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): January 4, 2024

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
Series A Preferred Stock Purchase Rights		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 January 4, 2024, Sensei Biotherapeutics, Inc. (the "Company") updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 and the exhibit attached hereto are being furnished and shall not be deemed "filed" for the 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 they be deemed incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933, as amended, whether filed before or after the date hereof and regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Sensei Biotherapeutics, Inc. corporate presentation, dated January 2024
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBRL

SIGNATURES

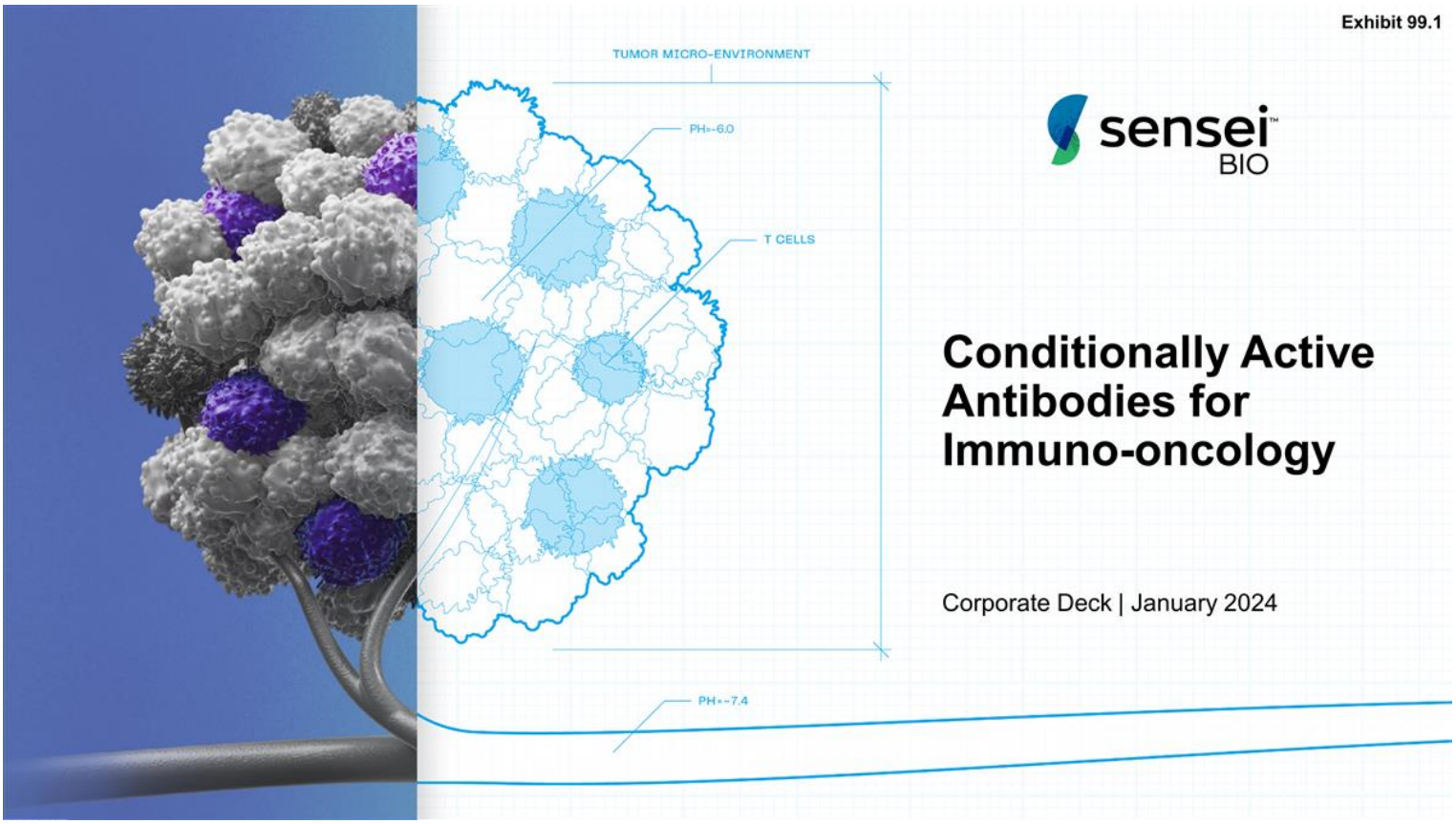
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Sensei Biotherapeutics, Inc.

Date: January 4, 2024

/s/ Christopher W. Gerry
Christopher W. Gerry
General Counsel and Secretary

Exhibit 99.1

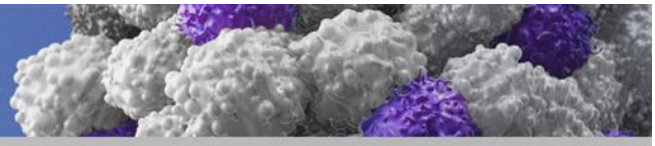


sensei BIO

Conditionally Active Antibodies for Immuno-oncology

Corporate Deck | January 2024

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, expectations regarding the development and potential therapeutic benefits of our product candidates; the expected safety, pharmacokinetic and efficacy profile of our product candidates, including SNS-101; the expected timing of clinical data from our Phase 1/2 clinical trial of SNS-101; the expansion of the Phase 1 clinical trial to include additional patients with specific tumor types; and our belief that our existing cash and cash equivalents will be sufficient to fund our operations at least into the fourth quarter of 2025 and reach midway into Phase 2 clinical studies of SNS-101.

When used in this presentation, the words and phrases "designed to," "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, including the risk of delay or cessation of any clinical trials of Sensei’s product candidates; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical trials and early results from the clinical trial of SNS-101, will not be replicated or will not continue in ongoing or future studies or clinical trials involving Sensei’s product candidates, including SNS-101; our reliance on third parties over which we may not always have full control; risks regarding the accuracy of our estimates of expenses, capital requirements and needs for additional financing; and other risk and uncertainties that are described in our Quarterly Report on Form 10-Q filed with the SEC on or about November 7, 2023 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.

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Company Highlights

- Sensei Bio's proprietary platform is designed to harness the unique acidic tumor microenvironment to widen the therapeutic window and enable druggability of promising oncology targets
- SNS-101, the company's lead asset, targets VISTA, a critical negative regulator of T-cell function and promising immune checkpoint target
- SNS-101 is currently in Phase 1 clinical testing with data to date displaying an attractive safety profile and potentially best-in-class pharmacokinetics
- Anticipated near-term milestones include topline Phase 1 monotherapy data in Q2 2024
- Three additional early-stage drug candidates
- Cash runway into the fourth quarter of 2025, which is expected to fund operations midway into Phase 2 studies of SNS-101

Leadership Team with History of Antibody Oncology Success

John Celebi, MBA
President and CEO

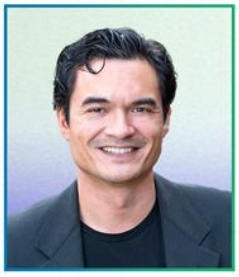
X4 Tutarik ArQule

Erin Colgan
Chief Financial Officer

Vertex Intarcia pwc

Christopher Gerry, J.D.
VP, General Counsel

AVROBIO Cooley



Edward van der Horst, Ph.D.
Chief Scientific Officer

AMGEN IGENICA oncomed

Stephanie Krebs, M.S., MBA
Chief Business Officer

SNIPRBIOME bluebirdbio Biogen

Ron Weitzman, M.D.
Chief Medical Officer (part-time)

EXELIXIS APROS THERAPEUTICS

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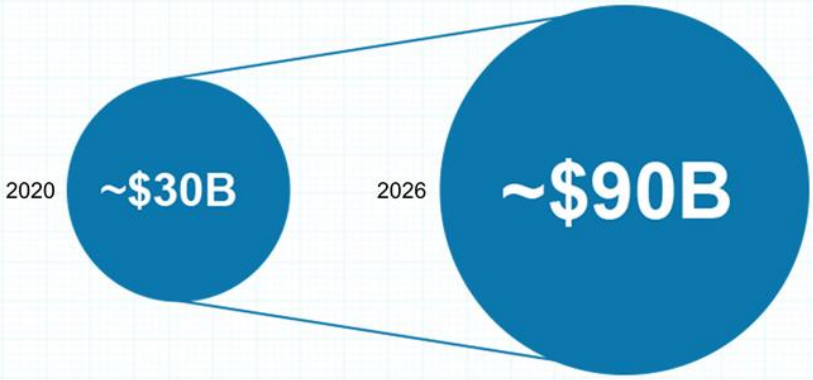
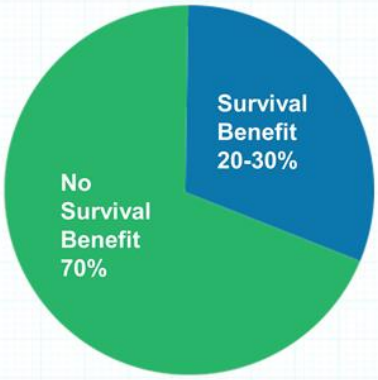
The Modern-Day Challenge in Immuno-Oncology (IO)

The PD-1/PD-L1 market is big and growing fast[1]



PD-1/PD-L1 monotherapy does not benefit 70% of patients[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

Lack of Tumor Targeting is a Major Obstacle in IO Innovation

Industry Problem	Sensei's Solution
Conventional antibodies target immune checkpoints that are highly expressed in normal tissues, resulting in:	**Conditionally active antibodies are selectively targeted to the tumor microenvironment, potentially providing:**
• Dose-limiting toxicities due to on-target/off-tumor action	• Little or no toxicity due to selective on-target/on-tumor action
• Pharmacological sink effect requires higher & more frequent dosing	• Lower & less frequent doses with tumor-specific binding
• Suboptimal activity due to poor PK & dose-limiting toxicities	• Powerful activity selectively focused on the tumor microenvironment

