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 3, 2023

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 November 3, 2023, Sensei Biotherapeutics, Inc. (the "Company") issued a press release titled "Sensei Biotherapeutics Reports Favorable Clinical Data for SNS-101 at 2023 SITC Annual Meeting." A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

On November 3, 2023, the Company updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Item 7.01 and the exhibits 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. press release, dated November 3, 2023
99.2	Sensei Biotherapeutics, Inc. corporate presentation, dated November 3, 2023
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: November 3, 2023

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

Exhibit 99.1

Sensei Biotherapeutics Reports Favorable Clinical Data for SNS-101 at 2023 SITC Annual Meeting

- Clinical dose escalation data for SNS-101 monotherapy show well tolerated safety profile, potentially best-in-class pharmacokinetics, and encouraging cytokine release profile across multiple dose cohorts -

- First VISTA-blocking antibody administered at a dose anticipated to be therapeutically relevant without eliciting dose-limiting toxicity -

- Monotherapy data from Phase 1/2 study to be presented in a late-breaking poster presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting -

BOSTON, MA – November 03, 2023 – Sensei Biotherapeutics, Inc. (Nasdaq: SNSE), a clinical stage immuno-oncology company focused on the discovery and development of next-generation therapeutics for cancer patients, today reported initial data from the monotherapy dose-escalation portion of its Phase 1/2 clinical trial for SNS-101, a conditionally active, human monoclonal antibody targeting the immune checkpoint VISTA (V-domain Ig suppressor of T cell activation). The data, to be presented in a late-breaker poster presentation at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting, suggest a potential best-in-class safety and pharmacokinetic profile among VISTA blocking antibodies and the potential to overcome long-standing pharmacological challenges encountered by first generation approaches to blocking VISTA.

“We are pleased to report favorable clinical data for SNS-101, a pioneering VISTA-blocking antibody that provides validation of our conditionally active approach. The data support that this highly innovative antibody is well tolerated across dose levels tested to date, shows linear, dose-dependent pharmacokinetics predicted preclinically to elicit immune-mediated anti-tumor activity, and a cytokine profile consistent with an absence of cytokine release syndrome,” said John Celebi, President and Chief Executive Officer of Sensei Biotherapeutics. “Data from this clinical study to date provides important initial evidence that SNS-101 can provide clinically meaningful and mechanistic differentiation from first generation anti-VISTA approaches, as indicated by SNS-101 dose levels that are at least 10 times higher than the first clinical study of a competitor VISTA antibody that was prematurely halted due to cytokine release syndrome and poor pharmacokinetics. We believe this represents a foundational clinical achievement in the pursuit of a transformational VISTA-blocking antibody, and we look forward to building on this success with additional data readouts, including efficacy analysis, expected next year.”

The multi-center Phase 1/2 clinical trial is a dose escalation study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of SNS-101 as both a monotherapy and in combination with Regeneron’s PD-1 inhibitor Libtayo® (cemiplimab) in patients with advanced solid tumors.

Summary of reported data (as of the October 3, 2023 cutoff date):

- A total of 13 patients were enrolled in the study.
  - In the monotherapy dose escalation arm, ten patients were enrolled across four dosing cohorts receiving SNS-101 treatment at 0.3, 1, 3, or 10 mg/kg.
  - In the combination arm, three patients were enrolled at the first dose level of 3.0 mg/kg of SNS-101 plus 350 mg of Libtayo® (cemiplimab).

- Safety, cytokine expression and pharmacokinetic data were presented for seven patients from the first three monotherapy cohorts, all of which have cleared the dose-limiting toxicity assessment period.
    - A total of 11 adverse events (including one serious adverse event not considered related to SNS-101) was reported in five patients, with no dose-limiting toxicities observed. Only one adverse event (Grade 2 dermatitis acneiform) was considered related to SNS-101.
    - There were no instances of cytokine release syndrome and no significant changes in key inflammatory cytokines over time, consistent with preclinical studies.
    - Pharmacokinetic data demonstrate dose-proportional exposure consistent with lack of target mediated drug disposition, no notable accumulation with repeat dosing, and linear elimination kinetics of SNS-101, in concordance with preclinical data.

“Too many patients remain underserved by existing immunotherapies. SNS-101 highlights the potential of targeting VISTA through an innovative concept, thoughtful approach and a well-executed study as Sensei has done,” said Shiraj Sen, M.D., Ph.D., a medical oncologist at NEXT Oncology and investigator on the Phase 1/2 SNS-101 clinical trial. “I’m encouraged by the patient experience so far in the SNS-101 trial, including a potentially best-in-class safety profile and an every-three-week dosing schedule that helps alleviate the logistical burden imposed on patients by agents requiring more frequent administration due to their unfavorable PK profiles.”

Sensei expects to report initial safety and pharmacokinetic combination data in Q1 2024, with topline monotherapy data in Q2 2024, and topline combination data in 2024.

Presentation at SITC:

Title: A phase 1/2 study of safety, tolerability and pharmacokinetics of SNS-101, a pH-sensitive anti-VISTA mAb, as monotherapy and in combination with cemiplimab in patients with advanced solid tumors

Presentation type: Poster (late breaking abstract)

Abstract Number: 1532

Date and time: Saturday, November 4, 2023, at 9 a.m. PT – 8:30 p.m. PT

Location: Exhibit Halls A and B1 – San Diego Convention Center

Lead authors: Shiraj Sen, M.D., Ph.D. and F. Donelson Smith, Ph.D.

A copy of the presentation materials will be added to the “Events & Presentations” section of the Company’s Investor Relations website at www.senseibio.com.

About Sensei Biotherapeutics:

Sensei Biotherapeutics (Nasdaq: SNSE) is a clinical stage immuno-oncology company focused on the discovery and development of next-generation therapeutics for cancer patients. Through its TMAb™ (Tumor Microenvironment Activated biologics) platform, Sensei develops conditionally active therapeutics designed to disable immunosuppressive signals or activate immunostimulatory signals selectively in the tumor microenvironment to unleash T cells against tumors. Sensei’s lead investigational candidate is SNS-101, a conditionally active antibody designed to block the V-domain Ig suppressor of T cell activation (VISTA) checkpoint selectively within the low pH tumor microenvironment, where VISTA acts as a suppressor of T cells by binding the receptor PSGL-1. The company is also developing SNS-102, a conditional binding monoclonal antibody targeting V-Set and Immunoglobulin Domain Containing 4 (VSIG-4), as well as SNS-103, also a conditionally active monoclonal antibody targeting ecto-nucleoside triphosphate diphosphohydrolase-1 (ENTPDase1), also known as CD39. For more information, please visit www.senseibio.com, and follow the company on Twitter @SenseiBio and LinkedIn.

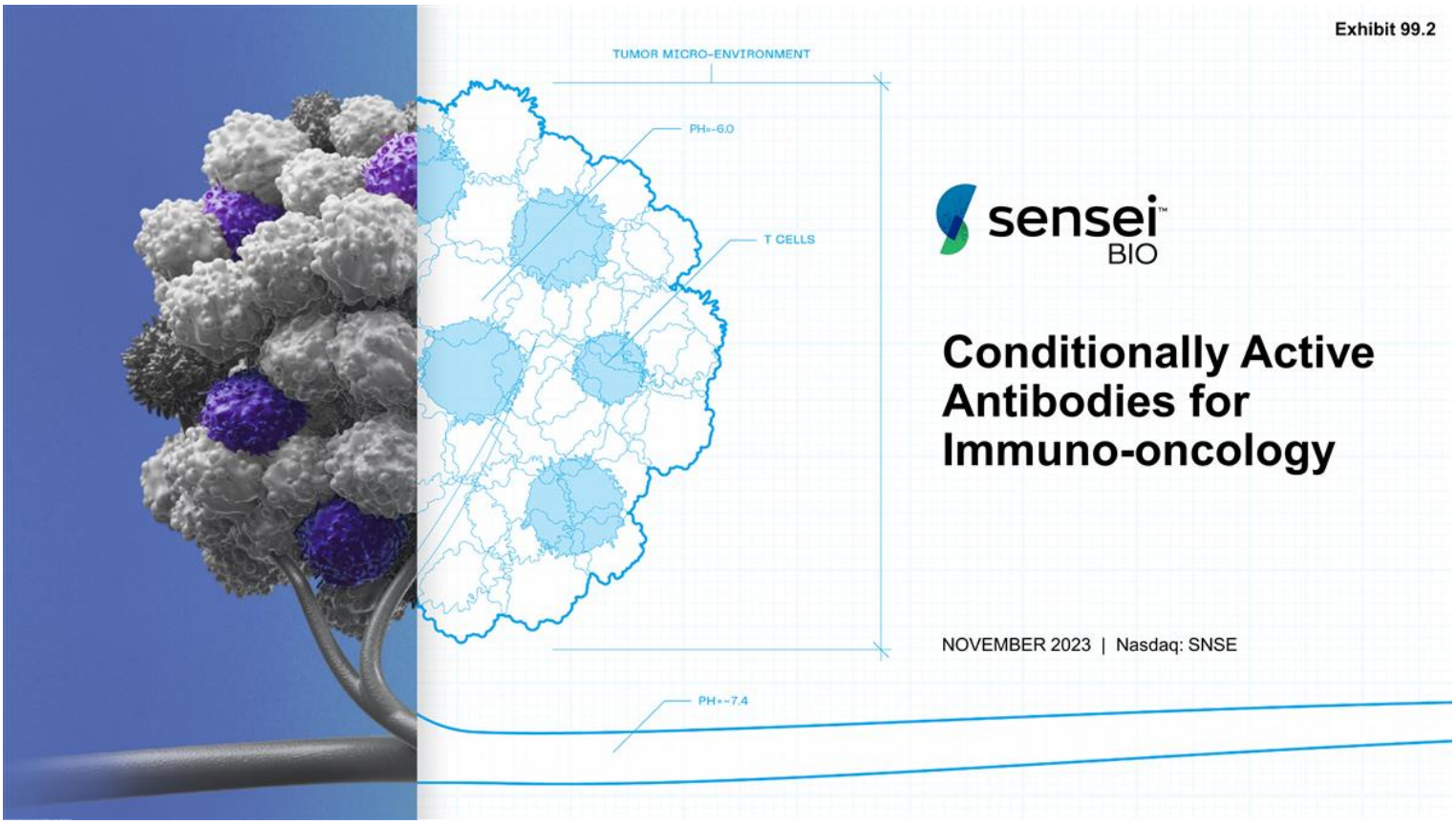
Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words and phrases such as “believe”, “designed to,” “expect”, “may”, “plan”, “potential”, “will”, and similar expressions, and are based on Sensei’s current beliefs and expectations. These forward-looking statements include expectations regarding the development and potential therapeutic benefits of Sensei’s product candidates, as well as the timing of Sensei’s Phase 1/2 clinical trial of SNS-101, including reporting of data therefrom. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the development of therapeutic product candidates, such as the risk that any one or more of Sensei’s product candidates will not be successfully developed or commercialized; the risk of delay or cessation of any planned 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, will not be replicated or will not continue in ongoing or future studies or clinical trials involving Sensei’s product candidates; the risk that Sensei’s product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that we anticipate; risks associated with Sensei’s dependence on third-party suppliers and manufacturers, including sole source suppliers, 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 risks and uncertainties that are described in Sensei’s Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission (SEC) on or about August 3, 2023 and Sensei’s other Periodic Reports filed with the SEC. Any forward-looking statements speak only as of the date of this press release and are based on information available to Sensei as of the date of this release, and Sensei assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

