



August 2023

Developing next-generation  
immunotherapies that address  
cancer immune resistance

**KA (Nasdaq)**

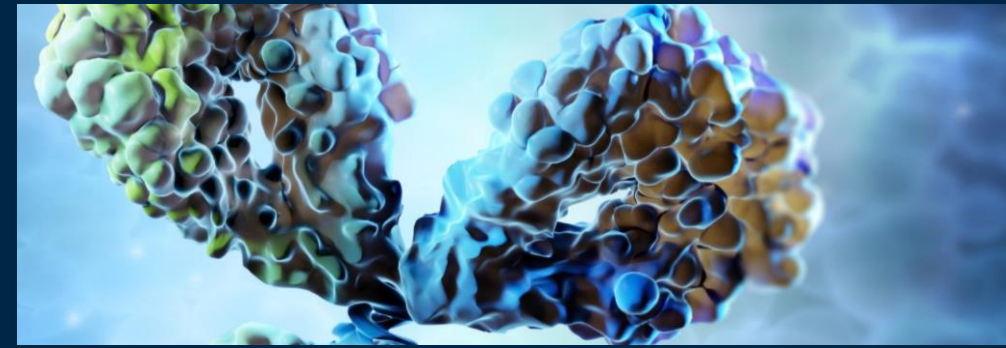
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# Kineta is developing next-generation immunotherapies that address cancer immune resistance



## Innate Immunity Focused Pipeline

### KVA12123

- VISTA blocking mAb to address immunosuppression in the TME
  - Phase 1/2 clinical study evaluating KVA12123 alone and in combination with pembrolizumab in advanced solid tumors
- Preclinical Anti-CD27 agonist mAb to address exhausted T cells

## Catalysts

3Q23 | KVA12123 initial clinical safety data  
4Q23 | KVA12123 initial clinical efficacy data

## Financial Position

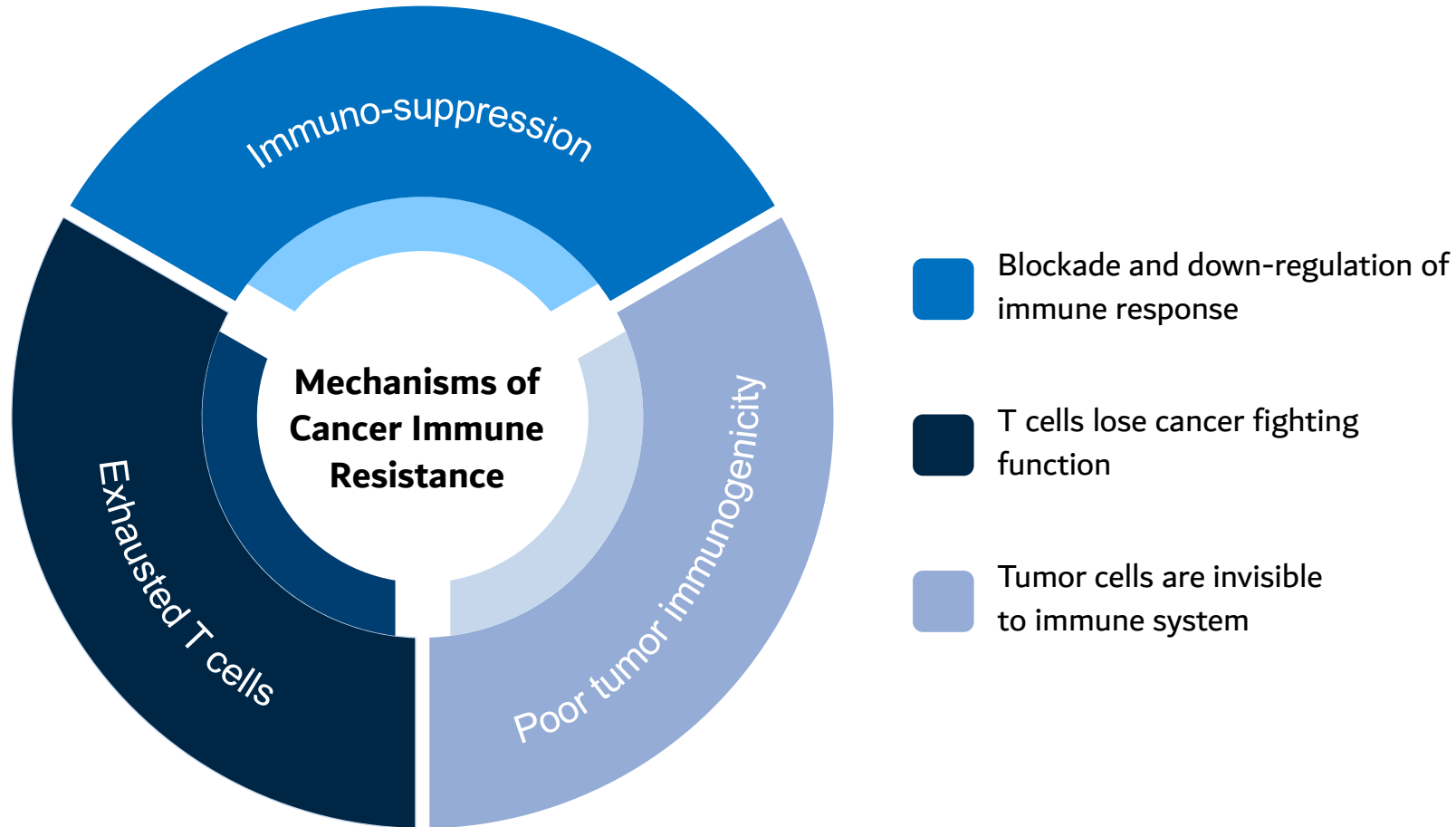
Cash runway into early 2025\*  
9.7 million outstanding shares (KA: Nasdaq)

## Partnerships



*\*includes \$7.8M cash as of Q2 23, \$6M registered direct closed 4/23, \$5M Merck milestone payment received 7/23 and \$22.5M PIPE financing expected to close 10/23*

