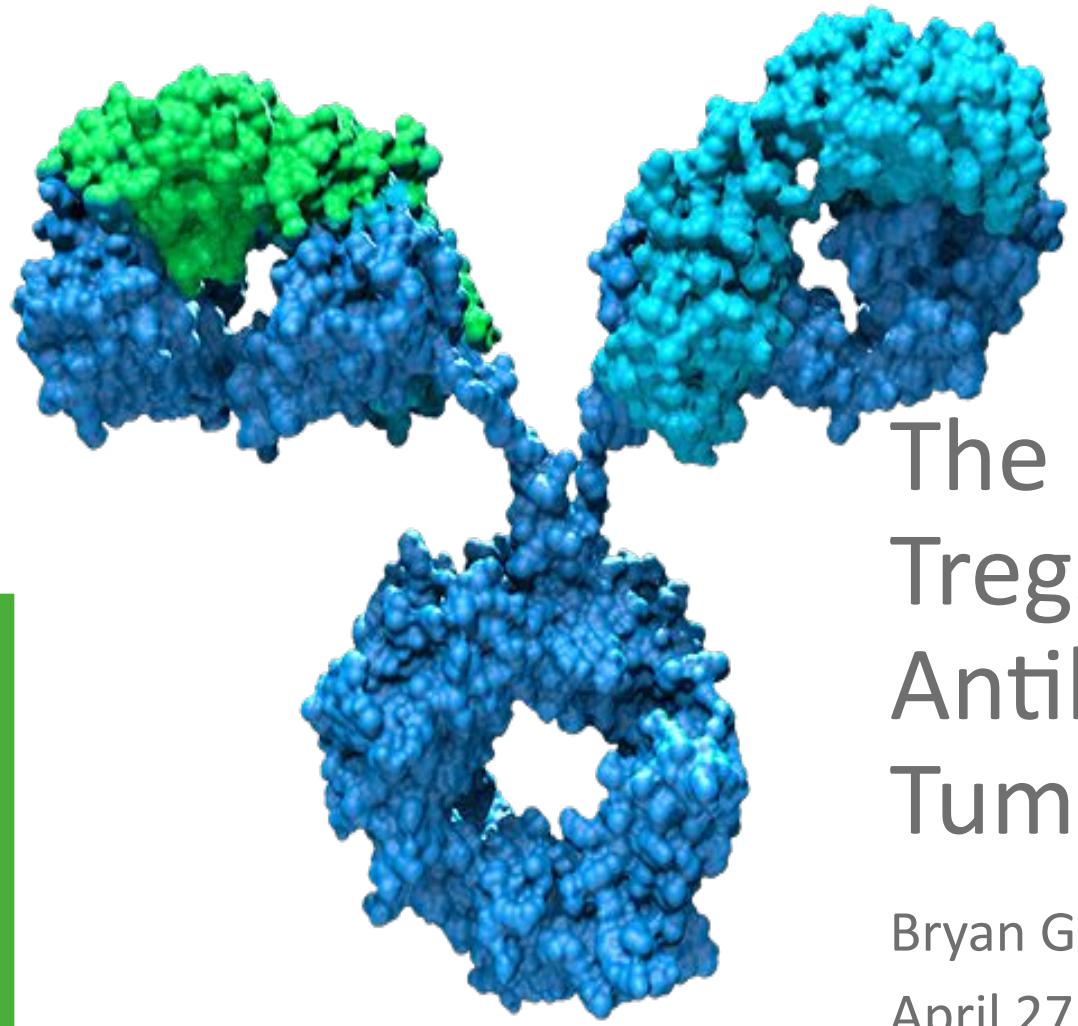


invenra

The Selective Elimination of Tumor Tregs by a Bispecific SNIPER Antibody Delivers a Strong Anti-Tumor Activity

Bryan Glaser, PhD

April 27, 2021

Biologics Europe: Online

Invenra's Guiding Strategy in Oncology

- *"For decades, new treatments for advanced cancer were considered successful if they could slow the cancer's growth and extend survival a few months. For all children with cancer, and for most adults with cancer, we should aim for more than a few months. Our goal must remain eliminating all cancer in these patients and preventing cancer from ever coming back. "*

Paul Sondel MD, PhD

Pediatric Oncologist and Immunotherapy Researcher

University of Wisconsin Carbone Cancer Center

The Three Lines of Attack for Effective I/O Therapy

Line 1– Trigger Immunogenic Tumor Cell Death

Line 2 – Eliminate Suppressive Immune Cells

Line 3 – Inflame the Tumor

We Believe All Three of These Lines Should be Pursued
To
Cure Late-Stage Metastatic Disease

