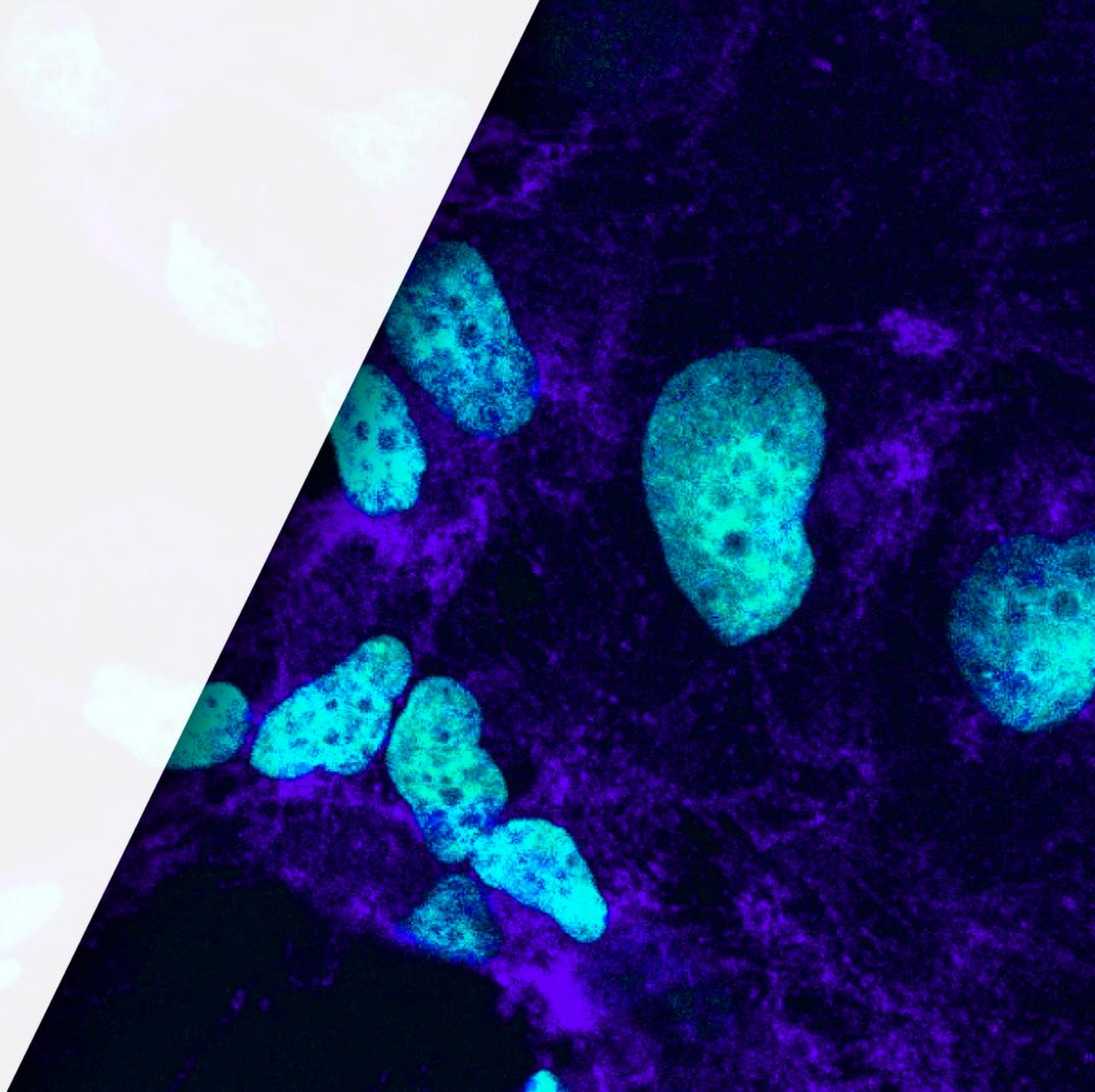
IMMUNITY.
RECRUITED.

# UNMASKING CANCER CELL CAMOUFLAGE

**COMPANY PRESENTATION | April 2021**



## SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This presentation contains forward-looking statements about our expectations, beliefs and intentions regarding, among other things, our product development efforts, business, financial condition, results of operations, strategies, plans and prospects. In addition, from time to time, we or our representatives have made or may make forward-looking statements, orally or in writing. Forward-looking statements can be identified by the use of forward-looking words such as “believe”, “expect”, “intend”, “plan”, “may”, “should”, “could”, “might”, “seek”, “target”, “will”, “project”, “forecast”, “continue” or “anticipate” or their negatives or variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical matters. Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements.

We believe these forward-looking statements are reasonable; however, these statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry’s actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements.

All forward-looking statements speak only as of the date hereof, and we undertake no obligations to update or revise forward-looking statements to reflect events or circumstances that arise after the date made or to reflect the occurrence of unanticipated events, except as required by applicable law. In evaluating forward-looking statements, you should consider these risks and uncertainties.

# INVESTMENT HIGHLIGHTS

## MIRP™
Multifunctional Immuno-Recruitment Proteins - A family of Immuno-therapeutic drugs for multiple cancer types

## CURRENT STATUS
- Robust preclinical results
- Phase I/II for solid tumors
- Collaboration with ROCHE to combine with Atezolizumab

## PIPELINE
**-1st product |** Phase I/II CD47/41BB
**-2nd & 3rd products |** IND H2 2022
**-Multiple future candidates in R&D**

## MARKET
Immuno-therapeutics
$56.5B by 2025

## IP
15 families
2 granted (US and other territories),
13 pending (NP worldwide and PCT stage)

## STRONG TEAM
Experienced management, supported by reputable KOLs, amongst which is technology inventor, Prof. Mark Tykocinski, Dean of the School of Medicine and Provost, Jefferson University.

IMMUNITY. RECRUITED.

# LEADERSHIP TEAM

## Management

**Yaron Pereg, PhD**
CEO
Genentech A Member of the Roche Group · BIOLINERX · CELLECT · GLOSENSE

**Adam Foley-Comer, MD**
CMO
Roche · BIOLINERX · QUINTILES · IMMUNE Pharmaceuticals · Quark Pharmaceuticals

**Ayelet Chajut, PhD**
CTO
Quantomics · Pluristem · ROSETTA GENOMICS · Quark Pharmaceuticals

**Oren Gez, MBA**
VP Strategy & Corporate Dev.
BARCLAYS · ING

**Iris Pecker, PhD**
VP CMC
InSight Biopharmaceutical

**Rinat Tabakman, PhD**
VP Development
BIOLINERX · XTLbio

## Scientific and Clinical Advisory Board

**Mark L. Tykocinski, M.D.**
KAHR technology inventor; BOD Observer; Provost Jefferson Thomas University

**Martin S. Tallman, MD**
Chief Leukemia Service, Memorial Sloan Kettering Cancer Center

**Ezra Cohen, M.D.**
Director San Diego Center for Precision Immunotherapy

**Manuel Hidalgo, M.D., Ph.D**
Chief Division of Hematology and Medical Oncology, Weill Cornell;

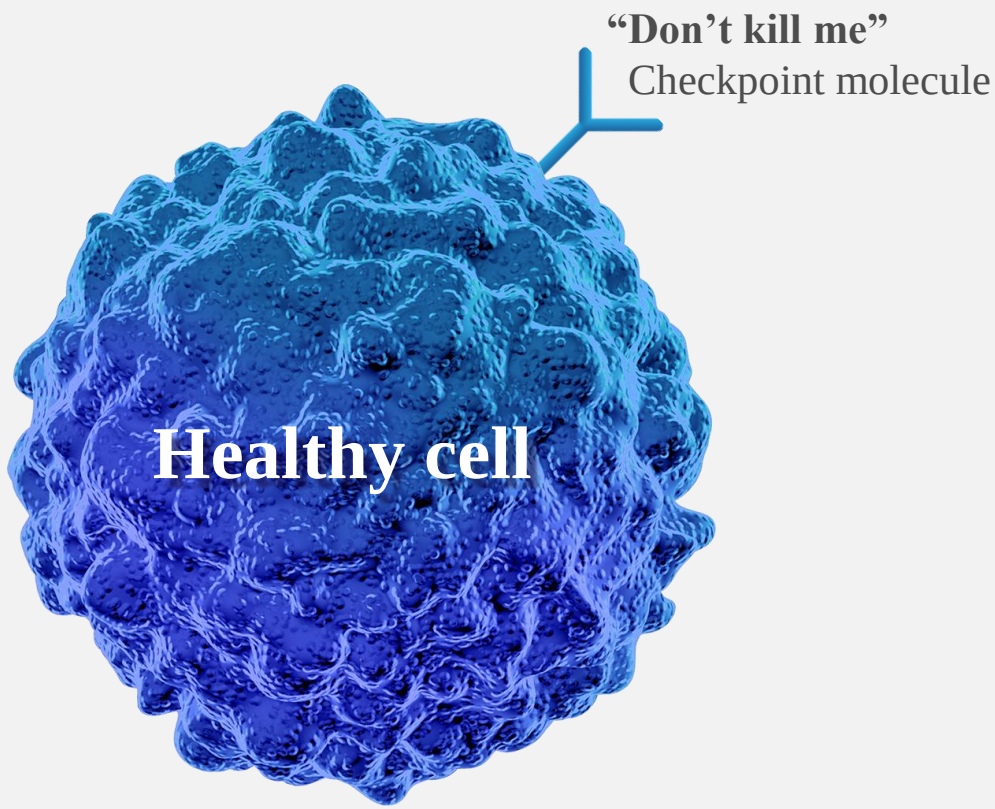
**Hagop Kantarjian, M.D.**
Chair Department of Leukemia at The University of Texas MD Anderson Cancer Center

**Edwin Bremer, PhD**
Professor at the Translational Surgical Oncology at the University Medical Center Groningen

**Samir Khelif, MD**
Director, Loop Immuno-Oncology Research Lab, Georgetown Lombardi Comprehensive Cancer Center

**Senthil Muthuswamy, PhD**
Associate Professor, Harvard Medical School and Director Cell Biology, Beth Israel Deaconess Medical Center

