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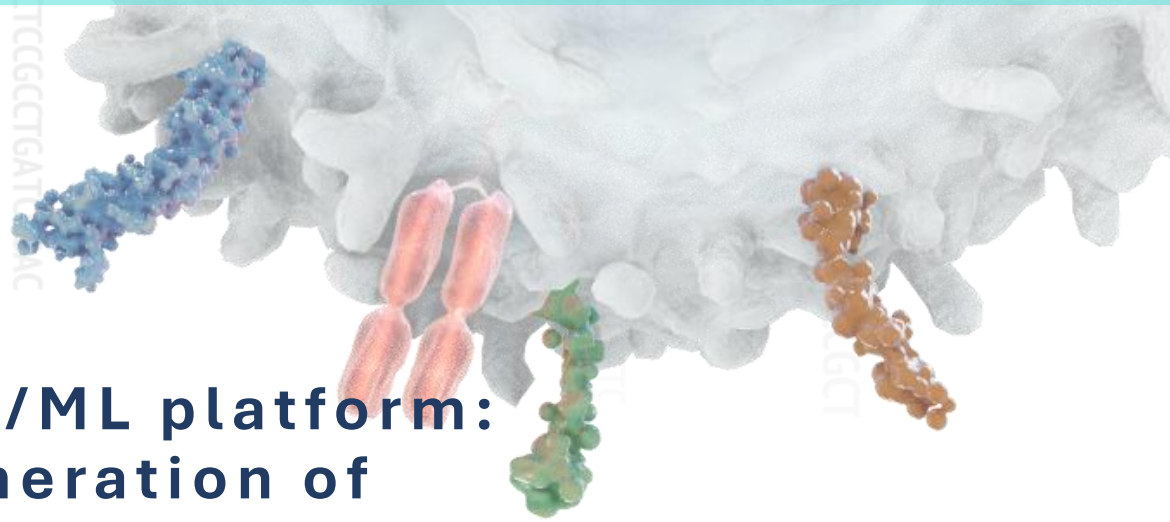

From Code to Cure with Unigen AI/ML platform: Compugen advancing the next generation of cancer immunotherapies

Festival of Biologics 2025 – Basel – 01 Oct 2025

Pierre Ferré – Chief Operating Officer

Safe Harbor Statement

This presentation contains “forward-looking statements” within the meaning of the Securities Act of 1933 and the Securities Exchange Act of 1934, as amended, and the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by the use of terminology such as “will,” “may,” “expects,” “anticipates,” “believes,” “potential,” “plan,” “goal,” “estimate,” “likely,” “should,” and “intends,” and similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements involve known and unknown risks and uncertainties that may cause the actual results, performance or achievements of Compugen to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements, including statements regarding the timing and success of our clinical trials, enrollment of patients, type of clinical trials, presentation of data and our cash position and expenditures. Among these risks: Clinical development involves a lengthy and expensive process, with an uncertain outcome and Compugen may encounter substantial delays or even an inability to begin clinical trials for any specific product, or may not be able to conduct or complete its trials on the timelines it expects; Compugen relies and expects to continue to rely on third parties to conduct its clinical trials and these third parties may not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, and Compugen may experience significant delays in the conduct of its clinical trials as well as significant increased expenditures; Compugen’s business model is substantially dependent on entering into collaboration agreements with third parties and Compugen may not be successful in generating adequate revenues or commercializing aspects of its business model; Compugen’s approach to the discovery of therapeutic products is based on its proprietary computational target discovery infrastructure, which is unproven clinically; and Compugen does not know whether it will be able to discover and develop additional potential product candidates or products of commercial value. These and other factors, including the ability to finance the Company, are more fully discussed in the "Risk Factors" section of Compugen’s most recent Annual Report on Form 20-F as filed with the Securities and Exchange Commission (“SEC”) as well as other documents that may be subsequently filed by Compugen from time to time with the SEC. In addition, any forward-looking statements represent Compugen’s views only as of the date of this presentation and should not be relied upon as representing its views as of any subsequent date. Compugen does not assume any obligation to update any forward-looking statements unless required by law. Certain studies and data presented herein have been conducted for us by other entities as indicated where relevant. Intellectual property, including patents, copyrights or trade secret displayed in this presentation, whether registered or unregistered, are the intellectual property rights of Compugen. Compugen's name and logo and other Compugen product names, slogans and logos referenced in this presentation are trademarks of Compugen Ltd. and/or its subsidiary, registered in the U.S.A., EU member states and Israel.

Disclosure

Employee of Compugen

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The birth of Compugen

The “Bioccelerator”



Illustration rendered from MS Copilot tool

Immune checkpoints in cancer immunotherapy

Anti-PD-1/L1 “revolution”

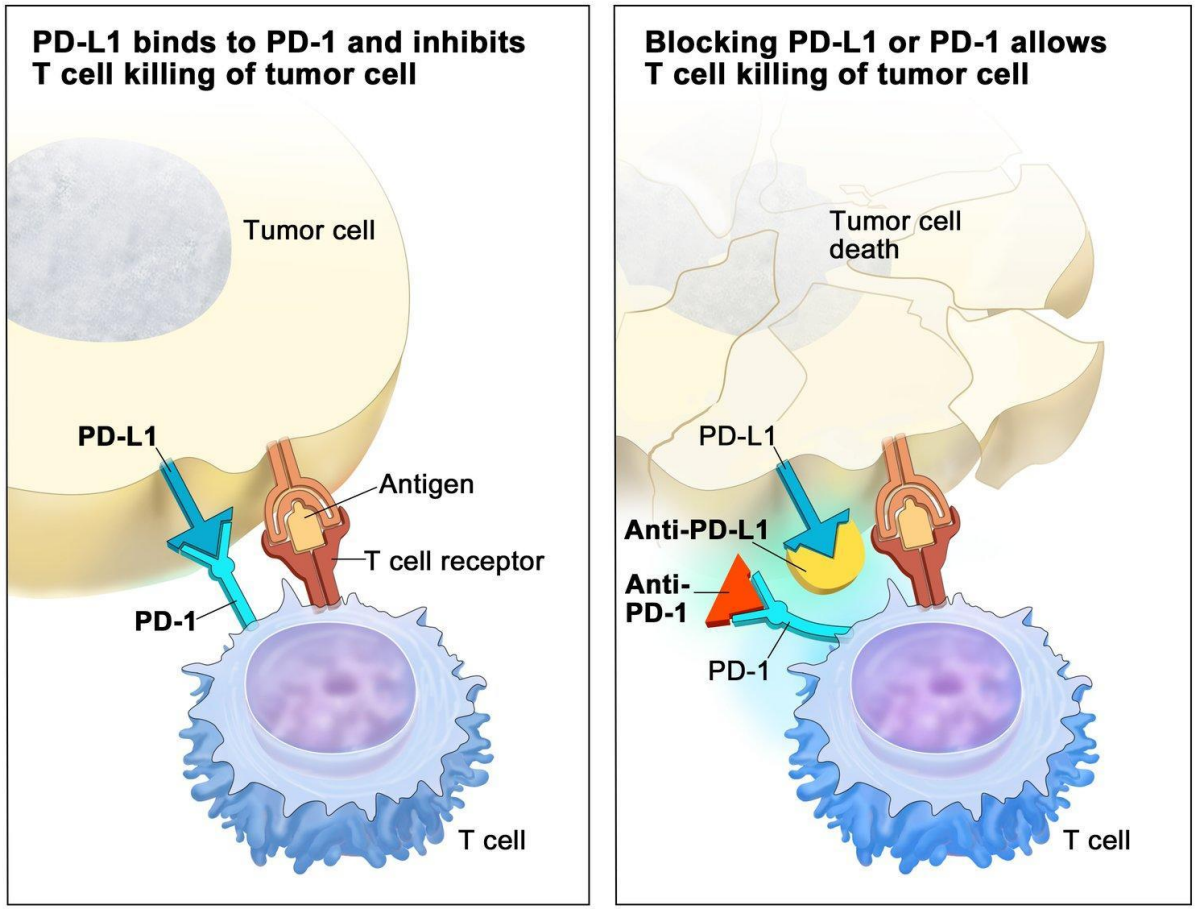

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Illustration from the National Cancer Institute website

But about 70-80% of patients still do not respond across solid tumor indications

What does Compugen bring to the immune checkpoint landscape?

Next generation immune checkpoint programs in clinical trials

Discovered by Compugen's computational discovery platform-Unigen™

1. Novel "Traditional" checkpoints antibodies

COM701
Potential 1st in-class
anti-PVRIG antibody

COM902
Potential best-in-class
anti-TIGIT antibody

2. Novel bispecific checkpoint Antibody

Rilvegostomig*

anti-PD1/TIGIT bispecific Ab,
TIGIT component derived
from COM902

Program by:

AstraZeneca

3. Novel "Soluble checkpoint" blocker Antibody

GS-0321 (previously COM503)**
Potential first-in-class
anti-IL-18BP antibody

licensed to:

GILEAD

* Rilvegostomig, an Fc-reduced, monovalent, bispecific humanized IgG1 monoclonal antibody targeting PD-1 and TIGIT. The anti-TIGIT component of rilvegostomig is derived from COM902 developed by Compugen Ltd.
** Compugen responsible for preclinical development and first- in-human Phase 1 trial evaluating the safety and tolerability of GS-0321. Thereafter, Gilead will have sole right to develop and commercialize GS-0321

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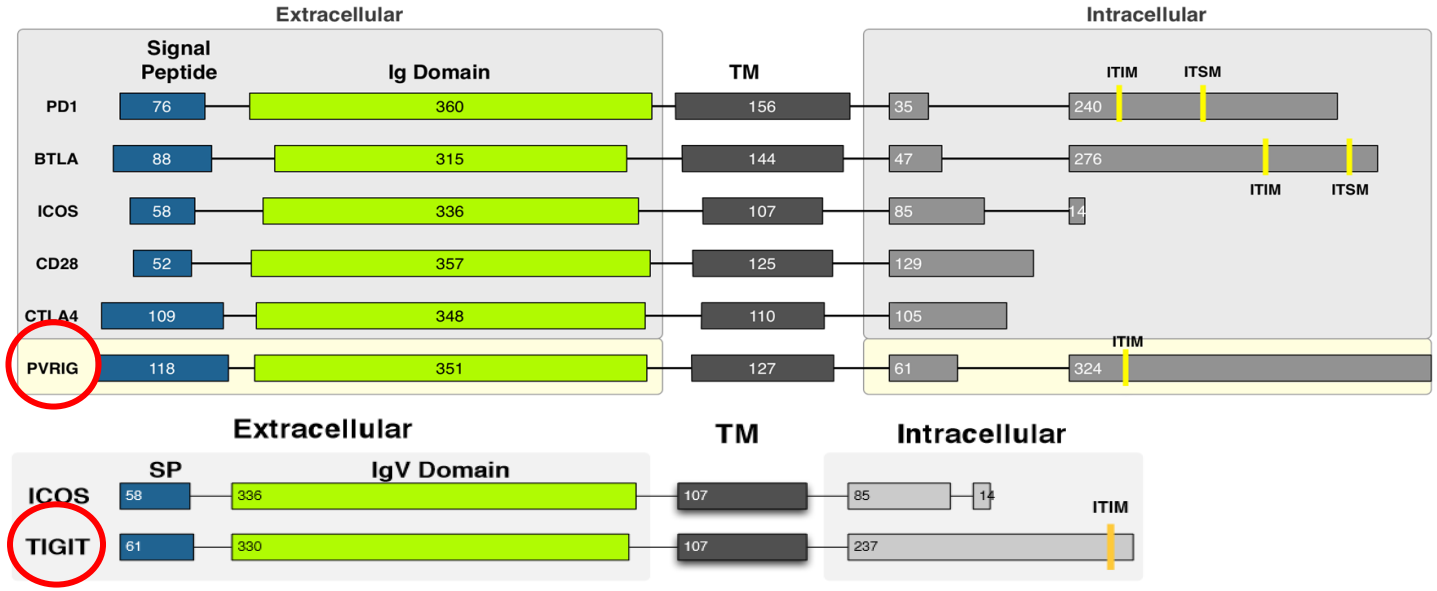
1. Novel immune checkpoints: TIGIT and PVRIG

1. TIGIT and PVRIG checkpoints

Discovered by Compugen's computational discovery platform

- "Functional homology": B7/CD28 immune checkpoints have a distinct extracellular gene structure
- TIGIT identified by Compugen as a potential immune checkpoint in 2009
- TIGIT (and PVRIG) functional gene structure matches known immune checkpoint receptors



