



Conditionally Active Antibodies for Immuno-oncology

Corporate Deck | January 2025

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Sensei Bio Key Highlights



LEAD PROGRAM

- Solnerstotug (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 bestin-class pharmacokinetic profile



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





EXPECTED MILESTONES

Dose expansion data in Q2 2025



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





Leadership Team with History of Oncology Antibody 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)











Cooley















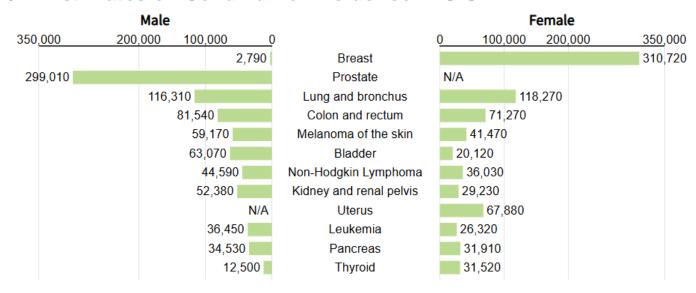




High Unmet Need Remains in Solid Tumors

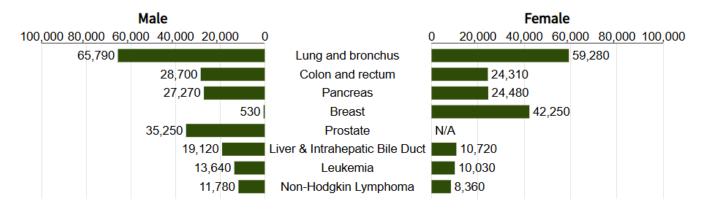
~2.0M+ New Solid Tumor Cases Per Year

2024 Estimates on Solid Tumor Incidence in U.S.



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

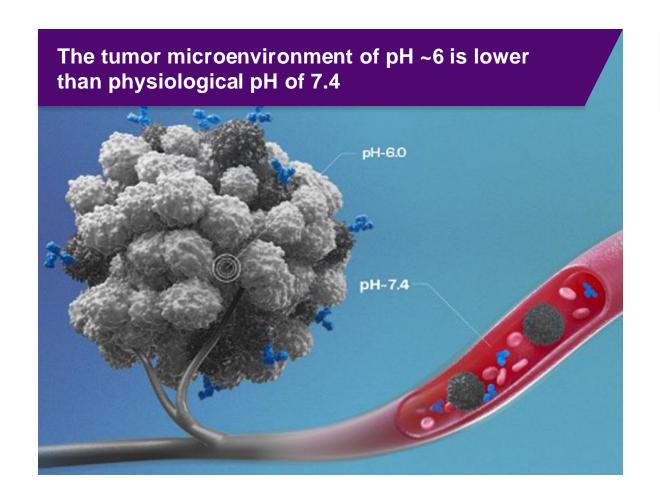
Industry Problem Sensei's Solution **Conventional antibodies target immune** Conditionally active antibodies are selectively checkpoints that are highly expressed in targeted to the tumor microenvironment, normal tissues, resulting in: potentially providing: Dose-limiting toxicities due to on-target/off-tumor action Little or no toxicity due to selective on-target/on-tumor action Pharmacological sink effect requires higher & more frequent Lower & less frequent doses with tumor-specific binding dosing Powerful activity selectively focused on the tumor Suboptimal activity due to poor PK & dose-limiting toxicities microenvironment





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



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

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



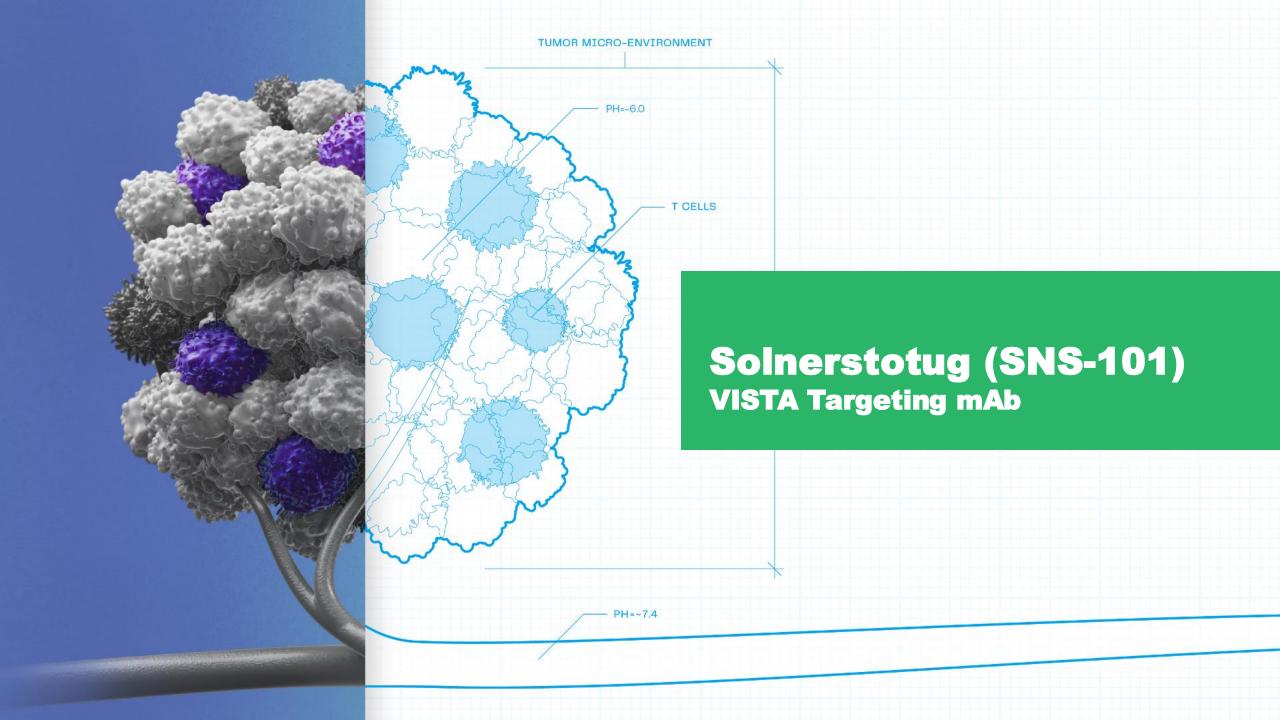
Innovative Pipeline of IO Drugs with Broad Commercial Potential

Program (Target)	Indication	Discovery	IND-enabling	Phase 1	Phase 2
Solnerstotug* (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 solnerstotug in combination with Regeneron's anti-PD-1 therapy Libtayo® (cemiplimab) in a Phase 1/2 clinical trial in solid tumors.

