



# Company Overview

**TRANSFORMING INNOVATIVE IMMUNOTHERAPIES TO ERADICATE CANCER**

Praveen Tyle, Ph.D.

President & CEO

October 24, 2022

# INVECTYS EXECUTIVE SUMMARY

## **Our Vision : Develop the Next Generation of Immunotherapies to Eradicate Cancer**

- Company originated from the well-known Pasteur Institute in Paris
- Our Strategy offers significant benefits
  - Targets most cancers, including solid tumors (90% of Cancers are Solid tumors)
  - Induces high and robust anti-tumor immune responses
  - Has a robust patent portfolio with clear FTO (Patents issued)
- HLA-G portfolio developed in house at Invectys
- Three investigational products entering clinical studies within next 1.5 years
  - HLA-G CART in 2H2022 with MD Anderson Cancer Center in Renal Cell Carcinoma, Ovarian Carcinoma etc
  - ILT4 Nanobody in 2H2023 for Solid Tumors
  - HLA-G monoclonal antibody in 2H2023 for Solid tumors
- Low risk profile: Multiple shots on goal
- Each program with significant market potential
- Close to exit (Potentially strategic in next 12-18 months or IPO in 24-30 months)

# Seasoned Executive and Management Team



**Praveen Tyle, Ph.D.**  
President & CEO,  
Invectys, Inc.



**Julien Caumartin, Ph.D.**  
Chief Scientific Officer  
Invectys, SAS



**Francois Lescure, Ph.D.**  
General Manager  
Invectys, SAS.



**Jian Cao, Ph.D.**  
VP, Pharma  
Development  
Invectys, Inc



**Rosie Williams, CPA**  
VP, Administration &  
Controller Invectys, Inc.



**Q. Melissa Yang, Ph.D.**  
VP, Scientific Affairs,  
Invectys, Inc.

# Experienced and Talented Board of Directors



**Cary McNair**  
Chairman of the Board, Investcys, Inc  
CEO of McNair Interests  
President of the McNair Medical Institute



**Shannon A. Fairbanks**

- Chair of the Fairbanks Investment Fund Holdings LLC
- Provides Investcys Inc. with her broad experience, including 25 years cross border private equity partnerships



**David Guyer, M.D.**

- CEO of several successful companies including Ophthotech
- Venture Partner at SV Health Investors.
- Recipient of several awards, including 2003 Ernst & Young's Entrepreneur of the Year Award in Life Science



**Praveen Tyle, Ph.D.**

- President & CEO of Investcys Inc.
- Former CEO & member of Board Directors of Osmotica Pharma. Has served in leading roles at Bausch+Lomb, Novartis OTC and Lexicon
- Currently serves on the Board of Kiora Pharma, Orient EuroPharma Ltd; Yolia Health, Maxwell Biosciences and SKYE Bioscience, Inc



**Maurizio Zanetti, M.D.**

- Professor of Medicine at the UCSD and Director of the Laboratory of Immunology at the UCSD Moores Cancer Center
- Pioneer of T cell responses to Telomerase reverse transcriptase in cancer patients
- Brings vast knowledge to Investcys' strategic decisions, especially in the domain of T cells.

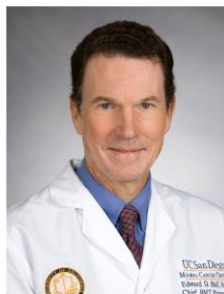
# Respected Chief Strategic Advisor and Scientific Board

## David Epstein, M.B.A.

Invectys Chief Strategic Advisor



Executive partner at Flagship Pioneering, Chairman of Axcella Health, Rubius Therapeutics and Evelo Biosciences, Board member at Tarus Therapeutics, Woolsey Pharma, Dynamics Special Purpose Corp. and Valo Health. Formerly, CEO of Novartis Pharmaceuticals (2010-2016), and previously led Novartis Oncology and Molecular Diagnostics Units, 25+ years of extensive drug development, deal making, commercialization and leadership experience on a global scale. Named one of the “25 most influential people in biopharma” by FierceBiotech



## Edward D. Ball, M.D.

Invectys Scientific Board Member  
Professor of Medicine  
University of California, San Diego, USA



## Michael Croft, Ph.D.

Invectys Scientific Board Member  
Professor, Director of Scientific Affairs  
La Jolla Institute for Immunology  
La Jolla, California, USA



## Theodore Friedmann, M.D.

Invectys Scientific Board Member  
Professor of Pediatrics Emeritus  
University of California, San Diego, USA



## Olivera (Olja) J. Finn, Ph.D.

Invectys Scientific Board Member  
Distinguished Professor of  
Immunology and Surgery  
University of Pittsburgh, USA



## Robert Jackson, Ph.D.

Invectys Scientific Board Member  
Founder & Director  
Pharmacometrics Ltd.



## Wayne A. Marasco, M.D., Ph.D.

Invectys Scientific Board Member  
Professor, Harvard Medical School, USA  
Lab Chief, Dept of Cancer Immunology &  
Virology at Dana-Farber Cancer Institute  
Founding Scientific Director of NFCR  
Scientific founder, Caladrius Biosciences  
Scientific advisory of several biotech  
companies



