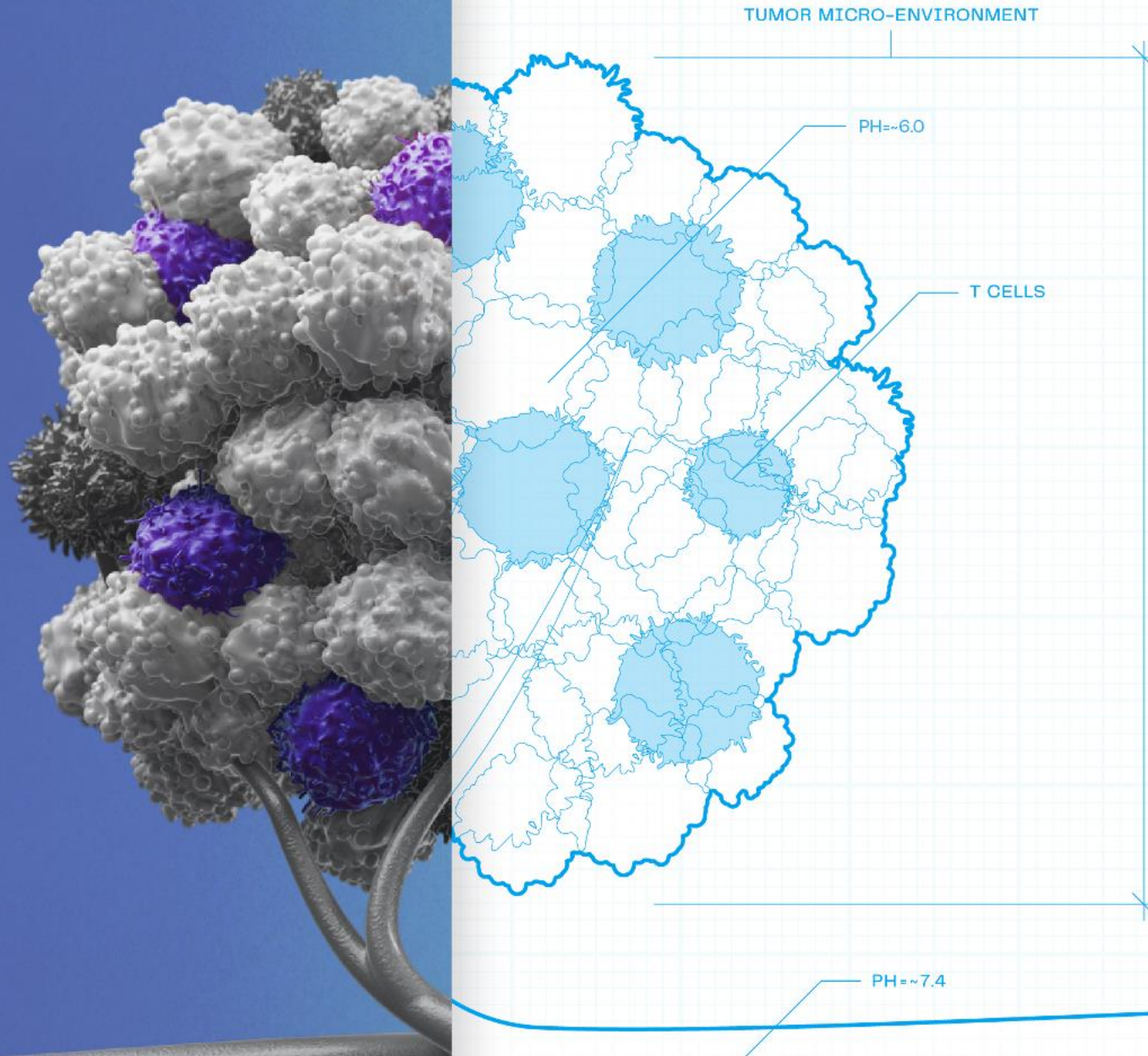


# Conditionally Active Antibodies for Immuno-oncology

Corporate Deck | November 2024



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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, pharmacokinetic and efficacy profile of our product candidates, including SNS-101; the expected timing of clinical data from our Phase 1/2 clinical trial of SNS-101; the expansion of the Phase 1 clinical trial to include additional patients with specific tumor types; and our belief that our existing cash and cash equivalents will be sufficient to fund our operations at least into the second quarter of 2026 and reach midway into Phase 2 clinical studies of SNS-101.

When used in this presentation, the words and phrases "designed to," "may," "believes," "intends," "seeks," "anticipates," "plans," "estimates," "expects," "should," "assumes," "continues," "could," "will," "future" and the negative of these or similar terms and phrases are intended to identify forward-looking statements. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the development of therapeutic product candidates, such as preclinical discovery and development; conduct of clinical trials and related regulatory requirements, including the risk of delay or cessation of any clinical trials of Sensei's product candidates; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical trials and early results from the clinical trial of SNS-101, will not be replicated or will not continue in ongoing or future studies or clinical trials involving Sensei's product candidates, including SNS-101; our reliance on third parties over which we may not always have full control; risks regarding the accuracy of our estimates of expenses, capital requirements and needs for additional financing; and other risk and uncertainties that are described in our Quarterly Report on Form 10-Q filed with the SEC on November 14, 2024 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 Key Highlights



## LEAD PROGRAM

- SNS-101, a conditionally active antibody targeting VISTA
- Clinical data demonstrated initial signs of promising clinical activity in multiple tumor types, a well-tolerated safety profile and potential best-in-class pharmacokinetic profile



## TMAb PLATFORM

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



## EXPECTED MILESTONES

- Dose expansion data in H1 2025



## FINANCIALS

- Ended Q3 2024: \$47M\*
- Cash runway into Q2 2026



# Leadership Team with History of Antibody Oncology Success



**John Celebi, MBA**  
President and CEO



**Josiah Craver, CPA**  
SVP, Finance



**Christopher Gerry, J.D.**  
SVP, General Counsel



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



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

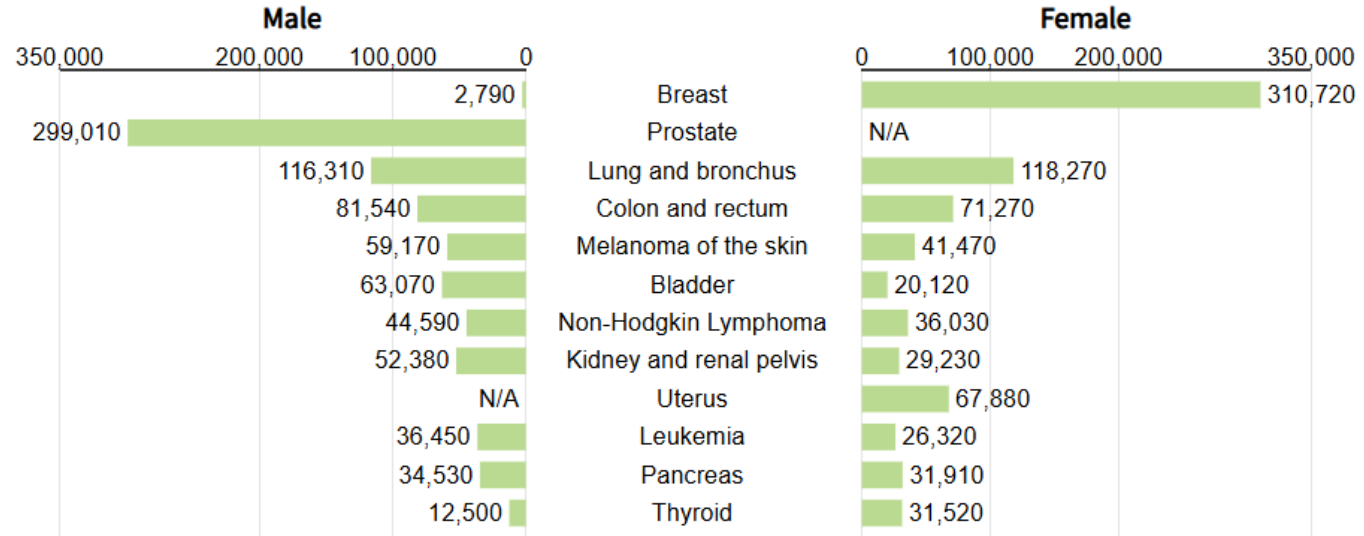


**Ron Weitzman, M.D.**  
Chief Medical Officer  
(part-time)



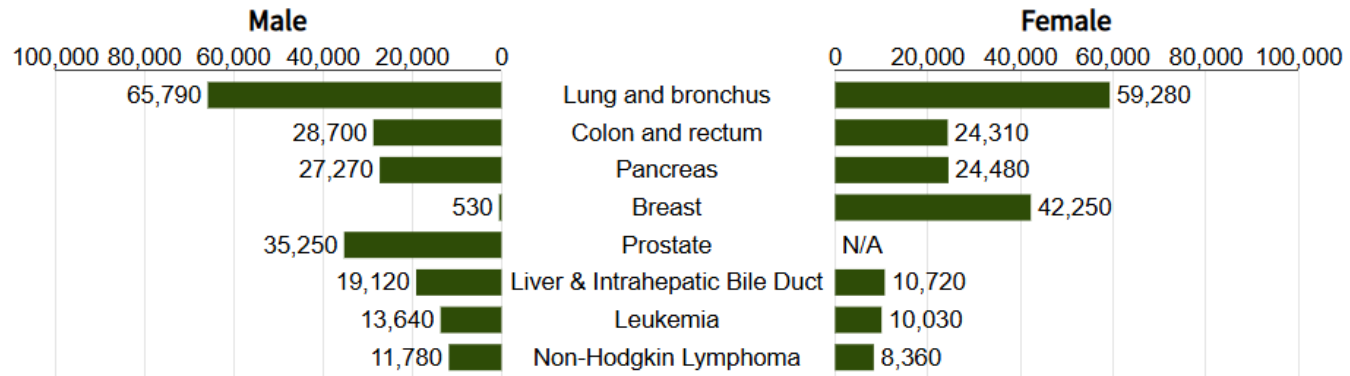
# High Unmet Need Remains in Solid Tumors

## 2024 Estimates on Solid Tumor Incidence in U.S.



**~2.0M+**  
New Solid Tumor  
Cases Per Year

## 2024 Estimates on Solid Tumor Deaths in U.S.



**~600K+**  
Solid Tumor  
Deaths Per Year

# Lack of Tumor Targeting is a Major Obstacle in IO Innovation

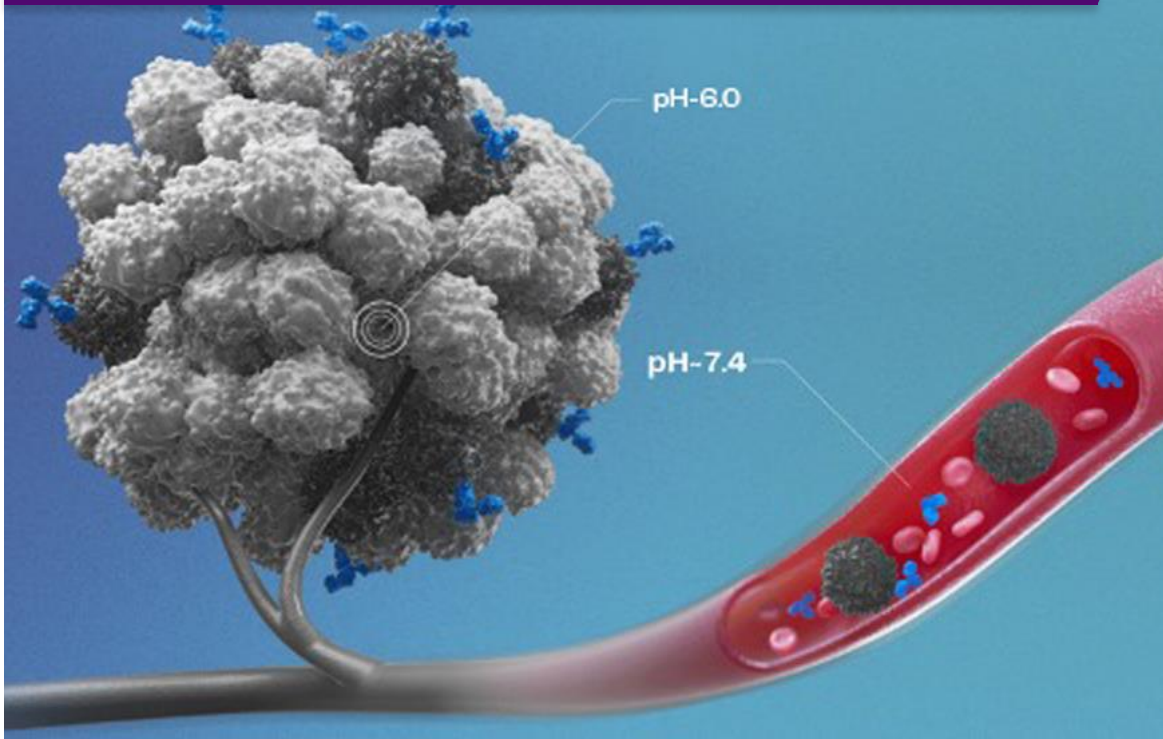
Industry Problem	Sensei's Solution
<p><b>Conventional antibodies target immune checkpoints that are highly expressed in normal tissues, resulting in:</b></p> <ul style="list-style-type: none"><li>• Dose-limiting toxicities due to on-target/off-tumor action</li><li>• Pharmacological sink effect requires higher &amp; more frequent dosing</li><li>• Suboptimal activity due to poor PK &amp; dose-limiting toxicities</li></ul>	<p><b>Conditionally active antibodies are selectively targeted to the tumor microenvironment, potentially providing:</b></p> <ul style="list-style-type: none"><li>• Little or no toxicity due to selective on-target/on-tumor action</li><li>• Lower &amp; less frequent doses with tumor-specific binding</li><li>• Powerful activity selectively focused on the tumor microenvironment</li></ul>