# Immune resistance is a major challenge with current cancer therapy



## Next-generation cancer treatments require:

Improving survival for checkpoint inhibitor (CPI) non-responders **(70-80%)\***

**Reprogramming** the immune system to attack cancer

Integrating **innate and adaptive immune** responses



# Kineta pipeline integrates innate and adaptive immunity to address mechanisms of cancer resistance

## Innate immunity

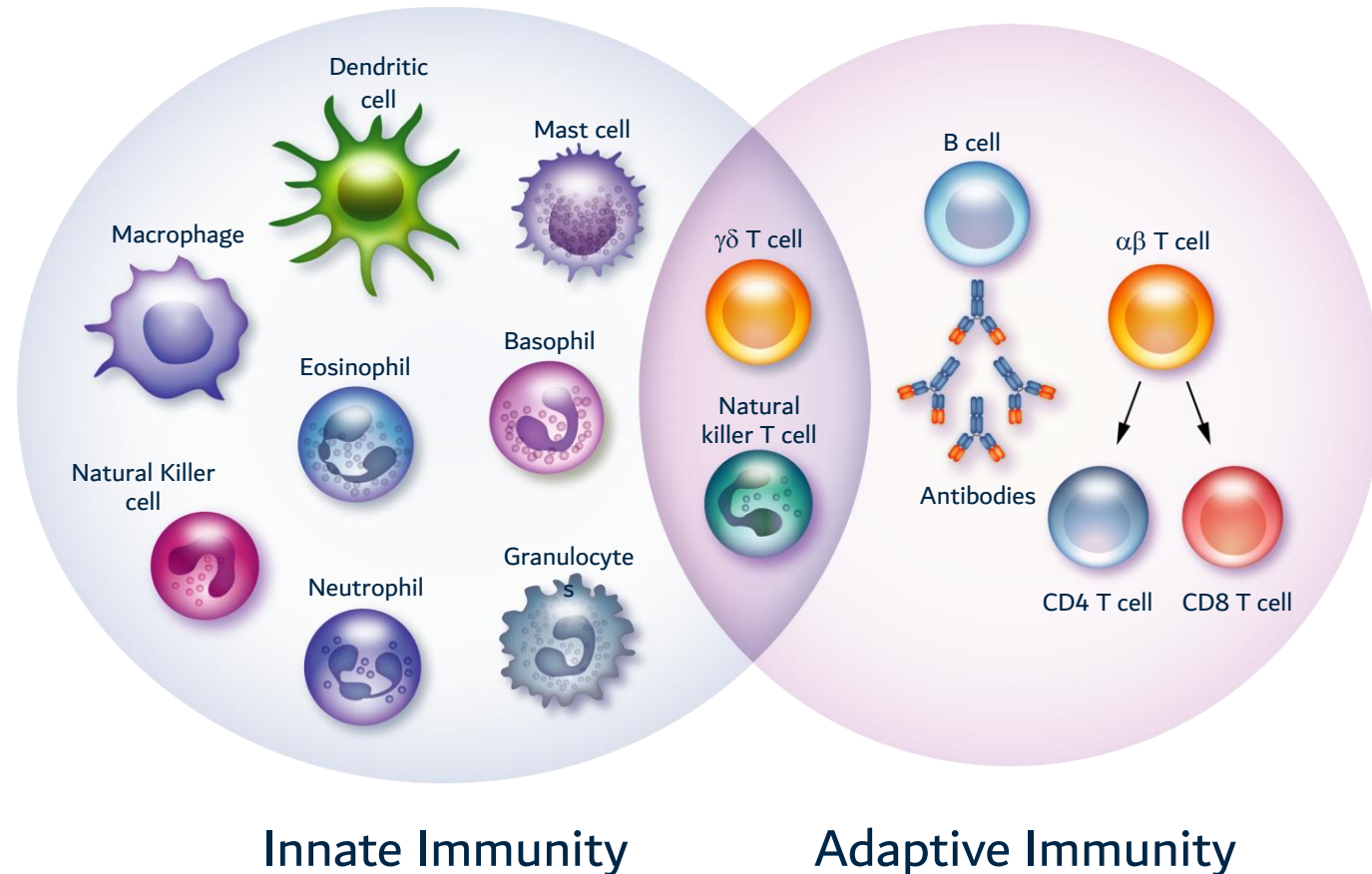
Involved in early response to cancer

Necessary driver for appropriate adaptive immunity

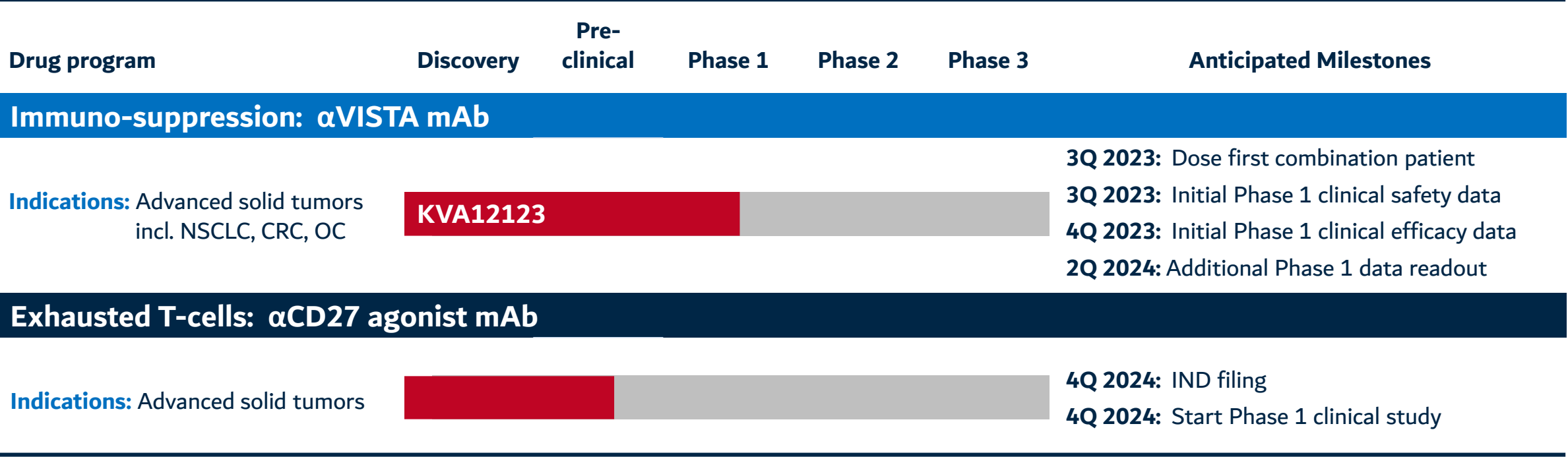
## Significant cause of cancer resistance

## Adaptive immunity

Most competitor drug development is focused **only** on T cell adaptive immunity



# Kineta’s immuno-oncology pipeline aims to address the mechanisms of cancer immune resistance





# KVA12123

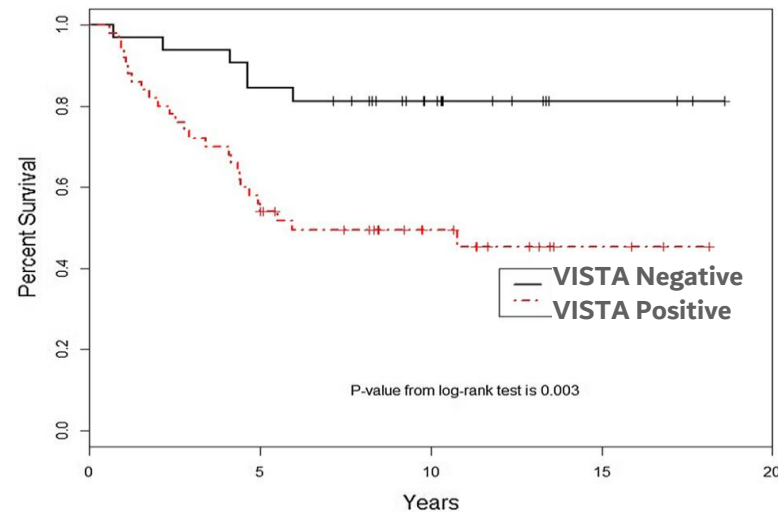
Potentially differentiated  
VISTA blocking immunotherapy



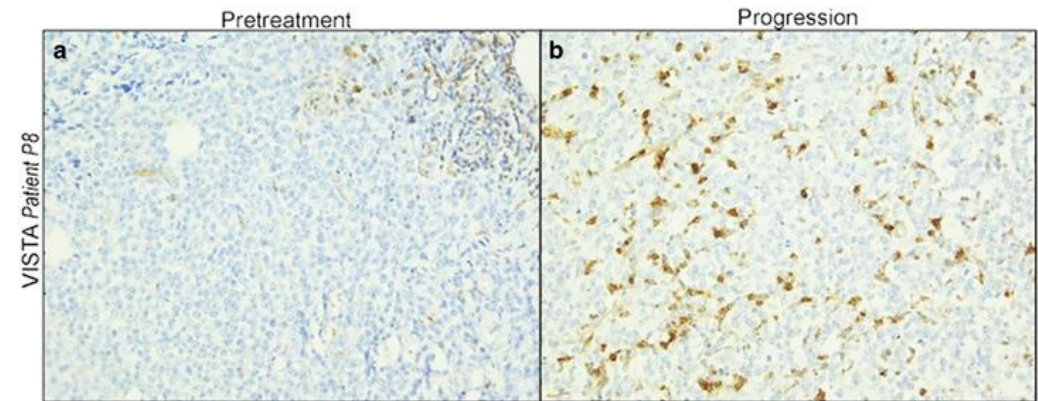
# VISTA is a key driver of immunosuppression in the tumor microenvironment

- Immunosuppressive protein expressed on **myeloid cells**
- Highly expressed in **cold tumors** including lung, colon and ovarian cancers
- Correlates with **poor outcomes** in cancer patients
- Up-regulated after CPI therapy and **associated with treatment failure**

Melanoma patient survival by  
VISTA expression in tumor-infiltrating immune cells <sup>1</sup>



VISTA expression increases in melanoma patient  
during pembrolizumab relapse/progression <sup>2</sup>



Brown staining in human tumors  
indicates VISTA expression



# KVA12123: Potentially differentiated VISTA blocking immunotherapy

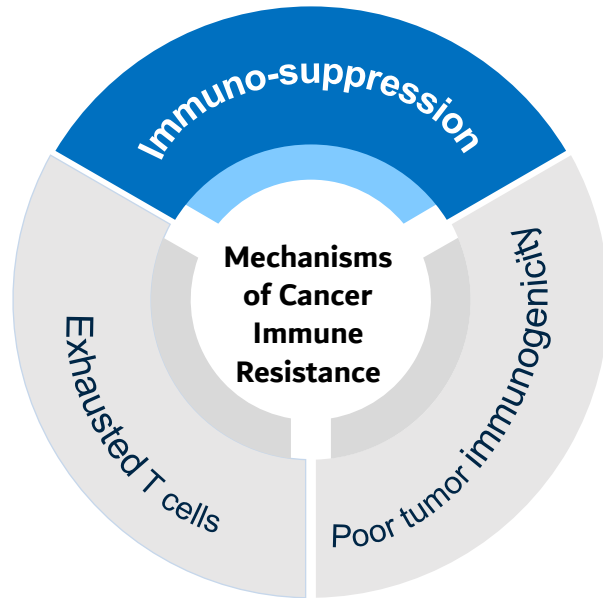
Product	Development stage	Isotype	pH Binding	Single Agent Tumor Model Efficacy	CRS Cytokine Release
<b>Kineta</b> KVA12123	Phase 1	Engineered IgG1 mAb that binds to a unique epitope	Binds at both physiologic pH and acidic pH in the TME	Strong single agent tumor growth inhibition and in combination with PD-1 in preclinical models	No CRS-associated cytokine release or neurotoxicity seen in preclinical models
<b>Hummingbird</b> HMBD002	Phase 1	IgG4	Physiologic & acidic	Moderate	IL-6
<b>Pierre Fabre</b> WO180	Phase 1				
<b>Sensei</b> SNS-101	Phase 1	IgG1	Acidic	Weak	TNF $\alpha$
<b>Curis*</b> CI-8993	Phase 1	IgG1	Physiologic	Moderate	TNF $\alpha$ , IFN $\gamma$ , IL2, IL-1 $\beta$
<b>Pharmabcine</b> PMC309	IND	IgG1	Physiologic & acidic	Moderate	IFN $\gamma$

Other discovery stage programs: Apexigen, Five Prime Therapeutics/BMS

Empty cells indicate no public data available

\*Curis announced 11/9/2022 : “Concentrating its resources to focus on and accelerate emavusertib”, the company’s lead asset and “deprioritization of other programs” (CI-8993)

# Blocking VISTA can reverse immunosuppression in the TME



Inhibits **MDSC** (myeloid-derived suppressor cells)

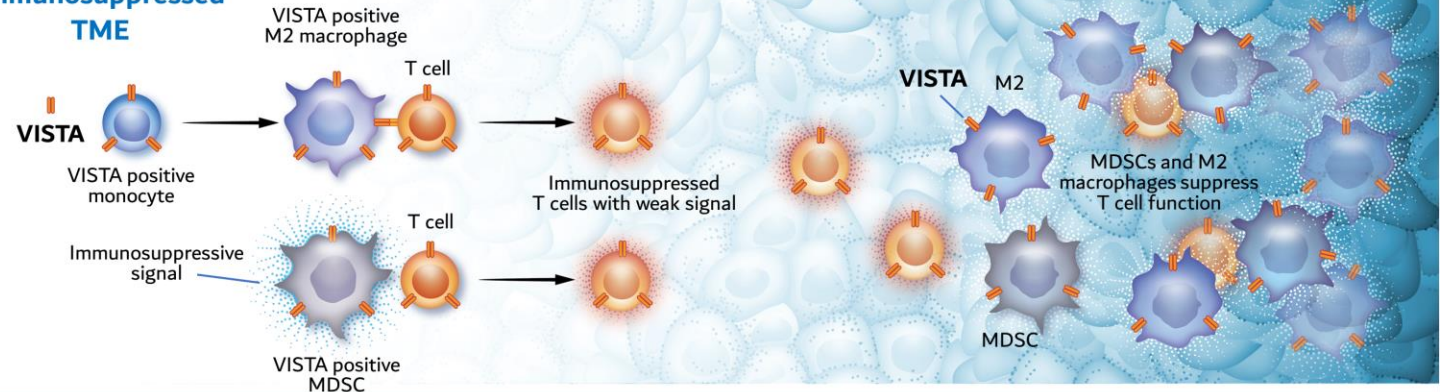
Promotes **T<sub>eff</sub>** function

Enhances **NK cell** activation

Enhances **monocyte** activation

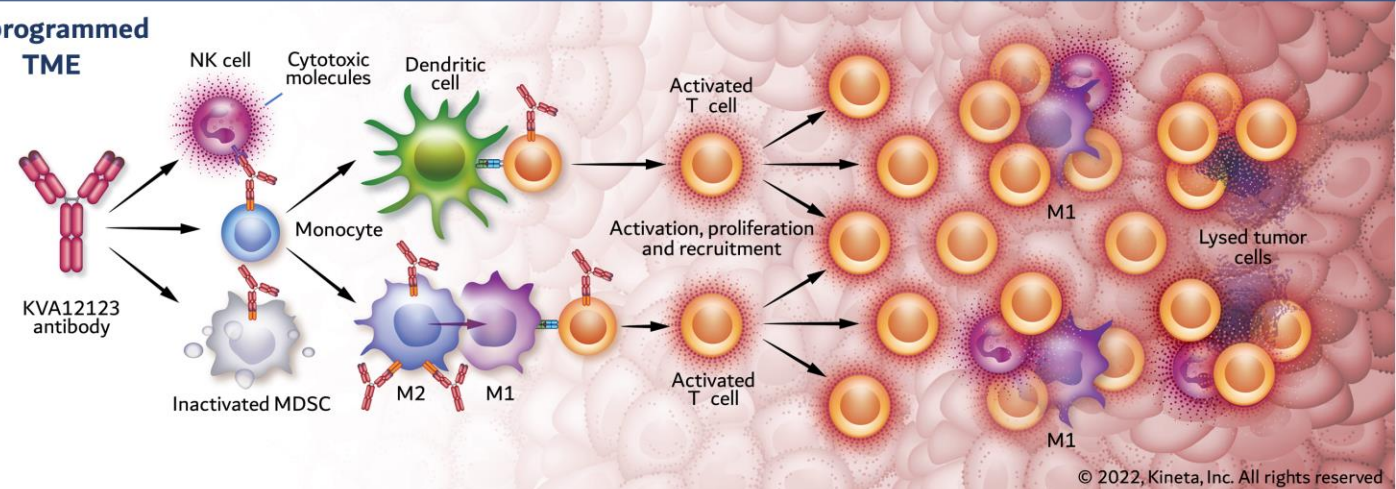
## VISTA causes immunosuppression by inactivating T cells

