Developing mab Therapies From Tumor Neoantigens

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PRECISION BIOLOGICS

October 28, 2021

Forward Looking Statements

Statements in this Presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and clinical development activities, plans and projected timelines, business strategy and plans, regulatory matters, objectives of management for future operations, market size and opportunity, our ability to complete certain milestones and our expectations regarding the relative benefits of our drug candidates versus competitive therapies. Words such as “believe,” “can”, “continue,” “anticipate,” “could,” “estimate,” “plan,” “predict,” “expect,” “intend,” “will,” “may,” “goal,” “upcoming,” “near term”, “milestone”, “potential,” “target” or the negative of these terms or similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation: our preclinical studies and clinical trials may not be successful; regulatory authorities, including the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our drug candidates; we may decide, or regulatory authorities may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our drug candidates, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; our drug candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our drug candidates could delay or prevent regulatory approval or commercialization; the COVID-19 pandemic may disrupt our business and that of third parties on which we depend, including delaying or otherwise disrupting our research and development activities; and we may not be able to obtain additional financing. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this Presentation is given. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

This Presentation discusses drug candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these drug candidates for the use for which such drug candidates are being studied.

Precision Biologics is a Biopharmaceutical Company

with an Enrichment Strategy, Developing

Tumor-Specific Monoclonal Antibodies

to Treat a Broad Variety of Cancers

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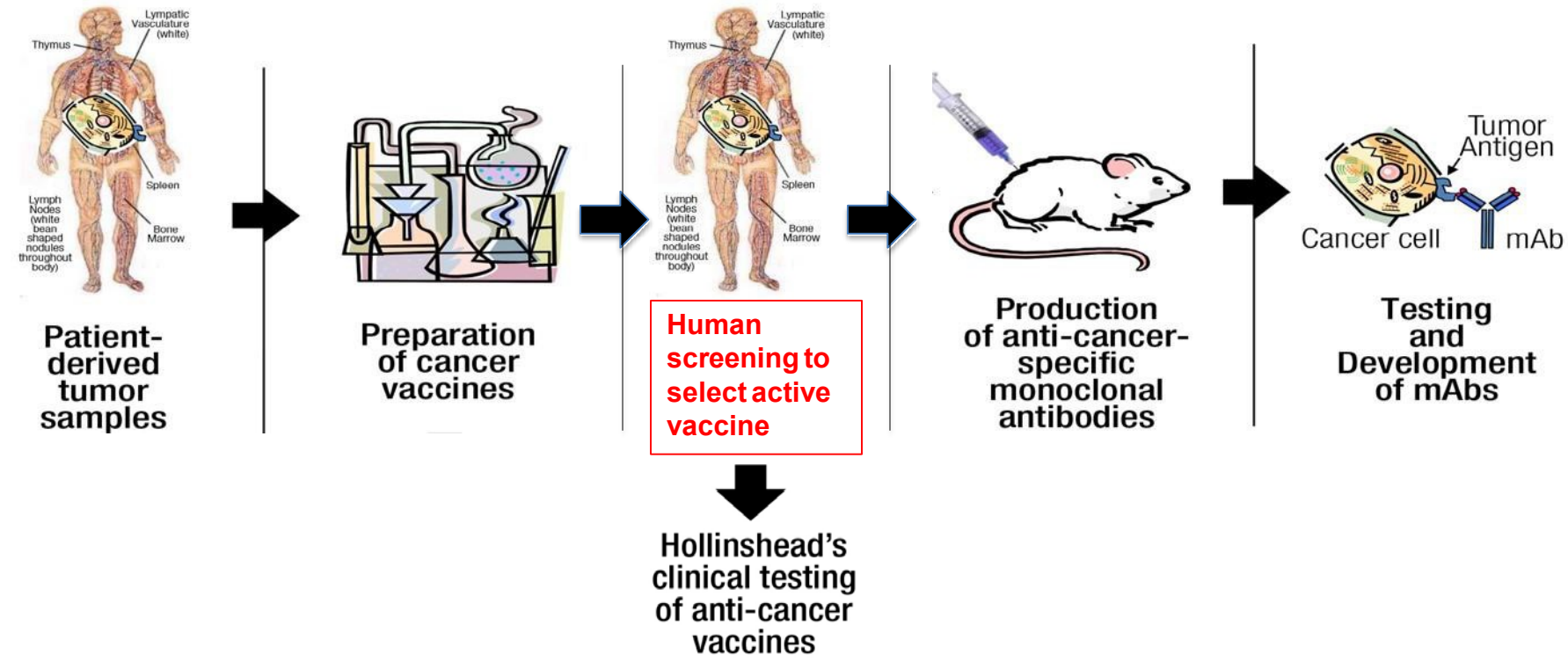
Only Human Derived and Human Tested Neo-Epitope Platform to Create Novel Therapeutics



- Only platform that has discovered functional neo-antigens that have been tested for immunogenic responses
- Validated targets with anti-tumor activity

Precision Biologics Wholly-Owned Oncology Pipeline
Lead Clinical Programs: NEO-201

Product	Indication	Preclinical	Pre-IND / IND	Phase 1	Phase 2	Phase 3
NEO-201	Phase I Solid Tumors					
NEO-201 + Pembrolizumab	2nd line metastatic Non Small Cell Lung Cancer (NSCLC)					
	2nd line metastatic Head and Neck (H&N) cancers					
	2nd line metastatic endometrial cancer					
	2nd line metastatic cervical cancer					
NEO-201 + IL-15	Refractory colorectal, pancreatic & mucinous ovarian cancer					
NEO-201	Blood tumors and Other malignancies (TBD)					

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Precision Biologics Wholly-Owned Oncology Pipeline
Lead Clinical Programs: NEO-102

Product	Indication	Preclinical	Pre-IND / IND	Phase 1	Phase 2	Phase 3
NEO-102	Phase I Solid Tumors					
NEO-102	Phase II 3rd line Colorectal cancer					
NEO-102 + IL-15	3rd line Colorectal cancer					
NEO-102 Antibody Drug Conjugate (ADC)	Refractory metastatic Colorectal and Pancreatic cancer					

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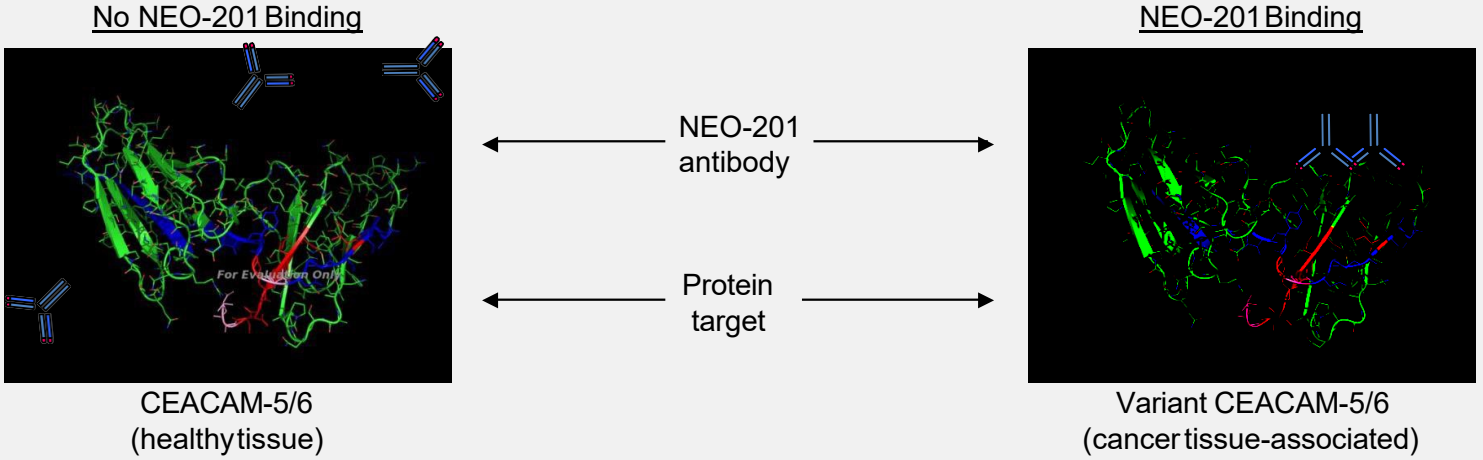
NEO-201 Monoclonal Antibody

Tumor specificity with Multiple Mechanisms of Action

Variant CEACAM-5, CEACAM-6 (cancer tissue-associated)



