

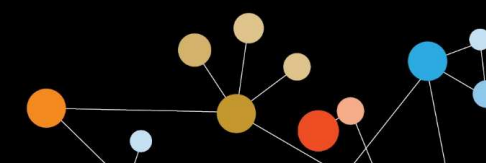
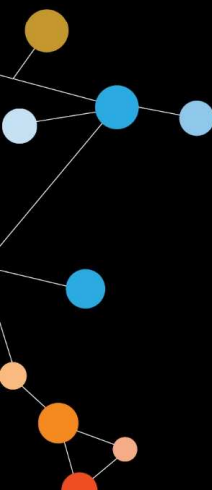


# SITC 2016

NATIONAL HARBOR, MD  
NOVEMBER 9-13, 2016



Society for Immunotherapy of Cancer





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NATIONAL HARBOR, MD  
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## Anti-Semaphorin4D VX15/2503 in Combination with Ipilimumab or Antibody to PD-1 or PD-L1

**Elizabeth Evans, PhD, Vice President, Preclinical Research**  
**Vaccinex, Inc. Rochester NY**



Society for Immunotherapy of Cancer

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# Presenter Disclosure Information

*Elizabeth Evans*

The following relationships exist related to this presentation:

*Full-time employee at Vaccinex, Inc.*

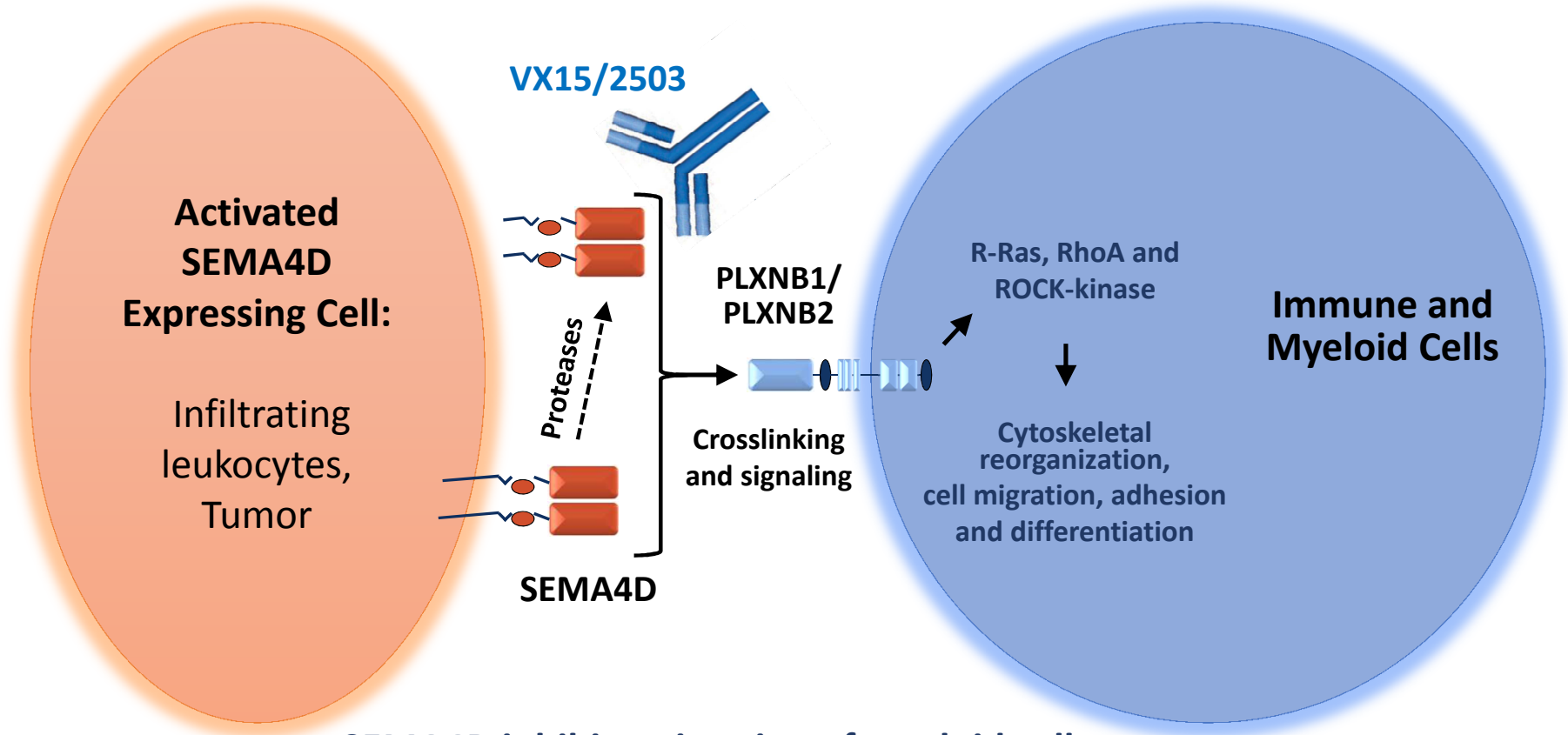


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# Forward Looking Statements

## *Cautionary Note on Forward-Looking Statements*

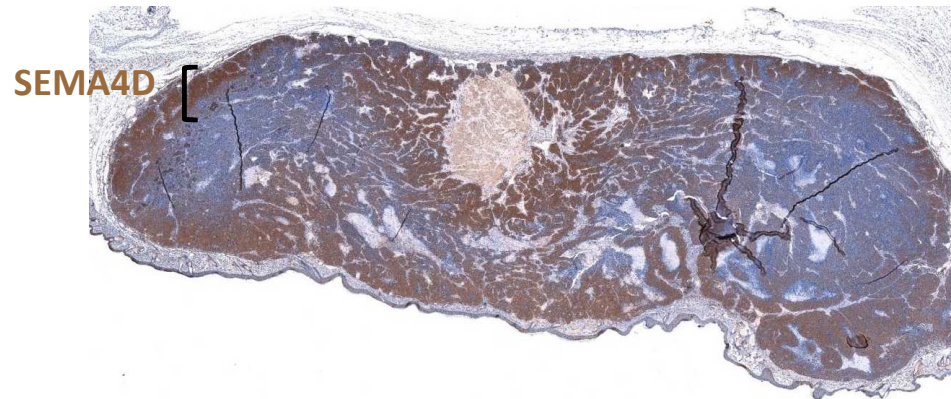
*This presentation contains forward-looking statements reflecting the current beliefs and expectations of Vaccinex management. Words such as “may,” “believe,” “will,” “expect,” “plan,” “anticipate,” “estimate,” “intend” and similar expressions, as well as other words or