

# A CD28/CD40-based chimeric costimulatory antigen receptor (CoStAR™) targeting folate receptor alpha enhances anti-tumour activity of tumour infiltrating lymphocytes.

John Bridgeman PhD.  
Director Discovery Research  
Instil Bio

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unTIL cancer is cured™

# Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this presentation, including statements regarding our strategy, the preclinical and clinical development of our product candidates, the timing of initiation, enrollment and patient dosing in and the expected design of our clinical trials, as well as the availability or disclosure of data from those clinical trials, the timing of planned regulatory submissions, the potential for our product candidates to receive regulatory approval from the FDA or other regulatory agencies, our expected manufacturing capabilities and the timing thereof, our cash runway, the anticipated sale-leaseback of our Tarzana, CA manufacturing facility, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. Words such as “anticipates,” “believes,” “expects,” “future,” “intends,” “plans,” “potential,” “projects,” and “will” or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning or implying the therapeutic potential of our product candidates, our research, development and regulatory plans for our product candidates, including our expectations of CTA clearance from the MHRA, the timing of our ongoing and potential future clinical trials and studies and the availability of data therefrom, including our expectations concerning the initiation of, and timing of updates, on our ITIL-306 clinical trial in the United Kingdom, the potential for us to make submissions concerning, and for our product candidates to receive, regulatory approval from the FDA, MHRA or equivalent foreign regulatory agencies and whether, if approved, these product candidates will be successfully distributed and marketed, the anticipated sale or lease of our Tarzana, California manufacturing facility, our cash runway and quarterly cash burn, and other statements that are not historical fact. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements, including risks and uncertainties associated with the costly and time-consuming cell therapy product development process and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating, enrolling, reporting data from or completing clinical studies, as well as the risks that results obtained in clinical trials to date may not be indicative of results obtained in ongoing or future trials and that Instil's product candidates may otherwise not be effective treatments in their planned indications; macroeconomic conditions, including as a result of the ongoing COVID-19 pandemic, the ongoing conflict between Russia and Ukraine, bank failures and other factors, which could materially and adversely affect Instil's business and operations, including Instil's ability to timely initiate, enroll and complete its ongoing and future clinical trials; the time-consuming and uncertain regulatory approval process; risks inherent in manufacturing and testing of cell therapy products; the sufficiency of Instil's cash resources, and other risks and uncertainties affecting Instil and its development programs, including those discussed in the section titled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2022 to be filed with the SEC. Additional information will be made available in other filings that we make from time to time with the SEC. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements speak only as the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

# Executive Summary

**1**

**Instil Bio has developed a platform technology called CoStAR (Costimulatory Antigen Receptor)**

**2**

**CoStAR enhances the function of T cells and TIL in vitro and in vivo**

**3**

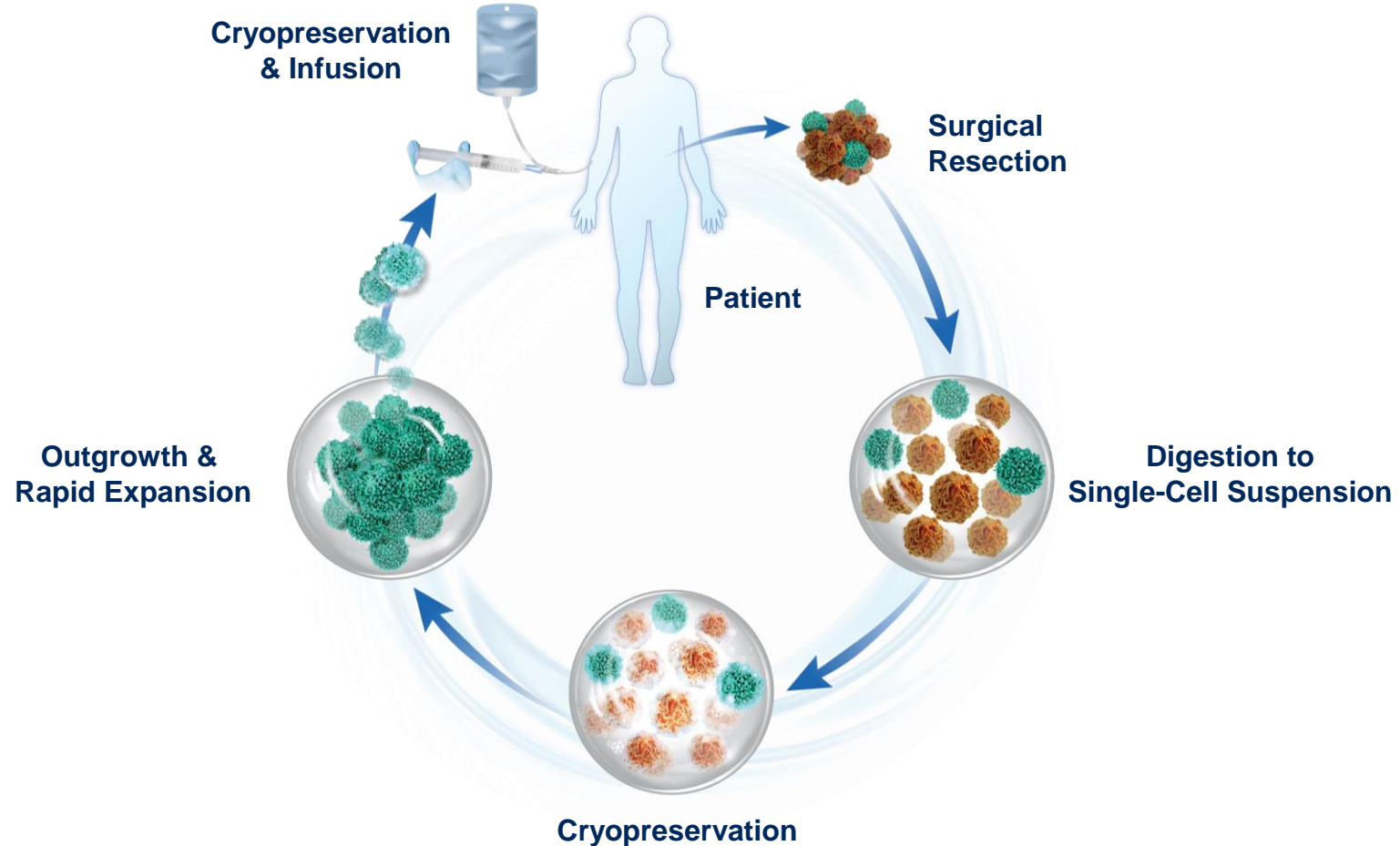
**Currently being evaluated as ITIL-306 in human clinical trials with first patient dosed**

