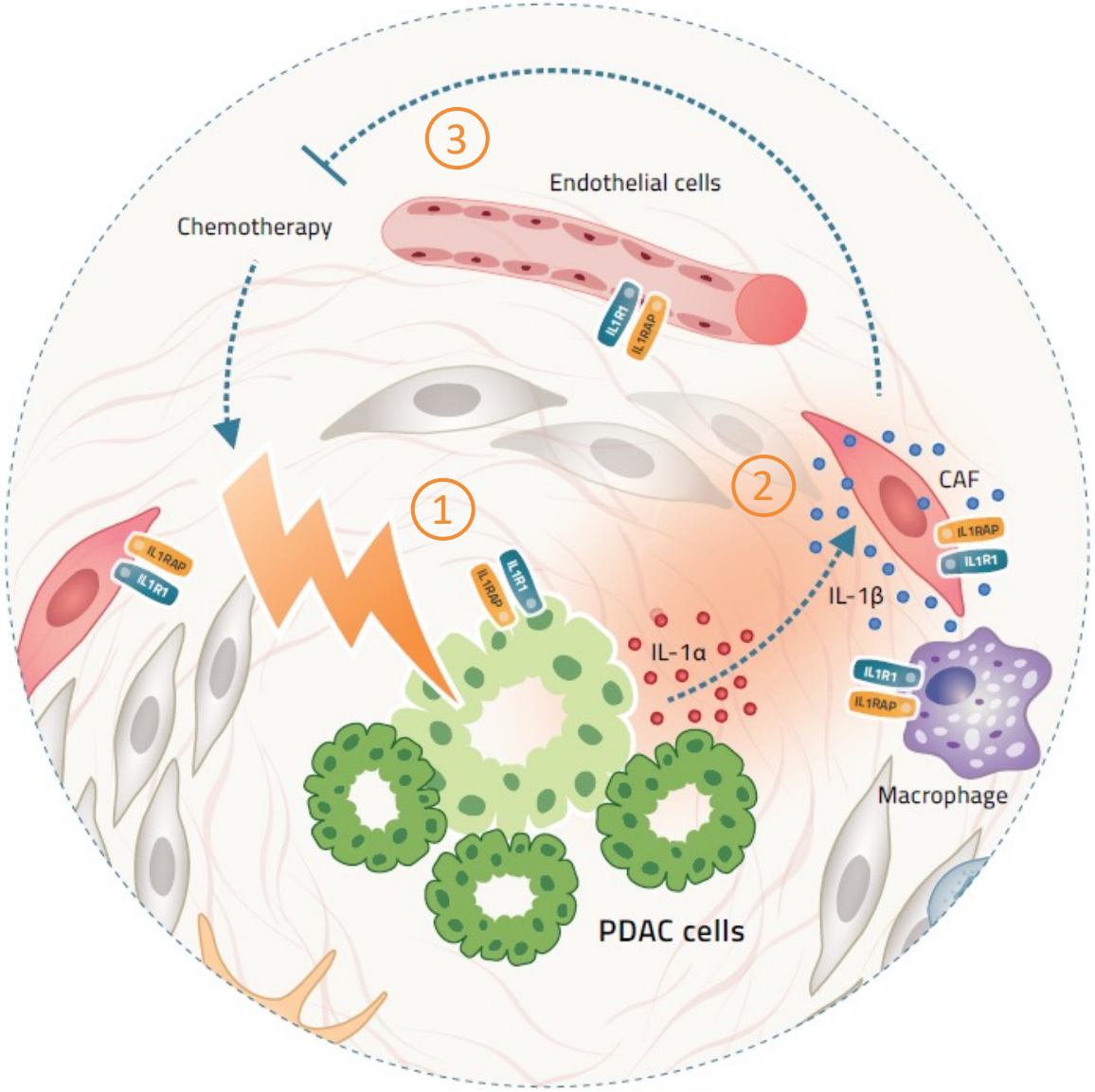
**Constitutive IRAK4 Activation Underlies Poor Prognosis and Chemoresistance in Pancreatic Ductal Adenocarcinoma**

Daoxiang Zhang[1], Lin Li[1], Hongmei Jiang[1], Brett L. Knolhoff[1], Albert C. Lockhart[1], Andrea Wang-Gillam[1], David G. DeNardo[1], Marianna B. Ruzinova[2], and Kian-Huat Lim[1]



Cantargia

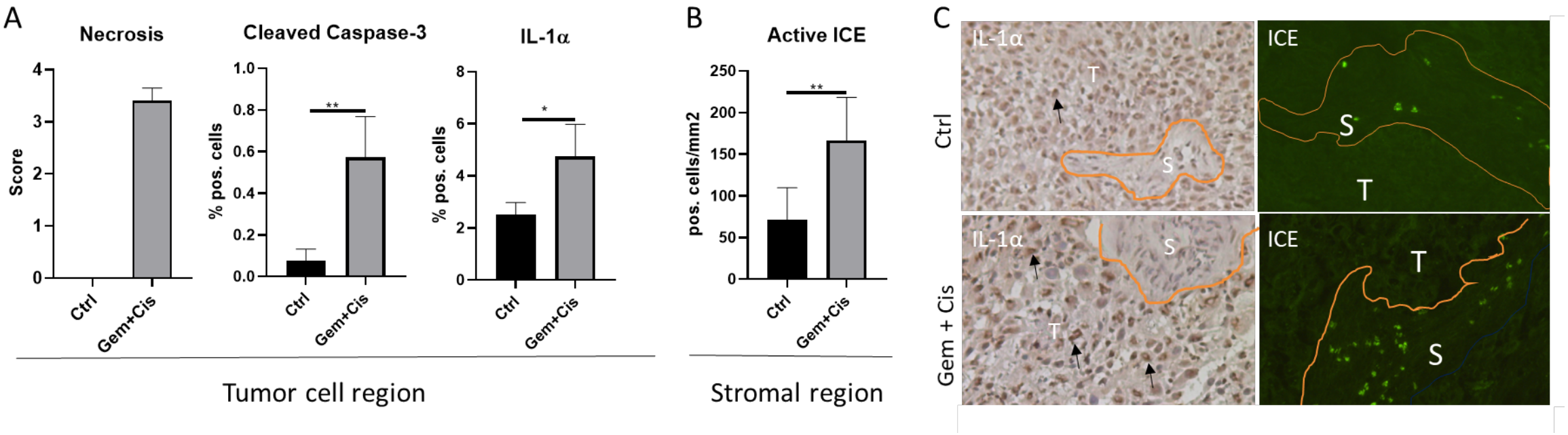
# The IL-1 system is induced by chemotherapy




1. Chemotherapy induces cell killing and IL1α upregulation in tumor cells
2. IL1β is induced in the tumor stroma
3. IL1α and IL1β mediates chemoresistance

# The IL-1 system is induced by chemotherapy

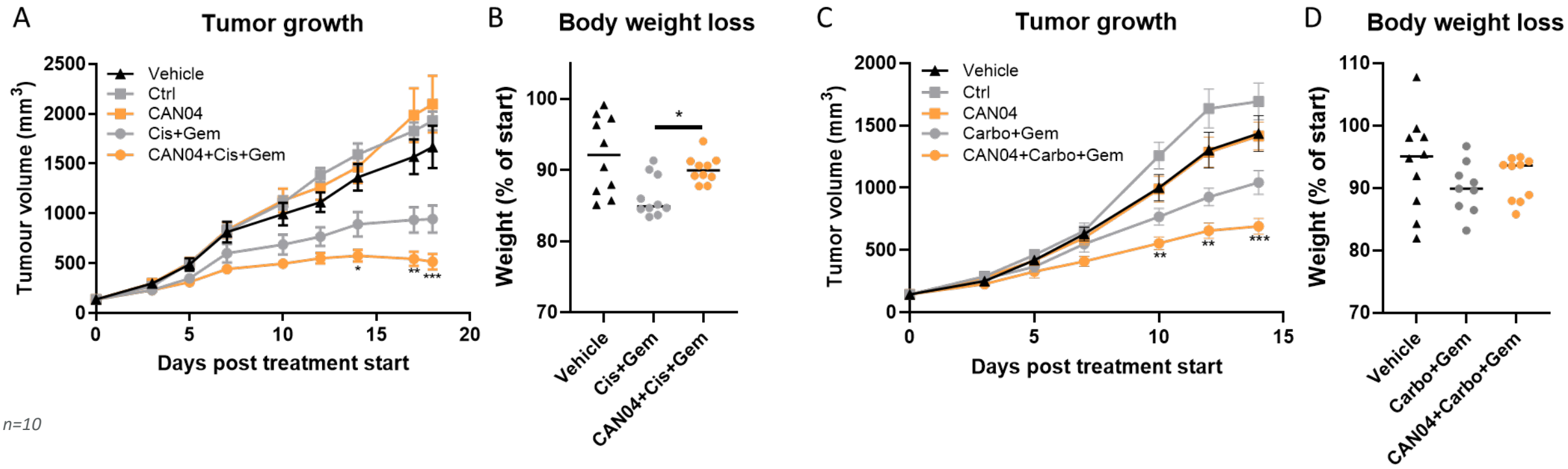
*Immunohistochemistry of tumor tissue in a NSCLC patient-derived xenograft model*




IL-1α is upregulated in tumor cells after chemotherapy and Interleukin 1β-converting enzyme (ICE/Caspase-1) in the tumor stroma

# CAN04 increases the efficacy of chemotherapy

*Tumor growth in a NSCLC patient-derived xenograft model*



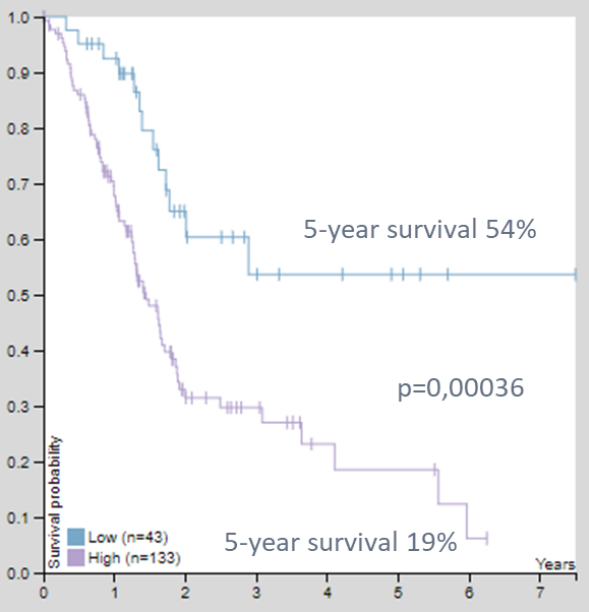

*n=10*

CAN04 increases efficacy of chemotherapy regimens and counteracts weight loss

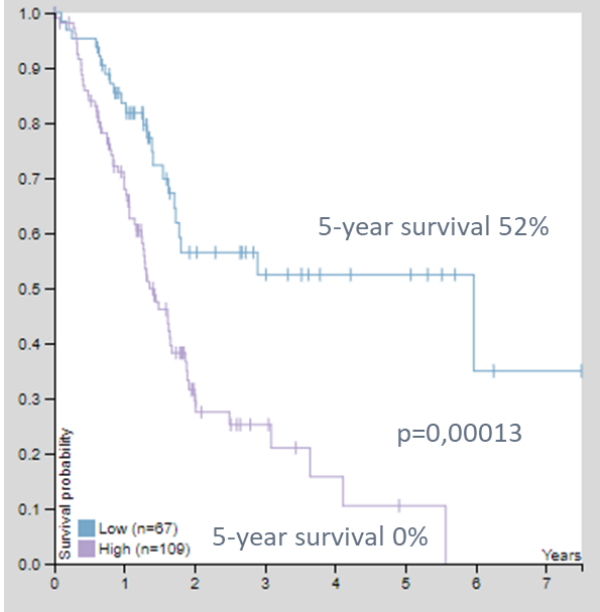
# Pancreatic cancer

*KRAS-driven inflammation and the potential of CAN04*

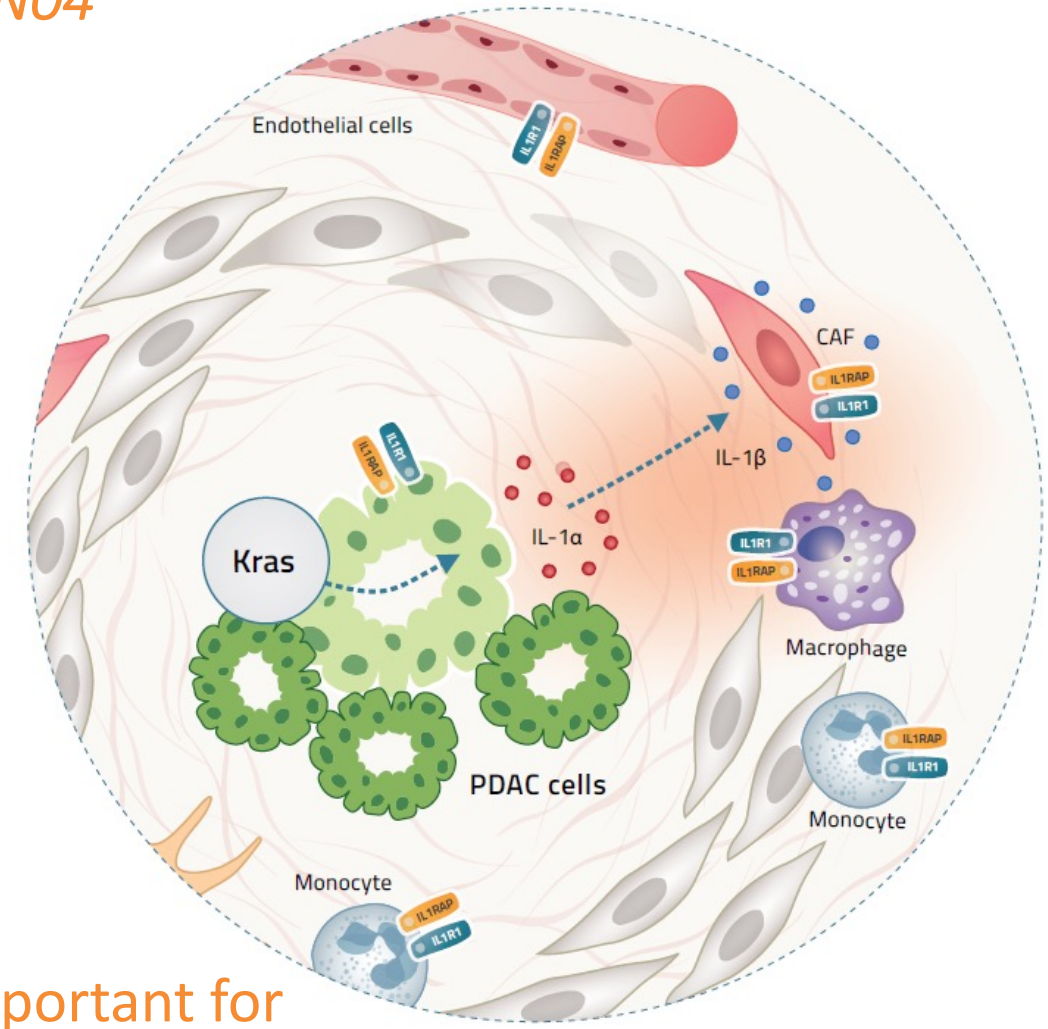
KRAS mRNA (TCGA) vs survival




IL1RAP mRNA (TCGA) vs survival




*https://www.proteinatlas.org/*




- > 90% of PDAC tumors have mutated KRAS
- IL1α induced by KRAS has been shown to be important for tumor development in PDAC

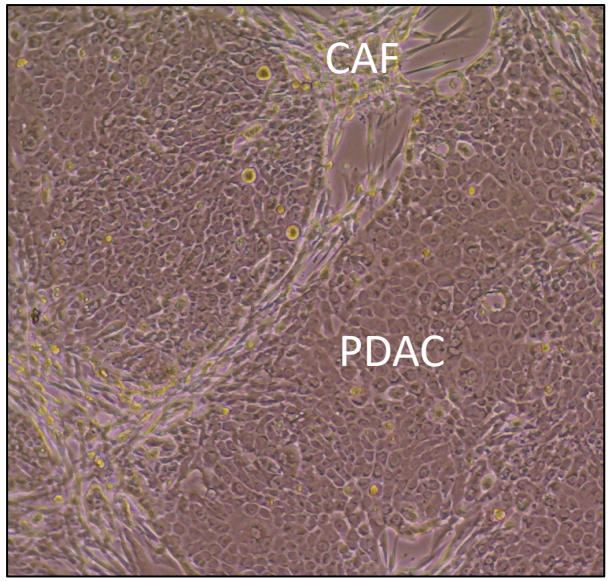


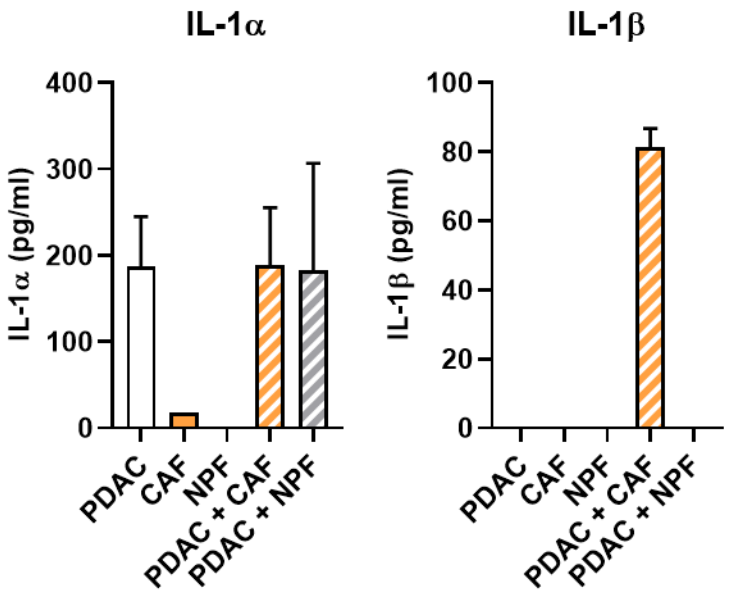


Cantargia

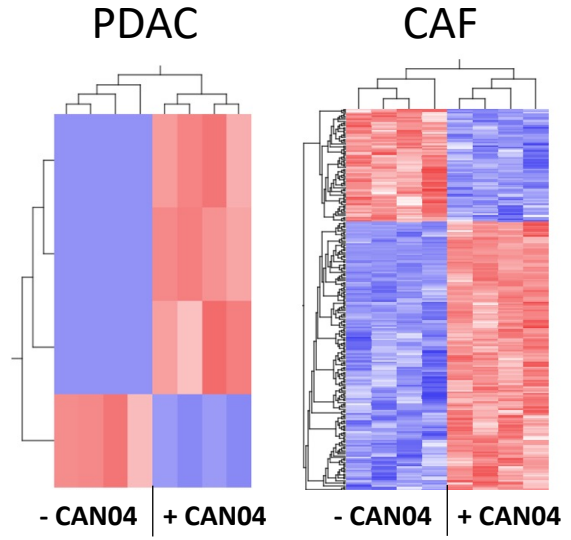
# The pancreatic tumor microenvironment in vitro

*Human pancreatic cancer cells cultured with human cancer associated fibroblasts*




