SNS-101 Dose Expansion Data

March 27, 2025

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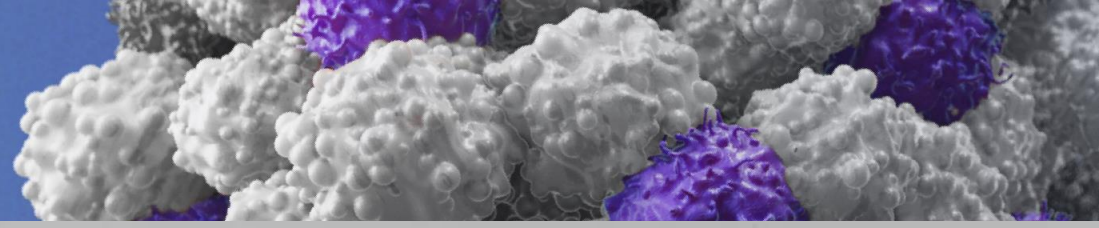

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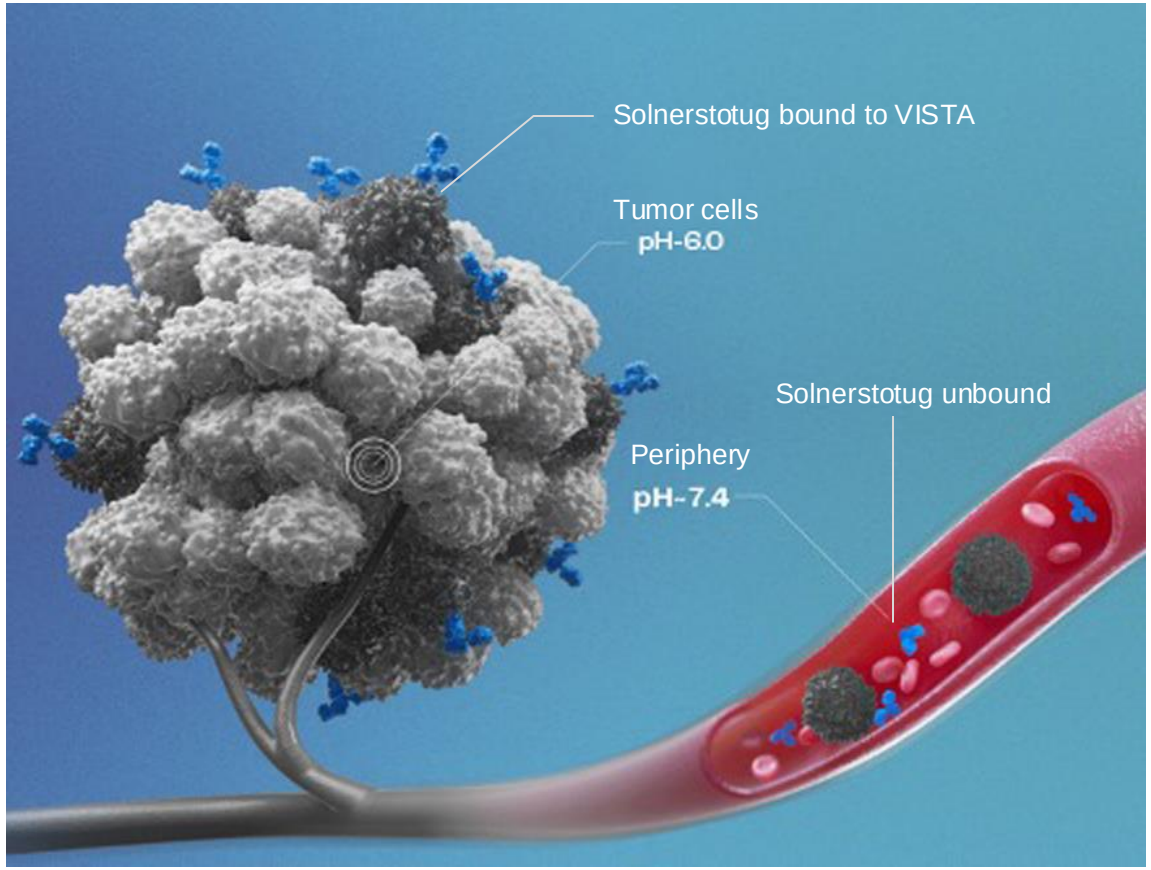
Solnerstotug is a Potential First-in-Class VISTA Targeting Mab That Binds Selectively in the Tumor Microenvironment



Targets VISTA:

- An immune checkpoint protein and B7 family member that drives immunosuppression analogous to PD-1/PD-L1
- Unique and extensive expression pattern, found on tumors and myeloid-lineage cells
- Acts in a pH-sensitive matter, engaging with its T-cell receptor PSGL-1 selectively under acidic conditions
- Plays a potentially key role in both primary (innate) and secondary (acquired) resistance to checkpoint blockade

Unique MOA:

- Selectively inhibits VISTA:PSGL-1 interaction within the acidic TME
- Drives anti-tumor activity by reversing immunosuppression

Solnerstotug is a pioneering approach designed to overcome toxicities associated with 1st-generation antibodies

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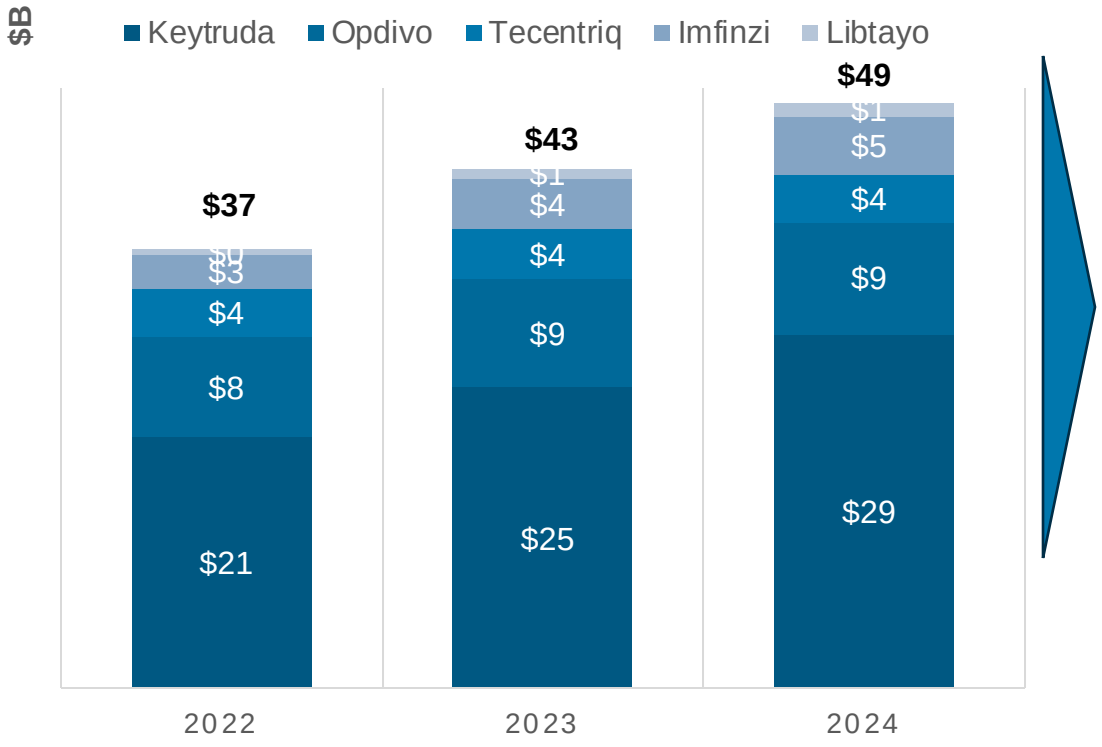
*Gao et al. Nat Med. 2017
Kakavand et al. Mod Pathol. 2017

The VISTA Commercial Opportunity

PD-(L)1 Targeted Therapies Are One of the Largest Classes of Drugs Across All Therapeutic Areas

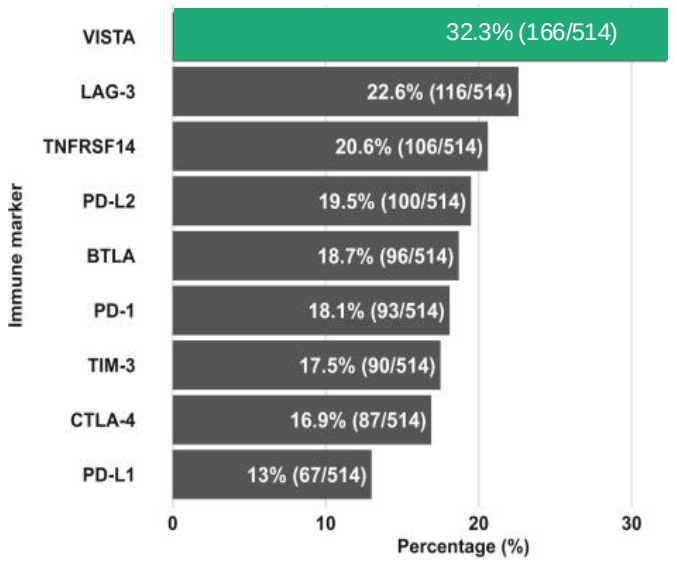
Sales of Top 5 PD-(L)1 Targeted Therapies



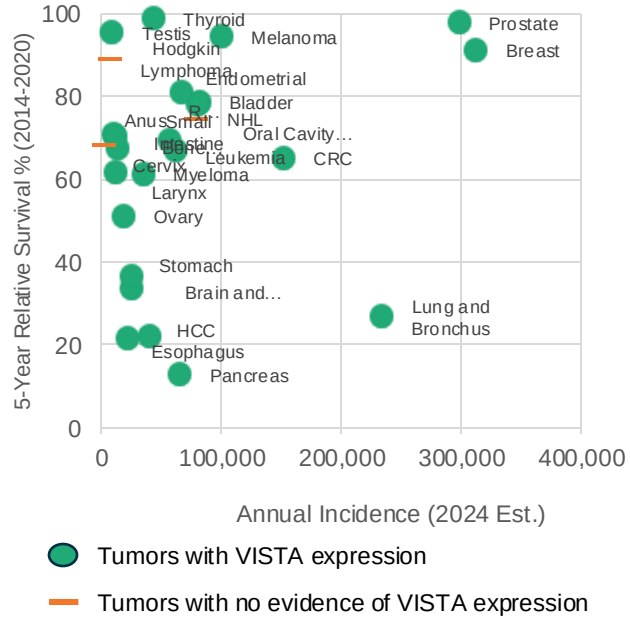
Source: Merck, BMS, Roche, AstraZeneca, Regeneron