Investor Contact:
Michael Biega
Senior Director, Investor Relations
Sensei Biotherapeutics
mbiega@senseibio.com

Media Contact:
Chris Railey
Ten Bridge Communications
chris@tenbridgecommunications.com

Exhibit 99.2

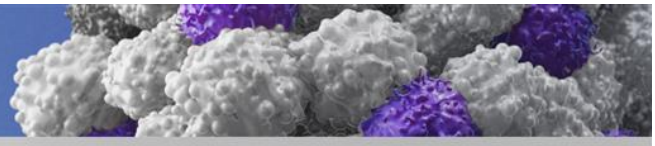


sensei™ BIO

Conditionally Active Antibodies for Immuno-oncology

NOVEMBER 2023 | Nasdaq: SNSE

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 profile and pharmacokinetic 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 availability of data from our preclinical studies; the timing of discovery and selection of product candidates; and our belief that our existing cash and cash equivalents will be sufficient to fund our operations at least into the second half 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, 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 August 3, 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

Engineered Selectivity to Extend the Clinical Reach of Immuno-oncology 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 data in Q1 2024

Topline monotherapy data in Q2 2024

Topline combination data in 2024

FINANCIALS

Ended Q2 2023: $78.8M*

Cash runway into 2H 2025

Cash currently sufficient to reach midway into Phase 2 clinical studies for SNS-101

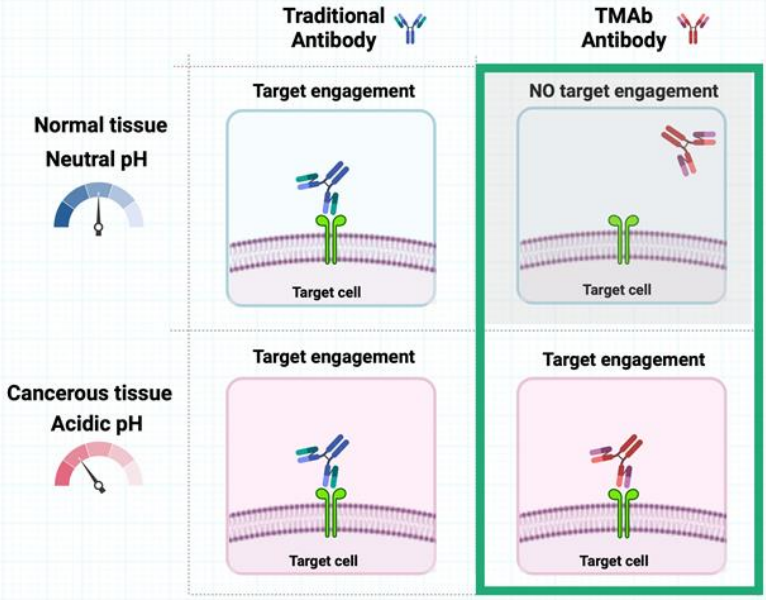
*Consists of cash, cash equivalents and marketable securities

Lack of Tumor Targeting is a Major Obstacle to 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 and more frequent dosing	Lower and less frequent doses by avoiding normal tissue binding
Suboptimal activity due to poor PK and dose-limiting toxicities	Powerful activity selectively focused on the tumor microenvironment

Only one new checkpoint inhibitor has been approved since the original CTLA-4 and PD-1/PD-L1 group

TMAb Antibodies are Designed to Bind Selectively in the Tumor Microenvironment



Lack of peripheral target engagement can improve safety and pharmacokinetic parameters while focusing action to the tumor microenvironment

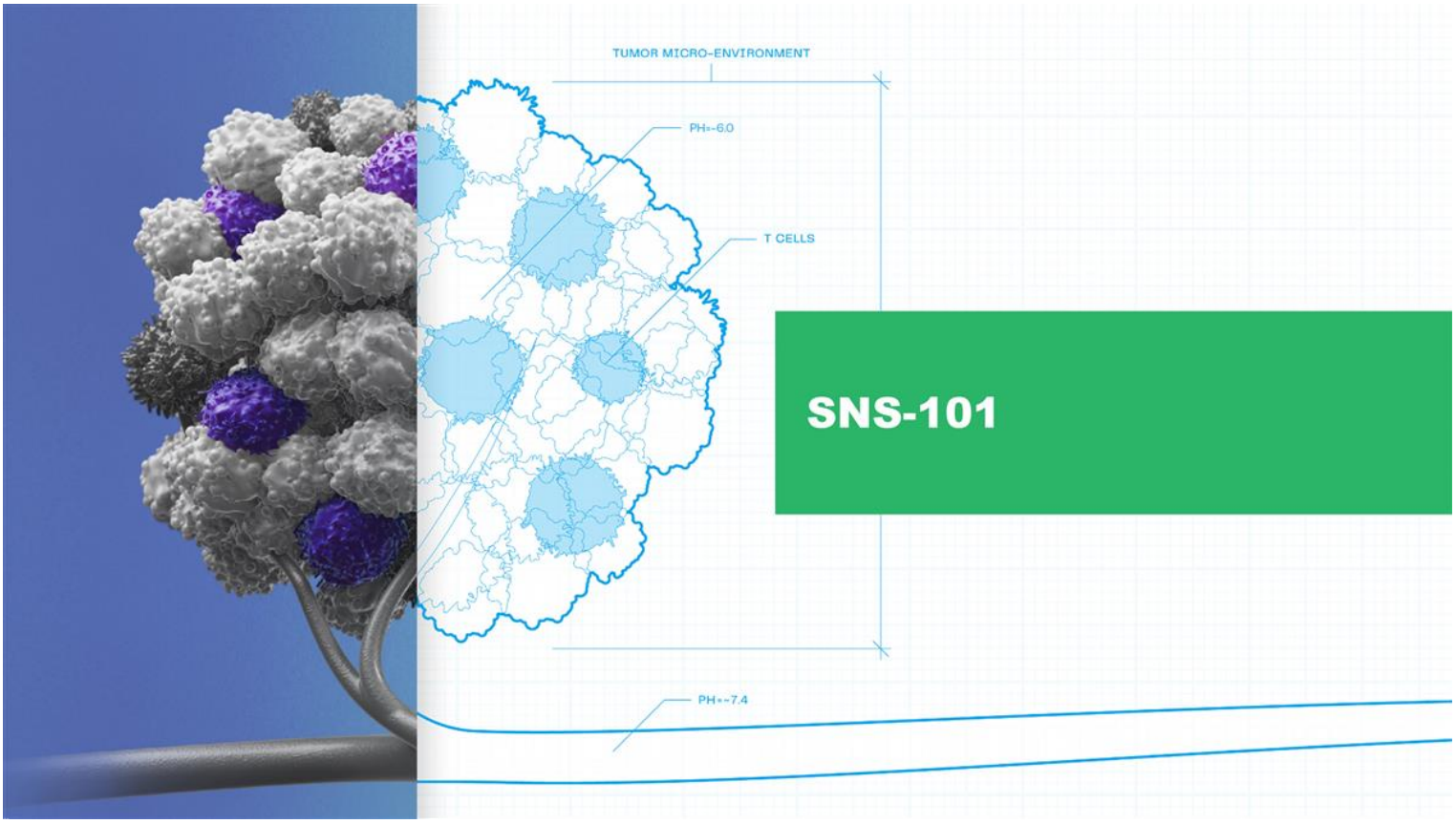
Innovative Pipeline of IO Drugs with Broad Commercial Potential

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.

