



**Targeted immune activation
with SIRP α antibody — TLR9 agonist
conjugate (SIRP α TRAAC)**

Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including without limitation, statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, results of clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, plans and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “believe,” “estimate,” “predict,” “potential,” or “continue” or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including, among other things: our history of incurring significant net losses since our inception and our expectation that we will continue to incur significant net losses for the foreseeable future; sufficiency of our cash and cash equivalents to fund our planned operations; the need for additional capital to finance our operations and our ability to obtain such financing, if at all, on terms that are favorable to us; our limited operating history and absence of products approved for commercial sale; our substantial dependency on the success of our lead product candidate, ALX148, which is in clinical development and which has not completed a pivotal trial; the fact that outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the Food and Drug Administration (“FDA”) or other comparable foreign regulatory authorities; the possibility that our product candidates may cause significant adverse events or other undesirable side effects when used alone or in combination with other treatments; the fact that the clinical trials of our product candidates are expensive, time consuming and difficult to design and implement and may fail to demonstrate adequate safety, efficacy and potency of our product candidates or provide the basis for marketing approval; the lengthy, time-consuming and inherently unpredictable nature of the regulatory approval processes of the FDA and comparable foreign regulatory authorities, which could lead to our inability to generate product revenue; our ability to obtain, maintain and enforce patent protection and other intellectual property for our product candidates and related technology; our dependency on our key personnel and our ability to successfully attract, motivate and retain highly qualified personnel; the fact that our preclinical research is conducted solely by Tallac Therapeutics, Inc. (“Tallac Therapeutics”) and that we are dependent on Tallac Therapeutics to perform its contractual research obligations on an effective or timely basis; the potential adverse impact of COVID-19 on our business, including our ongoing and planned clinical trials and preclinical research; and material weaknesses in our internal control over financial reporting. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management team to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Information regarding additional risks and uncertainties may be found in our filings with the SEC. Except as required by applicable law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

This presentation concerns drugs that are under clinical investigation and which have not yet been approved for marketing by the FDA. It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

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 α antibody – TLR9 agonist conjugate (SIRP α TRAAC)



Provides
SIRP α antibody

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



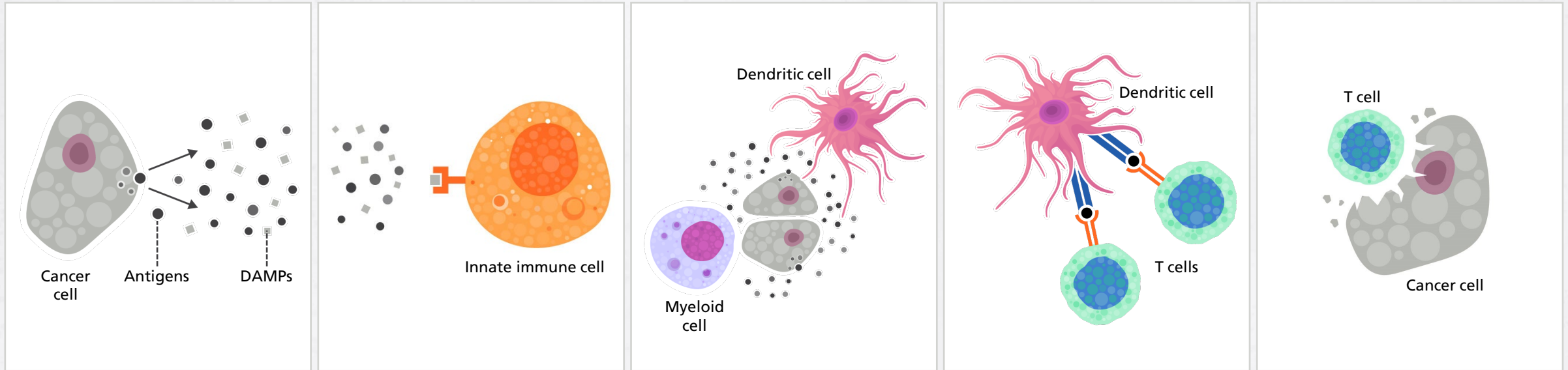
Provides
TRAAC platform
and TLR9 agonist

- 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 α TRAAC induces targeted immune activation, bridging innate and adaptive immune responses.