# Tumour Infiltrating Lymphocyte (TIL) Therapy

Tumour infiltrating lymphocytes (TIL) therapy depends upon:

1. Isolating TIL from a patient tumours
2. Expanding them to high numbers ex vivo in favourable growth conditions
3. Infusion back into the patient

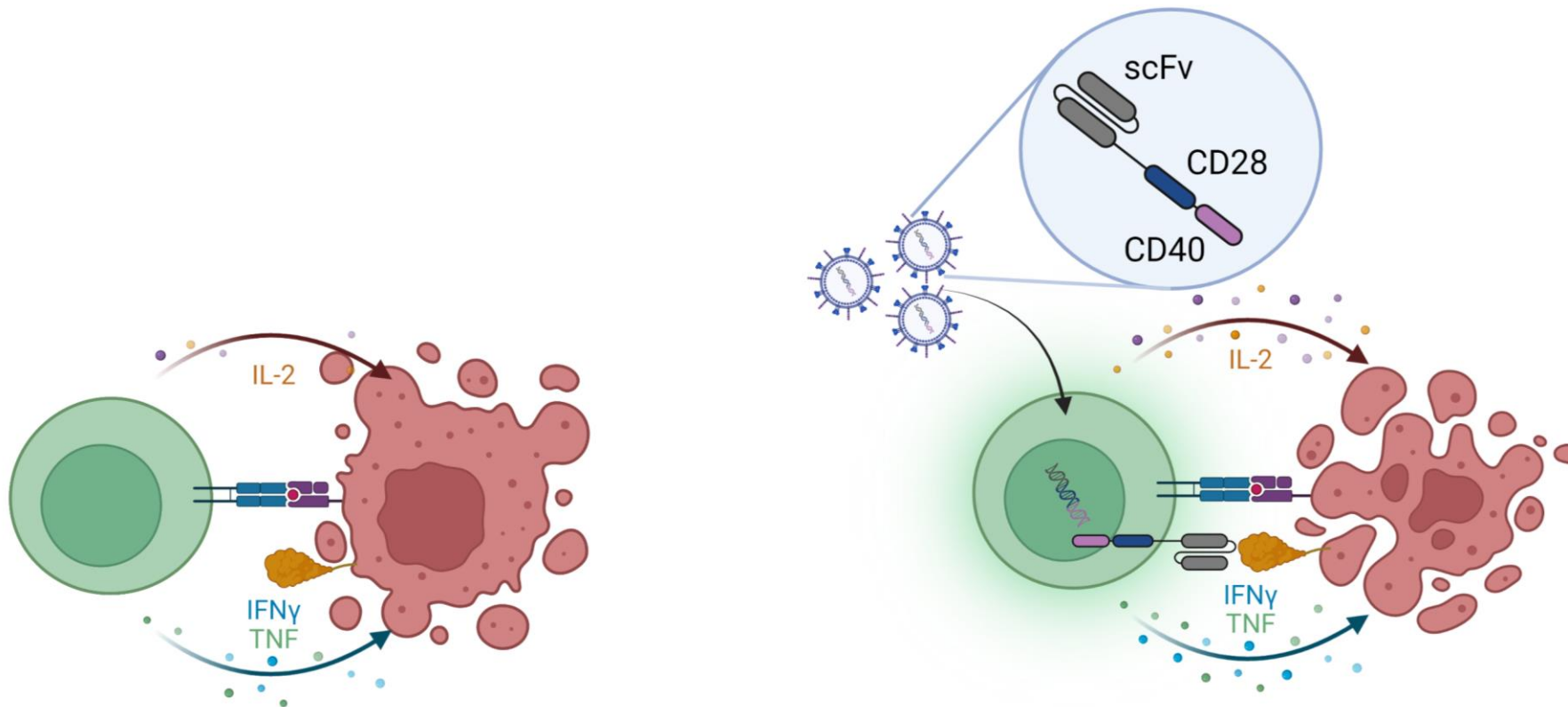
This process shifts the balance of tumour:immune system interplay in favour of the immune system leading to a high frequency of durable clinical responses