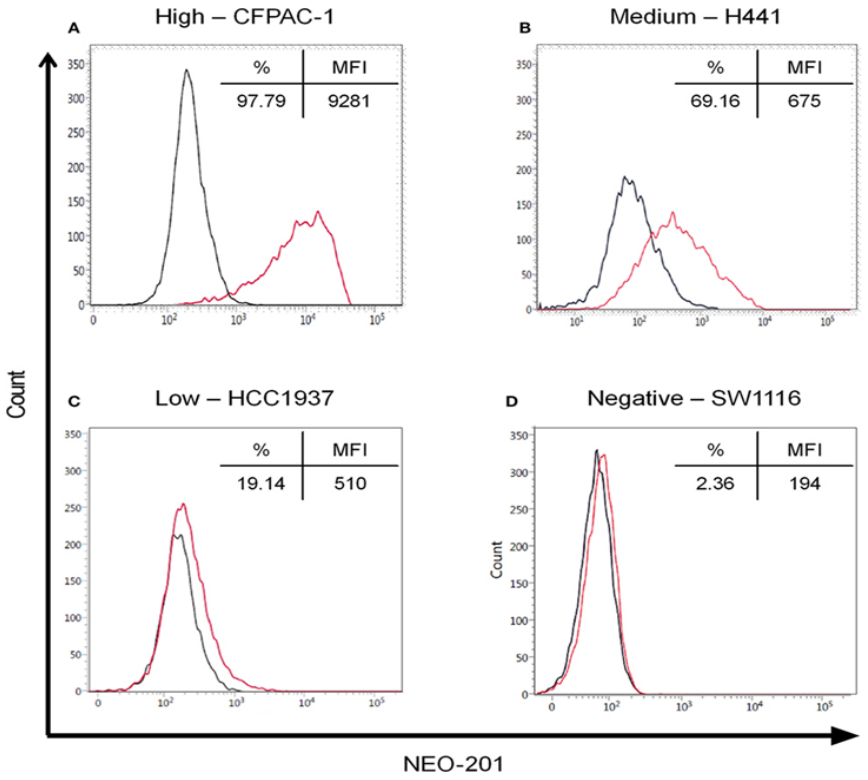
NEO-201: Direct Tumor Killing & Killing Through Immune Enhancement

- Kills target through **Antibody dependent cell-mediated cytotoxicity (ADCC)** and **Complement dependent cytotoxicity (CDC)** unlike other CEA antibodies
- Recognizes tumor-specific variants of CEACAM-5 and CEACAM-6,
- Does not cross-react significantly with healthy epithelial tissues that express normal CEACAM-5 or CEACAM-6
- Enhanced NK tumor killing through CEACAM5/CEACAM1 blockade
- Binding and killing of human regulatory T cells (Tregs) – supporting combination therapy with checkpoint therapy

NEO-201 Binds to Various Human Carcinoma Cell Lines

Flow cytometry analysis of NEO-201 binding to tumor cell lines derived from various types of solid tumors

CELL LINE	TUMOR TYPE	% POSITIVE	MFI
COLO 205	**Colon**	**10.33**	**245**
HT-29	**Colon**	**38.40**	**352**
LS174T	**Colon**	**46.46**	**345**
SW1116	Colon	2.36	194
SW1463	Colon	1.23	278
SW480	Colon	1.70	575
ASPC-1	**Pancreatic**	**79.26**	**8927**
BxPC-3	**Pancreatic**	**97.25**	**2584**
CAPAN-2	**Pancreatic**	**29.69**	**327**
CFPAC-1	**Pancreatic**	**97.79**	**9281**
PANC-1	Pancreatic	3.29	289
H441	**NSCLC (adenocarcinoma)**	**69.16**	**675**
H522	NSCLC (adenocarcinoma)	1.38	238
HCC4006	**NSCLC (adenocarcinoma)**	**99.27**	**9899**
HCC827	**NSCLC (adenocarcinoma)**	**77.46**	**692**
SK-LU-1	NSCLC (adenocarcinoma)	1.77	685
CALU-1	NSCLC (squamous)	4.22	571
H1703	NSCLC (squamous)	4.16	111
H226	NSCLC (squamous)	4.83	209
H520	**NSCLC (squamous)**	**61.78**	**443**
AU-565	**Breast (HER2+)**	**50.04**	**227**
BT-474	**Breast (PR+/HER2+)**	**68.79**	**591**
HCC1500	Breast (ER+/PR+)	1.53	597
SK-BR-3	Breast (HER2+)	1.61	329
T-47D	Breast (ER+/PR+)	8.00	161
ZR-75-1	**Breast (ER+/PR+/HER2+)**	**68.80**	**550**
BT-549	Breast (ER-/PR-/HER2-)	1.47	477
HCC1937	**Breast (ER-/PR-/HER2-)**	**19.14**	**510**
HCC38	Breast (ER-/PR-/HER2-)	2.15	226
MDA-MB-468	Breast (ER-/PR-/HER2-)	6.33	344



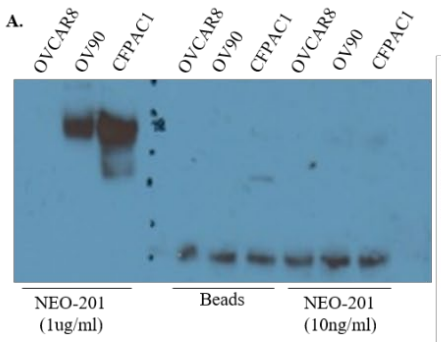
NEO-201 positive cell lines appear in bold text.

NEO-201 positivity was defined as % positive >10%

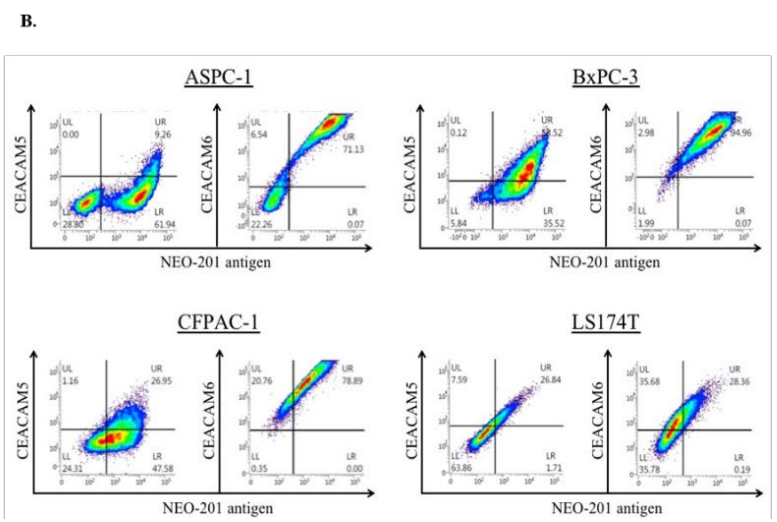
Fantini *et al.* ***Frontiers in Immunology*, 2018**

Positivity was determined using fluorescence minus one (FMO) controls. Positive cell lines were ranked according to their quantified expression level (% positive × MFI), and then sorted into groups of low (<200), medium (200-1000), and high (<1000) expression

NEO-201 Binds to a Tumor Associated Form of CEACAM-5 and -6



PEPTIDE	CFPAC1	OV90	#AAs	MW	Calc pi
CEACAM-6	4	3	344	37.2	5.82
CEACAM-5	1	2	702	76.7	5.69
CEACAM-7	1	2	265	29.4	5.54



CELL LINE (CANCER TYPE)	MARKER	% POSITIVE	MFI
ASPC-1 (pancreas)	NEO-201	**75.86**	**9,078**
	CEACAM5	20.04	869
	CEACAM6	**77.87**	**52,138**
BxPC-3 (pancreas)	NEO-201	**97.41**	**5,259**
	CEACAM5	**79.54**	**711**
	CEACAM6	**98.45**	**18,690**
CFPAC-1 (pancreas)	NEO-201	**85.21**	**1,728**
	CEACAM5	25.83	1,108
	CEACAM6	**96.50**	**27,792**
LS174T (colon)	NEO-201	29.15	858
	CEACAM5	36.34	1,030
	CEACAM6	**63.41**	**1.462**

From these screening the Carcinoembryonic Antigen-Related Cell Adhesion Molecule (CEACAM)5, also known as CEA, and CEACAM 6 were identified as the most likely targets of NEO-201

