SNS-101 Topline Monotherapy & Combination Dose Escalation Data

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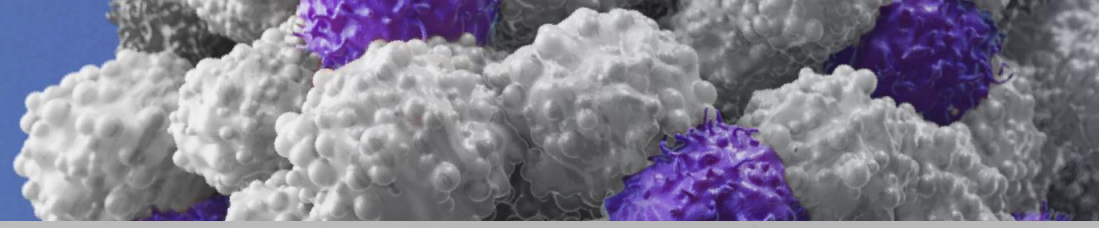

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VISTA is a Potent T cell Checkpoint Extensively Expressed on Myeloid Cells

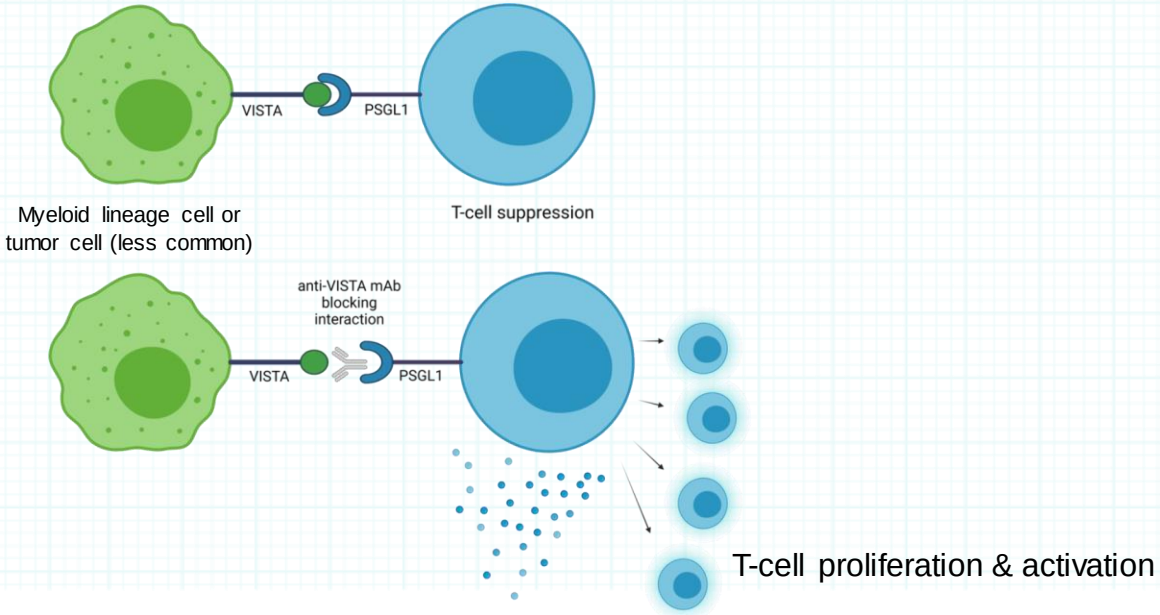
VISTA is a B7 family member that inhibits T cell activation[1]

Immunosuppressive function believed to be mediated by PSGL-1 receptor

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

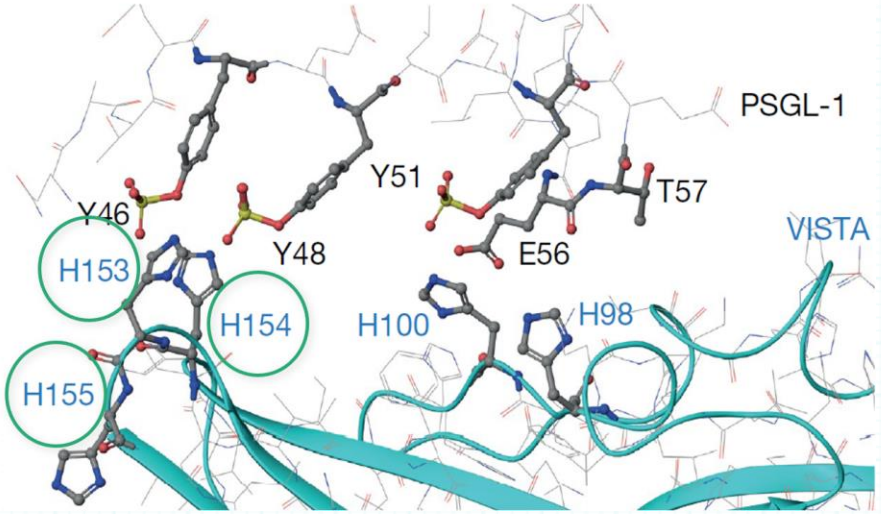
Increased expression on tissue infiltrating immune cells upon checkpoint therapy failure[3]

IS ACTIVATED IN A pH SENSITIVE MANNER



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

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



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

Competitors Previously Developing VISTA Antibodies Challenged by Severe Toxicities & Poor PK From Off-Tumor On-Target Activity

