

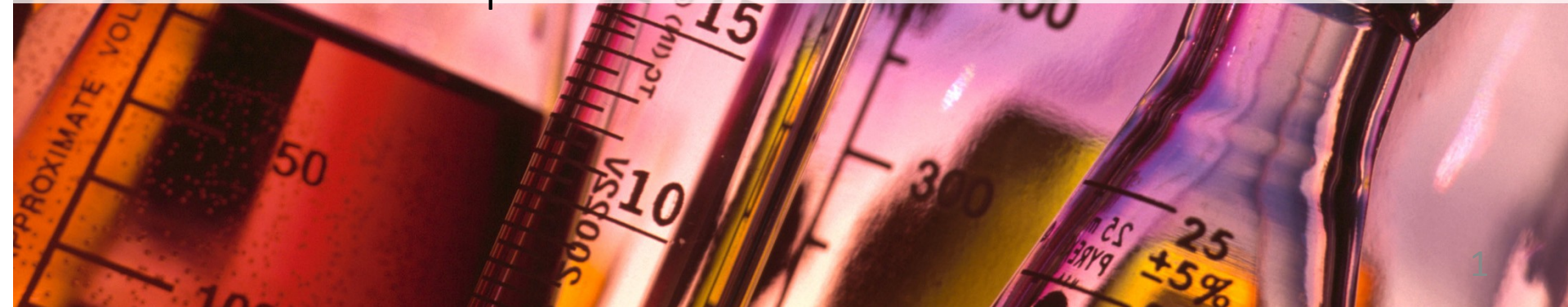


# PRECISION BIOLOGICS

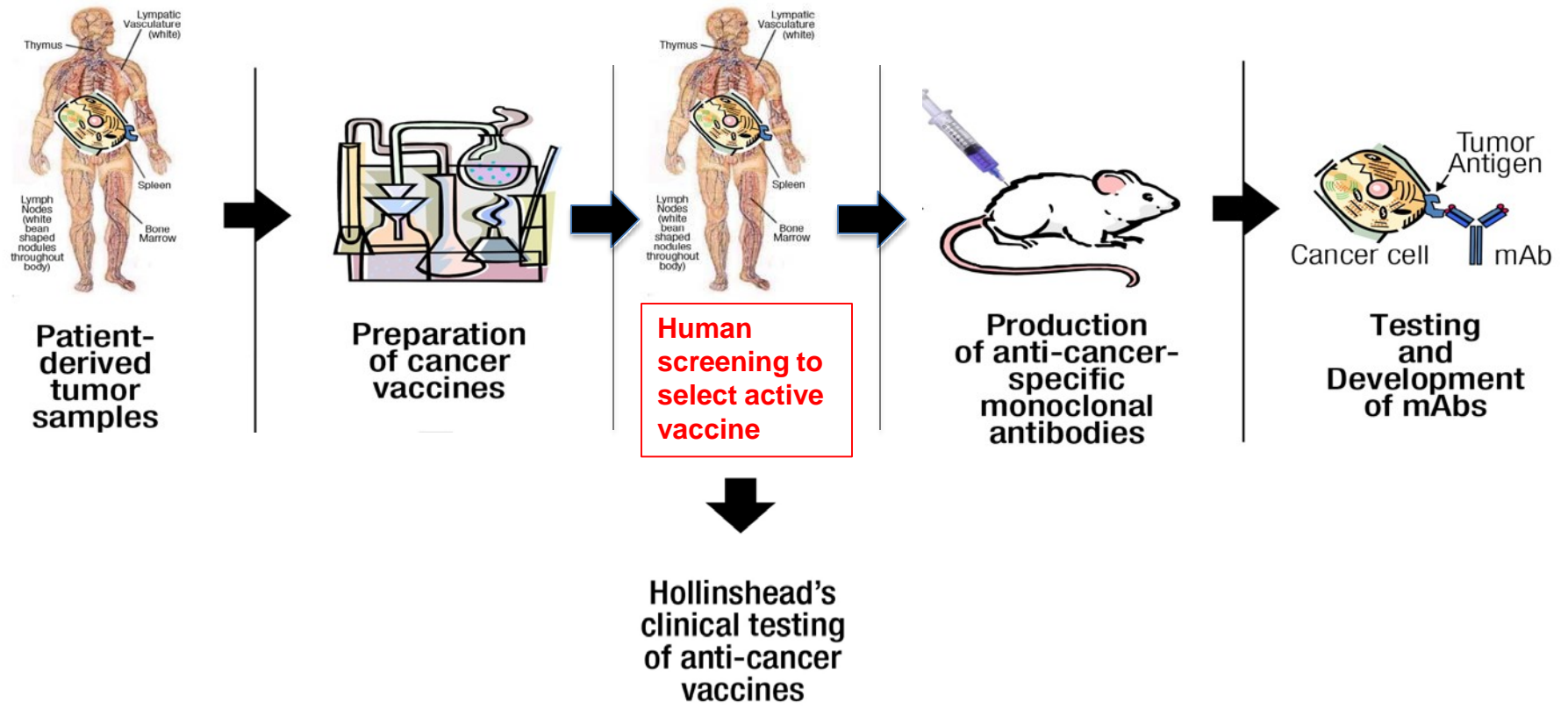
**The Discovery and Development of Novel Monoclonal Antibodies Targeting Neoantigens**

February 2017

Philip M. Arlen, M.D.







# Only Human Derived & Human Tested Neo-antigen Platform to Create Novel Therapeutics



# Pipeline

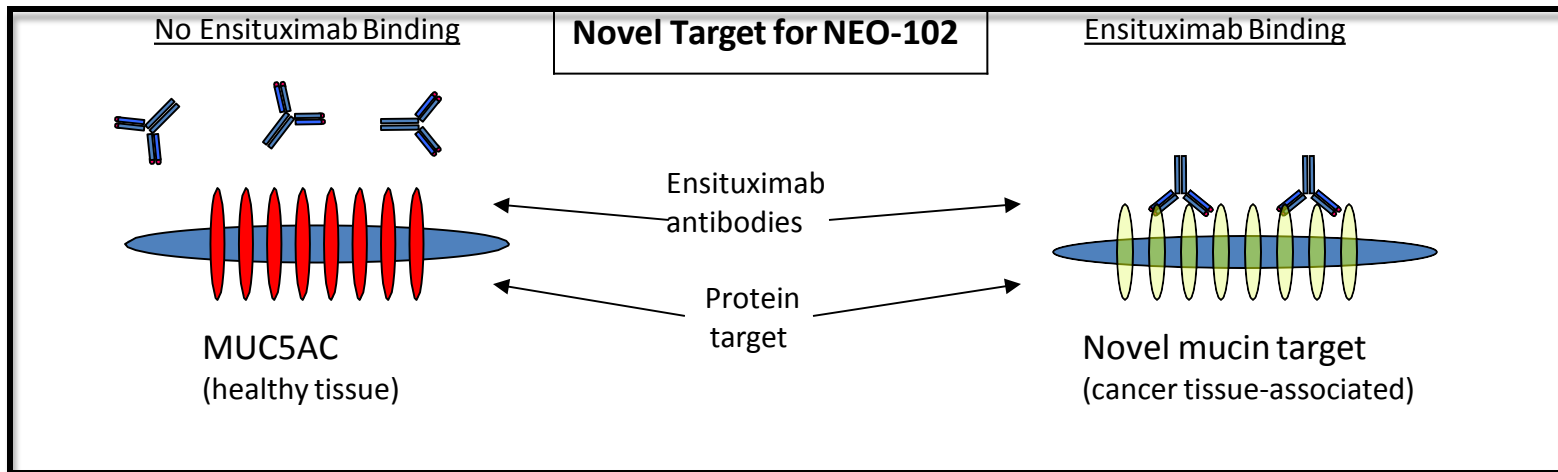
- NEO-102: Phase 2a colorectal and pancreatic ( NEO-102 monotherapy)- **COMPLETE**
- NEO-102: Phase 2b: pancreatic (randomized Gemzar/Abraxane ± NEO-102)
- NEO-201: IND-enabling studies, manufacturing underway and Phase 1 in planning for mid 2017

Product	Indication	Pre-Clinical	Pre-IND/IND	Phase 1	Phase 2	Phase 3
NEO-102	Pancreatic Cancer Randomized Phase 2B					
NEO-102	Colorectal and Pancreatic Cancer Phase 2A					
NEO-201	Pancarcinomas including GYN, Head and Neck, GI, Lung					
NEO-301	Pancreatic, Colorectal and other Cancers					

 Active  
 Projected

# Ensituximab (NEO-102) Binds to *Novel Cancer Target*

- Novel monoclonal antibody that specifically recognizes colorectal and pancreatic cancer.
- Recognizes a novel target which is a member of the mucin family of proteins, similar to BUT distinct from MUC5ac.
- Our novel target is not present in healthy tissues.





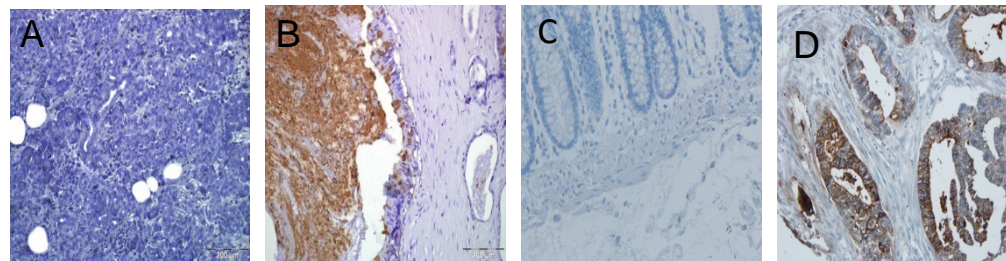
# Ensituximab Highlighted on Cover of Cancer Immunology, Immunotherapy

