A New Vista for Cancer Care:

Exploring SNS-101's Potential as a Transformative Treatment Option for Patients with Solid Tumors

June 27, 2023

Guest Speaker:

James Gulley, M.D., Ph.D., F.A.C.P.

Co-Director, Center for Immuno-Oncology

Clinical Director, National Cancer Institute, NIH

James Gulley, M.D., Ph.D., is an internationally recognized expert in cancer immunotherapy with a strong interest in prostate cancer. Since 1998 he has authored and run a variety of clinical trials at the National Cancer Institute (NCI). These innovative, investigator-initiated studies involve the use of cancer immunotherapy to (a) initiate immune responses, (b) expand immune responses and/or (c) allow the immune responses to be effective within the tumor microenvironment. In addition to his role as the CIO Co-Director, Dr. James L. Gulley is the Clinical Director, NCI.

Sensei Presenters:

John Celebi
Chief Executive Officer

Dr. Edward van der Horst
Chief Scientific Officer

Ron Weitzman
Consulting Chief Medical Officer

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 of SNS-101; the potential safety profile of SNS-101; the potential efficacy and other benefits of SNS-101; and expected clinical development timelines for 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, the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies, including the preclinical studies of SNS-101, will not be replicated or will not continue in ongoing or future studies or clinical trials involving SNS-101 or Sensei’s other product candidates, our reliance on third parties over which we may not always have full control, and other risk and uncertainties that are described in our Quarterly Report on Form 10-Q filed with the SEC on May 9, 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.

sensei™ BIO

Agenda

WELCOME

John Celebi
President & Chief Executive Officer, Sensei Biotherapeutics

IMPROVING TREATMENT FOR PATIENTS WITH CANCER

James Gulley, M.D., Ph.D., F.A.C.P.
Co-Director, Center for Immuno-Oncology, Clinical Director, National Cancer Institute, NIH

SNS-101 PHASE 1/2 CLINICAL TRIAL OVERVIEW

Edward van der Horst, Ph.D.
Chief Scientific Officer, Sensei Biotherapeutics
Ron Weitzman, M.D.
Consulting Chief Medical Officer, Sensei Biotherapeutics

Q&A

Lack of Tumor Targeting is a Major Obstacle to CI Innovation

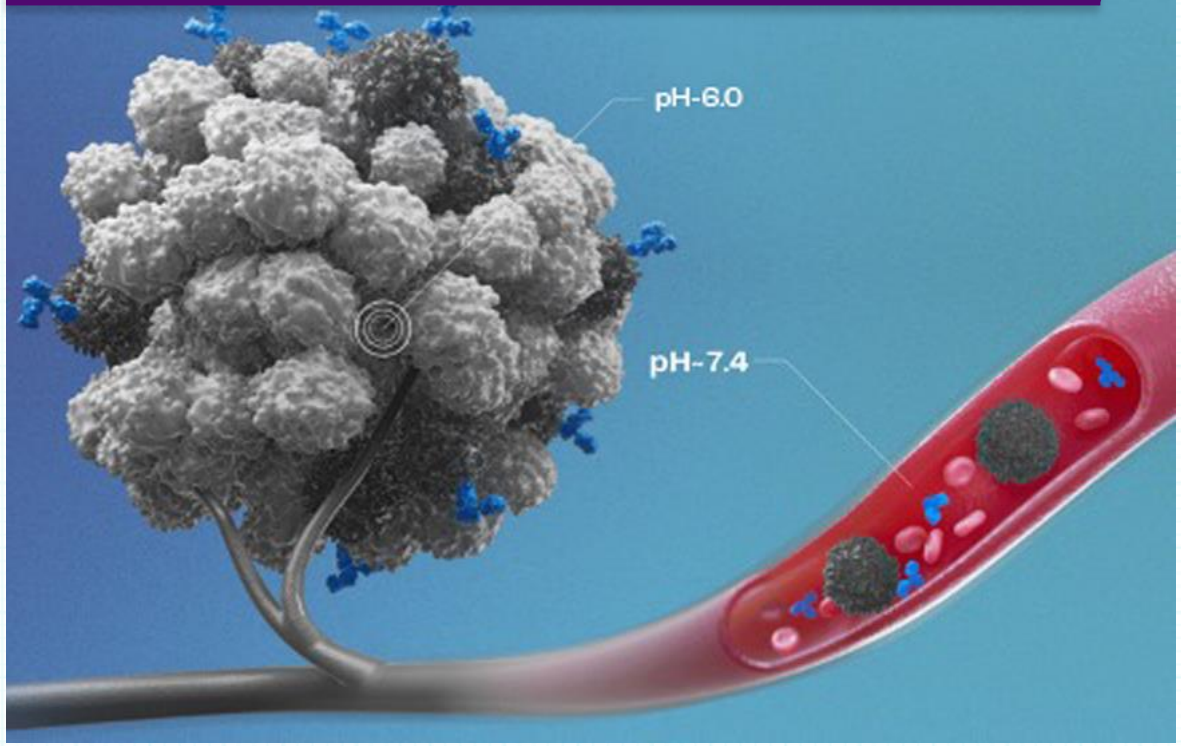
Industry Problem	Sensei's Solution
Conventional antibodies target immune checkpoints that are highly expressed in normal tissues, resulting in:	**Conditionally active antibodies are selectively targeted to the tumor microenvironment, potentially providing:**
Dose-limiting toxicities due to on-target/off-tumor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

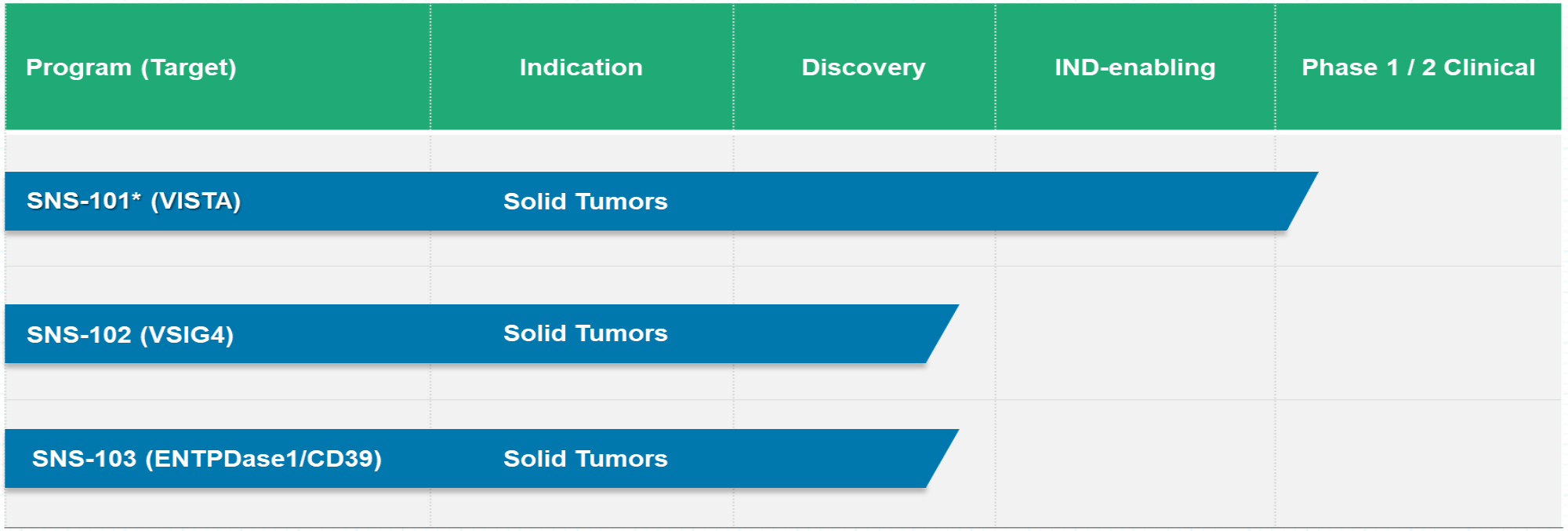
The tumor microenvironment of pH ~6 is lower than physiological pH of 7.4