*CAF = Cancer-associated fibroblast*
*NPF = Normal pancreatic fibroblast*




*4 genes changed by CAN04*

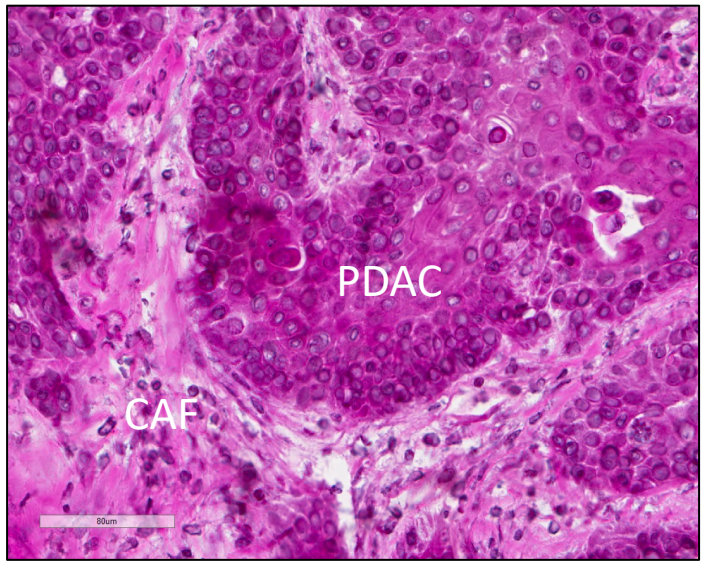
*230 genes changed by CAN04*

*RNAseq*

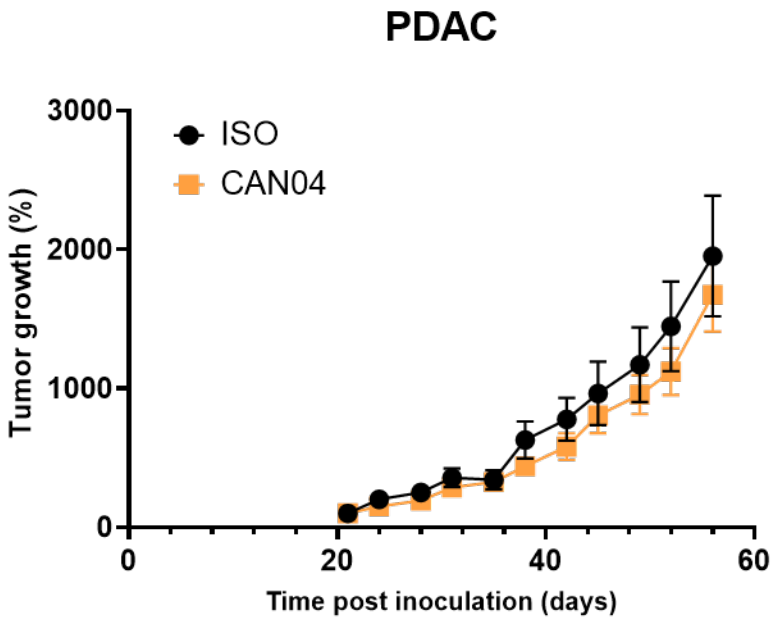
- Cross-talk between cancer cells and stromal cells involve IL1α/β
- CAN04 treatment has a major impact on tumor cell-induced reprogramming of cancer-associated fibroblasts

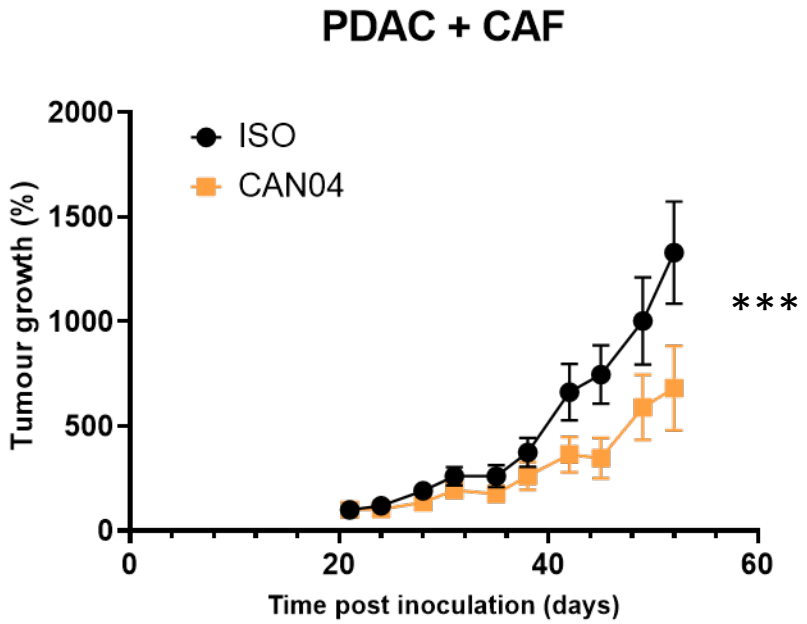
# Inhibition of pancreatic tumor growth by CAN04

## Tumor growth in a CAF-PDAC xenograft model of human pancreatic cancer




*PDAC – cancer cells*
*CAF – tumor stroma*




*n=10*

## The inhibition of tumor cell growth induced by CAN04 is mediated by cancer-associated fibroblasts (CAFs)

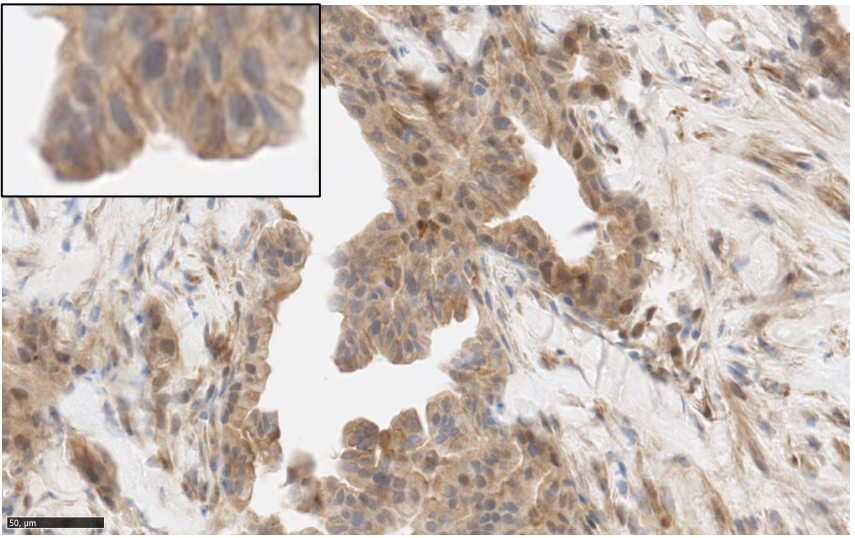
# Summary

- CAN04 (nadunolimab) blocks IL1α/IL1β signaling and induces antibody-mediated cell killing of IL1RAP-expressing cells
- IL1RAP is broadly expressed in solid tumors, both on tumor cells and in tumor stroma
- CAN04 targets both tumor cells and components of the tumor stroma
- Chemotherapy activates the IL1α/β-system in the tumor microenvironment
- CAN04 and chemotherapy act in synergy to inhibit tumor growth

Effects on tumor microenvironment and chemoresistance makes CAN04 an intriguing and unique compound for treatment of cancer, including pancreatic cancer

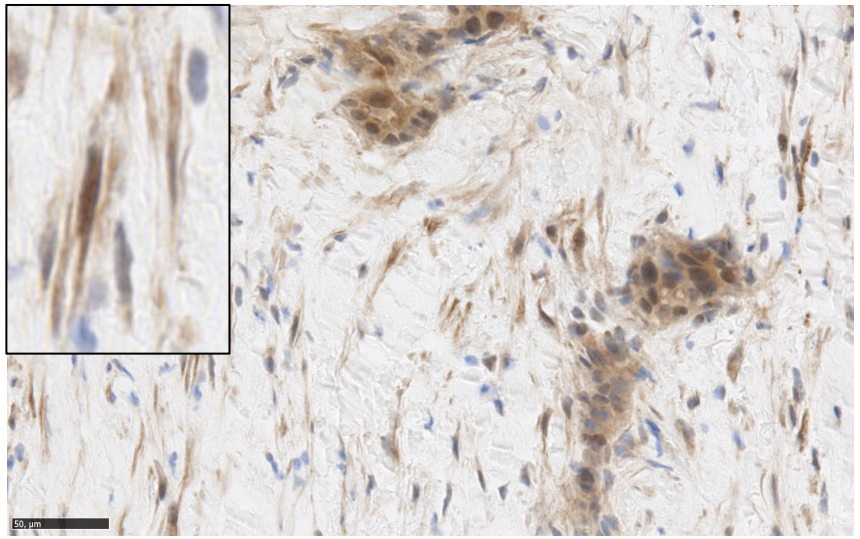
# CANFOUR - Pancreatic ductal adenocarcinoma

Tumor cells



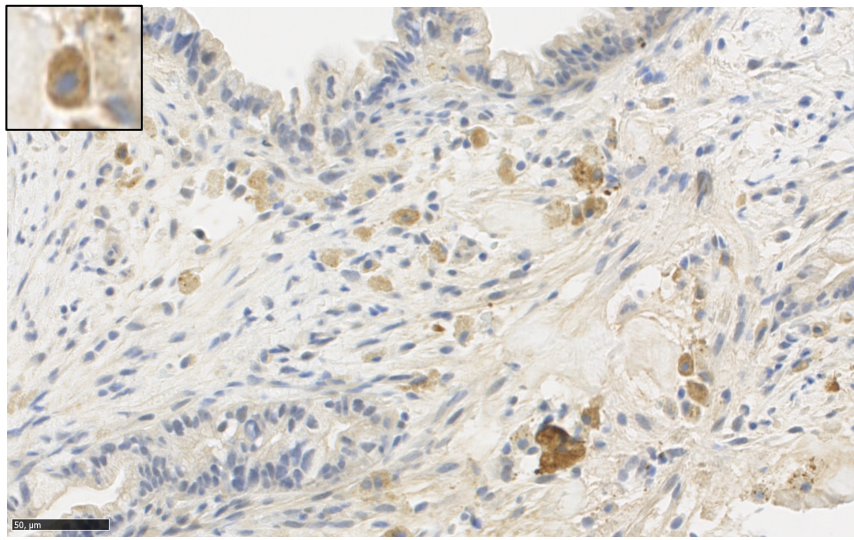
*CANFOUR pancreatic biopsy*

Cancer-associated Fibroblasts (CAFs)



*CANFOUR pancreatic biopsy*

Tumor-associated Macrophages (TAMs)



*CANFOUR liver biopsy*

- IL1RAP is expressed in tumor and stromal cells in primary and metastatic tumors from PDAC patients
- Analyses of plasma and tumor samples ongoing, to be presented at a scientific conference

# Nadunolimab (CAN04, anti-IL1RAP) in Pancreatic Cancer

*Interim analysis April 20 based ongoing trial*

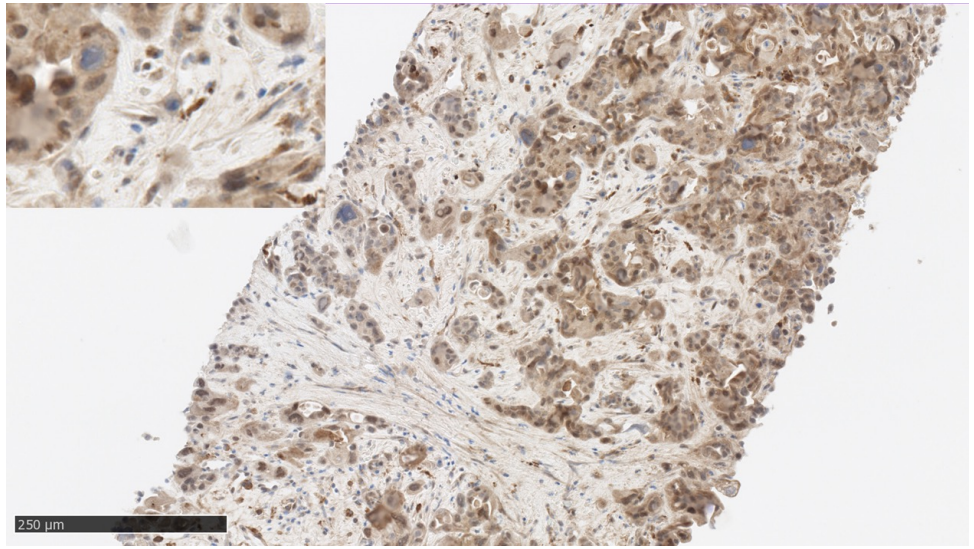
Professor Ahmad Awada

Institut Jules Bordet, Brussels

*20 May 2021*

# IL1RAP relevance in pancreatic cancer

- Pancreas cancer still an unmet medical need.
- One of the few indications where immunotherapy does not have a role.
- IL1RAP, overexpressed on pancreatic cancer cells and associated stroma
- IL1RAP and IL-1 system has documented roles in pancreatic cancer tumor microenvironment
- IL1RAP blockade synergizes with chemotherapy regimes used to pancreas cancer.




*CANFOUR PDAC patient biopsy showing IL1RAP expression on tumor cells and stroma*

# The first nadunolimab clinical trial CANFOUR

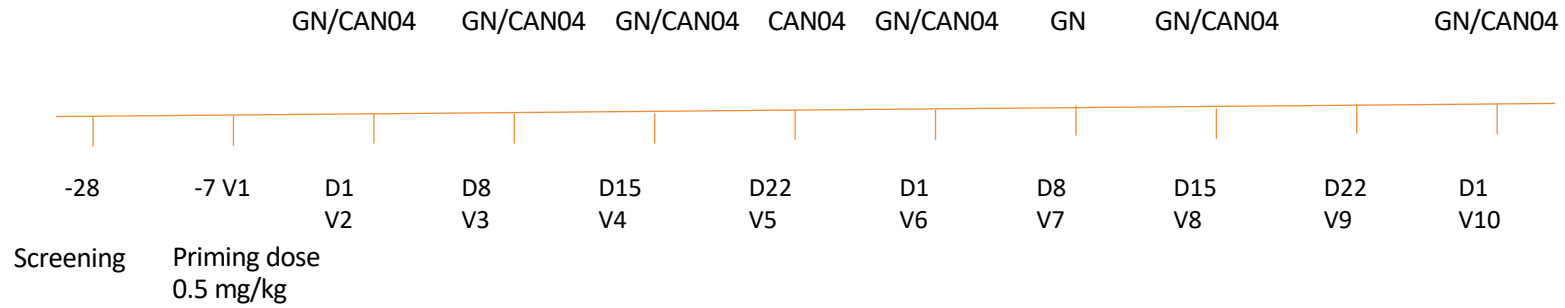
**Started 2017 with the aim to identify a safe dose, evaluate biomarkers and find early efficacy signals of:**

- Nadunolimab monotherapy (N=48)
- Nadunolimab in combination with gemcitabine/cisplatin in NSCLC (plan N=31)
- Nadunolimab in combination with gemcitabine/nab-paclitaxel as first line treatment of PDAC (N=36)

**CANFOUR trial is currently ongoing.**

# Nadunolimab with gemcitabine/nab-paclitaxel (GN) in PDAC

- Patient population: Stage III/IV PDAC in first line of systemic chemotherapy
- Patient Disposition:
  - 36 PDAC patients were treated in 10 sites in 5 EU countries from March 2019 up to October 2020.
  - 8 patients were treated initially at 7.5 mg/kg/week and 28 at 5 mg/kg/week. CAN04 at 5mg/kg was considered the maximum tolerated dose.
  - Infusion related reaction risk with 1st infusion was managed with a priming dose of 0.5 mg/kg and premedication.
  - Modified intention to treat (mITT) population(efficacy population): 33 patients. Three patients withdrew consent/discontinued due to IRR with priming dose and never received chemotherapy.





23

# Baseline patient characteristics vs. MPACT trial

| | | CANFOUR | *MPACT** |
|---|---|---|---|
| | | 36 | *431* |
| **Age** | Median | 62 | *62* |
| | Range | 46-87 | *27-86* |
| | <65 yr | 64% | *59%* |
| | >=65 yr | 36% | *41%* |
| **Sex** | Female | 53% | *43%* |
| | Male | 47% | *57%* |
| **PS** | 0 | 64% | *58%* |
| | 1 | 36% | *42%* |
| **Site of metastases** | Liver | 74% | *85%* |
| | Lung | 34% | *35%* |
| | Lymph nodes | 40% | *ND* |
| | Peritoneum | 28% | *4%* |
| **CA19-9** | N | 33 | *379* |
| | Median | 4483 | *2294* |
| | Range | 1-47 929 | *1.9-6 159 233* |
| **Previous treatment** | RT | 8% | *4%* |
| | Chemotherapy | 15% | *5%* |
| | Surgery | 36% | *7%* |
| | Biliary stent | 13% | *19%* |

*MPACT is the randomized gemcitabine/nab paclitaxel historical control data (von Hoff et al, 2013).
Data presented only for the gemcitabine/nab-paclitaxel arm

**CANFOUR population seems to be similar to MPACT**


24

# PDAC efficacy evaluation and summary

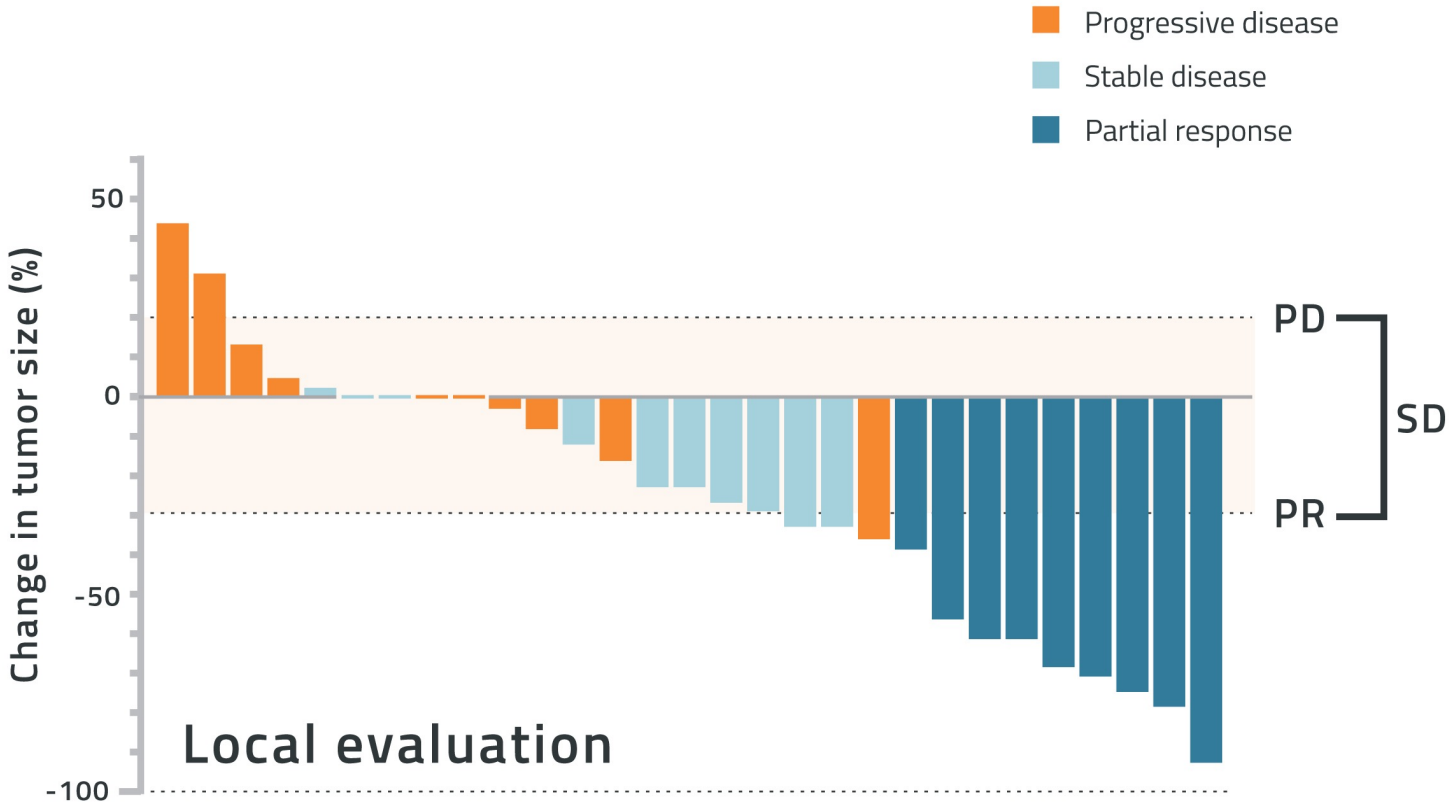
Efficacy evaluation:

- CT scan every 2nd month
- Serum CA19-9

Efficacy evaluation summary:

- Durable responses observed
- Promising PFS and OS
- Important finding of pseudoprogression-like response in 5 (15%) patients predicting long PFS.