Unlike, PD-(L)1, VISTA is Found in Nearly All Solid Tumors with High Unmet Need

VISTA Expression Levels Are Relatively High Across Cancer Indications



VISTA Expression is Found in the Majority of Solid Tumor Indications



Source: Nishizaki, D. et al. ESMO Open, Volume 9, Issue 4, 102942, Incidence and Survival: NCI SEER Data 2024, Expression: internal data and publications

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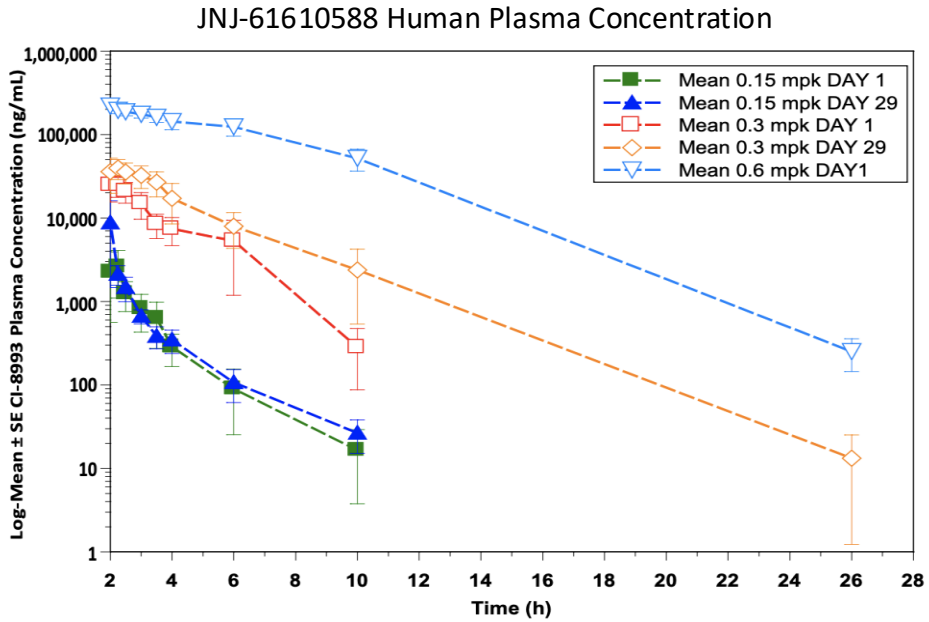
The Challenge of Targeting VISTA

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 $t_{1/2}$



Key issues likely driven by extensive off-tumor expression of VISTA

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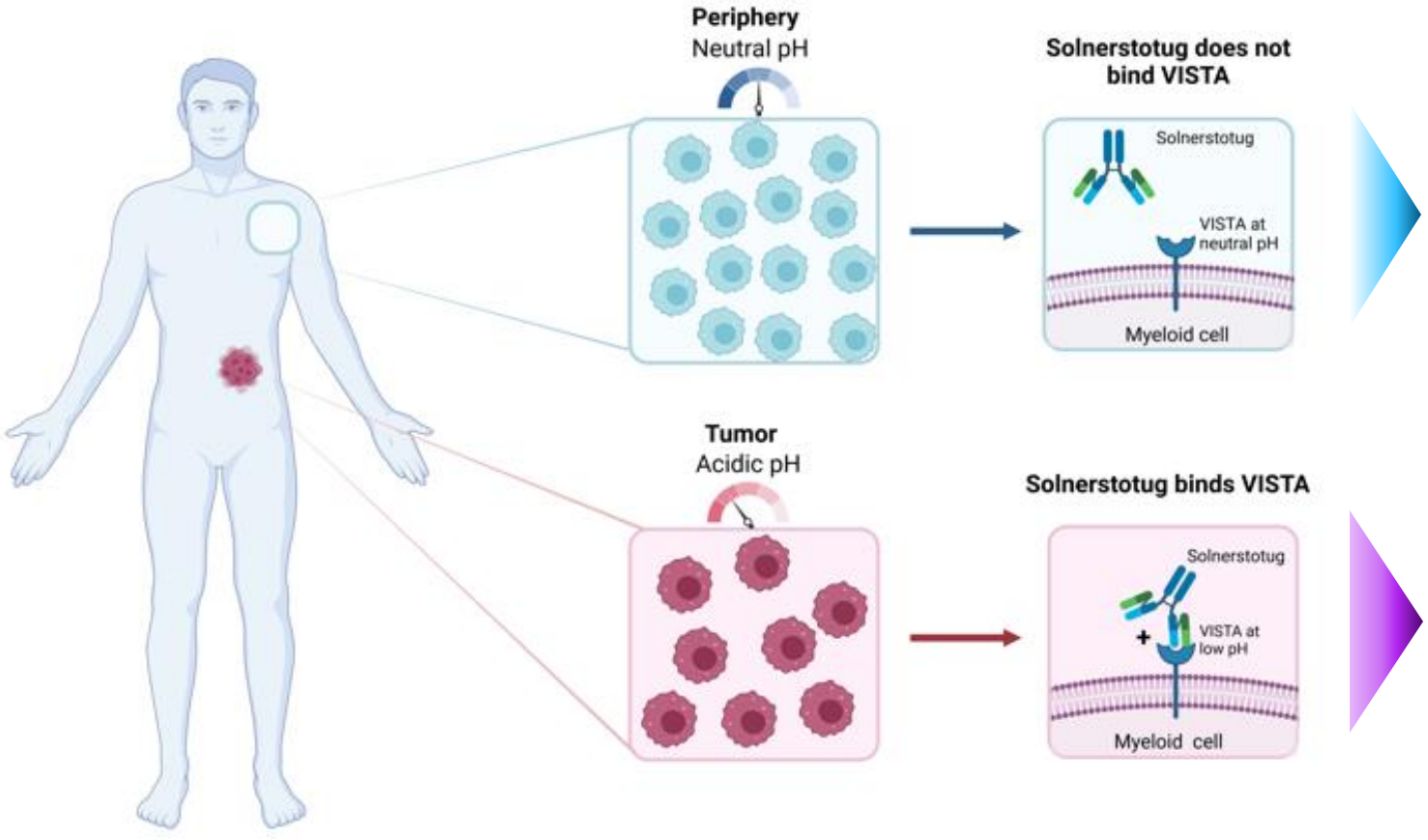
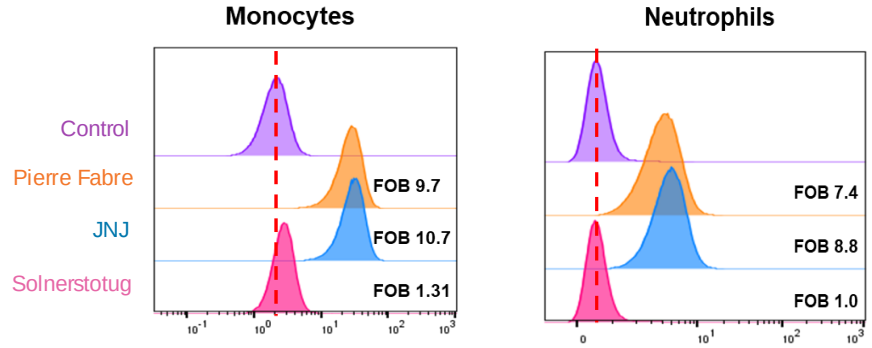
1 Curis, Inc., Corporate Presentation, Feb 2022