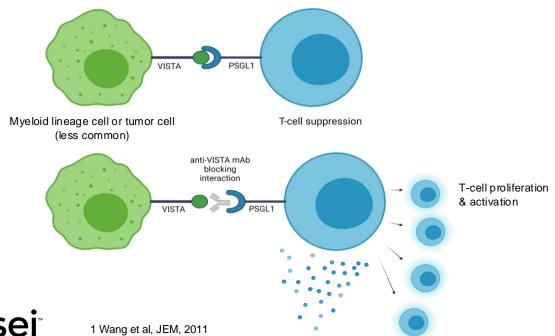




VISTA is a Potent T cell Checkpoint Extensively Expressed on Myeloid Cells

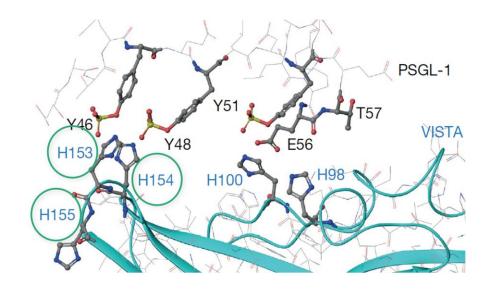
FUNCTION AND EXPRESSION PROFILE

- A B7 family member that inhibits T cell activation in a manner analogous to PD-1/PD-L1¹
- Immunosuppressive function believed to be mediated by PSGL-1 receptor
- Broad expression on MDSCs and also found on tumors; increased expression upon checkpoint therapy failure²



VISTA ACTIVATION IS pH SENSITIVE

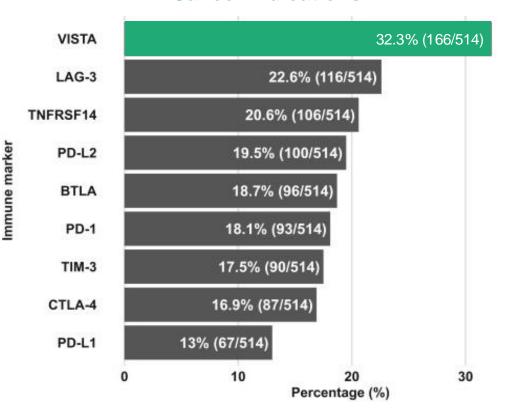
- Extensive VISTA expression on off-tumor myeloid-lineage cells demands a conditionally active antibody approach
- VISTA has inherent pH sensitivity: its extracellular domain is uniquely rich in histidines³



The VISTA Opportunity

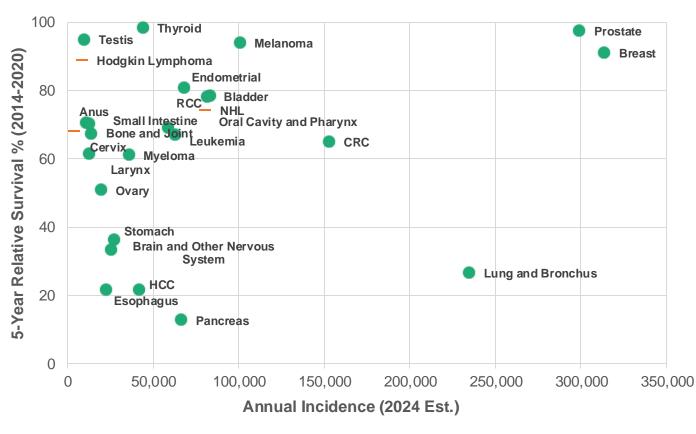
VISTA is Found in Nearly All Solid Tumors with High Unmet Need

Expression Levels Are Relatively High in Cancer Indications

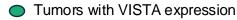


Source: Nishizaki, D. et al. ESMO Open, Volume 9, Issue 4, 102942

Expression is Detected in the Majority of Solid Tumor Indications



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



Tumors with no evidence of VISTA expression



The Challenge of Targeting VISTA

Competitors Halted Development of VISTA Antibodies as a Result of Toxicities and Poor PK

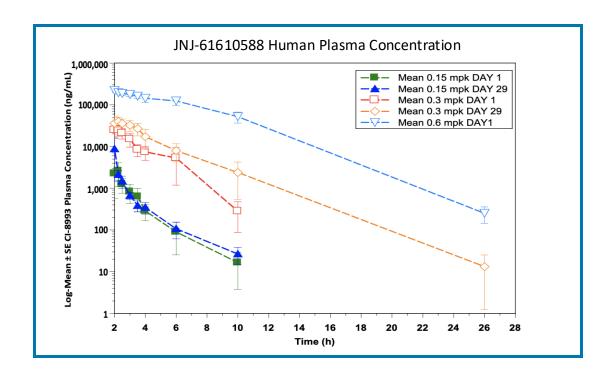
Dose-limiting toxicity

Grade 3 CRS-associated encephalopathy

- JNJ-61610588 (CI-8993) was the first anti-VISTA antibody to be studied in clinical trials in 2016 (NCT02671955) 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}



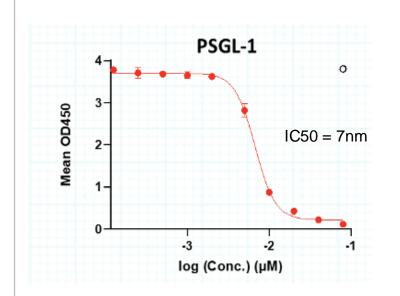


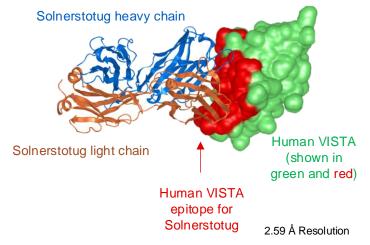
Solnerstotug Was Designed to Address the Challenges of VISTA