PNAS

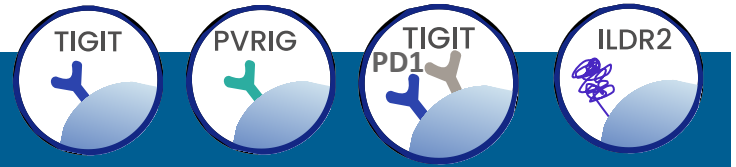
The interaction of TIGIT with PVR and PVRL2 inhibits human NK cell cytotoxicity

Noa Stanietsky[a], Hrvoje Simic[b], Jurica Arapovic[b], Amir Toporik[c], Ofer Levy[c], Amit Novik[c], Zurit Levine[c], Meirav Beiman[c], Liat Dassa[c], Hagit Achdout[a], Noam Stern-Ginossar[a], Pinhas Tsukerman[a], Stipan Jonjic[b,1,2], and Ofer Mandelboim[a,1,2]

[a]The Lautenberg Center for General and Tumor Immunology, IMRIC, Hadassah Medical School, Hebrew University, Jerusalem 91120, Israel; [b]Center for Proteomics, Faculty of Medicine, University of Rijeka, Brace Branchetta 20, Rijeka, Croatia; and [c]Compugen Ltd., 72 Pinchas Rosen Street, Tel Aviv 69512, Israel

Edited by Wayne M. Yokoyama, Washington University School of Medicine, St. Louis, MO, and approved September 1, 2009 (received for review March 30, 2009)

Four clinical programs based on this discovery platform



COM902 | COM701 | COM902 Rilvegostomig (COM902+aPD1 BS) | Bapotulimab

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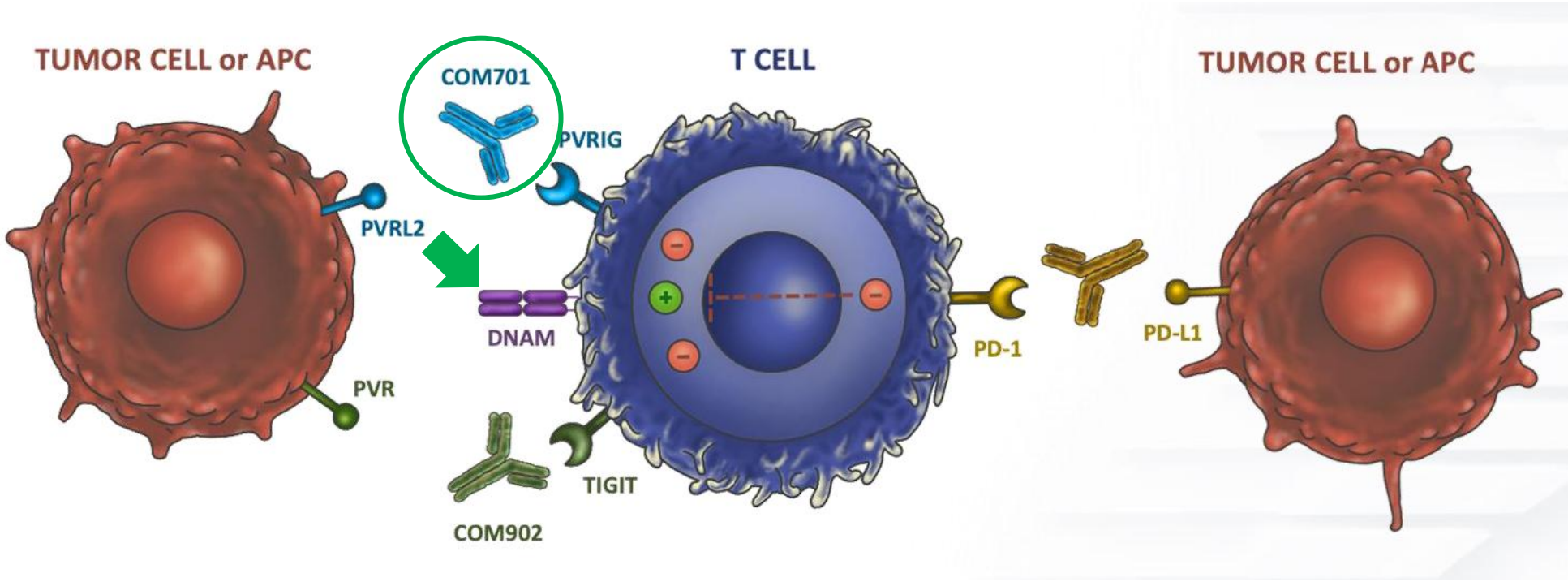
PVRIG, TIGIT and PD-1 are players in the DNAM-1 axis

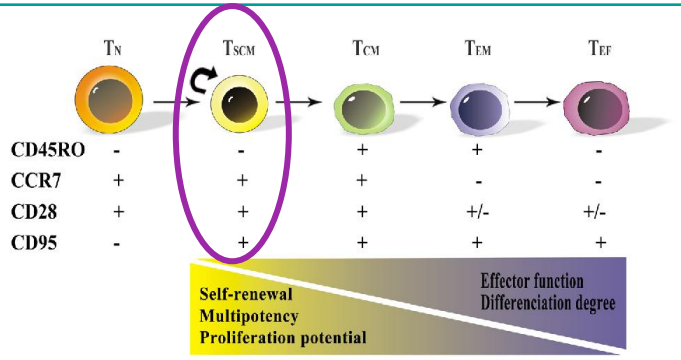
PVR and PVRL2 are broadly expressed in PD-L1 positive and negative tumors



Adapted from Alteber *et al.* Cancer Discov. 2021

PVRIG uniquely clusters with early differentiated/T_{SCM} genes

Early differentiated Tscm cells are potent inducers of anti-tumor activity following adoptive T cell transfer



Central memory self/tumor-reactive CD8⁺ T cells confer superior antitumor immunity compared with effector memory T cells

Christopher A. Klebanoff*†‡, Luca Gattinoni‡, Parizad Torabi-Parizi*§, Keith Kerstann¶, Adela R. Cardones§, Steven E. Finkelstein¶, Douglas C. Palmer¶, Paul A. Antony¶, Sam T. Hwang§, Steven A. Rosenberg¶, Thomas A. Waldmann||, and Nicholas P. Restifo¶**

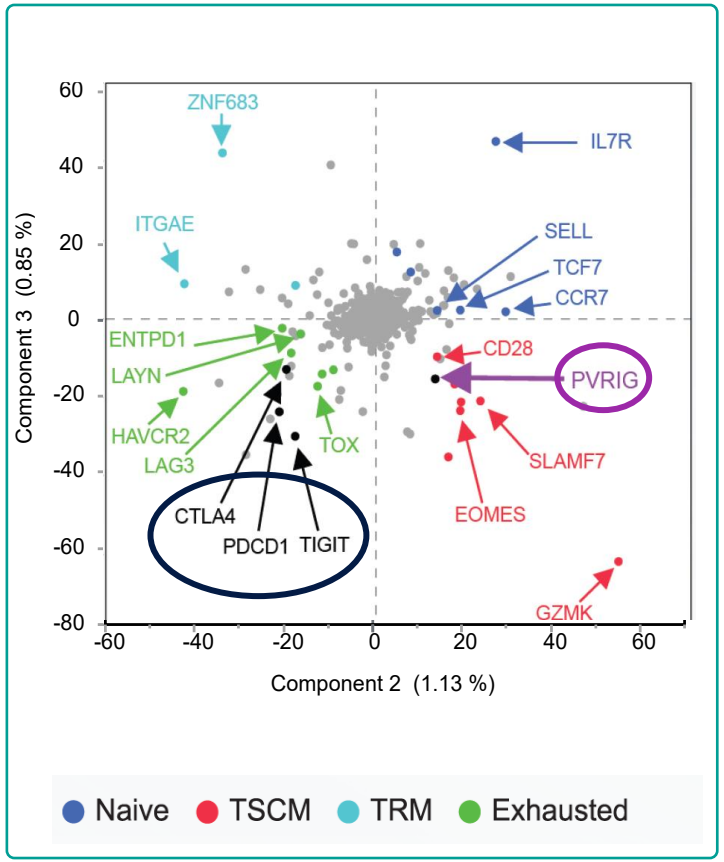
Klebbanoff et al., 2005, PNAS.

Stem-like CD8 T cells mediate response of adoptive cell immunotherapy against human cancer

Sri Krishna[1]*, Frank J. Lowery[1]*, Amy R. Copeland[1], Erol Bahadiroglu[2], Ratnadeep Mukherjee[2], Li Jia[3], James T. Anibal[2], Abraham Sachs[1], Serifat O. Adebola[2], Devikala Gurusamy[1], Zhiya Yu[1], Victoria Hill[1], Jared J. Gartner[1], Yong F. Li[1], Maria Parkhurst[1], Biman Paria[1], Pia Kvistborg[4], Michael C. Kelly[5], Stephanie L. Goff[1], Grégoire Altan-Bonnet[2], Paul F. Robbins[1]†, Steven A. Rosenberg[1]†

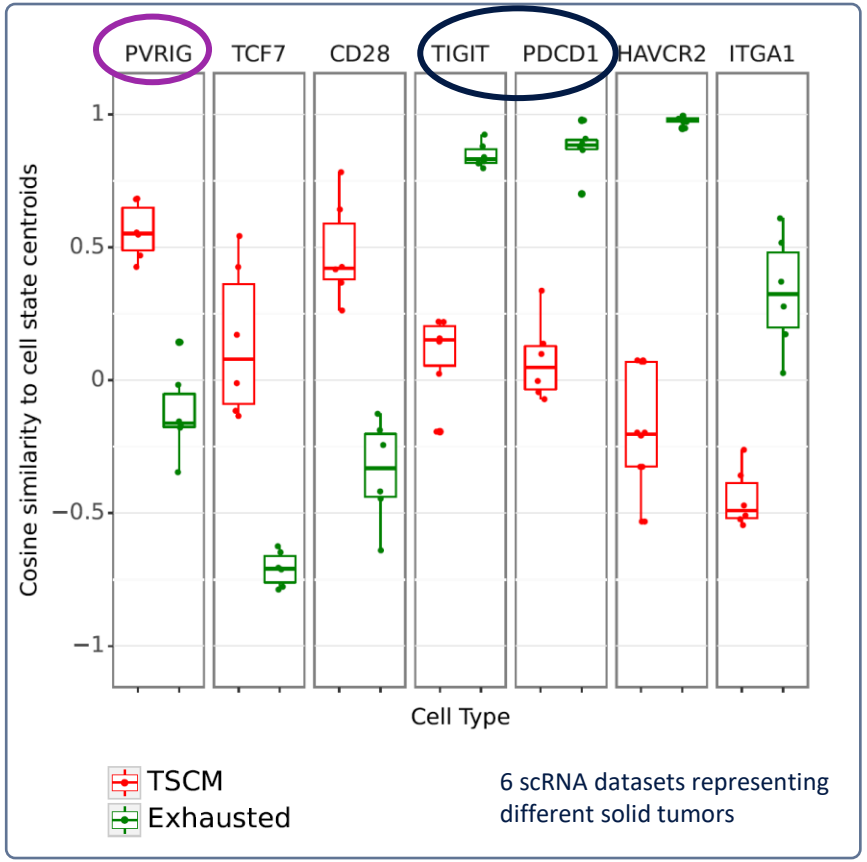
Krishna et al., 2020, Science

PCA analysis of scRNA of CD8⁺ T cell genes, NSCLC



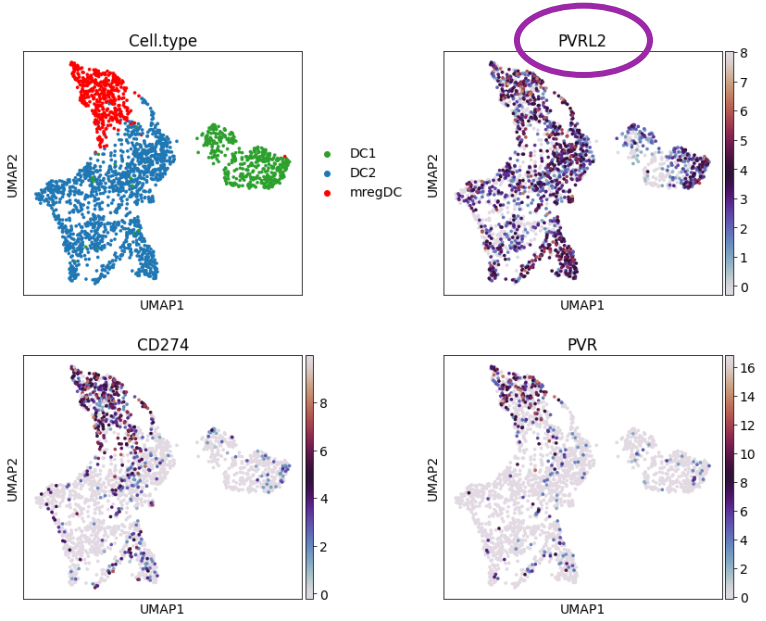
NSCLC: Non small cell lung cancer

PVRIG is expressed in T_{SCM} cells whereas other immune checkpoints are enriched in exhausted



