siamab therapeutics

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

Funding First Human Data

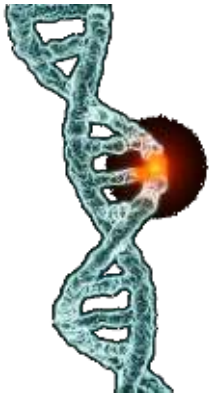
May 2018

Executive Summary

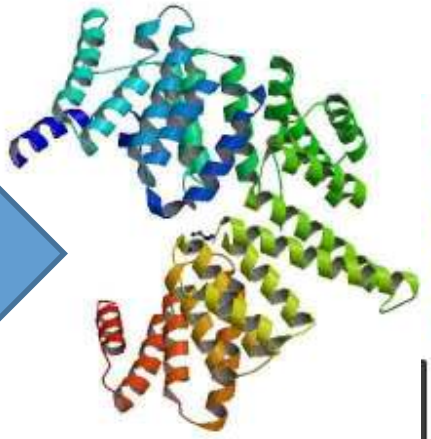
- **Siamab platform unlocks exciting but historically challenging target space**
  - Glycans: cancer specific & immunosuppressive/chemoresistant
  - Initiated discovery collaboration w/ Boehringer Ingelheim using Siamab's platform in 2017
- **Lead ST1-ADC program moving rapidly to clinical trials in 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

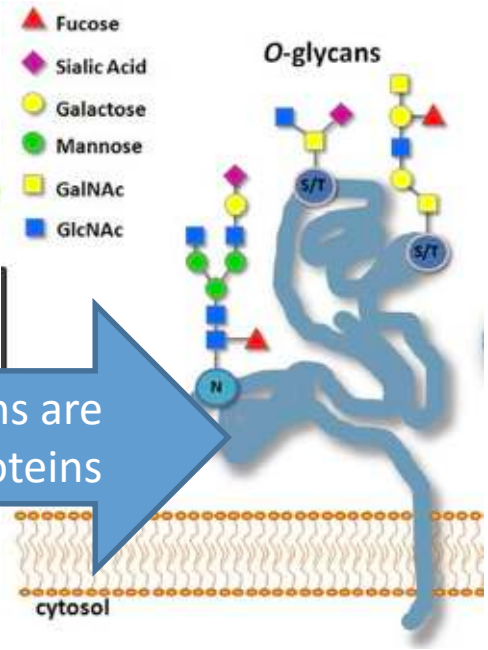
Multiple TACA Targets: Tumor Associated Carbohydrate Antigens



Mutated DNA alters proteins



Similarly, glycans are mutated on proteins



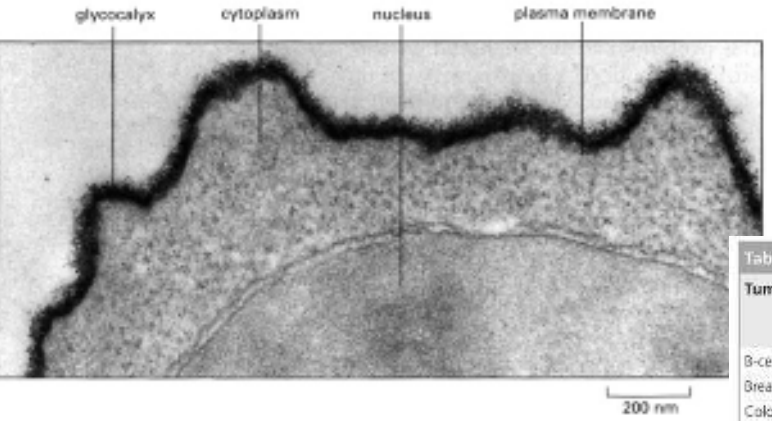


Table 1. Most prominent carbohydrate antigens and their associated tumor types.