June 2013

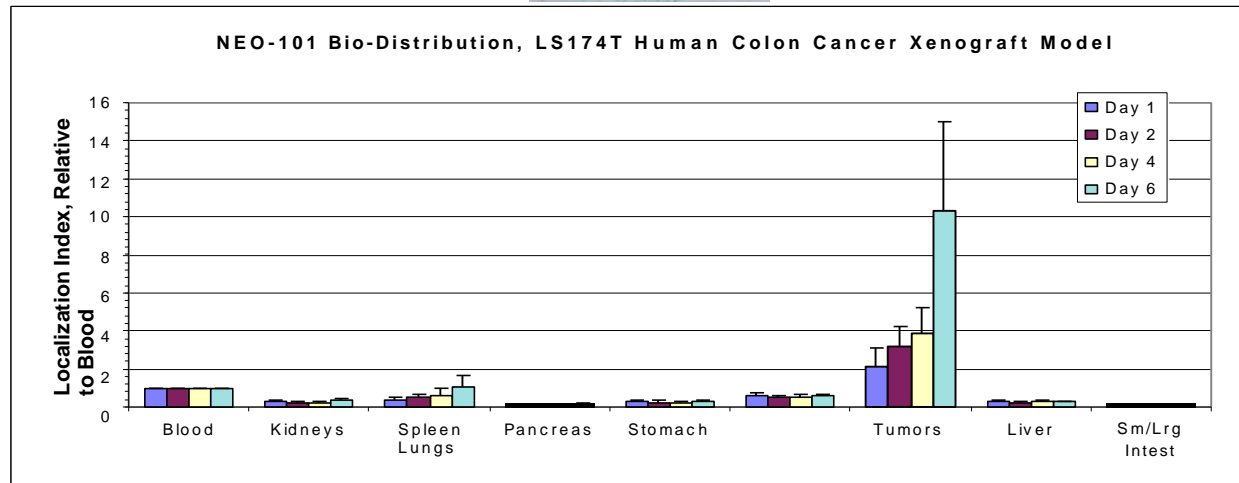
Anti-tumor activity of a novel monoclonal antibody, NEO-102, optimized for recognition of tumor antigen in preclinical models



Cancer Immunol  
Immunother (2013)  
62:1011–1019  
DOI 10.1007/s00262-013-1420-z



A) Normal pancreas  
B) Pancreas adenocarcinoma  
C) Normal Colon  
D) Colon Cancer

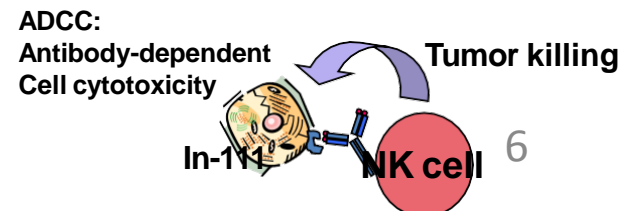


Mice with pre-established human colorectal tumors (LS174T) were injected iv with I-125 labeled NEO-101; mice were sacrificed on the indicated days and radioactivity was measured in selected tissues

# Tumor Cell Killing Activity- Antibody Dependent Cellular Cytotoxicity (ADCC) of (NEO-102)

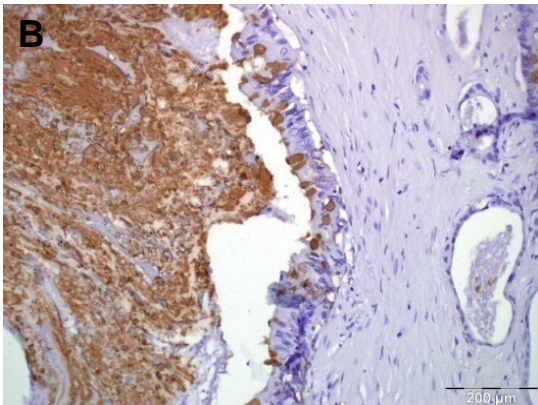
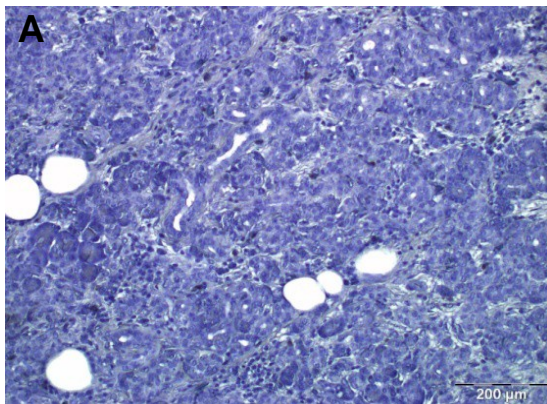
Tumor Cell Line	% Specific Killing ( $\pm$ SEM)		
	Eff/Tar get Ratio	Cont rol mAb	NEO-101
Colo-205 (Colorectal)	50:1	9.8 $\pm$ 1.9	66.7 $\pm$ 0.6
	25:1	0.8 $\pm$ 1.2	46.4 $\pm$ 1.6
	12.5:1	-0.5 $\pm$ 0.1	32.8 $\pm$ 2.0
SW620 (Colorectal)	50:1	1.6 $\pm$ 0.2	63.7 $\pm$ 2.9
	25:1	3.5 $\pm$ 1.8	61.0 $\pm$ 1.8
	12.5:1	0.0 $\pm$ 0.3	51.5 $\pm$ 0.9
SW1463 (Colorectal)	50:1	0.1 $\pm$ 1.1	33.8 $\pm$ 1.0
	25:1	-1.3 $\pm$ 0.2	25.5 $\pm$ 0.6
	12.5:1	-1.2 $\pm$ 0.1	17.9 $\pm$ 1.7
LS174T (Colorectal)	50:1	-1.2 $\pm$ 0.1	26.8 $\pm$ 2.9
	25:1	-0.8 $\pm$ 0.1	18.5 $\pm$ 4.1
	12.5:1	-1.1 $\pm$ 0.0	9.5 $\pm$ 0.5
AsPC-1 (Pancreatic)	50:1	-0.8 $\pm$ 2.9	44.5 $\pm$ 6.8
	25:1	-7.0 $\pm$ 2.2	36.2 $\pm$ 2.6
	12.5:1	-1.2 $\pm$ 0.9	26.5 $\pm$ 6.7

Tumor Cell Line	% Specific Killing ( $\pm$ SEM)		
	Eff/Tar get Ratio	Contr ol mAb	NEO-101
CFPAC-1 (Pancreatic)	50:1	-1.2 $\pm$ 2.3	26.9 $\pm$ 1.6
	25:1	-2.4 $\pm$ 0.1	23.2 $\pm$ 2.2
	12.5:1	-2.0 $\pm$ 0.4	11.1 $\pm$ 1.6
PANC-1 (Pancreatic)	50:1	-2.2 $\pm$ 0.4	46.8 $\pm$ 2.1
	25:1	-2.5 $\pm$ 0.4	33.2 $\pm$ 3.3
	12.5:1	-3.9 $\pm$ 0.3	21.2 $\pm$ 0.6
SK-MEL (Melanoma)	50:1	2.7 $\pm$ 0.7	4.6 $\pm$ 1.1
	25:1	1.5 $\pm$ 0.3	3.3 $\pm$ 1.1
	12.5:1	1.6 $\pm$ 0.4	2.3 $\pm$ 0.6
DU145 (Prostate)	50:1	-0.3 $\pm$ 0.2	-0.5 $\pm$ 0.3
	25:1	-0.7 $\pm$ 0.1	0.3 $\pm$ 0.8
	12.5:1	-0.2 $\pm$ 0.2	-0.3 $\pm$ 0.1

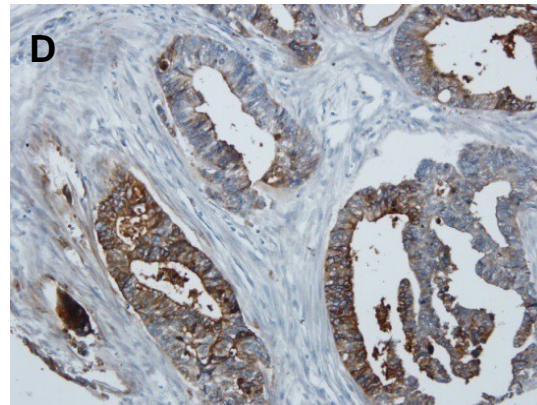
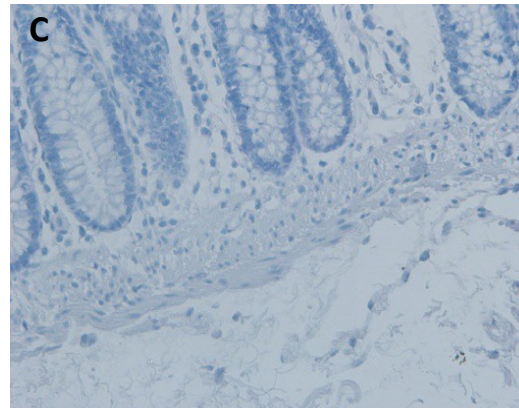


# 1. NPC-1 Antigen and Epitope

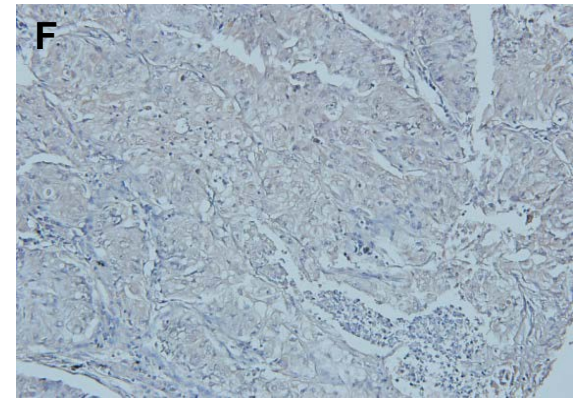
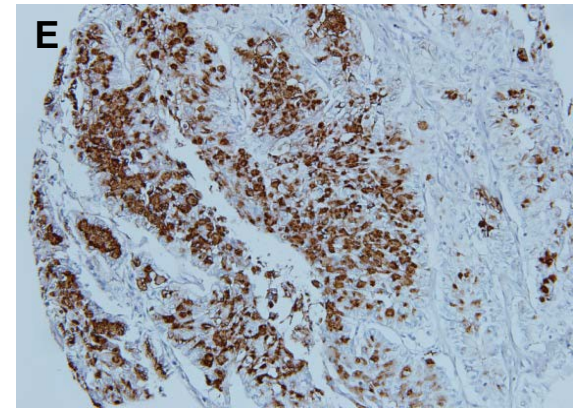
## Tissue-Specific Staining with Ensituximab (NEO-102)