**41%**

ORR in 410 patients with melanoma treated at multiple clinical sites since 1988<sup>1</sup>

# The CoStAR (CoStimulatory Antigen Receptor) principle



## Non-transduced TIL

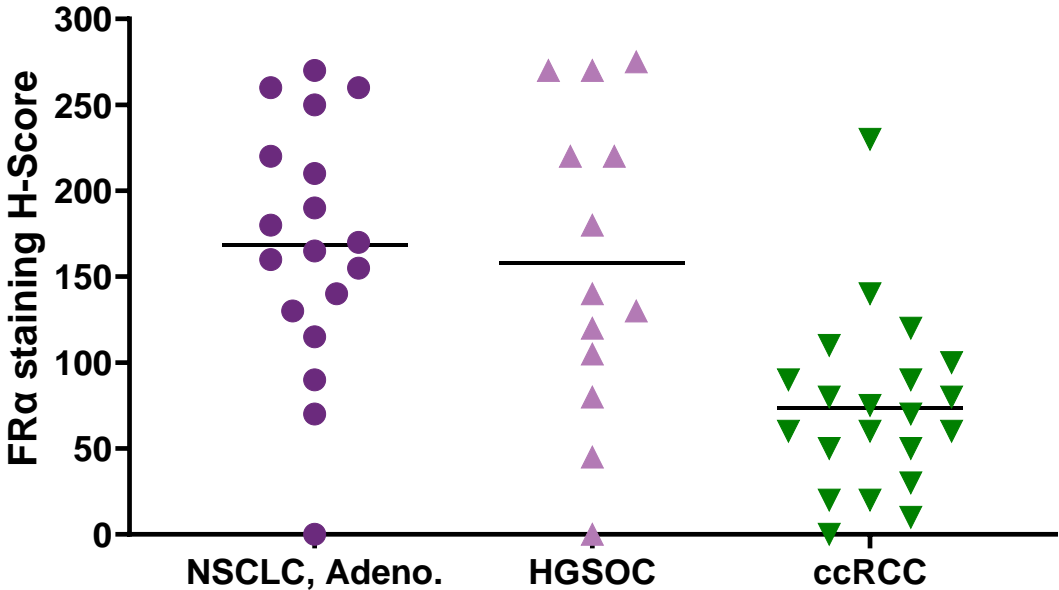
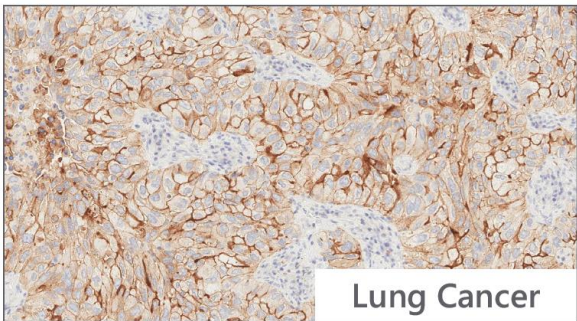
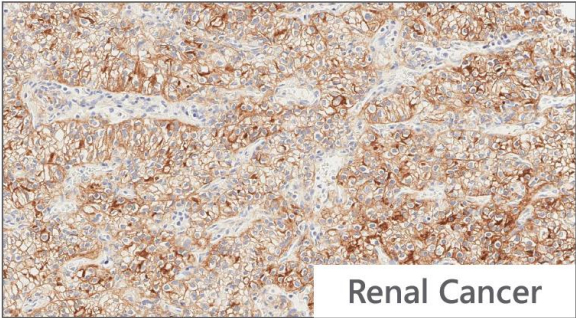
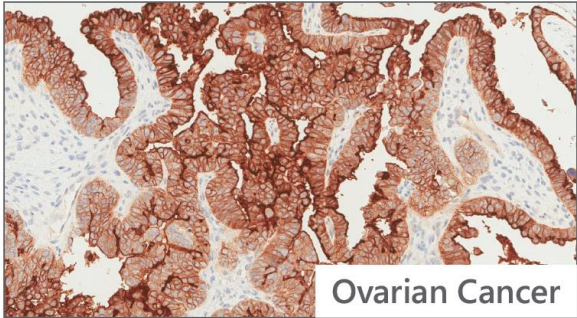
- Low level cytokine secretion
- Tumour killing
- Limited proliferative response
- Lack of costimulation leads to AICD

