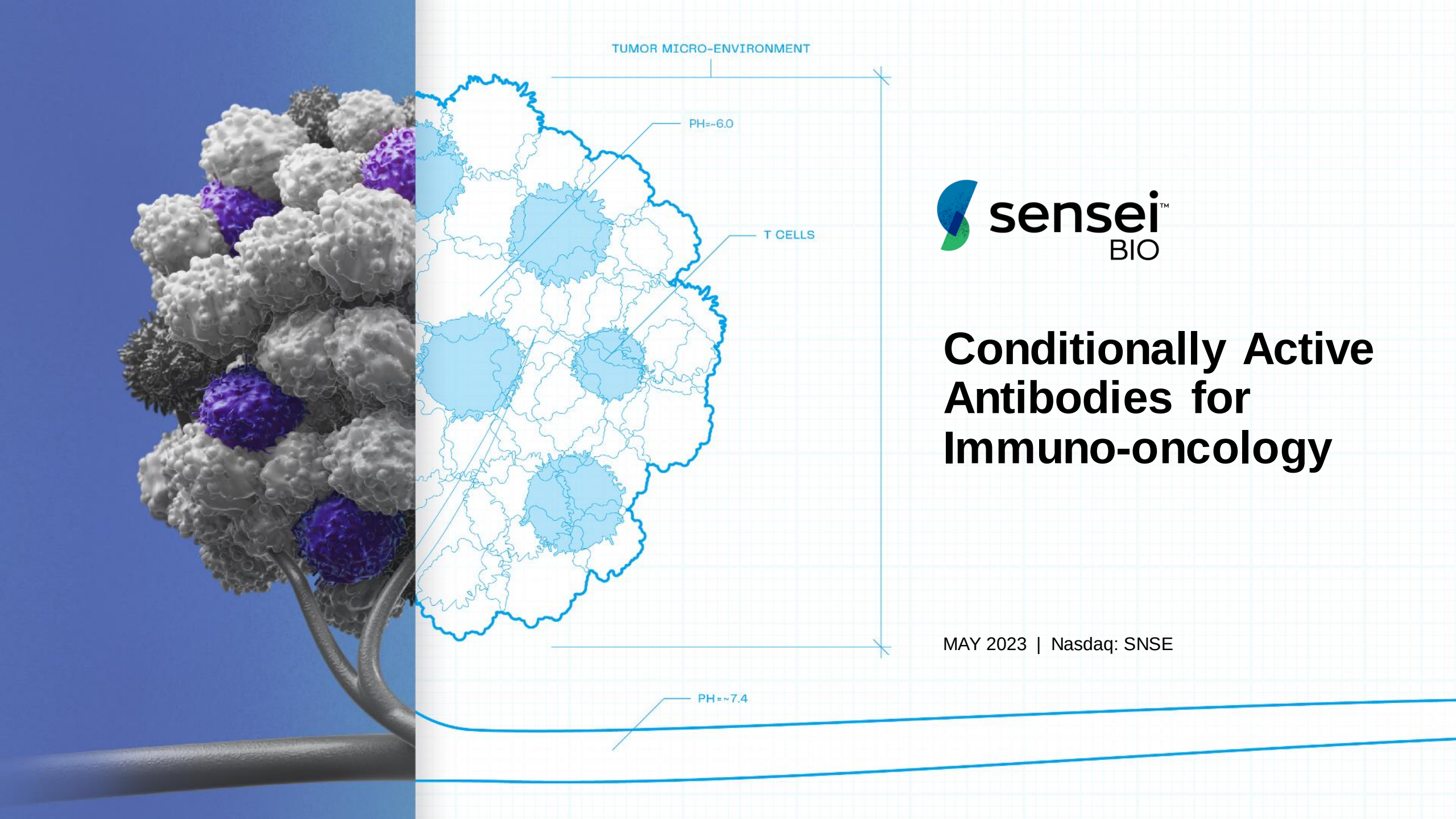
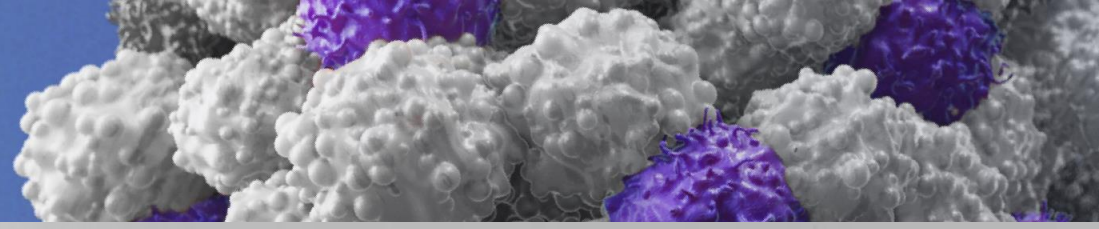


sensei™ BIO

Conditionally Active Antibodies for Immuno-oncology

MAY 2023 | Nasdaq: SNSE

Disclaimer



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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 of our product candidates; the expected timing and design of our Phase 1/2 clinical trial of SNS-101; the availability of data from our preclinical studies; the timing of 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.

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, 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 29, 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.

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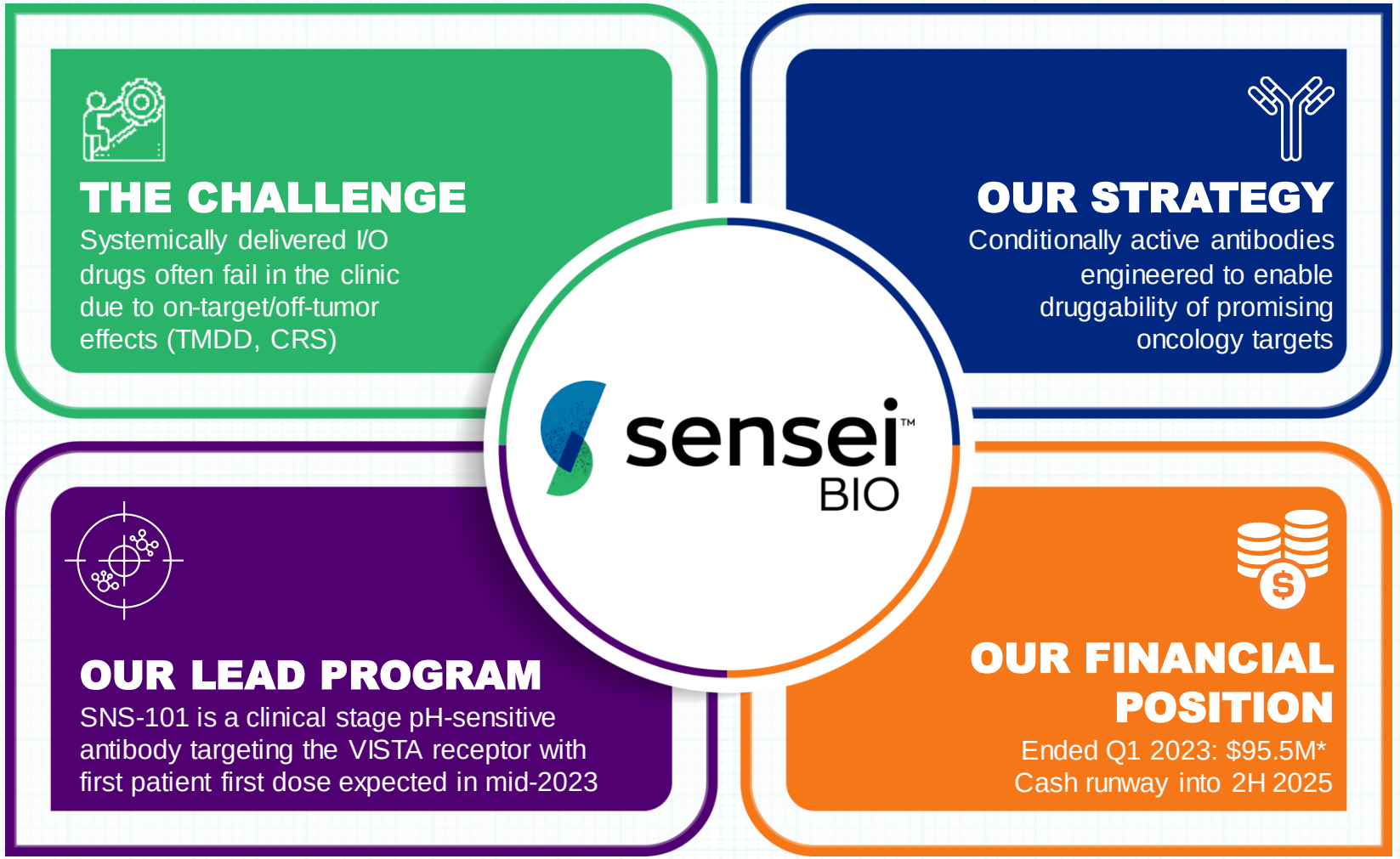
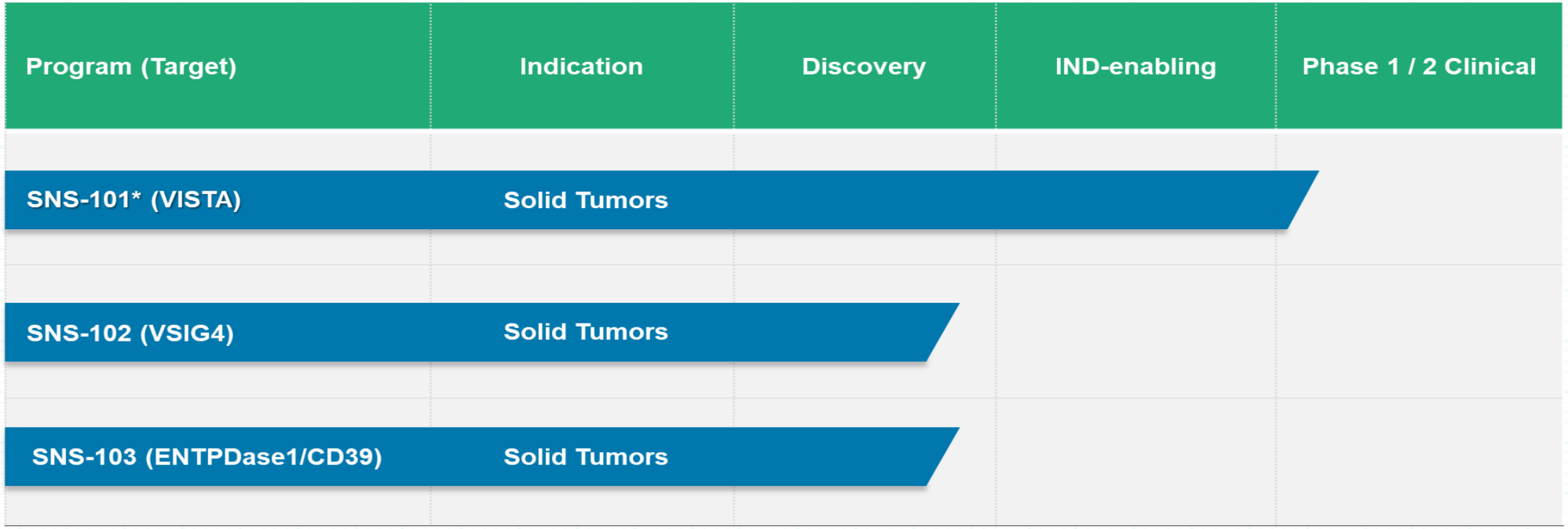
sensei™ BIO