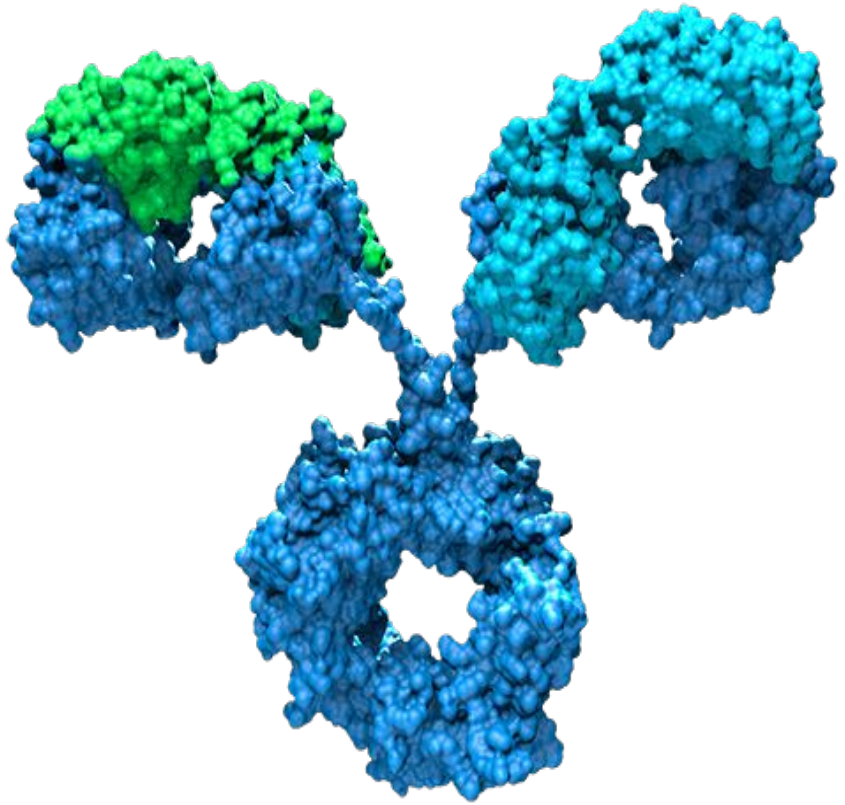
Two Preclinical Oncology Programs

Program	Line of Attack	Discovery	Lead Selection	Preclinical	Phase 1
INV721	Immunogenic Cell Death				
INV321	Eliminate Suppressive Tregs				

- Pipeline assets are focused on the three lines of attack
- Asset qualities:
  - Large standalone value
  - Synergy with each other
  - Can be building blocks for other Invenra Technologies

