



DFCs: a new class of drugs breaking ground in anti-virals and oncology

Forward-looking statements

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The words “may,” “will,” “estimate,” “plan,” “anticipate,” “expect,” “potential,” “could,” “project,” and similar expressions (including the negative thereof), are intended to identify forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding Cidara’s research and development efforts; preclinical and clinical development activities; plans, projections and expectations for and the potential effectiveness, safety and benefits of, its product candidates, including rezafungin, CD388, and other candidates from the Cloudbreak platform; Cidara’s ability to successfully commercialize its product candidates directly or through third parties; and potential ability to achieve milestones under its respective collaborations with Mundipharma and Janssen, and receipt of the related milestone payments; and advancement of its strategic plans.

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Research & Development Day

Thursday, July 7, 2022

Rezafungin and Cloudbreak platforms

REZAFUNGIN

- Echinocandin antifungal treatment & prevention
- Positive Phase 3 data
- Expected PDUFA Q1 2023

Product	Indications	IND-Enabling	Phase 1	Phase 2	Phase 3
REZAFUNGIN Treatment	Candidemia and Invasive Candidiasis Partnered with Mundipharma (Ex-U.S. and Ex-Japan)				>>
REZAFUNGIN Prevention	IFD in Blood & Marrow Transplant Patients Partnered with Mundipharma (Ex-U.S. and Ex-Japan)				>>

CLOUDBREAK

- Novel immunotherapy platform: antiviral & oncology
- Clinical stage (influenza)
- Opportunity to drive future value

Program	Indications	Discovery	Preclinical	IND-Enabling	Phase 1
CD388 Prevention & Treatment	Influenza – Single-Dose ~ 6 months Partnered with Janssen (Worldwide License)				>>
SARS-CoV-2 DFC Prevention & Treatment	SARS-CoV-2		>>		
ONCOLOGY DFC Treatment	Solid Tumors		>>		

Both platforms provide additional ongoing and future value



~\$568M Phase 2 data (2019)
REZAFUNGIN



~\$780M Preclinical data (2021)
CLOUDBREAK

Both platforms provide additional ongoing and future value



~\$568M Phase 2 data (2019)
REZAFUNGIN

PROGRAM: antifungal
RIGHTS: ex-US/Japan

- \$30M upfront
- \$9M equity investment
- \$42M in development support
- \$487M clin/reg/comm milestones
- Double-digit royalties in the teens



~\$780M Preclinical data (2021)
CLOUDBREAK

Both platforms provide additional ongoing and future value



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~\$780M Preclinical data (2021)
CLOUDBREAK

PROGRAM: influenza DFC
RIGHTS: global

- \$27M upfront
- \$58M in R&D support
- \$695M clin/reg/comm milestones
- Mid to high single digit royalties

Rezafungin update

REZAFUNGIN

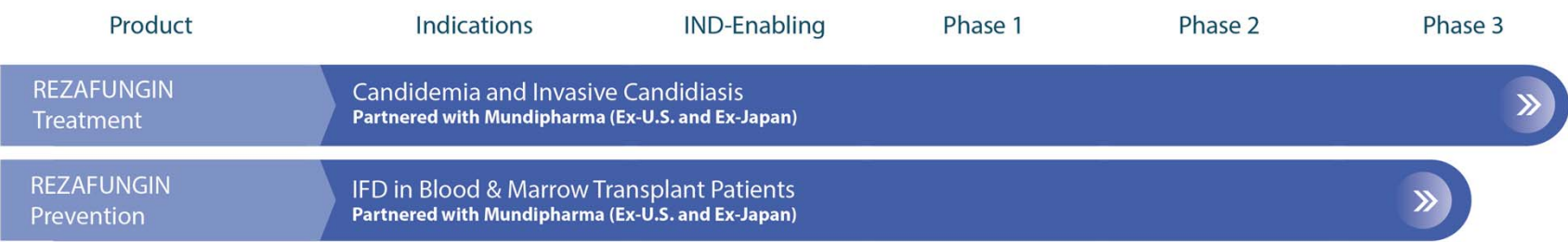
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Rezafungin update

REZAFUNGIN

- Echinocandin antifungal treatment & prevention
- Positive Phase 3 data
- Expected PDUFA Q1 2023



Rezafungin will be commercialized by third parties in US and Japan

- Cidara does not intend to fund commercialization costs
- In discussions for US licensing
- Will explore Japan licensing post NDA approval

Cidara’s new strategic focus: Cloudbreak DFC program

REZAFUNGIN

Anti-Fungal Treatment and Prevention

Product	Indications	IND-Enabling	Phase 1	Phase 2	Phase 3
REZAFUNGIN Treatment	Candidemia and Invasive Candidiasis Partnered with Mundipharma (Ex-U.S. and Ex-Japan)				»
REZAFUNGIN Prevention	IFD in Blood & Marrow Transplant Patients Partnered with Mundipharma (Ex-U.S. and Ex-Japan)				»

CLOUDBREAK

Drug Fc Conjugates with broad clinical application

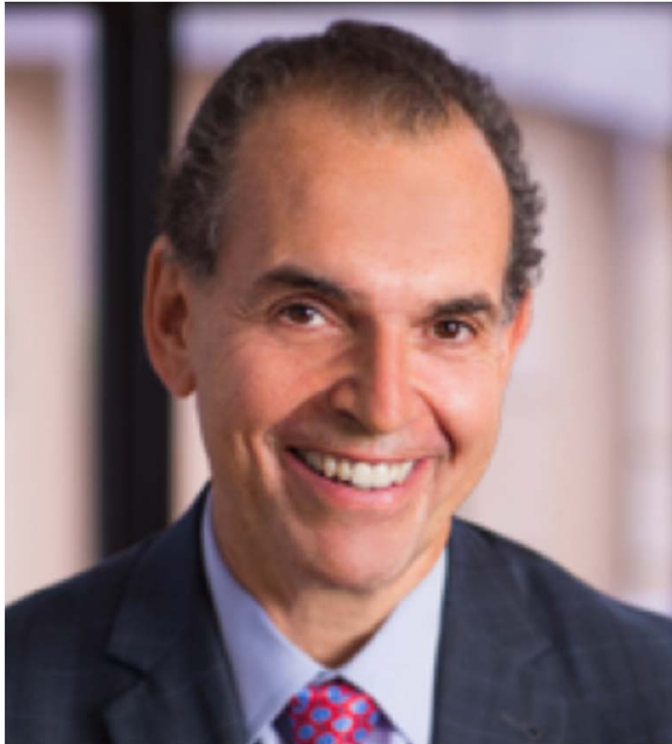
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Today's panel members



Ezra Cohen, MD

Chief of Hematology-Oncology UCSD



Perry Nisen, MD, PhD

CEO, Quanta Therapeutics

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Perry Nisen, MD, PhD

CEO, Quanta Therapeutics



Leslie Tari, PhD

Chief Scientific Officer, Cidara

Agenda

Drug Fc Conjugates

what they are (and are not) Les Tari, PhD

Advantages of DFCs

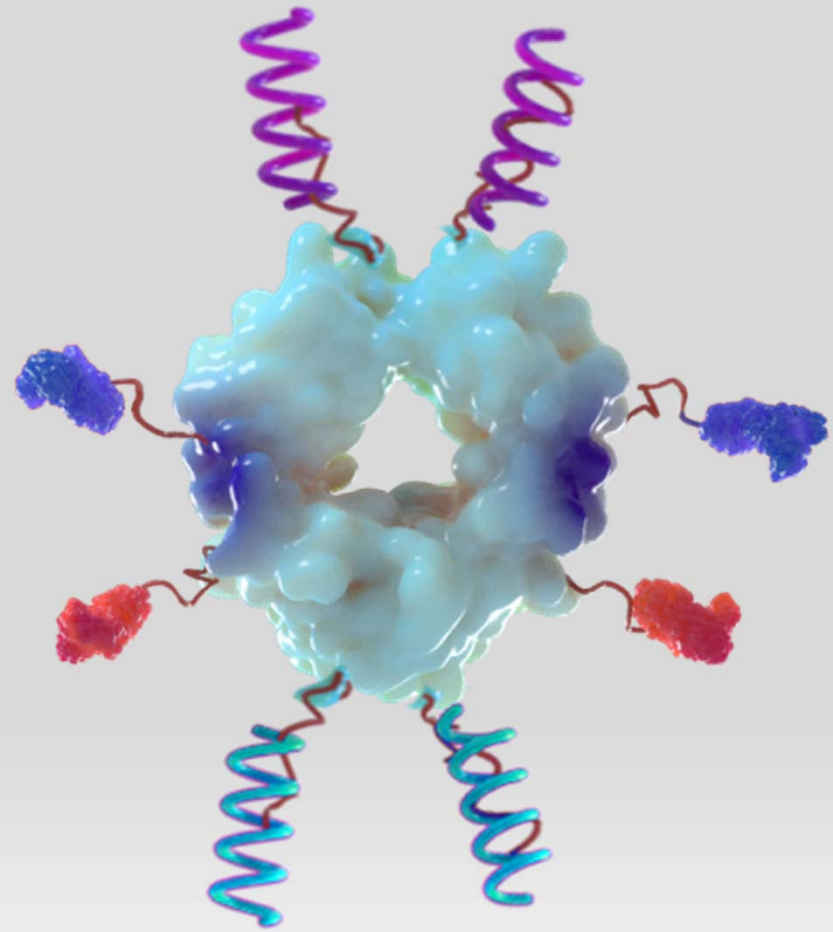
over conventional modalities in
Influenza, SARS and oncology Les Tari, PhD

Clinical Potential

in oncology Perry Nisen, MD, PhD
Ezra Cohen, MD

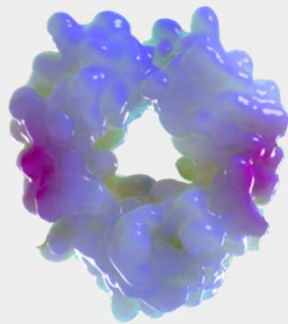
CLOUDBREAK® creates a new class of drug conjugates: “DFCs”

DFC
Drug Fc Conjugate



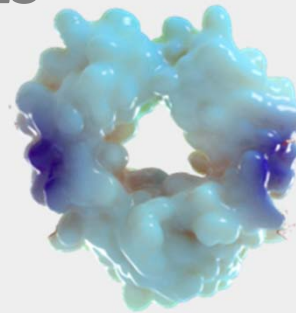
Fc moiety is tailored to to specific indications

Fc MOIETY



Wild type

ANTI-VIRALS



PK extended Fc

- IgG1
- Engineered to enhance FcRn binding
- Improves half-life compared to wt Fc
- Master cell bank established for manufacturing

CANCER

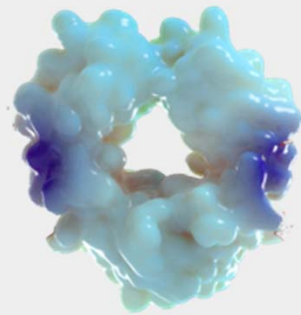


Immune silent Fc

- IgG1 and IgG4
- IgG1 versions mutated to reduce immune effector function
- IgG4 lacks effector function

Different types of targeting moieties (TMs) attach to the Fc moiety

Fc MOIETY

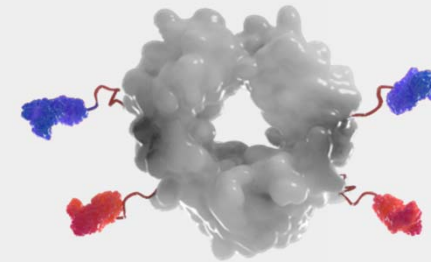


ANTI-VIRALS

SMALL MOLECULES

Directed against surface target active sites.

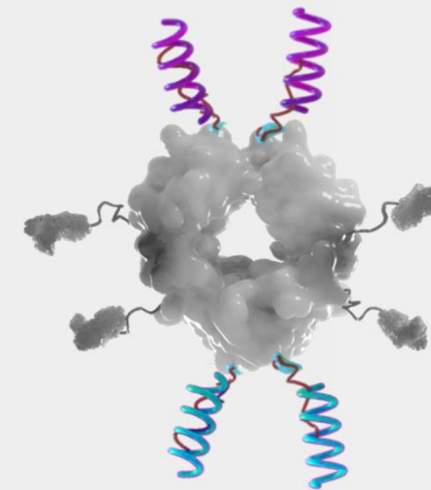
Example: Neuraminidase in CD388.



PEPTIDE FUSIONS

Designed to inhibit protein-protein interactions.