Engineered Selectivity to Extend the Clinical Reach of Immuno-oncology Agents



*Consists of cash, cash equivalents and marketable securities

Innovative Pipeline of IO Drugs with Broad Commercial Potential



NIH NATIONAL CANCER INSTITUTE

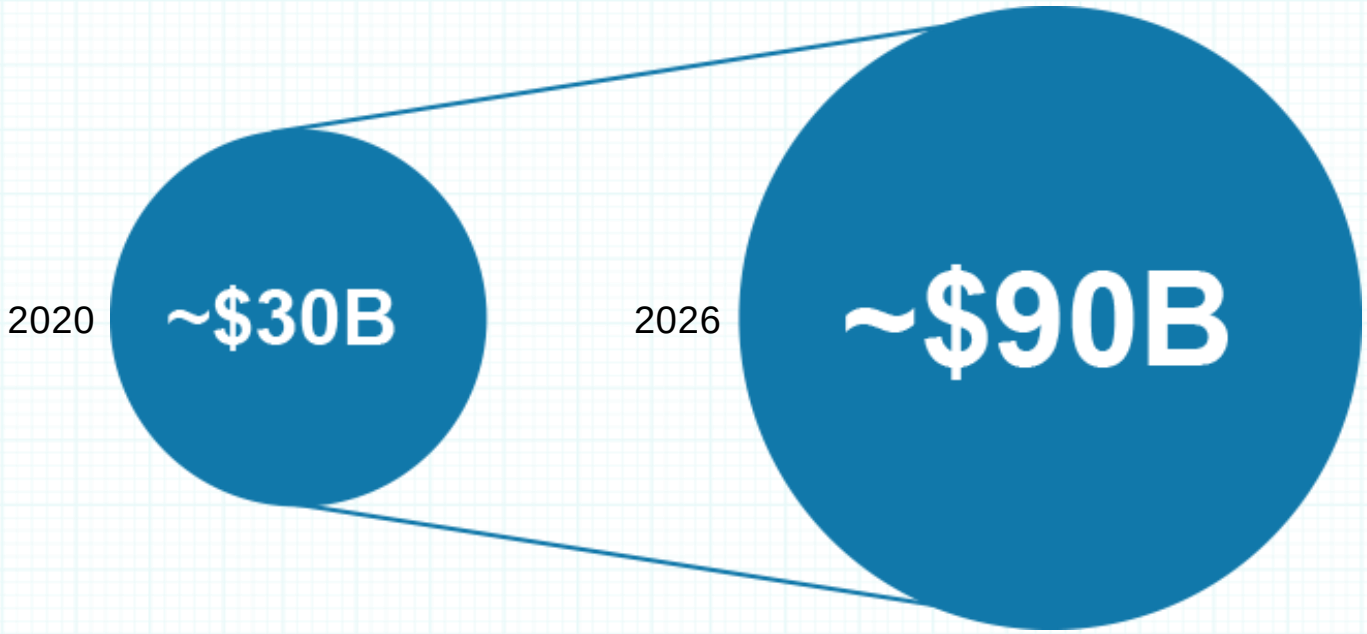
*Sensei has entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute. The goal of this collaborative effort is to further elucidate the role of VISTA in immune checkpoint resistance and expand the potential of SNS-101 as a combination therapy beyond anti-PD-1.

REGENERON

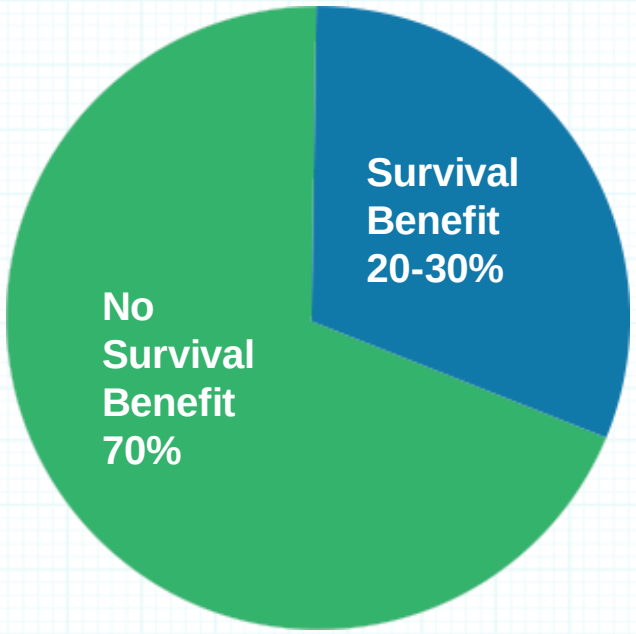
*Sensei has entered into a clinical supply agreement with Regeneron supporting the planned evaluation of SNS-101 in combination with Regeneron's anti-PD-1 therapy Libtayo® (cemiplimab) in a Phase 1/2 clinical trial in solid tumors.

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]



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 to CI Innovation

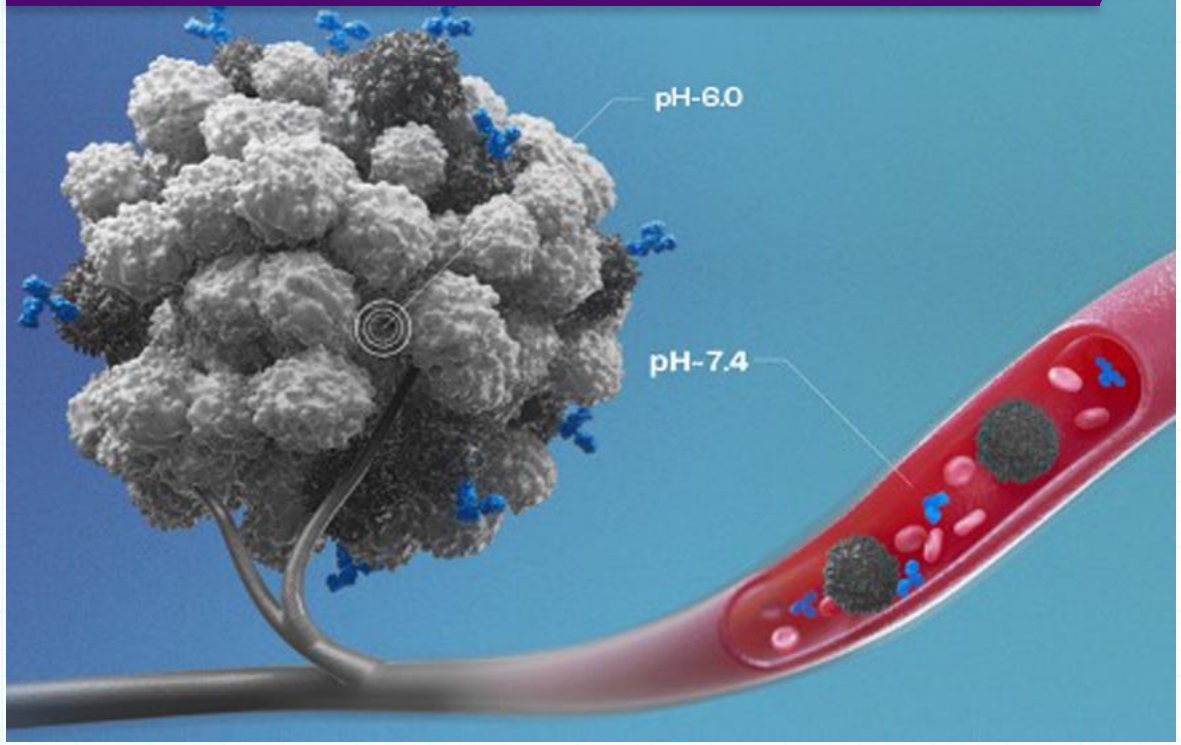
Industry Problem	Sensei's Solution
Conventional antibodies target immune checkpoints that are highly expressed in normal tissues, resulting in:	**Conditionally active antibodies are selectively targeted to the tumor microenvironment, potentially providing:**
Dose-limiting toxicities due to on-target/off-tumor 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

pH-sensitive Antibodies Have Potential to Selectively Bind Their Targets in the Low-pH Tumor Microenvironment

TMAb Platform

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 properties:
  - Dose-limiting toxicities due to on-target/off-tumor binding
  - Higher and more frequent dosing due to poor pharmacokinetics (Target-mediated Drug Disposition, or TMDD)
- Bolsters specific activities
- Goal is to unlock previously undruggable immune targets

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**

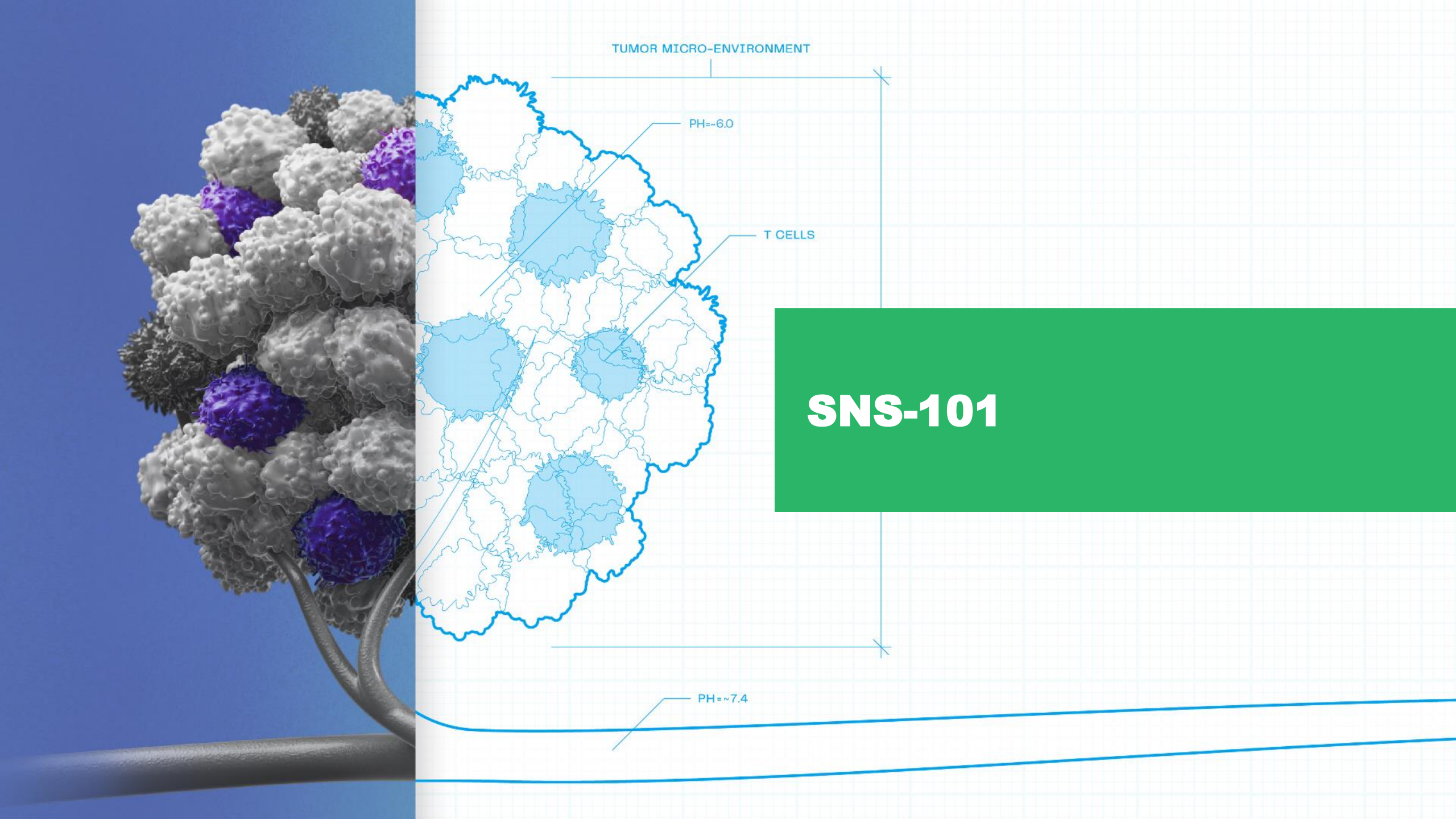
Revulizumab utilized histidine insertions into the CDR regions (VH_Y27H, VH_S57H) and Fc substitutions (M428L, N434S) of eculizumab