INV321

A Tumor Selective Treg SNIPER

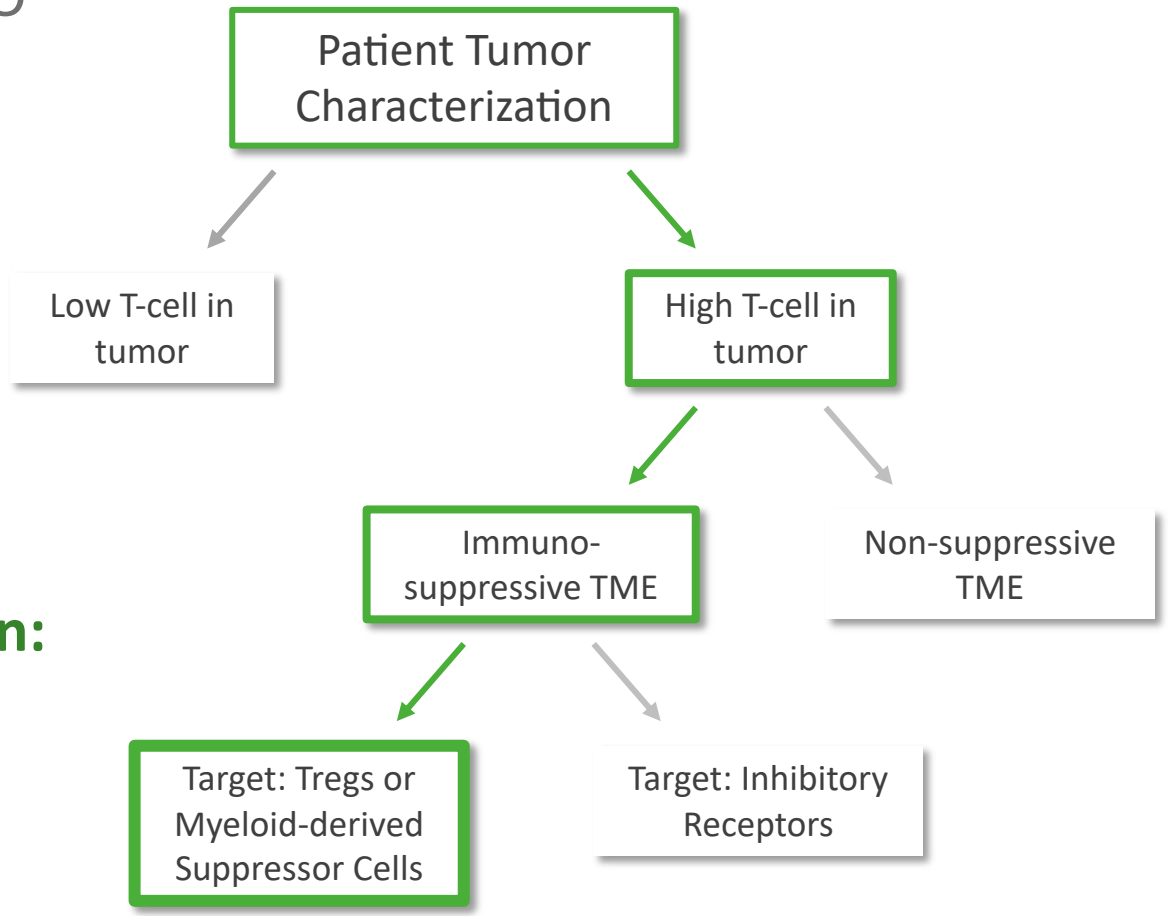


The Need for Targeted Treg Depletion

- Tumors can have a suppressive tumor microenvironment (TME) that limit Current IO therapies

- Monoclonal antibody challenges:
  - High affinity non-specific binding, toxicity
  - Depletion of other needed immune cells
  - Target-specific biology can change depending on cell type

- **Depletion of tumor Tregs with bispecifics can:**
  - Reduce suppressive TME and rebalance the immune response
  - Avoid global Treg depletion to prevent autoimmune disease
  - Improve the efficacy of IO therapies



INV321: A SNIPER™ Bispecific with Best-in-Class Potential

- Typical monoclonal antibody approaches use high affinity binding to target Tregs
  - Target expression is typically higher on Tregs than other immune cell populations
  - Target-specific biology (ligand blocking, agonism, etc.) could enhance efficacy
- Treg targets are often not exclusively found on one immune cell type
- Our SNIPER approach has comprehensively analyzed current Treg depletion targets
  - Screened primary cancer patient samples vis flow cytometry to identify promising double-positive target pairs
  - Comprehensively defined two targets of interest and confirmed biology in murine and human systems
  - Produced and tested 100s of B-Bodies™ to identify combinations of binding arms that achieve desired selectivity for tumor Tregs
- Have advanced INV321 through *in vitro* and *in vivo* testing against these 2 targets

The Invenra SNIPER™ Approach to Enhancing Specificity

- Bispecifics designed with weak monovalent affinity to each target, but strong avidity to the combination
- Maximizes specificity and efficacy
- Minimizes binding to non-target cells significantly reducing possible side effects/toxicity
- Can better direct ADCC, ADC, radionuclides, or T-cells to targeted cells while avoiding healthy cells

SNIPER™ Bispecifics

BENEFITS

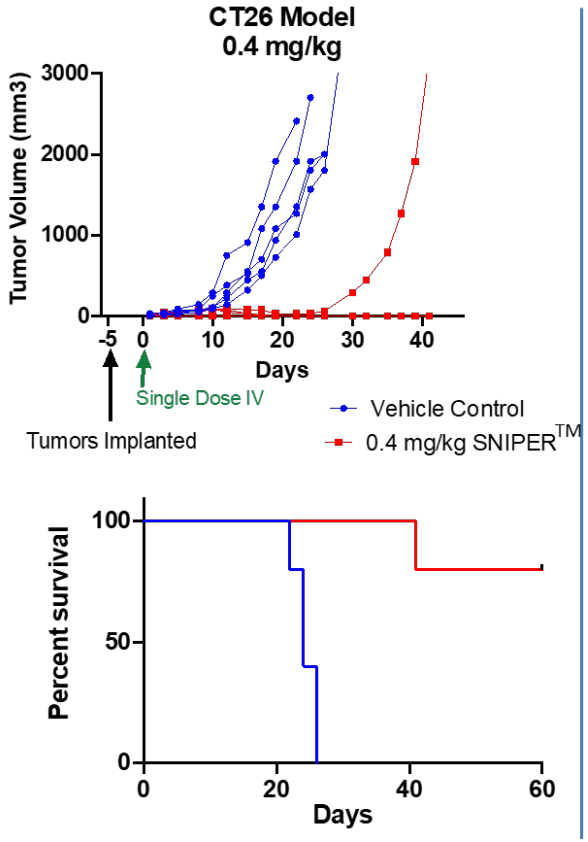
- ✓ On-disease specificity
- ✓ Multiple MOAs
- ✓ Increased therapeutic window