## CoStAR-transduced TIL

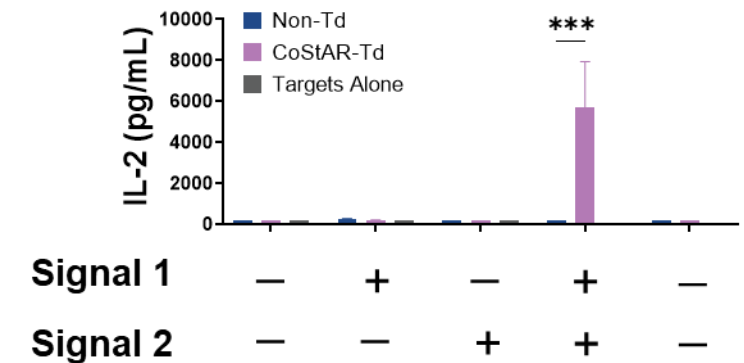
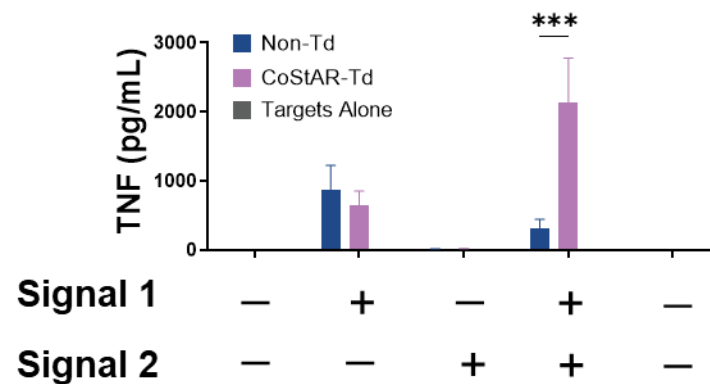
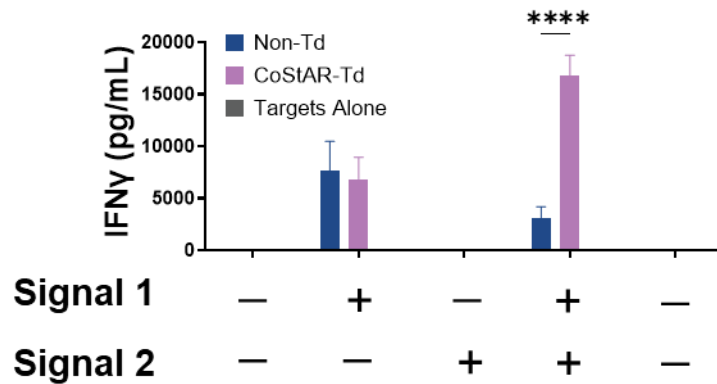
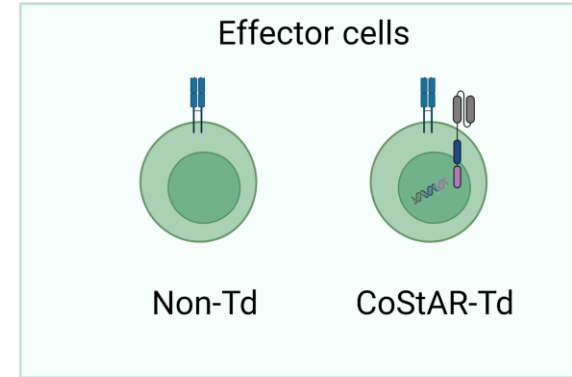
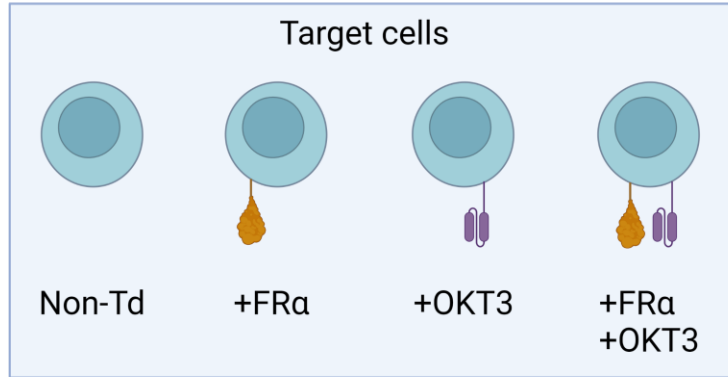
- **Elevated** cytokine secretion
- **Enhanced** tumour killing
- **Increased** proliferative response
- **Reduced** AICD