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

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

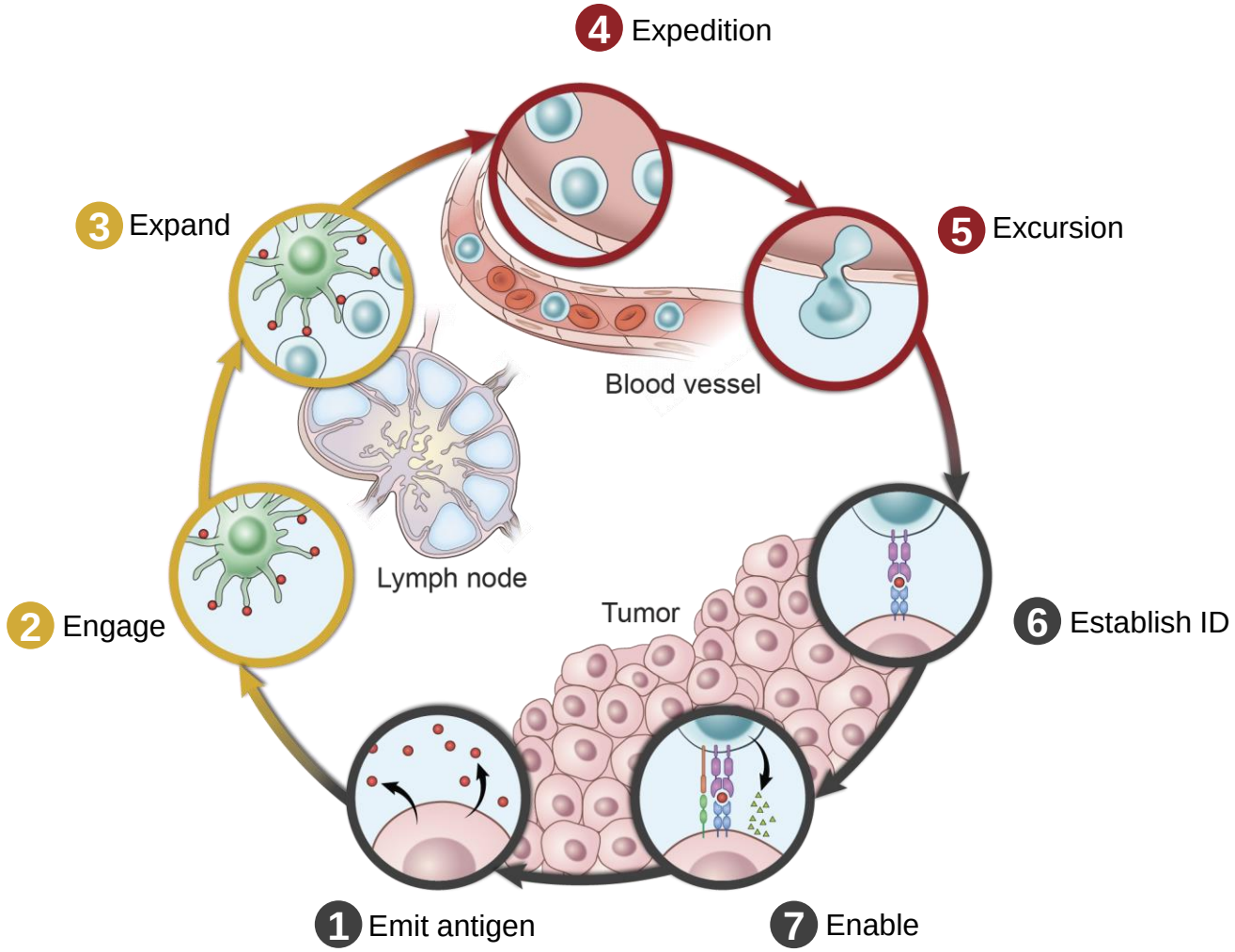
*Sensei has entered into a clinical supply agreement with Regeneron supporting the planned evaluation of SNS-101 in combination with Regeneron's anti-PD-1 therapy Libtayo® (cemiplimab) in a Phase 1/2 clinical trial in solid tumors.

Immuno-Oncology Landscape

James L. Gulley, M.D., Ph.D., F.A.C.P.
Co-Director, Center for Immuno-Oncology
Clinical Director, National Cancer Institute, NIH

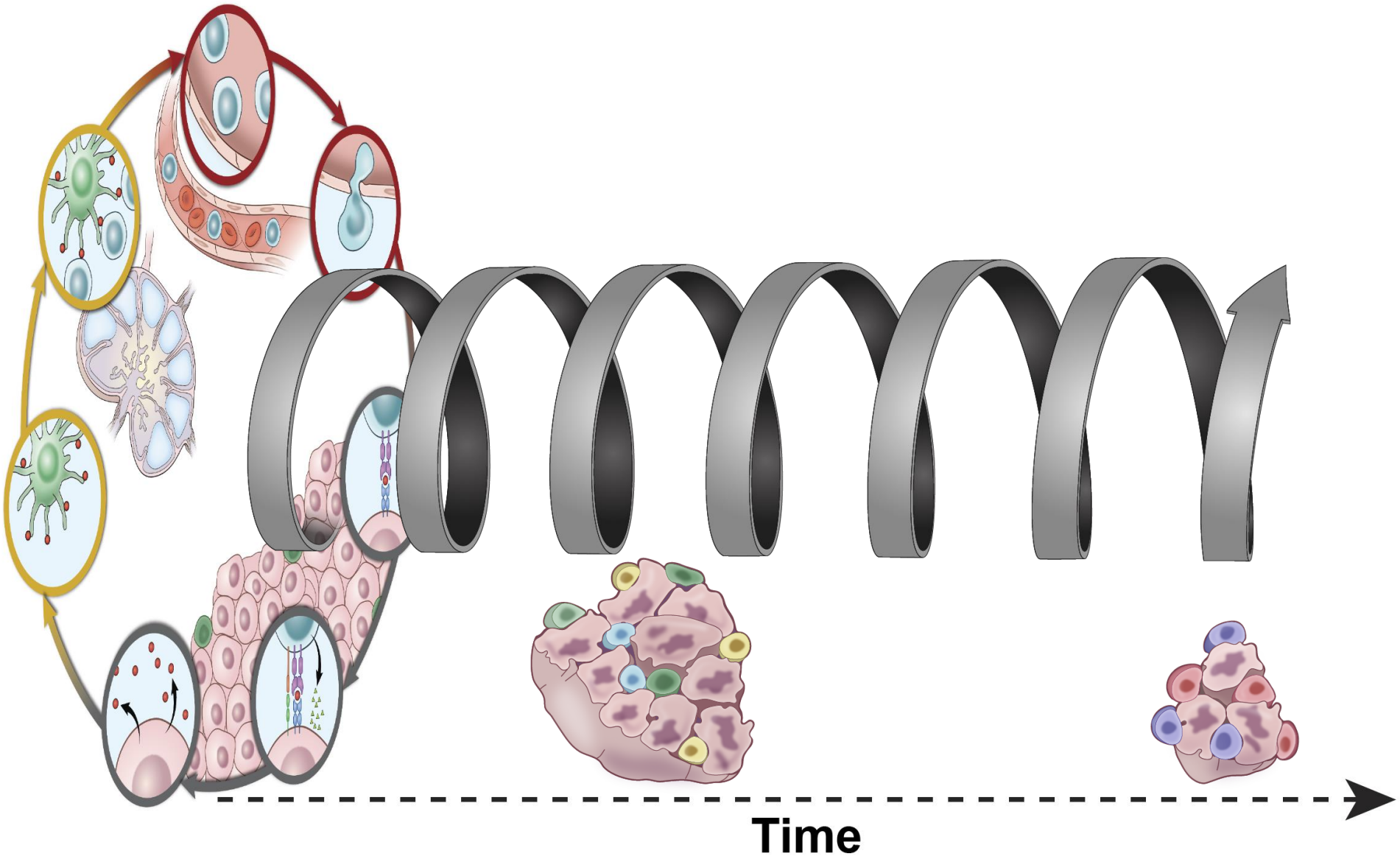
NIH NATIONAL CANCER INSTITUTE

Cancer Immunity Cyclical Evolution (E^8)