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

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

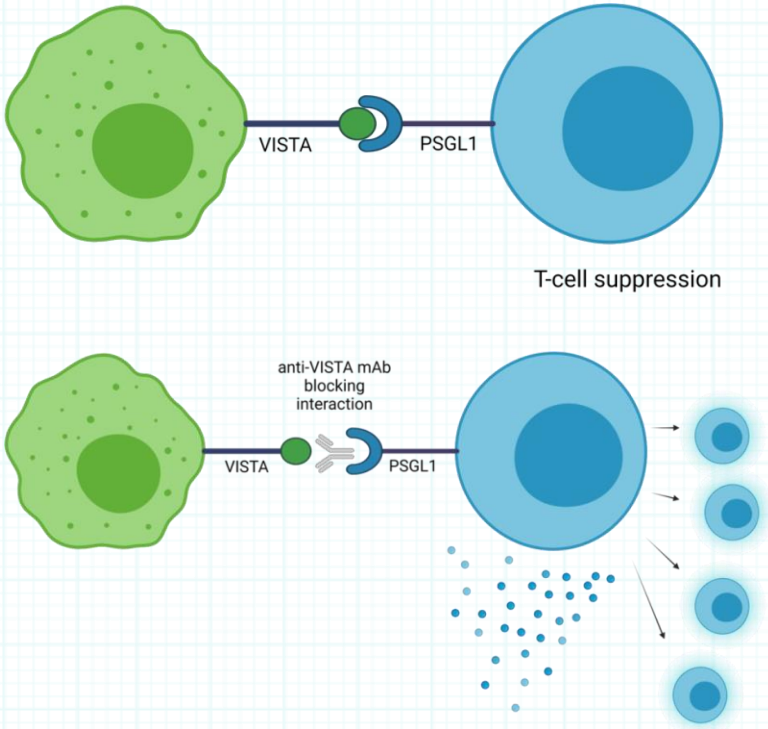


SNS-101

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

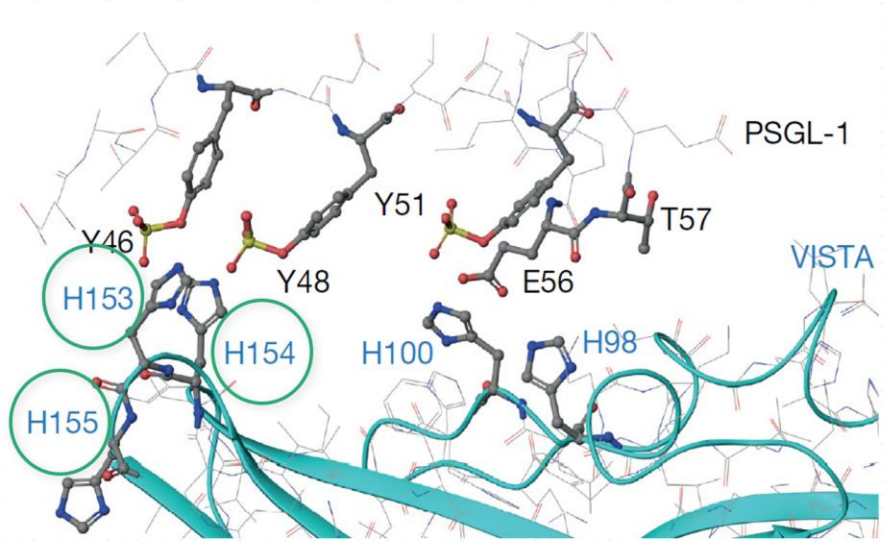
VISTA is a B7 family member that suppresses T cell function

Immunosuppressive function believed to be mediated by PSGL-1 receptor



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

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



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

SNS-101: Selectively Targeting VISTA with 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) [nM]

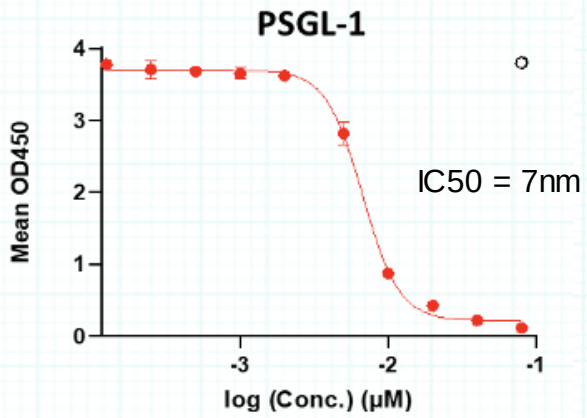
pH 6.0	pH 7.4
0.218	132 (~No binding)

Additional SNS-101 features

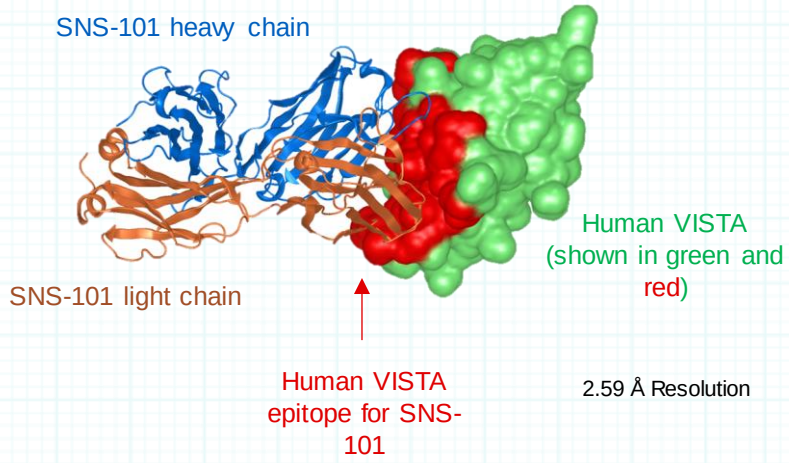
- IgG1 format
- Active Fc

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

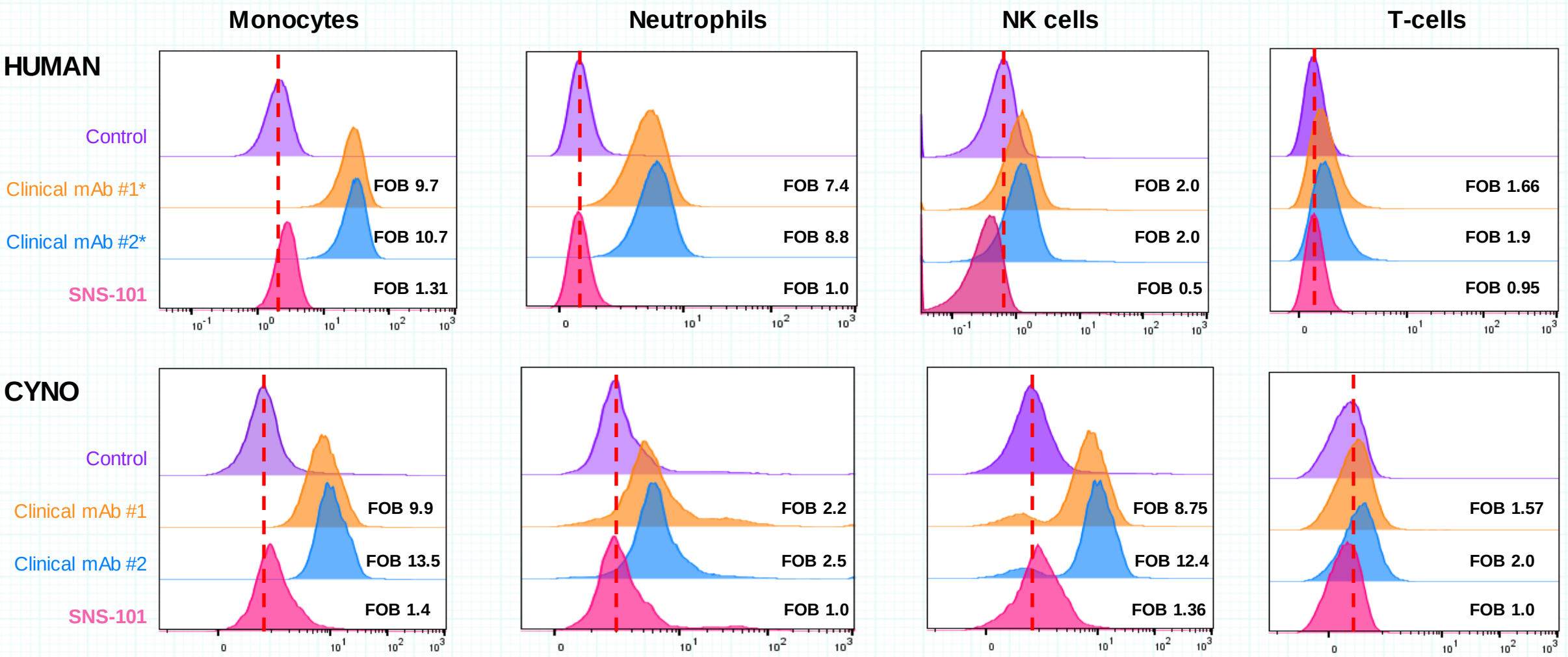
SNS-101 strongly inhibits the VISTA:PSGL-1 interaction and all other potential binding partners at pH 6.0 *in vitro*