SIRP α TRAAC simultaneously overrides “don’t eat me” signals by blocking CD47-SIRP α 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

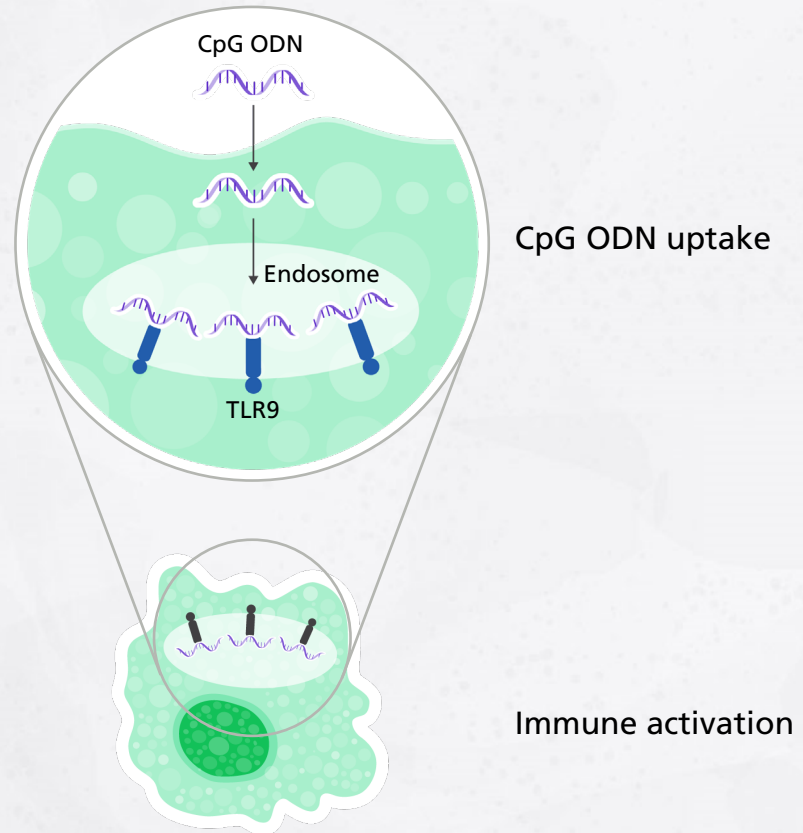
- Successful immune-mediated elimination of cancer requires coordination between the innate and adaptive arms of the immune system.
- Innate immune cells (macrophages, myeloid cells and dendritic cells) may utilize a variety of signaling pathways, including TLR9, TLR7 or 8, STING and CD40, to trigger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

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

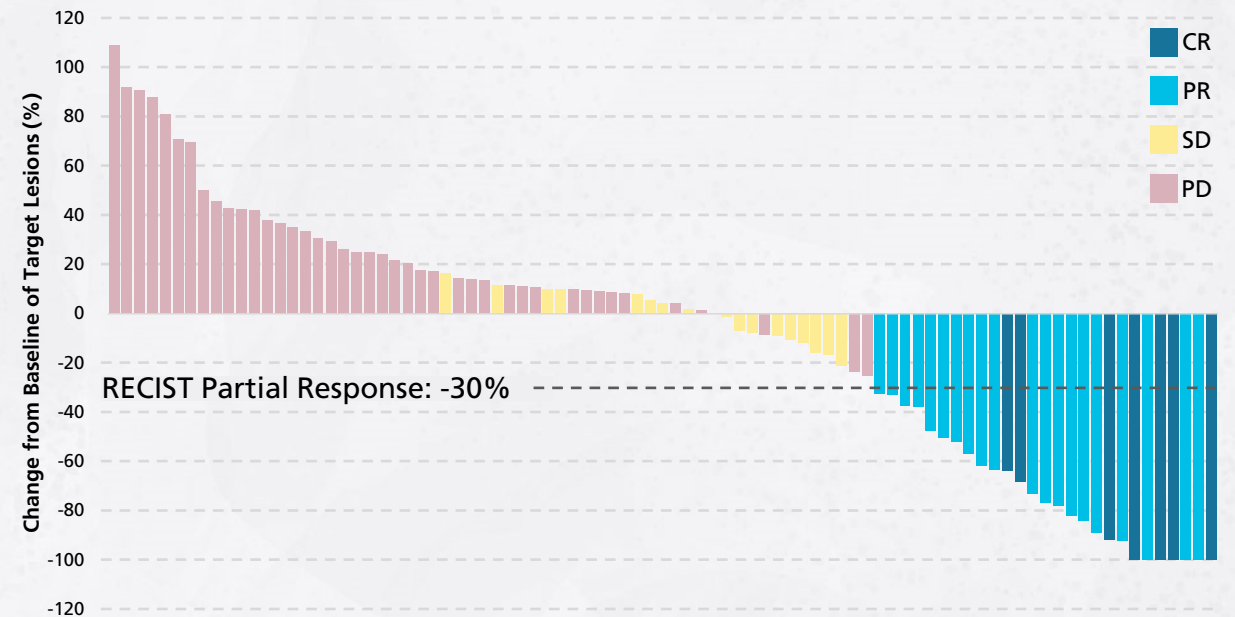
Toll-like Receptor 9 (TLR9): a key innate pathway

