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): November 16, 2021

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

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 November 16, 2021, Sensei Biotherapeutics, Inc. (the "**Company**") is hosting a virtual VISTA science symposium. A copy of the Company's presentation that is being presented during the symposium is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

In accordance with General Instruction B.2. of Form 8-K, the information in this Item 7.01 and Exhibit 99.1 hereto 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 liability of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, 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	Company Presentation.
104	The cover page from Sensei Biotherapeutics, Inc.'s Form 8-K filed on November 16, 2021, 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: November 16, 2021

/s/ John Celebi
John Celebi
President and Chief Executive Officer

Exhibit 99.1

VISTA Science Symposium

November 16, 2021

Guest Speaker:

Prof. Robert Schreiber

Andrew M. Bursky and Jane M. Bursky Distinguished Professor of Pathology and Immunology, Professor of Molecular Microbiology and co-leader of the tumor immunology program at the Siteman Comprehensive Cancer Center, Founding Director of the Center for Human Immunology and Immunotherapy Programs at The Washington University School of Medicine
Sensei IOAB member

Sensei Presenters:

John Celebi
Chief Executive Officer

Dr. Robert Pierce
Chief Scientific Officer

Dr. Edward van der Horst
SVP, TMAb Antibody Development

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, and the preclinical and clinical development of our product candidates. 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 30, 2021 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.

AGENDA

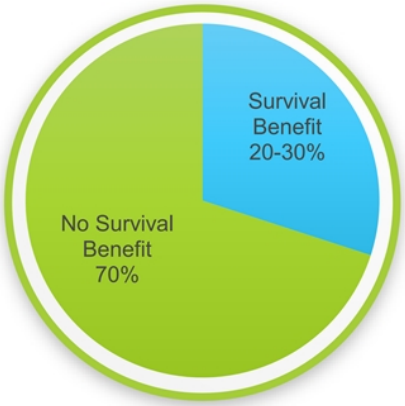
	Speaker	Topics
	**John Celebi** *President & CEO*	• Welcome/TMAb Mission
	**Professor, Robert Schreiber, Ph.D.** *Washington University School of Medicine* *Sensei IOAB member*	• VISTA biology
	**Robert Pierce, M.D.** *Chief Scientific Officer*	• SNS-101 preclinical data highlights from SITC
	**Edward van der Horst, Ph.D.** *SVP, TMAb Antibody Development*	• Join for Q&A

Our TMAb (Tumor Microenvironment Activated biologics) Platform Mission

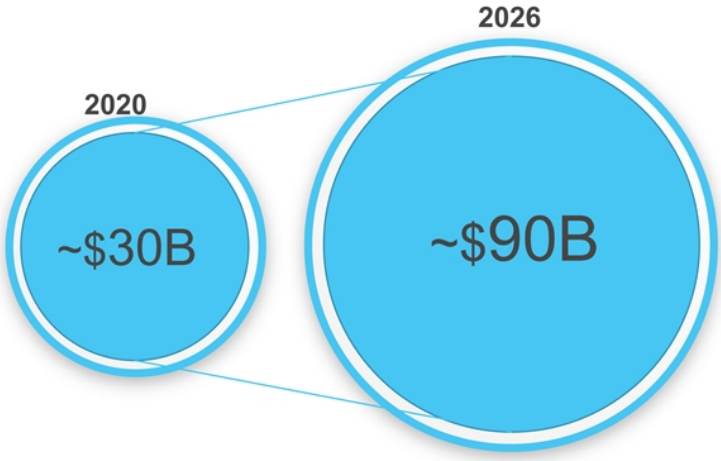
Leverage unique features of the tumor microenvironment to selectively activate biologics that unleash clinically meaningful anti-cancer immune responses

The Modern-Day Challenge in Immuno-Oncology

Majority of patients don't respond to PD-1/PD-L1 monotherapy[1]

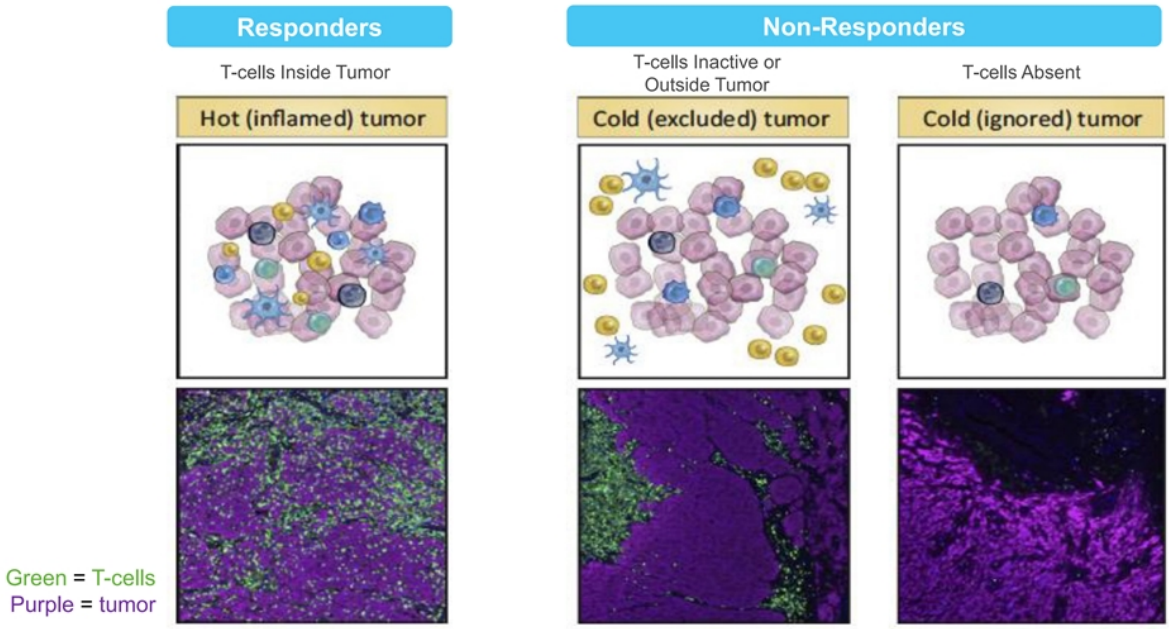


Global PD-1/PD-L1 Market[2]