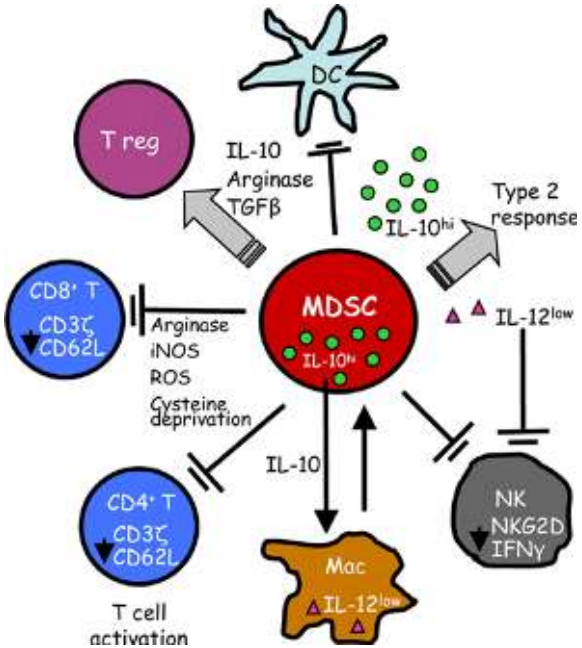
Tumor type	Carbohydrate antigen														
	Fucosyl GM1	GM2	GM3	*N*-Gc GM3	GD2	GD3	GD3L	Tn	sTn	TF	globo H	Le^y	Le^x	sLe^x	pSA
B-cell lymphoma		•			•										
Breast		•	•	•		•		•	•	•	•	•		•	
Colon		•						•	•	•		•		•	
Lung		•		•				•	•		•	•			
Melanoma		•	•	•	•	•	•								
Neuroblastoma		•		•	•	•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

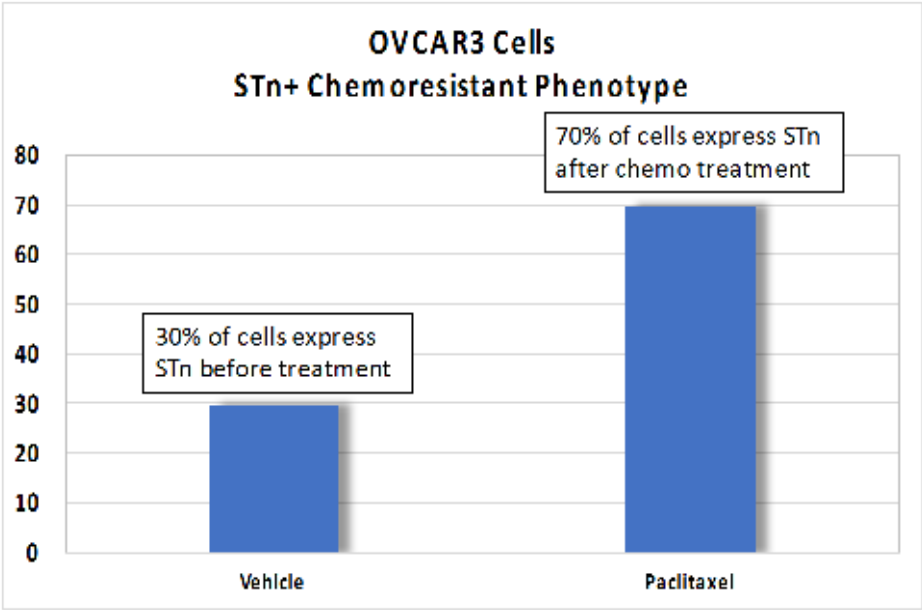
*Le^y: Lewis A; Le^x: Lewis X; Le^a: Lewis Y; *N*-Gc: *N*-glycolyl; pSA: Polysialic acid; SCLC: Small-cell lung cancer; sTn: Sialyl Thomsen-nouvelle; TF: Thomsen–Friedenreich; Tn: Thomsen nouvelle.*

Data from [32,48,51,145,164,313–315].

