TARGETING SIALYL THOMSEN NOUVEAU (STN) ANTIGEN WITH THE SGN-STNV ANTIBODY-DRUG CONJUGATE IS EFFECTIVE IN PRECLINICAL STUDIES

Alyssa Schwartz, Ph.D., Hector Rincon, Ph.D., Nanna Hansen, M.S., Robert Lawrence, Ph.D., Sarah Anderson, B.S., Nicole Stevens, B.S., Kerry Klussman, B.S., Angela Epp, B.S., Shyra Gardai, Ph.D., Bill Arthur, Ph.D.

Seagen Inc., Bothell WA

American Academy of Cancer Research (AACR) Annual Meeting; April 10-15 and May 17-21, 2021; Abstract No. 50

Important Note

- These are reformatted slides of an oral presentation presented at the American Academy of Cancer Research (AACR) 2021.
    - You may not alter content on any slide without having received approval from MeRLeN.
- This deck is intended for reactive scientific exchange.
- SGN-STNV is an investigational agent and its safety and efficacy have not been established. There is no guarantee it will receive regulatory approval.
- Information about potential future uses are intended only for discussion in response to an unsolicited question.
- The contents of this slide deck should not be used in any manner to directly or indirectly promote a product for unapproved uses.
- Seagen prohibits the promotion of unapproved uses and complies with all applicable laws, regulations, and company policies.

Disclosure Information

Alyssa Schwartz

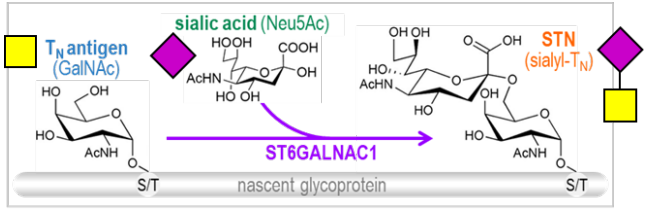
I have the following financial relationships to disclose:

Employee and Stockholder of Seagen

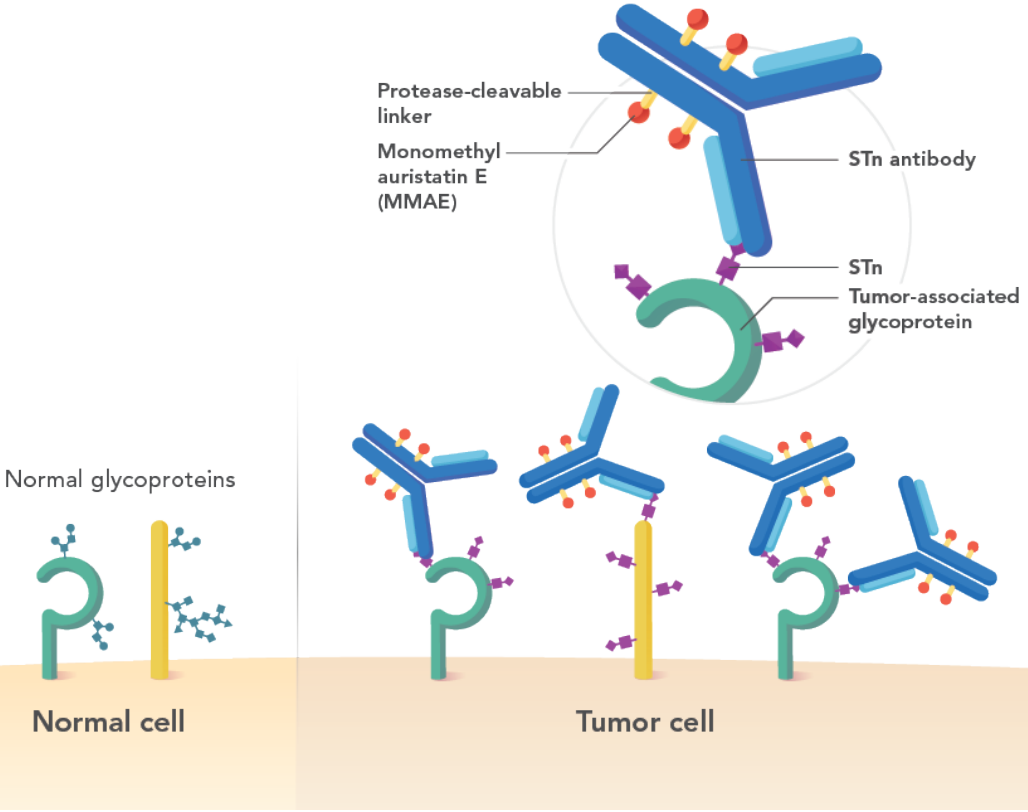
I will discuss the following investigational use in my presentation: SGN-STNV, under investigation in Ovarian, Gastric, NSCLC, and Endometrial carcinomas.