1. Gerber et al., Biochemical Pharmacology 2016
2. Market estimates from PD-1 and PDL-1 Inhibitors Market Size in 2021 – MarketWatch, 360 Research

Two Major Types of Non-Responders to PD-1 Blockade



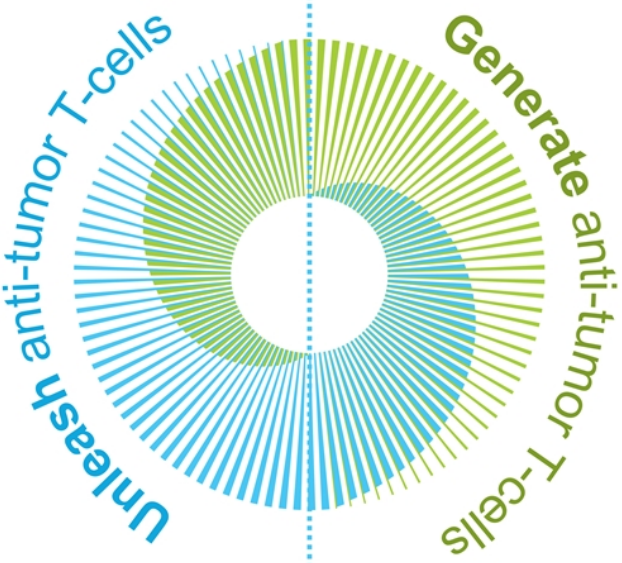
Adapted from Van der Woulde-LL, et al, Trends in Cancer, 2017

Two Platforms to Unleash Anti-Cancer T-cell Activity

TODAY'S DISCUSSION

TMAb™ (Tumor Microenvironment Activated Biologics) Platform

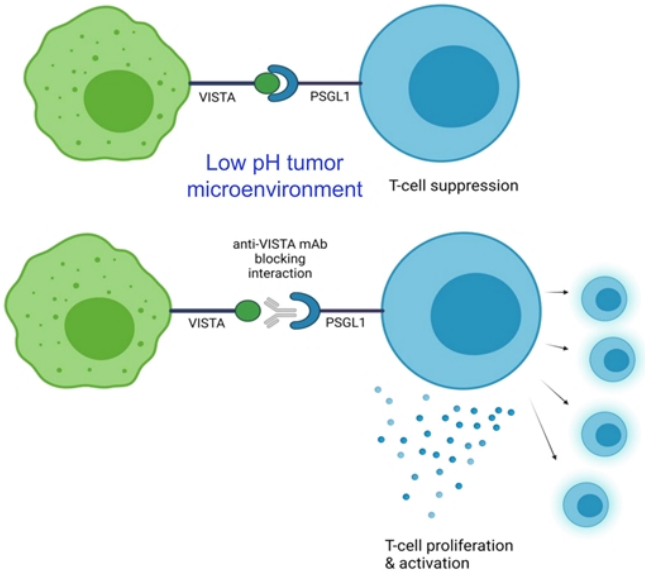
- Next-generation tumor activated mAbs



ImmunoPhage™ Platform

- Powerfully self-adjuvanted nanoparticle vaccine that drive tumor-specific T cell responses

VISTA (V-domain Ig suppressor of T cell activation)



Target Overview:

- Established immune checkpoint target to overcome checkpoint resistance
- Large market opportunity
- Extensive expression on normal myeloid cells

Sensei's Competitive Advantage:

Leverage extensive understanding of VISTA biology to deliver a differentiated approach

SNS-101:

- A fully human monoclonal antibody that selectively binds active (low pH) VISTA, but not inactive VISTA in the blood
- Potent inhibitor of PSGL-1 binding to VISTA
- Fc-competent framework to deliver positive "kick" to suppressive myeloid cells in the tumor microenvironment

Leveraging a Team with Decades of Experience

Dr. Schreiber

VISTA Biology

VISTA (B7-H5) is recognized an important immune checkpoint and B7 family member that is expressed on myeloid cells, a hub of immunosuppressive activity, and is activated via binding to its receptor on T-cells (PSGL-1) at sub-physiologic pH

The Promise and Challenge of Immunotherapy

Targeting Immunosuppressive myeloid cells is a promising strategy to overcome resistance to checkpoint Inhibitor therapy

THE PROMISE

- Using the body's own immune system to attack cancer
- Capitalizing on immunological specificity and long-term memory
- Achieving durable cures with minimal toxicity

THE CHALLENGE

- 70-80% of patients do not achieve increased survival with CPI monotherapy[1]
- The immunosuppressive tumor microenvironment (TME) influences response to immune checkpoint blockade
- Innate immune cells such as myeloid cells are a key driver of immunosuppressive TME

1 Gerber, et al Biochemical Pharmacology 2016

VISTA Has Emerged as an Important Checkpoint Regulator Target

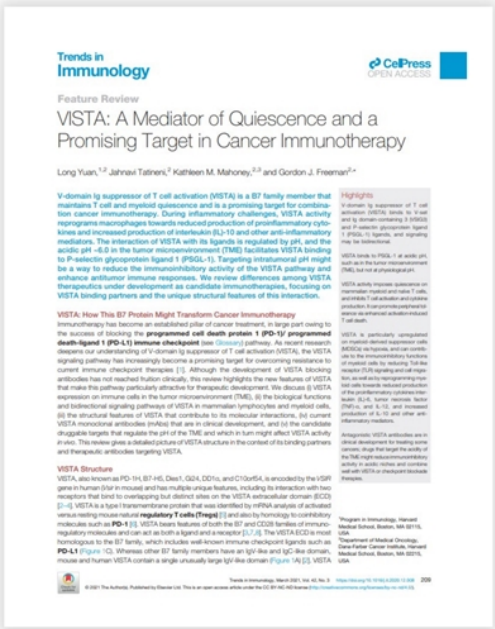
BRIEF COMMUNICATIONS

nature medicine

VISTA is an inhibitory immune checkpoint that is increased after ipilimumab therapy in patients with prostate cancer

nature medicine

Gao. J., et al



Trends in Immunology

CellPress OPEN ACCESS

Feature Review

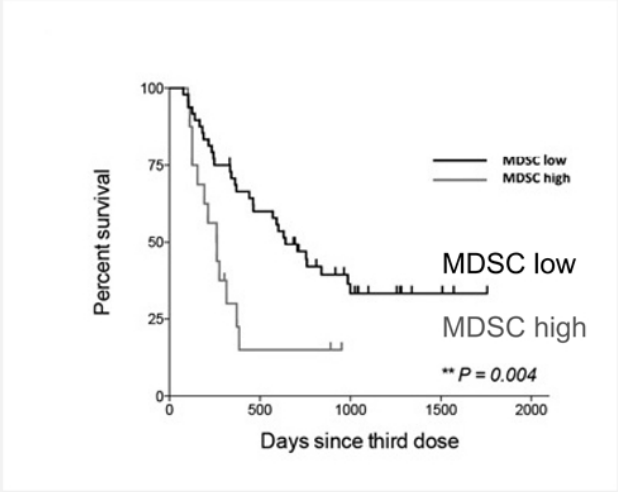
VISTA: A Mediator of Quiescence and a Promising Target in Cancer Immunotherapy