One new IO checkpoint inhibitor approved after the CTLA-4 and PD-1/PD-L1 group

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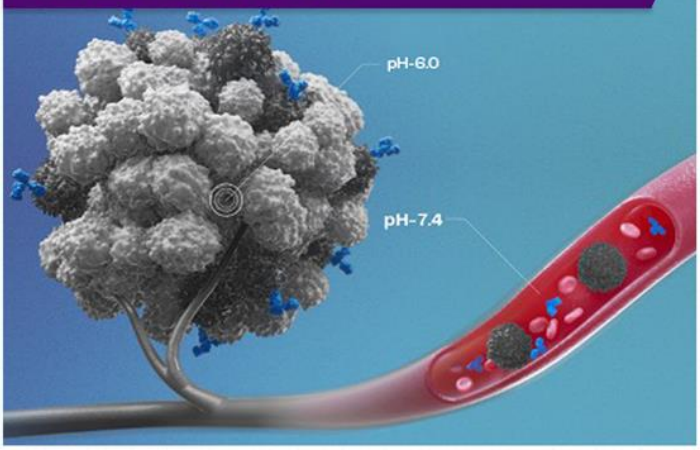
The TMAb Platform: pH-sensitive Antibodies Selectively Bind to Targets in the Low-pH Tumor Microenvironment

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



Sensei's technology identifies pH-sensitive antibodies designed to bind only at the tumor

- Exploits the tumor microenvironment using pH-selective properties
- Intended to alleviate undesirable PK/PD properties:
  - Dose-limiting toxicities due to on-target/off-tumor binding
  - Higher and more frequent dosing due to poor pharmacokinetics
- Bolsters specific activities
- Unlocks previously undruggable immune targets

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Innovative Pipeline of IO Drugs with Broad Commercial Potential

REGENERON

*Sensei has entered into a clinical supply agreement with Regeneron supporting the planned evaluation of SNS-101 in combination with Regeneron's anti-PD-1 therapy Libtayo® (cemiplimab) in a Phase 1/2 clinical trial in solid tumors.

NIH NATIONAL CANCER INSTITUTE

*Sensei has entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute. The goal of this collaborative effort is to further elucidate the role of VISTA in immune checkpoint resistance and expand the potential of SNS-101 as a combination therapy beyond anti-PD-1.

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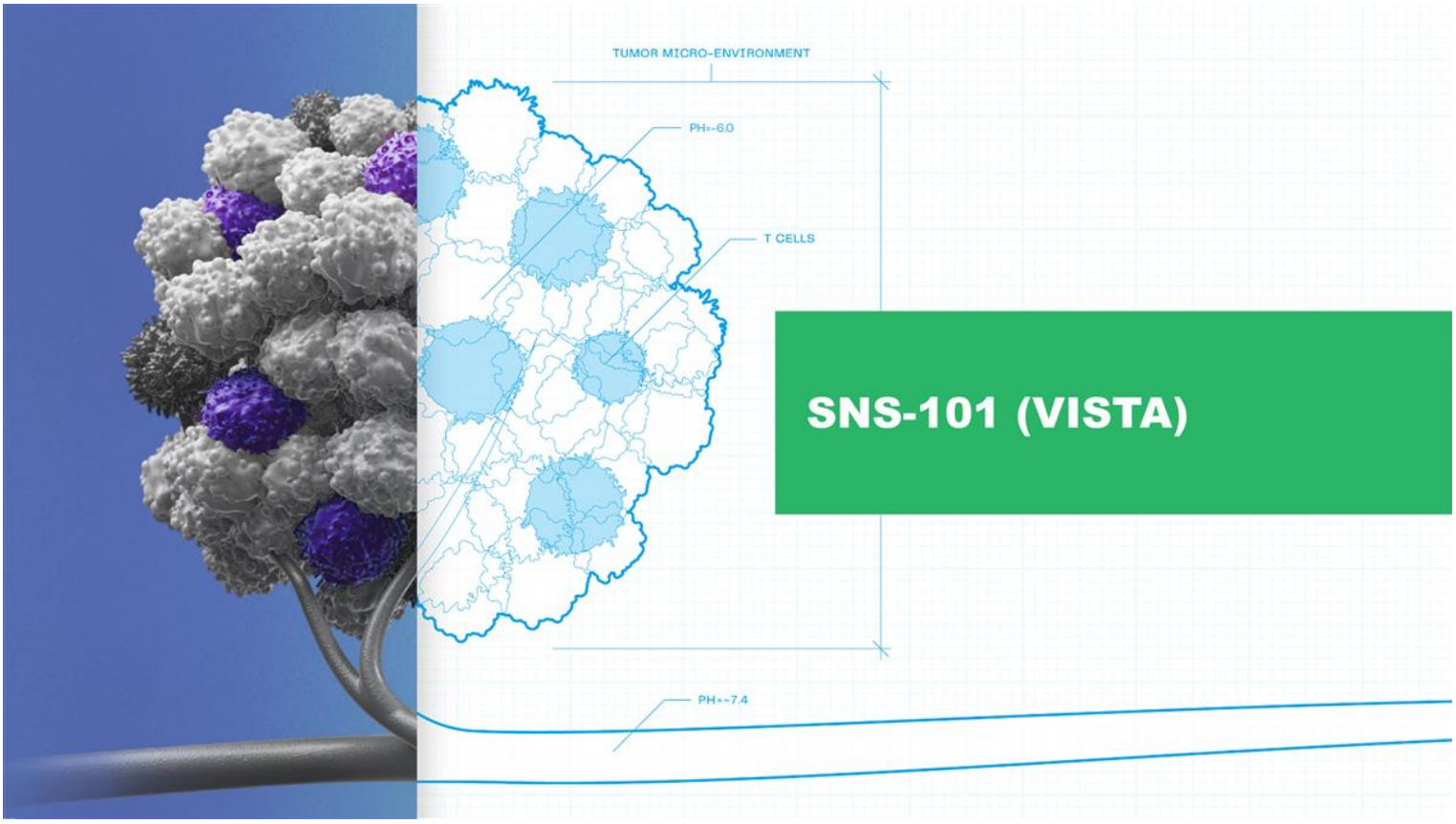


SNS-101 (VISTA)

VISTA is a Potent T cell Checkpoint Extensively Expressed on Myeloid Cells

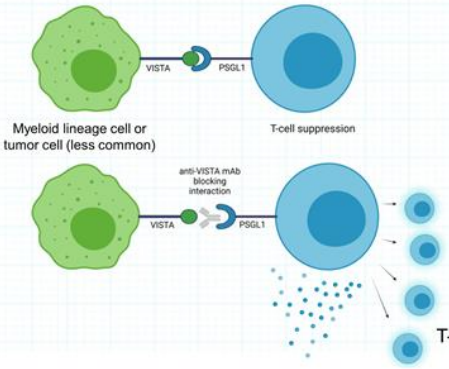
VISTA is a B7 family member that inhibits T cell activation[1]

Immunosuppressive function believed to be mediated by PSGL-1 receptor

Upregulated on immune suppressive myeloid-derived suppressor cells (MDSCs) via hypoxia[2]

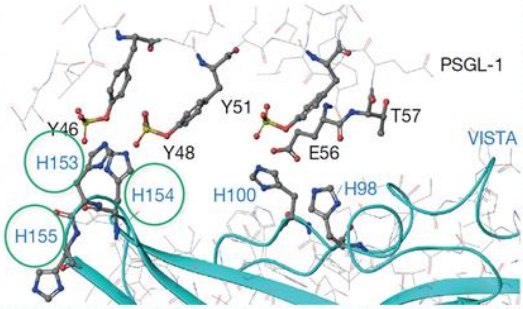
Increased expression on tissue infiltrating immune cells upon checkpoint therapy failure[3]

IS ACTIVATED IN A pH SENSITIVE MANNER



Extensive VISTA expression on off-tumor myeloid-lineage cells demands a conditionally active antibody approach

VISTA has inherent pH sensitivity: its extracellular domain is uniquely rich in histidines[4]



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1 Wang et al, JEM, 2011
2 Deng et al, Cancer Immunonol Res 2019
3 Gao et al., Nat Med. 2017
4 Johnston et al., Nature 2019

SNS-101: Selectively Targets VISTA via a pH-sensitive Antibody

SNS-101 is a differentiated, pH-sensitive antibody

Selectivity for active VISTA^{pH6} over VISTA$^{pH7.4}$

Monovalent Affinity (K_D)

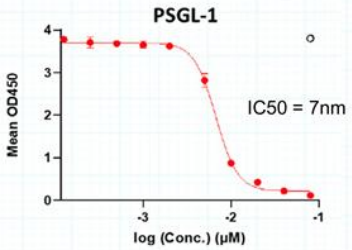
pH 6.0	pH 7.4
0.218 nM	132 nM (~No binding)

Additional SNS-101 features

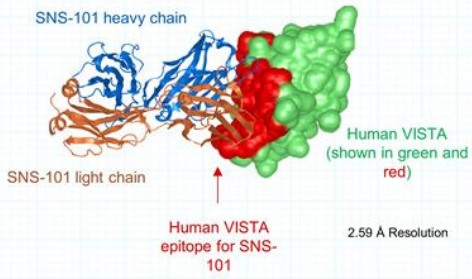
- IgG1 format
- Active Fc

SNS-101 blocks the key receptor regulating VISTA's immunosuppressive activity

SNS-101 strongly inhibits the VISTA:PSGL-1 interaction and all other potential binding partners at pH 6.0 *in vitro*



VISTA:SNS-101 co-crystal structure demonstrates epitope of SNS-101 encompasses VISTA's PSGL-1 epitope

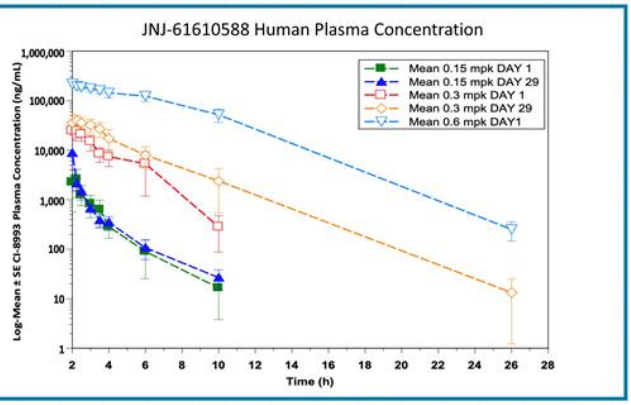


Competitors Halted Development of VISTA Antibodies as a Result of Severe Toxicities From Non-Tumor Activity & Poor PK