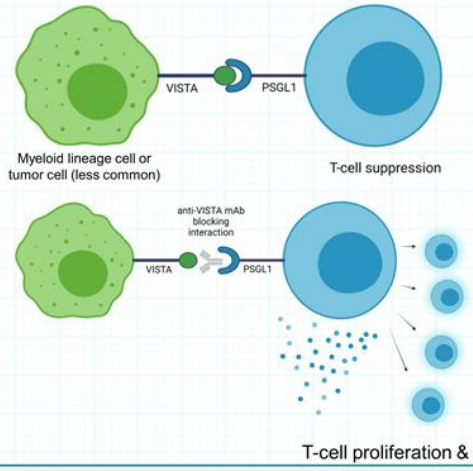


SNS-101

VISTA is a Potent T cell Checkpoint Extensively Expressed on Myeloid Cells[1]

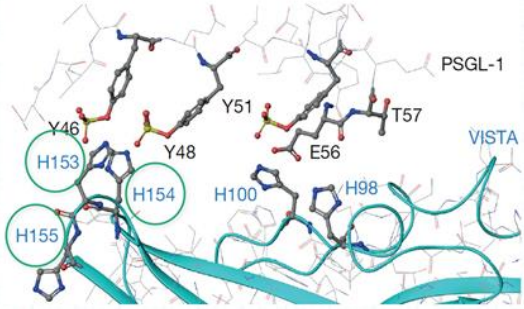
VISTA is a B7 family member that suppresses T cell function and is expressed extensively by myeloid cells

SNS-101 targets immunosuppressive function mediated by PSGL-1 and other receptors



VISTA has inherent pH sensitivity: its extracellular domain is uniquely rich in histidines[2]

SNS-101 has monovalent affinity of 0.218 nM at pH 6.0, with no observed binding at neutral pH



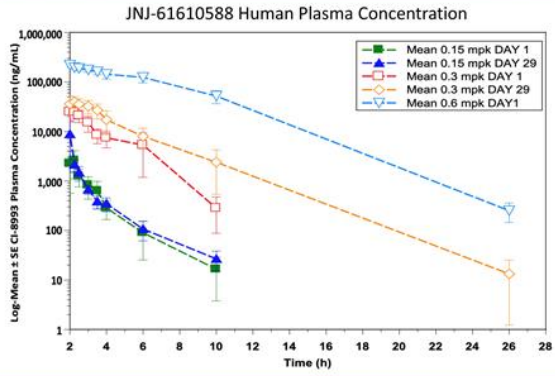
1. Lines et al. Cancer research vol. 74,7 (2014)
2. Johnston et al., Nature 2019

Historical Challenges Targeting VISTA-Positive Myeloid Cells Resulted in Early Clinical Trial Termination

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 a Differentiated, pH-Sensitive Antibody Designed to Overcome the Unique Challenges of VISTA

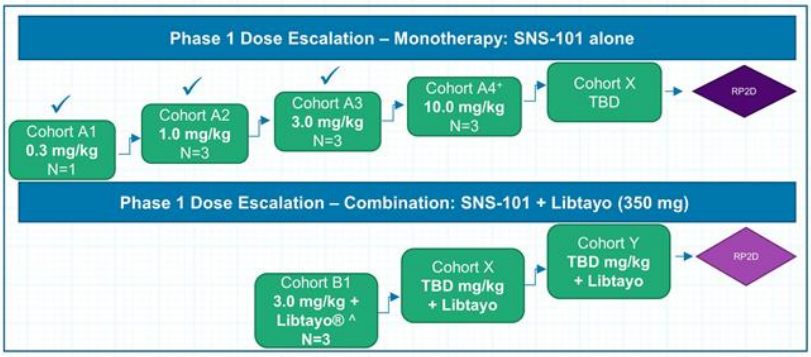
Differentiated Design and Mechanism	IgG1, Fc-active antibody designed to selectively block VISTA in the low-pH tumor microenvironment
Rapidly Enrolling Phase 1/2 Clinical Trial	Multi-center U.S. study as single agent and in combination with PD-1 inhibitor Libtayo®
Potential Best-in-Class Safety and PK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

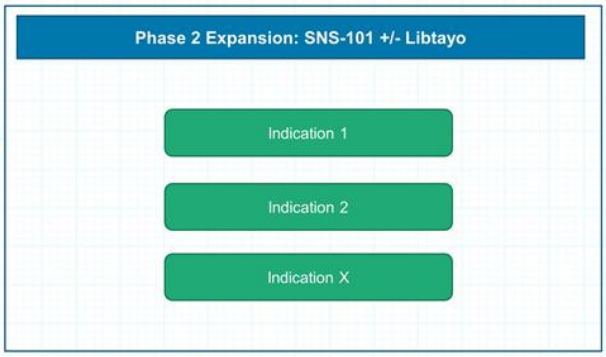
*As of safety cut-off date of October 3, 2023

SNS-101 Phase 1/2 Study

Phase 1 Study Design
Dose escalation using Bayesian Optimal Interval (BOIN) design

Anticipated Phase 2 Expansion Design
Single-arm, Simon two-stage minimax design incorporating an interim futility analysis





Patient Population	Study Objectives	Dosing
• Advanced solid tumors	• Primary endpoint: safety, tolerability & RP2D • Secondary endpoint: PK profile, immunogenicity & anti-tumor activity	• SNS-101 +/- Libtayo (350 mg) dosed as an IV infusion once every 3 weeks • Dose escalation/de-escalation will proceed following the BOIN design until the MTD/RP2D is determined

Patient Population	Study Objectives	Dosing
• Advanced solid tumors • Tumor types to be determined based on data from Ph1 dose escalation and emerging results from preclinical studies	• Primary endpoint: Anti-tumor activity • Secondary endpoint: Safety, tolerability, PK profile & immunogenicity	• SNS-101 +/- Libtayo (350 mg) dosed as an IV infusion once every 3 weeks • Dose will be determined from Ph1 dose escalation

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+ As of October 3, 2023, enrollment complete in Cohort A4 (10.0 mg/kg), pending DLT assessment period
^ As of October 3, 2023, enrollment complete in Cohort B1 (3.0 mg/kg of SNS-101 + 350 mg of Libtayo), pending DLT assessment period
RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose

SNS-101 Displayed Favorable Safety & Tolerability Profile

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

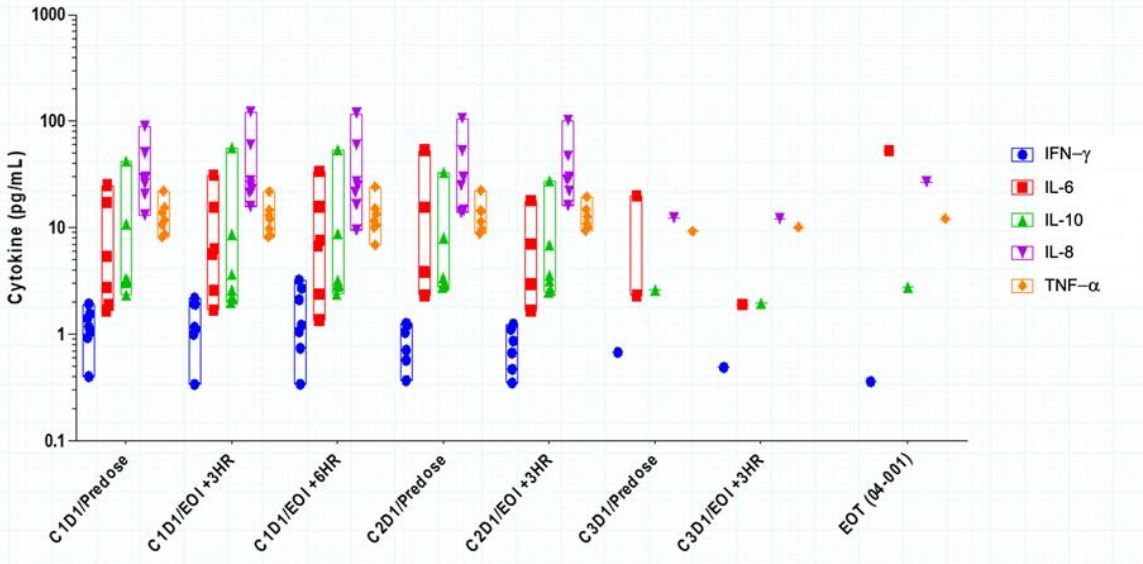
	0.3 mg/kg N=1 n (%)	1.0 mg/kg N=3 n (%)	3.0 mg/kg N=3 n (%)	Total N=7 n (%)
At least 1 TEAE	1	3	1	5 (71.4)
At least 1 SAE	0	0	1*	1* (14.3)
At least 1 TEAE leading to discontinuation	0	0	1*	1* (14.3)
DLTs	0	0	0	0
CRS events	**0**	**0**	**0**	**0**
≥Grade 3 TEAE	0	0	1*	1* (14.3)
Related TEAE	0	1#	0	1#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