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

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

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



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

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

# Innovative Pipeline of IO Drugs with Broad Commercial Potential

Program (Target)	Indication	Discovery	IND-enabling	Phase 1	Phase 2
SNS-101* (VISTA)	Solid Tumors				
SNS-102 (VSIG4)	Solid Tumors				
SNS-103 (ENTPDase1/CD39)	Solid Tumors				
SNS-201 (VISTAxCD28)	Solid Tumors				

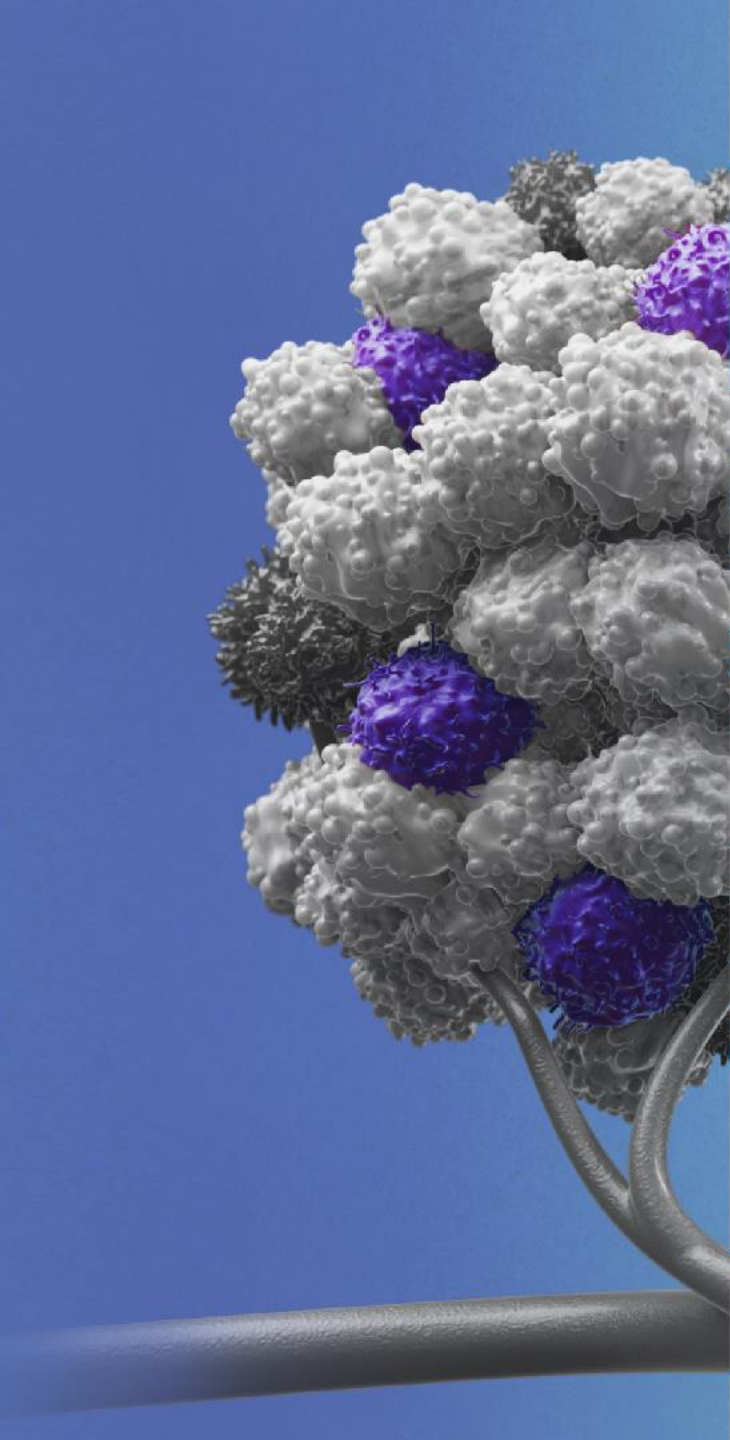
**REGENERON**

\*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.



\*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 Targeting mAb**

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

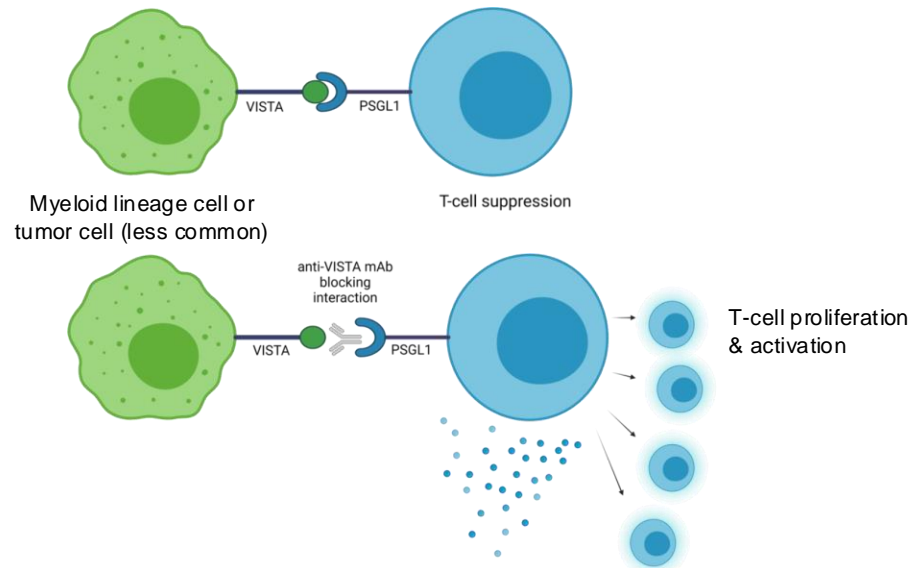
VISTA is a B7 family member that inhibits T cell activation<sup>1</sup>

Immunosuppressive function believed to be mediated by PSGL-1 receptor

Upregulated on immune suppressive myeloid-derived suppressor cells (MDSCs) via hypoxia<sup>2</sup>

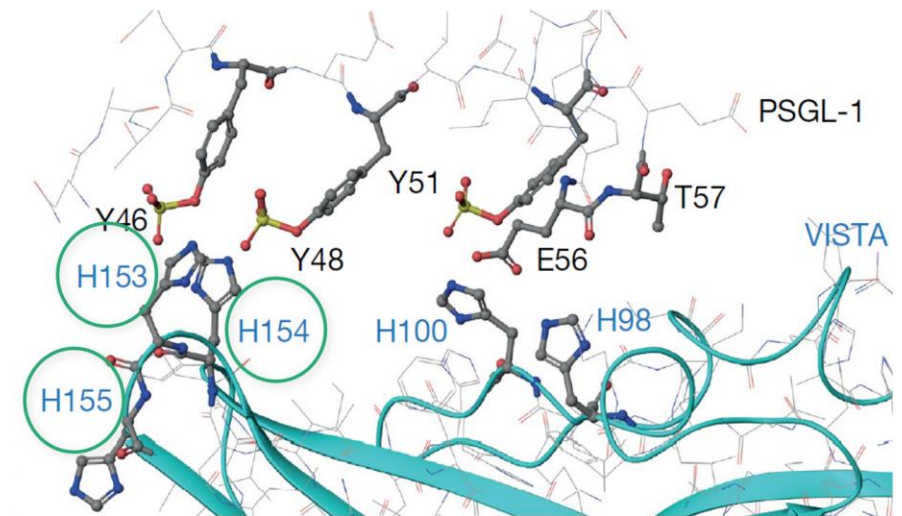
Increased expression on tissue infiltrating immune cells upon checkpoint therapy failure<sup>3</sup>

## IS ACTIVATED IN A pH SENSITIVE MANNER



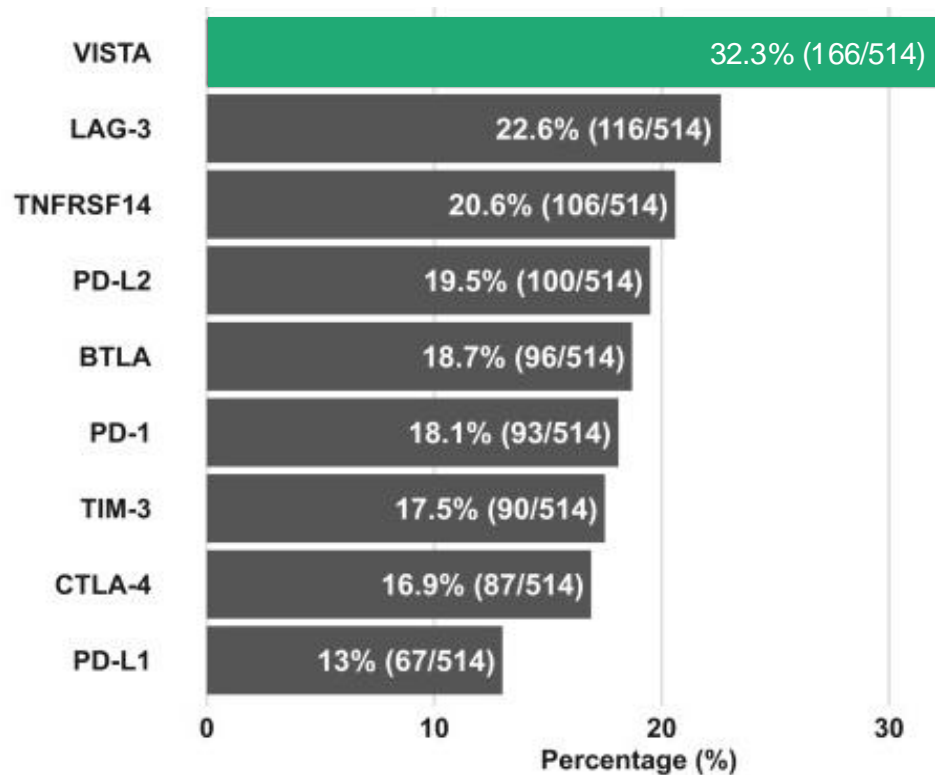
Extensive VISTA expression on off-tumor myeloid-lineage cells demands a conditionally active antibody approach

VISTA has inherent pH sensitivity: its extracellular domain is uniquely rich in histidines<sup>4</sup>