Dose-limiting toxicity
Grade 3 CRS-associated encephalopathy

- JNJ-61610588 (CI-8993) was the first anti-VISTA antibody to be studied in clinical trials in 2016 (NCT02671955) [1]
- Transient Cytokine Release Syndrome (CRS) observed in several patients at **0.15 mg/kg**
- Transient **Grade 3 CRS-associated encephalopathy** observed at **0.3 mg/kg**, after which Janssen halted the study

Challenging PK profile
Non-linear PK, short $t_{1/2}$



1 Curis, Inc., Corporate Presentation, Feb 2022

SNS-101 is Designed to Overcome VISTA's Unique Challenges

Differentiated Design and Mechanism	IgG1, Fc-active antibody designed to selectively block VISTA in the acidic tumor microenvironment
Enrolling Phase 1/2 Clinical Trial	Multi-center U.S. study as single agent and in combination with PD-1 inhibitor Libtayo®
Potential Best-in-Class Safety and PK Profile Supported by Initial Clinical Data	No observed CRS or dose-limiting toxicity and no evidence of target-mediated drug disposition through 3 mg/kg monotherapy*
Achieving "Firsts" for the VISTA Field	First VISTA-blocking antibody administered at a dose anticipated to be therapeutically relevant without eliciting dose-limiting toxicity**
Anticipated Near-Term Clinical Milestones	Initial combination PK/safety data in Q1 2024 Topline monotherapy dose escalation data in Q2 2024 Topline combination dose escalation data in Q3 2024 Initial dose expansion data by end of 2024

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*As of data cut-off of October 3, 2023
**Anticipate therapeutically relevant clinical doses at approximately 3mg/kg or higher based on preclinical studies

SNS-101 is Unique and Differentiated From Its Peers

	SNS-101 sensei BIO	CI-8993; JNJ-61610588 (J&J/Curis)	K01401-020; W0180 (Pierre Fabre)	HMBD-002 (Hummingbird)	KVA12123 (Kineta)	VISTA.18 (BMS)	(PMC-309) Pharm Abcine
Inhibit PSGL-1 Binding	✓	✓	✓	✗	✓	✓	✓
pH Sensitive Binding	✓	✗	✗	✗	✗	✓	✗
Fc Active	✓ (IgG1)	✓ (IgG1)	N/A	✗	✓ (IgG1)	✗ (IgG4)	✓ (IgG1)
Stage	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Preclinical	Phase 1

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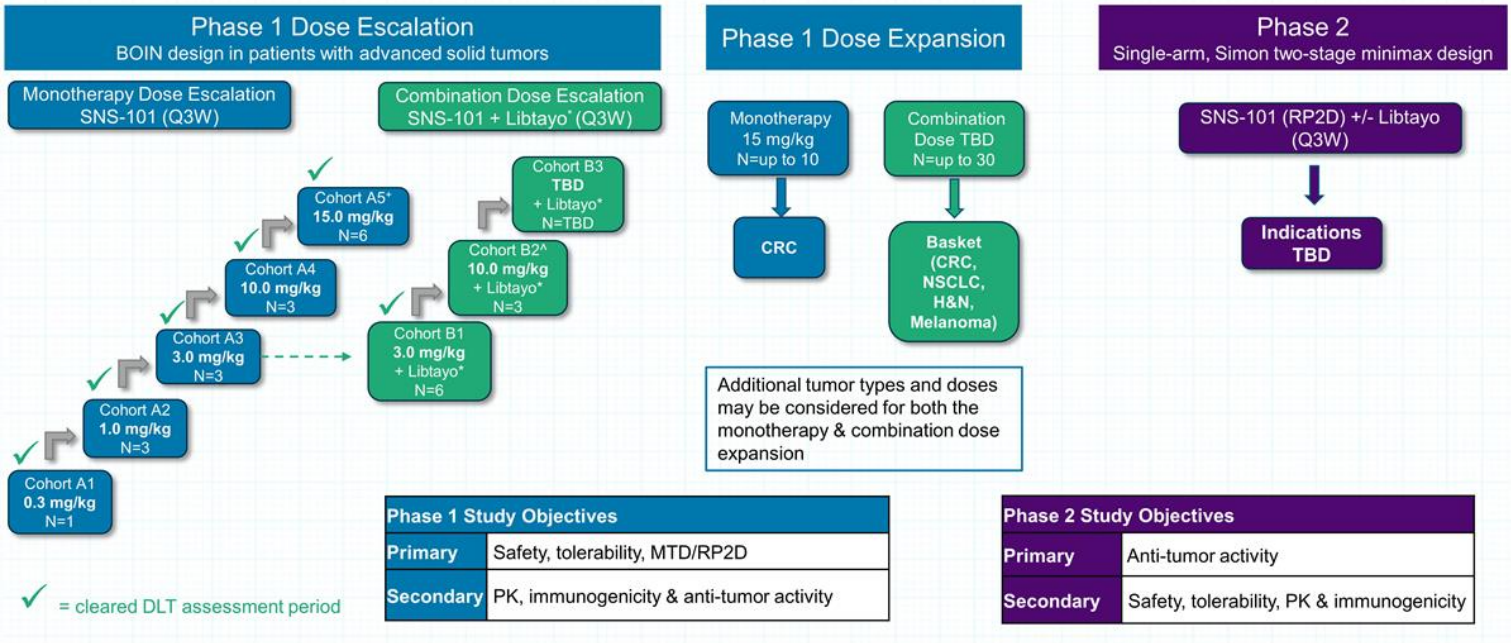
Johnston et al., Nature 2019; Kineta website; Snyder et al, AACR Annual Meeting 2016; Pierre Fabre website; Hummingbird website; Thakkar et al, J of Immunother Cancer, 2022; PharmAbcine website

SNS-101 Phase 1/2 Study



Phase 1 Study Objectives	
Primary	Safety, tolerability, MTD/RP2D
Secondary	PK, immunogenicity & anti-tumor activity

Phase 2 Study Objectives	
Primary	Anti-tumor activity
Secondary	Safety, tolerability, PK & immunogenicity

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* Libtayo 350 mg
+ As of January 2, 2024, cleared Cohort A5 (15.0 mg/kg)
^ As of January 2, 2024, Cohort B2 (10.0 mg/kg of SNS-101 + Libtayo) enrolled, pending DLT assessment period
RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose

CRC = colorectal cancer
NSCLC = non small cell lung cancer
H&N = head and neck cancer

SNS-101 Displayed Favorable Safety & Tolerability Profile Through 3 mg/kg Monotherapy

Well Tolerated with No Evidence of Cytokine Release Syndrome and No Dose-Limiting Toxicities Observed

	0.3 mg/kg N=1 n (%)	1.0 mg/kg N=3 n (%)	3.0 mg/kg N=3 n (%)	Total N=7 n (%)
At least 1 TEAE	1	3	1	5 (71.4)
At least 1 SAE	0	0	1*	1* (14.3)
At least 1 TEAE leading to discontinuation	0	0	1*	1* (14.3)
DLTs	0	0	0	0
CRS events	**0**	**0**	**0**	**0**
≥Grade 3 TEAE	0	0	1*	1* (14.3)
Related TEAE	0	1#	0	1# (14.3)

*One patient experienced an SAE, Grade 5 bronchial obstruction, that resulted in death; Event was considered related to disease progression, not SNS-101.
One patient experienced a Grade 2 dermatitis acneiform considered to be related to SNS-101. The event resolved following phototherapy treatment.

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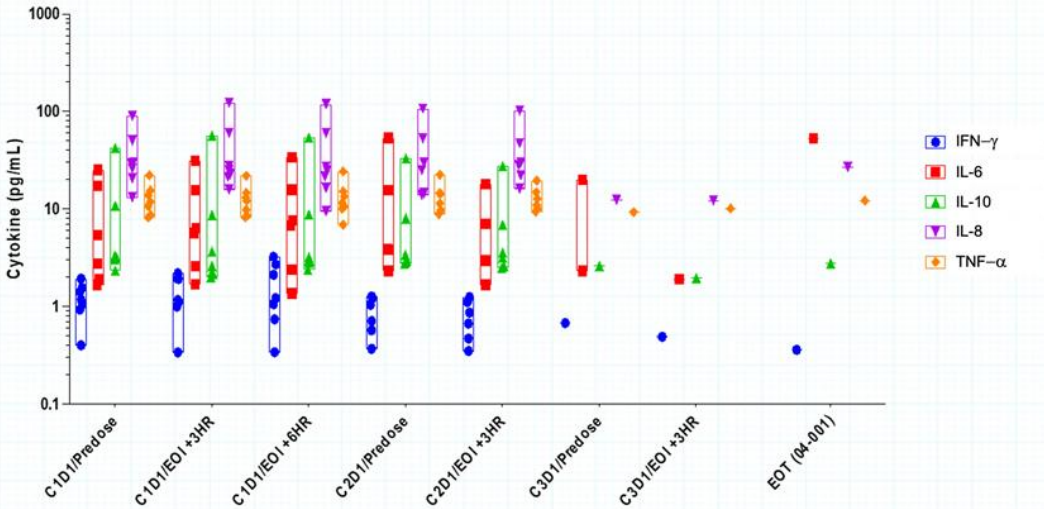
Data from monotherapy dose escalation arm as of cut-off date of October 3, 2023

DLT = Dose-limiting toxicity
CRS = Cytokine release syndrome
TEAE = Treatment emergent adverse event
SAE = Serious adverse event

Monotherapy Data Consistent with Lack of Observed Cytokine Release Syndrome Through 3.0 mg/kg

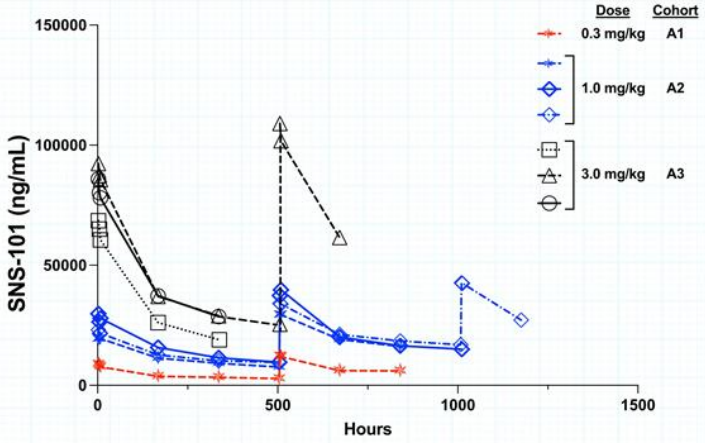
No Significant Changes in Key Inflammatory Cytokines



Cytokine analysis: Blood samples were taken pre-dose, 3 hours post-infusion and 6 hours post infusion at C1D1, and pre- and 3hr-post thereafter. Serum was assayed for indicated cytokines using a platform (MSD) that has been validated for clinical sample analysis.