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



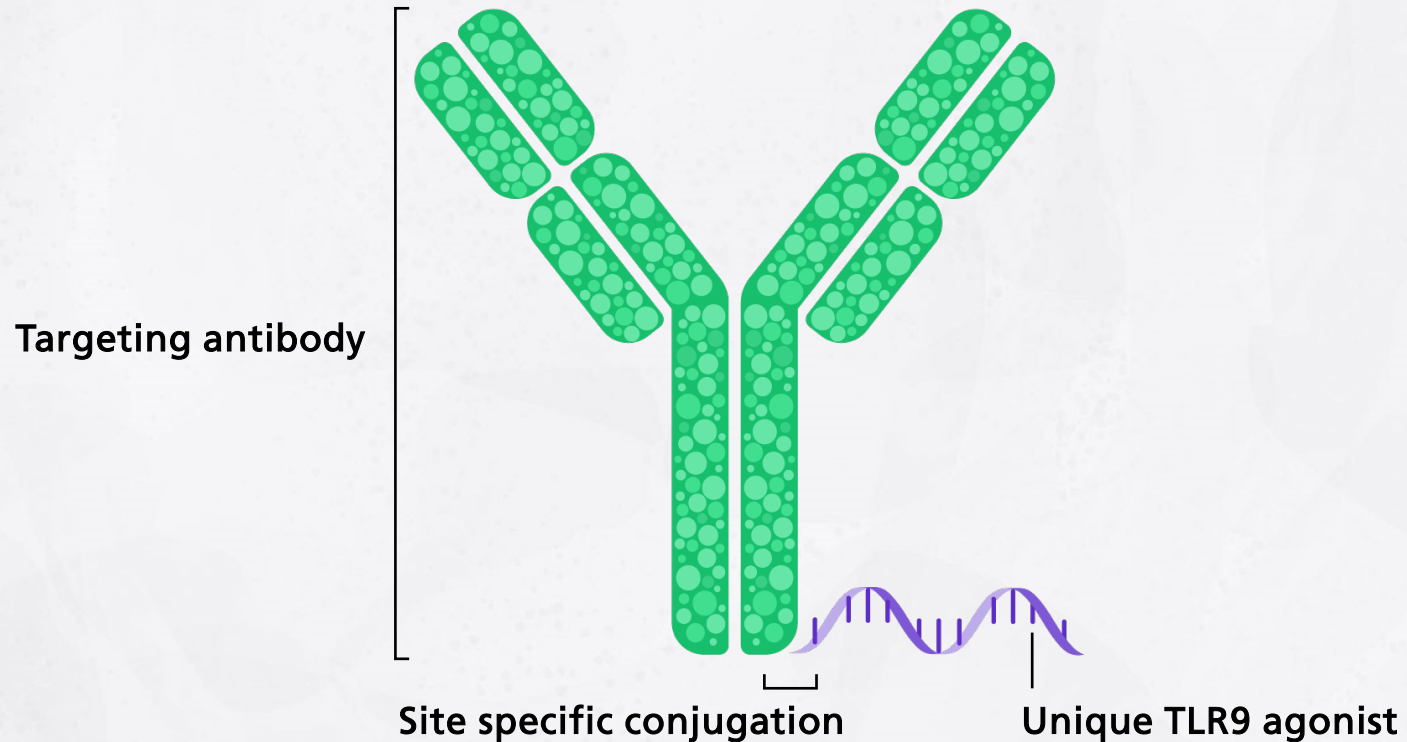
CMP-001 (Checkmate) + Pembrolizumab in Anti-PD-1 Refractory Melanoma, ¹⁻⁴Checkmate, S1 2020.