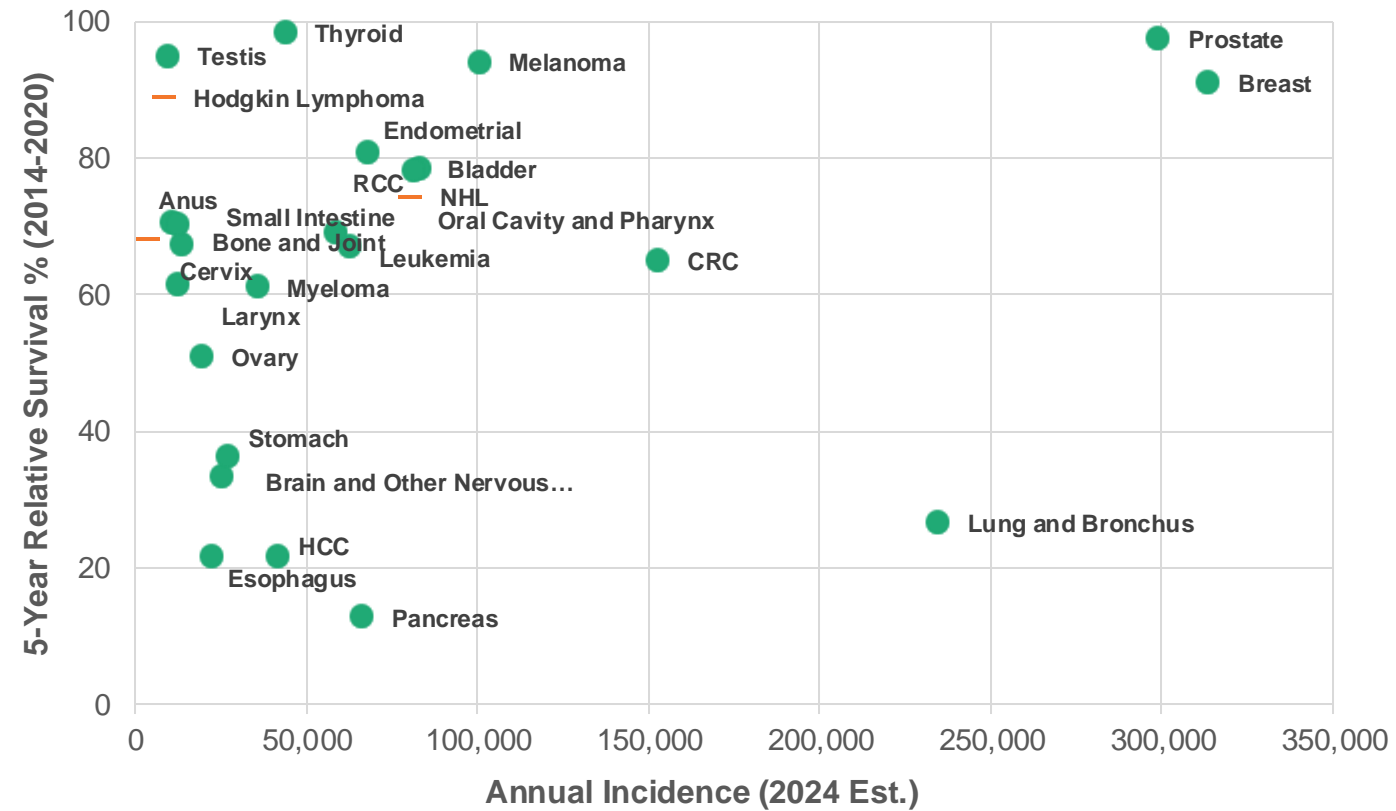


# VISTA is Found in Nearly All Solid Tumors with High Unmet Need

## VISTA Expression Levels Are Relatively High in Cancer Indications



## VISTA Expression is Detected in the Majority of Solid Tumor Indications

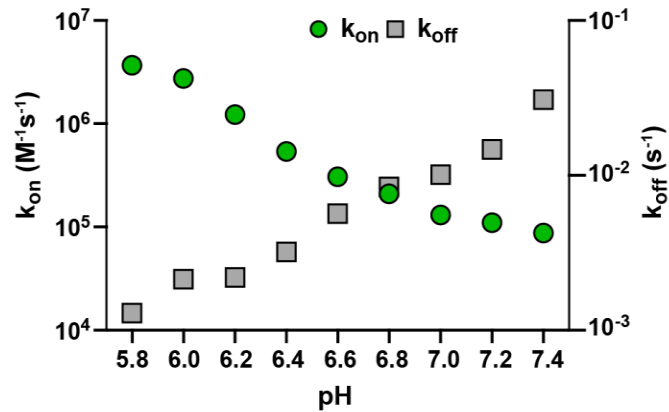


Source: Nishizaki, D. et al. ESMO Open, Volume 9, Issue 4, 102942

Source: Incidence and Survival: NCI SEER Data 2024, Expression: internal data and publications

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

## Selectivity for active VISTA<sup>pH6</sup> over VISTA<sup>pH7.4</sup>



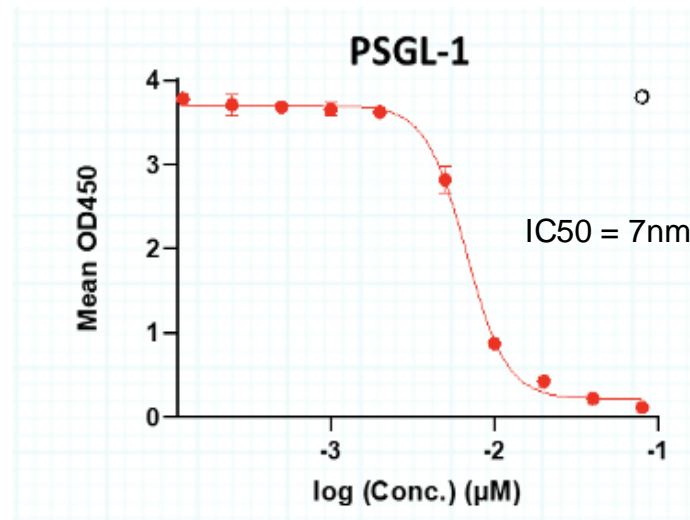
pH 6.0	pH 7.4
0.218 nM	132 nM (~No binding)

Monovalent Affinity (K<sub>D</sub>)

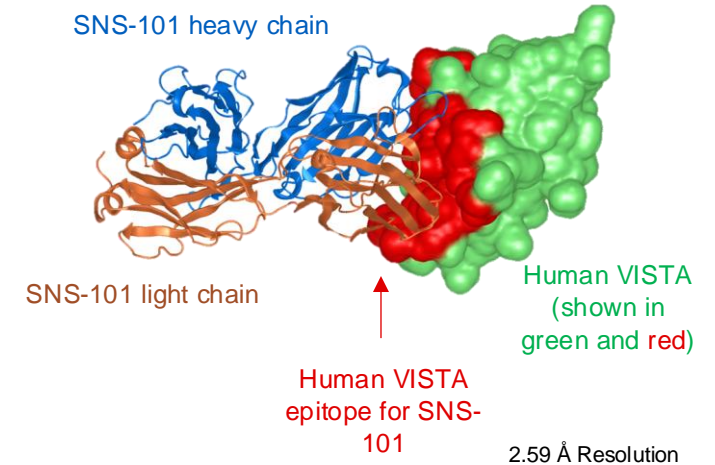
### Additional SNS-101 features

- IgG1 format
- Active Fc

## Blocks the key receptor regulating VISTA's immunosuppressive activity



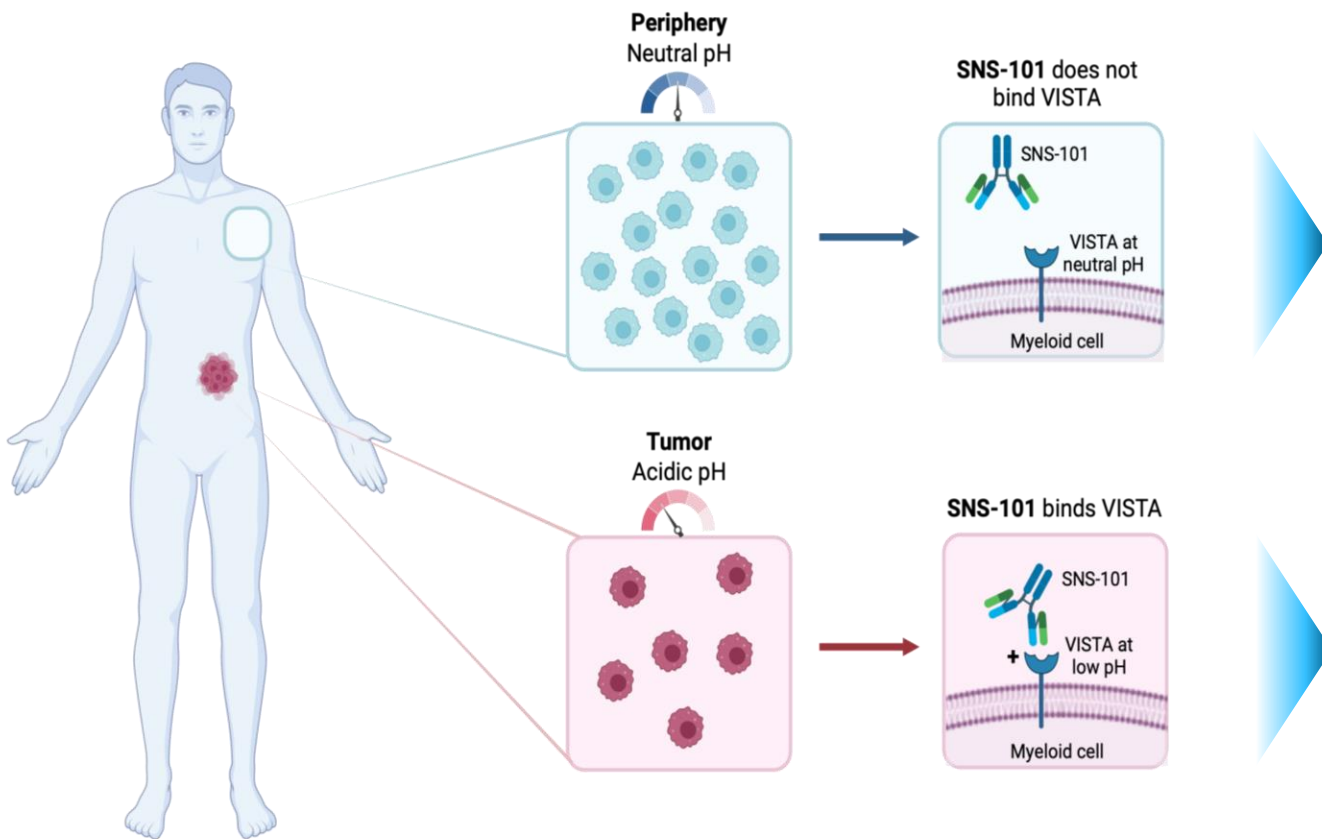
SNS-101 potently inhibits the VISTA:PSGL-1 interaction and all other potential binding partners at pH 6.0 *in vitro*



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

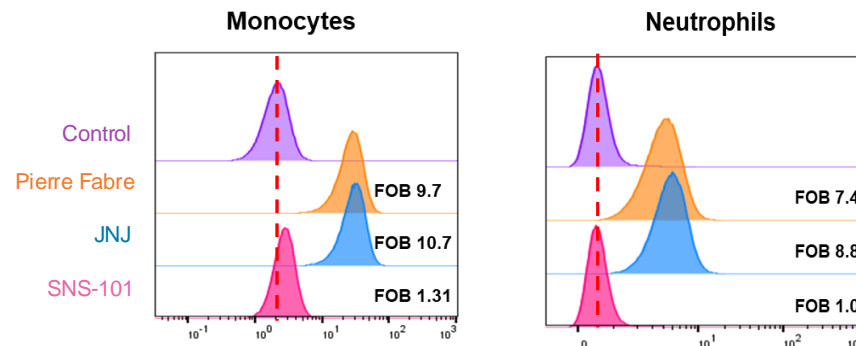


# SNS-101 Designed to Bind VISTA at the Tumor but Not in the Periphery



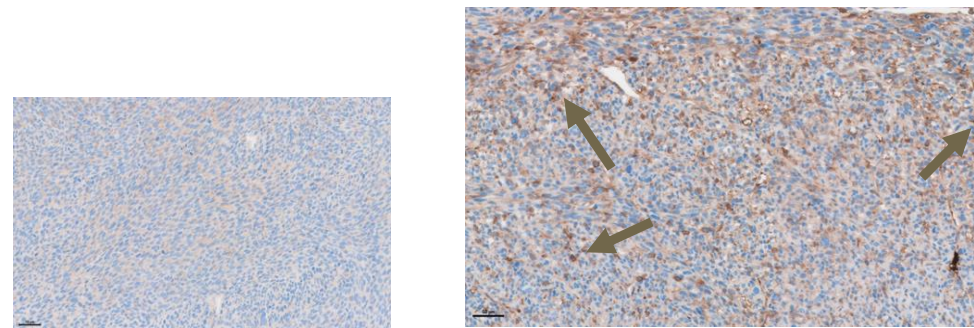
## Periphery (Neutral pH)

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



## Tumor (Acidic pH)

SNS-101 rapidly accumulates in the tumor



Isotype control  
6h post-dosing

SNS-101  
6h post-dosing

Blue = tumor  
Brown = SNS-101

# Competitors Halted Development of VISTA Antibodies as a Result of Severe Toxicities From Off-Tumor On-Target Activity & Poor PK

