UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 20, 2022

Sensei Biotherapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-39980**	**83-1863385**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

1405 Research Blvd, Suite 125 **Rockville, MD**	**20850**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (240) 243-8000

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Securities Exchange Act of 1934:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock	**SNSE**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On April 20, 2022, Dr. Robert Pierce, Chief R&D Officer of Sensei Biotherapeutics, Inc. (the "**Company**") will present a presentation regarding SNS-101 at the World Vaccine Congress 2022, including new preclinical data from a mouse model evaluating the pharmacokinetic profile of SNS-101 and new preclinical data from mouse models evaluating both activity and the pharmacokinetic profile of SNS-101. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Presentation.
104	The cover page from Sensei Biotherapeutics, Inc.'s Form 8-K filed on April 20, 2022, formatted in Inline XBRL.

SIGNATURES

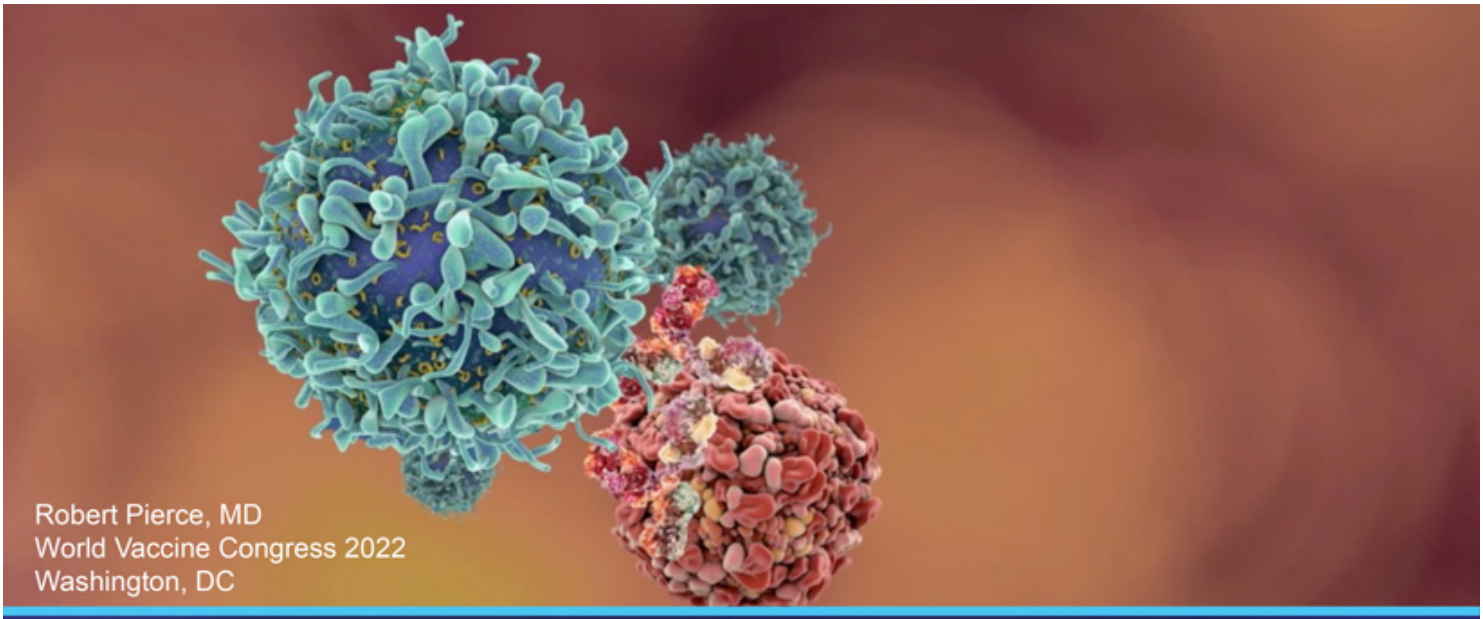
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Sensei Biotherapeutics, Inc.

Date: April 20, 2022

/s/ John Celebi

John Celebi
President and Chief Executive Officer



SNS-101, A Unique Tumor-selective Anti-VISTA Monoclonal Antibody with a Novel Mechanism of Action

SENSEI BIOTHERAPEUTICS

Disclaimer

This presentation has been prepared by Sensei Biotherapeutics, Inc. (the "Company," "we," "us") and is made for informational purposes only. The information set forth herein does not purport to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this presentation unless stated otherwise, and neither the delivery of this presentation at any time, nor any sale of securities, shall under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof.

This presentation contains estimates and other statistical data made by independent parties and by us relating to market shares and other data about our industry. This presentation also contains "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 that are based on our management's beliefs and assumptions and on information currently available to management. These forward-looking statements include, without limitation, statements regarding our industry, business strategy, plans, the preclinical and clinical development of our product candidates, and other financial and operating information. When used in this presentation, the words "may," "believes," "intends," "seeks," "anticipates," "plans," "estimates," "expects," "should," "assumes," "continues," "could," "will," "future" and the negative of these or similar terms and phrases are intended to identify forward-looking statements. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the development of therapeutic product candidates, such as preclinical discovery and development, conduct of clinical trials and related regulatory requirements, our reliance on third parties over which we may not always have full control, and other risk and uncertainties that are described in our Annual Report on Form 10-K filed with the SEC on March 15, 2022 and our other Periodic Reports filed with the SEC. Forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation and include all matters that are not historical facts. Our actual future results may be materially different from what we expect. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Certain information contained in this presentation relates to, or is based on, studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

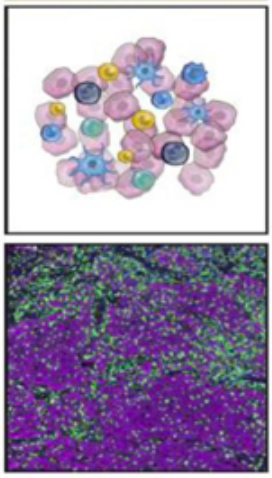
The Therapeutic Problem: PD-1/PD-L1 Non-Response