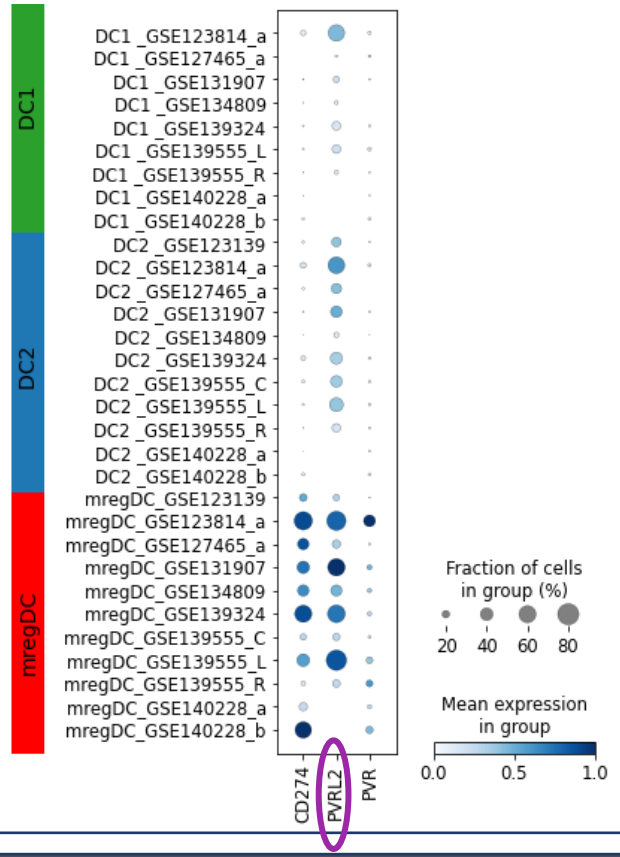
PVRL2 (PVRIG ligand) has a dominant expression on dendritic cells

PVRL2 is expressed on DCs

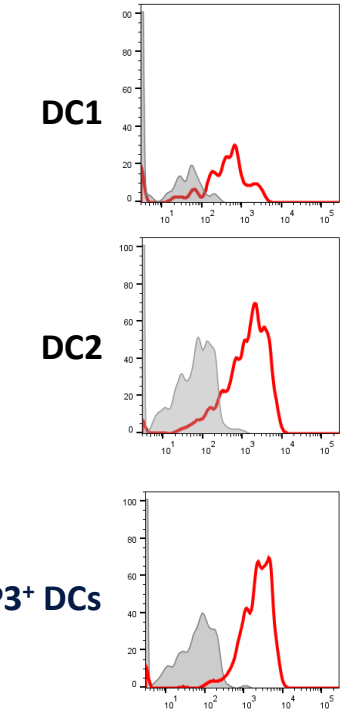


GSE123814 Dataset of SCC/BCC internally analyzed

PVRL2, PD-L1, PVR expression on DCs across multiple scRNA cancer datasets



PVRL2 protein expression on DCs in ovarian cancer



Internal protein data

PVRIG blockade may enhance T_{SCM} - DC interaction and induce potent T_{SCM} activation

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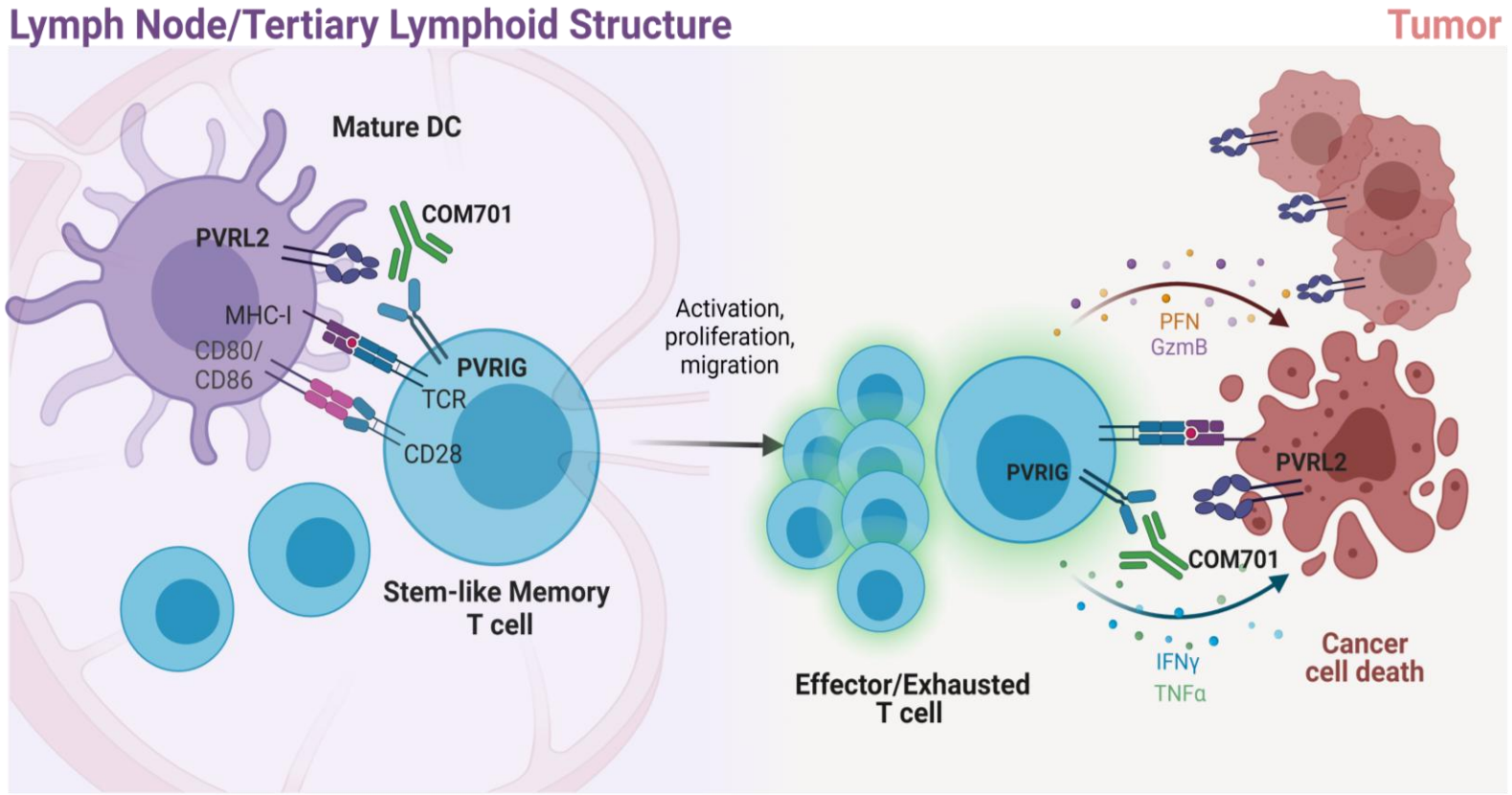
Alteber et al, Cancer Immunology Research, 2024

Unique biology for PVRIG checkpoint

And Strong biological rationale to target PVRIG in ovarian cancer

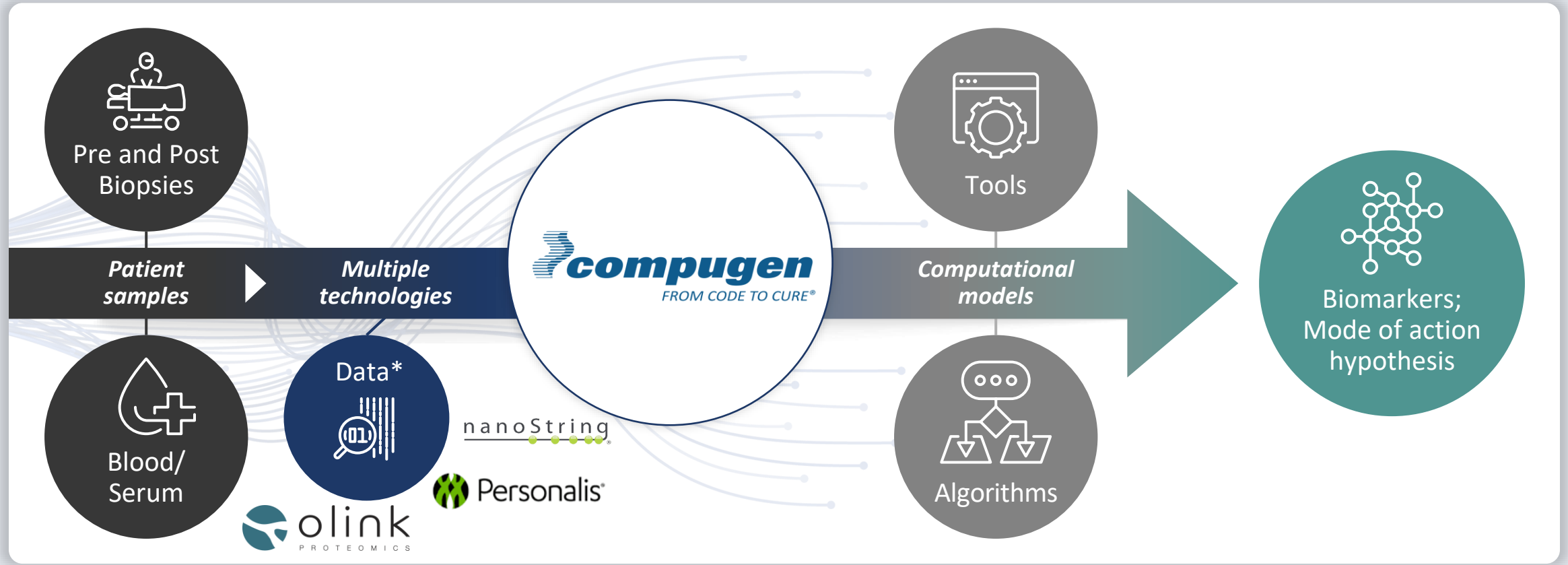
- High **PVRIG pathway** expression levels in **ovarian cancer**
- **PVRIG pathway** differentially expressed on early differentiated stem like memory T cells and dendritic cells compared to other immune checkpoints
- PVRIG blockade with **COM701** alters the tumor microenvironment including in less inflamed tumors **like ovarian cancer**



Alteber et al, Cancer Immunology Research, 2024

Translational insights from COM701 clinical studies

Translational exploration using multiple new technologies and data types

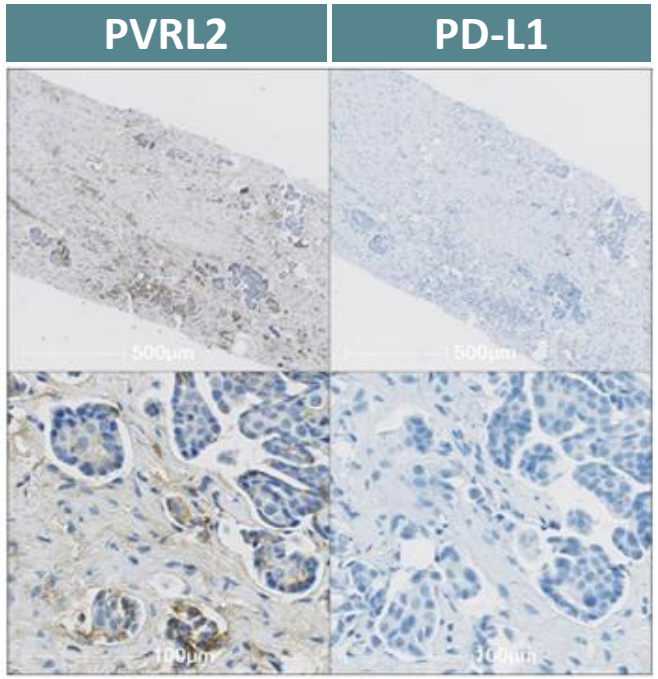


*Data: Olink – blood proteins, Personalis – DNA,RNAseq, TCR NanoString DSP – Spatial omics