### Immunosuppressed TME



## KVA12123 targets VISTA with the potential to promote T cell and NK cell anti-tumor function

### Reprogrammed TME



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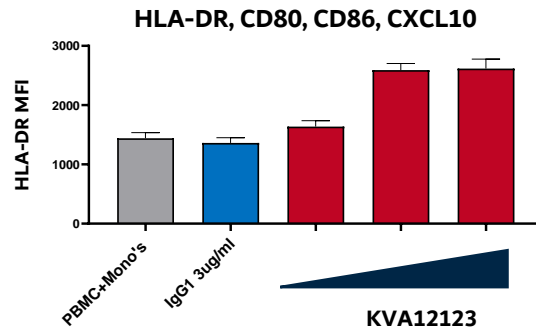
# KVA12123 activates both innate and adaptive immune cells *in vitro*



## Increases monocyte differentiation and activation



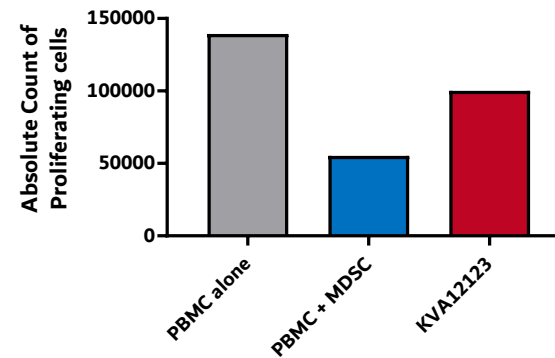
monocyte



## Reduces MDSC-mediated T cell suppression



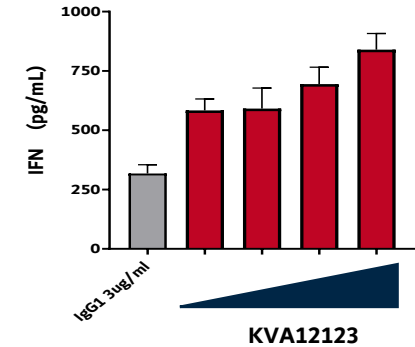
MDSC



## Increases HLA-dependent T cell activation



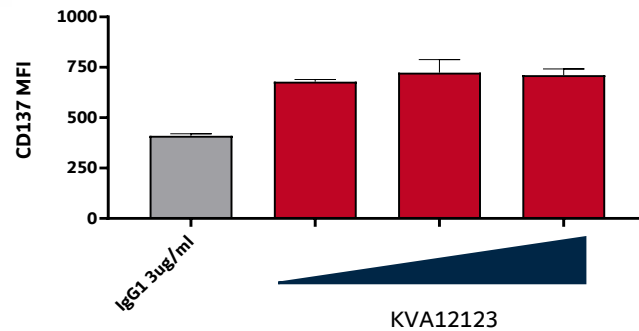
T cell



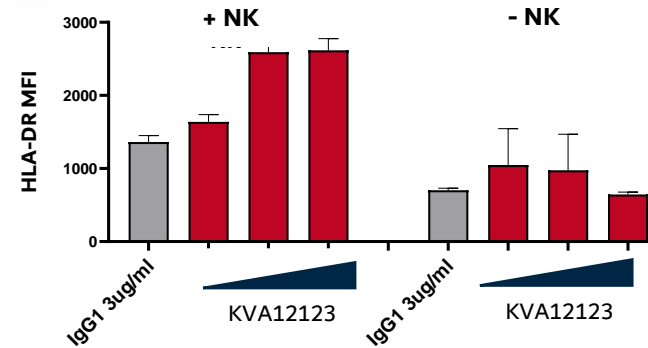
## Enhances NK cell activation



NK cell

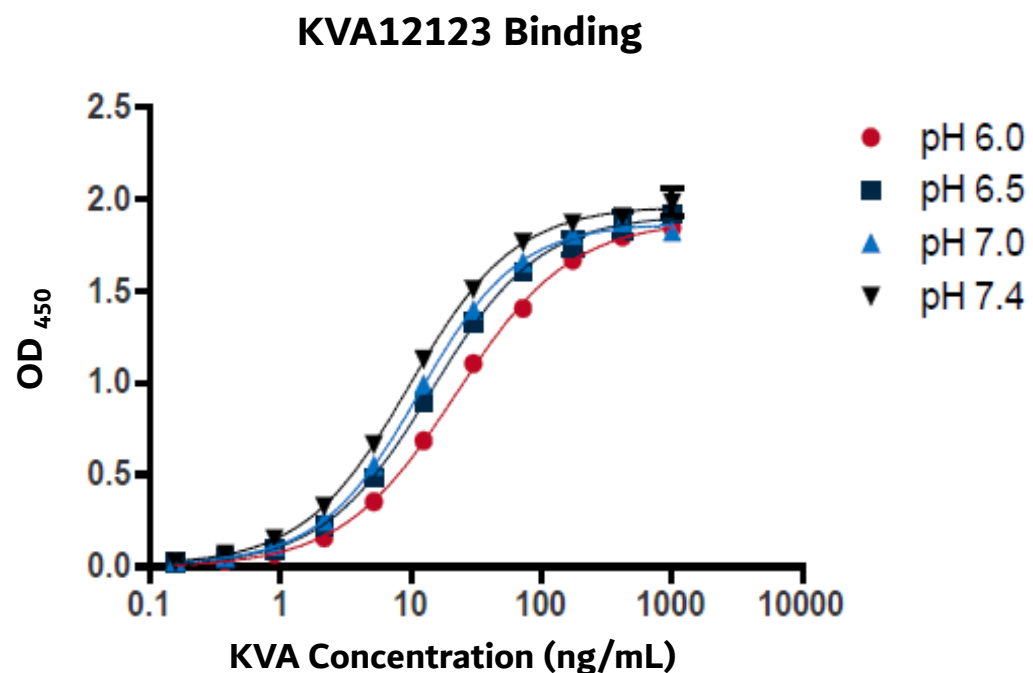


## NK dependent mechanism of action

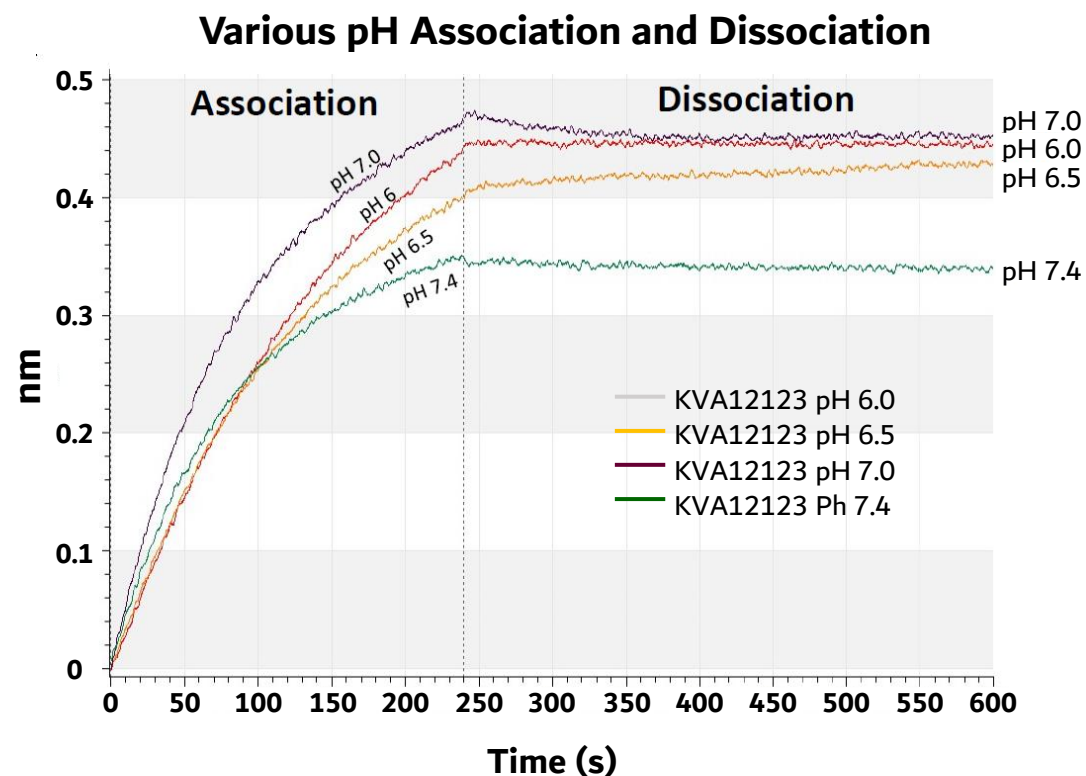


# KVA12123 binds at physiologic and acidic pH

## ELISA



## Octet



Binding studies by ELISA and Octet demonstrate rapid on-rate and slow off-rate from pH 7.4 to pH 6.0



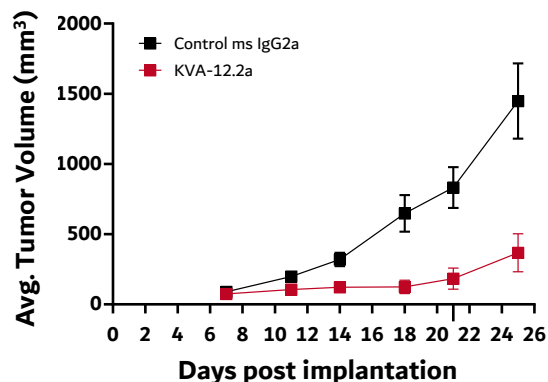
# KVA12123 demonstrates single agent tumor growth inhibition and in combination with PD-1 in preclinical models