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

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

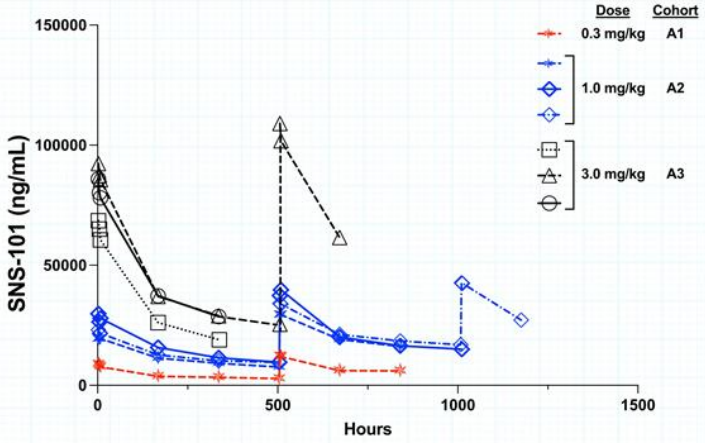
DLT = Dose limiting toxicity
CRS = Cytokine release syndrome
TEAE – Treatment emergent adverse event
SAE = Serious adverse event

Cytokine Data Consistent with Lack of Observed CRS



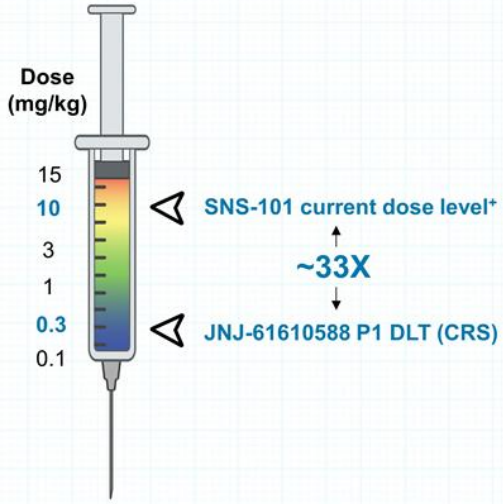
Cytokine analysis: Blood samples were taken pre-dose, 3 hours post-infusion and 6 hours post infusion at C1D1, and pre- and 3hr-post thereafter. Serum was assayed for indicated cytokines using a platform (MSD) that has been validated for clinical sample analysis.
Data from monotherapy dose escalation arm as of safety cut-off date of October 3, 2023

SNS-101 Clinical PK Data Show Linear Pharmacokinetics and Long Half-Life (Unlike Prior Anti-VISTA mAbs)



Supports Every 3 Week Dosing

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 cleared dose level (0.3 mg/kg) that caused CRS with JNJ
- No observed DLTs or CRS in Phase 1 study*
- No prophylaxis

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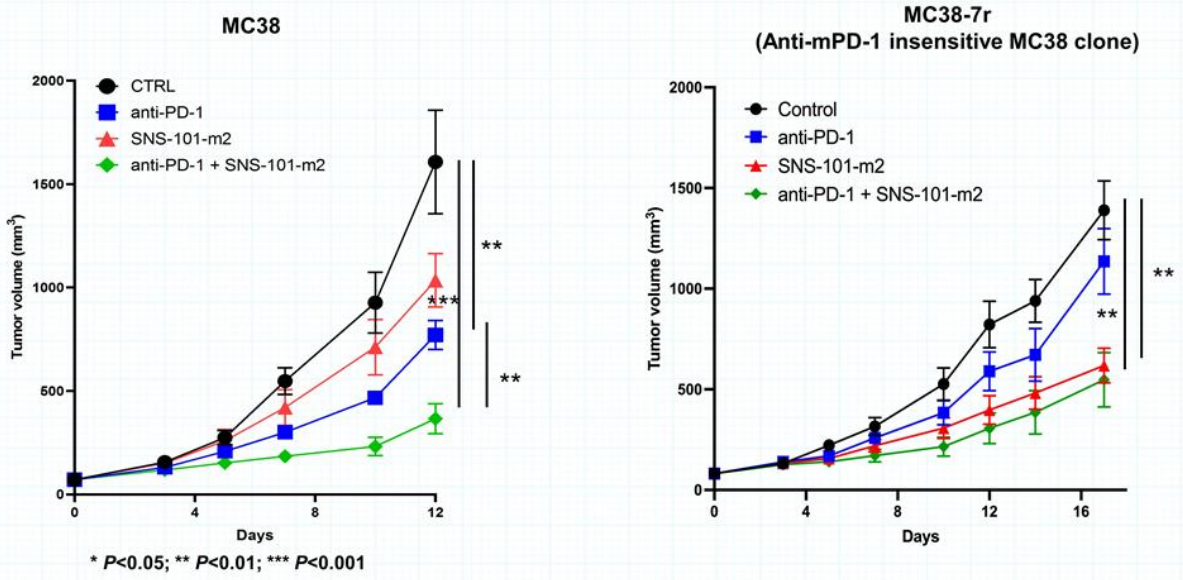
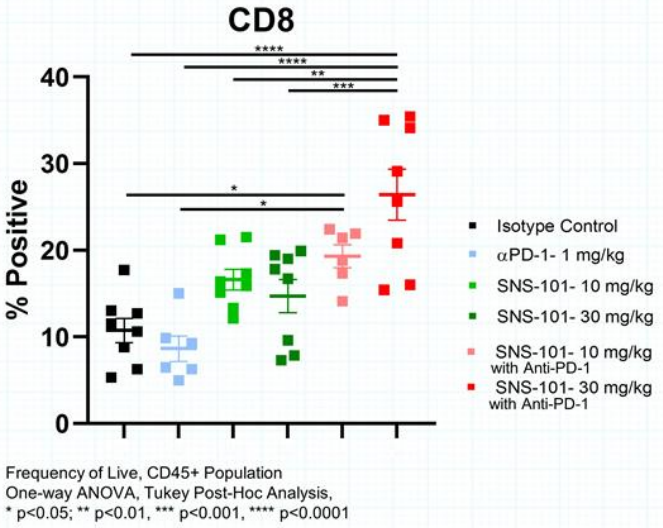
*Represents highest dose level in monotherapy arm as of October 3, 2023
*As of safety cut-off date of October 3, 2023

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

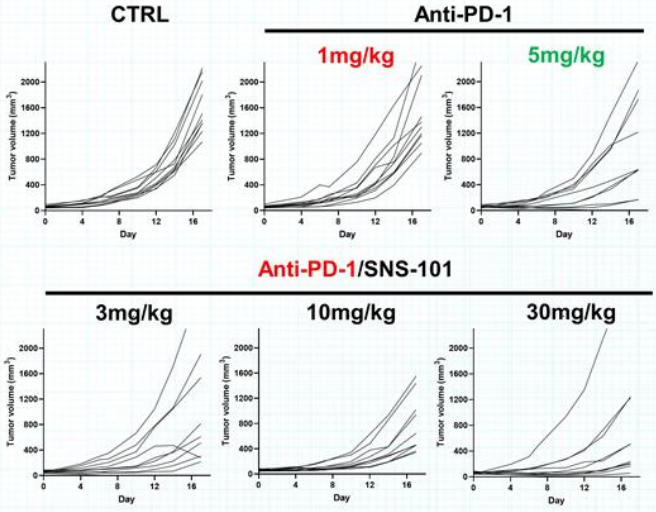


* *P*<0.05; ** *P*<0.01; *** *P*<0.001

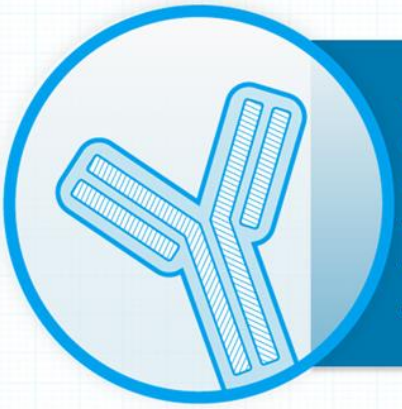
SNS-101 Increased CD8 T-cells in Combination With Anti-PD-1 in MC38 Tumors *In Vivo*



