Kadmon®

Targeted IL-15 Immunotherapy Platform

May 2021

About Kadmon

Kadmon®

Research

Clinical Pipeline

Commercial Operation

- **Late-stage biopharma company headquartered in New York, NY (Nasdaq: KDMN)**
- **Therapeutic focus areas:**
  - Immune and fibrotic diseases
  - Immuno-oncology (I-O)
- **Lead candidate: Belumosudil, a small molecule ROCK2 inhibitor for the treatment of chronic graft-versus-host disease (cGVHD)**

Executive Summary: Kadmon IL-15 Immuno-oncology (I-O) Platform

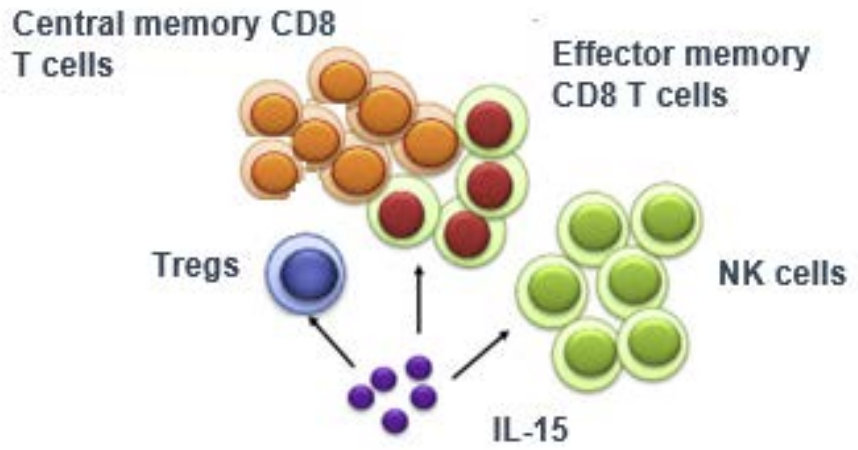
- **Kadmon's I-O platform seeks to harness the immuno-stimulatory activity of IL-15 to treat cancer**
- **Lead candidate: KD033, a proprietary anti-PD-L1 monoclonal antibody fused to IL-15**
  - Phase 1 clinical trial of KD033 ongoing in patients with metastatic or locally advanced solid tumors
  - Patent protection through 2035 (without extension)
- **Additional IL-15 fusion proteins in development**

IL-15 Stimulates Immune Response without Immunosuppression

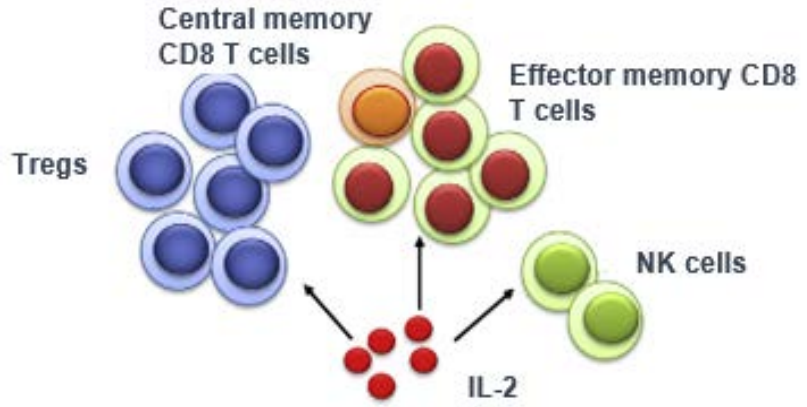
IL-15 May Offer Unique Advantages over IL-2

- **IL-15 is a selective immuno-stimulatory cytokine**
  - Promotes CD8 memory T, natural killer (NK), and NKT cells to induce long-lasting responses
  - Does not stimulate immunosuppressive Treg cells, promoting response durability
- **Engineered IL-2 is currently being studied in combination with I-O therapies**
  - Broadly stimulates immunosuppressive Treg cells, potentially reducing efficacy
  - Requires genetic engineering to skew activity toward immuno-stimulatory CD8 T cells

IL-15 promotes CD8 memory T cells without stimulating Tregs, promoting response durability



