Training the Immune System to Fight Cancer

The *ImmunoPhage*™ platform induces robust, focused immune responses

May 12, 2021

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FINANCIAL SUMMARY

- **February 2021 IPO:**
  - ~ $152M in gross proceeds
  - NASDAQ Ticker “SNSE”
  - Bookrunners: Citigroup, Piper Sandler, Berenberg
  - Manager: Oppenheimer

- **Cash position as of March 31, 2021**
  - $169.4M - runway at least into 2H 2023

- **Use of proceeds:**
  - Clinical development of SNS-301
  - Preclinical and clinical development of SNS-401
  - Preclinical and clinical development of SNS-VISTA
  - Development of ImmunoPhage™ platform & other pipeline programs
  - Working capital and other general corporate purposes

PROVEN TEAM WITH DEEP EXPERIENCE

MANAGEMENT

John Celebi, MBA
President and CEO

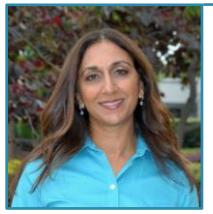
- Over 23 years of experience in biotechnology sector
- Former Chief Operating Officer of X4 Pharmaceuticals and Chief Business Officer of Igenica Biotherapeutics

Marie-Louise Fjaellskog, MD, PhD
Chief Medical Officer

- Over 25 years of experience in clinical oncology, translational research, and drug development
- Previously served as VP of Clinical Development at Merus where she lead the development of several bispecific antibody therapeutics in oncology

Robert Pierce, MD
Chief Scientific Officer

- Over 20 years of experience in immuno-oncology
- While at Merck, he led a team focused on the development of tissue-based biomarkers for its anti-PD- 1 therapeutic antibody, KEYTRUDA
- Medical lead of the clinical trials of KEYTRUDA in MCC and CTCL



Anu Hoey, MS, MBA
Chief Business Officer

Michael Boychyn, PhD
SVP, CMC

Erin Colgan
SVP, Finance and Administration

Pauline Callinan, PhD
VP, Business Operations and Strategy

Jean Campbell, PhD
VP, Biologics Discovery

Alice Drumheller
VP, Clinical Operations

Lora Pike
VP, Investor Relations and Communications

Edward van der Horst, PhD
VP, Preclinical Development

OUR IMMUNOPHAGE PLATFORM SOLVES THE TOUGHEST PROBLEMS IN IMMUNO-ONCOLOGY

- Proprietary ImmunoPhage platform programs and mAbs and nanobody programs
- Pipeline of immunotherapies for cancer with potential to expand into additional disease areas
- Ongoing Phase 1/2 clinical trial for SNS-301 in head and neck cancer that has shown promising anti-tumor activity and has been well-tolerated
- Collaborations with multiple academic institutions
- In-house GMP manufacturing capabilities

ROBUST PIPELINE UTILIZING PIONEERING IMMUNOPHAGE PLATFORM

Program	Approach/Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
ONCOLOGY								
SNS-301	 Targeting ASPH; HPV-specific E6/E7	1st Line+ Head & Neck Cancer	**In combination with pembrolizumab**					**YE 2021:** • Addition of HPV-specific E6/E7 ImmunoPhage combination • Phase 1/2 data readout from large subset of patients
		Head & Neck Cancer – Neoadjuvant	**Evaluating combination strategies**					**YE 2021:** Phase 2 trial initiation
SNS-401	 Cocktail with MCPyV	Merkel Cell Carcinoma						**1H 2022:** IND filing with FDA
SNS-VISTA	 Targeting VISTA	Solid Tumors						**YE 2021:** Initiate IND-enabling studies
Antibodies and Nanobodies		**Discovery and validation of multiple antibodies and nanobodies utilizing ImmunoPhage platform**						

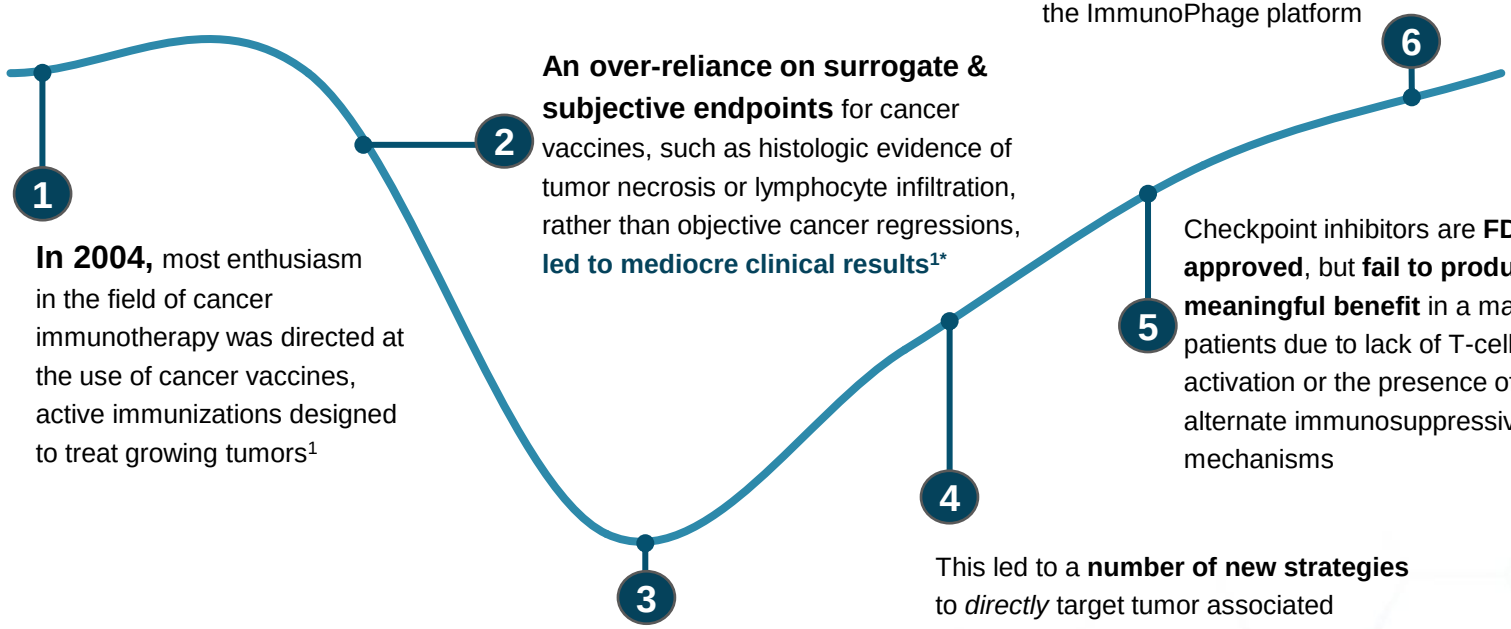
 ImmunoPhage  Antibody

ImmunoPhage Platform

IMMUNO-ONCOLOGY VACCINE HISTORY

The emergence of checkpoint inhibitors has rekindled interest in mechanisms that activate T-cells and block alternate immunosuppressive mechanisms

Immuno-oncology vaccine history



In 2004, most enthusiasm in the field of cancer immunotherapy was directed at the use of cancer vaccines, active immunizations designed to treat growing tumors[1]

An over-reliance on surrogate & subjective endpoints for cancer vaccines, such as histologic evidence of tumor necrosis or lymphocyte infiltration, rather than objective cancer regressions, **led to mediocre clinical results[1*]**

The conclusion by many is that cancer vaccines generally fail to immunologically destroy established tumors that lead to objective responses**