# Evaluation of tumor shrinkage by the investigator




- Waterfall plot is based on largest percentage tumor shrinkage (target lesions) and best overall response during study
- PD is >20% increase vs baseline and PR is >30% tumor shrinkage.
- Central review ongoing
  - 1CR
  - 7PR (incl 1 unconfirmed CR)
  - 3PR awaiting confirmatory scan

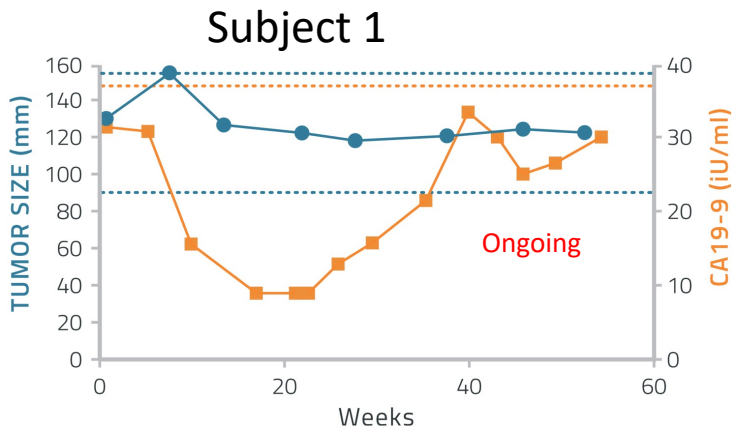
# Pseudoprogression (PsP) in PDAC

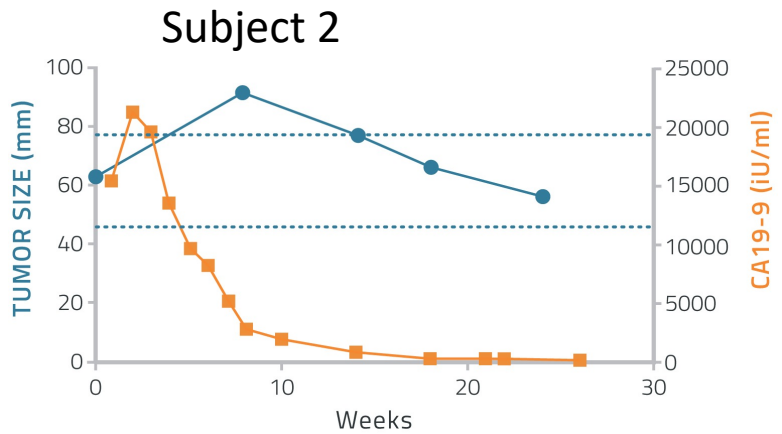
- Evidence of tumor growth (including the appearance of new lesions) not corresponding with treatment failure but with long-term benefit.
- In solid tumors, PsP is observed with checkpoint inhibitors. The apparent increase in tumor burden  may precede antitumor effects, resulting from immune cells infiltrating the tumor.
  - Specific response criteria have been developed to account for treatment benefit beyond progression (iRECIST)
  - CAN04 can activate the immune system against the tumor. For this reason, iRECIST is used to measure response and progression free survival.
- To our knowledge, PsP is not previously described for PDAC with chemotherapy or immunotherapy.

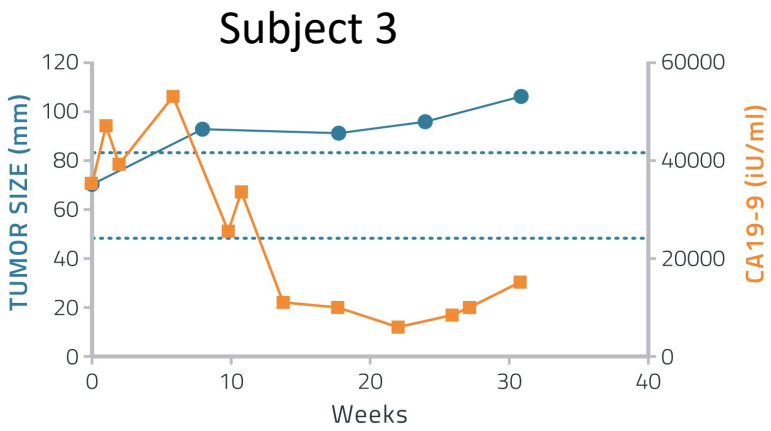

27

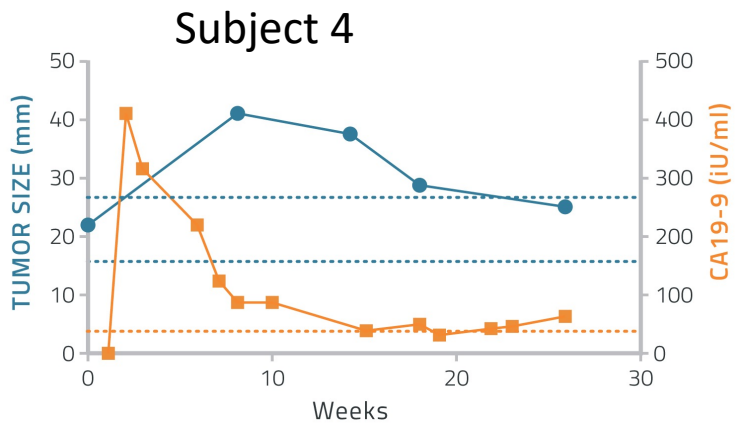
# Patients with Pseudoprogression-like response

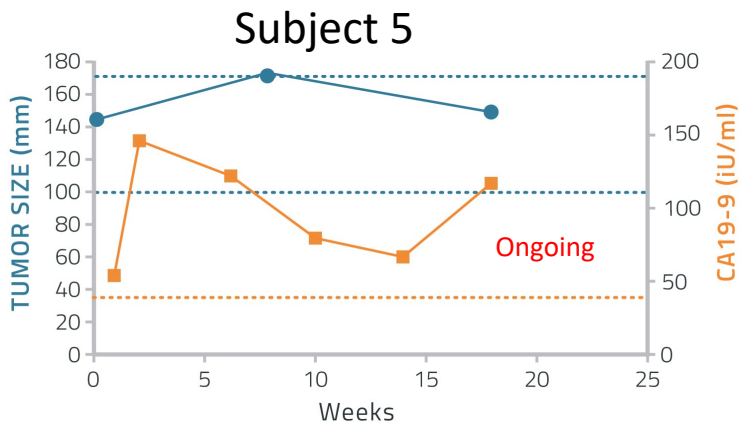
- All presented PD at 1st CT scan evaluation (8 weeks)
- All showed concomitant reduction of CA19-9



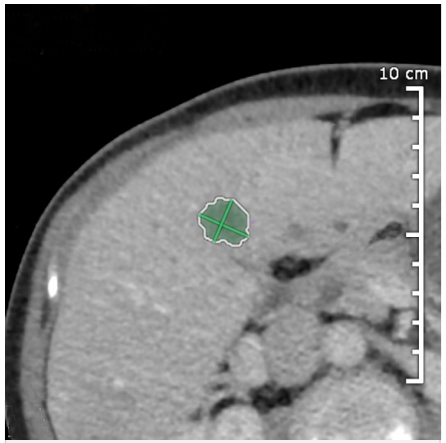



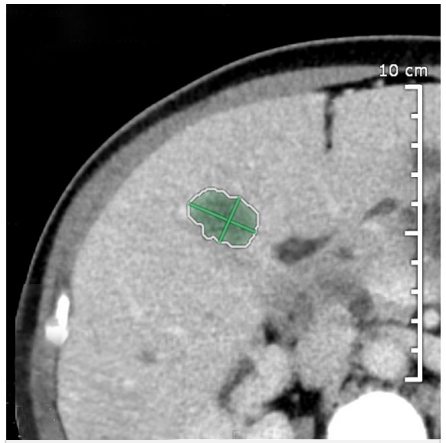



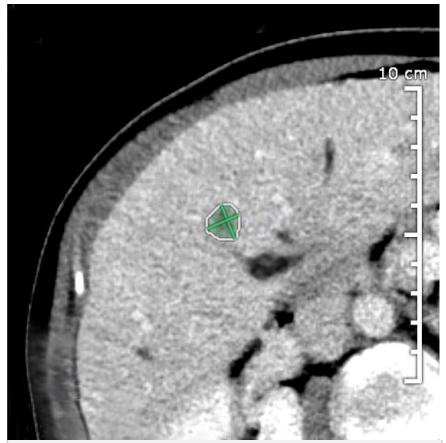
# Liver metastases evolution subject 1



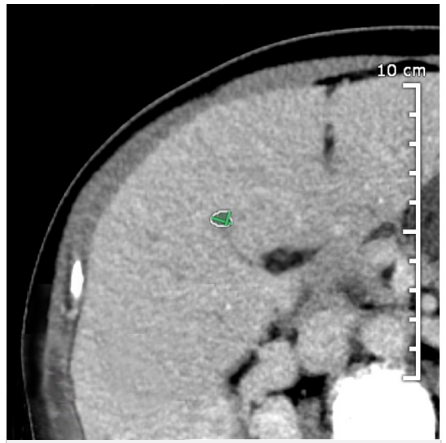

**Screening**
Target lesions



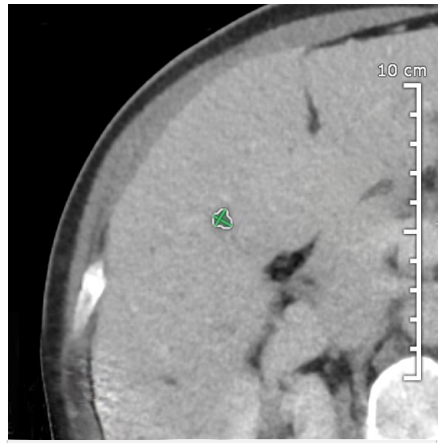

**2 months**
+32% (PD/iUPD)



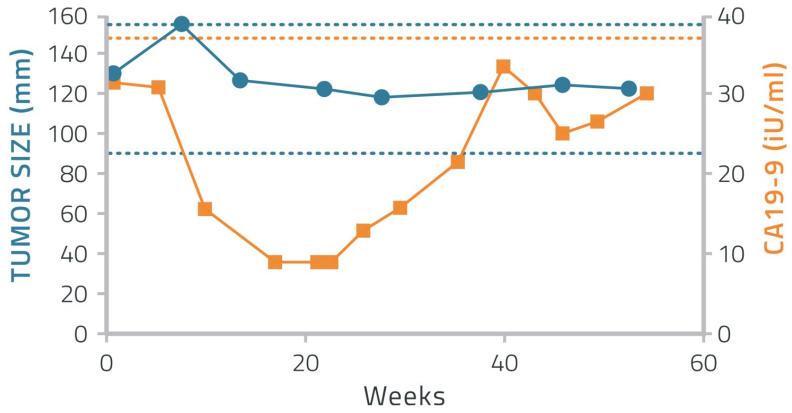

**3 months**
-35% (iPR)




**7 months**
-56% (iPR)

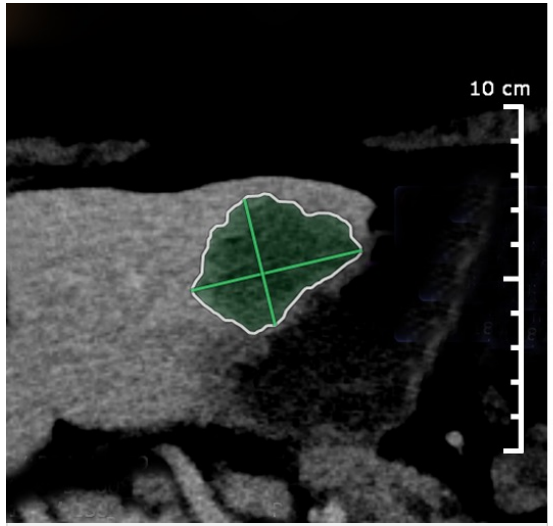



**12 months**
-62% (iPR)

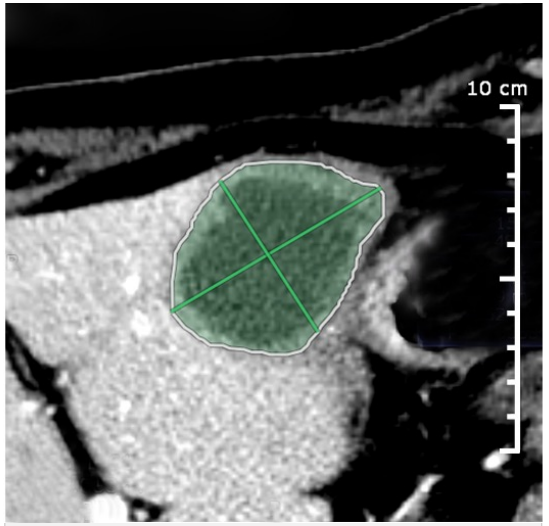



PD= progressive disease
iUPD= unconfirmed progressive disease by iRECIST
iPR= immune partial response by iRECIST

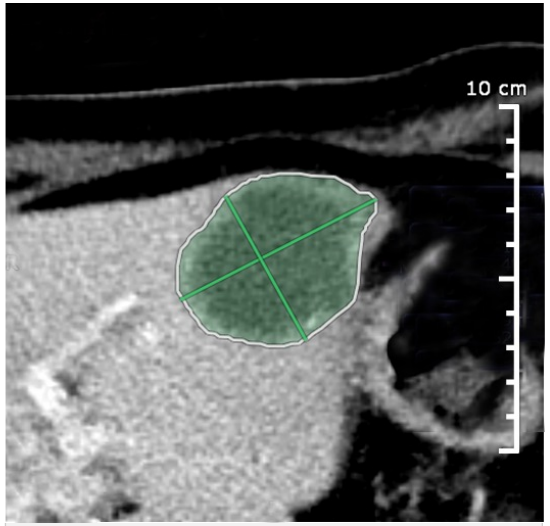
# Liver metastases evolution subject 2



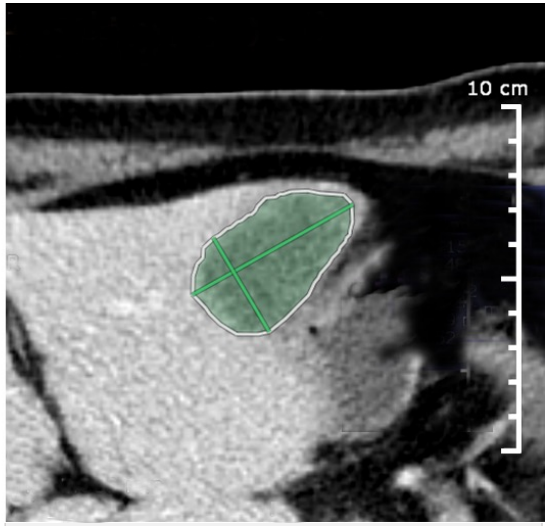

**Screening**
Target lesions



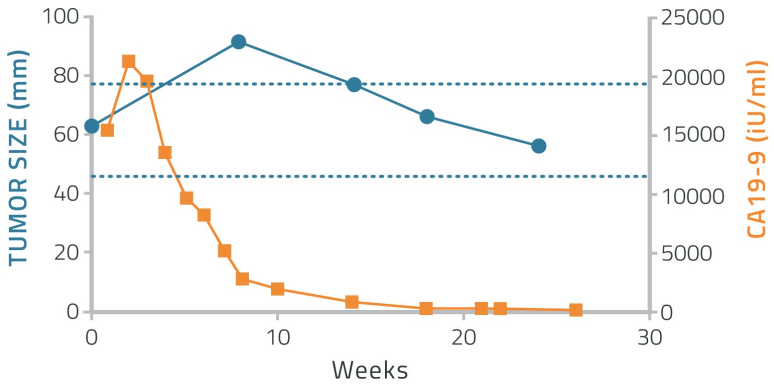

**2 months**
+25% (PD/iUPD)




**4 months**
+14% (iSD)




**5 months**
0% (iSD)




PD= progressive disease
iUPD= unconfirmed progressive disease by iRECIST
iSD= immune stable disease by iRECIST

# PDAC response parameters and benchmark

| Response parameter | CANFOUR (N=33) | Reference (von Hoff; Fernández) |
|---|---|---|
| **ORR per investigator** | 27 % (9 PR) | 29% (95%CI: 25-34) |
| **Pseudoprogression iRECIST** | 15% | 0% |
| **Disease control rate (PR+SD+ iRECIST iUPD/iSD)** | 72% | 48% (95% CI: 43-53) |
| **Median duration of response** | 6.8 months (range 1.9 to 13.8) | 3.5 months |

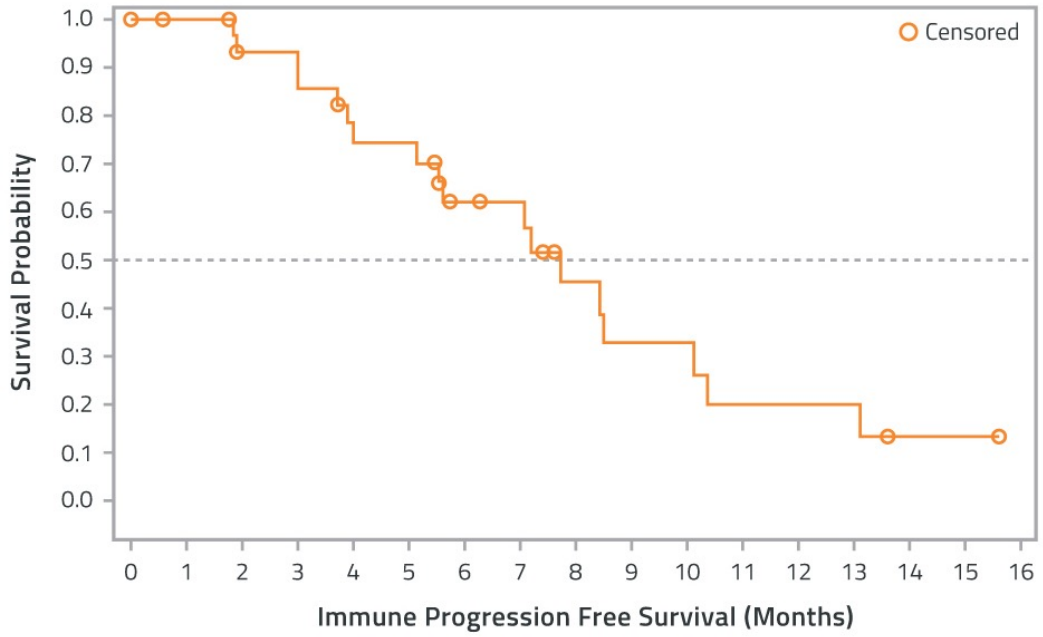
**Note 7/33 pts still being treated at cutoff date (20 April 2021)**

- von Hoff et al, 2013; Fernández et al, 2018. Data from gemcitabine/nab-paclitaxel arm only


31

# Progression Free Survival by iRECIST

- Median iPFS is 7.8 months (95% CI 5.2 to 10.2) with 55% of events. iPFS range 0 to 15.6 months
  - iPFS rate at 6 months: 62%; at 1 year: 19%
  - Seven patients at cut-off are still receiving treatment.