IL-2 induces Treg proliferation, resulting in immunosuppression

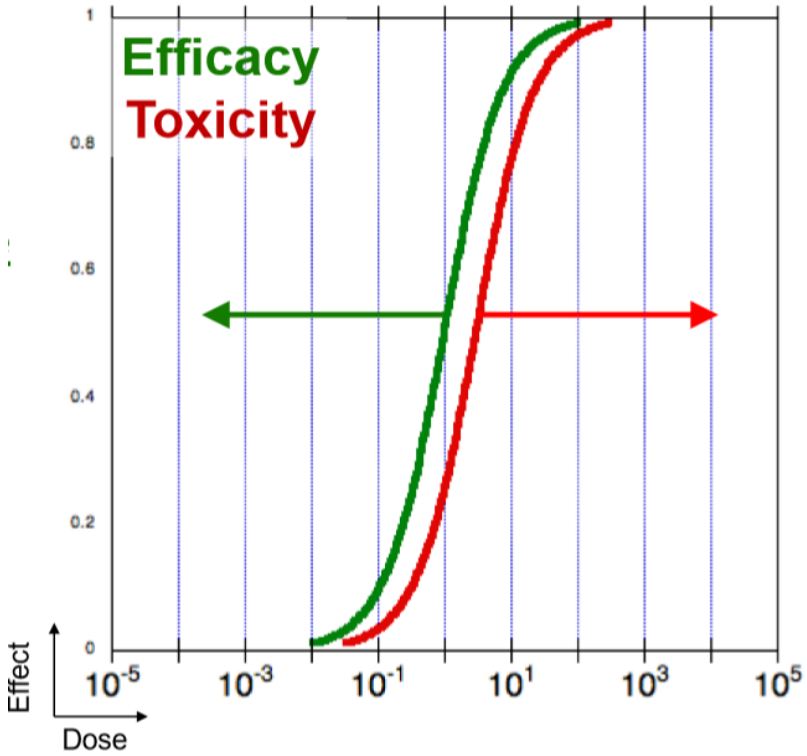


Sim GC et al. *Cytokine & growth factor reviews. 2014*

Challenge: Recombinant IL-15 Therapy has a Limited Therapeutic Window

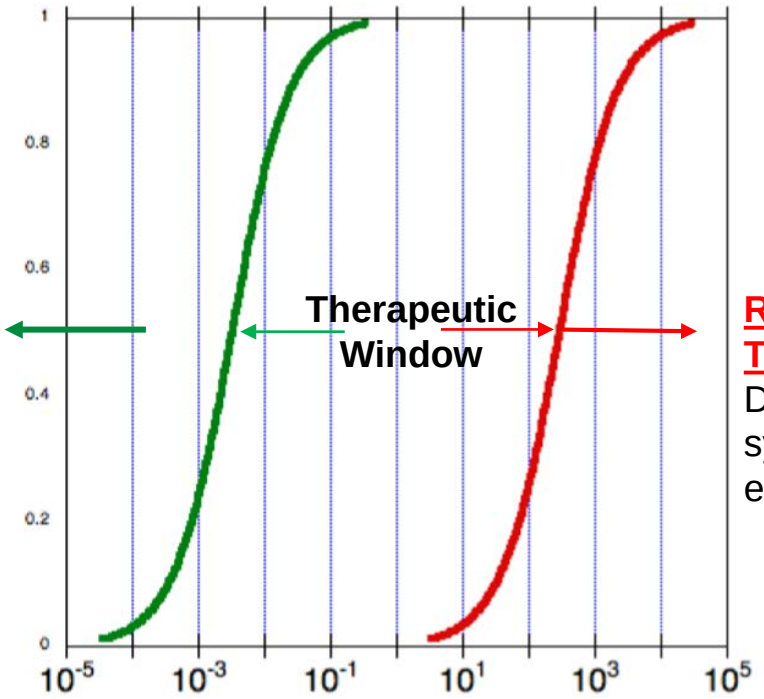
Opportunity: Targeting IL-15 to tumor microenvironment with a monoclonal antibody enhances efficacy and reduces toxicity, improving therapeutic index