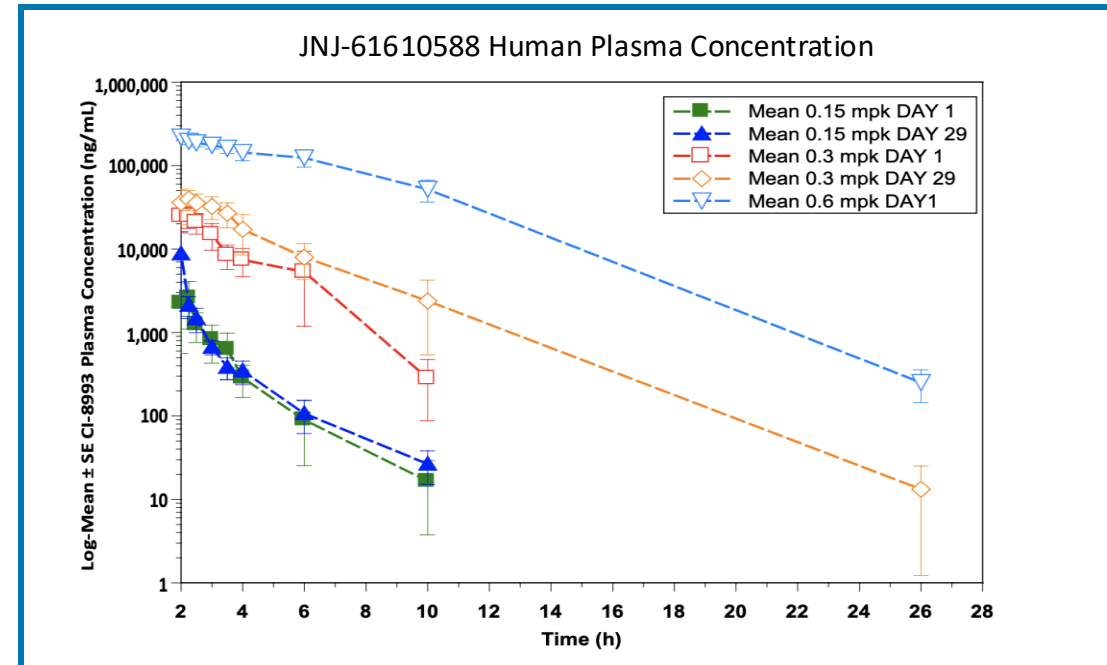
## Dose-limiting toxicity

Grade 3 CRS-associated encephalopathy

- JNJ-61610588 (CI-8993) was the first anti-VISTA antibody to be studied in clinical trials in 2016 (NCT02671955) <sup>1</sup>
- 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  $t_{1/2}$



# Early Development Plan is in Alignment with Corporate Objectives

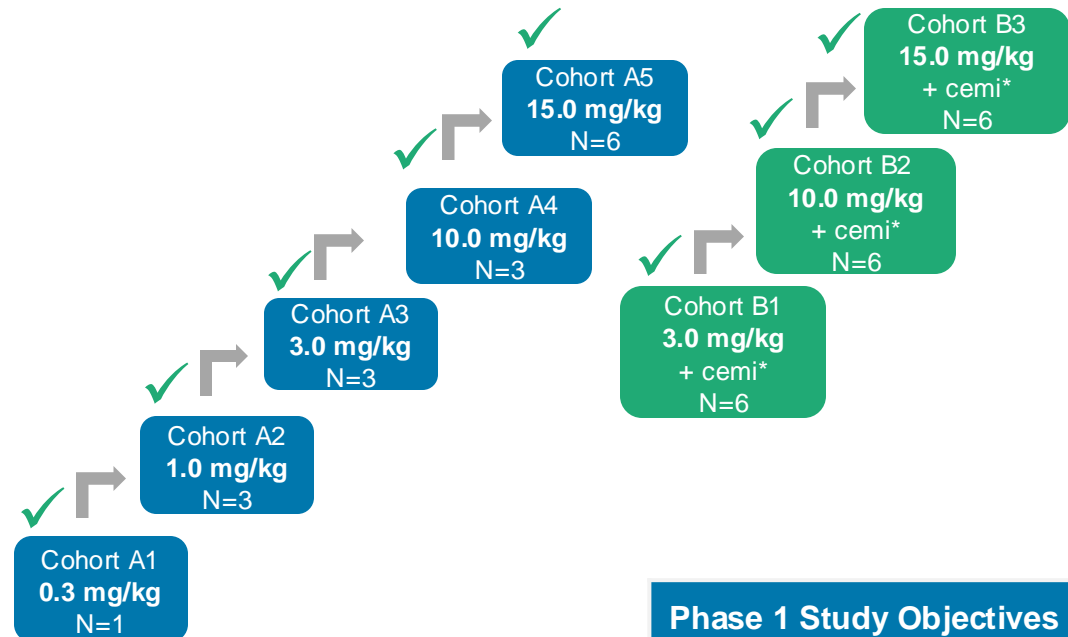
Corporate Objectives	Impact on Study Design
<p><b>PRIMARY</b></p> <p>Rapidly confirm conditionally active MOA through:</p> <ul style="list-style-type: none"><li>• Lack of severe CRS</li><li>• Absence of TMDD</li><li>• Reach doses several folds higher than doses where prior anti-VISTA mAbs experienced DLT</li></ul>	<ul style="list-style-type: none"><li>• Enroll <b>all-comer</b> solid tumor population during <b>dose escalation</b> which included both "hot" and "cold" tumor histologies, allowing for efficient enrollment</li></ul>
<p><b>SECONDARY</b></p> <ul style="list-style-type: none"><li>• 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</li><li>• Identify RP2D</li></ul>	<ul style="list-style-type: none"><li>• Enroll <b>selected patient populations</b> to balance cold/hot tumor ratio</li><li>• Explore more discreet range of doses</li></ul>

# SNS-101 Phase 1/2 Study

## Phase 1 Dose Escalation BOIN design in patients with advanced solid tumors

Monotherapy Dose Escalation  
SNS-101 (Q3W)

Combination Dose Escalation  
SNS-101 + cemiplimab\* (Q3W)



✓ = cleared DLT assessment period

## Phase 1 Dose Expansion ~ 50 to 70 patients

Monotherapy  
15 mg/kg

Combination  
3 mg/kg and  
15 mg/kg +  
cemi

CRC

Basket  
(CRC,  
NSCLC,  
H&N,  
Melanoma)

Additional tumor types and doses may be considered for both the monotherapy & combination dose expansion

## Phase 2

SNS-101 (RP2D) +/- cemi  
(Q3W)

Indications  
TBD

### Phase 1 Study Objectives

<b>Primary</b>	Safety, tolerability, MTD/RP2D
<b>Secondary</b>	PK, immunogenicity & anti-tumor activity

### Phase 2 Study Objectives

<b>Primary</b>	Anti-tumor activity
<b>Secondary</b>	Safety, tolerability, PK & immunogenicity



# 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 <sup>#</sup>
Withdrew Consent	0	1
Death Regardless of Causality	1 <sup>*</sup>	0
Death Related to Study Therapy	0	0
Clinical Progression	0	1

<sup>\*</sup> Related to disease progression, not related to SNS-101 (1 mg/kg dose level)

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

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

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

## Summary of Adverse Events

	SNS-101 n=16 (%)	SNS-101 + Combo 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 <sup>^</sup>	0	4 (22)
CRS <sup>#</sup>	1 (6)	1 (6)

- 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

## 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 30 April 2024

\*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

<sup>^</sup>One patient experienced Grade 2 rash maculo-papular at 3 mg/kg + cemi

<sup>^</sup>One patient experienced Grade 3 Diabetic Ketoacidosis at 3 mg/kg + cemi

<sup>^</sup>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)

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

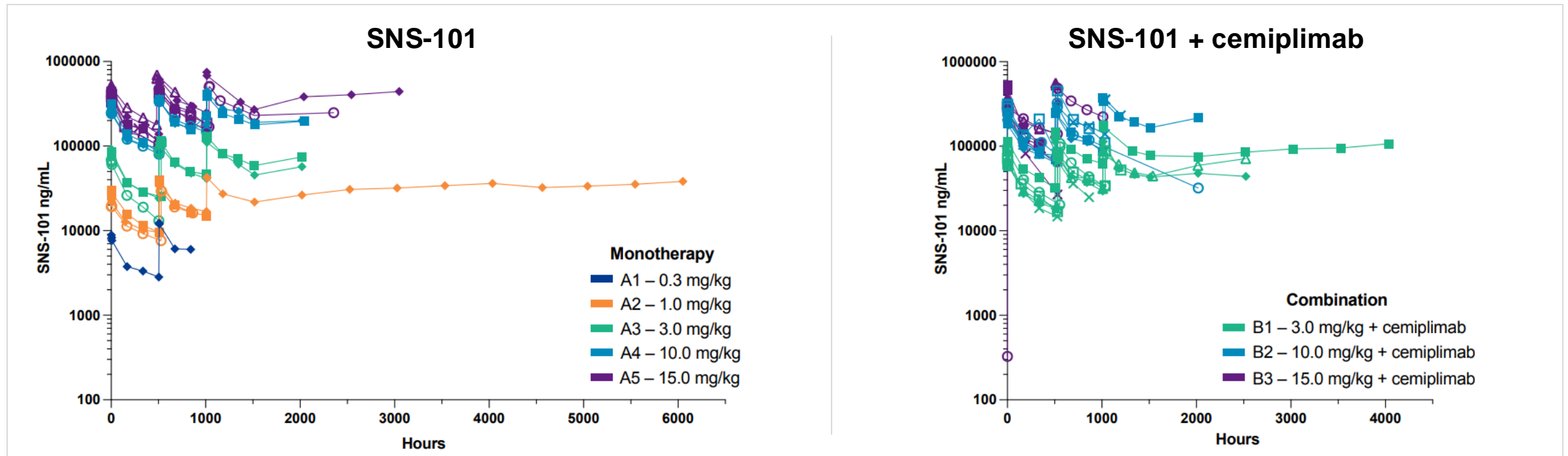
Subject Number	Dose Level	Adverse Event Preferred Term (Event description)	Severity (Grade)	Time of Onset Relative to Start of Infusion
01-010	SNS-101 15.0 mg/kg	Cytokine Release Syndrome (Chills and fever)	Grade 1	C1D1 ~4 hours post SNS-101 Infusion
01-013	SNS-101 15.0 mg/kg + cemi	Cytokine Release 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) <i>Patient also reported grade 1 itching and flushing about 1 hour after C1D1</i>	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



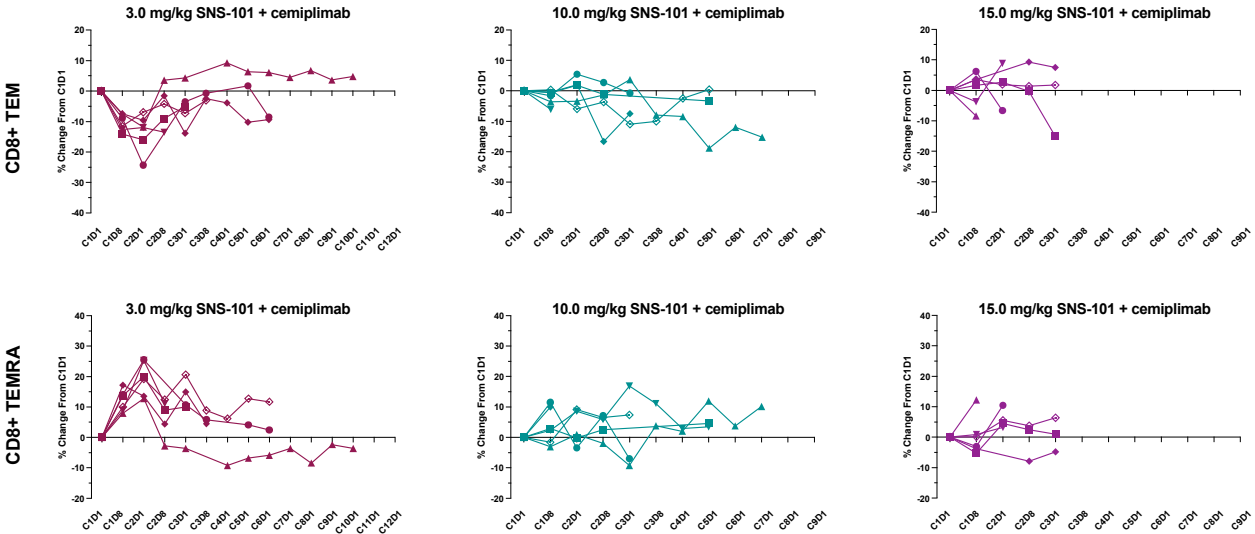
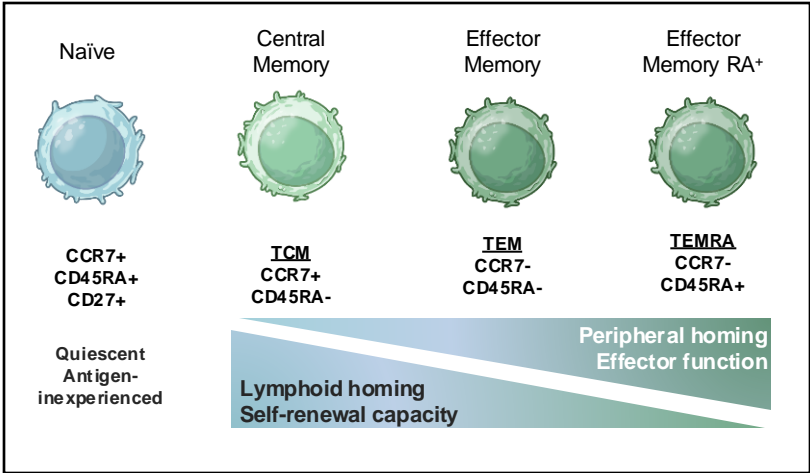
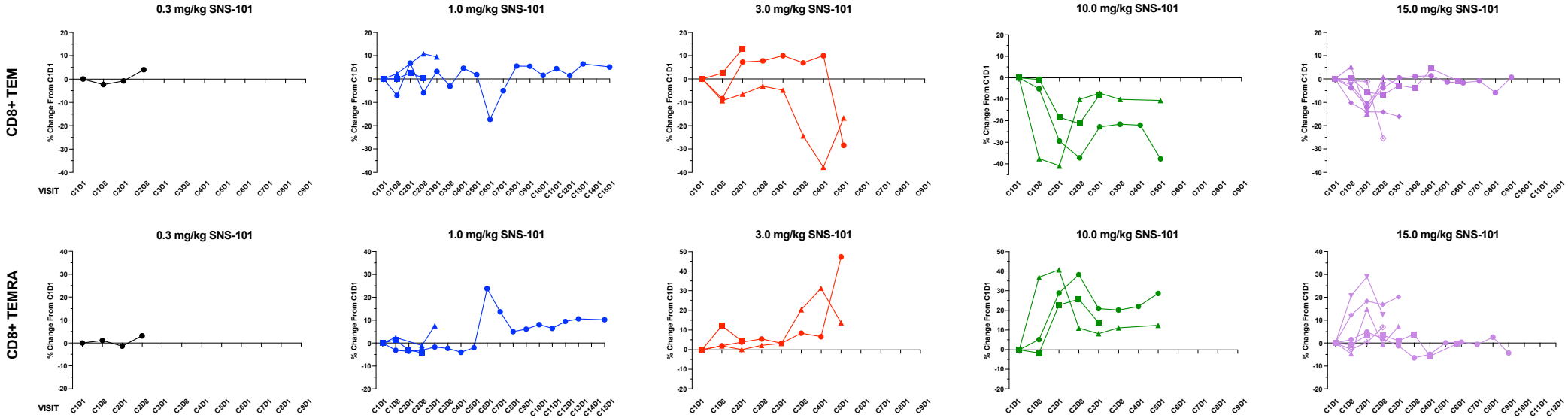
# Pharmacokinetic Data Show Linear Elimination Kinetics with Long Half-Life