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**

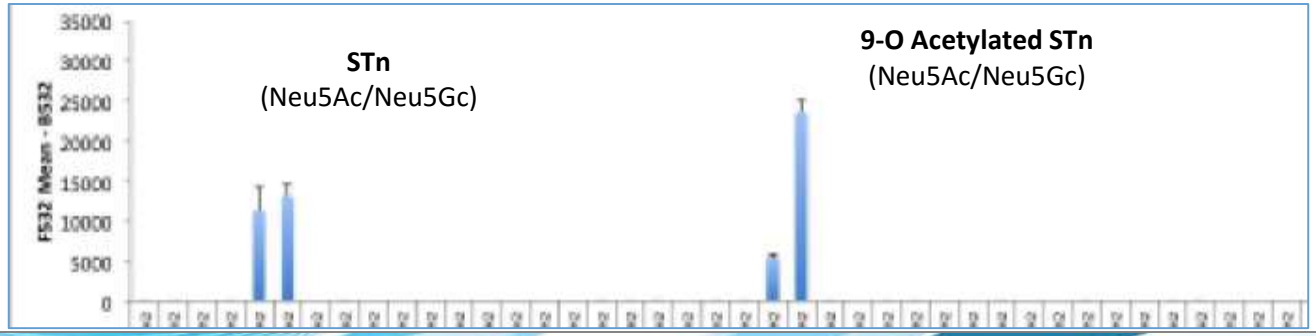




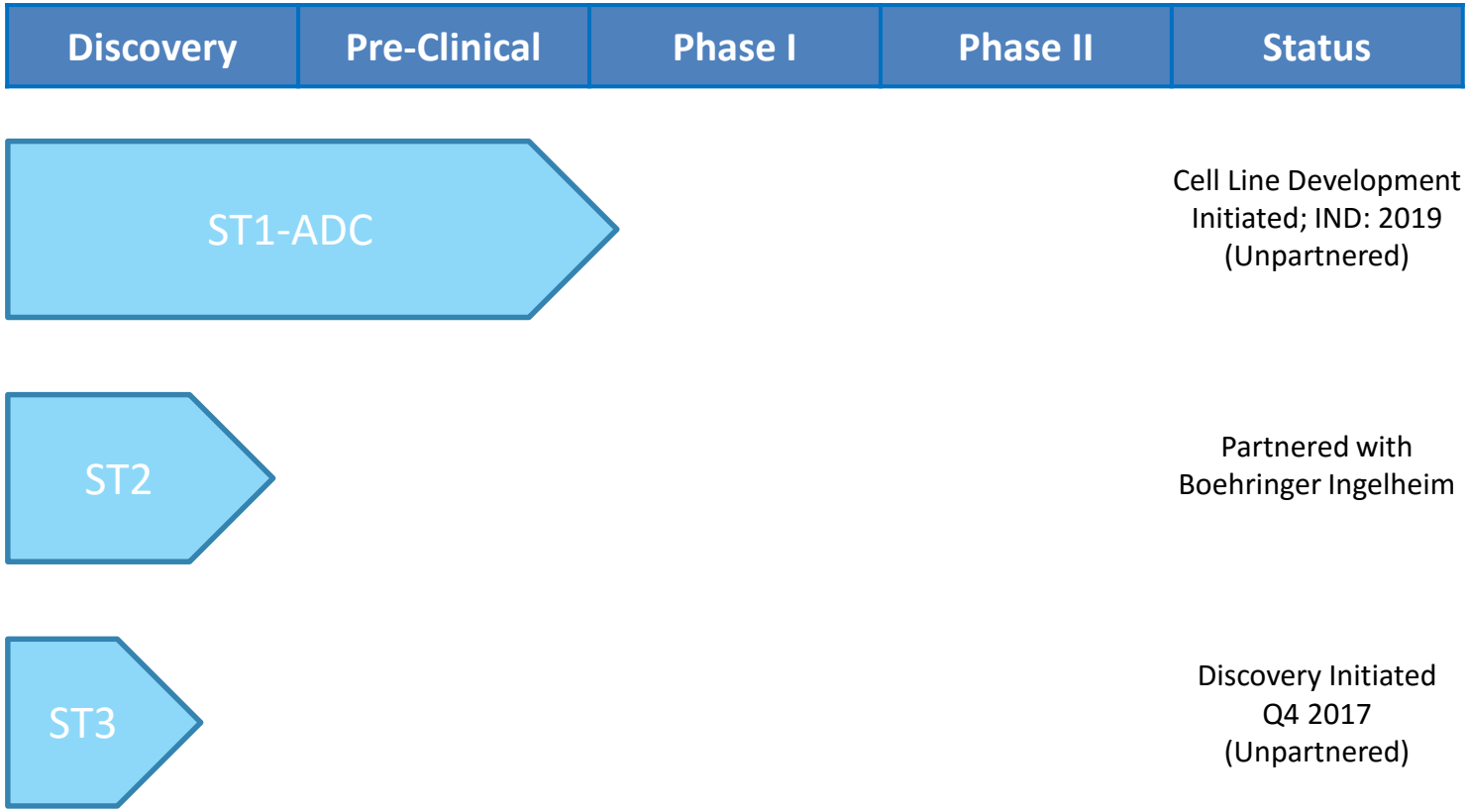
Siamab's Platform Unlocks TACA Targeting Enables Unprecedented Specificity