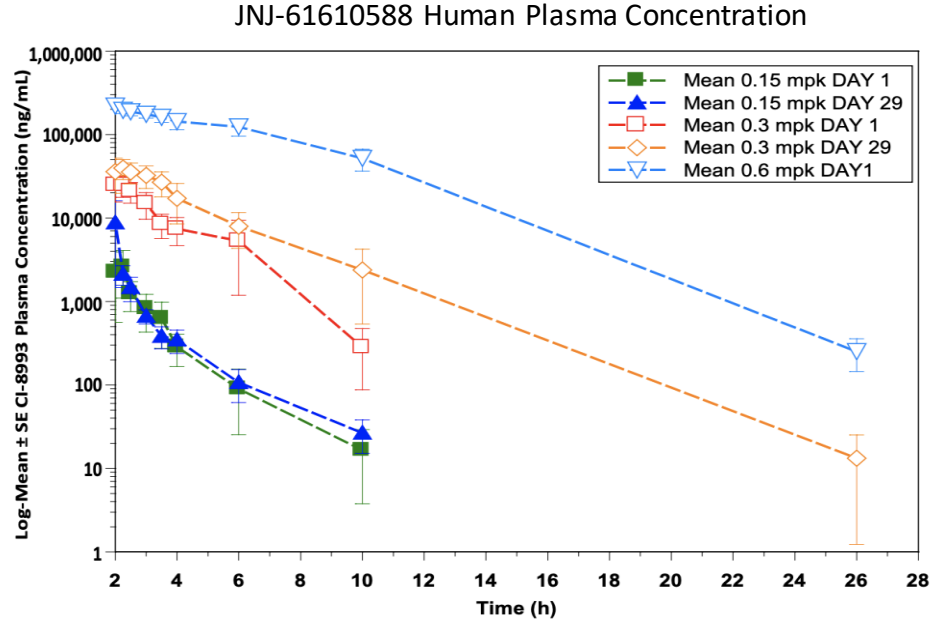
Dose-limiting toxicity

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

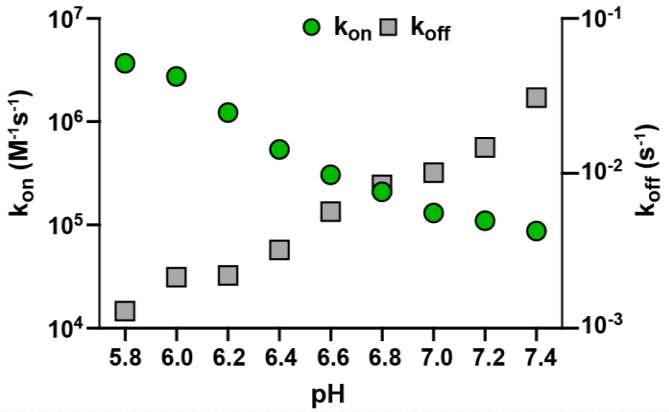
Non-linear PK, short $t_{1/2}$



1 Curis, Inc., Corporate Presentation, Feb 2022

SNS-101 is a pH-sensitive Antibody Selective for VISTA

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



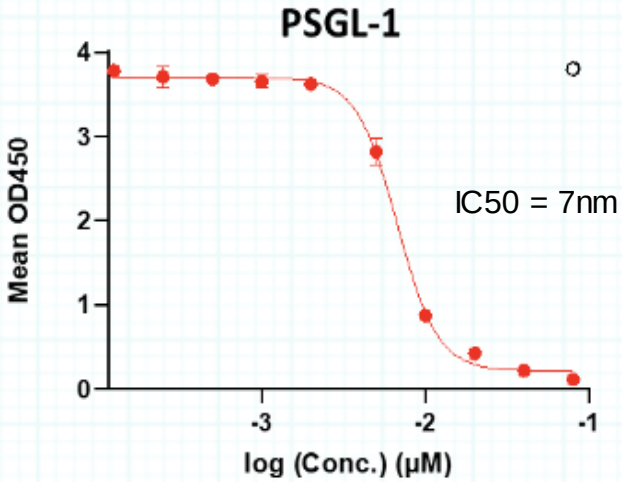
pH 6.0	pH 7.4
0.218 nM	132 nM (~No binding)

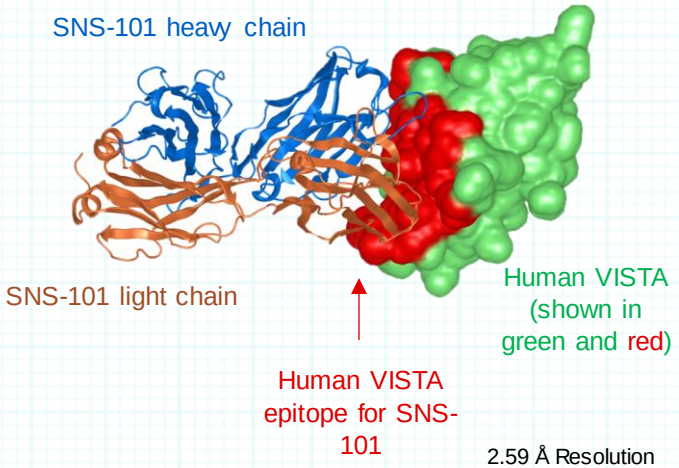
Monovalent Affinity (K_D)

Additional SNS-101 features

- IgG1 format
- Active Fc

Blocks the key receptor regulating VISTA's immunosuppressive activity





SNS-101 potently 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 SNS-101 encompasses VISTA's PSGL-1 epitope

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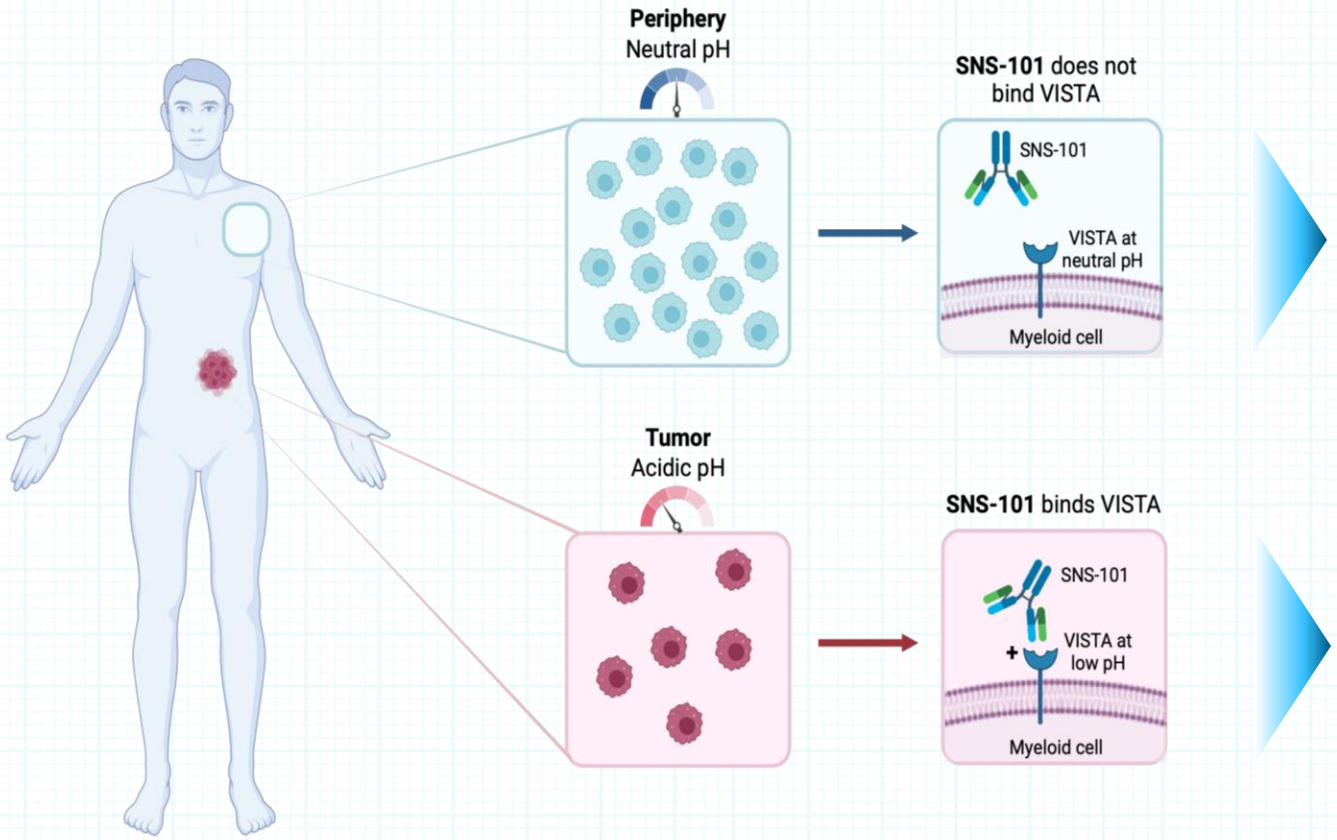
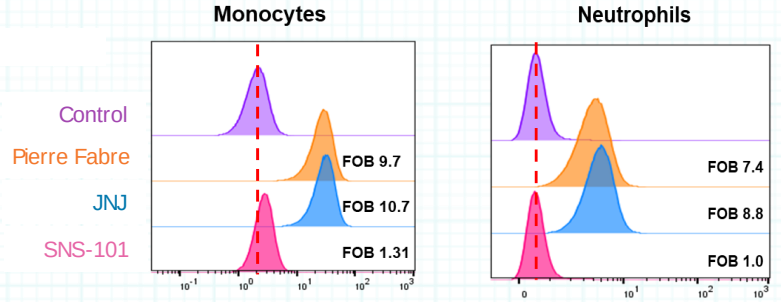
Thisted T. et al. *Nature Communications* 2024