Data from monotherapy dose escalation arm as of cut-off date of October 3, 2023

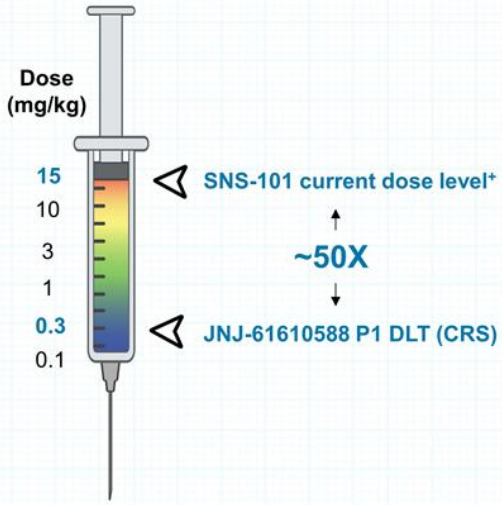
SNS-101 Monotherapy Data Show Linear Pharmacokinetics and Long Half-Life in Stark Contrast to Prior Anti-VISTA mAbs



Supports Every 3 Week Dosing

Data from monotherapy dose escalation arm as of cut-off date of October 3, 2023

Key SNS-101 Differentiators: Potential Best-in-Class Therapeutic



Potential Best-In-Class PK Profile

- Dosing every 3 weeks vs. every 1 or 2 weeks for competitors
- Linear elimination kinetics vs. non-linear for competitors

Safety Parameters On Track

- Highest dose to date for any anti-VISTA antibody
- SNS-101 at a dose ~50x higher than the JNJ dose (0.3mg/kg) that caused DLT and termination of trial
- No observed DLTs or CRS through 3.0mg/kg monotherapy*
- No routine prophylaxis per protocol

Anti-Tumor Activity

- Preclinical data demonstrate monotherapy activity in PD-1 resistant tumor model and deepened anti-tumor responses to PD-1 combo
- Topline monotherapy data expected in Q2 2024 with topline combination data to follow in Q3 2024

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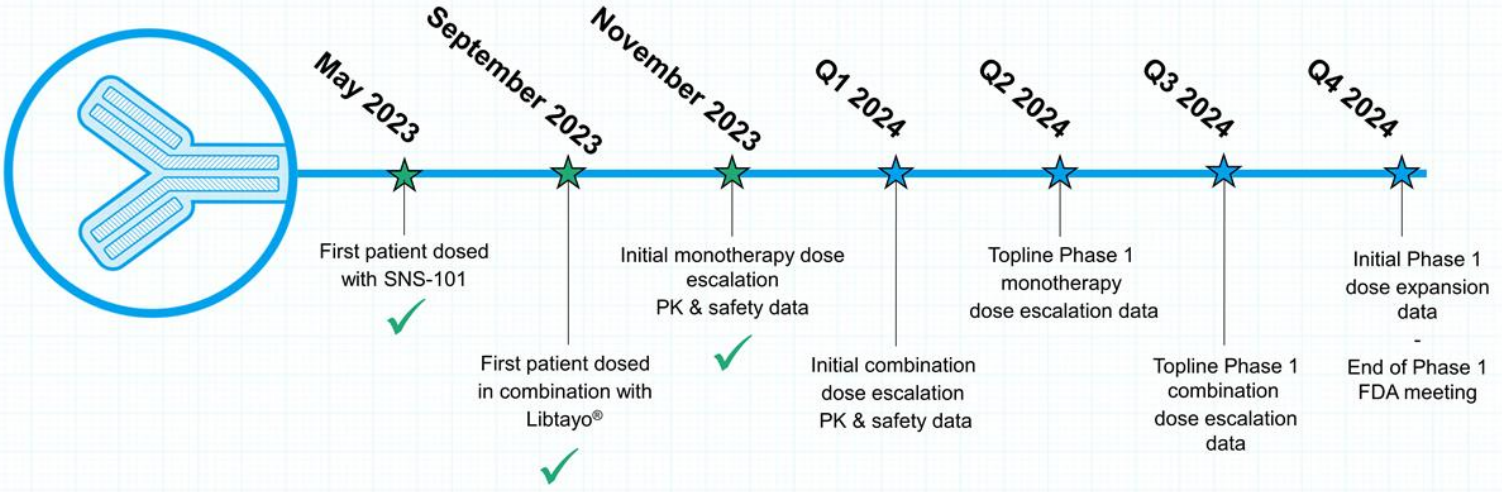
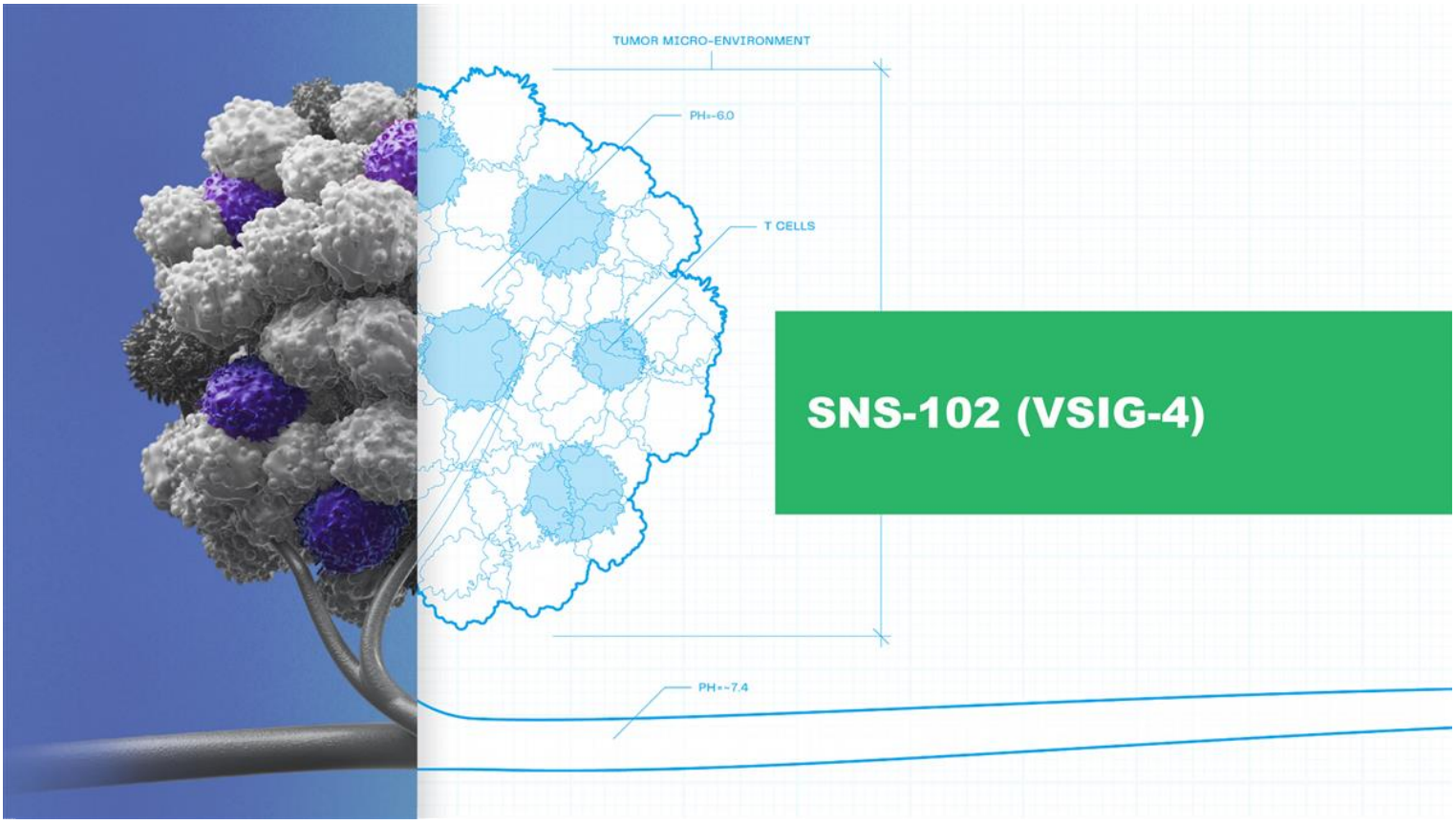
*Represents highest dose level in monotherapy arm as of January 2, 2024
*As of cut-off date of October 3, 2023

Completed and Anticipated SNS-101 Clinical Milestones

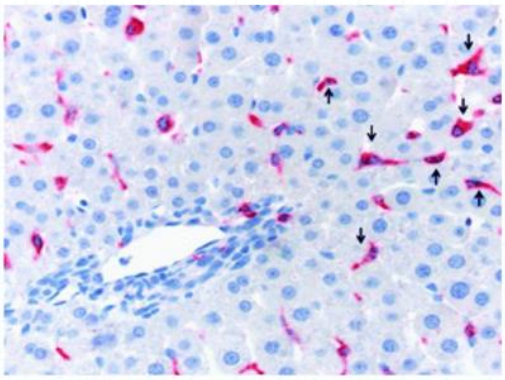




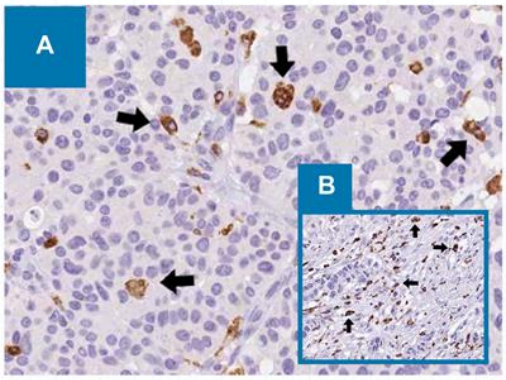
SNS-102 (VSIG-4)