Tumor Targeting through pH Dependent Binding

Selectivity for active VISTA^{pH6} over VISTA^{pH7.4} 10⁷--10⁻¹ • k_{on} ■ k_{off} k_{on} (M⁻¹s⁻¹) 5.8 6.0 6.2 6.4 6.6 6.8 7.0 7.2 7.4 pН pH 6.0 pH 7.4 132 nM 0.218 nM (~No binding) Monovalent Affinity (K_D) **Additional Solnerstotug features** IgG1 format

Blocks the key receptor regulating VISTA's immunosuppressive activity





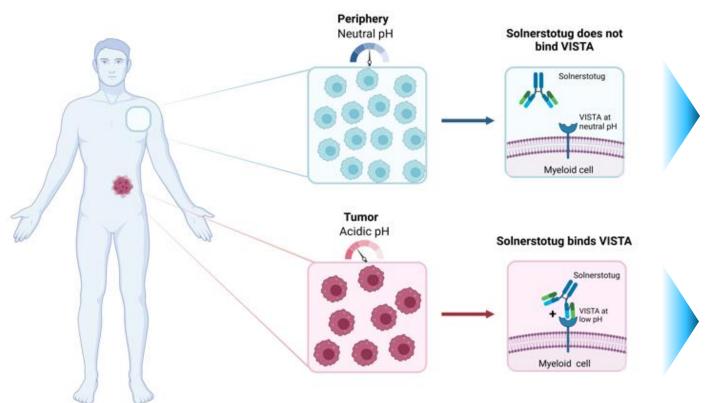
Solnerstotug potently inhibits the VISTA:PSGL-1 interaction and all other potential binding partners at pH 6.0 *in vitro*

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



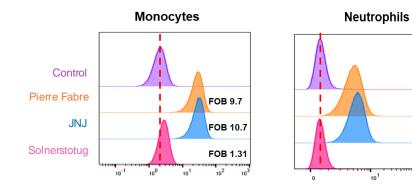
Active Fc

Solnerstotug Binds VISTA Selectively at the Tumor



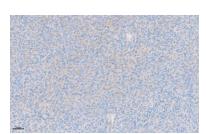
Periphery (Neutral pH) = No Binding

Solnerstotug has no detectable binding in peripheral or normal tissues

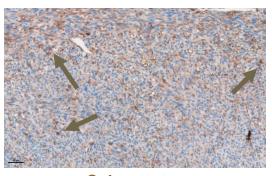


Tumor (Acidic pH) = Binding

Solnerstotug rapidly accumulates in the tumor



Isotype control 6h post-dosing



FOB 7.4

FOB 8.8

FOB 1.0

Solnerstotug 6h post-dosing



Solnerstotug is Unique and Differentiated

	Solnerstotug 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		X					
pH Sensitive Binding		X	X	X	X	X	
Fc Active	IgG1	IgG4	IgG1	IgG1	IgG1	IgG1 ^{mut}	IgG4
Most Advanced Stage	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Phase 1	Preclinical



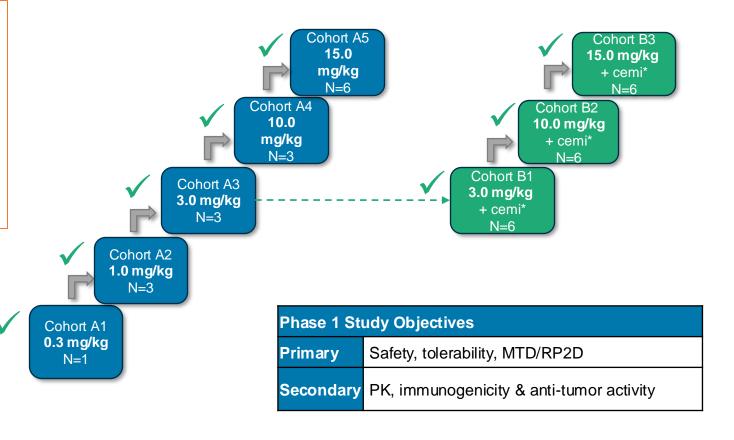
Solnerstotug Phase 1 Dose Escalation Study

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

Monotherapy Dose Escalation Solnerstotug (Q3W) Combination Dose Escalation Solnerstotug + cemiplimab* (Q3W)

Designed to rapidly confirm conditionally active MOA through:

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





RP2D = Recommended Phase 2 Dose MTD = Maximum Tolerated Dose * cemi = Libtayo (cemiplimab) 350 mg

Patient Demographics and Disease Characteristics Solnerstotug - Phase 1 Dose Escalation

	Solnerstotug n=16 (%)	Solnerstotug + Libtayo 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)

	Solnerstotug n=16 (%)	Solnerstotug + Libtayo n=18 (%)
Baseline ECOG, n (%)		
0	6 (37)	4 (22)
1	10 (63)	14 (78)
Prior lines metastatic therapy		
Median	2	2.5
Min, Max	0,7	1,7



Solnerstotug Was Well Tolerated Phase 1 Dose Escalation

Summary of Adverse Events

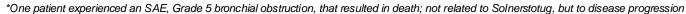
	Solnerstotug n=16 (%)	Solnerstotug + cemi Combo n=18 (%)
At least 1 TEAE	13 (81)	14 (78)
At least 1 SAE	1 (6)	8 (44)
≥Grade 3 TEAE	2 (13)	8 (44)
At least 1 TEAE leading to discontinuation	1* (6)	1 (5)
DLTs	0	0
AESI	1 (6)	5 (28)
Immune-mediated [^]	0	4 (22)
CRS#	1 (6)	1 (6)

- 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	Solnerstotug Mono n=16	Solnerstotug + cemi 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



[#]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)