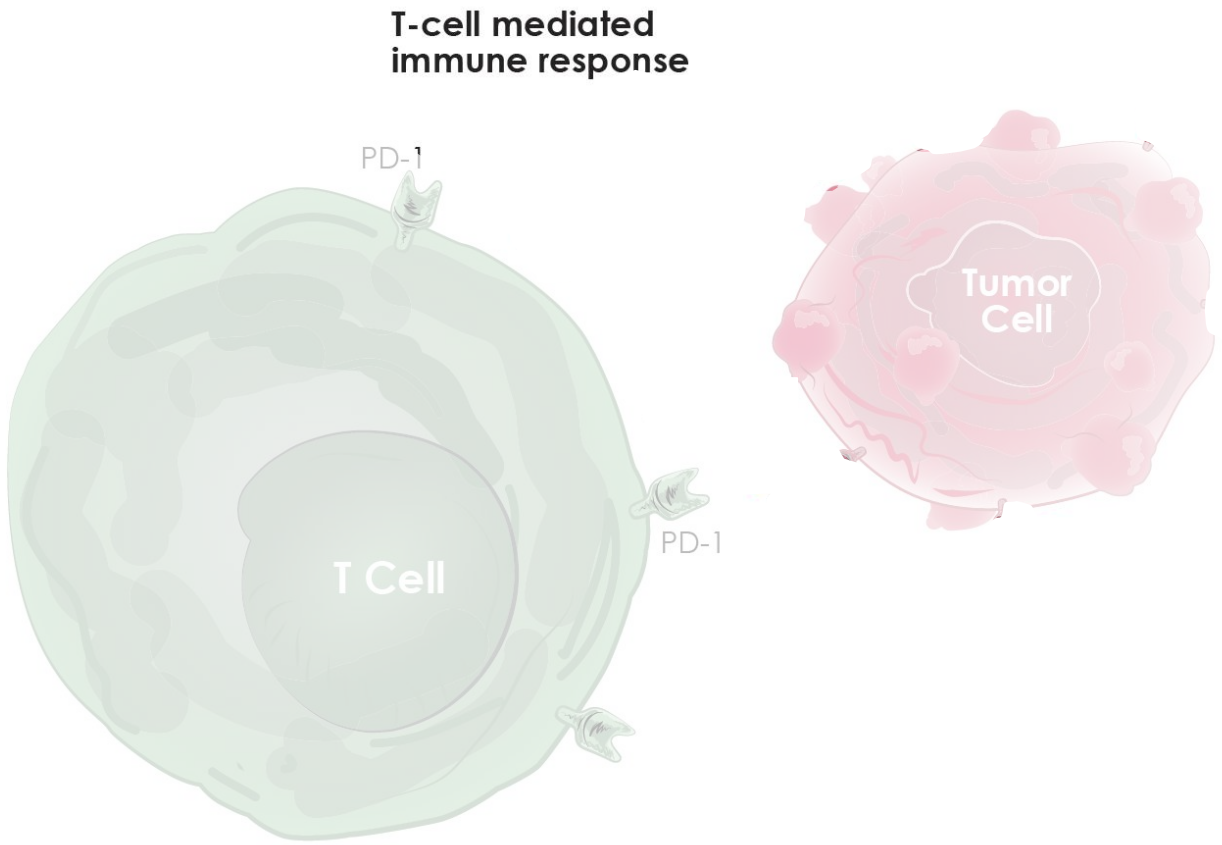


Modified from Chen and Mellman, *Immunity* 2013

Cancer Immunity Cyclical Evolution (E^8): Antigen spreading



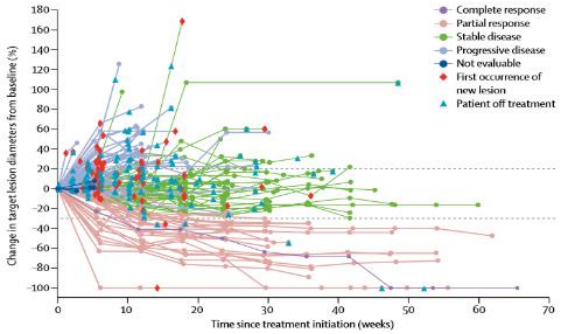
Importance of PD-1/PD-L1 blockade



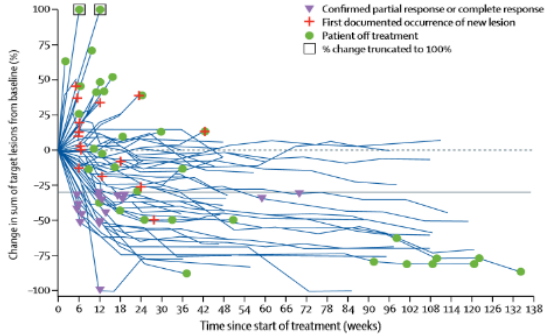
NIH. News Headlines: https://ccr.cancer.gov/news/article/investigators-lead-first-human-trials-of-new-immunotherapy-drug (accessed August 2017)

PD-1/PD-L1 inhibition

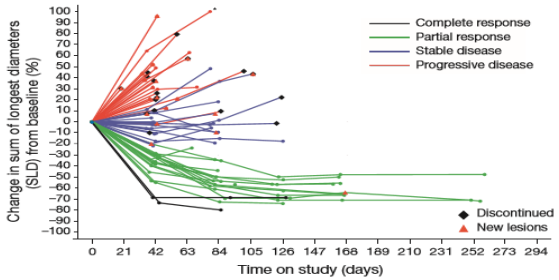
Rapid, deep, durable responses
Across a wide range of tumors
Seen in a subset of patients



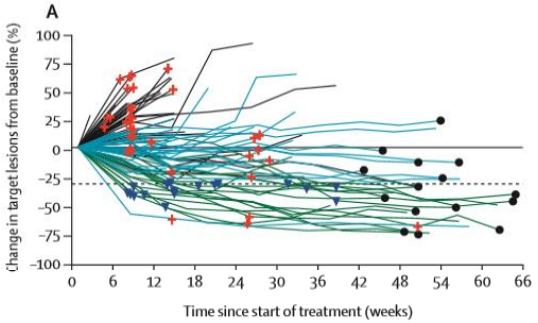
NSCLC: avelumab
Gulley JL et al. Lancet Oncol 2017



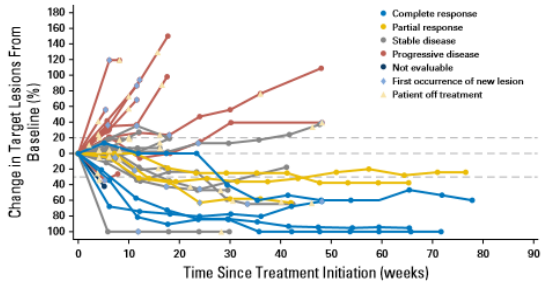
MSI hi CRC: nivolumab
Overman MJ et al. Lancet Oncol 2017



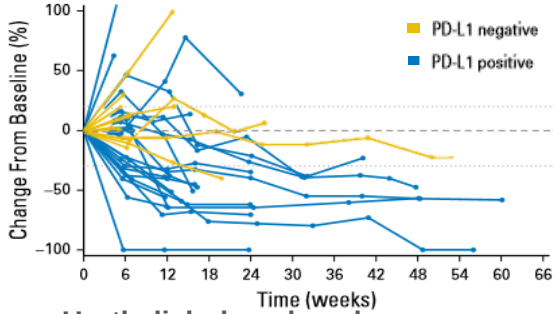
Urothelial: atezolizumab
Powles T et al. Nature 2014



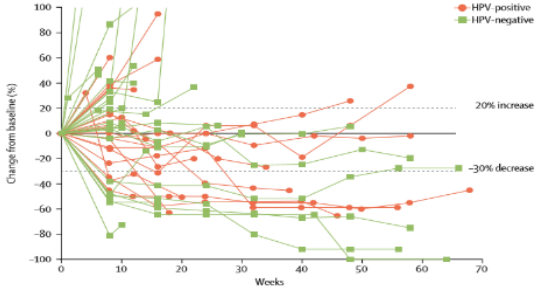
NSCLC (squamous only): nivolumab
Rizvi NA et al. Lancet Oncol 2015



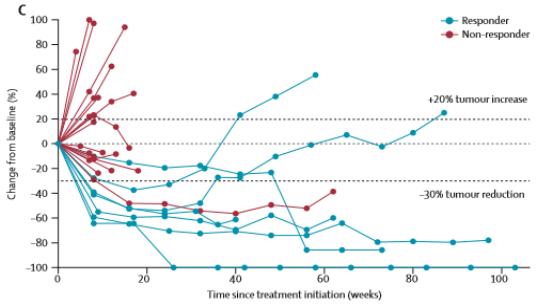
Urothelial: avelumab
Apolo AB et al. J Clin Oncol 2017