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

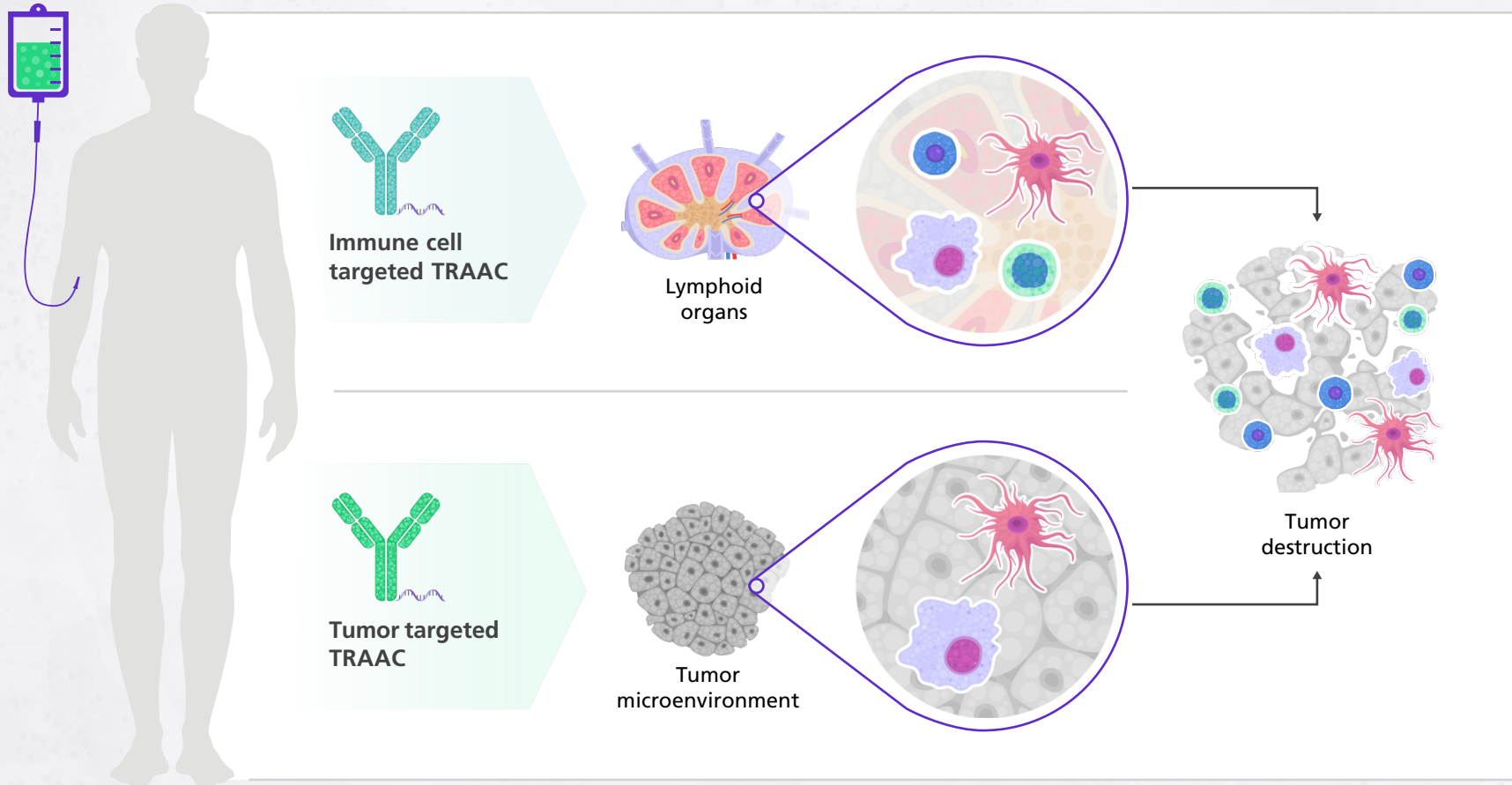
Antibody directs TLR9 agonist (T-CpG) to specific immune cells