A) Normal pancreas  
B) Pancreas adenocarcinoma



C) Normal Colon  
D) Colon Cancer



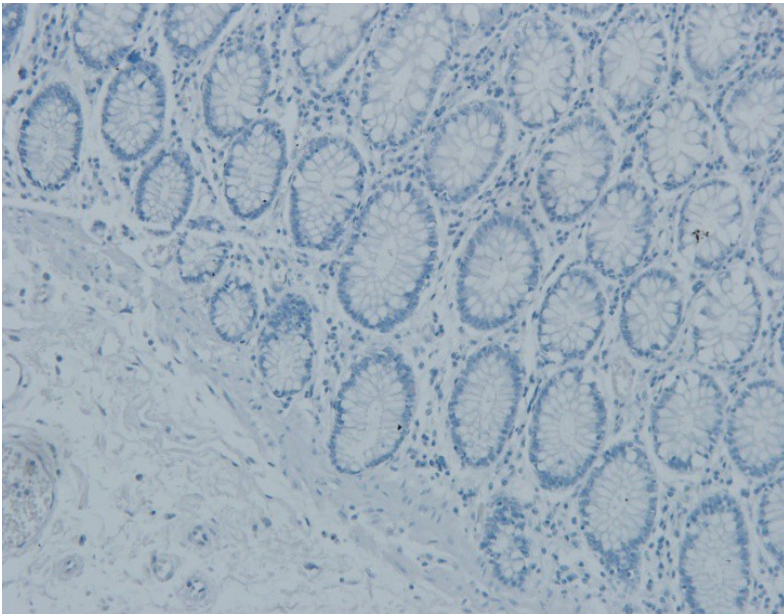
E) Lung Cancer (anti-MUC5AC)  
F) Lung Cancer (NEO-101)



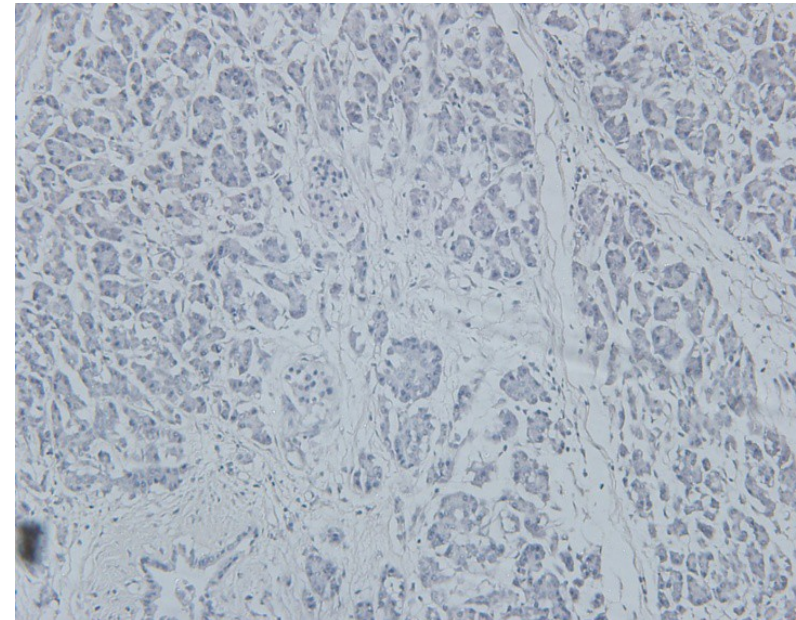
## 2. NPC-1 IHC Results from Normal Tissue

### NPC-1 IHC Staining in Normal Tissue

**Normal colon**

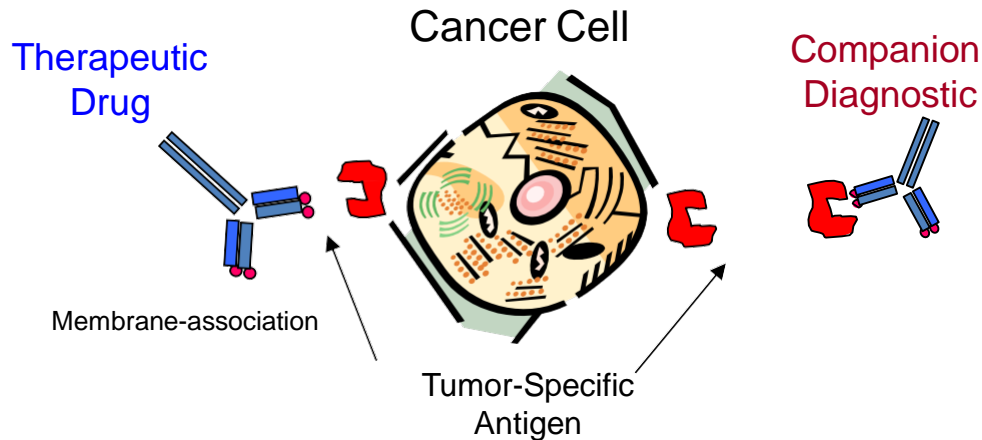


**Normal pancreas**





# Identification Tumor-specific Antigen (TSA) in a Companion Diagnostic



- Tumor-specific antigen detected by companion diagnostic-immunohistochemistry (IHC).
- Herceptin success in breast cancer based on similar concept.
- Companion diagnostic currently used to test formalin-fixed, paraffin embedded (FFPE) tumor tissue to pre-select for clinical trial eligibility.
- Clinical IHC testing is being conducted at the Pathology Department of UT Southwestern, Duke University Medical Center and Johns Hopkins University.
- Eligibility for clinical trial requires IHC staining  $\geq 20\%$  of tissue with at least 2+ intensity positive for NEO-102.
- Pre- IDE held with the FDA in early 2016; Risk Determination submitted 12/2016.

# NEO-102 Monotherapy - Highlights of Clinical Data

- Phase 2a, open label, multicenter clinical trial with NEO-102 for patients with refractory pancreatic or metastatic colorectal cancer (mCRC).
- Primary endpoint- overall survival (OS) will be compared with their respective historical controls to determine if there is improvement in OS with administration of NEO-102.
- FDA recently approved Regorafenib for treatment of 3<sup>rd</sup> line colorectal cancer based on Phase 3 data demonstrating an increase in OS from 5.0 to 6.4 months, despite a significant toxicity profile.
- Literature estimates a 4.5 month median survival with gemcitabine for patients with recurrent or refractory pancreatic cancer.
- Summary of IHC: 382 subjects with mCRC or pancreatic cancer had tumor screened by immunohistochemistry (IHC) for overexpression of NPC-1 (positive results defined as  $\geq 20\%$  tumor cells stain  $\geq 2+$  intensity) .
  - 142 (60%) of 238 patients with mCRC were positive
  - 88 ( 61%) of 144 patients with pancreatic cancer were positive

# NEO-102 Monotherapy - Highlights of Clinical Data for Phase 1/2 Study in Colorectal and Pancreatic Cancer

- During the Phase 1 portion of this study: NEO-102 was administered IV every two weeks X 4 doses (D1, D15, D29, D43) and evaluated D57 (1 course)
  - 3 patients with mCRC at **1.5** mg/kg
  - 1 patient with mCRC and 2 patients with pancreatic cancer at **2** mg/kg
  - 3 patients with mCRC at **3** mg/kg
  - 6 patients with mCRC and 1 patient with pancreatic cancer at **4** mg/kg
    - 2 dose limiting toxicities (DLTs) occurred, grade 3 anemia and grade 3 hyperbilirubinemia
  - Dose de-escalated and 3 additional patients treated at **3** mg/kg with one DLT (grade 3 hypoxia)
- Maximum Tolerated Dose (MTD) established at 3 mg/kg



# NEO-102 Phase 1/2 Monotherapy in Treatment Refractory Colorectal Cancer Patients- Patient Summary

## Phase 1 and 2:

- 63 patients with recurrent or metastatic recurrent colorectal cancer received at least 1 dose of NEO-102
- Gender: 35 male (56%), 28 female (44%)
- Age: range 32-83, median 60 years
- Number of Prior Therapies: range 1-9, average 3.7, **median 4.0**
- Number of doses of NEO-102: range 1 – 16, average 4
- Overall survival (OS) of patients with colorectal cancer enrolled in Phase 1/2 who were evaluable for response (57 patients received  $\geq 2$  doses of NEO-102):
  - ✓ 6.77 months (range 1-30 months after start of therapy)
  - ✓ 15 patients lived greater than 1 year from start of therapy
  - ✓ 3 patients remain alive (20-21 months after start of therapy)