Urothelial: durvalumab
Massard C et al. JCO 2016

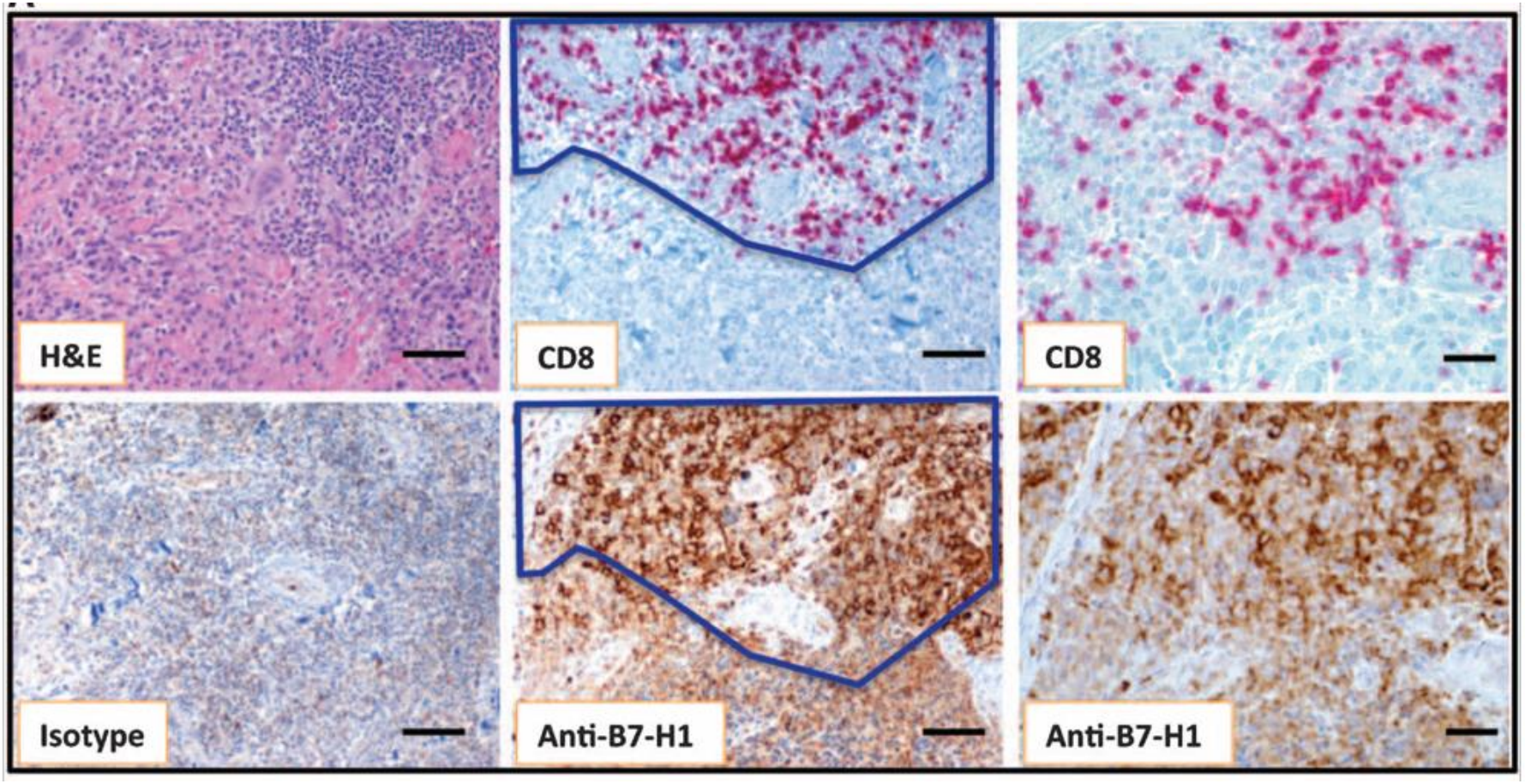


HNSCC: pembrolizumab
Seiwert TY et al. Lancet Oncol 2016



Urothelial: pembrolizumab
Plimack ER P et al. Lancet Oncol 2017

Co-localization of inflammatory response and PDL1 expression: TILs are being blocked at tumor site (Enable)



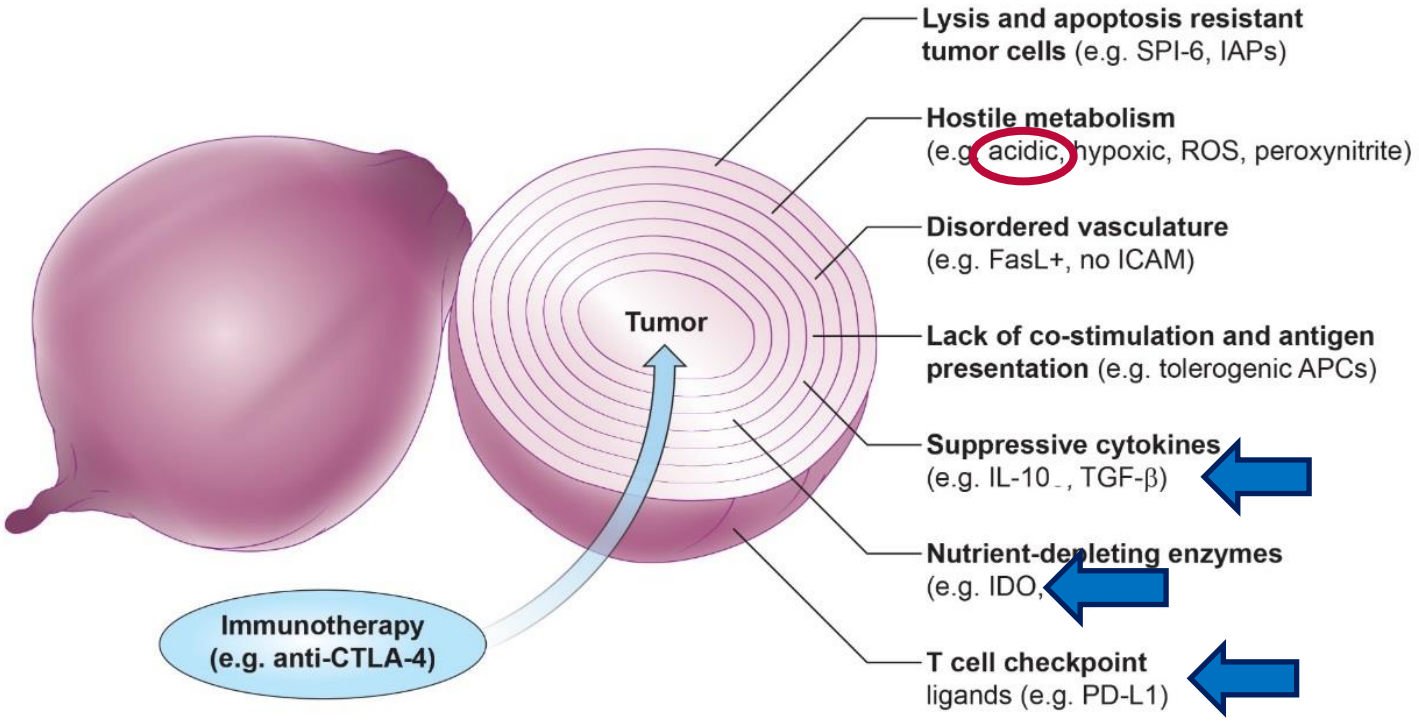
IFN-γ upregulates PDL1 expression in vitro

Taube et al., *Sci Trans Med* 2012

What happens when there is little / no immune recognition

- Strategies to enhance immune recognition include
  - Generating new cells to recognize tumor
    - ACT, vaccine, non-T-cell approaches etc.
  - Expanding effector cells / bringing them to TIME
    - Bi-specific Ab, cytokines etc.
  - Addressing other negative aspects of the TIME
    - TGF-beta, other checkpoints, IL10, etc.
  - Making use of unique properties of TME to engineer specificity
    - pH, proteases, low O_2