Solnerstotug Binds VISTA Selectively at the Tumor



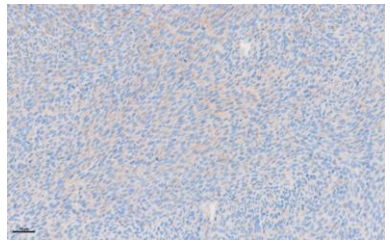
Periphery (Neutral pH) = No Binding

Solnerstotug has no detectable binding in peripheral or normal tissues

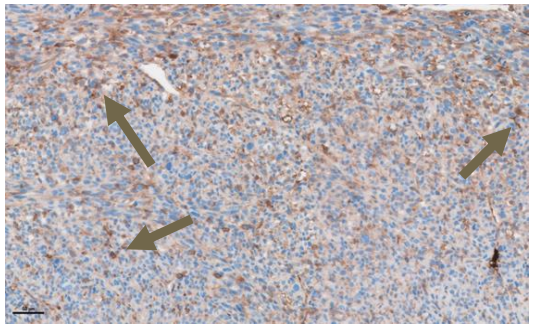


Tumor (Acidic pH) = Binding

Solnerstotug rapidly accumulates in the tumor



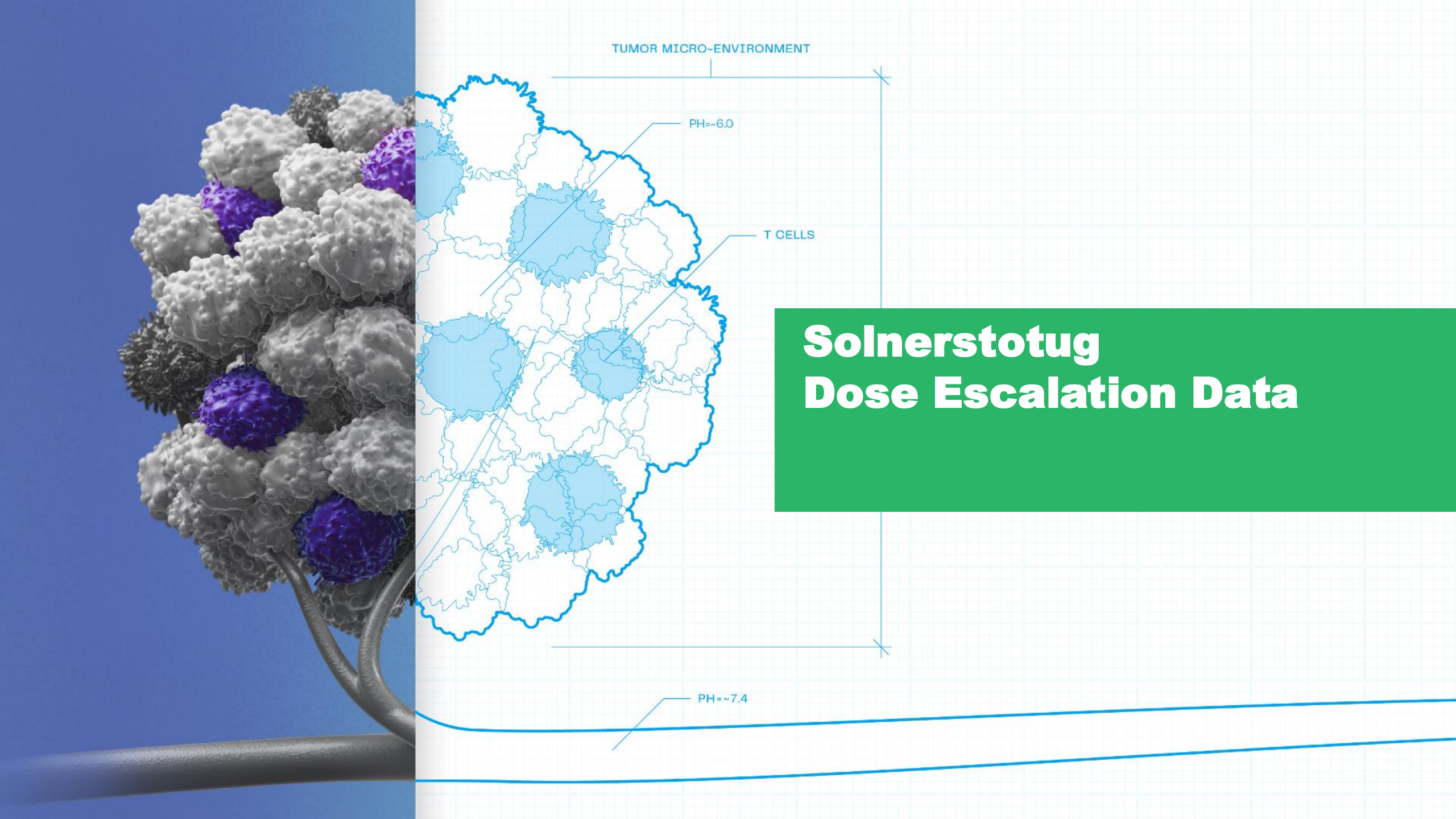
Isotype control
6h post-dosing



Solnerstotug
6h post-dosing

Solnerstotug minimizes off-tumor binding, providing potential for an improved tox and PK profile

Blue = tumor
Brown = Solnerstotug



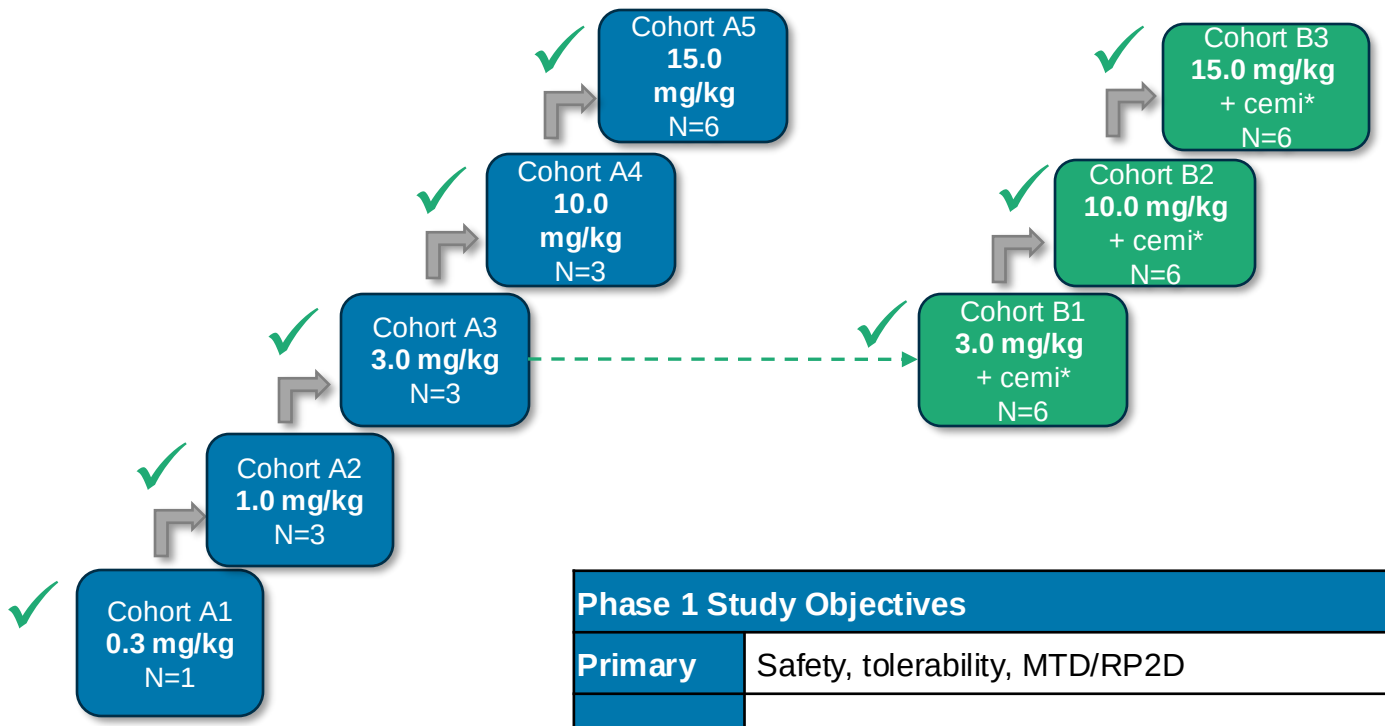
Solnerstotug
Dose Escalation Data

Solnerstotug Phase 1 Dose Escalation Study

Given prior history of VISTA antibodies, Sensei prioritized establishing:

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

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

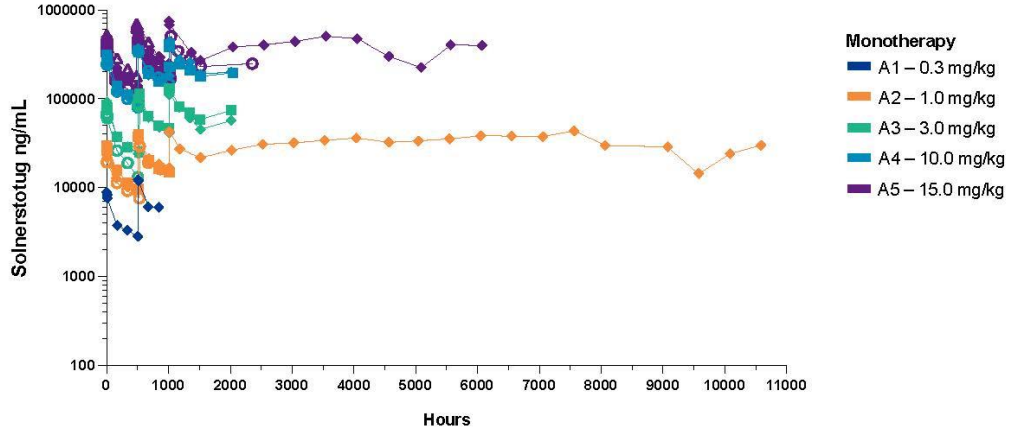
✓ = cleared DLT assessment period

Phase 1 Dose Escalation Data Affirms Solnerstotug's MOA and Focused Patient Population in Dose Expansion

- **Well-tolerated**
- **Commercially acceptable and potentially best-in-class PK profile**
- **First and only agent to be dosed at pharmacologically relevant levels**
- **Forward focus on patients with "hot" tumors more likely to respond to immunotherapy**

Safety Profile Summary (Dose Escalation)

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



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

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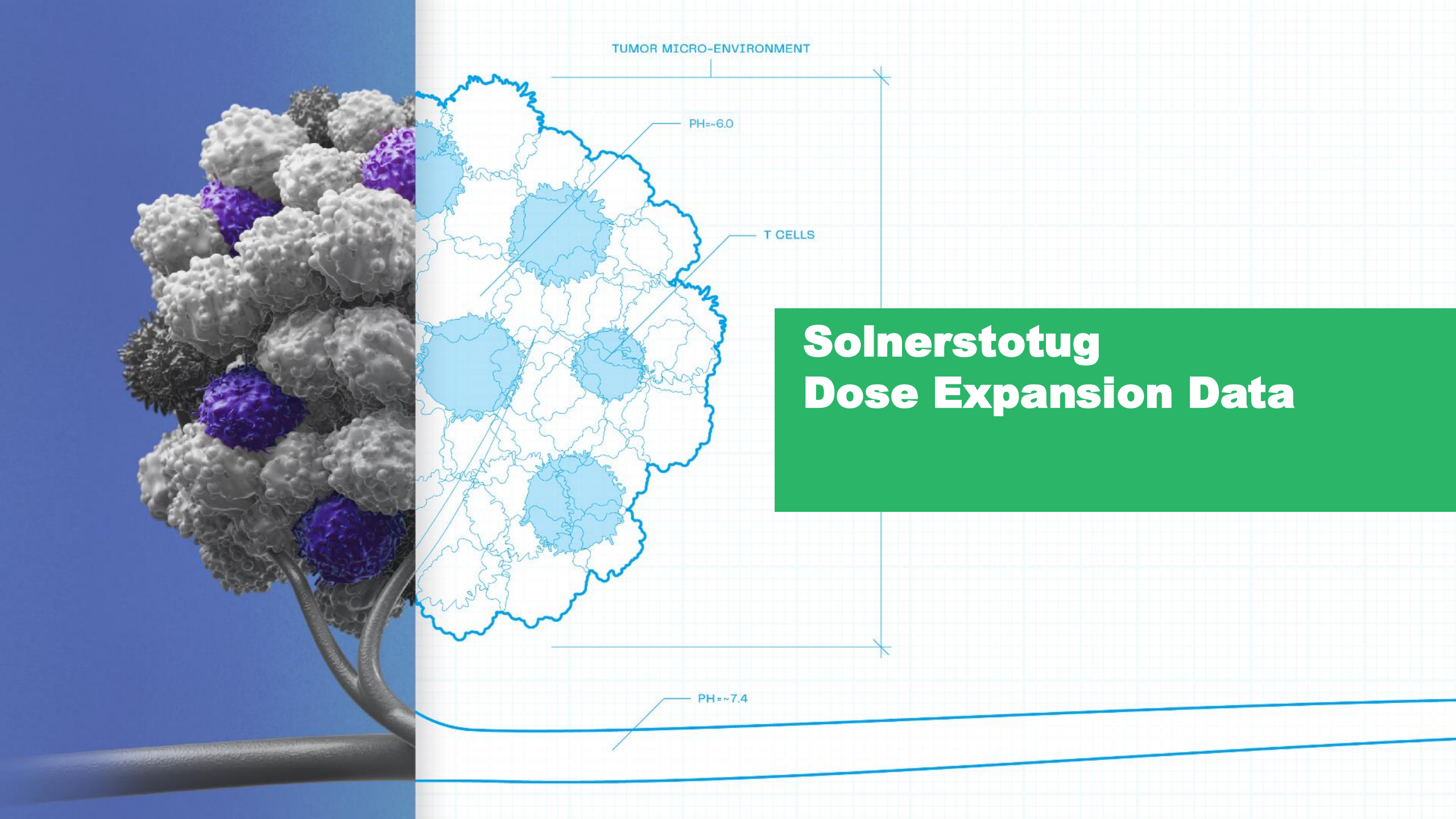
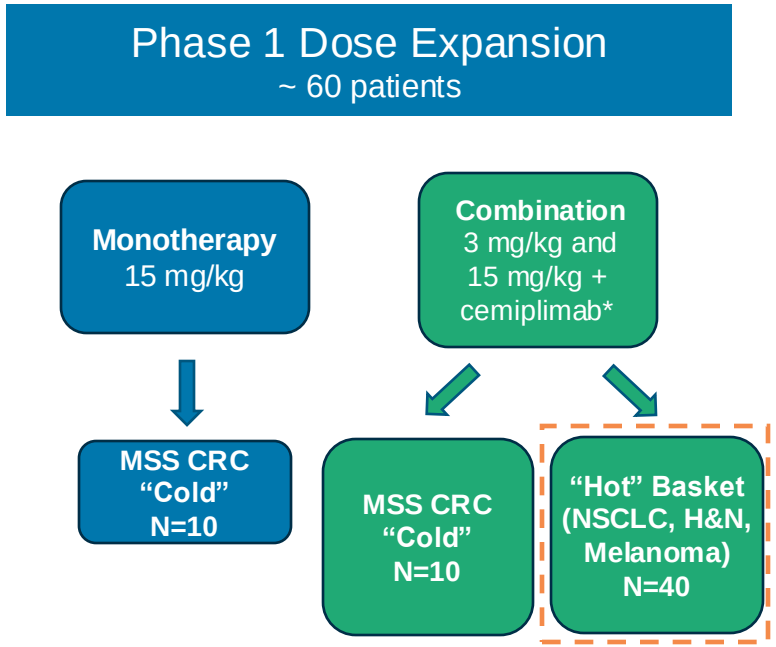