This led to a **number of new strategies** to *directly* target tumor associated antigens, including the advancement of TCR and CAR-T therapies, and checkpoint inhibitors

Checkpoint inhibitors are **FDA approved**, but **fail to produce meaningful benefit** in a majority of patients due to lack of T-cell activation or the presence of alternate immunosuppressive mechanisms

In 2019, Sensei Bio launches the ImmunoPhage platform

*At the NCI, among 440 patients treated with cancer vaccines, the objective response rate was 2.6%[1]

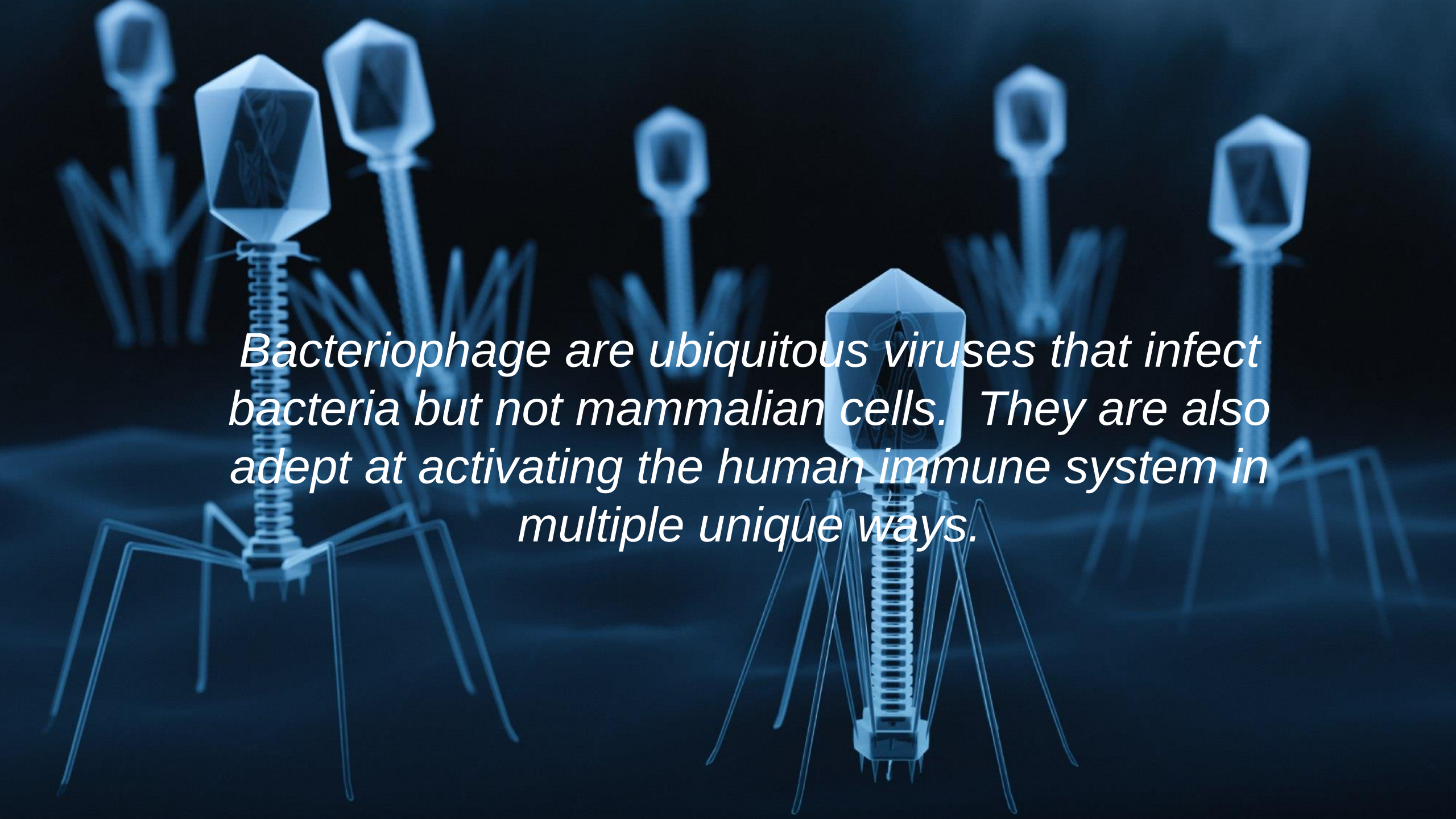
** Due to insufficient numbers of high avidity T-cells with recognition of tumor antigens, trafficking and infiltration of T-cells to the tumor and stroma, and activation of T-cells at the site of the tumor.

1 Rosenberg SA, Nature Medicine, 2004; 2 McKinsey report, “The next wave of innovation in oncology”

What if we could **engineer** a virus to **target** the key mechanisms of **checkpoint resistance?**

What if we could do this in a **personalized** way**,** with an **off-the-shelf** product concept?

At ***Sensei Biotherapeutics***, we have built the ***ImmunoPhage*** platform dedicated to **develop** therapeutics that induce a **robust, focused** and **coordinated immune response** to treat cancer



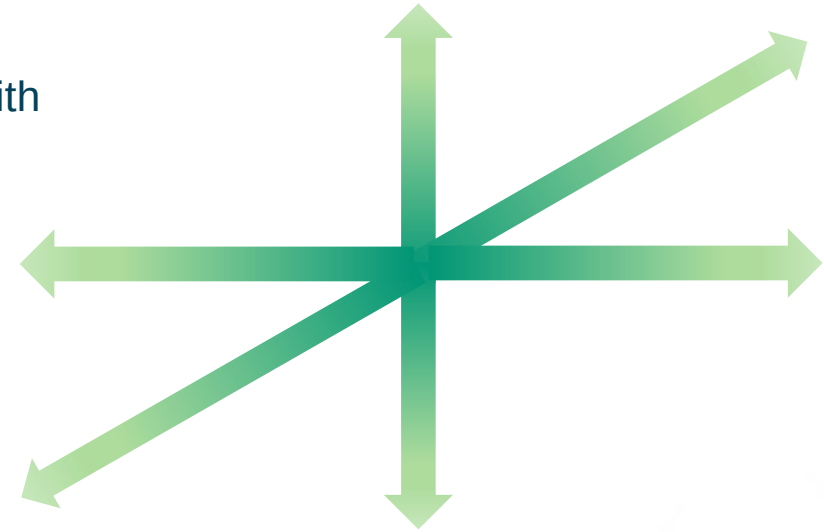
Bacteriophage are ubiquitous viruses that infect bacteria but not mammalian cells. They are also adept at activating the human immune system in multiple unique ways.

THREE AXES OF INNOVATION TO FIGHT CANCER

Cancer is a complex problem requiring a multi-pronged solution. Our *ImmunoPhage*s can mount a multi-modal attack on cancer, combining the benefits of a traditional vaccine with localized gene therapy.

