



**Targeted immune activation  
with SIRP $\alpha$  antibody — TLR9 agonist  
conjugate (SIRP $\alpha$  TRAAC)**

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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

# ALX Oncology and Tallac Therapeutics 50/50 joint collaboration on novel SIRP $\alpha$ antibody – TLR9 agonist conjugate (SIRP $\alpha$ TRAAC)



Provides  
SIRP $\alpha$  antibody

- CD47-SIRP $\alpha$  is a dominant myeloid checkpoint mechanism where SIRP $\alpha$  is expressed on myeloid and dendritic cells as well as on a range of tumor cells.
- SIRP $\alpha$  expression on tumor cells enables tumor microenvironment localization of SIRP $\alpha$  TRAAC.



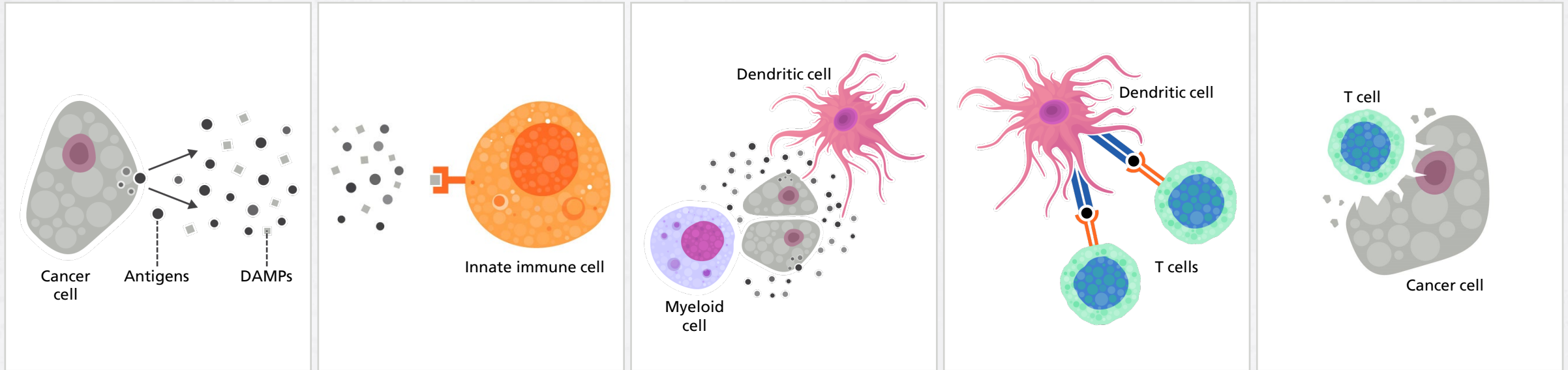
Provides  
TRAAC platform  
and TLR9 agonist

- Toll-like receptor 9 (TLR9) is a key receptor in the innate immune response.
- Synthetic CpG oligonucleotides (CpG ODNs) are potent TLR9 agonists that stimulate antitumoral cytokine production and immune activation.
- Novel Toll-like receptor agonist antibody conjugation platform (TRAAC) enables systemic delivery of targeted TLR9 activation.

**SIRP $\alpha$  TRAAC induces targeted immune activation, bridging innate and adaptive immune responses.**

**SIRP $\alpha$  TRAAC simultaneously overrides “don’t eat me” signals by blocking CD47-SIRP $\alpha$  myeloid checkpoint pathway and induces TLR9-based immune activation in antigen presenting cells (APCs).**