# NEO-102 Monotherapy - Highlights of Clinical Data for Colorectal Cancer

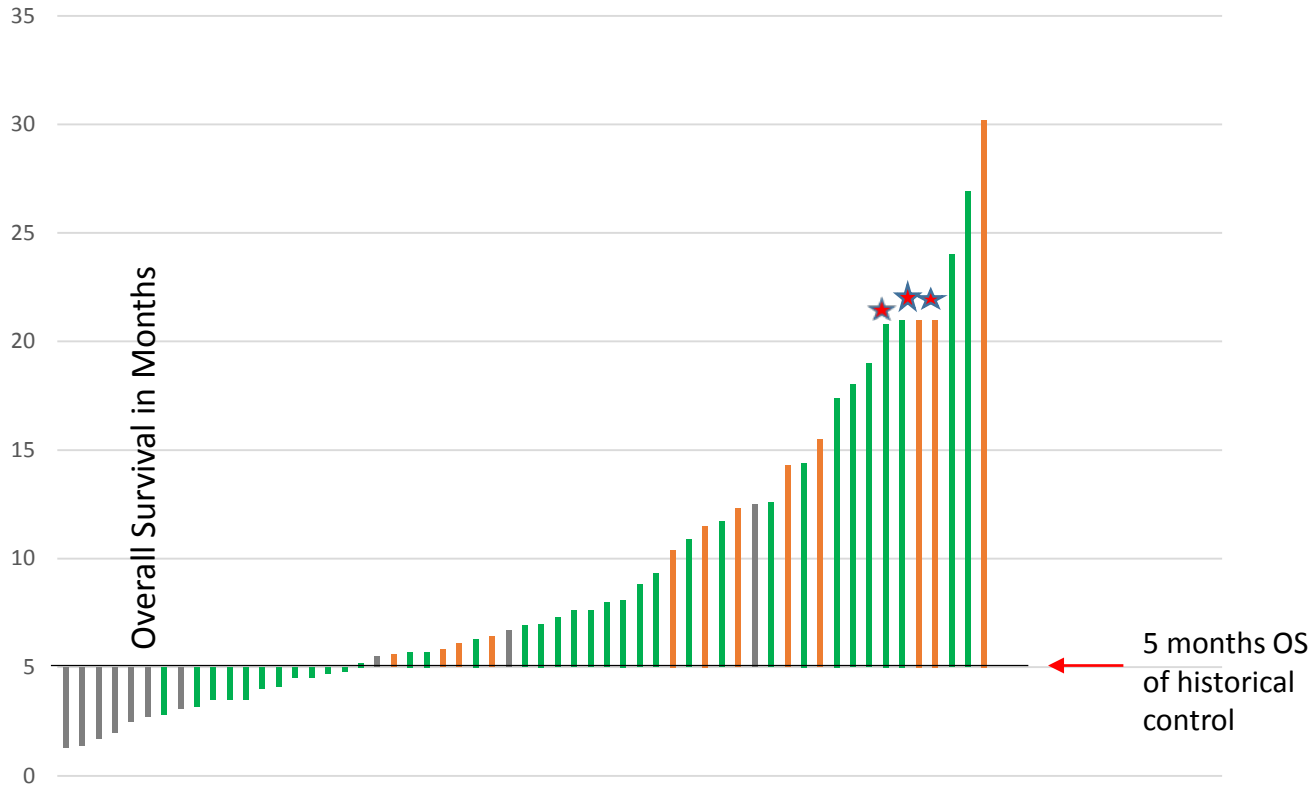
- **Phase 2:** 54 patients with mCRC were enrolled (including 6 from Phase 1)
  - 1 patient withdrew prior to the first dose
  - 53 patients received  $\geq 1$  dose of NEO-102 and were evaluable for toxicity
  - 48 patients received  $\geq 2$  doses of NEO-102 and were evaluable for response and overall survival (OS)
  - 41 patients were evaluated at D57 for response per RECIST
    - ✓ 9/41 (22%) had stable disease (SD) by RECIST at D57.
    - ✓ 7 patients were taken off treatment for other reasons: subject decision, investigator decision, prolonged intercurrent illness
    - ✓ 2 patients were taken off treatment for treatment-related toxicity: 1 for prolonged anemia and 1 for grade 3 hypoxia

# NEO-102 Phase 2 Monotherapy in Treatment Refractory Colorectal Cancer Patients- Patient Summary

- 48 evaluable patients; Gender: 26 male (54%), 22 female (46%)
- Age: range 33-79, median 59 years
- Ethnicity: 32 (67%) Caucasian; 3 (6%) Hispanic; 11 (23%) Black/African Am; 2 (4%) Asian
- Number of Prior Therapies: range 2-9, average 3.7, **median 4**
- 12 of 48 (**25%**) patients in this trial had received prior therapy with Stivarga (regorafenib)
- Number of doses of NEO-102: range 2 – 16, average 3
- Number of subjects removed from therapy for treatment related toxicity: 1 (recovery from anemia delayed >14 days)
- Number of grade 3 / 4 toxicities were limited: anemia (1.3%), hyperbilirubinemia (0.9%), fatigue (0.9%), hemolysis, and nausea, vomiting, headache and hypoxia (0.4 %), respectively.



# Overall Survival of Evaluable Colorectal Cancer Patients ( $\geq 2$ doses of NEO-102) in NEO-0901 Compared with 5 months OS in the CORRECT Study (Grothey, et al. 2013)



█ Not evaluated (ND) at C1D57   
 █ Progressive Disease (PD) at C1D57   
 █ Stable Disease (SD) at C1D57   
 ★ Alive as of October, 2016

# Evaluable Colorectal Cancer Patients in Clinical Study NEO0901

Table sorted by # of Prior Chemotherapies

Patient #	# Prior chemotherapy	Regorafenib (Stivarga)	# NEO-102 doses	RECIST at C1D57	OS months	% of NPC-1C
304	2		3	PD	3.2	25
253	2		4	PD	3.5	50
260	2		4	PD	4.1	30
275	2		7	PD	4.5	80
259	2		4	PD	5.2	100
262	2		8	SD	6.1	25
258	2		4	PD	7.0	25
296	2		4	PD	7.6	40
287	2		4	PD	21+	25
313	2		2	PD	19.0	20
288	2		12	SD	21+	30
285	3		3	ND	1.7	60
249	3		4	PD	4.7	20
276	3		4	PD	6.3	20
284	3		13	SD	6.4	40
239	3		4	PD	7.6	75
280	3		4	PD	8.0	20
303	3		4	PD	8.8	50
243	3		3	ND	12.5	20
298	3		8	SD	14.3	20
316	3	Yes	4	PD	18.0	50
286	3		7	SD	21.0	100
238	3		4	SD	30.2	30

# Evaluable Colorectal Cancer Patients in Clinical Study NEO0901

Patient #	# Prior chemotherapy	Regorafenib (Stivarga)	# NEO-102 doses	RECIST at C1D57	OS months	% of NPC-1C
240	4		2	ND	1.3	90
233	4		2	ND	1.4	60
305	4	Yes	2	ND	2.0	40
256	4		3	ND	2.5	70
266	4	Yes	4	PD	4.0	80
283	4	Yes	9	SD	5.6	90
250	4		4	PD	5.7	40
299	4		8	SD	5.8	40
252	4		2	ND	6.7	75
295	4	Yes	4	PD	9.3	80
302	4		4	PD	10.9	80
230	4	Yes	8	SD	11.5	30
308	4		4	PD	14.4	30
273	4		8	SD	15.5	60
292	4		4	PD	20.8+	50
242	4		4	PD	24.0	40
232	4	Yes	4	PD	26.9	70
241	5	Yes	4	PD	2.8	60
236	5	Yes	2	ND	3.1	40
289	5		3	PD	3.5	25
257	5		4	PD	3.5	30
274	5		3	PD	4.8	30
255	5	Yes	4	PD	6.9	80
231	5		8	SD	12.3	25
294	5	Yes	4	PD	17.4	30
248	6	Yes	3	ND	2.7	80
311	6		4	PD	4.5	20
277	6		4	ND	5.5	40
291	6	Yes	4	PD	5.7	20
267	6		4	PD	7.3	20
282	6	Yes	4	PD	12.6	60
306	7	Yes	4	PD	8.1	40
270	7		4	PD	11.7	50
237	9		4	SD	10.4	100

Table sorted by # of Prior Chemotherapies



**Primary Objective:** Analyze overall survival (OS) of colorectal cancer patients comparing with CORRECT study (5 months OS) using one sample log-rank test

<b>Groups</b>	<b>Updated Median Survival (Months)</b>
1: __NPC_1C_doses>=2 and upcase(Evaluable_Y_N)='Y'	6.77 (5.39, 8.67), $p=0.019$

CRC patients with all dose levels

**Kaplan-Meier Plot for TimeToDeath**

# NEO-102 Combination Therapy for 2nd line Pancreatic Cancer

- Phase 2b, randomized, multicenter clinical trial with NEO-102 for patients with refractory pancreatic cancer.
- Phase 3 Study-FOLFIRINOX vs Gemcitabine showed overall survival (OS) 11.1 months vs 6.8 months (NEJM 2011) as first line therapy.
- Phase 3 Study-Gemcitabine/Abiraxane vs Gemcitabine alone showed OS 8.5 months vs. 6.7 months (NEJM 2013).
- 30% of pancreatic cancer patients in U.S. receive FOLFIRINOX as frontline therapy, and Gemcitabine/Abiraxane as 2<sup>nd</sup> line. Preliminary OS data suggests a median of approximately 5-6 months in 2<sup>nd</sup> line therapy.
- Therefore, 2<sup>nd</sup> line therapy remains an unmet need with a short OS and few ongoing clinical studies in this population.
- Based on preliminary safety data combining Gemcitabine with NEO-102 in this setting, we have an ongoing 90 patient multicenter randomized study using Gemcitabine/Abiraxane vs Gemcitabine/Abiraxane + NEO-102.

# NEO-102 Combination Therapy

- Title: *A multicenter randomized phase II study of NEO-102 in combination with Gemcitabine and Nab-Paclitaxel versus Gemcitabine and Nab-Paclitaxel alone in patients with metastatic or locally advanced pancreatic cancer previously treated with FOLFIRINOX.*
- NCI CRADA covers clinical trial costs at NCI Clinical Center (Bethesda).

Arm	Gemcitabine (mg/m <sup>2</sup> IV on days 1, 8, and 15 of a 28-day cycle)	Nab-paclitaxel (mg/m <sup>2</sup> IV on days 1, 8, and 15 of a 28-day cycle)	NEO-102 (mg/kg IV every other week on days 1 and 15 of a 28- day cycle)**
A (n=45)	1000	125	1.5
B (n=45)	1000	125	No NEO-102

# NEO-102 Combination Therapy

- Enrollment is ongoing
- Total of 75 patients have been enrolled; 38 in Arm A and 37 in Arm B.
- Most common side effects are myelosuppression. No additional side effects reported solely attributable to NEO-102. Doses of gemcitabine and abraxane have frequently been delayed or reduced due to myelosuppression.
- Interim Safety Analysis performed by NCI DSMB in May 2016 showed comparable toxicity in both arms.
- Efficacy and Futility interim analysis by DSMB to be completed by March 2017.

## NEO-102 is well tolerated and convenient for both colorectal and pancreatic cancer patients

- Over 125 patients have been exposed to increasing doses of NEO-102 (ranging from 1.5 mg/kg to 4.0 mg/kg), with or without chemotherapy.
- Infrequent serious adverse events (SAEs) have been reported possibly related to NEO-102 at the MTD of 3.0mg/kg.
- Dose-limiting toxicity in phase 1 was noted at the 4.0 mg/kg dose that included Grade 3 transient hyperbilirubinemia and anemia.
- In Phase 2: It is very well tolerated with no grade 3 myelosuppression, skin rashes, GI, renal or cardiopulmonary toxicity.
- Dosing interval is administered IV every 2 weeks.