Targeted therapeutic vaccine

- MHC-mediated immunity
- Bacteriophage have natural tropism for APCs
- Can be further targeted to APCs with non-antigen capsid modifications



Phortress™ library

- Personalized - yet off the shelf - medicines
- Pre-manufactured cost effectively - then combined based on genetic profile

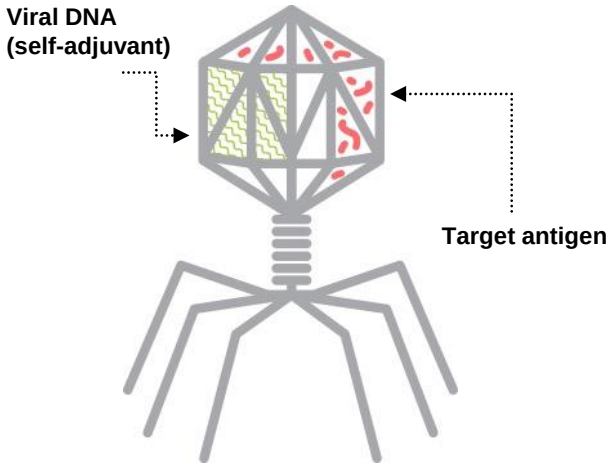
Gene therapy vehicle

- Phage containing self-replicating RNA
- Used to deliver payloads consisting of immunomodulatory proteins or nanobodies

GENERATING STRONG ANTIBODY AND T-CELL RESPONSES

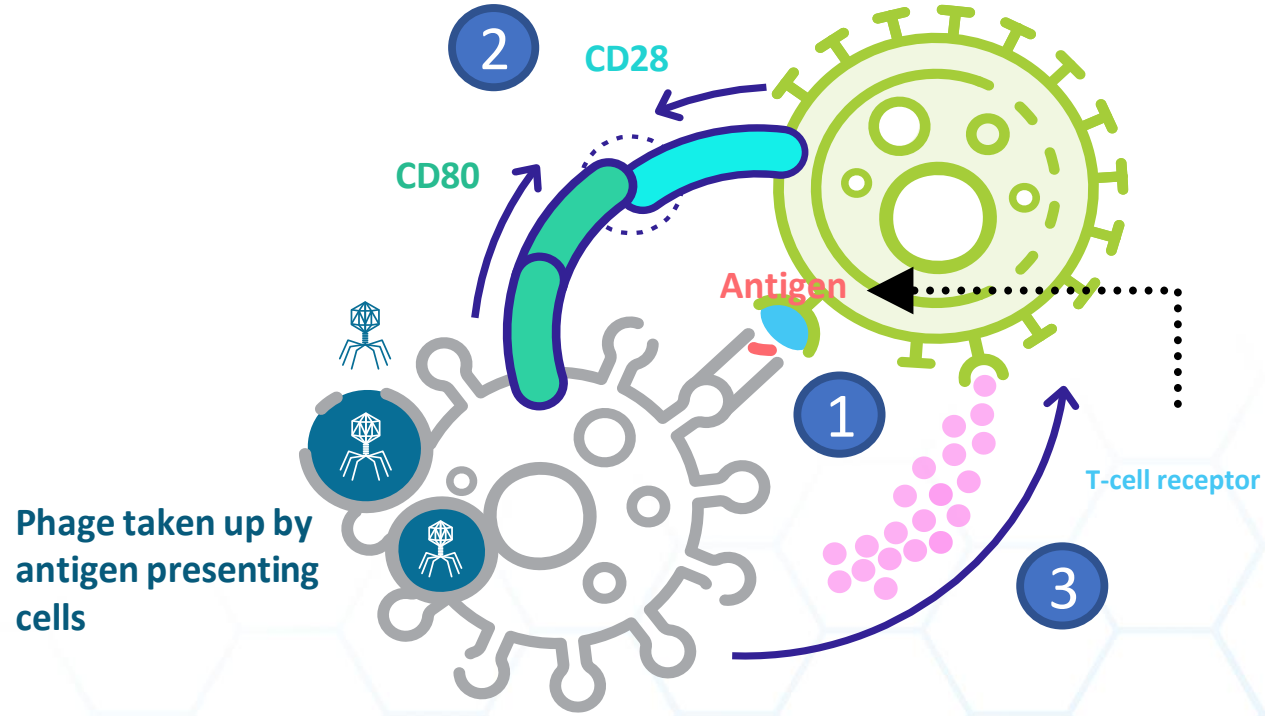
Our *ImmunoPhages* contain an **engineered display of target antigens on the surface of a bacteriophage.** We use non-infectious lambda bacteriophage viruses to mimic a pathogenic virus, driving strong T cell and B cell mediated antibody responses**.**

1 **Bacteriophage virus is engineered and manufactured with both antigen and immune stimulatory viral DNA**



The *ImmunoPhage* bacteriophage is an icosahedron with a tail. This configuration can be viewed as an activating signal to the immune system.

2 **ImmunoPhages are taken-up by APCs and deliver the three critical signals required to drive activation of T cells. 1) Activation of CD8 T cells through cross presentation 2) Positive Co-stimulation of T cells 3) Generation of a Th1-biased immune response and cytotoxic T-lymphocytes**



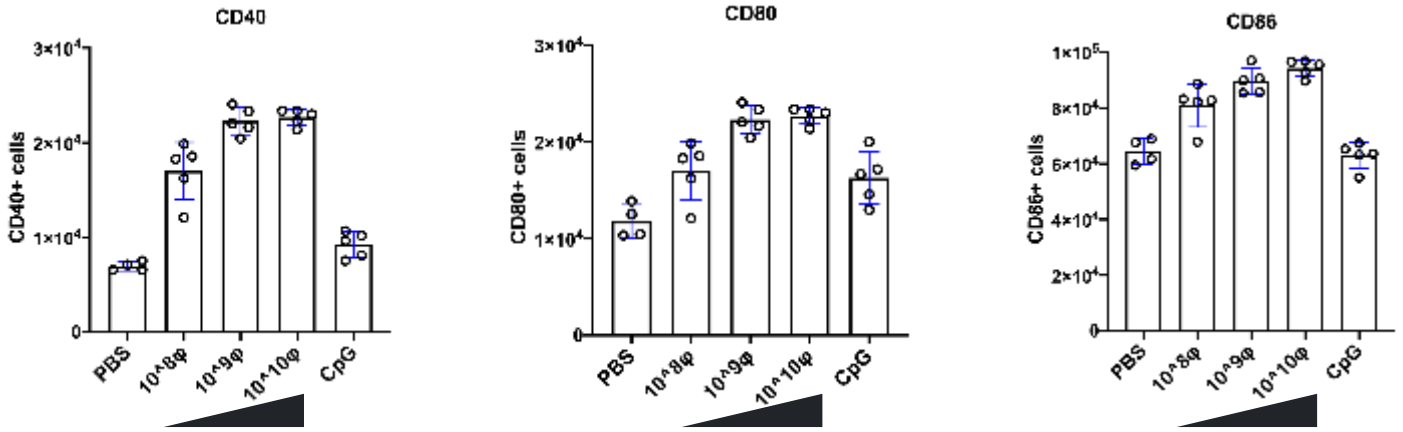
MECHANISM OF ACTION: ACTIVATION AND MATURATION OF DENDRITIC CELLS

Critical signals of dendritic cell activation show **dose-dependent increases** when dendritic cells are exposed to increasing amounts of *ImmunoPhages*