***Zeligs** et al. **Frontiers in Oncology**, 2020*

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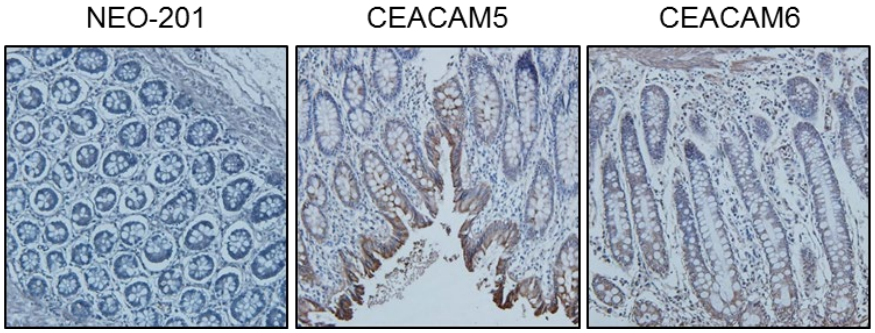
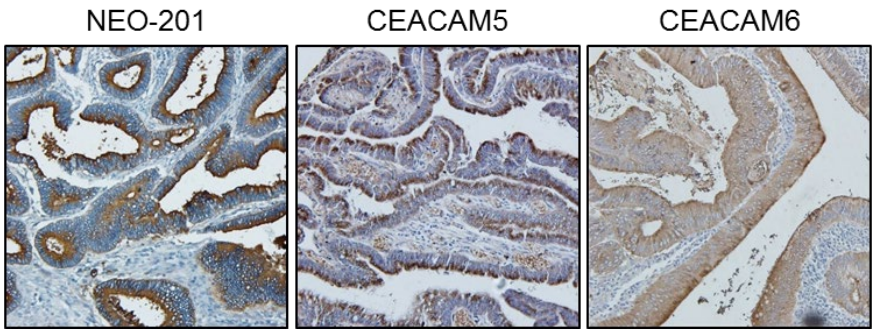
IHC Confirmed that NEO-201 Reactivity is Specifically Tumor-Associated

Normal Colon Tissue



Tumor Tissue



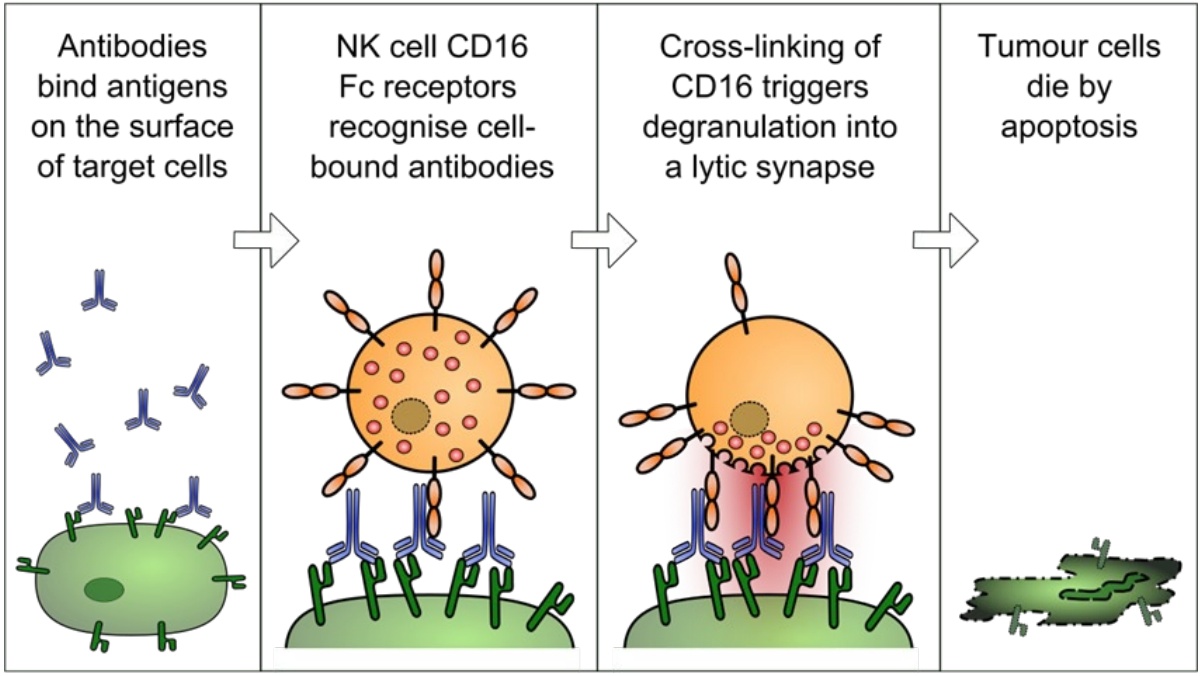
- NEO-201 does not react against normal epithelial tissue CEACAM5/6 positive.
  - Majority of normal tissues stained CEACAM5$^+$ and/or CEACAM6$^+$
  - Colon (29/31, 94%), pancreatic (26/28, 93%), lung (30/32, 94%)

- NEO-201 reacts against tumor tissue CEACAM5/6 positive.
  - Majority of sampled tumors stained “triple positive” – NEO-201$^+$ CEACAM5$^+$ CEACAM6$^+$
  - Colon (28/32, 88%), pancreatic (23/30, 77%), lung (16/32, 50%)

MECHANISMS OF ACTION OF NEO-201

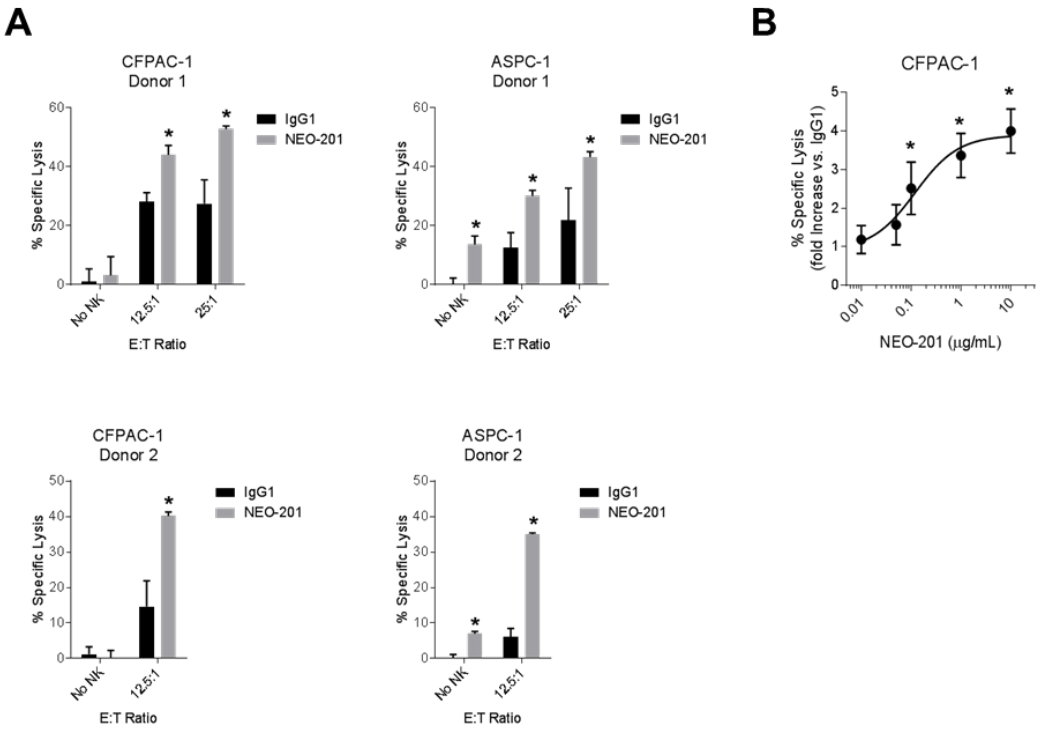
Mechanisms of Action

1) NEO-201 mediates Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) against human tumor cell lines