COM701 single agent activity: Partial response >18 months*

PD-L1 negative ovarian cancer patient supported by immune activation

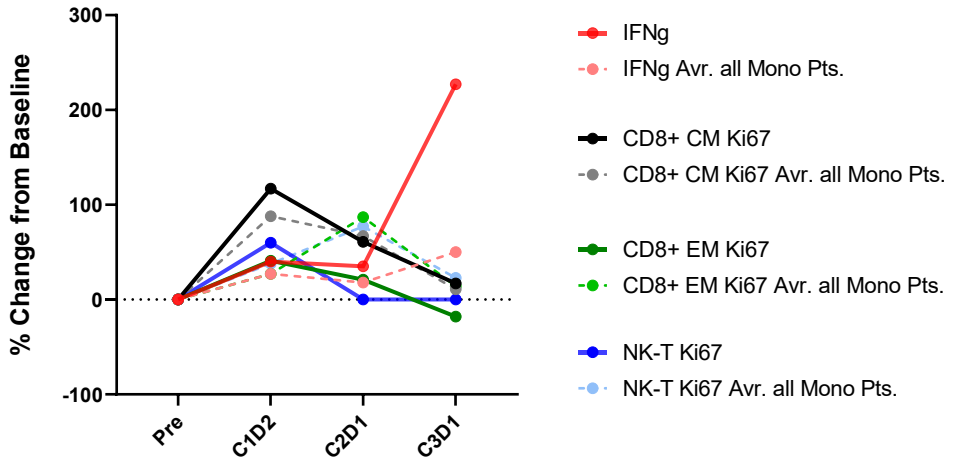
Patient received 3 prior lines of therapy



Pre- treatment archival biopsy (>1 year)

- **Immune "desert":** no immune cells in the biopsy
- **Negative PD-L1 staining**
- PVRL2 (PVRIG ligand) expressed on tumor and endothelial cells

Increase in IFNγ induction and immune activation in peripheral blood



ASCO, June 2021, Vaena et al., Oral presentation

COM701 single agent immune modulation of the tumor microenvironment also demonstrated

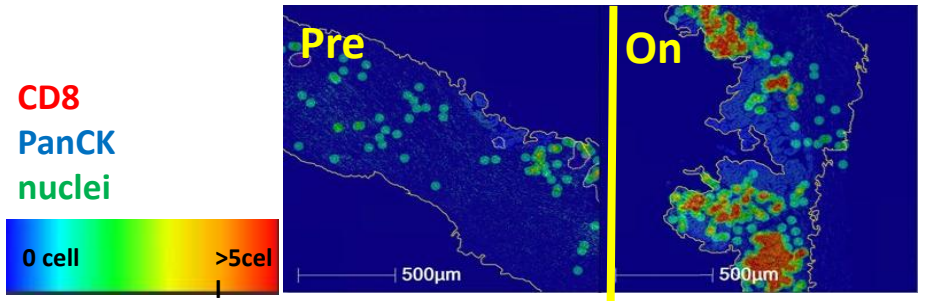
Ophir E et al SITC 2022; Alteber E et al Cancer Immunology Research 2024

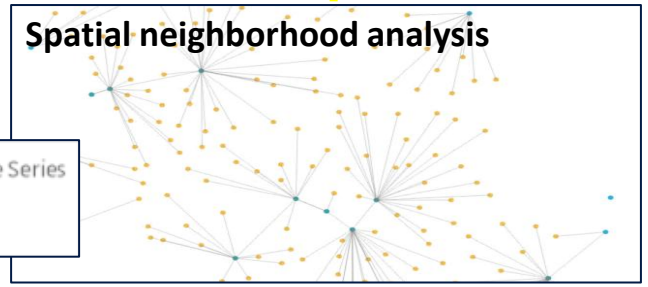
* This patient was on study treatment for 24 months i.e., she completed her treatment course allowed per protocol

Incorporating cutting-edge technologies with computational capabilities to support end-to-end R&D inquiries

nanoString

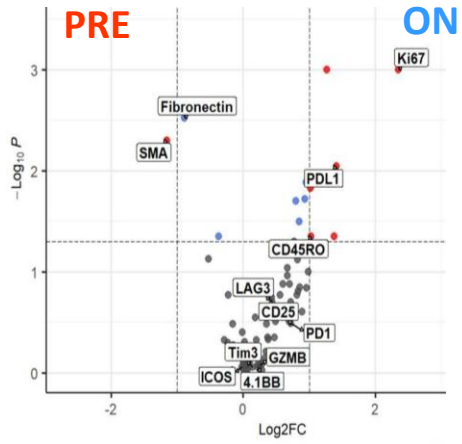
CD8 distribution in TME



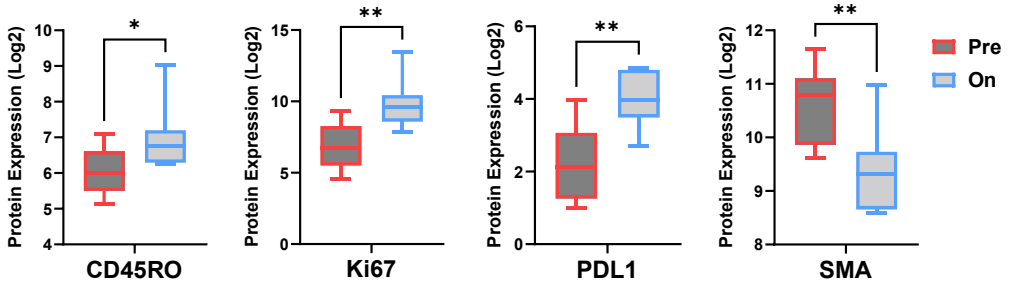


% CD8 cells	5.2	15.8
Maximum CD8 Density (CD8/µm²)	0.005	0.012
Av. Distance Tumor-CD8 (µm)	51.027	23.190

Protein expression in CD8 regions (NanoString, DSP)



Protein expression in CD8 regions



SMA = Smooth Muscle Actin

Patient with ovarian cancer demonstrating shift from stromal markers towards immune activation in TME following COM701 monotherapy

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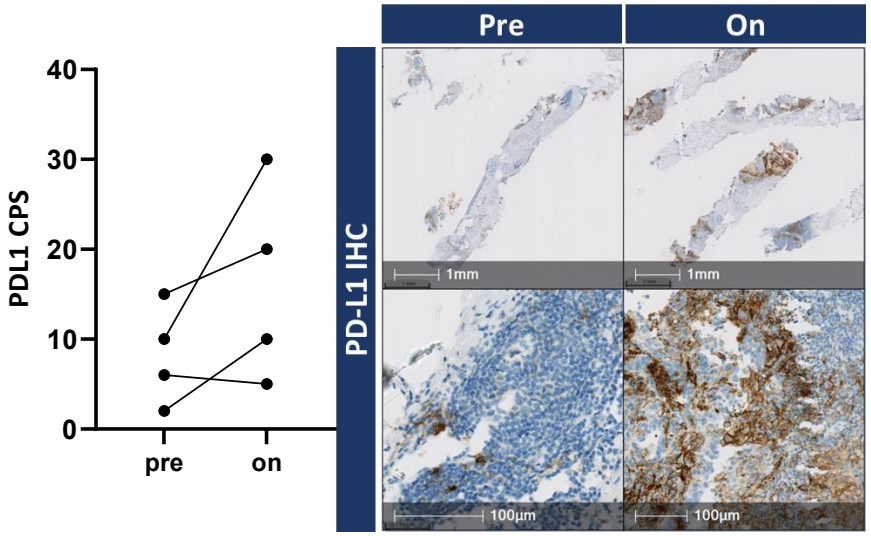
Alteber et al, Cancer Immunology Research, 2024

TME immune activation is induced by PVRIG blockade in patients with ovarian cancer

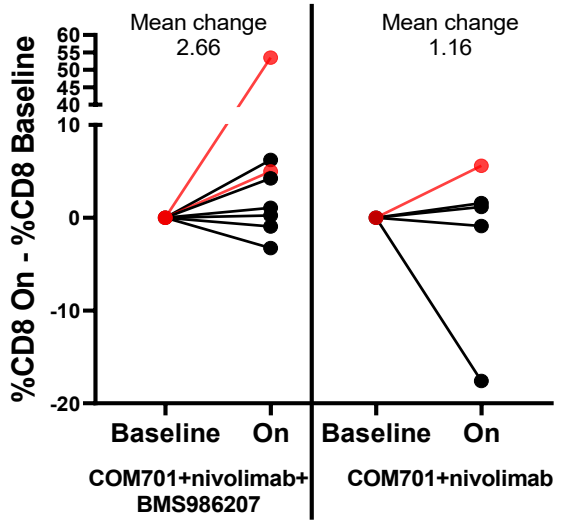
COM701 monotherapy induces TME immune activation in patients with ovarian cancer



- 3 / 4 patients showed an increase in PD-L1
- PD-L1 upregulation and increased CD8 infiltration indicate immune activation induced by COM701 monotherapy

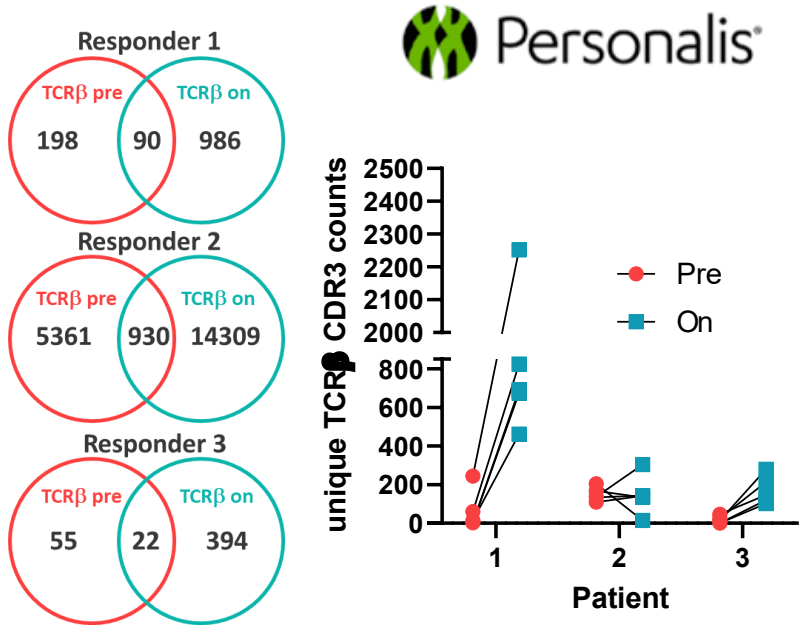
COM701+nivolumab ± anti-TIGIT (BMS-986207) in PROC patients

% of CD8 infiltration on treatment



- 8/13 patients with increased CD8
- Most prominent in patients with clinical benefit (marked in red)

TME T cell clonal expansion in patients with clinical benefit from COM701+ nivolumab± BMS-986207



PROC: Platinum Resistant Ovarian Cance ; TME: Tumor Microenvironment

Definition: Clinical Benefit (CB)= CR+PR+SD>180 days on study; No Clinical Benefit (NCB) = PD +SD<180 days on study

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Consistent efficacy & safety with COM701 combination

In platinum resistant ovarian cancer patients who have exhausted all options

Efficacy

Investigator assessed by RECIST v1.1	COM701+ nivolumab + BMS-986207[1] (N=20)	COM701+ pembrolizumab+ COM902[2] (N=24)
Overall Response rate % (CR+PR)	4 (20%)	4 (17%)
Disease control rate % (CR+PR+SD)	9 (45%)	11 (46%)

- Responses were also observed in PDL1 negative
- Benchmark results reported for anti-PD-1 ± anti-TIGIT [3,4,5]
  - ORR <10% in all-comers
  - ORR 0% in PD-L1 <1

The safety and tolerability profile generally consistent with approved anti-PD-(L)1s

- Most common reported AEs grade 1/2 fatigue, diarrhea and nausea
- Grade ≥3 TRAEs 20%
- No grade 4/5 TRAEs
- Tx related discontinuations 4.4%

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BMS-986207 (Bristol Myer's Squibb, anti-TIGIT)
TRAE: Treatment related adverse event
AE: Adverse event

1. Moroney J, et al, ESMO IO 2022 Modified
2. Yeku O, et al, SITC 2024 Modified
3. Matulonis et al ASCO 2022,
4. Holmes et al JCO ASCO 2022,
5. Perets et al ACCR 2022