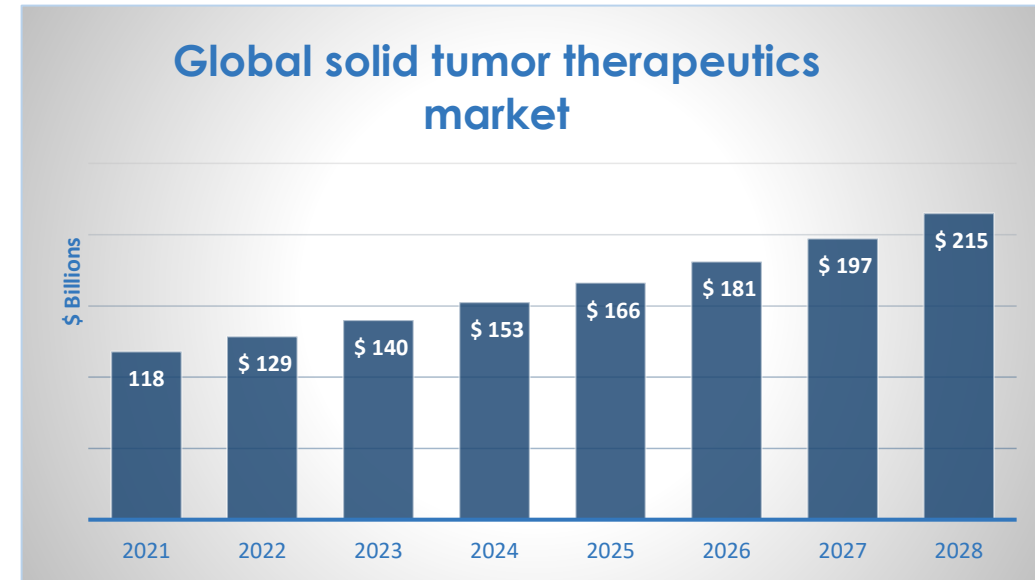
## Maurizio Zanetti, M.D.

Invectys Scientific Board Member  
Senate Emeritus, Medicine  
University of California, San Diego,  
USA



# Treating Solid Tumor Remains as Large Unmet Medical Need Today!

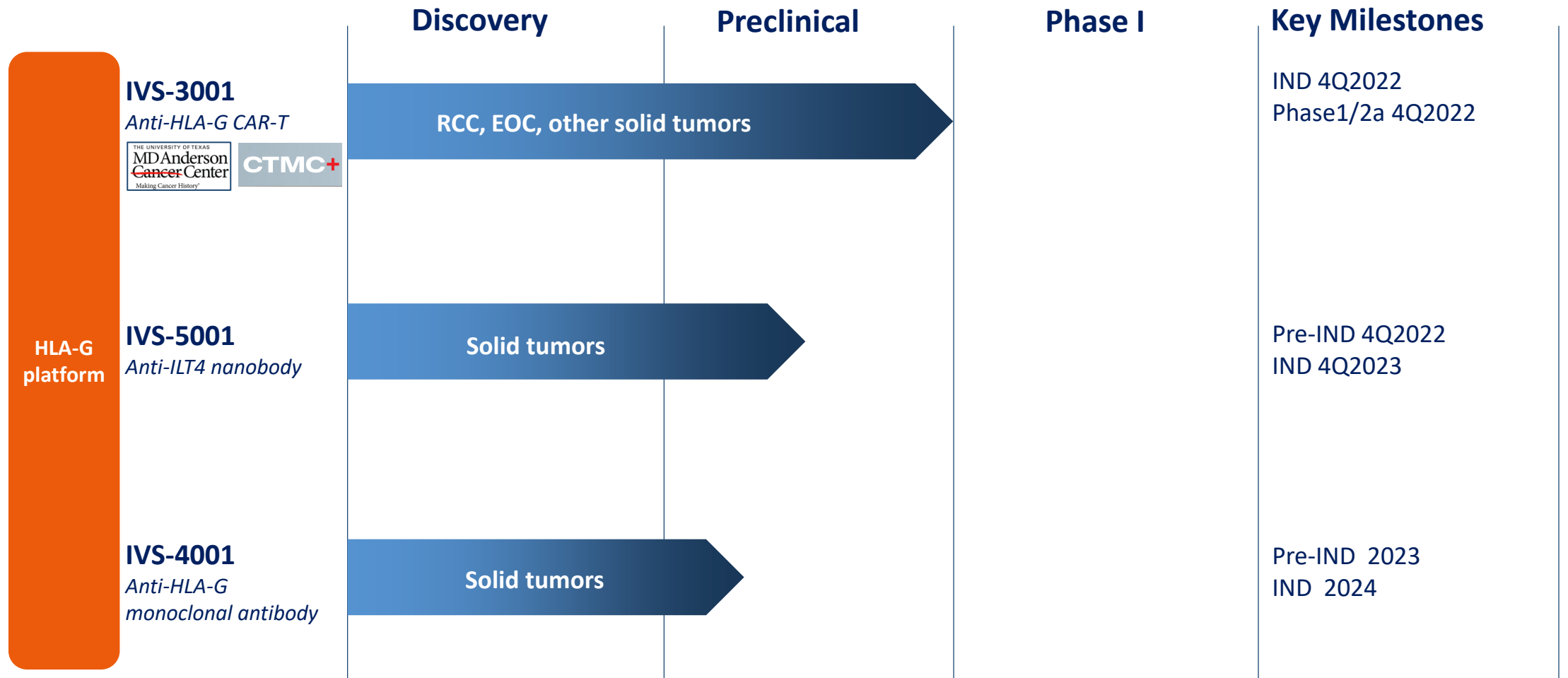
- The global Solid Tumor Therapeutics market is estimated \$215B by 2028 with a CAGR of 8.5% due to
  - Increasing incidence of solid tumor cancer patients
  - Growing prevalence of various types of metastatic cancers
- Current anti-tumor immunotherapies are limited due to
  - Scarce tumor specific antigens (TSA)
  - Inhibition by immune checkpoint molecules(ICP)
- Only 10-30% of patients show long-term and sustained efficacy to date
- The majority of patients have no clear evidence of treatment efficacy or will remain resistant to it or will relapse
- Immune-related adverse events (irAE) are commonly seen in patients treated with immunotherapies (e.g. Keytruda®, Opdivo®, Yervoy®)
- Challenges: Tumor escape applied medicines and mutate to resist current treatments.