Solnerstotug
Dose Expansion Data

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



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

Focused on the activity profile and optimizing dose / patient population for Phase 2

- Focused on a basket of "hot" tumors (combination therapy) and one "cold" tumor type (monotherapy and combination therapy)
- Nearly all patients in "hot" tumor cohort:
  - Will have received and progressed on a prior anti-PD-1 therapy; or
  - Are PD-L1 negative
  - Historical response rates to PD-1 rechallenge following progression on PD-1 are in the **single digits**[1,2]
- Favorable activity was observed in patients with "hot" tumors
- No signal of activity was observed in patients with "cold" tumors (MSS CRC; see appendix)

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* 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
MSS = Microsatellite stable
CRC = Colorectal cancer
NSCLC = Non small cell lung cancer
H&N = Head and neck cancer

1. Livanou et al., *Cancers* 2024
2. Kluger H, et al. J Immunother Cancer 2023

Patient Disposition
Phase 1 Dose Expansion

Entire Expansion Cohort

	Monotherapy	Combination
	solnerstotug N = 10 (%)	**solnerstotug + cemi N = 50 (%)**
Enrolled	10	50
Dose Received		
3 mg/kg	0	16 (32)
15 mg/kg	10 (100)	34 (68)
Treatment Ongoing	1 (10)	23 (46)
Discontinued	9 (90)	27 (54)
Reason for Discontinuation		
Progressive Disease	6 (60)	20 (40)
Adverse Event	0 (0)	0 (0)
Withdrew Consent	0 (0)	1 (2)
Death	1 (10)*	2 (4)**
Clinical Progression	0 (0)	3 (6)
Physician Decision/Lack of clinical benefit	1 (0)	1 (2)
Lost to Follow-up	1 (10)	0 (0)

Expansion Cohort Basket of "Hot" Tumors

	Combination
	solnerstotug + cemi N = 40 (%)
Enrolled	40
Dose Received	
3 mg/kg	16 (40)
15 mg/kg	24 (60)
Treatment Ongoing	23 (58)
Discontinued	17 (42)
Reason for Discontinuation	
Progressive Disease	10 (25)
Adverse Event	0 (0)
Withdrew Consent	1 (3)
Death	2 (5)**
Clinical Progression	3 (8)
Physician Decision/Lack of clinical benefit	1 (3)
Lost to Follow-up	0 (0)

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*Death due to Myocardial Infarction, that resulted in death; not related to SNS-101
**Death due to Hypoxia that resulted in death; secondary to the overall event of disease progression, not related to SNS-101 or Cemi; death due to PD

Patient Demographics (Patients with "Hot" Tumors)
Phase 1 Dose Expansion

	solnerstotug + cemi N = 40 (%)
Gender, n (%)	
Male	29 (73)
Female	11 (27)
Age, years	
Median (min, max)	73.5 (28, 85)
Baseline ECOG, n (%)	
0	11 (27)
1	29 (73)
Prior lines *metastatic* therapy	
Median (min/max)	2 (0, 7)
Prior PD-1/PD-L1, n (%)	
% Yes*	**36 (90)**
Prior PD-1/PD-L1 regimen preceding enrollment in the study, n (%)	
% Yes	24 (60)

	solnerstotug + cemi N = 40 (%)
Cancer Type, n (%)	
Responsive to PD-1 (e.g. "hot" tumors)	
Head and Neck	11 (28)
NSCLC	10 (25)
Melanoma	5 (13)
Renal	5 (13)
Merkel Cell	2 (5)
CRC- MSI High	2 (5)
Cholangiocarcinoma- MSI High	1 (3)
Endometrial	1 (3)
Esophageal	1 (3)
Hepatocellular	1 (3)
Pleomorphic Spindle cell	1 (3)

90% of patients received and progressed on a prior PD-1/PD-L1 therapy

*Two NSCLC patients were I/O naïve because 1 had very low PD-L1 expression and the other was EGFR mutant. One pleomorphic cancer patient was I/O naïve due to PD-1 not being approved in that setting. 1 patient does not have data entered about prior treatment with PD-1.

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Data as of March 17, 2025

Historical Response Rates Highlight Difficulties of Re-Challenging with PD-(L)1

NSCLC Example [1]

	Fujita et al, 2018		Watanabe et al, 2019		Katayama et al, 2019		Fujita et al, 2020	
No. of Patients	12		14		35		15	
Reason for discontinuation	PD		PD		PD		PD	
	1st course	**Re-challenge**	**1st course**	**Re-challenge**	**1st course**	**Re-challenge**	**1st course**	**Re-challenge**
Treatment used	Anti-PD-1	Anti-PD-1	Anti-PD-(L)1	Anti-PD-(L)1	Anti-PD-(L)1	Anti-PD-L1	Anti-PD-1	Anti-PD-1
ORR, N (%)	7 (58.3)	1 (8.3)	3 (21.4)	1 (7.1)	12 (34.3)	1 (2.9)	0 (0)	0 (0)

Aligned with SITC definition of acquired resistance, which defines ≤5% chance of benefit with ICI therapy past progression [2]

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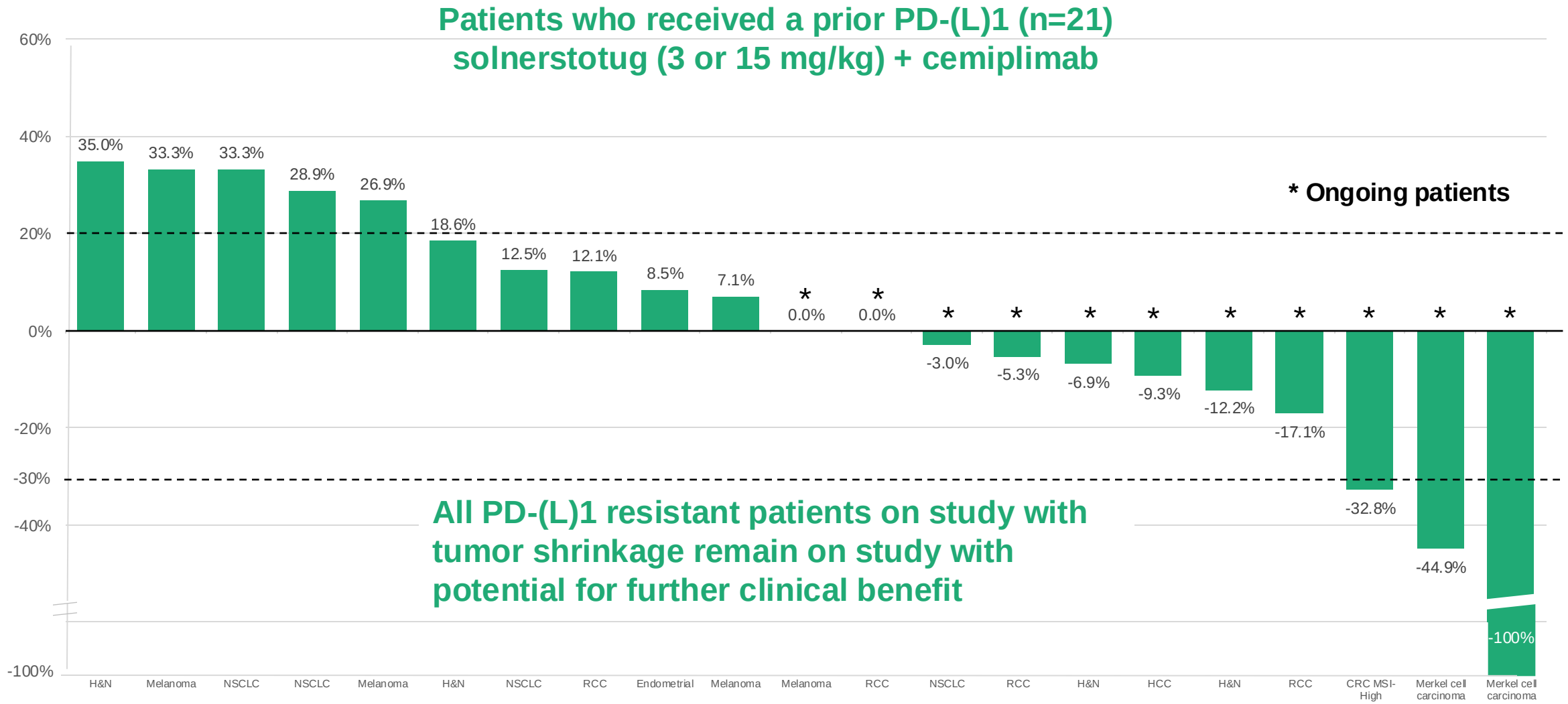
1 Livanou et al., 2024
2 Kluger H, et al. J immunother Cancer 2023
Spagnolo et al., BMC Cancer 2021

Preliminary Efficacy Data in PD-(L)1-Refractory "Hot" Tumor Patients is Favorable

Phase 1 Dose Expansion



21 "hot" tumor PD-(L)1 refractory patients were considered evaluable for efficacy having received at least one post-baseline scan. An additional 11 patients have not yet reached first baseline scan, with an additional 8 patients discontinued study prior to initial scan.