MAIA-ovarian: COM701 adaptive platform trial in relapsed platinum sensitive ovarian cancer in maintenance setting

Key eligibility criteria

Relapsed platinum sensitive ovarian cancer

Complete or partial response following platinum-based chemotherapy

Maintenance therapy post bevacizumab and/or PARP inhibitor or not a candidate for bevacizumab and/or PARP inhibitor

Sub-trial 1
Single agent activity of COM701 versus placebo (standard of care)

Adaptive trial n= 60
2:1 Randomization

Sub-trial 2 and beyond
COM701 combination studies e.g.
anti-PD-1/TIGIT or bevacizumab or PARPi or others

Endpoints

Primary: Efficacy- median progression free survival

Secondary: Safety

Exploratory: Biomarkers

Trial initiation: Q2 2025

First patient dosed: Mid July 2025

Projected Interim analysis: H2 2026

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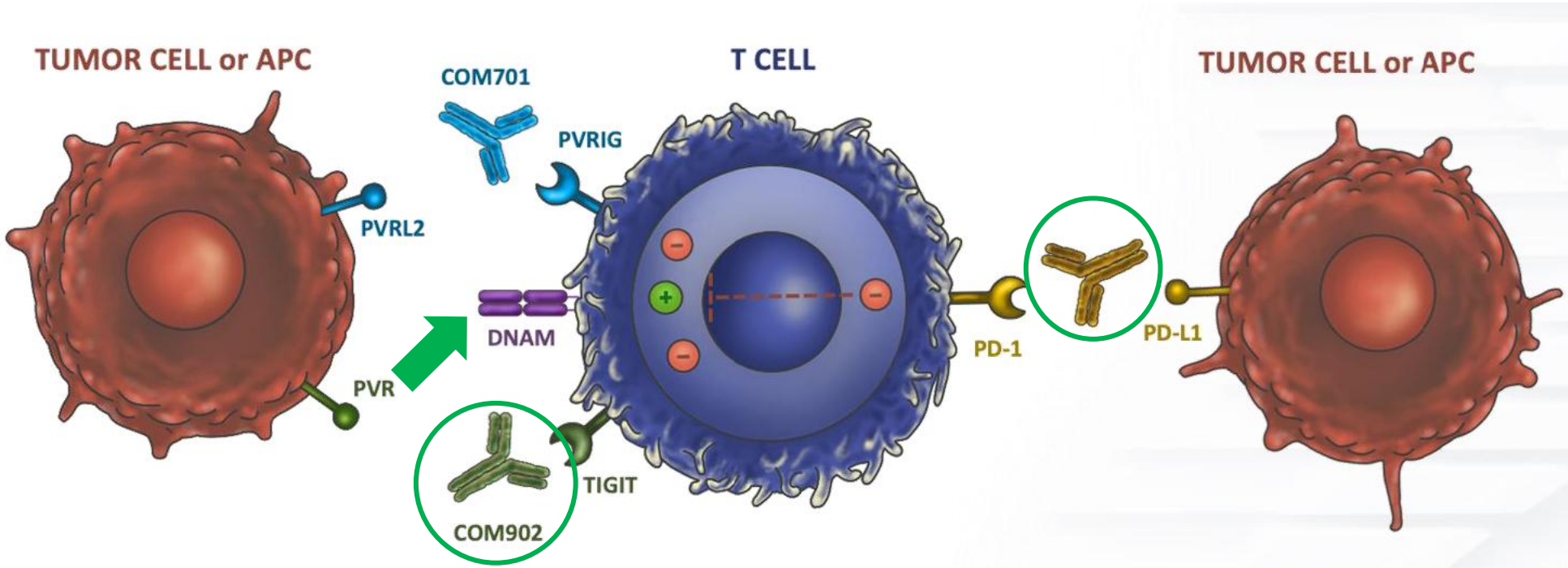
2. Novel strategy for TIGIT immune checkpoint

2. Novel strategy in the TIGIT pathway

Taking advantage of best-in-class Compugen anti-TIGIT antibody COM902

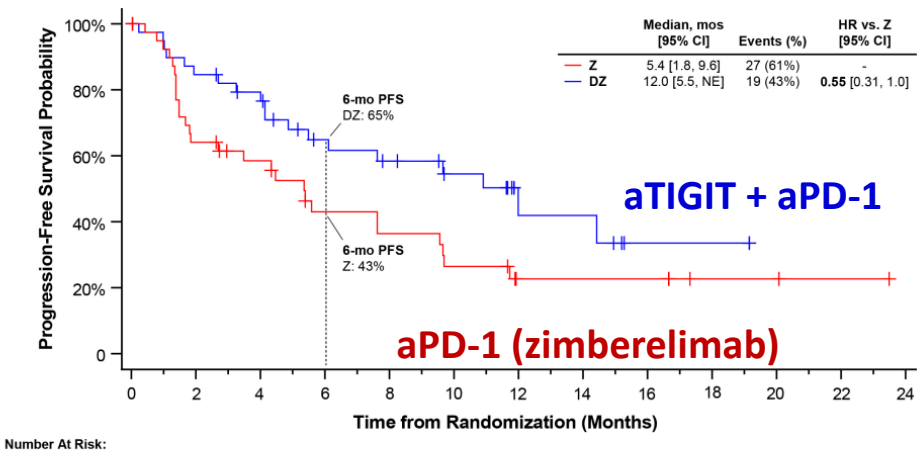


Adapted from Alteber *et al.* Cancer Discov. 2021

TIGIT – A validated target in randomized clinical trials

Domvanalimab (Ph2) "ARC-7" Lung

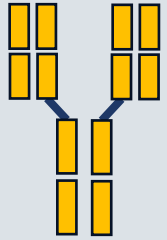
PD-L1≥50%



Tiragolumab (Ph3)

potential first-in-class anti-TIGIT

Anti-TIGIT Fabs

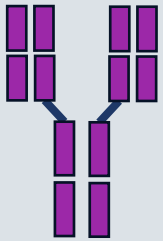


IgG1 Fc*

COM902 (Ph1/2)

potential best-in-class anti-TIGIT

Anti-TIGIT Fabs



IgG4 Fc**

Fab functionality	Moderate affinity for TIGIT (nM)	Better affinity / increased EC50 (pM)
Fc functionality	Active FcgR, ADCC CDC	LOW FcgR, Low ADCC

* Other Fc active anti-TIGIT antibodies : Vibostolimab (Ph3), Ociperlimab (Ph3), Belrestotug (Ph2)
** Other Fc reduced anti-TIGIT antibodies : Domvanalimab (Ph3), BMS 986207 (Ph2)

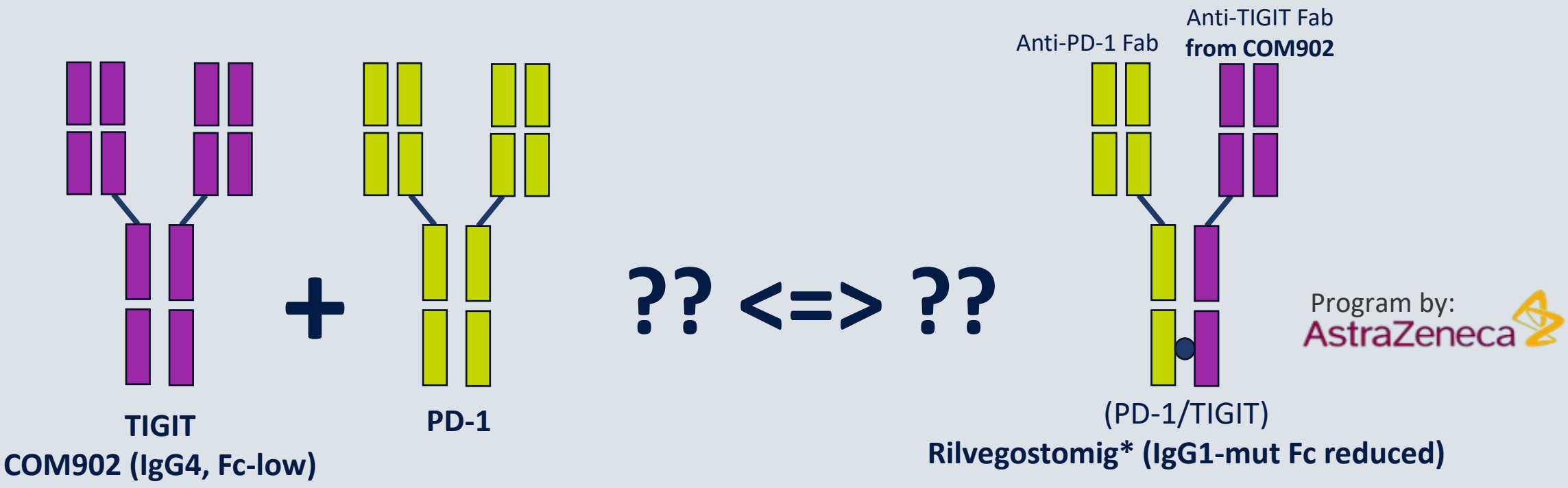
Anti-TIGIT antibodies bring some additional activity to anti-PD-(L)1

The nature of the Fc may matter ; best-in-class with Fc-low or reduced

Sources:
Gubens MA, et al. ARC-7: Phase 2 study of domvanalimab and zimberelimab ± etrumadenant vs zimberelimab in first-line, PD-L1–high, locally advanced or metastatic NSCLC. J Clin Oncol. 2023;41(suppl 16; abstr 9002).

Novel strategy in the TIGIT pathway

What would a bispecific antibody bring?



Source: compugen FROM CODE TO CURE®

* Rilvegostomig, an Fc-reduced, monovalent, bispecific humanized IgG1 monoclonal antibody targeting PD-1 and TIGIT. The anti-TIGIT component of rilvegostomig is derived from COM902 developed by Compugen Ltd.

TIGIT-PD1 bispecific unique pharmacology

Rilvegostomig's *ex vivo* activity was assessed in comparison with pharmacy-grade reagents to explore its differentiated mechanism of action

Key comparisons	Mechanistic Comparators	Method
1 Comparison against bivalent PD-(L)1 inhibitors	Pembrolizumab & Atezolizumab Pharmacy grade αPD-1 and αPD-L1	Fresh tumor collection and baseline testing
2 Comparison against co-administration of the single components	αPD-1 (LO115) bivalent OR monovalent +/- αTIGIT (COM902) bivalent OR monovalent	Processing
3 Activity with different Fc backbones	αPD-(L)1 Pembrolizumab OR Atezolizumab +/- αTIGIT (COM902) Fc-active OR Fc-reduced OR Rilvegostomig Fc-active OR Fc-reduced	Rilvegostomig → *Ex vivo* culture → Data analysis

The tumors in this study are not sourced from rilvegostomig clinical trials.

