



Developing a clinically important class of glycan-targeted biologics with unprecedented tumor specificity

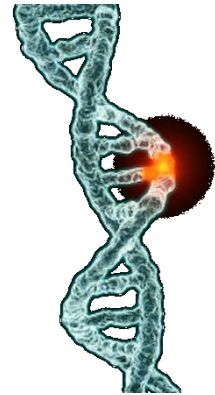
Funding First Human Data

May 2018

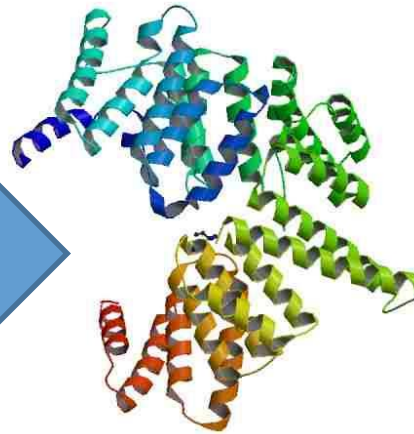
- **Siamab platform unlocks exciting but historically challenging target space**
 - Glycans: cancer specific & immunosuppressive/chemoresistant
 - Initiated discovery collaboration w/ Boehringer Ingelheim using Siamab's platform in 2017
- **Lead ST1-ADC program moving rapidly to clinical trials in ovarian cancer**
 - Compelling efficacy in multiple xenograft & PDX models
 - Favorable safety profile in pilot cyno tox study
- **Raising \$15-20m B-round to fund through clinical proof of concept**
 - Raised \$14m A round from Novartis, Momenta, family offices to date
 - \$3m+ in grants won to date
- **Seeking lead institutional investor**
 - Alternative funding history – highly capital efficient but challenging to transition

Cancers Consistently Alter Glycosylation

Multiple TACA Targets: Tumor Associated Carbohydrate Antigens



Mutated DNA alters proteins



- ▲ Fucose
- ◆ Sialic Acid
- Galactose
- Mannose
- GalNAc
- GlcNAc

Similarly, glycans are mutated on proteins

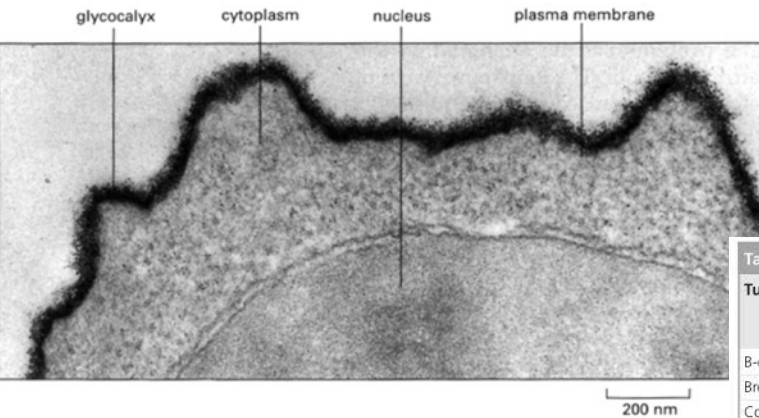
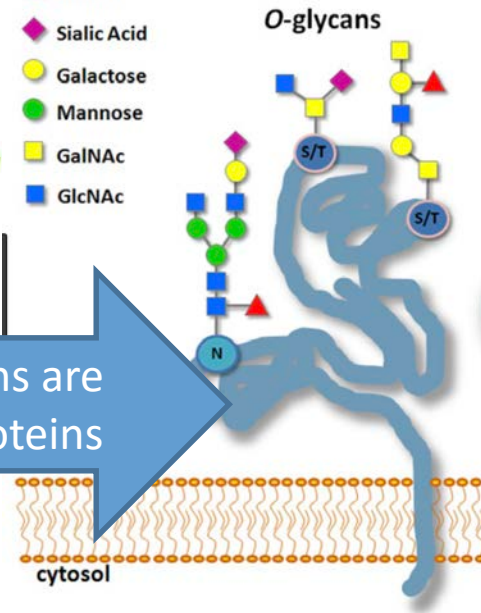