VSIG4 is an Immunosuppressive Receptor with On-Target, Off-Tumor Challenges

Tissue macrophages (Kupffer cells) in the liver



Tumor-associated macrophages in tumors & stroma (inset)



In the liver, VSIG-4 …
Is expressed on Kupffer cells[1-2]

Appears to drive significant target-mediated drug disposition (TMDD) and clearance

In the tumor microenvironment, VSIG-4 …
Correlates with immunosuppressive "M2" macrophage infiltration[3]

Inhibits T cell activation[4]

Promotes tumor growth based on data from a syngeneic Lewis lung carcinoma model in knockout mice[5]

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1. doi: 10.1016/j.cell.2005.12.039.
2. doi: 10.4049/jimmunol.2101109.
3. doi: 10.4414/smw.2016.14301.
4. doi: 10.1172/JCI25673.
5. doi: 10.1038/labinvest.2014.73.

SNS-102 is a pH-sensitive Antibody Designed With the Goal of Reversing T-cell Suppression within the Tumor Microenvironment

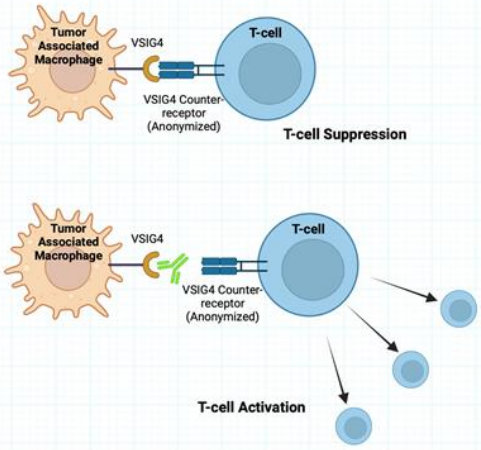
SNS-102 blocks the interaction of VSIG4 with its novel counter-receptor, which has been provisionally identified

Monovalent Affinity (K_D)

pH 6.0	pH 7.4
0.7nm	410 nm (~No binding)

Ratio = 585

SNS-102 is **585-fold more selective** for VSIG4 at low pH conditions



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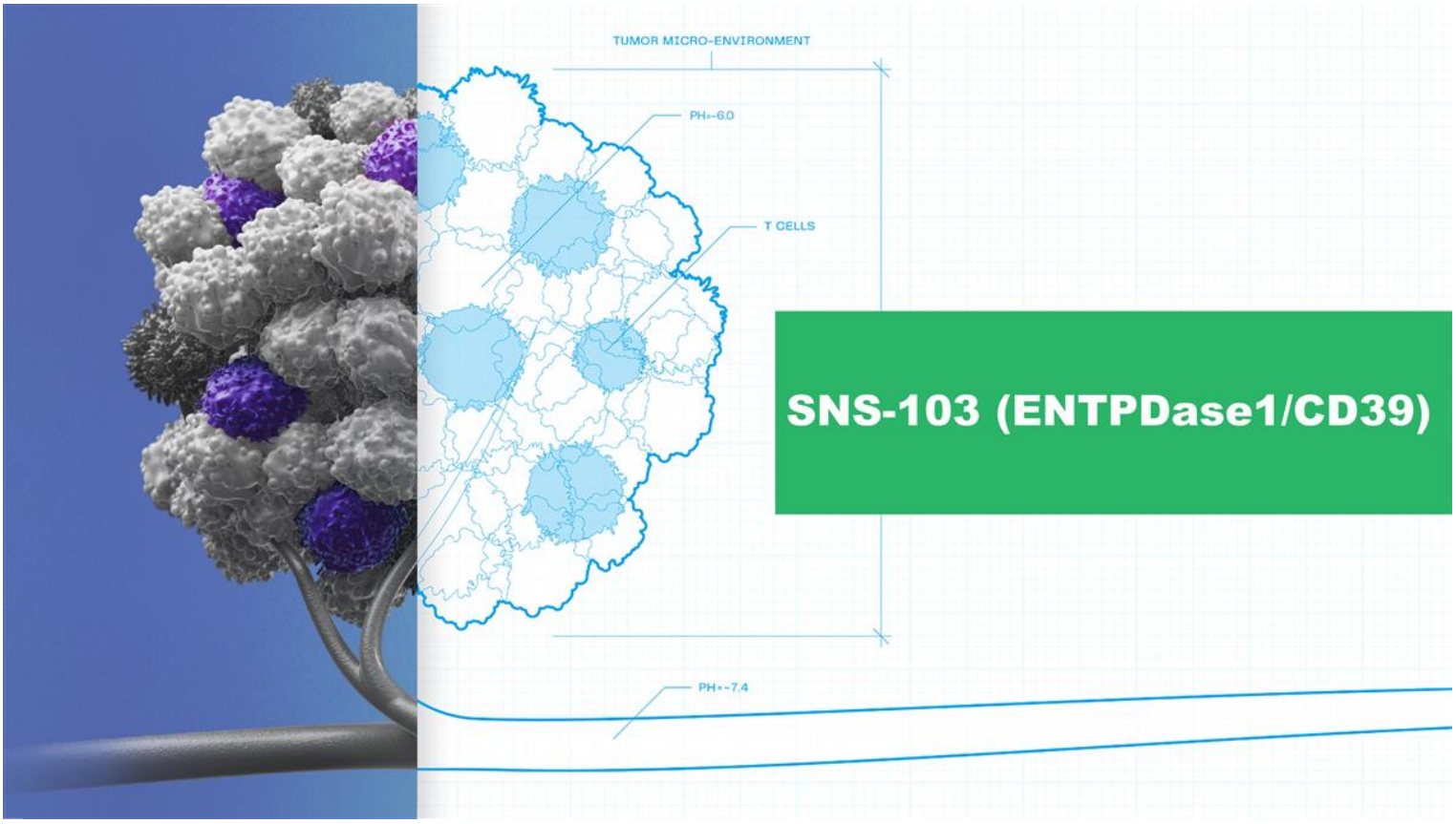
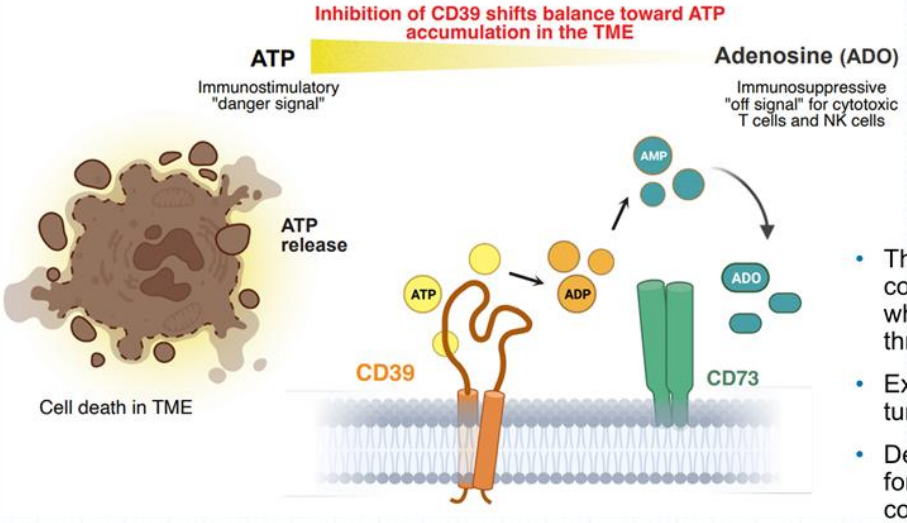
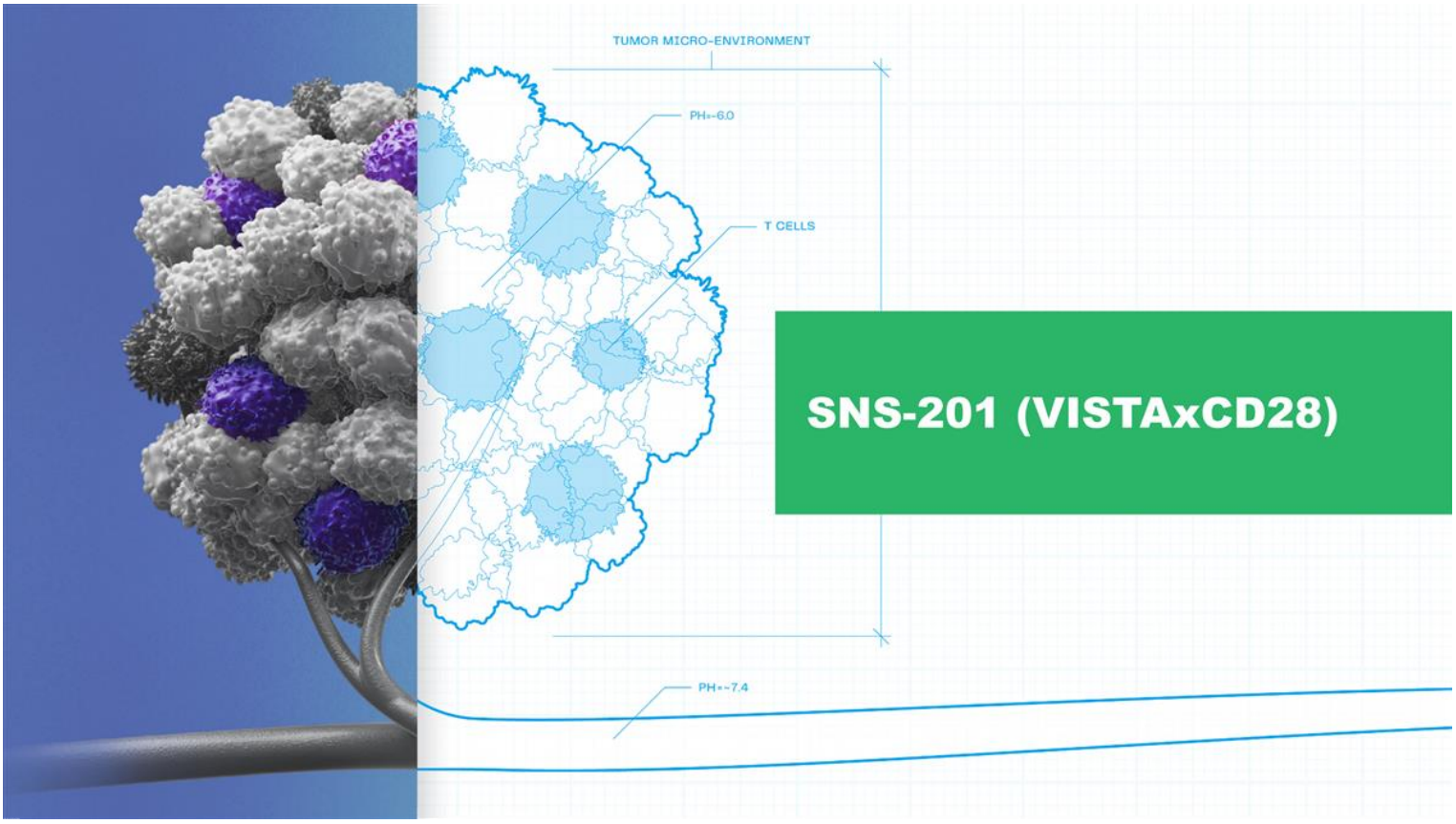