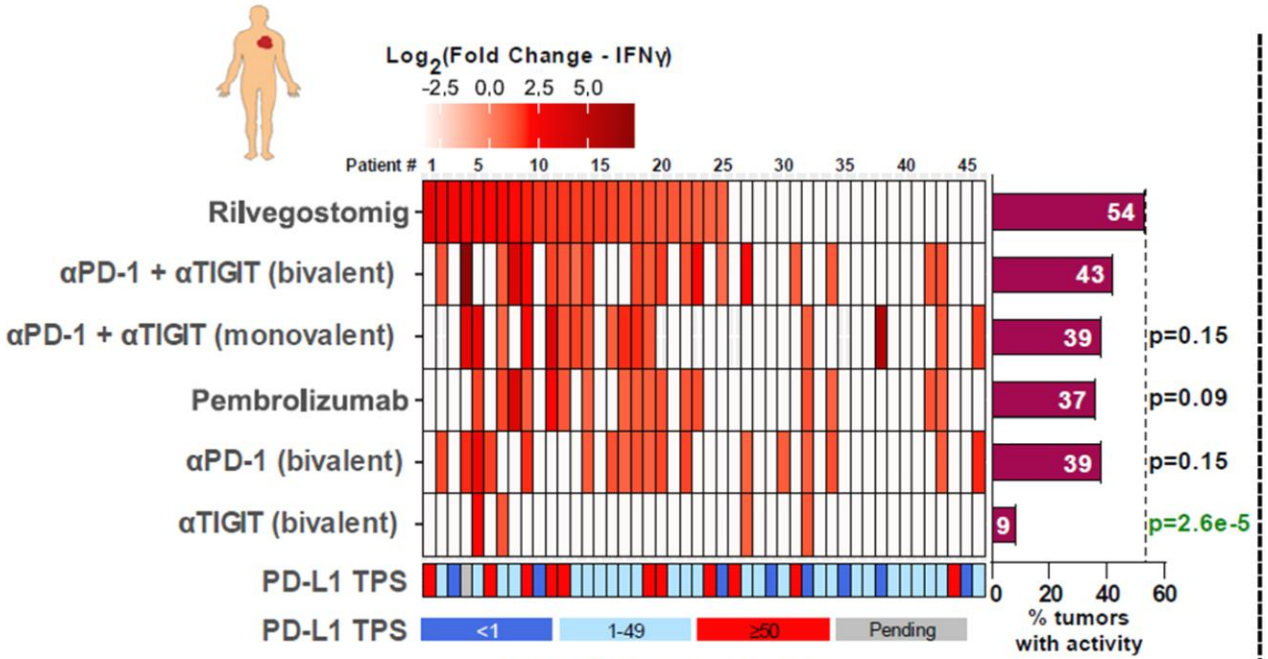
From Ratiu et al. (2025) - Rilvegostomig Enhances Ex Vivo Immune Activation in Patient-Resected NSCLC Tumors Over PDx or PDX/αTIGIT Combination Therapy

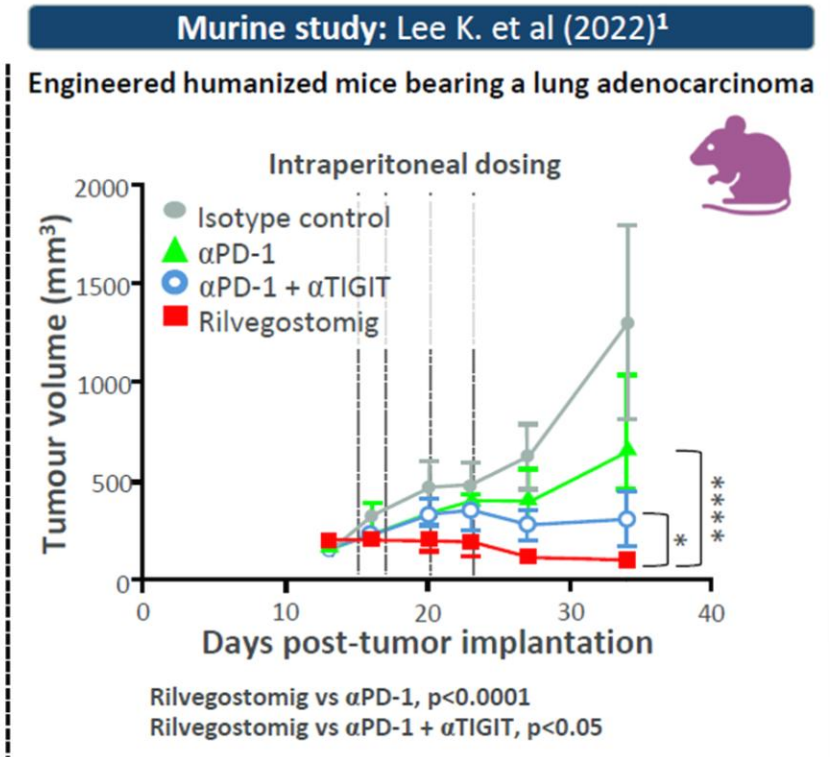
Source: compugen FROM CODE TO CURE®

Program by: AstraZeneca

TIGIT-PD1 bispecific unique pharmacology

Rilvegostomig's coordinated inhibition of PD-1/TIGIT induces greater *ex vivo* and *in vivo* activity than its components





From Ratiu et al. (2025) - Rilvegostomig Enhances Ex Vivo Immune Activation in Patient-Resected NSCLC Tumors Over PDx or PDX/αTIGIT Combination Therapy

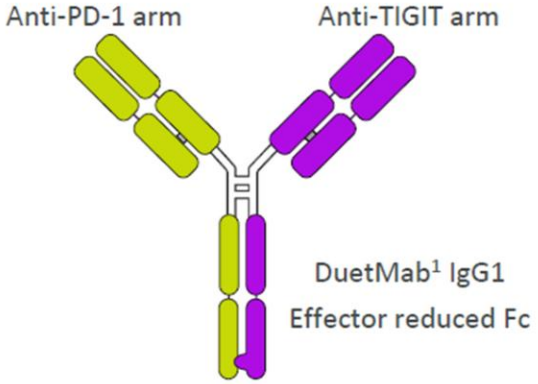
Source: compugen FROM CODE TO CURE®

Program by: AstraZeneca

TIGIT-PD1 bispecific antibody is clinically active

Rilvegostomig is a Fc-reduced anti-PD-1/TIGIT monovalent bispecific antibody that showed preliminary encouraging activity in NSCLC in the phase 1/2 ARTEMIDE-01 trial

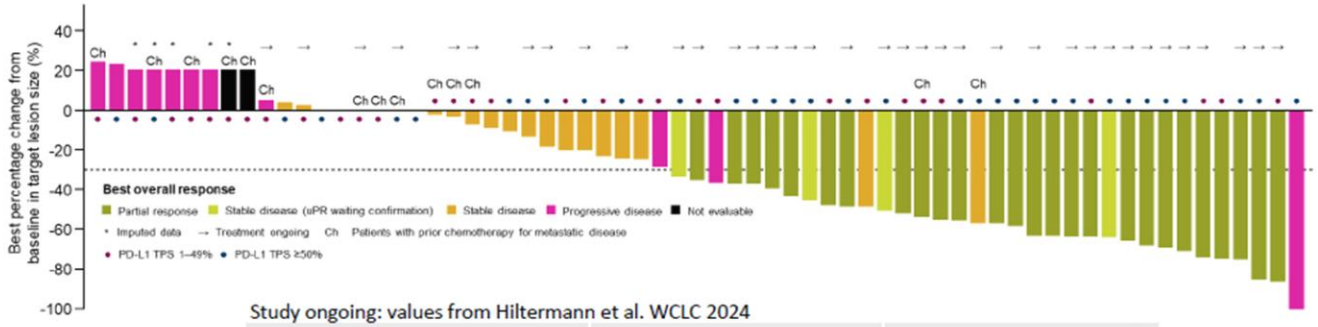
Rilvegostomig (PD-1/TIGIT bispecific Ab)



Rilvegostomig's bispecific format enables the synchronous, localized, and coordinated inhibition of both targets on the same cell to enhance CD8/NK cells anti-tumor activity

ARTEMIDE-01[2]

Overall response rate of rilvegostomig 750 mg Q3W in CPI-naïve, PD-L1 TPS ≥1% NSCLC



Study ongoing: values from Hiltermann et al. WCLC 2024

n (%)	PD-L1 1–49% TPS (n=31)	PD-L1 ≥50% TPS (n=34)
ORR, confirmed + pending [95%CI]	9 (29%) [14.2, 48.0]	21 (61.8%) [43.6, 77.8]
Continuing treatment	12 (38.7%)	24 (70.6%)

10 Ph2 and 10 Ph3 clinical trials are ongoing with Rilvegostomig

From Ratiu et al. (2025) - Rilvegostomig Enhances Ex Vivo Immune Activation in Patient-Resected NSCLC Tumors Over PDx or PDX/αTIGIT Combination Therapy

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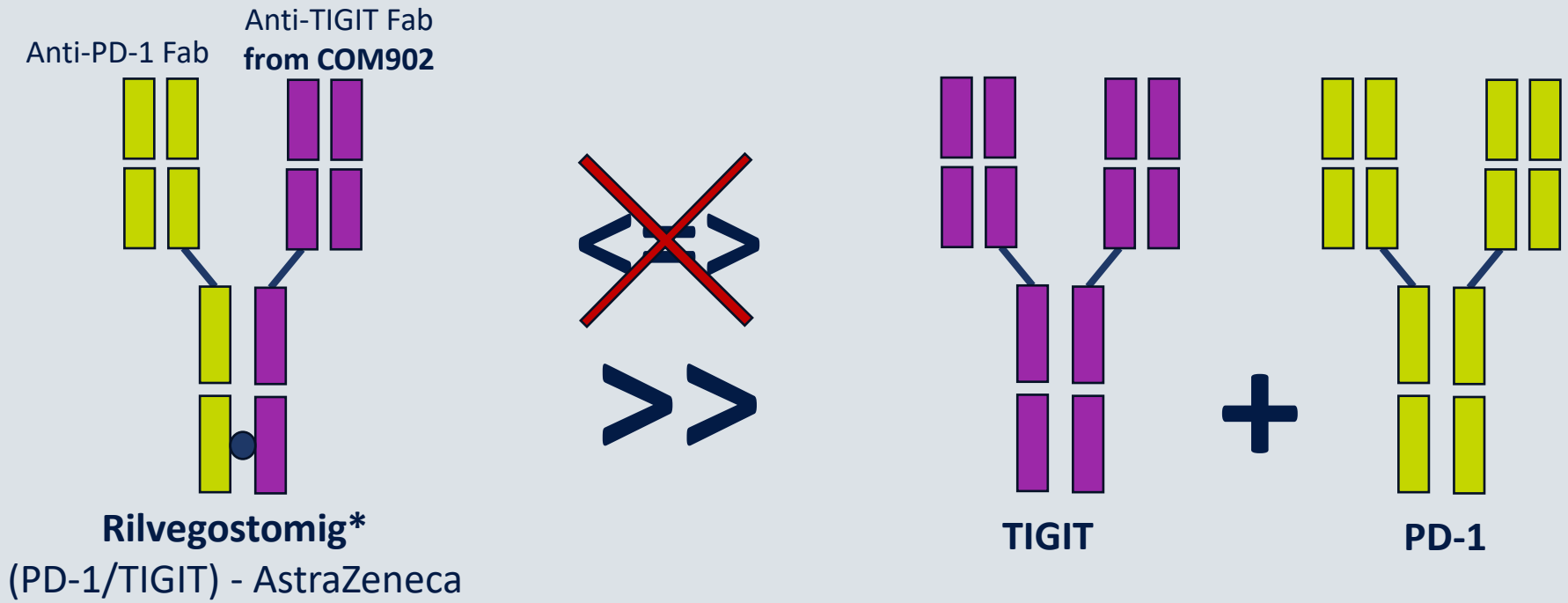
TIGIT-PD1 bispecific unique pharmacology

Rilvegostomig preclinical data from AZ suggest that the inhibition of PD-1 and TIGIT is “coordinated”



From Ratiu et al. (2025) - Rilvegostomig Enhances Ex Vivo Immune Activation in Patient-Resected NSCLC Tumors Over PDx or PDX/αTIGIT Combination Therapy

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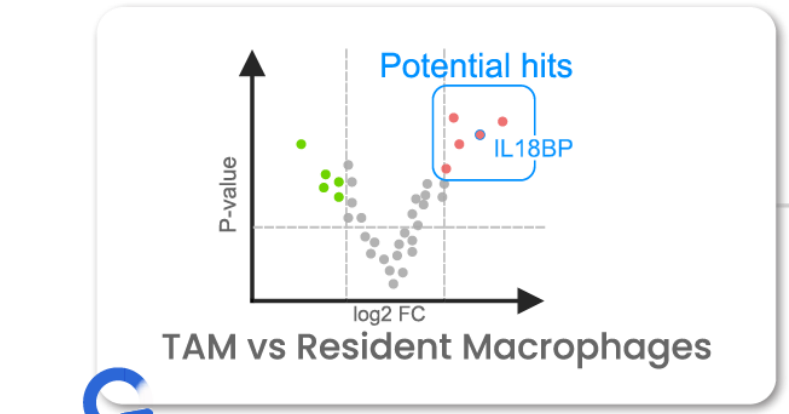
* Rilvegostomig, an Fc-reduced, monovalent, bispecific humanized IgG1 monoclonal antibody targeting PD-1 and TIGIT. The anti-TIGIT component of rilvegostomig is derived from COM902 developed by Compugen Ltd.