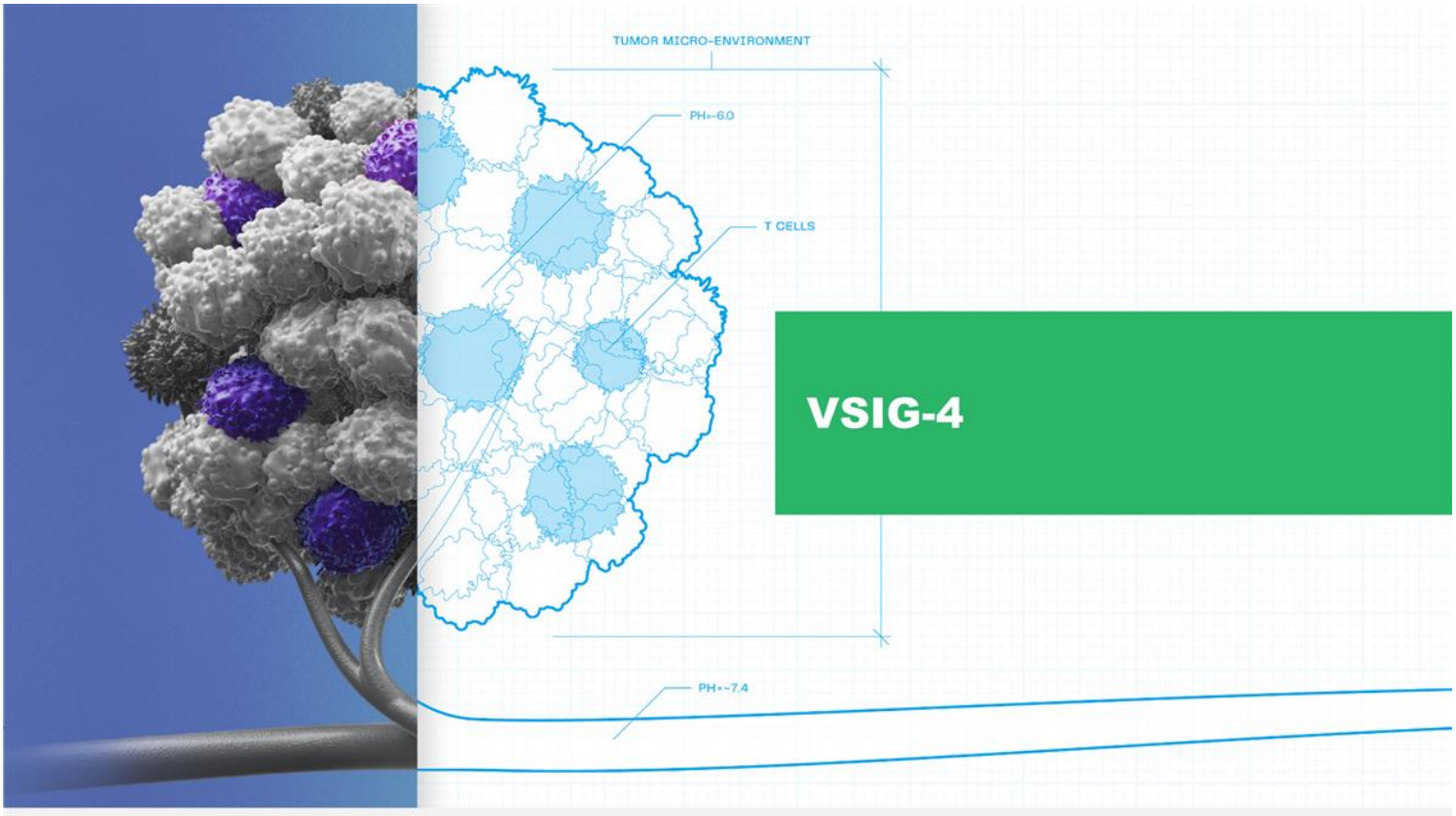
Frequency of Live, CD45+ Population
One-way ANOVA, Tukey Post-Hoc Analysis,
* p<0.05; ** p<0.01, *** p<0.001, **** p<0.0001



SNS-101 Completed and Anticipated Clinical Milestones



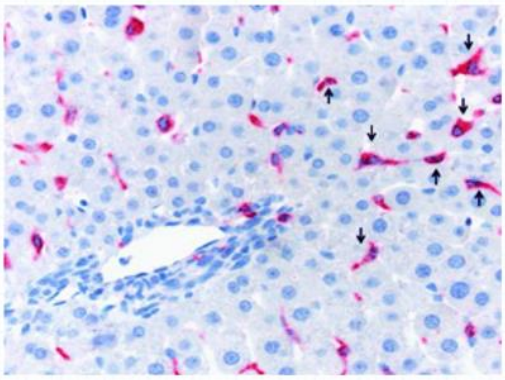
- ✓ **May 2023:** First patient dosed
- ✓ **Sept 2023:** First patient dosed in combination with Libtayo®
- ✓ **Q4 2023**: Initial monotherapy PK and safety data
- • **Q1 2024**: Initial combination PK and safety data
- • **Q2 2024:** Topline Phase 1 monotherapy data
- • **2024:** Topline combination data



VSIG-4

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

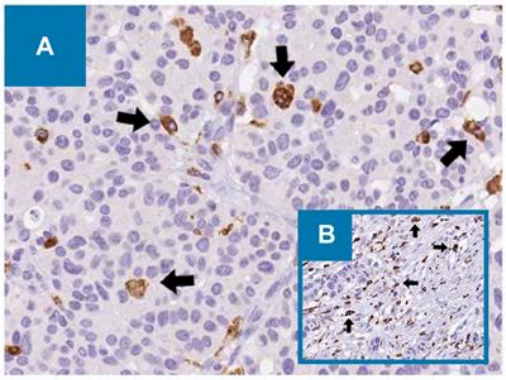
Tissue macrophages (Kupffer cells) in liver



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

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

Tumor-associated macrophages in tumor and stroma (inset)



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

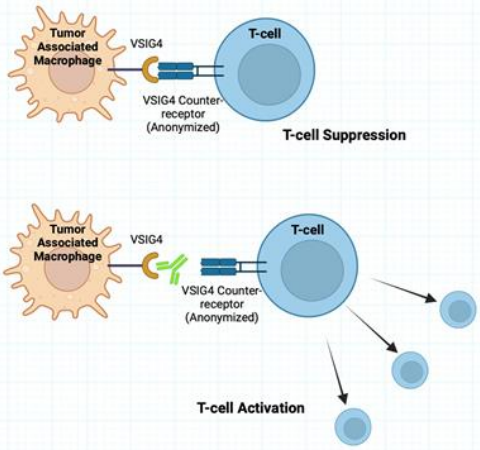
Inhibits T cell activation[4]

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

See references in Appendix

SNS-102 is a Highly pH-sensitive Antibody that Could Reverse T-cell Suppression within the Tumor Microenvironment

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



Plan to select product candidate in 2023

pH-Sensitive VSIG4 Parental Antibodies Selected for Further Optimization

Antibody Reference #	Ratio of pH Selectivity (6.0 vs 7.4)	Blockage of Immobilized VSIG4-T-cell Inhibition	Blockage of Cellular VSIG4-T-cell Inhibition
1	1	+	+
2	7	+	+
3	1	+	+
4	3	+	+
5	3	+/-	+
6	25	+	+
7	1	+	+
8	2	-	+