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

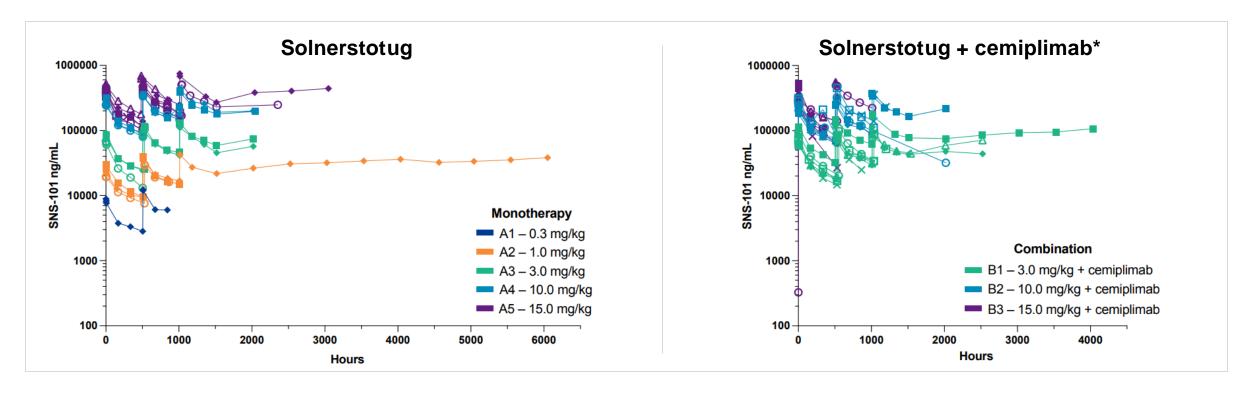
Subject Number	Dose Level	Adverse Event Preferred Term (Event description)	Severity (Grade)	Time of Onset Relative to Start of Infusion
01-010	Solnerstotug 15.0 mg/kg	Cytokine Release Syndrome (Chills and fever)	Grade 1	C1D1 ~4 hours post Solnerstotug Infusion
01-013	Solnerstotug 15.0 mg/kg + cemi	Cytokine Release Syndrome (Chills, no fever)	Grade 1	C1D1 ~5 hours post Solnerstotug Infusion
01-009	Solnerstotug 3.0 mg/kg + cemi	Infusion-related reaction (Chills and flushing)	Grade 2	C2D1 At the end of the Solnerstotug Infusion
04-015	Solnerstotug 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 Solnerstotug infusion

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



Solnerstotug Has a Long Half-Life Phase 1 Dose Escalation

- Supports once every three week (or greater) dosing in humans
- No significant immunogenicity detected in analysis of ADAs



Data as of 30April2024

^{*} Libtayo (cemiplimab) administered on Cycle 1 Day 2; co-administration thereafter



Phase 1 Dose Escalation Data Affirms Solnerstotug's MOA

Solnerstotug 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 doselimiting CRS at pharmacologically relevant dose levels
- Initial signals of anti-tumor activity







Solnerstotug is well positioned to be the first VISTA-targeted mAb to test the VISTA IO hypothesis



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

Soln	erstotug	Phase 1	Dose	Escalation

	Solnerstotug Mono n=16 (%)	Solnerstotug 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

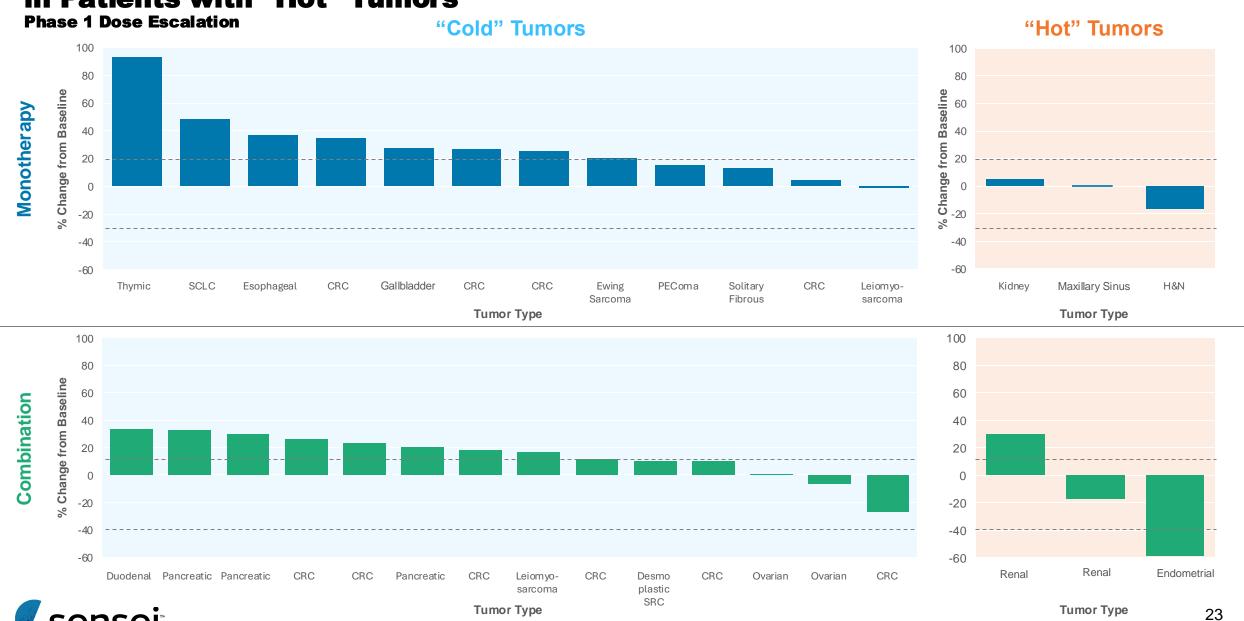
85% of enrolled patients had tumors typically unresponsive to PD-1/PD-L1 therapy