Program by: AstraZeneca

3. “Soluble” immune checkpoint discovery and development

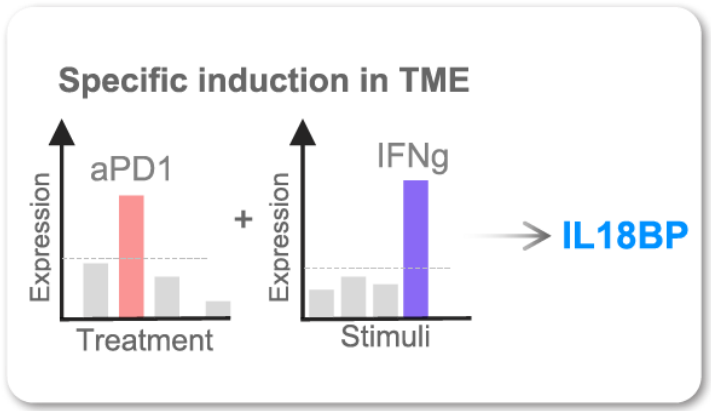
3. Discovery of IL-18 Binding Protein as a novel IO target





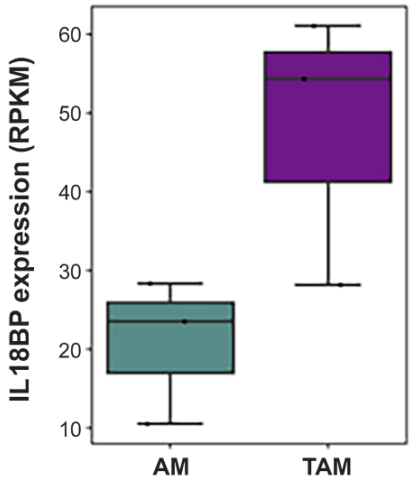
Filter top recurring membrane or secreted targets

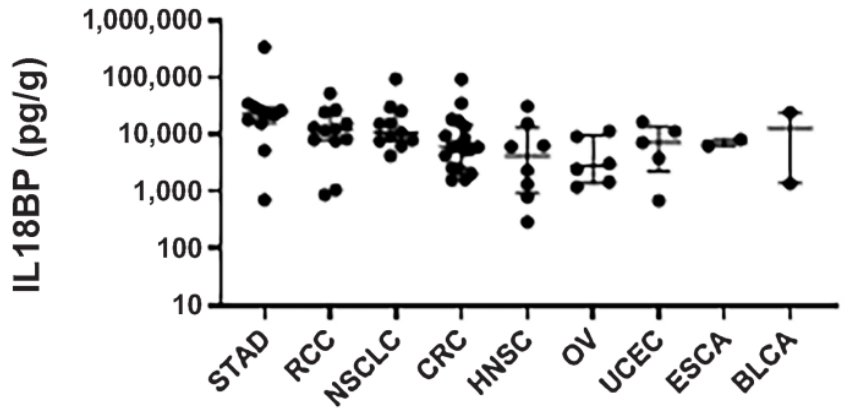




unigen Data pipeline

Lung adenocarcinoma TAMs express significantly higher IL-18BP than normal alveolar macrophages



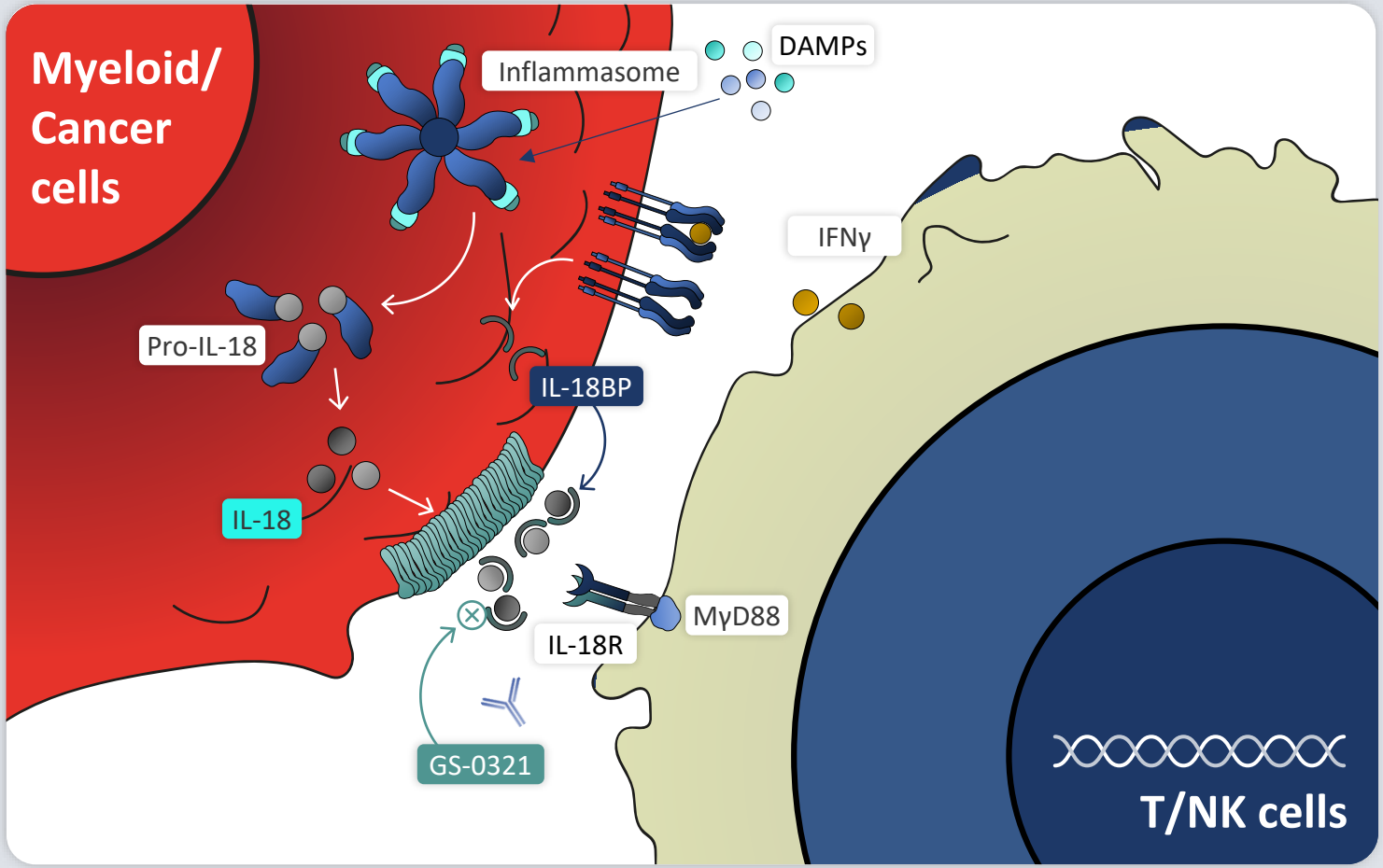


High levels of IL-18BP protein were detected in the TME across a wide range of solid tumor indications

Menachem et al, Cancer Immunology Research, 2024

Compugen identified potential dominant immunosuppression mechanism and antibody therapeutic

Interleukin-18 binding protein, an endogenous inhibitor of interleukin-18



IL-18 immune stimulatory cytokine upregulated endogenously in tumor microenvironment

IL-18BP blocks IL-18 activity

GS-0321 (COM503) potential first-in-class high affinity antibody releases IL-18 to enhance T and NK cell activation in the tumor

DAMPs- Damage-associated molecular patterns . GS-0321 is licenced to Gilead, Compugen responsible for ongoing Phase 1 development, Thereafter, Gilead will have sole right to develop and commercialize GS-0321

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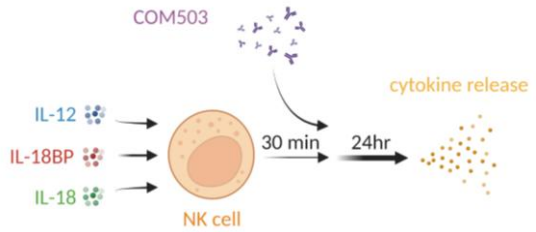
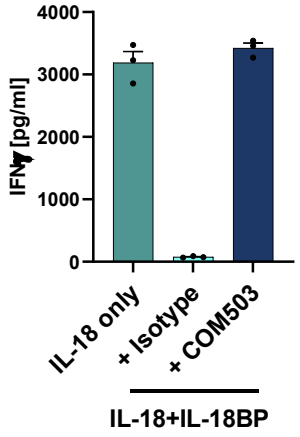
GILEAD Creating Possible

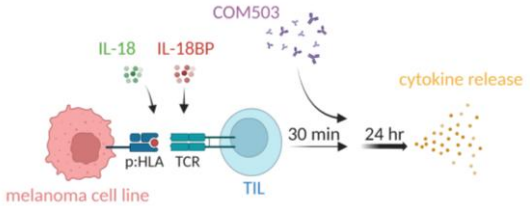
COM503, fully human, high affinity anti-IL-18BP antibody restores human TIL and NK cell activity in human assays