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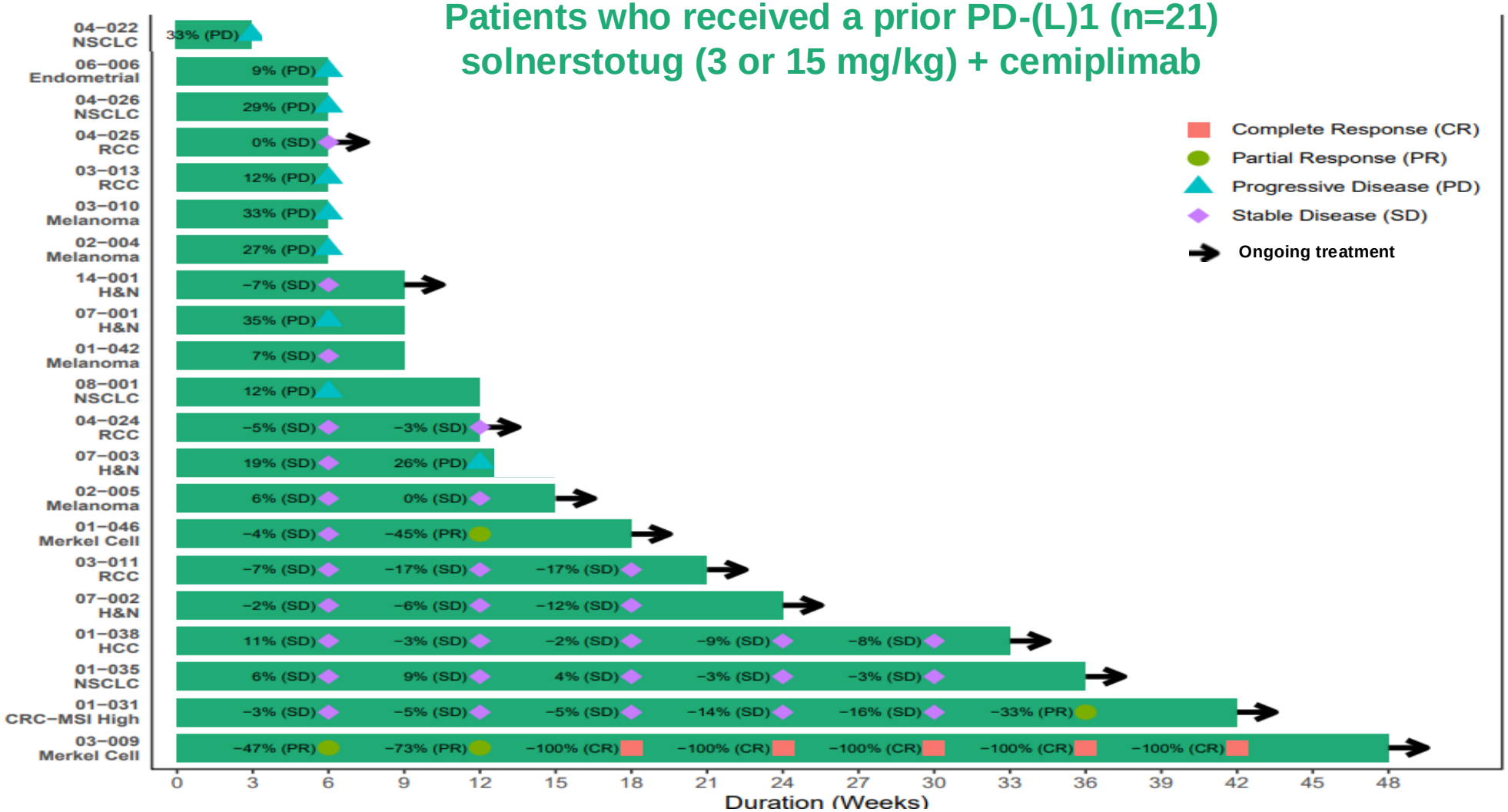
“Hot” Tumor PD-(L)1 Refractory Patients Have Favorable Duration on Study and Achieved Responses or Long-Term Stable Disease



07-001 (H&N) and 08-001 (NSCLC): continued beyond progression

Data as of March 17, 2025

Merkel Cell Carcinoma Patient (03-009)

Complete Response

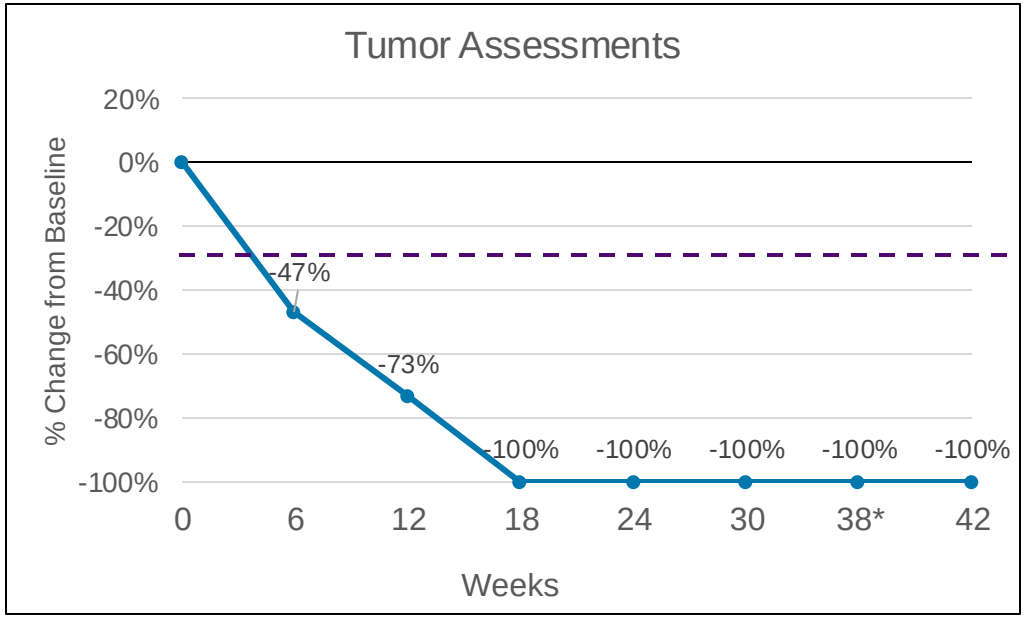
15 mg/kg solnerstotug + cemiplimab

- **85 yo male with Merkel Cell Carcinoma of skin (right nasal sidewall)**
  - Diagnosed June 2022
  - **TMB 91**, MSS. ATR, BLM, RB1 TP53 RASA1, CDKN1B and ARID1B K1250fs

- **Prior treatment:**
  - **20Oct2022 to 18Jan2024: Avelumab (Bavencio)** with Signatera of 553 MTM/ml, best response stable disease, stopped due to progression.
  - 06Dec2022 to 24Jan2023: underwent RT (36 Gy) to nose and neck; sustained a prompt and robust response (PR) to Rx

- **Cycle 1 Day 1:** 24Apr2024

- **Treatment ongoing**



*Missed 2 cycles (Cycle 12 and 13) of drug due to extended vacation.

Merkel Cell Carcinoma Patient (01-046)

Partial Response

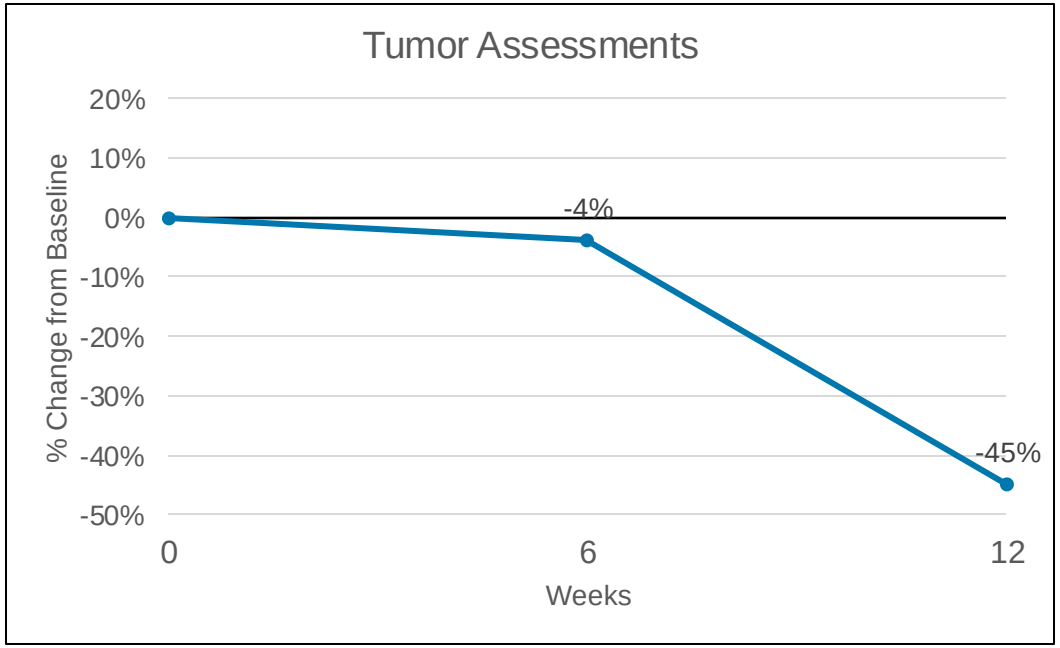
15 mg/kg solnerstotug + cemiplimab

- **58 yo female with Metastatic Merkel cell carcinoma**
  - Diagnosed 2Dec2022
  - TMB 15.16 mut/Mb
  - KMT2D, DPTOR, EPHA5, CREBBP+
  - Hx of follicular lymphoma (received chemo followed by Zydelig maintenance until 2021, remission)

- **Prior Treatment:**
  - March 2023 to July 2023: **Pembro** (adjuvant setting), best response unknown, stopped due to progression
  - Aug 2023 to Oct 2023: **Nivolumab + Ipilimumab**, best response and reason for stopping unknown
  - Nov 2023 to Apr 2024: Continued on **Nivolumab** alone, best response SD, stopped due to progression
  - May 2024 to October 2024: DM919 (MICA/B Antibody), best response SD, stopped due to progression