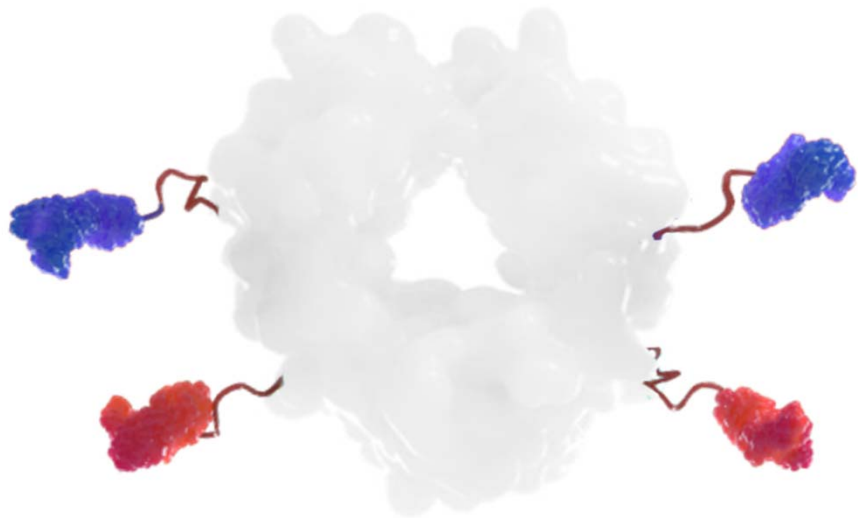
Example: SARS spike-binding/ACE-2 interaction.



Targeting moieties are directed against validated targets

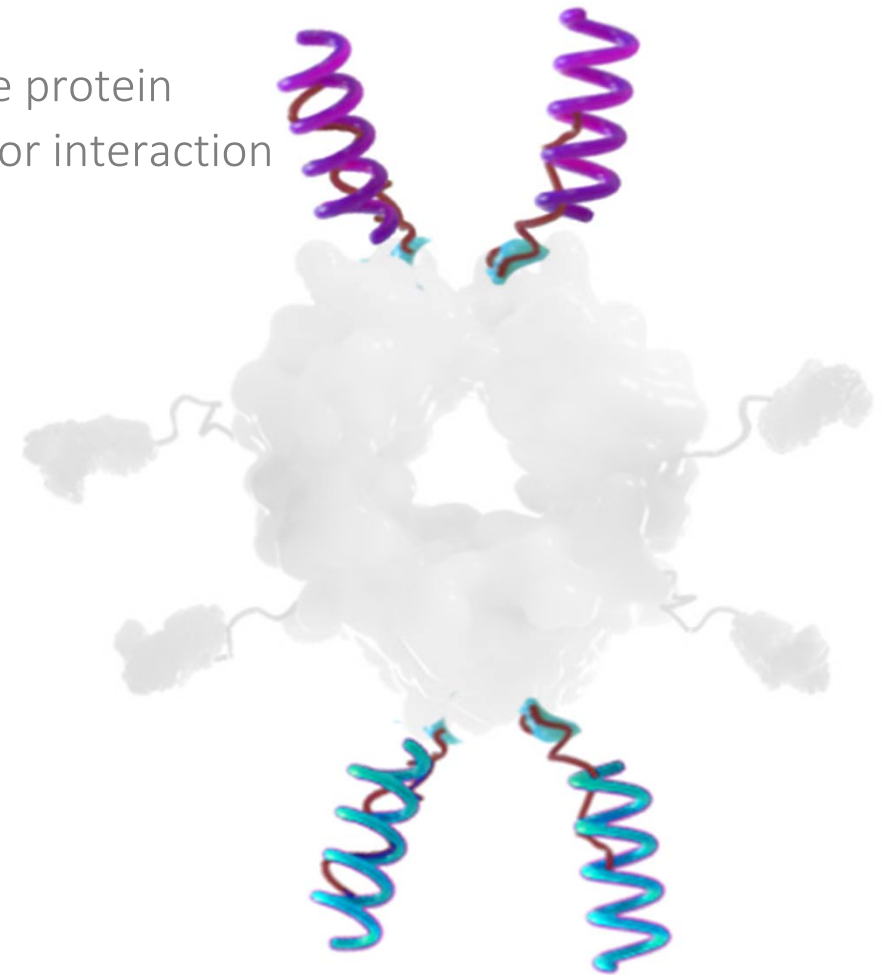
INFLUENZA: neuraminidase

CANCER: adenosine-signaling pathway



SARS: spike protein

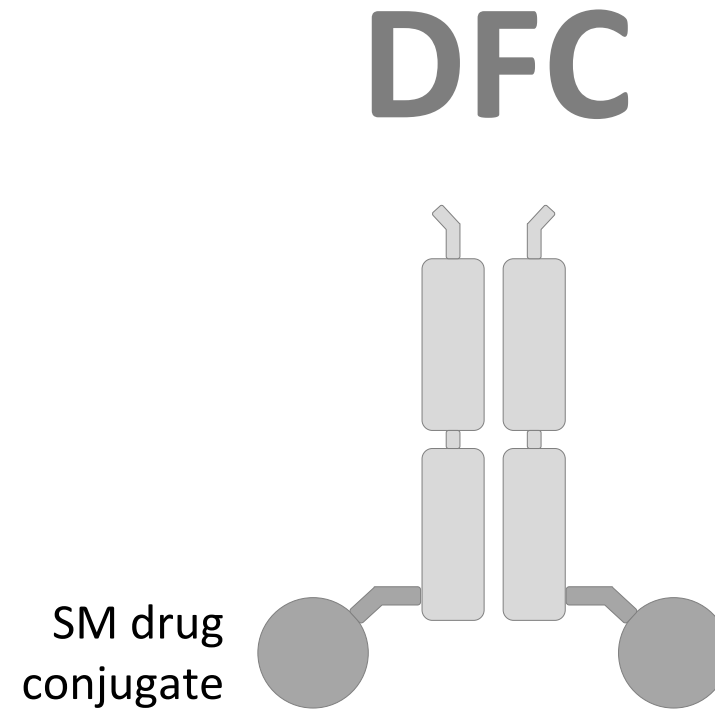
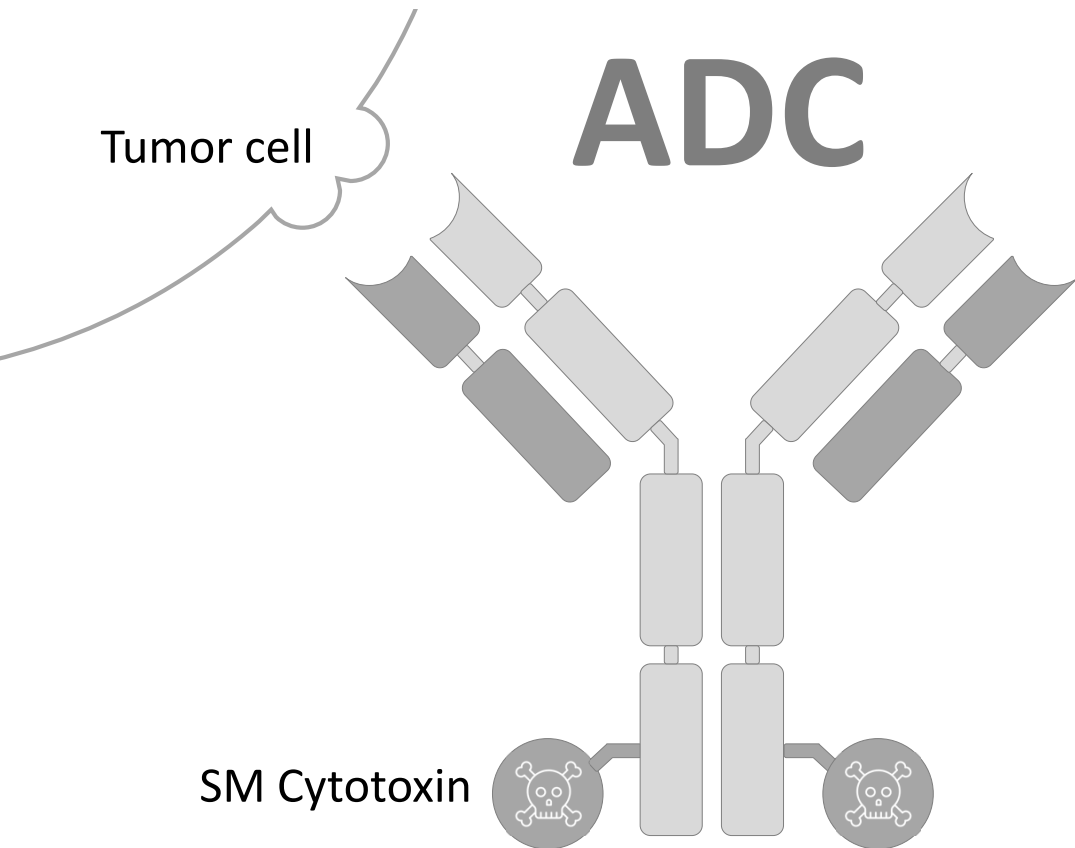
ACE-2 receptor interaction



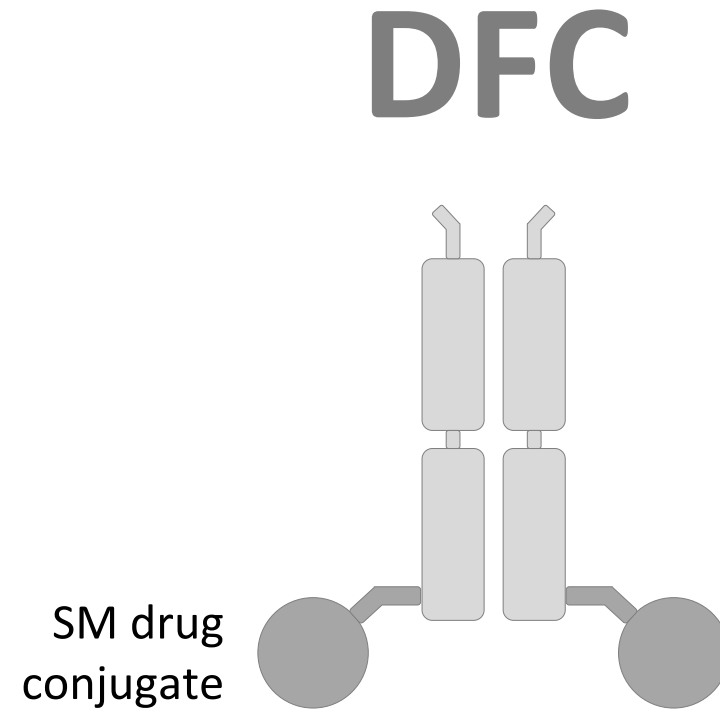
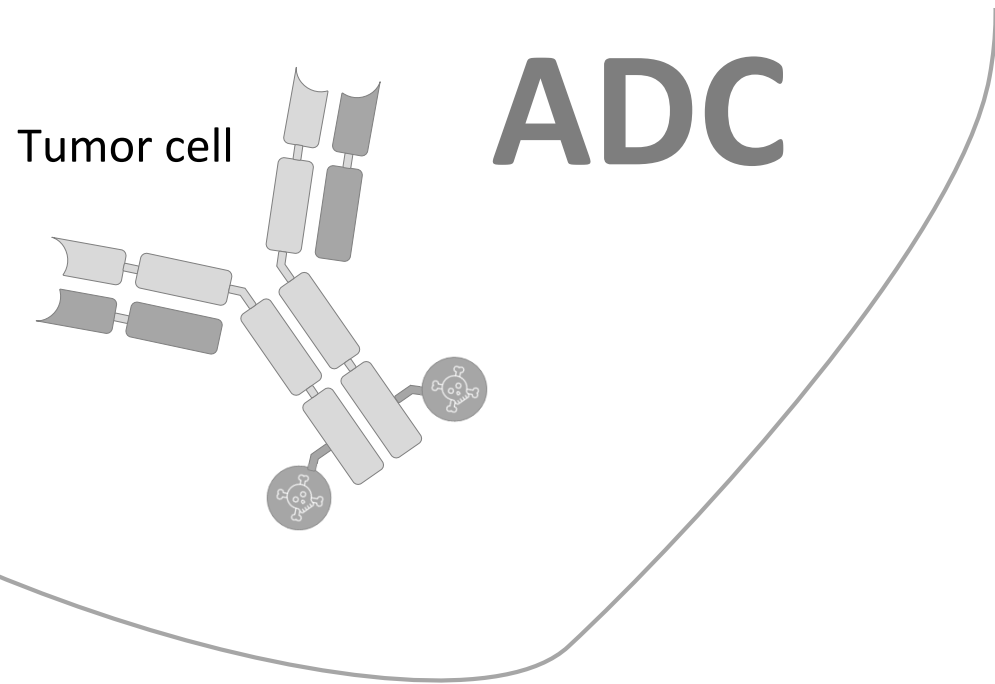