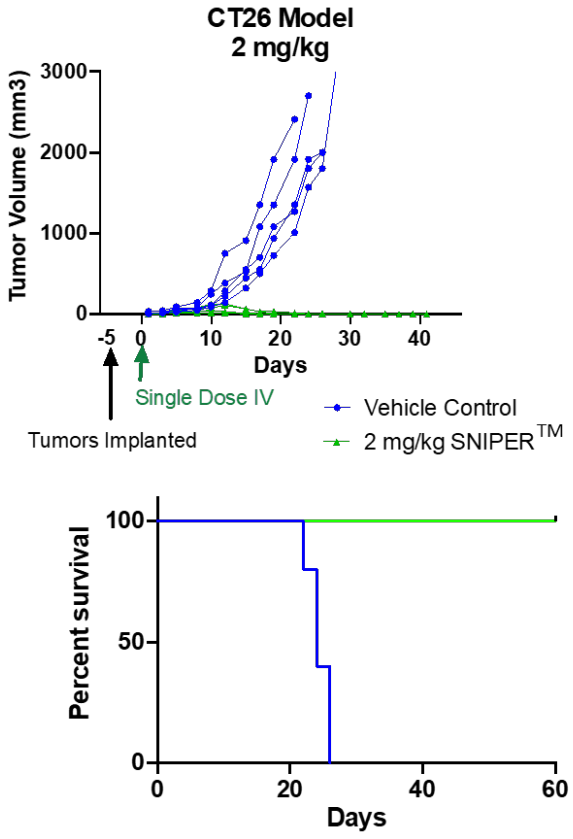
Monospecific Antibodies

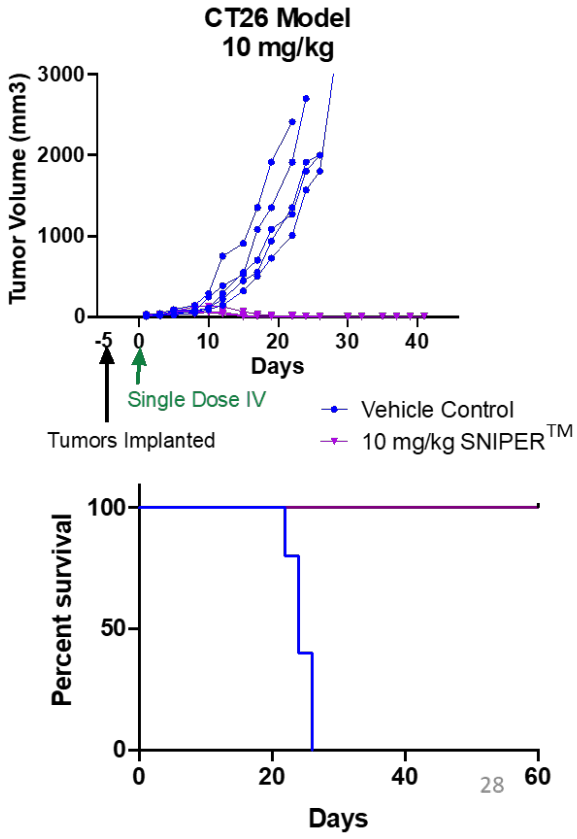
LIABILITIES

- ✓ Limited MOA
- ✓ On-target efficacy, but off-target toxicities

INV321: CT26 Efficacy Model





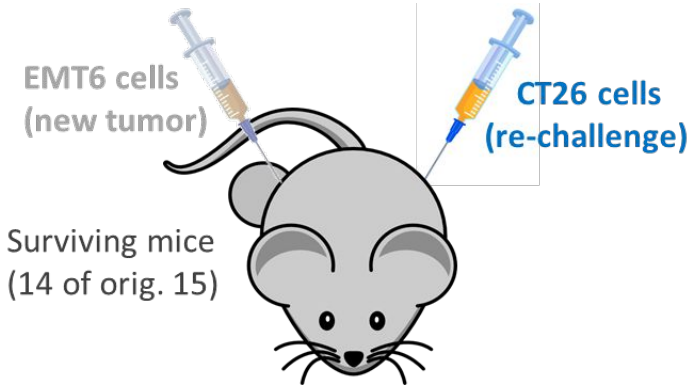