- **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



Siamab's Leadership Team

- **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

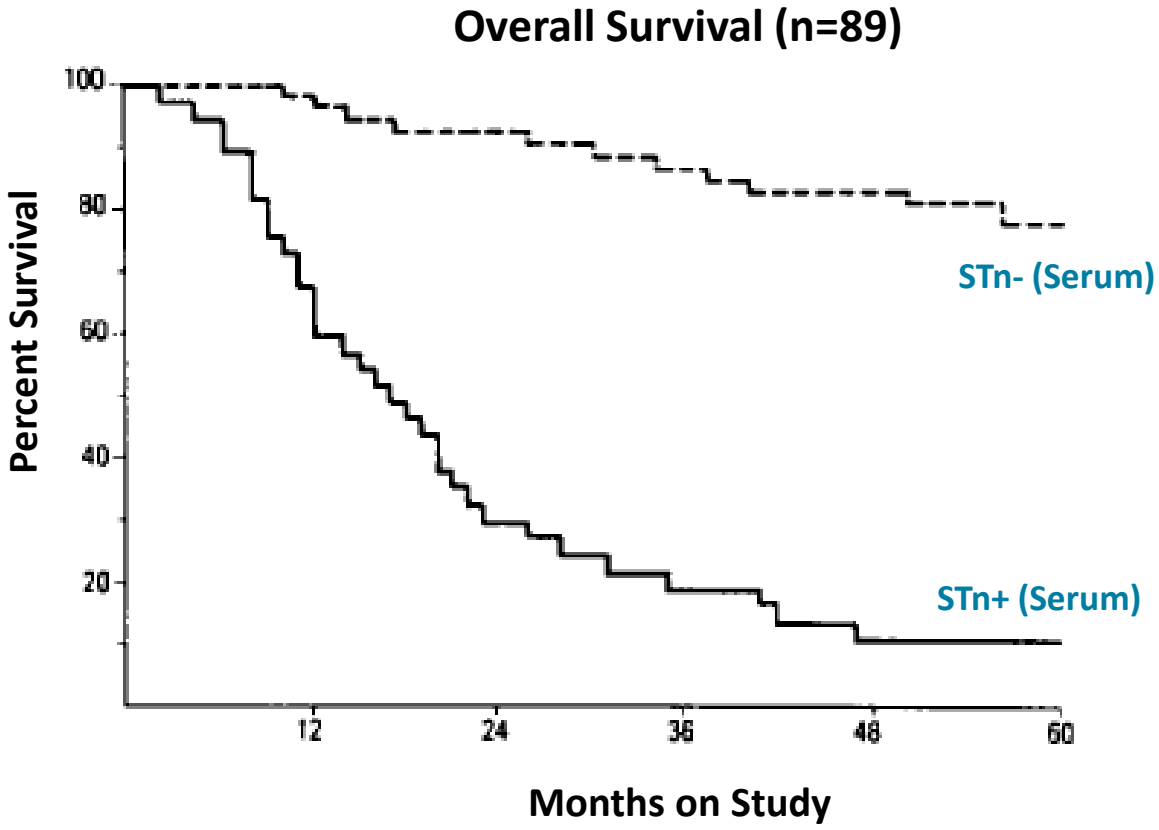
- **Morris Rosenburg, PhD** – former EVP, Seattle Genetics
- **Peter Kiener, PhD** – CSO, Sucampo Pharmaceuticals
- **Haifeng Bao, PhD** – Preclinical Consultant, former MedImmune
- **John Edwards** – Genzyme, Genetics Institute, TKT, Adnexus, F-Star