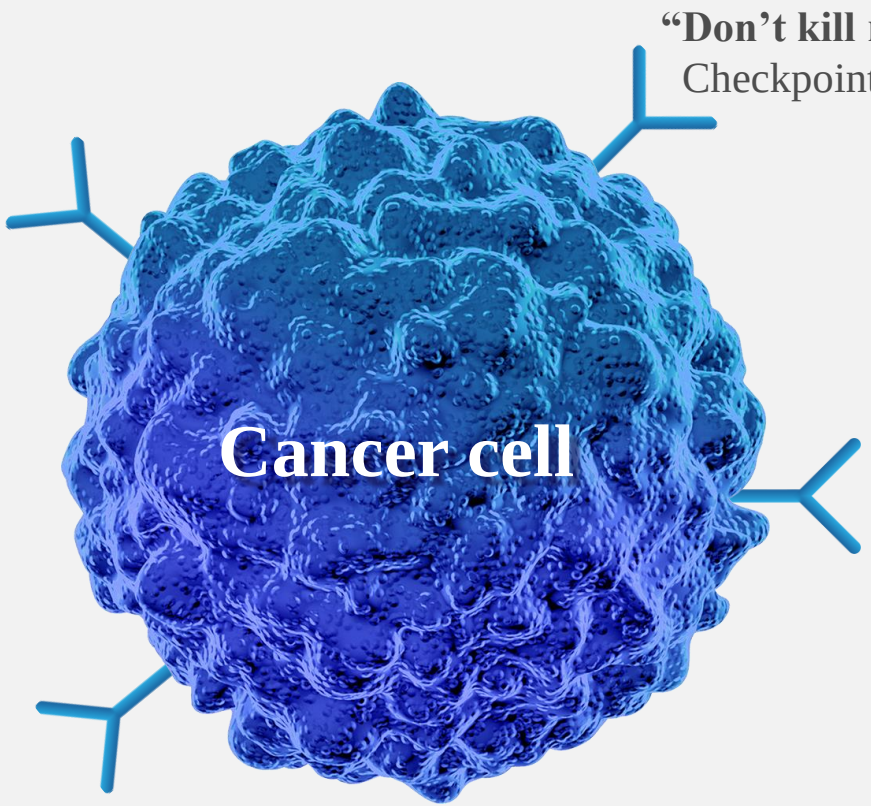
# THE CAMOUFLAGE CHALLENGE IN TREATING CANCER




**Immune checkpoints** are molecules expressed on all cells in the body that regulate the immune system’s self-tolerance, to **prevent indiscriminate attack** of healthy cells.

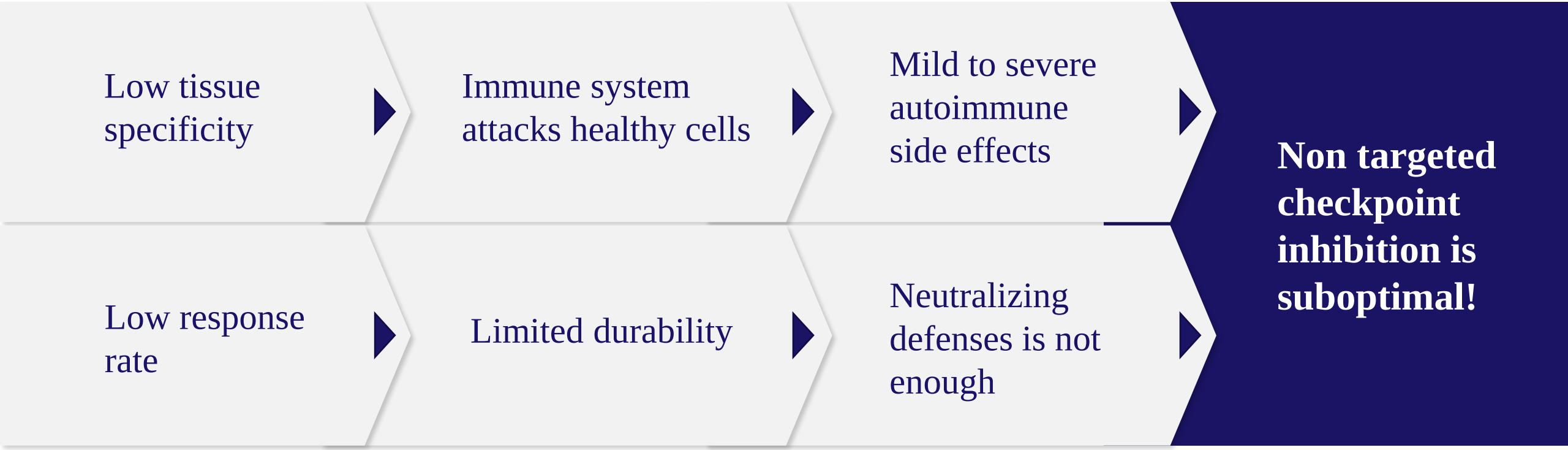
When immune cells bind to checkpoint molecules, their activity is inhibited

# THE CAMOUFLAGE CHALLENGE IN TREATING CANCER




**Cancer cells** overexpress immune checkpoint molecules to camouflage themselves from the immune system by **pretending to be healthy cells**, thus evading immune recognition and attack.

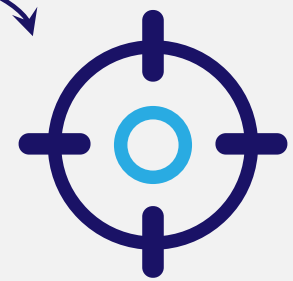
# CURRENT CHECKPOINT IMMUNOTHERAPY HAS ITS DOWNSIDES



# EFFECTIVELY TREATING CANCER REQUIRES A MULTIFACETED APPROACH

Selectively disabling cancer defense mechanism

WHILE



Recruiting a local targeted immune attack

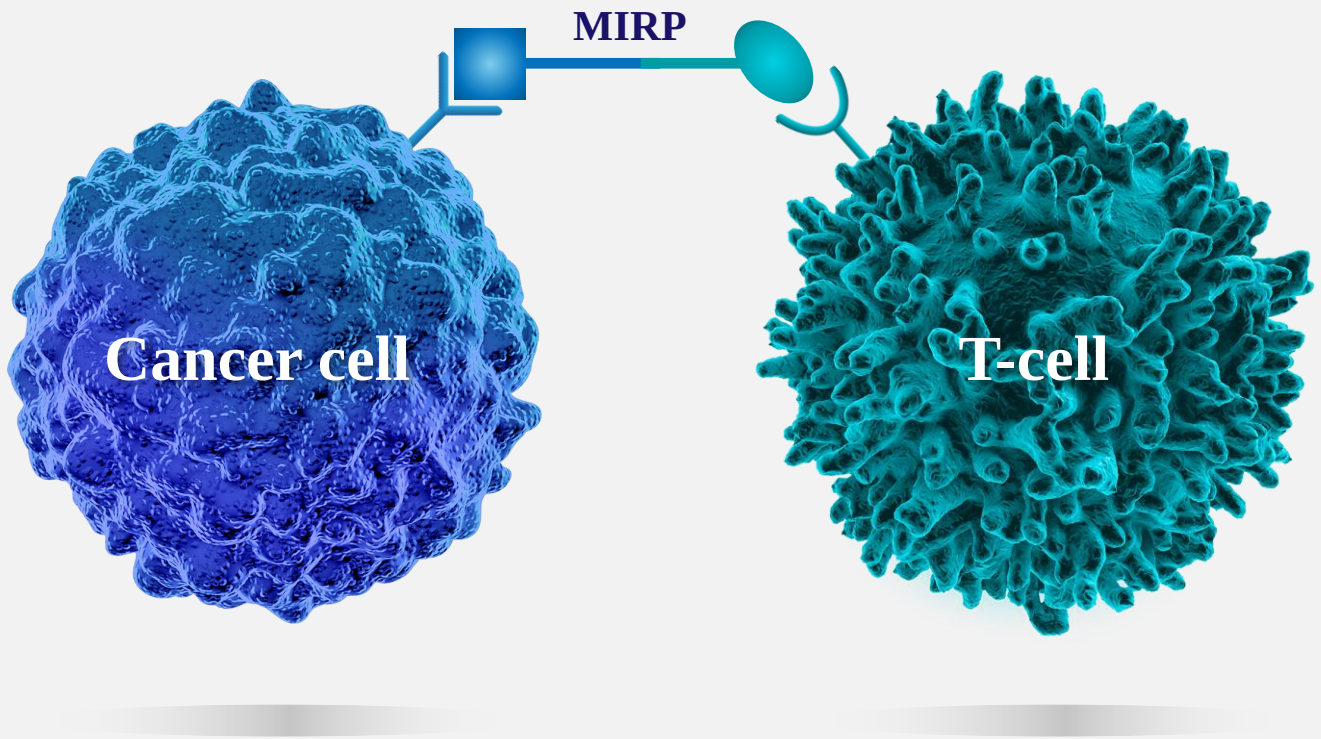
IMMUNITY. RECRUITED.

IMMUNITY.
RECRUITED.

KAHR develops smart immune-recruitment cancer drugs that activate a targeted immune response by converting cancer camouflage into beacons for the immune system to attack

# **MIRP** (MULTI-FUNCTIONAL IMMUNE-RECRUITMENT PROTEINS)

MIRPs deliver a multilayered attack by binding cancer cells and T-cells to produce a targeted synergistic effect, combining immune checkpoint inhibition with selective T-cell activation.