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

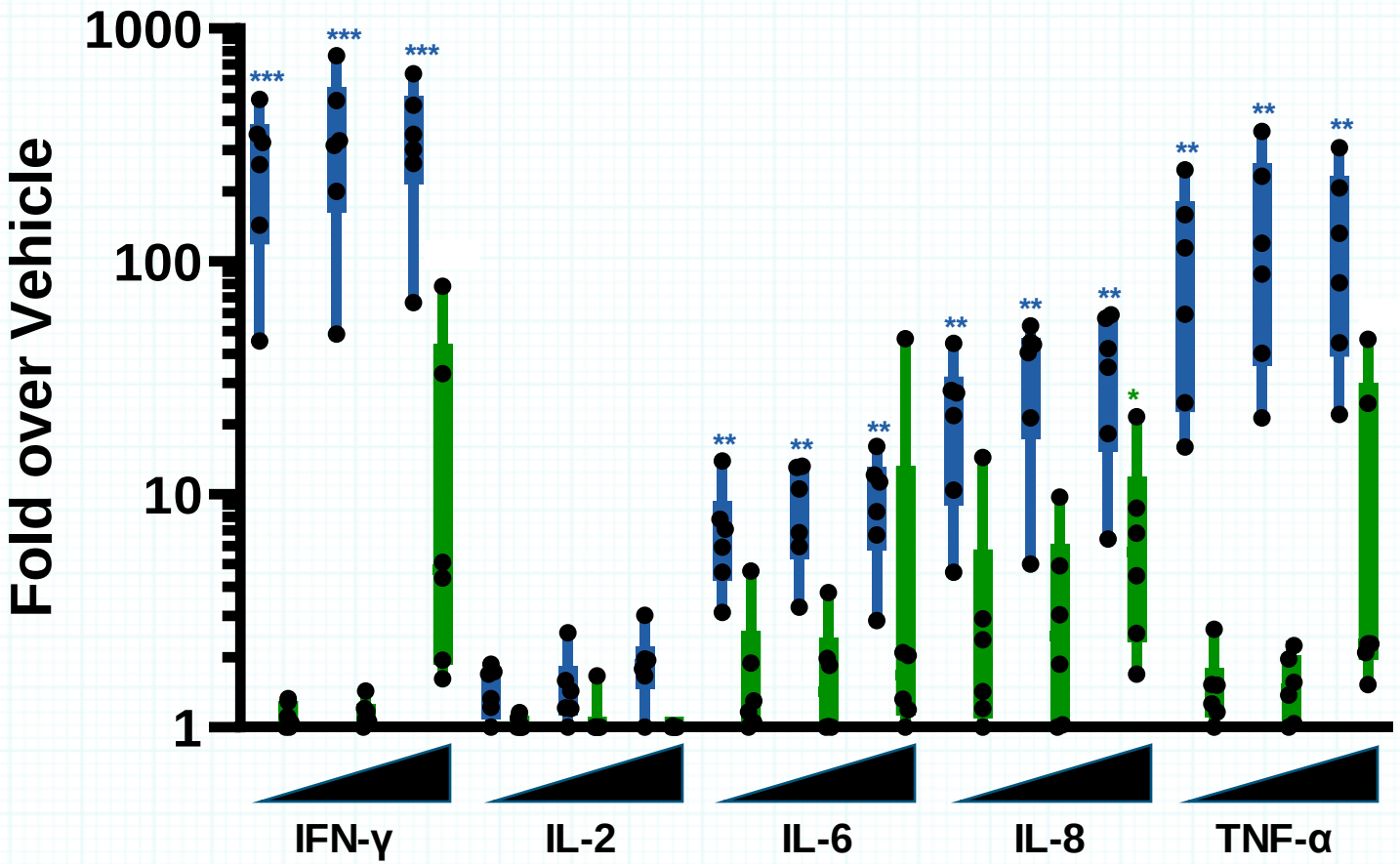


No Significant Binding of SNS-101 to Monocytes, Neutrophils, NK Cells and T-cells in Whole blood at Physiological pH



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

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

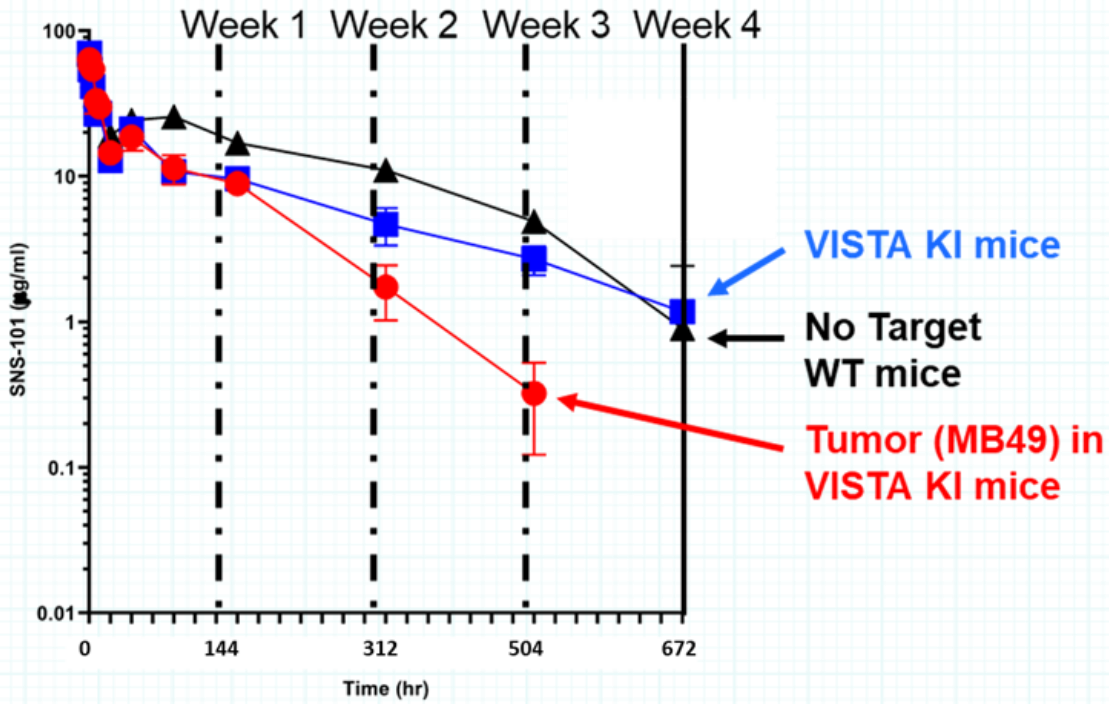


Dose ranges: 1, 10, and 100 ug/ml

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

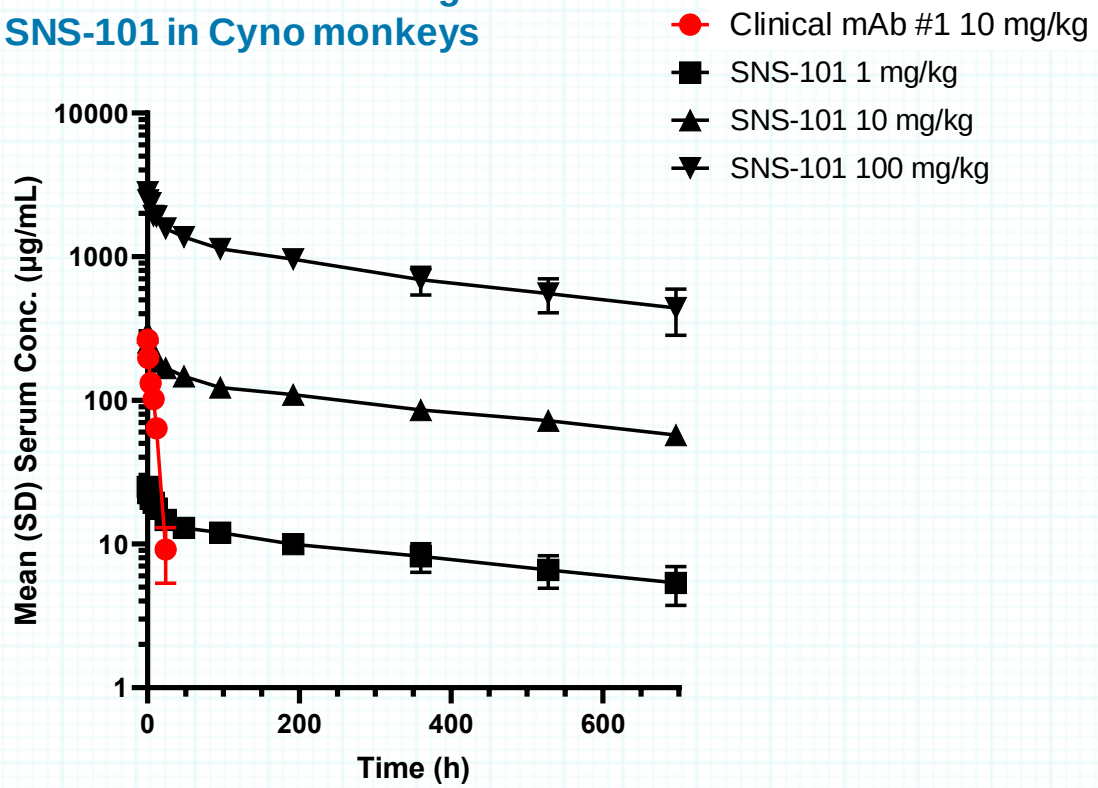
SNS-101 Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - *No Significant TMDD in Human VISTA KI Mice or Non-human Primates*

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



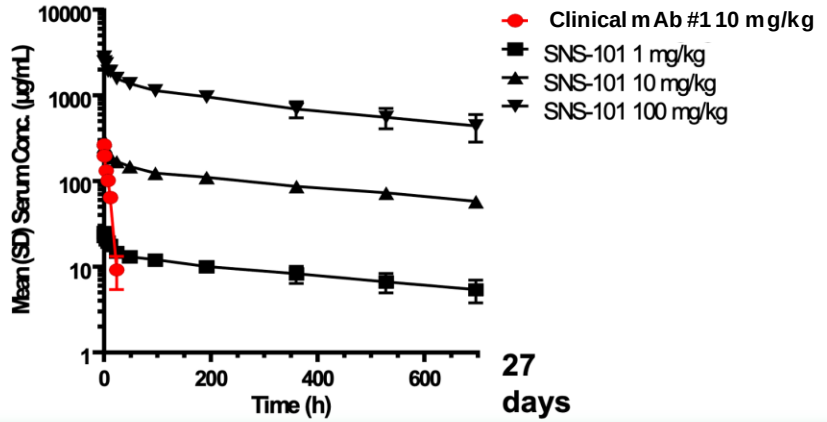
SNS-101 displayed linear elimination kinetics unlike a pH-independent anti-VISTA mAb, which demonstrated TMDD and rapid clearance