- 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





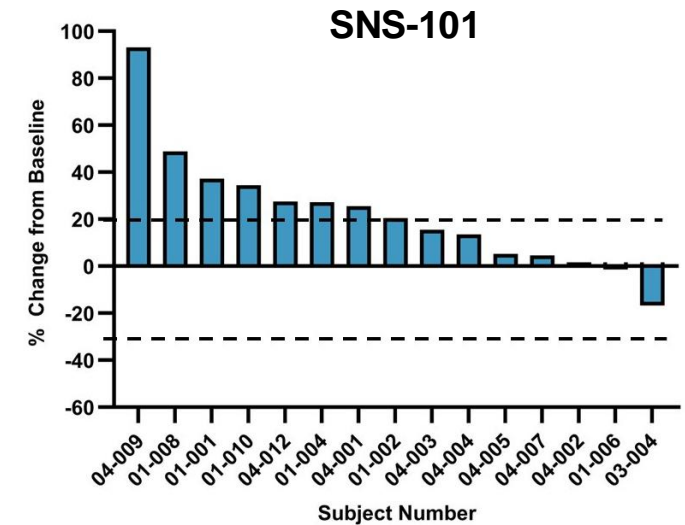
# Dose-dependent Changes in Specific T-cell Populations Indicate Potential SNS-101-Related Pharmacological Effect



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

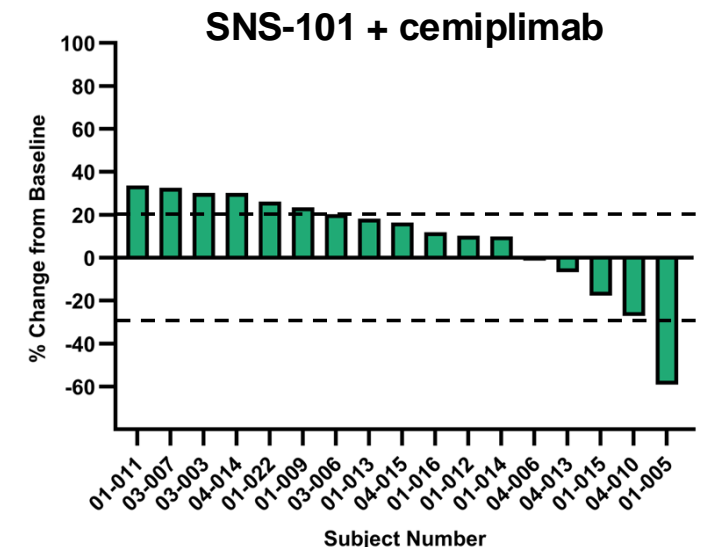
## Monotherapy Dose Escalation

- 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 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



# 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 yr old female with endometrial carcinoma, diagnosed Dec 2020, ECOG 0

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

### Prior Treatment/Surgery

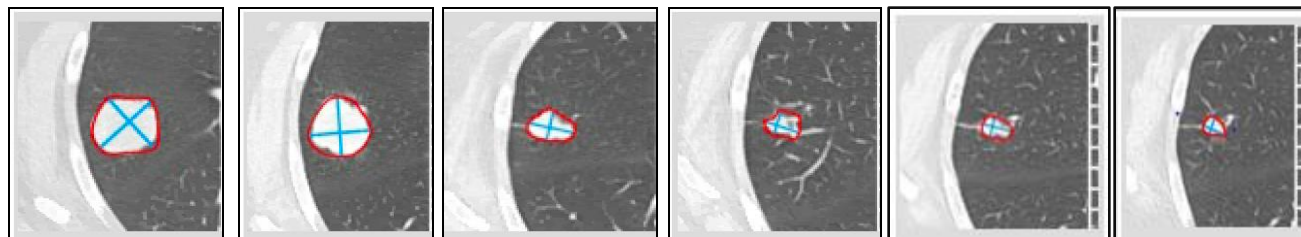
- Total laparoscopic hysterectomy with bilateral salpingo-oophorectomy, and additional sentinel lymph node dissection, Dec 2020
- Paclitaxel/Carboplatin (adjuvant setting), Feb 2021 to Aug 2021
- Anastrozole (metastatic setting), Aug 2023 to Sep 2023

### Adverse Events

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

### Tumor Assessments in Solitary Target Lesion

Baseline      6-Week SD (-0.6%)      12-Week PR (-34%)      18-Week (-45%)      24-Week PR (-52%)      30-Week PR (-59%)



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

62 yr old male with colon cancer; diagnosed 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 Libtayo
- Grade 2 rash maculo-popular, related to SNS-101 and Libtayo, AESI (immune-mediated), resolved after treatment with prednisone
- Grade 2 pruritis, related to SNS-101 and Libtayo

### 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



# SNS-101 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**



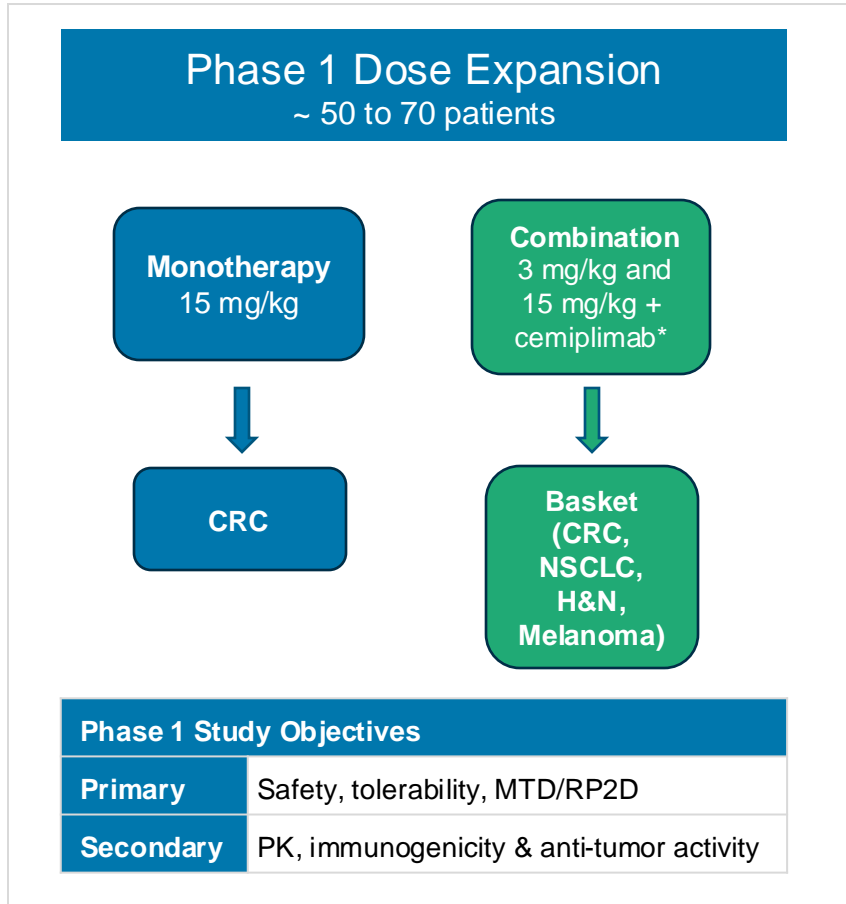
**Potentially best-in-class PK**



**Initial signs of encouraging clinical activity**

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

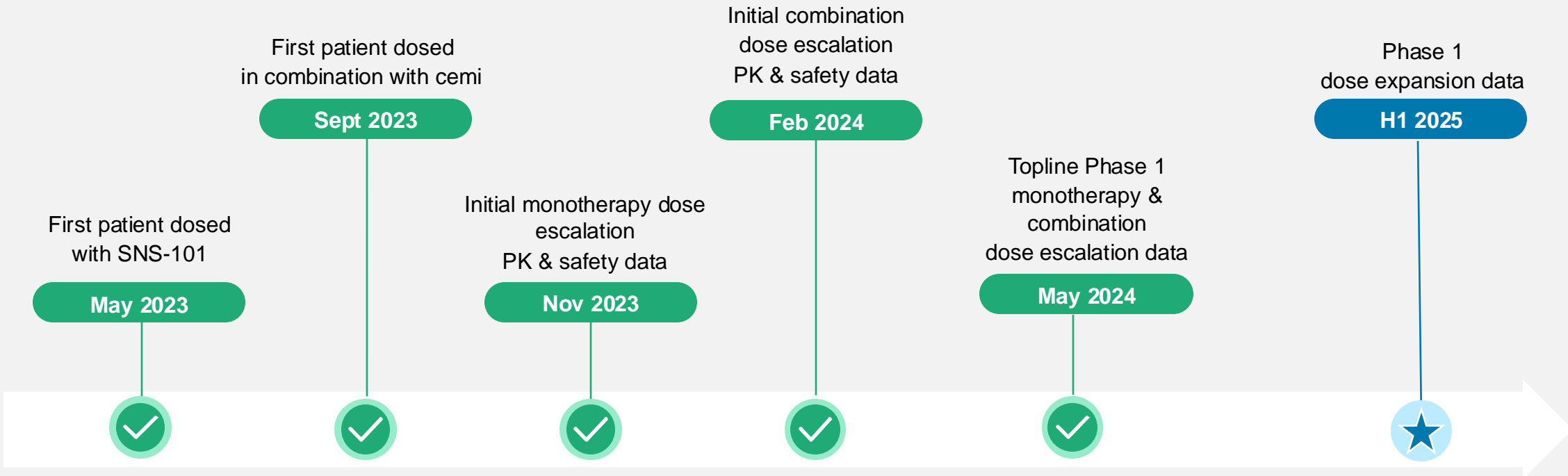
# SNS-101 Next Steps



- 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 extended to Q2 2026

Data from dose expansion expected in H1 2025

# Completed and Anticipated SNS-101 Clinical Milestones



# SNS-101 is Unique and Differentiated From Its Peers

	SNS-101 Sensei Bio	HMBD-002 (Hummingbird)	PMC-309 (PharmAbcine)	CI-8993; JNJ-61610588 (J&J/Curis)	K01401-020; WO180 (Pierre Fabre)	KVA12123 (Kineta)	VISTA.18 (BMS)
Inhibit PSGL-1 Binding	✓	✗	✓	✓	✓	✓	✓
pH Sensitive Binding	✓	✗	✗	✗	✗	✗	✓
Fc Active	✓ IgG1	✗ IgG4	✓ IgG1	✓ IgG1	✓ IgG1	✗ IgG1 <sup>mut</sup>	✗ IgG4
Most Advanced Stage	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Preclinical