Multi-layered immunosuppression

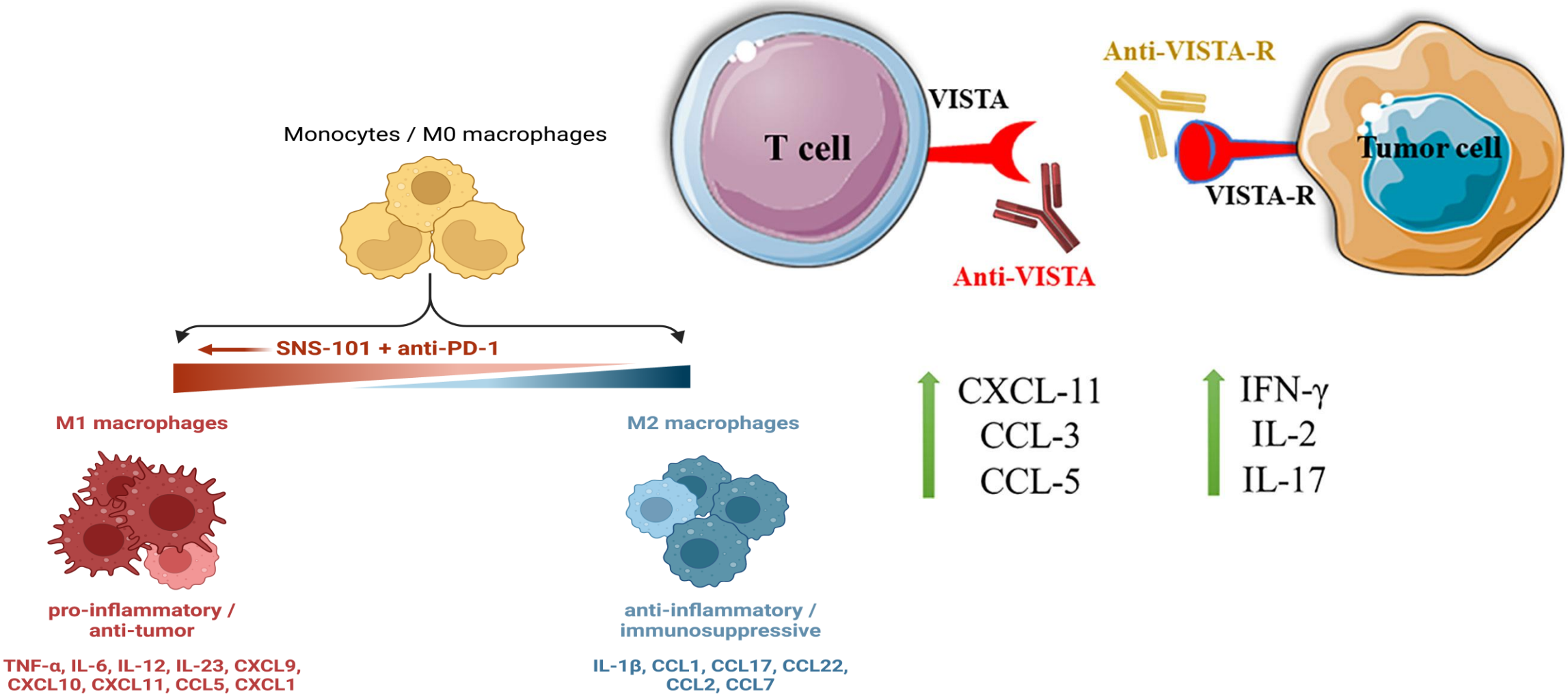


- Tumors insulate themselves with dense layers of immunosuppressive stroma
- Overcoming the many layers of interconnected and often functionally redundant immune suppressive mechanisms represents a daunting challenge for tumor-specific T cells
- Immunotherapy can "peel back" the layers of local immune suppression, thereby restoring the capacity of T cells to eradicate the tumor

sitc

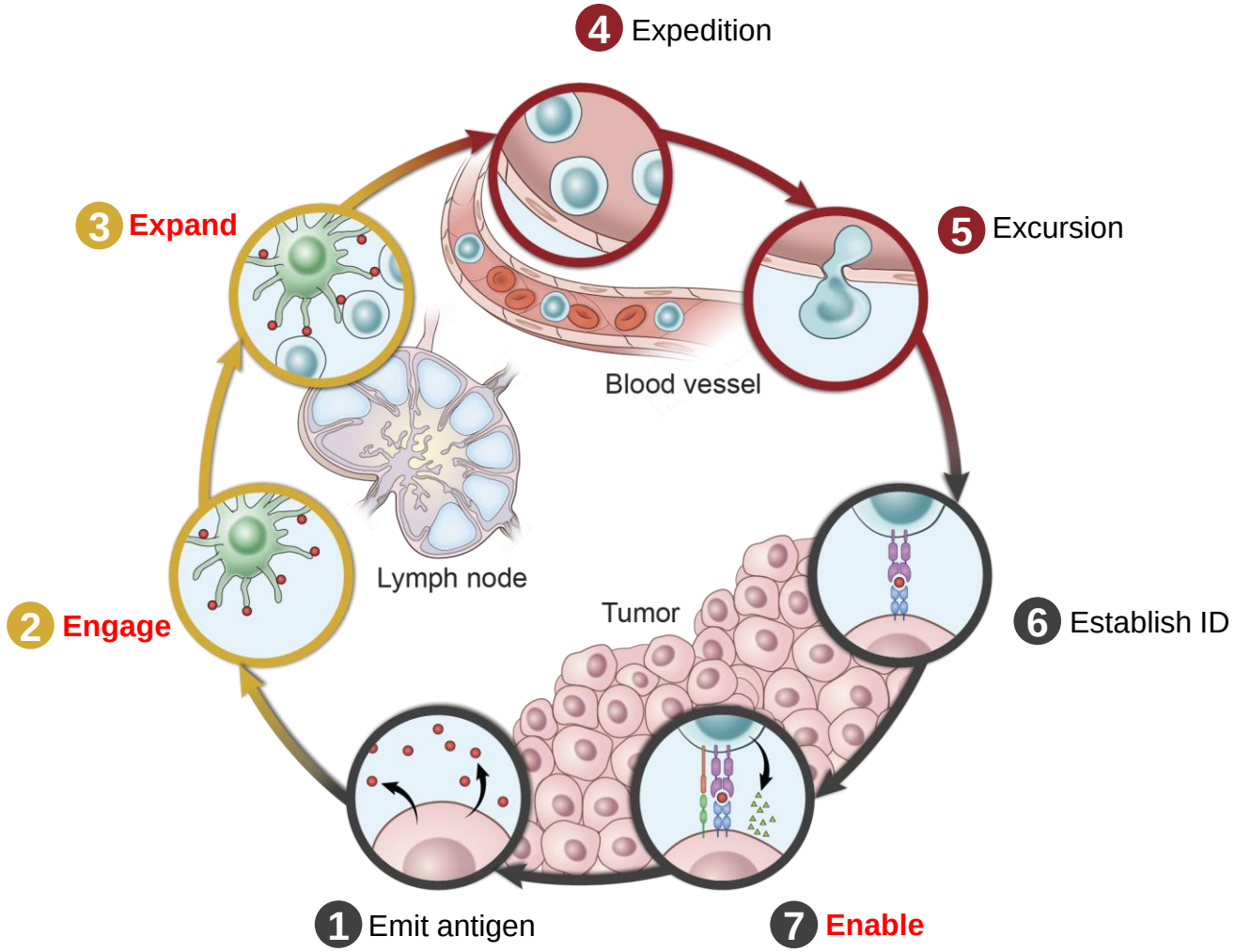
NIH NATIONAL CANCER INSTITUTE

Impact of targeting VISTA



Hosseinkhani *et al, Font. Immunol*. 2021

Universal Strategy for Immunologically Cold Tumors?



Examples of some combination approaches at NCI

- QuEST (vaccine, IL-15, bintrafusp alfa) ESMO and AACR
- HPV Triple (vaccine, IL-12, bintrafusp alfa) ASCO
- BEST (HDACi, IL-12, bintrafusp alfa)

NCI's Center for Immuno-Oncology

- Formed in 2022 from parts of 3 groups
  - Serves as a nidus for future immuno-Oncology growth at the CCR
  - Has about 100 personnel
- Has CRADAs with 22 companies (pharma/biotech)
  - Cooperative Research and Development Agreement
  - Allows for novel/novel combinations from different companies
  - Only mechanism to provide resources for co-development of agents
- Preclinical/translational and Clinical Programs in
  - Therapeutic Cancer Vaccines
  - Immune Checkpoint inhibitors
  - Immunocytokines
  - Bispecific Antibodies
  - Cell Therapies (TCR-T, CAR-T, CAR-NK, others)
  - **Combination IO approaches**