Link to Leadership Team

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



Kobayashi et al. 1992

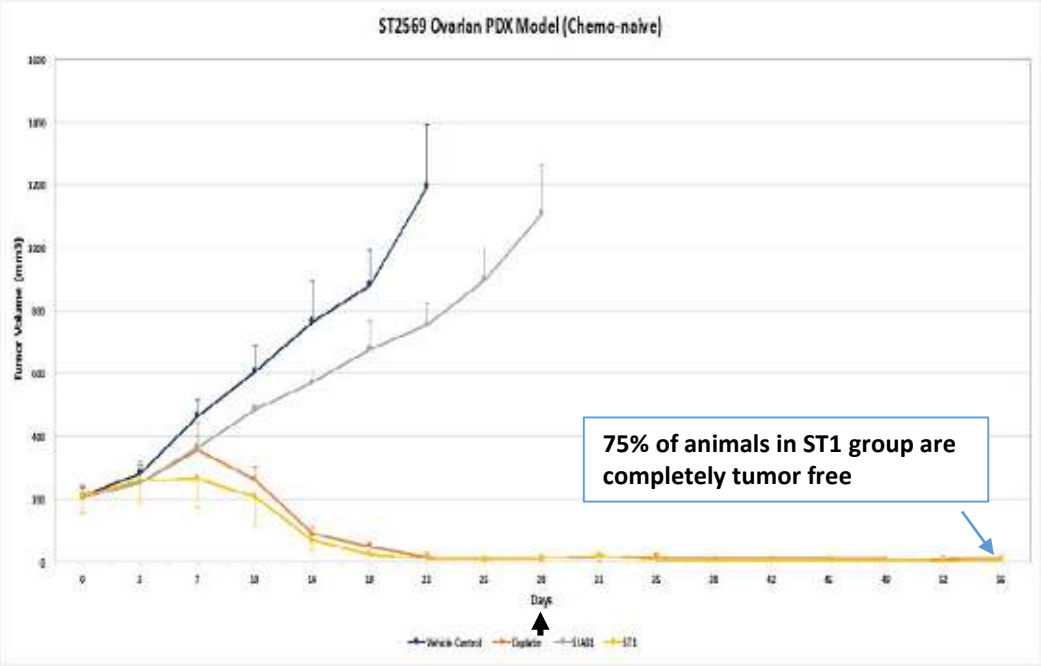
Myleoid-Derived Suppressor Cells (MDSCs) are STn+ and Offer Immune Reengagement Potential

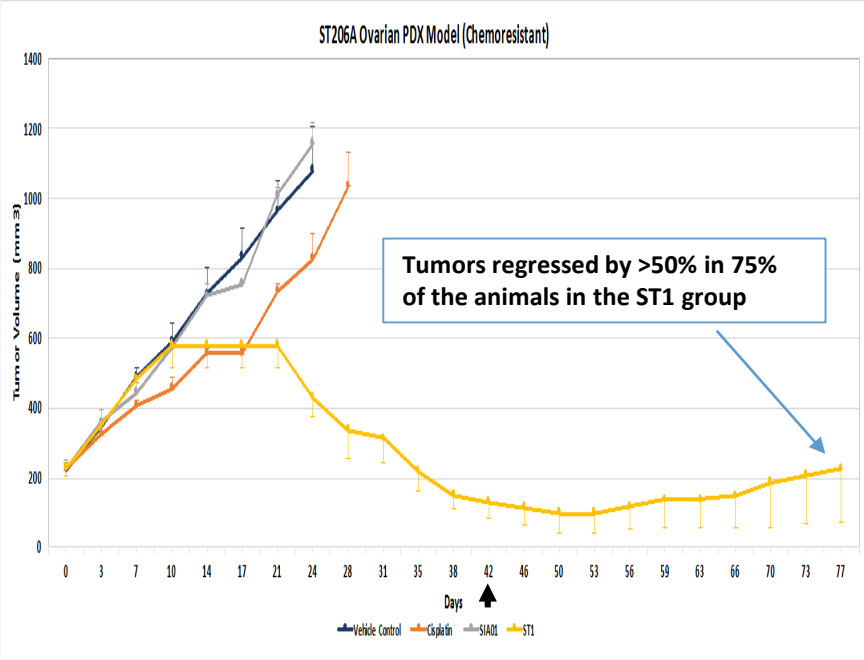
- **Quantified STn expression on primary patient tumor samples and MDSCs**
  - Fresh samples analyzed by flow cytometry
  - Both tumor cells and tumor infiltrating MDSCs express STn in patient samples