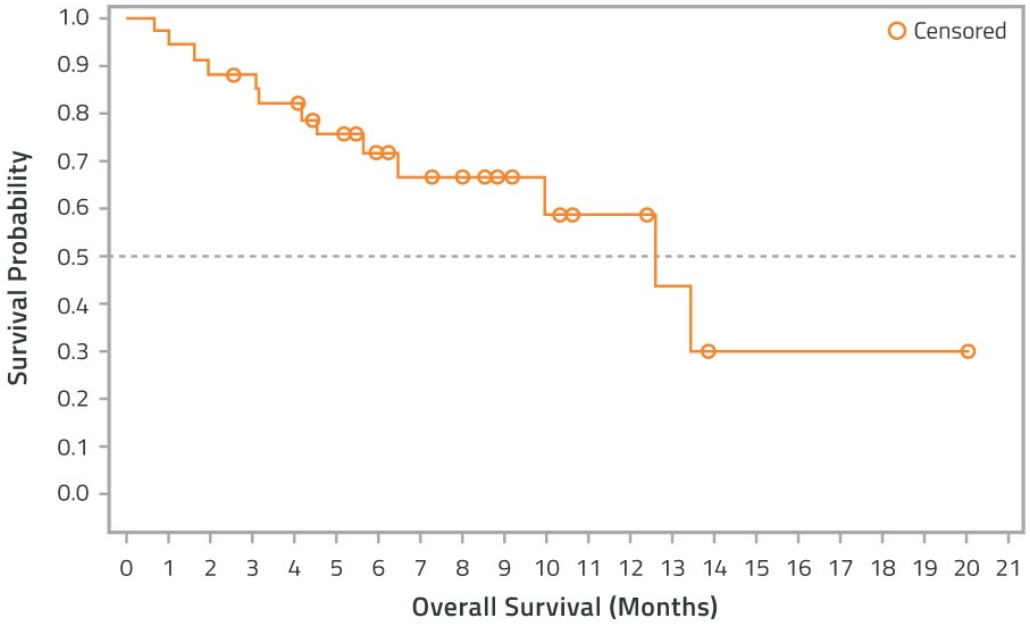



**The observed iPFS is longer than expected from chemotherapy alone**


32

# Overall Survival

- Median OS is 12.6 months (95% CI not estimable) with 42% of OS events.
- 6-month survival rate: 71%, 1-year survival rate: 55%
- Data needs further maturation before firm conclusions




**Early survival data compare favourable to benchmark, but needs longer follow up**


33

# PDAC efficacy parameters and benchmark

| Efficacy parameter | CANFOUR (N=33) | MPACT trial* (N=431) |
|---|---|---|
| **Median iPFS (iRECIST)/PFS (RECIST1.1)** | Median iPFS 7.8 mo [95%CI: 5.2-10.2]<br>iPFS at 6 months: 62% | Median PFS: 5.5 mo (95% CI: 4.5-5.9)<br>PFS at 6 months: 44% |
| **Mean duration of treatment** | 4.8 months | 3.9 months |
| **Overall survival (OS)** | Median OS 12.6 mo [95% CI not estimable]<br>1-year survival 55%. | Median OS 8.5 mo [95%CI: 7.9 to 9.5)<br>1-year survival 35%. |

**Note 7/33 pts still being treated at cutoff date (20 April 2021)**

- von Hoff et al, 2013; Data from gemcitabine/nab-paclitaxel arm only

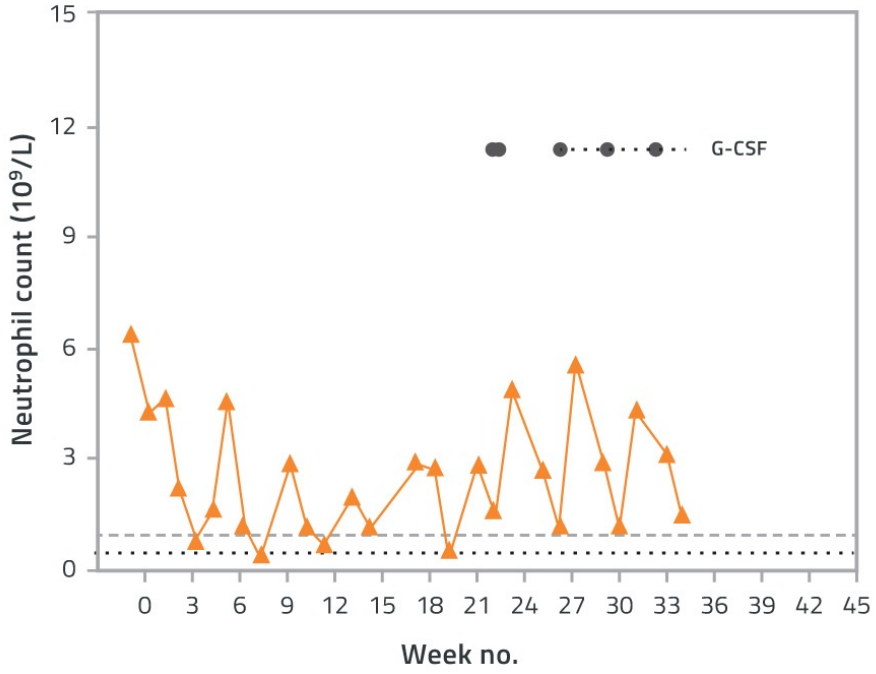

34

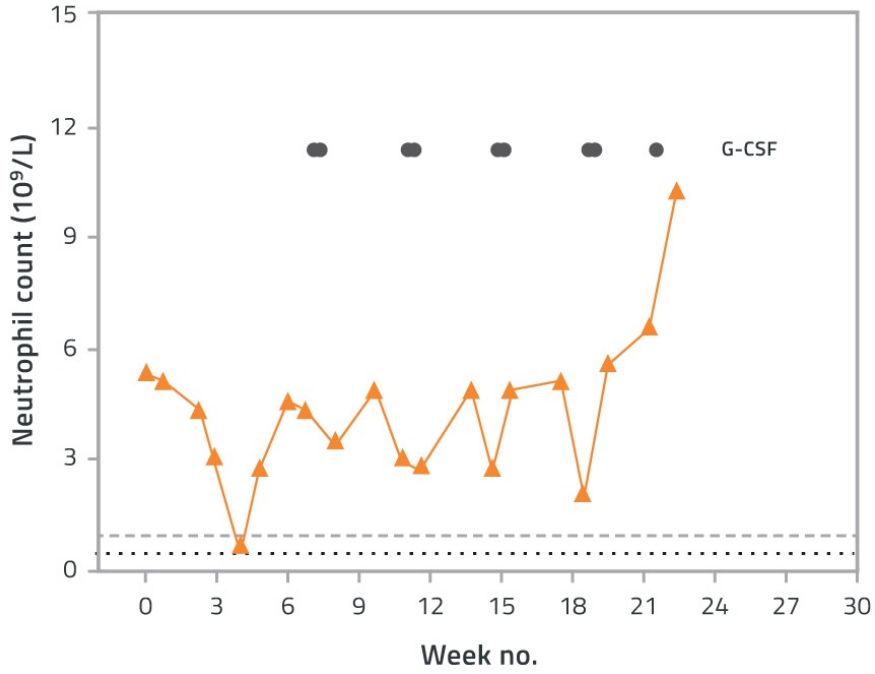
# Nadunolimab/GN in PDAC safety summary

- Only infusion related reaction (IRR) and neutropenia are considered nadunolimab safety findings.
- Both reflect pharmacodynamic effects of nadunolimab.
- Infusion Related Reactions:
  - IRR in 16/36 (44%) of the patients. Mild in 38% and moderate in 56% of these. Only 1 patient had a severe (Grade 3) reaction.
  - Managed with premedication and a prolonged 1$^{st}$ infusion.
- Neutropenia and febrile neutropenia:
  - Grade 3/4 neutropenia in 67% of the patients and Grade 3 febrile neutropenia in 17%
  - It can be prevented and managed with G-CSF and dose reductions.

# G-CSF is effective for neutropenia prevention

- There is greater than expected frequency of neutropenia and febrile neutropenia with the addition of CAN04
- G-CSF accelerates recovery and seems to be effective at preventing future episodes.




For patients currently treated, G-CSF is used proactively to counteract neutropenia

# CAN04/GN in PDAC safety summary and benchmark

| Grade 3 or higher AEs | Gem/Abraxane (von Hoff) N=421 | CANFOUR CAN04/GN N=36 | FOLFIRINOX (Conroy 2011) N=171 |
|---|---|---|---|
| Neutropenia | 38% | 67% | 46% |
| Febrile neutropenia | 3% | 17% | 5% |
| Thrombocytopenia | 13% | 19% | 9% |
| Anemia | 13% | 14% | 8% |
| Fatigue | 17% | 6% | 24% |
| Peripheral neuropathy | 17% | 0% | 9% |
| Diarrhea | 6% | 3% | 13% |
| Elevated ALT | ND | 3% | 7% |
| IRR | ND | 3% | ND |

The beneficial effect in fatigue and chemotherapy-induced neuropathy[2] (nab-paclitaxel or oxaliplatin) can be mediated by IL-1 blockade.

[1] Al-Mazidi et al. Eur J Pain, 2018

# Conclusions

- Adding nadunolimab to gemcitabine/nab-paclitaxel in first line treatment of metastatic PDAC:
  - Promising efficacy:
  - Long duration of response
  - Identification of a pseudoprogression-like phenomena that predicts longer treatment benefit
  - Emerging PFS and OS seems to be better than historical controls
- Manageable safety:
  - Neutropenia can be managed with G-CSF and GN dose modifications
  - Mild/moderate infusion related reactions during first infusion that are manageable same as other commercialized drugs.
  - Notably decreased levels of fatigue and nab-paclitaxel neuropathy

- Combination should be advanced towards randomized trial to verify effects.

# Therapeutic Opportunities in Pancreatic Cancer

Manuel Hidalgo, M.D., Ph.D.

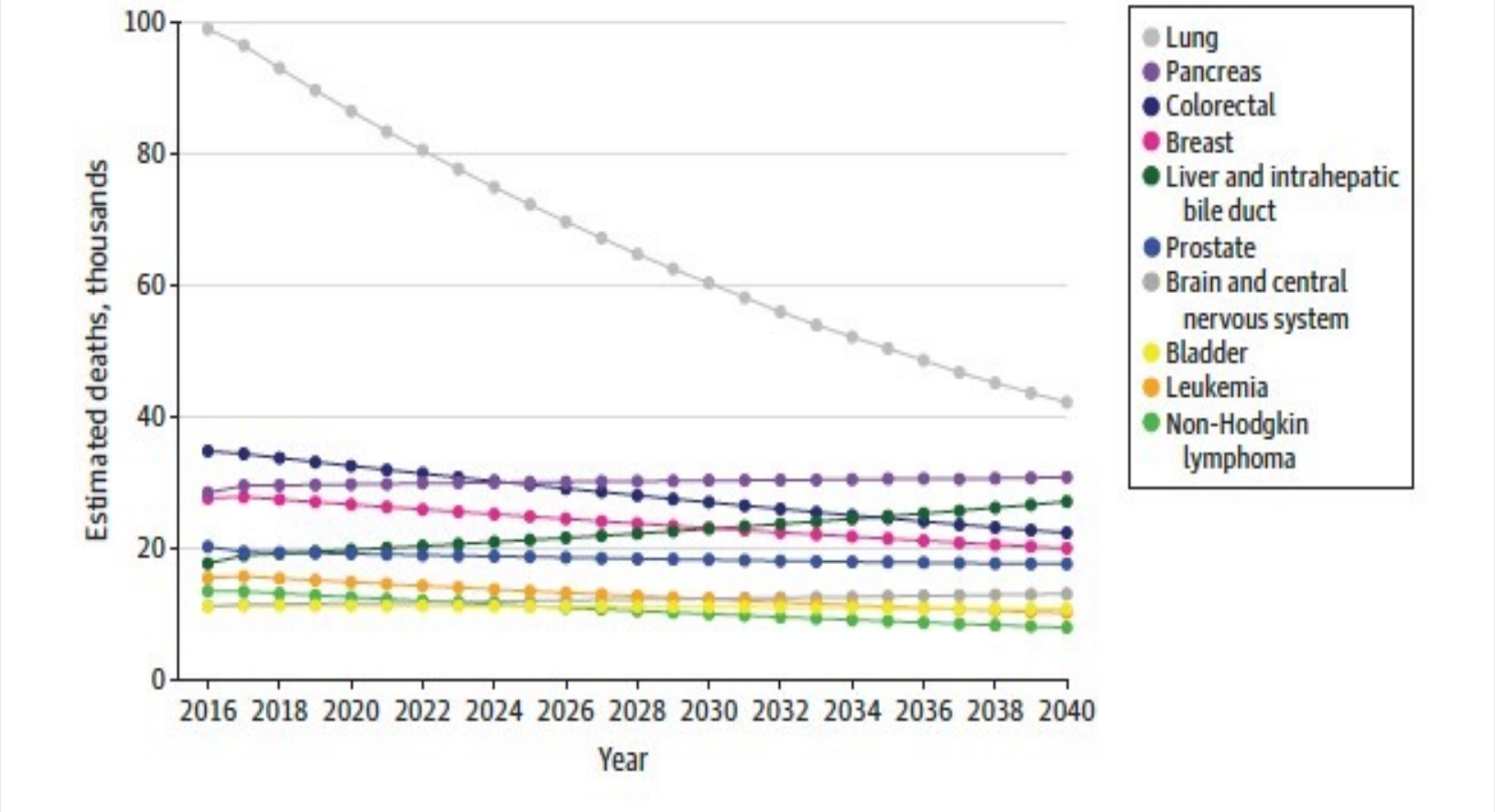
Weill Cornell Medicine

NewYork-Presbyterian

# COI Disclosure

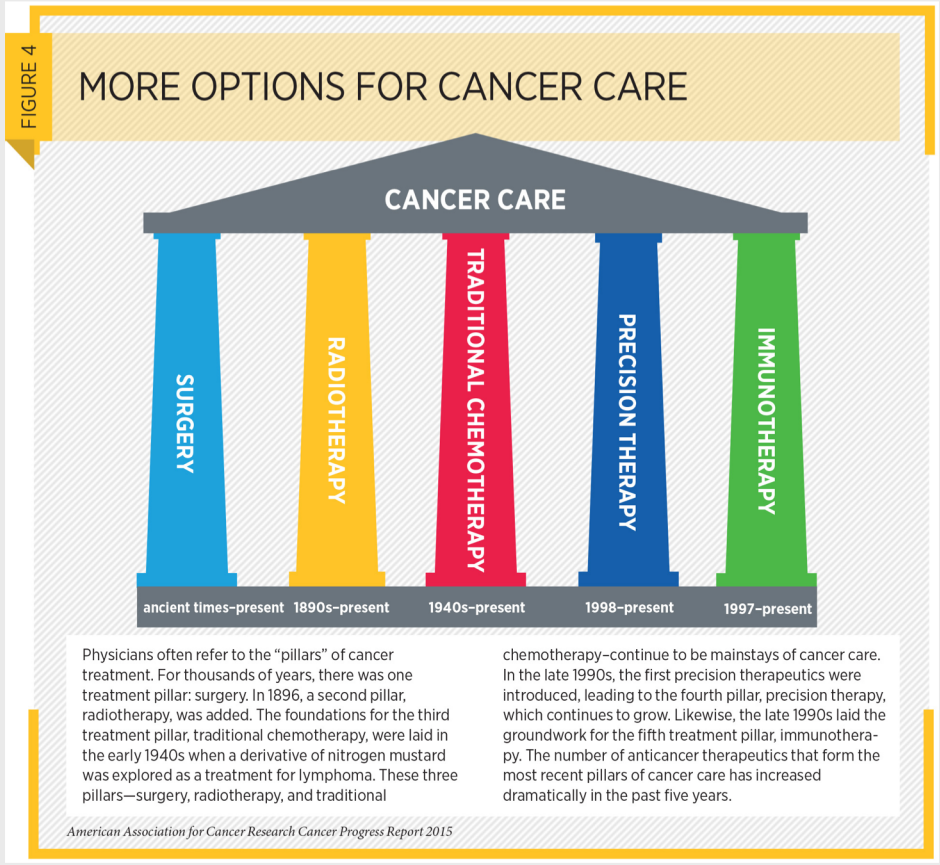
- **Board of Directors**
  - BMS
- **Founder:**
  - Champions Oncology, Nelum Pharmaceuticals
- **Stock holder:**
  - Champions Oncology, Agenus, Nelum Pharmaceuticals, Highlight Pharmaceuticals, Oncomatrix, Inxmed, Pharmacyte, BMS.
- **Research support:**
  - Erytech, PanCan, TBA alliance
- **Honorarium:**
  - Agenus, Oncomatrix, Inxmed, Khar, Genechem, Cantargia, BMS
- **Royalties:**
  - Myriad, Kahr