# Sensei Bio Key Highlights



## LEAD PROGRAM

- SNS-101, a conditionally active antibody targeting VISTA
- Clinical data demonstrated initial signs of promising clinical activity in multiple tumor types, a well-tolerated safety profile and potential best-in-class pharmacokinetic profile



## TMAb PLATFORM

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



## EXPECTED MILESTONES

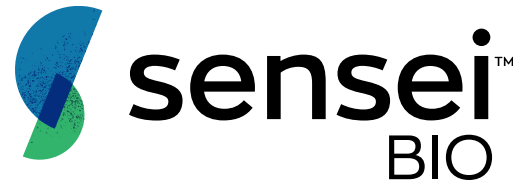
- Dose expansion data in H1 2025



## FINANCIALS

- Ended Q3 2024: \$47M\*
- Cash runway into Q2 2026





**Headquarters**

1405 Research Blvd  
Suite 125, Rockville  
MD 20850

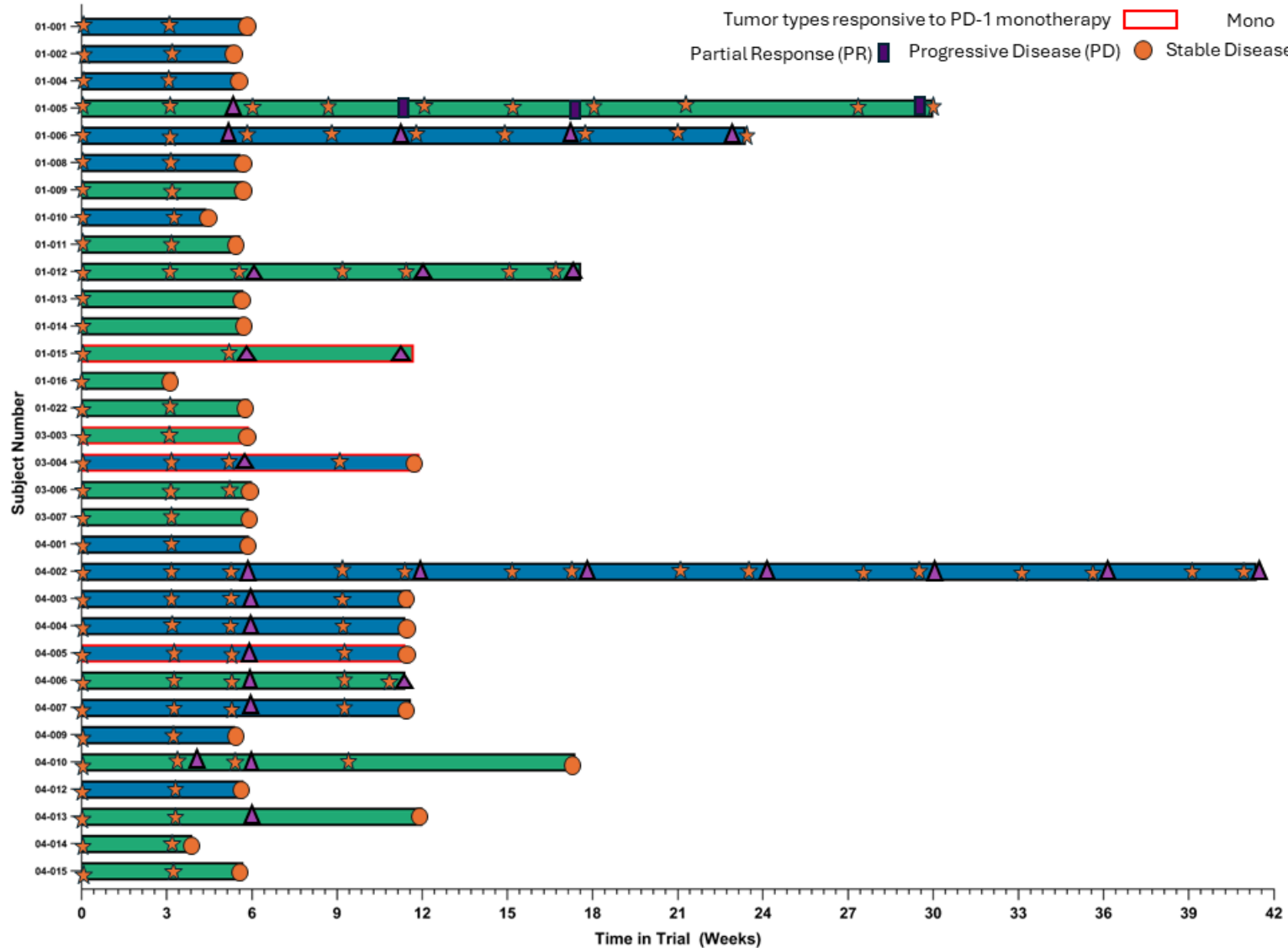
**Massachusetts**

22 Boston Wharf Rd  
7<sup>th</sup> floor  
Boston, MA 02210

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**[senseibio.com](https://www.senseibio.com)**

# SNS-101 Duration of Treatment



# Key Partnerships Supporting SNS-101's Clinical Development

*Potential opportunities for combination therapy and biomarker identification*

Partner / Collaborator	Goal	Description
  Clinical Supply Agreement	Support evaluation of SNS-101 in combination with Libtayo <sup>®</sup> (cemiplimab) in planned Phase 1/2 clinical trial	<ul style="list-style-type: none"> <li>• Sensei to fund planned clinical trial</li> <li>• Regeneron to provide Libtayo<sup>®</sup></li> <li>• Sensei maintains global development and commercial rights to SNS-101</li> </ul>
  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	<ul style="list-style-type: none"> <li>• Sensei collaborating with NCI Center for Immunology Co-Directors, Jeffrey Schlom, Ph.D., and James Gulley, M.D., Ph.D.</li> <li>• Preclinical studies will assess SNS-101 mechanism of action in combination with therapies beyond anti-PD-1</li> </ul>
  Research Collaboration	Further study the mechanism of SNS-101's anti-tumor activity	<ul style="list-style-type: none"> <li>• Sensei collaborating with laboratory of immuno-oncology KOL, Robert Schreiber, Ph.D.</li> <li>• Preclinical studies will include identification of SNS-101 response biomarkers</li> </ul>

# 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 <sub>D</sub> pH 7.4 (nM)	0.03		0.49
K <sub>D</sub> pH 6.0 (nM)	0.6		22
t <sub>1/2</sub> (d)	3.9		13.4

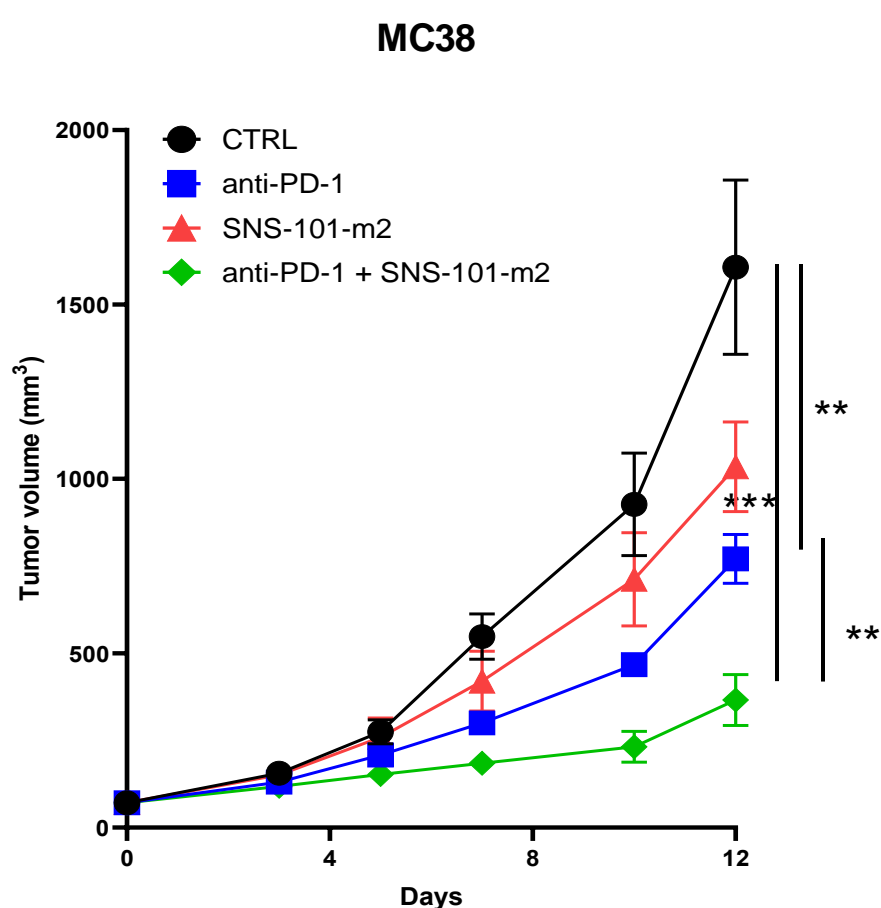
Ravulizumab utilized histidine insertions into the CDR regions (VH\_Y27H, VH\_S57H) and Fc substitutions (M428L, N434S) of eculizumab

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

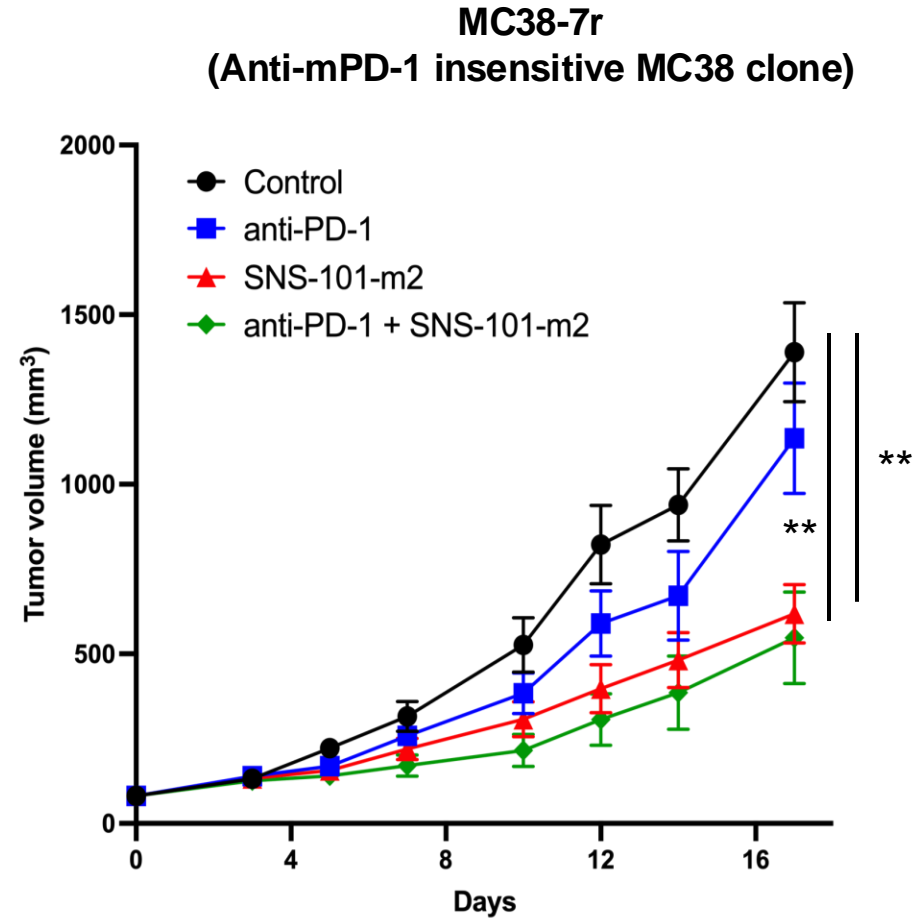
2018: FDA approves Ultomiris® (ravulizumab, ALXN1210)