Anti-PD-1 or PD-L1 Treatment →

More Likely to Respond

T-cells Inside Tumor

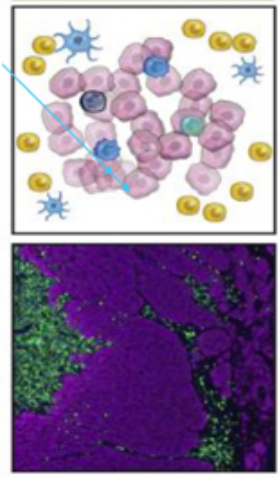
Hot (inflamed) tumor



Less Likely to Respond

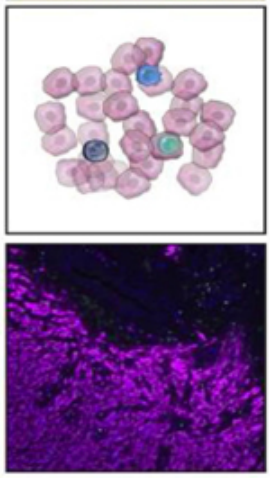
T-cells Outside Tumor

Cold (excluded) tumor



T-cells Absent

Cold (ignored) tumor



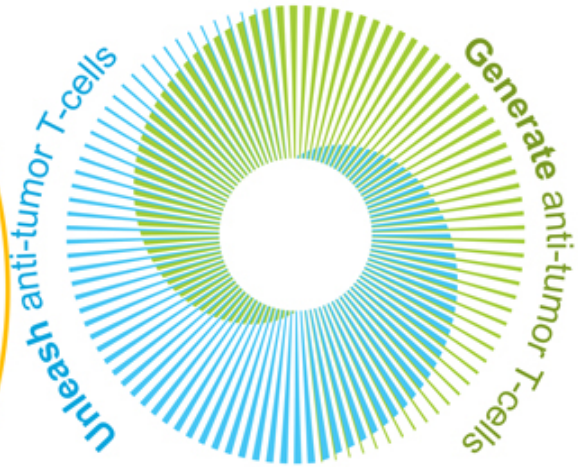
Green = T-cells
Purple = tumor

Adapted from Van der Woulde-LL, et al, Trends in Cancer, 2017

Two Platforms to Unleash Anti-Cancer T-cell Activity

TMAb™ (Tumor Microenvironment Activated Biologics) Platform

- Next-generation tumor activated mAbs
- Binding only in the low-pH tumor microenvironment
- Target checkpoints and/or other immune pathways
- Enable improved PK/PD and toxicity profiles



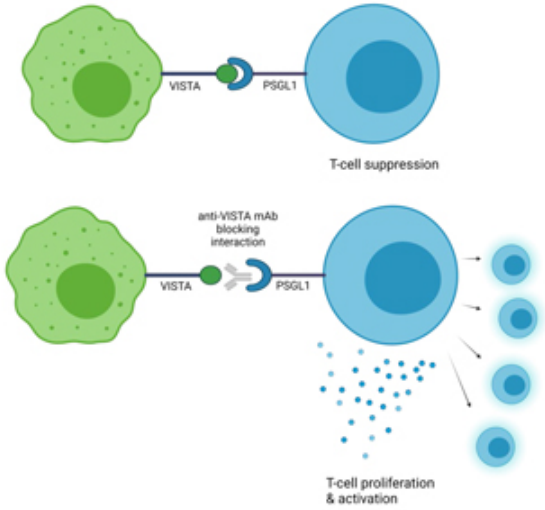
ImmunoPhage™ Platform

- Powerfully self-adjuvanted nanoparticle vaccine can drive B cell and T cell responses
- Multi-antigen vaccine enables personalized approach from "off-the-shelf" components
- Targets APCs
- Enhanced through addition of immunostimulatory nanobodies & cytokines

VISTA: A Promising but Difficult Target on Myeloid Cells

- VISTA (aka B7-H5; PD-1H) is B7 family ligand with homology to PD-L1
- VISTA suppresses T cell activation[1]
- Expressed on myeloid cells including macrophages and neutrophils; NK cells and T-regs[2]
- Inhibition of VISTA may "convert" myeloid cells to a proinflammatory/immune activating state
- Excellent therapeutic combinability with CTLA-4 or PD-1/PD-L1 ICIs, especially in cold tumors[3]
- Identity of critical VISTA binding partner/receptor remains subject of debate.

VISTA is a Negative Regulator of T cell Function

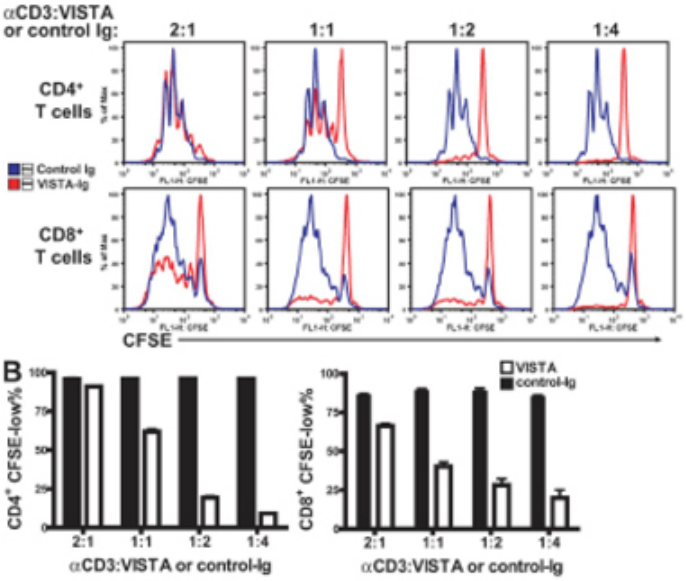


1 Wang et al, *JEM*, 2011
2 Lines et al. *Cancer research* vol. 74,7 (2014)
3 Gao et al. *Nature medicine* vol. 23,5 (2017)