# HOW IT WORKS

**Targeting checkpoint overexpression**

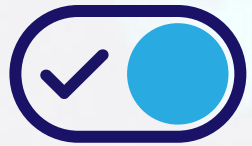
MIRPs utilize cancer cell overexpression of checkpoint surface antigens to selectively target and bind to the cancer

**Inhibiting cancer checkpoints**

Checkpoint binding and inhibition unmasks the cancer cell's camouflage and enables immune response

**Recruiting adaptive immunity**

MIRPs bind to T-cells and activate them in the tumor environment

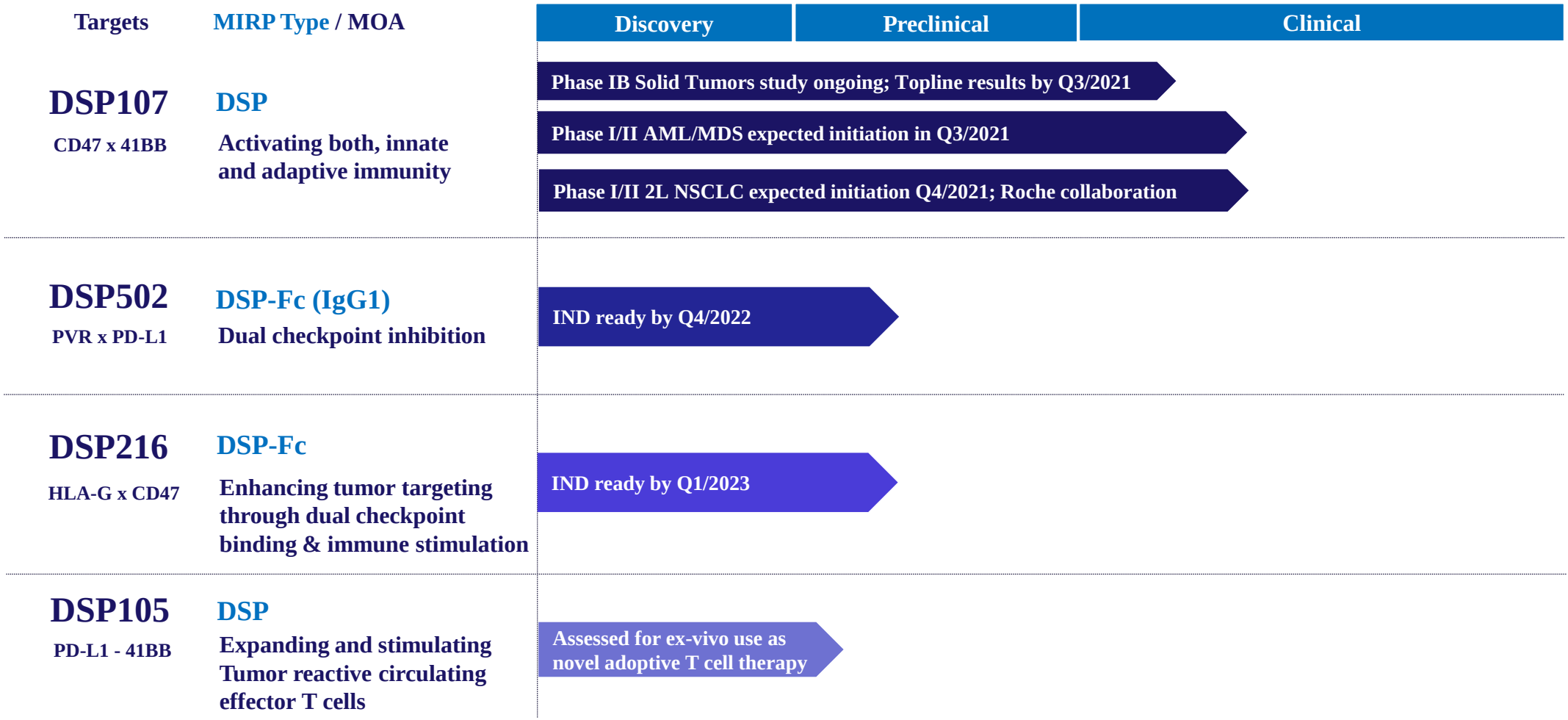


**Activating immune response**

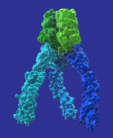
Activated T-cells initiate a selective and locally restricted immune response to kill the cancer cells

IMMUNITY. RECRUITED.

# PIPELINE



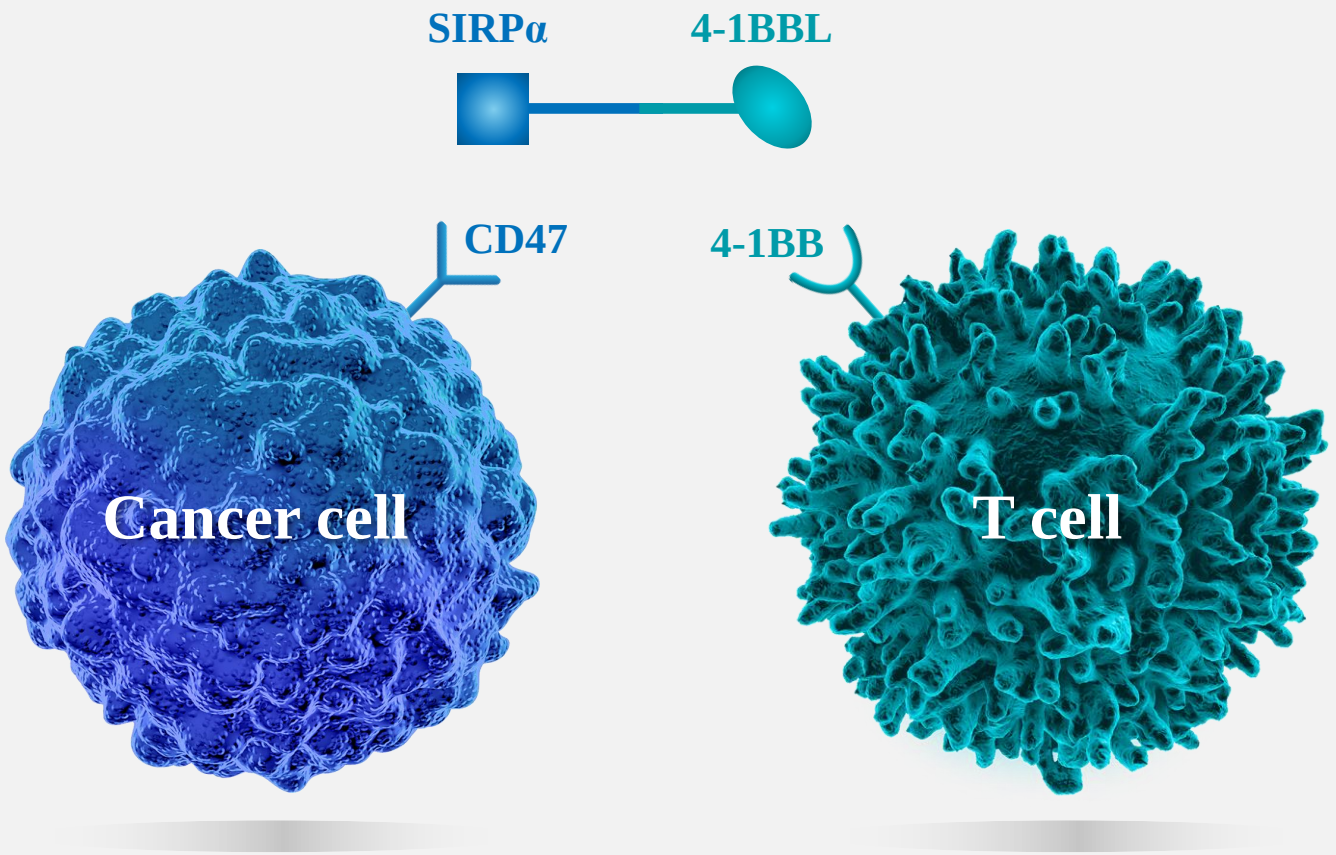

IMMUNITY. RECRUITED.



# LEAD MIRP PRODUCT – **DSP107**

# **DSP107** (MIRP type - Dual Signaling Protein)

**SIRPα** binds to **CD47** overexpressed on cancer cells, disabling their "don't eat me" signal




**4-1BBL** side binds to **4-1BB** on tumor-antigen specific T cells, stimulating their expansion, cytokine production, and the development of cytolytic effector functions

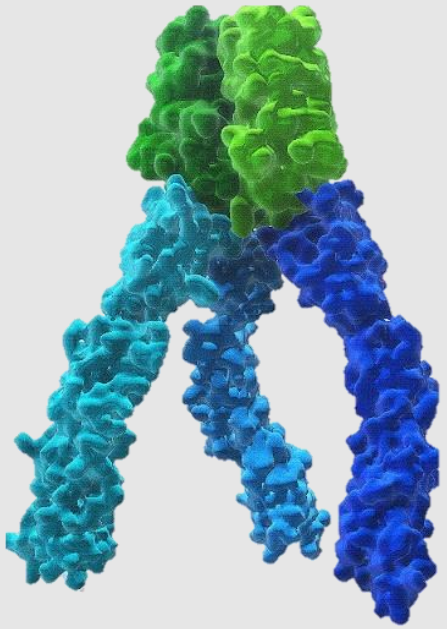
# UNIQUE TRIMERIC STRUCTURE ENABLE SPECIFICITY AND SELECTIVITY

## DSP107 Structure

**Trimeric ligand ends enable both:**

- High tissue specificity by binding overexpressed checkpoint molecules driven by affinity and high avidity
- Selective activation of immunity by recruiting and co-stimulating local immune cells