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

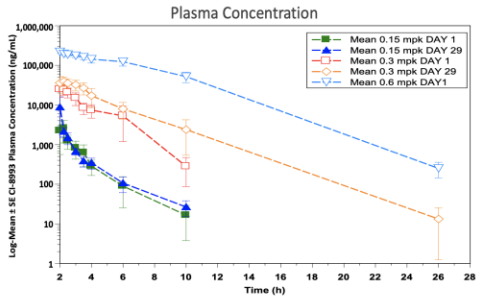
Linear

SNS-101 Cyno PK

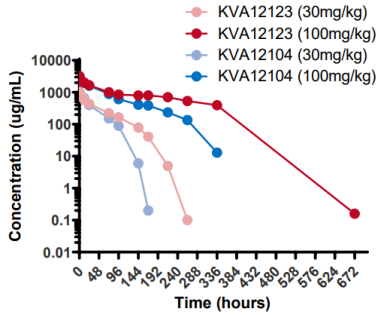


Non-linear

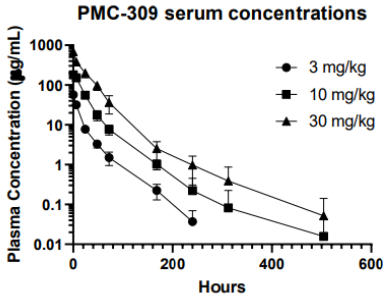
Curis CI-8993 Plasma Concentration



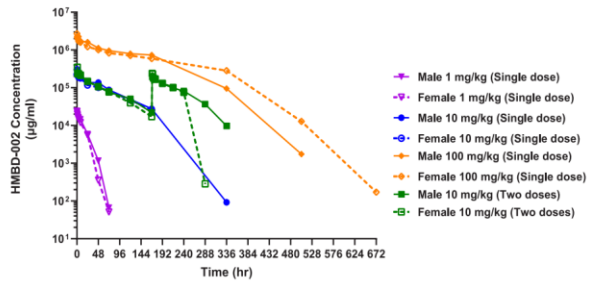
Kineta KVA12123 Cyno PK



Abcine PMC-309 Serum Conc Cyno



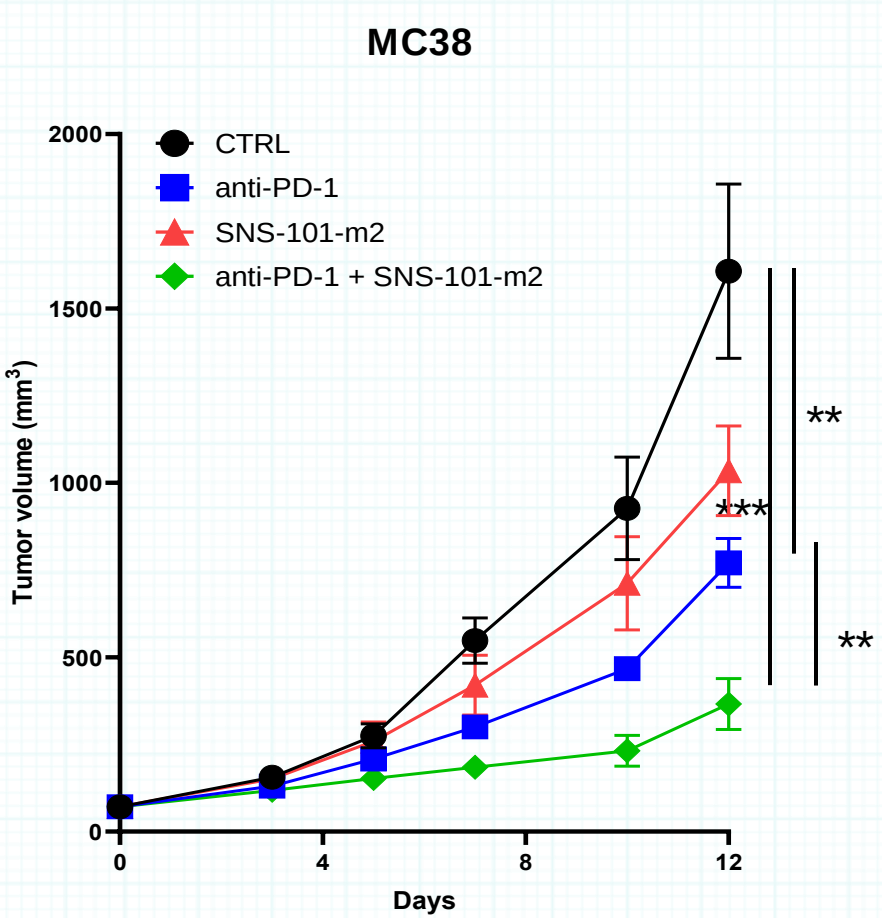
Hummingbird HMBD-002 Preclinical PK



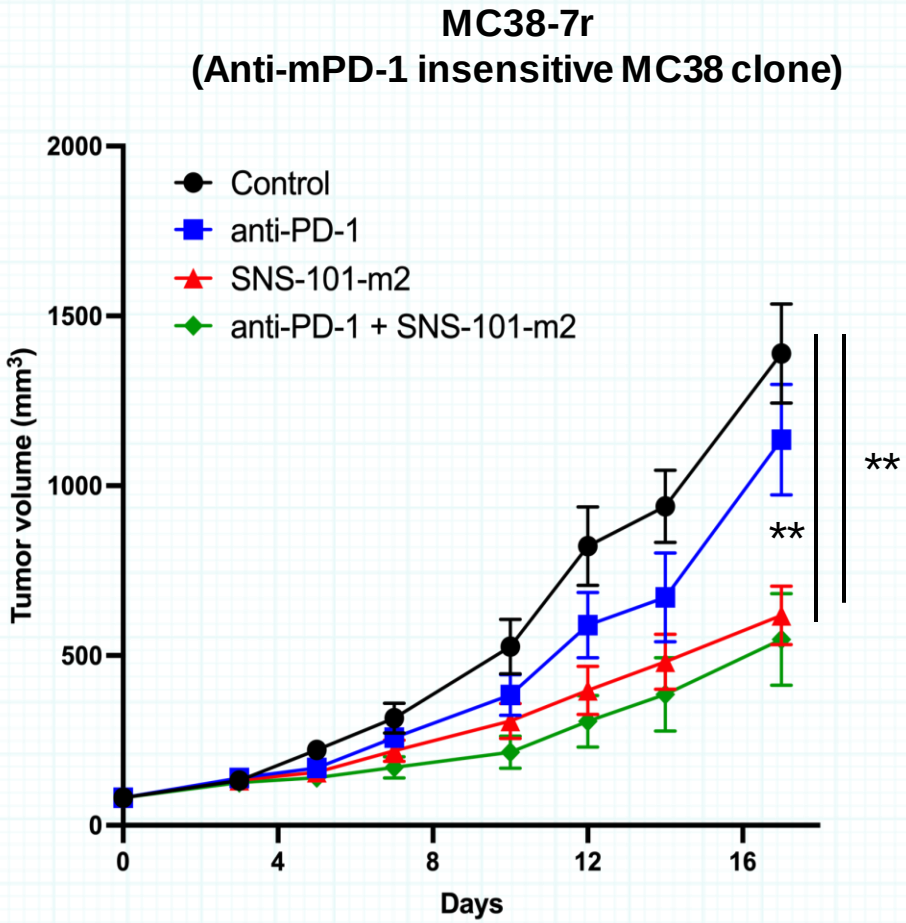
1. Hummingbird SITC 2022; 2. Kineta Corporate Presentation; 3. Abcine, SITC 2022; 4. Curis, SITC 2022

*Each graph differs by time course based on data presented

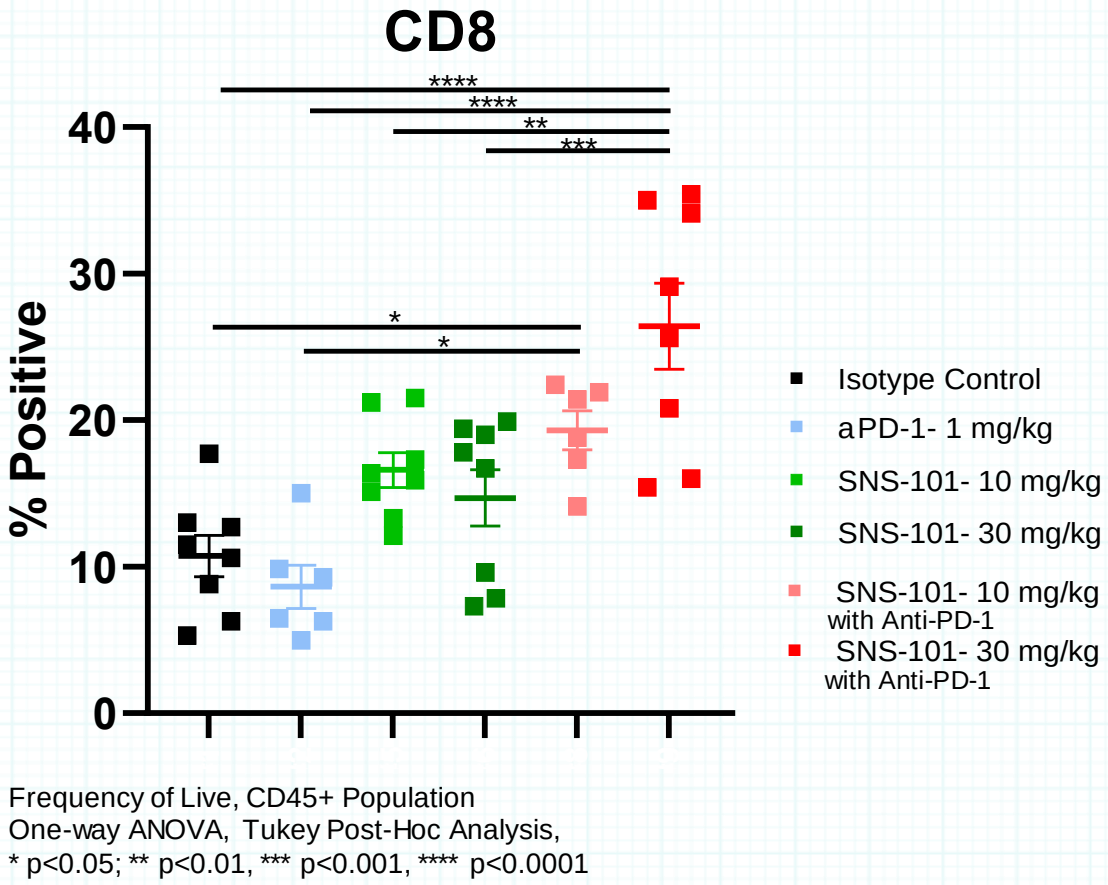
SNS-101 Drove Single-agent Activity and Deepened Anti-tumor Responses to PD-1 in Human VISTA KI Mice