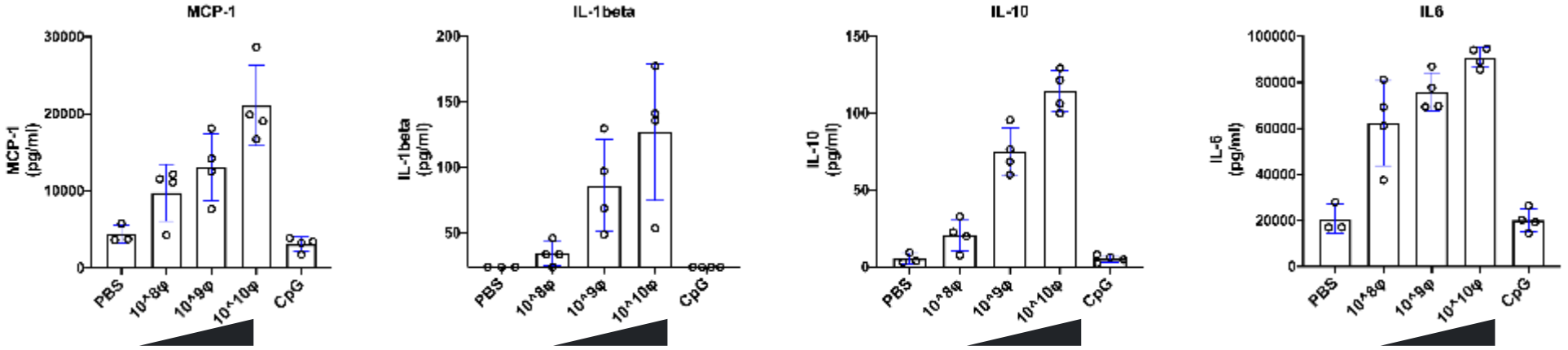
Bacteriophage-expressed antigens are then processed and presented efficiently by MHC class I and class 2 pathways, leading to **robust CD4 and CD8 T cell responses**

Dose-response of engineered lambda phage on human skin-derived DC cultures

Signal 2
Dendritic cell co-stimulatory molecules



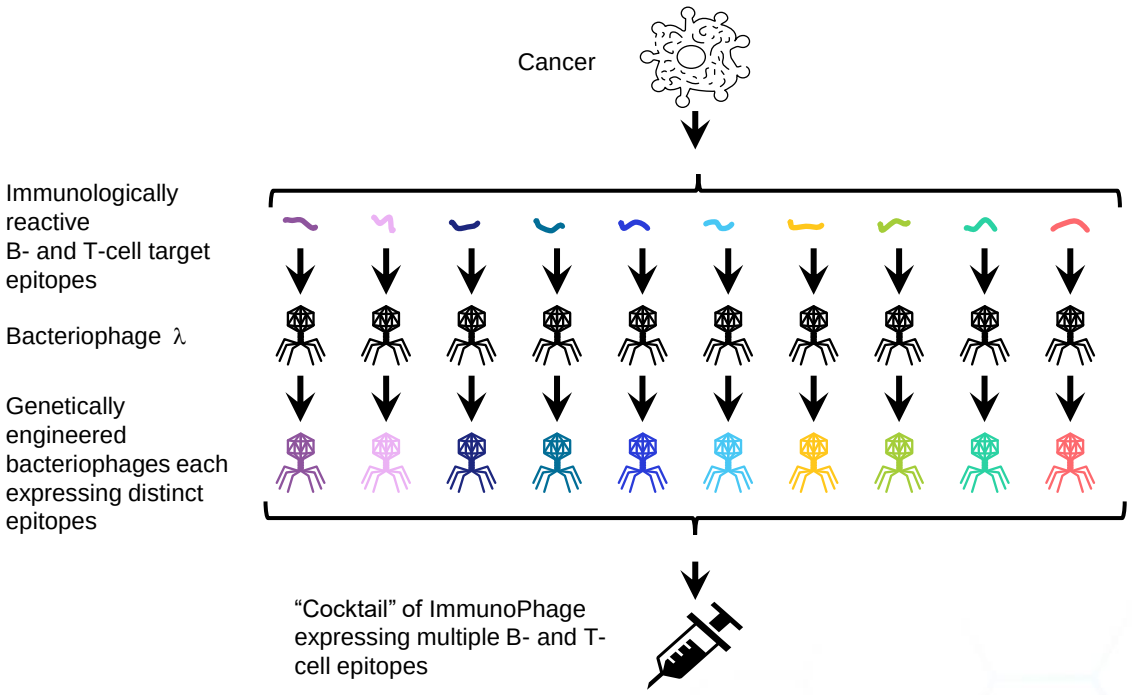
Signal 3
Cytokine secretion



COMBINATIONS CAN BE CUSTOMIZED FOR PERSONALIZED IMMUNOTHERAPY

Our proprietary library of *ImmunoPhage* – *Phortress* – harnesses the intrinsic immunostimulatory characteristics and capabilities of bacteriophage to create a personalized, coordinated, and nuanced multi-modal immune response.

Phortress is our proprietary library of personalized vaccine cocktails with off-the-shelf *ImmunoPhage* "ingredients"



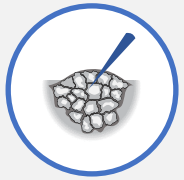
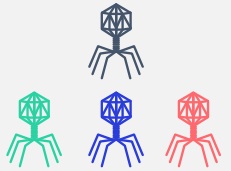
- These "cocktails" are defined by the disease or patient genetics
- Combinations are customized to cover multiple epitopes, protein domains or targets
- Each *ImmunoPhage* is pre-manufactured to target a discrete antigen

PERSONALIZED IMMUNOTHERAPY APPROACH

High speed and low cost-of-goods of ImmunoPhage allows a broader array of antigens

Personalized yet Off-the Shelf TAA Therapy

Off-the-Shelf + Patient-specific Neoantigen Therapy

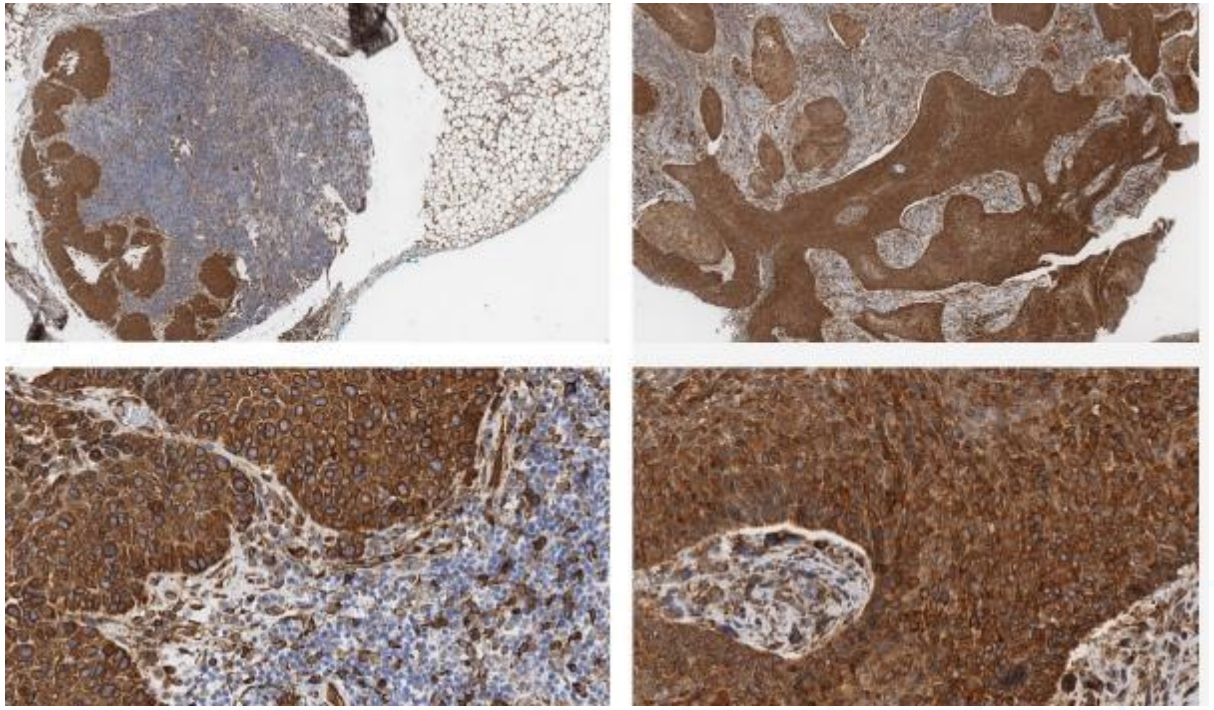
1	2	3	4	5	6
Routine Biopsy	**Tumor Sequencing**	**Personalized yet Off-the-shelf ImmunoPhage Cocktail**	**Neoantigen Prediction**	**Neoantigen ImmunoPhage Manufacturing**	**ImmunoPhage Injection Including Neoantigens**
					