Sialyl-Thomsen nouveau (STn) Antigen is an O-linked Glycan Overexpressed in Cancer

Sialyl-Tn antigen (STn) is a short *O*-glycan containing a sialic acid residue α2,6-linked to GalNAcα-*O*-Ser/Thr



ST6GALNAC1 converts T_N to STn

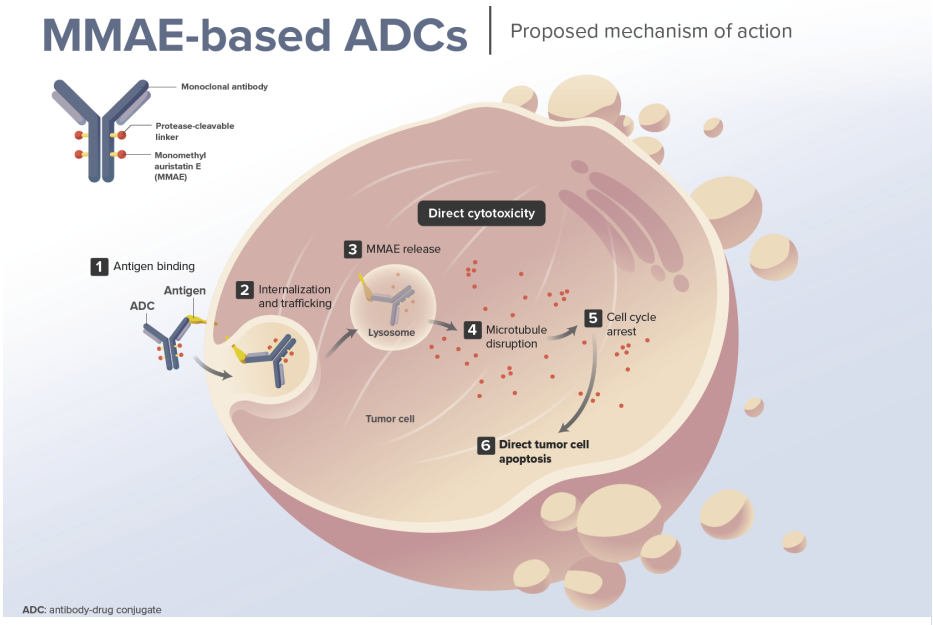


Schultz et al, Cancer and Metastasis Rev 2012
Pinho et al, Nat Rev Cancer 2015
Eavarone et al, PLOS One 2018

Seagen®

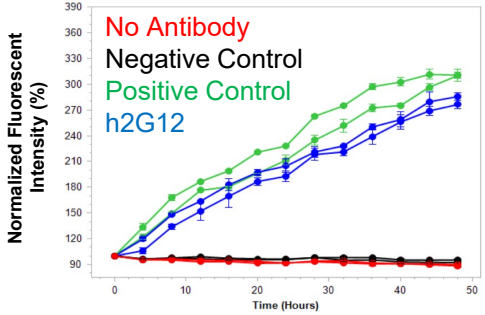
SGN-STNV is an STn-targeted ADC using Vedotin Platform Technology