## Monotherapy

### Bladder Cancer Model MB49

*hVISTA KI mice*

#### Mean Tumor Volume



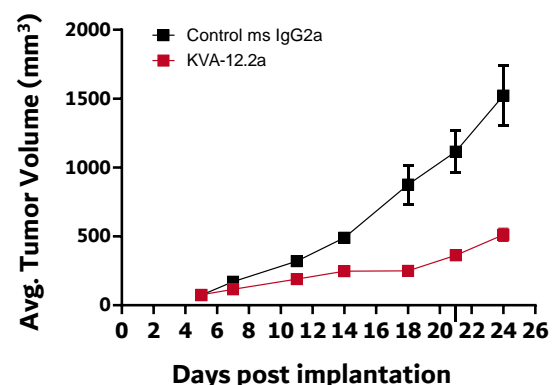
#### Tumor Growth Inhibition

Anti-VISTA: **75%**

### T Cell Lymphoma Model EG7

*hVISTA KI mice*

#### Mean Tumor Volume



#### Tumor Growth Inhibition

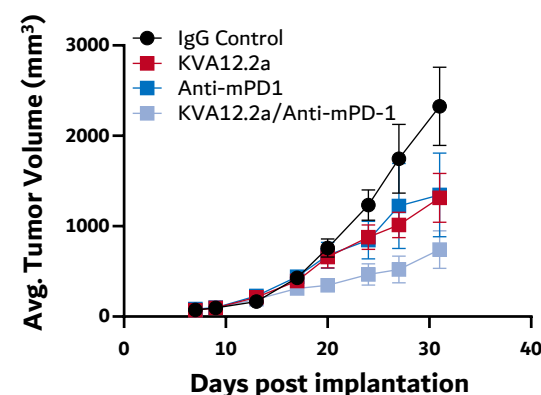
Anti-VISTA: **66%**

## Combination therapy

### Colon Carcinoma Model MC38\*

*hVISTA KI mice*

#### Mean Tumor Volume



#### Tumor Growth Inhibition

Anti-VISTA: **35-42%**

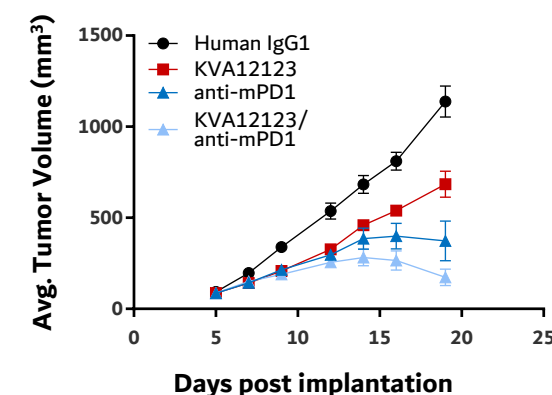
Anti-PD1: **42-60%**

Combination: **68%**

### Bladder Cancer Model MB49\*

*hVISTA KI mice*

#### Mean Tumor Volume



#### Tumor Growth Inhibition

Anti-VISTA: **40%**

Anti-PD1: **67%**

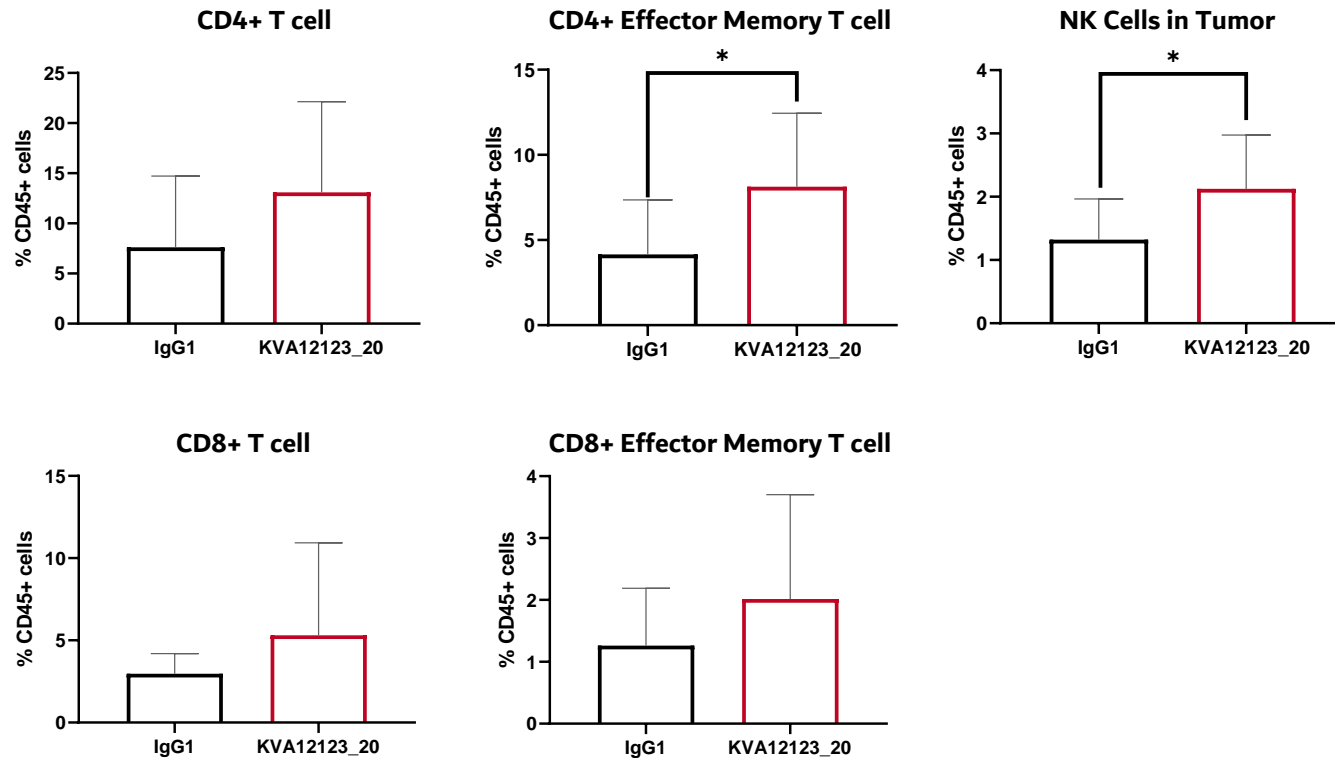
Combination: **85%**

\*Combination therapy studies used sub-optimal doses of each agent

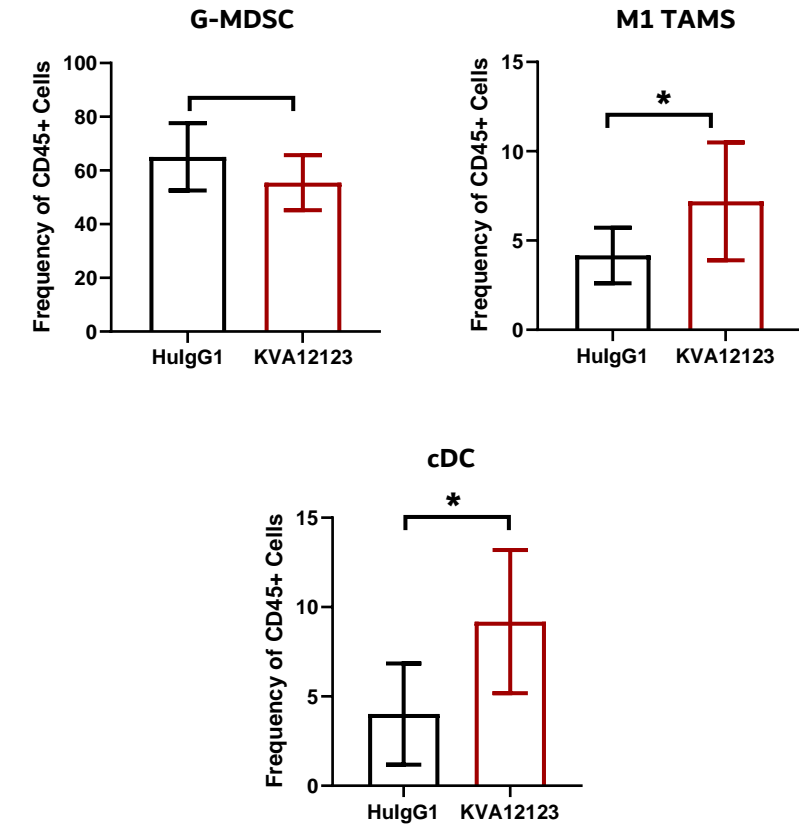
KVA12.2a: mouse isotype equivalent of KVA12123

# KVA12123 drives an integrated innate and adaptive anti-tumor immune response in MB49 model (*ex vivo*)

## Lymphoid compartment



## Myeloid compartment



# KVA12123 was observed to be well-tolerated in NHP toxicology studies



No  
mortality



No change in CRS cytokine  
levels (IL6 or TNF $\alpha$ )