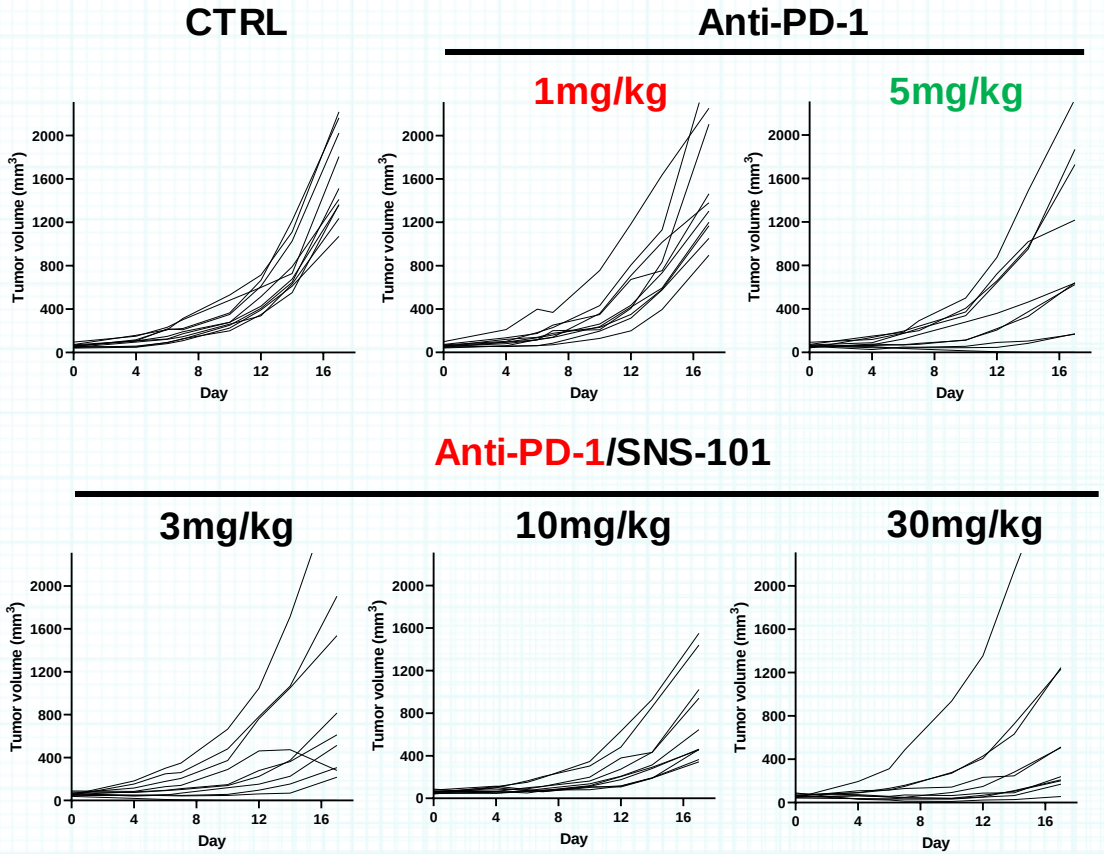
* *P*<0.05; ** *P*<0.01; *** *P*<0.001



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



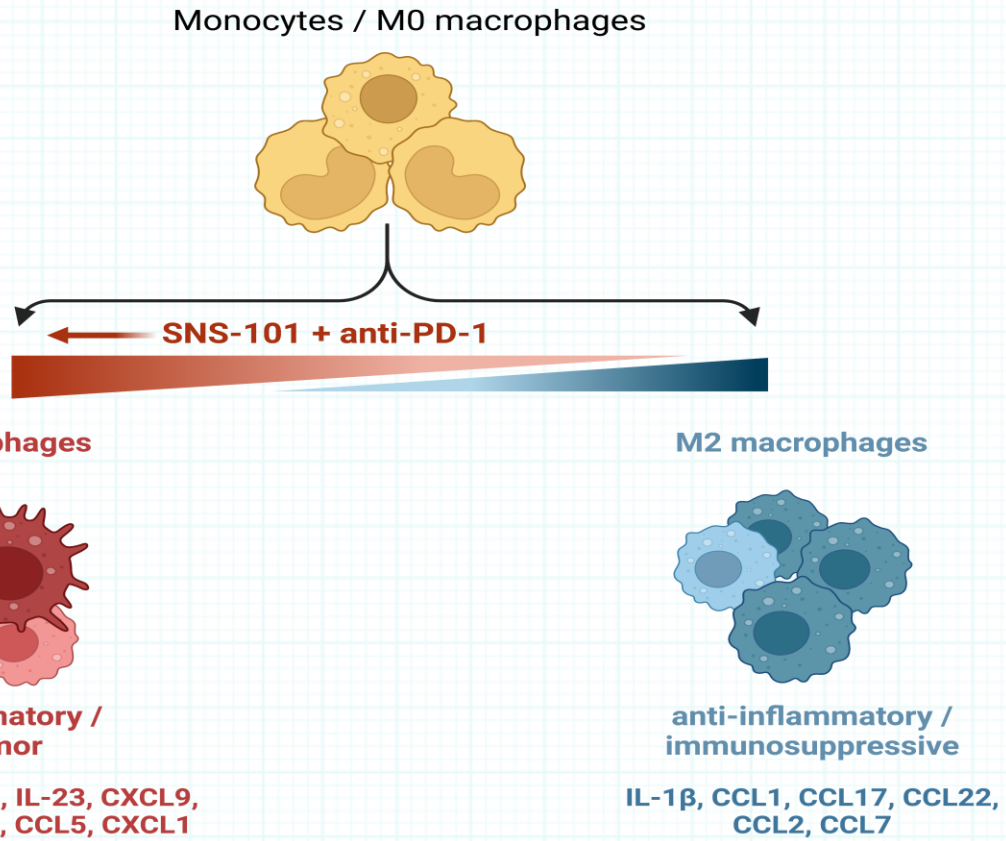
Frequency of Live, CD45+ Population
One-way ANOVA, Tukey Post-Hoc Analysis,
* p<0.05; ** p<0.01, *** p<0.001, **** p<0.0001



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

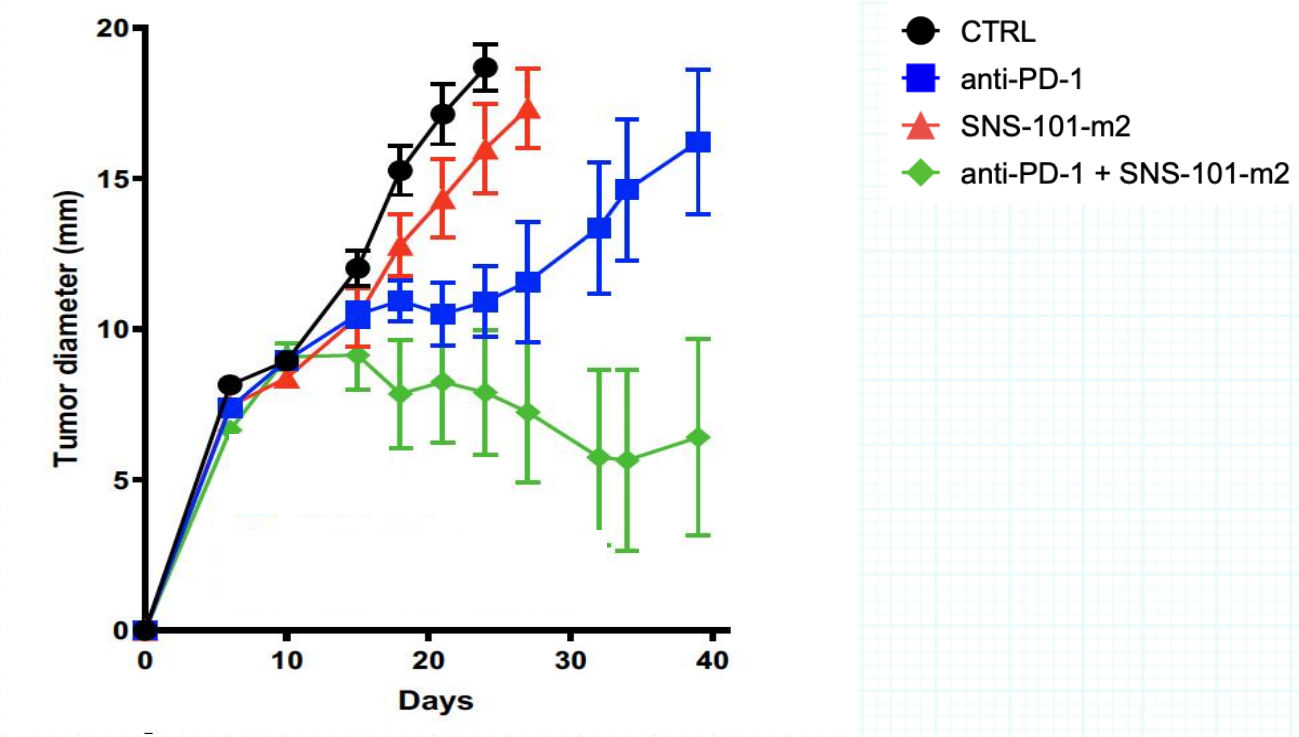
SNS-101 targets suppressive signaling in the myeloid compartment, and in combination with anti-PD-1 may help shift the balance of macrophage polarization toward an anti-tumor M1 phenotype

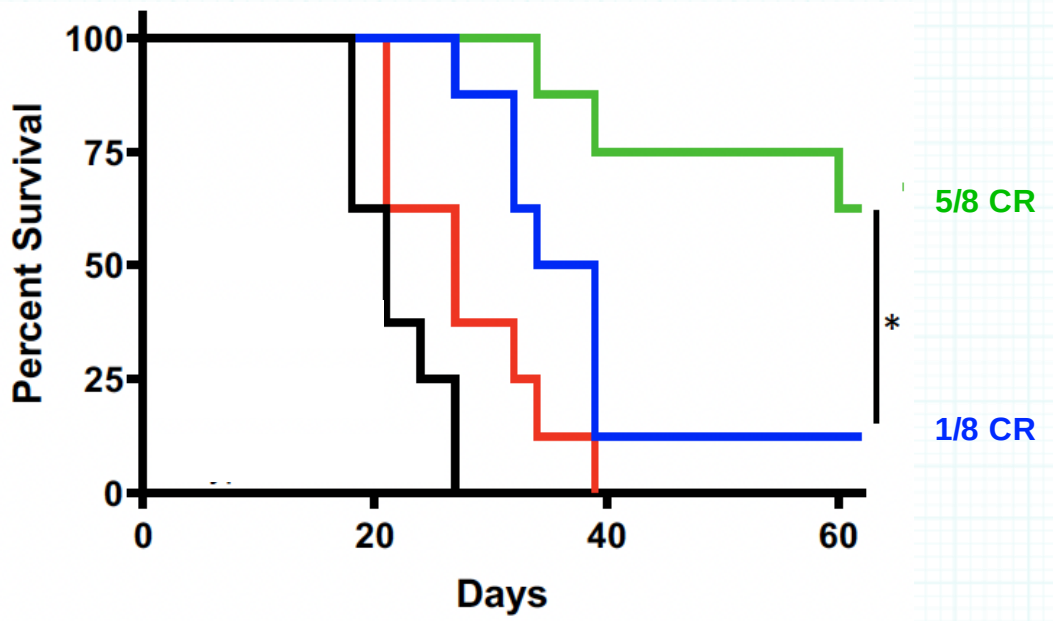
M1 macrophages are anti-tumorigenic through secretion of pro-inflammatory cytokines and chemokines, and driving of Th1 CD4+ T cell responses



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

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



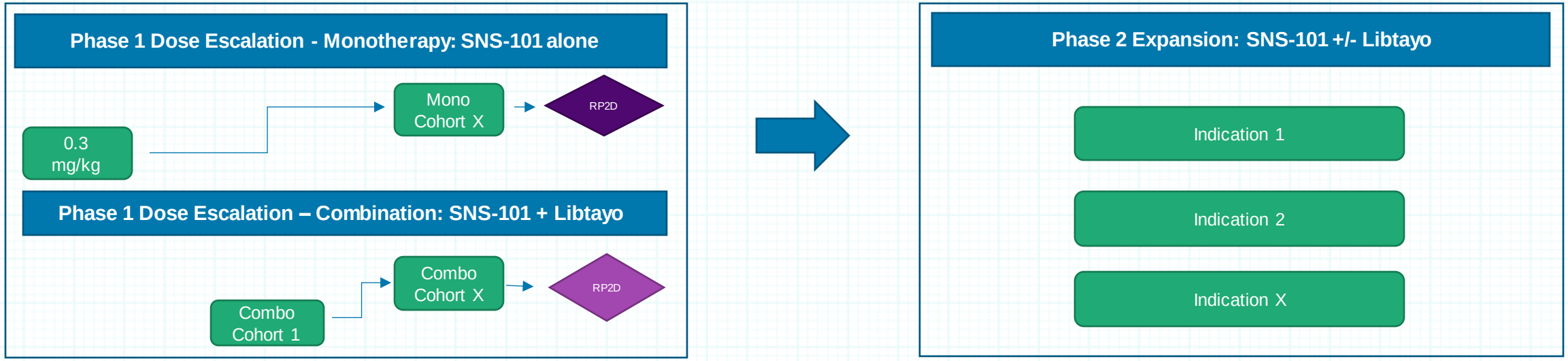


* p<0.05

SNS-101 Phase 1/2 Study

Phase 1 Study Design
Dose escalation using Bayesian Optimal Interval (BOIN) design; plan to initiate combo dosing prior to monotherapy RP2D*

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 • SNS-101 starting dose = 0.3 mg/kg; 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 Phase 1 study and emerging results from preclinical studies	• Primary endpoint: Anti-tumor activity • Secondary endpoint: Anti-tumor activity, safety, tolerability, PK profile & immunogenicity	• SNS-101 +/- Libtayo (350 mg) dosed as an IV infusion once every 3 weeks • Dose will be determined from the Phase 1 study

* Safety Monitoring Committee (SMC) to determine initiation of combination arm based on emerging clinical data
RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose

Key Partnerships Supporting SNS-101's Clinical Development

Potential opportunities for combination therapy and biomarker identification

Partner / Collaborator	Goal	Description
REGENERON Clinical Supply Agreement	Supports 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

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)	KVA12.1 (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	Preclinical