Clinical biopsy of tumor as input material	Tumor DNA Tumor RNA Normal DNA	Assemble a personalized cocktail from off-the-shelf TAA ImmunoPhage for administration	Identify additional tumor specific neoantigens	Engineer novel ImmunoPhages expressing distinct tumor specific epitopes	Deliver neoantigen ImmunoPhage cocktail for administration and add neoantigen phages to bank for future use

Pipeline Programs

SNS-301 ONGOING PHASE 1/2 TRIAL IN HEAD AND NECK CANCER

OBJECTIVES
Evaluate safety, tolerability, and anti-tumor activity; immune responses and tumor/immune biomarkers
PATIENT POPULATION (n=60)
• ~30 difficult to treat patients without observed tumor reductions on PD-1 blockade • ~30 patients with no prior PD-1 blockade
DATA
Phase 1/2 study data • Well tolerated & encouraging clinical activity observed • Tumor samples collected from ~30 screened patients showed strong ASPH expression
STATUS
• New data accepted for poster presentation at ASCO 2021 • Anticipate substantial data readout by end of 2021

Patients enrolled in the SNS-301 Phase 1/2 trial strongly express the tumor-associated antigen ASPH



ASPH = TUMOR-ASSOCIATED ANTIGEN

SNS-301 CLINICAL DEVELOPMENT PATH

Phase 1/2 data readout expected by YE 2021

PHASE 1/2
COMBINATION SAFETY AND EFFICACY

TRIAL POPULATION FOR SNS-301/ PEMBROLIZUMAB COMBO

INCLUSION CRITERIA

1. Locally advanced / metastatic SCCHN
2. PD-1 blockade > 12 weeks
3. SD or unconfirmed PD

STAGE 1

Cohort A (n=15)

★ ***If Cohort A achieves ≥ 1 partial or complete response, add additional patients***

STAGE 2

ADD Additional n=15

ADD Cohort B
PD-1 blockade naïve patients (1st Line)

ADD Cohort C
E6/E7 HPV+ cocktail approach

RANDOMIZED PHASE 2/3
COMBINATION THERAPY VS. PEMBROLIZUMAB

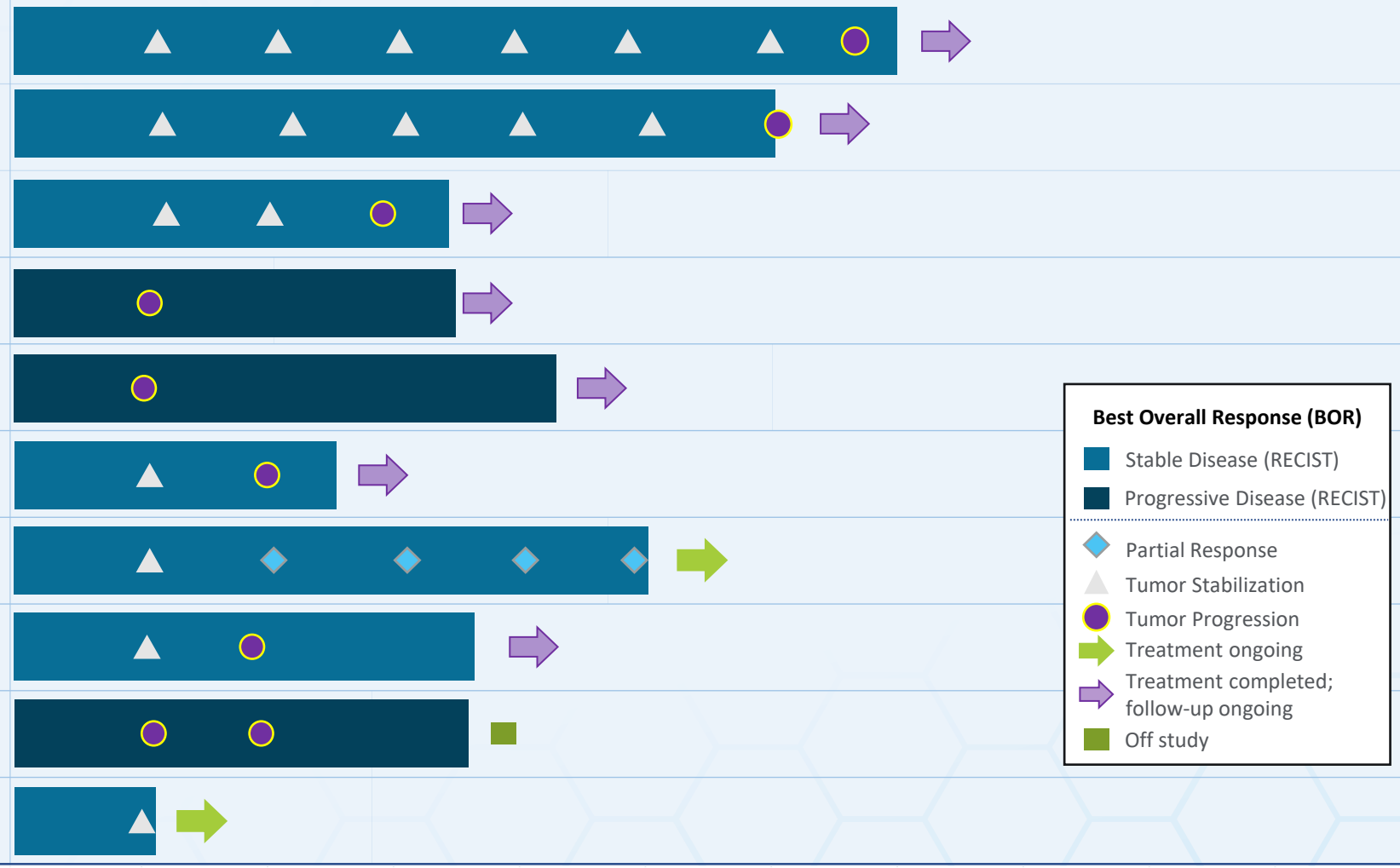
PATIENTS RANDOMIZED TO

A — **SNS-301/ pembrolizumab combo**

B — **Pembrolizumab monotherapy**

RESULTS FROM PHASE 1/2 TRIAL IN HEAD AND NECK CANCER (AS OF DECEMBER 10, 2020)

PD-L1 Status	Status Pre-Trial*	BOR On Trial	Patient
–	SD	SD	A
+	SD	SD	B
Unknown	uPD	SD	C
+	uPD	PD	D
Unknown	uPD	PD	E
+	SD	SD	F
–	SD	PR	G
Unknown	SD	SD	H
Unknown	SD	PD	I
Unknown	uPD	SD	J



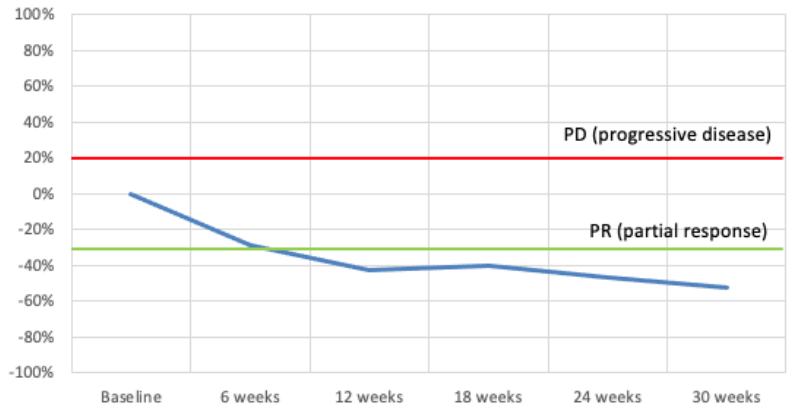
uPD = unconfirmed Progressive Disease
BOR = Best Overall Response
* Disease status at enrollment after ≥ 12 weeks of PD-1 blockade

PATIENT G DETAIL

The partial response is highly likely to be attributed to the addition of SNS-301 to pembrolizumab, given that the tumor was PD-L1 negative prior to study and no objective response was observed after >3 months of prior pembrolizumab.