1. [https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRma\\_Cancer\\_Research\\_7142020.pdf](https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRma_Cancer_Research_7142020.pdf)
2. <https://www.marketwatch.com/press-release/solid-tumor-therapeutics-market-2022-covid-19-impact-analysis-key-insights-based-on-product-type-end-user-application-driver-segmentation-and-regional-demand-till-2028-2022-03-08>
3. [Real-World Clinical and Economic Outcomes in Selected Immune-Related Adverse Events Among Patients with Cancer Receiving Immune Checkpoint Inhibitors.Zheng et al 2021 Oncologist. PMID: 34327774](#)
4. [PD-1/PD-L1 Checkpoint Inhibitors in Tumor Immunotherapy. Liu et al 2021 Front Pharmacol. PMID 34539412](#)

**Invectys investigational immunotherapeutics have demonstrated results against the solid tumor barrier, with an ability to reprogram the tumor microenvironment and unleash the host immune system to eradicate tumors both at the primary and metastatic sites**

# HLA-G Platform Projects and Key Milestones (Oct 2022)

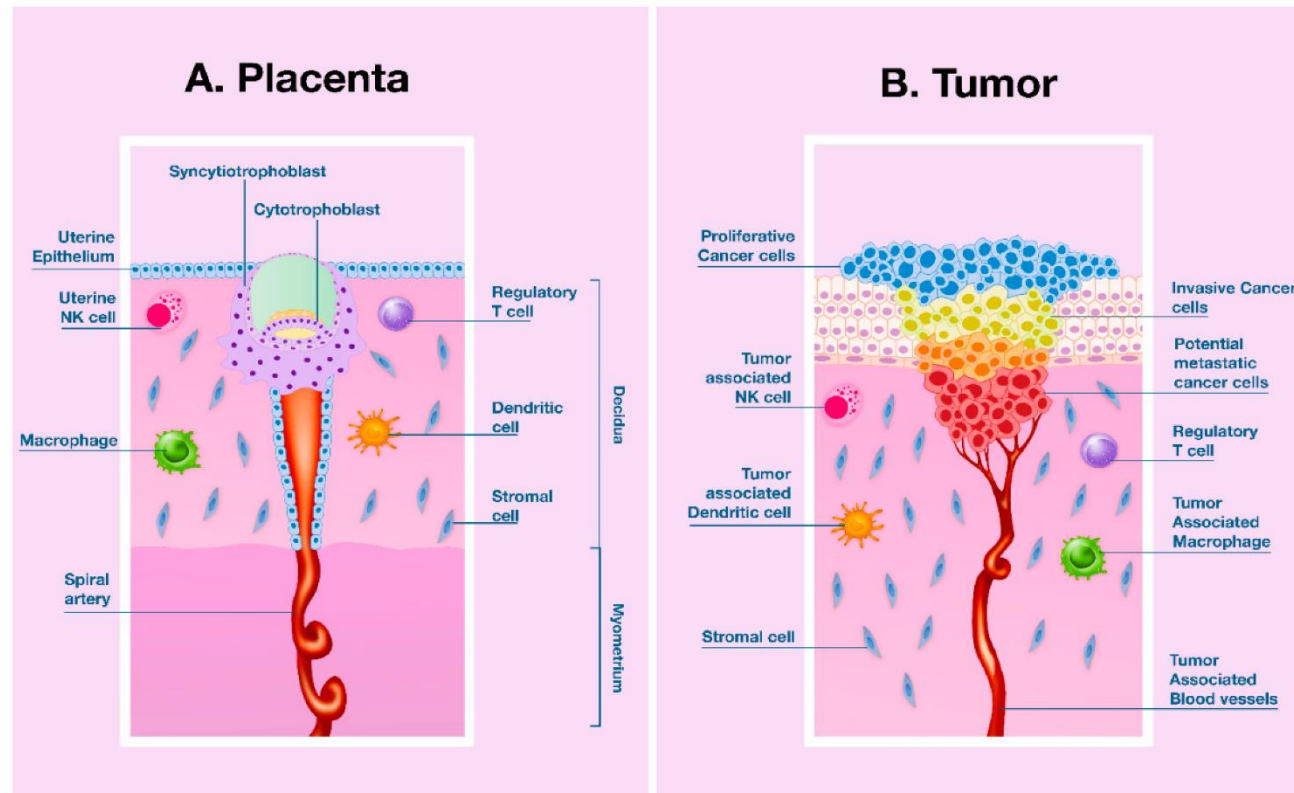


## TARGET OVERVIEW: HLA-G AND ILT4



# HLA-G Is An Immune Checkpoint (ICP)

## HLA-G IS INVOLVED IN PREGNANCY TOLERANCE AND TUMOR IMMUNE ESCAPE



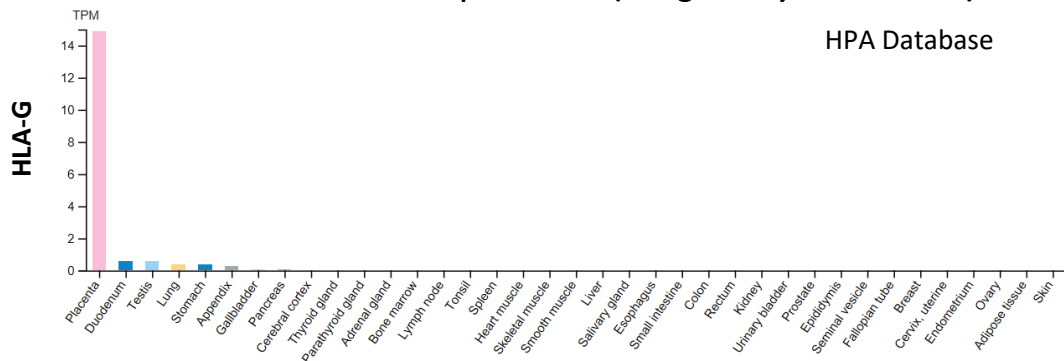
- HLA-G expression on placenta protects the semi-allogenic fetus from the mother's immune response.
- Tumors profit from the HLA-G expression to evade immune responses by mimicking pregnancy.
- ILT-4 is a key receptor for HLA-G and present on the surface of most tumor cells