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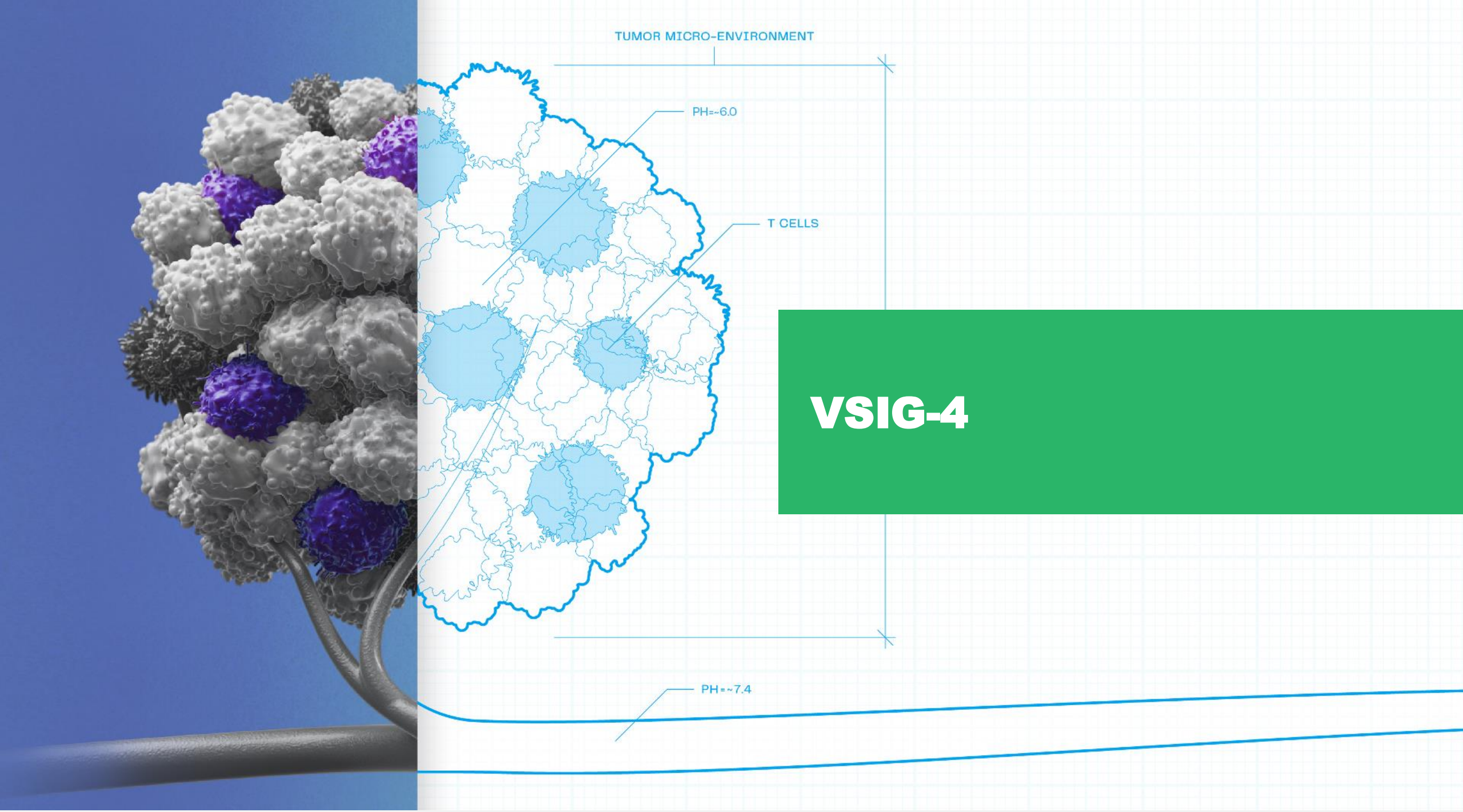
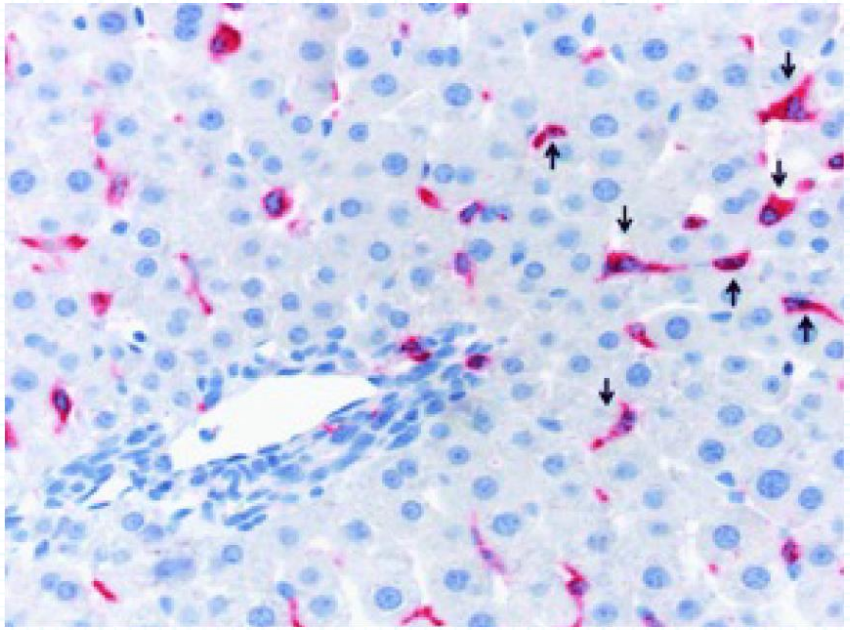
Johnston et al., Nature 2019; Kineta website; Snyder et al, AACR Annual Meeting 2016; Pierre Fabre website; Hummingbird website; Thakkar et al, J of Immunother Cancer, 2022; PharmAbcine website



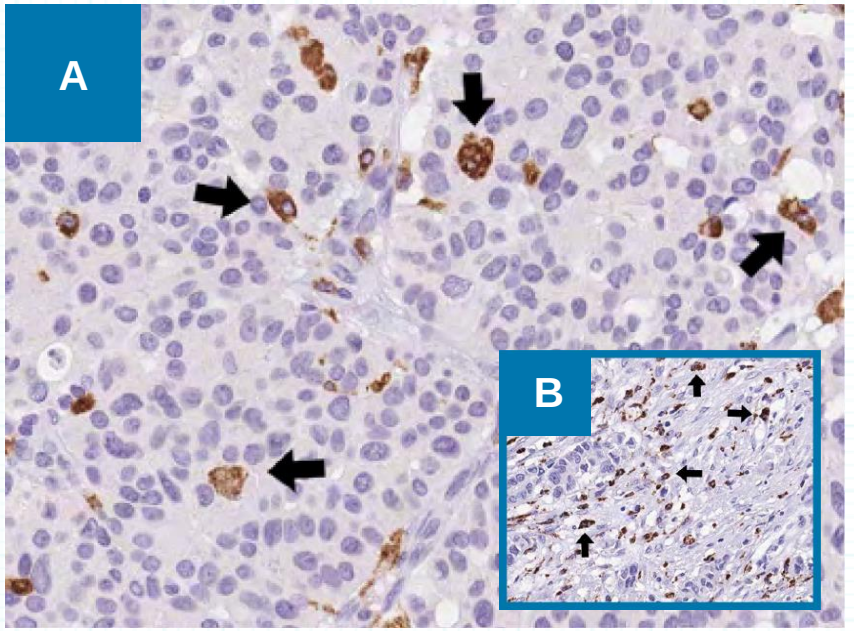
VSIG-4

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

Tissue macrophages (Kupffer cells) in liver



Tumor-associated macrophages in tumor and 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]

See references in Appendix

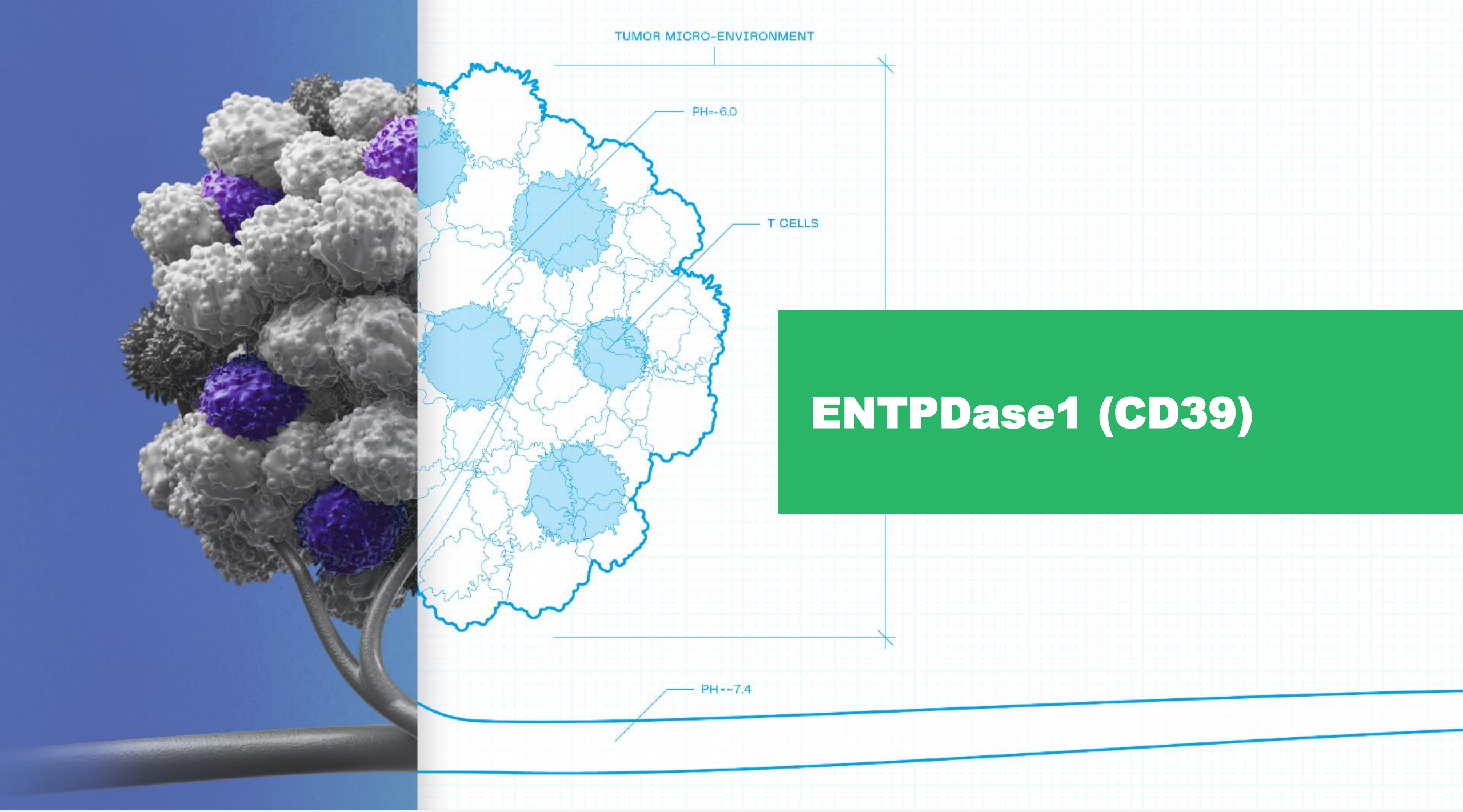
Sensei Has Identified pH-sensitive VSIG4 Antibodies

- Program milestones to date:
  - Identified 8 parental antibodies for optimization and are currently testing progeny antibodies;
  - Identified pH-sensitive antibodies highlighting the potential breadth of the TMAb platform;
  - Identified novel VSIG4 receptors on primary T-cells by Hi-Res proteomics, which are currently in verification stage.
- Plan to select product candidate in 2023

pH-Sensitive VSIG4 Parental Antibodies Selected for Further Optimization

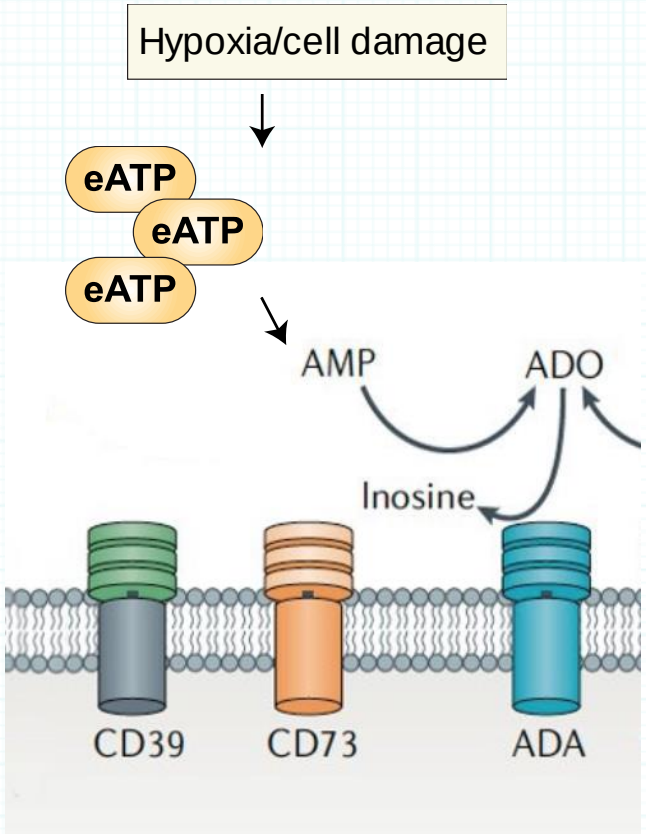
Antibody Reference #	Ratio of pH Selectivity (6.0 vs 7.4)	Blockage of Immobilized VSIG4-T-cell Inhibition	Blockage of Cellular VSIG4-T-cell Inhibition
1	1	+	+
2	7	+	+
3	1	+	+
4	3	+	+
5	3	+/-	+
6	25	+	+
7	1	+	+
8	2	-	+