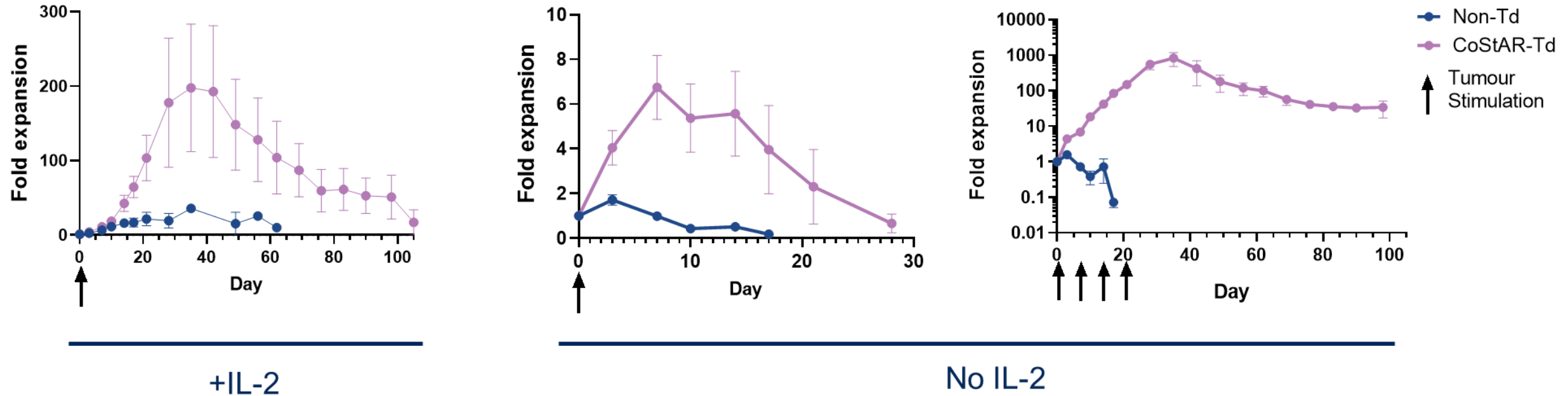
# ITIL-306 CoStAR Targets FR $\alpha$



# CoStAR enhances T cell effector function

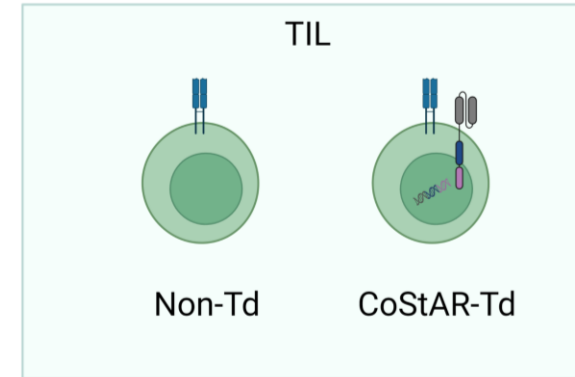
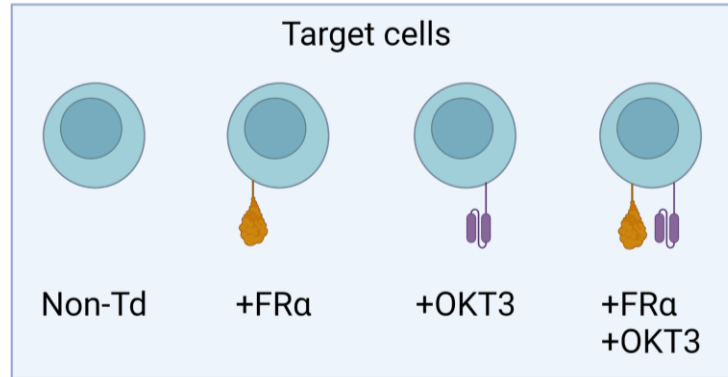


# CoStAR greatly enhances in vitro T cell proliferation

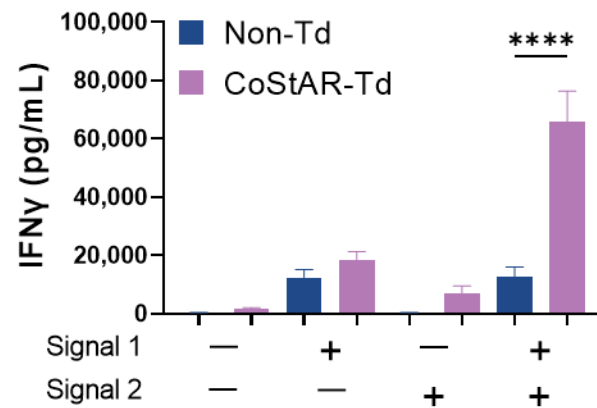




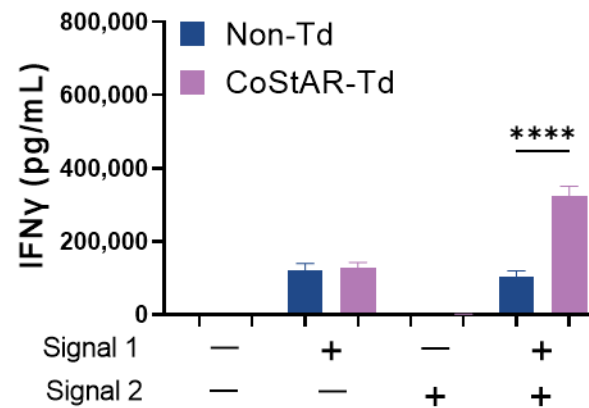
# CoStAR is active in TIL from multiple indications