VISTA Negatively Regulates CD4 and CD8 T Cell Responses

VISTA, a novel mouse Ig superfamily ligand that negatively regulates T cell responses

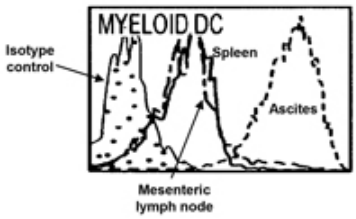
Li Wang,[1] Rotem Rubinstein,[4,5] Janet L. Lines,[1] Anna Wasiuk,[1] Cory Ahonen,[1] Yanxia Guo,[1] Li-Fan Lu,[1] David Gondek,[1] Yan Wang,[1] Roy A. Fava,[3] Andras Fiser,[4,5] Steve Almo,[5] and Randolph J. Noelle[1,2]



Wang_L, et al, *JEM*, 2011

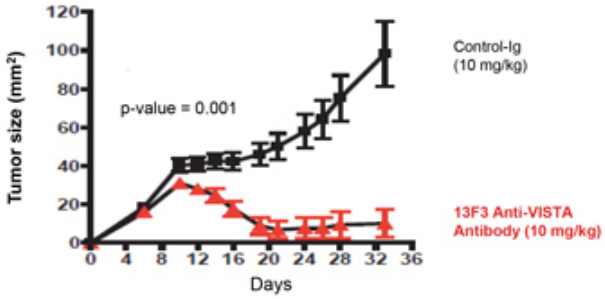
Anti-VISTA mAb Treatment Leads to Tumor Growth Inhibition in Multiple Syngeneic Mouse Tumor Models

VISTA Expression on Myeloid Cells in Tumor-Bearing Mice

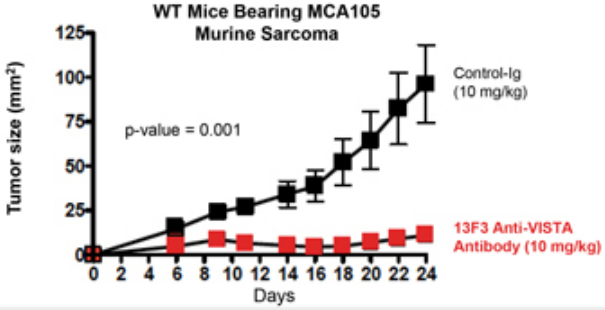


- An anti-murine VISTA antibody (13F3) was administered to WT mice bearing tumors
- Myeloid cells from these mice were assessed and found to have high levels of VISTA expression

WT Mice Bearing MB49 Murine Bladder Carcinoma



WT Mice Bearing MCA105 Murine Sarcoma

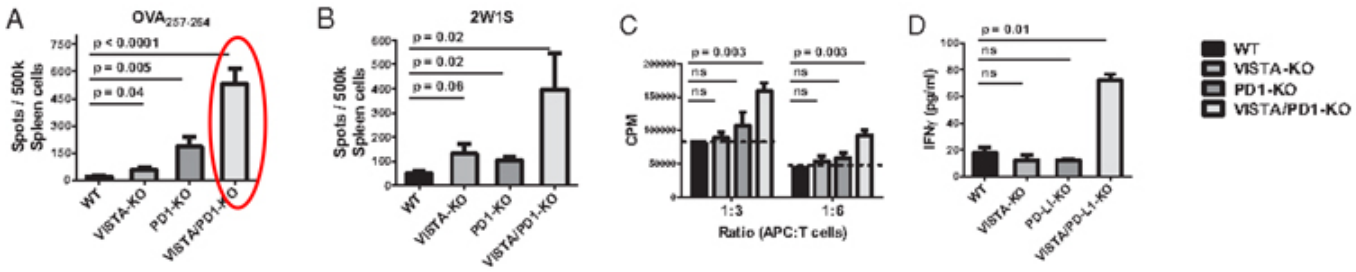


Noelle et. al., US 2013/0177557

PD-1/VISTA Double Knock-out Mice Have Increased Antigen-specific T cell Responses

Immune-checkpoint proteins VISTA and PD-1 nonredundantly regulate murine T-cell responses

Jun Liu[a,b], Ying Yuan[a,1], Wenna Chen[a], Juan Putra[c], Arief A. Suriawinata[c], Austin D. Schenk[d], Halli E. Miller[a], Indira Guleria[e], Richard J. Barth[d], Yina H. Huang[c], and Li Wang[a,2]

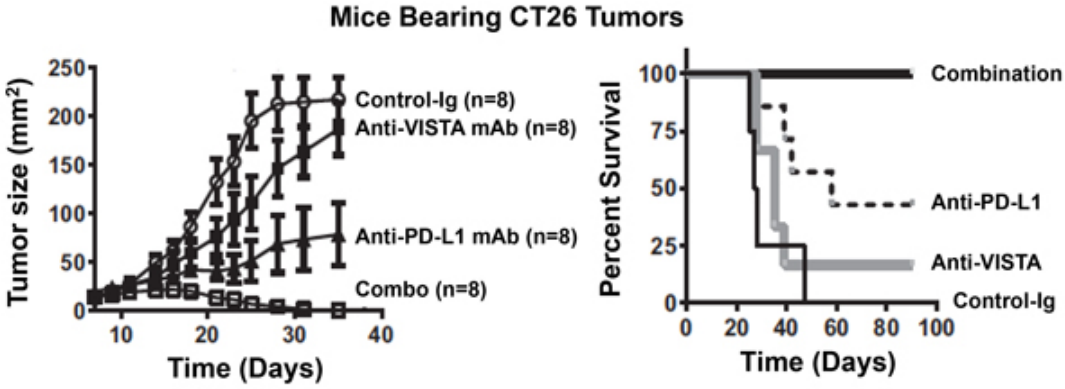


Liu J. et al. PNAS 2015

Combination of VISTA Inhibition and PD-1 Blockade Yields Synergistic Anti-tumor Responses