No treatment-related  
adverse events



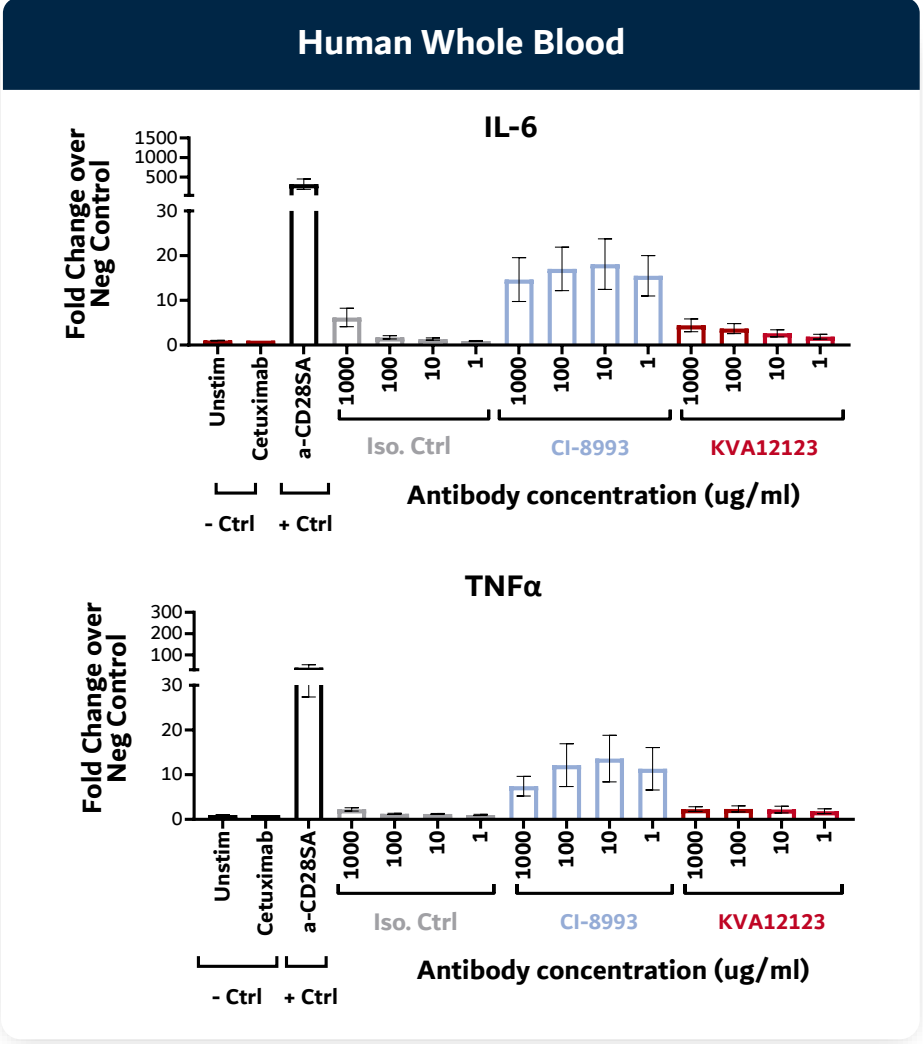
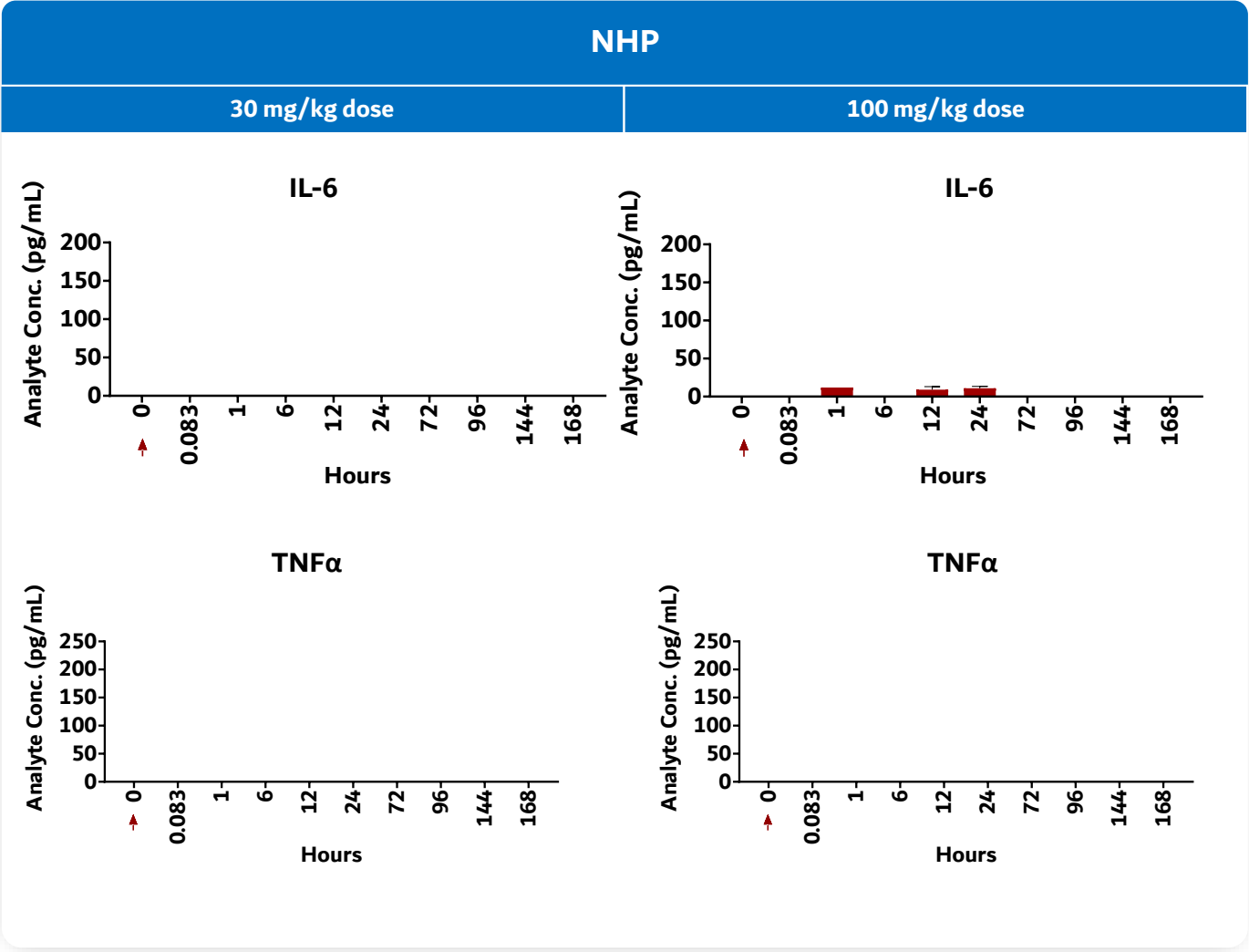
Well  
tolerated



No overt clinical signs  
or weight loss

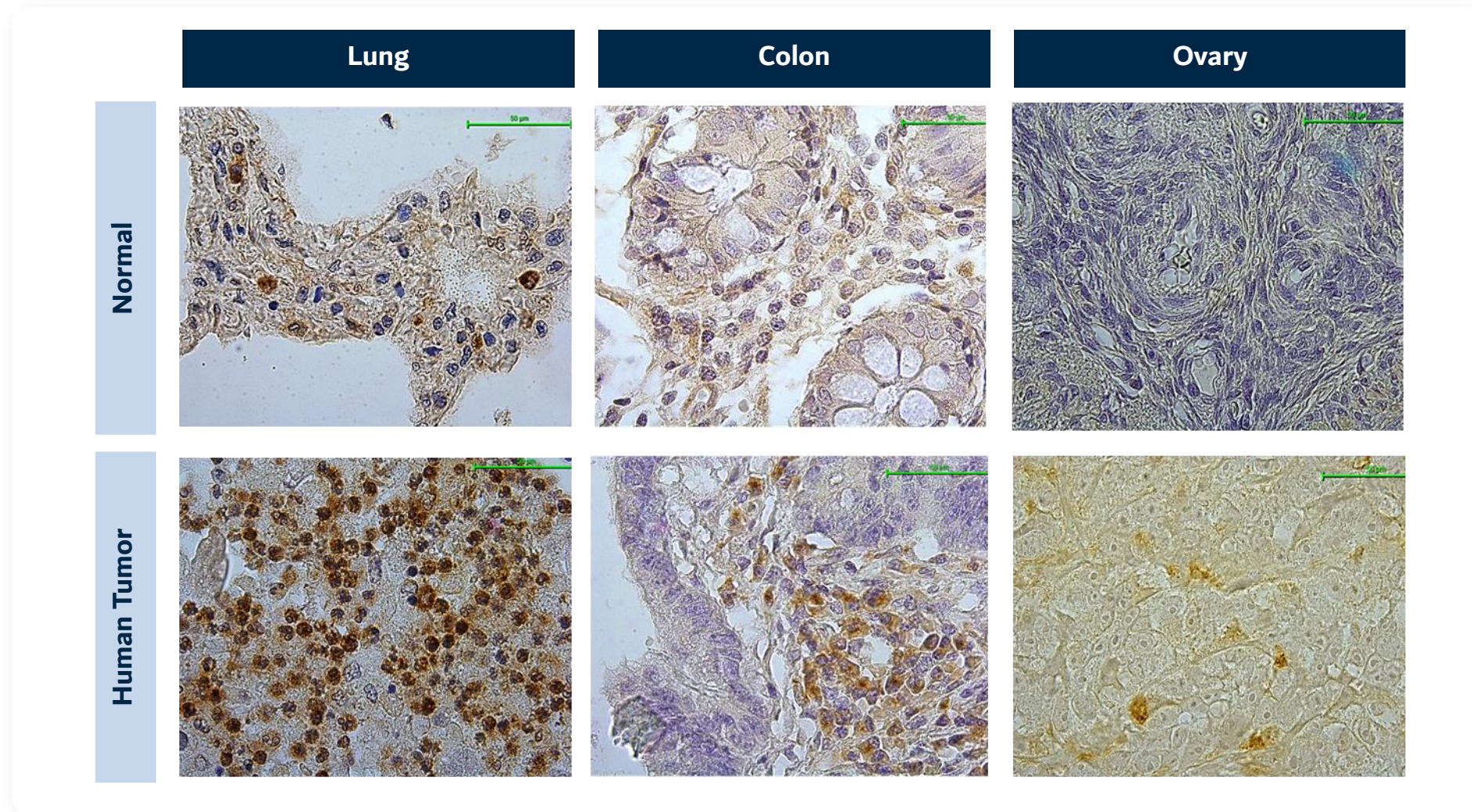
**Kineta has completed multiple, single and repeat-dose toxicology studies in NHP  
with doses of KVA12123 up to 100 mg/kg  
(>100-fold safety margin over target human exposure)**