expressions referencing future events, conditions or circumstances, are intended to identify forward-looking statements. Forward-looking statements contained in this presentation include statements about expectations related to a clinical trial for the Company’s lead monoclonal antibody, VX15/2503. Forward-looking statements in this presentation involve substantial risks and uncertainties that could cause the Company’s performance or achievements to differ significantly from those expressed or implied by the forward-looking statements, including as a result of the inherent challenges in clinical development. All forward-looking statements are based on Vaccinex’s expectations and assumptions as of the date of this presentation, and actual results may differ materially. Except as required by law, Vaccinex expressly disclaims any responsibility to update any forward-looking statement contained herein, whether as a result of new information, future events or otherwise.*



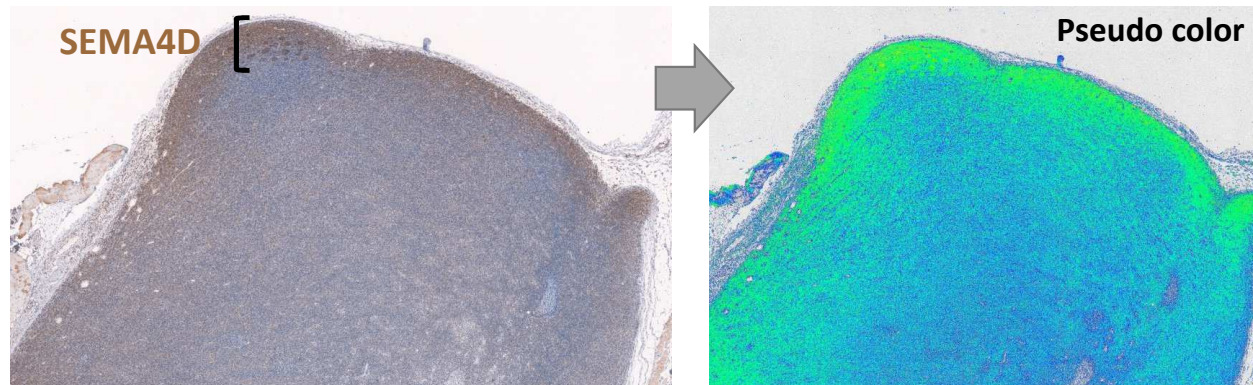
**SEMA4D inhibits migration of myeloid cells.**  
**Blockade of SEMA4D promotes infiltration of potent APC**  
**and inhibits differentiation/expansion of MDSC, M2 TAM and Treg.**  
 ADVANCING CANCER IMMUNOTHERAPY WORLDWIDE