2020: Ultomiris sales = \$1.08 billion

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

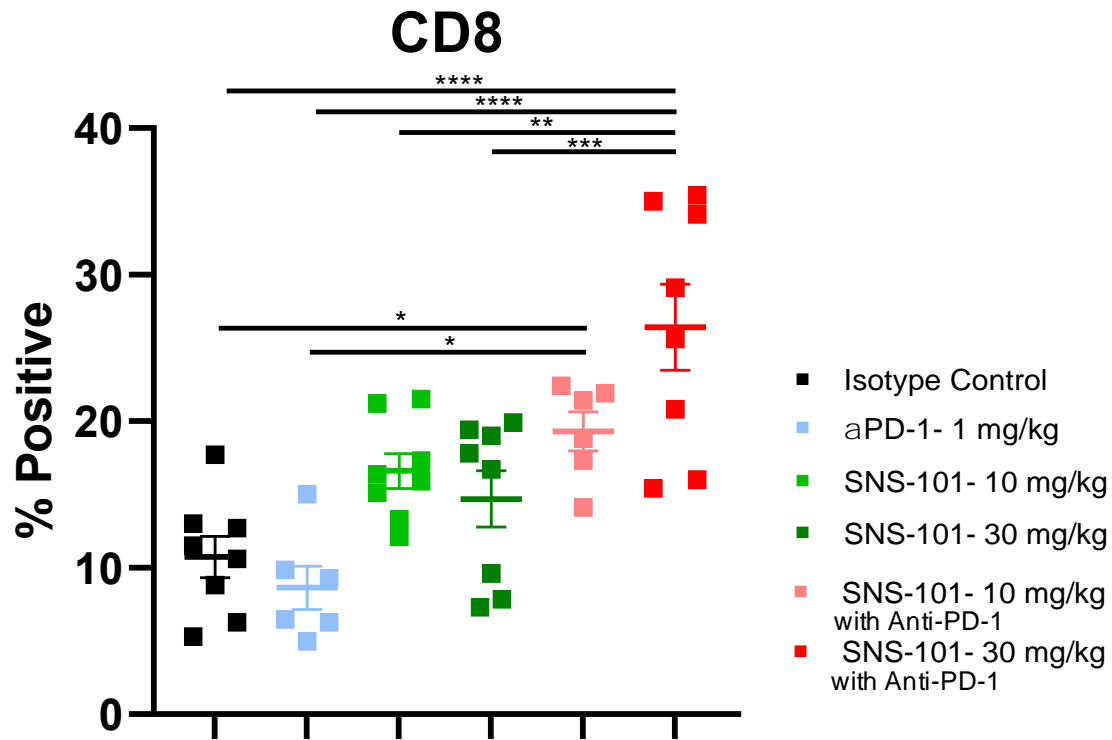


\*  $P < 0.05$ ; \*\*  $P < 0.01$ ; \*\*\*  $P < 0.001$

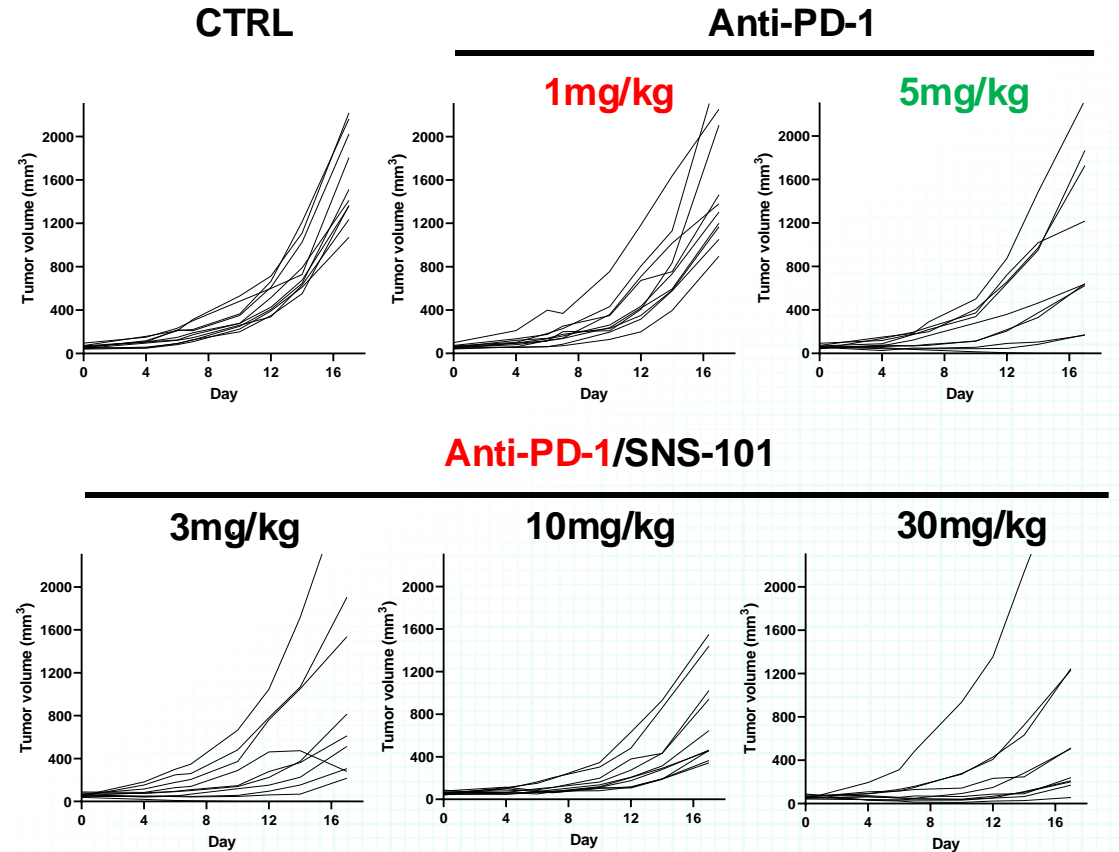




# SNS-101 Increased CD8 T-cells in Combination With Anti-PD-1 in MC38 Tumors *In Vivo*



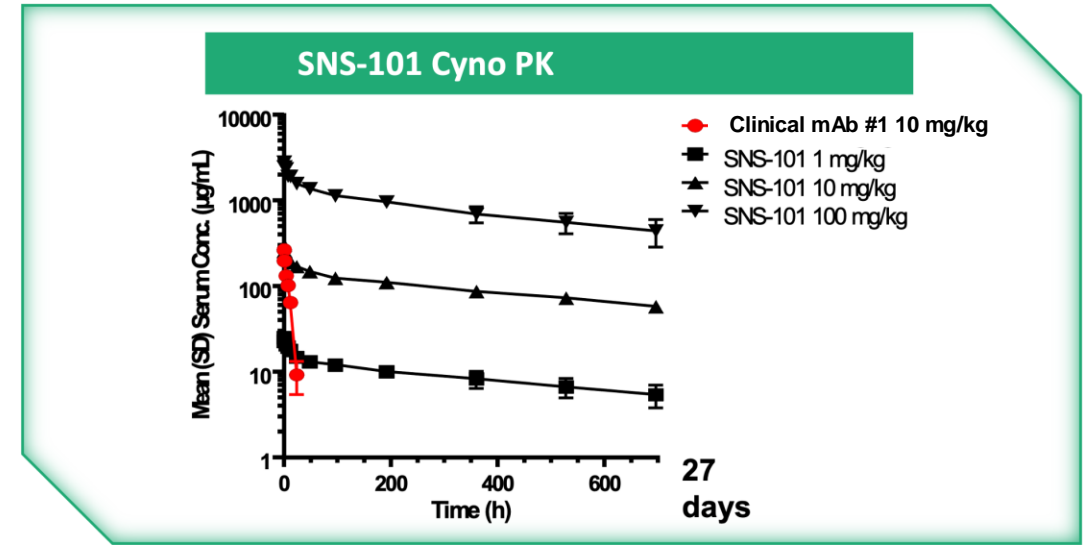
Frequency of Live, CD45+ Population  
 One-way ANOVA, Tukey Post-Hoc Analysis,  
 \* p<0.05; \*\* p<0.01, \*\*\* p<0.001, \*\*\*\* p<0.0001



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

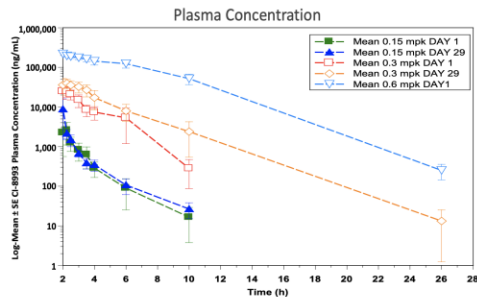
SNS-101 is designed to overcome elimination kinetics and half-life related to PK sink observed in non-pH-sensitive VISTA programs

Linear

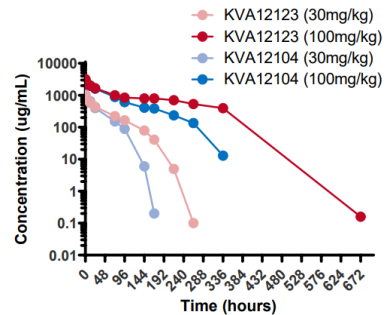


Non-linear

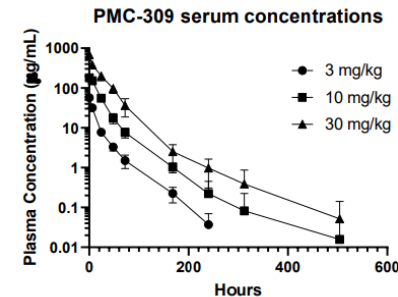
Curis CI-8993 Plasma Concentration



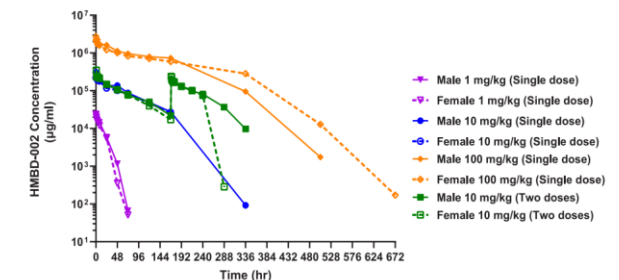
Kineta KVA12123 Cyno PK



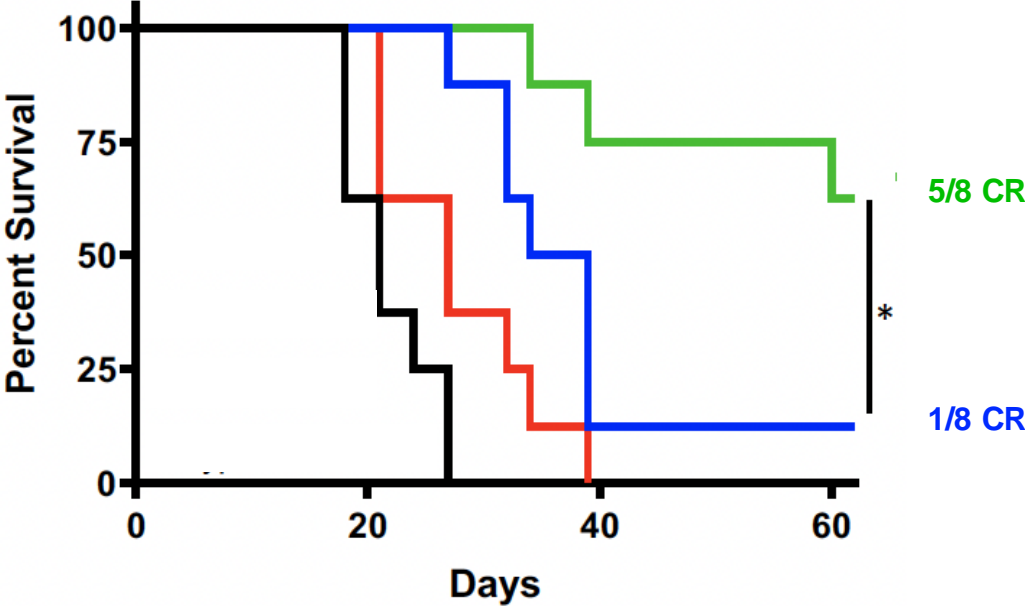
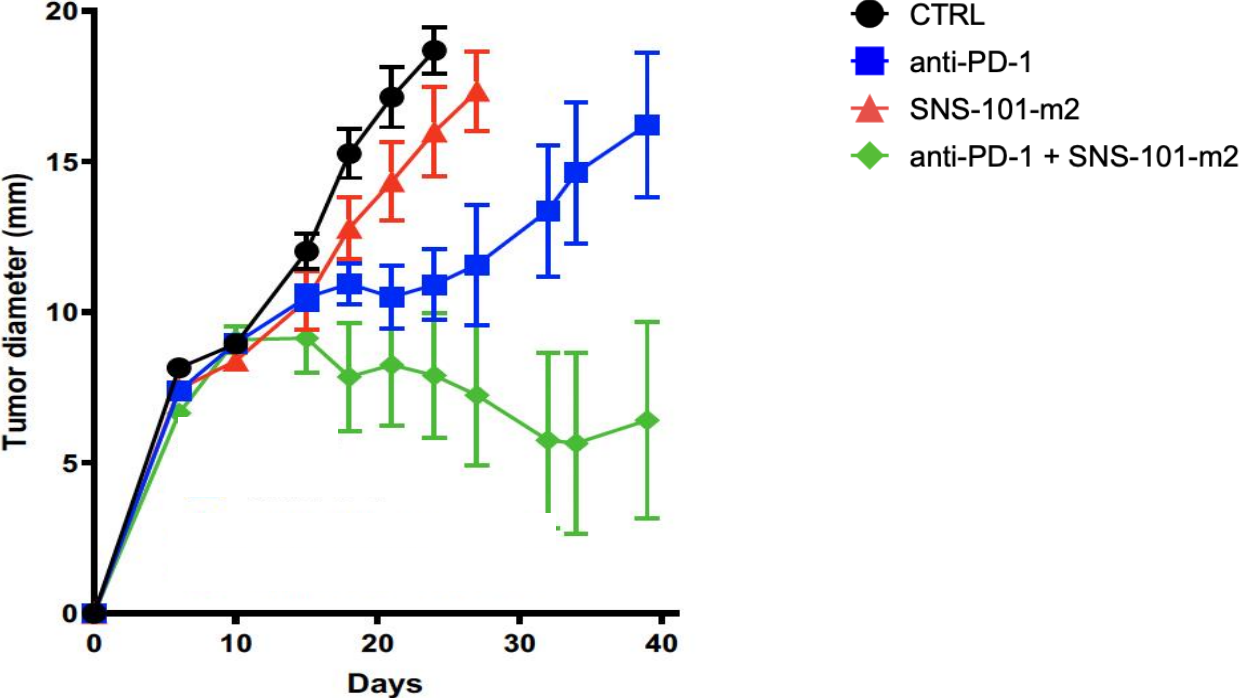
Abcine PMC-309 Serum Conc Cyno