SGN-STNV is an investigational antibody-drug conjugate (ADC), comprised of the STn-targeted antibody h2G12 and Seagen vedotin linker technology, designed to deliver MMAE to STn-expressing cells

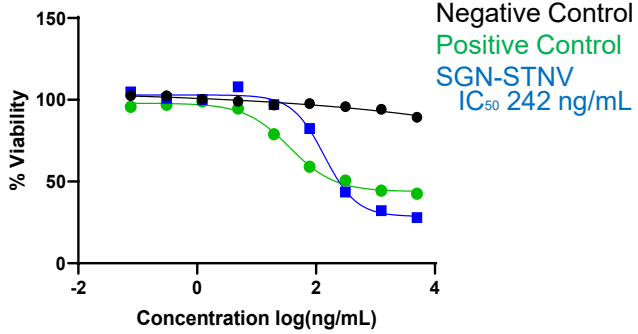


Cell Line Overexpressing ST6GALNAC1

Antibody Internalization: h2G12 internalizes into STn+ cells

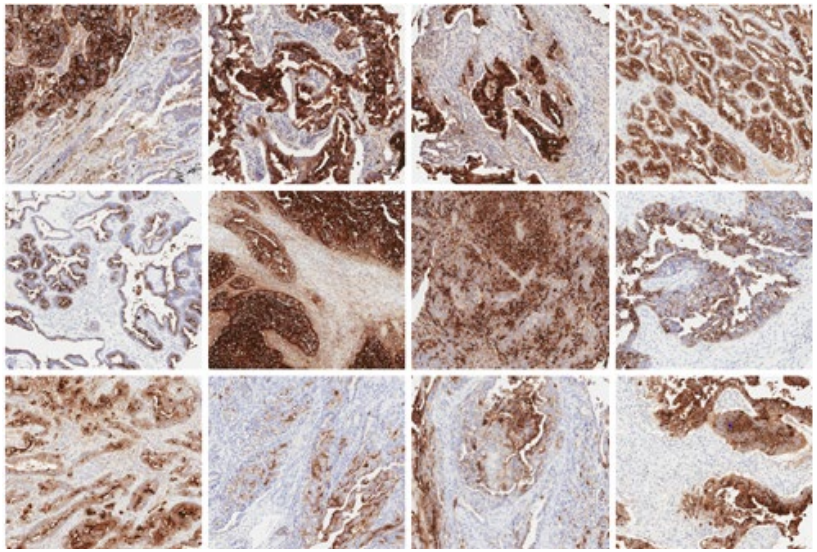


In vitro cytotoxicity: SGN-STNV delivers MMAE to STn+ TNBC cells



STn is Expressed in Many Solid Tumors

Immunohistochemistry staining confirms expression in NSCLC, ovarian, and gastric carcinomas