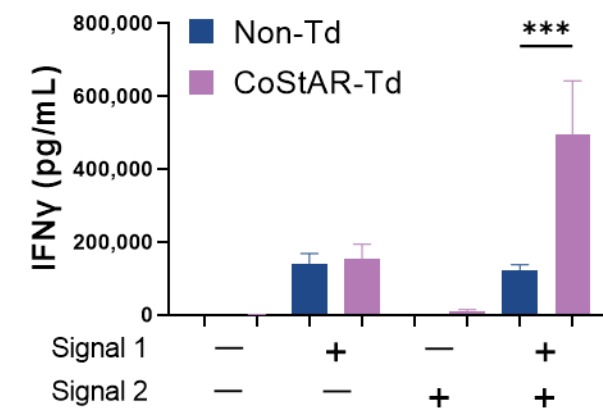
## Ovarian cancer



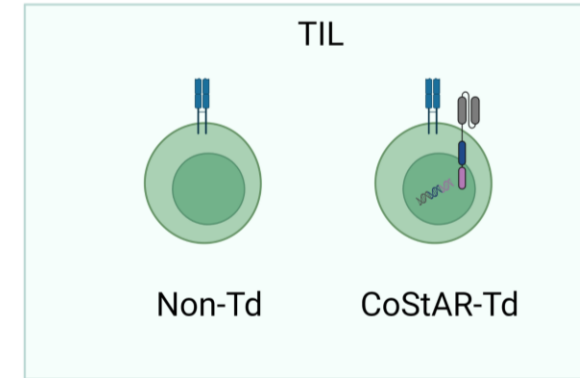
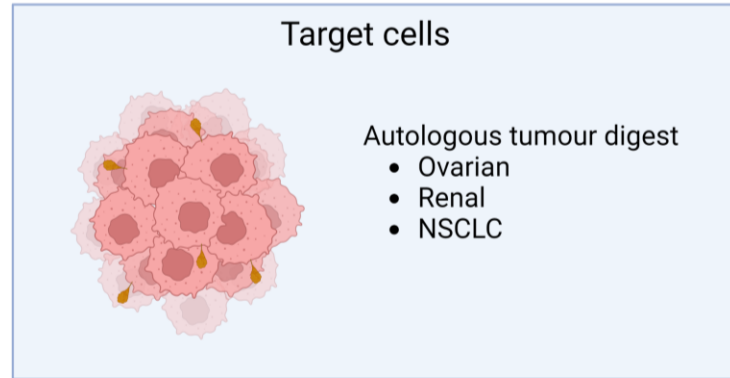
## Renal cancer



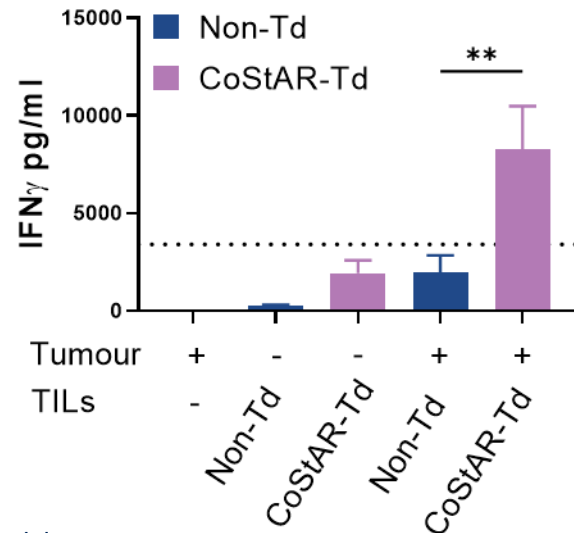
## Non-small cell lung cancer



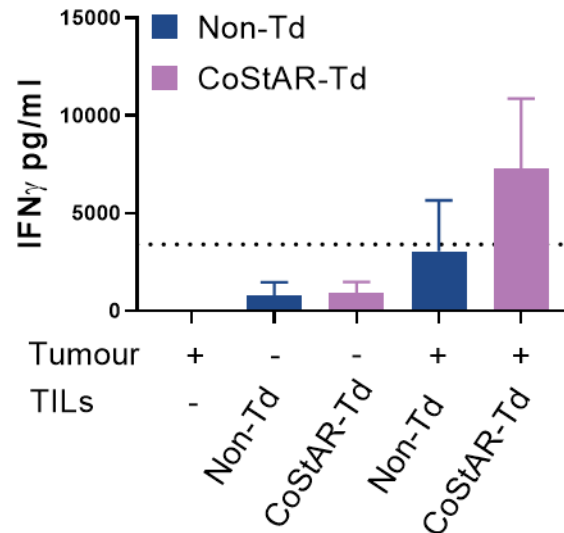
# CoStAR enhances TIL activity towards autologous tumour