https://www.genscript.com/ADCC-and-CDC-assay-services.html

NEO-201 Mediates ADCC Against Human Pancreatic Tumor Cell Lines

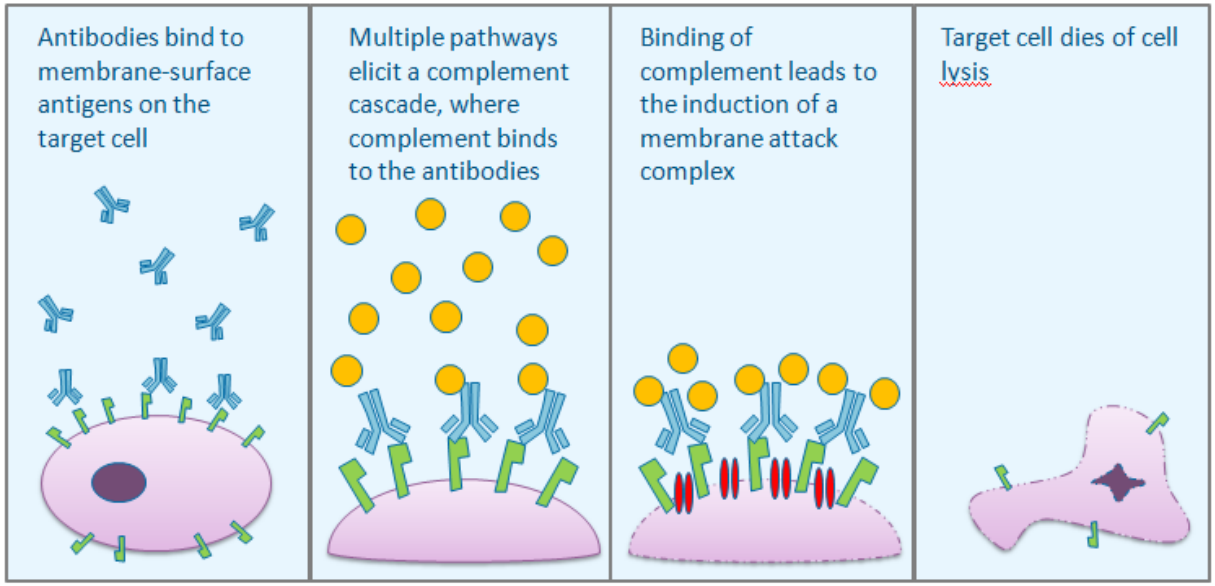


- (**A**) ADCC activity using CFPAC-1 or ASPC-1 cells as target cells. Cells were treated with 10µg/mL of NEO-201 or human IgG1 (negative control). Purified NK cells from two healthy donors were used as effector cells at the indicated E:T ratios. (**B**) ADCC assay using CFPAC-1 cells treated with increasing doses of NEO-201. NK cells were used at an E:T ratio of 12.5:1.
- * statistically significant ($p < 0.05$) by T-test.

Fantini *et al.* ***Frontiers in Immunology*, 2018**

Mechanisms of Action

2) NEO-201 Mediates Complement-Dependent Cytotoxicity (CDC) Against Human Tumor Cell Lines



https://www.genscript.com/ADCC-and-CDC-assay-services.html

NEO-201 Mediates CDC Against Human Tumor Cell Lines

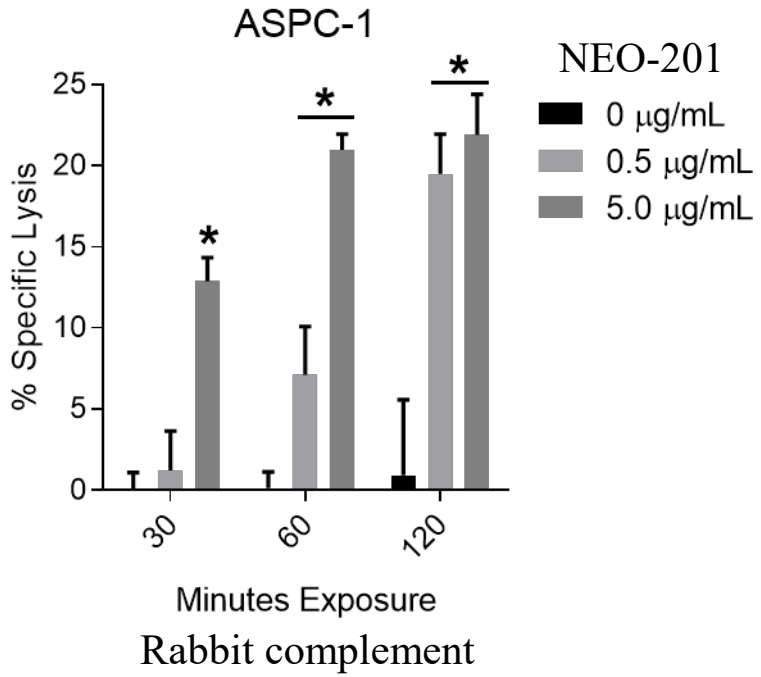
Target cells: ASPC-1

↓

Target cells treated with NEO-201 (0.5 and 5µg/mL) for 15 minutes (OSPONIZATION)

↓

Rabbit complement (1:8) for 30, 60, 120 minutes

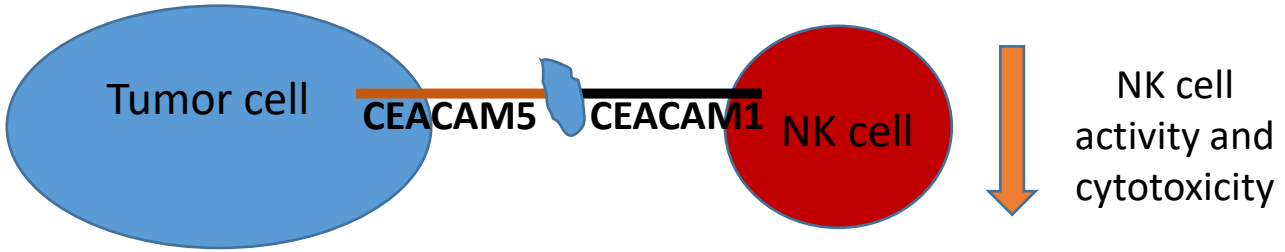


- CDC assay using ASPC-1 cells treated with rabbit complement (1:8 dilution) and the indicated doses of NEO-201 for the indicated durations.
- * statistically significant ($p < 0.05$) by T-test.

Fantini *et al.* ***Frontiers in Immunology*, 2018**

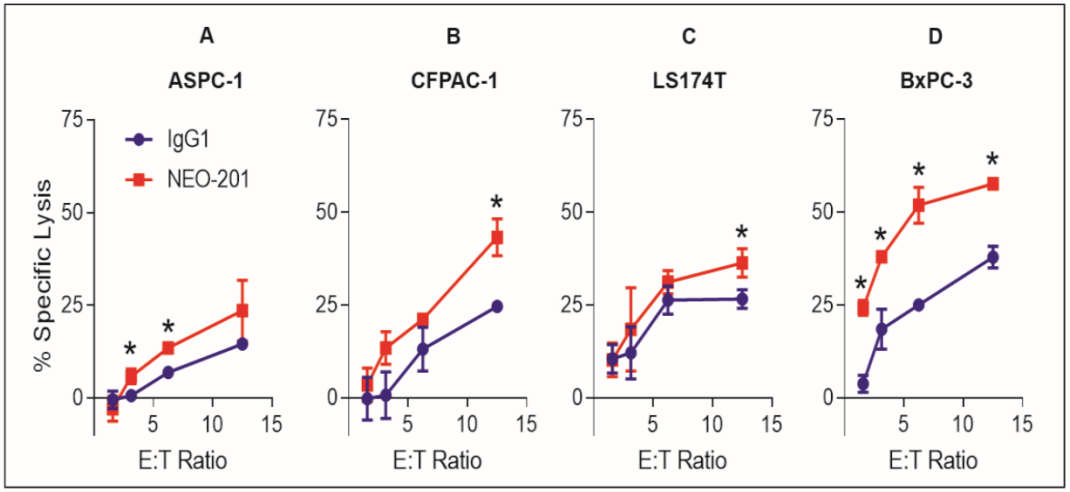
Mechanisms of Action

3) NEO-201 Enhances Natural Killer Cell Cytotoxicity Against Tumor Cells Through Blockade of the Inhibitory CEACAM5/CEACAM1 Immune Checkpoint Pathway



NEO-201 Enhances NK-92 Cell Cytotoxicity Against CEACAM5+/NEO-201+ Tumor Cells

Cell line	CEACAM1$^+$	CEACAM5$^+$/NEO-201$^+$
	% positive (MFI)	
ASPC-1	**61.15** (707)	9.26 (869/9,078)
BxPC-3	2.45 (1,471)	**58.52** (1,447/6,420)
CFPAC-1	**18.67** (1,938)	**26.95** (1,108/1,728)
LS174T	2.43 (3,287)	**26.84** (1,030/858)