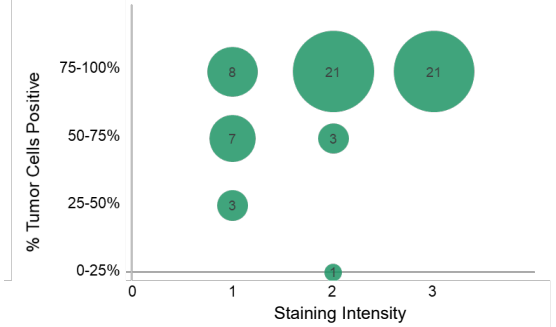


NSCLC

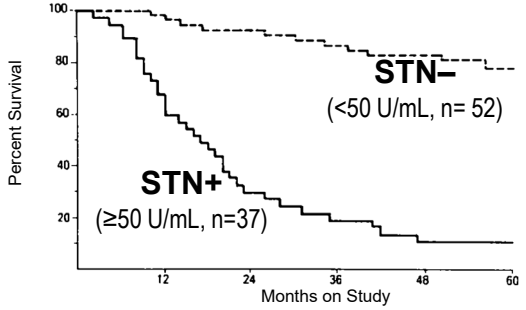
Ovarian cancer

Gastric cancer

The mucinous subtype of many solid tumors is enriched for STn expression



STn detected in patient serum is a prognostic marker for survival



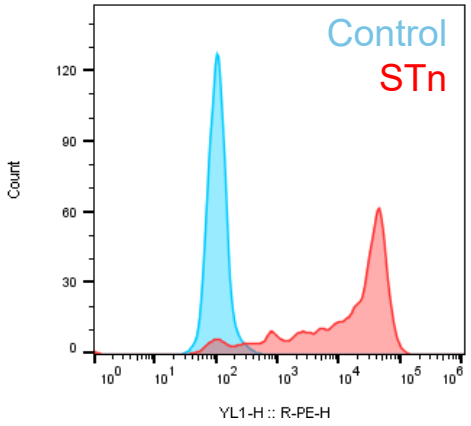
STn+/- serum vs. OS in ovarian cancer patients[1]

[1]Kobayashi. (1992) J. Clin. Onc., 10:95[6]

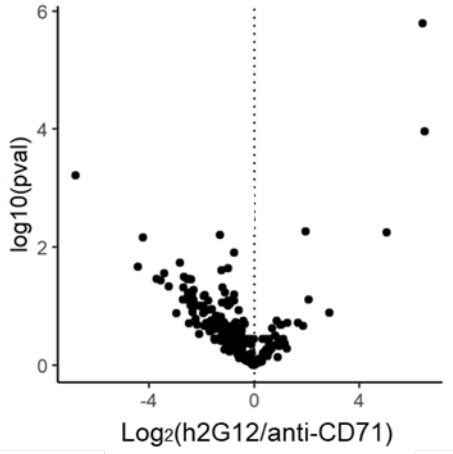
SGN-STNV Antibody Binding is Independent of Protein Backbone

- STn-targeted antibody, h2G12, is specific for STn, independent of target protein identity
- Present on multiple tumor associated glycoproteins (e.g. CA-125, MUC1, Integrin β_1)
- Novel surface proteins were identified that are also able to internalize and turnover, likely contributing to SGN-STNV efficacy

ST6GALNAC1 Expressing Cells
Engineered Overexpression of STn



Flow cytometry confirming surface STn expression

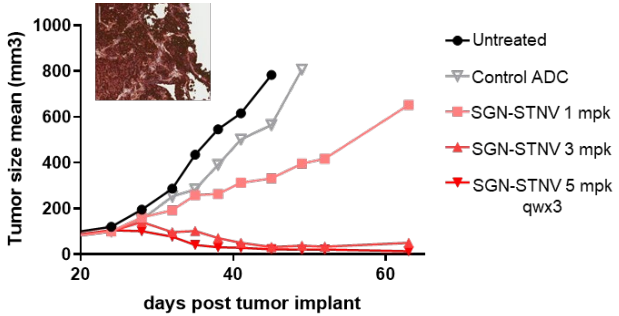


Relative protein enrichment from antibody pulldowns comparing *anti-STn (enriched further right)* compared to *anti-CD71 (enriched further left)*