Non-targeted IL-15



Targeted IL-15

Enhanced Efficacy
Increased tumor exposure

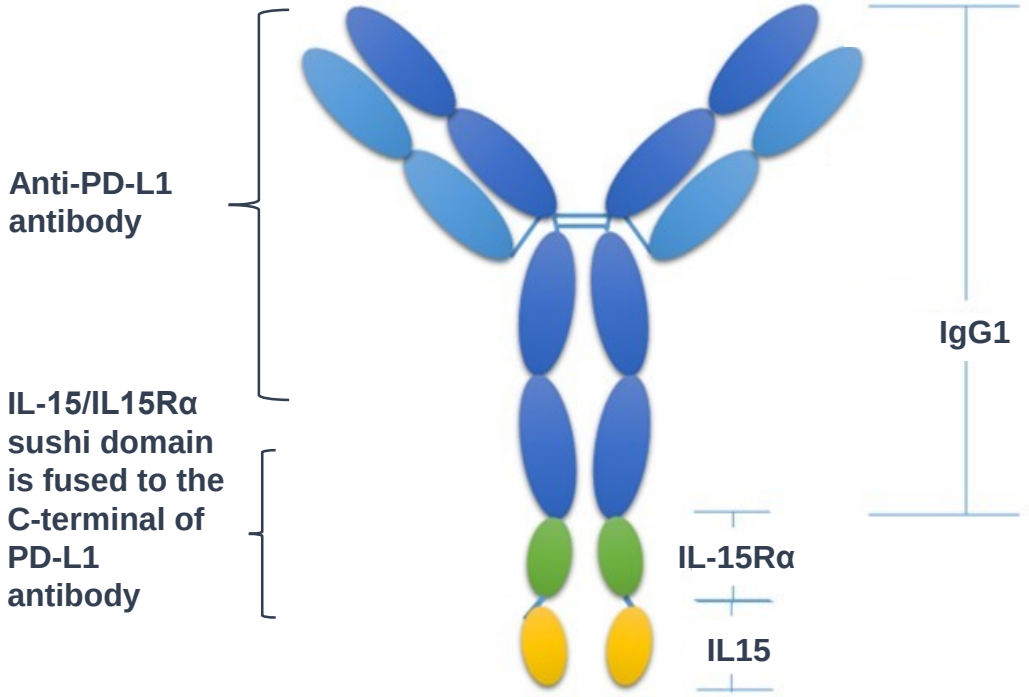


Reduced Toxicity
Decreased systemic exposure

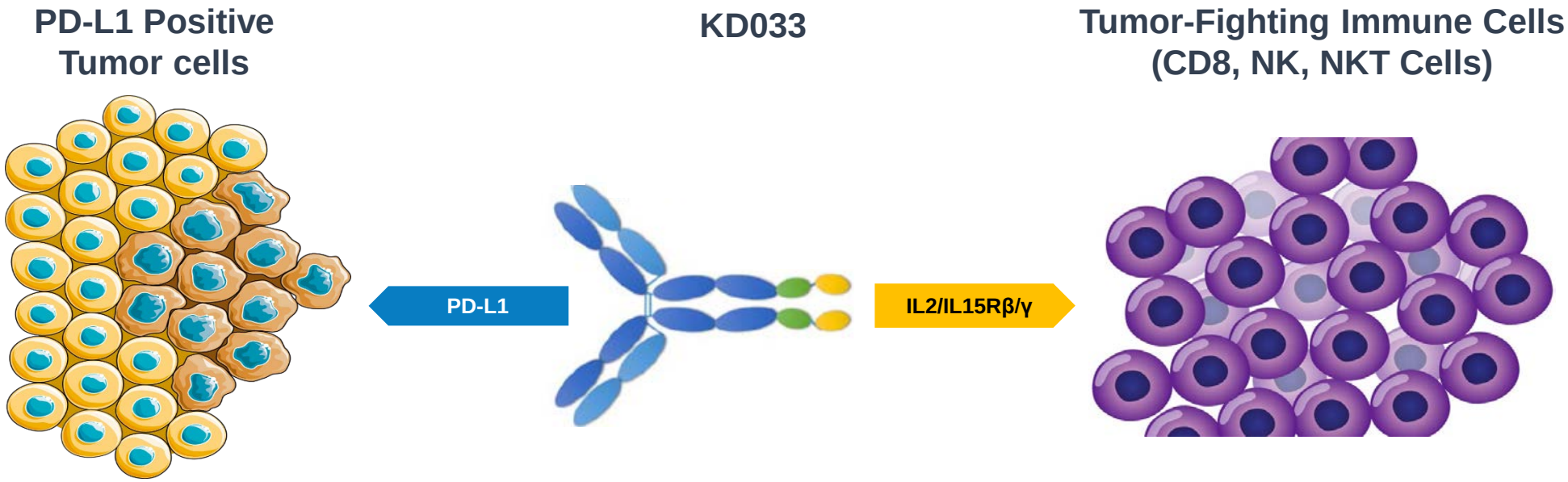
KD033: Anti-PD-L1/IL-15 Fusion Protein

- **KD033: Anti-PD-L1 antibody fused to two IL-15 cytokines**
  - **IL-15 cytokines:**
    - Stimulate immune response without immuno-suppression
    - Expand tumor-fighting NK and memory CD8+ T cells to induce long-lasting responses
    - IL-15 fusion to IL-15 receptor alpha sushi domain enhances stability of the antibody complex
  - **PD-L1 antibody:**
    - Targets IL-15 to the tumor microenvironment to mitigate safety concerns

KD033 Structure



KD033 Trans-presentation Optimizes Activity of PD-L1 and IL-15

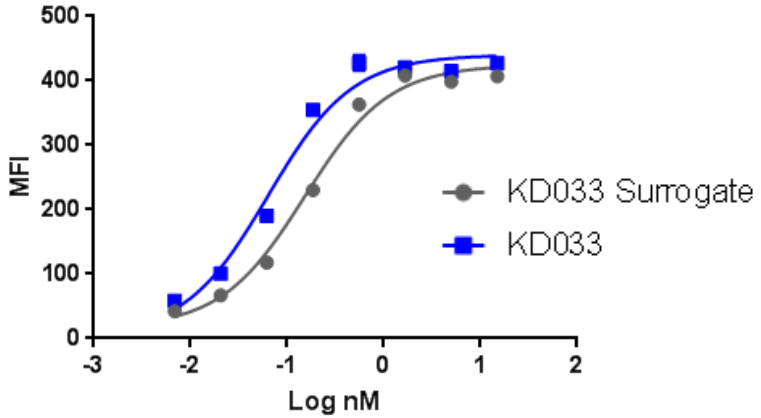


- Trans-presentation localizes immuno-stimulatory activity of IL-15 to PD-L1 positive tumors
- KD033 blocks PD-1/PD-L1 inhibitory signaling and stimulates IL2/IL15Rβ/γ signaling in immune cells

Comparable Binding to Surrogate in Human Tumor and Immune Cells

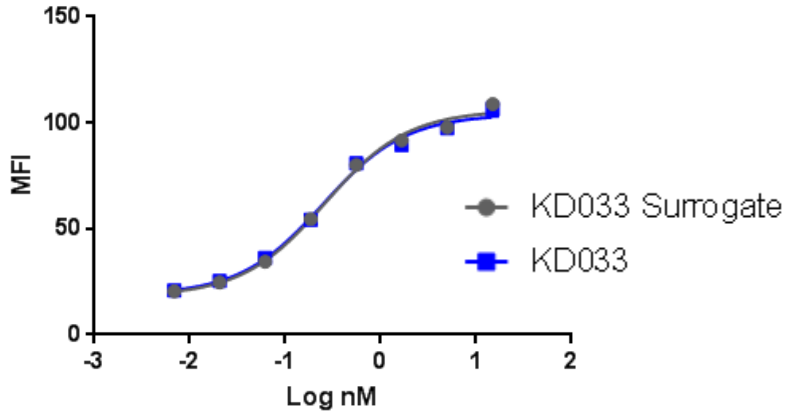
KD033 and Surrogate Binding to Tumor Cells Expressing PD-L1

PD-L1 high human breast cancer cell line (MDAMB231)