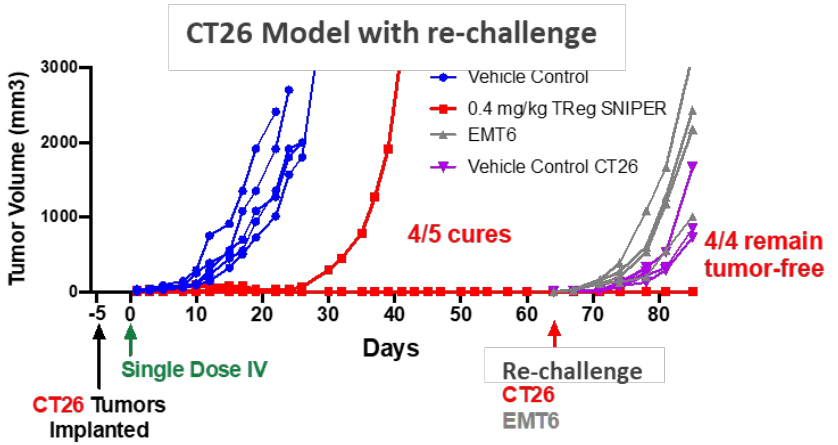
- Strong avidity requires presence of Target 1 AND Target 2
- Target 1 and Target 2 ligands blocked only during avid binding

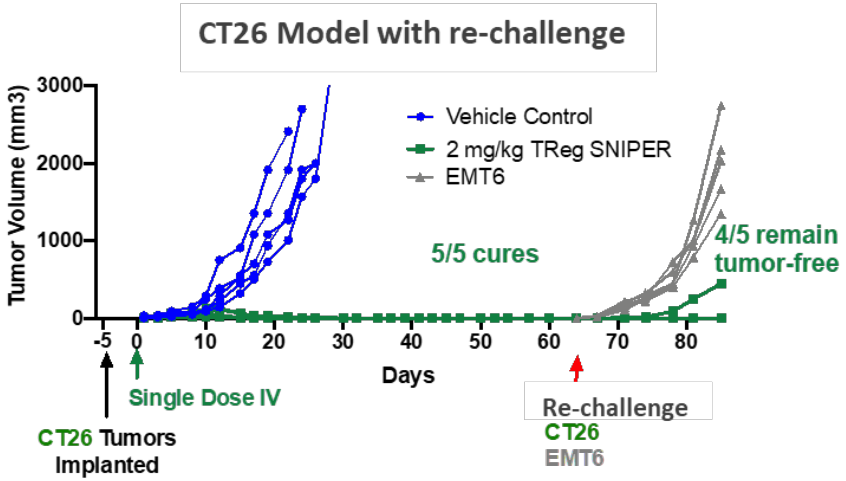
28

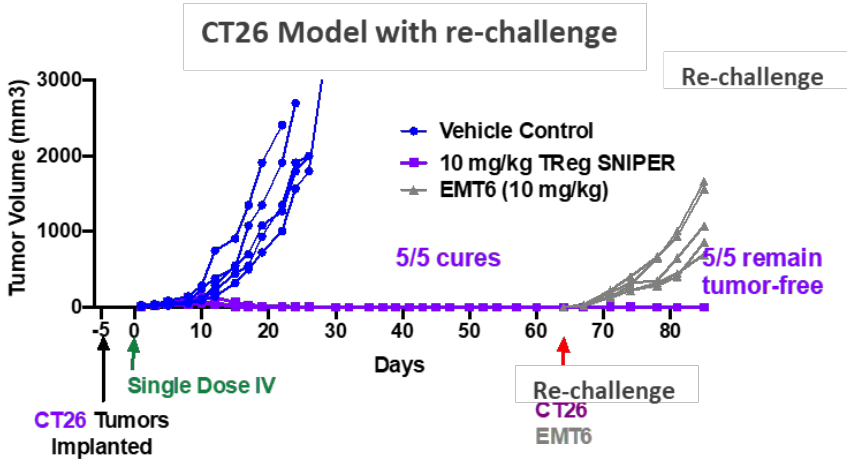
A Single Dose of INV321 Eliminated Most Tumors