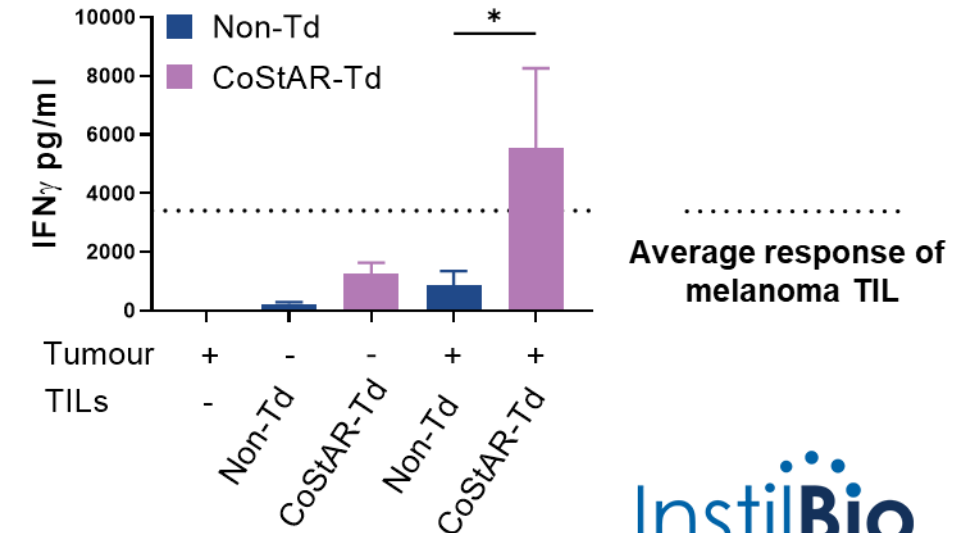
## Ovarian cancer



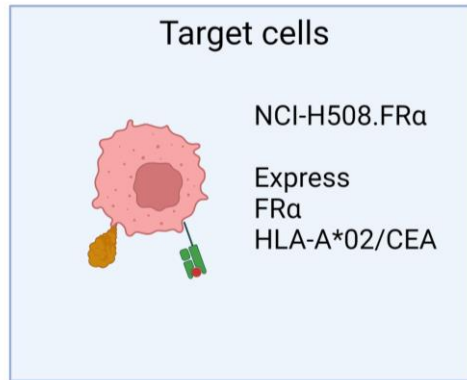
## Renal cancer



## Non-small cell lung cancer

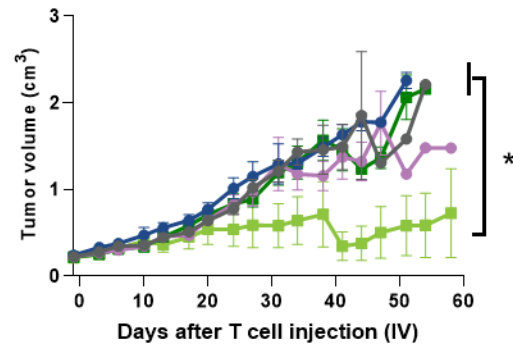


# CoStAR Enhances the Function of T cells *in vivo*

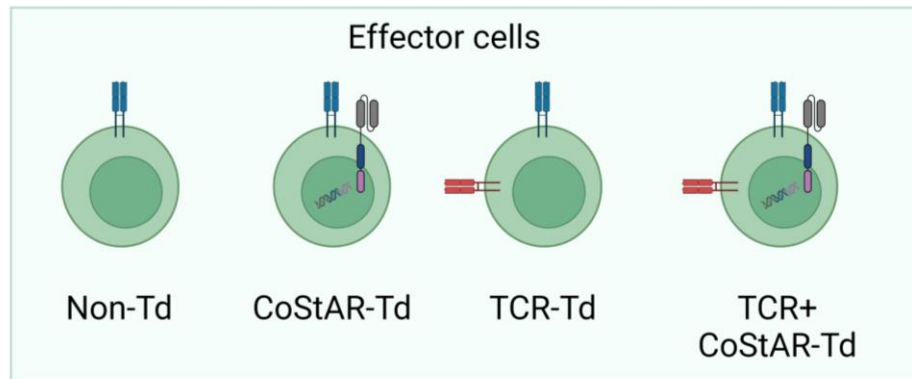
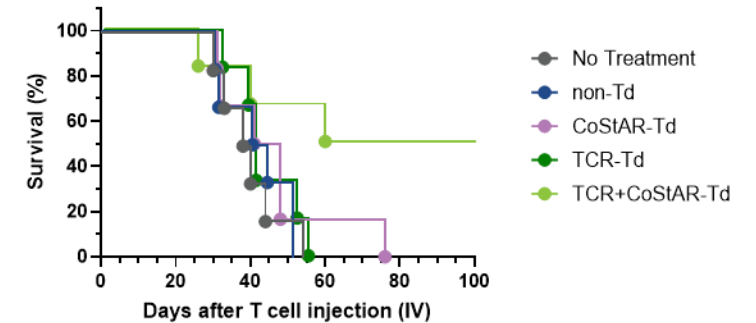