TUMOR MICRO-ENVIRONMENT
PH=~6.0
T CELLS
PH=~7.4
SNS-103 (ENTPDase1/CD39)

ENTPDase1 (CD39) is the Rate Limiting Enzyme in the Production of Immunosuppressive Adenosine



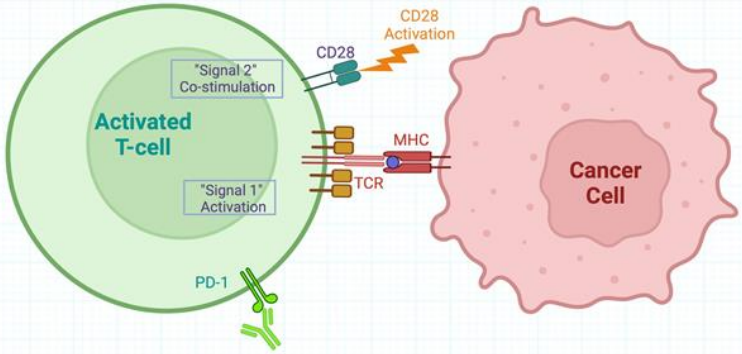
- The primary function of ENTPDase 1 is conversion of extracellular ATP to adenosine, which exerts immunosuppressive properties through binding to A2a/A2b receptors
- Expressed on various immune cells in both tumors and normal tissues
- Development of a TMAb antibody has potential for improved safety and PK profile compared to competitor CD39 mAbs



SNS-201 (VISTAxCD28)

Overcoming Toxicity Challenges Associated with Targeting CD28

CD28 is a major co-stimulatory pathway for T cells and a clinically validated therapeutic target for activating T cells in the tumor microenvironment



The Challenge

Targeting CD28 has shown clinical evidence of efficacy, but has been limited by dose-limiting toxicities resulting from systemic CD28 activation

Sensei's Solution

Leverage TMAb approach to potentially restrict CD28 activation to the tumor microenvironment, with no co-stimulation in the periphery

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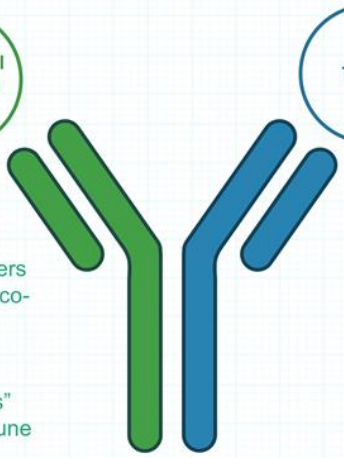
Bispecific TMAb Approach Can Generate T Cell Co-Stimulation Selectively Within the TME



pH-Sensitive anti-VISTA Arm

pH-sensitive arm confers tumor selective CD28 co-stimulation

Can be used in “cis” (tumor cell) or in “trans” (myeloid or other immune infiltrate)

Anti-CD28

CD28 agonist drives signal 2

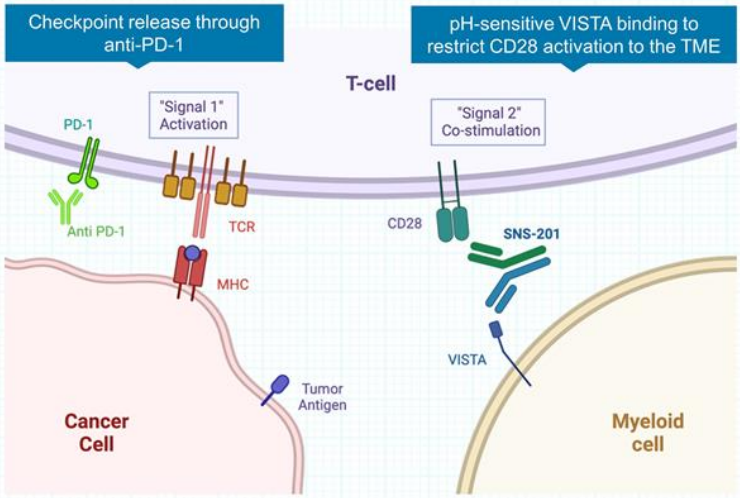
Co-Stimulatory VISTAxCD28 Bispecific

- ✓ Powerful co-stimulatory “signal 2” selectively within the TME
- ✓ Potential for little or no toxicity due to selective targeting
- ✓ No linkers or masks
- ✓ A single, off-the-shelf bispecific approach
- ✓ Avoids use of "tumor associated" antigens

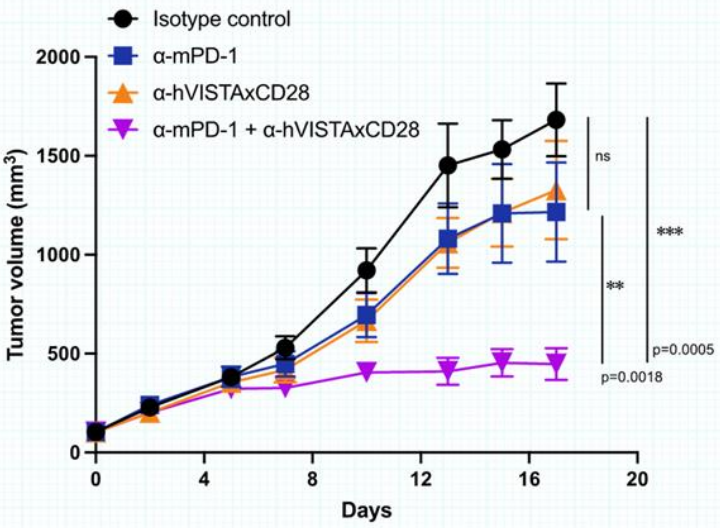
SNS-201 Provides Potential for Profound Anti-Tumor Activity By Selectively Co-Stimulating T Cells

SNS-201 (VISTAxCD28)

- Bispecific format with monovalent CD28 engagement
- Bivalent pH-selective VISTA binding for efficient engagement at low pH with cells displaying moderate VISTA copy numbers
- IgG1 backbone with silencing mutations abolishing Fc receptor interactions



In Vivo Study Shows Prototype Bispecific CD28xVISTA Induces Significant Tumor Growth Inhibition in Combo with anti-mPD-1



NS = not significant
*** = P<0.001
** = P<0.01

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Engineered Selectivity to Extend the Clinical Reach of IO Agents

LEAD PROGRAM

- SNS-101, a conditionally active antibody targeting VISTA
- Initial Phase 1 data demonstrate well tolerated safety profile & potentially best-in-class pharmacokinetics (PK)

TMAb PLATFORM

- Conditionally active antibodies designed to widen therapeutic window and enable druggability of promising oncology targets

EXPECTED MILESTONES

- Initial PK & safety combination dose escalation data in Q1 2024
- Topline monotherapy dose escalation data in Q2 2024
- Topline combination dose escalation data in Q3 2024
- Initial dose expansion data by end of 2024

FINANCIALS

- Ended Q3 2023: $72M*
- Cash runway into Q4 2025
- Cash currently expected to reach midway into Phase 2 clinical studies for SNS-101

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*Consists of cash, cash equivalents and marketable securities

Key Partnerships Supporting SNS-101's Clinical Development

Potential opportunities for combination therapy and biomarker identification

Partner / Collaborator	Goal	Description
REGENERON Clinical Supply Agreement	Support evaluation of SNS-101 in combination with Libtayo® (cemiplimab) in planned Phase 1/2 clinical trial	• Sensei to fund planned clinical trial • Regeneron to provide Libtayo® • Sensei maintains global development and commercial rights to SNS-101
NIH NATIONAL CANCER INSTITUTE Cooperative Research & Development Agreement	Further elucidate role of VISTA in immune checkpoint resistance and expand potential of SNS-101 as a combination therapy beyond anti-PD-1	• Sensei collaborating with NCI Center for Immuno-Oncology Co-Directors, Jeffrey Schlom, Ph.D., and James Gulley, M.D., Ph.D. • Preclinical studies will assess SNS-101 mechanism of action in combination with therapies beyond anti-PD-1
Washington University in St. Louis Research Collaboration	Further study the mechanism of SNS-101's anti-tumor activity	• Sensei collaborating with laboratory of immuno-oncology KOL, Robert Schreiber, Ph.D. • Preclinical studies will include identification of SNS-101 response biomarkers

Commercially Validated Precedent for pH-sensitive Approach

Soliris® (eculizumab), an anti-C5 monoclonal antibody (mAb), was considered standard of care for patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome, but had a short half-life as a result of extensive TMDD.