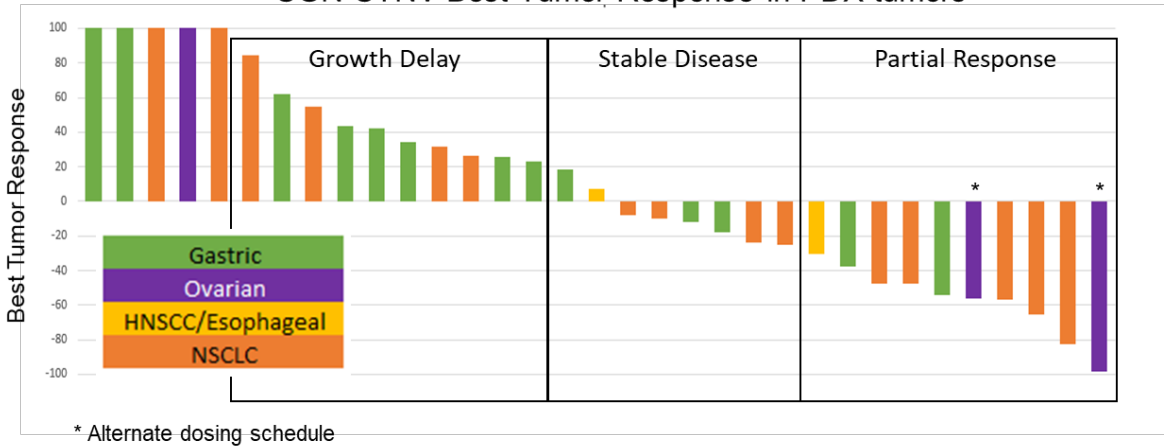
SGN-STNV is Active in Preclinical *In Vivo* Models

- A broad set of xenograft and PDX models were selected across key tumor types including gastric, ovarian, esophageal, and non-small cell lung carcinomas
- Efficacy observed was similar to other vedotin-platform ADCs

OV90 xenograft
Sub-Cutaneous
(ovarian model)

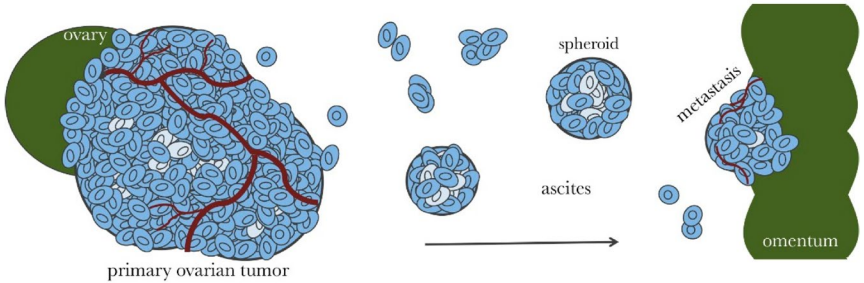


SGN-STNV Best Tumor Response in PDX tumors



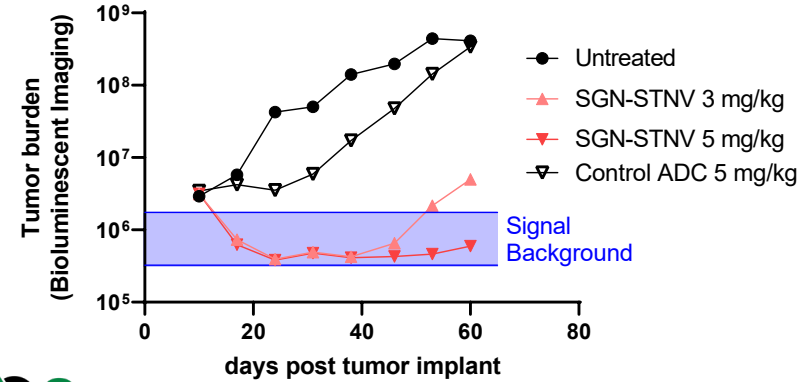
* Alternate dosing schedule

SGN-STNV Retains Activity in an Ascites-like Ovarian Model

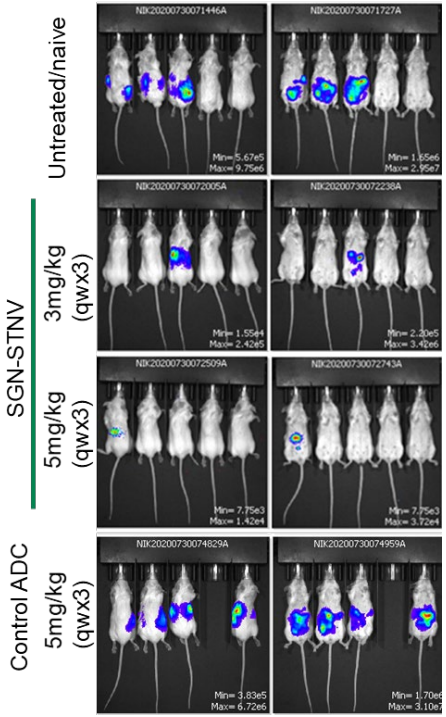


Emmings et al. (2019) Int. J. Mol. Sci. 20(1), 229

OV90 xenograft
Intraperitoneal
(ovarian model)