Binding of IL15 to IL2Rβ overexpressing cell line: a measure of IL-15 affinity

Binding: 293 IL2Rβ

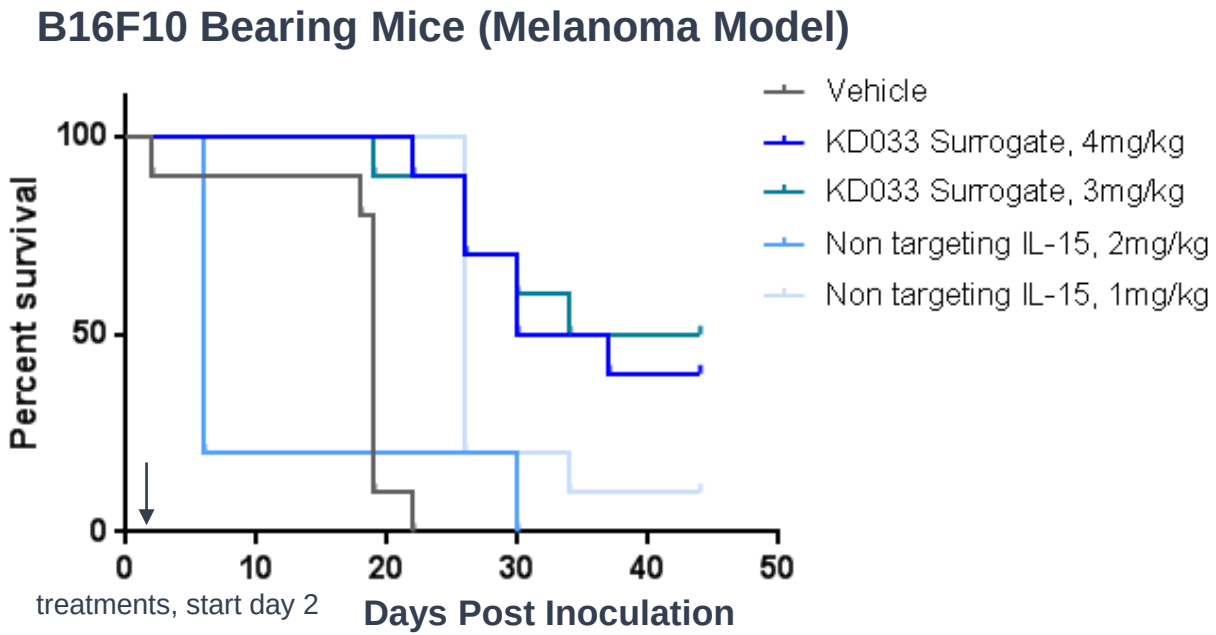


- KD033 Surrogate was generated to test pharmacology of KD033 in mouse syngeneic models
- KD033 and KD033 Surrogate bind to PD-L1 expressing human cells
- KD033 and KD033 Surrogate have high affinity binding to IL-2/IL-15Rβ

AACR 2020 poster #2827; internal data

KD033 is Better Tolerated at a Higher Dose than Non-targeting IL-15

KD033 Surrogate Tolerability is 4-Fold Higher than Non-targeting IL-15



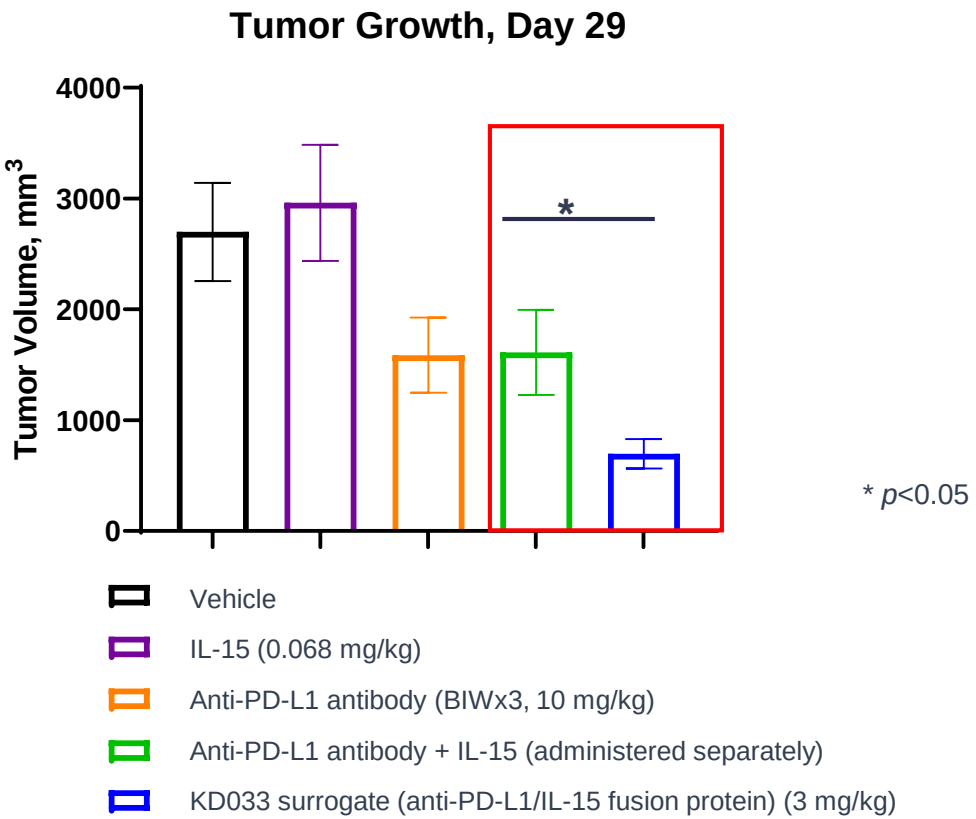
- **Mice treated with non-targeting IL-15 at 2 mg/kg died 4 days after treatment (MTD is 1 mg/kg)**
- **KD033 surrogate is tolerated up to 4 mg/kg**