Immune-checkpoint proteins VISTA and PD-1 nonredundantly regulate murine T-cell responses

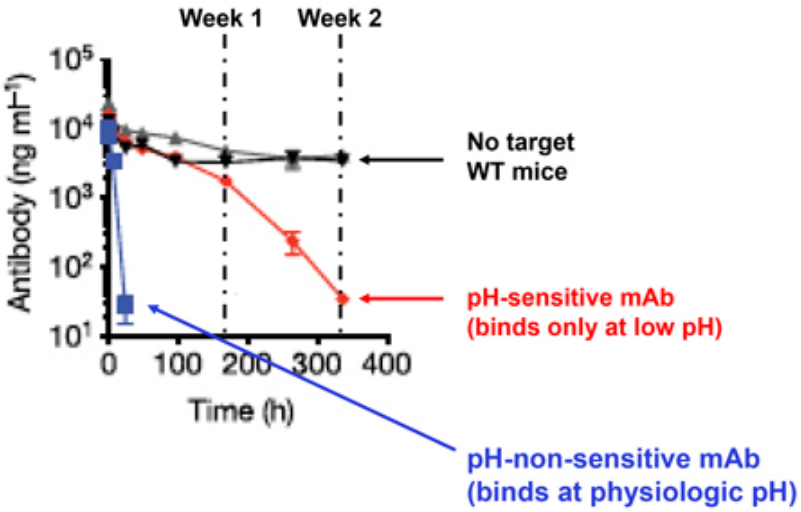
Jun Liu[a,b], Ying Yuan[a,1], Wenna Chen[a], Juan Putra[c], Arief A. Suriawinata[c], Austin D. Schenk[d], Halli E. Miller[a], Indira Guleria[a], Richard J. Barth[d], Yina H. Huang[c], and Li Wang[a,2]



Liu J. et al. PNAS 2015

Anti-VISTA mAb Binding on Myeloid Cells in Blood Results in Significant Target-mediated Drug Disposition (TMDD)

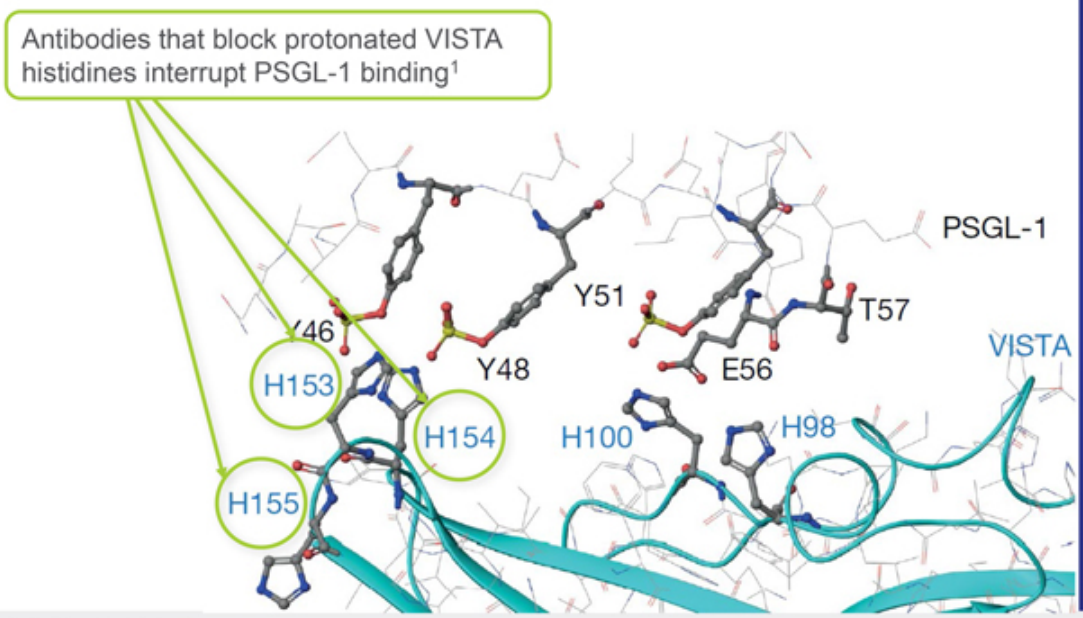
Mouse Pharmacokinetics of Anti-VISTA Antibodies (BMS) at 5 mg/kg



- Antibodies binding VISTA⁺ cells (e.g. monocytes) at physiological pH are eliminated from circulation through targeted-mediated drug disposition (TMDD)
- An antibody binding at pH 6 will accumulate in the TME resulting in an improved PK and safety profile

Johnston et al, Nature, 2019

VISTA Binding to PSGL-1 is pH-dependent Due to a Unique Histidine-rich Extracellular Binding Domain