# KVA12123: No CRS-associated signal in preclinical models in NHP toxicology studies as well as in human whole blood





# Clinical applications for KVA12123 are primarily focused on solid tumors with high levels of VISTA expression



Brown staining in human tumors indicates VISTA expression

# Phase 1 / 2 open-label clinical trial of KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors

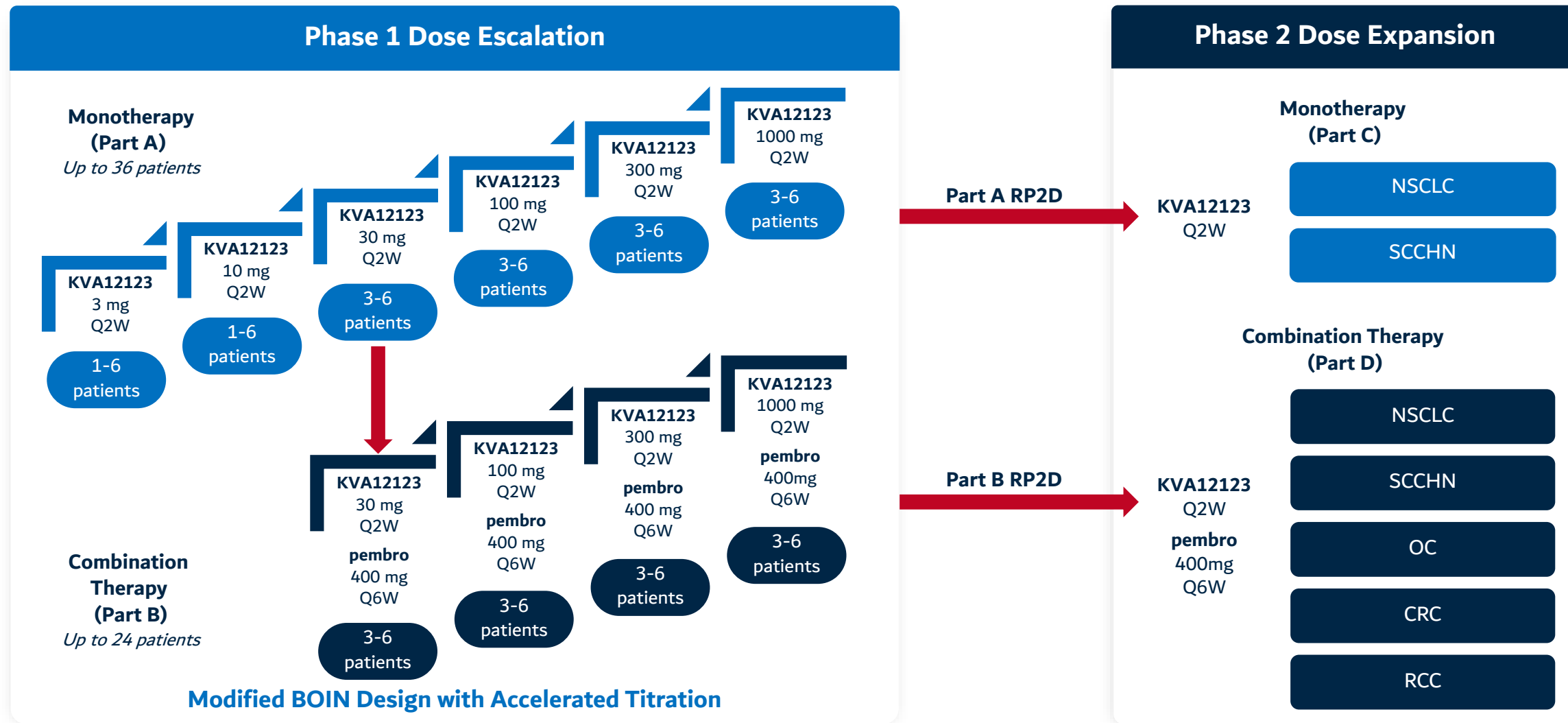
## Patient population:

- Phase 1 basket trial in patients with advanced solid tumors (up to 60 patients)
- Phase 2 in NSCLC, HNSCC, OC, CRC, RCC and TBD other patients

## Study objectives:

- Primary: Safety and tolerability, recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of KVA12123
- Secondary: Pharmacokinetics, immunogenicity, tumor response in subjects with advanced solid tumors per iRECIST (ORR)
- Exploratory: Biomarker and receptor occupancy

# Phase 1 / 2 open-label clinical trial of KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors





# KVA12123

## Clinical trial strategy

### Clinical research sites

- Selected to provide diverse advanced solid tumor patients

### Merck research collaboration

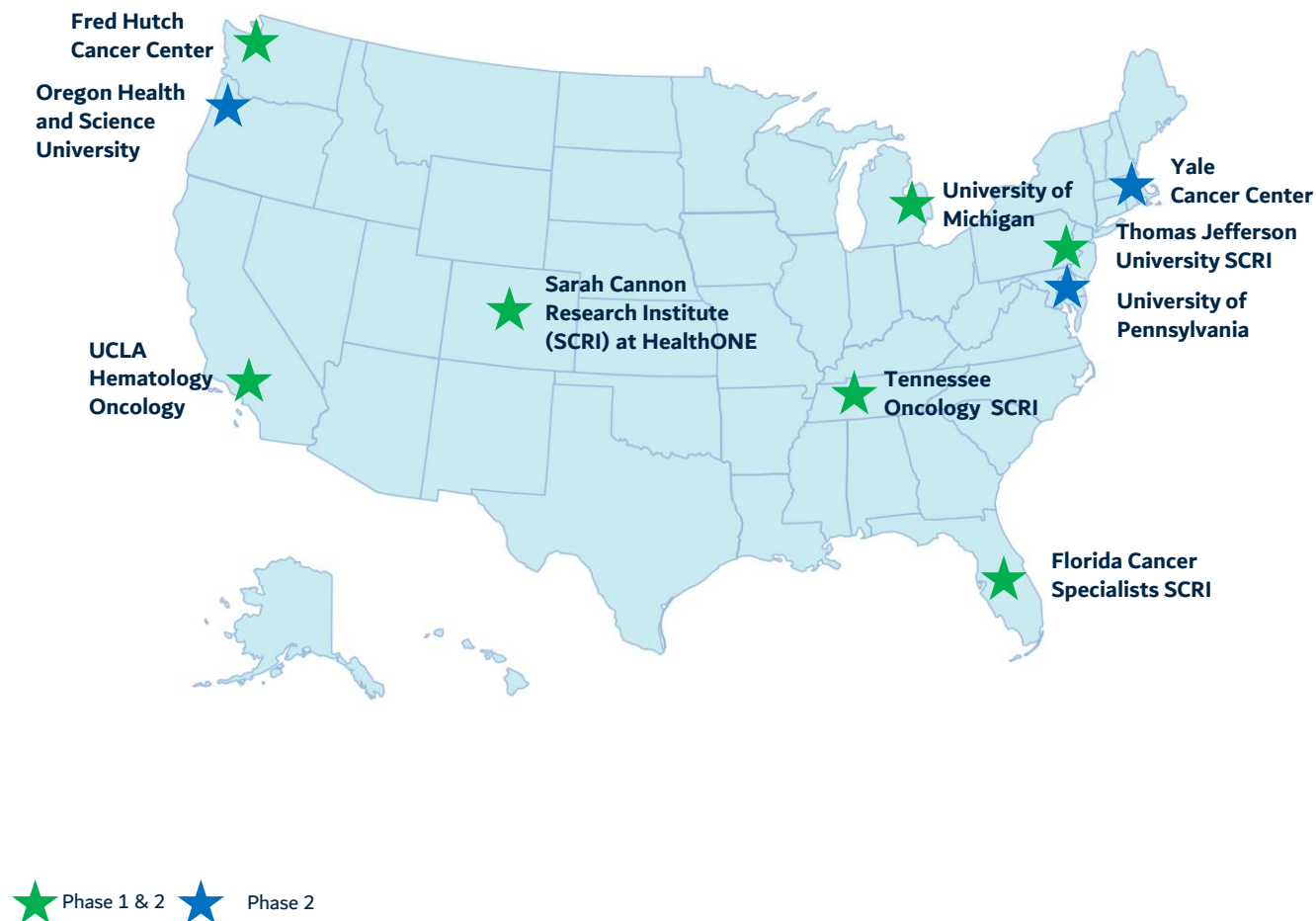
- Clinical trial collaboration and KEYTRUDA® supply agreement



### Exploratory biomarkers:

- Receptor Occupancy (RO)
- Chemokine and cytokine levels in blood
- Immune cell populations in blood
- VISTA expression in tumor pre- and post-treatment

### Clinical sites





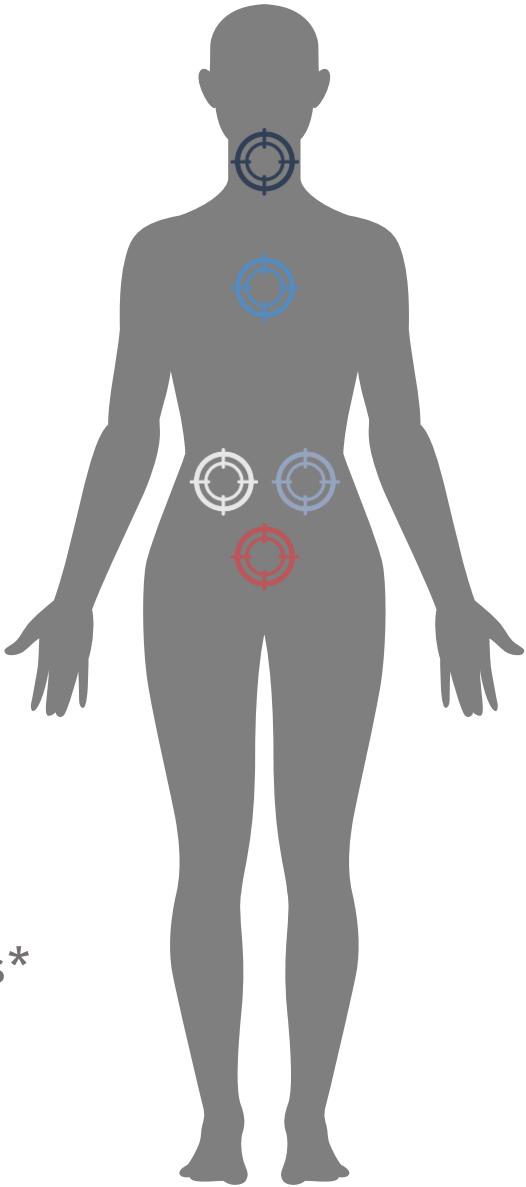
Large commercial market opportunity in potential solid tumor indications for KVA12123 in 2027