SNS-101 Designed to Bind VISTA at the Tumor but Not in the Periphery



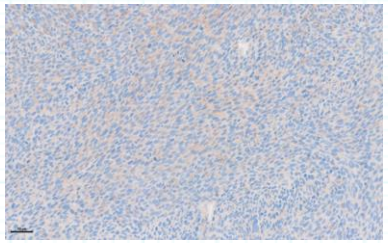
Periphery (Neutral pH)

SNS-101 had no detectable binding in peripheral or normal tissues

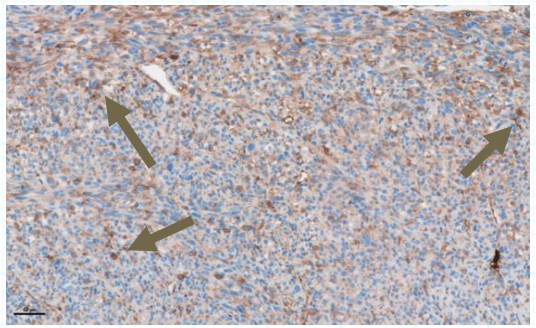


Tumor (Acidic pH)

SNS-101 rapidly accumulated in the tumor



Isotype control
6h post-dosing



SNS-101
6h post-dosing

Blue = tumor
Brown = SNS-101

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Early Development Plan is in Alignment with Corporate Objectives

Corporate Objectives	Impact on Study Design
PRIMARY Rapidly confirm conditionally active MOA through: • Lack of severe CRS • Absence of TMDD • Reach doses several folds higher than doses where prior anti-VISTA mAbs experienced DLT	• Enroll **all-comer** solid tumor population during **dose escalation** which included both "hot" and "cold" tumor histologies, allowing for efficient enrollment
SECONDARY • Explore VISTA's role in both "cold" and "hot" tumor settings to allow for efficient enrollment and to explore signs of activity in both settings • Identify RP2D	• Enroll **selected patient populations** to balance cold/hot tumor ratio • Explore more discreet range of doses

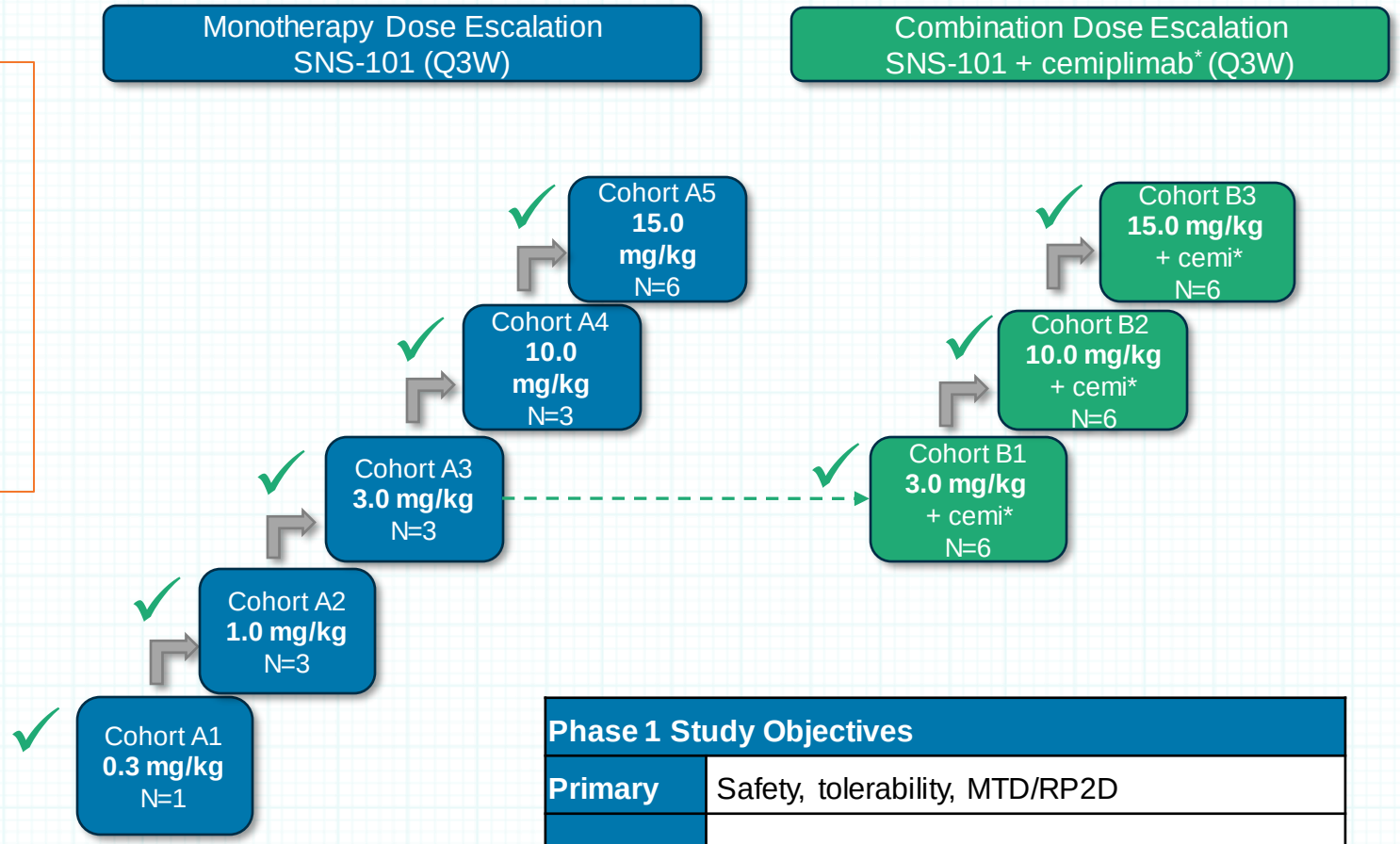
SNS-101 Phase 1 Study

Designed to rapidly confirm conditionally active MOA through:

1. **Lack of severe CRS**
2. **Acceptable PK**
3. **Dosing at pharmacologically relevant levels**

Phase 1 Dose Escalation

BOIN design in patients with advanced solid tumors



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

* cemi = Libtayo (cemiplimab) 350 mg

RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose
CRC = colorectal cancer
NSCLC = non small cell lung cancer
H&N = head and neck cancer

✓ = cleared DLT assessment period

Patient Disposition

	Monotherapy	Combination
	SNS-101 n=16 (%)	SNS-101 + cemi n=18 (%)
Enrolled	16 (100.0)	18 (100.0)
Treatment Ongoing	2 (13)	2 (11)
Discontinued	14 (88)	16 (89)
Progressive Disease	13	13
Adverse Event	0	1#
Withdrew Consent	0	1
Death Regardless of Causality	1*	0
Death Related to Study Therapy	0	0
Clinical Progression	0	1

** Related to disease progression, not related to SNS-101 (1 mg/kg dose level)*
 # Patient discontinued due to immune mediated AEs of Grade 3 AST and ALT (10 mg/kg + cemi)