# The Problem

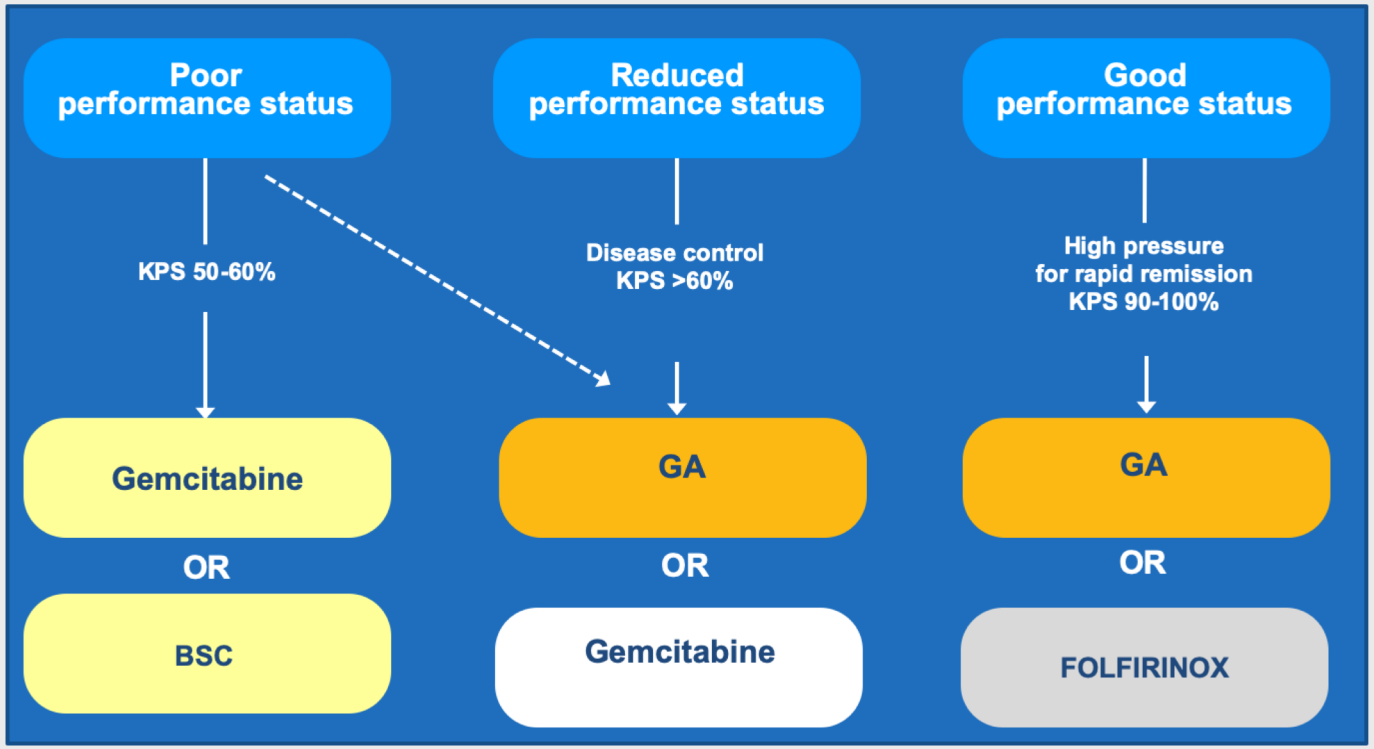



Rahib et al, JAMA Net 2014

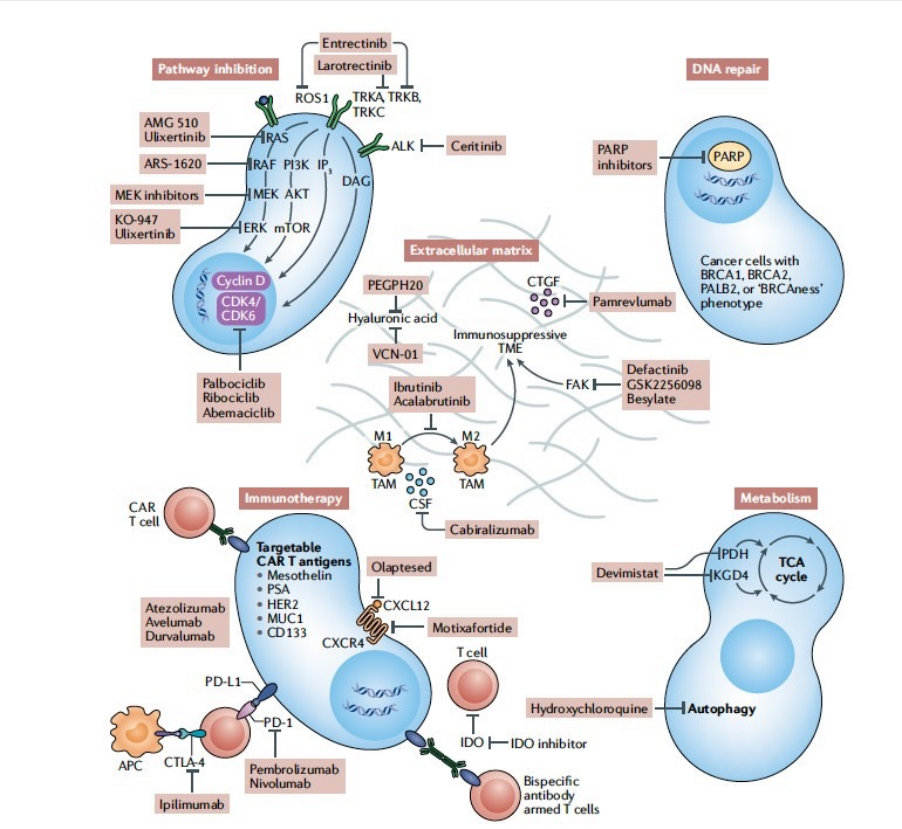
# Pillars of Cancer Treatment



# Stage IV Management Algorithm



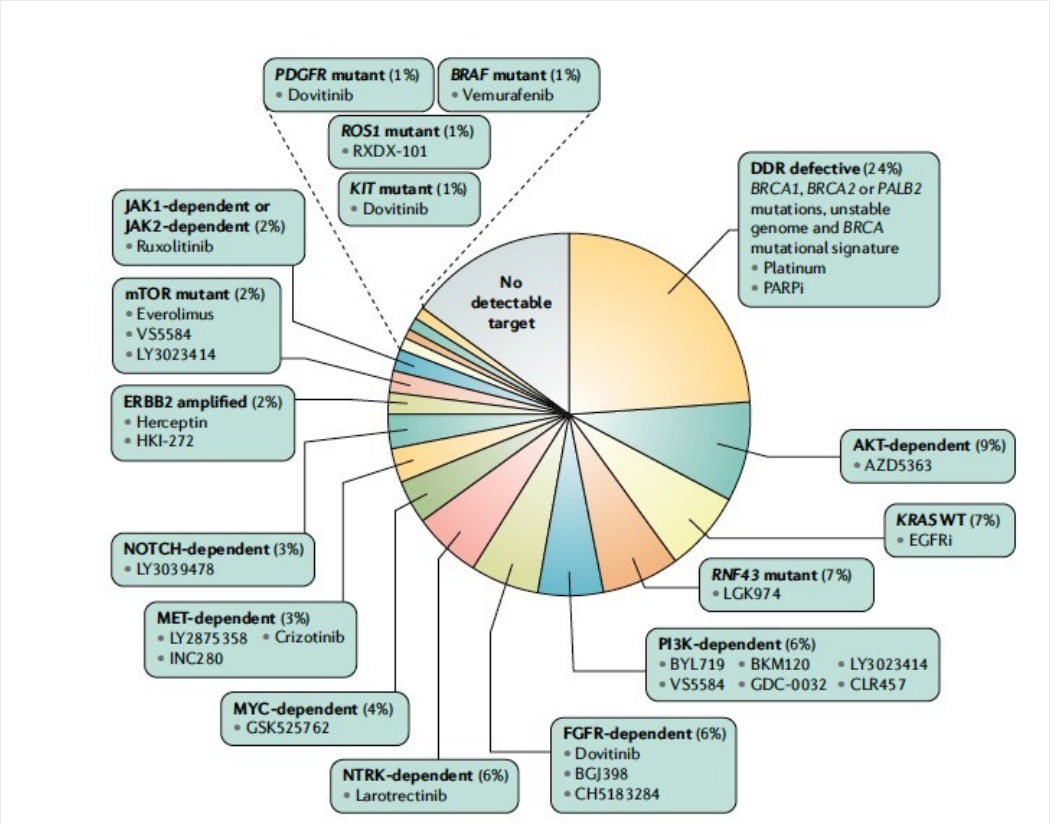
# Selected Agents in Development




Nevala Plagemann et al, Nat Can Rev 2019

# PDAC Genetics

# Putative Targets and Inhibitors



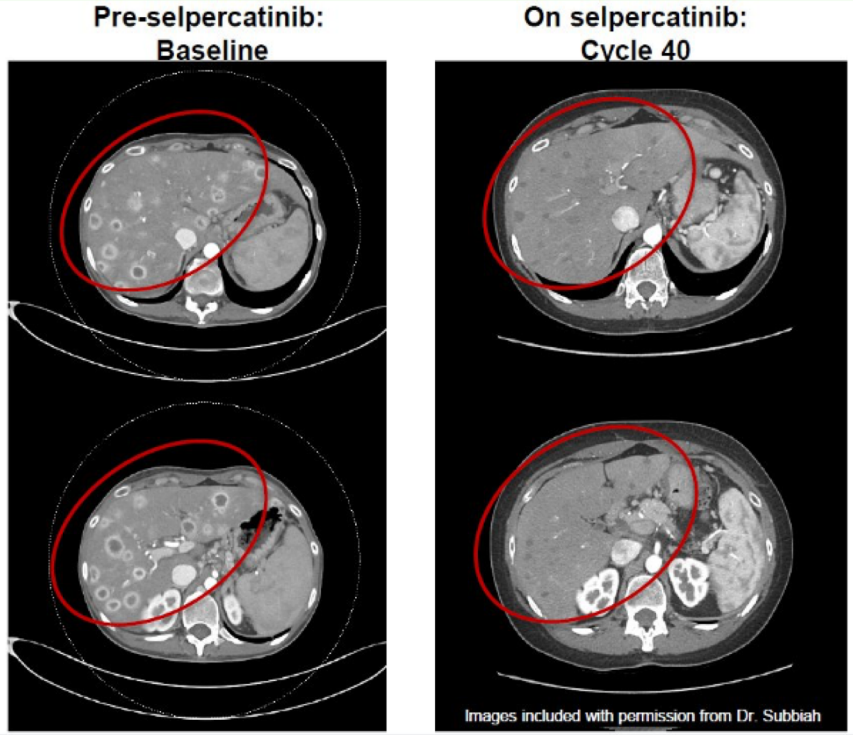

Collisson et al, Nat Can Rev 2019

# Example of Precision Medicine

## Case Study: 31-year-old Woman with Pancreatic Cancer

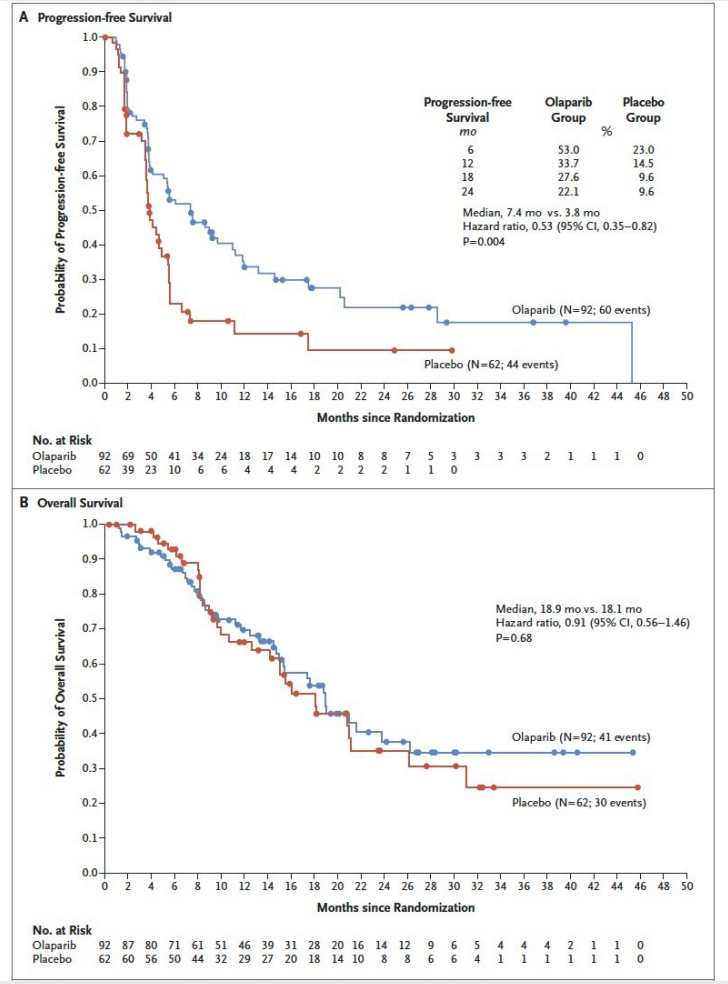
AACR American Association for Cancer Research
FINDING CURES TOGETHER

- Pancreatic metastatic ductal adenocarcinoma:
  - *PRKAR1A-RET* fusion
  - Microsatellite stable
  - *KRAS/BRAF* wildtype
- Prior therapy:
  - FOLFIRINOX/FOLFIRI, 6 months
  - Discontinued due to PD
- Selpercatinib started:
  - Partial response (-51%)
  - Manageable low-grade AEs
  - Response ongoing at 37 months



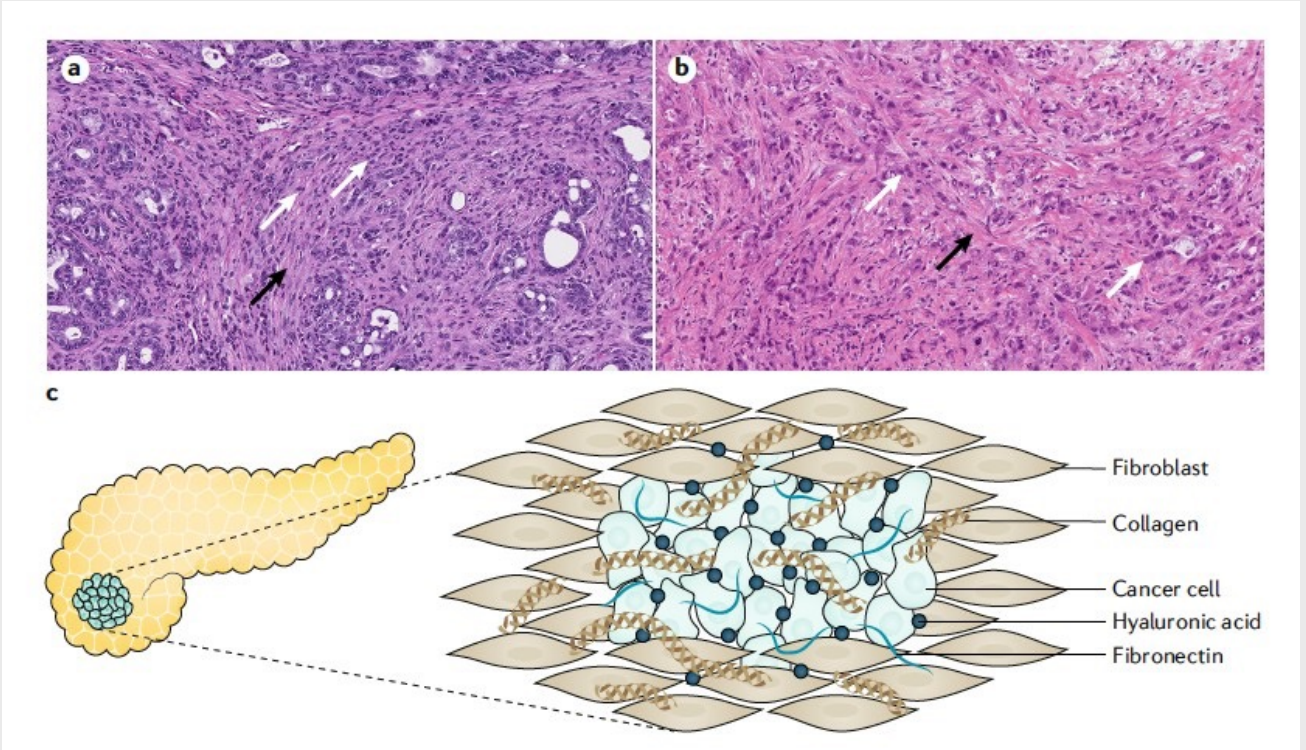

**AACR ANNUAL MEETING 2021:** APRIL 10-15, 2021 AND MAY 17-21, 2021

# Olaparib in BRCA mut PDAC



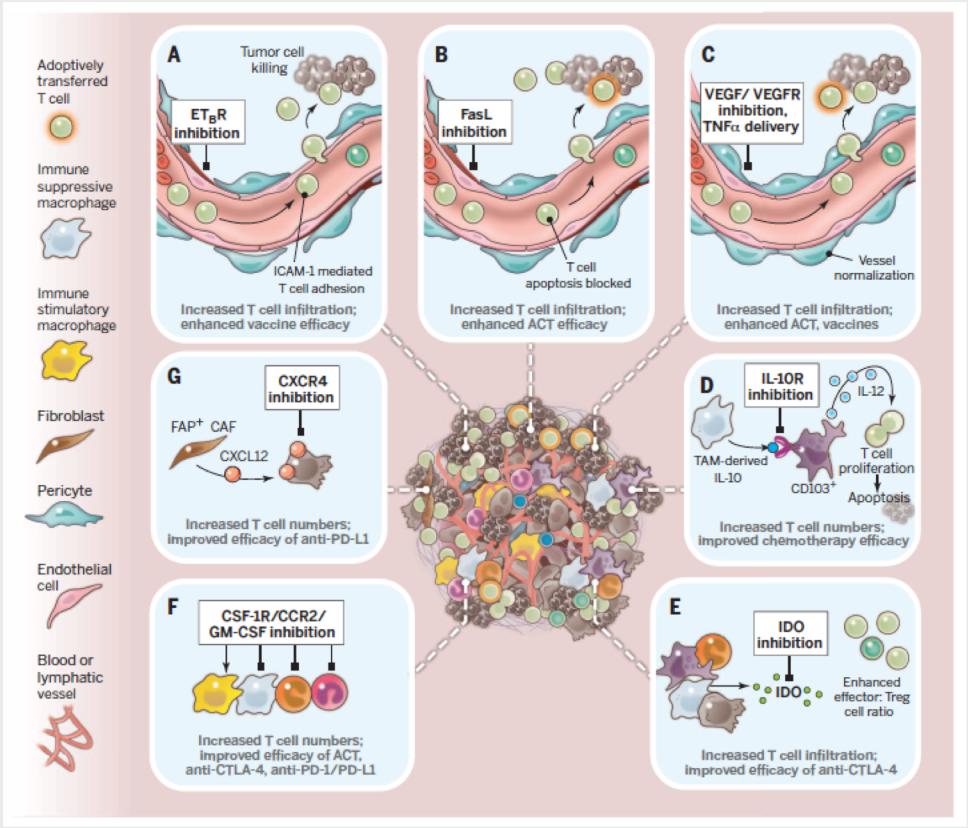

Golan et al, NEJM 2019

# PDAC TME



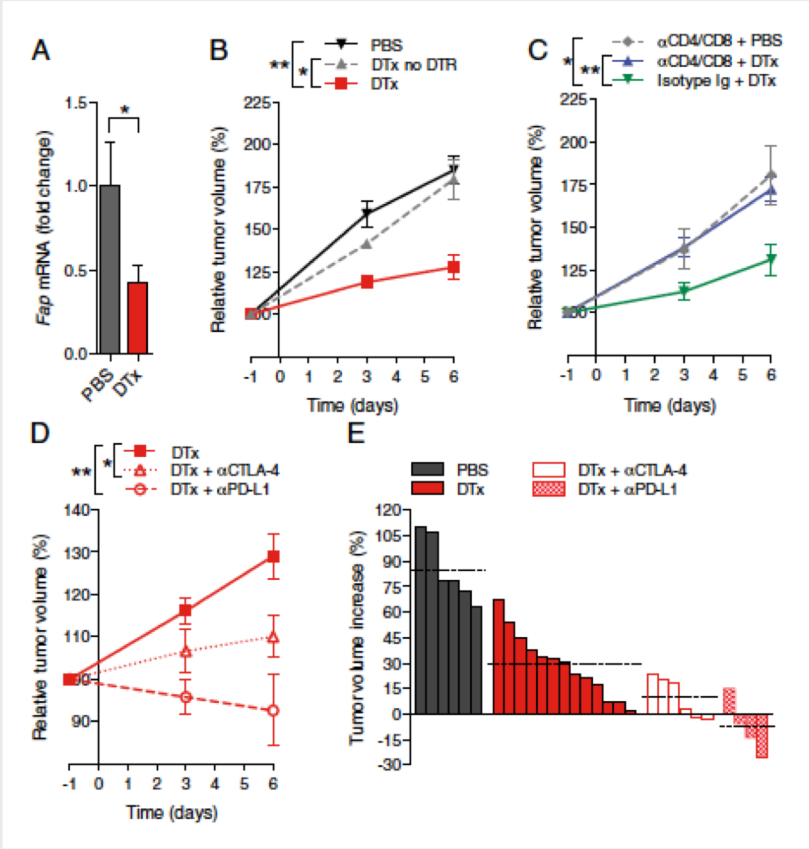

Hosein et al, Nat Rev Gastroenterology and Hepatology 2020

# IO in PDAC



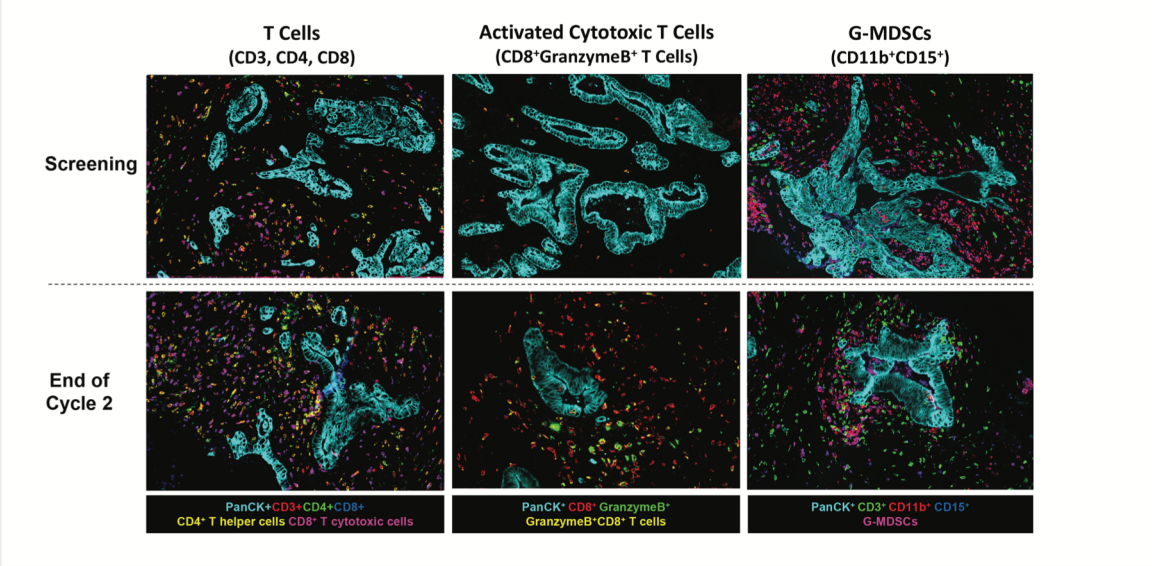

Joyce at al, Science 2015

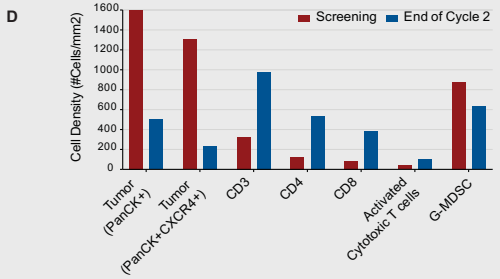
# Depletion of FAP+ Cells and Immune Response