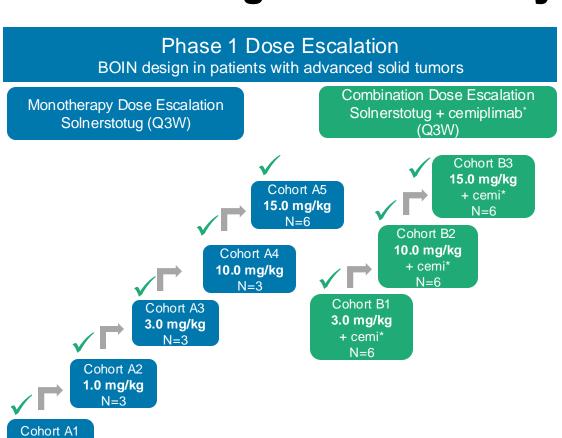
Data as of 30April2024

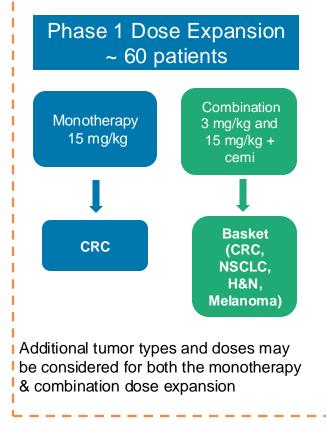
^{*}Sarcoma: Leiomyosarcoma, Ewing Sarcoma, PEComa, Hemangiopericytoma (mono) and Leiomyosarcoma and Desmoplastic small round cell (combo) **Other Tumor Types: Small cell lung carcinoma, Gallbladder, Adenocystic carcinoma maxillary sinus, and mediastinal carcinoma (mono) and Ovarian, Duodenal, granulosa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

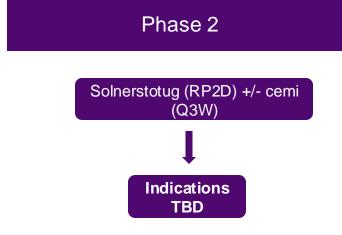
Dose Escalation Data Supports Advancement into Dose Expansion Predominantly in Patients with "Hot" Tumors



Solnerstotug Phase 1/2 Study







Phase 1 Study Objectives

Primary Safety, tolerability, MTD/RP2D

Secondary PK, immunogenicity & anti-tumor activity



= cleared DLT assessment period

0.3 mg/kg

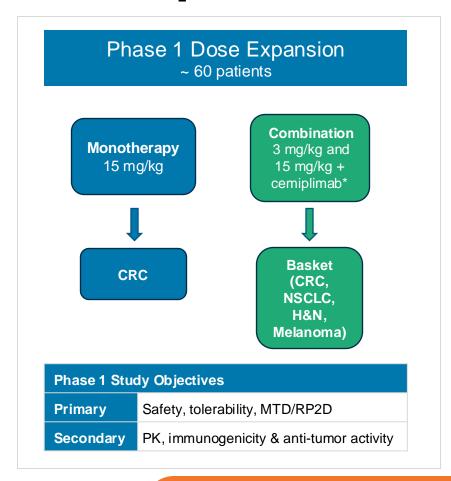
N=1

* cemi = Libtayo (cemiplimab) 350 mg Patient enrollment is ongoing for the monotherapy & combination expansion cohorts

Phase 2 Study Objectives				
Primary	Anti-tumor activity			
Secondary	Safety, tolerability, PK & immunogenicity			

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

Dose Expansion Cohort Designed to Explore Efficacy in "Hot" Tumor Population



Dose expansion cohort is focused on the activity profile of solnerstotug & optimizing the dose and patient population for Phase 2

- 45 out of ~60 patients enrolled in dose expansion cohorts^
- Anticipate full enrollment by end of Q1 2025
- Exploring two dose levels (3 and 15mg/kg) 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
 - The majority of patients with "hot" tumors will have received and progressed on a prior anti-PD-1 therapy or are PD-L1 negative

Data from dose expansion expected in Q2 2025



^ as of 1/1/2025

* Libtayo (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

Completed and Anticipated Solnerstotug Clinical Milestones





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- Clinical data demonstrated initial signs of promising clinical activity in multiple tumor types, a well-tolerated safety profile and potential bestin-class pharmacokinetic profile



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





EXPECTED MILESTONES

Dose expansion data in Q2 2025



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







Massachusetts Maryland

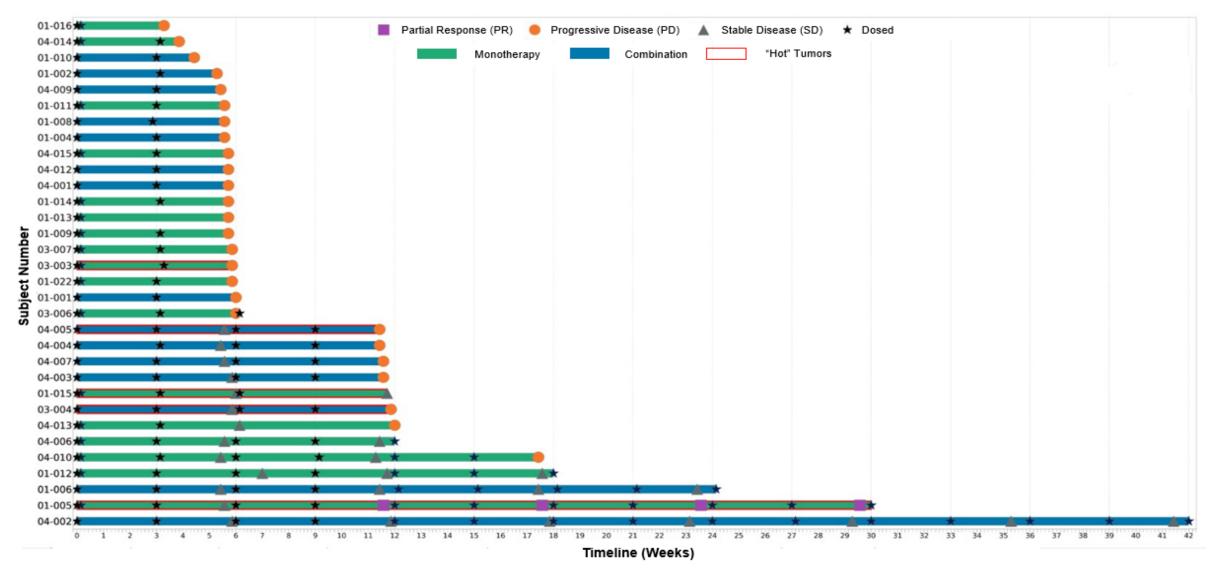
22 Boston Wharf Rd 1405 Research Blvd

7th floor Suite 125, Rockville

Boston, MA 02210 MD 20850

senseibio.com

Solnerstotug Duration of Treatment





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

I/O-naïve MSS Endometrial Cancer with PR
3.0 mg/kg Solnerstotug + 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