Potential DFC advantages

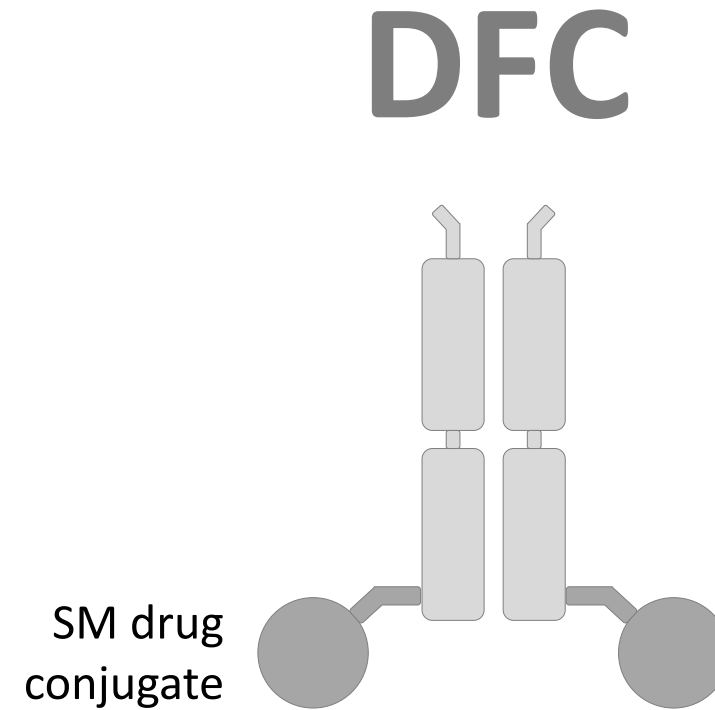
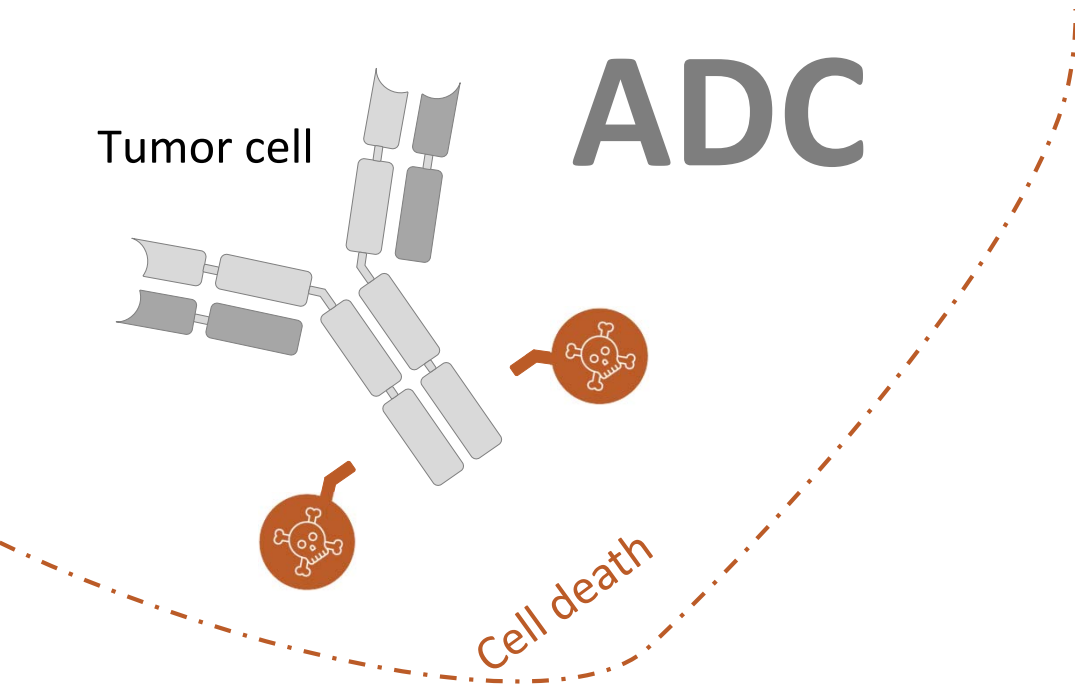
DFCs are fundamentally different from ADCs



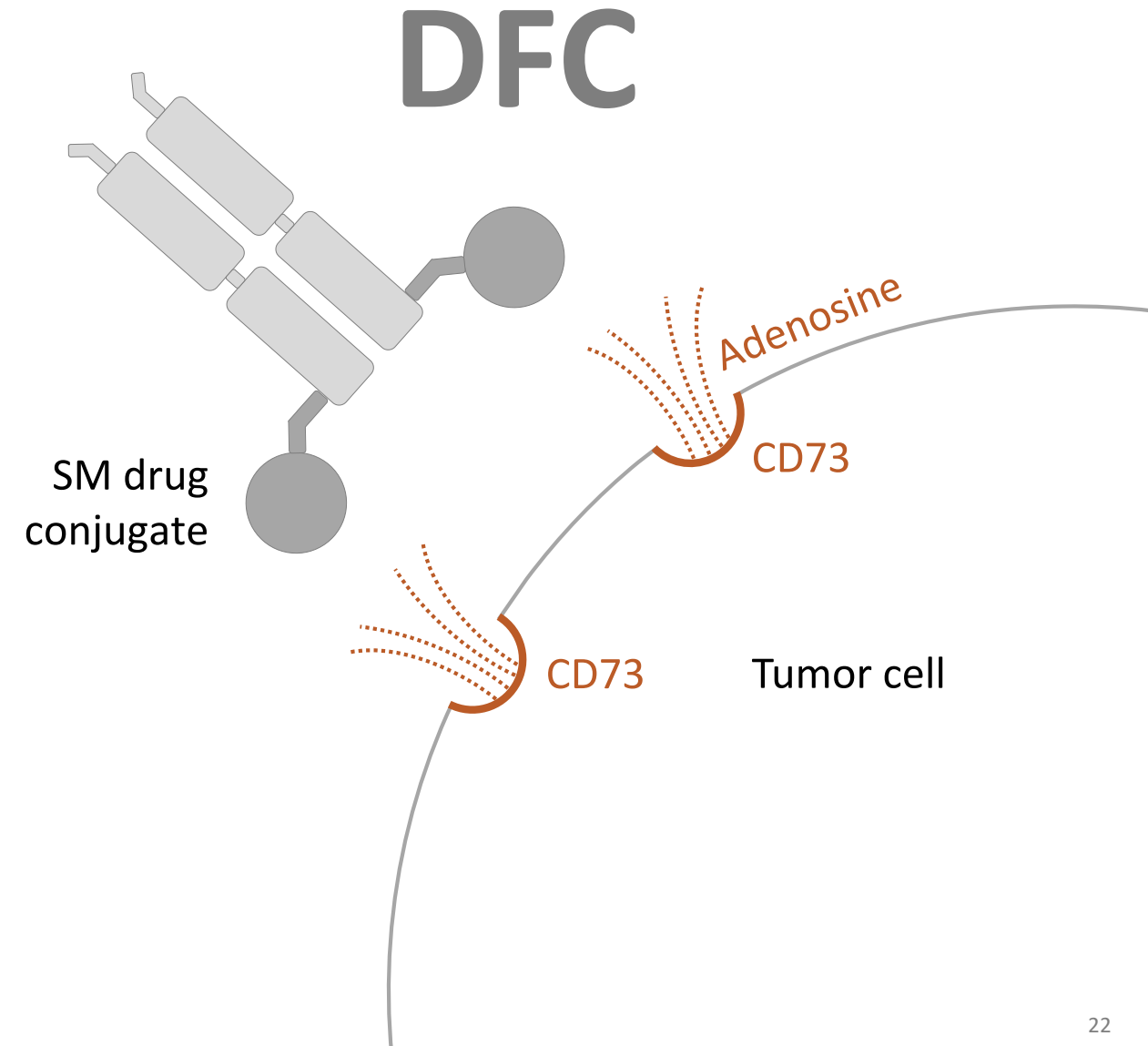
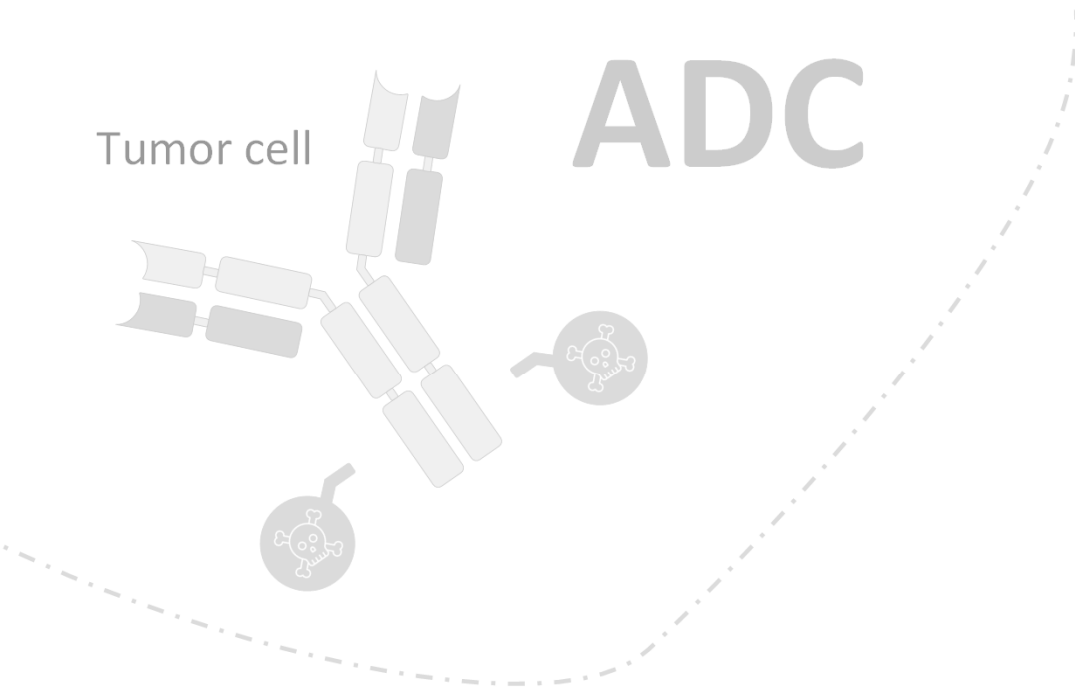
ADCs employ mAbs directed to cell surface epitopes...