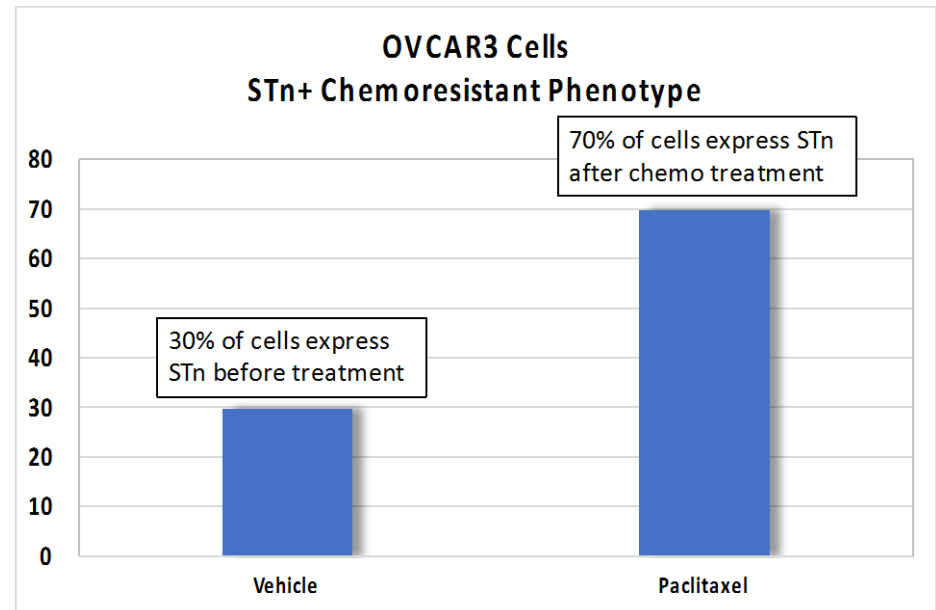
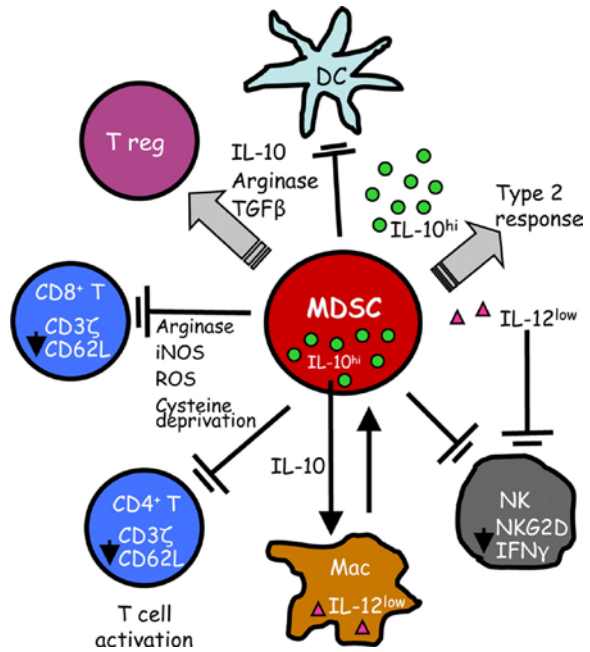
Table 1. Most prominent carbohydrate antigens and their associated tumor types.