## SEMA4D expression is concentrated at Invasive Tumor Margin, creating a barrier to immune cell penetration

Mammary carcinoma  
Tubo.A5



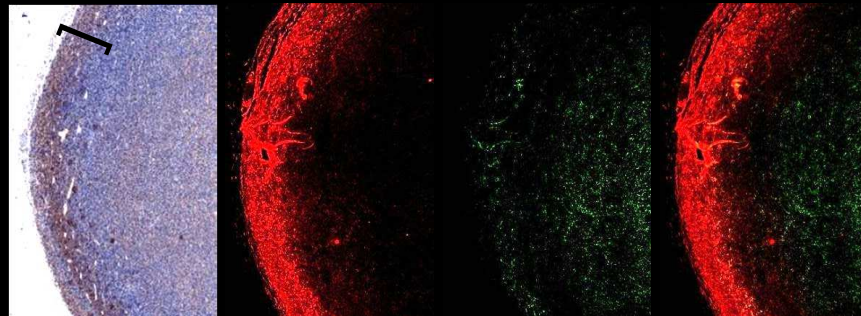
Colorectal  
Colon26





## SEMA4D Regulates Migration and Activation of Immune Cells in Tumor Microenvironment in Preclinical Models

Control IgG



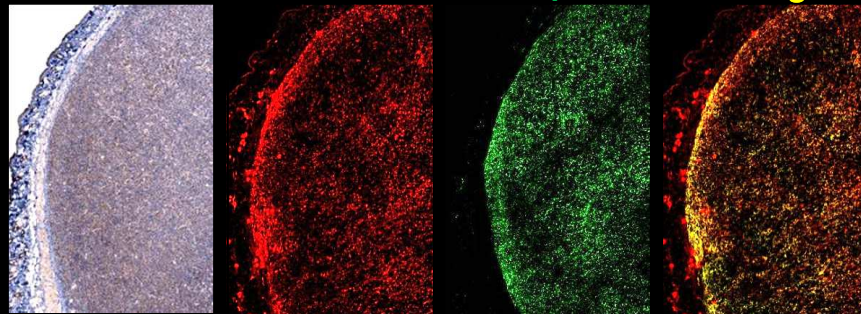
SEMA4D

CD11c

F4/80

Merge

$\alpha$ Sema4D  
Mab67



The Sema4D  
gradient is  
neutralized

Inflammatory  
APC's migrate into  
tumor

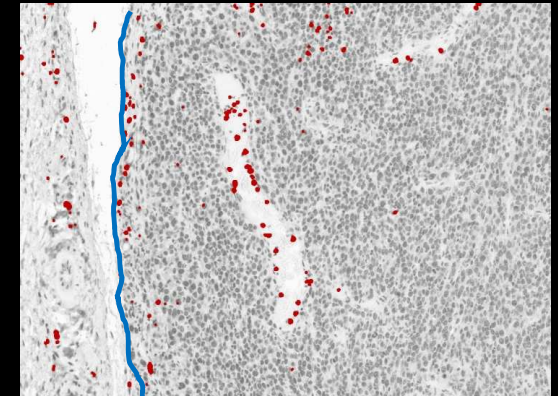
Increase in  
APC

APC mature to  
pro-inflammatory  
CD11c, F4/80  
double positive



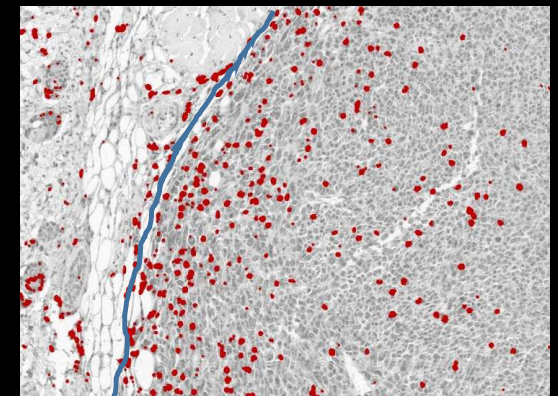
Control IgG:

CD8+ T cells (red)  
do not penetrate  
the tumor. Most  
CD8+ cells are  
within the stroma  
and vessels.



Anti-  
SEMA4D/MAb67:

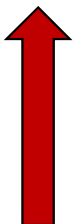
CD8+ T cells  
infiltrate the  
interior of the  
tumor.



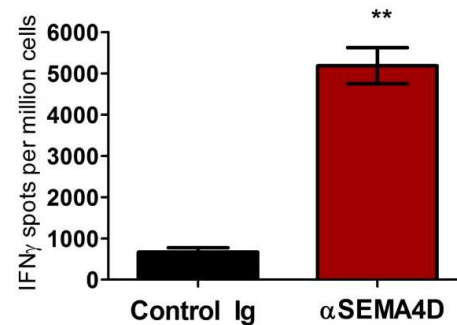
Evans EE et al. Cancer Immunol Res. 2015. 3(6): 689-701.