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

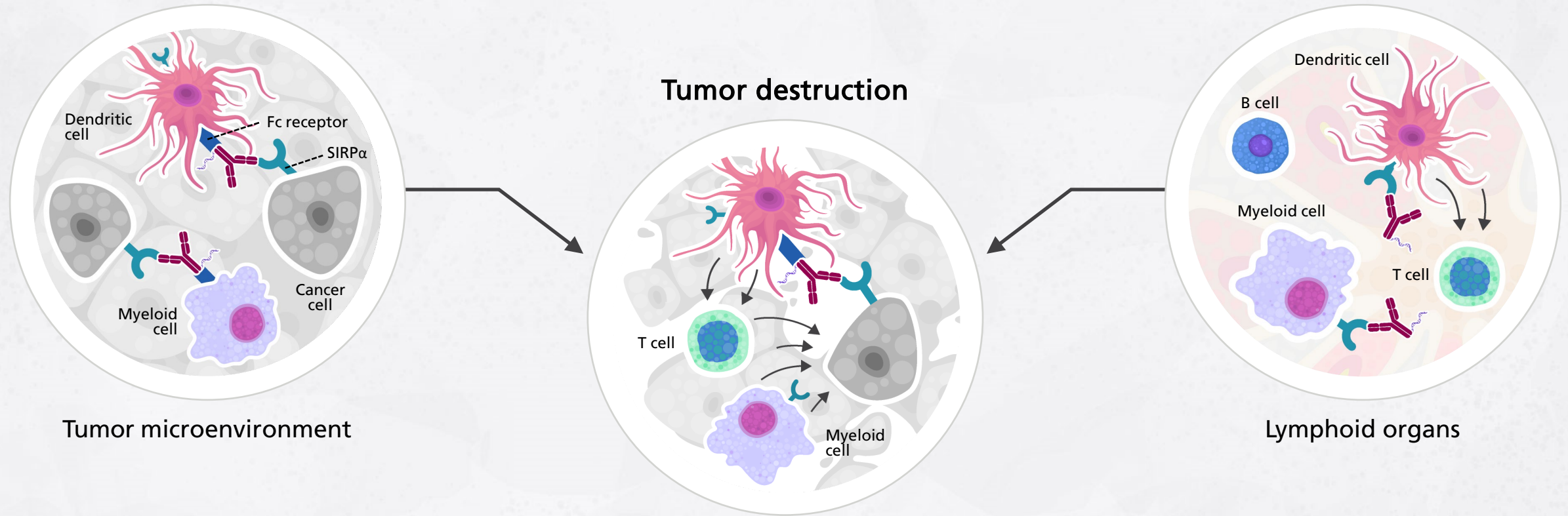


Targeted-CpG (T-CpG) designed specifically for compatibility with antibody conjugation, superior PK, receptor-mediated uptake and TLR9 stimulation

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



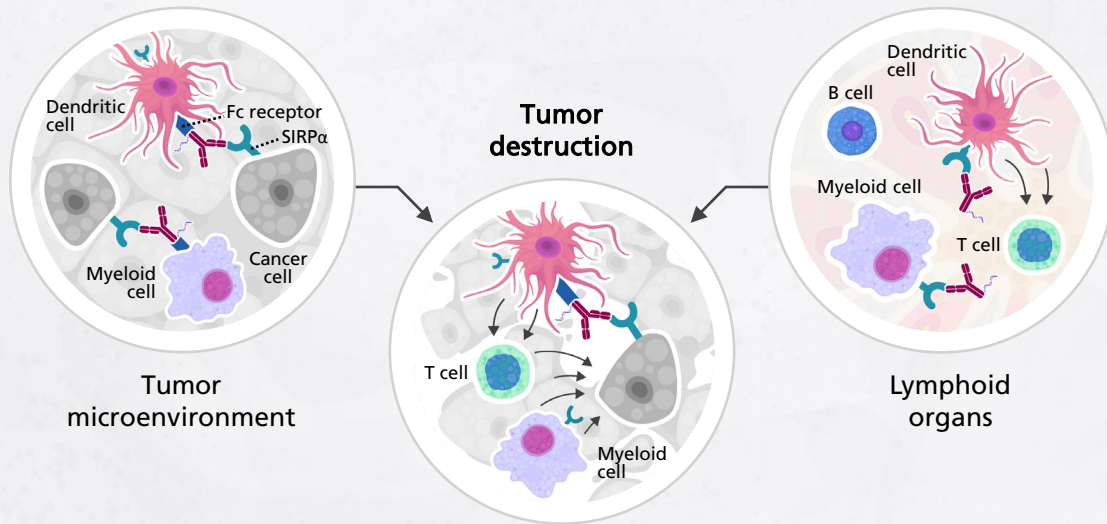
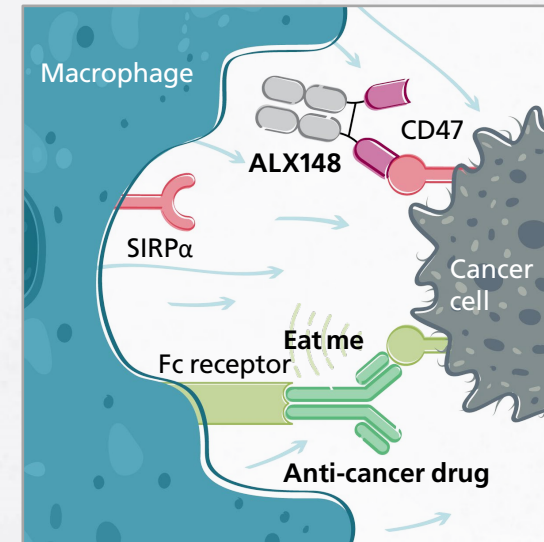
SIRP α is expressed on myeloid and dendritic cells as well as tumor cells