# NEO-102 Planned Studies

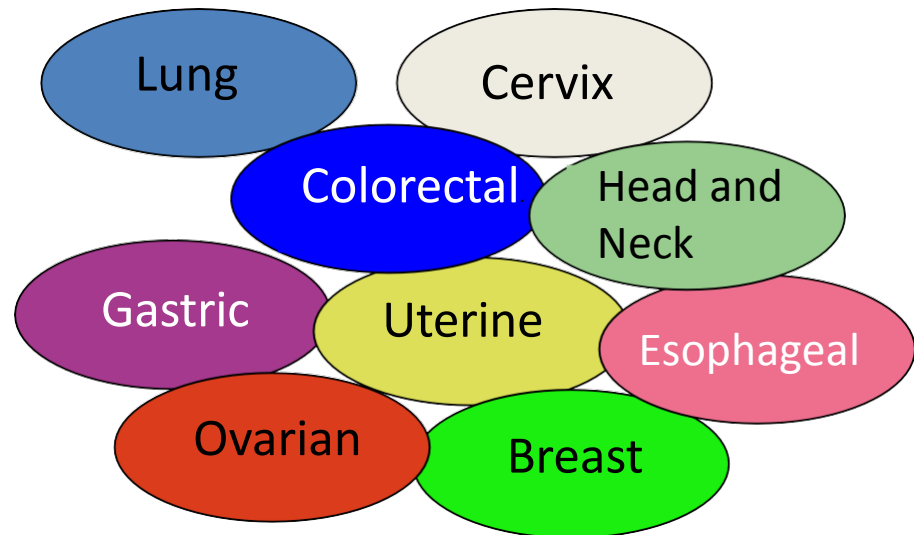
- NEO-102 - patient samples from all clinical trials, pre and post treatment: measure relevant genomic and proteomic targets on patient PBMC.
- NEO-102 in combination with ALT-803 and Ad5-CEA
  - Preclinical testing to include:
    - Cellular immune monitoring assays (phenotype and functional [killing and suppression] assays with NK, Treg and MDSC; CD16 phenotype of NK/haNK cells);
    - Humoral immune monitoring assays (multi-plex cytokine and chemokine analysis; soluble factors such as MICA, arginase, soluble PD-1 and soluble PD-L1 and IDO, *in vivo* assay- HAMA /HACA analysis)
  - Phase IIb/III Clinical Trial
    - Safety evaluation: NEO-102 with ALT-803 followed by NEO-102 with ALT-803 and Ad5-CEA
    - Efficacy: Randomized trial with Immunotherapy versus standard of care (SOC) [LONSURF or Regorafenib] in 3<sup>rd</sup> line metastatic colorectal cancer

# NEO-102 Summary

- Promising Phase I/II results in treatment of chemotherapy refractory colorectal and pancreatic patients in monotherapy clinical trial using NEO-102.
  - **Median OS in monotherapy Phase 1/2a study was 6.7 months for colorectal cancer patients, compares favorably to historical control of OS of 5.0 months.**
- Phase I of both the monotherapy and combination studies was completed in less than anticipated time. Enrollment onto phase II of the monotherapy completed. Since expansion of the combination study to include new collaborators, UNC Chapel Hill, Yale University and Dana Farber Cancer Institute, accrual has been steady in this niche patient population receiving first line FOLFIRINOX.
- IHC companion diagnostic: pre-IDE meeting completed and based on meeting, the IDE FDA submission is set for late 2016.
- Exploring opportunities with new technologies based on NEO-102 such as haNK, antibody drug conjugates (ADC), Bi-specific t-cell engagers (BiTEs) antibody, and other combination therapies.

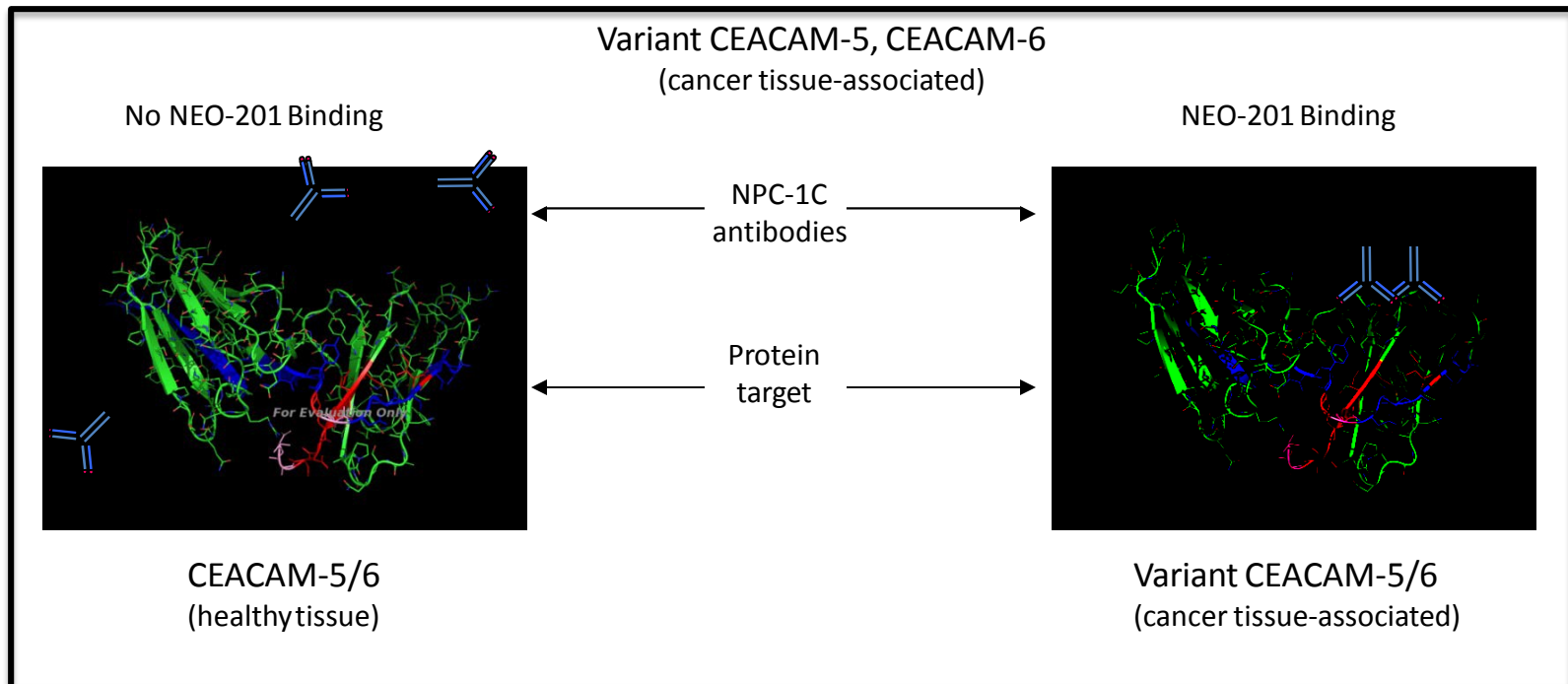
# NEO-201

- Humanized mAb targeting a variant of CEACAM-5/6.
- Target patient population includes GYN, Head and Neck, GI and Lung



- Initial CHO clone development and cell line manufacturing have been completed in collaboration with Catalent Pharma Solutions and Millipore.
- GMP manufacturing underway at Catalent Pharma Solutions
- IND-enabling studies ongoing
- First in human clinical trial anticipated to start Q3 2017

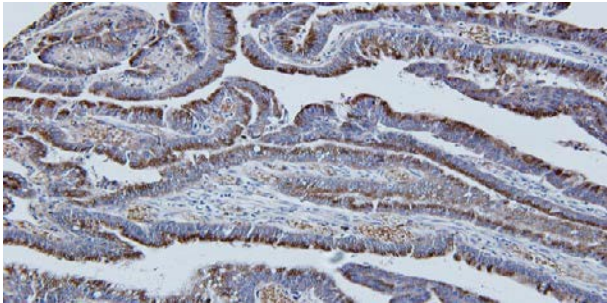
# NEO-201 Target



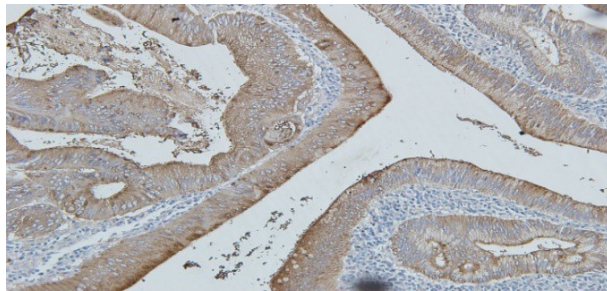
- NEO-201 recognizes tumor-specific variants of CEACAM-5 and CEACAM-6, members of the carcinoembryonic antigen (CEA) family of proteins. These proteins are expressed in normal epithelial tissues, and over-expressed in many solid tumor types (colon, pancreatic, breast, lung, ovarian)
- NEO-201 does not cross-react significantly with healthy tissues that express normal CEACAM-5 or CEACAM-6

# Comparison Binding Specificity of NEO-201 with Commercial CEACAM5/6 Antibodies by IHC

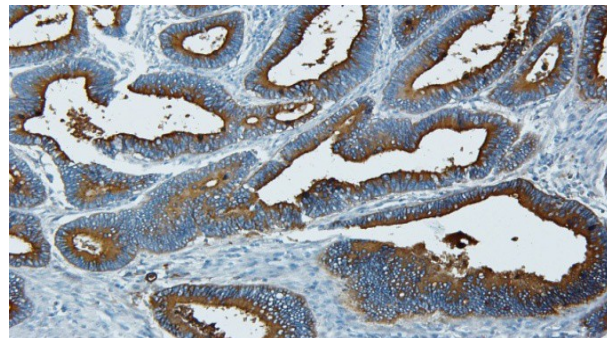
**Colon cancer**



**Anti-CEACAM6  
(9A6 from Cell Signal)**

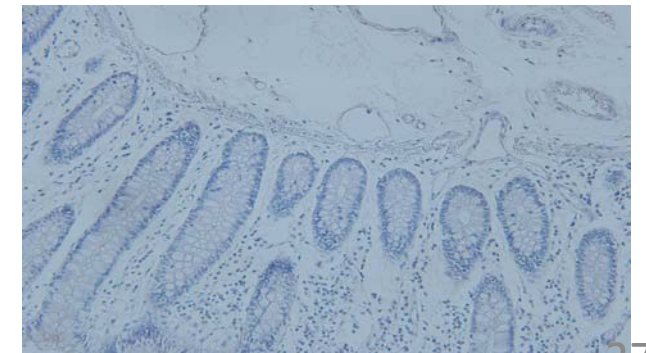
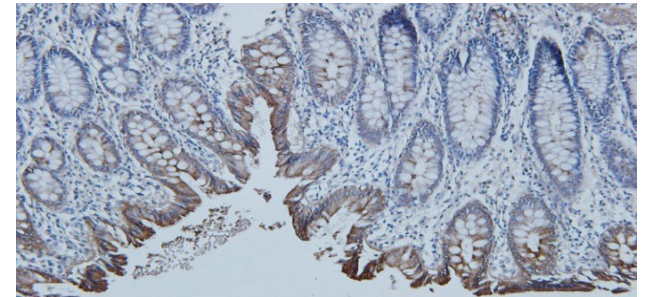
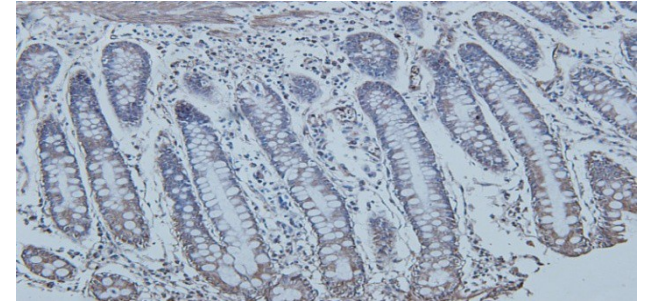