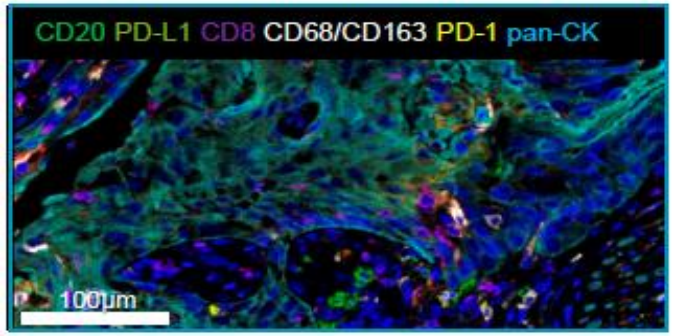
PATIENT
• 69-year-old woman / HPV and PD-L1 negative • Stage II T2N0M0 HNSCC (supraglottic larynx)
STATUS AT TRIAL ENTRY
• ECOG 1; PD-1 blockade (pembrolizumab) >3 months
PHASE 2 TRIAL OVERVIEW
• IMRT (2 - 54 Gy) 09JUL- 08AUG2018 • CARBO/PACLI/CETUX 08AUG-15AUG2019 (2 cycles) with best response PR • Pembrolizumab JAN2020 ongoing

Patient G Tumor Measurements

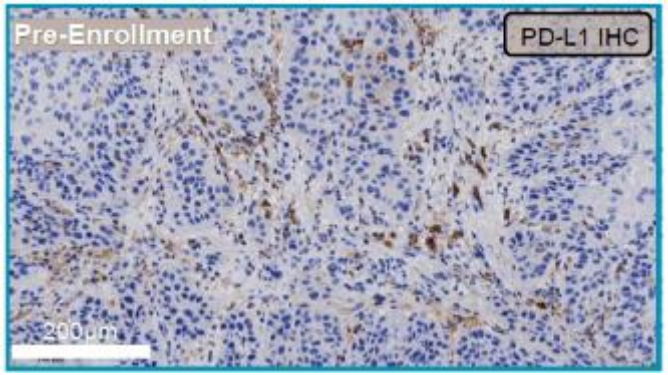


Pre-Treatment

Immune Markers by Multiplex IHC Pre-Treatment

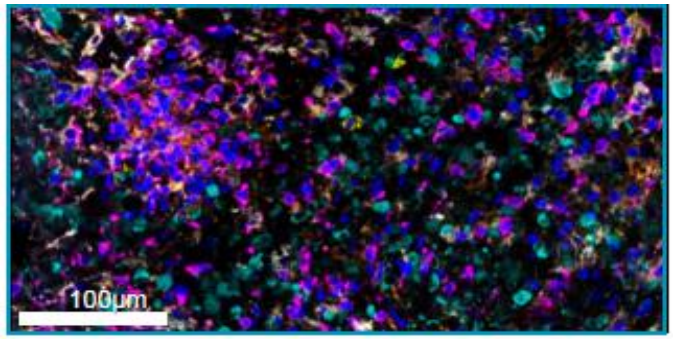


PD-L1 Negative Pre-Treatment

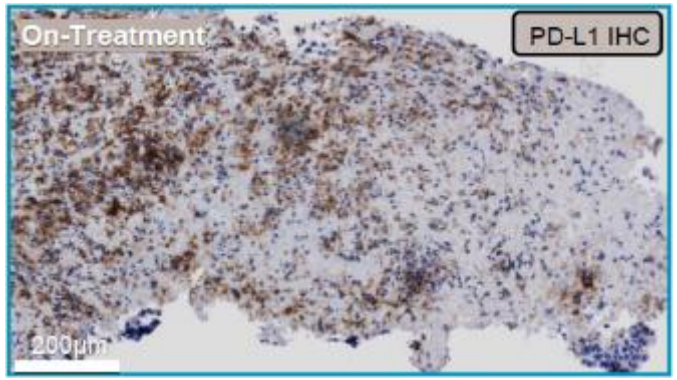


Post-Treatment

Increase in Immune Markers by Multiplex IHC



Strongly PD-L1 Positive Post-Treatment



SNS-301 HAS BEEN WELL TOLERATED IN COMBINATION WITH PEMBROLIZUMAB

	(n=11)					
Related Events	**Grade 1 n (%)**	**Grade 2 n (%)**	**Grade 3 n (%)**	**Grade 4 n (%)**	**Grade 5 n (%)**	**All Grades n (%)**
Decreased appetite	1(9.1)	1(9.1)	0	0	0	2 (18.2)
Fatigue	2(18.2)	0	0	0	0	2 (18.2)
Pruritus	2(18.2)	0	0	0	0	2 (18.2)
Back pain	0	1(9.1)	0	0	0	1 (9.1)
Constipation	0	1(9.1)	0	0	0	1 (9.1)
Dehydration	0	0	1(9.1)	0	0	1 (9.1)
Diarrhea	1(9.1)		0	0	0	1 (9.1)
Dizziness	0	1(9.1)	0	0	0	1 (9.1)
Electrocardiogram QT prolonged	0	0	1(9.1)	0	0	1 (9.1)
Erythema	1(9.1)	0	0	0	0	1 (9.1)
Headache	1(9.1)	0	0	0	0	1 (9.1)
Injection site pain	1(9.1)	0	0	0	0	1 (9.1)
Nausea	0	1(9.1)	0	0	0	1 (9.1)
Non-cardiac chest pain	0	1(9.1)	0	0	0	1 (9.1)
Urine output decreased	1(9.1)	0	0	0	0	1 (9.1)
Weight decreased	1(9.1)	0	0	0	0	1 (9.1)

Data as of December 10, 2020

- No DLTs and mostly Grade 1-2 unrelated adverse events.
- Two Grade 3 events were reported: hypertension (not related) and dehydration (related), reported as a serious adverse event (SAE). An additional SAE, Systemic Inflammatory Response Syndrome (G1), occurred during follow-up.

BUILDING THE FIRST CUSTOM MERKEL CELL POLYOMA VIRUS (MCPyV) IMMUNOPHAGE

An exclusive collaboration with the University of Washington to build the **first custom Merkel Cell Carcinoma (MCC) vaccine consisting of Merkel Cell Polyoma Virus epitopes** and other patient specific antigens

1 MCC is a rare, aggressive neuroendocrine skin cancer

- 33-46% disease-specific mortality
- 2,500 cases/yr with disease-specific mortality approaching 50%
- Vaccine combination therapy in adjuvant or neoadjuvant is attractive and feasible
  - PD-1/PD-L1 refractory MCC remains unmet medical need with aggressive clinical course
  - ~40% MCC patients recur <24 months following definitive local treatment

2 Integration of MCPyV is present in ~80% of U.S. cases

- In these cases, expression of a viral antigen (oncogenic T-antigen) **appears to be a strictly required tumor driver**
- Researchers at UW have mapped MCPyV epitopes and **determined CD8 T-cell, CD4 T-cell, and B-cell epitopes that are antigenic** in the context of MCPyV+ MCC tumors.