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

SIRP α TRAAC program is complementary to ALX148

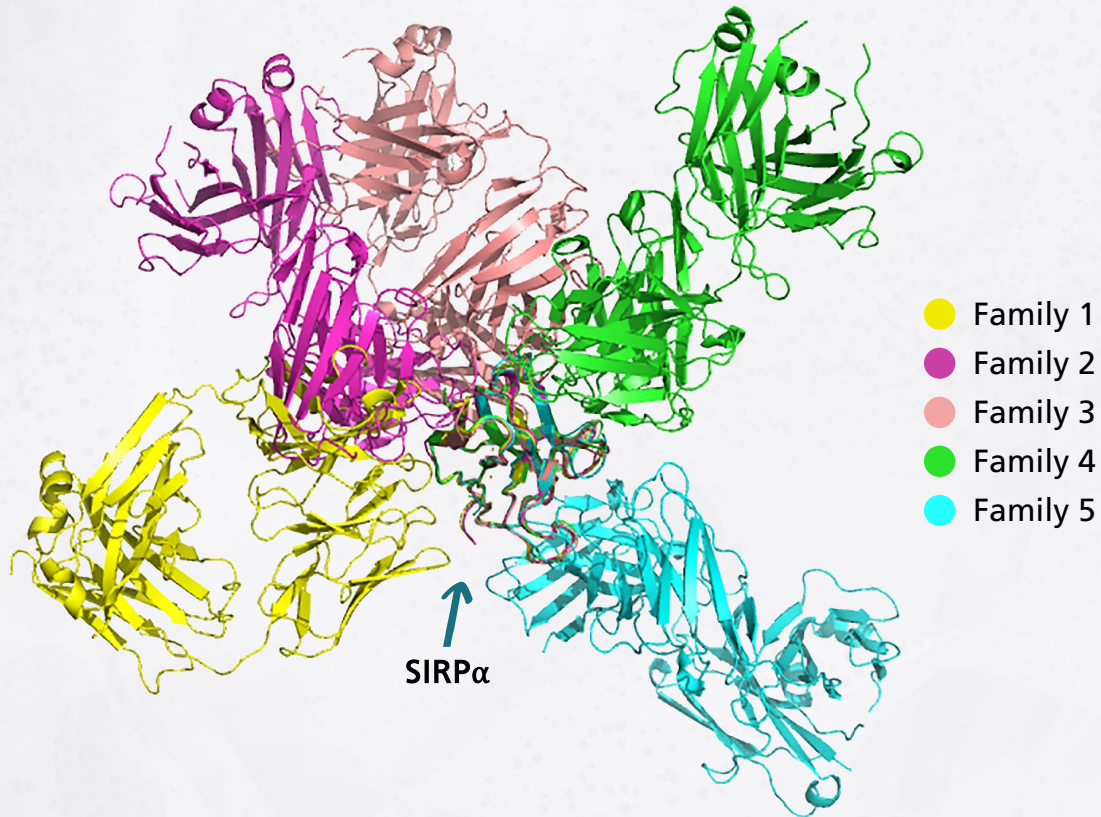
ALX148 is an antagonistic molecule designed to maximize the activity of a wide array of anti-cancer agents by blockade of the CD47 myeloid checkpoint. Removal of the CD47 inhibitory signal requires constant, full blockade of the pathway.



SIRP α 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 α antibodies: high affinity and diverse epitopes



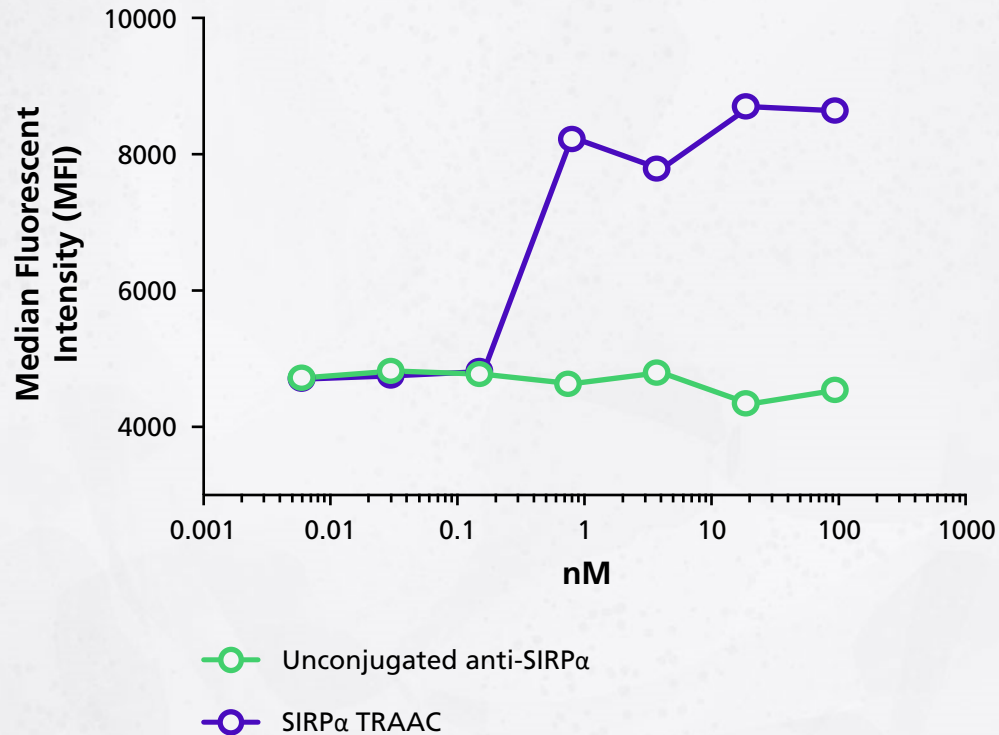
ALX's diverse range of SIRP α antibodies