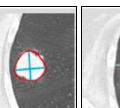
- Total laparoscopic hysterectomy with bilateral salpingo-oophorectomy, and additional sentinel lymph node dissection, Dec 2020
- Paclitaxel/Carboplatin (adjuvant setting), Feb 2021 to Aug 2021
- Anastrozole (metastatic setting), Aug 2023 to Sep 2023

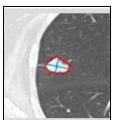
Adverse Events

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

Tumor Assessments in Solitary Target Lesion

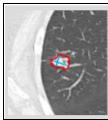
Baseline 6-Week SD (-0.6%)





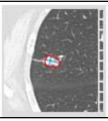
12-Week

PR (-34%)



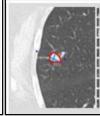
18-Week

(-45%)



24-Week

PR (-52%)



30-Week

PR (-59%)

I/O-naïve MSS Colon Cancer
3.0 mg/kg Solnerstotug + 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 Solnerstotug, not related to Libtayo
- Grade 2 rash maculo-popular, related to Solnerstotug and Libtayo,
 AESI (immune-mediated), resolved after treatment with prednisone
- Grade 2 pruritis, related to Solnerstotug and Libtayo

Tumor Assessments

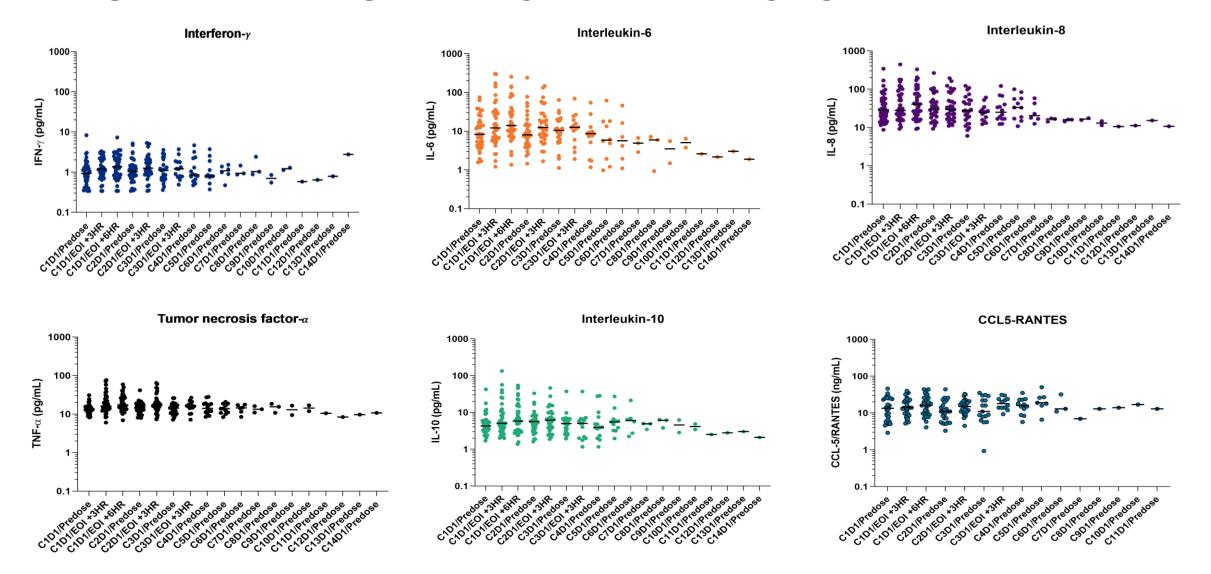
- 6-Week Scans: Stable Disease (19% decrease)
- 12-Week Scans: Stable Disease (27% decrease)
- 18-Week Scans: Progressive Disease (23% increase from nadir)