CellPress
Science that inspires

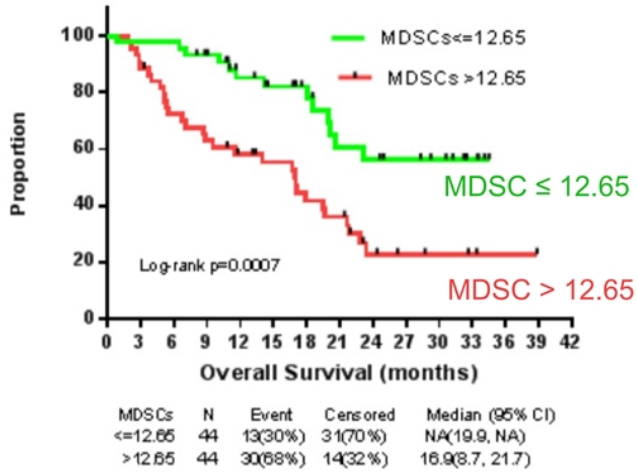
Yuan, L., et.al

Patients with High Circulating Myeloid Cells Have Shown Lower Overall Survival When Treated with Checkpoint Blockade

Ipilimumab-treated Melanoma Patients



Nivolumab-treated Melanoma Patients

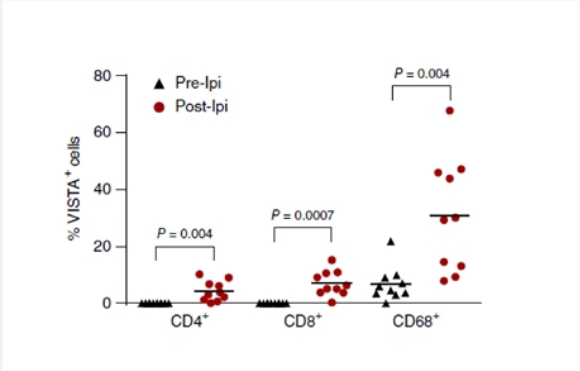


Kitano et al., *Cancer Immunol Res.* 2012
Weber et al., Cancer Immunol Res. 2016

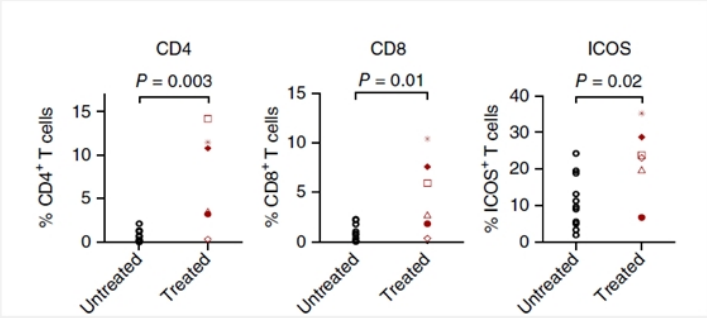
VISTA may be a Compensatory Pathway Following Checkpoint Therapy

Can targeting VISTA augment T-cell checkpoint blockade in refractory tumors?

VISTA Increases on Prostate Tumor Cell Infiltrates Following Ipilumimab Treatment

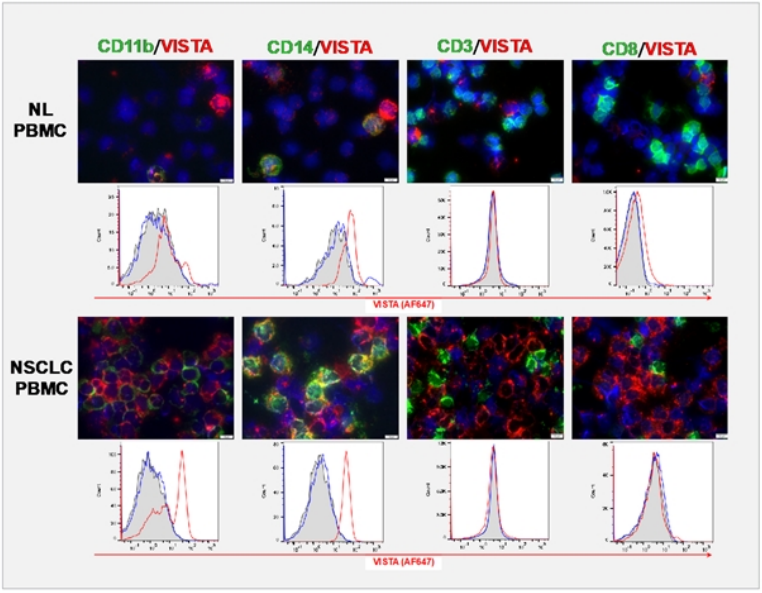


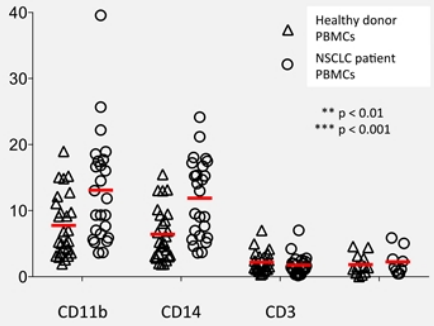
Prostate Tumor Cell Infiltrates Increase Following Ipilumimab Treatment