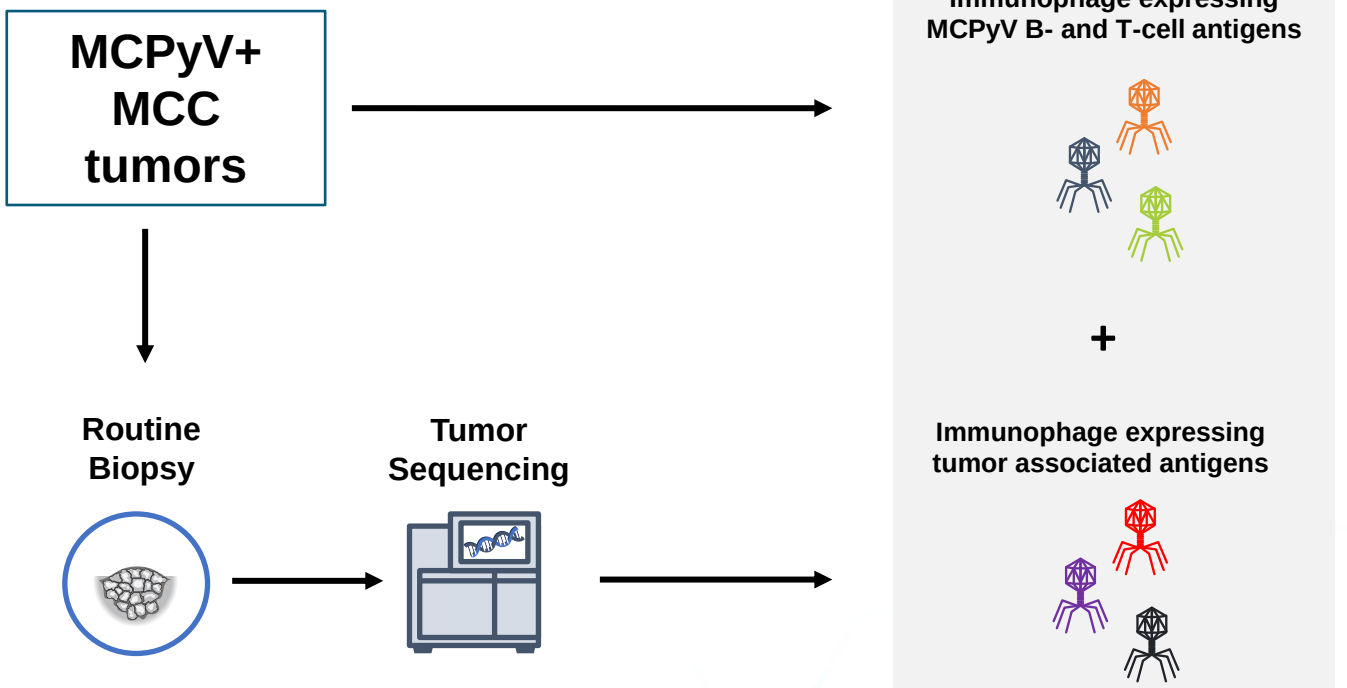
3 Discovery partnership with University of Washington

- UW will design MCPyV T-cell constructs and will determine the immunogenicity and mechanism of candidate *ImmunoPhages*
- Sensei will develop *ImmunoPhages* specifically targeting MCPyV T-cell constructs and other tumor associated antigens (TAAs) using a cocktail approach

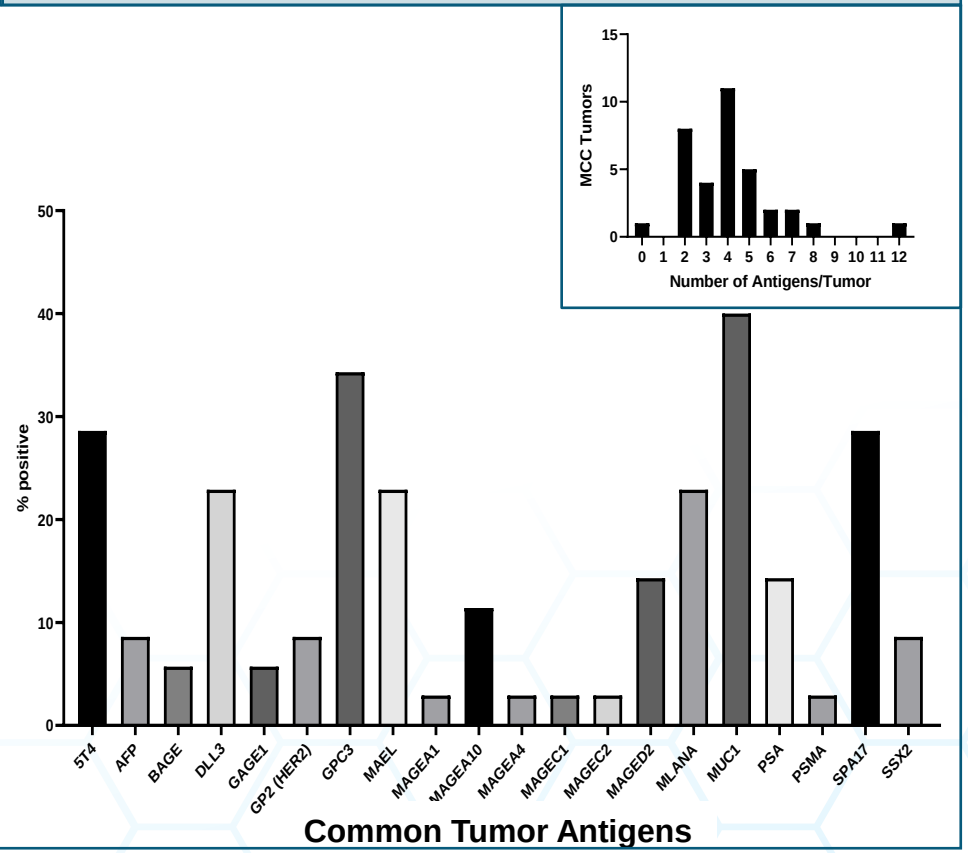
BUILDING THE FIRST CUSTOM MERKEL CELL POLYOMA VIRUS (MCPyV) IMMUNOPHAGE

SNS-401 has the potential to be the first **fully customized, yet off-the-shelf**, product.