INV321: CT26 Rechallenge







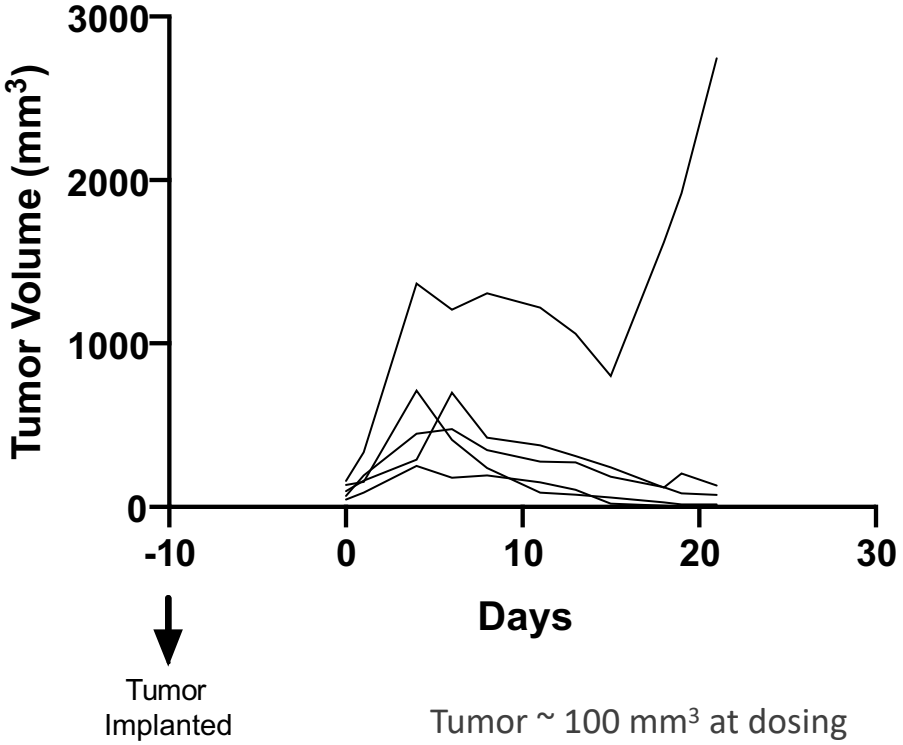


INV321 Stimulates a Strong Immune Response and Immune Memory

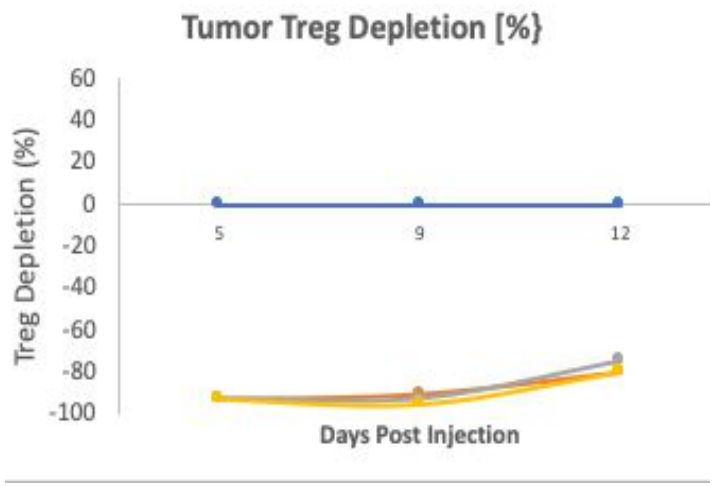
INV321: Treg Depletion in CT26 Efficacy Models

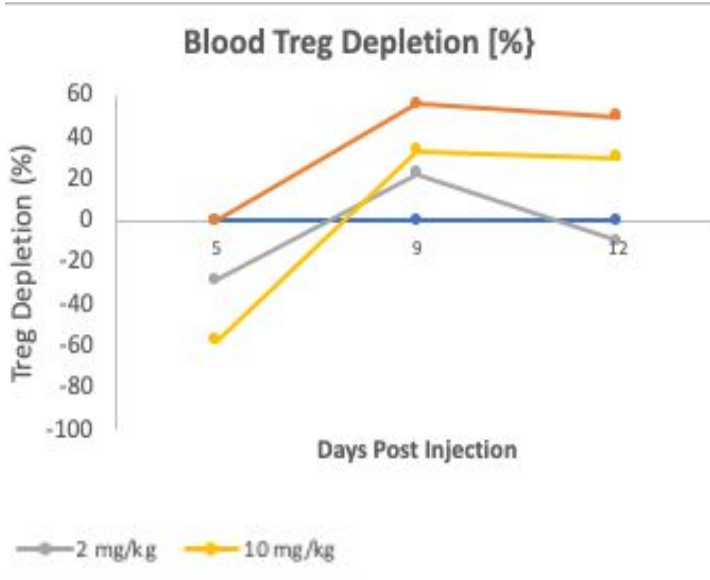
INV321 in CT26 Murine Model

2 mg/kg (single dose, IV)