# Harnessing the power of innate and adaptive immune responses to cancer



1. Release of PAMPs/DAMPs and tumor antigens

2. Detection by PRRs on innate immune cells

3. Amplification of innate immune cell activation

4. Antigen presentation and activation of T cells

5. Recognition and elimination of tumor by T cells

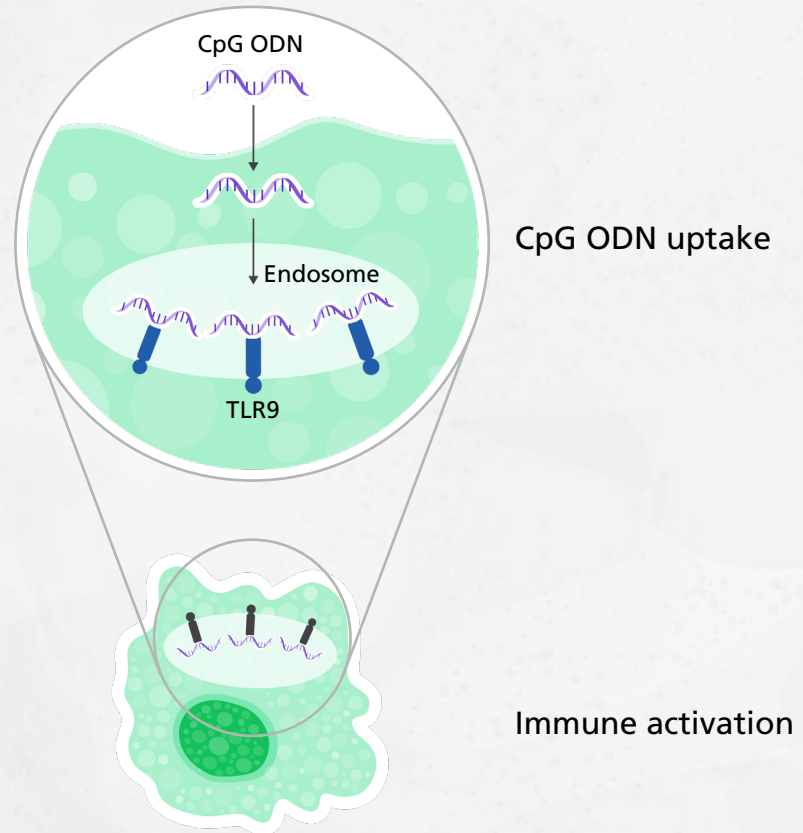
- Successful immune-mediated elimination of cancer requires coordination between the innate and adaptive arms of the immune system.
- Innate immune cells (macrophages, myeloid cells and dendritic cells) may utilize a variety of signaling pathways, including TLR9, TLR7 or 8, STING and CD40, to trigger proinflammatory programs and engage the adaptive immune system.

DAMPs: damage-associated molecular patterns  
PAMPs: pathogen-associated molecular patterns  
PRRs: pattern recognition receptors

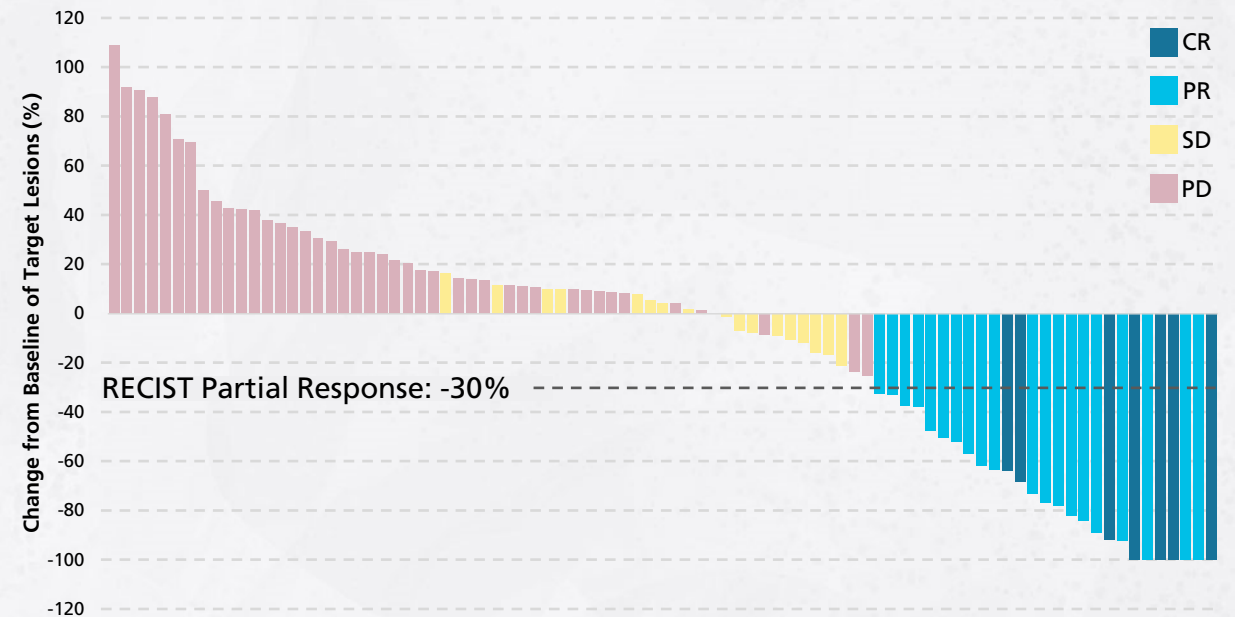
# Toll-like Receptor 9 (TLR9): a key innate pathway

Proof-of-concept data in melanoma patients with intratumoral TLR9 agonists

TLR9 stimulation by CpG ODN leads to immune cell activation



Intratumoral programs have demonstrated clinical activity



CMP-001 (Checkmate) + Pembrolizumab in Anti-PD-1 Refractory Melanoma, <sup>1-4</sup>Checkmate, S1 2020.