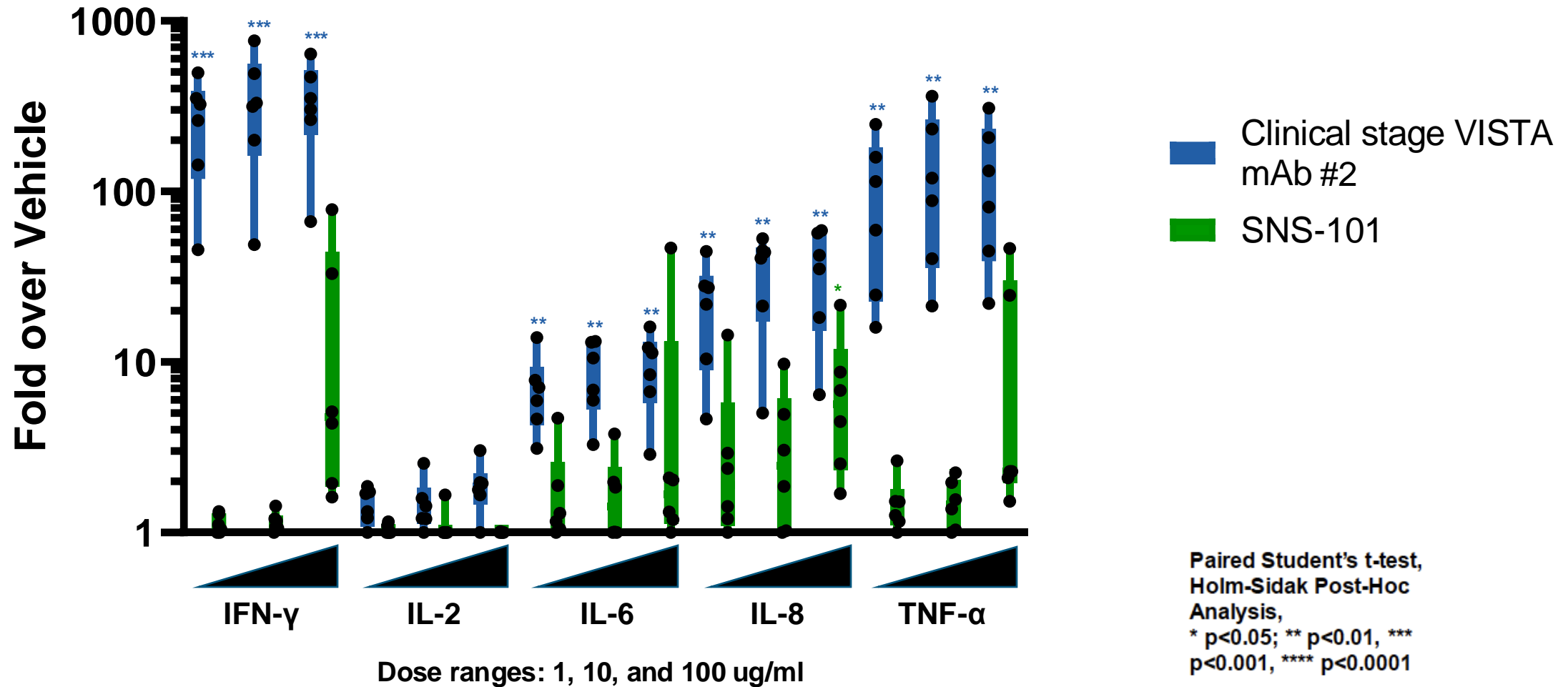
Hummingbird HMBD-002 Preclinical PK



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

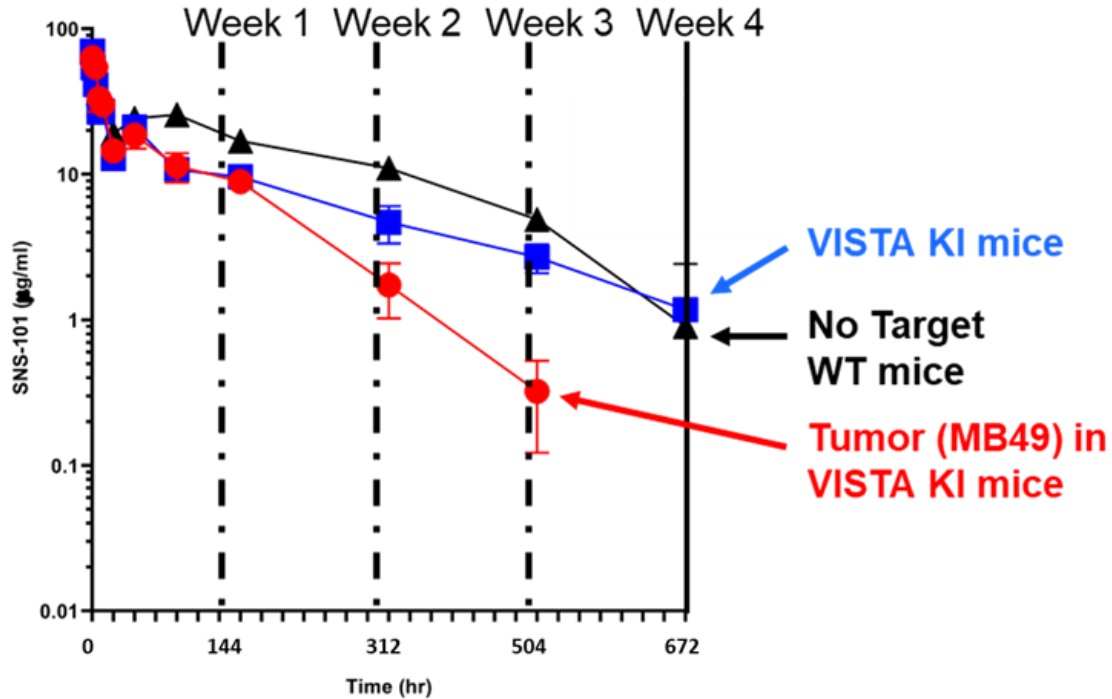


# SNS-101 Induced Substantially Lower Cytokine Release in Whole-blood Assay at Neutral pH Compared to pH-independent VISTA Antibody



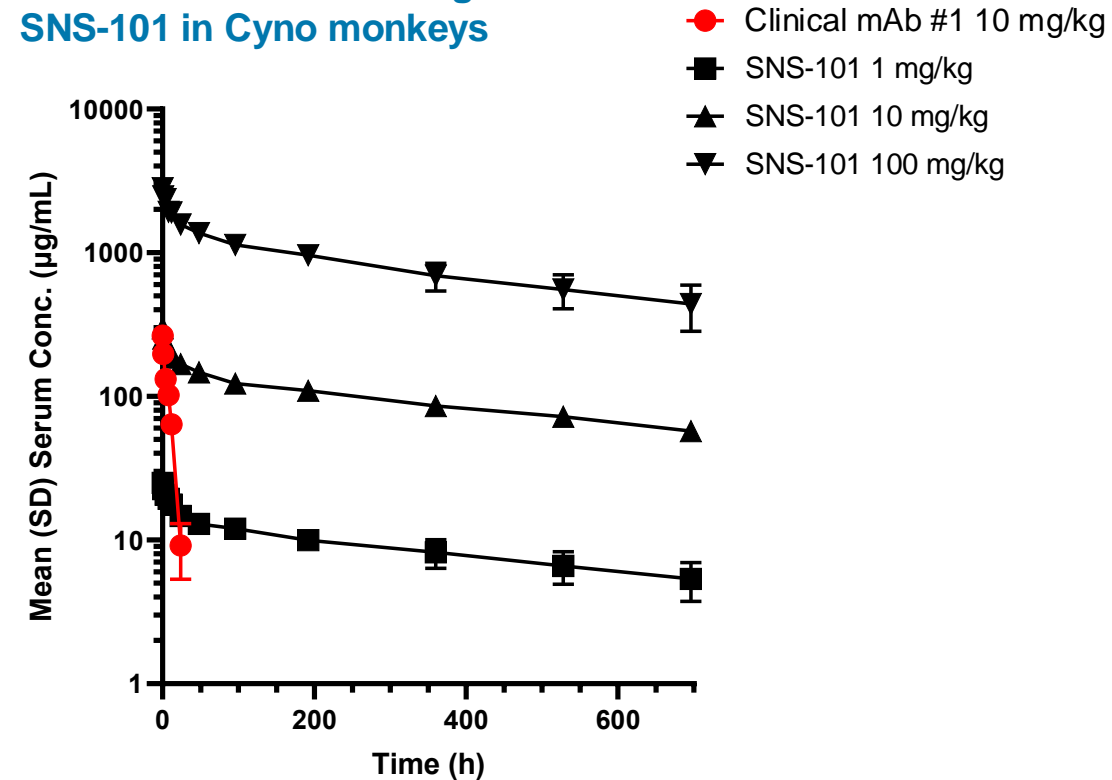
# SNS-101 Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - *No Significant TMDD in Human VISTA KI Mice or Non-human Primates*

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

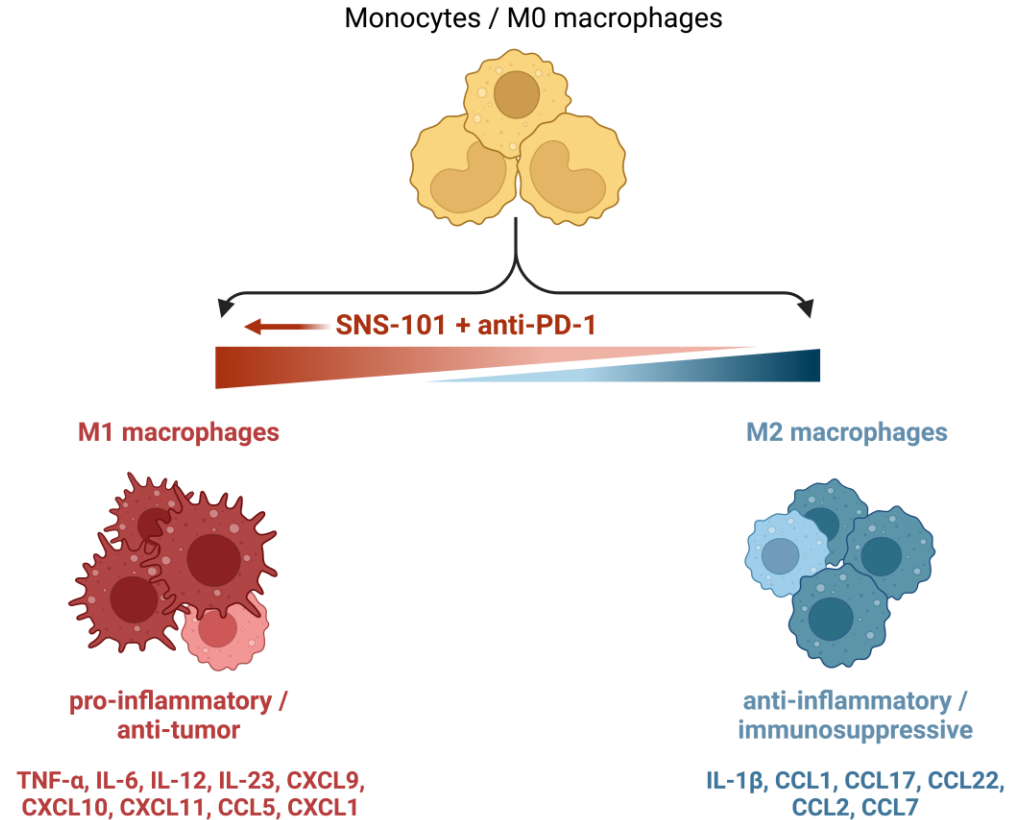


SNS-101 displayed linear elimination kinetics unlike a pH-independent anti-VISTA mAb, which demonstrated TMDD and rapid clearance



# 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