# HLA-G Is Also A Tumor Specific Antigen (TSA)

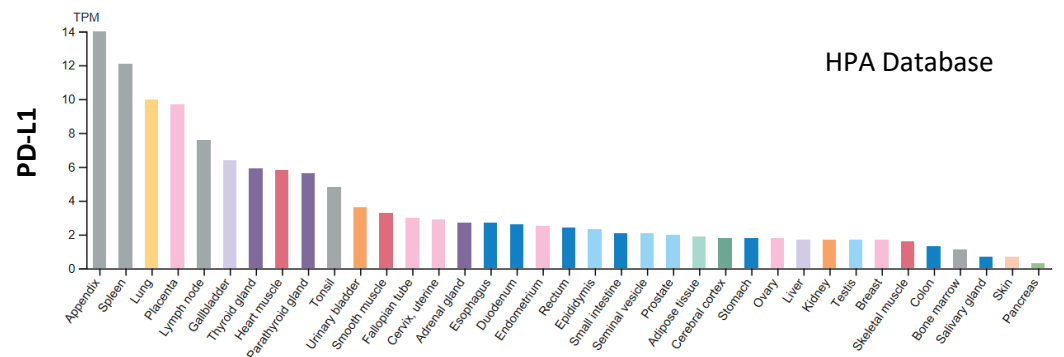
## HLA-G EXPRESSION: HIGH ON CANCERS; LOW OR ABSENT ON MAJOR HEALTHY TISSUES

HLA-G normal expression (*Pregnancy Tolerance*)

HPA Database

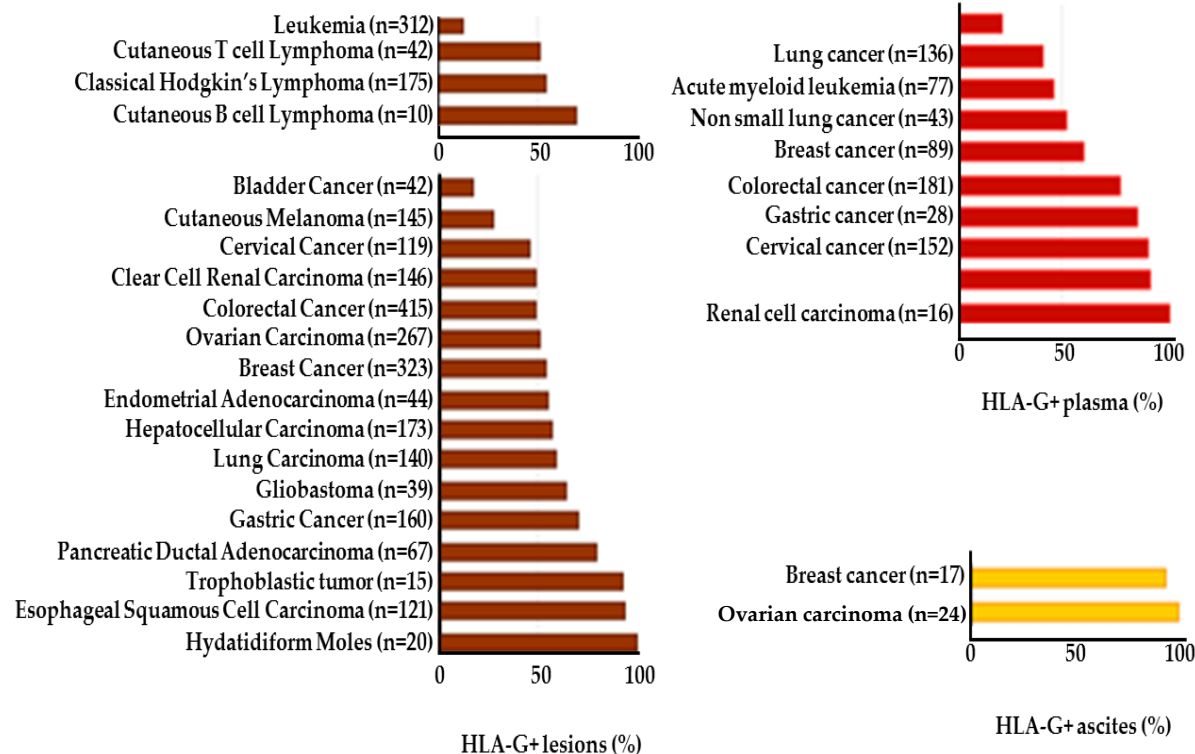


HPA Database



HPA = Human Protein Atlas; TPM = Transcripts per million

HLA-G abnormal expression (*Tumor Immune escape*)