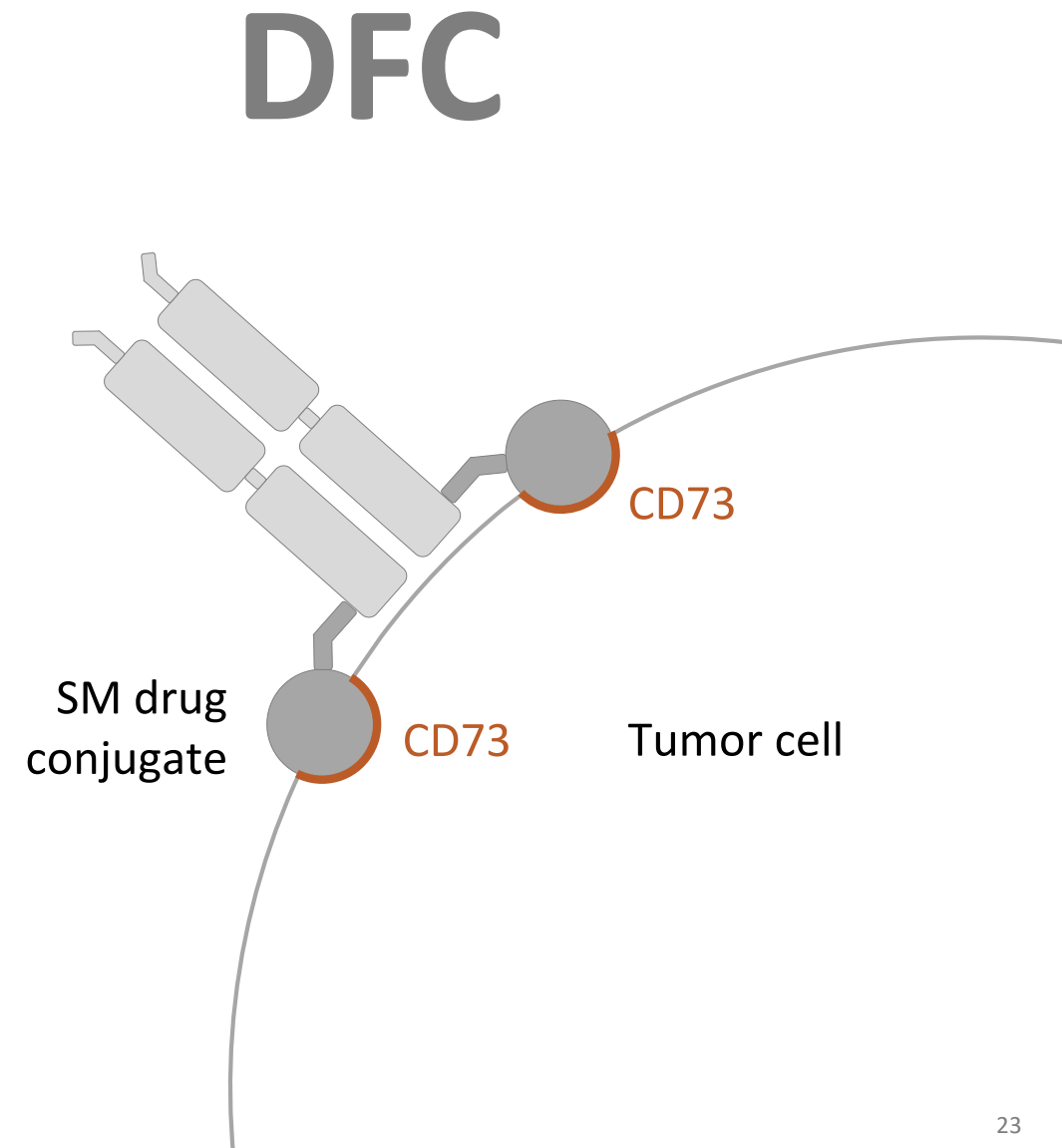
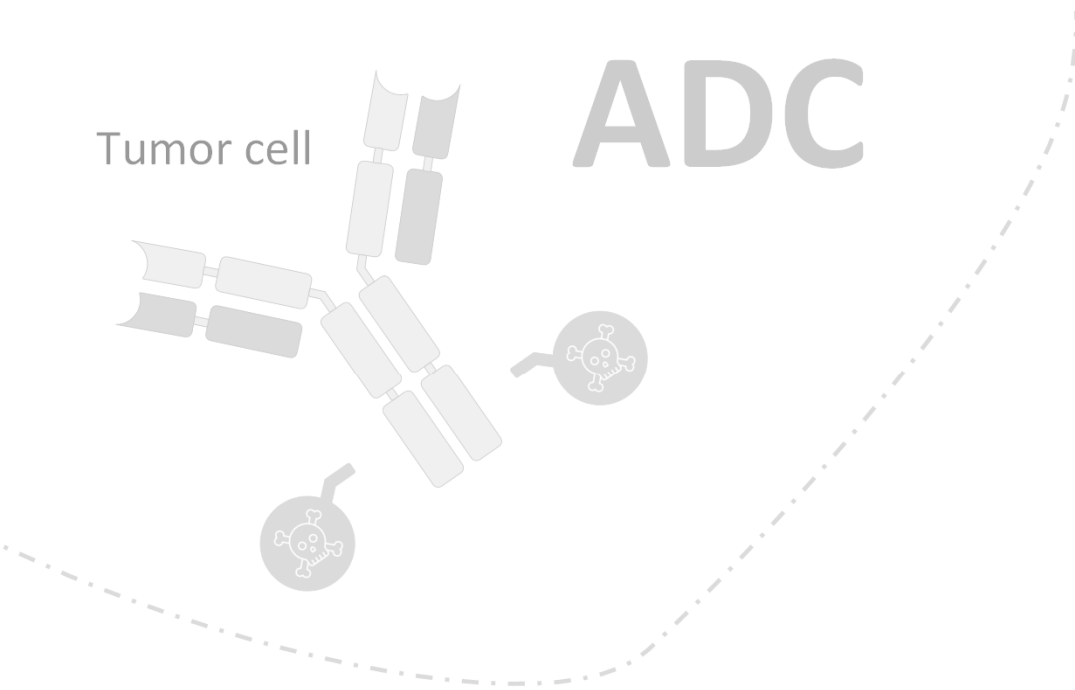
...and are internalized by cancer cells to release cytotoxic payloads



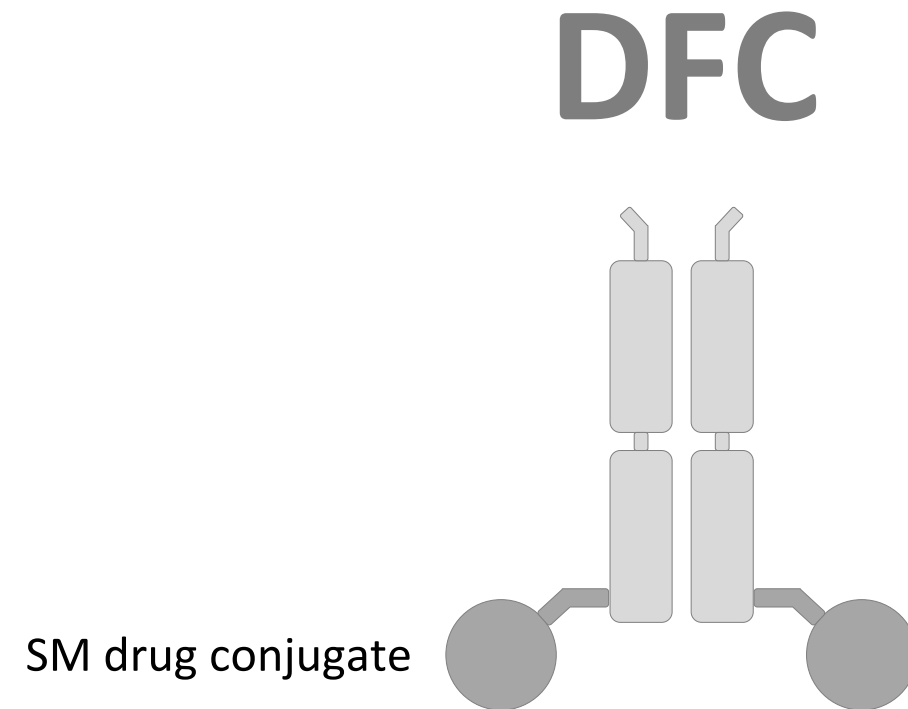
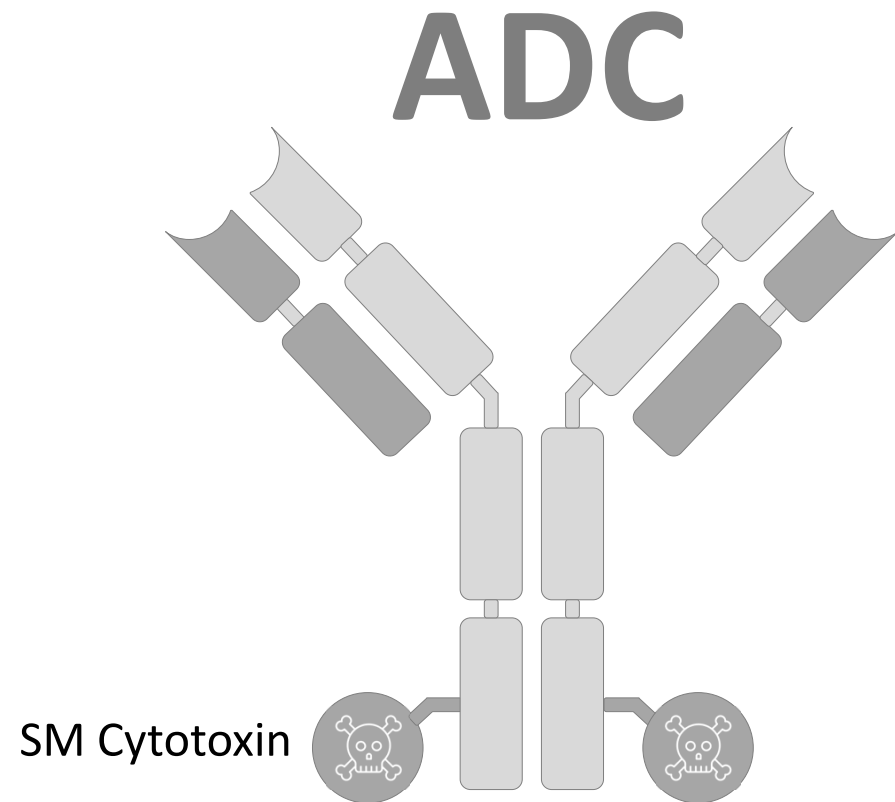
DFCs inhibit catalytic activity of surface exposed targets...



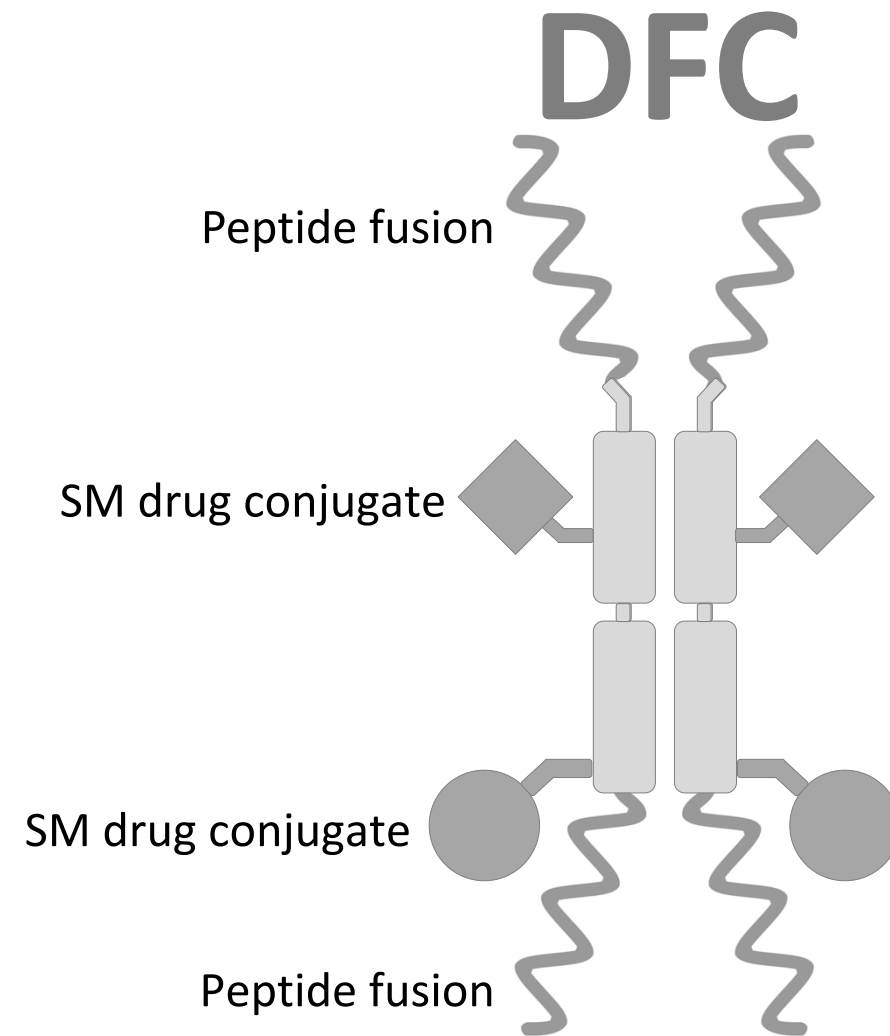
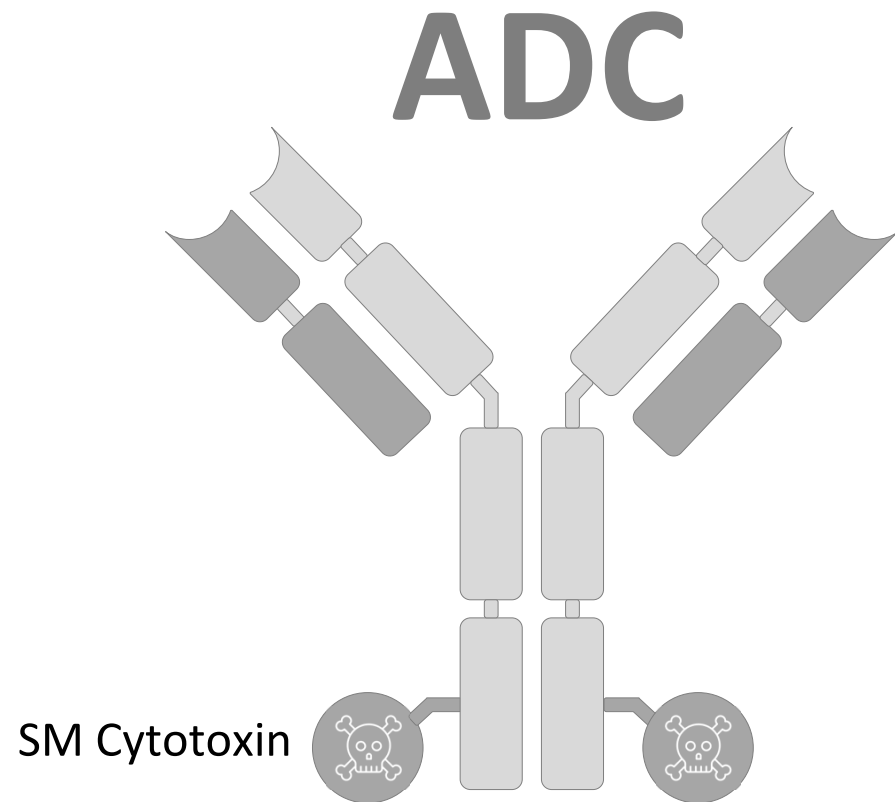
... and are inherently less toxic than ADCs