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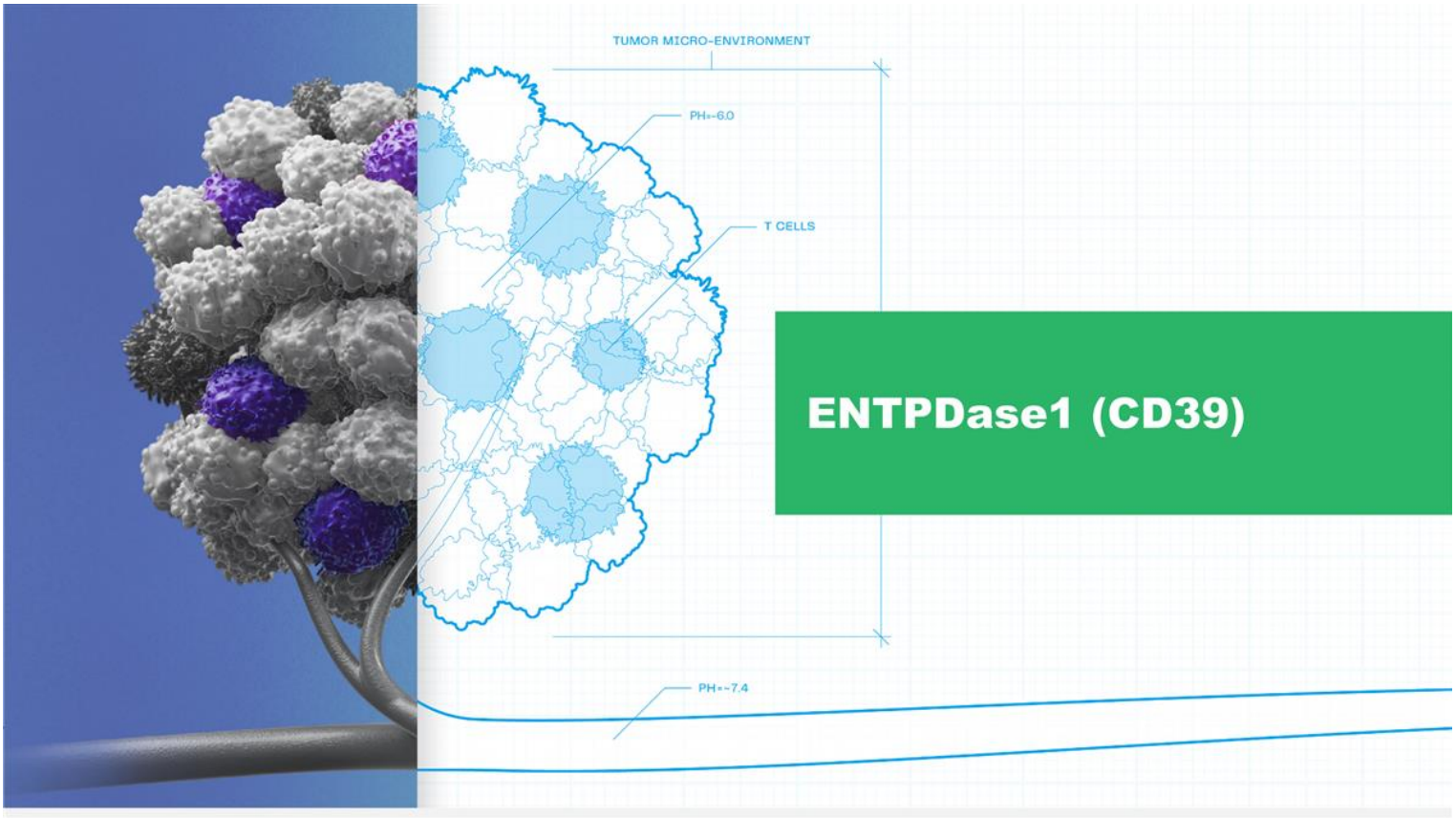
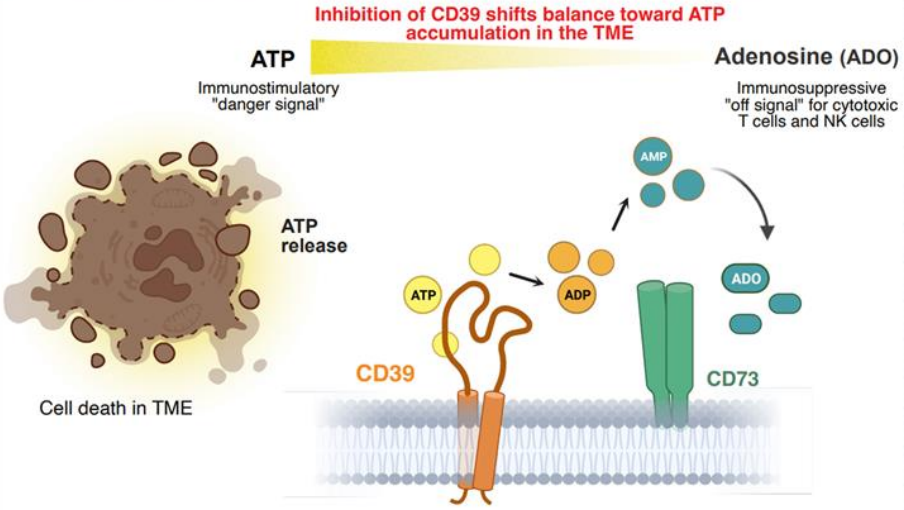


ENTPDase1 (CD39)

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



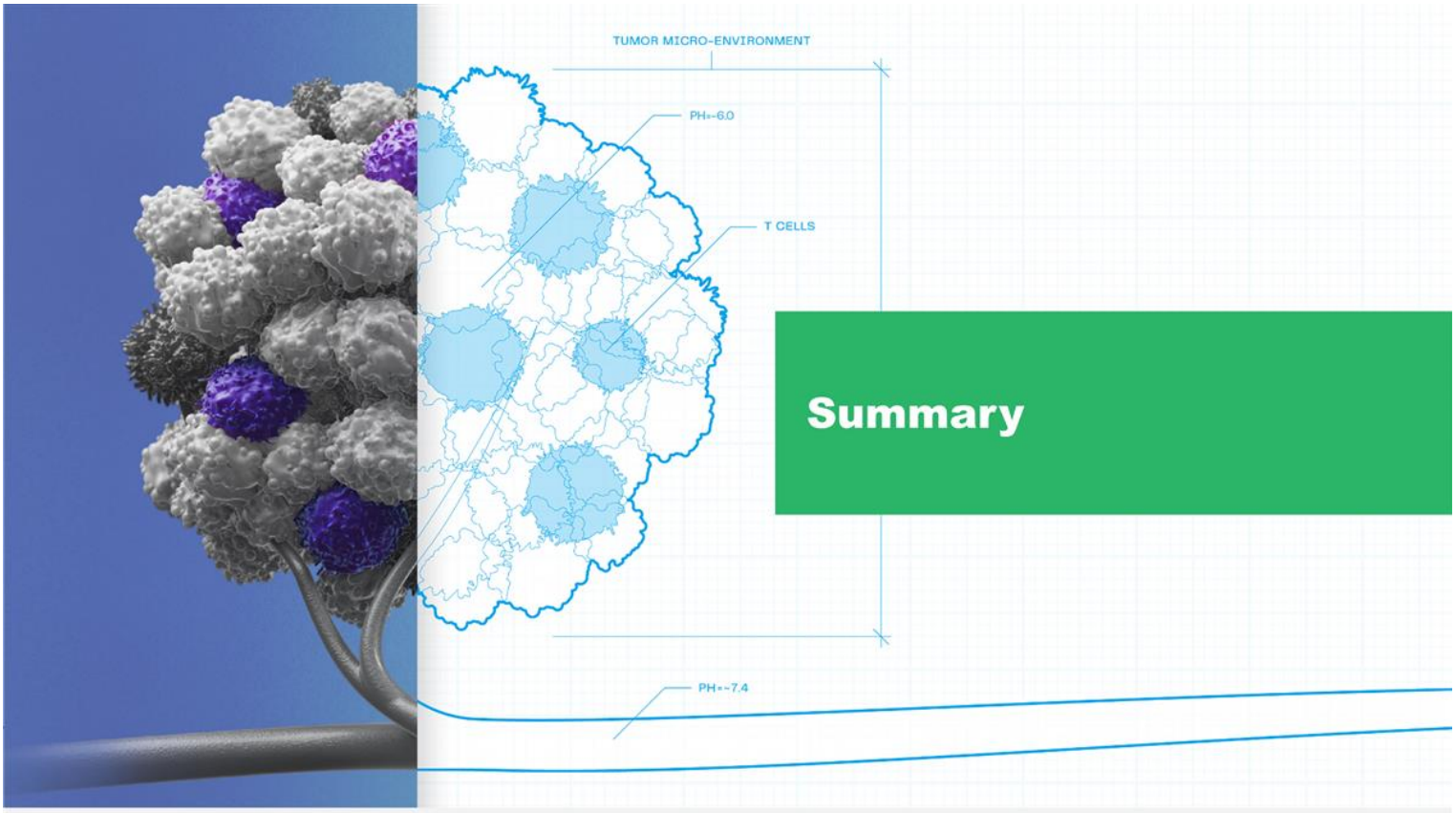
- Primary function is conversion of extracellular ATP (eATP) to adenosine (ADO), which exerts immunosuppressive properties through binding to A2a/A2b receptors (ADA)
- Expressed on various immune cells in both tumors and normal tissues

Sensei Has Identified pH-sensitive ENTPDase1 (CD39) Antibodies

- Development of a TMAb antibody has potential for improved safety and PK profile compared to competitor CD39 mAbs
- Plan to select product candidate in 2023

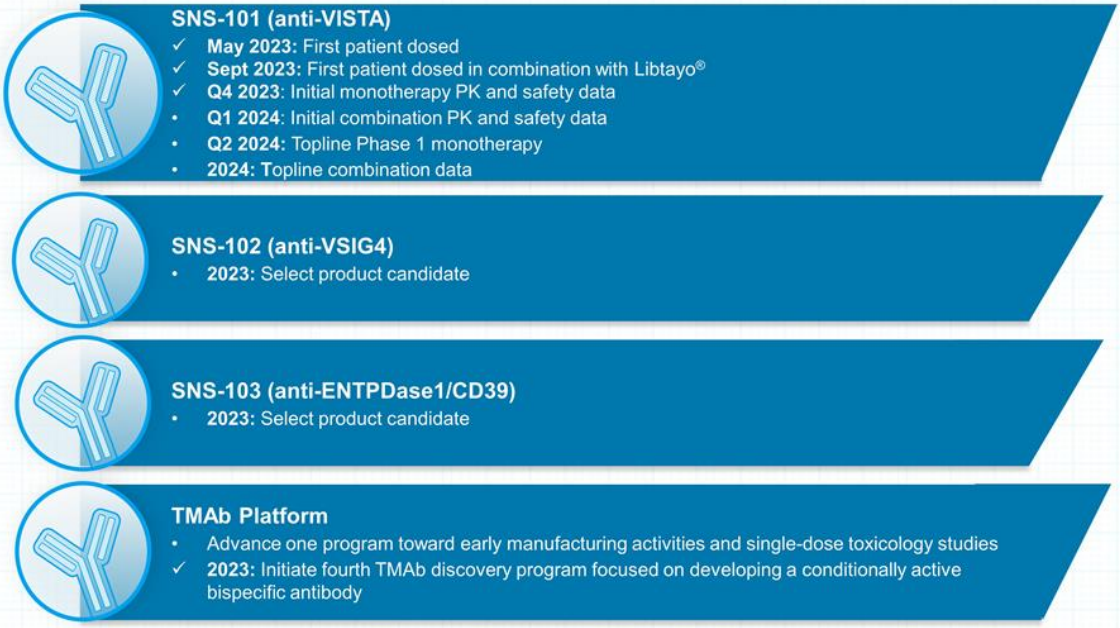
pH-Sensitive CD39 Parental Antibodies Selected for Further Optimization