**Anti-CEACAM5  
(CB30 from Abcam)**



**NEO-201**

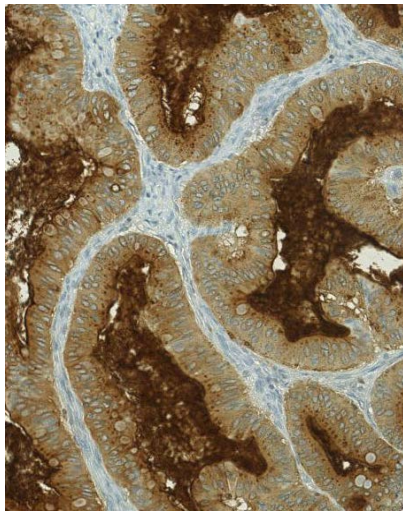
**Normal Colon**



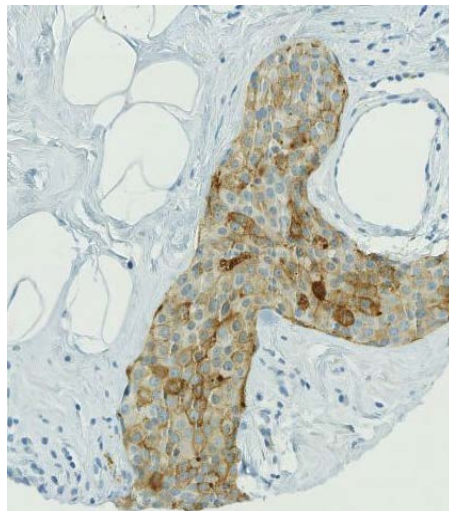


# Collaborative Research Project – Precision Biologics and Christina Annuziata, MD, NCI

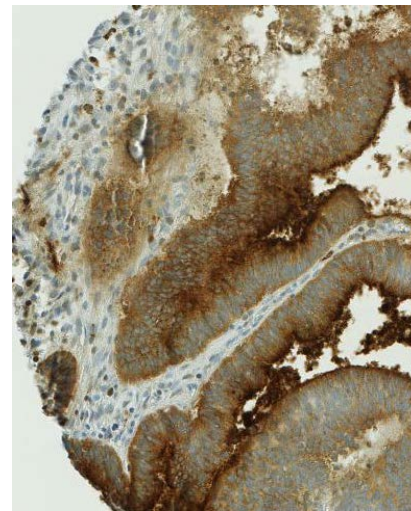
- Binds to tumor-associated antigen
- Minimal binding to healthy tissue



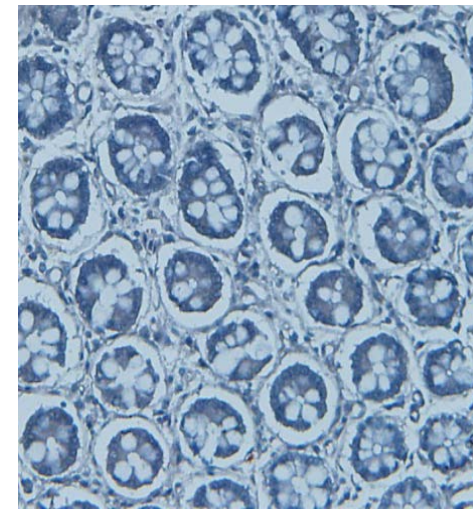
**Ovarian Cancer**



**Breast Cancer**



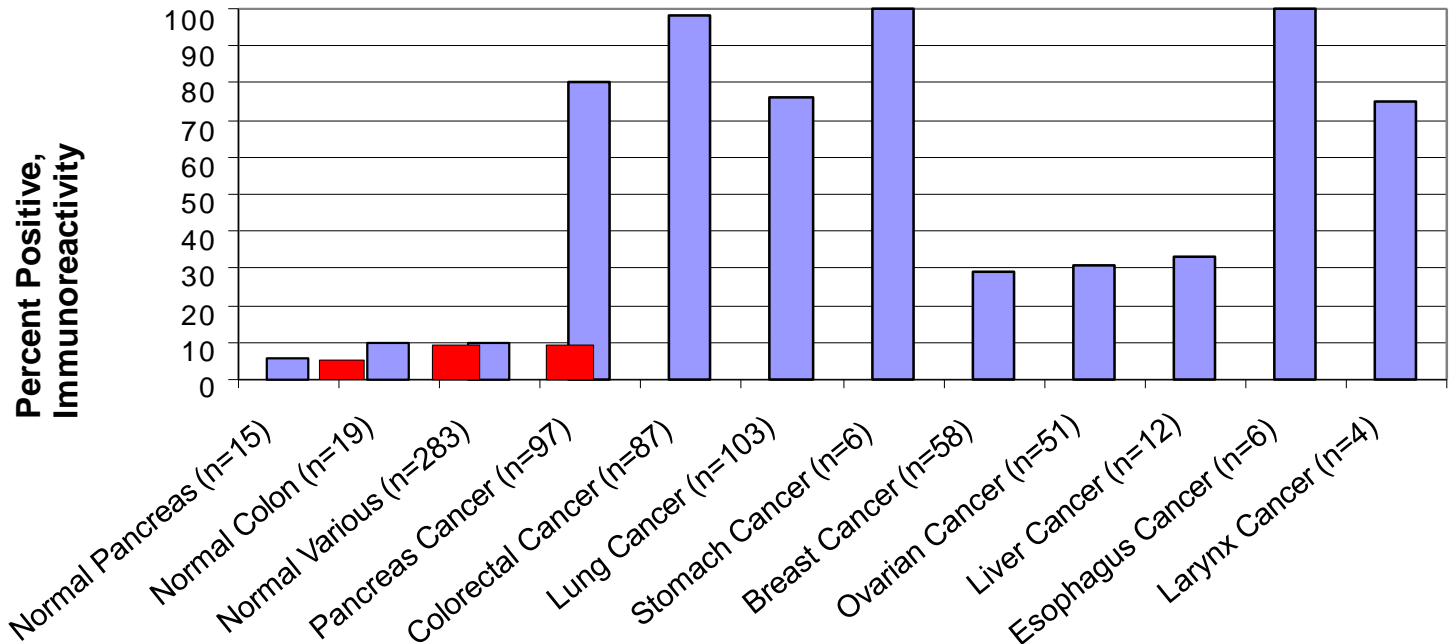
**Colon Cancer**



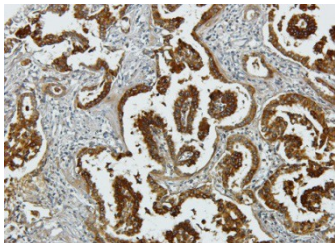
**Normal colon**

# NEO-201 Tumor Tissue-Specific Staining

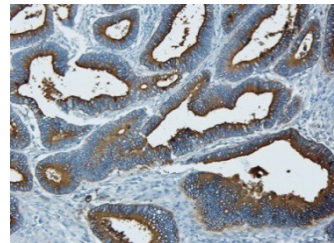
**Preliminary NEO-201 Immunohistochemical Staining Incidence**



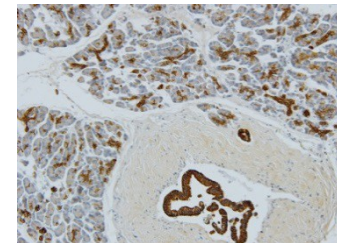
No reactivity in:  
 Melanoma (n=11)  
 GBM (n=7)  
 Lymphoma (n=11)