Gao et al., Nat Med. 2017

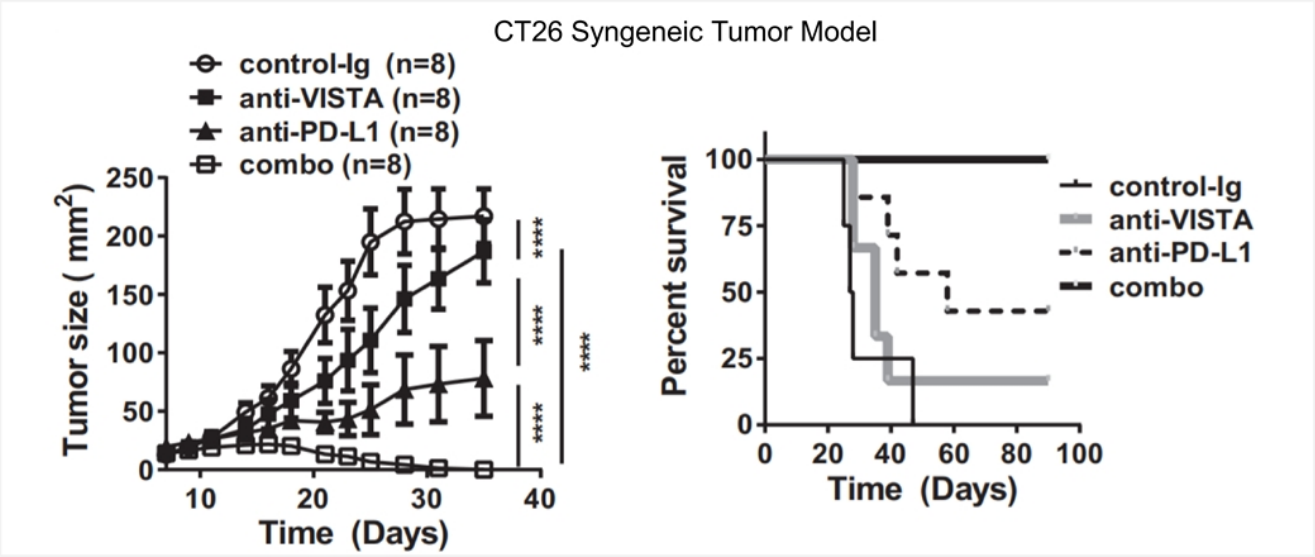
VISTA Expression Increases in PBMC Subsets of Patients with Non-Small Cell Lung Cancer (NSCLC)





Cell Subset	VISTA [Copy Numbers]	
	Normal	NSCLC
CD11b+	102611	***141143***
CD14+	102937	***191727***
CD3+	Below Level of Quantitation	
CD8+	Below Level of Quantitation	

VISTA Blockade Synergizes With PD-1/L-1 Pathway Inhibition

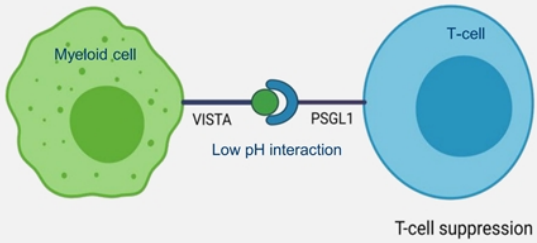


Liu J. et al. *PNAS* 2015

VISTA is An Emerging Target on Myeloid Cells and Key Resistance Mechanism for PD-1/PD-L1 Blockade

- VISTA is a B7 family (e.g., same protein family as PD-L1) ligand expressed on **myeloid cells**, a hub of immunosuppressive activity[1]
- VISTA is a key player in controlling checkpoint blockade
- VISTA has been implicated in **resistance to PD-1/PD-L1 inhibitors** [2]

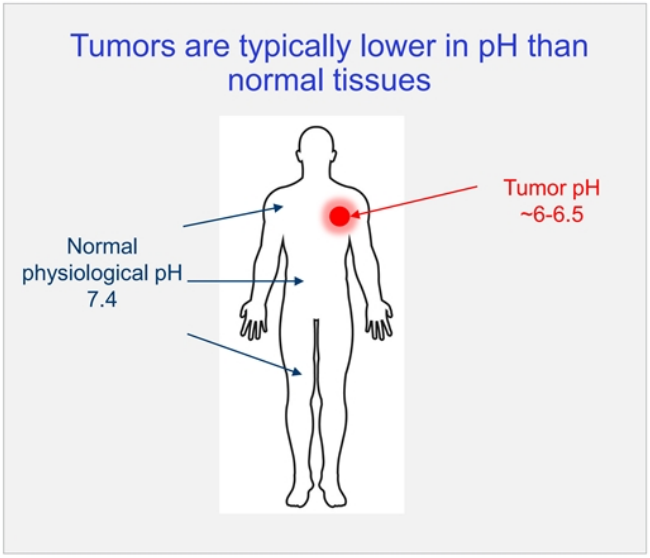
VISTA is a Negative Regulator of T cell Function at Low pH



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

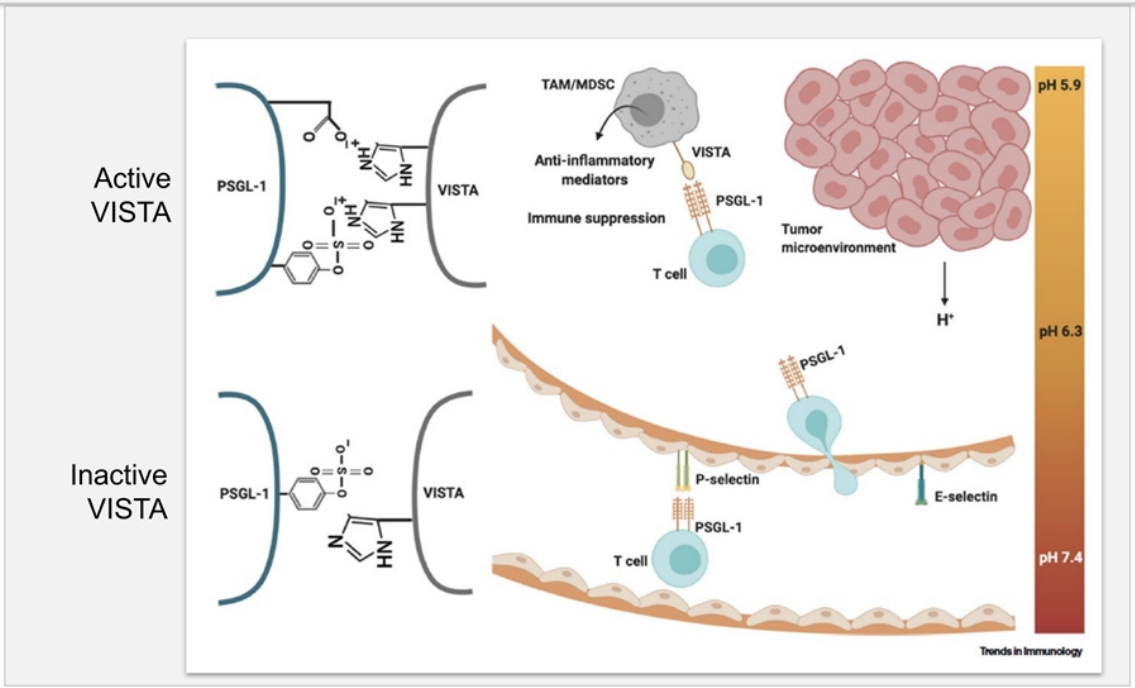
VISTA is an Emerging Target on Myeloid Cells and Key Resistance Mechanism for PD-1/PD-L1 Blockade