Joyce at al, Science 2015

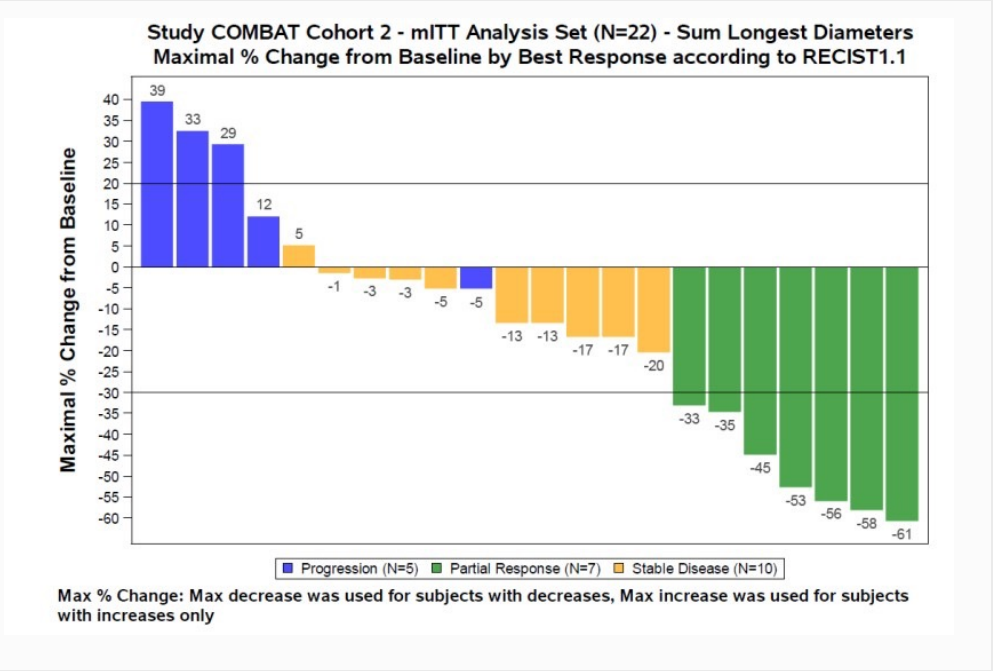
# Effects on T cell Infiltrate in Tumor Tissues




Bockorny et et al, Nat Med 2020

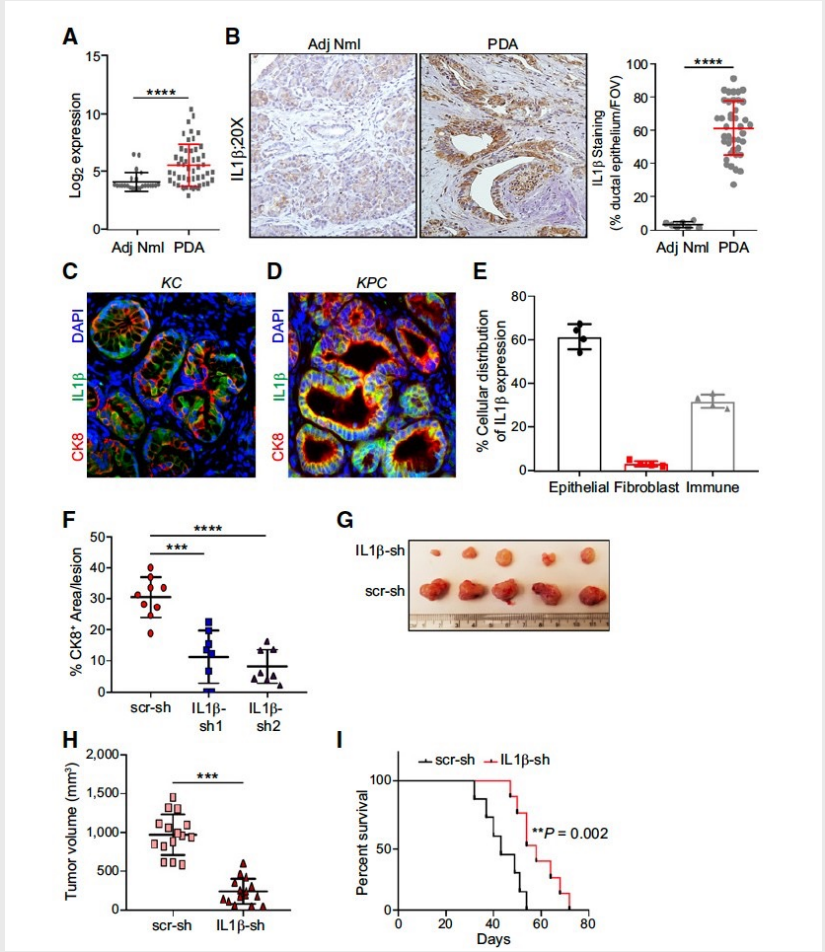
# Responses Water Fall Plot




| | N | % |
|---|---|---|
| Evaluable patients | 22 | 100% |
| ORR | 7 | 32% |
| DCR (PR + SD) | 17 | 77% |
| PR | 7 | 32% |
| SD | 10 | 45% |

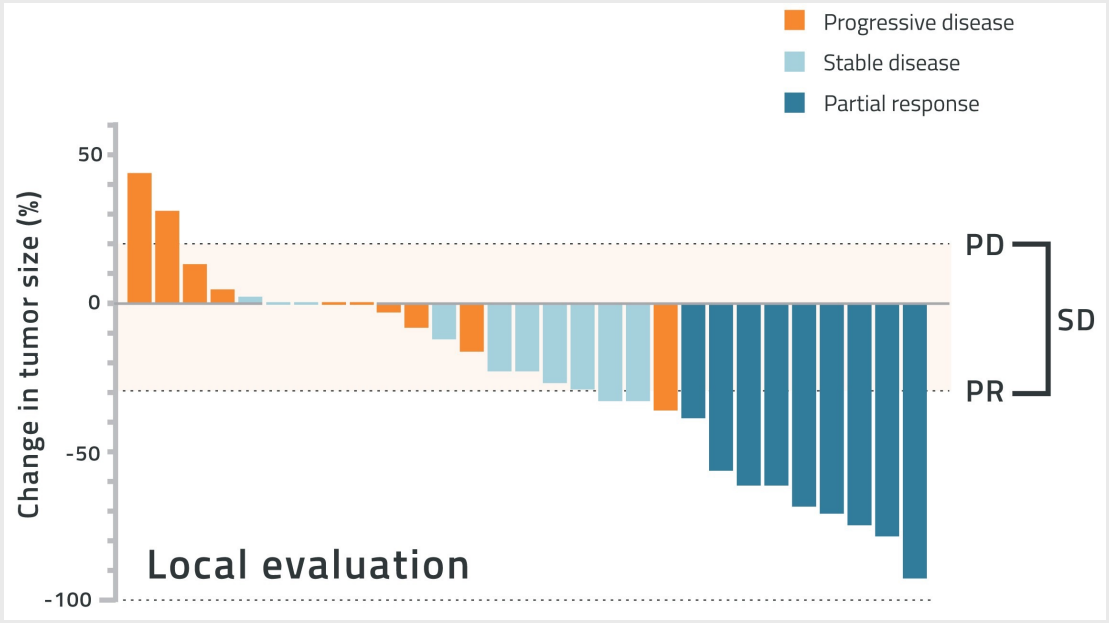
Bockorny et et al, Nat Med 2020

# Tumor cell-derive IL1 in PDAC




Das et et al, Can Res 2021

# Evaluation of tumor shrinkage by the investigator

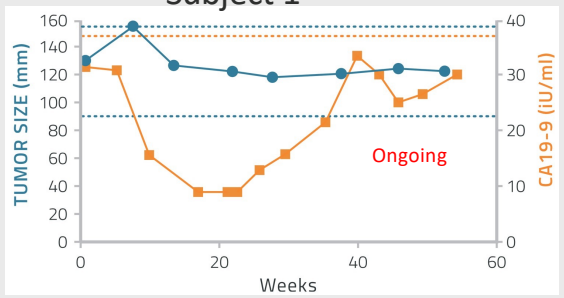



- Waterfall plot is based on largest percentage tumor shrinkage (target lesions) and best overall response during study
- PD is >20% increase vs baseline and PR is >30% tumor shrinkage.
- Central review ongoing
  - 1CR
  - 7PR (incl 1 unconfirmed CR)
  - 3PR awaiting confirmatory scan

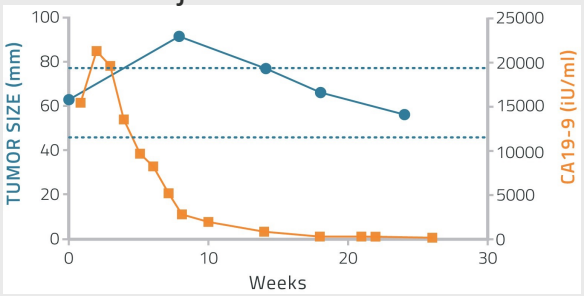
# Patients with Pseudoprogression-like response

- All presented PD at 1st CT scan evaluation (8 weeks)
- All showed concomitant reduction of CA19-9

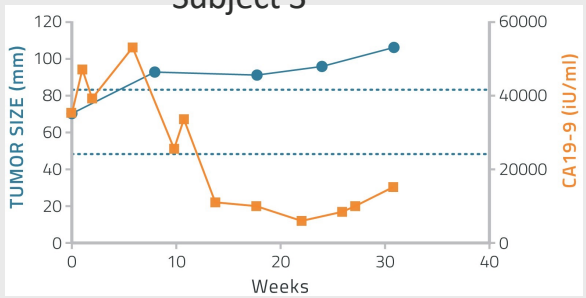
Subject 1



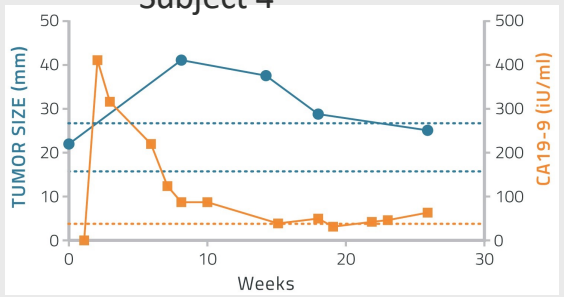

Subject 2



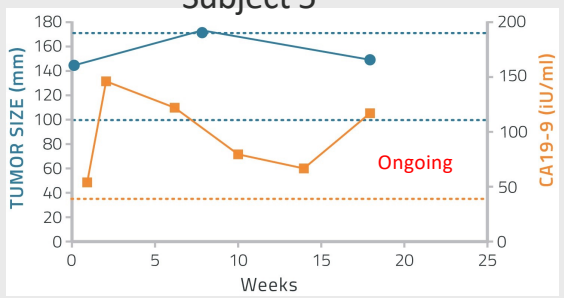

Subject 3



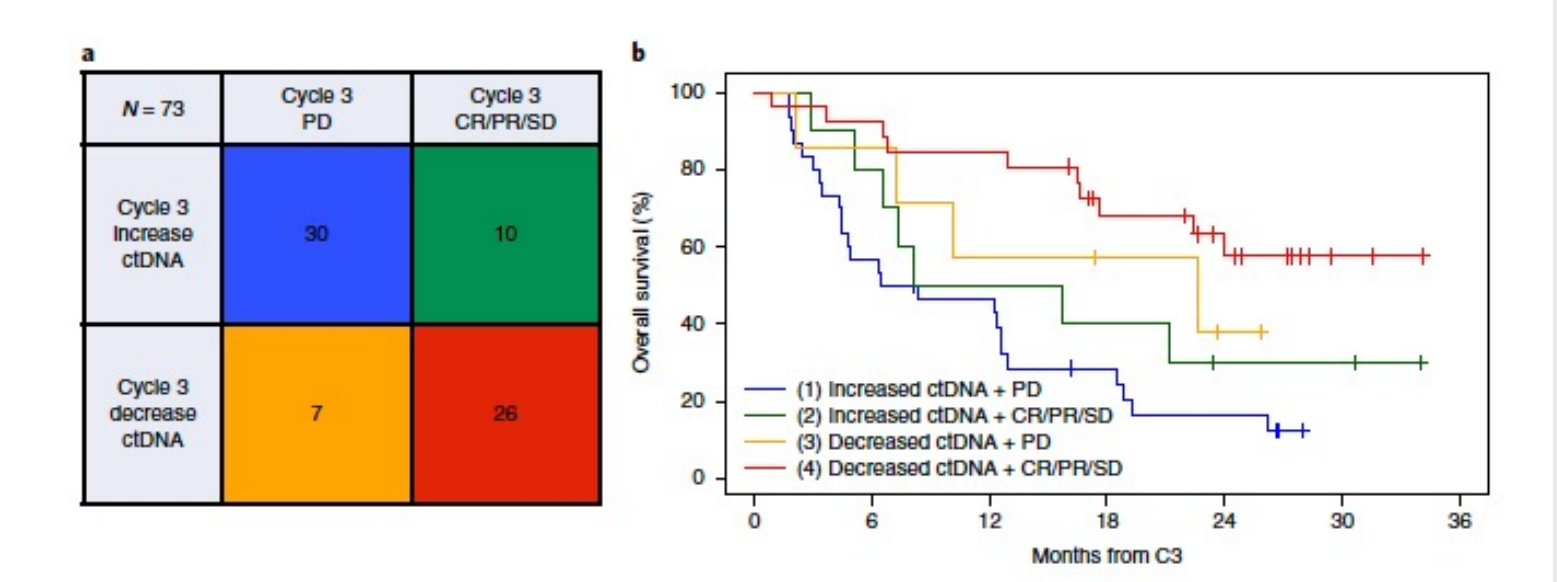

Subject 4




Subject 5

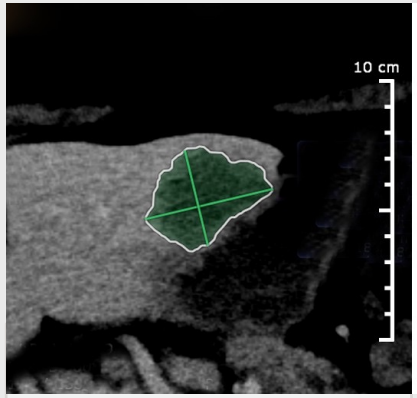


# Monitoring Pseudoprogression

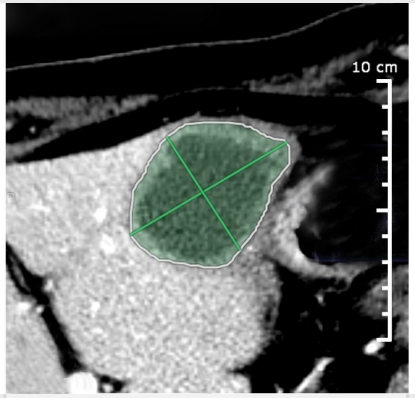



Bratman et et al, Can Res 2021

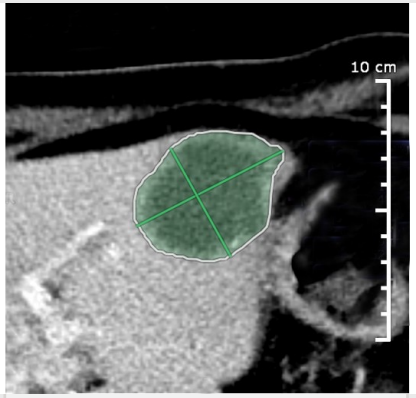
# Liver metastases evolution subject 2



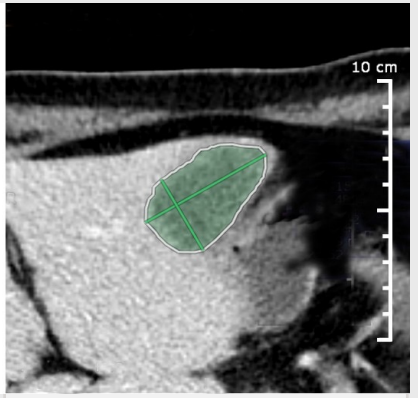

**Screening**
Target lesions



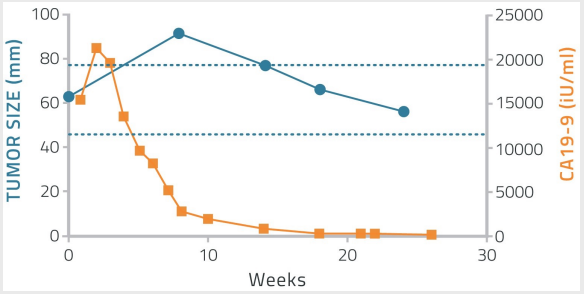

**2 months**
+25% (PD/iUPD)




**4 months**
+14% (iSD)




**5 months**
0% (iSD)




PD= progressive disease
iUPD= unconfirmed progressive disease by iRECIST
iSD= immune stable disease by iRECIST

Weill Cornell Medicine

NewYork-Presbyterian


# Nadunolimab, ongoing and upcoming clinical trials

Ignacio Garcia-Ribas, CMO

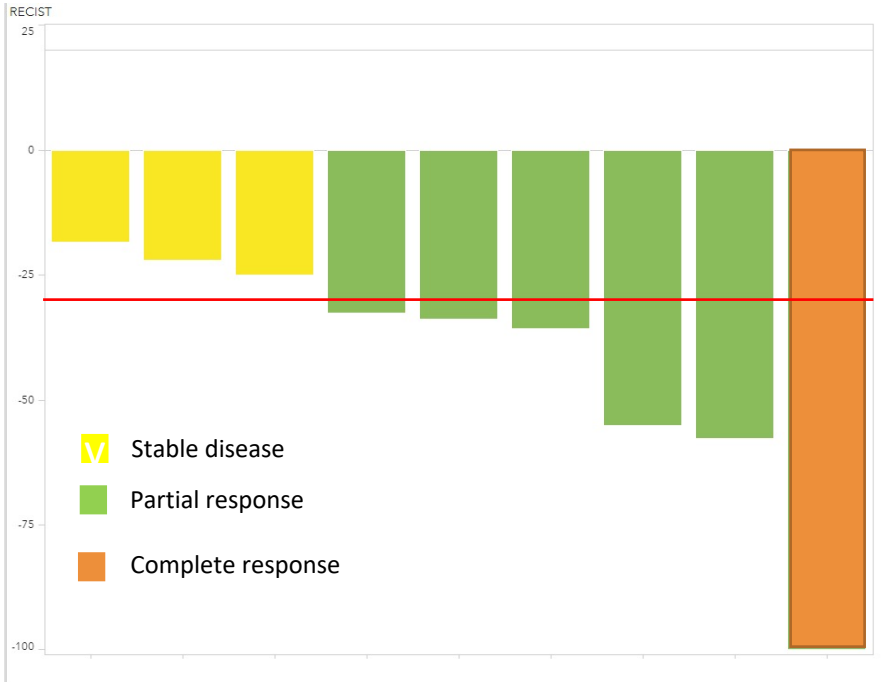
# Nadunolimab PDAC highlights

- Nadunolimab appears to increase the efficacy of gemcitabine and nab-paclitaxel (Abraxane®) in patients with metastatic PDAC.
- Several patients benefit with durable responses or pseudoprogression (benefit after initial disease progression). These patient populations contribute to a positive impact in progression free survival that may be translated in improved survival.
- This is the first time pseudoprogression has been described in PDAC and it is a distinctive feature of nadunolimab.
- The new clinical results fit well with a chemosensitization mechanism as observed in animal models.
- On the safety side, infusion related reactions and neutropenia are the identified toxicities of CAN04 with chemotherapy. Neutropenia can be effectively prevented with G-CSF and dose modifications.
- Nadunolimab may be beneficial in preventing/delaying nab-paclitaxel neuropathy and cancer-related fatigue.