Engineering eculizumab using histidine substitutions resulted in a pH-sensitive mAb with markedly improved half-life.

Antibody Engineering of Solaris Led to pH Sensitivity and Half-Life Improvements

	Soliris (Eculizumab)	→	Ultomiris (Ravulizumab, ALXN1210)
K_D pH 7.4 (nM)	0.03		0.49
K_D pH 6.0 (nM)	0.6		22
$t_{½}$ (d)	**3.9**		**13.4**

Revulizumab utilized histidine insertions into the CDR regions (VH_Y27H, VH_S57H) and Fc substitutions (M428L, N434S) of eculizumab

Due to its longer half-life (13.4d vs 3.9d), ravulizumab given every 8w achieved noninferiority compared with eculizumab given every 2w for all efficacy endpoints, while maintaining a similar safety profile.

2018: FDA approves Ultomiris® (ravulizumab, ALXN1210)

2020: Ultomiris sales = $1.08 billion

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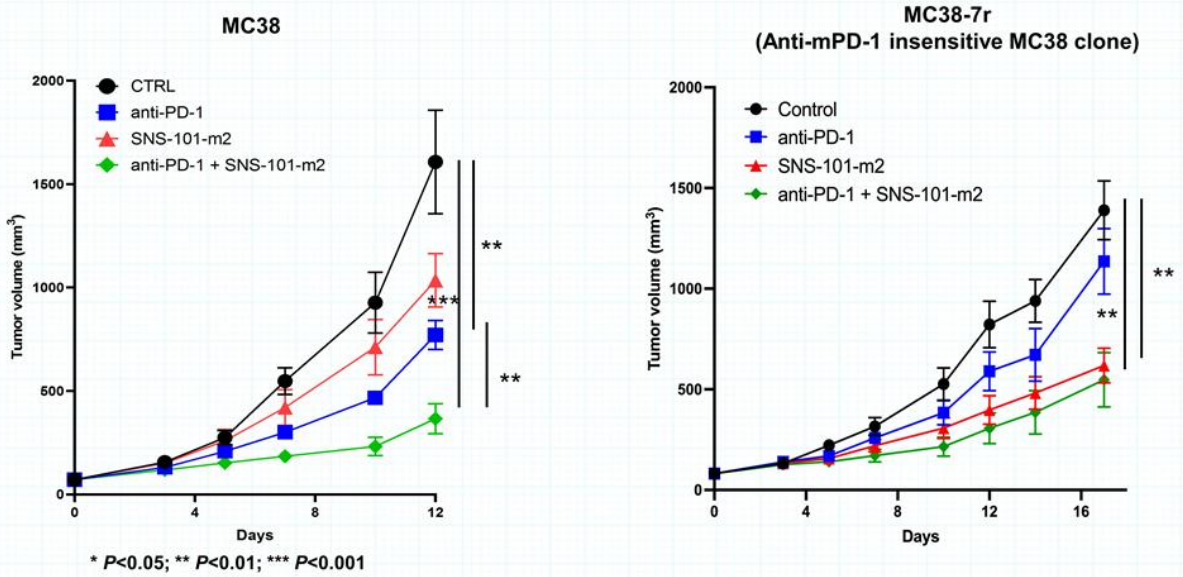
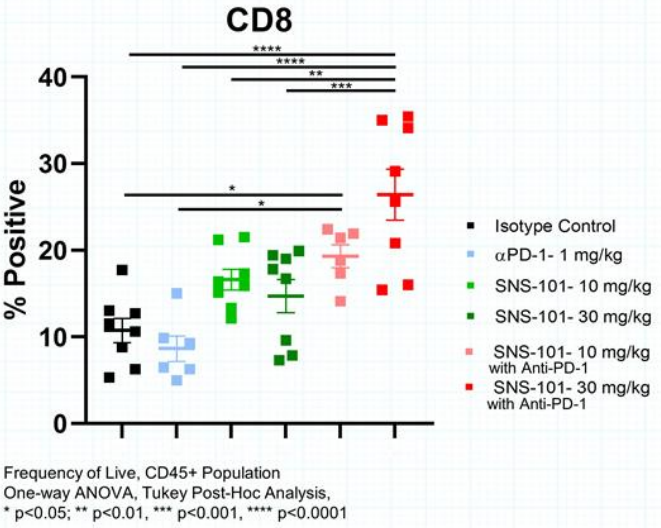
Sheridan et al, PLOS One, April 2018 (https://doi.org/10.1371/journal.pone.0195909)
Lee et al, Blood, (doi:10.1182/blood-2018-09-876136)
Sales figures: https://media.alexion.com/news-releases/news-release-details/alexion-reports-fourth-quarter-and-full-year-2020-results

Single-agent Activity and Deepened Anti-tumor Responses to PD-1 Combo in Human VISTA KI Mice *In vivo*

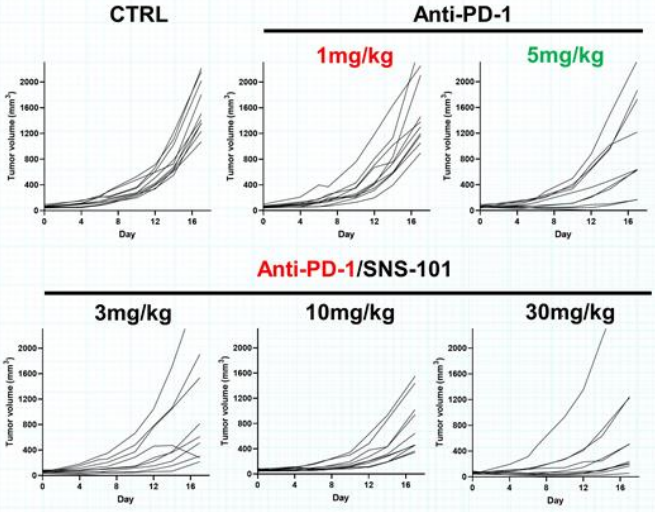


* *P*<0.05; ** *P*<0.01; *** *P*<0.001

SNS-101 Increased CD8 T-cells in Combination With Anti-PD-1 in MC38 Tumors *In Vivo*



Frequency of Live, CD45+ Population
One-way ANOVA, Tukey Post-Hoc Analysis,
* p<0.05; ** p<0.01, *** p<0.001, **** p<0.0001



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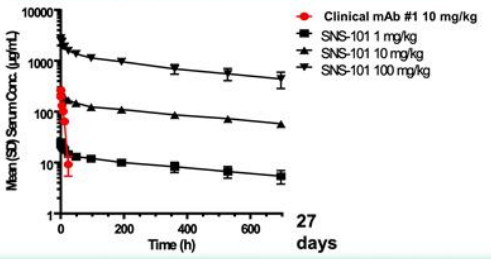
PK Sink Continues to be an Issue with Non-pH-Sensitive VISTA programs*

SNS-101 is designed to overcome elimination kinetics and half-life related to PK sink observed in non-pH-sensitive VISTA programs