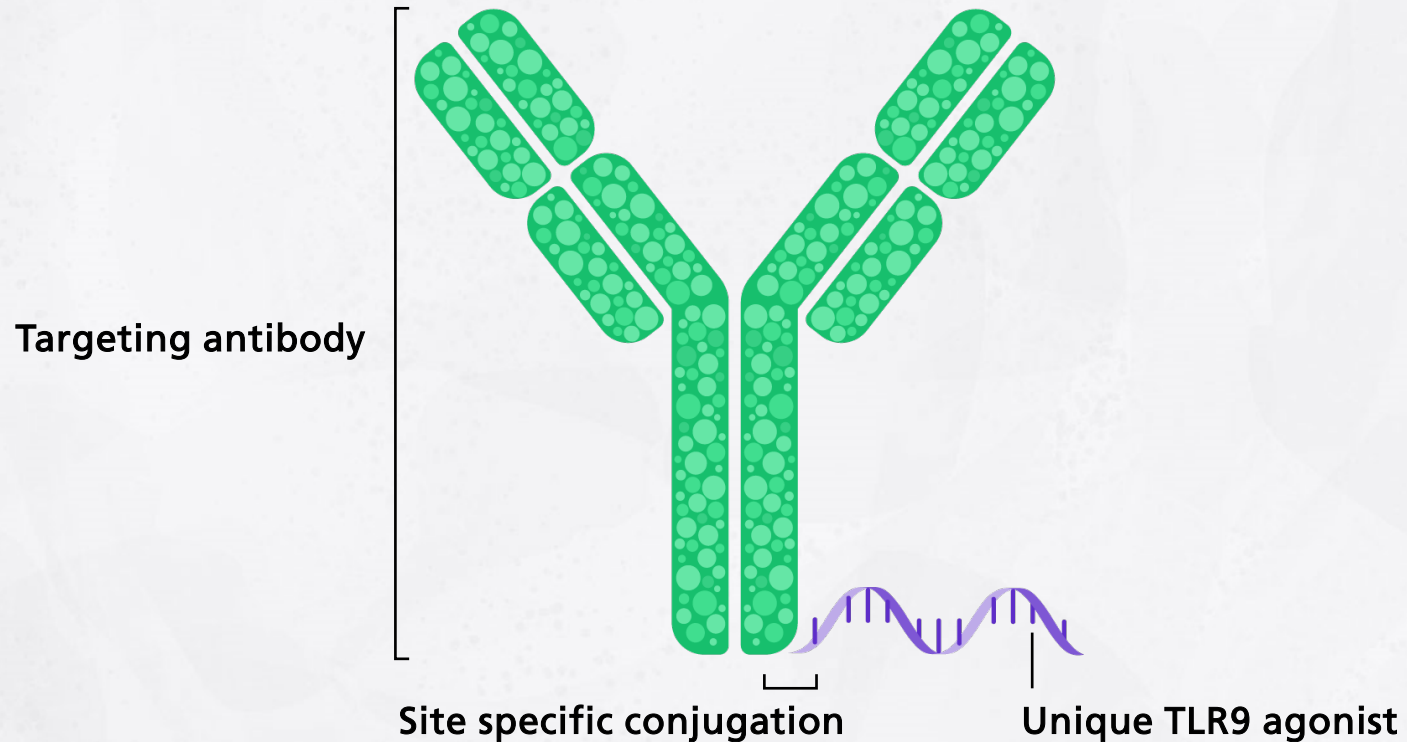
Additional clinical data from SD-101 (Dynavax), IMO-2125 (Idera) and AST-008 (Exicure) further validate TLR9 agonism in cancer.