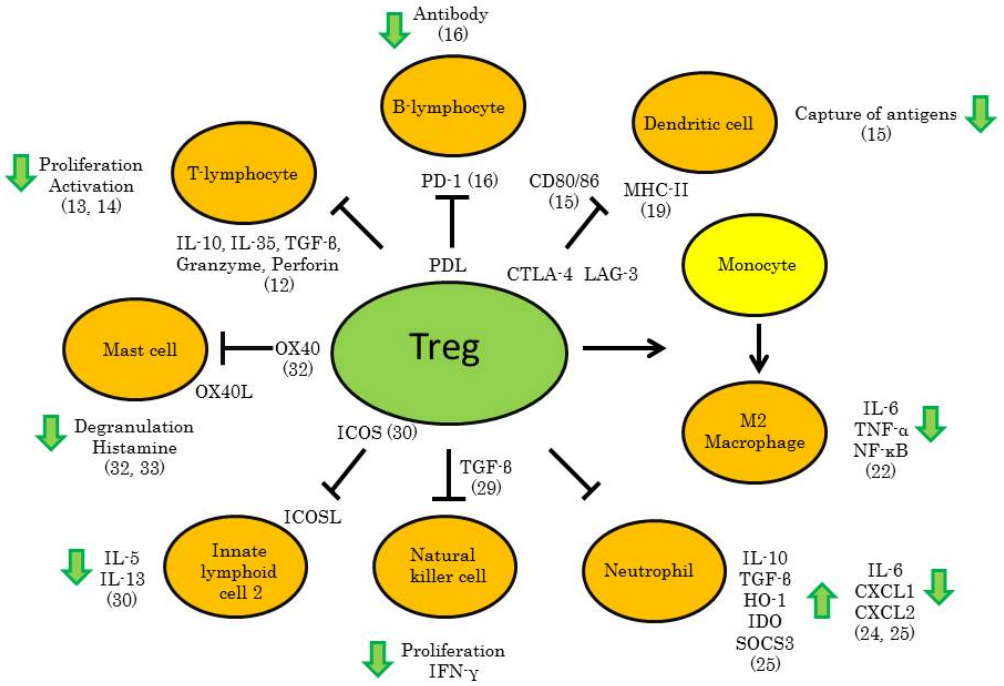


The addition of NEO-201 resulted in a **greater enhancement of NK-92 killing at all E:T ratio only against BxPC-3 cell line** (high CEACAM5$^+$/NEO-201$^+$ /CEACAM1$^-$), while in in both CFPAC-1 (low CEACAM1/ low CEACAM5$^+$/NEO-201$^+$) and LS174T (low CEACAM5$^+$/NEO-201$^+$/CEACAM1$^-$) cell lines, the addition of NEO-201 enhanced NK-92 killing only at the highest E:T ratio (12.5:1).

Fantini *et al.* ***Cancer Biother Radiopharm*, 2020**

Mechanisms of Action

4) NEO-201 Targets and Eliminates Human Immunosuppressive Regulatory T cells



- Foxp3-expressing Treg cells can suppress the activation of T cells, the function of NK, neutrophils, dendritic cells, monocytes and macrophages in the tumor microenvironment (TME).
- Depletion of Treg cells is an effective strategy to enhance the anti-tumor immunity

Seike M. ***J Dermatological Research*****, 2019**

NEO-201 targets human immunosuppressive Tregs: comparison between healthy donors and cancer patients

	CD4+/NEO-201+	CD25+/CD127-	Foxp3+ /CD15s+	Foxp3+ /CD15s-
Healthy donor #	% positive (MFI)	% positive (MFI)	% positive (MFI)	% positive (MFI)
1	**3.54** (2,444/889)	**97.22** (1,054/82)	**5.00** (2,236/1,180)	**84.64** (1,895/229)
2	**2.75** (3,222/2,691)	**99.33** (2,324/109)	**5.39** (3,746/1,617)	**94.61** (3,600/709)
3	**2.71** (248/532)	**96.73** (415/109)	**4.22** (293/1,323)	**88.19** (271/893)
4	**2.55** (255/428)	**98.61** (765/99)	**14.55** (443/2,477)	**80.28** (364/1,089)
5	**1.85** (193/375)	**96.35** (3,705/98)	**37.12** (545/3,986)	**49.24** (484/1,252)
6	**1.73** (3,183/1,437)	**88.82** (1,152/79)	**72.22** (5,179/2,277)	**27.78** (2,786/231)
Average	**2.52** (1,591/1,059)	**96.18** (1,569/96)	**23.08** (2,074/2,143)	**70.71** (1,567/553)
Cancer patient #	% positive (MFI)	% positive (MFI)	% positive (MFI)	% positive (MFI)
1	**4.80** (355/747)	**94.35** (1,359/260)	**61.25** (1,993/818)	**34.11** (1,851/220)
2	**3.74** (404/2,136)	**94.19** (1,244/371)	**78.63** (907/885)	**18.80** (807/316)
3	**4.83** (924/266)	**94.56** (221/194)	**85.38** (4,072/1,726)	**11.46** (3,542/446)
4	**2.38** (3,699/1,067)	**92.72** (839/159)	**61.57** (2,716/2,513)	**34.71** (2,394/1,151)
5	**5.66** (1,589/672)	**92,67** (970/158)	**84.85** (2,297/1,113)	**14.14** (2,308/438)
Average	***4.28** (1,394/978)	**93.70** (927/228)	**#74.33** (2,397/1,411)	**22.64** (2,180/553)

The percentage of **CD4+/NEO-201+ cells** in PBMCs from cancer patients as compared to healthy donors is significantly higher (4.28% vs 2.52%; $p<0.01$)

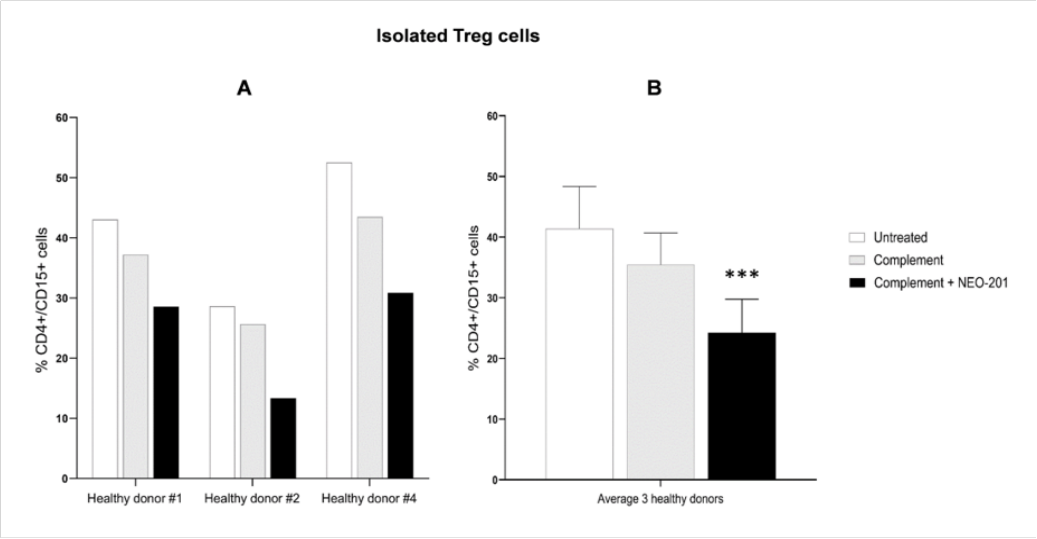
The percentage of **CD4+/NEO-201+ /CD127neg/CD25+Foxp3+CD15s** Treg (highly suppressive) cells were significantly higher in cancer patients as compared to normal donors (74.33% vs 23.08%; ($p<0.01$)

CD4+/NEO-201+ cells gated from live PBMCs; CD25+/CD127- gated from CD4+/NEO-201+ cells; Foxp3+/CD15s+ and Foxp3+/CD15s+ cells gated from CD25+/CD127- cells.