SITC 2018 poster #P414

KD033 is More Efficacious than IL-15, Anti-PD-L1, or Anti-PD-L1 + IL-15

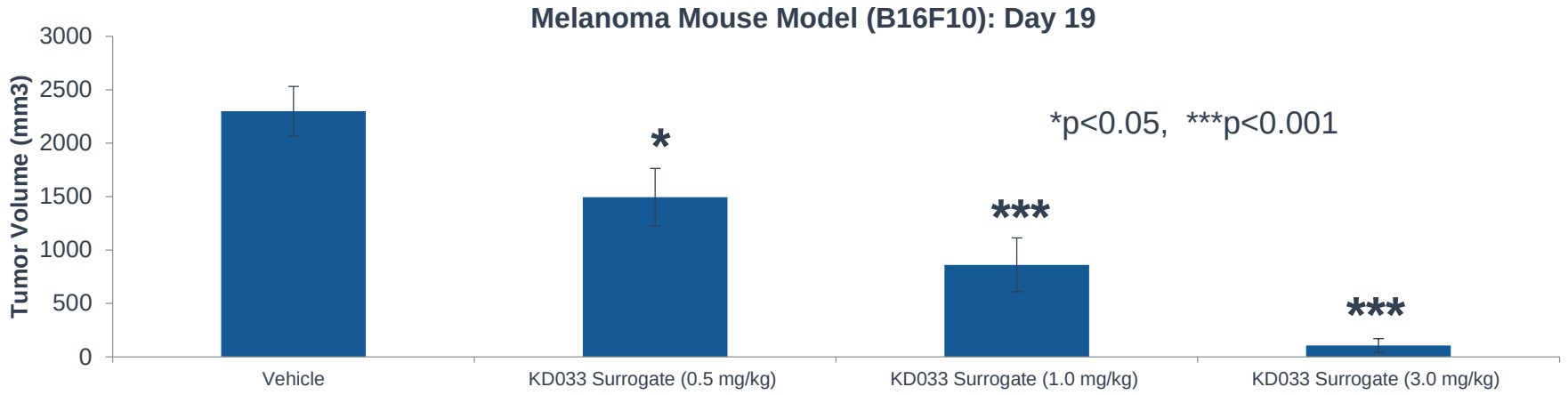
Better together:
KD033 surrogate was significantly more efficacious vs. anti-PD-L1 alone or anti-PD-L1 + IL-15 in animal studies

KD033 Surrogate Efficacy in CT26 Colon Carcinoma Model

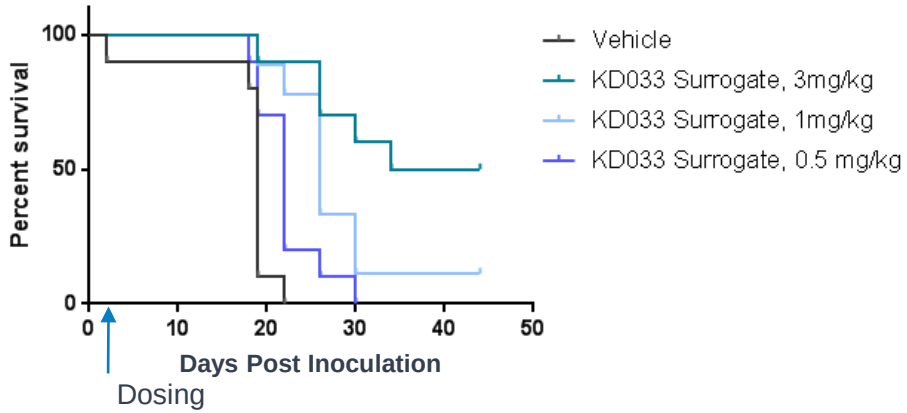


AACR 2020 poster #2827

Dose-Dependent Efficacy in PD-1/PD-L1-Resistant Melanoma Model



Melanoma Model: Survival



Group	Median Survival (Days)
Vehicle	19
KD033 Surrogate **0.5 mg/kg**	22
KD033 Surrogate **1.0 mg/kg**	26
KD033 Surrogate **3.0 mg/kg**	39

SITC 2018 poster #P414

Significant Tumor Growth Inhibition (TGI)