- Tumors are typically lower in pH than normal tissues
- At low pH, key amino acids in VISTA become protonated, changing its charge, and likely, its shape
  - This change activates VISTA **enabling VISTA to** bind to PSGL-1 on T cells, engaging its checkpoint function



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

The Binding of VISTA to PSGL-1 is pH Dependent



Adapted from Gao et al. *Nature medicine* vol. 23,5 (2017)

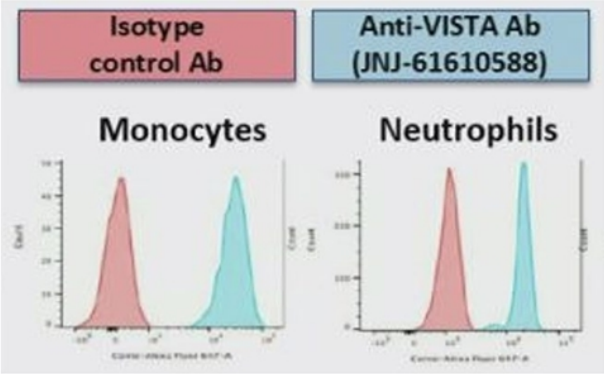
Dr. Schreiber

VISTA has been difficult to drug due to its unique biology

SENSEI BIOTHERAPEUTICS

VISTA is Expressed at High Levels on Human Monocytes and Neutrophils

Flow Cytometry Analysis of VISTA Expression on Normal Human Peripheral Immune Cells



High VISTA Expression on Monocytes and Neutrophils Results in Sub-Optimal PK and may Decrease the Therapeutic Window

- Antibodies binding VISTA^{+} cells (e.g. monocytes) at physiological pH result in rapid elimination from circulation through **targeted-mediated drug disposition (TMDD)**
- Efficacious drug occupancy levels may be difficult to reach and potentially narrow the therapeutic window

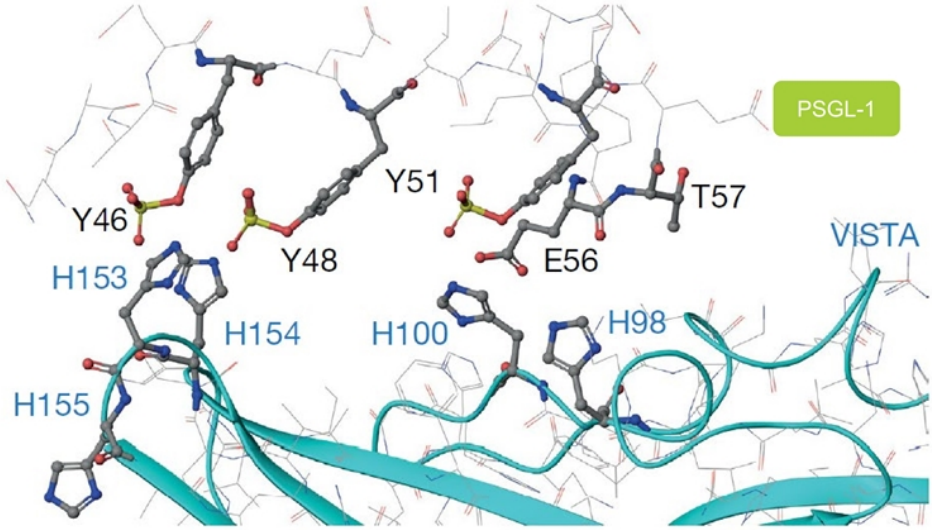
Case Study

CI-8993 Clinical Ongoing Clinical Study

- Phase 1 Dose Escalation Study
- 12 patients enrolled with advanced refractory solid tumors
- Initial dose of 0.005 mg/kg and above
- Low-grade transient Cytokine Release Syndrome (CRS) seen at 0.15 mg/kg and above
- Study halted after 1 DLT at sub-therapeutic dose level

The VISTA Checkpoint Itself is Only "ON" Under Low pH Conditions

Antibodies that block VISTA histidines H153, H154 and H155 interrupt PSGL-1 binding[1]



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

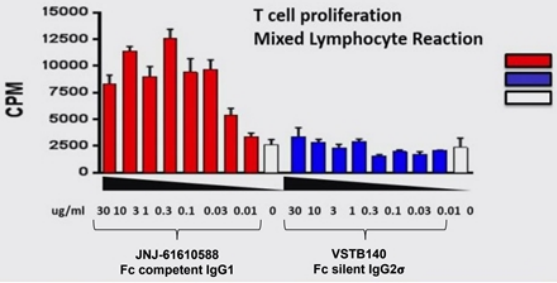
Histidines are protonated at low pH enabling VISTA to distinguish the active (acidic pH) and inactive (neutral pH) PSGL-1 interface

1. Johnston et al., Nature 2019

Engagement of FcγR may be Required for Optimal Activity of Anti-VISTA Monoclonal Antibodies