Majority of Patients had Tumor Type Typically Unresponsive to PD-1 Monotherapy

	SNS-101 Mono n=16 (%)	SNS-101 Combo n=18 (%)
Gender, n (%)		
Male	12 (75)	11 (61)
Female	4 (25)	7 (39)
Age, years		
Median	61.5	62
Min, Max	35, 79	33, 81
Race, n (%)		
Asian	1 (6)	1 (6)
Black or African American	0	2 (11)
Not Reported	1 (6)	1 (6)
White	14 (88)	14 (77)
Ethnicity, n (%)		
Not Hispanic or Latino	14 (88)	14 (77)
Hispanic or Latino	1 (6)	3 (17)
Not reported	1 (6)	1 (6)
Baseline ECOG, n (%)		
0	6 (37)	4 (22)
1	10 (63)	14 (78)

	SNS-101 Mono n=16 (%)	SNS-101 Combo n=18 (%)
Prior lines metastatic therapy		
Median	2	2.5
Min, Max	0,7	1,7
Prior PD-1/PDL-1 YES%		
% Yes	**8 (50)**	**4 (22)**
Cancer Type, n (%)		
Responsive to PD-1 monotherapy (e.g. "hot" tumors)	**3 (19)**	**2 (11)**
Head and Neck	2	0
Kidney	1	2
Typically Unresponsive to PD-1 monotherapy (e.g. "cold" tumors)	**13 (81)**	**16 (89)**
MSS Colon	4	7
MSS Endometrial	0	1
Esophageal	1	0
Pancreatic	0	3
*Sarcoma**	4	2
*Other***	4	3

~85% of enrolled patients had tumors typically unresponsive to PD-1/PD-L1 therapy

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Data as of 30April2024

*Sarcoma: Leiomyosarcoma, Ewing Sarcoma, PEComa, Hemangiopericytoma (mono) and Leiomyosarcoma and Desmoplastic small round cell (combo)
**Other Tumor Types: Small cell lung carcinoma, Gallbladder, Adenocystic carcinoma maxillary sinus, and mediastinal carcinoma (mono) and Ovarian, Duodenal, granulosa cell tumor (germ cell)

SNS-101 Was Well Tolerated as Monotherapy and in Combination with Cemiplimab

- No dose-limiting toxicities observed
- Majority of AEs were Grade 1 or 2
- Two patients experienced Grade 1 CRS, suggesting that CRS is a class effect of VISTA-targeting antibodies

Summary of Adverse Events

	SNS-101 n=16 (%)	SNS-101 + cemi n=18 (%)
At least 1 TEAE	13 (81)	14 (78)
At least 1 SAE	1 (6)	8 (44)
≥Grade 3 TEAE	2 (13)	8 (44)
At least 1 TEAE leading to discontinuation	1* (6)	1 (5)
DLTs	0	0
AESI	1 (6)	5 (28)
Immune-mediated^	0	4 (22)
CRS#	1 (6)	1 (6)

**One patient experienced an SAE, Grade 5 bronchial obstruction, that resulted in death; not related to SNS-101, but to disease progression*
#Two patients experienced Grade 1 CRS
^One patient experienced Grade 2 rash maculo-papular at 3 mg/kg + cemi
^One patient experienced Grade 3 Diabetic Ketoacidosis at 3 mg/kg + cemi
^Two patients experienced elevated liver enzymes both at 10 mg/kg + cemi (one pt with Grade 3 ALT and Grade 1 AST and one pt with Grade 3 AST and ALT which resulted in discontinuation from treatment)

Most Frequently Occurring AEs (≥ 2 Overall) Regardless of Causality

Preferred Term	SNS-101 Mono n=16	SNS-101 Combo n=18	Total n=34
Fatigue	0	5	**5**
Cough	3	1	**4**
Pleural effusion	1	2	**3**
Pyrexia	2	1	**3**
Rash maculopapular	1	2	**3**
Alanine aminotransferase increased	0	2	**2**
Anaemia	0	2	**2**
Aspartate aminotransferase increased	0	2	**2**
Blood bilirubin increased	0	2	**2**
Chills	1	1	**2**
COVID-19	1	1	**2**
Cytokine release syndrome	1	1	**2**
Dermatitis acneiform	2	0	**2**
Hypokalemia	1	1	**2**
Hypomagnesemia	1	1	**2**
Infusion related reaction	0	2	**2**
Lymphocyte count decreased	0	2	**2**
Nausea	0	2	**2**
Pruritis	0	2	**2**

Data as of 30April2024

SNS-101 Has Only Been Associated with Mild IRR/CRS-like Adverse Events (Unlike First Generation VISTA Antibodies)

Subject Number	Dose Level	Adverse Event Preferred Term (Event description)	Severity (Grade)	Time of Onset relative to start of Infusion
01-010	SNS-101 15.0 mg/kg	Cytokine Release Syndrome (Chills and fever)	Grade 1	C1D1 ~4 hours post SNS-101 Infusion
01-013	SNS-101 15.0 mg/kg + cemi	Cytokine Release Syndrome (Chills, no fever)	Grade 1	C1D1 ~5 hours post SNS-101 Infusion
01-009	SNS-101 3.0 mg/kg + cemi	Infusion-related reaction (Chills and flushing)	Grade 2	C2D1 At the end of the SNS-101 Infusion
04-015	SNS-101 15.0 mg/kg + cemi	Infusion-related reaction (chest tightness, muscle aches, hypotension) *Patient also reported grade 1 itching and flushing about 1 hour after C1D1*	Grade 2	C2D1 ~6 minutes after start of SNS-101 infusion

- **All CRS events have been low grade and manageable**
- **Demonstrates that SNS-101 has the potential to overcome a key hurdle that impeded development of first-generation VISTA mAbs**

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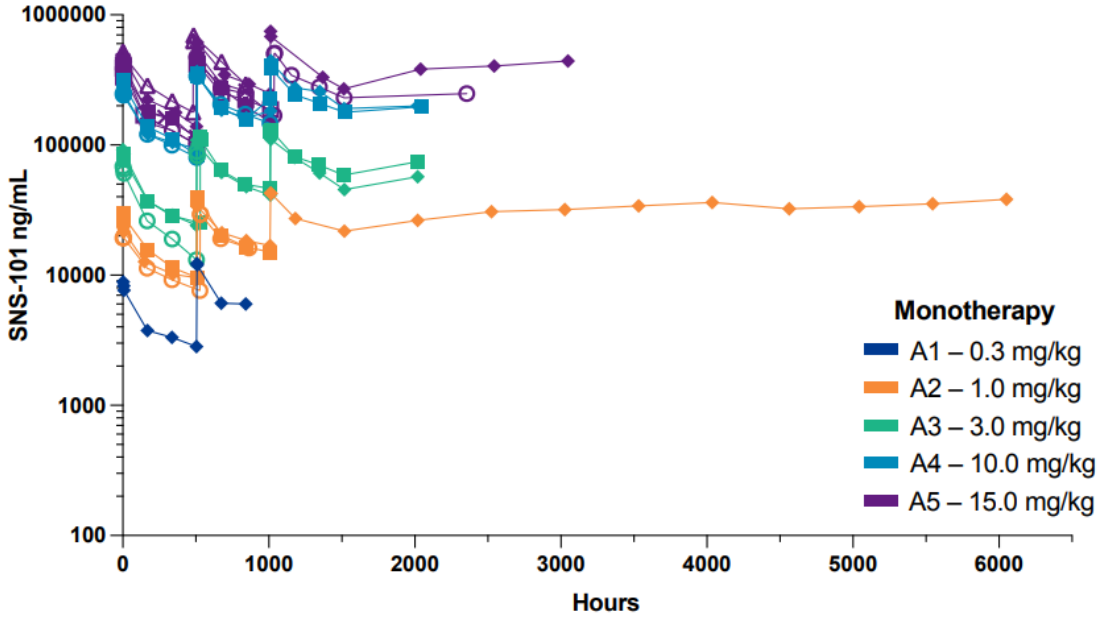
Data as of 30April2024