# Tallac TRAAC platform: systemic, targeted immune activation

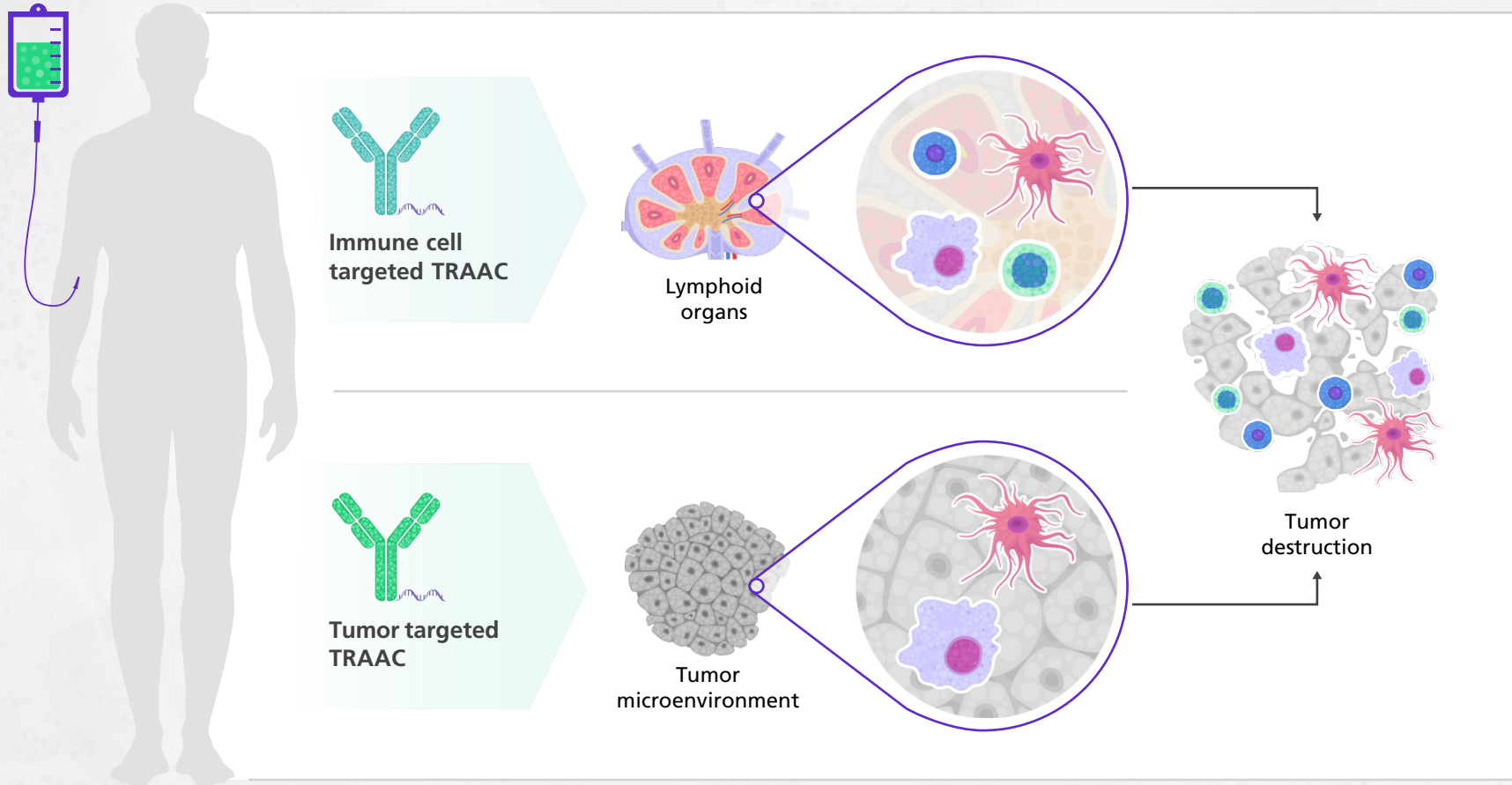
Antibody directs TLR9 agonist (T-CpG) to specific immune cells

**TLR9 Agonist Antibody Conjugate (TRAAC):  
Systemic dosing with cell specific TLR9 activation**

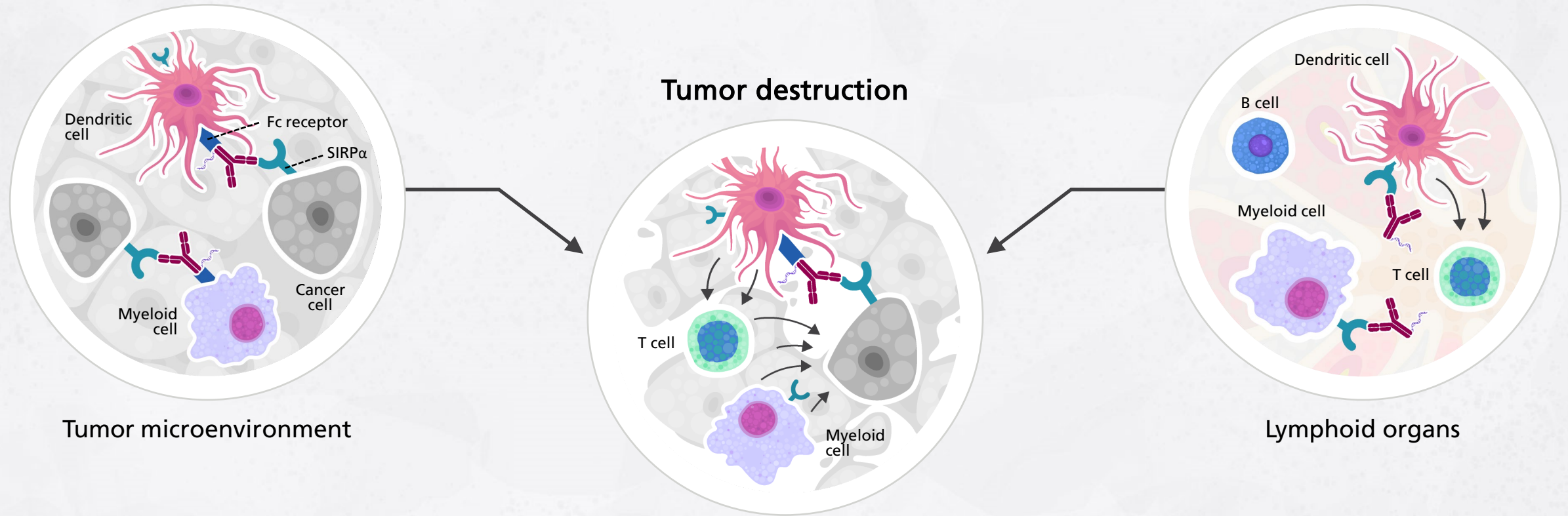


Targeted-CpG (T-CpG) designed specifically for compatibility with antibody conjugation, superior PK, receptor-mediated uptake and TLR9 stimulation