# Nadunolimab clinical development status

| Study | Indication | CAN04 combination | Status | Planned milestone(s) |
|---|---|---|---|---|
| **CANFOUR** | NSCLC | Gemcitabine/cisplatin | Recruitment ongoing, | Results planned for Q3 2021 |
| **CANFOUR** | PDAC | Gemcitabine/nab-paclitaxel | Extension phase ongoing.<br>(Dosing schedule, lower doses, G-CSF) | Main study results presented 20 May<br>LPI extension phase expected Q3 2021 |
| **CIRIFOUR** | NSCLC, HNSCC, melanoma, bladder cancer | Pembrolizumab | Recruitment ongoing | LPI Q3 2021<br>Results H2 2021 |
| - | PDAC | mFOLFIRINOX | Regulatory review ongoing | FPI Q2 2021 |
| - | Triple negative breast cancer | Gemcitabine/carboplatin | Preparation together with GEICAM. | Submission Q2 |
| - | Colorectal cancer | mFOLFOX | Preparation | Submission Q2 |
| - | Biliary tract cancer | Gemcitabine/cisplatin | Preparation | Submission Q2 |
| - | NSCLC | Docetaxel | Preparation | Submission Q2 |

# CANFOUR: Tumor shrinkage – NSCLC combination




CAN04/GC. Maximal target lesion reduction versus baseline

- CAN04 in combination with gem/cis in 1st line chemotherapy
- Press release September 2020: 6 of 9 evaluable patients with metastatic non-small cell lung cancer (NSCLC) showed objective response including 1 complete response (67% vs historical control data 22–28%)
- The complete response has lasted more than 1 year
- 5 patients were second line to pembrolizumab monotherapy, 4 patients first line
- No major side effects observed except those from chemotherapy or CAN04 alone. *Neutropenia frequency higher than expected from chemo (treated with dose reductions/GCSF*

**POSITIVE INTERIM DATA, RECRUITMENT CONTINUE FOR PRIMARY ANALYSIS**
**BROADENING OF NSCLC DEVELOPMENT INTO ADDITIONAL MARKET SEGMENTS**

# CIRIFOUR: US Phase I clinical trial

- First patient started 2020. Enrollment according to plan, results expected H2.
- Combination with checkpoint inhibitor in patients no longer responding to PD1/PDL-1 therapy.
  - Investigating the safety of the combination
  - Exploring CAN04 as immune-oncology drug
  - Building block for the development of platinum doublet/pembro/CAN04
- Primary endpoint safety, secondary endpoints include biomarkers and efficacy
- Indications include NSCLC, HNSCC, malignant melanoma and bladder cancer (up to 18 patients).
- Strong US centres, Coord investigator Prof Roger Cohen, UPenn
- https://clinicaltrials.gov/ct2/show/NCT04452214

**TRIAL DESIGNED TO ADVANCE NADUNOLIMAB OUTSIDE CHEMOTHERAPY COMBINATIONS**
**IMPORTANT STEP FOR COMBINING CAN04 WITH IO AND CHEMOTHERAPY, E.G. IN NSCLC**

# Nadunolimab clinical trials to be started

→ **First line combination with modified FOLFIRINOX in pancreatic cancer**

- Up to 30 patients, initial dose escalation followed by dose expansion
- Approximately 9 centres in France and Spain
- First patient planned June 2021

→ **“Basket trial” in new indications and combinations**

- Including NSCLC (docetaxel), CRC (mFOLFOX) and biliary tract cancer (gemcitabine/cisplatin)
- Protocol submission planned Q2 2021
- Performed in Europe

→ **CAN04 in triple negative breast cancer**

- In combination with gemcitabine/carboplatin
- In collaboration with the Spanish Breast Cancer Group (GEICAM)

**TRIALS DESIGNED TO EXPAND THE CHEMOSENSITIZATION HYPOTHESIS**

# Rationale for the novel indications/combinations (1)

**Colorectal cancer:**

- → 3rd most common tumor, incidence 150.000 per year USA.
- → Oxaliplatin is a cornerstone in CRC. Immunotherapy doesn't work in 90% of CRC.
- → Potential clinical synergy of CAN04 with oxaliplatin
- → IL-1β is required for macrophages to promote growth and support survival of colon cancer cells[1]. Thus, CAN04, may reduce tumor inflammation and tumor progression

**Biliary tract cancer (BTC)**

- → Less common cancer, incidence 12.000 per year USA
- → Standard first line is gemcitabine and cisplatin: right spot for assessing CAN04[3]
- → CPIs do not work. Recently isocitrate dehydrogenase (IDH) inhibitor has been approved for IDH-mutant intrahepatic cholangiocarcinoma (10% BTC)
- → Several exploratory studies report a promoting role of exogenous IL-1β on the proliferation and migration of gallbladder cancer cell lines and the importance of IL1 pathway[2]

[1] Kaler P, et al. Oncogene 2009. [2] Guo R, et al. Oncol Lett 2016. [3] Vallle JW, et al. Ann Oncol 2016

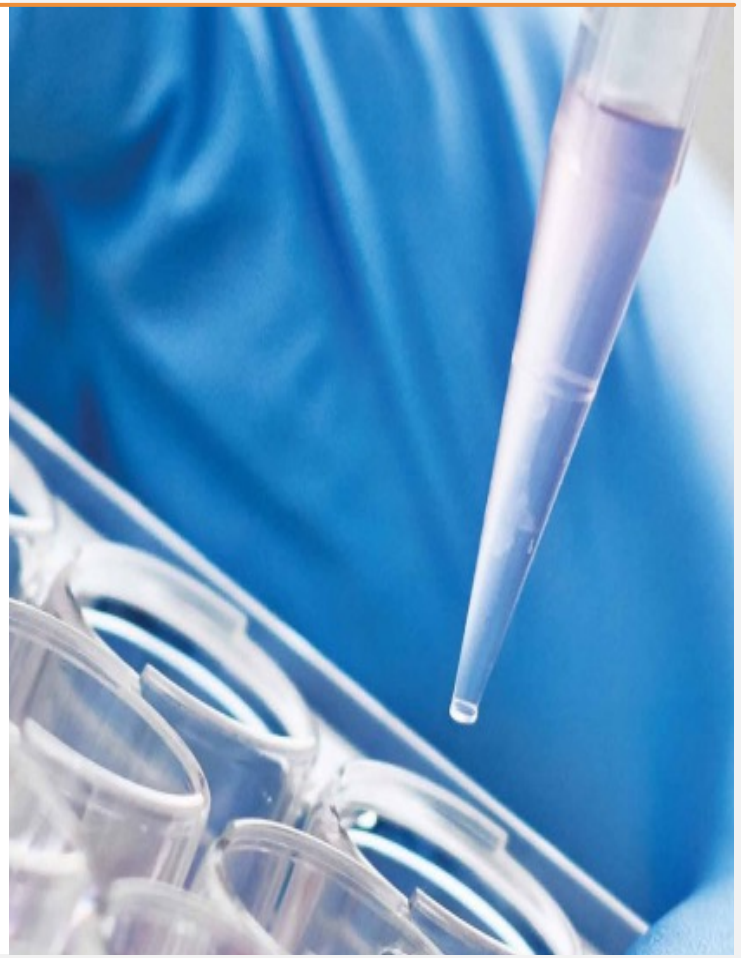
# Rationale for the novel indications/combinations (2)

**NSCLC**

- Docetaxel standard therapy in late stage patients
- Based on CANFOUR results and chemosensitization hypothesis, an interesting opportunity for CAN04
- IL-1 system has a well described role in NSCLC development

**Triple negative breast cancer (TNBC)**

- Breast cancer incidence 284.000 per year USA. TNBC is approximately 15% of cases.
- Affects younger women, more aggressive. Associated with BRCA mutations.
- It is the BC subtype in which IL1RAP has the highest level of expression
- Platinums and polychemotherapy is widely accepted for metastatic disease.
- Excellent opportunity for exploring CAN04 synergy with platinums



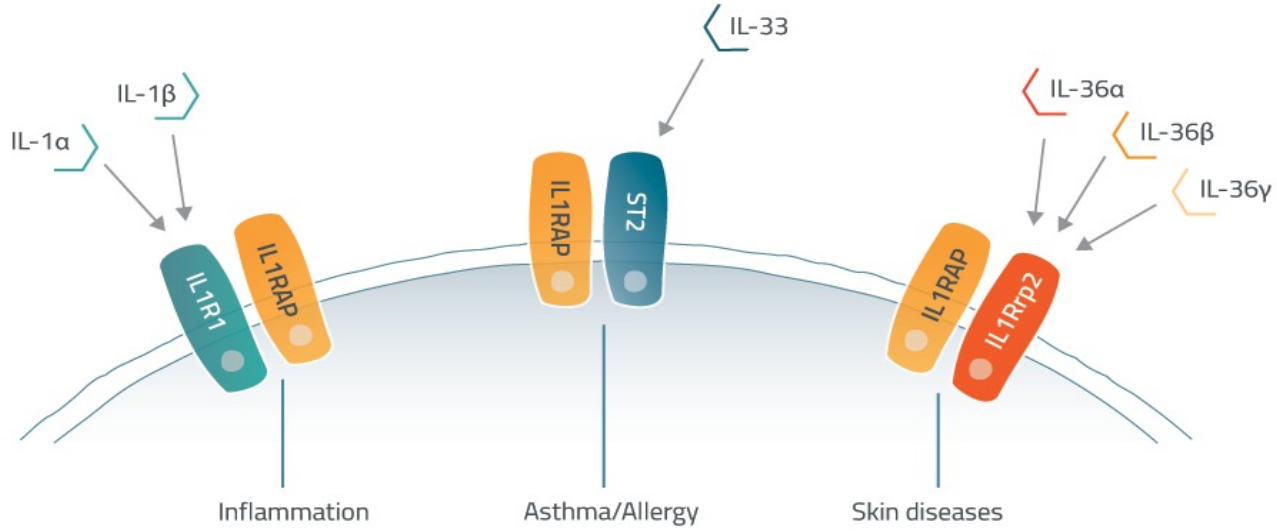
# CAN10 RESEARCH AND DEVELOPMENT

# CAN10 – indications and preclinical development


- → Inflammation of muscular tissues of the heart that can lead to fibrosis and loss of contractile function
- → Characterized by initial acute inflammation that can progress to fibrosis and loss of contractile function
- → 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

# CAN10 – rationale




*Opportunity: target all IL1RAP-dependent signaling pathways*

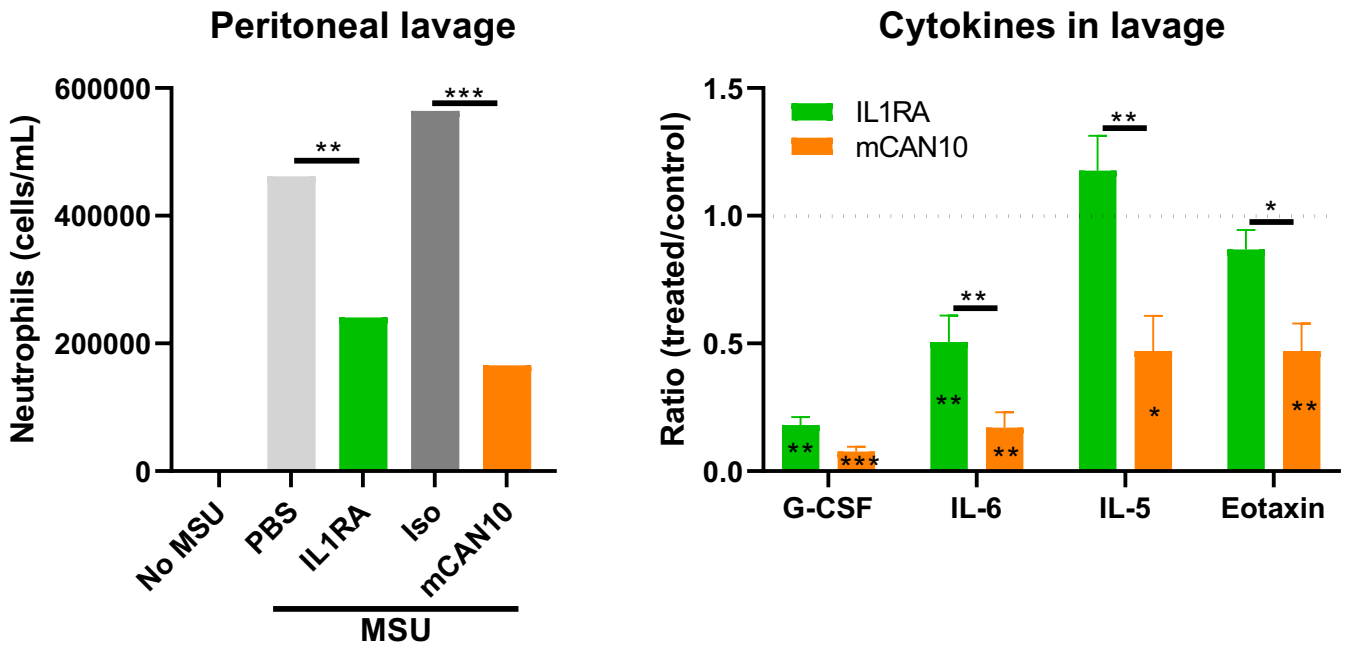
*IL1RAP binding and signaling inhibition*

*Engineered to minimize FcγR binding*

- → The CAN10 antibody is developed as a therapy for inflammatory/autoimmune diseases
- → CAN10 blocks all signaling pathways mediated by IL1RAP and does not induce antibody-dependent cell killing
- → Conceptual studies in vitro and in vivo with the aim to understand the potential of IL1RAP targeting
- → Development focused on myocarditis and systemic sclerosis

# IL1RAP inhibition is a potent strategy to block inflammation

MSU-induced peritonitis (i.p. injection with MSU-crystals, measure cells and cytokines after 6h)

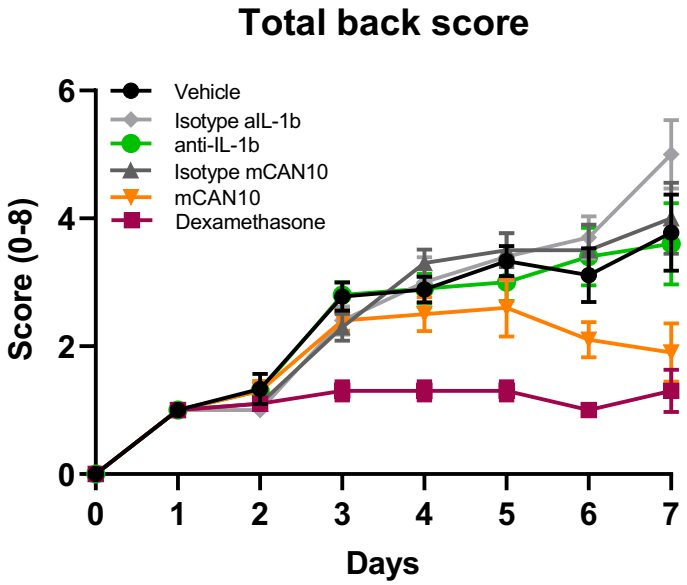


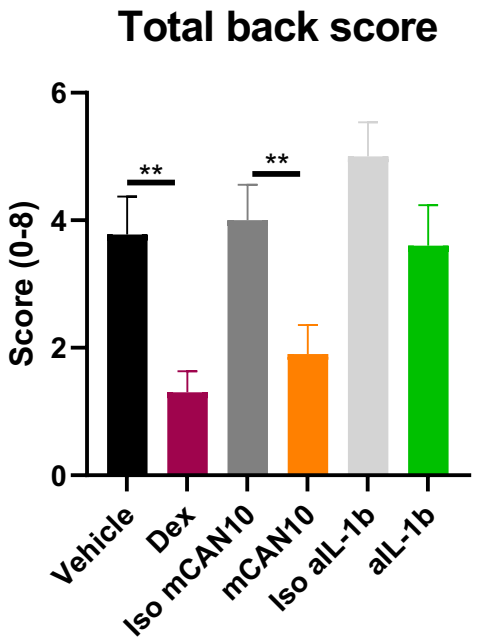

…in a way that is not recapitulated by IL1α/β-blockade alone

*MSU, monosodium urate*
*IL1RA/anakinra, blocks IL1α/β signaling*

# IL1RAP inhibition modulates local and systemic inflammation

IMQ-induced Psoriasis (topical daily administration of IMQ, biweekly i.p treatment with ab or daily topical with dex)



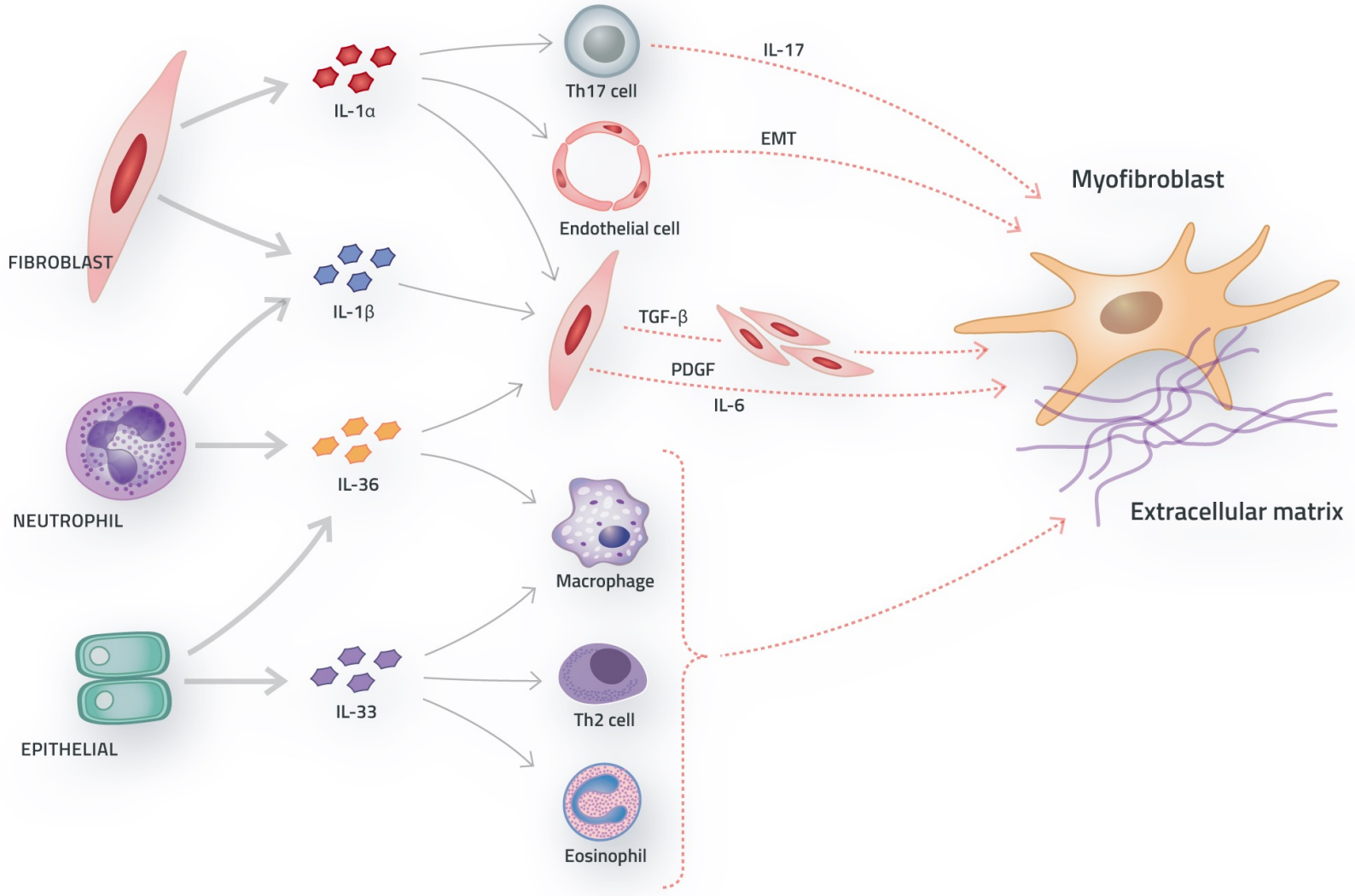

- Skin inflammation involves IL1, IL33 and IL36
- Experiments performed to study inhibition of local and systemic inflammation by systemic antibody
- CAN10 is a feasible treatment for skin inflammation

*IMQ, imiquimod*

# CAN10 – indications and preclinical development

# CAN10 – indications and preclinical development

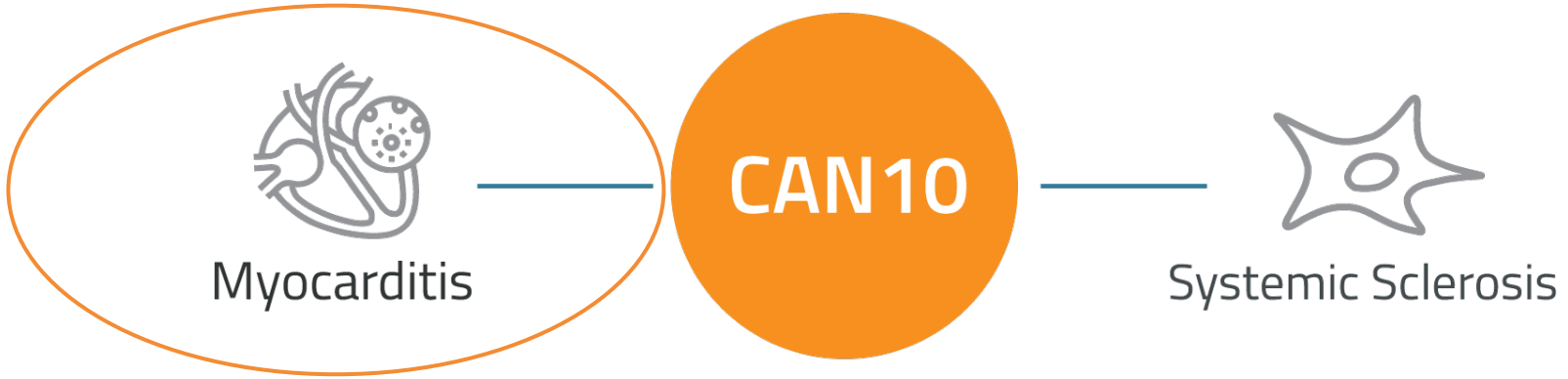
# Systemic sclerosis and fibrotic disease