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

sensei

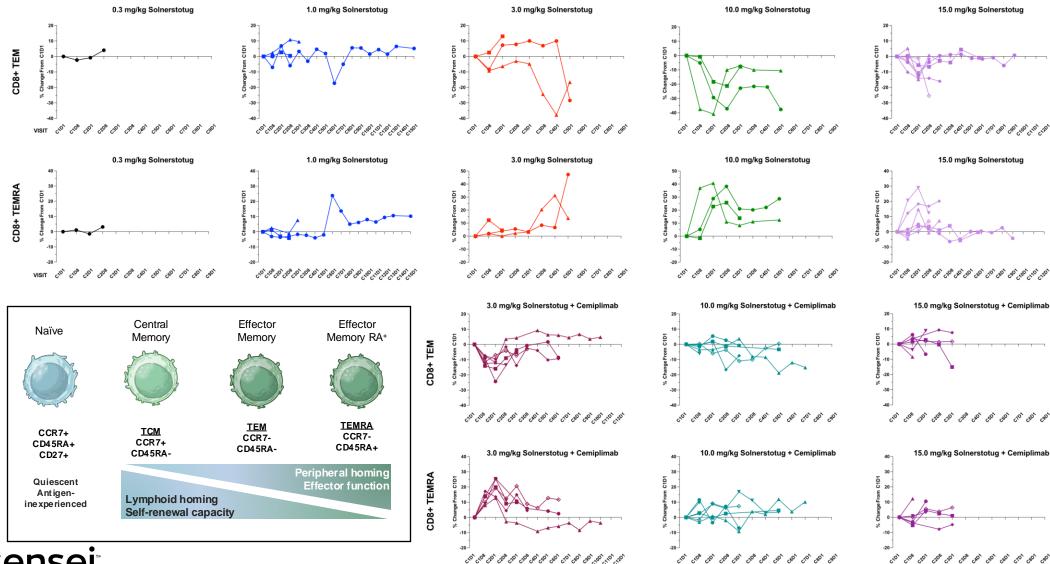
Data as of 30April2024

No Significant Changes in Key Inflammatory Cytokines





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





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

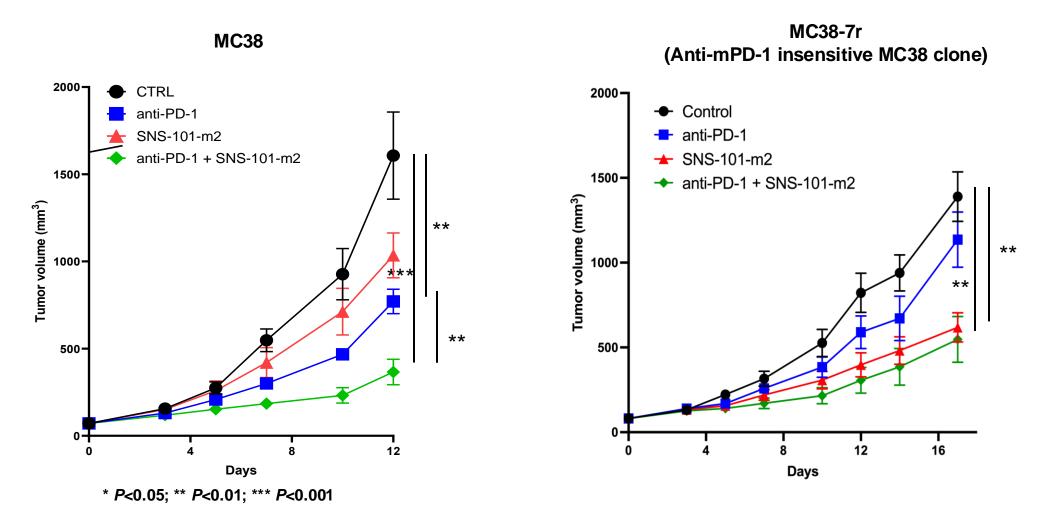
Due to its longer half-life (13.4d vs 3.9d), ravulizumab given every 8w achieved noninferiority compared with eculizumab given every 2w for all efficacy endpoints, while maintaining a similar safety profile.

2018: FDA approves Ultomiris® (ravulizumab, ALXN1210)

2020: Ultomiris sales = \$1.08 billion

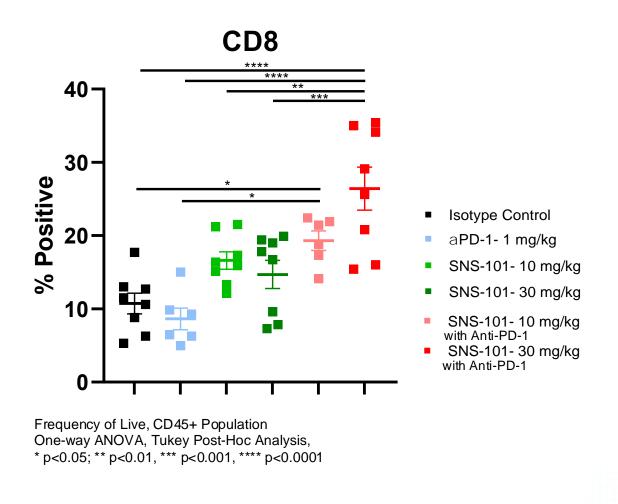


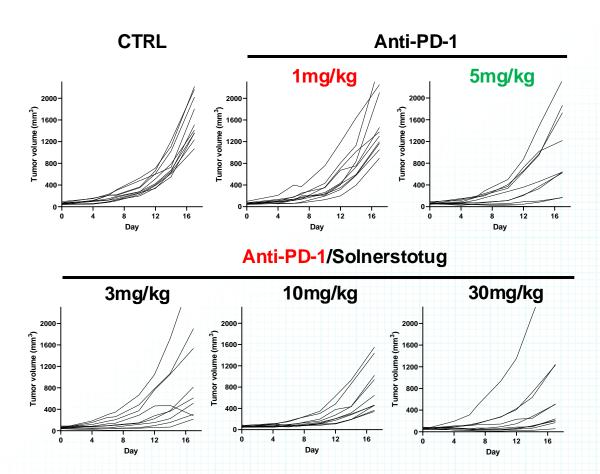
Single-agent Activity and Deepened Anti-tumor Responses to PD-1 Combo in Human VISTA KI Mice *In vivo*





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



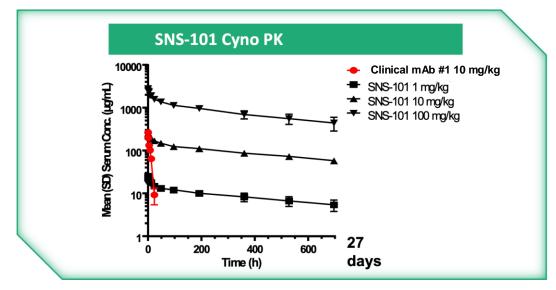




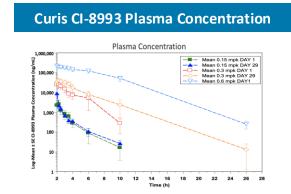
PK Sink Continues to be an Issue with Non-pH-Sensitive VISTA programs*

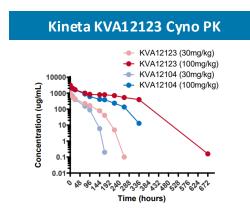
Linear

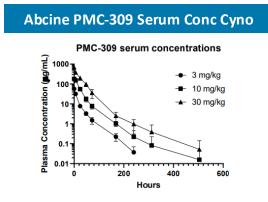
Solnerstotug is designed to overcome elimination kinetics and half-life related to PK sink observed in non-pH-sensitive VISTA programs