- **Cycle 1 Day 1: 20Nov2024**

- **Treatment ongoing**



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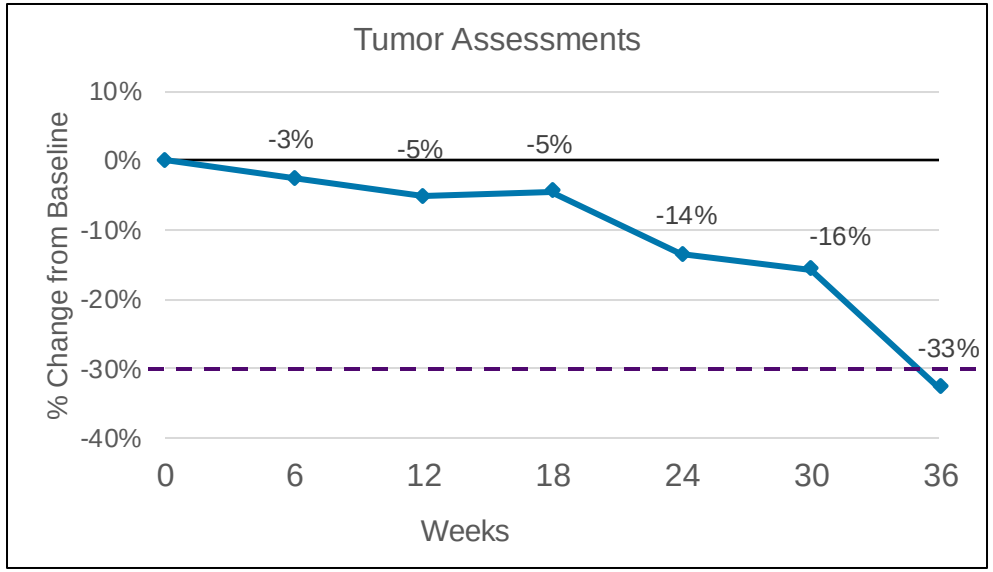
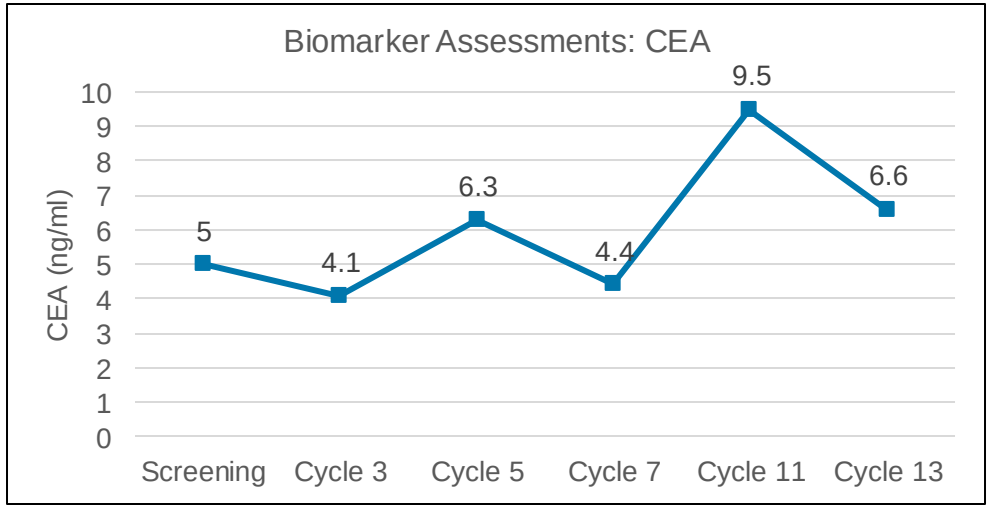
MSI-High CRC Patient (01-031)

Partial Response

15 mg/kg solnerstotug + cemiplimab

- **51 yo male with MSI High CRC (adenocarcinoma of the transverse colon)**
  - Diagnosed 18Nov2019
  - RAS (wild type); NRAS (wild type); BRAF(wild type); MSI-High; MMR- Deficient; MSH2 (S77fs)
- **Prior anti-cancer treatment**
  - Dec 2019 to Feb 2020: FOLFOX + Avastin, best response progression
  - **Feb 2020 to Apr 2024: Pembrolizumab,** best response complete response, stopped due to progression
- **Cycle 1 Day 1:** 22May2024
- **Treatment ongoing**





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Renal Cell Carcinoma Patient (03-011)

Stable Disease (SD) with Tumor Regression

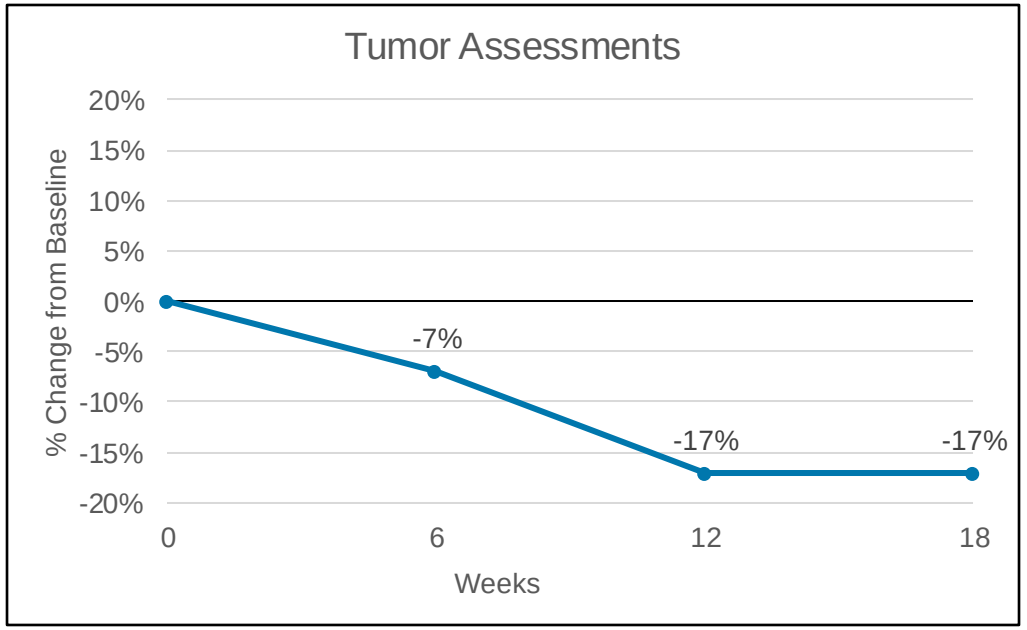
3 mg/kg solnerstotug + cemiplimab

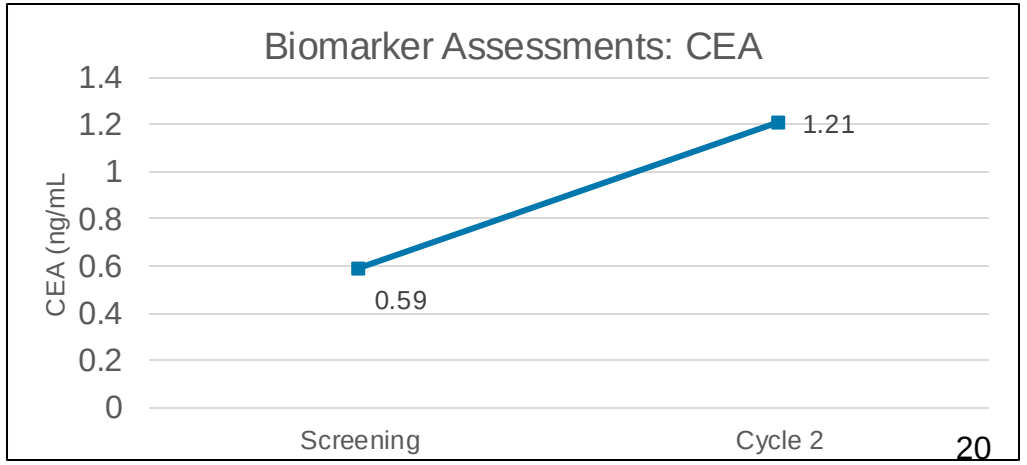
- **59 yo male with metastatic Renal Clear Cell Carcinoma (malignant neoplasm of left kidney, except renal pelvis)**
  - Diagnosed 8Mar2017
  - Evidence of a PTEN deletion in his tumor
  - MSI-high not detected

- **Prior Treatment/Surgery:**
  - Apr 2018 to Feb 2019: **Pembro** + Lenvatinib, best response SD, stopped due to progression
  - Mar 2019 to Jul 2020: Sutent, best response progression
  - Aug 2019 to Sep 2019: CB-839 (Glutaminase Inhibitor) + Talazoparib, best response progression
  - Oct 2019 to Dec 2019 : **Nivo + Ipi**, best response progression
  - Jan 2020 for 3 weeks: Cabometyx, stopped due to adverse event/toxicity
  - Feb 2020 to Aug 2023: XL092 (TKI), best response partial response, stopped due to progression
  - Aug 2023 to Sep 2024: AB521 (HIF-alpha Inhibitor), best response partial response, stopped due to progression

- **Cycle 1 Day 1:** 21Oct2024

- **Treatment Ongoing**





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Data as of March 17, 2025

Hepatocellular Patient (01-038)

Durable Stable Disease and Tumor Kinetics and AFP Consistent with a Pattern of Pseudo-Progression