Antibody Reference #	Ratio of pH Selectivity (6.0 vs 7.4)
1	1
2	6
3	4
4	5
5	18
6	1
7	1
8	1



Summary

Completed and Anticipated Program Milestones



Engineered Selectivity to Extend the Clinical Reach of Immuno-oncology 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 data in Q1 2024

Topline monotherapy data in Q2 2024

Topline combination data in 2024

FINANCIALS

Ended Q2 2023: $78.8M*

Cash runway into 2H 2025

Cash currently sufficient to reach midway into Phase 2 clinical studies for SNS-101

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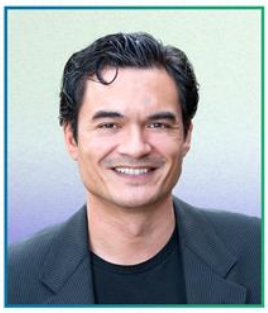
*Consists of cash, cash equivalents and marketable securities

Seasoned Leadership Team

John Celebi, MBA
President and CEO

Erin Colgan
Chief Financial Officer



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

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

Christopher Gerry, J.D.
VP, General Counsel

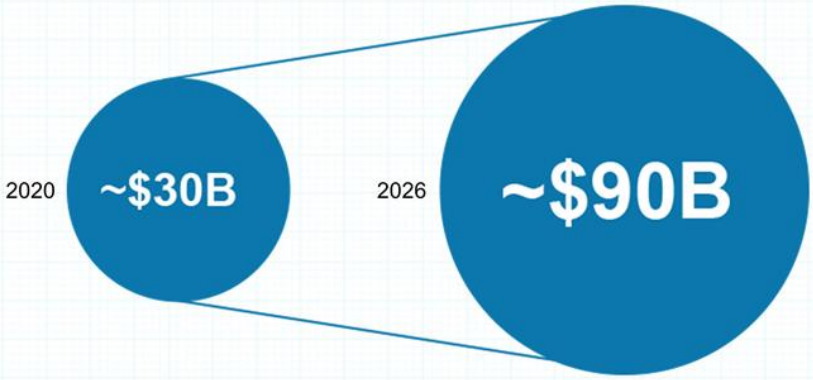
Appendix

References for Slide 20

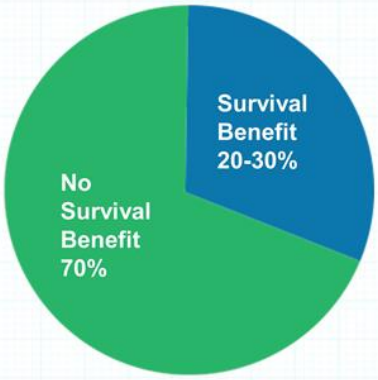
1. Helmy KY, Katschke KJ Jr, Gorgani NN, Kljavin NM, Elliott JM, Diehl L, Scales SJ, Ghilardi N, van Lookeren Campagne M. CRIg: a macrophage complement receptor required for phagocytosis of circulating pathogens. Cell. 2006 Mar 10;124(5):915-27. doi: 10.1016/j.cell.2005.12.039. PMID: 16530040.
2. Voillet V, Berger TR, McKenna KM, Paulson KG, Tan WH, Smythe KS, Hunter DS, Valente WJ, Weaver S, Campbell JS, Kim TS, Byrd DR, Bielas JH, Pierce RH, Chapuis AG, Gottardo R, Rongvaux A. An In Vivo Model of Human Macrophages in Metastatic Melanoma. J Immunol. 2022 Aug 1;209(3):606-620. doi: 10.4049/jimmunol.2101109. Epub 2022 Jul 11. PMID: 35817516; PMCID: PMC9377377.
3. Reviewed in Small AG, Al-Baghdadi M, Quach A, Hii C, Ferrante A. Complement receptor immunoglobulin: a control point in infection and immunity, inflammation and cancer. Swiss Med Wkly. 2016 Apr 5;146:w14301. doi: 10.4414/smw.2016.14301. PMID: 27045607.
4. Vogt L, Schmitz N, Kurrer MO, Bauer M, Hinton HI, Behnke S, Gatto D, Sebbel P, Beerli RR, Sonderegger I, Kopf M, Saudan P, Bachmann MF. VSIG4, a B7 family-related protein, is a negative regulator of T cell activation. J Clin Invest. 2006 Oct;116(10):2817-26. doi: 10.1172/JCI25673. PMID: 17016562; PMCID: PMC1578631.
5. Liao Y, Guo S, Chen Y, Cao D, Xu H, Yang C, Fei L, Ni B, Ruan Z. VSIG4 expression on macrophages facilitates lung cancer development. Lab Invest. 2014 Jul;94(7):706-15. doi: 10.1038/labinvest.2014.73. Epub 2014 May 26. PMID: 24862966.

The Modern-Day Challenge in Immuno-Oncology

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



PD-1/PD-L1 monotherapy does not benefit 70% of patients[2]



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

Key Partnerships Supporting SNS-101's Clinical Development

Potential opportunities for combination therapy and biomarker identification

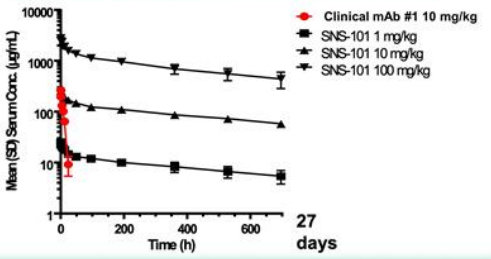
Partner / Collaborator	Goal	Description
REGENERON Clinical Supply Agreement	Support evaluation of SNS-101 in combination with Libtayo® (cemiplimab) in planned Phase 1/2 clinical trial	• Sensei to fund planned clinical trial • Regeneron to provide Libtayo® • Sensei maintains global development and commercial 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