Trimeric 4-1BBL



**Immune cell stimulation**

**Proliferation**

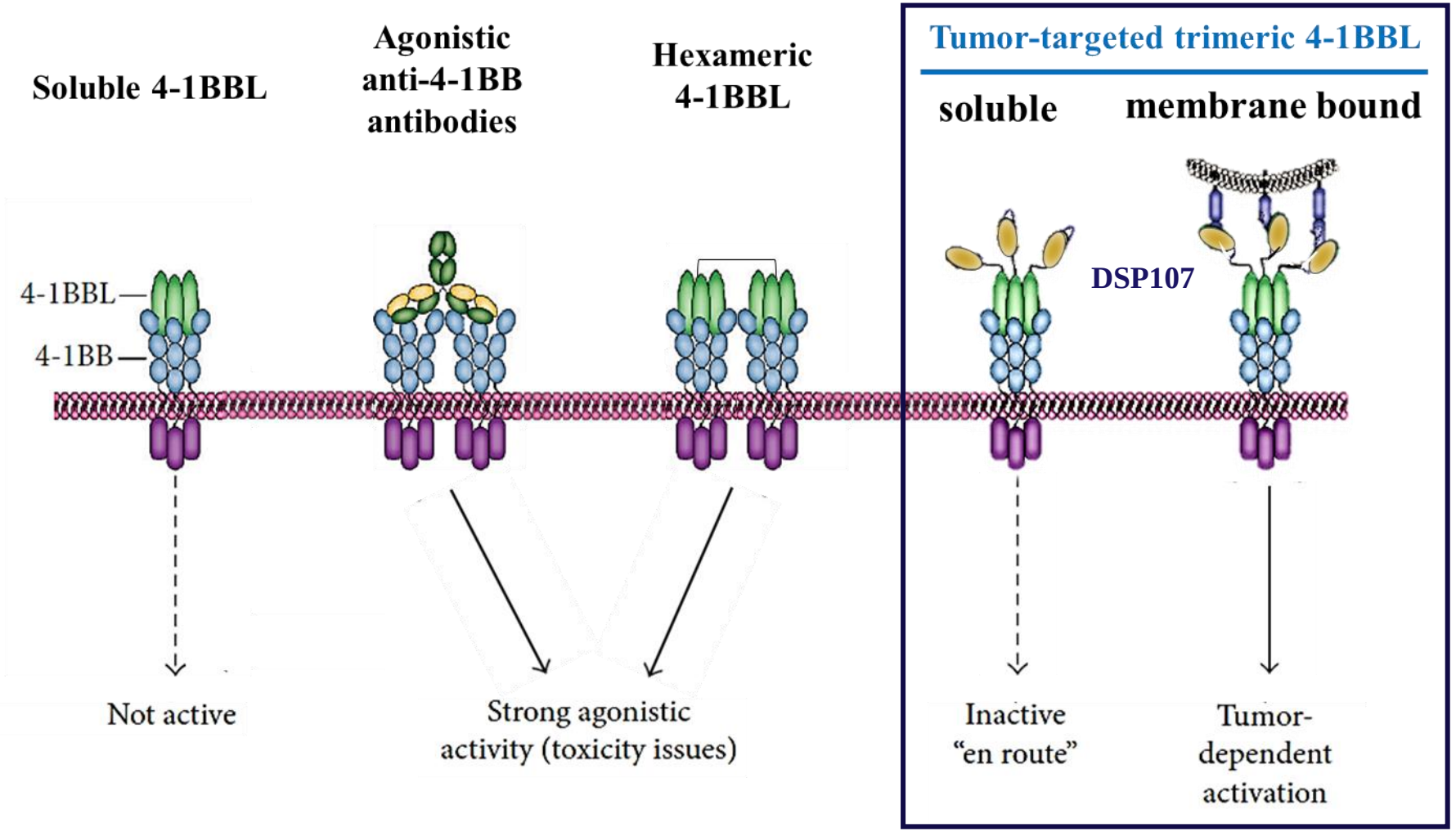
**Checkpoint inhibition**

**Tumor microenvironment modulation**

3 SIRPα for
CD47 Checkpoint Targeting

IMMUNITY. RECRUITED.

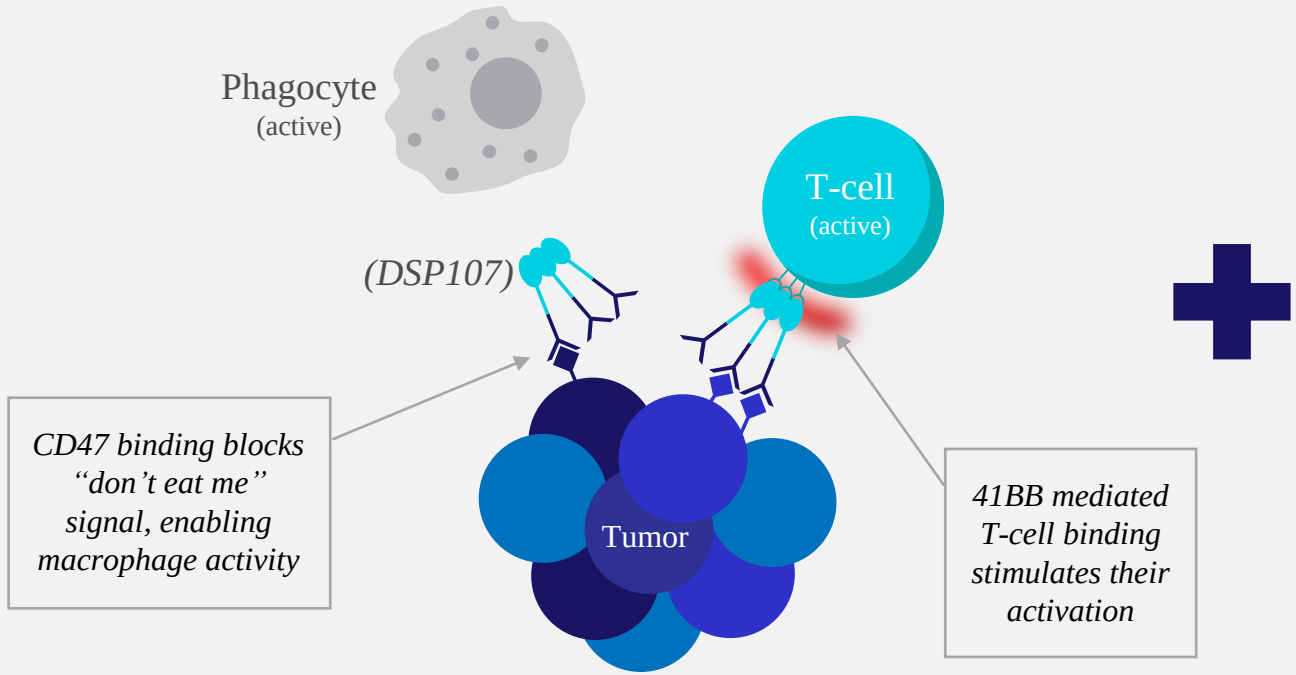
# UNIQUE TRIMERIC STRUCTURE ENABLE TUMOR TARGETED 4-1BB CONDITIONAL ACTIVATION



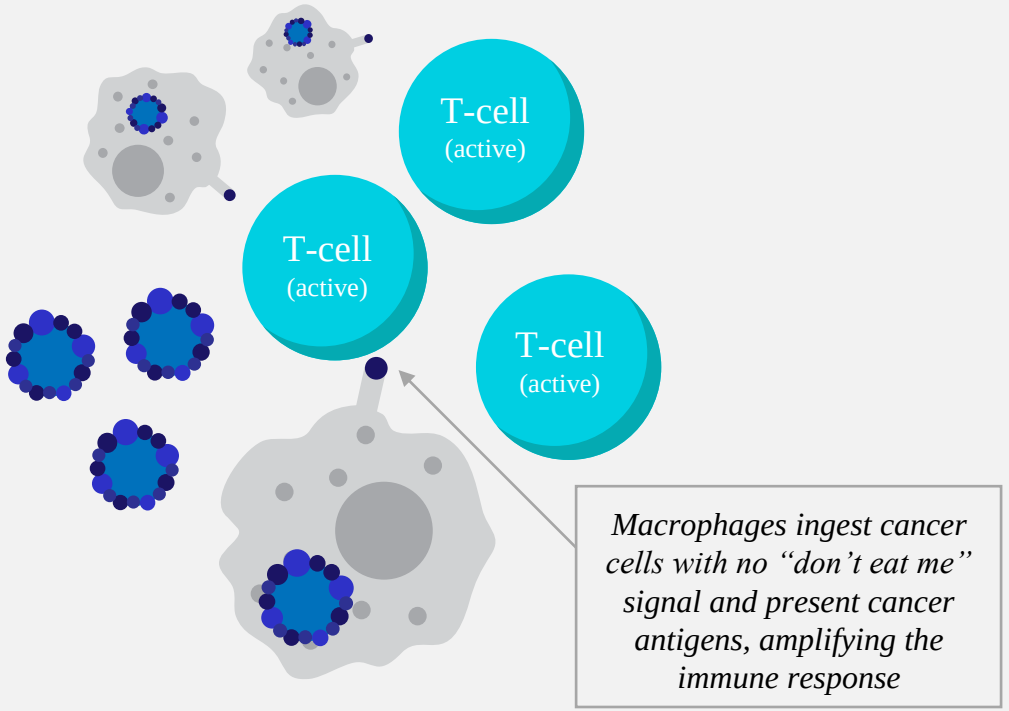

Modified from: Bremer E.; ISRN Oncology; Volume 2013, Article ID 371854

# **DSP107** – SYNERGISTIC IMMUNE ACTIVATION

*Innate immunity enabled + mediated activation of adaptive immunity*



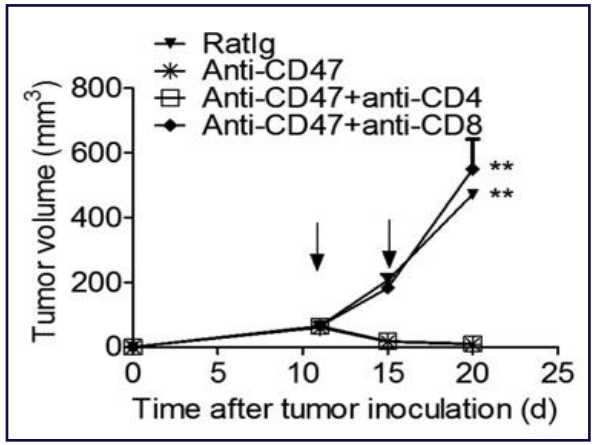

*Natural adaptive immune response*



# COMBINING CD47 AND 4-1BB – RATIONALE

## COMBINING CD47 BLOCKADE WITH T-CELL STIMULATION HOLDS CLEAR PROMISE

- T-cell activation is a pre-requisite for CD47 therapy, with T-cell depletion abrogating its anti tumor activity[1]
- Blockade of CD47 reactivates macrophages against cancer cells, enhances antigen presentation and induces specific anti-tumor T-cell activity[2]
- 4-1BB has been used in various studies to identify tumor-reactive T-cells in the tumor microenviroment[3]
- DSP107 is designed to activate macrophages and stimulate T-cells by activation of 4-1BB, a costimulatory receptor transiently upregulated on tumor reactive T-cells[4]




Liu X et al. Nat Med. 2015 21:1209-15

**DSP107 is a first-in-class therapeutic agent that effectively combines CD47 checkpoint inhibition with 4-1BB-mediated activation of tumor specific T-cells**

[1] Liu X et al. Nat Med. 2015 21:1209-15; [2] Tseng T et al. PNAS 2013 110: 11103-11108; [3] Chacon JA et al. PLoS ONE. 2013;8(4). [4] Bartkowiak T & Curran MA. Frontiers in Oncology. 2015 5:1-16;

IMMUNITY. RECRUITED.