Representative bioluminescent images to show IP tumor burden

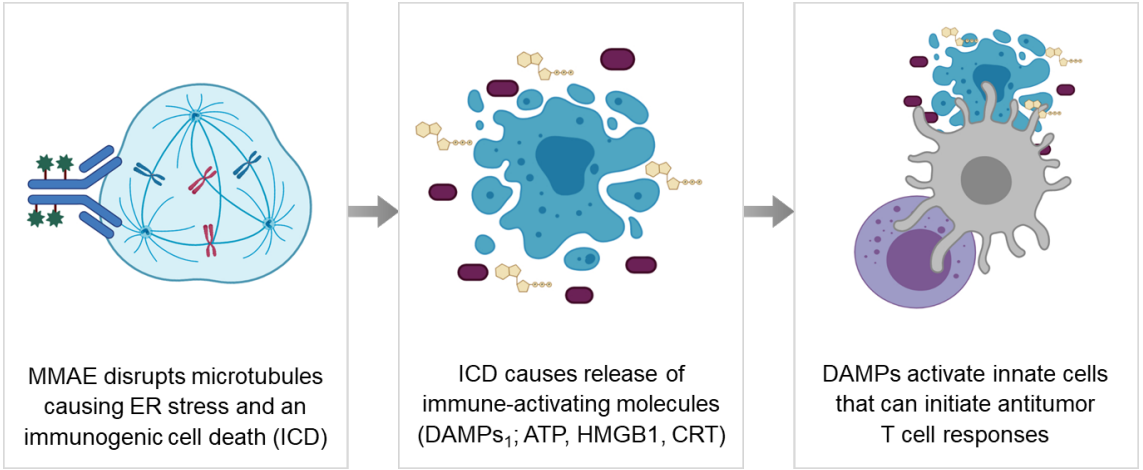


- Most tumor models are implanted subcutaneously, which provides a rough approximation of solid TME
- Seagen developed an ascites-like orthotopic model where tumor cells were implanted into the IP compartment
- SGN-STNV retains robust activity when tumor cells are implanted into the IP compartment

TME; Tumor Microenvironment
IP; Intraperitoneal

Immune-Mediated Mechanisms of Action Driven by Both Antibody and Linker Selection