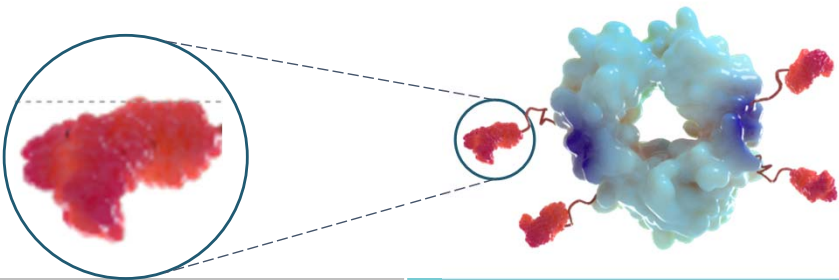
DFCs can accommodate multiple targeting moieties



DFCs can accommodate multiple targeting moieties



DFCs have advantages over small molecule therapeutics

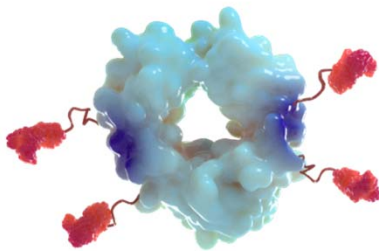
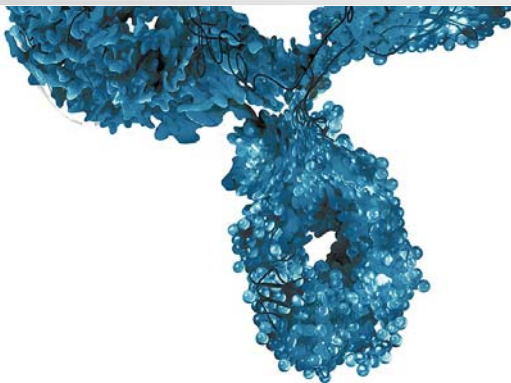


	SM Inhibitors	DFCs ¹
Potency	Single binding pocket, single target	Multivalent binding Multiple targets
Toxicity, Drug-Drug-Interactions (DDIs)	Extra- and intra-cellular compartments	Only in extra-cellular compartment
Oral bioavailability, cell penetration	Lipinski's rules	Fewer constraints, not required for activity
Distribution to compartments outside plasma (e.g., lung)	Potentially limited by cell penetration, properties	Good—dictated by Fc domain

Unlike SMs, DFC optimization can be focused primarily on potency.

1. DFC assessments are based on pre-clinical study results and estimates

DFCs have advantages over antibodies

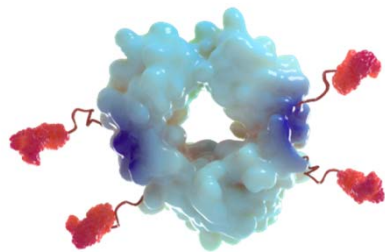
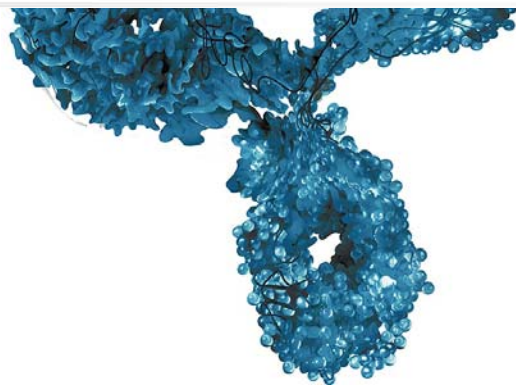


	Monoclonal Antibodies	DFCs
Able to target cryptic sites, small molecule binding pockets	No	Yes
Able to modulate drug-Fc-ratio to increase potency	No	Yes
Able to install 2 or more discrete targeting moieties	Challenging	Multiple Options
Distribution to compartments outside plasma (e.g., lung)	Limited, slow kinetics	High, rapid kinetics

DFCs advantages over mAbs: they're smaller and can target multiple sites

Janssen collaboration on CD388 DFC

Janssen recognized the shortcomings of the flu vaccine and antibodies



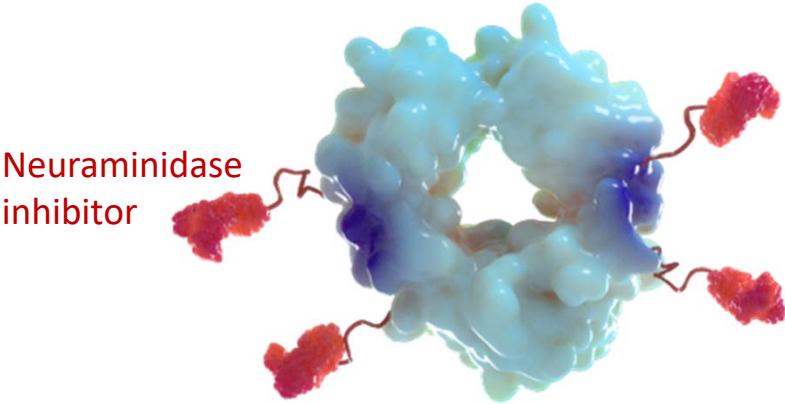
	Vaccines	Monoclonal Antibodies	DFCs
Universal protection: multiple viruses	No	No	Yes
Potential to protect all high risk groups	Low	High	High
Potential for prevention and treatment	No	Limited	Yes
Scale and cost	Attractive	Expensive	Attractive

CD388 is in clinical trials for universal influenza prevention

INFLUENZA

	DFCs
Universal protection: all strains	Yes
Potential to protect all high risk groups	High
Potential for prevention and treatment	Yes
Scale and cost	Attractive

CD388 is being developed for universal, season-long flu protection in all patient populations.

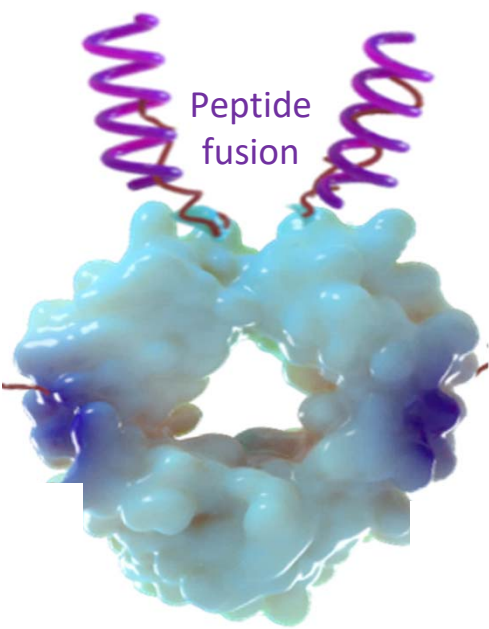


- Single dose /~4-6 months
- Mutant Fc (attenuated immune engagement, improved PK, and extended duration of action)

DFCs designed for “Universal” SARS-2 prevention

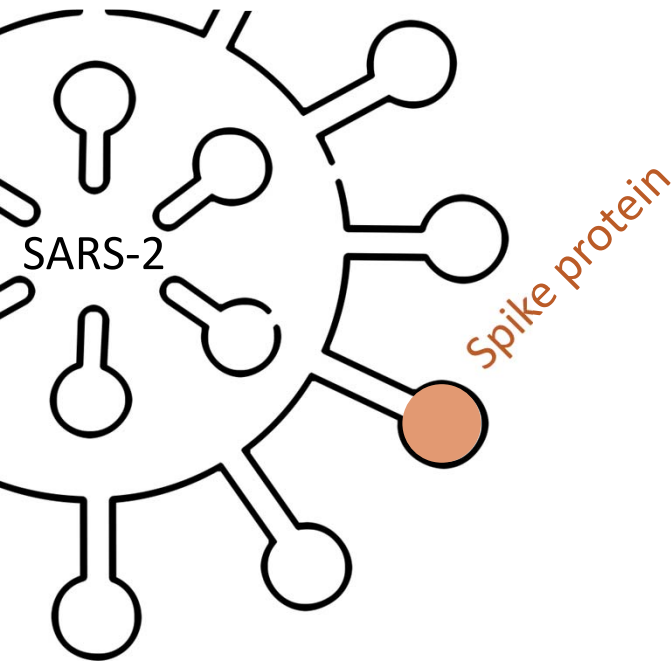
SARS-2

	DFCs
Universal protection: multiple viruses	Yes
Potential to protect all high risk groups	High
Potential for prevention and treatment	Yes
Scale and cost	Attractive



- Peptide engineered to maximize antiviral spectrum and *in vivo* stability
- Fc being optimized to tailor for inhaled delivery

Targeting the ACE2-spike protein interaction limits viral escape options



In development for treatment and long-term prophylaxis via inhalation

Peptide is being optimized for stability



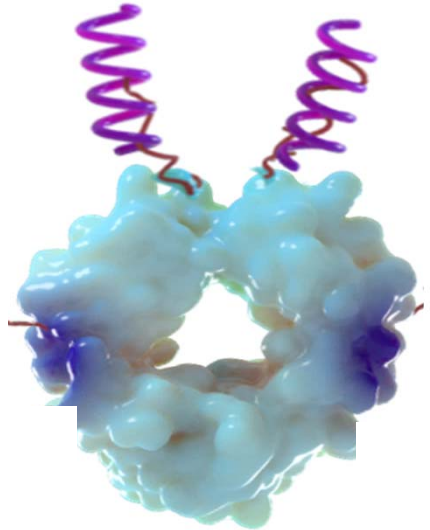
Peptide has been engineered for compatibility with small molecule conjugation – allows addition of other antivirals