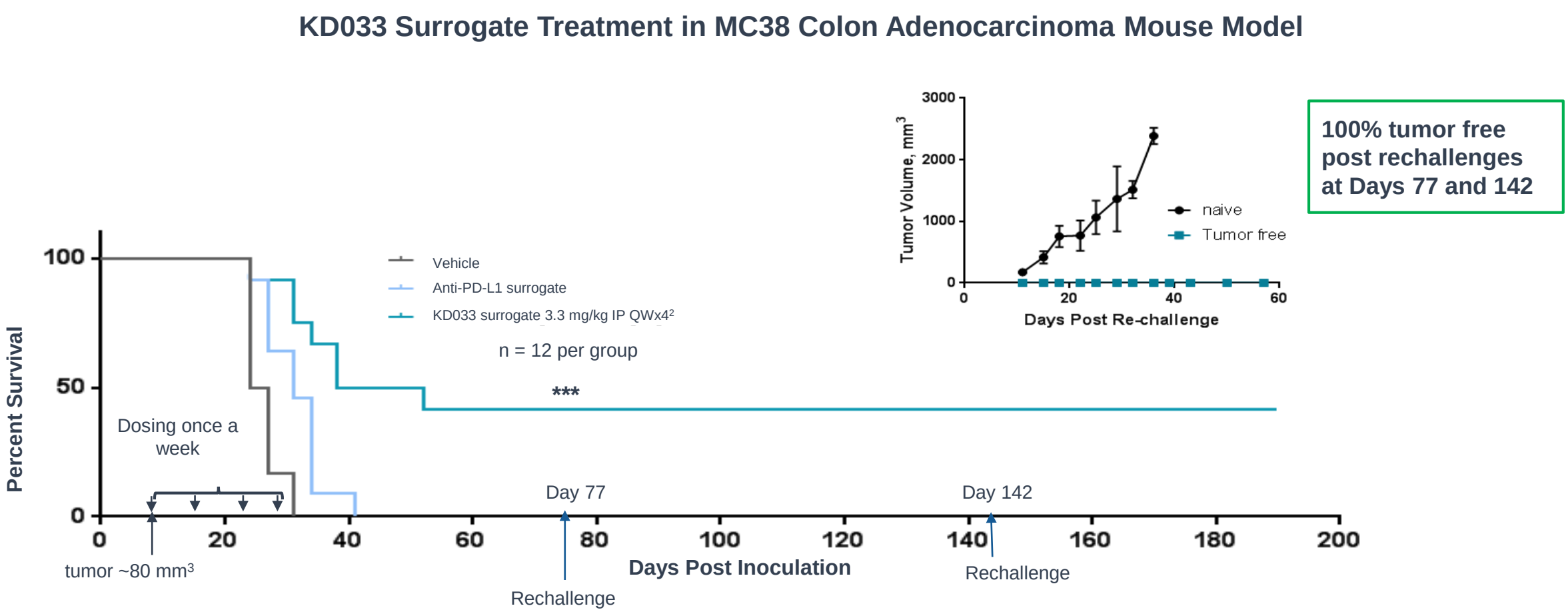
Nonclinical Efficacy Screening of KD033 in 10 Syngeneic Models		
Model	Tumor Type	Single-dose KD033 surrogate treatment
		TGI (%)
CT26-WT	**Colorectal**	**79**
MC38	**Colorectal**	**72**
MBT-2	**Bladder**	**63**
H22	Liver	58
A20	Lymphoma	46
RM-1	**Prostate**	**44**
Pan02	Pancreatic	37
B16F10	**Melanoma**	**34**
B16BL6	**Melanoma**	**32**
LL/2	Lung	28

- Single-Dose KD033 Surrogate Treatment 3mg/kg, tumor volume ~100mm^3
- Purple indicates syngeneic models used as tool models; dark blue indicates significantly better efficacy than historical anti-PD-L1 efficacy

Mol Cancer Ther February 1 2021 (20) (2) 347-356

KD033 Triggers Tumor Cell Killing Memory

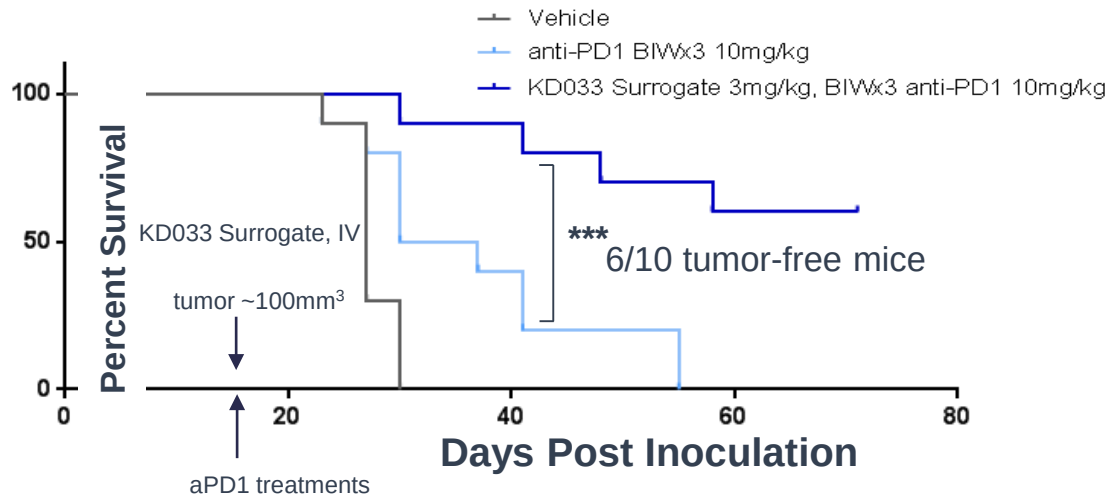
- **KD033 induced immune system memory:**
  - Mice treated with KD033 surrogate survived tumor rechallenges at Day 77 and Day 142 post inoculation