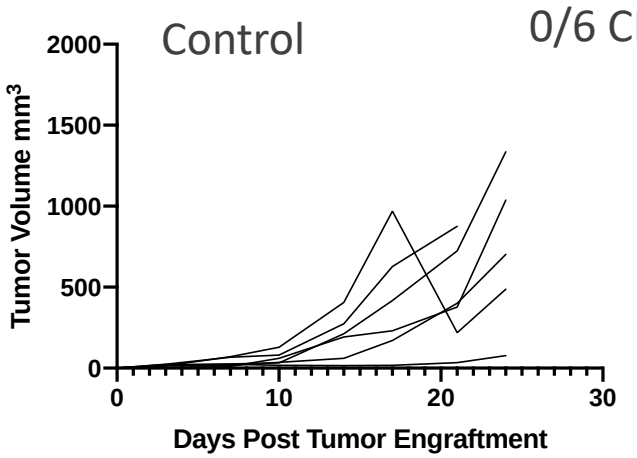
Tumor ~ 100 mm^3 at dosing

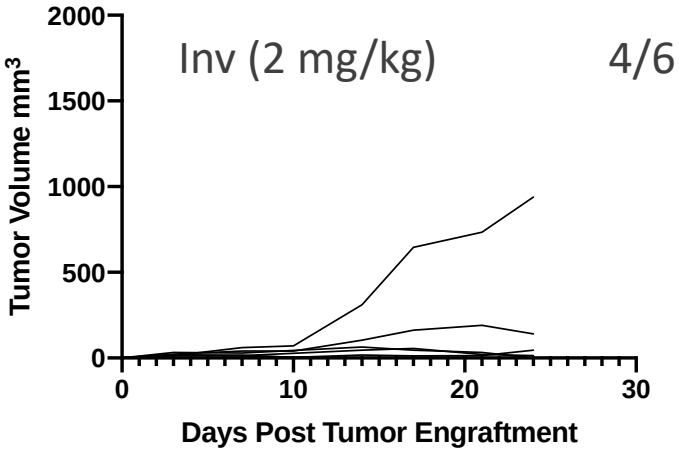


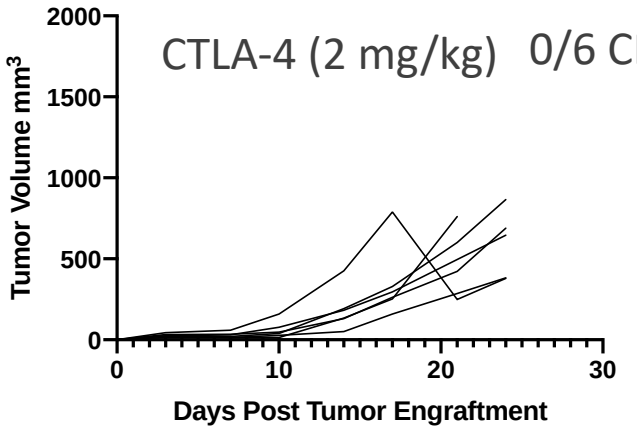


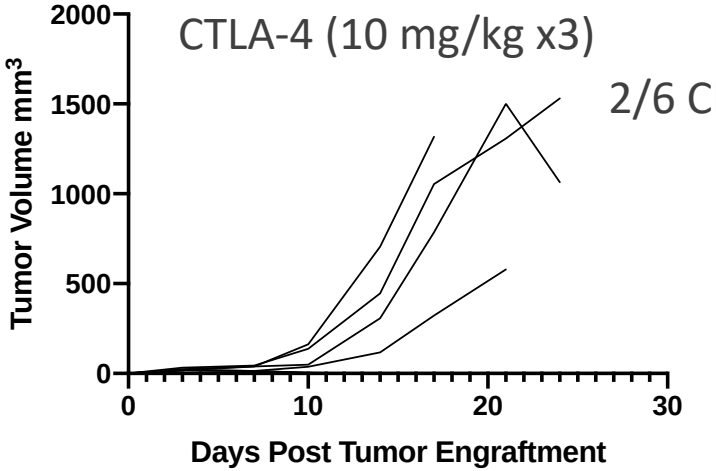
INV321 Specifically Depletes Tregs in the Tumor and not the Blood