- → Characterized by diffuse fibrosis and vascular abnormalities in the skin, joints, and internal organs
- → Lung fibrosis and Pulmonary Arterial Hypertension often accounts for death
- → IL1/33/36 are involved in several aspects of fibrosis
- → Experiments on human tissue and animal models ongoing, results to be presented at a scientific conference

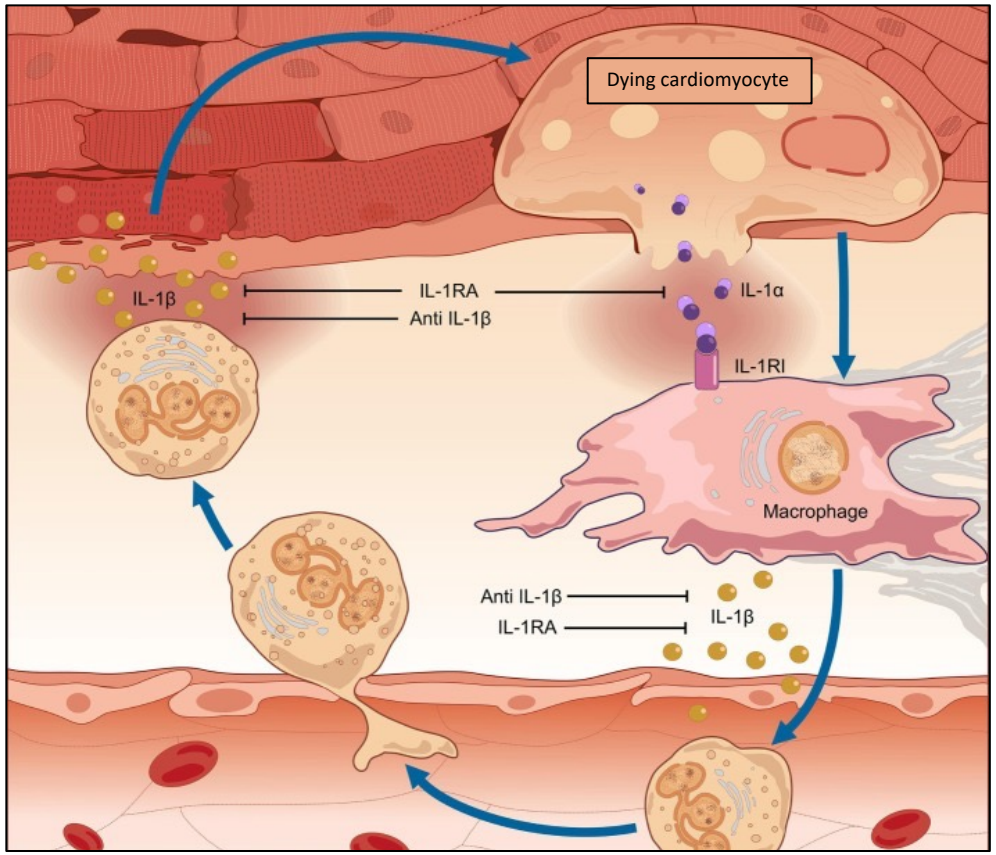
# CAN10 – indications and preclinical development

# CAN10 – indications and preclinical development



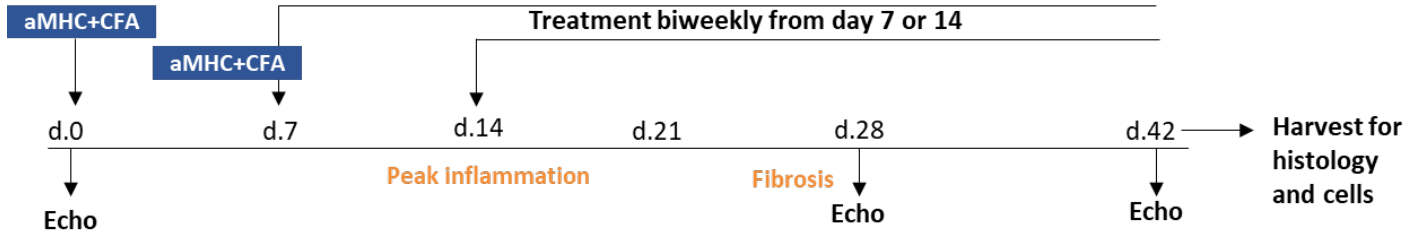
# The IL-1 family in Cardiovascular Inflammation

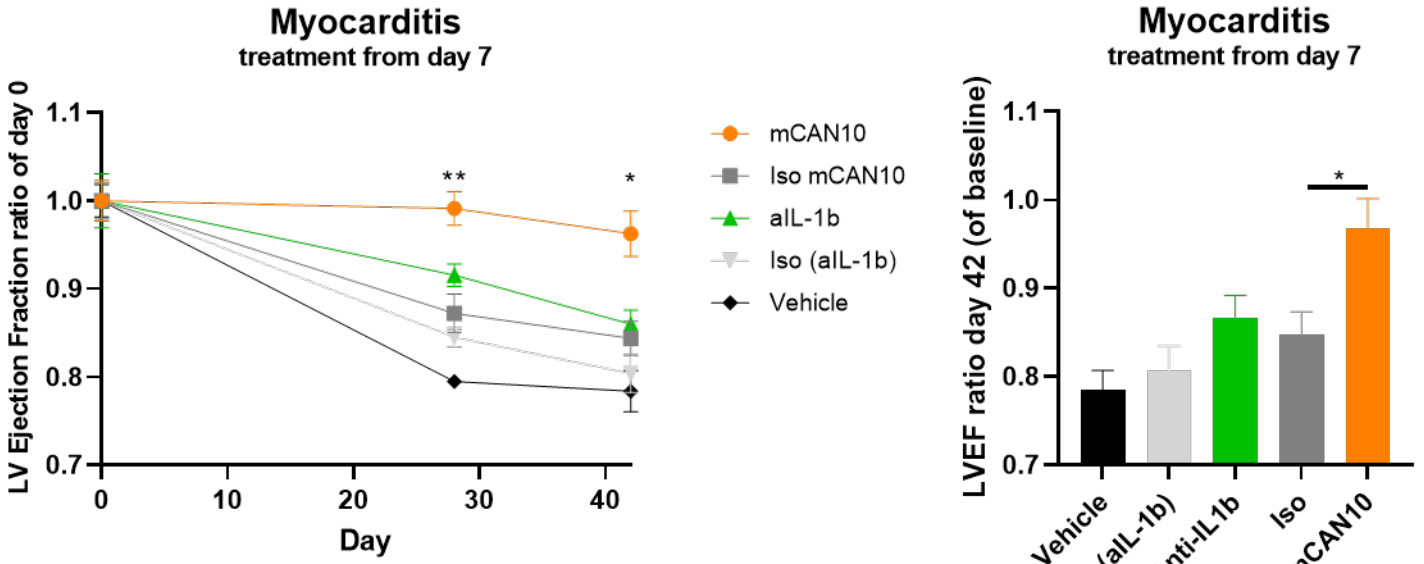
- → Inflammation of muscular tissues of the heart that can lead to fibrosis and loss of contractile function
- → IL-1 is central to the development of cardiac inflammation and is a potential driver of Myocarditis, ongoing clinical trial with Anakinra in patients with Acute Myocarditis
- → IL-33 and IL36 are emerging in cardiovascular disease but is not as thoroughly described
- → Does IL1RAP inhibition have benefits compared to only IL-1 blockade?



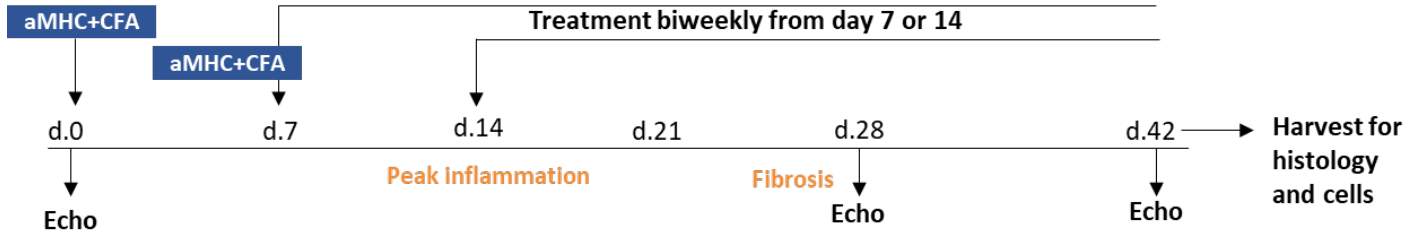

*Da Luca et al., Front Immunol. 2018*

# mCAN10 improves heart function in experimental autoimmune myocarditis



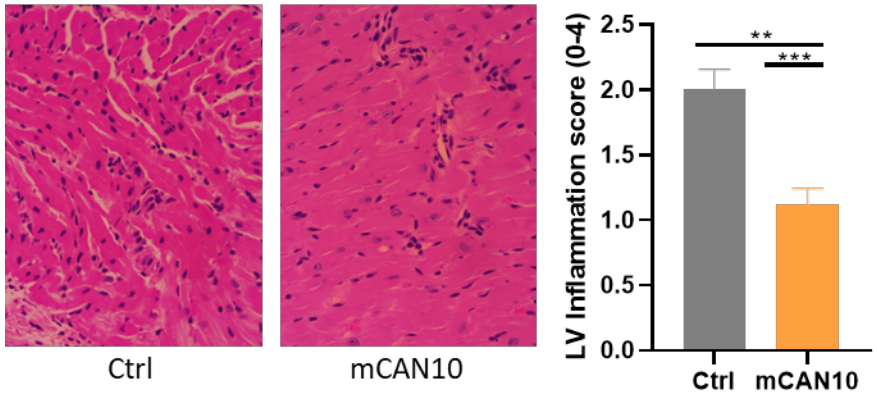



# mCAN10 reduces inflammation and fibrosis in experimental autoimmune myocarditis



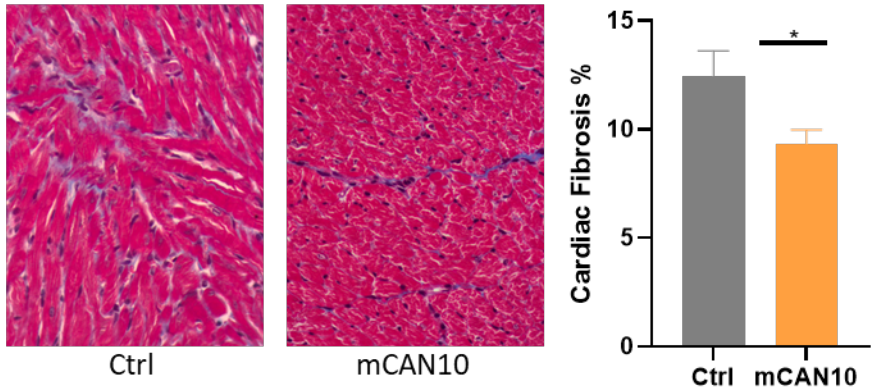

**H&E staining**

Treatment from day 14




**Masson Trichrome staining**

Treatment from day 14

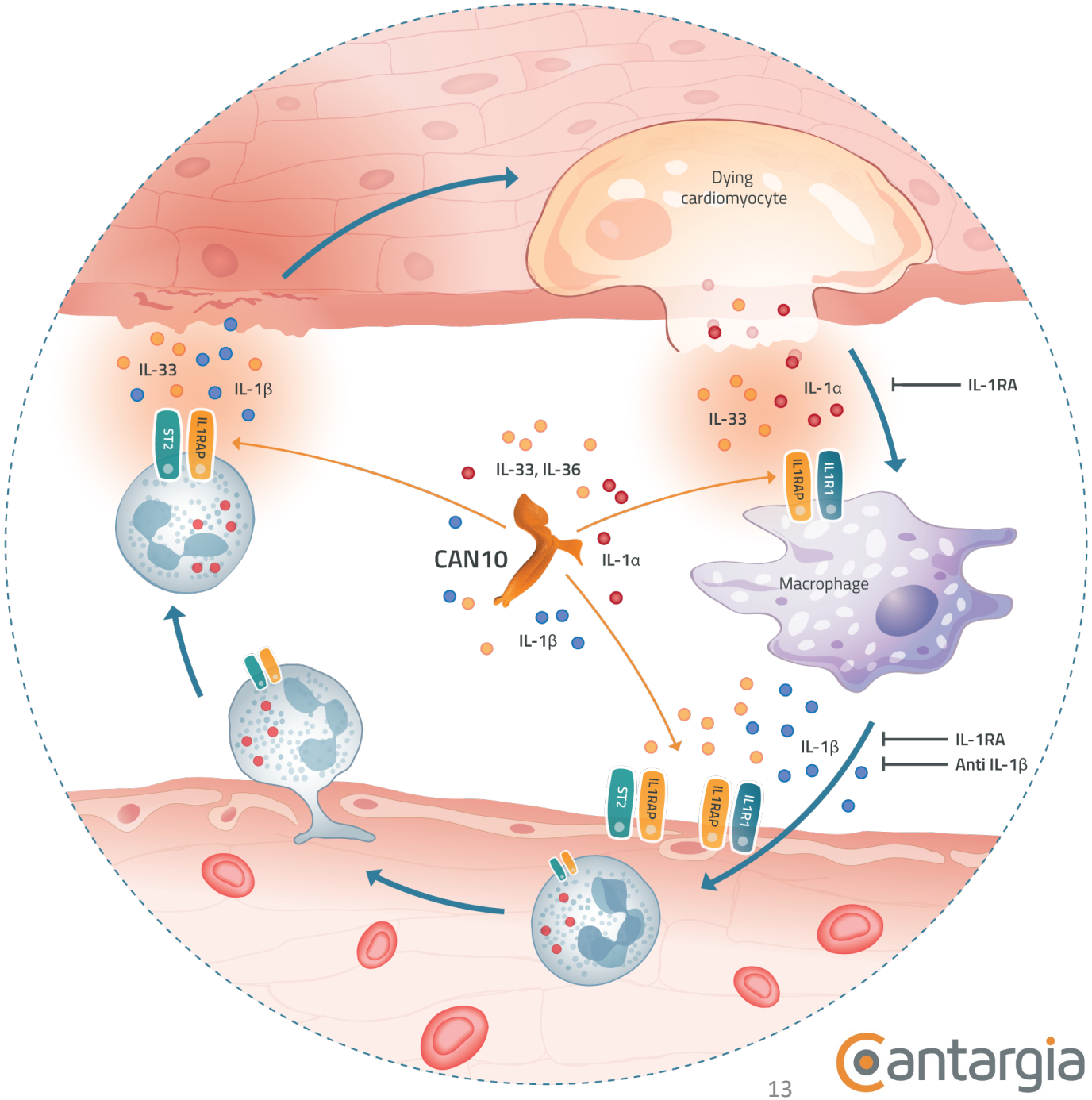


# CAN10 – summary

→ CAN10 blocks IL1α/β, IL33 and IL36α/β/γ signaling through targeting of IL1RAP and is in late-stage preclinical development for clinical trials

→ Blocking IL1RAP is a potent anti-inflammatory strategy that is qualitatively different from pure IL1α/β blockade.

→ IL1RAP-blockade counteracts inflammation, fibrosis and the decrease in heart function with additional value compared to IL-1 blockade or prednisone



# CAN10 – milestones

**2021**

→ CMC development and production for safety and clinical studies

→ Completion of safety program

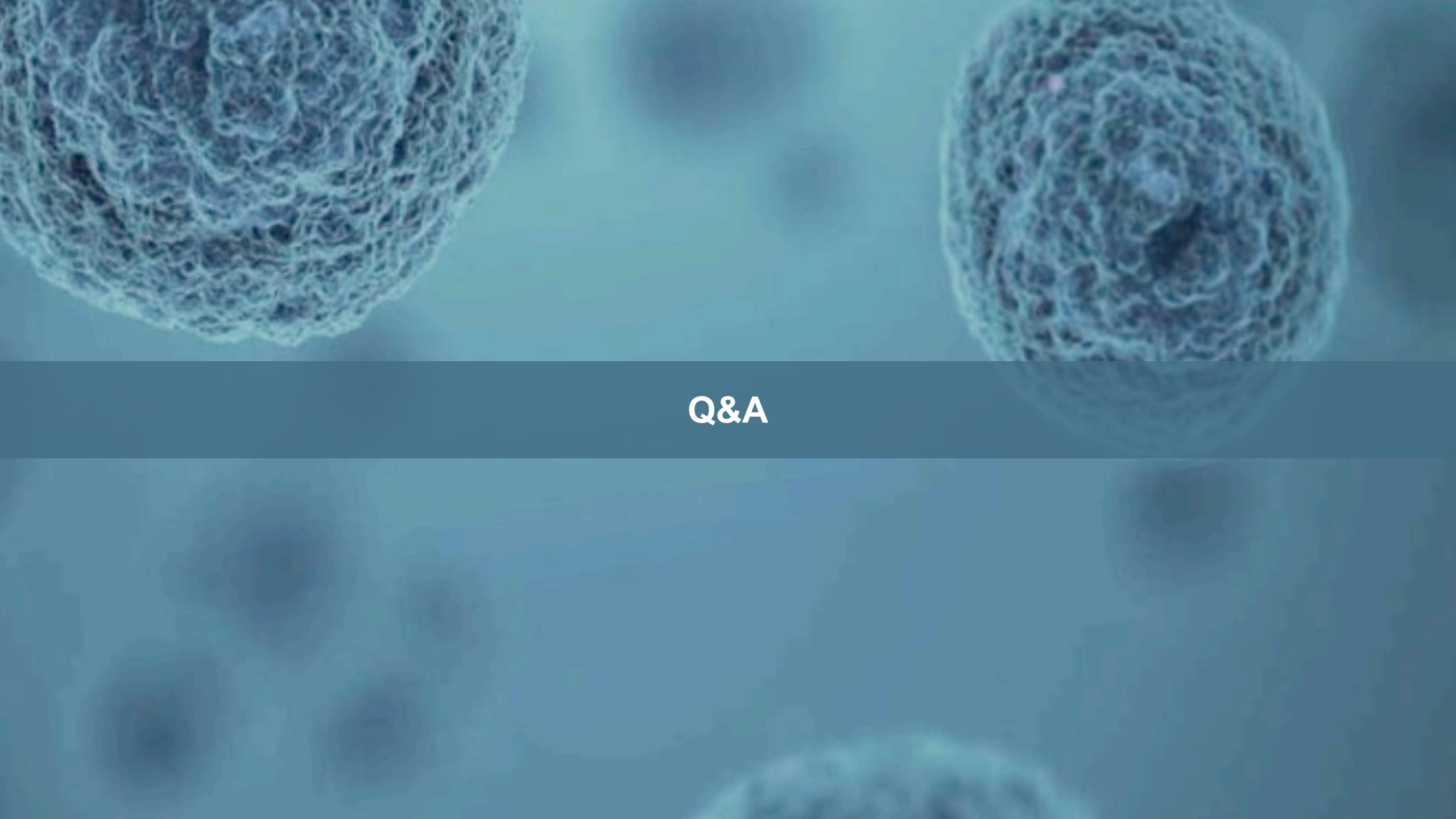
→ Interactions with health authorities

**2022**

→ CTA submissions

→ Initiation of clinical studies

→ Preparations for clinical development in myocarditis and/or SSc



# Q&A