## Anti-SEMA4D Shifts the Balance of Immune Cells in Tumor Microenvironment

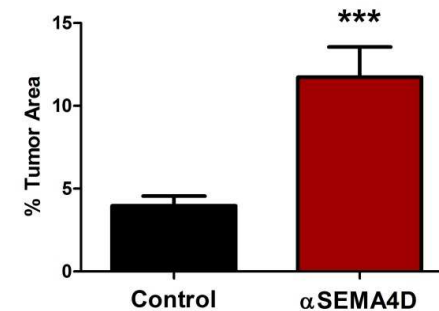
Tumoricidal  
Cells



Tumor-specific Cytotoxic T Cells



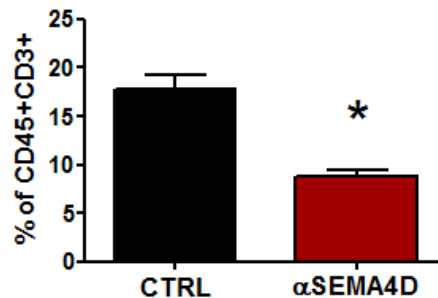
Anti-tumorigenic APC  
F4/80+CD11c+



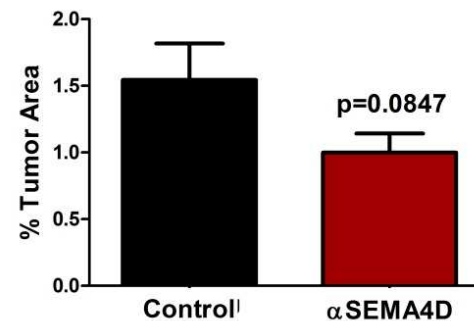
Immuno-  
suppressive  
Cells



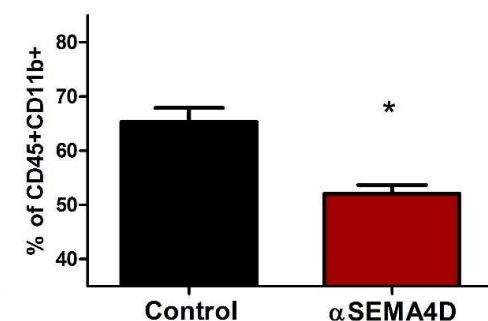
T<sub>regulatory</sub> CD4+CD25+