Tumor type	Carbohydrate antigen														
	Fucosyl GM1	GM2	GM3	N-Gc GM3	GD2	GD3	GD3L	Tn	sTn	TF	globo H	Le ^x	Le ^a	sLe ^a	pSA
B-cell lymphoma		•			•										
Breast		•	•	•		•		•	•	•	•	•		•	
Colon		•						•	•	•		•		•	
Lung				•				•	•		•	•			
Melanoma		•	•	•	•	•	•								
Neuroblastoma		•		•	•	•	•								•
Ovary		•							•	•	•	•			
Prostate		•						•	•	•	•	•			
Sarcoma		•			•	•	•								
SCLC	•	•									•			•	•
Stomach		•							•	•		•	•	•	•

Le^x: Lewis X; Le^y: Lewis Y; N-Gc: N-glycolyl; pSA: Polysialic acid; SCLC: Small-cell lung cancer; sTn: Sialyl Thomsen-nouvelle; TF: Thomsen-Freidenreich; Tn: Thomsen nouvelle.
Data from [32,48,51,145,148,313-315].

TACAs Promote an Aggressive, Immunosuppressive Phenotype Attractive but Challenging Targets

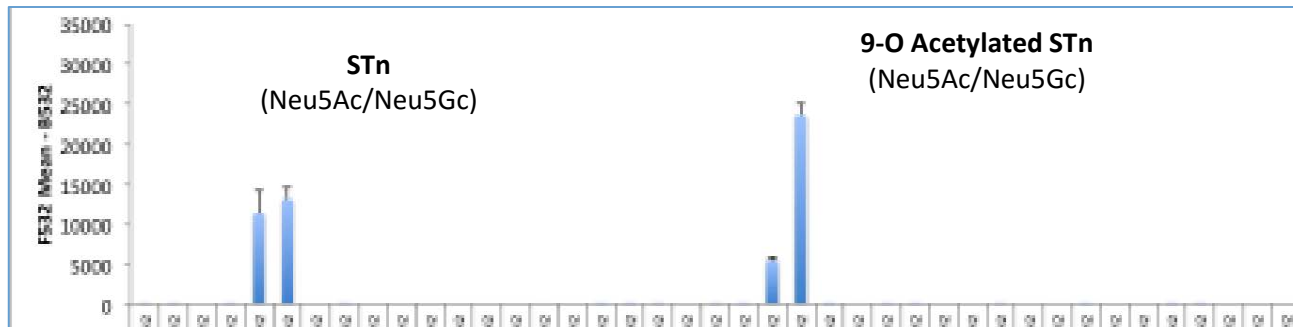
- Suppress innate immunity (MDSCs and NK cells)
- Confer chemoresistance and a cancer stem-cell phenotype
- Enable tissue invasion & metastases



Siamab's Platform Unlocks TACA Targeting Enables Unprecedented Specificity

- **Target is the glycan itself – not the glycoprotein**
 - Binds multiple glycoproteins
- **Glycan-binding mAbs – rare to find with high affinity and specificity**
 - Multiple format potential – ADC, TCR/bispecific, CAR-T
- **Siamab's platform solves this problem**
 - Validated with lead program and Boehringer Ingelheim collaboration
- **Pharma needs new targets!**

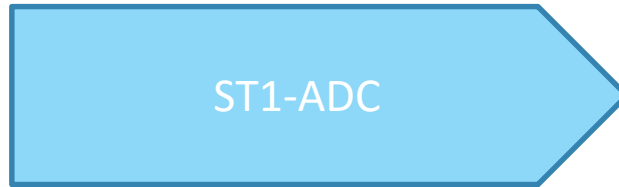
Siamab's glycan microarray confirms anti-glycan binding specificity



Siamab Pipeline



Glycan Target: STn
Ovarian & Other Solid Tumors



Cell Line Development Initiated; IND: 2019 (Unpartnered)

Glycan Target: N/D
Solid Tumors



Partnered with Boehringer Ingelheim

Glycan Target: N/D
Breast, Colon & Other Solid Tumors



Discovery Initiated Q4 2017 (Unpartnered)