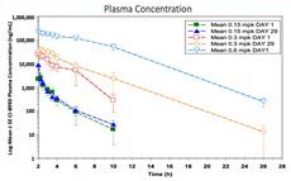
Linear

SNS-101 Cyno PK

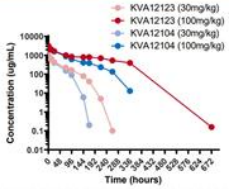


Non-linear

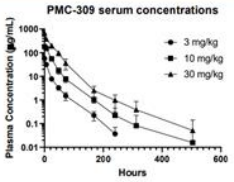
Curis CI-8993 Plasma Concentration



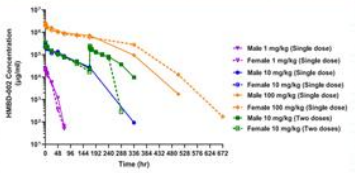
Kineta KVA12123 Cyno PK



Abcine PMC-309 Serum Conc Cyno



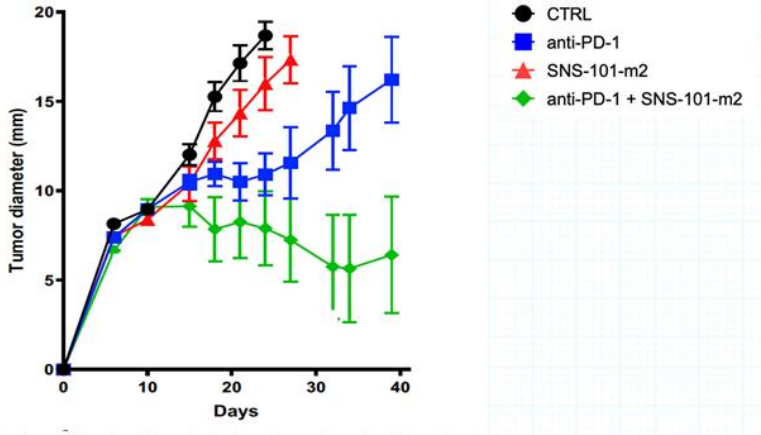
Hummingbird HMBD-002 Preclinical PK

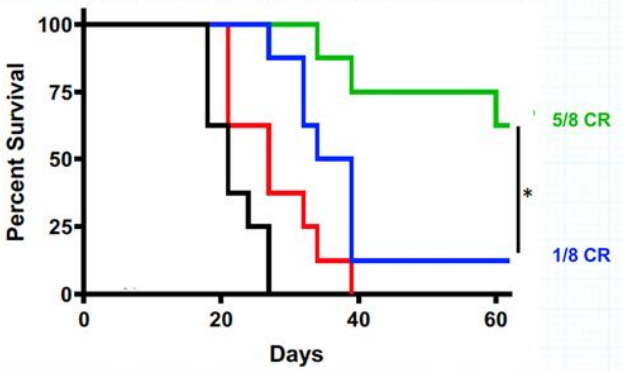


1. Hummingbird SITC 2022; 2. Kineta Corporate Presentation; 3. Abcine, SITC 2022; 4. Curis, SITC 2022

Each graph differs by time course based on data presented

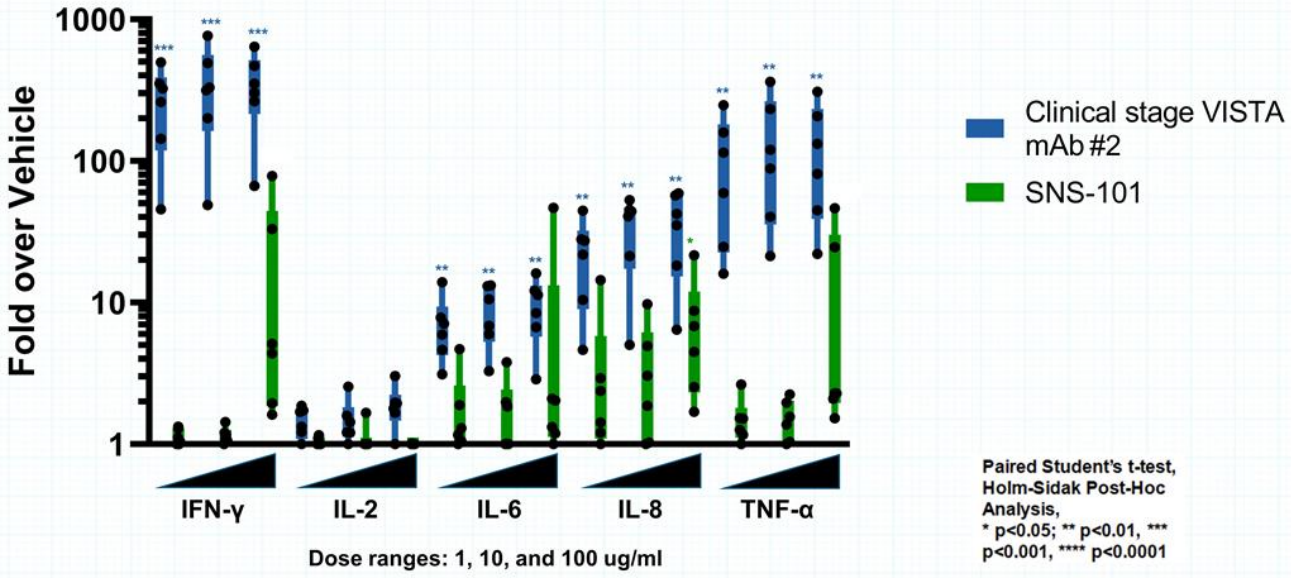
SNS-101 Re-sensitized Anti-PD-1 Insensitive Sarcoma Tumors in Human VISTA Knock-in Mice





* p<0.05

SNS-101 Induced Substantially Lower Cytokine Release in Whole-blood Assay at Neutral pH Compared to pH-independent VISTA Antibody



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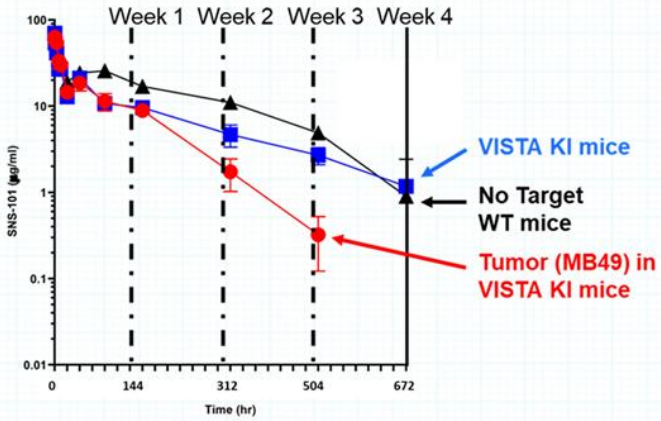
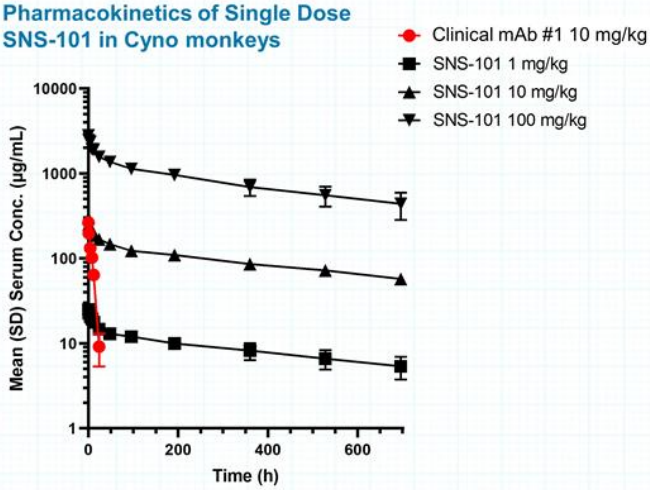
SNS-101 Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - *No Significant TMDD in Human VISTA KI Mice or Non-human Primates*

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



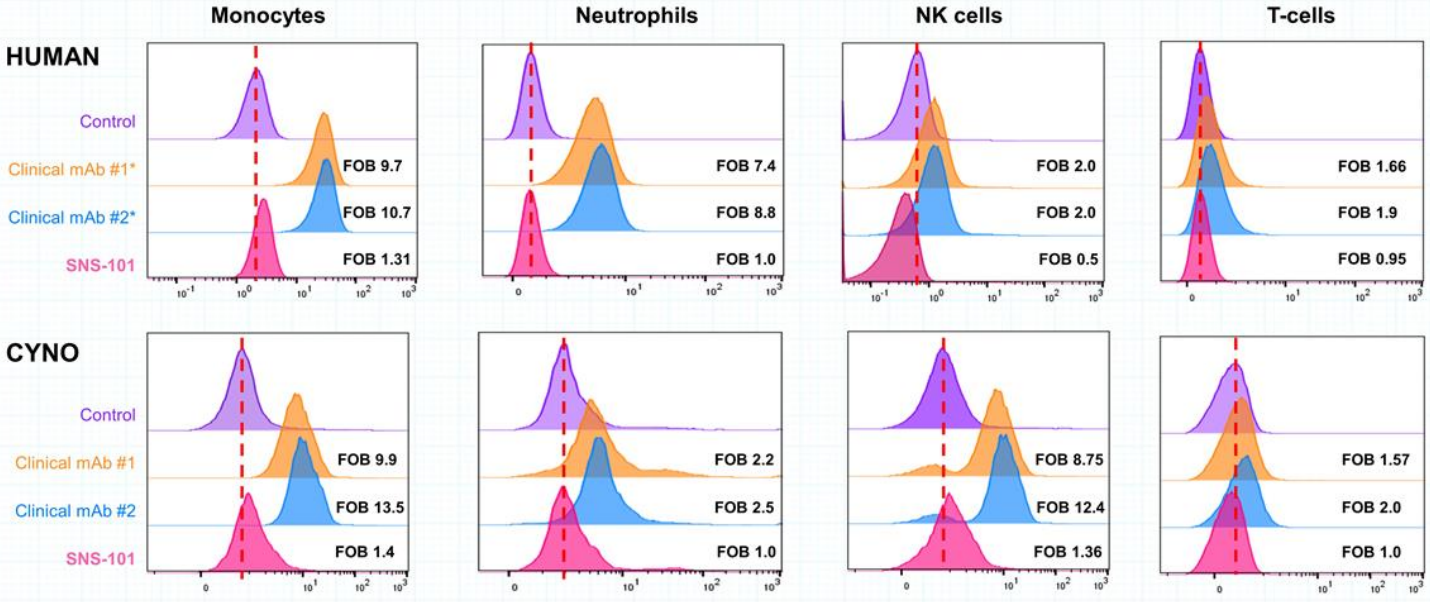
Demonstrated a long mean residence time in the blood, indicating a lack of significant target-mediated drug disposition (TMDD) and clearance in non-malignant tissues

Pharmacokinetics of Single Dose SNS-101 in Cyno monkeys



SNS-101 displayed linear elimination kinetics unlike a pH-independent anti-VISTA mAb, which demonstrated TMDD and rapid clearance

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

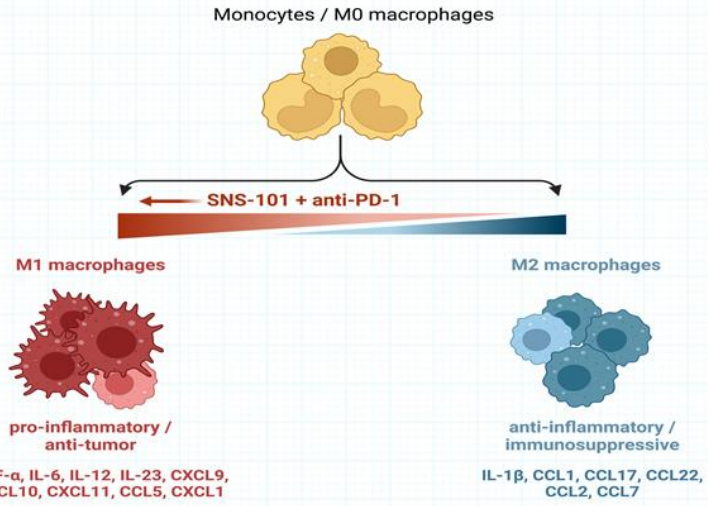


*Clinical mAb #1 & #2 are pH-independent VISTA antibodies

Targeting VISTA and PD-1 Checkpoints in the TME Promotes Anti-tumoral M1 Macrophage Polarization

SNS-101 targets suppressive signaling in the myeloid compartment, and in combination with anti-PD-1 may help shift the balance of macrophage polarization toward an anti-tumor M1 phenotype

M1 macrophages are anti-tumorigenic through secretion of pro-inflammatory cytokines and chemokines, and driving of Th1 CD4+ T cell responses



M2 macrophages are immunosuppressive; pro-tumor TAMs are a subset of M2-type cells