Diversity allows selection of best-in-class SIRP α antibodies:

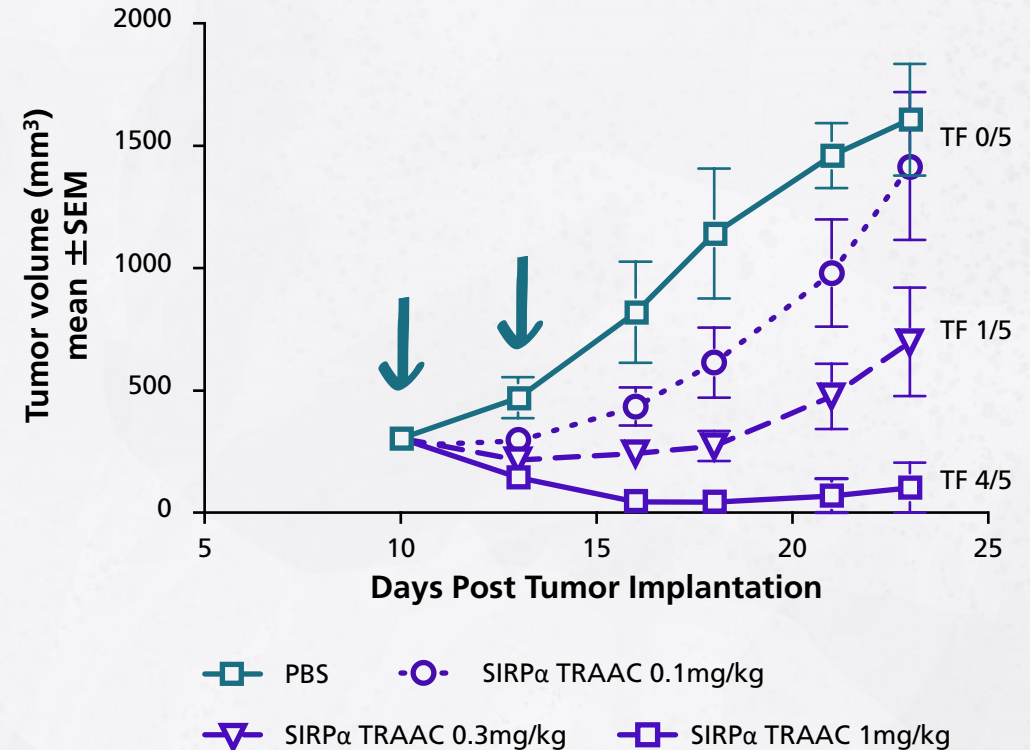
- Binds human SIRP α variants V1 and V2
- Cross reacts with rodent, monkey and human SIRP α
- Wide range of affinities
- Full coverage of SIRP α domain 1 surface allows selection for optimal epitope

SIRP α TRAAC induces potent and selective immune activation and leads to potent single agent activity in tumor models