* $p<0.01$, CD4+/NEO-201+ cancer patients vs healthy donors

\# $p<0.01$, Foxp3+/CD15s+ cancer patients vs healthy donors

NEO-201 Eliminates Human Immunosuppressive Regulatory T cells (Tregs) Through CDC



B. Flow cytometry analysis of NEO-201 CDC activity against isolated Treg cells from PBMCs from 3 healthy donors using the EasySep™ Human CD4+CD127lowCD25+ Regulatory T Cell Isolation Kit. Isolated Treg cells were used as target cells in the presence of 10μg/mL of NEO-201 plus complement or complement alone in the CDC assay
Data are presented as percentage of viable cells expressing cell-surface Treg cells markers. Asterisks denote statistical significance of complement + NEO-201 vs untreated cells (unpaired t-test). *** $p < 0.001$. Positivity was determined by using fluorescence-minus-one controls. Positivity was defined as % of positive cells ≥ 10%.

Figure panel A: in Treg cells incubated with complement plus NEO-201, there was a reduction of 33.56% (28.59% vs 43.03%), 53.4% (13.34% vs 28.60%) and 41.32% (30.82% vs 52.52%) of CD4+/CD15s+ cells compared to untreated Tregs in healthy donor #1, #2 and #4, respectively.

Figure panel B: When the average of CD4+/CD15s+ cells after incubation with complement plus NEO-201 was analyzed compared to untreated Treg cells from these 3 healthy donors, we observed that the reduction was statistically significant ($p<0.001$)

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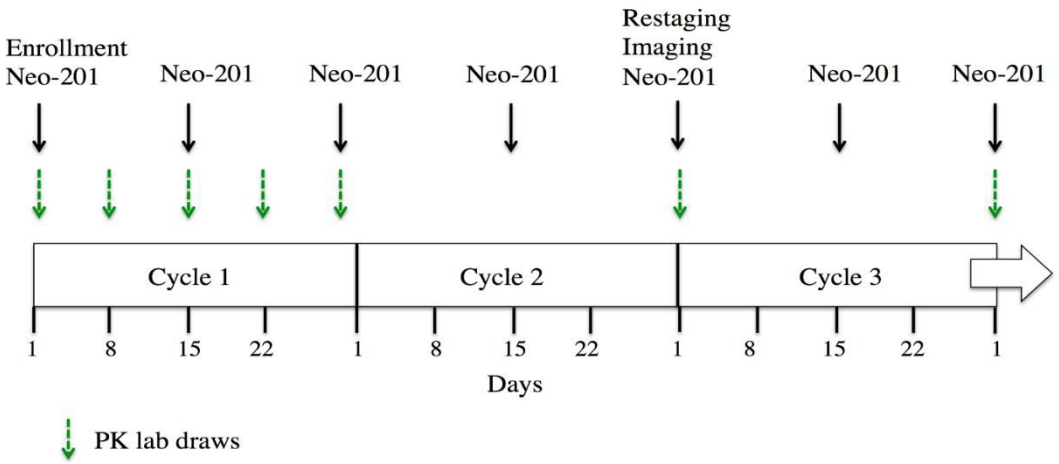
NEO-201 Completed Clinical Trial

Completed NEO-201, 1st in Human Clinical Trial

- NEO-201- 1st in human studies treated patients with colon ca, pancreatic ca, breast ca, NSCLC, and mucinous ovarian ca, who are no longer eligible for standard therapy
- Completed first in-human clinical studies at the NCI in patients with refractory solid tumors

Study Schema



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Phase 1 Dose Escalation of NEO-201

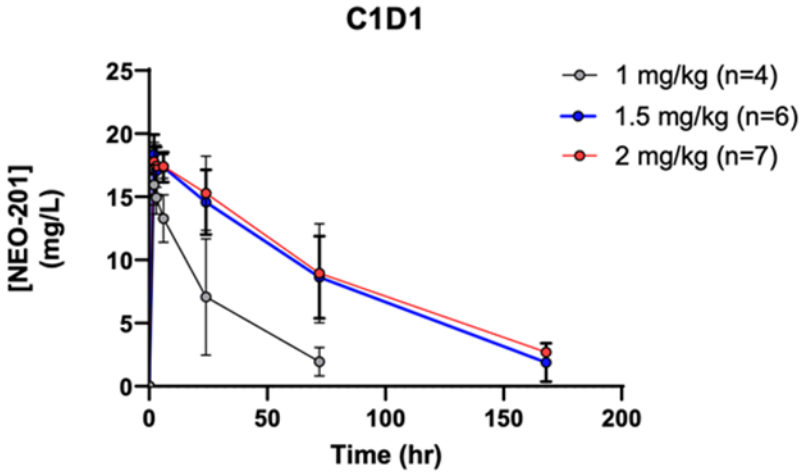
Gender	Male: 6 (35%)	Female: 11 (65%)			
Age (years)	30-50: 5 (29%)	51-60: 4 (24%)	61-70: 5 (29%)	71-80: 2 (12%)	> 80: 1 (6%)
Cancer Type	Colorectal: 11 (65%)	Pancreatic: 4 (24%)	Breast: 2 (12%)		
Race	White: 15 (88%)	African American: 2 (12%)			
Ethnicity	Non-Hispanic: 17 (100%)				
Performance Status	ECOG 0: 6 (35%)	ECOG 1: 9 (53%)	ECOG 2: 2 (12%)		

17 subjects who failed all standard therapies were enrolled in this 1st in human study with 9 evaluable for clinical response

- **4 received NEO-201 at dose level 1 (1 mg/kg)**
- **7 received NEO-201 at dose level 2 (2 mg/kg)**
- **6 received NEO-201 at dose level 1.5 (1.5 mg/kg)**

4 of the 9 evaluable subjects with durable stable disease (up to 15 doses)

Phase 1 Dose Escalation of NEO-201: PK Analysis



- **PK analysis showed no difference between 1.5 mg/kg and 2 mg/kg cohorts**
- **1.5 mg/kg and 2 mg/kg cohort: it is very likely at these dose levels, NEO-201 could be cleared from the blood between C1D7 and C1D9.**
- **NEO-201 was chosen at the recommended Phase 2 dose at 1.5mg/kg IV every 2 weeks**

Phase 1 Dose Escalation of NEO-201: Toxicity

Body System, Adverse Event	Dose Level 1 mg/kg (n= 4 subjects/12 doses)				Dose Level 2 mg/kg (n= 7 subjects/34 doses)				Dose Level 1.5 mg/kg (n= 6 subjects/23 doses)				Cumulative Incidence (n =17 subjects/69 doses)
	Gr 1	Gr 2	Gr 3	Gr 4	Gr 1	Gr 2	Gr 3	Gr 4	Gr 1	Gr 2	Gr 3	Gr 4	
Blood and Lymphatic System Disorders													
Anemia	2 (17%)	4 (33%)	--	--	4 (12%)	9 (26%)	2 (6%)	--	3 (13%)	3 (13%)	--	--	27 (39%)
Febrile Neutropenia	--	--	--	--	--	--	2 (6%)	1 (3%)	--	--	1 (4%)	--	4 (6%)
General Disorders and Administration Site Conditions													
Chills/Rigors	2 (17%)	1 (8%)	--	--	2 (6%)	1 (3%)	--	--	--	--	--	--	6 (9%)
Fatigue	1 (8%)	1 (8%)	--	--	--	2 (6%)	--	--	2 (9%)	--	--	--	6 (9%)
Fever	6 (50%)	1 (8%)	--	--	4 (12%)	1 (3%)	--	--	4 (17%)	--	--	--	16 (23%)
Injury, Poisoning and procedural complications													
Infusion related reaction	--	8 (66%)	--	--	--	7 (21%)	--	--	--	3 (13%)	--	--	18 (26%)
Investigations													
Lymphocyte count decreased	1 (8%)	--	1 (8%)	--	--	6 (18%)	4 (12%)	2 (6%)	2 (9%)	1 (4%)	--	1 (4%)	18 (26%)
Neutrophil count decreased	--	--	2 (17%)	4 (33%)	1 (3%)	--	2 (6%)	10 (29%)	2 (9%)	--	1 (4%)	7 (30%)	29 (42%)
Platelet count decreased	1 (8%)	--	--	--	5 (15%)	1 (3%)	--	--	2 (9%)	--	--	--	9 (13%)
Weight loss	--	--	--	--	2 (6%)	--	--	--	--	--	--	--	2 (3%)
White blood cell decreased	4 (33%)	--	2 (17%)	--	2 (6%)	3 (9%)	7 (21%)	2 (6%)	--	2 (9%)	1 (4%)	4 (17%)	27 (39%)

Overall, of 17 subjects receiving a total of 69 doses of NEO-201, the most common toxicities included:

neutropenia (42%), **anemia (**Gr1 and Gr2**,** 39%), **decreased white blood cell count** (39%), **infusion related reactions** (Gr2, 26%), **decreased lymphocytes** (26%), **fever** (Gr1 and Gr2, 23%), and **thrombocytopenia** (Gr1 and Gr2, 13%)