1 Patients would receive a bespoke mixture of ImmunoPhage that included antigens from the MCPyV and a subset of TAA-expressing ImmunoPhage



2 Most MCC tumors contain five or fewer TAAs[1]



1 Based on internal data.

PARTNERSHIP WITH ADIMAB TO DEVELOP LEAD anti-VISTA ANTIBODY

A VISTA is recognized as an important immune checkpoint regulator

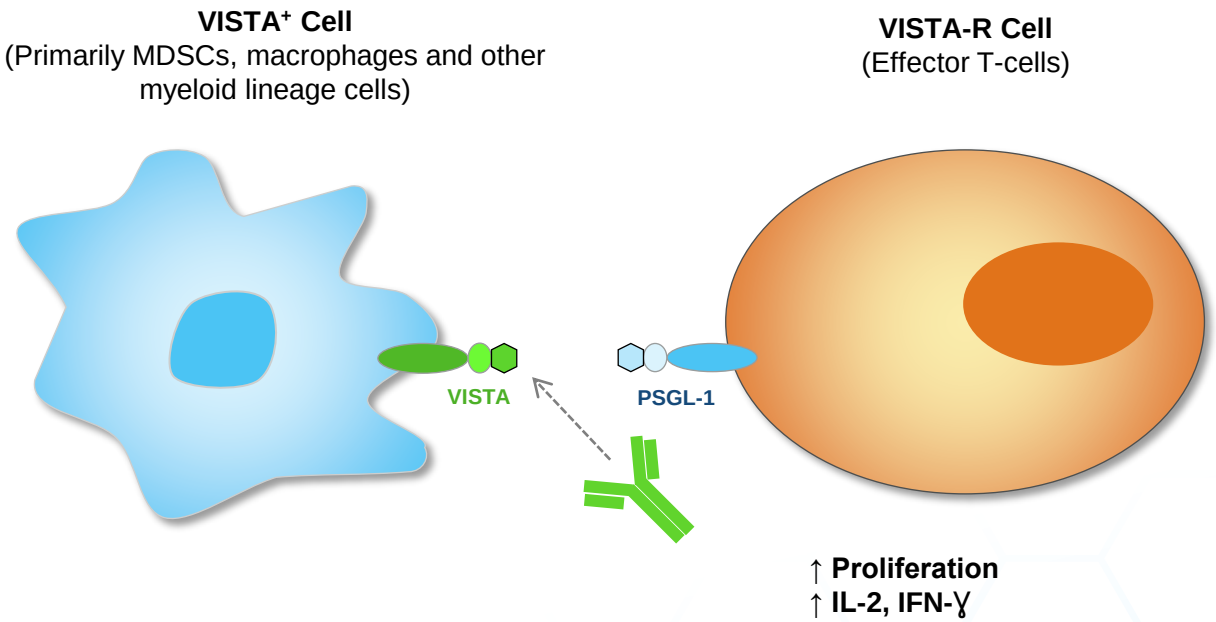
- Member of B7 family of proteins
- A negative regulator of T cell responses
- Blockade significantly enhances immune-mediated tumor rejection in vivo[1]
- Agonists exert protective effect in autoimmune models
- Plays a role in immune surveillance through phagocytic dead cell clearance[2]
- Mice lacking VISTA and PD-1 display enhanced ability to control tumor outgrowth[3]

[1] Le Mercier et al. VISTA Regulates the Development of Protective Antitumor Immunity. Cancer Res. 2014 Apr 1;74(7):1933-44.

[2] K. W. Yoon et al., Science 349, 1261669 (2015). DOI: 10.1126/science.1261669

[3] Liu J. et al. PNAS 2015

B Disruption of the extracellular VISTA-PSGL-1 interaction enhances T-cell proliferation and induces cytokine production

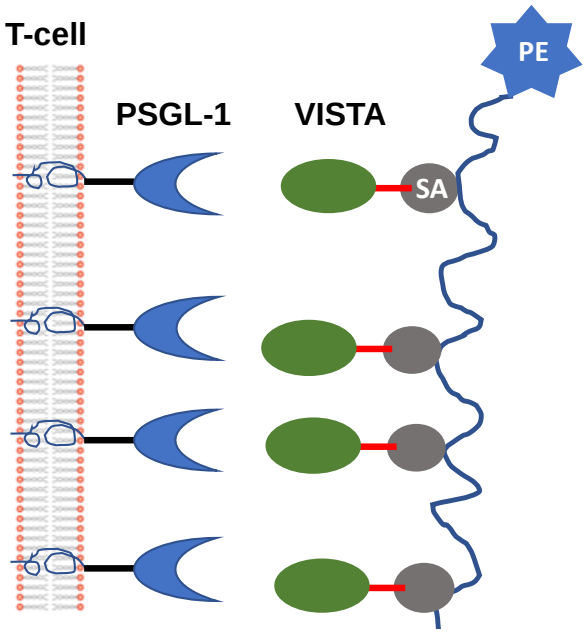


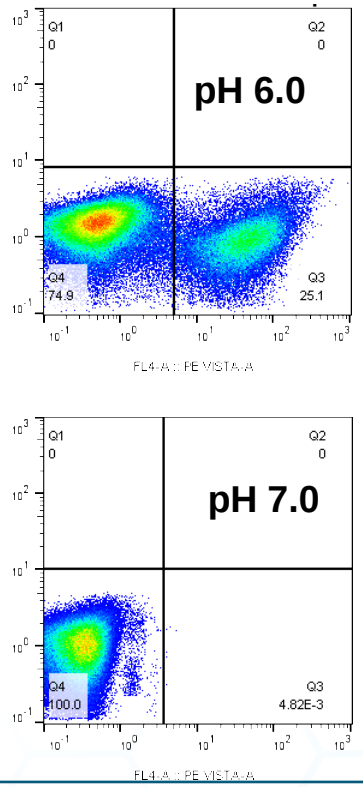
Knowledge of functional epitope between VISTA and PSGL-1 and potential patient population decreases development timeline and enhances early signal detection in Ph I trial

ASSESSMENT OF LEAD ANTIBODIES

A Assessment of anti-VISTA mAbs through interaction of VISTA and native PSGL-1 at varying pH

- Assay shows binding of VISTA protein to native PSGL-1 on activated CD4 T-cells

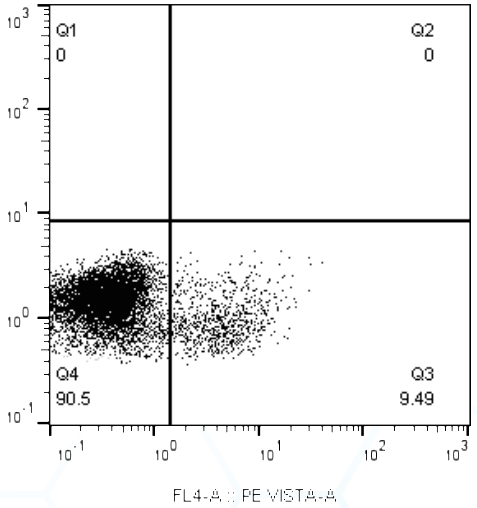




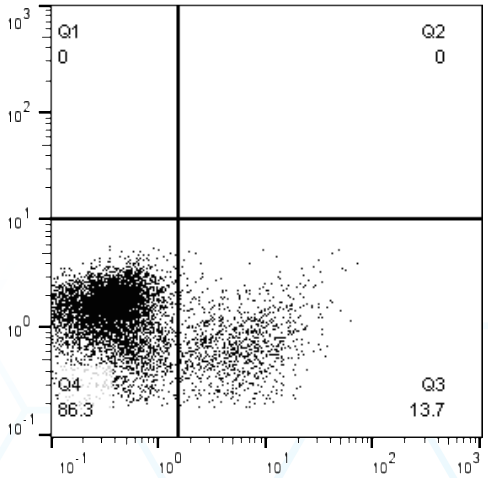
B Disruption of the VISTA-PSGL-1 interaction at pH 6 enhances T-cell proliferation and induces cytokine production

- Screened >80 mAb candidates
- Multiple candidates **inhibited VISTA binding** to cell surface of CD4+ T-cells at **pH 6.0,** including:

mAb 921



mAb 140



PH1/2 IN SCCHN TOPLINE READOUT BY YE 2021; NEW PROGRAMS ENTERING THE CLINIC IN 2022