JNJ-61610588 induces T cell proliferation in MLR *in vitro*

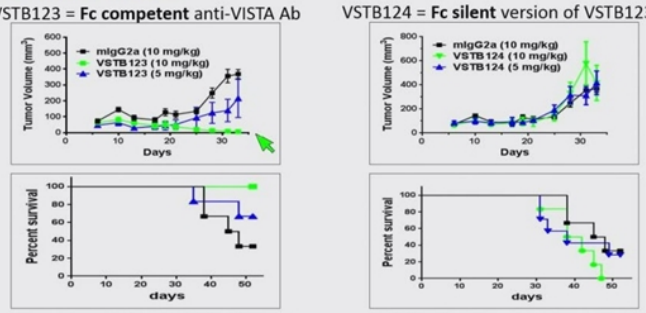
Active Fc is required



JNJ-61610588 murine surrogate inhibits tumor growth in a syngeneic mouse tumor model

VSTB123 = **Fc competent** anti-VISTA Ab

VSTB124 = **Fc silent** version of VSTB123



Model: MB49 bladder carcinoma grown in female VISTA KI mice

Summary

Reasons Why VISTA Has Been Difficult to Drug Historically

- VISTA is expressed at high levels on monocytes and neutrophils
- For non-pH-dependent blocking antibodies, high expression on monocytes and neutrophils results in a sub-optimal PK due to target-mediated clearance and may decrease the therapeutic window
- The VISTA checkpoint itself is only "ON" under low pH conditions
  - VISTA's immune checkpoint function is only active (i.e. capable of binding PSGL-1 at low pH)
  - Other receptors for VISTA are active at physiologic pH but do not appear to function as immune checkpoints
- Engagement of FcɣR may be a prerequisite for optimal activity of anti-VISTA antibodies
  - Fc silent antibodies are not effective at T cell proliferation ex vivo or anti-tumor activity in vivo despite picomolar binding affinity to VISTA
  - Engagement in the blood may result in untoward "off tumor" activation (i.e. CRS)

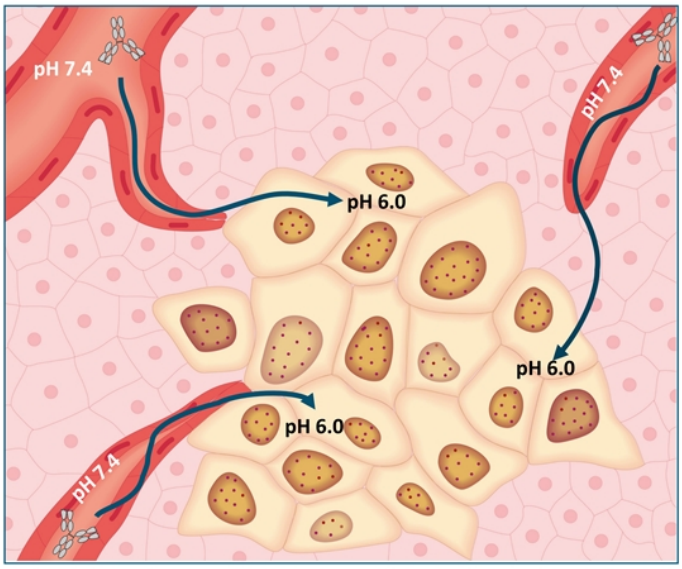
Dr. Rob Pierce

SITC 2021: SNS-101 Preclinical Data

Poster Presentation

pH-sensitive Antibodies Primarily Bind Their Antibodies in the Low pH Tumor Microenvironment

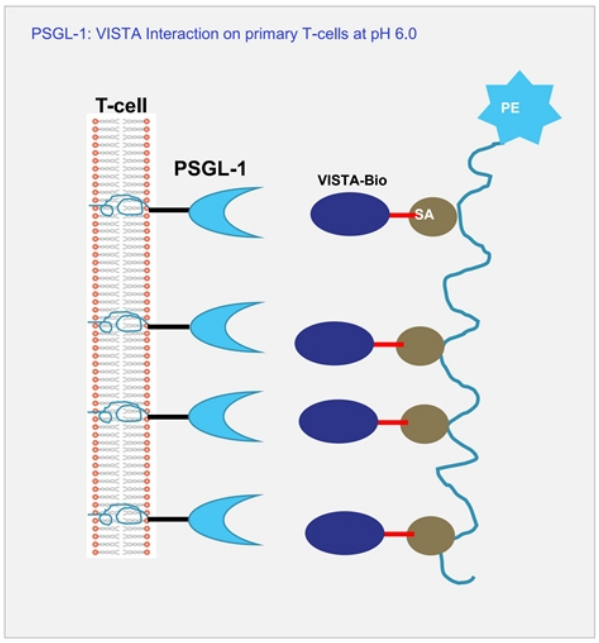
The tumor microenvironment of pH~6.0 is lower than physiological pH of 7.4

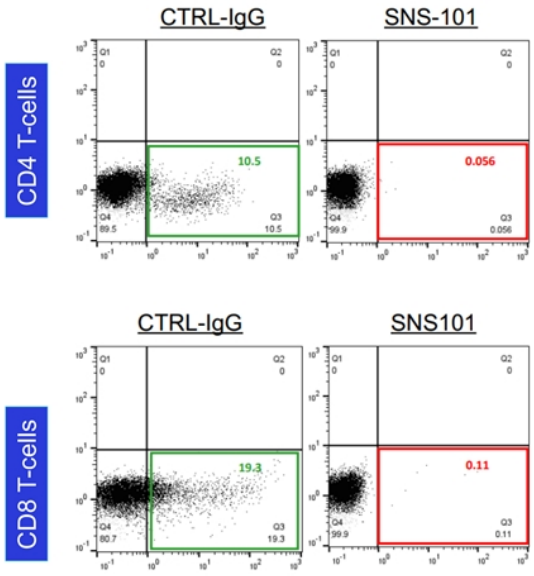


Sensei's technology identifies pH-sensitive antibodies that bind primarily at the tumor

- Antibodies that bind at physiological pH may encounter a "sink"
  - Prevents effective binding at the tumor and may lead to toxicity
- Sensei's technology selectively targets pH-sensitive antibodies to bypass tissue compartments other than the low-pH tumor microenvironment:
  - Potential for improved safety and clinical activity profile