# **DSP107** – BEST IN CLASS CD47 TARGETING COMPOUND

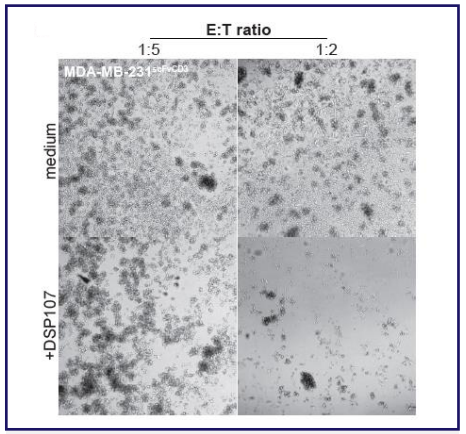
## Next generation capabilities

**Dual MOA**
activates innate and adaptive immunity

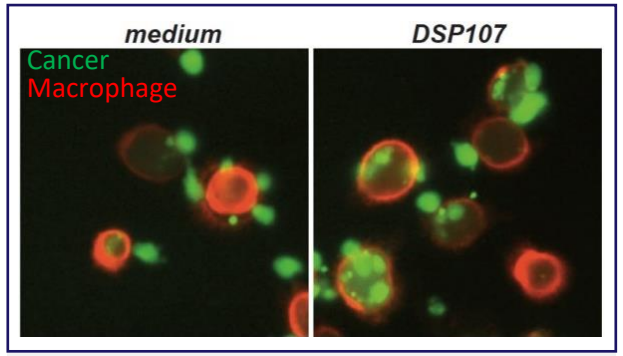
**Excellent safety**
without hematological toxicities

**Strongly positioned**
for treatment of solid and hematological malignancies

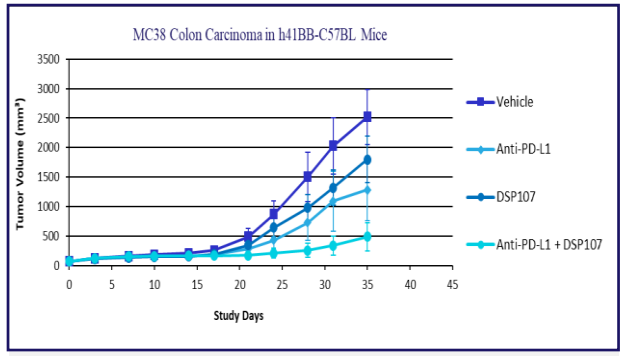
## Unique synergistic effects



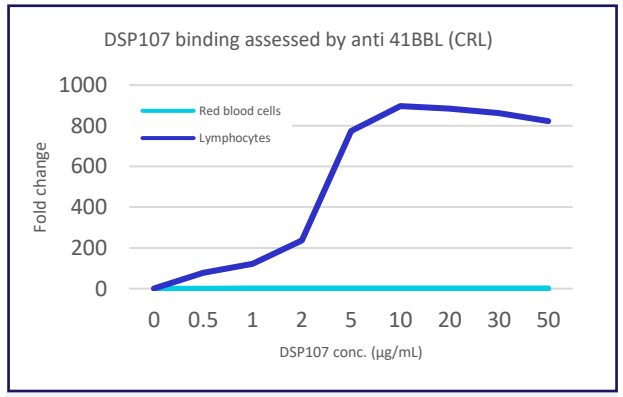

Activates T cells to secrete IFN-γ and augment their cancer cell killing potential




Augments macrophages-mediated phagocytosis of tumor cells as a single agent and synergizes with mAb's




Strong anti tumor activity as a single agent and synergizes with PD1/PD-L1 checkpoint inhibitors in-vivo




Does not bind red blood cells, avoiding antigen sink issues, resulting in a best-in-class safety profile

# CD47 AGENT PIPELINE



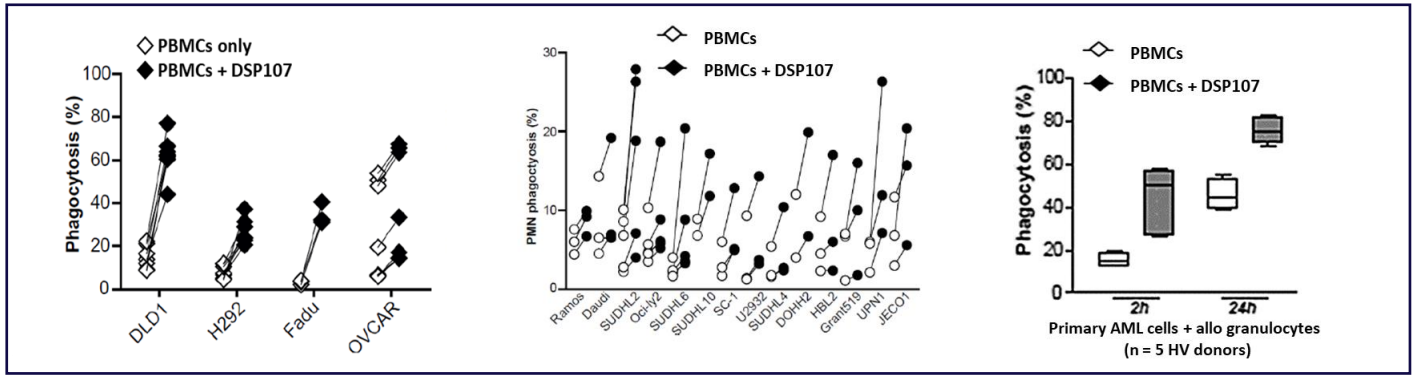
| Candidate | DSP107 | Magrolimab | ALX148 | TTI-622 | AO-176 | TG-1801 | SL-172154 |
|---|---|---|---|---|---|---|---|
| **Type** | **SIRPα-41BBL** fusion protein | CD47 mAb | SIRPα-Fc fusion protein | SIRPα-Fc fusion protein | CD47 mAb | CD47/CD19 BisAb | SIRPα-Fc-CD40L Fusion protein |
| **Mechanism** | **Bi-functional** | Monovalent | Monovalent | Monovalent | Monovalent | Bi-specific | Bi-functional |
| **Immune activation** | **Innate and adaptive** | Innate | Innate | Innate | Innate | Innate | Innate |
| **RBC binding**<br>- **Antigen Sink issue**<br>- **Heme toxicities** | **No** | Yes | Low | No | Low | No | ?? |
| **Monotherapy** (preclinical) | **Yes** | No | No | Yes | Yes | Yes | Yes |
| **Clinical indication** | **NSCLC, AML, MDS** | MDS, AML, NHL and Solid tumors | NHL, HNSCC, G/GEJ | NHL | Solid tumors | NHL | Ovarian |

*Other companies with phase I stage CD47-targeting agents: Innovent Bio, Surface Oncology, Seattle Genetics, Novimmune, I-Mab/Abbvie, OSE, Hengrui,

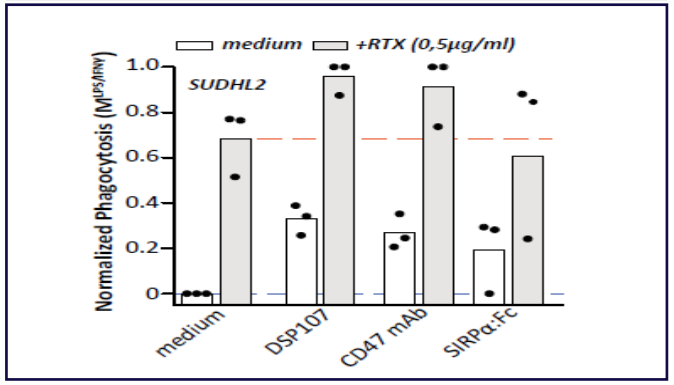
# DSP107 - PRE-CLINICAL OVERVIEW

# SIRPα – BINDS TUMOR AND INDUCES PHAGOCYTOSIS

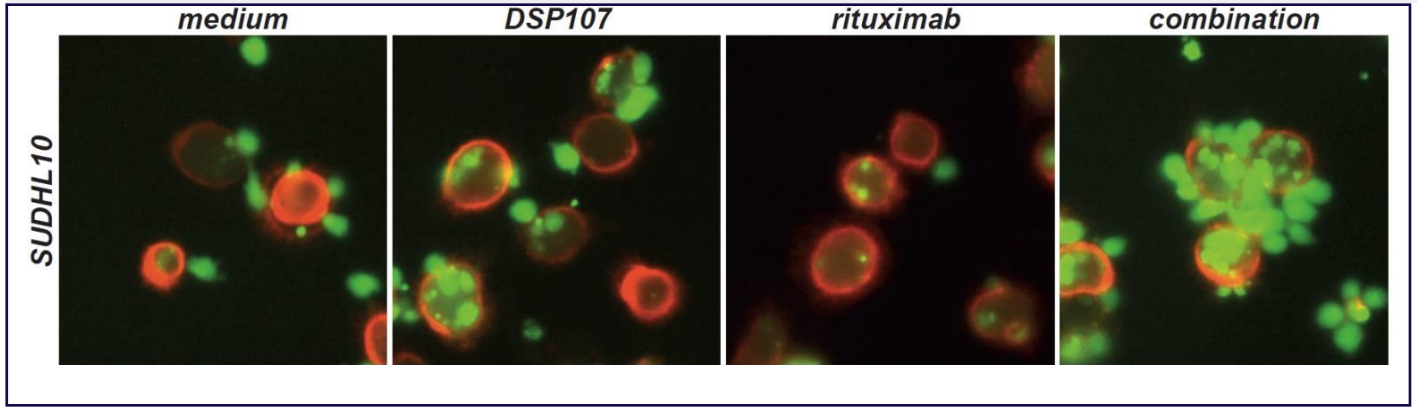
## Triggers cancer cell death by phagocytosis as a single agent