Lung adenocarcinoma

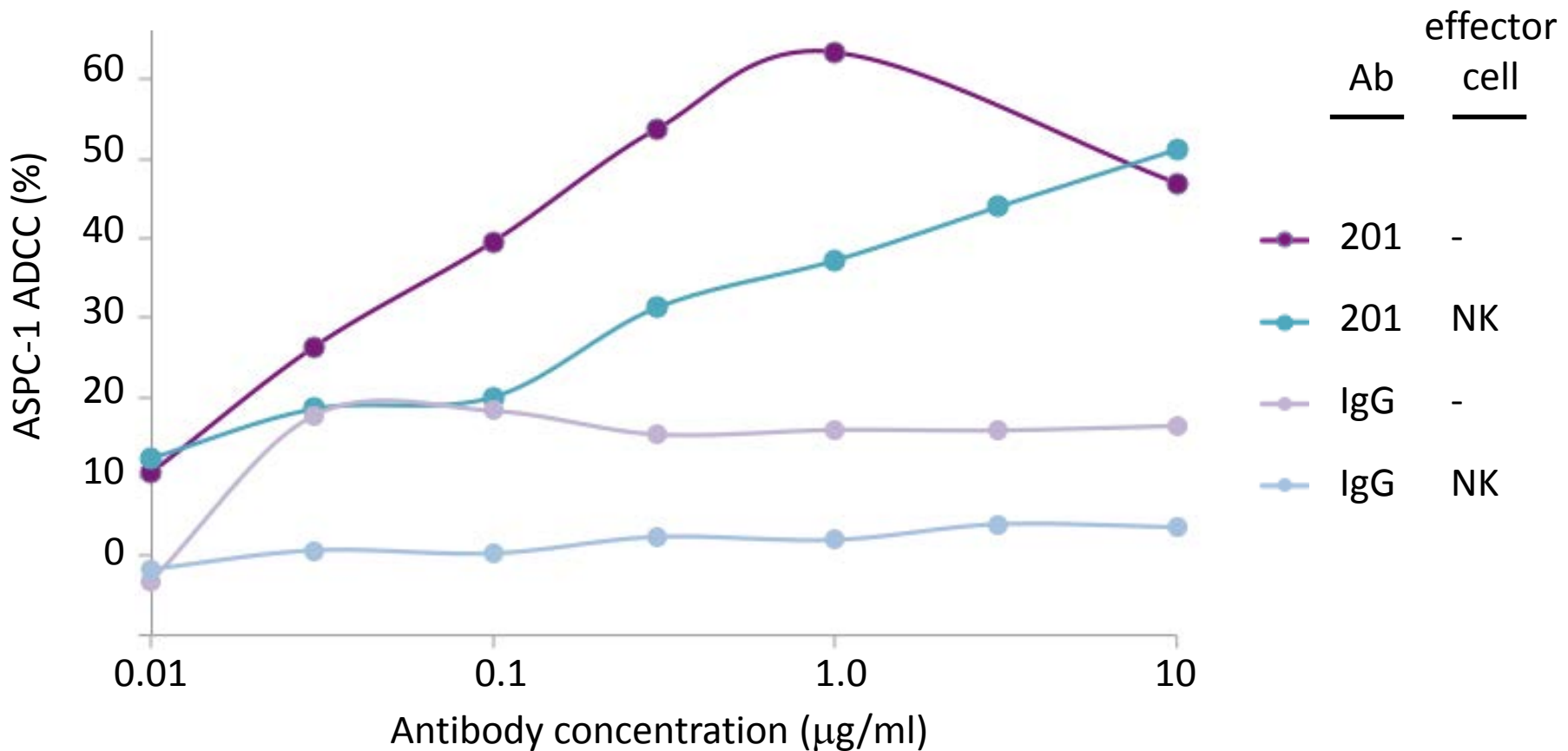


Colon adenocarcinoma

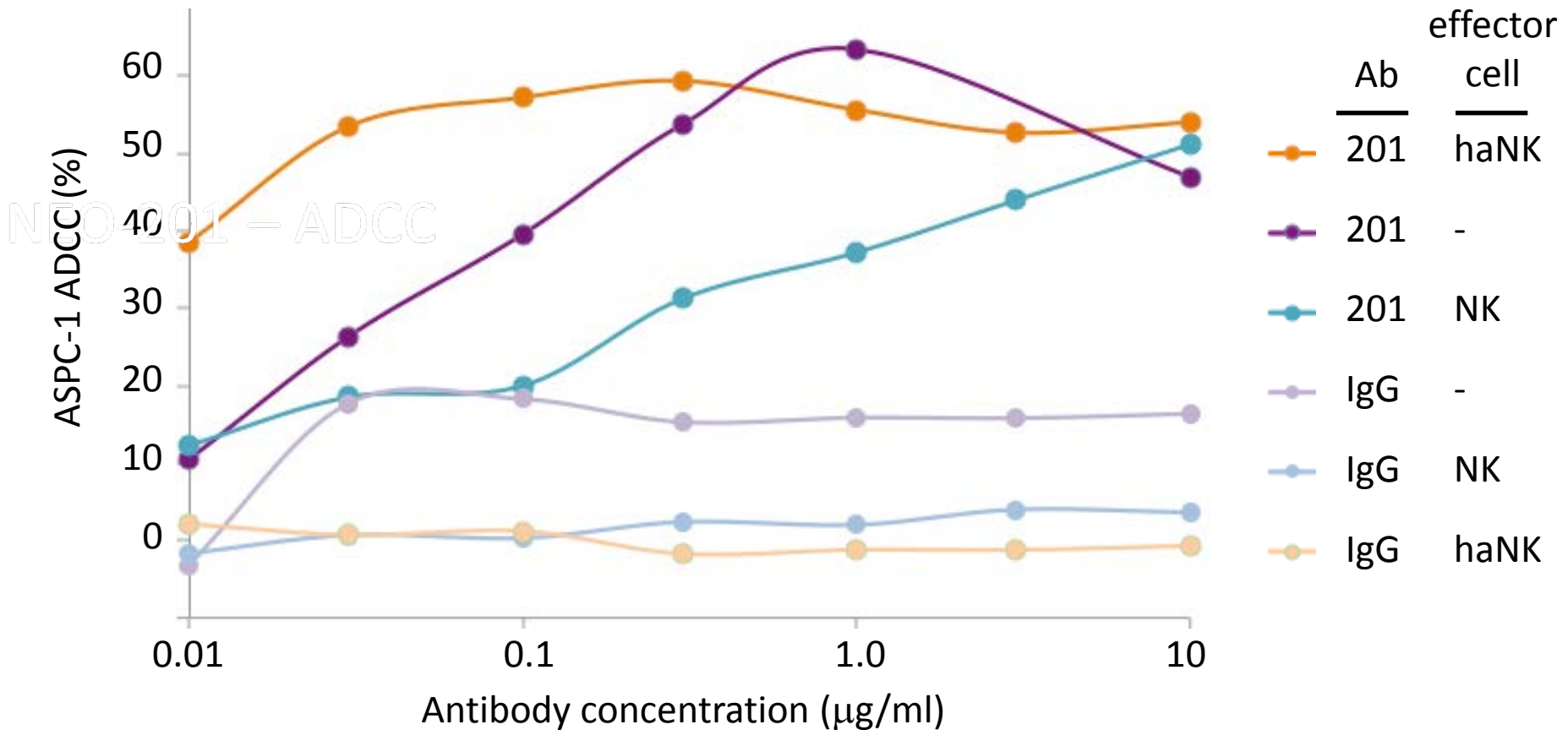


Pancreatic adenocarcinoma

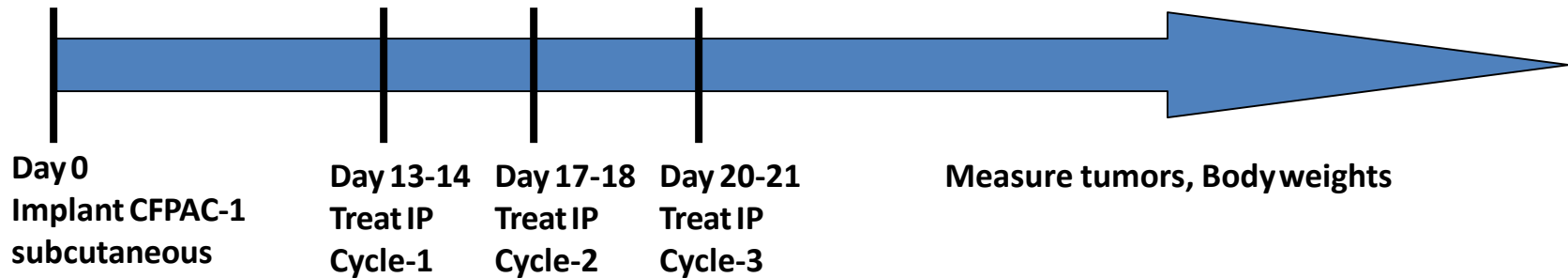
# NEO-201 (h16C3) Anti-tumor Efficacy- ADCC with or without NK using the ASPC-1 human Pancreatic Cancer Cell Line as the Target



# NEO-201 (h16C3) Anti-tumor Efficacy- ADCC with or without NK and haNK using the ASPC-1 human Pancreatic Cancer Cell Line as the Target



# NEO-201 Anti-tumor Efficacy in CFPAC-1 Tumor Xenograft Mouse Model

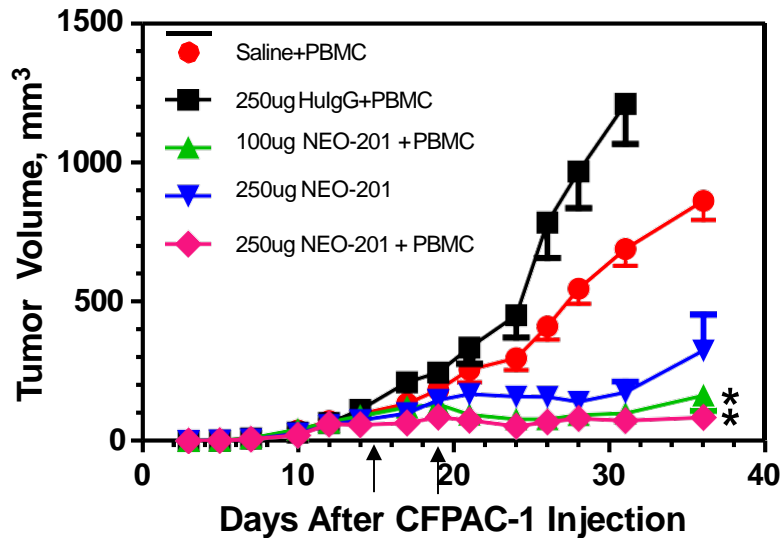


Group (n=10)	Antibody, dose	IL-2 Activated PBMC (NK cells)
1	Saline	$\sim 1 \times 10^7$
2	Human IgG, 250ug	$\sim 1 \times 10^7$
3	h16C3, 100ug	$\sim 1 \times 10^7$
4	h16C3, 250ug	No PBMC
5	h16C3, 250ug	$\sim 1 \times 10^7$



# NEO-201 Anti-tumor Efficacy Results

**NEO-201 Treatment of CFPAC-1 Tumor-Bearing Mice, March 2009**



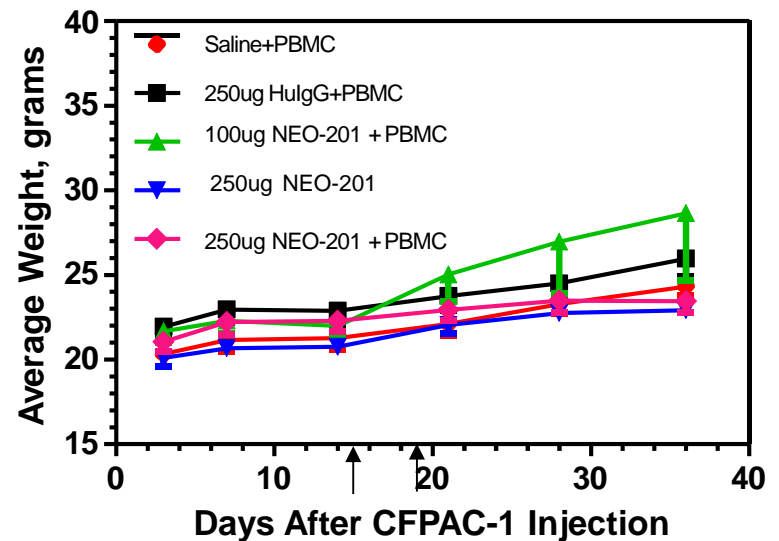
\*, indicates  $p < 0.05$  vs. saline group