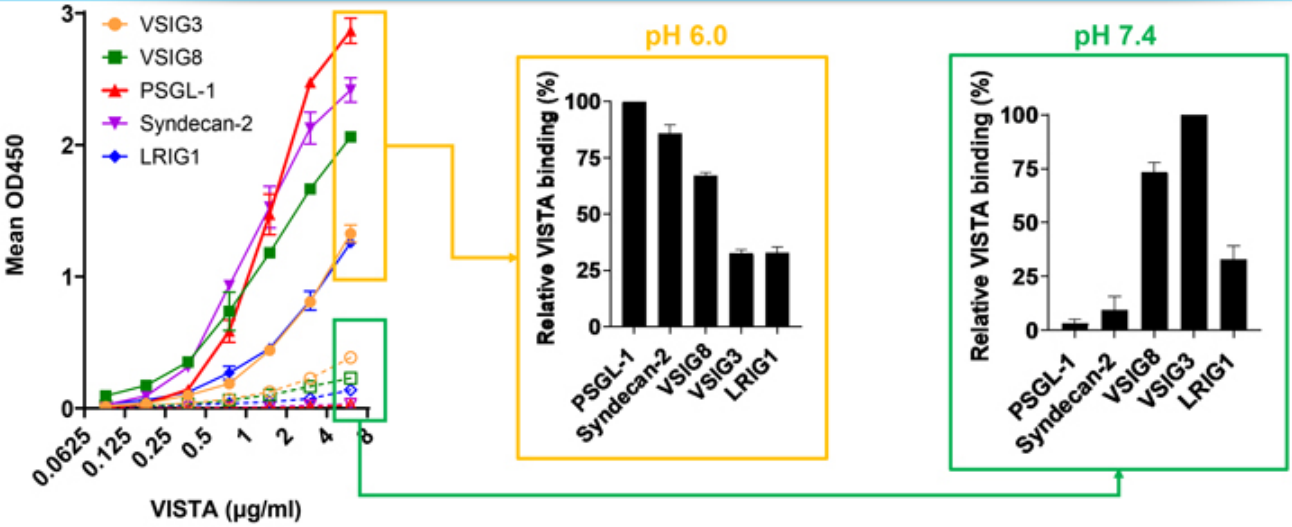


VISTA's extracellular domain is uniquely rich in histidines[1]

Histidines are protonated at low pH enabling VISTA to distinguish the active (acidic pH) and inactive (neutral pH) PSGL-1 binding interface

1. Johnston et al., Nature 2019

Strongest Interaction between Candidate VISTA Binding Partners is VISTA/PSGL-1 at Low pH

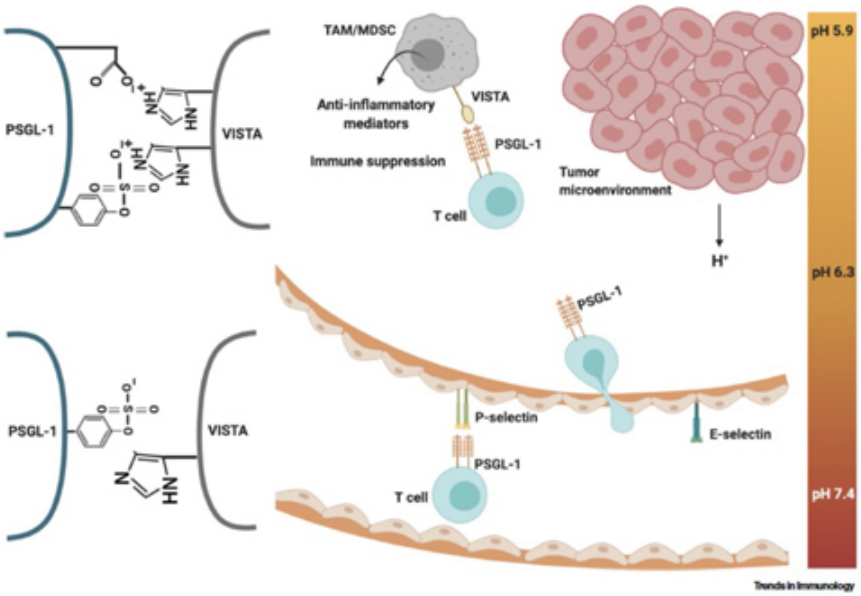


- **VISTA binds specifically to PSGL-1 and Syndecan-2 in a pH-dependent manner**
- VSIG-3, VSIG-8 and LRIG-1 interactions are very weak (pH 7.4)
  - The VSIG-3 interaction (pH 7.4) is 1/7 the affinity of PSGL-1 (pH 6.0)

Active “Protonated” VISTA Binds the T cell Checkpoint PSGL-1 in the Tumor Microenvironment

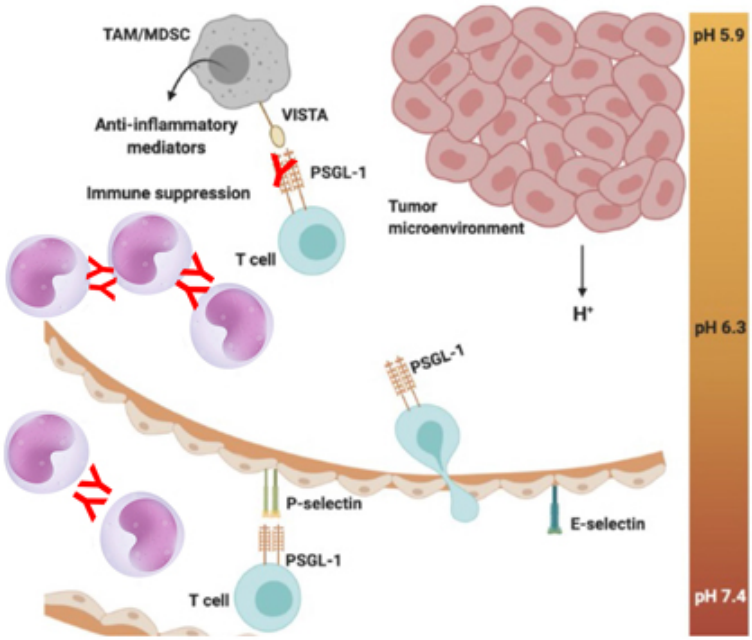
“Active”
VISTA Protonated

“Inactive”
VISTA
Unprotonated



Adapted from Yuan-L, Trends Immunol, 2021 Mar;42(3):209-227

pH-dependent mAb Binding to VISTA May Mitigate On-Target/Off-tumor Reactivity



	Low pH-selective Binder	pH Non-selective Binder
Tumor	• Blocks VISTA/PSGL-1 checkpoint • IgG1 Fc → myeloid activation	• Blocks VISTA/PSGL-1 checkpoint • Active Fc → myeloid activation • TMDD → low tumor drug exposure
Blood	• No significant VISTA binding • No significant TMDD • No significant myeloid activation • Decreased risk of CRS	• Binds VISTA on myeloid cells in blood → TMDD • Potential for myeloid activation AND CRS