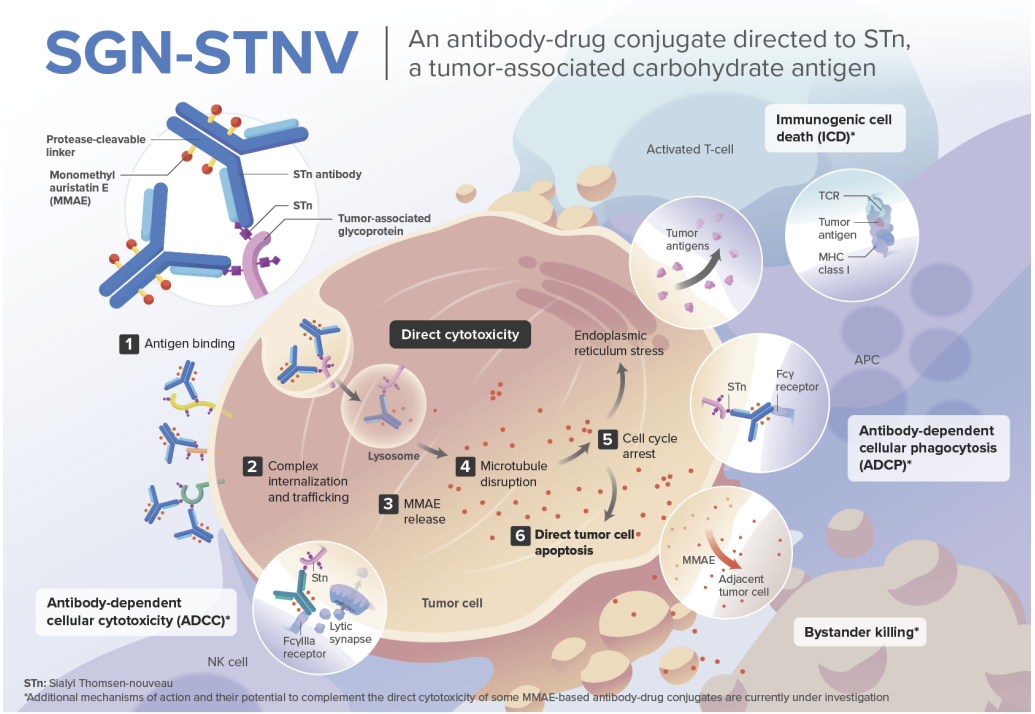
- Antibody-Dependent Cellular Cytotoxicity (ADCC):
  - SGN-STNV antibody backbone engages FCγRIII on natural killer cells to drive ADCC
- Antibody-Dependent Cellular Phagocytosis (ADCP):
  - Antibody backbone of SGN-STNV engages FCγRI on macrophages, leading to ADCP
- Immunogenic Cell Death (ICD):
  - Vedotin-platform ADCs have been well-characterized as driving ICD via ER-stress response
  - ICD contributes to dendritic cell maturation and priming of tumor-specific cytotoxic lymphocytes



DAMP=Damage-associated molecular patterns

1. Cao et al. AACR 2016. **2**. Cao et al. Cancer Res 2017;77(13 suppl): Abstract 5588. **3.** Cao et al. Cancer Res 2018;78(13 Suppl): Abstract 2742. **4.** Alley et al. Cancer Res 2019;79(13 Suppl): Abstract 221.

Conclusions



SGN-STNV is an investigational agent, and its safety and efficacy have not been established.

- STn is expressed in various solid tumors
- h2G12 is specific for STn and allows cell-targeted MMAE delivery through multiple surface proteins
- SGN-STNV leverages clinically validated vedotin-platform technology to deliver cytotoxic payload to tumor cells
- SGN-STNV induces antibody-dependent effector functions and vedotin-mediated immunogenic cell death
- SGN-STNV is well tolerated in non-human primate studies and there is an ongoing phase 1 trial, SGNSTNV-001 (NCT04665921)

Acknowledgements

Research
Hector Rincon
Nanna Hansen
Rob Lawrence
Sarah Anderson
Kerry Klussman
Angela Epp
Shyra Gardai
Bill Arthur
Bob Thurman
Aly Smith
Sasha Lucas
Lauren Bou
Jamie Mitchell
Dave Meyer
Allana Ubben
Michelle Wuerth
Serena Wo
Scott Peterson

Translational Sciences
Jess Simmons
Nicole Stevens
Jason Schrum
Sean Allred
Kelly Hensley
Vineet Kumar
Jackie Stilwell
Nancy Everds
Christine O'Day
Vaishali Chudasama
Paul Crosby
Anne Grosse-Wilde

CMC
John Valliere Douglass
Michael Pastorello

Regulatory
Mahnaz Irani
Tara Bumgarner
Dave Bhattacharya
John Redue
Chris Whalley
Linda Bowen

Development
Suzanne McGoldrick
Megan O'Meara
Biao Xing
Joy Jiang
Colleen Stromatt
Margaret Macdonald
Matthew Onsum

Project Management
Deb Gilbertson
Kerrie McLaughlin

Marketing
Nick Osgood

Corporate Development
Roland Gendron
Kelly Callahan