Fc is being optimized to bind respiratory mucosa for inhaled dosing

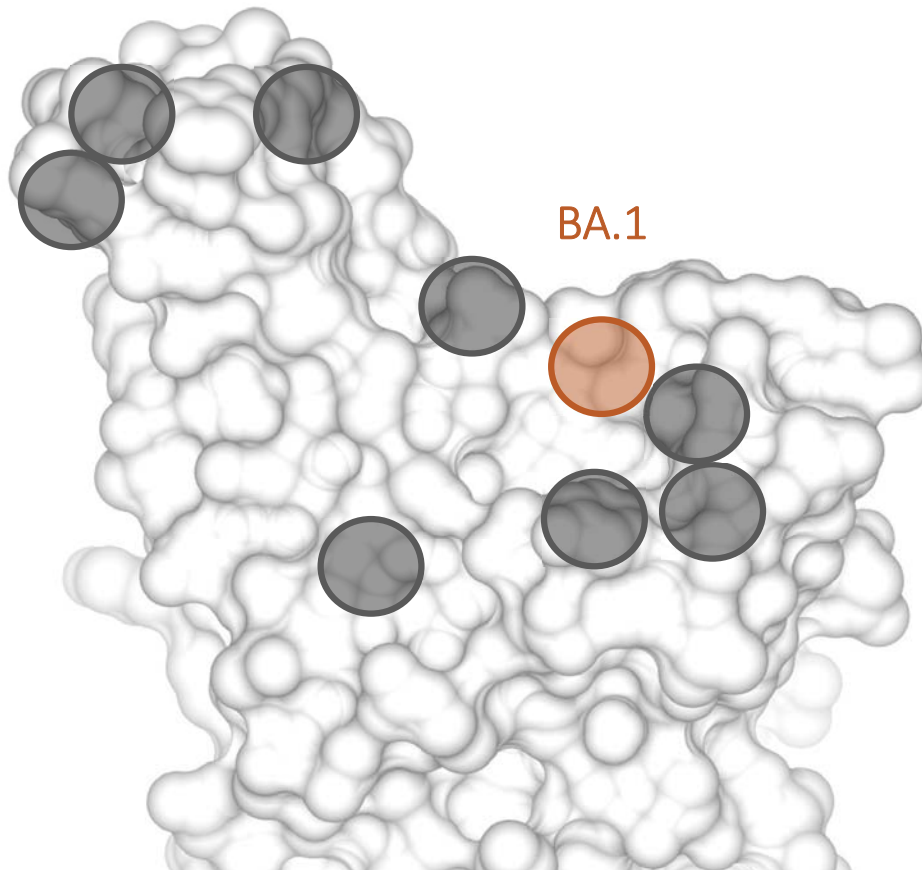
ACE2 Receptor

Cidara's SARS-2 DFC covers all known variants



Delta variant spike protein



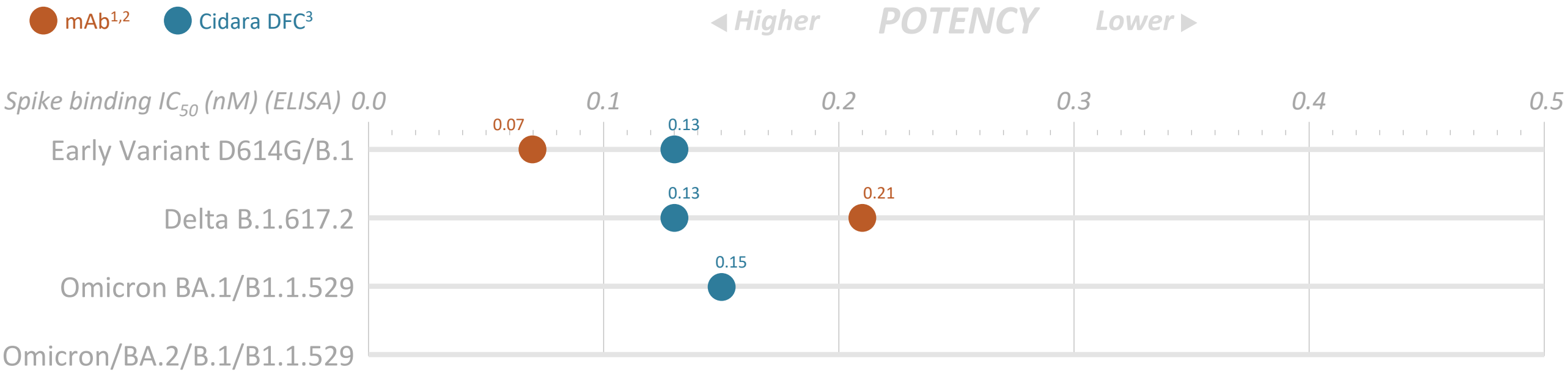
CTP-A



Mutations in CTP-A binding site
mapped on the delta variant spike
(PDB code 7WBQ)

-  observed in all omicron sub-lineages
-  observed only in BA.1

Potential for universal coverage of all SARS-2 strains

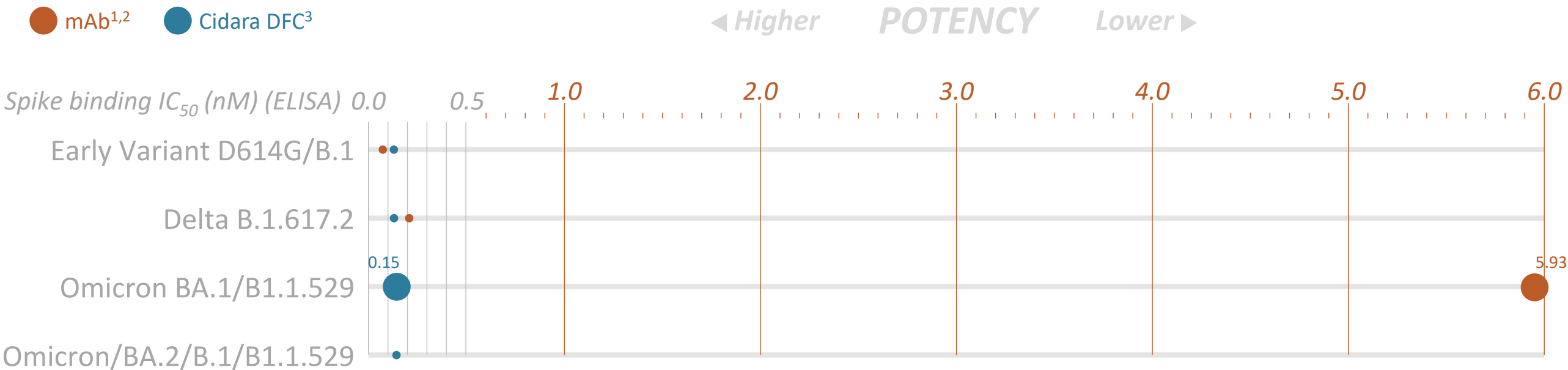


1. The mAb control is an anti-SARS-CoV-2 RBD neutralizing IgG1 antibody isolated from a SARS-CoV-2 infected patient that inhibits the SARS-CoV-2 spike/ACE2 interaction with an IC_{50} of 0.98 μ g/mL

2. Iketani *et al.* Nature, 604, 553, 2022

3. Molecule CTP-A

Potential for universal coverage of all SARS-2 strains

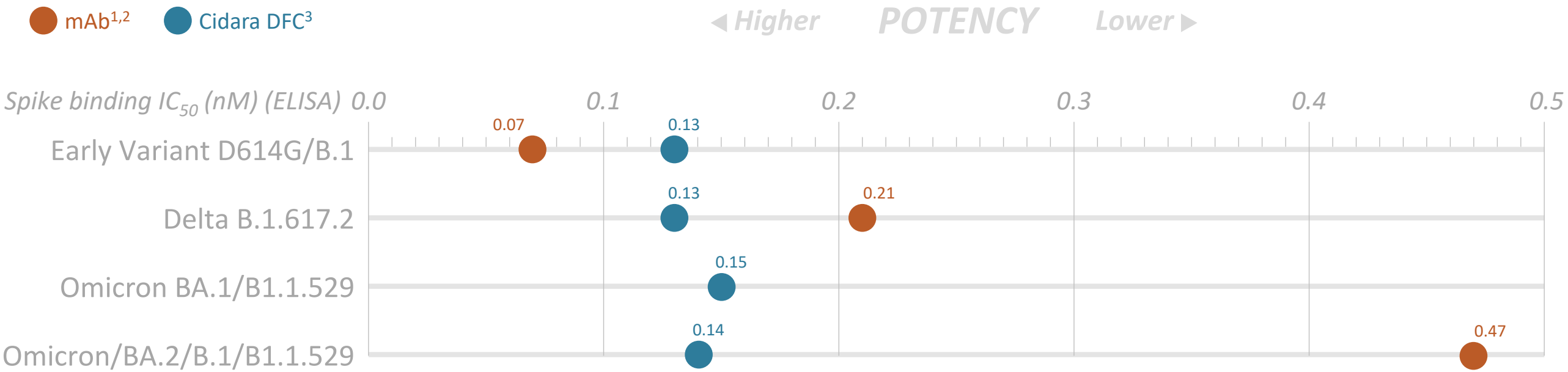


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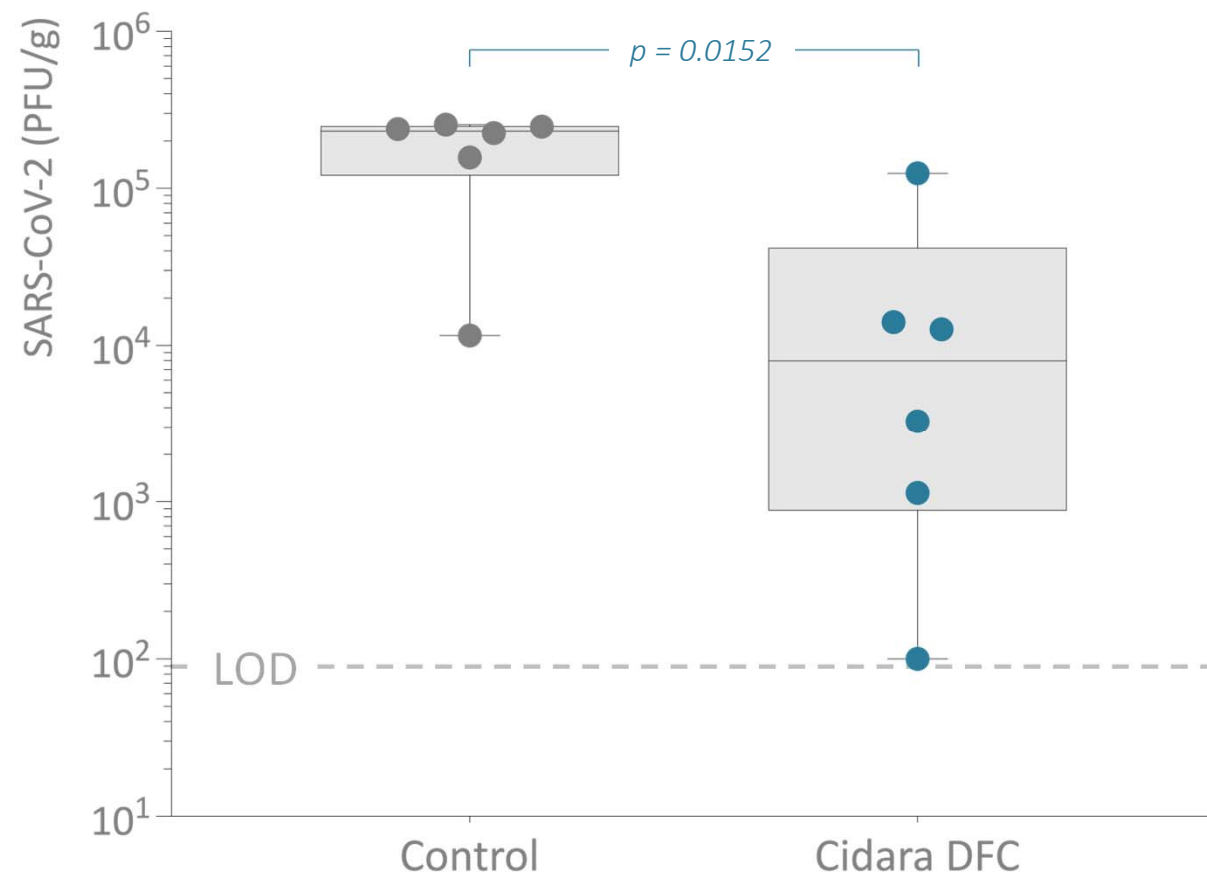
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3. Molecule CTP-A

Spike-binding data is supported by *in vivo* efficacy

Lung burden 4 days post-infection

Intranasal dosing Omicron BA.1/B1.1.529, in Syrian Hamsters
1mg dose, 6 hrs prior to infection

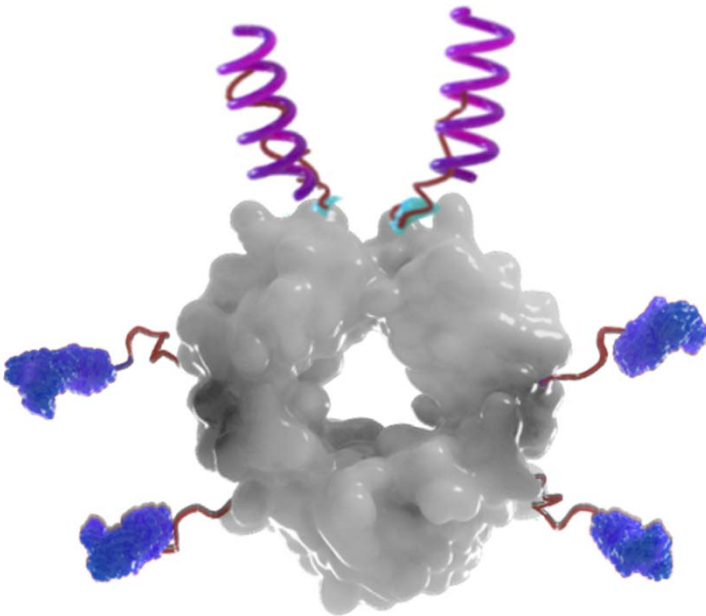


SARS-’Flu DFCs could protect against the two major respiratory viruses

SARS-’FLU

	DFCs
Universal protection: multiple viruses	Yes
Potential to protect all high risk groups	High
Potential for prevention and treatment	Yes
Scale and cost	Attractive