Adapted from Yuan-L, Trends Immunol, 2021 Mar;42(3):209-227

Critical Design Features for SNS-101

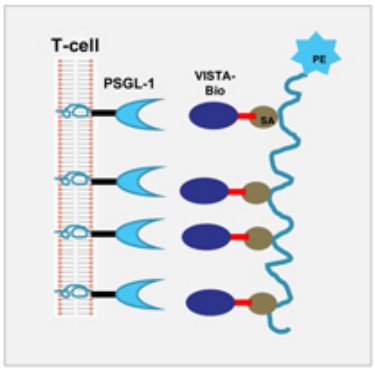
1. Block the critical checkpoint (pH-dependent binding of VISTA to PSGL-1 on T cells)

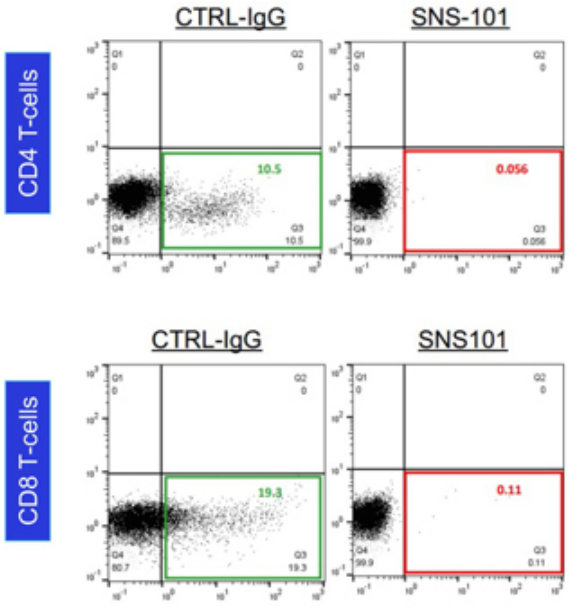
2. Selectively bind “active”/protonated VISTA at low pH to avoid:
   - target mediated drug disposition (TMDD)
   - on-target/off-tumor side effects