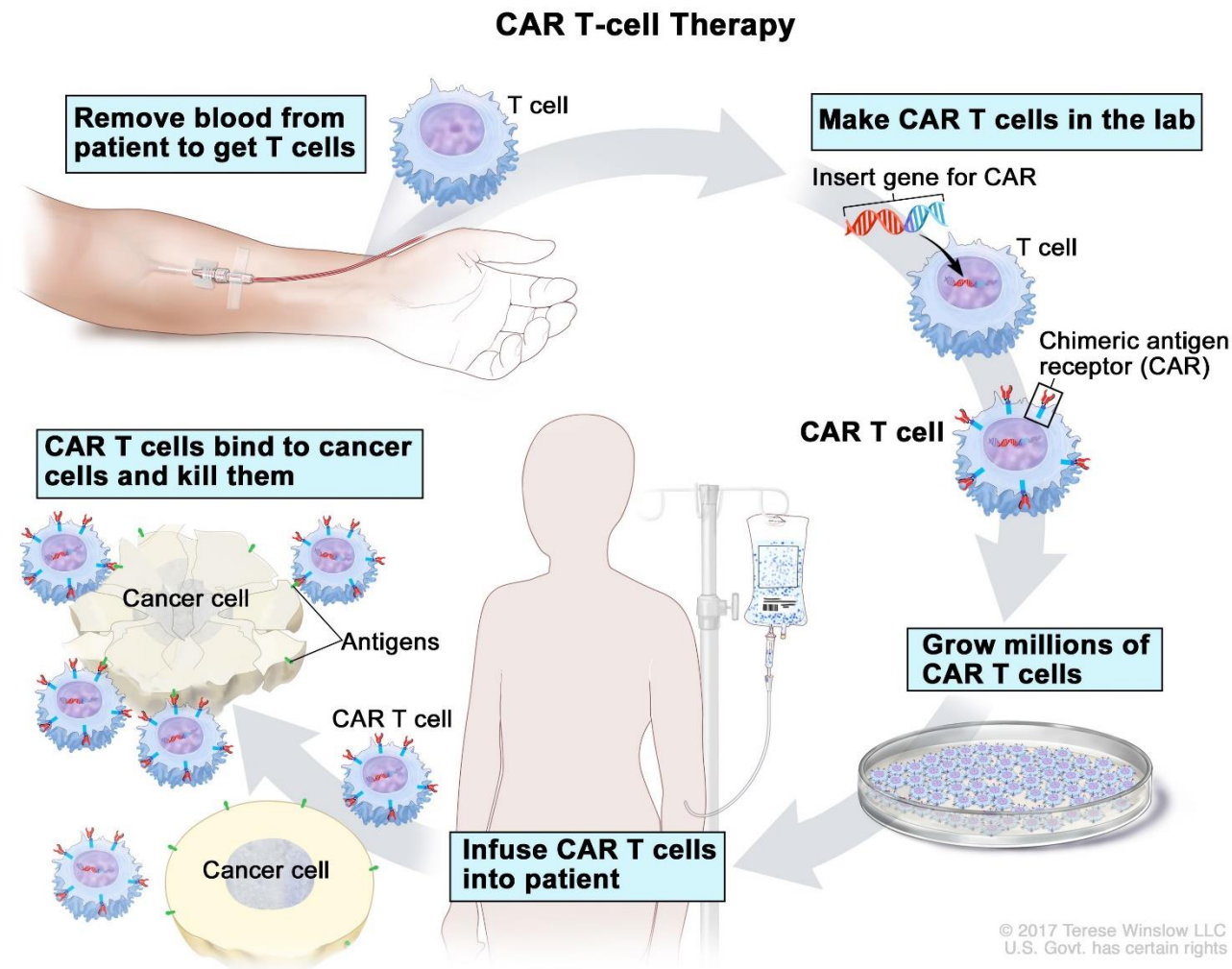
- Strongly neo-expressed on multiple hematopoietic and solid cancers: HLA-G expression on more than 70% of Human cancers
- Lack of expression on healthy tissues – In sharp contrast to PDL-1 – by passes off tumor toxicity problems.

# ILT-4 (LILRB2): An Immune Checkpoint

- ILT-4 is also known as Leukocyte Immunoglobulin Like Receptor B2 (LILRB2)
- ILT-4 expression :
  - Non-pathologic context: basal expression myeloid cells
  - Pathological context: upregulation on suppressive myeloid cells and on tumor cells
    - Suppressive myeloid cells are key cells of the protective tumor microenvironment (TME)
    - TME prevents effector immune cells to access and kill tumor cells
- Inhibition of ILT4, the new immune checkpoint, results in the repolarization of human macrophages from an M2 (suppressive) to an M1 (pro-inflammatory) phenotype, therefore, enhancing anti-tumor immunity
- 2 main ligands: HLA-G and ANGPTL-2

## IVS-3001 (CARGo): anti-HLA-G CART Cell Therapy

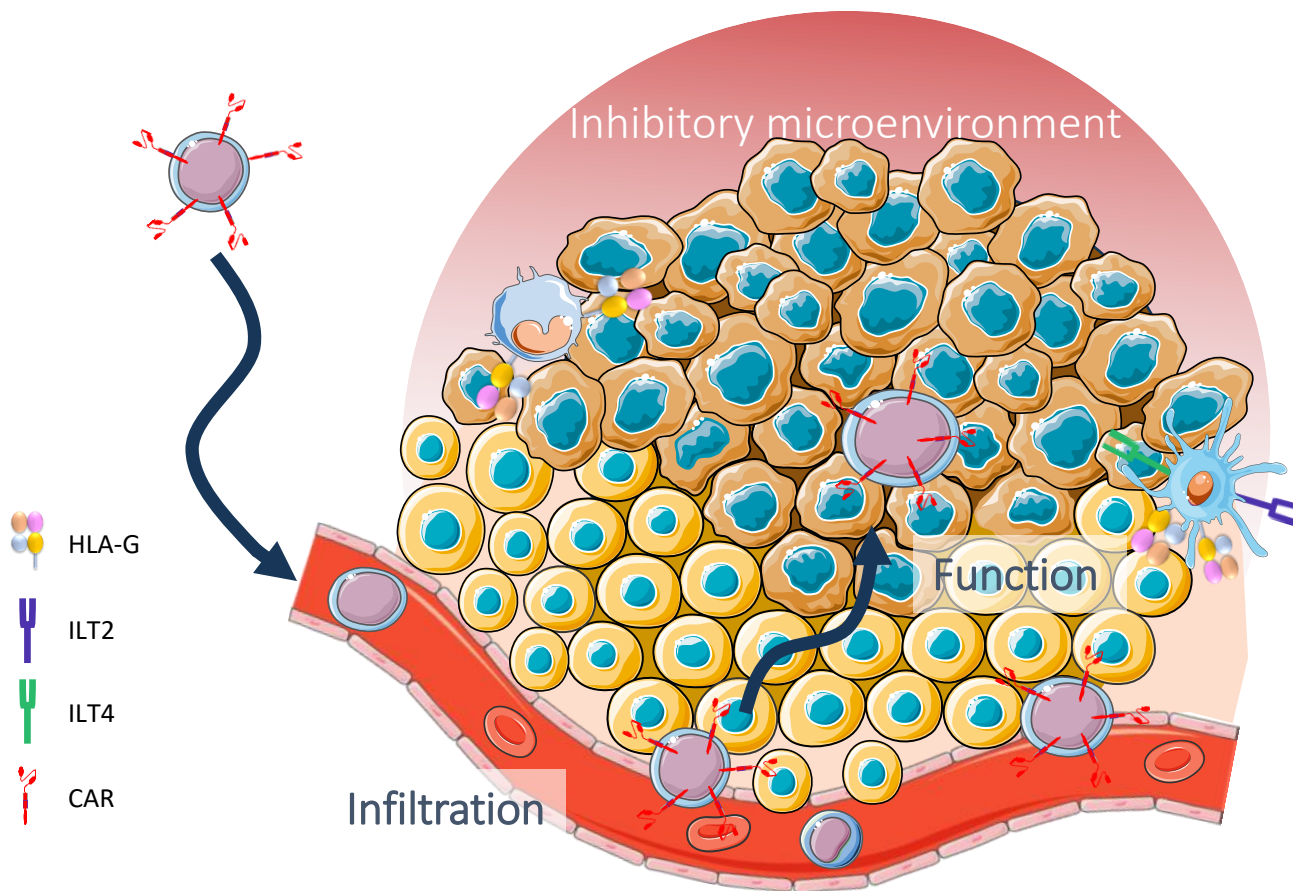
# CAR-T cells immunotherapy principle: Successfully applied to Liquid Tumors