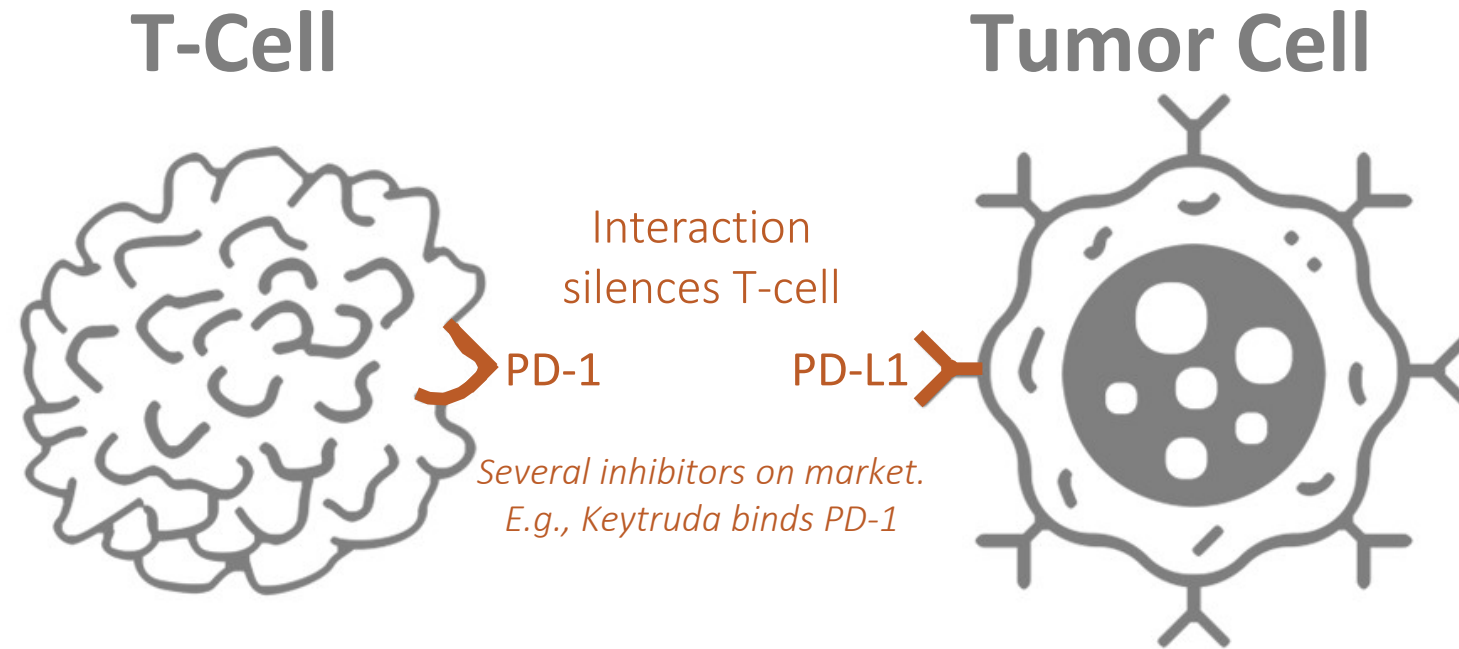
Flu and SARS clinically present the same way. Prevention or early treatment with DFCs could dramatically reduce the incidence of severe disease.



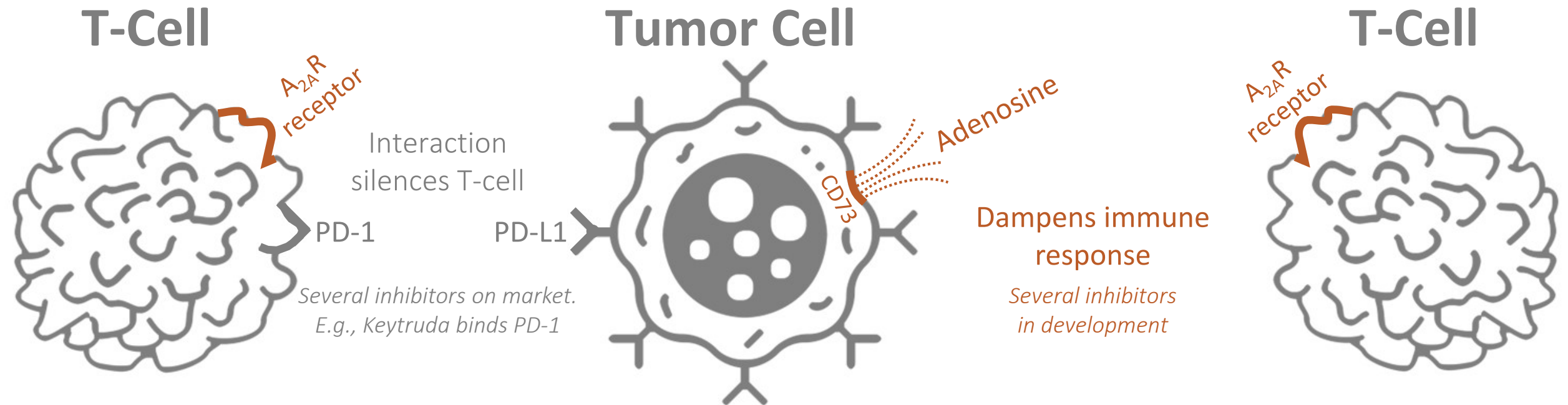


Immune checkpoint pathways

Fewer than 15% of patients respond to checkpoint monotherapies¹



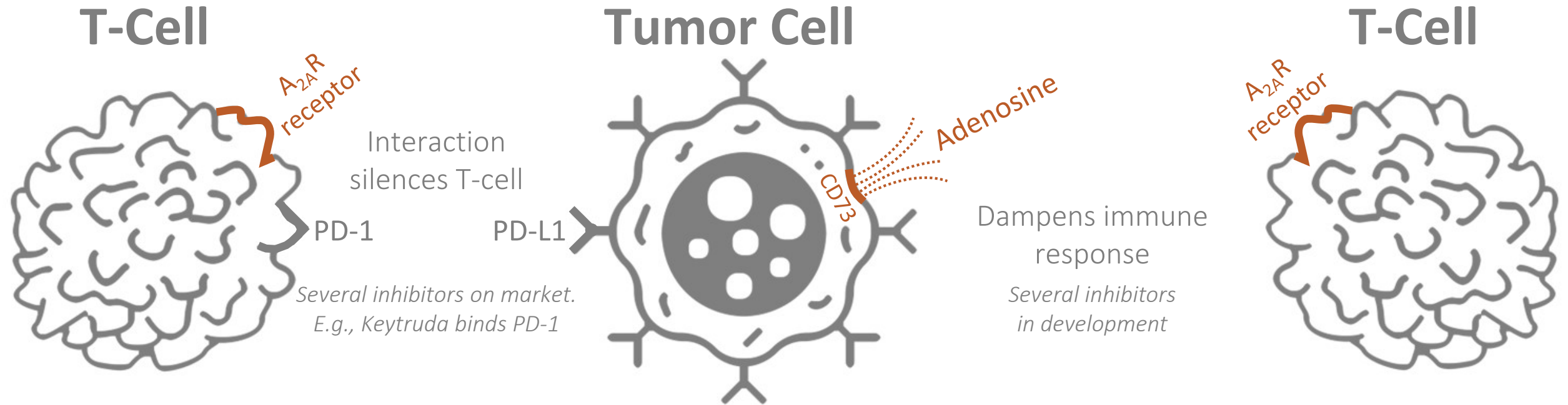
Fewer than 15% of patients respond to checkpoint monotherapies¹



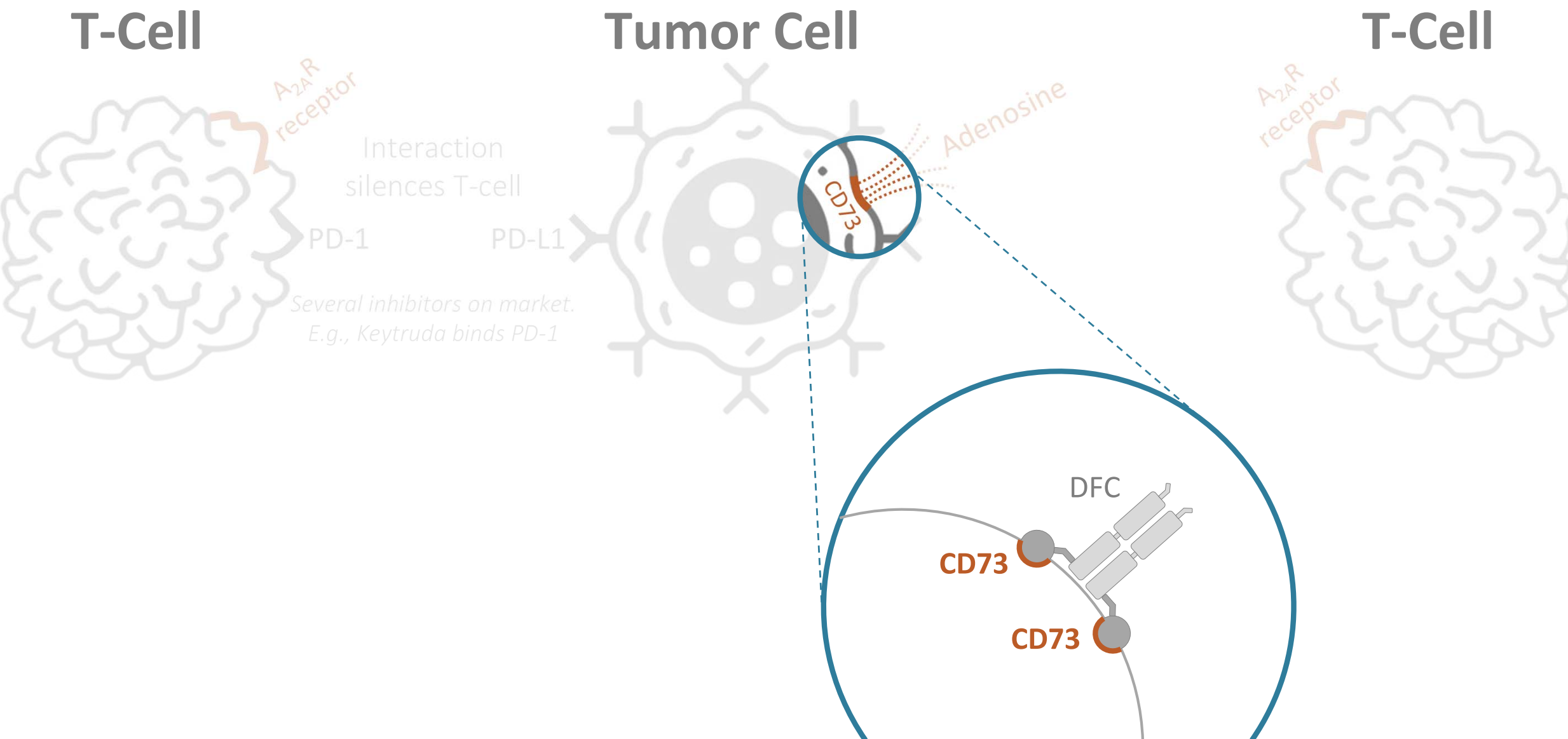


Discussion

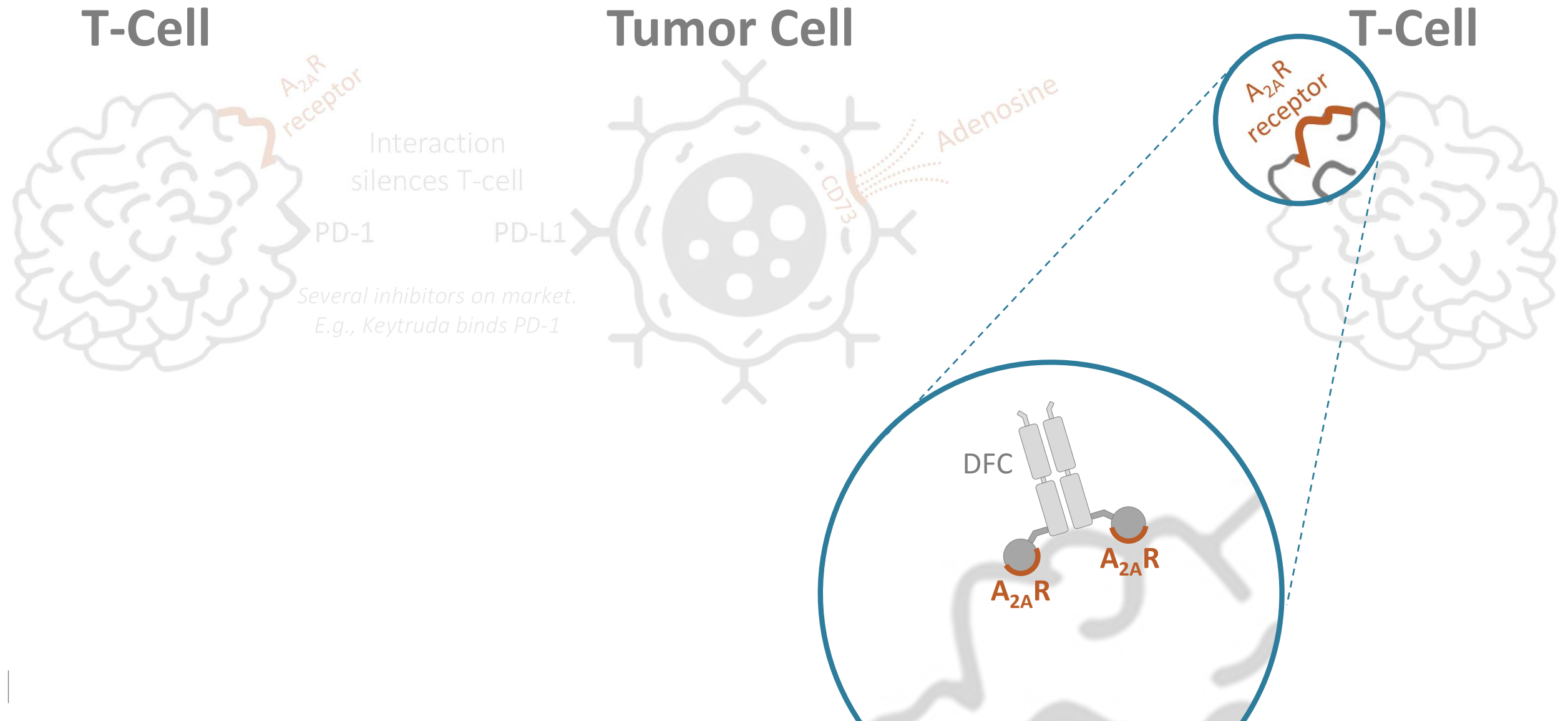
DFCs have the potential to augment PD-1/PD-L1 therapies