3. Utilize an Fc-competent IgG (e.g. IgG1) backbone to engage and activate FcɣR on tumor-infiltrating myeloid cells

SNS-101 Inhibits VISTA/PSGL-1 Interaction

PSGL-1: VISTA Interaction on Primary T-cells at pH 6.0

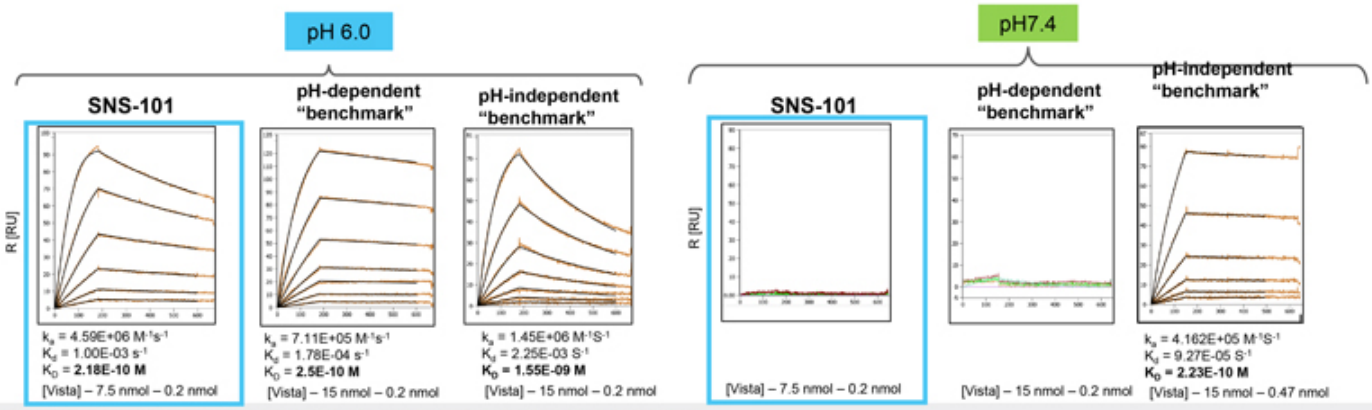




SNS-101 Has >600-Fold Selectivity for VISTA^{pH6}

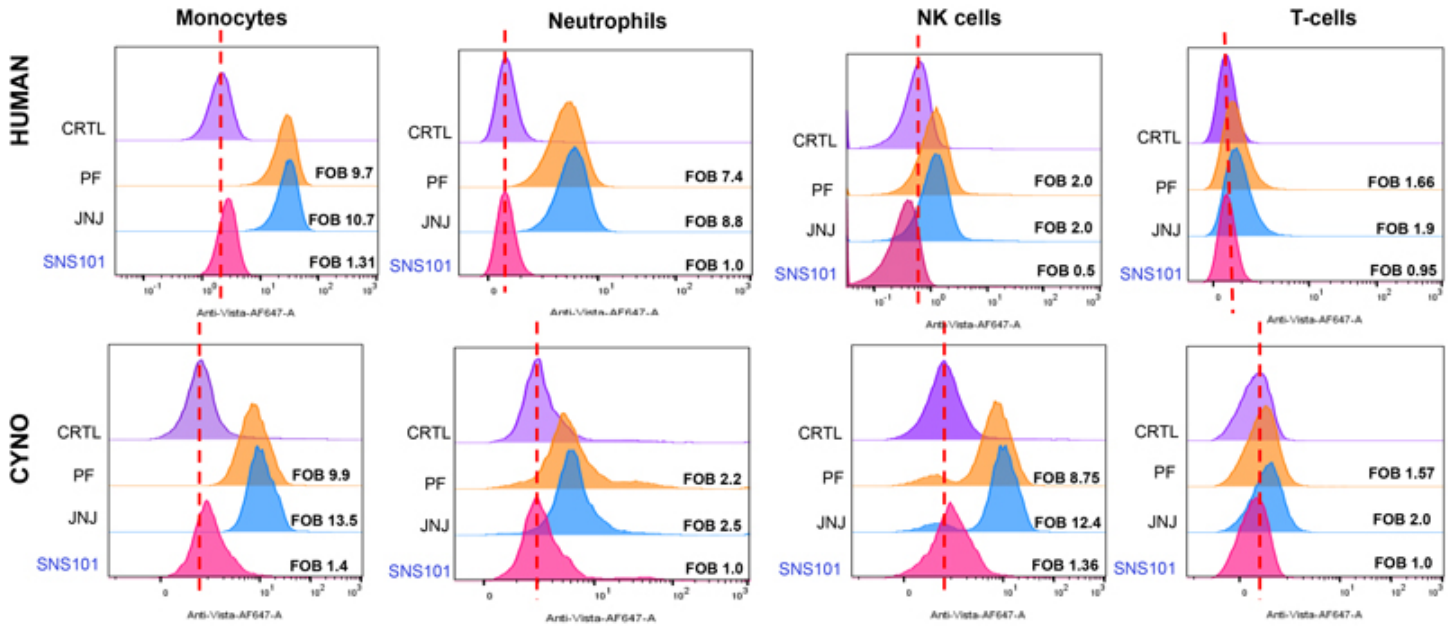
- **>600-fold selectivity for VISTA at pH 6.0**
- **Subnanomolar binding at low pH**
- **No significant binding observed at physiological pH (7.4)**

	pH 6.0	pH 7.4
Monovalent Affinity (K_D) [nmol]	0.218	132 (~No binding)



SITC 2021: Poster titled: Antagonistic pH-selective VISTA antibody SNS-101 potentiates anti-PD-1/PD-L1-induced anti-tumor immunity

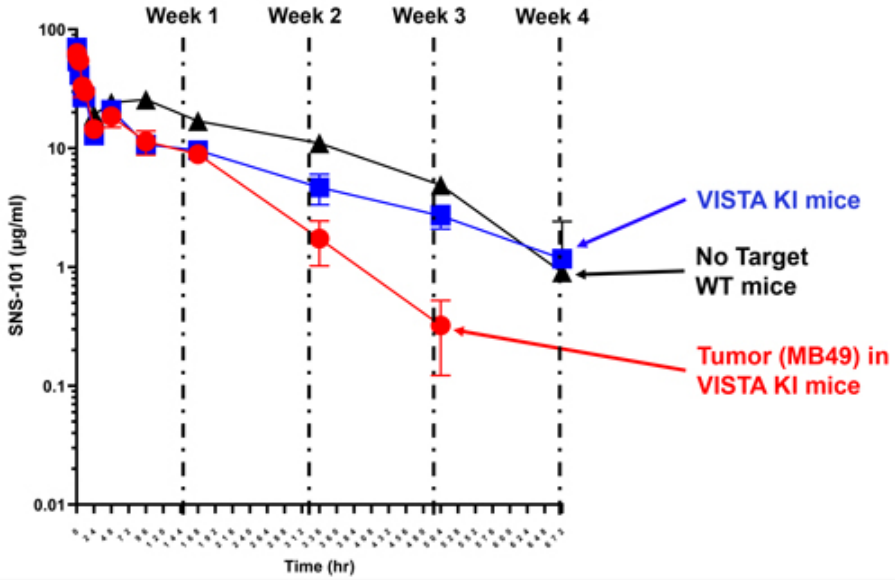
No Significant Binding of SNS-101 to Monocytes, Neutrophils, NK Cells and T-cells in Whole blood at Physiological pH



SNS-101 Displays Favorable PK Profile

No significant TMDD in human VISTA KI mice

Pharmacokinetics of Single Dose 5 mg/kg SNS-101 in VISTA Knock-in Mice

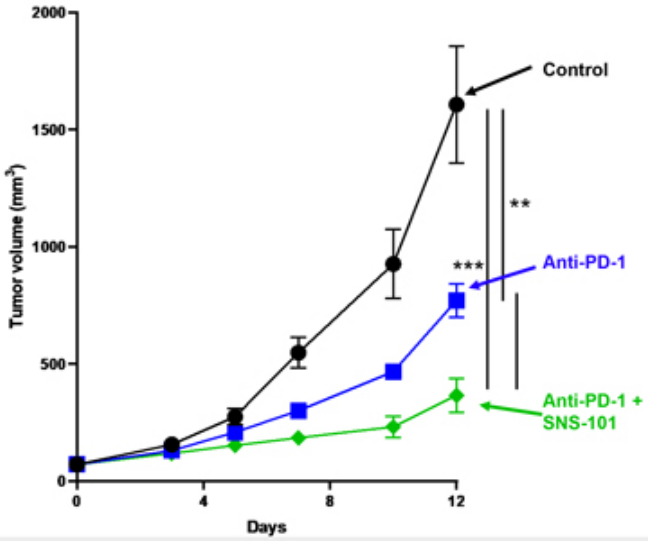


- **Tumor bearing mice have a favorable PK profile**
- **Non-tumor bearing mice demonstrate no TMDD**