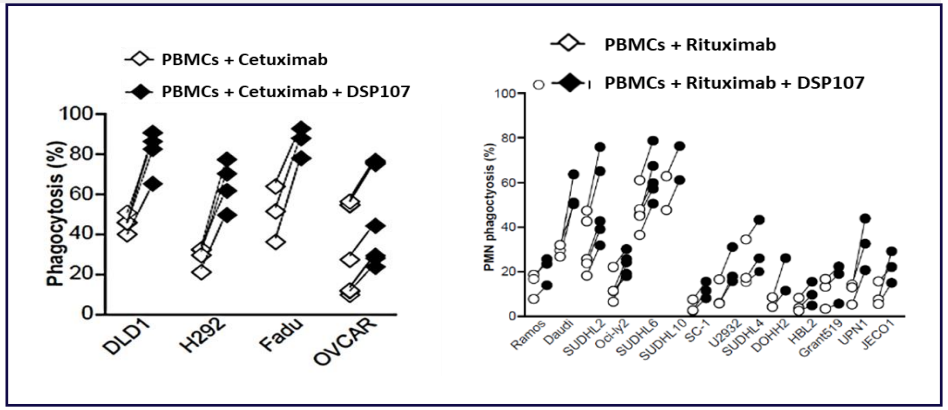



## Phagocytic effect better than other CD47 targeting agents




## Augments mAb's ADCP-mediated phagocytosis of cancer cells

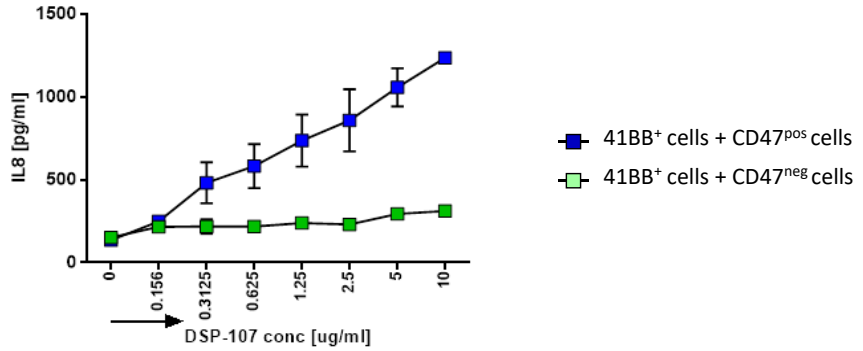


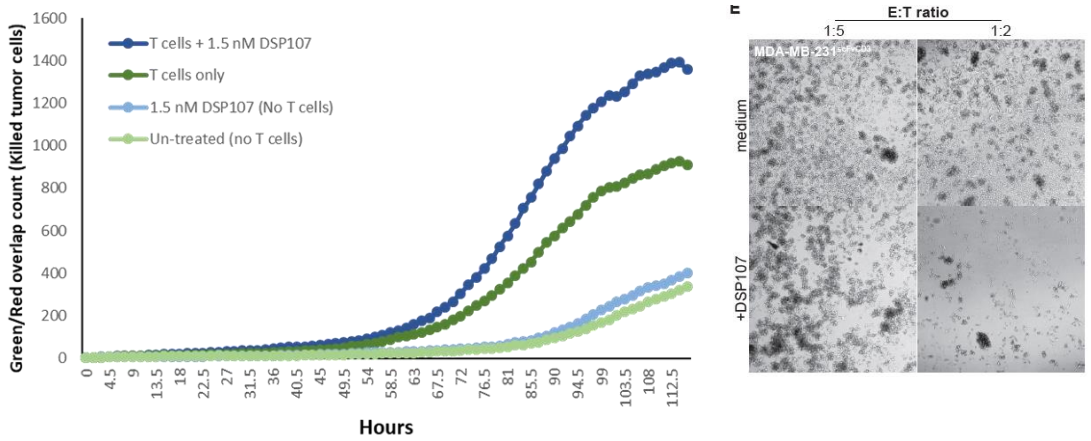

IMMUNITY. RECRUITED.

# 41BBL – ACTIVATES T-CELLS

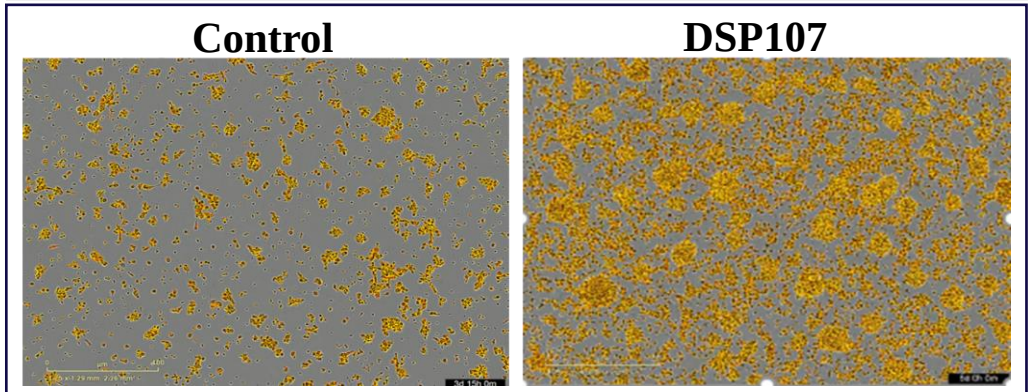
## Tumor selective cross presentation activates 41BB signaling