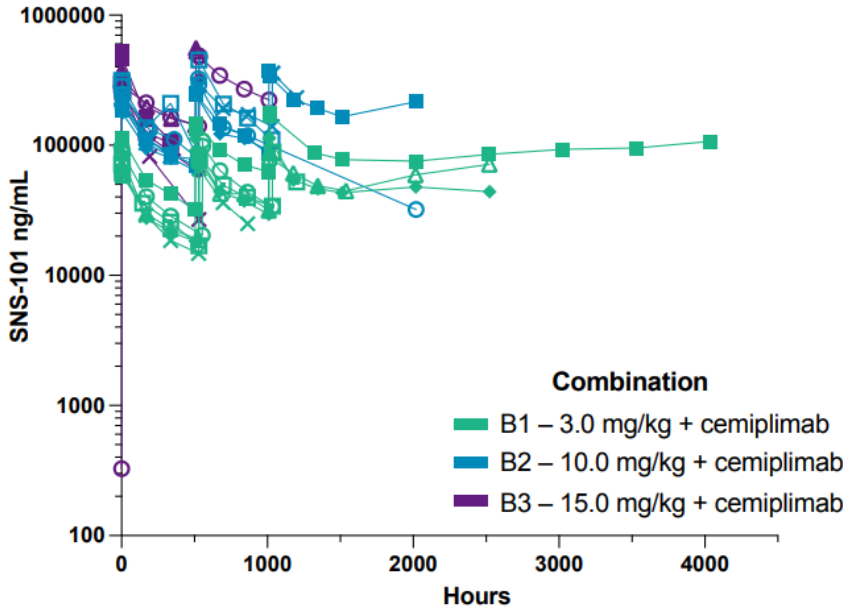
Pharmacokinetic Data Show Linear Elimination Kinetics with Long Half-Life

- Dose proportional exposure through 5 dose levels of SNS-101 (0.3 to 15.0 mg/kg)
- Consistent with lack of TMDD and supports Q3W dosing in humans
- No apparent effect on PK with combination
- Some increase with repeat dosing, but no notable accumulation
- No significant immunogenicity detected in analysis of ADAs

SNS-101



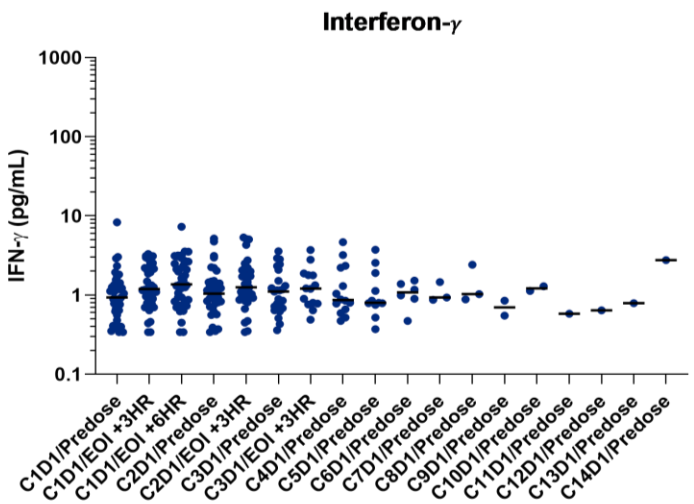
SNS-101 + cemiplimab

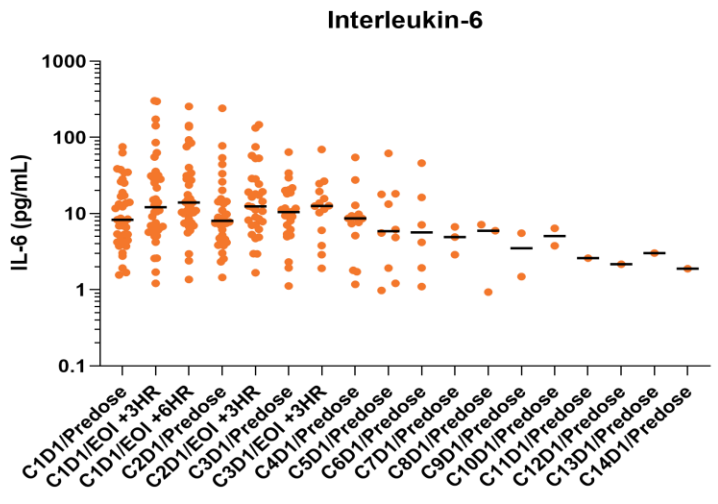


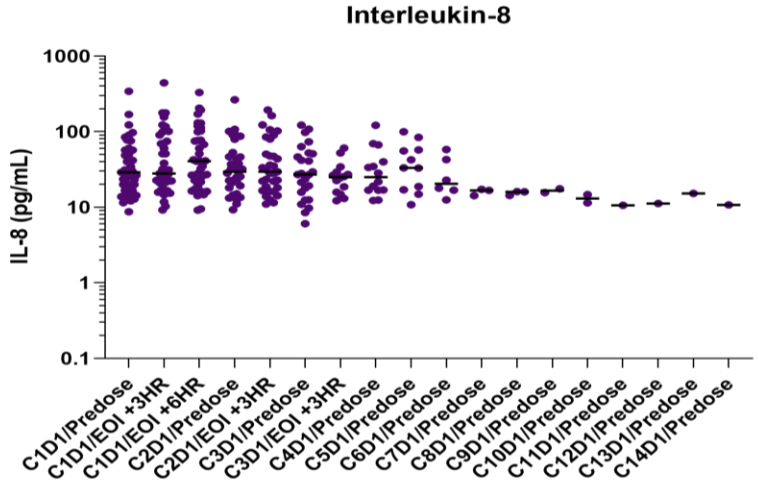
* Cemiplimab administered on Cycle 1 Day 2; co-administration thereafter