Internal data on file

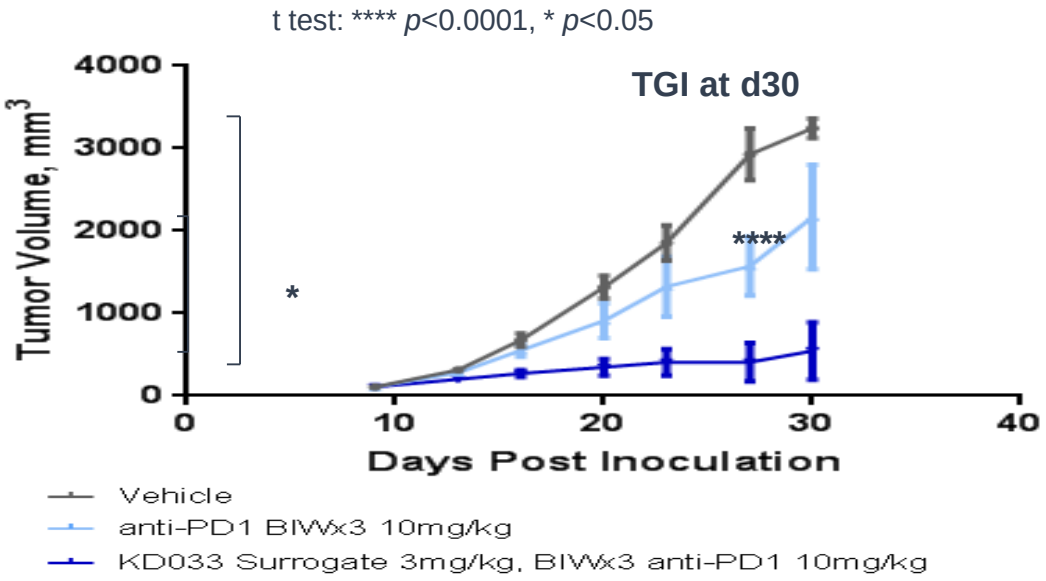
Synergistic Efficacy with Combined with Anti-PD-1

CT26



Log-rank (Mantel Cox) test: *** $p<0.001$

Mean Tumor Growth



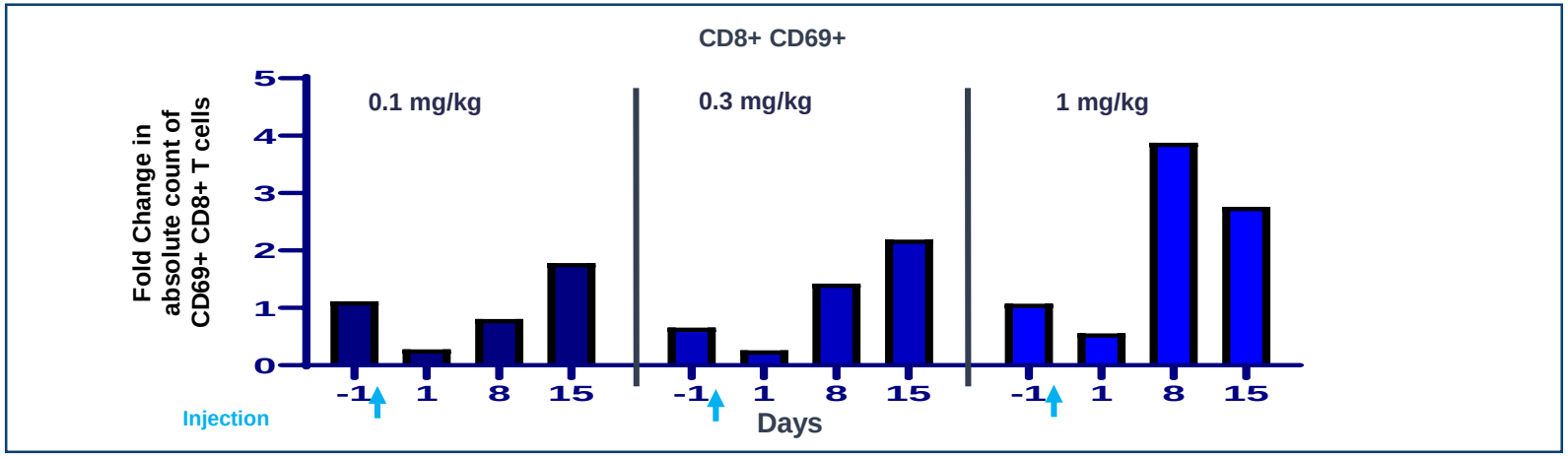
- **Adding anti-PD1 therapy to KD033 surrogate demonstrated strong anti-tumor activity (6/10 tumor-free mice)**
- **Combination of KD033 surrogate and anti-PD1 demonstrated acceptable safety**

Mol Cancer Ther February 1 2021 (20) (2) 347-356; *SITC 2018 poster #P414*

Activates Lymphocytes and Induces Proliferation of CD8+ T and NK Cells in PBMCs

Sustained T, CD8 and NK cell activation and proliferation in cynomolgus monkeys after a single dose of KD033

Increase in Activated CD8+ T Cells Observed After KD033 Infusion



Increase In Cell Numbers Observed At Day 7 Post Infusion

	Total T	CD8+T	NK	NKT-Like
0.1 mg/kg	1	1	1.3	1.5
0.3 mg/kg	2.3	2.8	2.5	3
1 mg/kg	6.1	8.1	5.1	5.8