- **Jeff Behrens, MBA, MS, President & CEO**
 - Biogen Idec Incubator: co-founder, led 3 deals
 - Alnylam, led alliance with Takeda pharmaceuticals
 - Edimer, Third Rock Ventures
- **Dan Dransfield, PhD, SVP R&D**
 - Dyax, ArQule, Tokai
 - Tufts, Yale, Medical College of Georgia
- **Gregg Beloff, JD, MBA, CFO**
 - Cerulean Pharma, Immunogen, Archemix
- **Rebecca Dabora, PhD, Consulting Head of CMC**
 - Biogen, Altus, Merck
- **William Slichenmyer, MD, Consulting CMO**
 - Pfizer, Merrimack, Aveo

Siamab Board & Key Advisors

Board of Directors

- **Jeff Behrens** - President & CEO
- **Brad Curley** - Boston Harbor Angels (Chair)
- **Adam Feire** - Novartis
- **Ganesh Kaundinya** - Momenta Pharma
- **Peter Kroon** - Exan Capital
- **Gary Pforzheimer** - PG Calc
- **Todd Zion** - SmartCells

Glycobiology Advisors

- **Ajit Varki, MD, PhD (Founder)** – UCSD
- **Joy Burchell, PhD** – Kings College London
- **Zach Shriver, PhD** – VP Research, Visterra

Oncology Advisors

- **Ron Drapkin, MD, PhD** – UPenn
- **Bo Rueda, PhD** – Mass General Hospital

Lead Program Development & Company Building

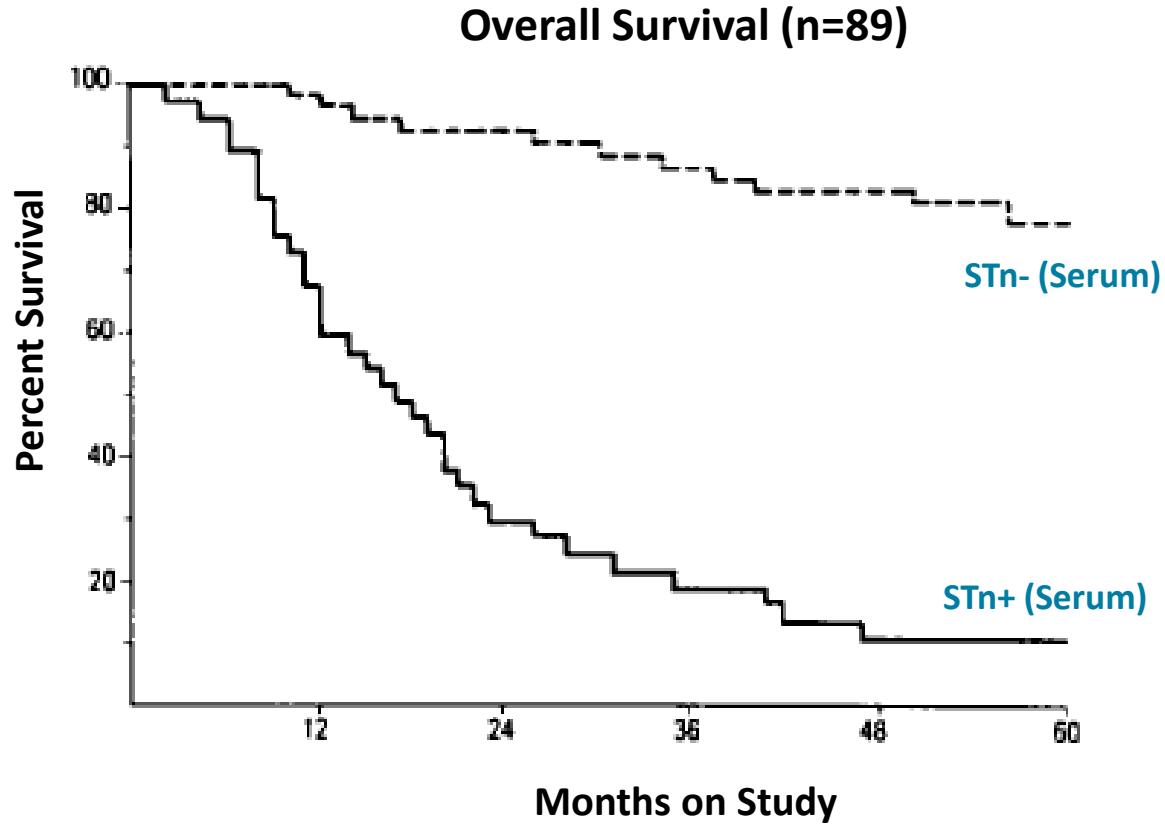
- **Morris Rosenberg, PhD** – former EVP, Seattle Genetics
- **Peter Kiener, PhD** – CSO, Sucampo Pharmaceuticals
- **Haifeng Bao, PhD** – Preclinical Consultant, former MedImmune
- **John Edwards** – Genzyme, Genetics Institute, TKT, Adnexus, F-Star