2.9M

annual newly diagnosed patients

2.0M

70% checkpoint inhibitor non-responders\*



NSCLC

984K newly diagnosed patients



Head and neck

243K newly diagnosed patients



Ovarian

142K newly diagnosed patients



Colorectal

1.2M newly diagnosed patients

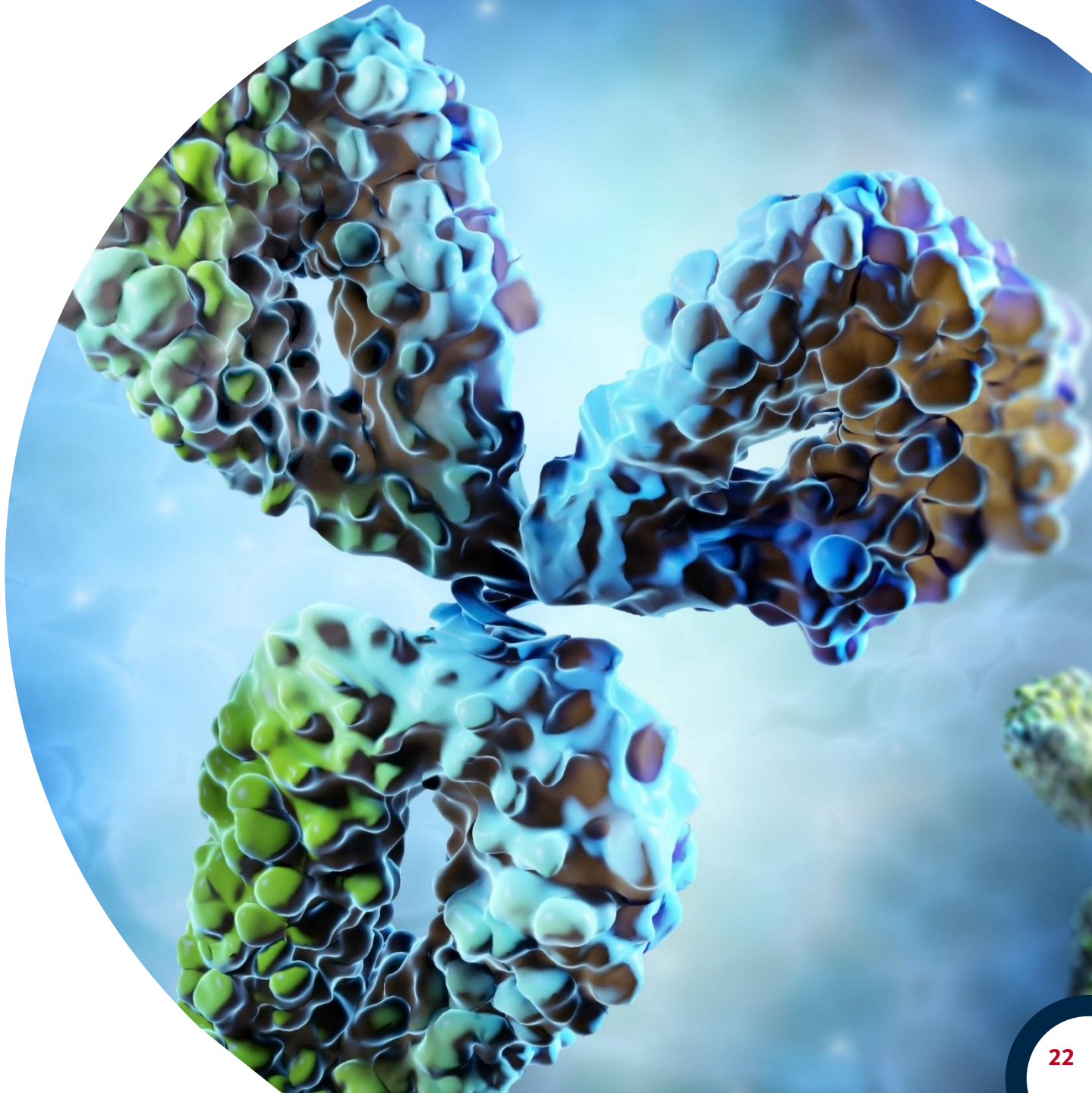


Renal cell carcinoma

372K newly diagnosed patients

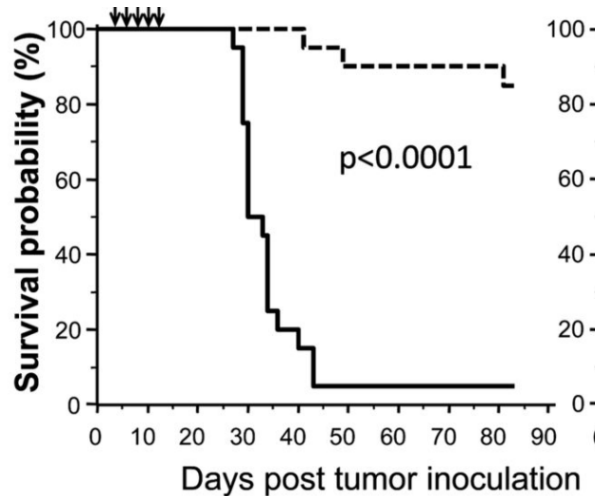


Anti-CD27 agonist  
mAb immunotherapy

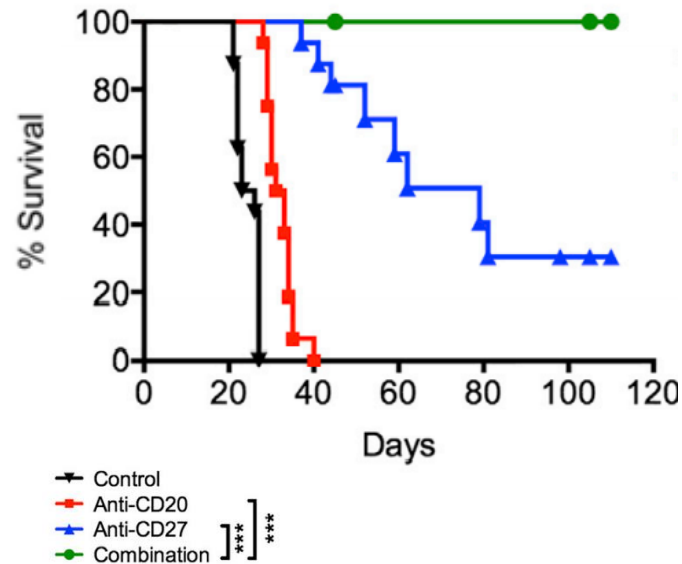


# Anti-CD27 agonist antibodies can drive tumor growth inhibition as a monotherapy and in combination with CPIs

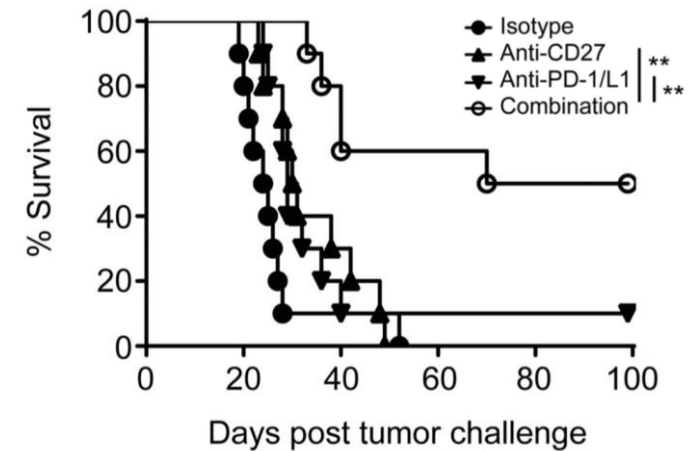
**Monotherapy**  
CT26 Colorectal Cancer <sup>1</sup>



**Combination Therapy**  
BCL-1 B cell lymphoma <sup>2</sup>

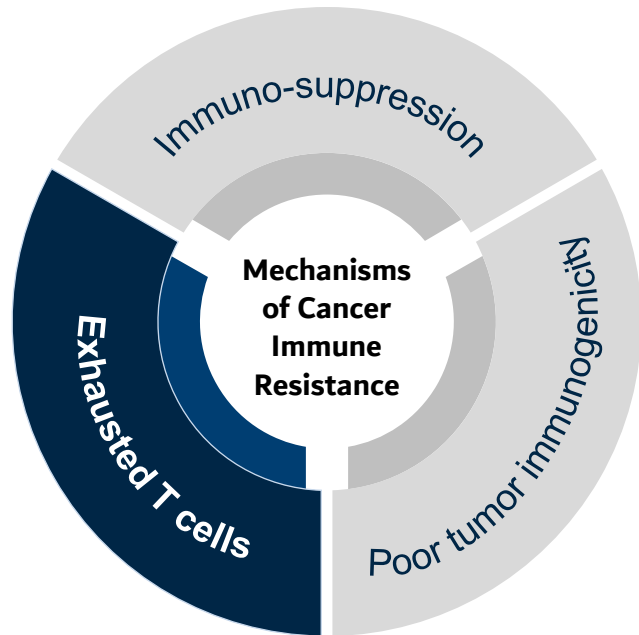


**Combination Therapy**  
B16-BL6 Melanoma <sup>3</sup>





# Anti-CD27 agonist to address exhausted T cell mechanism of cancer immune resistance



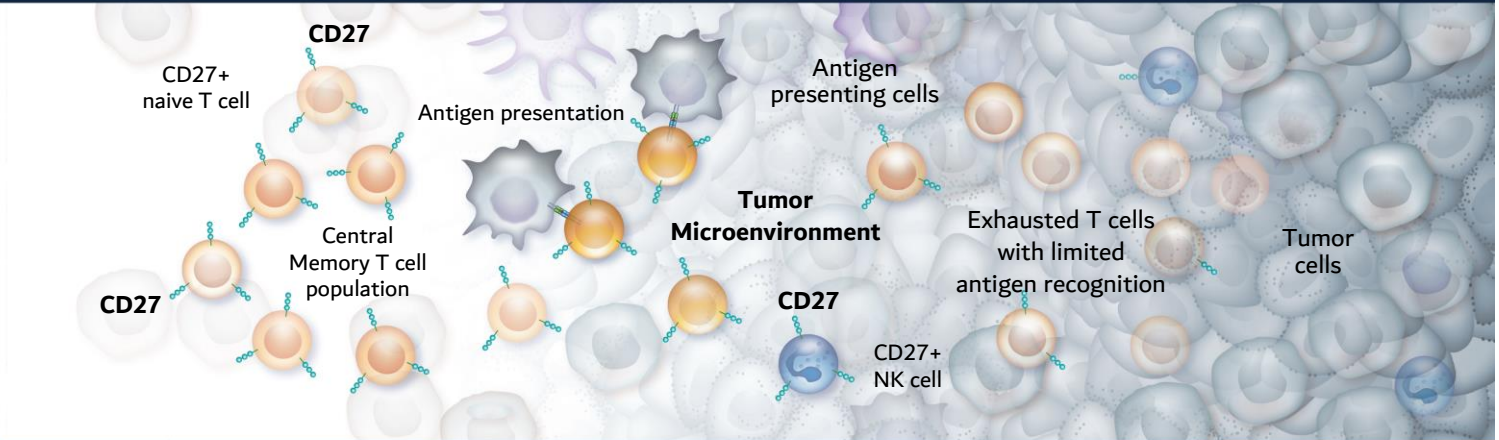
Activates and induces the maturation and migration of naïve **T cells**