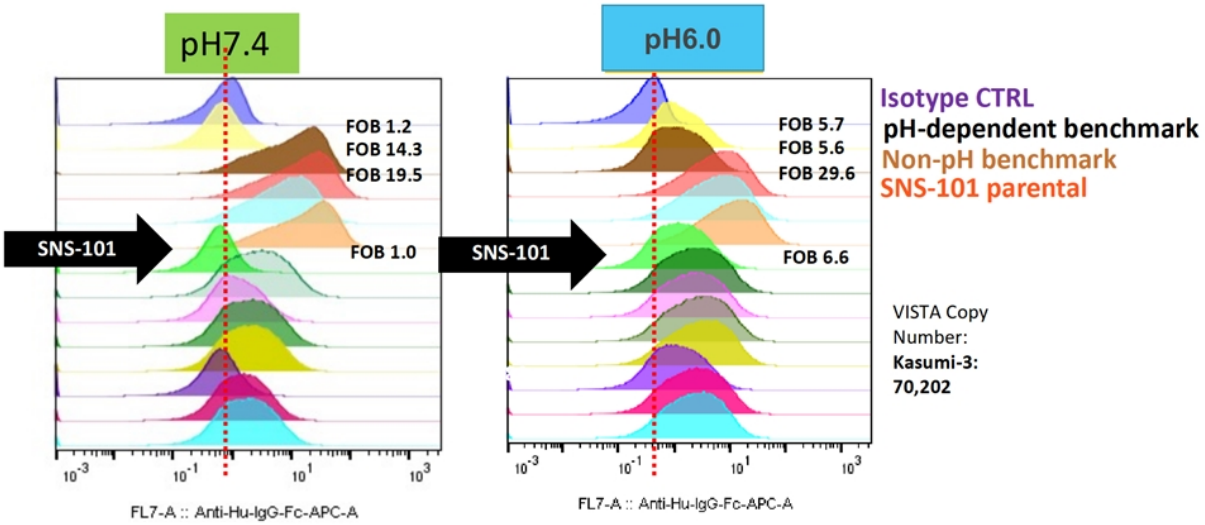
SNS-101 Inhibited Interaction of VISTA to its Receptor, PSGL-1, in CD4/CD8 T-Cells at Low pH 6.0





SNS-101 Identified Based on Stringent Cell-Based Assay

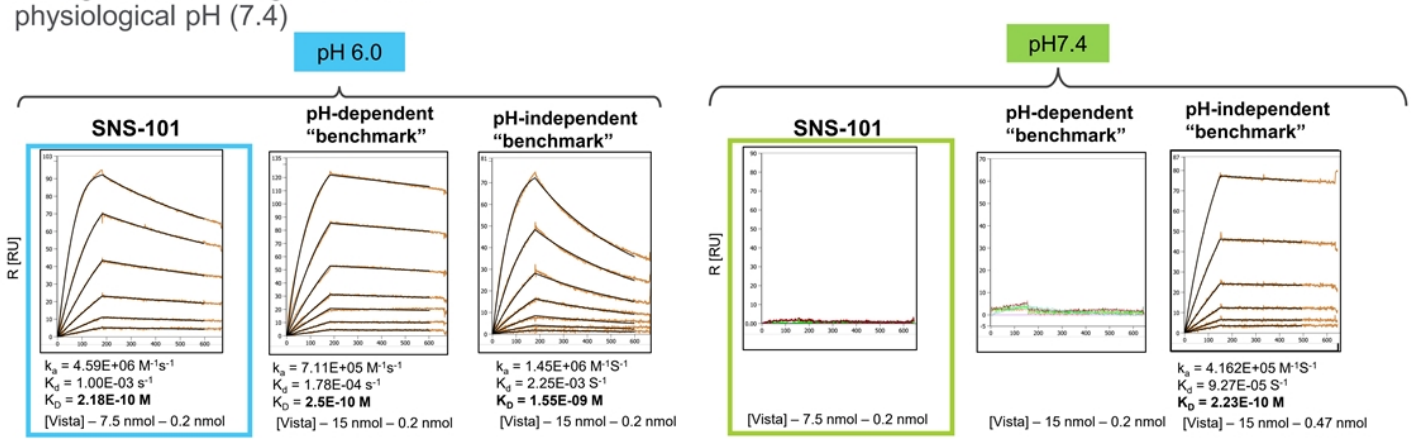
Candidate profile: no significant binding at pH 7.4



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

- Biophysical characterization demonstrates >600-fold selectivity for VISTA at pH 6.0
- Picomolar binding at low pH
- No significant binding observed at physiological pH (7.4)

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

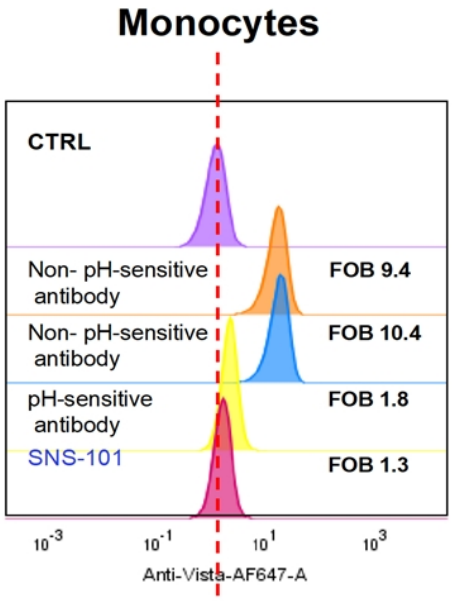


SITC 2021: Poster titled: Antagonistic pH-selective VISTA antibody SNS-101 potentiates anti-PD-1/PD-L1-induced anti-tumor immunity