Siamab's Lead ST1 Program (SIA01-ADC) IND-ready for FIM in 2019; Initiated Backup TCE Program

- **Platform discovered multiple mAbs against top priority target: STn**
- **MGH collaboration ongoing → chemoresistant/CSC phenotype**
- **Humanized leads conjugated to vc-MMAE → ADC format**
 - Excellent therapeutic window for ADC approach
- **Compelling xenograft & PDX efficacy data**
- **IHC and tissue cross reactivity (TCR) studies completed**
- **Pilot cyno tox study → excellent safety profile**

STn Target Opportunity

Serum STn+ Associated with Poor Prognosis



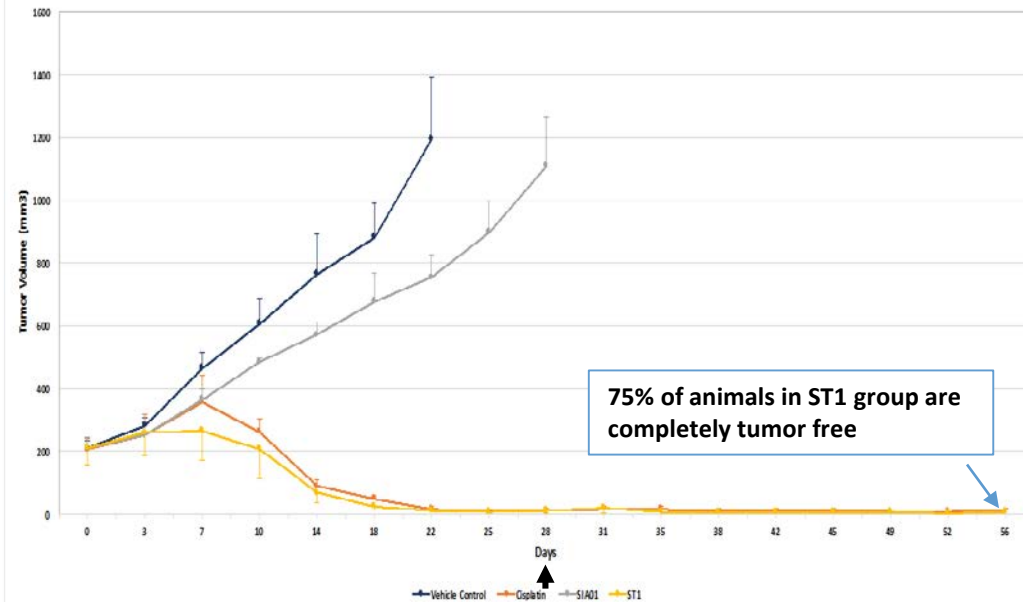
Myeloid-Derived Suppressor Cells (MDSCs) are STn+ and Offer Immune Reengagement Potential

- **Quantified STn expression on primary patient tumor samples and MDSCs**
 - Fresh samples analyzed by flow cytometry
 - Both tumor cells and tumor infiltrating MDSCs express STn in patient samples
- **STn+ MDSCs linked to STn+ tumors in MDA-MB-231 STn+/- model**
- **ST1 ADC depletes STn+ MDSCs in OVCAR3 mouse xenografts**