Pro-tumorigenic TAM  
CD206+ TAM



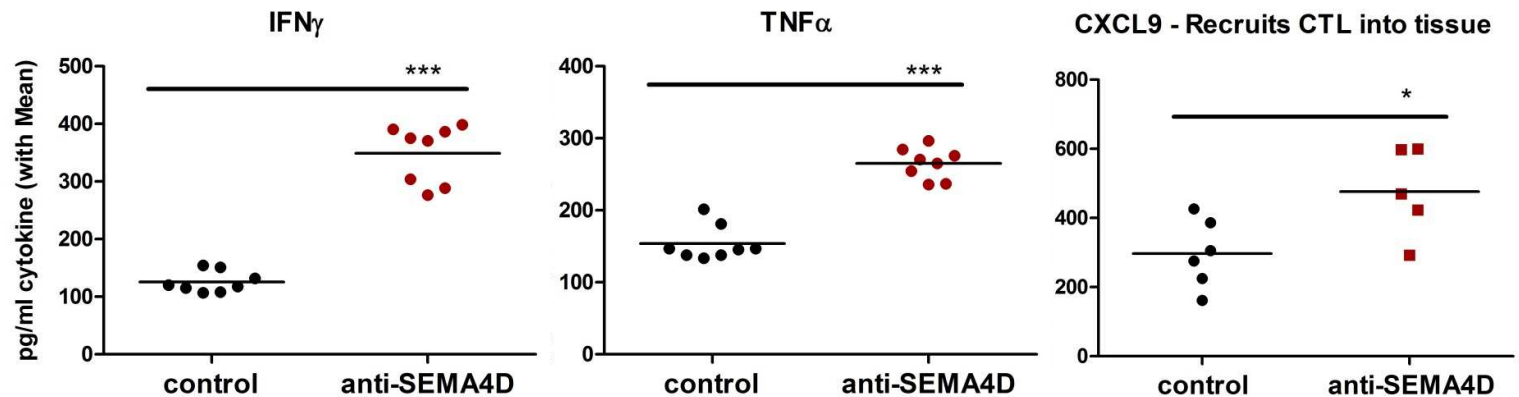
MDSC  
Gr1+CD11b+ MDSC



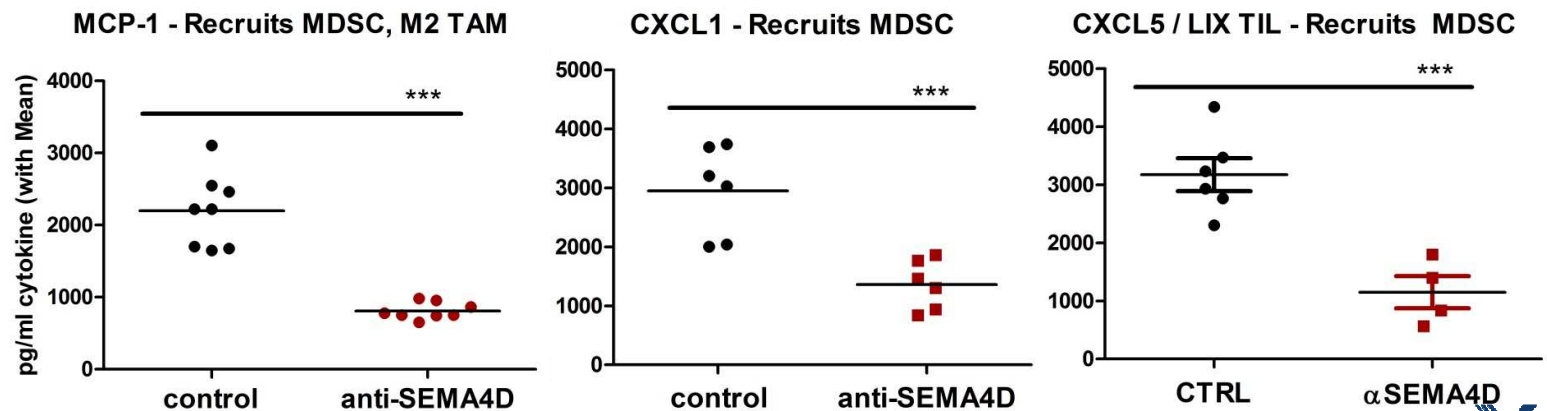


## Anti-SEMA4D Shifts the balance of Immunity in Tumor Microenvironment

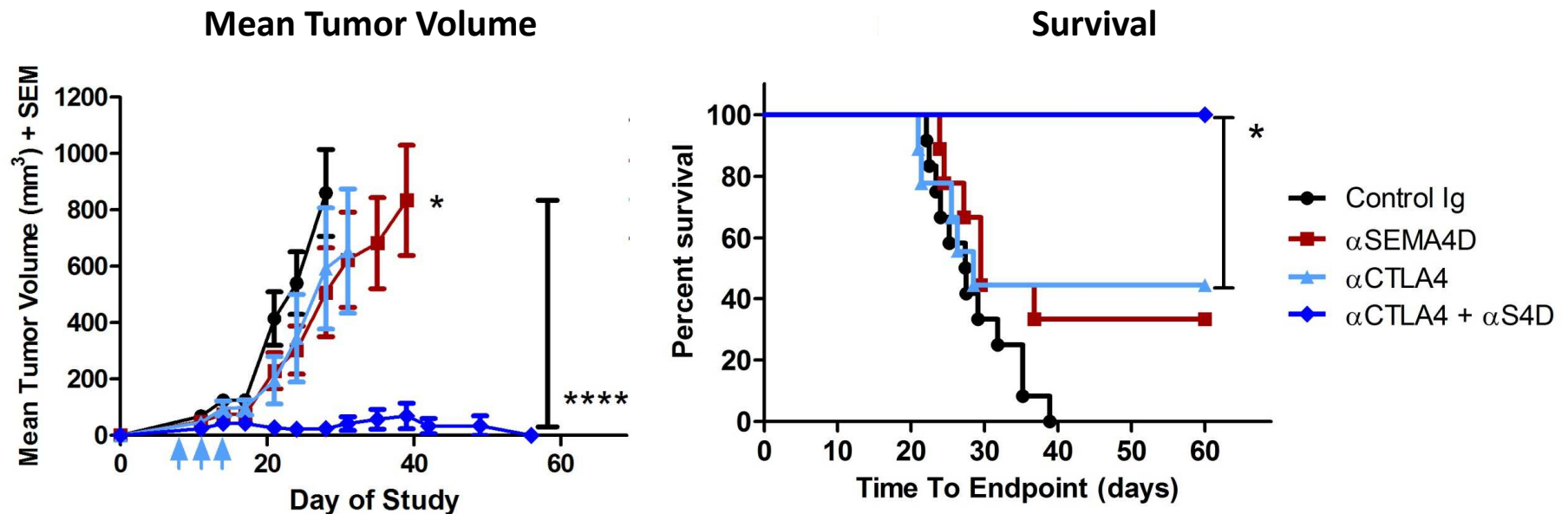
Tumoricidal  
Factors



Immuno-  
suppressive  
Factors



## Anti-SEMA4D enhances Immune Checkpoint blockade

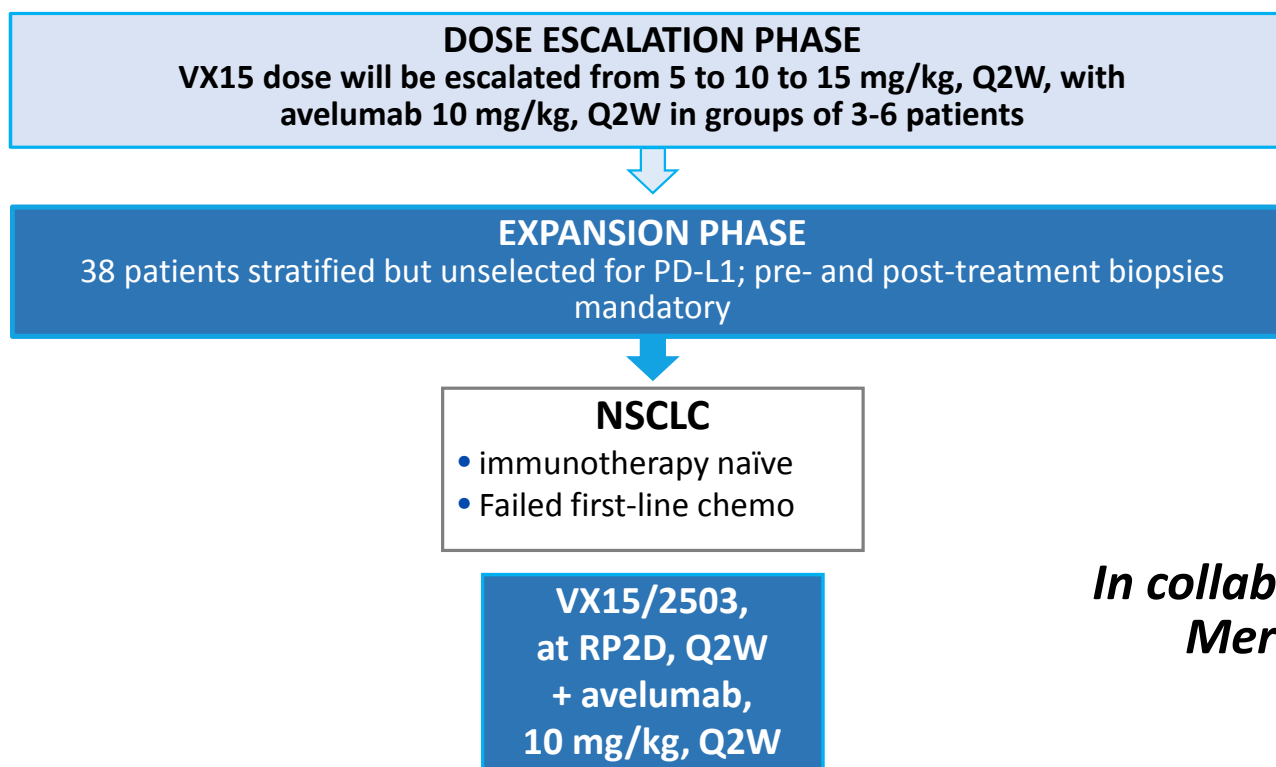


Durable responses, and regressor mice resist subsequent tumor challenge.

Anti-SEMA4D also enhances activity of chemotherapy (cyclophosphamide, etc.)  
and other immune checkpoint antibodies (anti-PD-1) in preclinical models

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## Vaccinex IND, Phase 1b/2 Combination Trial VX15/2503 (humanized IgG4) with Avelumab (anti-PD-L1): NSCLC (2L)