*** Ratio assessed by flow cytometry on VSIG4 overexpressing cells**



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
- Development of a TMAb antibody has potential for improved safety and PK profile compared to competitor CD39 mAbs

Blocking CD39 leads to: → **ATP** → **AMP** → **Adeno-sine** → **Immune Activation**

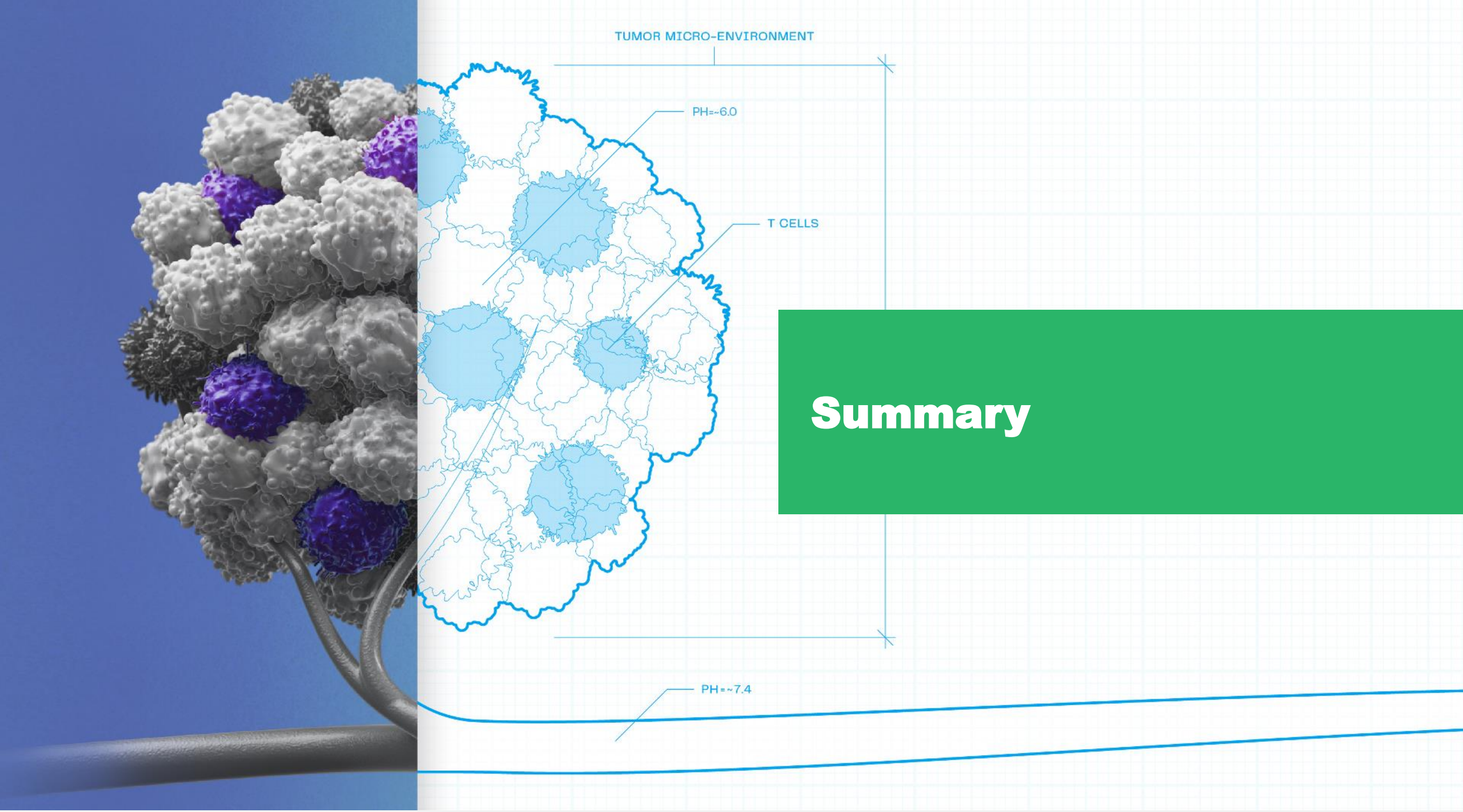
Figure adapted from: Moesta et al, *Nat Rev Immunol.* 2020;20 (12)

Sensei Has Identified pH-sensitive ENTPDase1 (CD39) Antibodies

- Program milestones to date:
  - Identified 8 parental antibodies for further optimization, and currently testing progeny antibodies
  - Identified pH-sensitive parental antibodies for lead optimization
- Plan to select lead product candidate in 2023

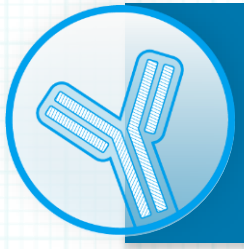
pH-Sensitive CD39 Parental Antibodies Selected for Further Optimization

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



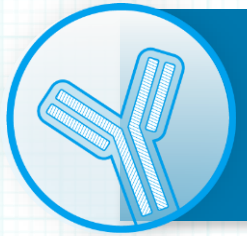
Summary

Expected Program Milestones



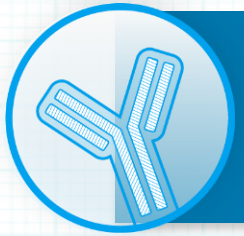
SNS-101 (anti-VISTA)

- **Mid-year 2023:** First patient first dose
- **2024:** Topline Phase 1 monotherapy data
- **2024:** Initial Phase 1 combination data



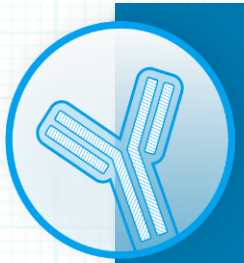
SNS-102 (anti-VSIG4)

- **2023:** Select product candidate



SNS-103 (anti-ENTPDase1/CD39)

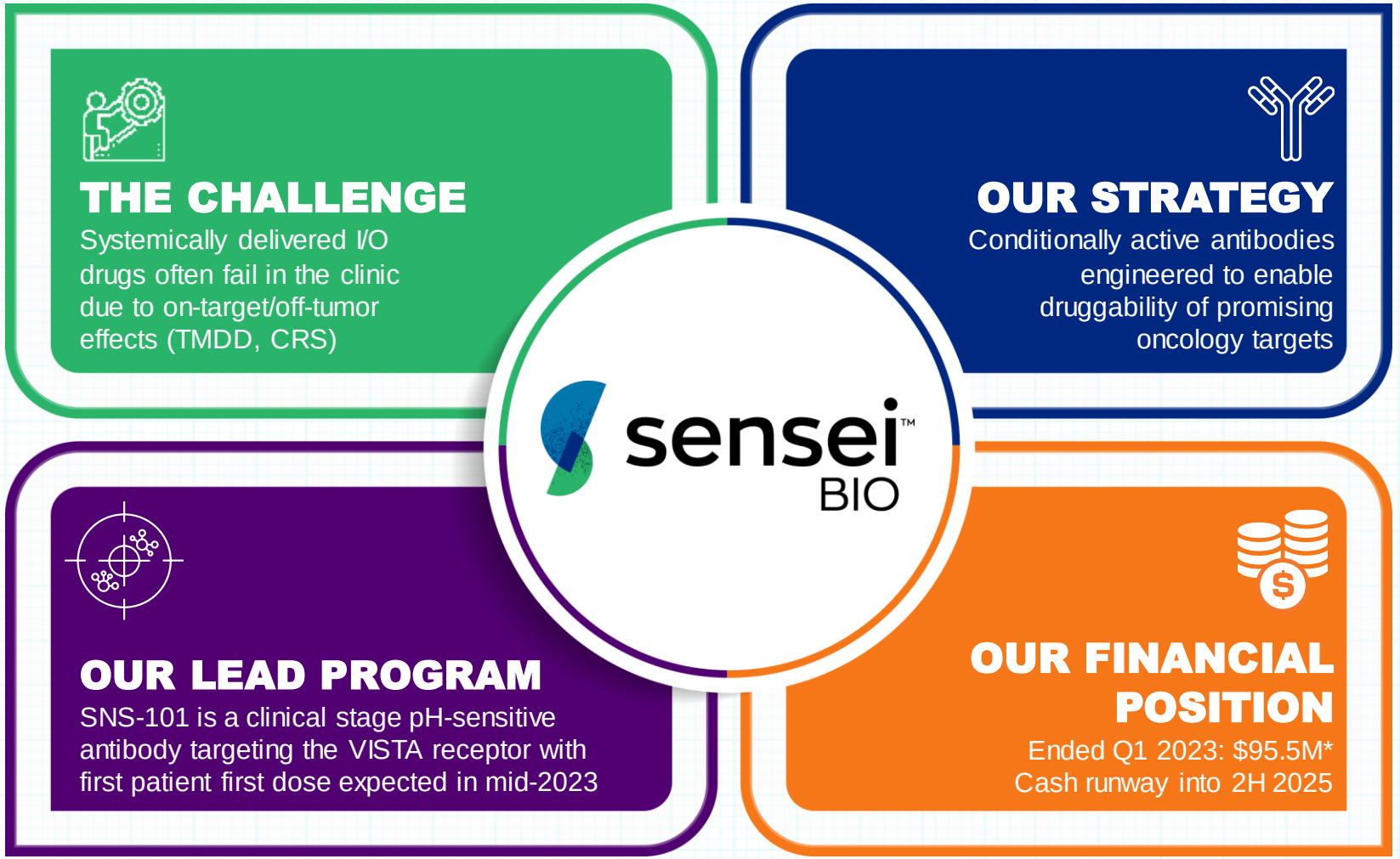
- **2023:** Select product candidate



TMAb Platform

- Advance one program forward to IND-enabling studies following product candidate selection
- ✓ **2023:** Initiate fourth TMAb discovery program focused on developing a conditionally active bispecific antibody

Engineered Selectivity to Extend the Clinical Reach of Immuno-oncology Agents



*Consists of cash, cash equivalents and marketable securities

Seasoned Leadership Team

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President and CEO

X4 Pharmaceuticals · Tularik · ArQule

Erin Colgan
Chief Financial Officer

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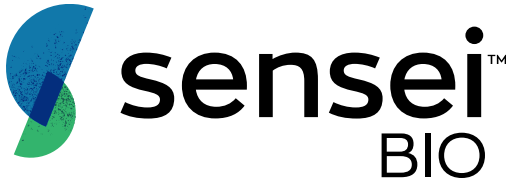
Edward van der Horst, Ph.D.
Chief Scientific Officer

AMGEN · IGENICA BIOTHERAPEUTICS · oncomed

Christopher Gerry, J.D.
VP, General Counsel

AVROBIO · Cooley



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Appendix

References for Slide 24

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