CORRELATION BETWEEN HIGH SOLUBLE FACTORS AND ACTIVATED NK STATUS SUMMARY SOLUBLE MICA

PROGRESSIVE DISEASE

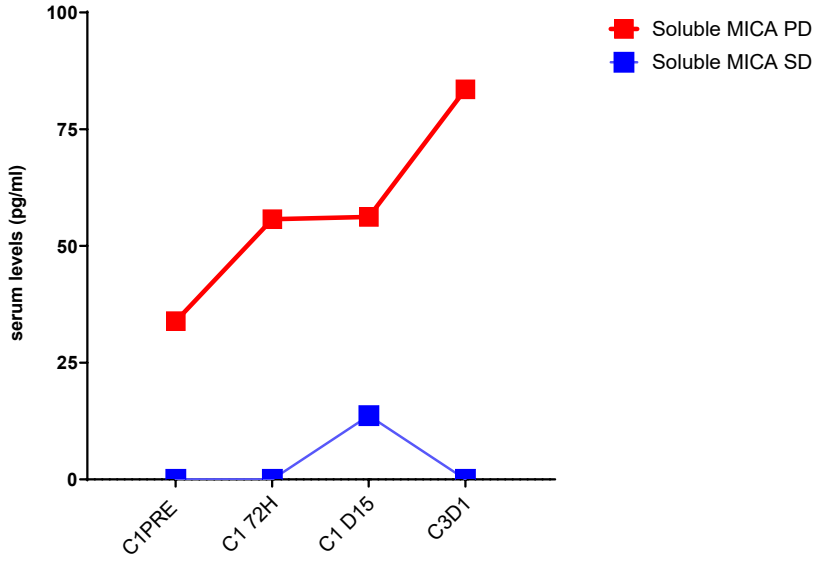
3 COLON CANCER PATIENTS
1 PANCREATIC CANCER PATIENTS

- 2 treated with 2 mg/kg NEO-201, 2 treated with 1.5 mg/kg NEO-201.
- >90% tissue positive for NEO-201 at 3+ intensity

STABLE DISEASE

3 COLON CANCER PATIENTS

- 2 treated with 2 mg/kg NEO-201, 1 treated with 1.5 mg/kg
- >90% tissue positive for NEO-201 at 3+ intensity



Analysis of sMICA in sera of 512 individuals revealed significantly ($p < 0.0001$) higher levels in **patients with various malignancies** (n = 296, median **161 pg/ml**) than in **healthy individuals** (n = 62, median **<30 pg/ml**). In cancer patients, elevated sMICA levels correlated significantly with cancer stage and metastasis

Stieber et al. Int J Cancer 2006

SOLUBLE MICA is higher in PD patients compared to SD patients

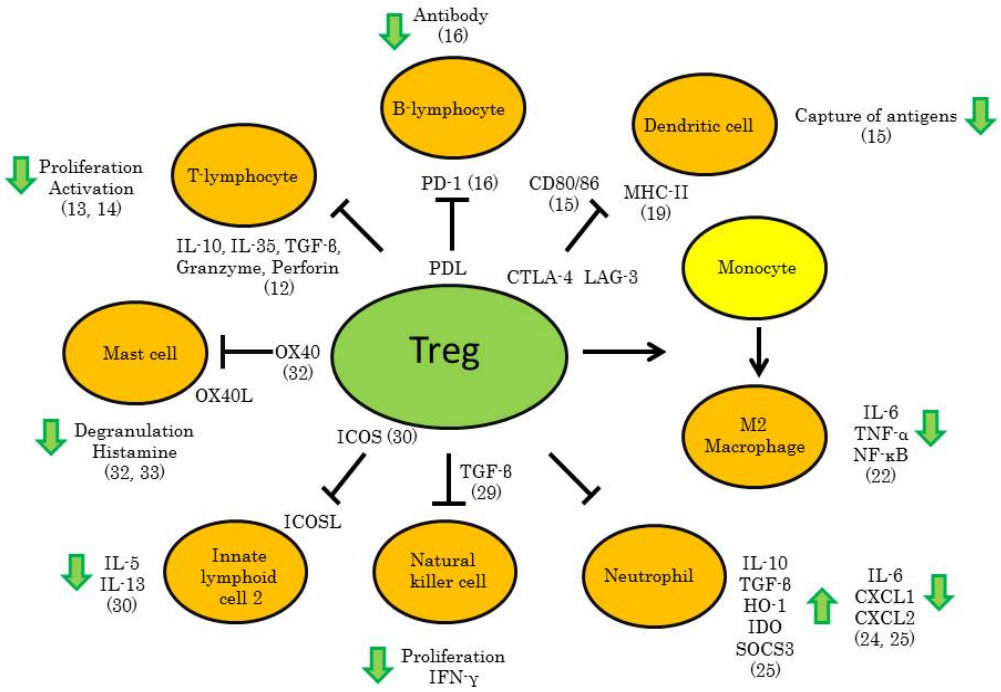
Conclusions

- NEO-201 has several mechanisms of action. NEO-201 is able to mediate both ADCC and CDC.
- In addition, NEO-201 can block the interaction between tumor cell CEACAM5 and NK cell CEACAM1 to reverse CEACAM1-dependent inhibition of NK cytotoxicity in patients whose tumors express the NEO-201-reactive variant of CEACAM5.
- NEO-201 can also target and eliminate human immunosuppressive regulatory T cells (Tregs)
- Our studies proved the NEO-201 anti-tumor efficacy in animal models
- Phase 1 trial concluded in December 2020: main side effect is Neutropenia, which is manageable with G-CSF administered after 5-6 days from infusion
- **NEO-201 CLINICAL EFFECT: stable disease in 4 patients**: low sMICA , high expression of activation and cytotoxicity markers in NK cells

Rationale for Combination of NEO-201+ Pembrolizumab

- The response rate of PD-1/PD-L1 blockade against solid cancers is around 15%-30% in front line therapy. It is significantly lower in **2nd line approved** indications (10-15%).
- The low response rates and resistance to PD-1/PD-L1 blockade may be due to the action of **Regulatory T (Tregs) cells** in the TME. Tregs cells have been demonstrated to **play a role in increase resistance to PD-1/PD-L1 blockade**
- **Our preliminary data showed that NEO-201 can target and eliminate Tregs cells through CDC**
- Based on this data we **hypothesize that combining NEO201 with PEMBROLIZUMAB may overcome resistance to PD-1/PD-L1 checkpoints inhibitors by depleting negative regulatory T-regs and enhancing immune system mediated anti-tumor activity in subjects for whom pembrolizumab is currently indicated**

NEO-201 Targets and Eliminates Human immunosuppressive Regulatory T Cells (Tregs)



- Foxp3-expressing Treg cells can suppress the activation of T cells, the function of NK, neutrophils, dendritic cells, monocytes and macrophages in the tumor microenvironment (TME).
- Data suggests that increased Tregs in the tumor microenvironment diminishes the efficacy of checkpoint blockade therapy
- Depletion of Treg cells is an effective strategy to enhance the anti-tumor immunity
- **Eliminating Tregs justifies combining NEO-201 with other immunotherapies (i.e., checkpoint inhibitors)**

Seike M. ***J Dermatological Research*****, 2019**

NEO-201 + Pembrolizumab

Pembrolizumab is a potent humanized immunoglobulin G4 (IgG4) monoclonal antibody (mAb) with high specificity of binding to the programmed cell death 1 (PD 1) receptor