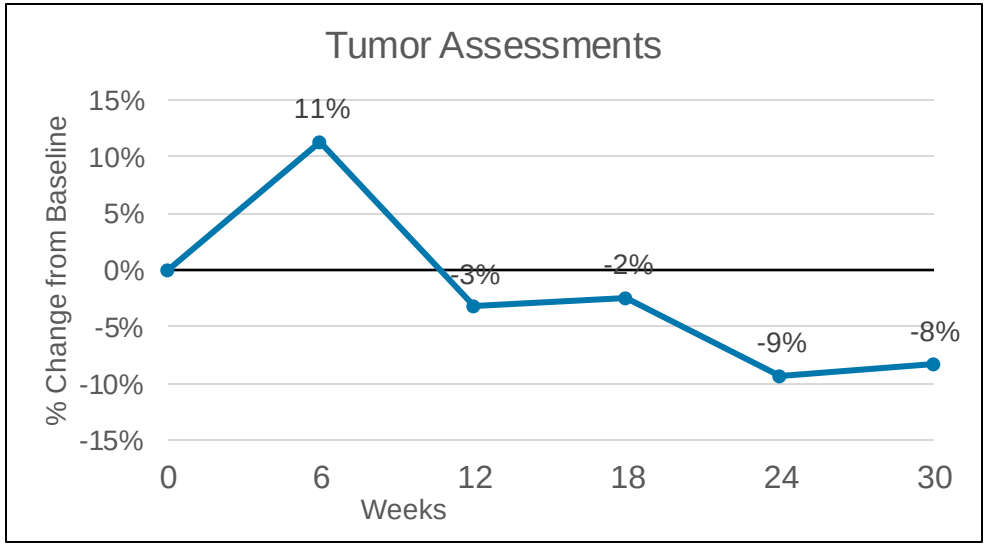
15 mg/kg solnerstotug + cemiplimab

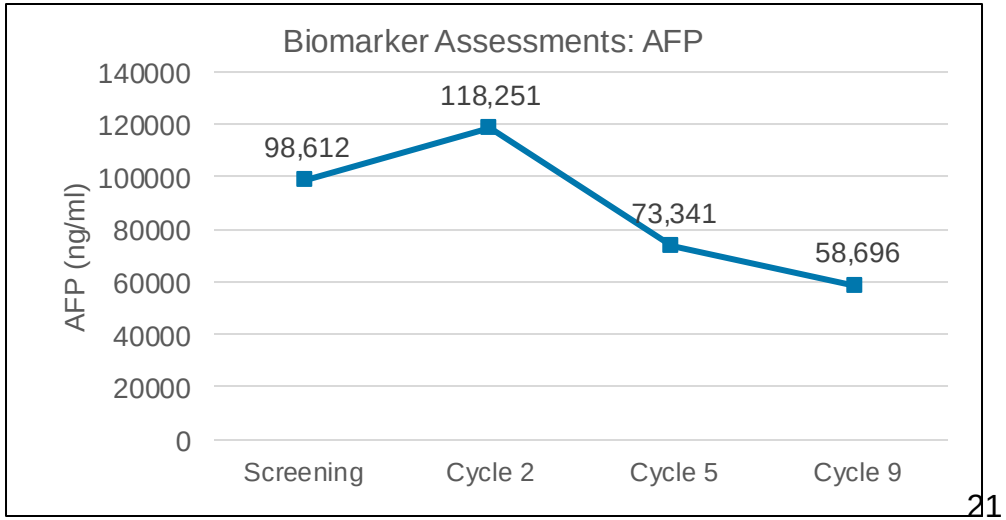
- **67 yo male with hepatocellular carcinoma**
  - Diagnosed 2017
  - RAD51C; ATM; TP53; CTNNB1

- **Prior Treatment/Surgery:**
  - 2017 and 2018: Chemoembolization x 2, Radiofrequency Ablation.
  - Jun-Aug 2019 : Sorafenib, stopped due to Toxicity
  - Sep 2019 to Dec 2019: **Nivolumab**, best response progression
  - Dec 2019 to 2020: Lenvima, best response stable disease, stopped due to progression
  - Aug 2020 to Jan 2022: **Pembrolizumab**, best response stable disease, stopped due to progression
  - Feb 2022 to Jan 2024: Cabozantinib, best response stable disease, stopped due to progression
  - **Mar 2024 to Jun 24: OR502 (anti-LILRB mAB) + Cemiplimab**, best response stable disease, stopped due to progression

- **Cycle 1, Day 1:** 14Aug2024

- **Treatment ongoing**





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Data as of March 17, 2025

Solnerstotug Continues to be Well Tolerated as Monotherapy and in Combination with Cemiplimab

Phase 1 Dose Expansion

Dose Expansion Safety Profile Summary

	Monotherapy	Combination
	Solnerstotug 15 mg/kg n=10 (%)	Solnerstotug 3 or 15 mg/kg* + cemi N=50* (%)
At least 1 TEAE	9 (90)	37 (74)
At least 1 SAE	3 (30)	12 (24)
≥Grade 3 TEAE	2 (20)	14 (28)
At least 1 TEAE leading to discontinuation	0 (0)	2 (5)**
AESI	1 (10)	3 (6)
Immune-mediated	0 (0)	2 (4)
CRS	**1 (10)**	**3 (6)**

- Majority of adverse events were Grade 1 or 2
- All CRS events were Grade 1 (4 of 60 patients; all at 15 mg/kg)

*16 patients received 3 mg/kg and 34 patients received 15 mg/kg solnerstotug in combination with cemiplimab
**1 patient had Grade 3 acute kidney injury, not related to solnerstotug or cemi; the primary reason for discontinuation is clinical progression. 1 patient had Grade 3 ischemic stroke, not related to solnerstotug or cemi; the primary reason for discontinuation is progressive disease.

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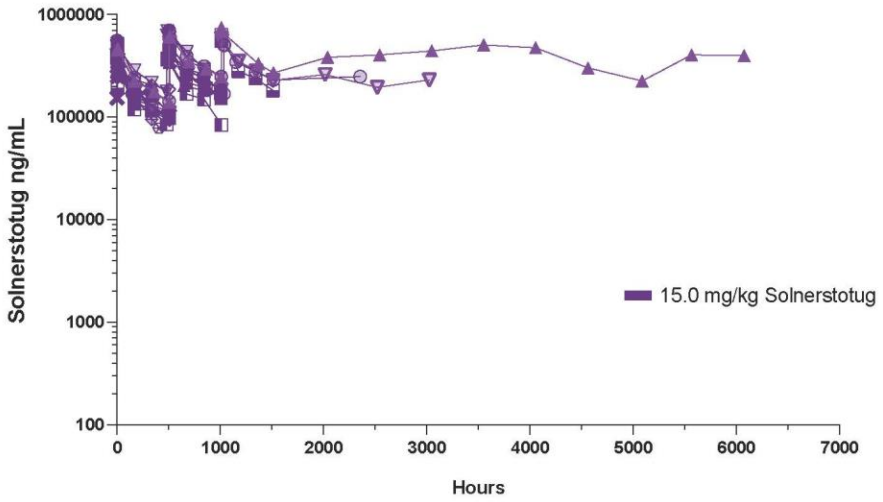
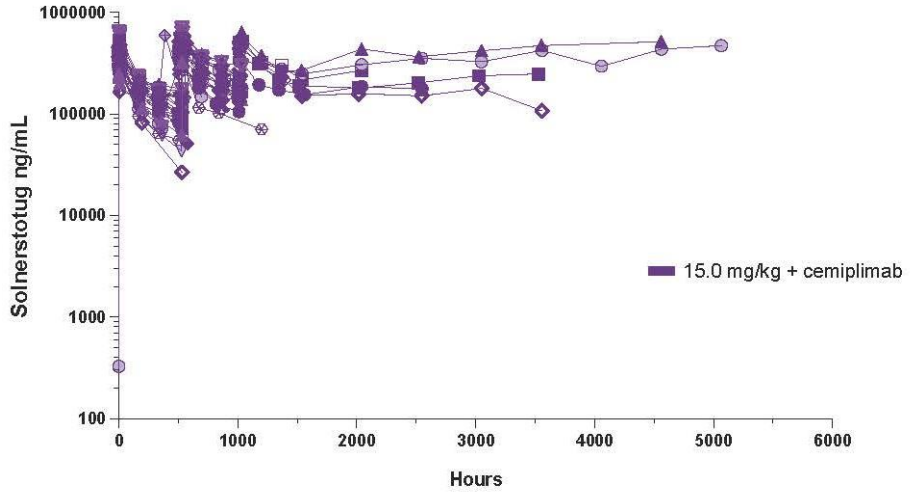
Data as of March 17, 2025

Pharmacokinetic Data Support Once Every Three Week (or Greater) Dosing

Solnerstotug Monotherapy (15 mg/kg)
Includes Dose Escalation + Expansion

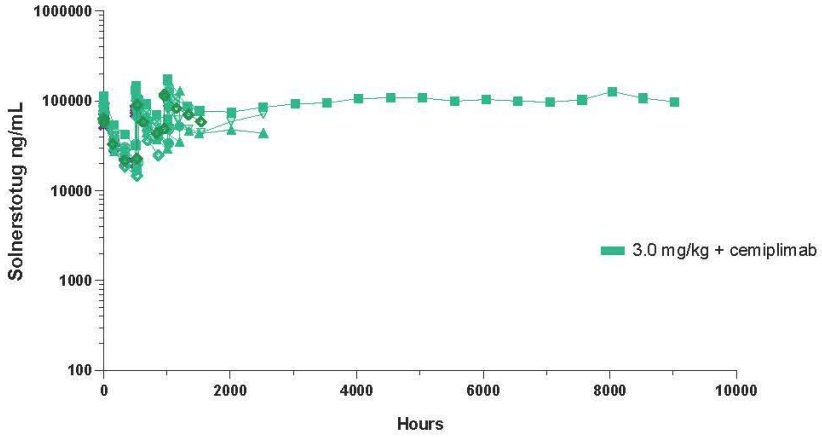


Solnerstotug (15 mg/kg) + cemiplimab
Includes Dose Escalation + Expansion



- Detectable in blood for thousands of hours (e.g., weeks)
- Supports Q3W dosing in humans
- No apparent effect on PK with combination
- Some increase with repeat dosing, but no notable accumulation

Solnerstotug (3 mg/kg) + cemiplimab
Includes Dose Escalation + Expansion



Data as of December 26, 2024

Approved Checkpoint Inhibitor Treatment Options

Studies Performed in PD-(L)1 Resistant Patients

Checkpoint Target(s)	Therapy	ORR	DCR	Duration of Response (Months, Median)	Tolerability	Stage
Benchmark: Anti-PD-1 Rechallenge	Various	≤5% [4]	Not reported	Not reported	Comparable to initial anti-PD-1 therapy	Standard of care (No formal approval for anti-PD-1 resistant tumors)
Anti-VISTA + Anti-PD-1	Solnerstotug (SNSE) + Cemiplimab (REGN)	14% (Ongoing, 3x higher than historical PD-1)	62%	Too soon to assess; Durable responses still evolving	Well-tolerated	Phase 1/2 ongoing
Anti-CTLA-4 + Anti-PD-1	Nivolumab + Ipilimumab (BMS)	28%[1]	Not reported	40.9[1]	High toxicity[3] (~40% discontinue early)	Approved for 1st line therapy in several tumor types (melanoma, NSCLC, RCC)*
Anti-LAG-3 + Anti-PD-1	Relatlimab + Nivolumab (BMS)	~12%[2] (9–12% across cohorts)	~40%[2]	12.8[2]	Well-tolerated	Approved for 1st line unresectable or metastatic melanoma*

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1 VanderWalde, A. et al., Nat Med. 2023 (SWOG S1616)
2 Ascierto et al, J Clin Onc, 2023 (RELATIVITY-020)
3 Albrecht et al, Current Oncology Reports 2023
4 Kluger H, et al. J Immunother Cancer 2023