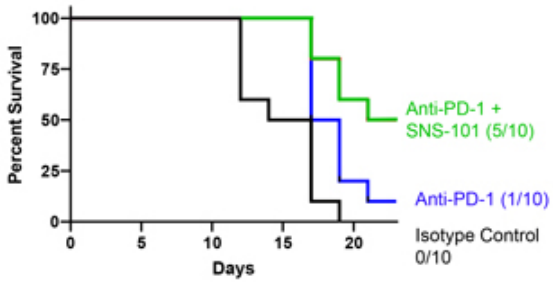
MC38 Syngeneic Tumor Model in huVISTA Knock-in Mice Confirms Combinatorial Activity of SNS-101

SNS-101* in Combination with Anti-mouse PD-1

Tumor Growth Inhibition



Survival



SNS-101 was grafted on to a mouse IgG2a framework to decrease anti-drug antibody production

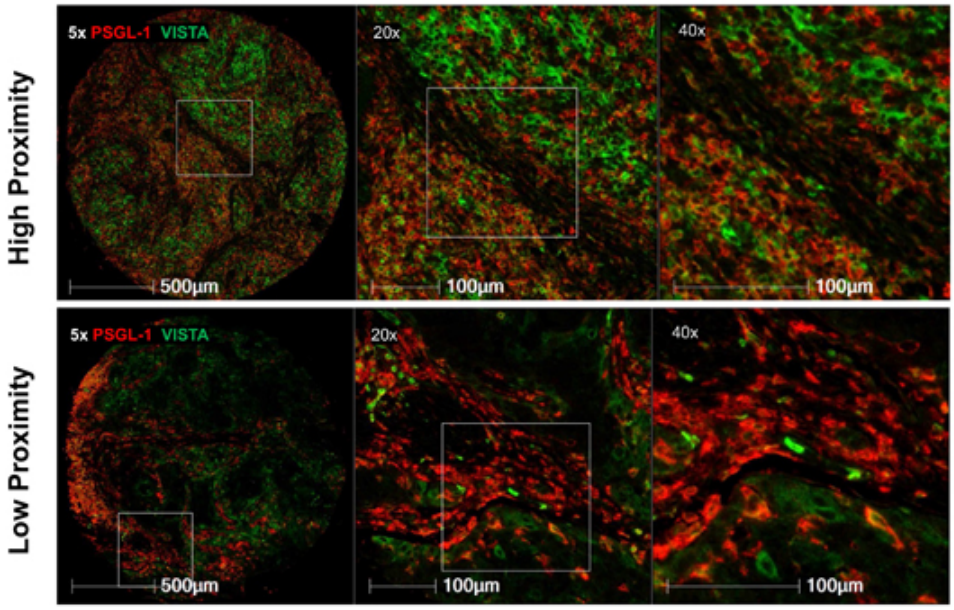
Preclinical Development Summary

- **Manufacturing of SNS-101 is ongoing**
  - No “developability” issues to date
  - Cell line has demonstrated great productivity/quality (~ 9 grams/liter and low % aggregates)

- **IND-enabling studies have been initiated**
  - Single-dose mouse and non-human primate PK
  - Optimized preclinical efficacy models in huVISTA-KI mice
  - GLP multi-dose PK and toxicology studies contracted
  - In vitro and In vivo CRS risk assessment models

- **Translational Medicine studies are underway to support FIH clinical trial in 2023**
  - Generate SNS-101 responder hypothesis → rationalize early development plan/focus on high probability of success indications

Preliminary PSGL-1/VISTA Proximity Assay on HNSCC Tumor Samples



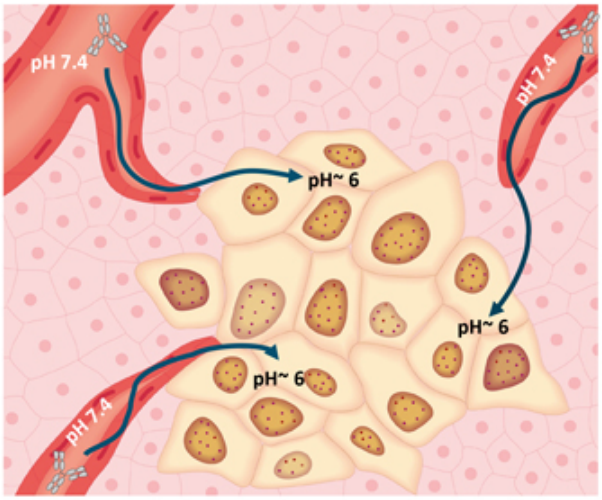
H&N (HN483a)
Core C6,R7

H&N (HN483a)
Core C5,R4

Beyond VISTA:

Tumor Microenvironment Activated Biologics (TMAbs)

The tumor microenvironment of pH ~6 is lower than physiological pH of 7.4



Sensei's technology identifies antibodies that selectively bind in the distinct biochemical milieu of the tumor, for example, sub-physiologic pH

- Antibodies that bind at physiological pH may encounter a "sink"
  - Prevents effective binding at the tumor and may lead to toxicity
- TMAb antibodies bypass tissue compartments other than the low-pH tumor microenvironment
- Goal is to unlock previously undruggable immune targets through potential for improved safety and clinical activity profile

Acknowledgements

Sensei Biotherapeutics

TMAb

Edward van der Horst
Thomas Thisted
Yuliya Kleschenko
Zuzana Biesova
Kanam Malhotra
Arnab Mukherjee
Anokhi Cifuentes

Translational Medicine

Jean Campbell
Lauren Abel
Rachel La Selva

Collaborators

Fred Hutchinson Cancer Research Center

Kimberly Smythe
Cecilia Yeung
Brandon Seaton

Adimab

Nadthakarn Boland
Nels Nielson