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

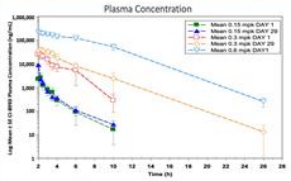
Linear

SNS-101 Cyno PK

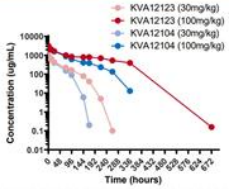


Non-linear

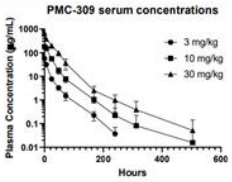
Curis CI-8993 Plasma Concentration



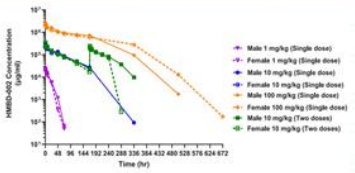
Kineta KVA12123 Cyno PK



Abcine PMC-309 Serum Conc Cyno



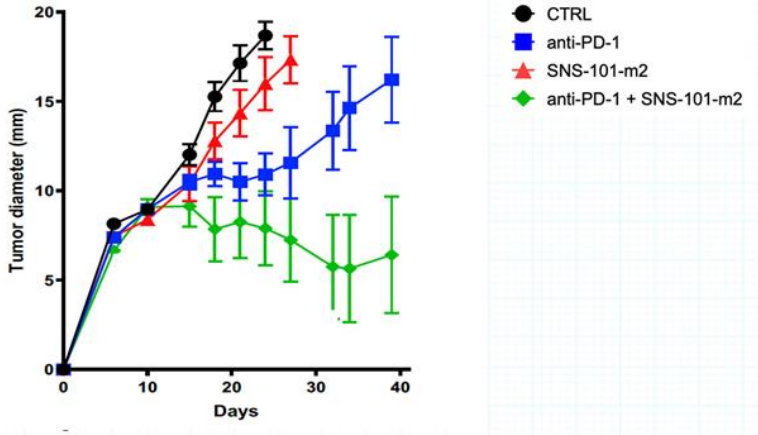
Hummingbird HMBD-002 Preclinical PK

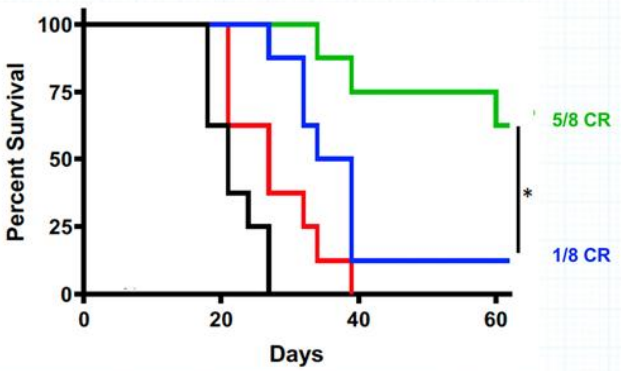


1. Hummingbird SITC 2022; 2. Kineta Corporate Presentation; 3. Abcine, SITC 2022; 4. Curis, SITC 2022

Each graph differs by time course based on data presented

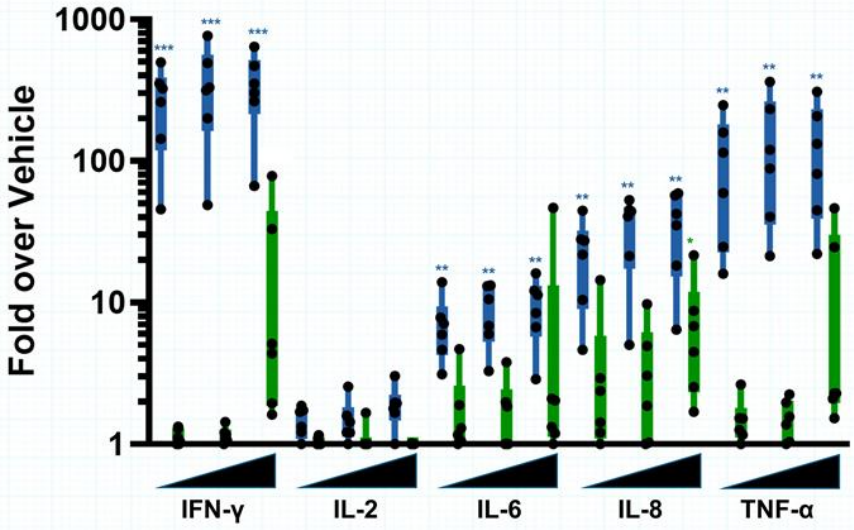
SNS-101 Re-sensitized Anti-PD-1 Insensitive Sarcoma Tumors in Human VISTA Knock-in Mice





* p<0.05

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



Clinical stage VISTA mAb #2

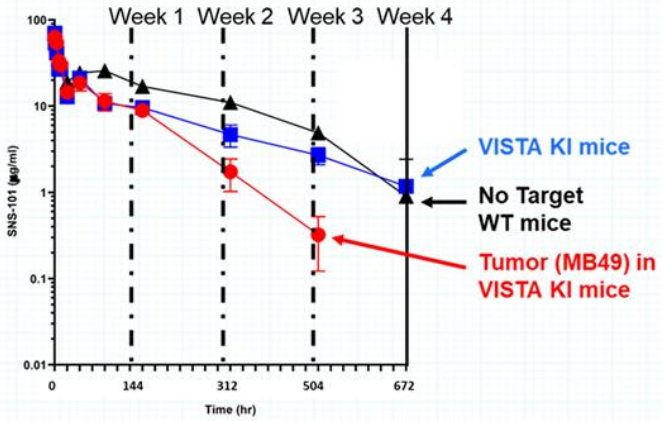
SNS-101

Dose ranges: 1, 10, and 100 ug/ml

Paired Student's t-test, Holm-Sidak Post-Hoc Analysis,
* p<0.05; ** p<0.01, *** p<0.001, **** p<0.0001

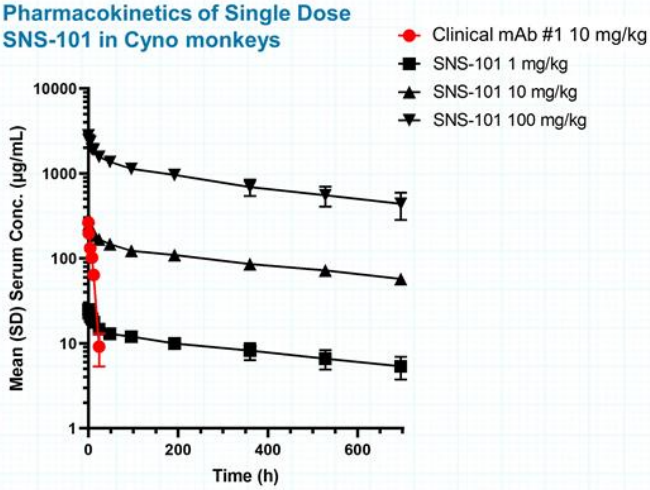
SNS-101 Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - *No Significant TMDD in Human VISTA KI Mice or Non-human Primates*

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



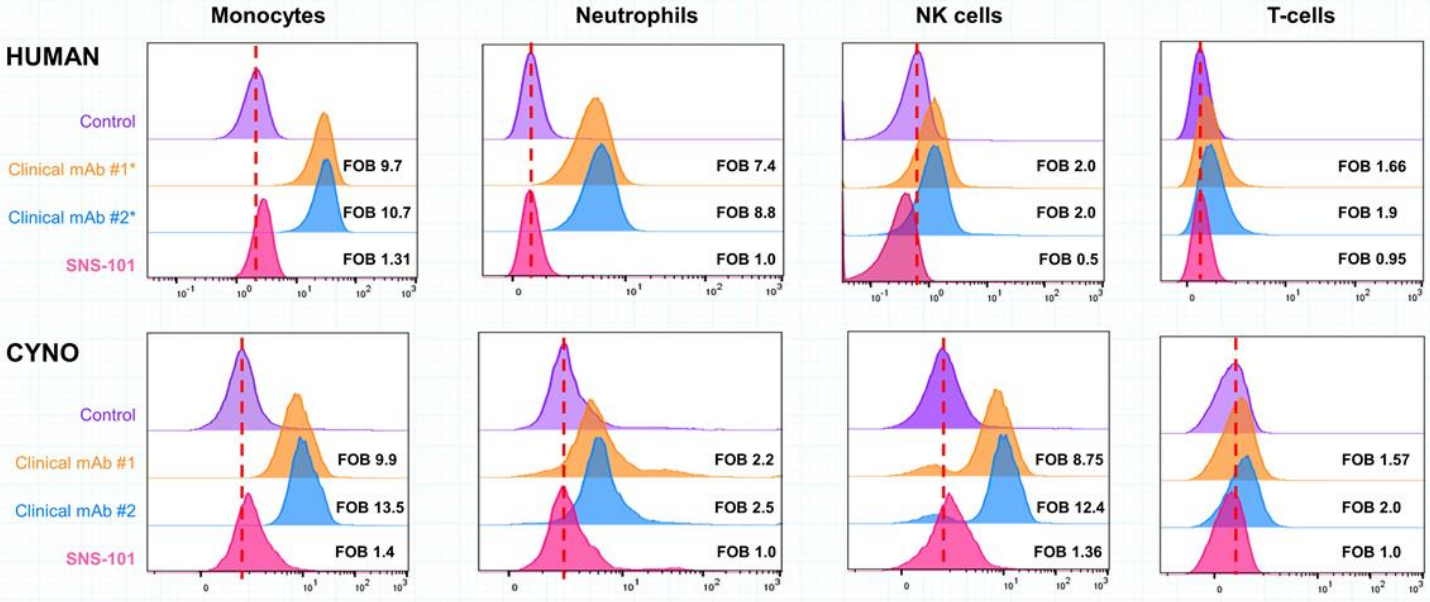
Demonstrated a long mean residence time in the blood, indicating a lack of significant target-mediated drug disposition (TMDD) and clearance in non-malignant tissues

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

SNS-101 Is a Fully Differentiated Anti-VISTA Antibody

	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

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

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 (13.4 d vs 3.9 d), ravulizumab given every 8 weeks achieved noninferiority compared with eculizumab given every 2 weeks 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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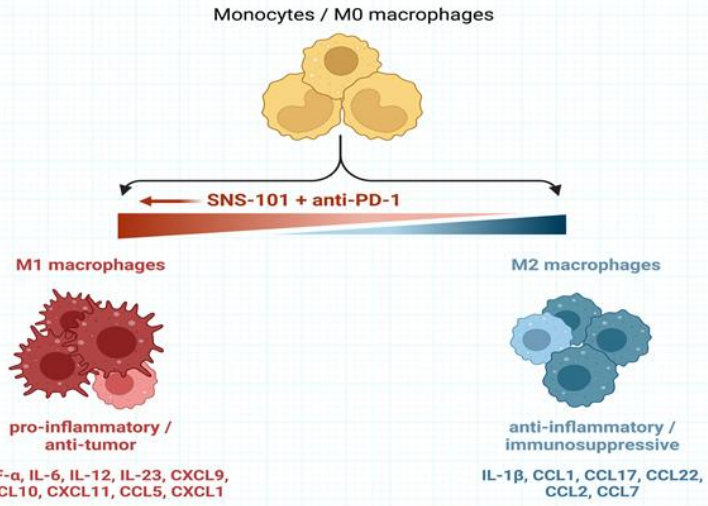
Sheridan et al, PLOS One, April 2018 (https://doi.org/10.1371/journal.pone.0195909)
Lee et al, Blood, (doi:10.1182/blood-2018-09-876136)
Sales figures: https://media.alexion.com/news-releases/news-release-details/alexion-reports-fourth-quarter-and-full-year-2020-results

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