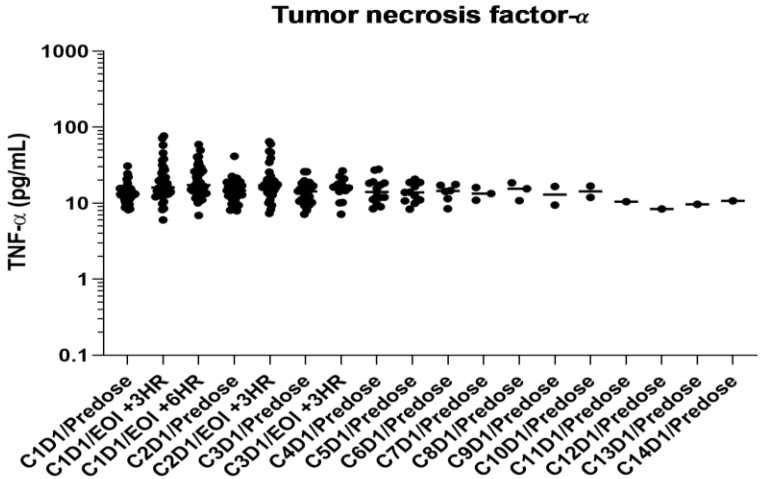
Data as of 30April2024

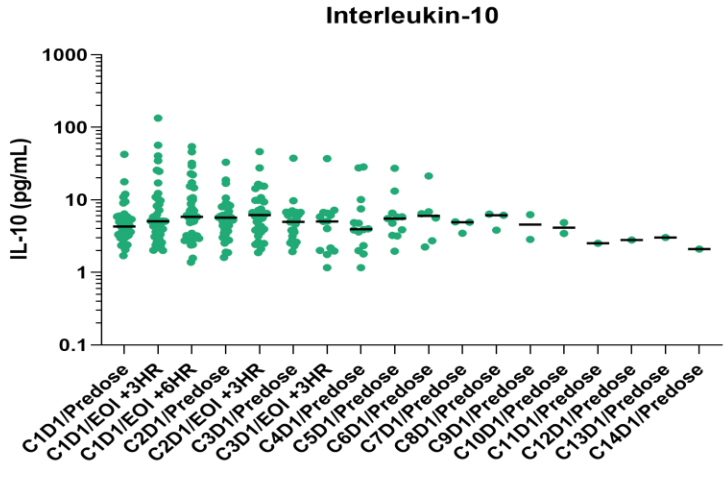
No Significant Changes in Key Inflammatory Cytokines

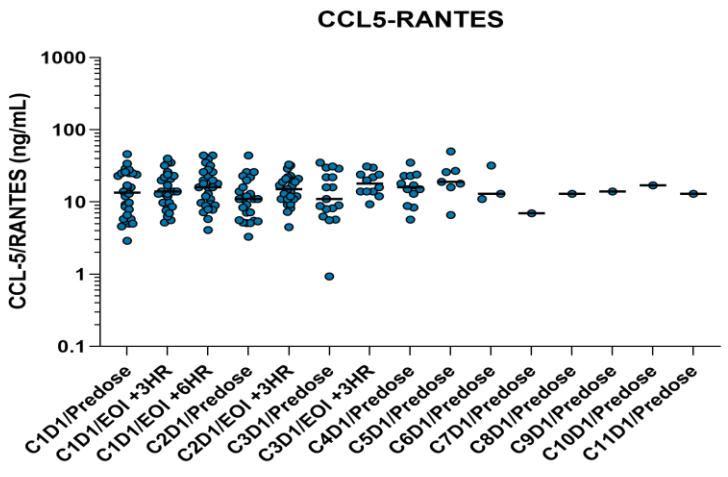












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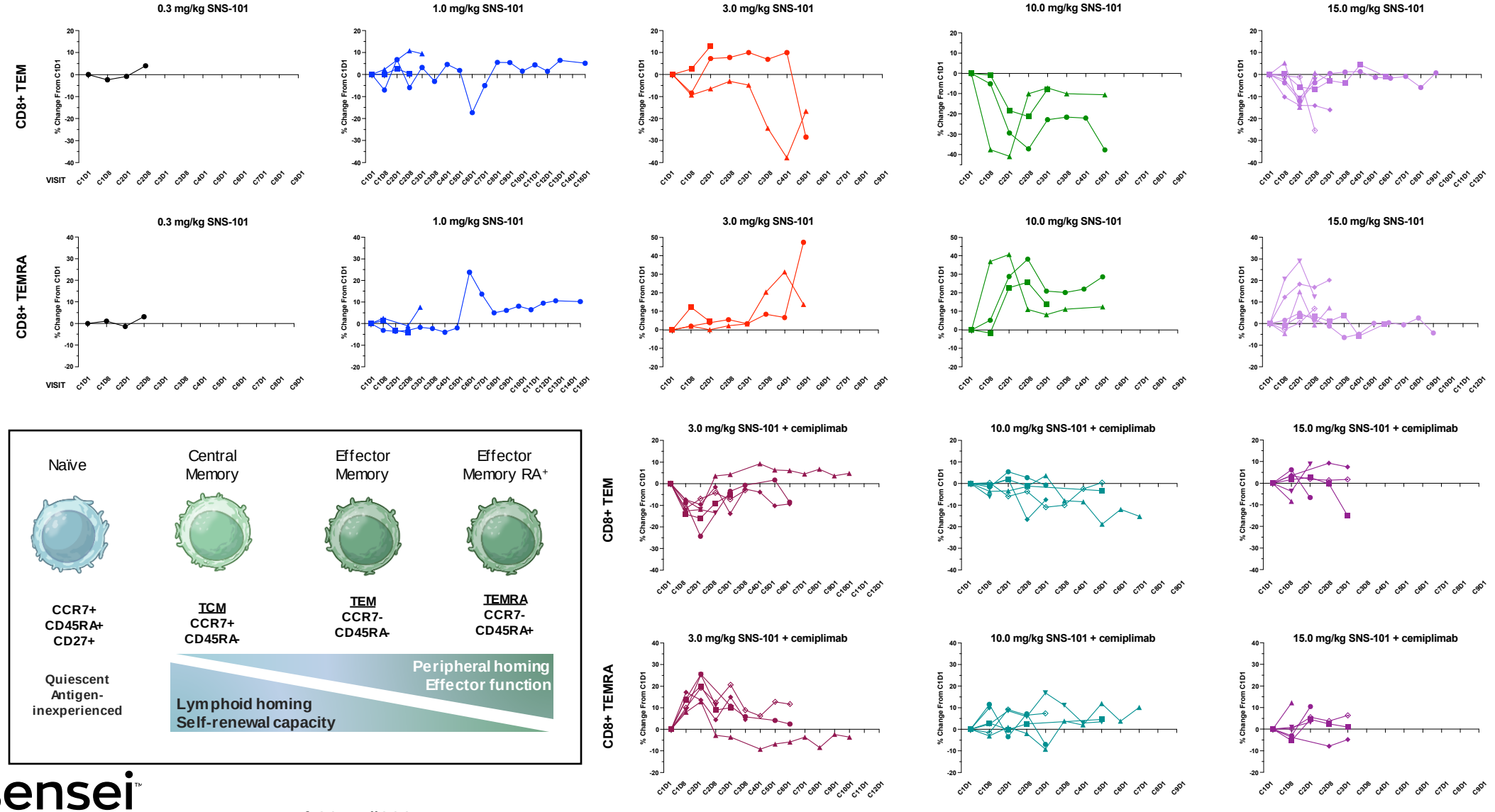
Dose-dependent Changes in Specific T-cell Populations Indicate Potential SNS-101-Related Pharmacological Effect



Data as of 30April2024

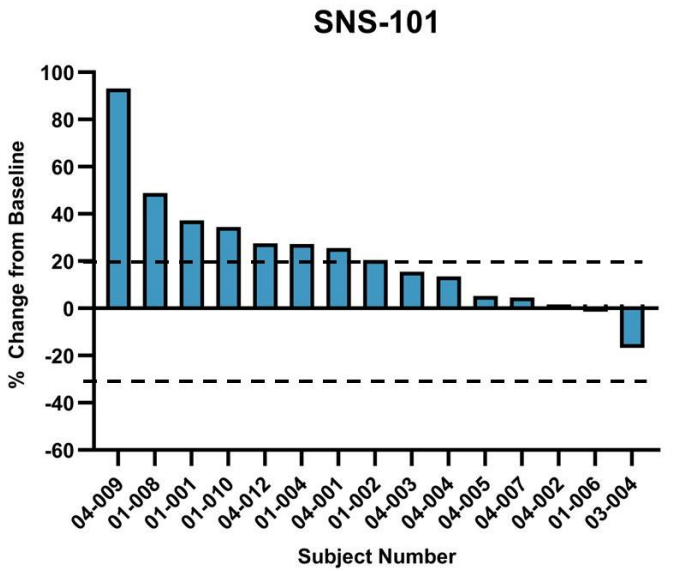
SNS-101 Alone or in Combination with Cemiplimab Has Shown Early Signs of Clinical Activity