## CAR-T cells success: Leukemia

- Successful in circulating Leukemia tumors:
  - Accessible to CAR-T cells
  - No physical barriers preventing CAR-T cells interaction
- These therapies target spread specific CD19 antigen
- There are already 6 proved high-rate success FDA approved CAR-T cells therapies:
  - **Kymriah**: B-ALL, B cell lymphoma, DLBCL.
  - **Yescarta**: DLBCL, B cell lymphoma
  - **Tecartus**: mantle cell lymphoma (MCL).
  - **Breyanzi**: DLBCL
  - **Abecma**: relapsed or refractory multiple myeloma
  - **CARVYKTI**: relapsed or refractory multiple myeloma

# CAR-T Cell Limitations in Solid Tumors: Invectys has the Solution



## CAR-T cells challenges: solid tumors

Solid tumor CAR-T cells immunotherapy defy several limitations:

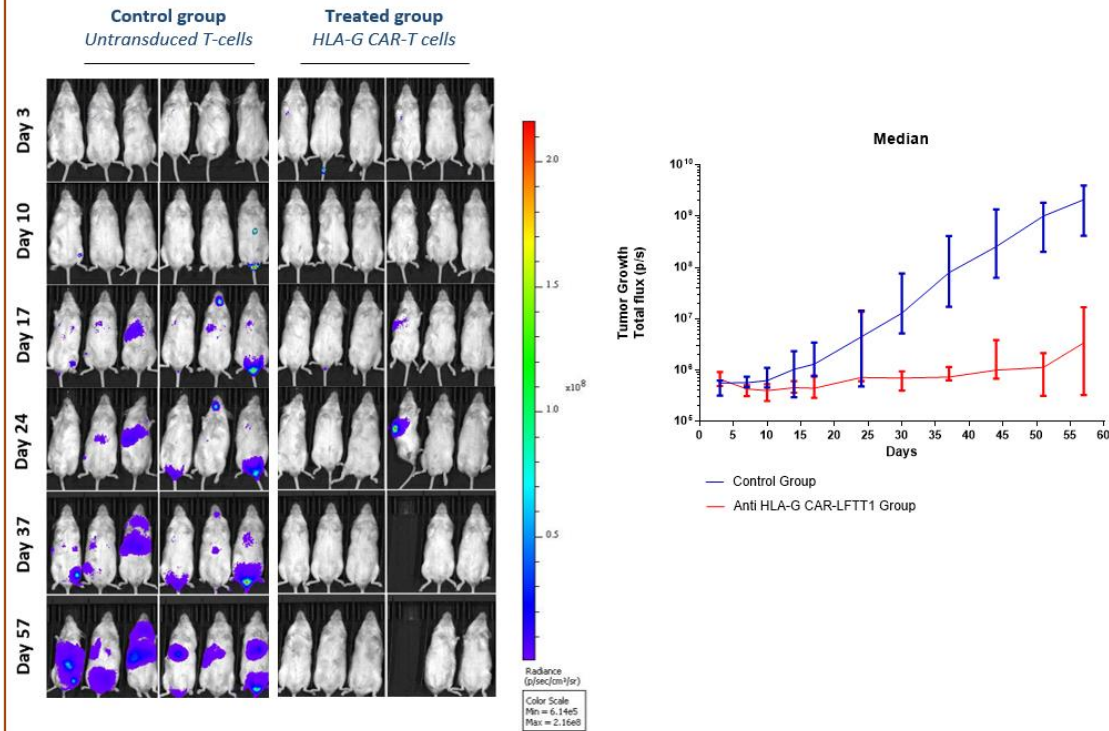
- No tumor-specific antigen (TSA): leak in healthy tissues
- No universal tumor-antigen: cannot be used against multiple solid tumors
- Restrained access:
  - Solid tumors are not in circulation contrary to Leukemia
  - Physical barrier (fibroblast) preventing CAR-T cells infiltration
  - Immunosuppressive barrier preventing (tumor microenvironment) CAR-T cells function

Solid tumors are protected by physical and suppressive barriers blocking preventing immune infiltration and functions: **Invectys has cracked the code to infiltrate and resolve Solid Tumors.**