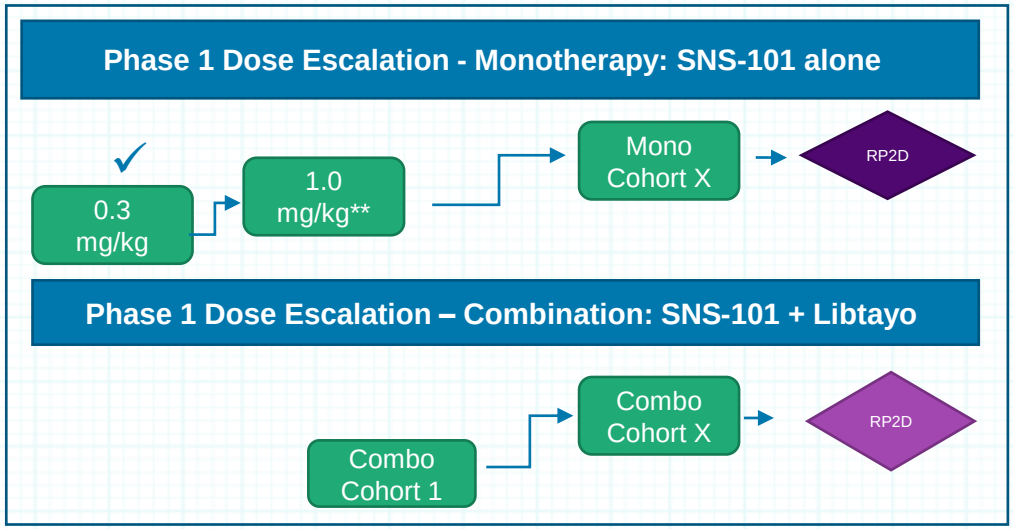
CRADA with Sensei

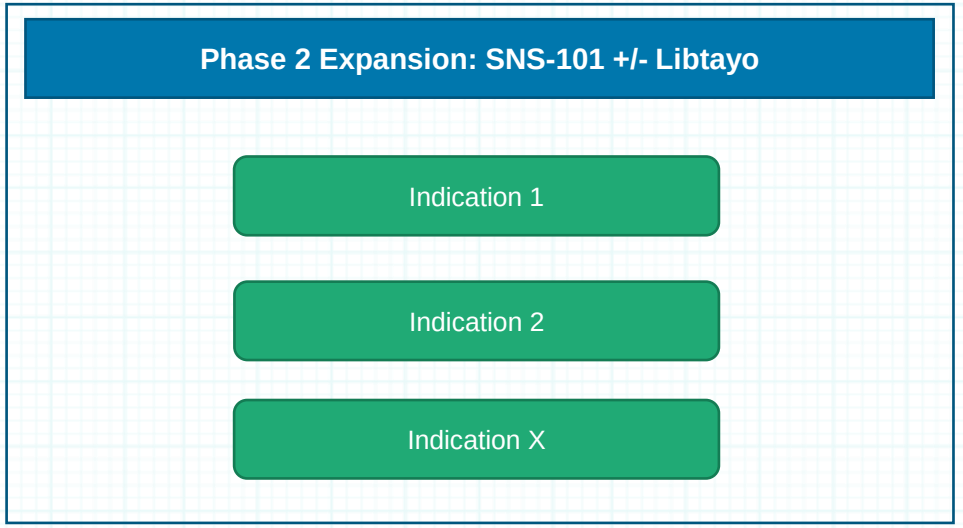
- Executed Feb 2, 2023
- Ongoing preclinical studies exploring combination approaches
  - Led by Jeff Schlom
- Clinical trial
  - NCI to act as clinical trial site for SNS-101
  - Scientific review (branch 6/28 then institute) → IRB

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
** Currently screening patients in Cohort 2 (1.0 mg/kg)
RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose

New VISTAs for our partnership

- Potential for novel / novel combination approaches in the clinic

Edward van der Horst, Ph.D.

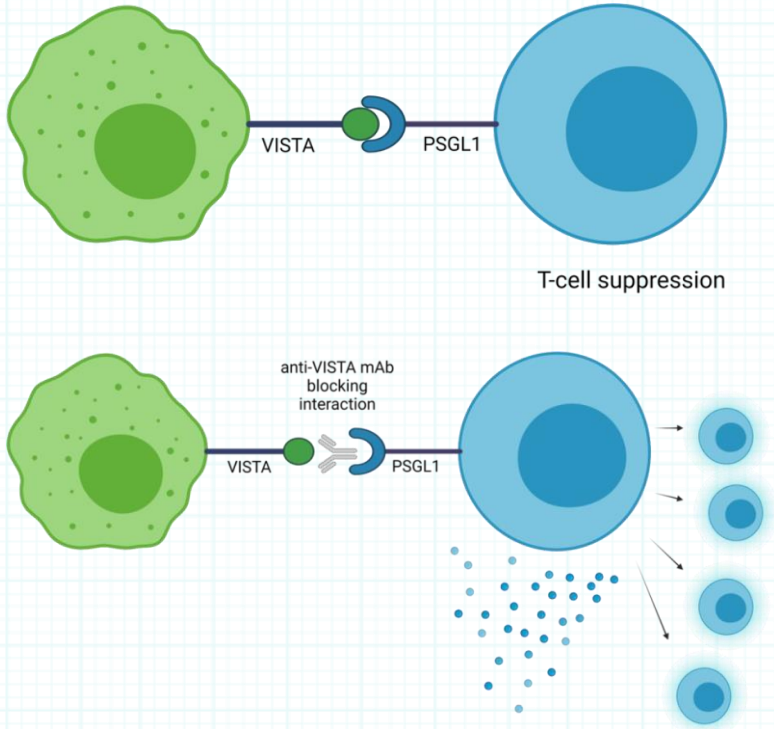
SNS-101 Overview

sensei BIO

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

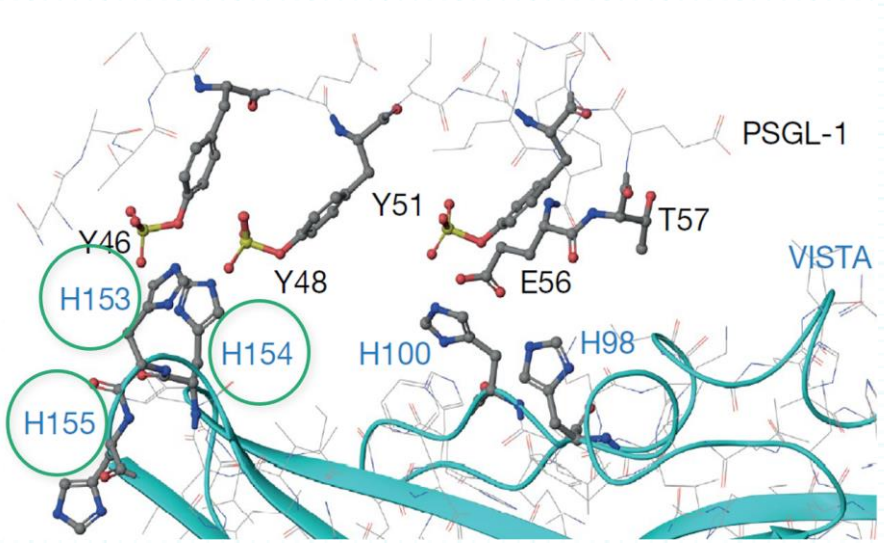
VISTA is a B7 family member that suppresses T cell function

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]

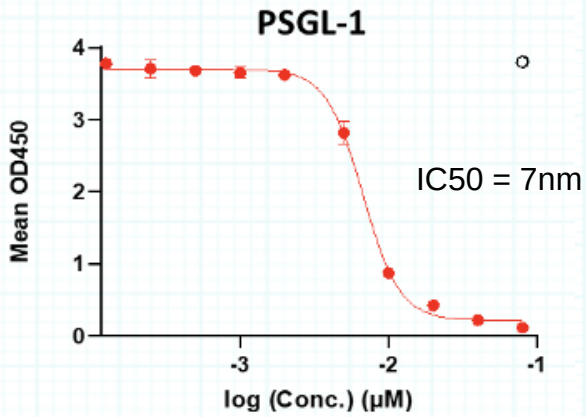
pH 6.0	pH 7.4
0.218	132 (~No binding)