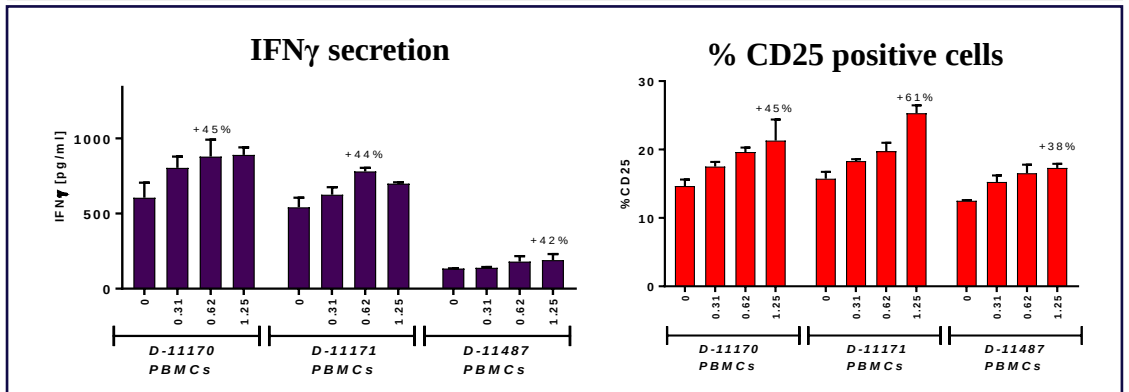

## Induces T-cell killing potential against cancer cells




## Augments T-cell proliferation

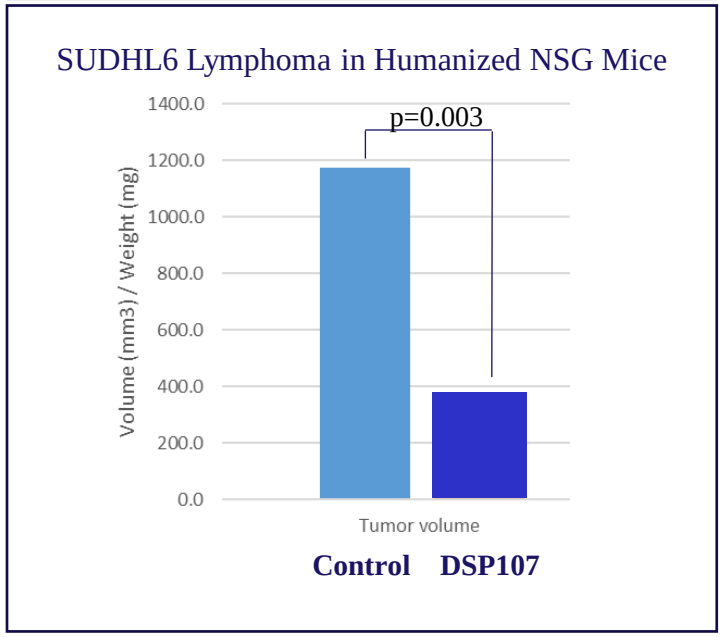



## Activates T cells and increases IFNγ secretion

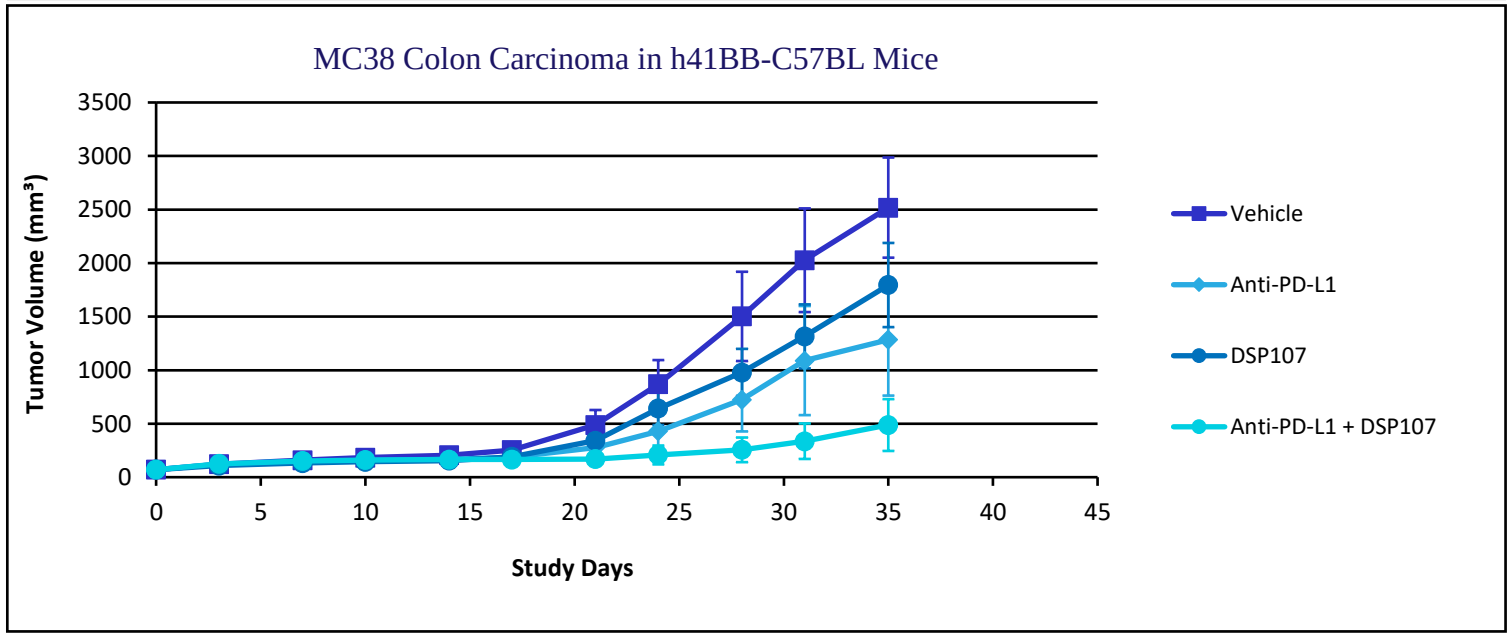


# DSP107 DEMONSTRATES POTENT IN VIVO EFFICACY

## Shows strong anti tumor activity as a single agent




## Significant tumor inhibition and extended survival when combined with anti PD-L1

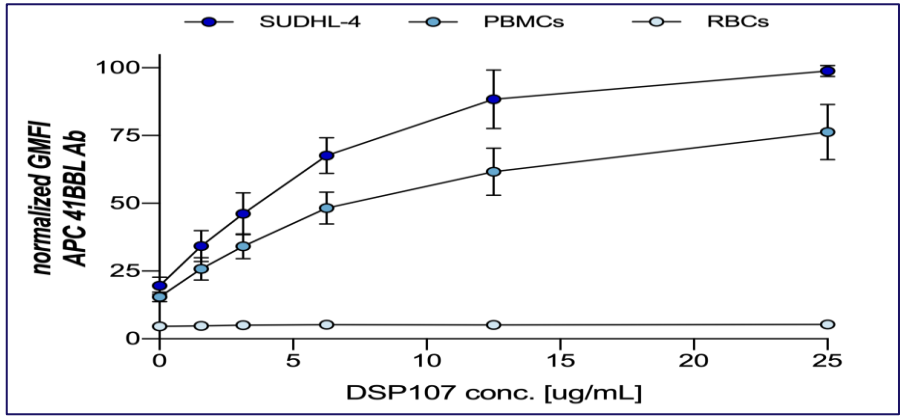


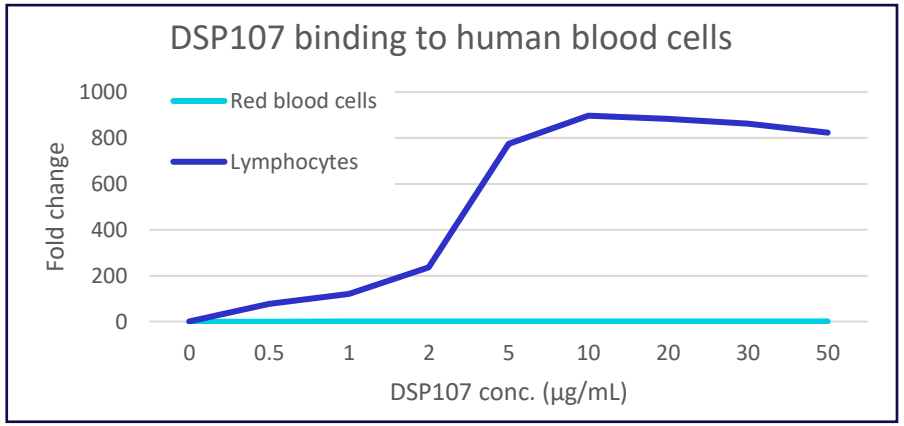
# EXCELLENT SAFETY - NO HEMATOLOGICAL TOXICITIES

## GLP Toxicology - Monkey study results

- Repeated administrations (up to 4) with doses of up to 50 mg/kg were safe & well tolerated
- No reduction in RBC count and Hb and no effect on platelets or white blood cells
- No changes in clinical chemistry parameters following repeated administration of DSP107
- No DSP107 related microscopic/macroscopic changes or findings (liver, spleen, kidneys, lung, lymph node)
- No treatment related changes in the cytokine levels

## Increased Affinity to Cancer Cells and Negligible binding to RBCs

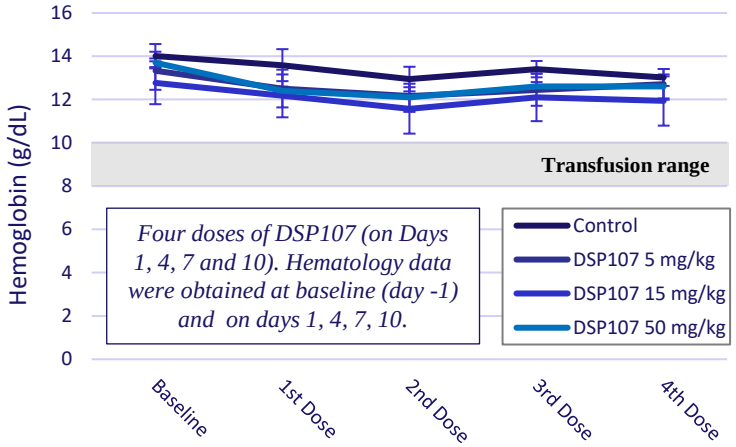


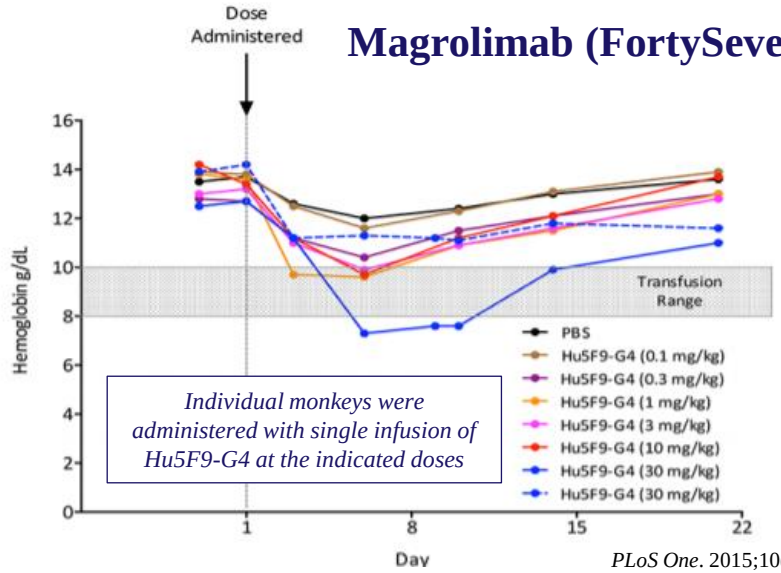



# BETTER SAFETY COMPARED TO OTHER CD47 AGENTS

Reported cynomolgus monkey's safety data

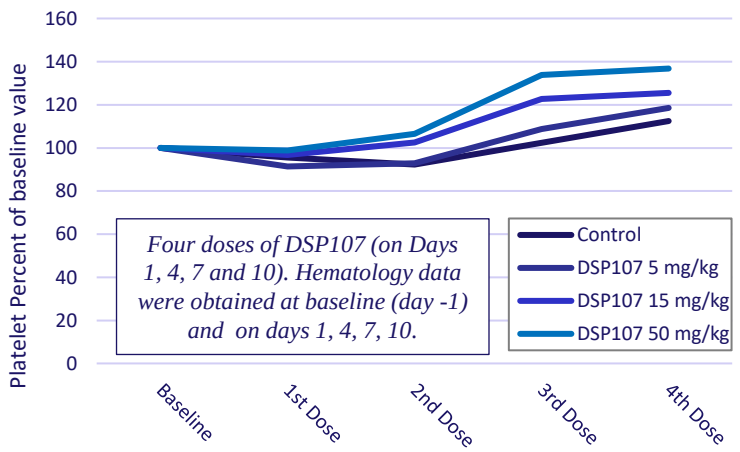
## Hemoglobin

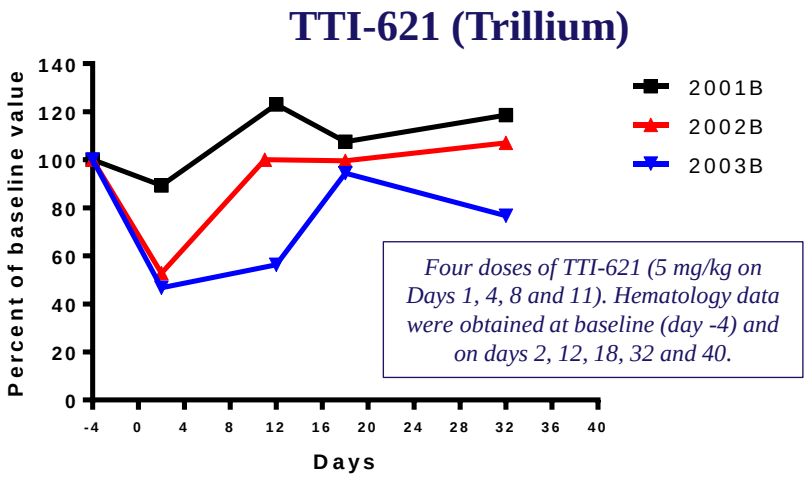



*PLoS One*. 2015;10(9):e0137345.

## Platelets

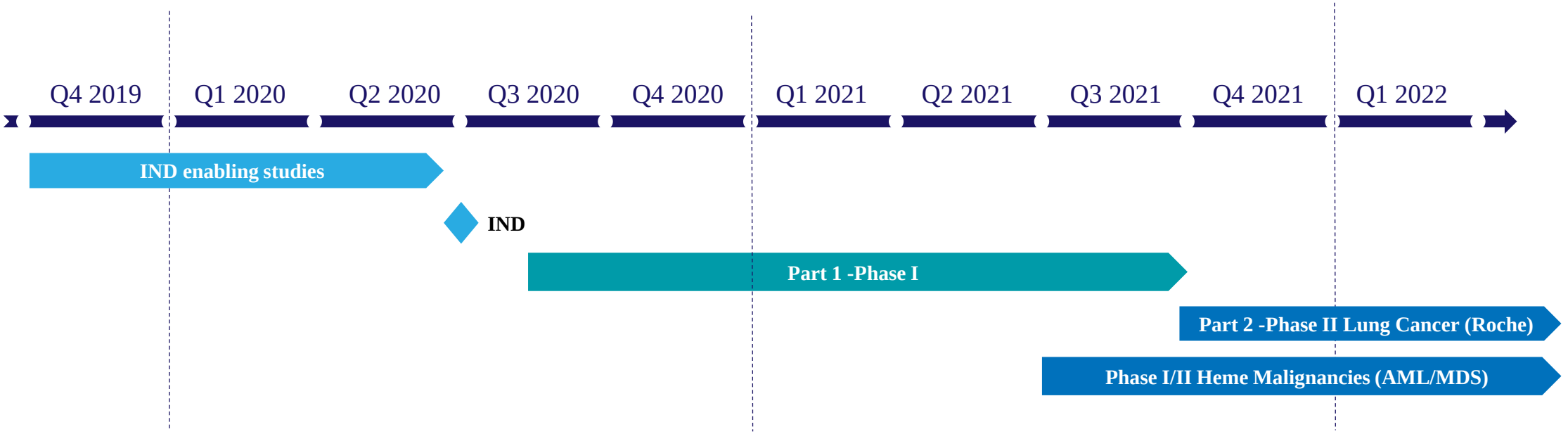



IMMUNITY. RECRUITED.

# DSP107 – CLINICAL DEVELOPMENT

# CLINICAL DEVELOPMENT PLAN




## Two Phase I/II studies to commence H2/2021:

- 2L NSCLC patients who progressed on PD1/PD-L1 therapies to evaluate safety and efficacy of DSP107 monotherapy and when combined with Atezolizumab
- High risk MDS/AML patients to evaluate safety and efficacy of DSP107 either as monotherapy or when combined with azacitidine

IMMUNITY. RECRUITED.