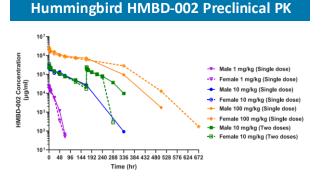


Non-linear



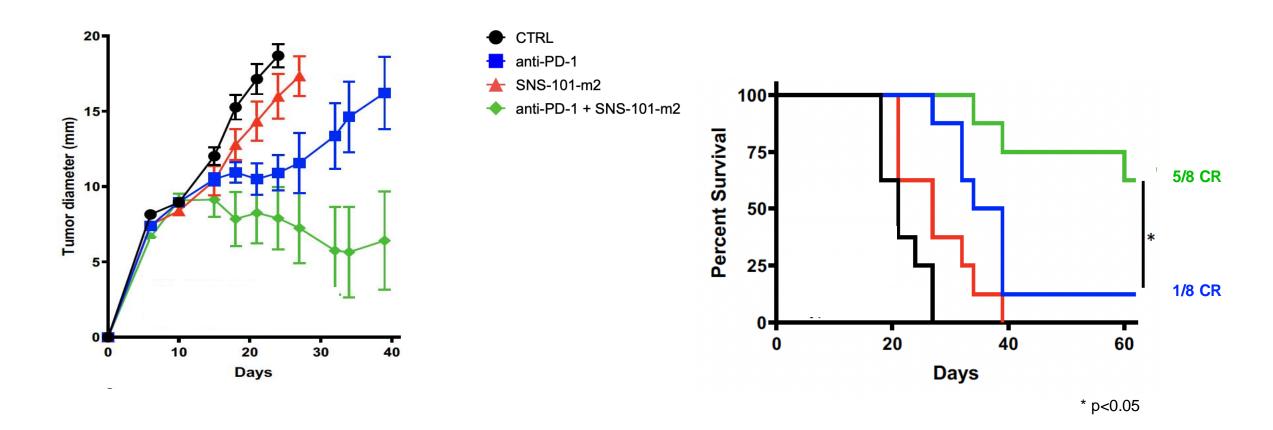






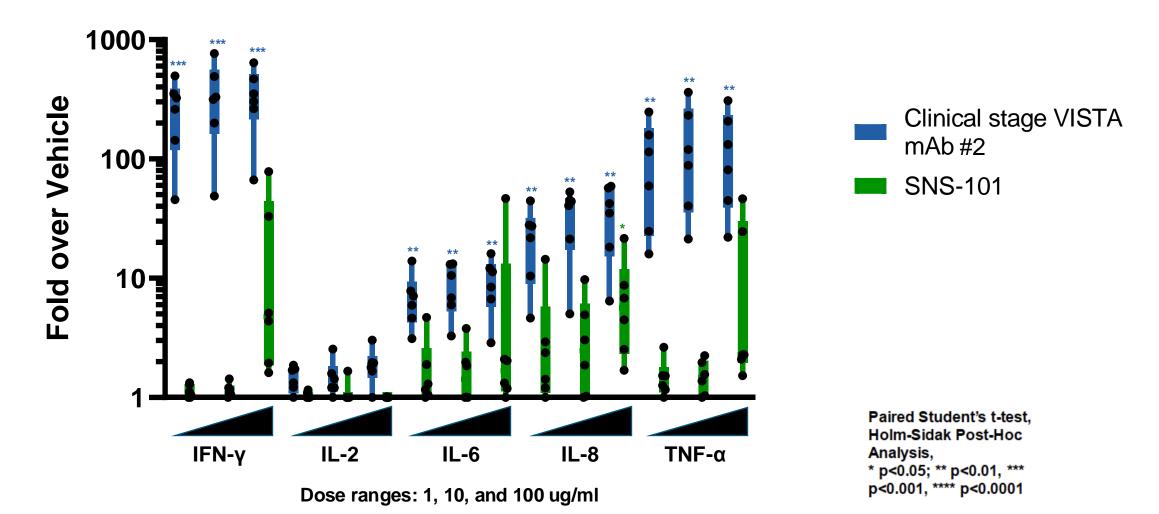


Solnerstotug Re-sensitized Anti-PD-1 Insensitive Sarcoma Tumors in Human VISTA Knock-in Mice





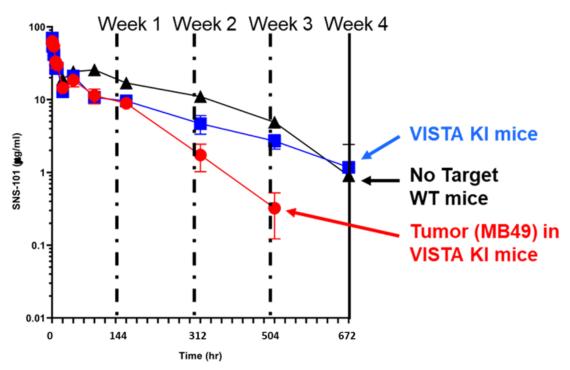
Solnerstotug Induced Substantially Lower Cytokine Release in Whole-blood Assay at Neutral pH Compared to pH-independent VISTA Antibody



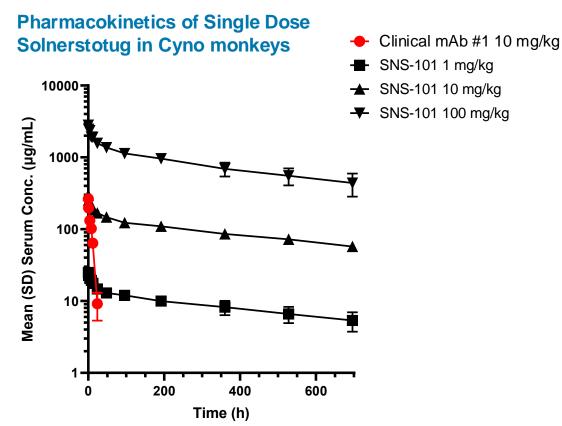


Solnerstotug Has Displayed a Favorable Single-dose PK Profile in Preclinical Studies - No Significant TMDD in Human VISTA KI Mice or Non-human Primates

Pharmacokinetics of Single Dose 5 mg/kg Solnerstotug 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

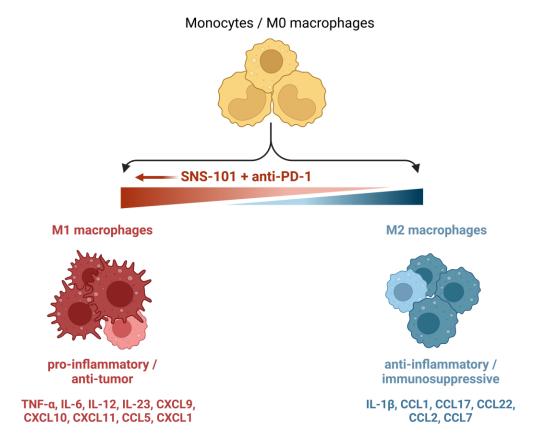


Solnerstotug displayed linear elimination kinetics unlike a pH-independent anti-VISTA mAb, which demonstrated TMDD and rapid clearance



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

Solnerstotug 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 antitumorigenic 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