Additional SNS-101 features

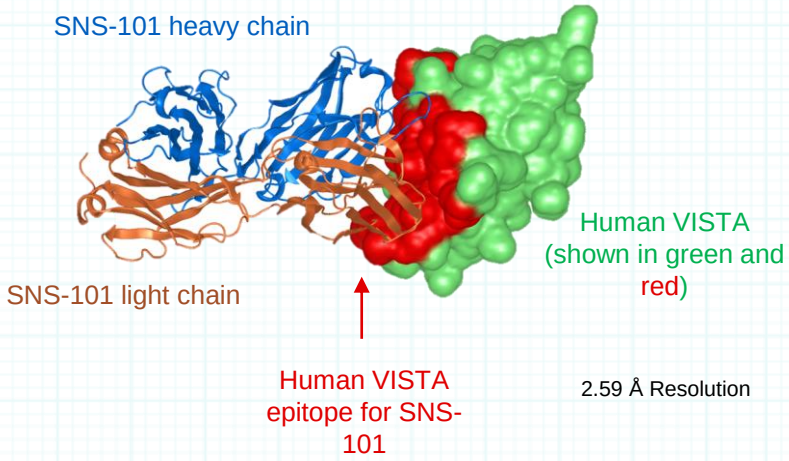
- IgG1 format
- Active Fc

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*

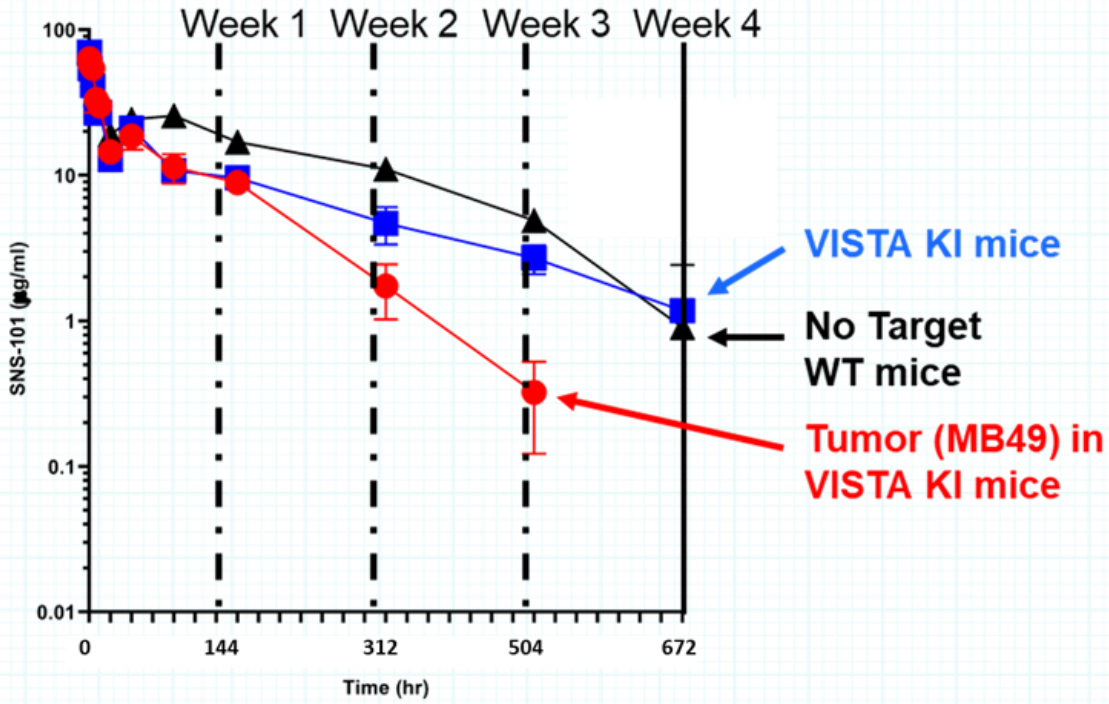


VISTA:SNS-101 co-crystal structure demonstrates epitope of SNS-101 encompasses VISTA's PSGL-1 epitope



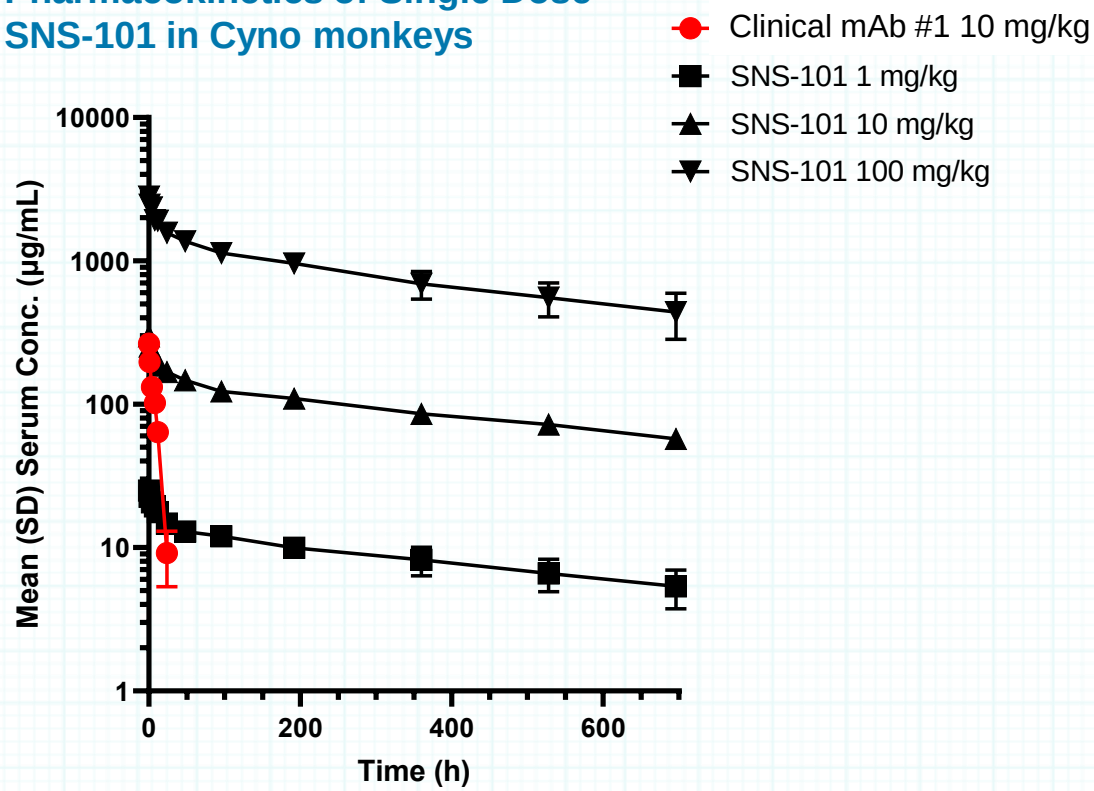
SNS-101 Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - *No Significant TMDD in Human VISTA KI Mice or Non-human Primates*

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



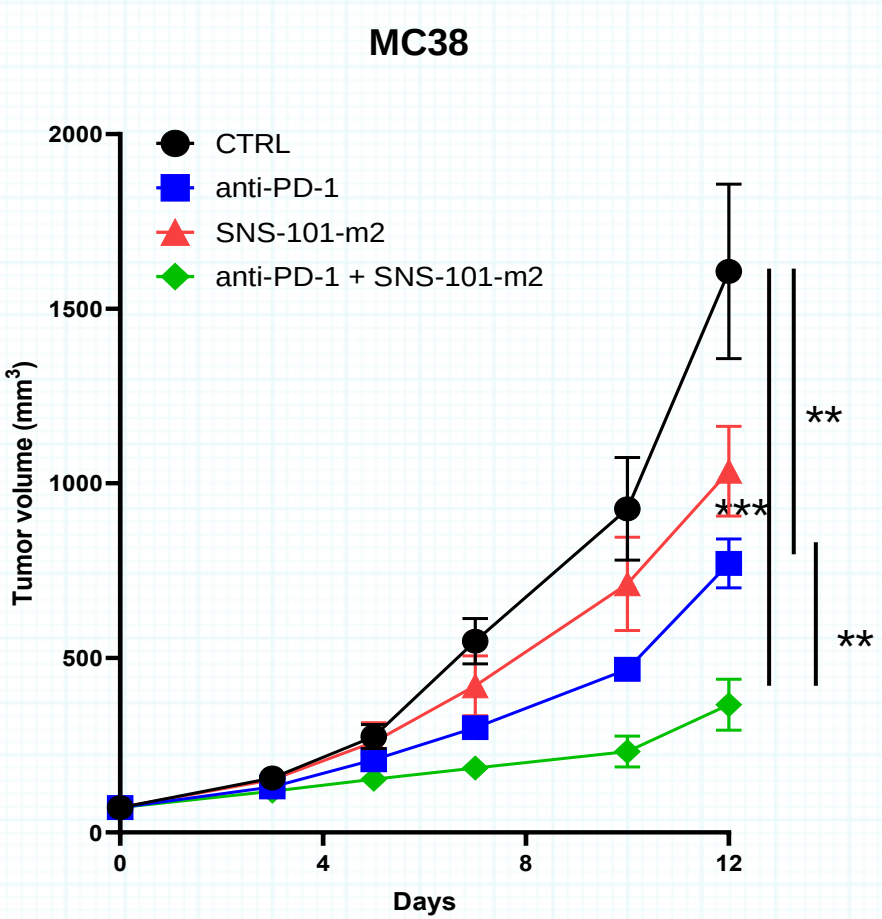
Demonstrated a long mean residence time in the blood, indicating a lack of significant target-mediated drug disposition (TMDD) and clearance in non-malignant tissues