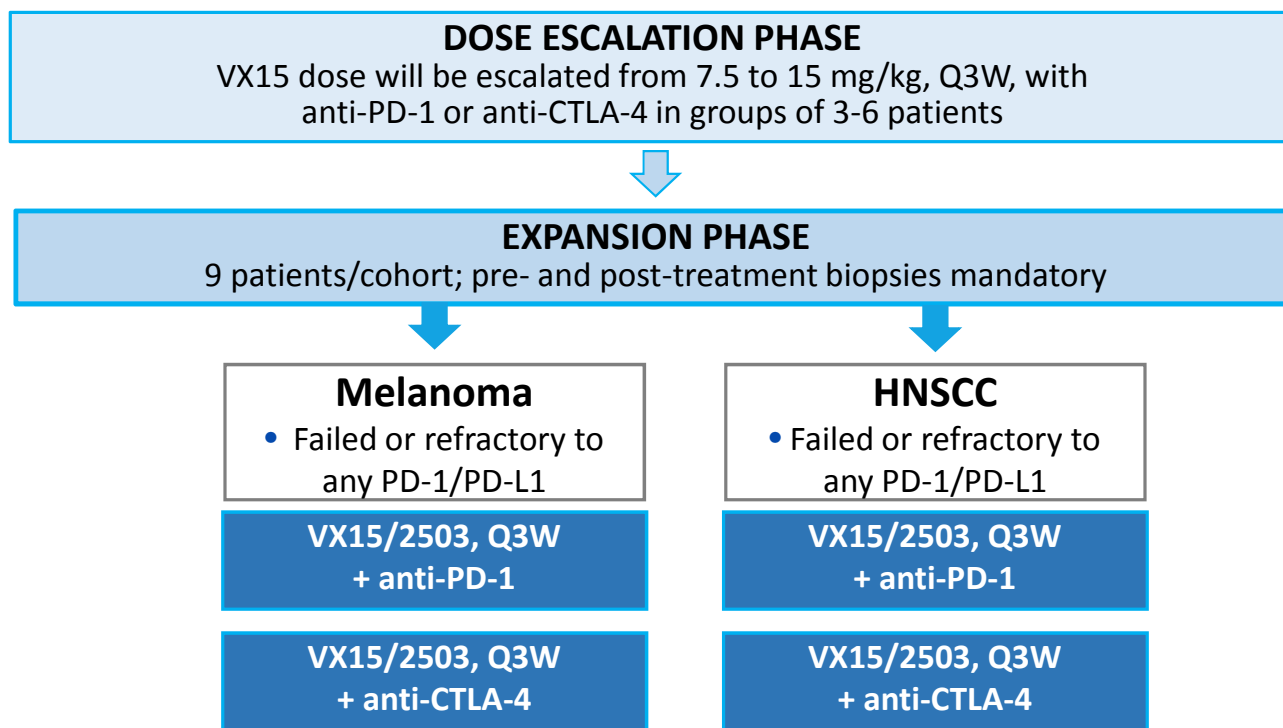


*In collaboration with  
Merck KGaA*

**Evaluate immune infiltration in tumor biopsies and ORR, DOR**

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## Investigator sponsored, Phase 1b/2 Combination Trial VX15/2503 (human IgG4) with anti-PD-1 or anti-CTLA-4



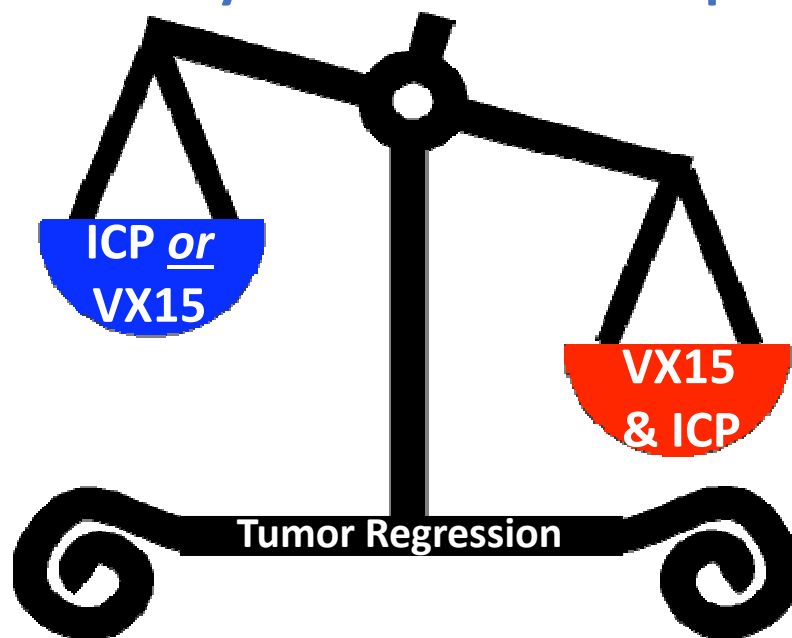
Evaluate immune infiltration in tumor biopsies and ORR, DOR

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## Anti-SEMA4D Shifts the Immune Balance to Enhance Activity of Immune Checkpoint Inhibitors

### Effects of ICP or anti-SEMA4D:

- $\uparrow T_{\text{effectors}}$
- $\uparrow$  Th1 cytokines: IFN $\gamma$ , TNF $\alpha$
- $\uparrow$  CXCL9, CXCL10



### Combination enhances effects and adds benefits of anti-SEMA4D to facilitate infiltration and reverse suppressive APC:

- $\downarrow$  M2 TAM
- $\downarrow$  MDSC
- $\downarrow T_{\text{regulatory}}$
- $\downarrow$  Chemokines that recruit M2 and polarize Treg: CCL2, CXCL1, CXCL5, IL-10

- **Potential Impact on Field:** The unique mechanism of action, facilitating penetration of activated immune cells, enhances activity immune checkpoint inhibition.
- **Take Home Message:** VX15/2503 was well-tolerated with a favorable safety profile in Phase I clinical trial; Phase1/2b combination trials with immune checkpoint inhibitors will be initiated in 2017.