SNS-101 Does Not Significantly Bind to VISTA+ Monocytes at pH 7.4

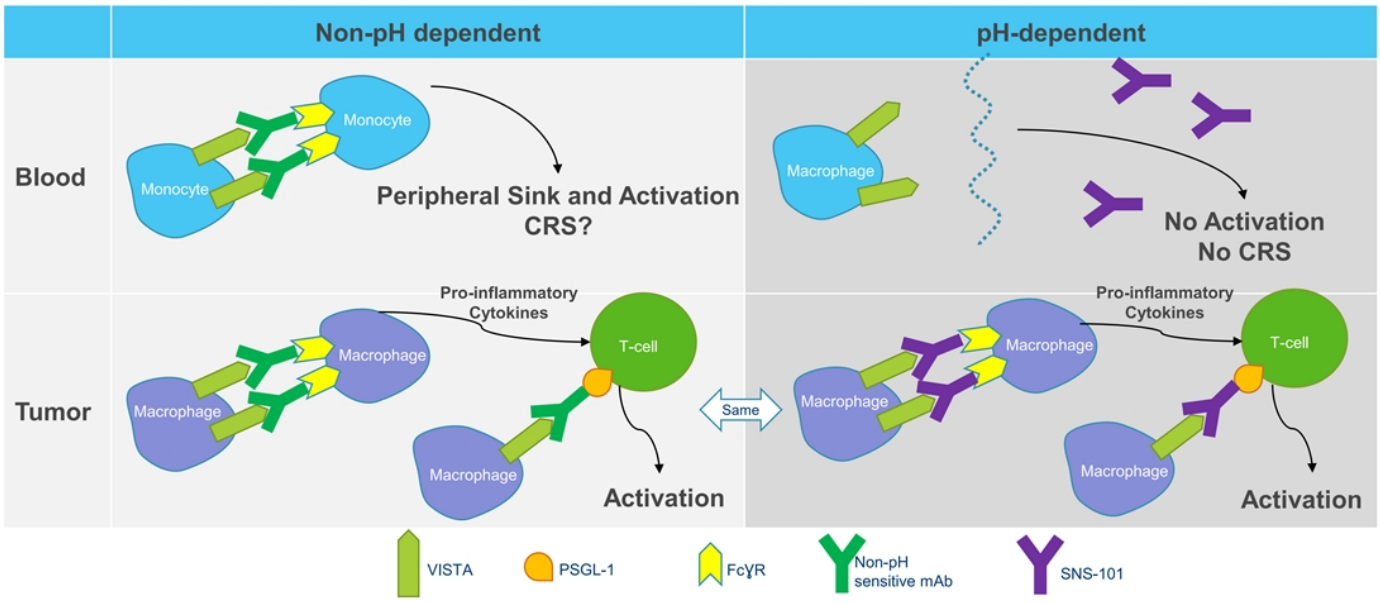
- VISTA+ monocytes are one of the main causes of TMDD
- Non-pH sensitive VISTA mAbs bind to monocytes at pH 7.4 thus allowing TMDD and have potential for on-target/off-tumor toxicity

VISTA Copy Number:	
Kasumi-3:	70,202
CD14+ Monocytes:	~103,000

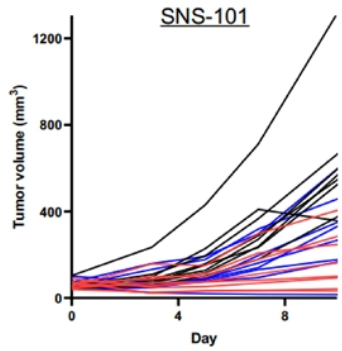


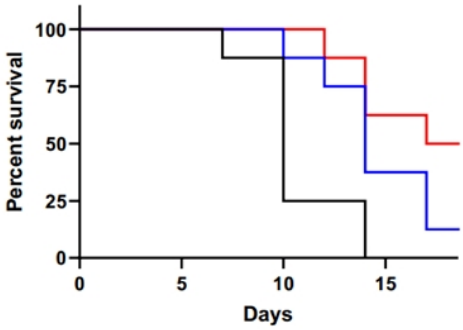
Proposed Mechanism of Action for SNS-101

Fc-competent framework is required for optimal activity, but FcγR engagement in the blood may result in untoward “off tumor” activation (i.e. CRS)



‘High-bar’ *In Vivo* Screening Test of SNS-101 Activity
1-week Administration





Antibodies were administered I.P. 2/wk **for 1 week** at 40 mg/kg total (20 mg/kg each)

Black Line (IgG Control human & ratI)
Blue Line (IgG Control human & rat anti-mPD-1)
Red Line (rat anti-mPD-1 & anti-VISTA)

SNS-101 Is a Differentiated Anti-VISTA Antibody

TMAb Platform

	SNS-101	VISTA.18 (BMS)	KVA12.1 (Kineta)	CI-8993; JNJ-61610588 (J&J/Curis)	K01401-020; W0180 (Pierre Fabre)	HMBD-002 (Hummingbird)
Inhibit PSGL-1 Binding	Yes	Yes	unknown	Yes	unknown	unknown
pH Sensitive Binding	Yes	Yes	No	No	No	No
Fc Active	Yes (IgG1)	No (IgG4)	Yes (IgG1)	Yes (IgG1)	N/A	No (IgG4)
Stage	Preclinical	Preclinical	Preclinical	Phase I	Phase I	IND submission
Clinical Data / Notes	• Preclinical data presented at STIC • IND-enabling studies underway	• N/A	• N/A	• JNJ initiated Phase I study in 2016 • 12 pts enrolled; initial dose 0.005 mg/kg • Only patient treated at 0.3 mg/kg experienced grade 3 CRS-associated encephalopathy; trial was halted	• Ongoing; no data reported	• First-patient to be dosed in 4Q'21

Johnston et al, Nature, 2019; Kineta website; Snyder et al, AACR Annual Meeting 2016; Pierre Fabre website; Hummingbird website

Key to Unlocking the Power of VISTA

1. Block VISTA's interaction with PSGL-1 at pH 6 within the tumor microenvironment

2. Selectively bind VISTA at low pH to avoid:
   - target mediated drug disposition
   - on-target/off-tumor side effects

3. Design an Fc-competent IgG engaging with FcɣR on tumor-infiltrating myeloid cells

IND-Enabling Studies are Underway for SNS-101

Question & Answer Session

VISTA Science Symposium

November 16, 2021

Guest Speaker:

Prof. Robert Schreiber

Andrew M. Bursky and Jane M. Bursky Distinguished Professor of Pathology and Immunology, Professor of Molecular Microbiology and co-leader of the tumor immunology program at the Siteman Comprehensive Cancer Center, Founding Director of the Center for Human Immunology and Immunotherapy Programs at The Washington University School of Medicine
Sensei IOAB member

Sensei Presenters:

John Celebi
Chief Executive Officer

Dr. Robert Pierce
Chief Scientific Officer

Dr. Edward van der Horst
SVP, TMAb Antibody Development