+IL-2

Tumor volume

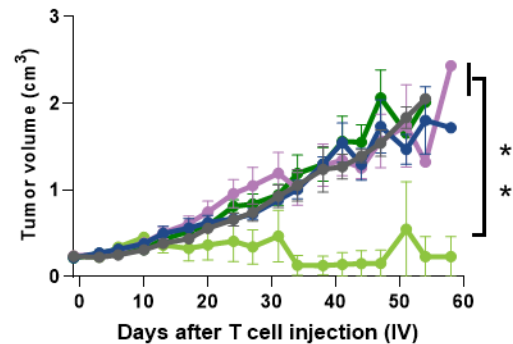


Survival

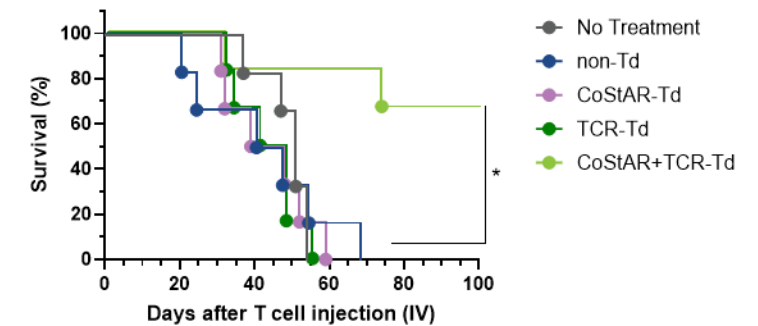


No IL-2

Tumor volume



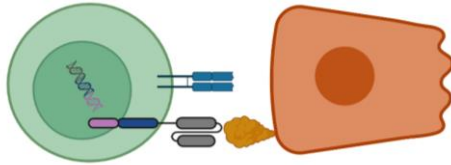
Survival



# CoStAR activity summary

CoStAR-Td TIL

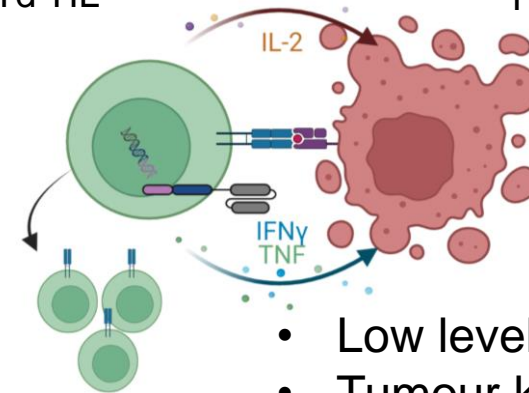
FR $\alpha$ + Normal tissue



- No effector activity

CoStAR-Td TIL

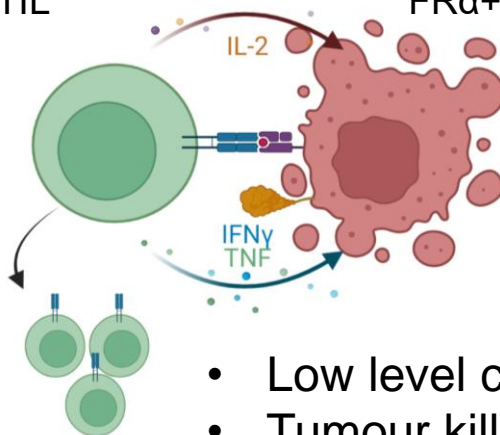
FR $\alpha$ - Tumour



- Low level cytokine secretion
- Tumour killing
- Limited proliferative response

Non-Td TIL

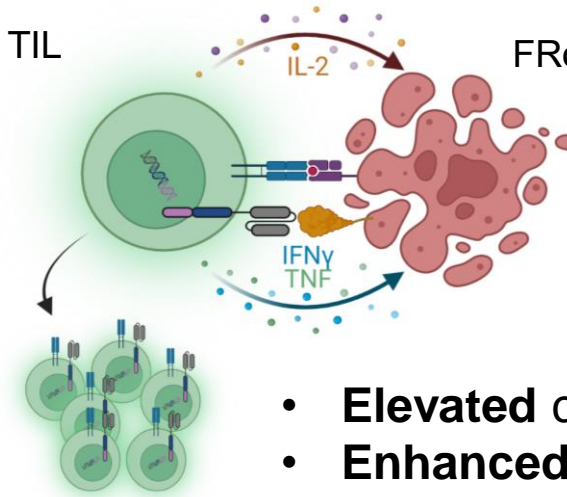
FR $\alpha$ + Tumour



- Low level cytokine secretion
- Tumour killing
- Limited proliferative response

CoStAR-Td TIL

FR $\alpha$ + Tumour



- **Elevated** cytokine secretion
- **Enhanced** tumour killing
- **Increased** proliferative response

# Summary

**1**

**Instil Bio has developed a platform technology called CoStAR (Costimulatory Antigen Receptor).**

**2**

**CoStAR enhances T cell effector function and proliferation in an IL-2 independent manner.**

**3**

**CoStAR is strictly dependent on provision of signal 1, and is not activated by membrane anchored or soluble FR $\alpha$ , nor is blocked by soluble FR $\alpha$ .**

**4**

**CoStAR enhances control of established tumours in vivo, even in the absence of IL-2.**

**5**

**CoStAR enhances activity of TIL towards autologous tumour.**

# Thank you!

John.bridgeman@instilbio.com  
[www.instilbio.com](http://www.instilbio.com)