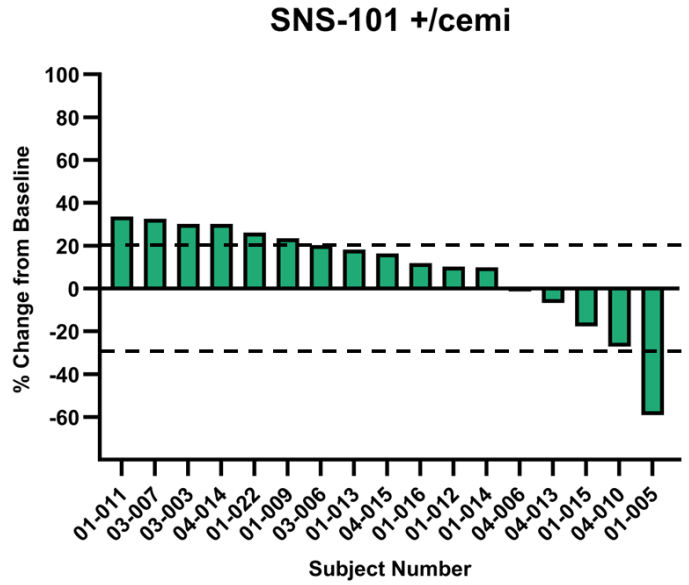
Monotherapy Dose Escalation

- 16 patients enrolled: 15 patients received both baseline and at least one follow-up scan
- 7 patients achieved stable disease as best overall response
- Patients of interest:
  - One pembrolizumab-resistant HPV+ H&N pt had tumor regression of 17% at a dose level of 15.0 mg/kg; discontinued at Week 12 due to PD
  - One pt with adenocystic carcinoma (maxillary sinus) continues on treatment with SD at 42+ weeks at a dose level of 1.0 mg/kg
  - One pt with leiomyosarcoma (kidney) continues on treatment with SD at 24+ weeks at a dose level of 15.0 mg/kg

Combination Dose Escalation

- 18 patients enrolled: 17 patients received both baseline and at least one follow-up scan.
- Patients of interest:
  - One **MSS** endometrial pt at 3 mg/kg + cemi had a confirmed PR (59% decrease); ongoing 30+ weeks
  - One **MSS** colon pt at 3 mg/kg + cemi had tumor regression of 27%; discontinued at Week 18 due to PD
  - One RCC pt at 10 mg/kg + cemi had tumor regression of 18%; discontinued due to immune-mediated toxicity





Data as of 30April2024

Two Examples of Patients with MSS Solid Tumors and Objective Tumor Regression

I/O-naïve MSS Endometrial Cancer with PR
3.0 mg/kg SNS-101 + cemiplimab (Patient 01-005)

68 yo female with endometrial carcinoma, dx Dec 2020, ECOG 0

- ER/PR positive, HER negative; PD-1/PD-L1: Not tested

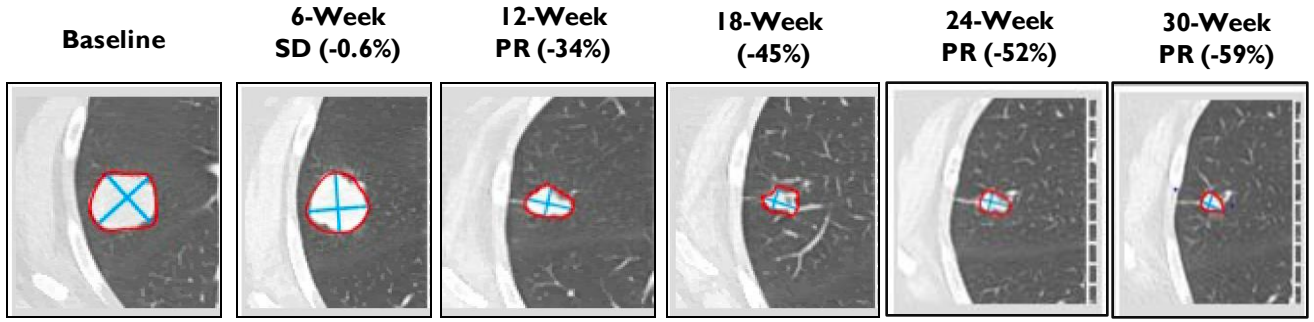
Prior Treatment/Surgery

- Total laparoscopic hysterectomy with bilateral salpingo-oophorectomy, and additional sentinel lymph node dissection, Dec 2020
- Paclitaxel/Carboplatin (adjuvant setting), Feb 2021 to Aug 2021
- Anastrozole (metastatic setting), Aug 2023 to Sep 2023

Adverse Events

- Grade 3 diabetic ketoacidosis 4 days after Cycle 3 infusions, related to SNS-101 and cemiplimab, AESI (immune-mediated) and SAE (hospitalization)
  - Patient recovered and maintained on Insulin and continued study therapy

Tumor Assessments in Solitary Target Lesion



I/O-naïve MSS Colon Cancer
3.0 mg/kg SNS-101 + cemiplimab (Patient 04-010)

62 yo male with colon cancer; dx Jan 2017, ECOG 1

- PD-1/PD-L1: Negative

Prior Treatment/Surgery

- Received 7 prior lines of therapy in the metastatic setting with the last 3 therapies investigational

Adverse Events

- Grade 2 dry skin, related to SNS-101, not related to cemiplimab
- Grade 2 rash maculo-popular, related to SNS-101 and cemiplimab, AESI (immune-mediated), resolved after treatment with prednisone
- Grade 2 pruritis, related to SNS-101 and cemiplimab

Tumor Assessments

- 6-Week Scans: Stable Disease (19% decrease)
- 12-Week Scans: Stable Disease (27% decrease)
- 18-Week Scans: Progressive Disease (23% increase from nadir)

Microsatellite stable (MSS) colon and endometrial tumors are typically unresponsive to PD-1/PD-L1 single agent therapy

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Data as of 30April2024

SNS-101 ASCO 2024 Summary

SNS-101 is a conditionally active VISTA targeting mAb that has demonstrated promising early clinical data consistent with its mechanism of action, including:

- First VISTA-targeting mAb without dose-limiting CRS at pharmacologically relevant dose levels
- Initial signals of anti-tumor activity in a predominantly "cold" solid tumor patient population