# IVS-3001 (HLA-G CAR-T): In Vivo Proof of Concept (Hematopoietic and Solid Tumors/metastasis)

## In vivo: hematopoietic tumors killing

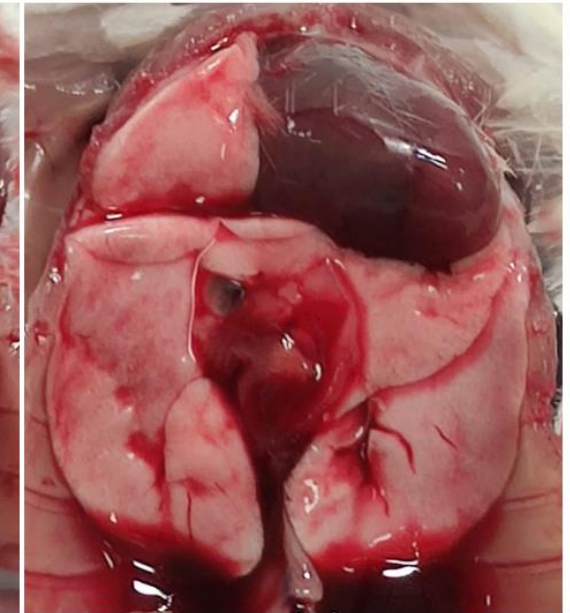


**IVS-3001 (Anti-HLA-G CAR-T cells) are potent cytotoxic T cells which lyse hematopoietic HLA-G tumor cells *in vivo***

Lung metastasis  
Autologous Control T cells



Lung metastasis  
Anti-HLA-G CAR-T cells (IVS-3001)



- IVS-3001 (HLA-G CART) eliminate HLA-G positive primary solid tumor and prevent dissemination and metastasis *in vivo*
- IVS-3001 (HLA-G CART) are activated in primary tumor and in metastasis *ex vivo*



# IVS-3001 (HLA-G CAR-T): Program Externally Validated & Next Steps

## ➤ External validation:

- Received coveted \$14.2 million Cancer Prevention & Research Institute of Texas “CPRIT” grant in 2020 from the State of Texas
- Established prestigious Strategic Industry Venture partnership with MD Anderson Cancer Center in 2022
- Aligned with FDA on pre-clinical, CMC and clinical plan via pre-IND interaction with FDA 2H2021
- EMA scientific advice completed

## ➤ Next steps:

- Preclinical, CMC and clinical activities are on target to support IND filing 4Q2022

# MD Anderson, Invectys and CTMC announce strategic collaboration for CAR T cell therapy development

## PUBLIC RELATIONS OFFICE

713-792-0655 • [publicrelations@mdanderson.org](mailto:publicrelations@mdanderson.org)  
[www.mdanderson.org/newsroom](http://www.mdanderson.org/newsroom)

THE UNIVERSITY OF TEXAS

**MD Anderson  
Cancer Center**

Making Cancer History®

**For immediate release:** June 16, 2022

## MD Anderson, Invectys and CTMC announce strategic collaboration for CAR T cell therapy development

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Contact: Laura Torgerson

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[Press@CTMC.com](mailto:Press@CTMC.com)

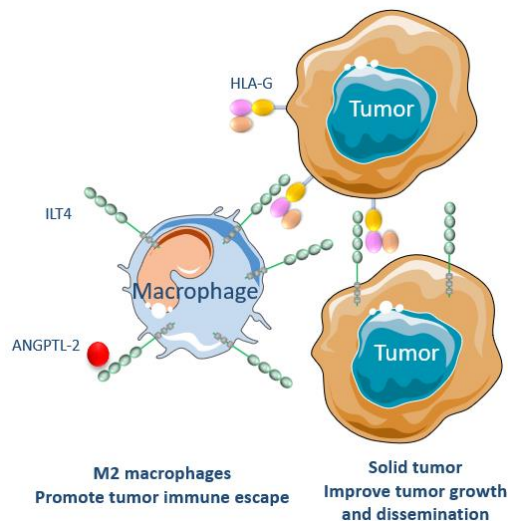
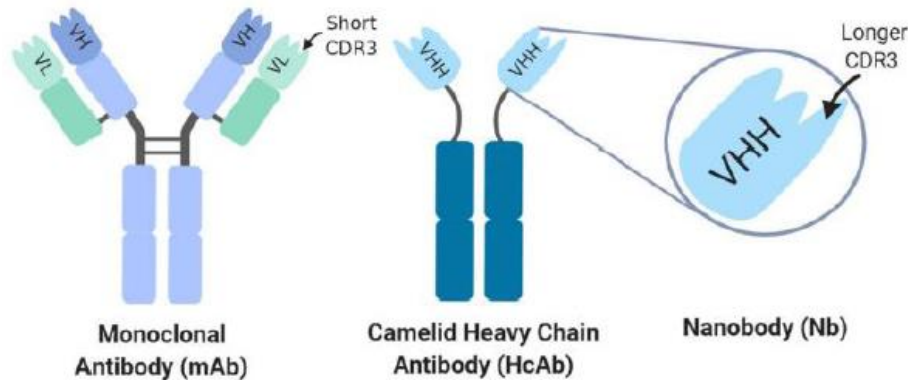
HOUSTON — [The University of Texas MD Anderson Cancer Center](http://www.mdanderson.org), Invectys, Inc., and the Cell Therapy Manufacturing Center (CTMC), a joint venture between MD Anderson and National Resilience, Inc., today announced a strategic collaboration to jointly develop a reliable, compliant and scalable process for human leukocyte antigen (HLA)-G targeted chimeric antigen receptor (CAR) T cell therapy for solid tumors.

The collaboration will build upon the HLA-G platform pioneered by Invectys to advance novel [CAR T cell therapies](#) through preclinical development with CTMC into early-phase clinical studies at MD Anderson. The collaboration brings Invectys' technology together with the cell therapy development and manufacturing expertise of CTMC and the clinical trials expertise of MD Anderson.