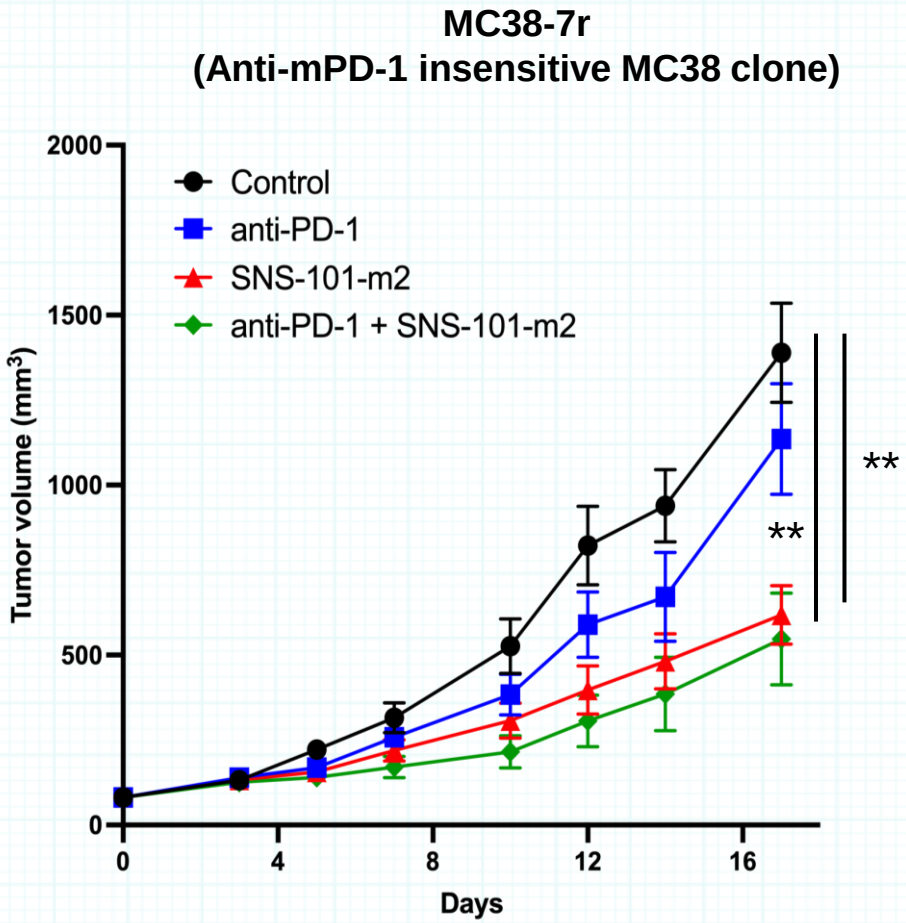
Pharmacokinetics of Single Dose SNS-101 in Cyno monkeys



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

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





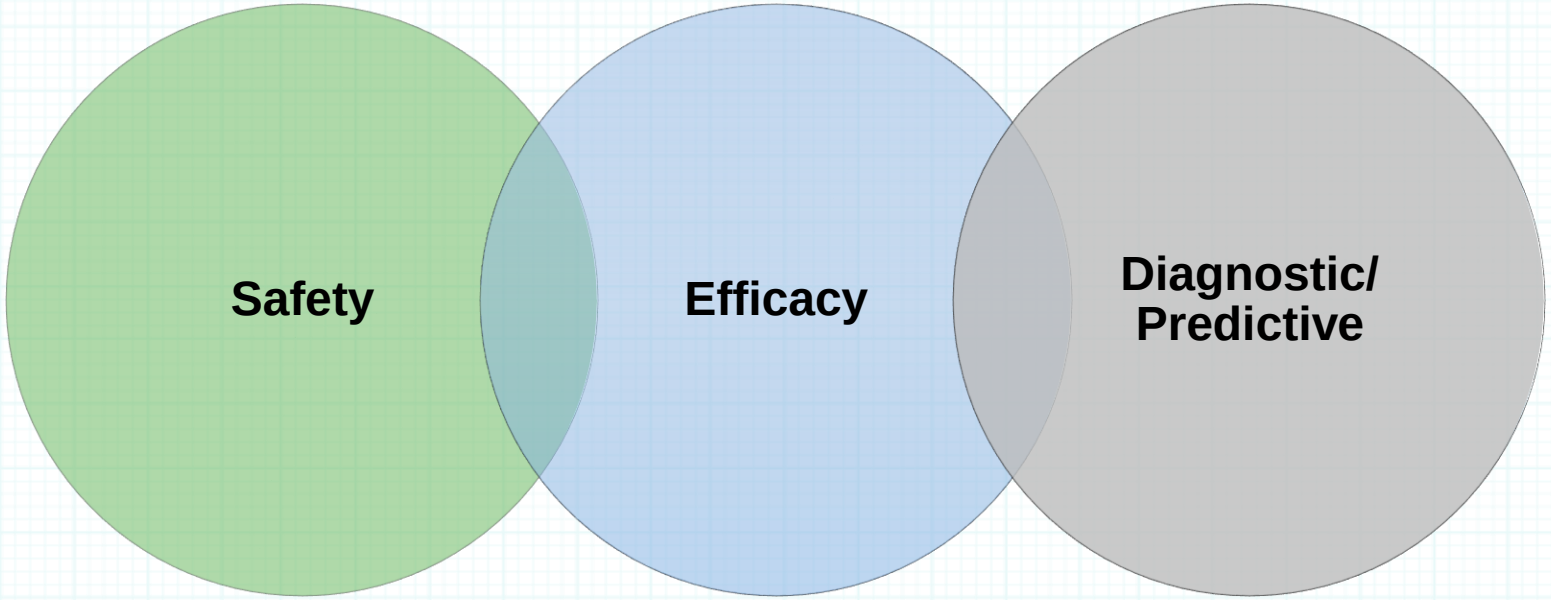
* *P*<0.05; ** *P*<0.01; *** *P*<0.001

SNS-101 “Responder Hypothesis”

Preclinical and Clinical/Translational Data to Inform Patient and Indication Selection

Hypothesis		Potential Clinical Direction
Combination therapy with SNS-101 and approved anti-PD-(L)1 drugs can overcome adaptive resistance induced by CPI treatment	→	Patients with hot tumors refractory to CPIs
SNS-101 can unleash CPI response in immunologically active yet refractory tumors	→	Patients with inflamed but cold tumors
Tumor types with high VISTA and PSGL-1 expression & proximity have VISTA-PSGL-1 checkpoint engaged	→	CPI-naïve patients

Phase 1/2 Clinical Trial Biomarker Plan



Pharmacokinetics
Is PK profile linear?

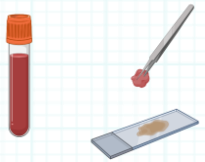
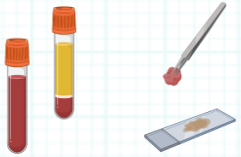
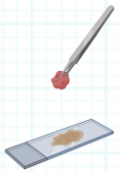
Safety/Toxicology
What are key toxicity issues related to SNS-101?

Pharmacodynamics
Does target engagement with protonated VISTA in the TME modulate directly and/or indirectly cellular activity?

Patient Selection/Stratification
What population is likely to experience positive benefit from SNS-101 treatment?

Does variability in target population affect efficacy and safety?

Anticipated SNS-101 Immuno-oncology Biomarkers

	Blood Serum	**PK/Safety** **PK & ADA**	Immunoassays	• SNS-101 exposure in blood • Anti-SNS-101 antibody detection
	Blood Serum PBMCs	**Biomarker**	Immunoassays Flow cytometry	• Cytokine analysis • Immunophenotyping
	Whole blood FFPE tissue (pre/on-treatment)	**Biomarker**	DNA sequencing RNA sequencing	• HLA typing • TCR / BCR repertoire analysis • Gene expression • Mutation identification / TMB • MSI status • Neoantigen prediction
	FFPE tissue (pre-treatment) Whole blood Cell-free plasma	**Biomarker**	DNA sequencing	• ctDNA tracking • Variant tracking of clinically relevant mutations • MRD detection
	FFPE tissue (pre/on-treatment)	**Biomarker**	Multiplex IF	• Cellular phenotyping (*52-plex*) • Spatial analysis of immune cell infiltration and interactions

Expected SNS-101 Program Milestones

May 2023: First patient dosed ✓

In or before Q1 2024: Dose first patient in combination with Libtayo®

2024: Topline Phase 1 monotherapy data

2024: Initial Phase 1 combination data

Question & Answer Session

sensei™ BIO

A New Vista for Cancer Care:

Exploring SNS-101's Potential as a Transformative Treatment Option for Patients with Solid Tumors

June 27, 2023

Guest Speaker:

James Gulley, M.D., Ph.D., F.A.C.P.

Co-Director, Center for Immuno-Oncology

Clinical Director, National Cancer Institute, NIH

James Gulley, M.D., Ph.D., is an internationally recognized expert in cancer immunotherapy with a strong interest in prostate cancer. Since 1998 he has authored and run a variety of clinical trials at the National Cancer Institute (NCI). These innovative, investigator-initiated studies involve the use of cancer immunotherapy to (a) initiate immune responses, (b) expand immune responses and/or (c) allow the immune responses to be effective within the tumor microenvironment. In addition to his role as the CIO Co-Director, Dr. James L. Gulley is the Clinical Director, NCI.

Sensei Presenters:

John Celebi
Chief Executive Officer

Dr. Edward van der Horst
Chief Scientific Officer

Ron Weitzman
Consulting Chief Medical Officer