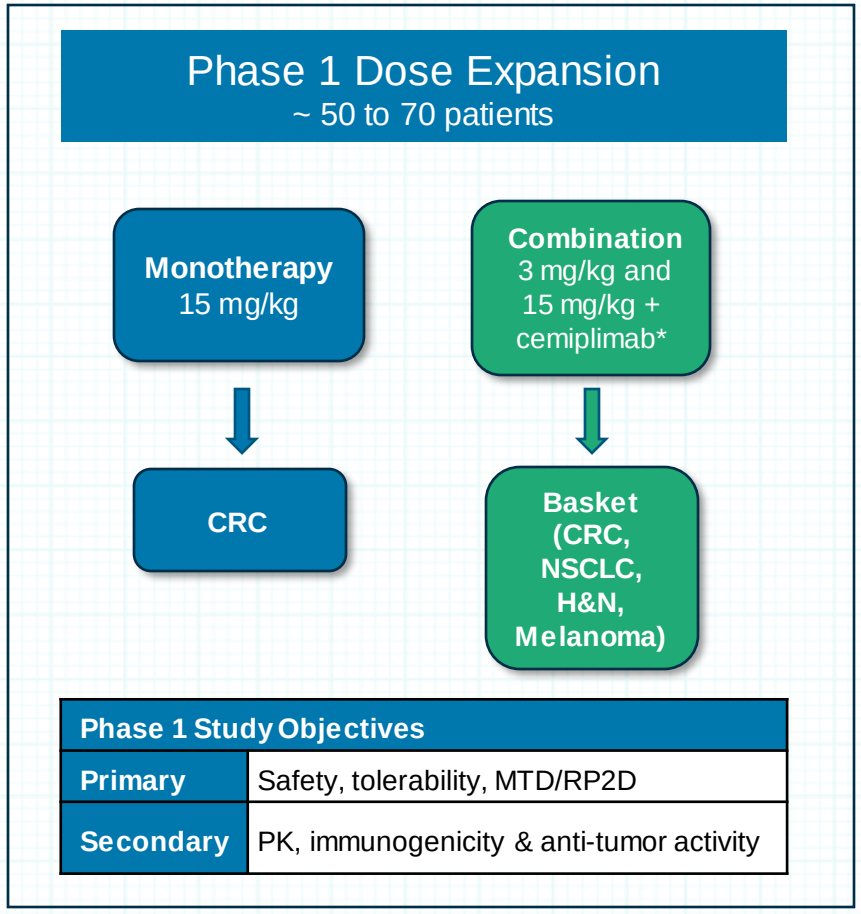
Well tolerated

Potentially best-in-class PK

Initial signs of encouraging clinical activity

SNS-101 well positioned to be the first VISTA-targeted mAb to test the VISTA IO hypothesis

SNS-101 Next Steps



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

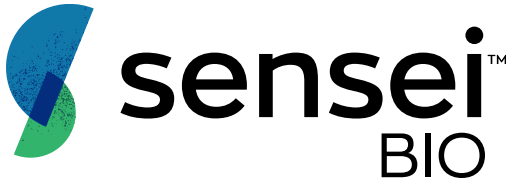
- Patient enrollment advancing in dose expansion cohorts
- Exploring two dose levels in the combination cohort to further optimize study design for Phase 2
- Expansion tumor types focused on a basket of “hot” tumors and one “cold” tumor, to rebalance between cold/hot given ~85% of patients in dose escalation had “cold” tumor types.
  - Additional tumor types and doses may be considered
  - All patients with “hot” tumors will have received and failed a prior PD-1/PDL-1
- Expansion phase expected to include ~50 to 70 patients
- Cash runway guidance unchanged (Q4 2025)

Initial data from dose expansion expected in Q4 2024

sensei BIO

* cemiplimab 350 mg
"Hot" tumors: Responsive to PD-1 monotherapy
"Cold" tumors: Unresponsive to PD-1 monotherapy

RP2D = Recommended Phase 2 Dose
MTD = Maximum Tolerated Dose
CRC = colorectal cancer
NSCLC = non small cell lung cancer
H&N = head and neck cancer



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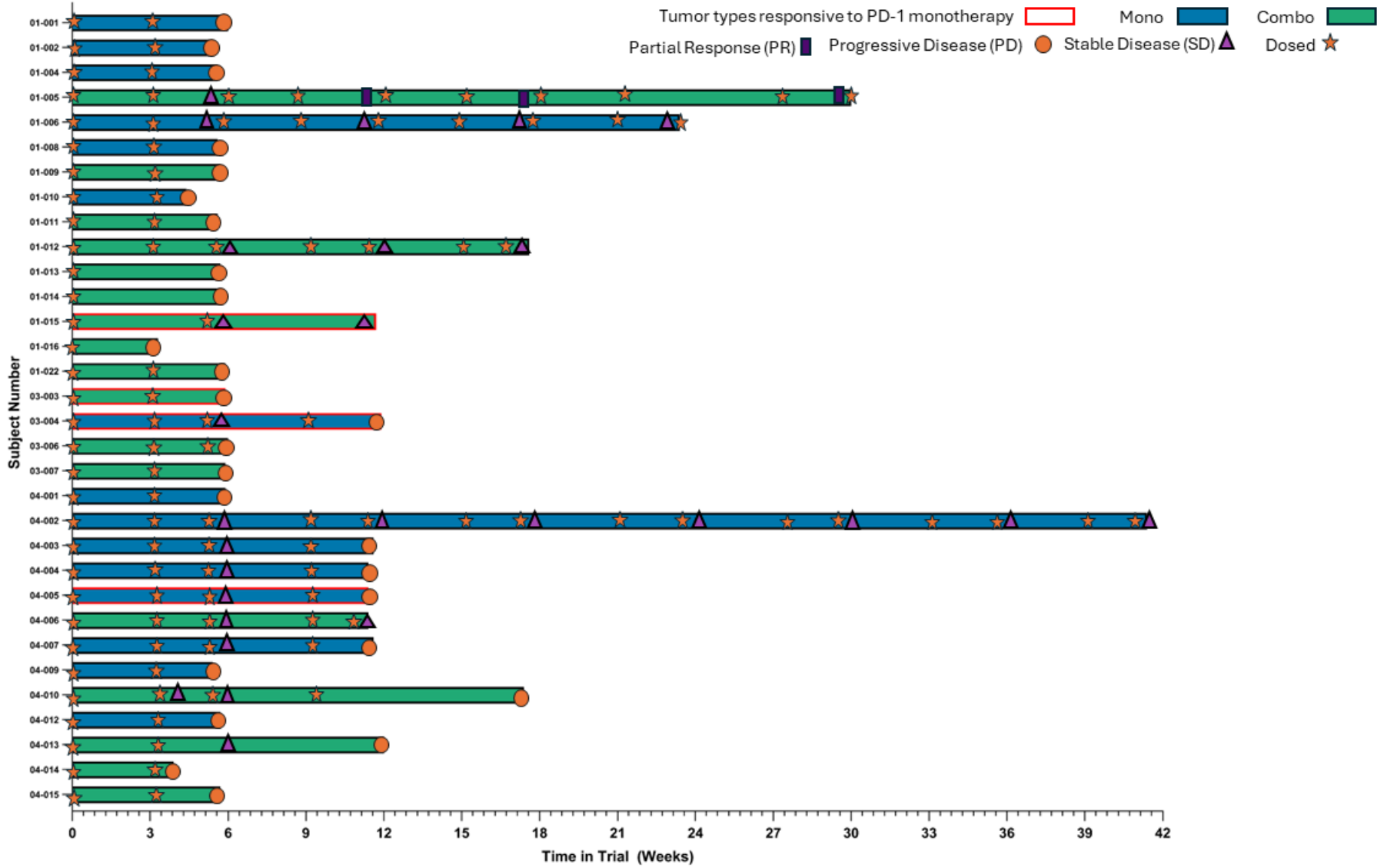
SNS-101 Duration of Treatment



Data as of 30April2024