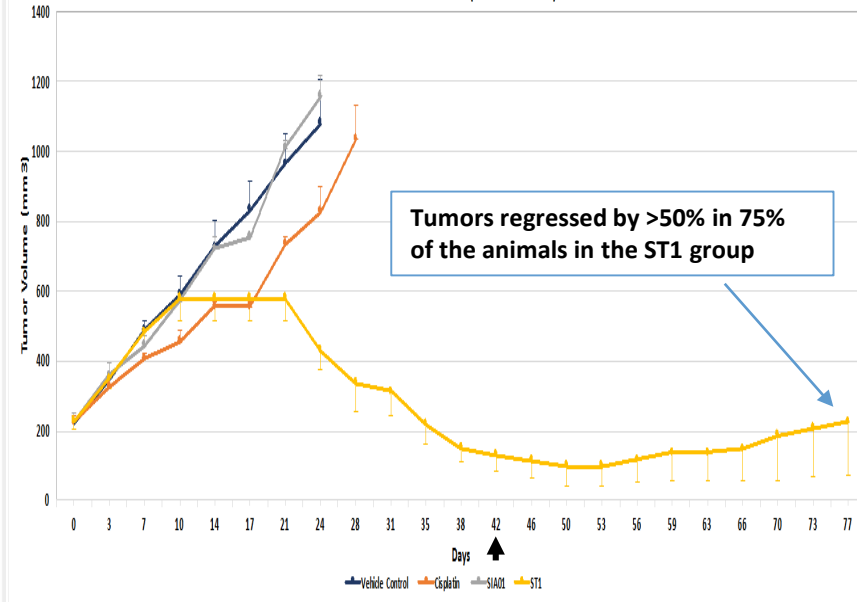
ST1-ADC Lead Program Results

Dramatic PDX Efficacy in Ovarian Cancer PDX Models

ST2569 Ovarian PDX Model (Chemo-naïve)



ST206A Ovarian PDX Model (Chemoresistant)



Cisplatin 3mg/kg, q7dx3
 SIA01/ST1 5mg/kg (IV), QW (arrow indicates when treatment ended)
 # of animals/group = 3-5

ST1 Lead Program Results

Pilot Cyno PK/Tox Study Demonstrates Safety & Therapeutic Window

- **2 doses ST1-ADC administered: Days 1, 22 @ 1, 3, 6mg/kg**
 - Designed based on MMAE history/Adcetris® preclinical package
- **Results demonstrate excellent safety profile of ST1**
 - No deaths, no body weight loss (animals maintained weights between 2.20-2.47 kgs)
 - No gross pathologic changes across all organs assessed
 - Histopathologic changes limited to the bone marrow (MMAE class effect)
 - All clinical chemistry results (e.g., LFT's (ALT/AST/ALP), kidney function (CREAT)) normal throughout study
- **Half-life ~4 days; exposure data in-line with published findings for other MMAE ADCs**
- **Derisked IND-enabling GLP tox → solid therapeutic window**

mg/kg allometric scaling			
Mouse	Cyno	Human	
1.00	0.21	0.07	
2.50	0.52	0.19	Efficacy (mouse)
5.00	1.03	0.37	Strong efficacy (mouse)
14.56	3.00	1.09	
29.13	6.00	2.17	Tox signs (low/cyno)
38.83	8.00	2.90	MTD? (not tested yet)