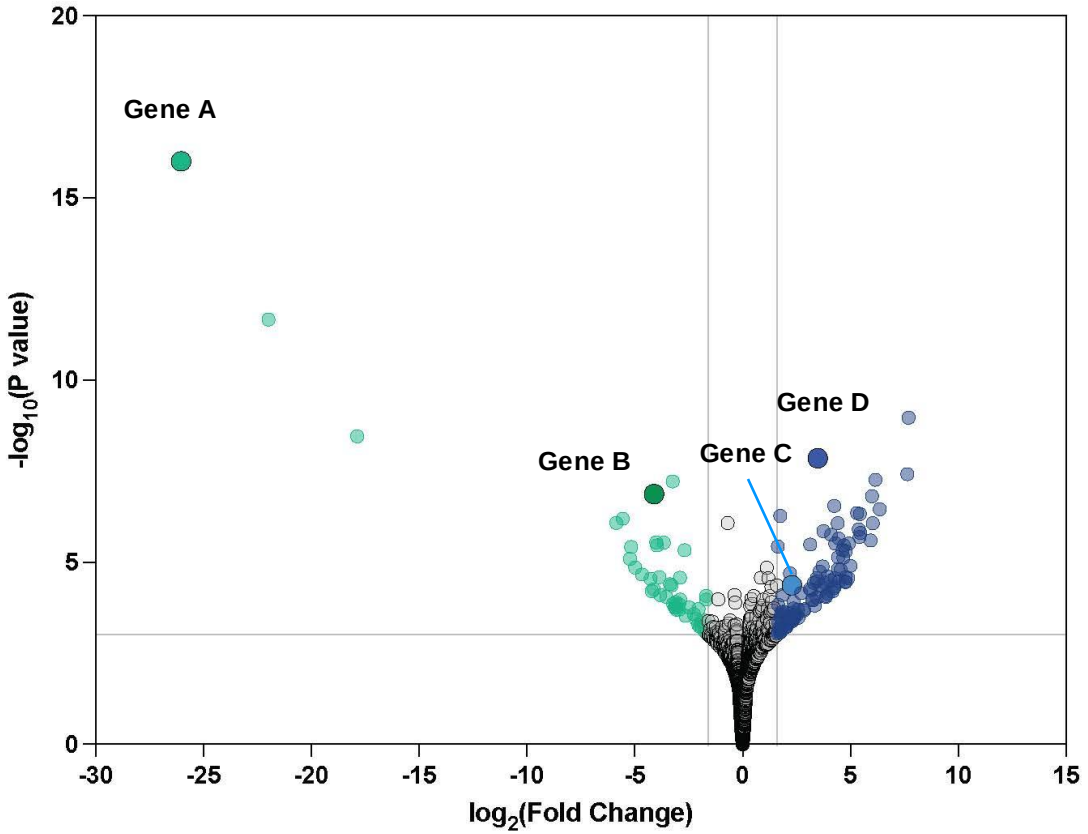
*No formal approval for PD-(L)1 resistant patients

Exploratory Gene Expression Analysis Identifies Potential Biomarkers of Clinical Benefit

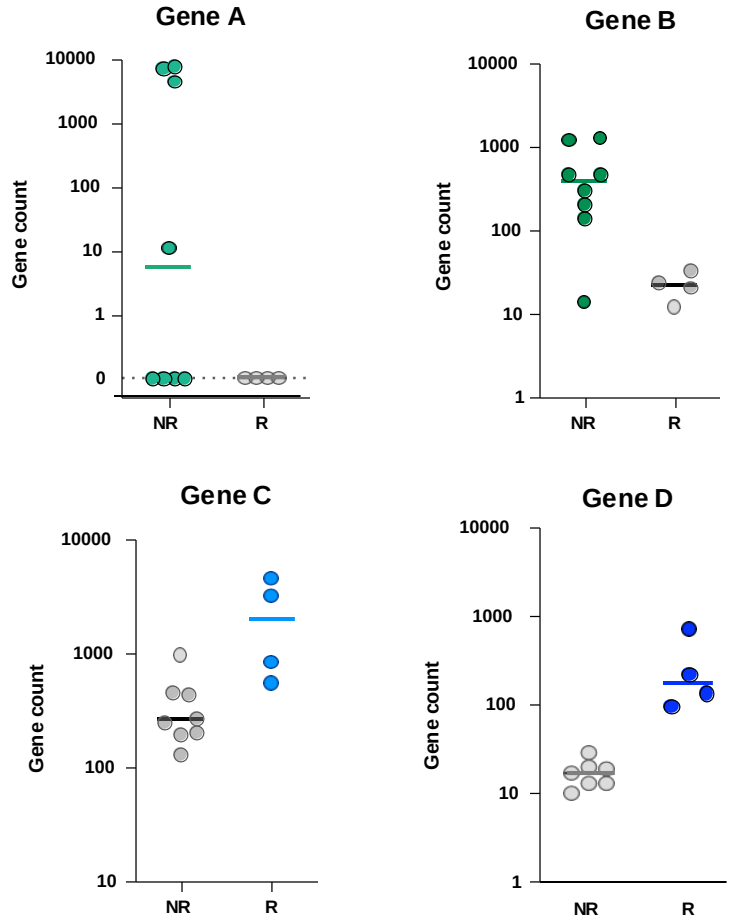
Compares baseline tumor RNA expression between a cohort of patients with observed clinical benefit (“response”) and a subset of non-responders with similar tumor types and demographics

- Preliminary analysis that is subject to change with additional patient data

Baseline Gene Expression

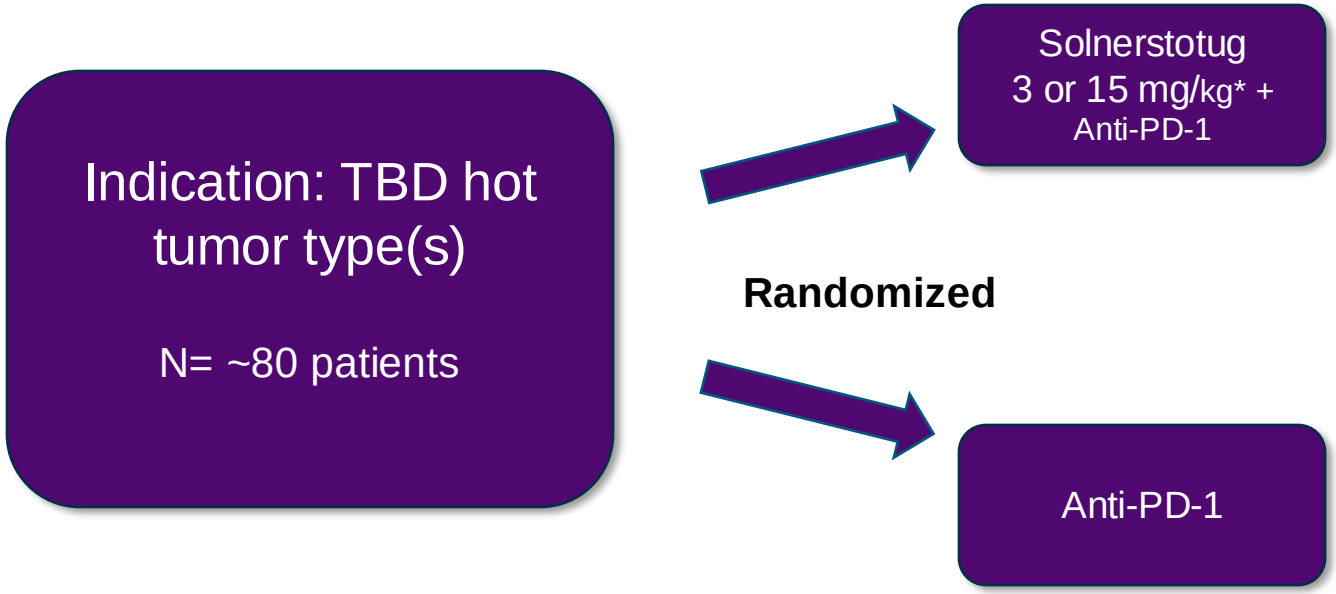


Patient Detail by Gene



NR – “no response”; R – “response” based on potential clinical benefit of drug/combo as defined by CR, PR, or tumor shrinkage
Responder group included 1 CR, 1 PR, and 4 SD patients with tumor shrinkage ranging from -12.3% to -27%

Phase 2 Strategy



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

Patient Population:

- Current considerations:
  - NSCLC
  - H&N
  - Melanoma
  - RCC
- May consider a second indication (e.g., Merkel Cell carcinoma) in a single arm study to pursue accelerated path to approval

* Phase 2 dose dependent on FDA feedback and additional data from dose expansion; possibility that 2 dose levels will be required in Phase 2

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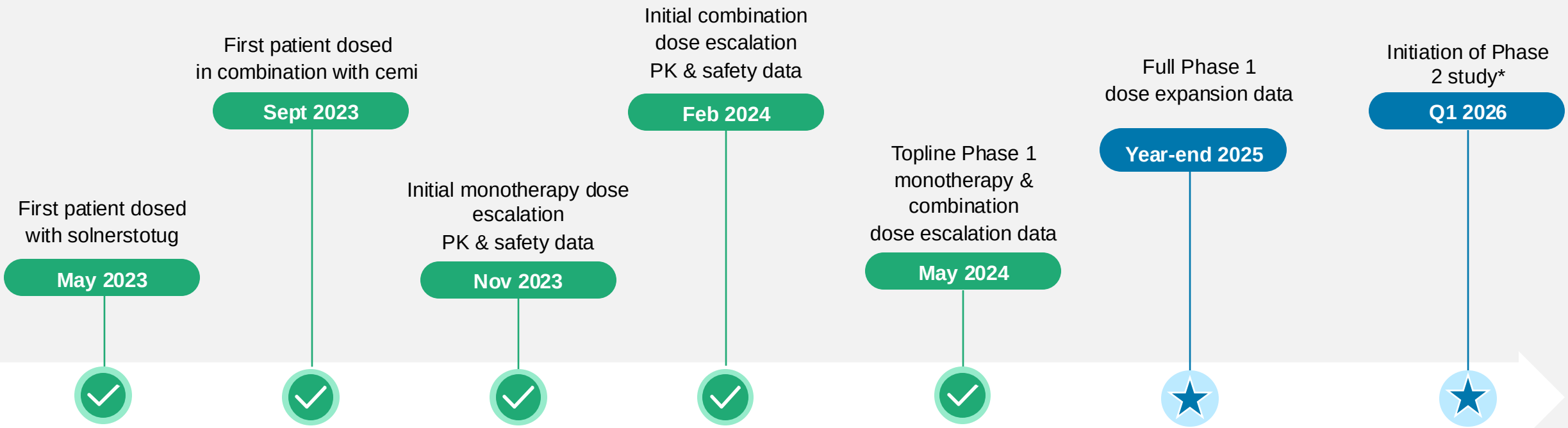
Completed and Anticipated Solnerstotug Clinical Milestones



*Subject to execution of clinical and financial objectives

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