# TLR9 Agonist Antibody Conjugate (TRAAC) enables versatile targeting of immune cells that matter



# SIRP $\alpha$ is expressed on myeloid and dendritic cells as well as tumor cells

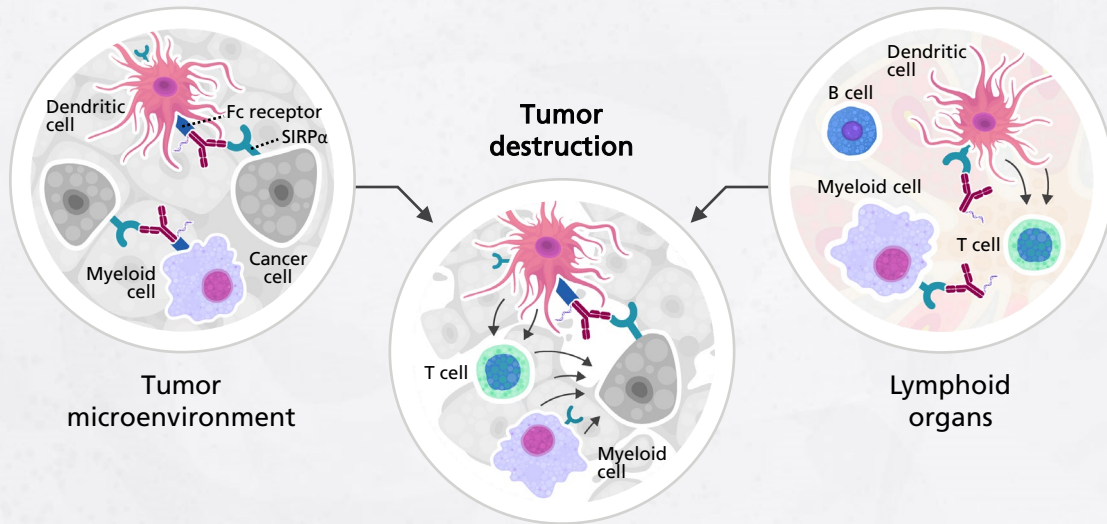
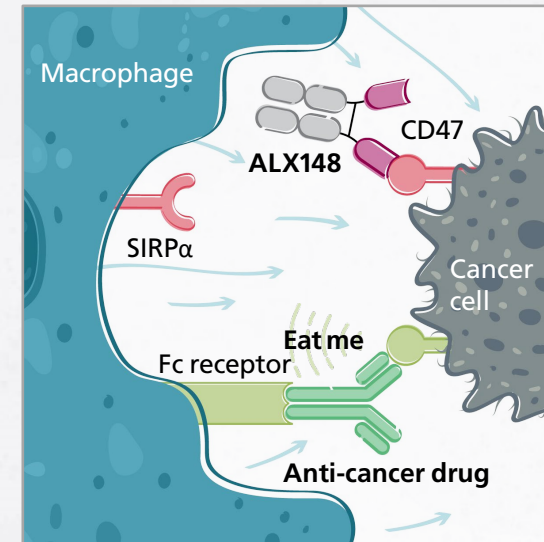


- SIRP $\alpha$  TRAAC binding to myeloid cells targets TLR9 activation in myeloid cells that matter (e.g. dendritic cells).
- SIRP $\alpha$  expression on tumor cells enables tumor microenvironment localization of SIRP $\alpha$  TRAAC.
- SIRP $\alpha$  TRAAC blocks CD47-SIRP $\alpha$  myeloid checkpoint pathway.