Comparing INV321 to Anti-CTLA-4 in a RENCA Tumor Model





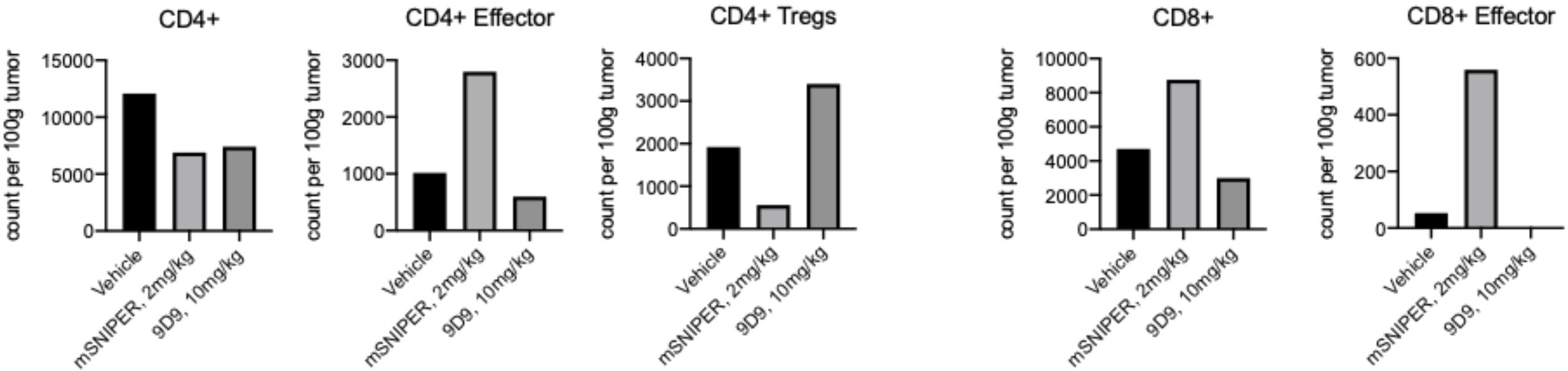




D0 – RENCA i.d.
D9 – Abs i.v. (mg/kg)
INV321 (Hu IgG_1)
9D9 (mu IgG_{2b})
Randomized ~ 40 mm^3

INV321 has Similar Efficacy to CTLA-4 Therapies

Tumor Immunophenotyping: Day 12 Post Dosing



Tregs: FoxP3^{+}CD127^{lo} & Effectors: CD44^{hi}CD62L^{lo}

Note: No significant changes observed in the periphery

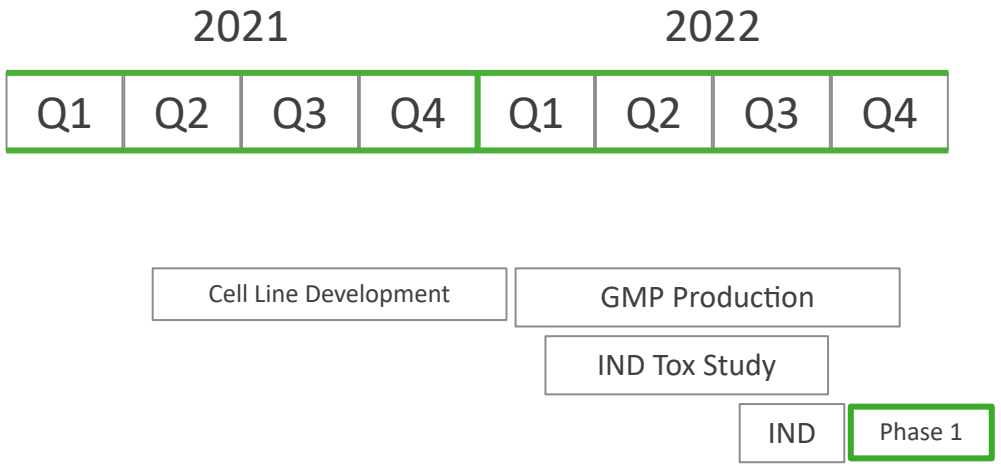
INV321 Specifically Eliminates Tumor Tregs and Increase Effector T-cells

INV321: Promising Proof-of-Concept Established

- Multiple MOAs
  - Enhanced ADCC (antibody-dependent cell-mediated cytotoxicity)
  - Specific disruption of two target-ligand interactions
  - May alter surface expression of targets through induced degradation

- Significant market opportunities in broad oncology indications
  - Primary focus on SCLC; secondary on non-small cell lung cancer, melanoma and head & neck cancers
  - Single agent activity
  - Suitable for combinations
    - PD-1/PD-L1
    - T cell-redirecting bispecifics
    - CAR-T therapeutics

Invenra's Path to the Clinic



Additional Indications: NSCLC, Melanoma, Head and Neck

Combinations: Anti-PD1/PD-L1, Car-T, T-cell redirecting bispecifics

Acknowledgements

The Whole Invenra Team

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