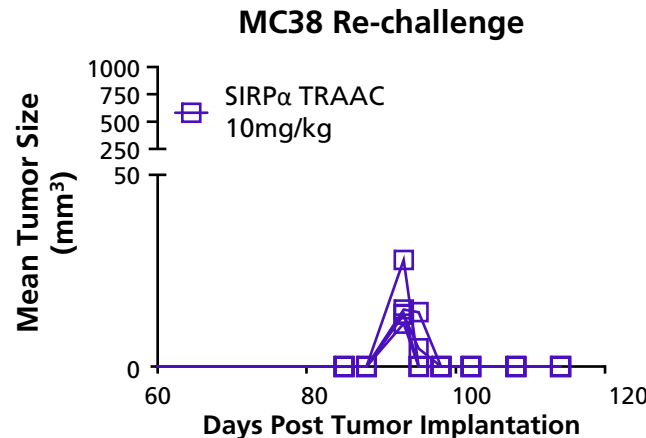
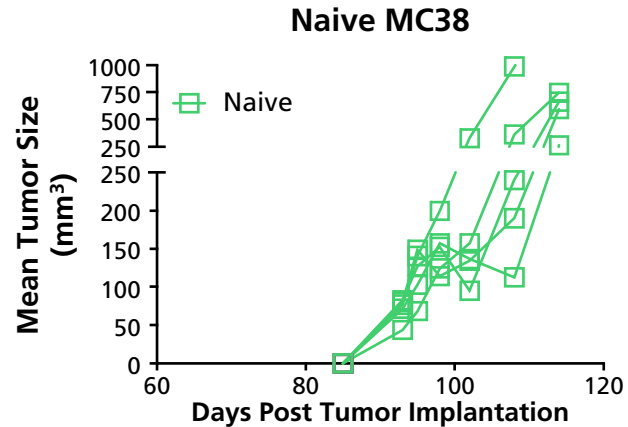
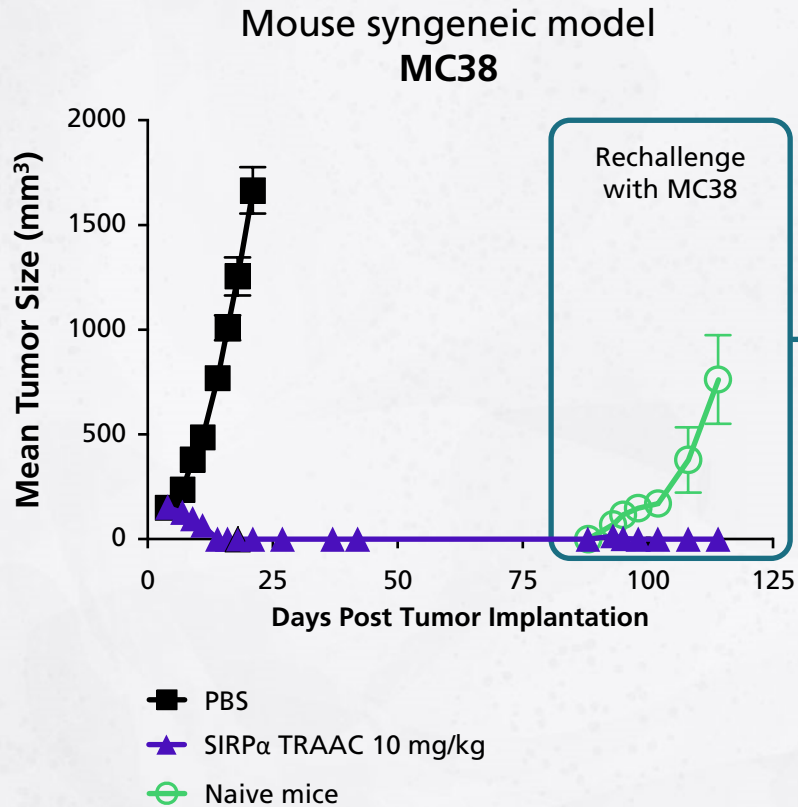
Human dendritic cells
Activation Marker CD86



Mouse syngeneic model
CT26

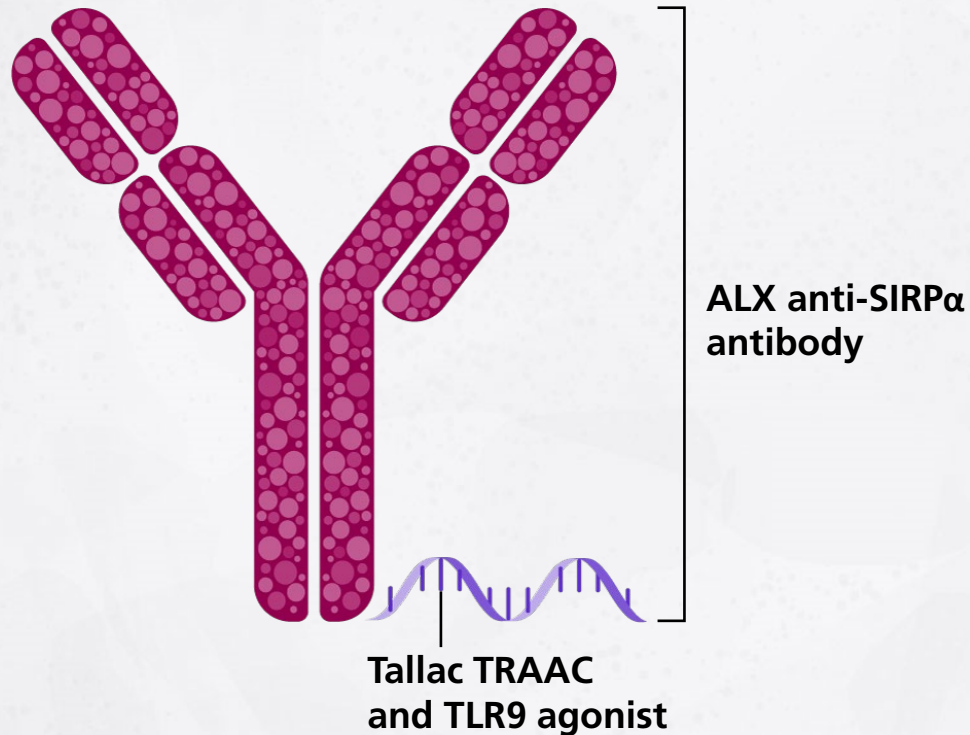


Systemic administration of SIRP α TRAAC generates durable anti-tumor response and immunological memory



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

SIRP α TRAAC: targeting immune activation to where it matters



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

IND expected end of 2022