## **IVS-5001 (B8): anti-ILT-4 Nanobody**

# IVS-5001 Is a High Affinity Nanobody to ILT-4: In vitro PoC demonstrated

- IVS-5001 has high affinity and specificity to ILT-4 with apparent  $K_d < 1\text{pM}$
- In vitro PoC demonstrated, expect various antitumor functions in vivo
- Nanobody has therapeutic advantages compared to conventional monoclonal antibodies, as listed below



## Advantages of Nanobodies

- High antigen specificity and affinity
- High solubility and robustness
- High BBB permeability
- High vascular permeability and low “binding site barrier” effect
- High tumor penetrability with low local drainage
- High tumor and metastasis uptake
- ROA: oral, IP, IV or intra-tumoral
- High stability and lower production costs
- High human identity (85-95%) → low immunogenicity (humanization may lead to affinity loss)
- Short bloodstream half-life (high renal clearance)
- Toxicity: high kidney, liver and intestine uptake

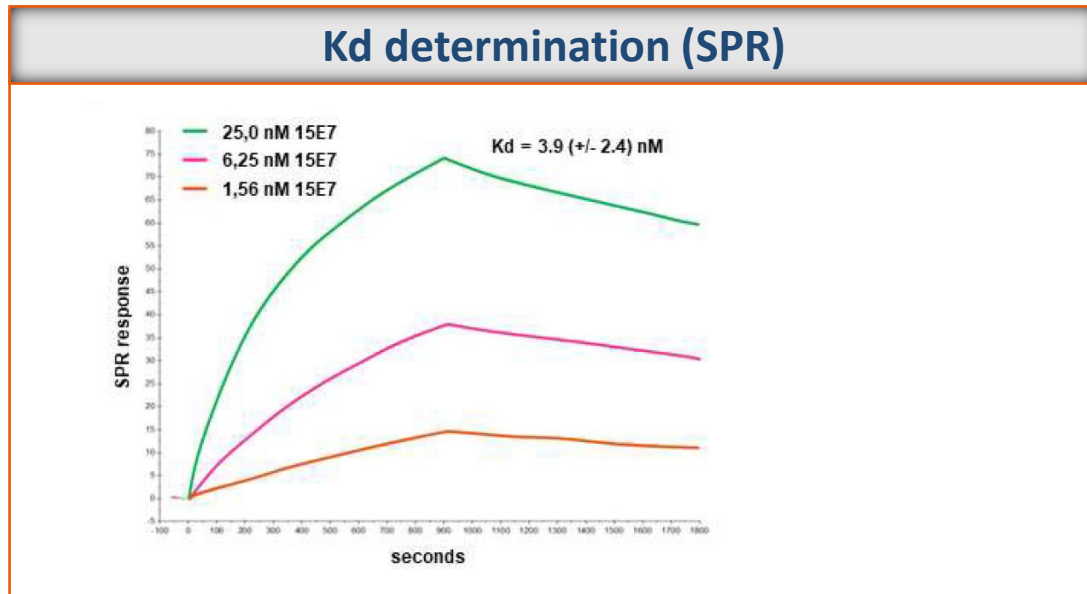
Preclinical, CMC and clinical activities are on target to support

- Pre-IND 1Q2023
- IND filing 2H2023

## **IVS-4001 (15E7): anti-HLA-G monoclonal antibody**

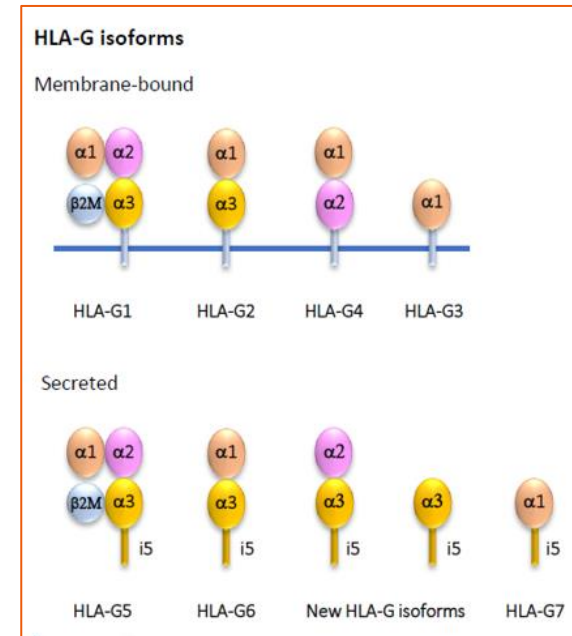
# IVS-4001 (HLA-G mAb) Shows High Affinity to Novel HLA-G Isoforms

- 1st antibody to target b2m-free HLA-G1, HLA-G2, HLA-G5 and HLA-G6 suppressive isoforms
  - Binds specifically to HLA-G-a3 region that mediates the interaction with ILT-4 inhibitory receptor
- Does not cross react with classical HLA molecules





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- IVS-4001 (15E7) presents an apparent Kd of 3.9 nM
- **Expected IVS-4001 (15E7) blocking functions:**
  - angiogenesis
  - innate responses
  - humoral responses
  - cellular responses
  - APC responses
  - Inhibition of suppressive immune cells (Tregs, suppressives NK and APC) and of TME inductions

# Invectys R&D Pipeline: HLA-G Platform (Oct 2022)

Program	Indication	Partners/ Collaborators	Anticipated Milestones			
			2021	2022	2023	2024
IVS-3001 HLA-G CAR-T	ccRCC EOC Solid tumors	 	PoC ✓ Pre-IND meeting ✓ IND-enabling studies initiation ✓	<b>IND filing</b> Phase 1/2a Initiation	Continue Phase 1/2a Fast-track designation	Phase 2a initiation RMAT designation
IVS-5001 ILT-4 Nb	Solid tumors	In discussion	In vitro PoC ✓ Lead optimization ✓	Clinical candidate ✓ PoC (in vitro) ✓ PoC (in vivo) Pre-IND meeting	IND enabling studies <b>IND filing</b> Phase 1 initiation	Fast-track designation Phase 2 initiation
IVS-4001 HLA-G mAb	Solid tumors	In discussion	In vitro PoC ✓ mAb humanization Initiation ✓	PoC (in vitro) PoC (in vivo)	Pre-IND meeting IND enabling studies	<b>IND filing</b> Phase 1 initiation Fast-track designation





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