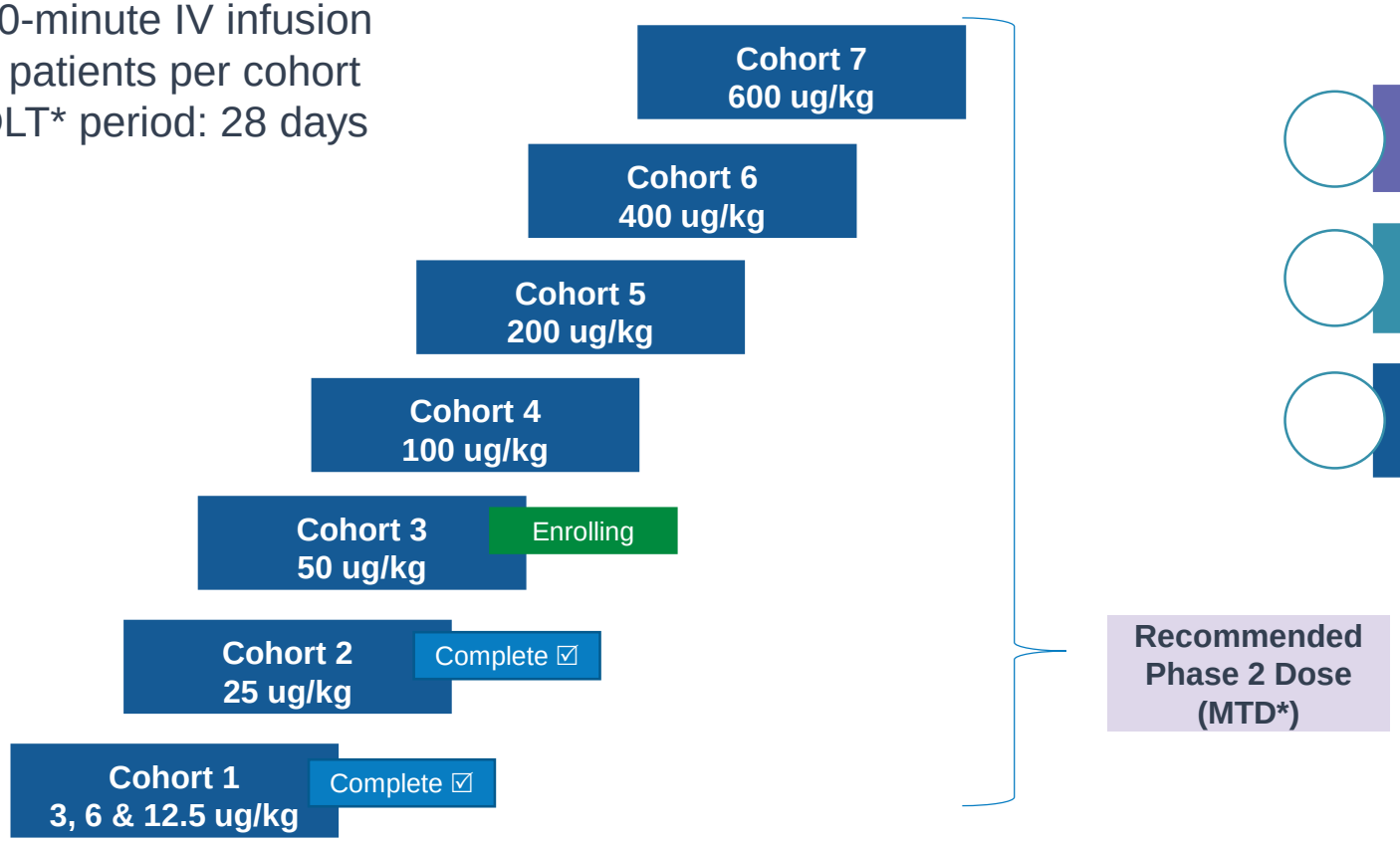
Values represent fold increases in lymphocyte cell numbers

Mol Cancer Ther February 1 2021 (20) (2) 347-356; *SITC 2018 poster #P414*

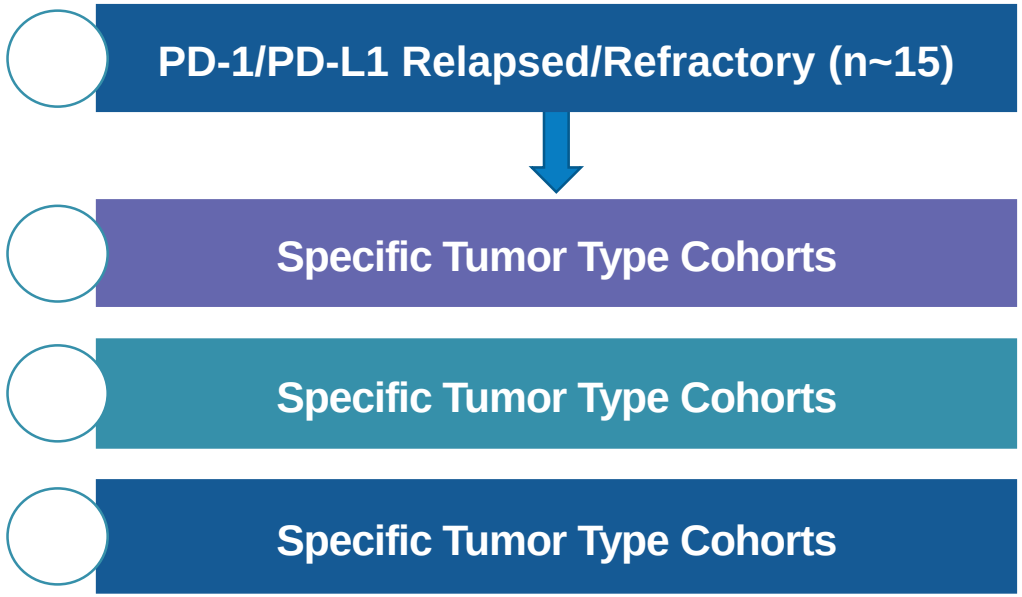
KD033-101: Phase 1a/1b Clinical Trial

Phase 1a: Escalation (KD033 monotherapy)

- Subjects with metastatic or locally advanced solid tumors
- Dosing every 2 weeks as a 30-minute IV infusion
- 3 patients per cohort
- DLT* period: 28 days



Phase 1b: Expansion (KD033 +/- Anti-PD-1 Antibody)



Endpoints

- Safety
- Efficacy
- Pharmacokinetics (PK)
- Anti-drug antibodies (ADA)
- Pharmacodynamics (PD)

Initial safety data to be presented at ASCO (June 2021); Additional clinical data in Q4 2021

**Dose-limiting toxicity*
**Maximum tolerated dose*