- **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





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**

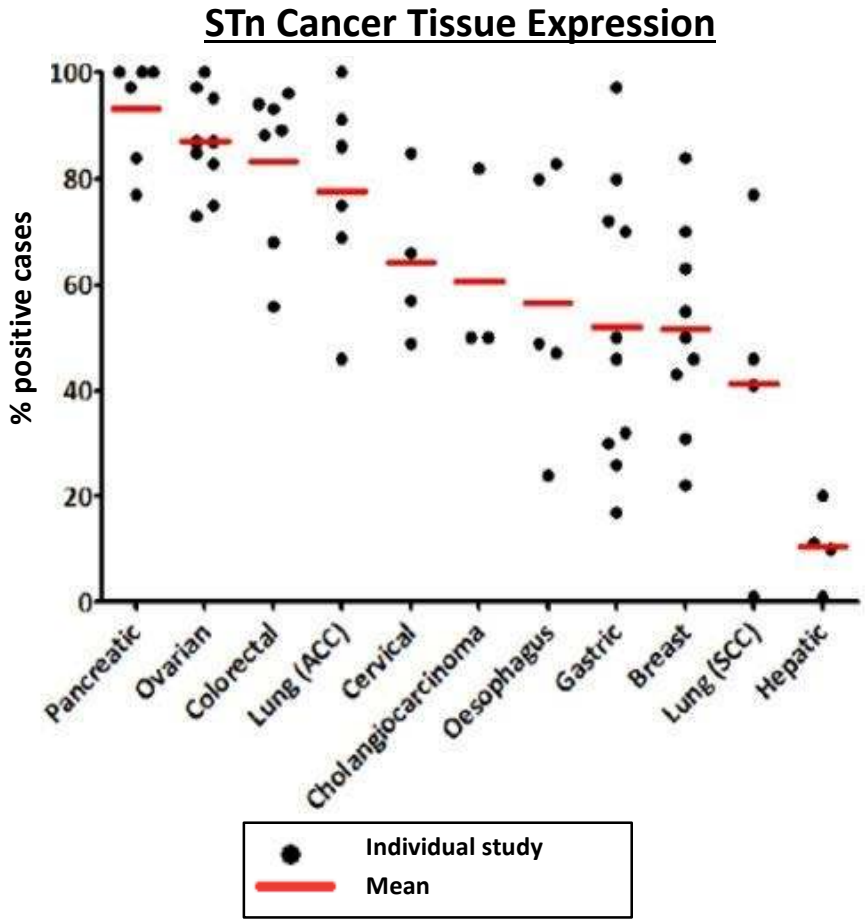
mg/kg allometric scaling			
Mouse	Cyno	Human	
1.00	0.21	0.07	
2.50	0.52	0.19	Efficacy (mouse)
5.00	1.03	0.37	Strong efficacy (mouse)
14.56	3.00	1.09	
29.13	6.00	2.17	Tox signs (low/cyno)
38.83	8.00	2.90	MTD? (not tested yet)
* Shaded boxes = in vivo data			

ST1-ADC – Ready to Enter the Clinic

- **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)



Julien et al, Biomolecules 2012

Siamab Series B Investment Summary

- **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