# SIRP $\alpha$ TRAAC program is complementary to ALX148

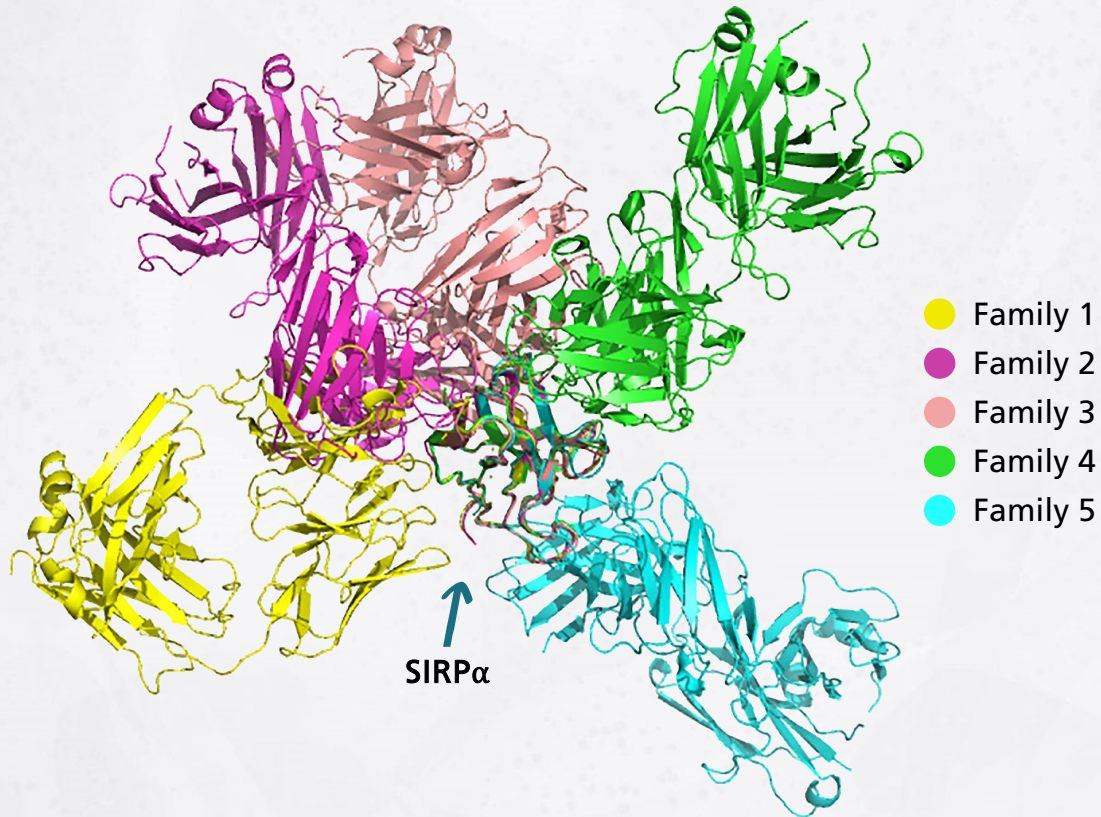
ALX148 is an antagonistic molecule designed to maximize the activity of a wide array of anti-cancer agents by blockade of the CD47 myeloid checkpoint. Removal of the CD47 inhibitory signal requires constant, full blockade of the pathway.



SIRP $\alpha$  TRAAC is an agonistic molecule that directly activates dendritic cells and initiates a coordinated innate and adaptive immune response against cancer.

In the case of agonistic molecules (TLR9 agonist), constant blockade is not required.

# ALX Oncology's SIRP $\alpha$ antibodies: high affinity and diverse epitopes



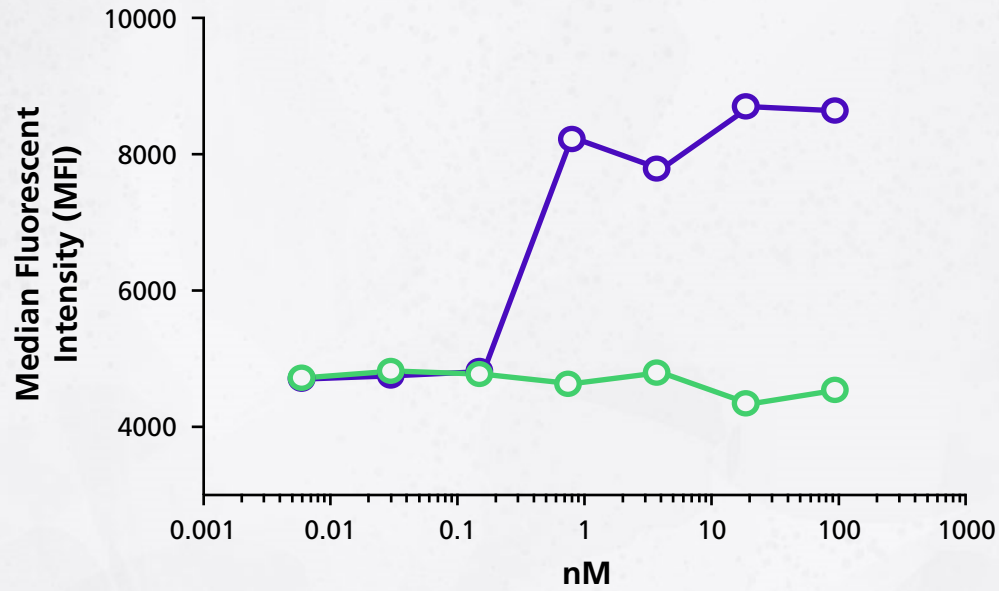
## ALX's diverse range of SIRP $\alpha$ antibodies

Diversity allows selection of best-in-class SIRP $\alpha$  antibodies:

- Binds human SIRP $\alpha$  variants V1 and V2
- Cross reacts with rodent, monkey and human SIRP $\alpha$
- Wide range of affinities
- Full coverage of SIRP $\alpha$  domain 1 surface allows selection for optimal epitope