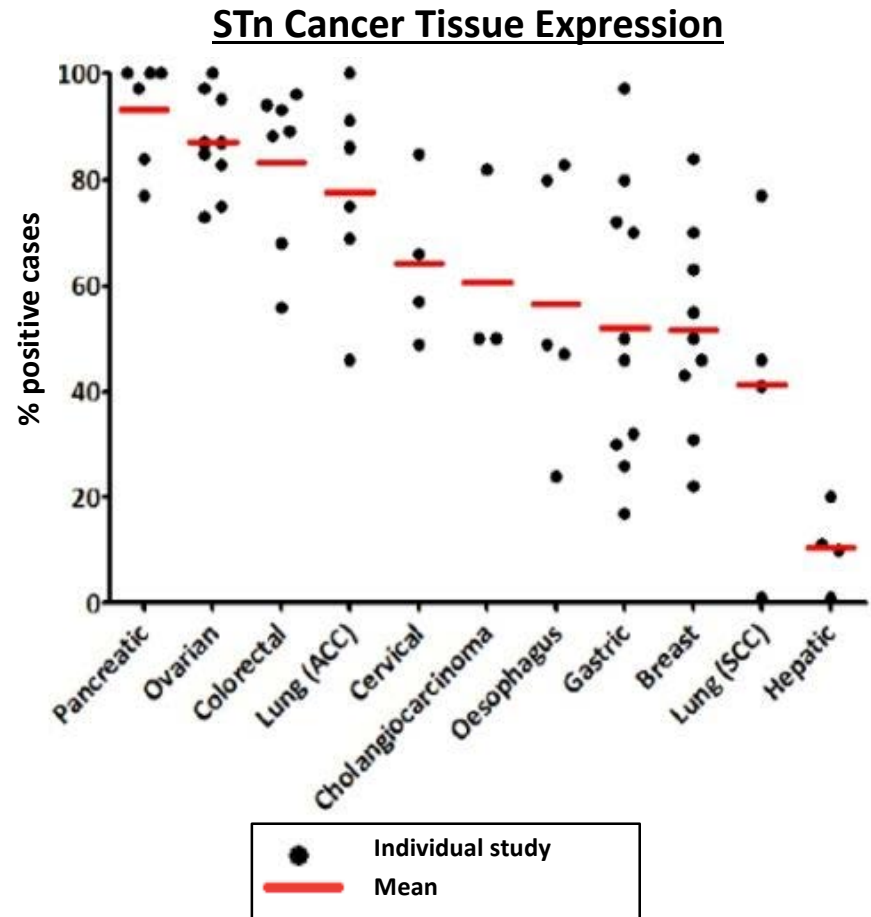
* Shaded boxes = in vivo data

- **Cell line development complete in early Q2 2018**
- **Next steps**
 - Select CMO and initiate GMP scaleup
 - IND-enabling GLP tox studies designed
 - Pre-IND meeting w/FDA in Q3 2018
- **Phase I/Ib studies design in place**
 - Standard 3x3 study with single patient cohorts at lowest doses
 - Expansion cohorts for phase Ib
 - Ovarian
 - Confirmed STn+ tumors
 - Possible 3rd cohort: pancreatic or gastric
 - STn expression to be assessed in serum and by IHC when samples available

Lead ST1-ADC Program: Large Commercial Potential

STn Glycan Present in Many Carcinomas (and Rare In Normal Tissue)

- **Ovarian cancer – Potential first indication**
 - High unmet medical need
 - Chemoresistant recurrence common
 - 5 year survival rate: 30%
 - US incidence: 22,500 cases diagnosed/yr
 - Peak sales potential approaches \$1b/yr
- **Other key indications**
 - Pancreatic
 - Gastric (diffuse subtype)
 - Prostate (>80% expression)



- **Advance lead program to clinical proof-of-concept (phase Ib)**
 - 3 years
 - \$17M program-specific costs: CMC, GLP tox, PhI/Ib studies
 - Australia strategy could reduce this by ~\$5m (tax rebate)
 - G&A \$3M
- **Advance pipeline**
 - 1-2 lead candidate programs → \$5M pipeline costs
- **Complete second pharma deal**
 - >\$10M free cash flow (2018-2020)
 - Incremental to raise and budget

Lead ST1 Program Development Timeline