# ONGOING DSP107_001 PHASE I/II SOLID TUMOR STUDY

Enrolling sites: Pittsburgh, Colorado, Kansas, Thomas Jefferson and San-Diego Universities

## PART I — Dose escalation study

- DSP107 administered as monotherapy and in combination with Atezolizumab
- Dosing regimen - iv administration once weekly
- Population (N=~30) - patients with advanced solid tumors not suitable for curative therapy and without approved treatment options
- Accelerated dose escalation in single patient cohorts until pre-determined safety signals observed, followed by standard 3+3 design

## PART II — Expansion cohort

- Dose selection based on safety results from part 1
- Single expansion cohort comparing DSP107 monotherapy to combination with Atezolizumab in patients with NSCLC who progressed after PD-1/PD-L1 targeting agents (N=~70 patients)

IMMUNITY. RECRUITED.

# CLINICAL COLLABORATION WITH ROCHE

***KAHR and Roche entered clinical collaboration agreement to evaluate DSP107 in combination with Atezolizumab in Advanced Lung Cancer patients***


Roche

Study will evaluate the potential of DSP107 and Atezolizumab (PD-L1 inhibitor) in NSCLC patients who have progressed following first line treatment with PD1/PD-L1 inhibitors

Patient enrollment expected to commence in H2/2021

KAHR IMMUNITY. RECRUITED.

# PLANNED **DSP107_002 PHASE I/II AML/MDS** STUDY DESIGN

Lead site: MD Anderson Cancer Center

## PART I — Dose escalation study

DSP107 administered as monotherapy (treatment cycle 1) and in combination with Azacitidine (treatment cycle 2)

DSP107 dosing regimen - iv administration once weekly

Population (N=18-36) – patients R/R with AML or MDS/CMML who have failed up to 2 prior therapeutic regimes

Dose selection based on solid tumor RP2D, dose level -1 RP2D, and dose level +1 for DSP107

## PART II — Expansion cohorts

Dose and regime (monotherapy or azacitidine combination or azacitidine and ventoclax combinations) selection based on safety and efficacy results from part 1

Three expansion cohorts with Simon 2-stage design and clear "go/no-go" decisions in patients with:

Cohort I - **FRONTLINE AML** (N=14+14)

Cohort II – **FRONTLINE MDS/CMML** (N=14+14)

Cohort III – **R/R MDS/CMML** (N=14+14)

Cohort IV **- R/R T-cell lymphoproliferative diseases** (N=14+14)

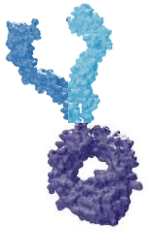
**Endpoints**

Safety – maximum tolerated dose, DLTs, RP2D of DSP107 monotherapy and Combination with azacitidine

Efficacy – (1) Overall response rate (CR+CRi+PR) within 3 months
(2) PFS (Time to next treatment), EFS and OS
(3) Exploratory biomarkers – 81-gene mutational profiling at MDACC, MRD by flow and NGS, CYTOF (Mass cytometry) customized panel for macrophages and T-cells in AML, TCR repertoire (Adaptive).

IMMUNITY. RECRUITED.

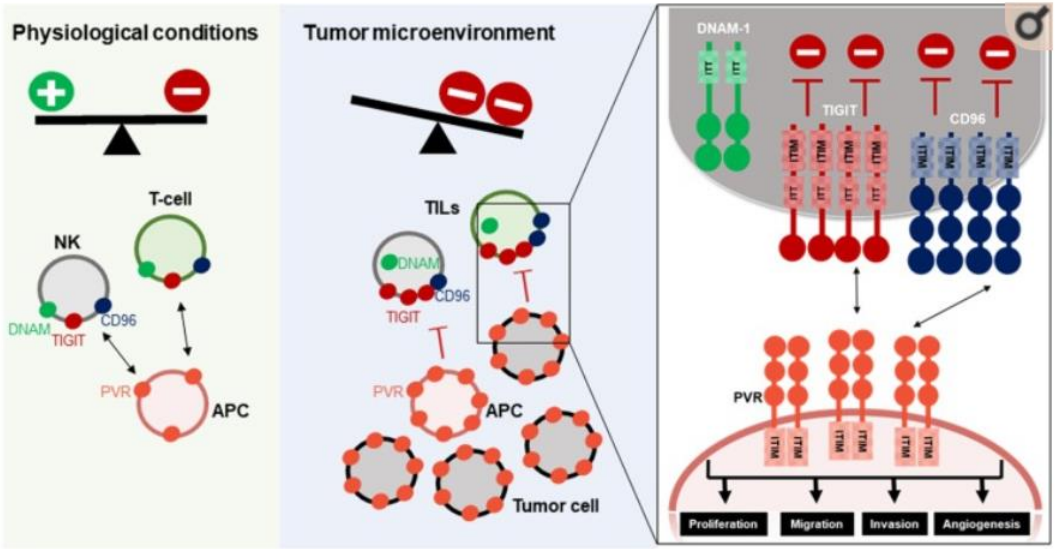
# PRECLINICAL PIPELINE



# DSP502 (TIGIT-Fc-PD1)

# TIGIT (PVR) – BACKGROUND

- PVR is the ligand of TIGIT, CD96 and DNAM1
- Under physiological conditions, PVR is expressed at low levels and limited to certain cell types
- Balance between activating and inhibitory PVR mediated signals maintains normal function of immune cells
- In the tumor microenvironment PVR is dramatically overexpressed and acts in trans to reduce DNAM1 protein levels
- Balance between immune activating and inhibitory signals is often disturbed in the TME: inhibitory receptors (TIGIT and CD96) are upregulated while activating receptor (DNAM1) is downregulated
- PVR blockade by mAb or genetic ablation increases DNAM1 in both NK and T cells in vivo

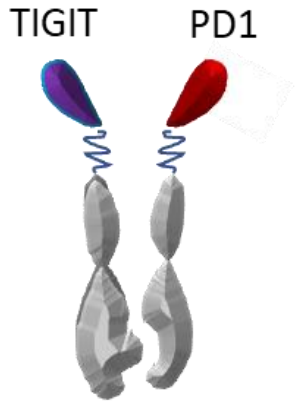



[1] Brlić et al. Cellular & molecular immunology (2019) 16, 40–52.

[2] Li, X. et al. The Journal of clinical investigation (2018) 128, 2613–2625.

[3] Stengel at al. PNAS (2012) 109 , 5399-5404.

# DSP502 – TIGIT-PD1




**Unique concept**

- Enhancing tumor targeting through dual checkpoint inhibition
- Tumor selectivity by dual binding relying on avidity (‘AND GATE’)
- Multiple activities to overcome resistance pathways affecting both TIGIT/PVR and PD/PD-L1 to activate effector T and NK cells and reduce Treg cells
- DSP502 is based on an IgG1 and expected to have Fc-mediated ADCC activity
- Inhibition of TIGIT/PVR pathway in clinical studies shows efficacy only when combined with PD-1 blockade

**Mechanism of Action – Targeting PVR and PD-L1**

- **TIGIT** will block endogenous **PVR** on cancer cells unleashing the activity of the adaptive immune system to attack the tumor cells
- **PD1** will block **PD-L1** on tumor cells to activate effector T cells and increase tumor specificity

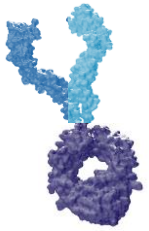
# DSP502- DIFFERENTIATION

- KAHR's TIGIT based product **targets PVR and PD-L1 on tumors**
- PVR blockade provides dual stimulatory mechanism to enhance anti-tumor immunity and promote DNAM1 costimulatory signaling for effective anti-tumor immunity
- High PVR expression was recently found to predict non-responders to PD1 therapy in NSCLC patients (with 100% accuracy)[1] and in melanoma[2]
- **Inhibition of TIGIT/PVR pathway in clinical studies shows efficacy only when combined with PD-1 blockade**

| **MoA** | **PVR targeting** (KAHR's approach) | **TIGIT Ab** (Competitors) |
|---|---|---|
| Inhibit TIGIT signaling | ✓ | ✓ |
| Inhibit CD96 signaling | ✓ | – |
| Increase DNAM1 surface expression and signaling | ✓ | – |

[1] *Lee et al. JCI insight* (2020). 10.1172
[2] *Lepletier et al. Clinical Cancer Research* (2020)

IMMUNITY. RECRUITED.



# DSP216 (LILRB2-Fc-SIRPα)

# LILRB2(ILT4)/HLA-G – BACKGROUND

- Leukocyte Immunoglobulin Like Receptor B (LILRB; ILT) are immune checkpoint proteins expressed on macrophages and other myeloid cells
- HLA-G, the main ligand for LILRB1 (ILT2) and LILRB2 (ILT4), is a critical protein responsible for immunotolerance in placenta preventing the mother's immune system from destroying the fetus
- By over-expressing HLA-G, tumor cells use the same escape mechanism to evade immune surveillance
- HLA-G expression is associated with cancer immune evasion, disease progression and poor prognosis

- HLA-G serves as a broad-range Immune Checkpoint protein which:
  - inhibits all immune cell subsets including macrophages, NK, B and APCs, as well as T cells
  - recruits suppressive immune cells inducing an immunosuppressive microenvironment for tumors

# DSP216 – LILRB2-SIRPA

## Unique concept

- Enhancing tumor targeting through dual checkpoint inhibition
- Tumor selectivity by dual binding relying on avidity (‘AND GATE’)
- Multiple activities to overcome resistance pathways:
  - Affecting both LILRB1 and LILRB2 to avoid redundancy compensation
  - Activating both innate (macrophages) and adaptive (T cells) immune systems
  - Blocking CD47 to trigger phagocytosis of tumor cells


## Mechanism of Action – Targeting HLA-G and CD47

- **LILRB2 (ILT4)** will block over-expresses **HLA-G** on cancer cells unleashing the activity of innate and adaptive immune systems
- **SIRPα** will block **CD47** on tumor cells inhibiting ‘don’t eat me’ signals to activate macrophages

# DSP216 - LILRB2-SIRPA – UNIQUE CONCEPT

- KAHR's LILRB based products target HLA-G expressed exclusively on tumors
- HLA-G blockade will interfere with both LILRB1 and LILRB2 binding to avoid redundancy compensation
- HLA-G blockade activates both innate (macrophages) and adaptive (T cells) immune systems

| **MoA** | **HLA-G targeting** (KAHR's approach) | **LILRB1/2 Ab** (Competitors) |
|---|---|---|
| Inhibit both LILRB1 and LILRB2 | ✔ | — |
| Tumor selectivity (HLA-G expression) | ✔ | — |
| Activates both innate (macrophages) and adaptive (T cells) | ✔ | ✔ |

# THANK YOU!