NEO-201 injected intraperitoneally on Days 13, 17, 20  
 PBMC injected intraperitoneally on Days 14, 18, 21

On Day 36:

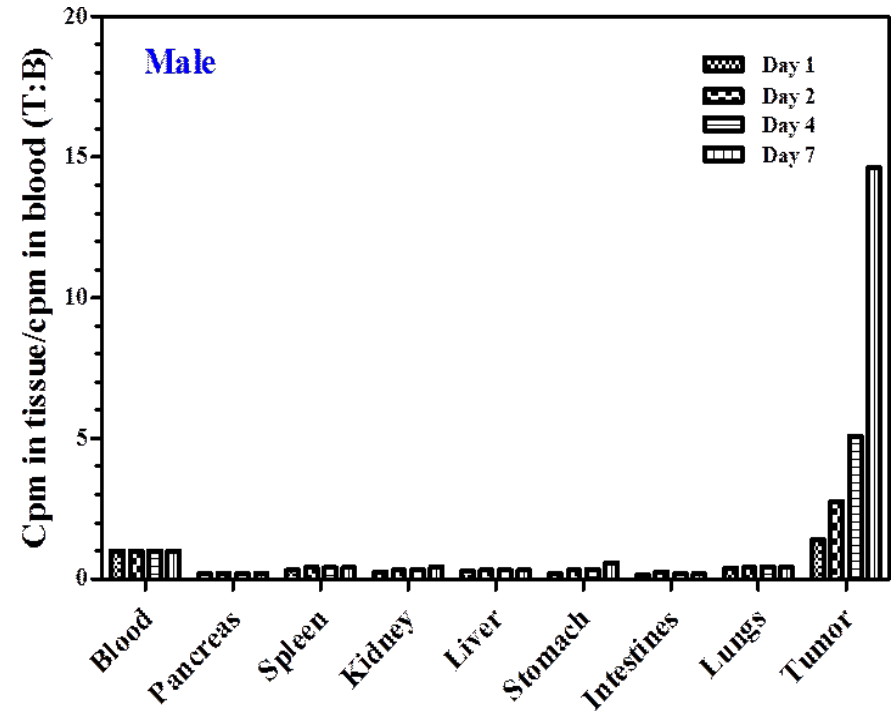
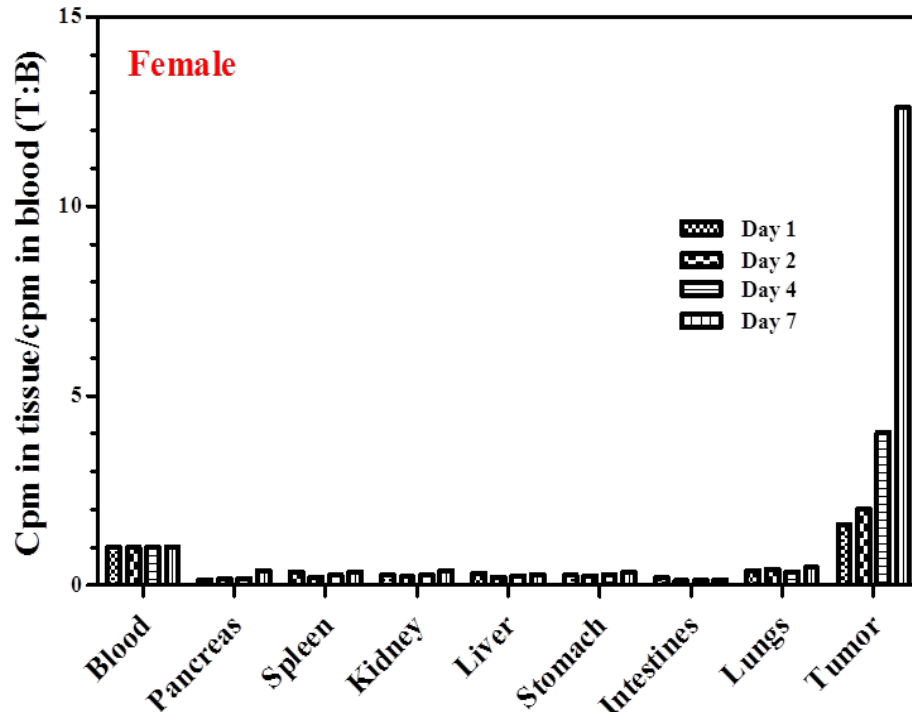
100ug NEO-201+PBMC, 1/10 mice tumor-free  
 250ug NEO-201 +PBMC, 4/10 mice tumor-free

**Body Weights, CFPAC-1 Tumor-Bearing Mice**



NEO-201 injected intraperitoneally on Days 13, 17, 20  
 PBMC injected intraperitoneally on Days 14, 18, 21

# NEO-201 Biodistribution Studies



Biodistribution studies show the distribution of NEO-201 in male and female mice with pre-established CFPAC-1 tumors. The mice were injected via tail vein with 20uCi of [<sup>125</sup>I] labeled NEO-201 monoclonal antibody and necropsied after 1, 2, 4 and 7 days. Blood and tumors were collected. The following organs were removed: lungs, kidneys, liver, spleen, pancreas, intestines, and stomach. All tissues were weighed. Radioactivity in tissues was measured in a gamma counter, and data were calculated as cpm/mg tissue. The data shown above represent the normalization of tissue cpm relative to blood cpm.

# NEO-201 Anti-tumor Efficacy Results

**NEO-201  
treated  
mouse**



**Control/Saline treated  
mice**

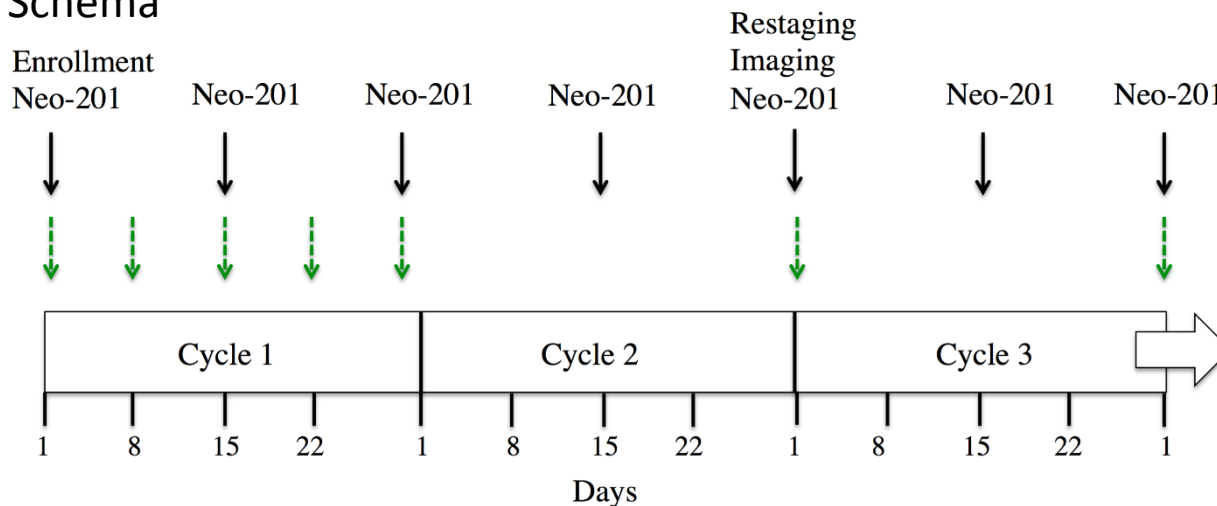
# NEO-201 Summary


- Promising pre-clinical results with complete regression of tumor in animal models.
- Target is broadly expressed in multiple solid tumors.
- Exhibits both immune and direct tumor killing.
- High expression cell line is ready for GMP manufacturing.
- Pre-clinical testing is 12-15 months from FDA IND filing.
- Strong clinical site network to move to Phase I clinical trials using GMP NEO-201.

# NEO-201 Planned Studies

- NEO-201- patient samples from all clinical trials, pre and post treatment: measure relevant genomic and proteomic targets on patient PBMC.
- Phase I first in human study at NCI, open label, dose escalation study to determine safety and recommended phase 2 dose (RP2D) in patients with refractory cancers expressing NEO-201 antigen. RP2D will be explored in expansion cohorts in several targeted disease states at multiple centers.

## Study Schema



 PK lab draws



# NEO-201 Planned Studies

## ➤ Phase I first in human study at NCI:

### ○ Planned doses:

Dose Escalation Schedule	
Dose Level	NEO-201 (mg/kg) *
Level 1	1.5
Level 2	2
Level 3	3
Level 4	4

\* Doses are stated as exact dose in units (e.g., mg/m<sup>2</sup>, mcg/kg, etc.) rather than as a percentage.

### ○ Correlative studies to include:

- Cellular immune monitoring assays (phenotype and functional [killing and suppression] assays with NK, Treg and MDSC; CD16 phenotype of NK/haNK cells);
- Humoral immune monitoring assays (multi-plex cytokine and chemokine analysis; soluble factors such as MICA, arginase, soluble PD-1 and soluble PD-L1 and IDO, *in vivo* assay- HAMA /HACA analysis)

# NEO-201 Planned Studies

## ➤ Future Studies

- Combinatorial approaches with NEO-201 to be determined based on analysis of the Phase 1 study and *in vitro* laboratory tests.

# Summary

- Novel immunotherapy platform utilizing tumor-specific monoclonal antibodies and companion diagnostics.
- Early phase II data in colorectal cancer is strongly suggestive of improved overall survival with well tolerated antibody.
- Precision Biologics has the **only** human tumor derived & human tested antibody platform.
- Future activities:
  - Lead novel antibody (NEO-102 mono and combination therapies) program through end of phase II discussions with the FDA
  - Continued development of novel antibody (NEO-201 and NEO-301) program through phase I development and clinical trials
  - Additional novel antibodies from Hollinshead proprietary platform