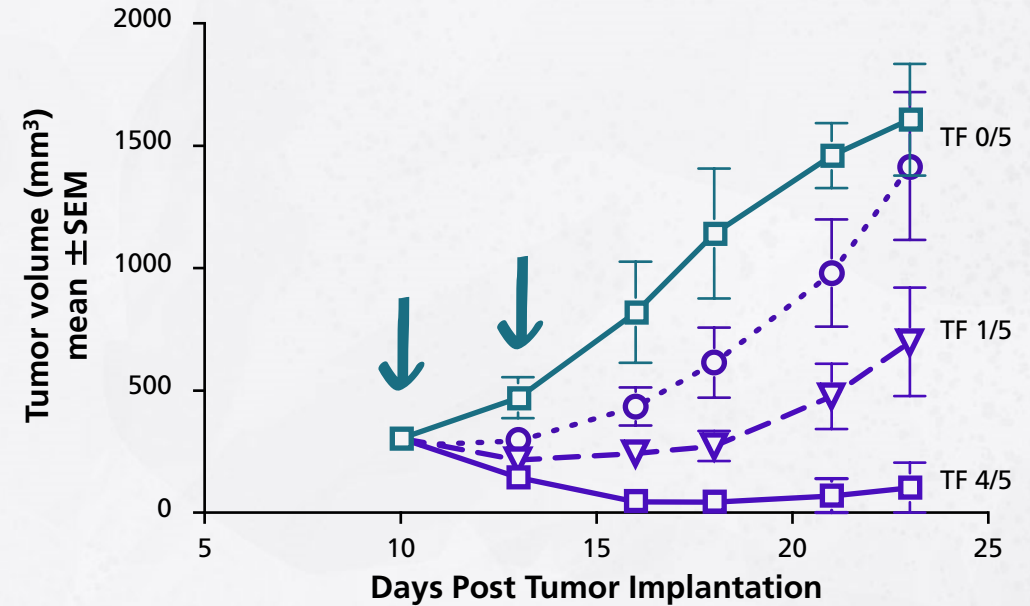
# SIRP $\alpha$ TRAAC induces potent and selective immune activation and leads to potent single agent activity in tumor models

Human dendritic cells  
Activation Marker CD86



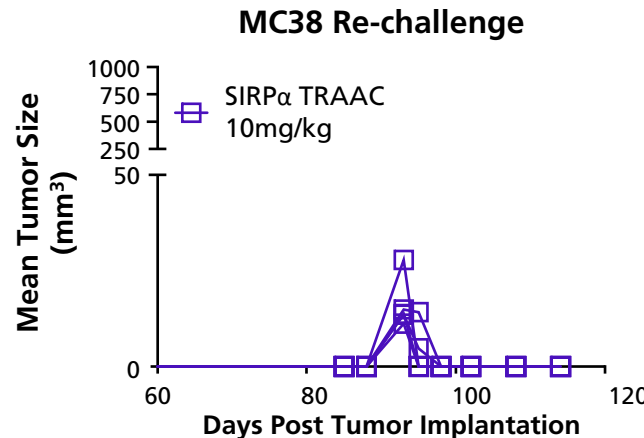
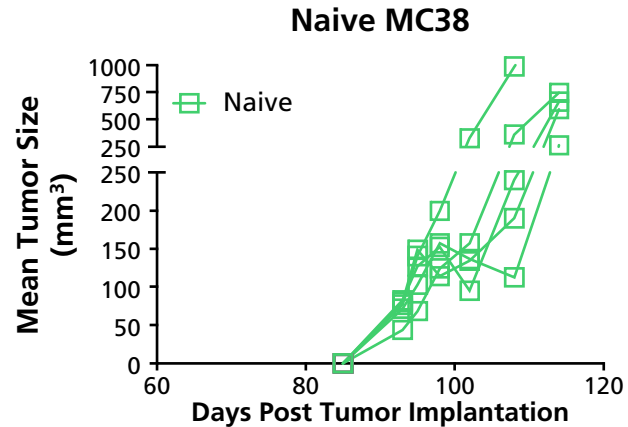
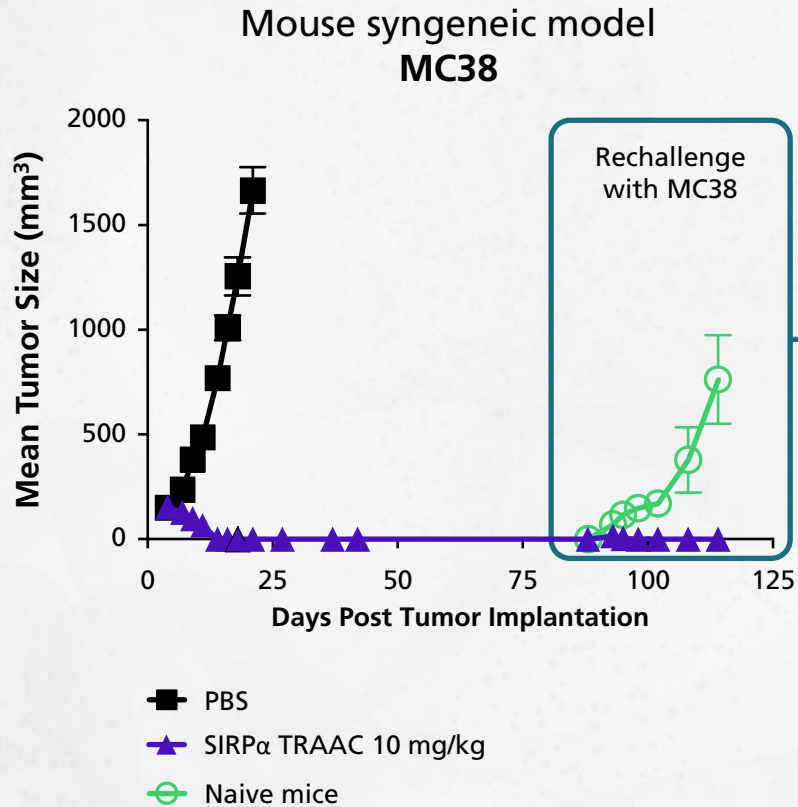
- Unconjugated anti-SIRP $\alpha$
- SIRP $\alpha$  TRAAC