Drives the **diversification of the T cell** repertoire

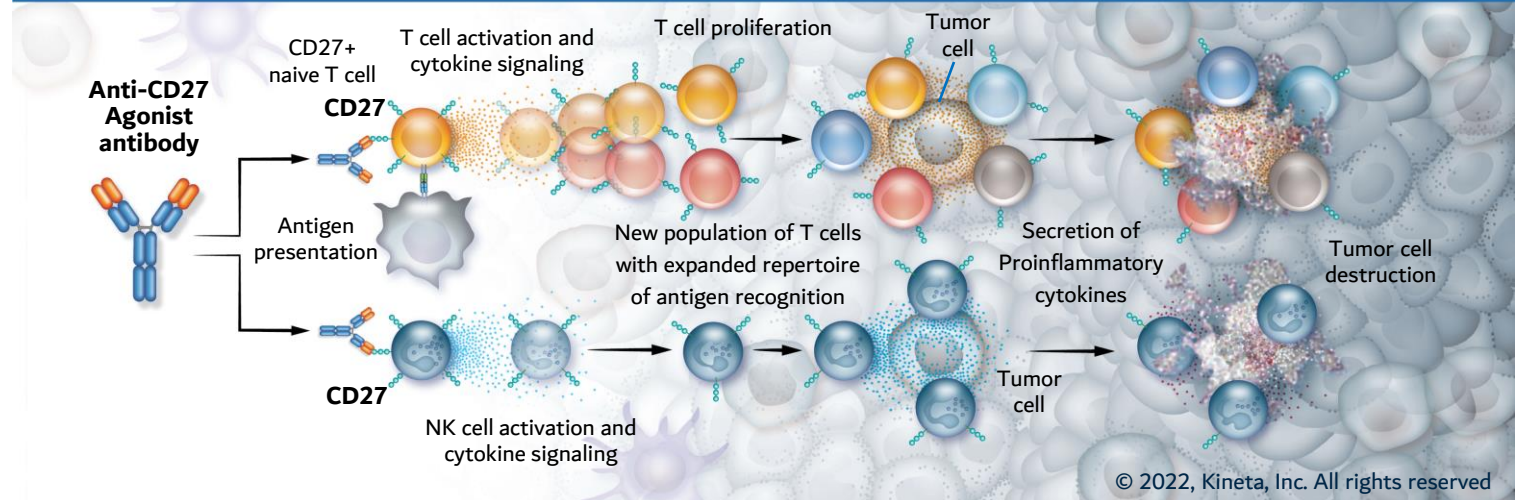
Enhances **NK cell** activation

Activates **low affinity antigens**

## Exhausted T cells



## CD27 agonist has the potential to generate new populations of functional anti-tumor immune cells



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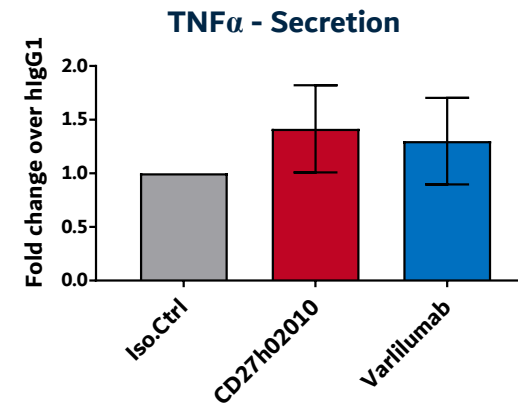
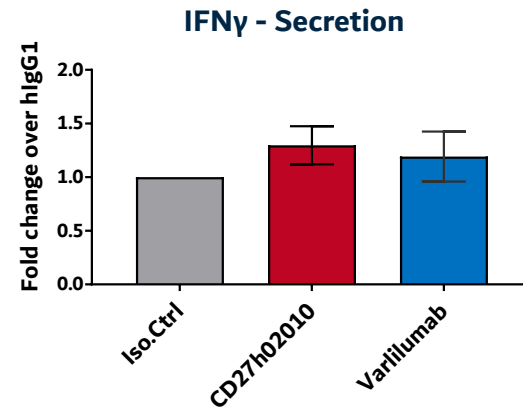
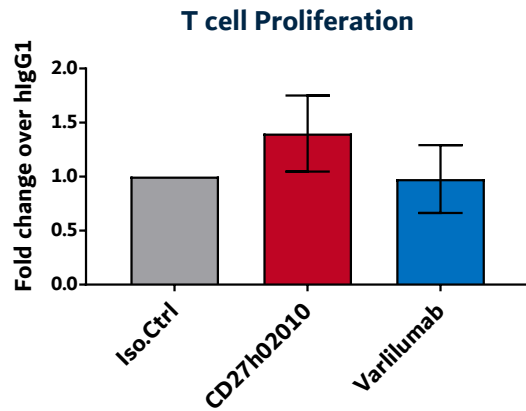
# Lead anti-CD27 mAb demonstrates robust agonist activities on T and NK cells in *in vitro* studies



## Increases T cell proliferation and activation



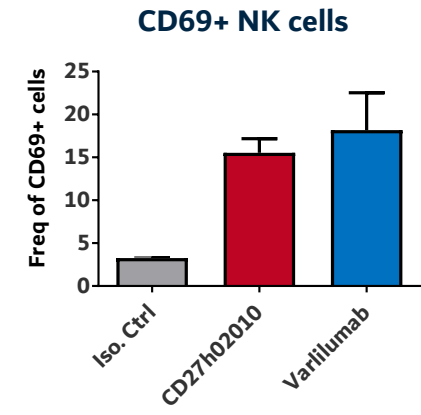
T cell



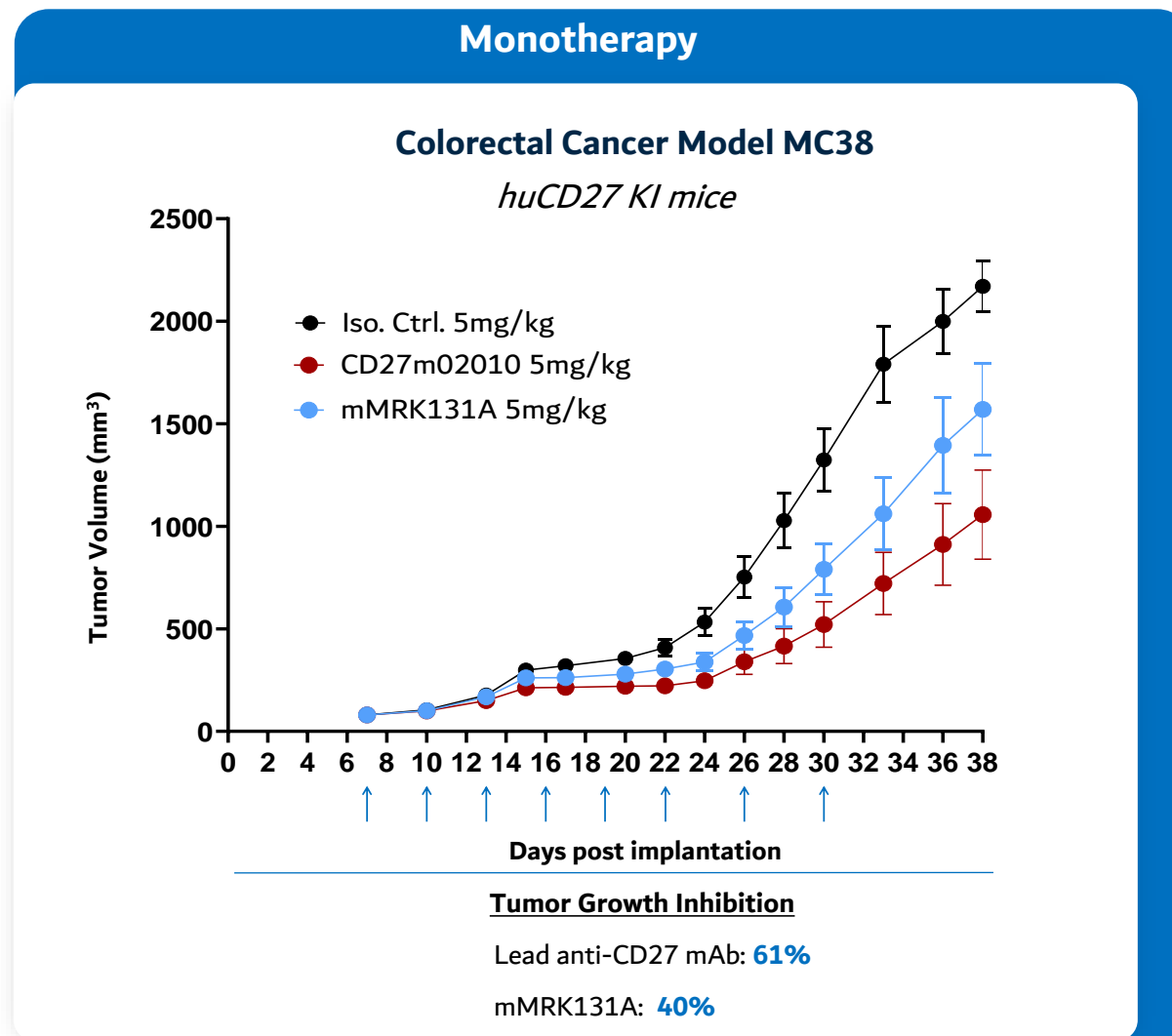
## Increases NK cell activation



NK cell



# Lead anti-CD27 agonist mAb demonstrates single agent tumor growth inhibition (TGI) in preclinical models



# Significant catalysts anticipated over the next 18 months

Anticipated Milestones		2023		2024			
		3Q	4Q	1Q	2Q	3Q	4Q
KVA12123	Dose first combination patient	●					
	Initial Phase 1 clinical safety data	●					
	Initial Phase 1 clinical efficacy data		●				
	Additional Phase 1 data readout				●		
	Initiate Phase 2 clinical study					●	
αCD27 agonist mAb	IND filing						●
	Start Phase 1 clinical study						●

# Experienced leadership team



**Shawn Iadonato, PhD**

Chief Executive Officer



**Craig Philips**

President



**Thierry Guillaudeau, PhD**

Chief Scientific Officer



**Keith Baker**

Chief Financial Officer



**Pauline Kenny**

General Counsel



**Jacques Bouchy**

EVP Investor Relations  
& Business Development

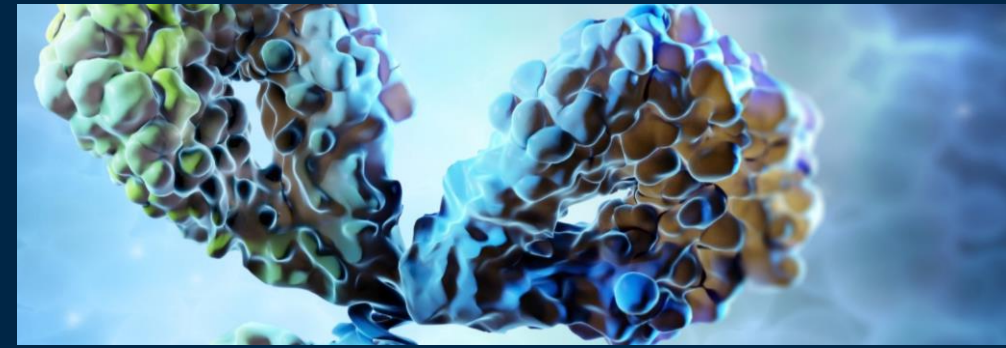


Schering-Plough





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Developing next generation  
immunotherapies for cancer patients

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## Appendix



# Strategic partnerships provide potential for a significant revenue stream

License Agreements with no research obligations by Kineta			
Program	Neuromuscular diseases-ALS	Oncology	Cystic fibrosis
Partner		 <small>A Member of the Roche Group</small>	
Key deal terms	Received <b>\$5M</b> milestone payment in July 2023	Up to <b>\$96M</b> in milestones	Up to <b>\$965M</b> in commercial only milestones
	Up to <b>\$255M</b> in milestones	Royalties on net sales	Royalties on net sales
	Royalties on net sales		Revenue share on sub-license payments