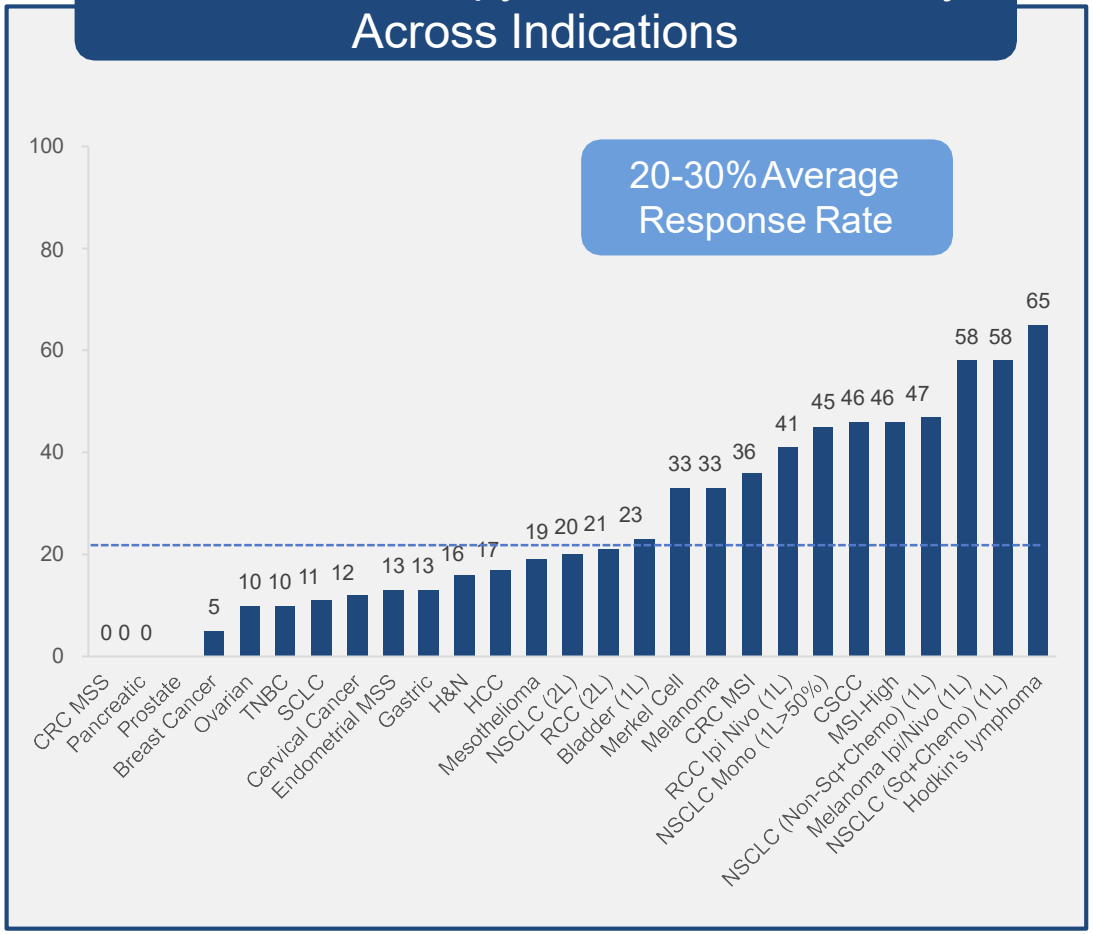
EFFICACY OF PEMBROLIZUMAB:

- **NSCLC**: substantial, clinically meaningful benefits in OS, PFS, and ORR in participants with NSCLC who progressed after platinum-containing chemotherapy and whose tumor cells expressed PD-L1 and do not have any sensitizing EGFR mutations or ALK rearrangements
- **HNSCC**: On June 2019, the FDA approved pembrolizumab (KEYTRUDA, Merck) for the first-line treatment of patients with metastatic or unresectable recurrent HNSCC
- **UTERINE CANCER**: On September 17, 2019 the FDA granted accelerated approval to **pembrolizumab plus lenvatinib** for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
- **CERVICAL CANCER**: On 12 June 2018, the FDA approved pembrolizumab (Keytruda, Merck and Co. Inc.) for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumours express PD-L1 (CPS ≥1)

Significant Unmet Need: Anti PD-1 Therapy Failure

70-80% of Patients Non-responsive to Approved Cancer Immunotherapies – Lower in 2nd line indications

PD-1 Monotherapy/Combination Activity Across Indications



Efficacy of NEO-201

- NEO-201 addresses non-responsive patient populations
- Mechanism-driven first-in-class combinations
- Anti PD-1 mAb response rates:
  - 2nd Line NSCLC <10% (post prior therapy), endometrial cancer 13%, H&N cancer 16%, and cervical cancer 12%

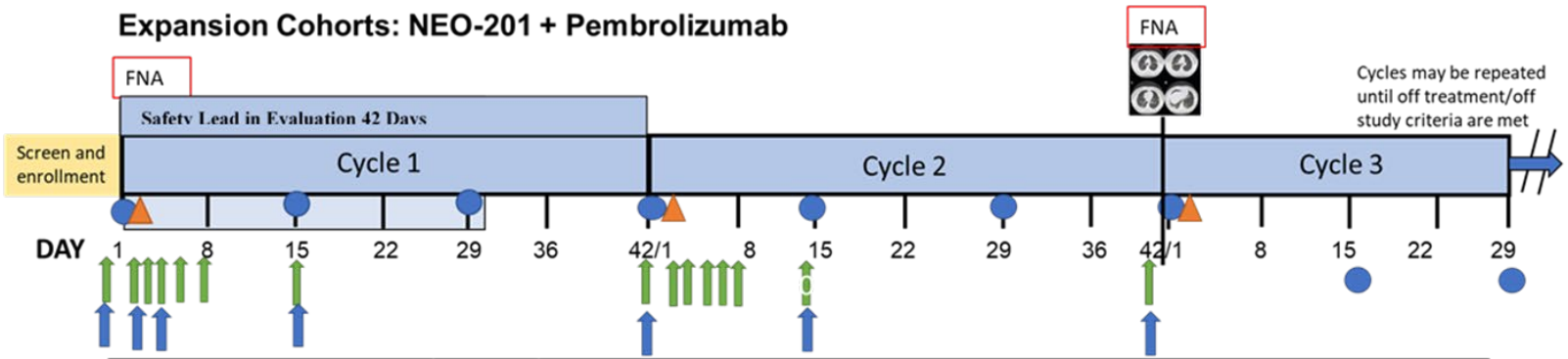
PRECISION BIOLOGICS

NEO-201 + Pembrolizumab Phase 2b Clinical Trial

Objectives

- Determine Objective Response Rate (ORR = CR, PR, SD) as determined by RECIST v1.1 guidelines and progression free survival (PFS) in four cohorts of subjects (subjects with NSCLC, HNSSC, uterine and cervical cancers) receiving NEO-201 at the RP2D in combination pembrolizumab at the FDA approved adult dose
- Assess immunogenicity of NEO-201 in adults with relapsed or chemo-resistant solid tumors participating in the dose escalation cohort and in the first 10 subjects receiving combination therapy.

Study Schema



PRECISION BIOLOGICS

NEO-201 + Pembrolizumab Phase 2b Clinical Trial: Study Design Overview

- Enrollment into Four Expansion Cohorts

❑ Up to 228 subjects will be screened and, if eligible, treated with NEO-201 at 1.5 mg/kg every 2 weeks in combination with Pembrolizumab, given 1 day after the NEO-201, at 400 mg IV every 6 weeks.

❑ Including the number of subjects required to determine the RP2D of NEO-201, a minimum of 74 (17 + 57) and maximum of 121 (17 + 104) subjects will participate in this study. Allowing for an additional 5 subjects to replace potentially in-evaluable subjects, the maximum accrual on this study will be 126 subjects.

❑ Using a Simon minimax two-stage design for the accrual to each disease cohort the following accrual targets have been established.

Enrollment to two-stage design per expansion cohort

Disease Cohort	Initial Stage	Acceptable Response Rate % (N/Total)	Second Stage	Sufficiently interesting Response Rate
NSCLC	12	20% (≥1/12)	21	14.3% (≥3/21)
HNSCC	16	25% (≥2/16)	31	19.4% (≥6/31)
Endometrial	16	25% (≥2/16)	31	19.4% (≥6/31)
Cervical	13	25% (≥1/13)	20	15% (≥3/20)

NEO-201 Studies

Phase 1/2b Using 2nd Line Checkpoint in Combination with NEO-201

- Targeting 2nd line therapy for NSCLC, H&N cancer, endometrial cancer, and cervical cancer (**Ongoing)**
- Strong scientific data supporting ability of NEO-201 to improve antitumor responses of Pembrolizumab (Keytruda) in 2nd line FDA approved indications where there is a significant unmet need (multibillion dollar annual market)
- Approximately **$25M of trial costs** (including Pembrolizumab) **are subsidized**

Phase 2 Clinical Trials Using NEO-201 + IL-15 in Refractory Solid Tumors

- Targeting refractory solid tumors, including colorectal cancer, pancreatic cancer, and mucinous ovarian cancer, expressing antigen recognized by NEO-201 mAb (Planned)

NEO-201 Phase 2 Hematological Malignancies

- Preclinical data supports binding and killing to hematological malignancies with NEO-201 antibody
- Provisional Patent protection filed in May 2021