Mouse syngeneic model  
CT26



- PBS
- SIRP $\alpha$  TRAAC 0.1mg/kg
- ▽ SIRP $\alpha$  TRAAC 0.3mg/kg
- SIRP $\alpha$  TRAAC 1mg/kg

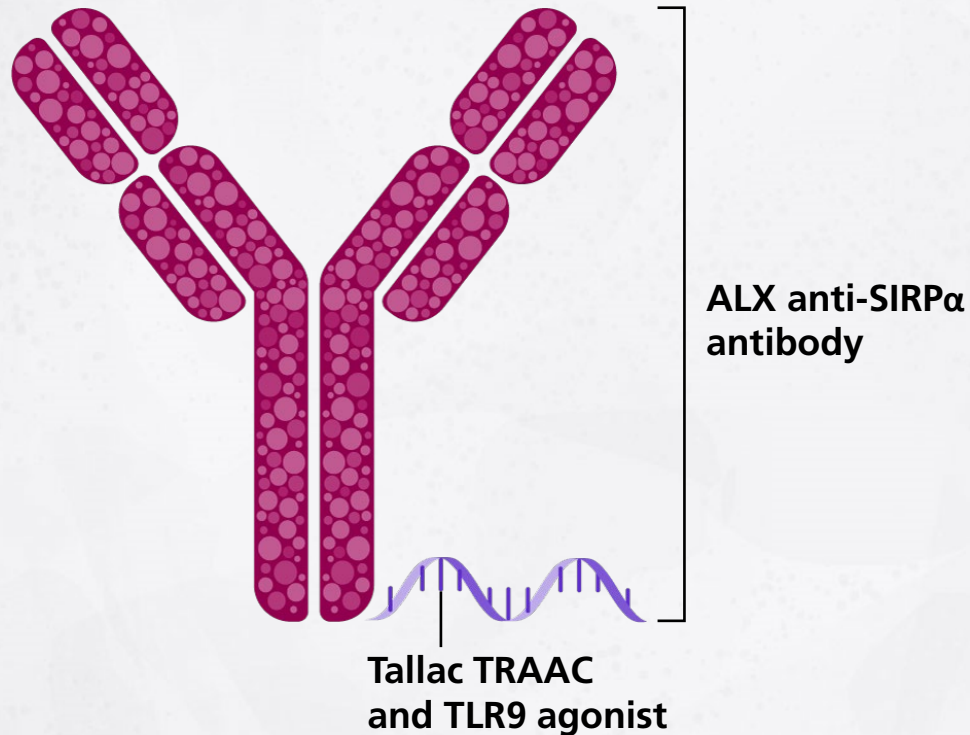
# Systemic administration of SIRP $\alpha$ TRAAC generates durable anti-tumor response and immunological memory



- Established MC38 tumors were eradicated following 10 mg/kg 2q3d systemic treatment with SIRP $\alpha$  TRAAC.
- These tumor free mice were then re-challenged 60-70 days post tumor clearance.
- SIRP $\alpha$  TRAAC treatment group demonstrated immune protection from the tumor re-challenge.
- Naïve age-matched mice were used as control for tumor growth.



# SIRP $\alpha$ TRAAC: targeting immune activation to where it matters



- SIRP $\alpha$  TRAAC binding to myeloid cells targets TLR9 activation in key myeloid cells (e.g. dendritic cells).
- SIRP $\alpha$  expression on tumor cells enables localization of SIRP $\alpha$  TRAAC to tumor microenvironment.
- SIRP $\alpha$  TRAAC blocks CD47-SIRP $\alpha$  myeloid checkpoint pathway.
- Antibody-like PK profile allows for convenient dosing.
- Antibody conjugate produced through established manufacturing processes.

IND expected end of 2022