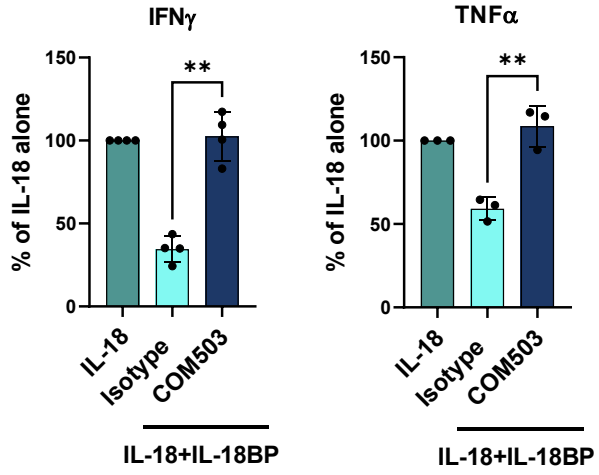
COM503 restored NK cell activity



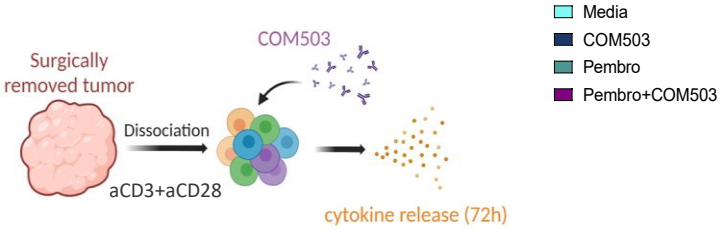


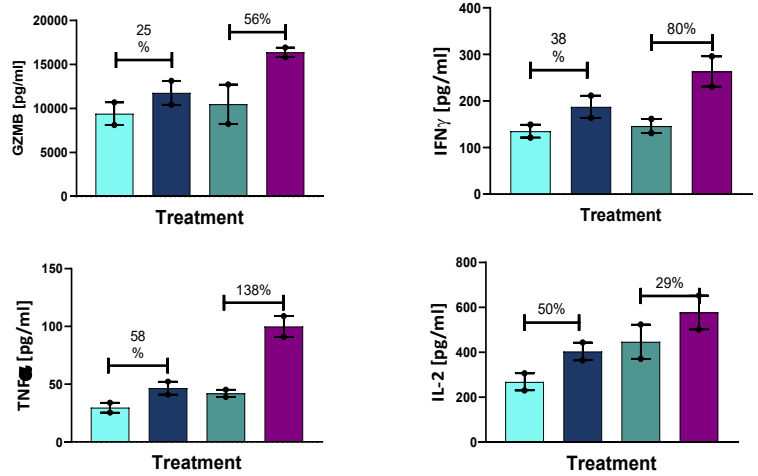
COM503 restored TILs activity





COM503 enhanced T cell activation in human dissociated tumor cells assay



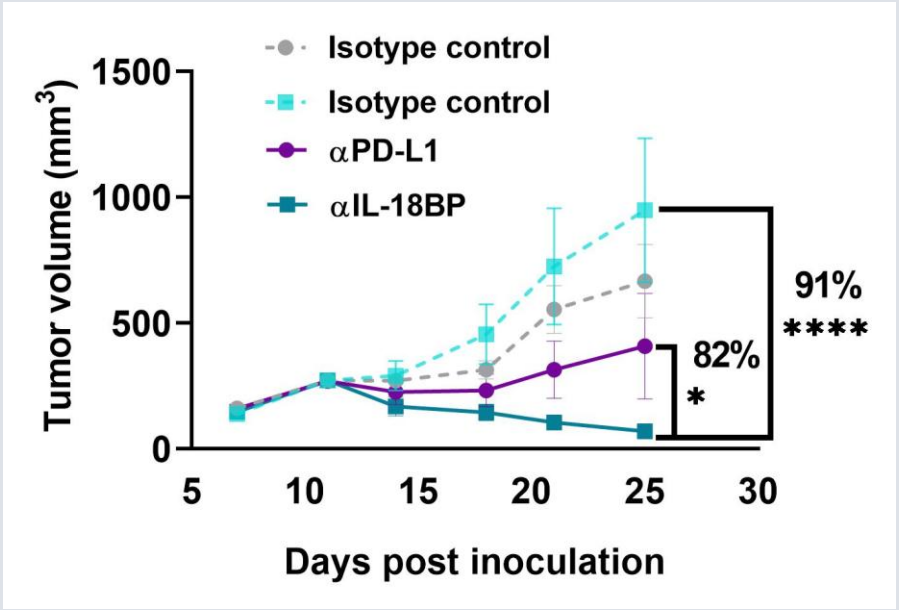


Menachem et al, Cancer Immunology Research, 2024

TILs- tumor infiltrating lymphocytes
Ferre P, presentation, SITC, 2023, modified

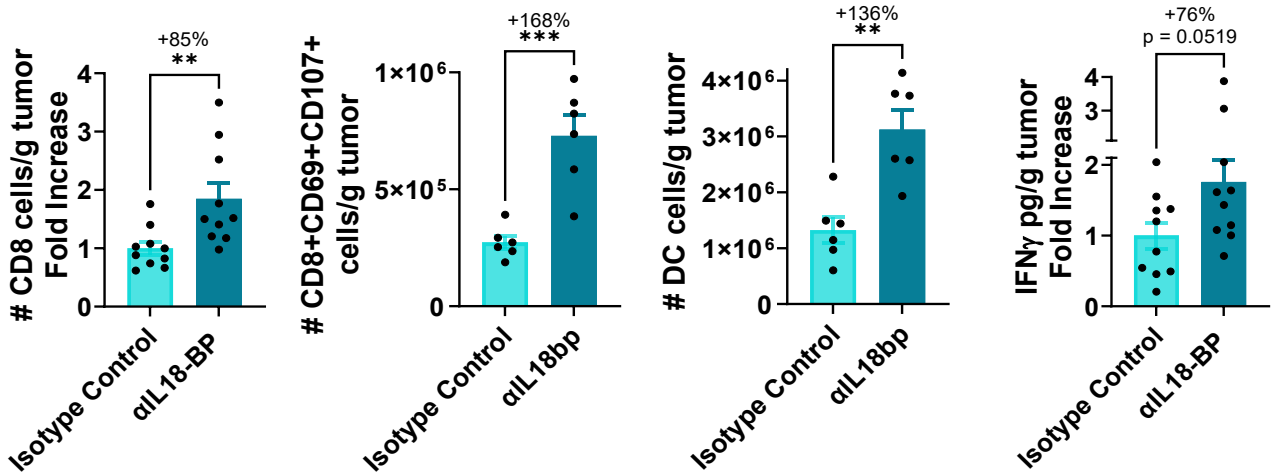
IL-18BP antibody demonstrates monotherapy efficacy and pharmacodynamic activity restricted to the tumor

A

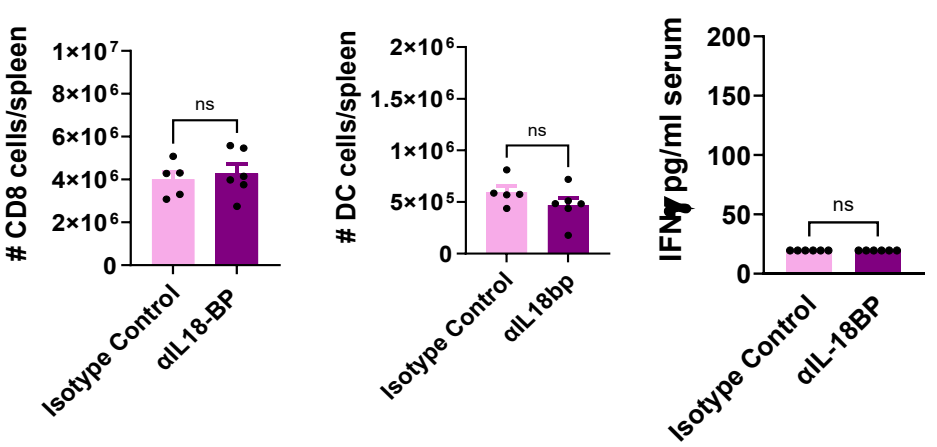


E0771 orthotopic mouse breast tumor model
Anti-mouse IL18BP antibody

B



C



IL-18BP antibody is currently investigated in Phase 1 trial

Menachem et al, Cancer Immunology Research, 2024

Ophir E, presentation, CIMT 2023, modified

Summary

Compugen's computational discovery and validation platform, Unigen, allowed:

- Discovery of novel IO targets that address mechanisms to enhance anti-cancer immunity, resulting in programs advancing in clinical trials
  - **PVRIG** (COM701), **TIGIT** (COM902, rilvegostomig[#]), **IL-18BP** (GS-0321[&]/COM503)

- Translational insights from patients' tumors or patients treated with novel IO agents
  - PVRIG unique expression in Tscm CD8 T cells, in immune aggregate structures in the TME
  - Anti-PVRIG effect: CD8+ T cell infiltration and immune modulation associated with clinical benefit, including in PDL1 negative tumors

Unigen continually evolves while adopting latest technologies (including AI/ML) and data to enhance its drug target discovery and validation capabilities

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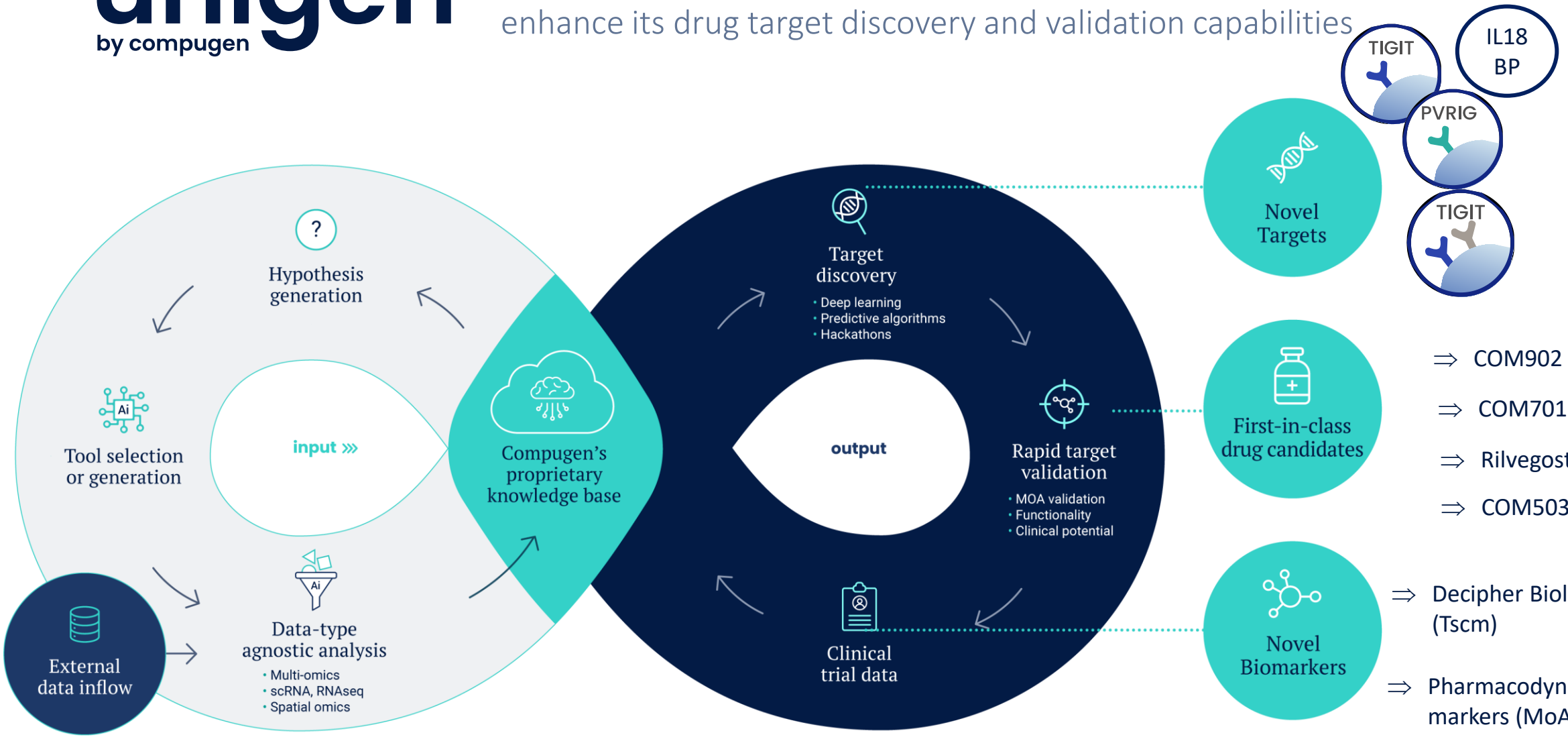
AstraZeneca's PD-1/TIGIT bi-specific antibody, the TIGIT component of which is derived from Compugen's COM902
& GS-0321 (previously COM503) licensed to Gilead

unigen™ by compugen

a flexible-loop platform for novel IO drug target discovery & development ; continually evolves while adopting additional technologies and data to enhance its drug target discovery and validation capabilities



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THANK YOU!

Compugen - 3 decades of evolving, refined computational biology, from Bioccelerator to Unigen



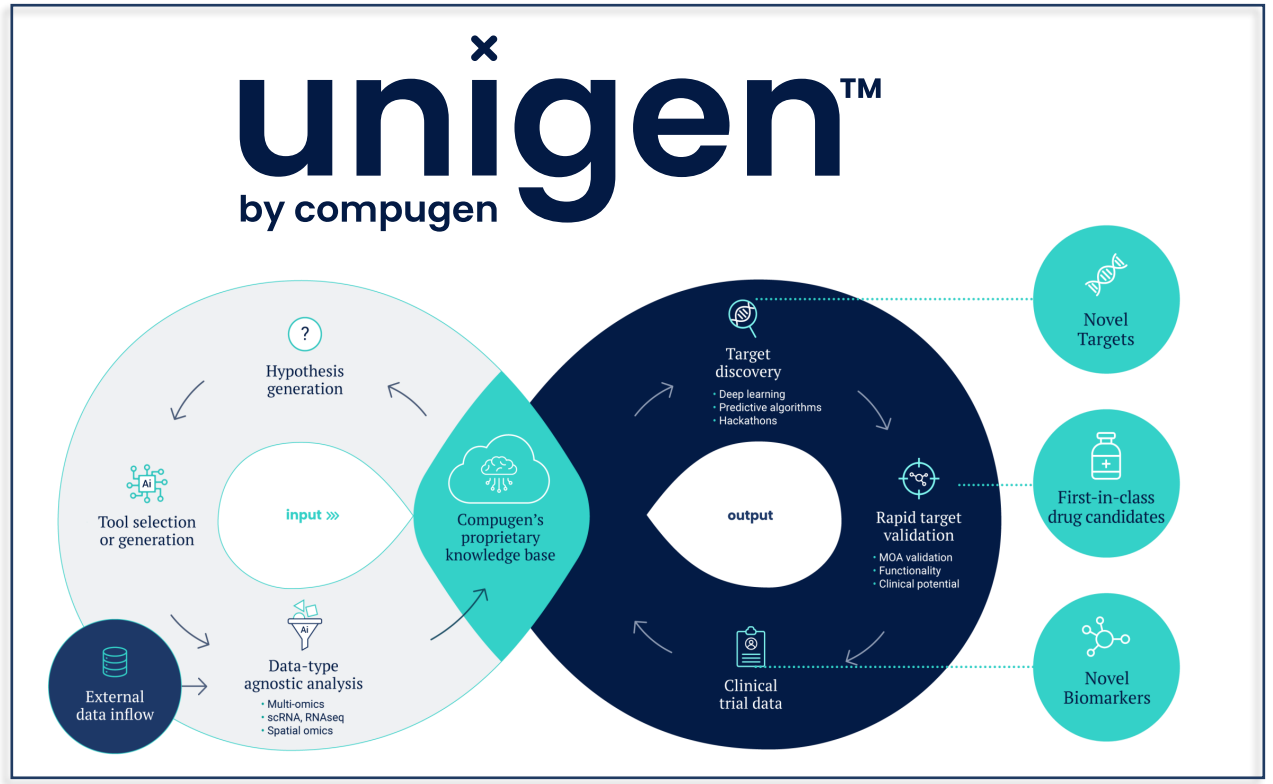

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Illustration rendered from MS Copilot tool