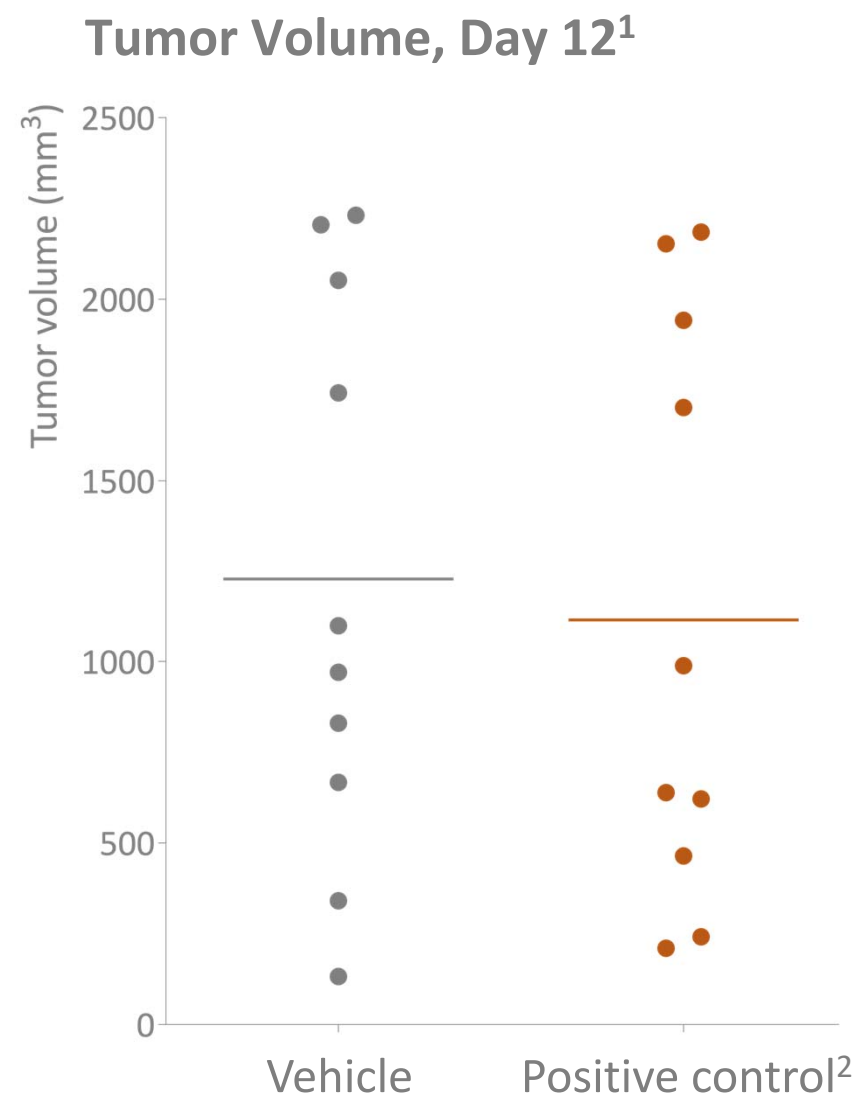
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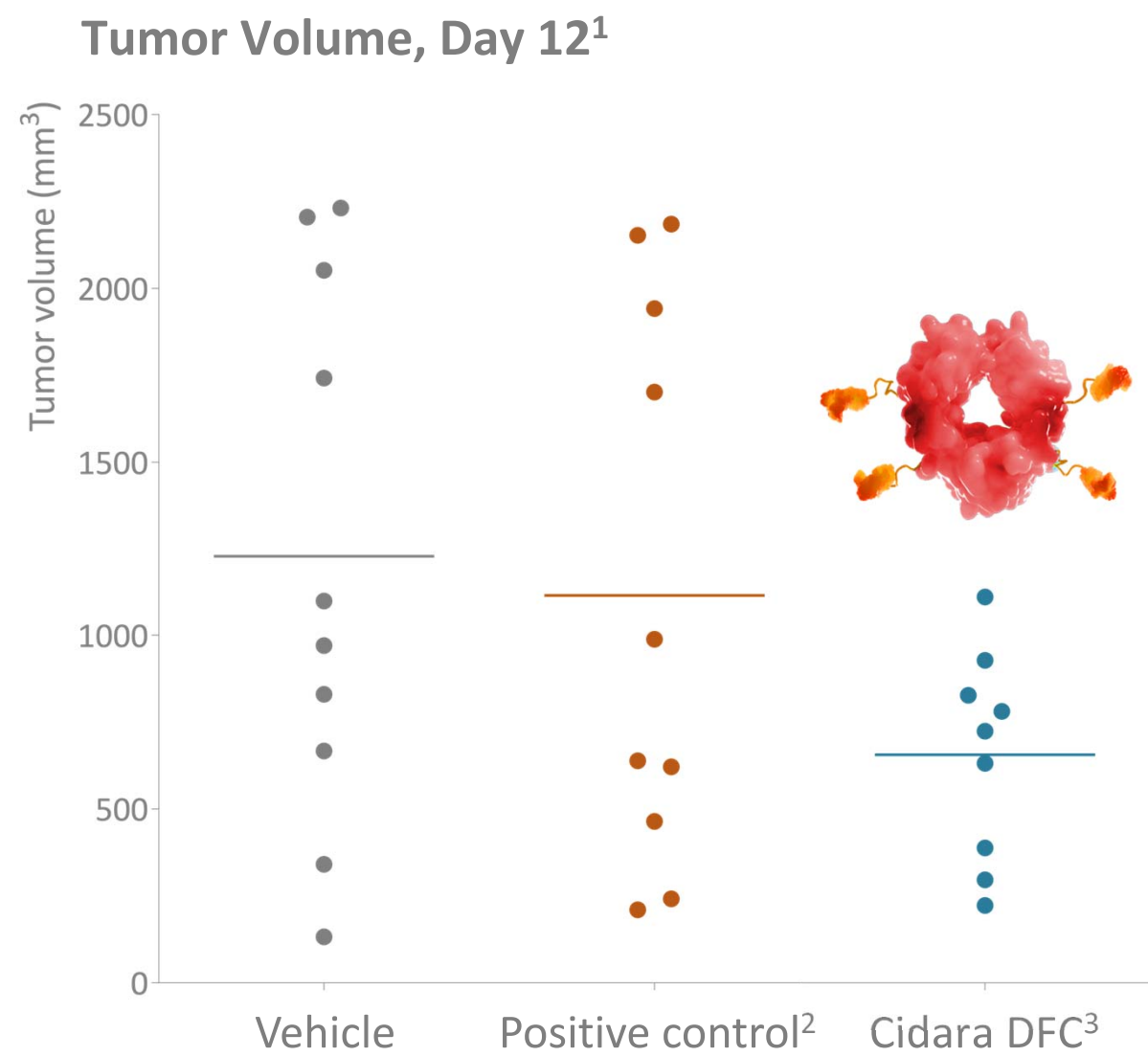
CD73 DFCs demonstrate robust anti-tumor activity in mouse models



1. Mouse syngeneic model with a colon tumor cell line (CT26). Scatter plot of individual animals on Day 12 post-treatment (N=9-10).

2. Small molecule AB680 in clinical trials

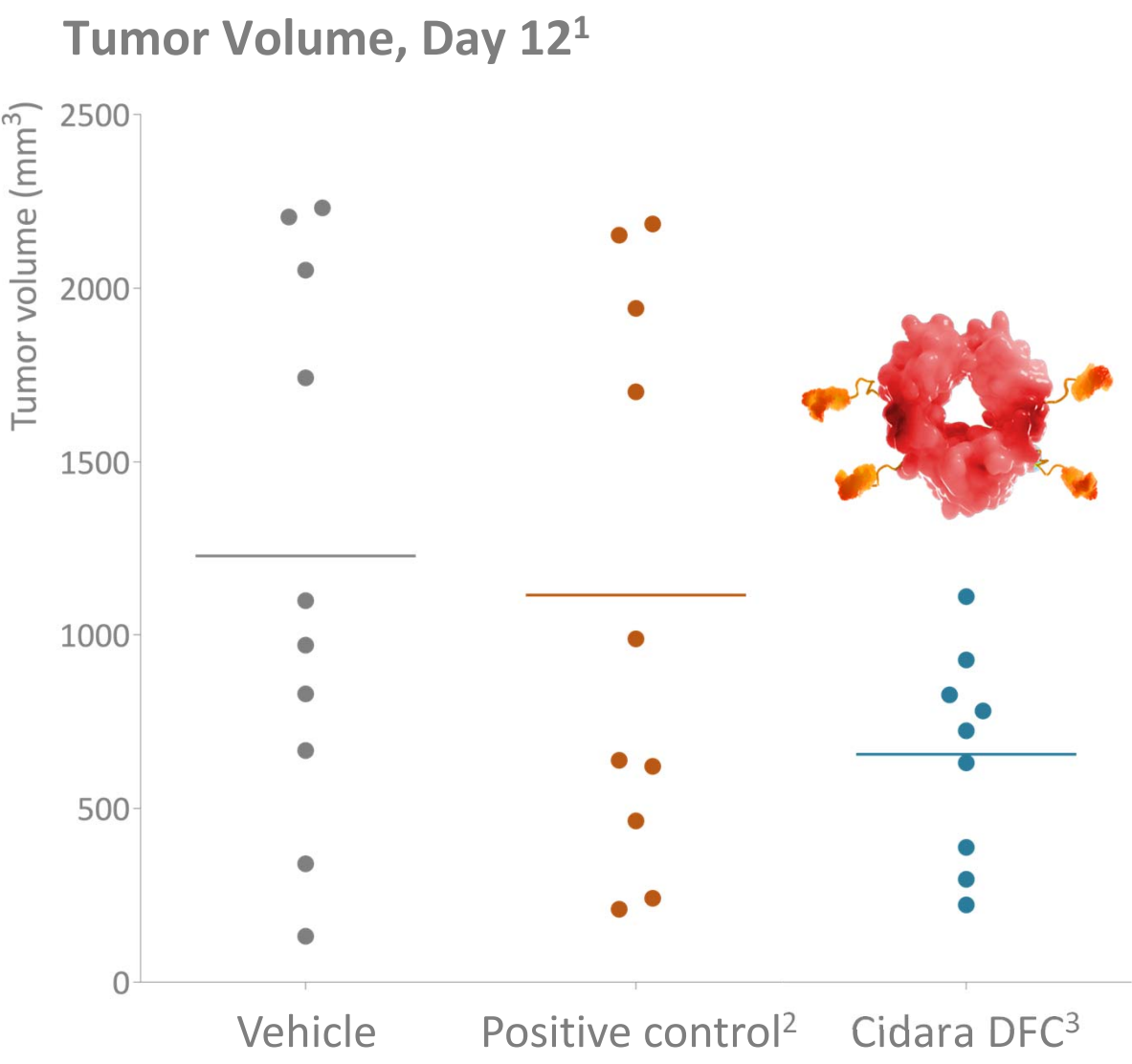
CD73 DFCs demonstrate robust anti-tumor activity in mouse models





















1. Mouse syngeneic model with a colon tumor cell line (CT26). Scatter plot of individual animals on Day 12 post-treatment (N=9-10).

2. Small molecule AB680 in clinical trials
3. Molecule CBO-A

CD73 DFCs demonstrate robust anti-tumor activity in mouse models



DOSING

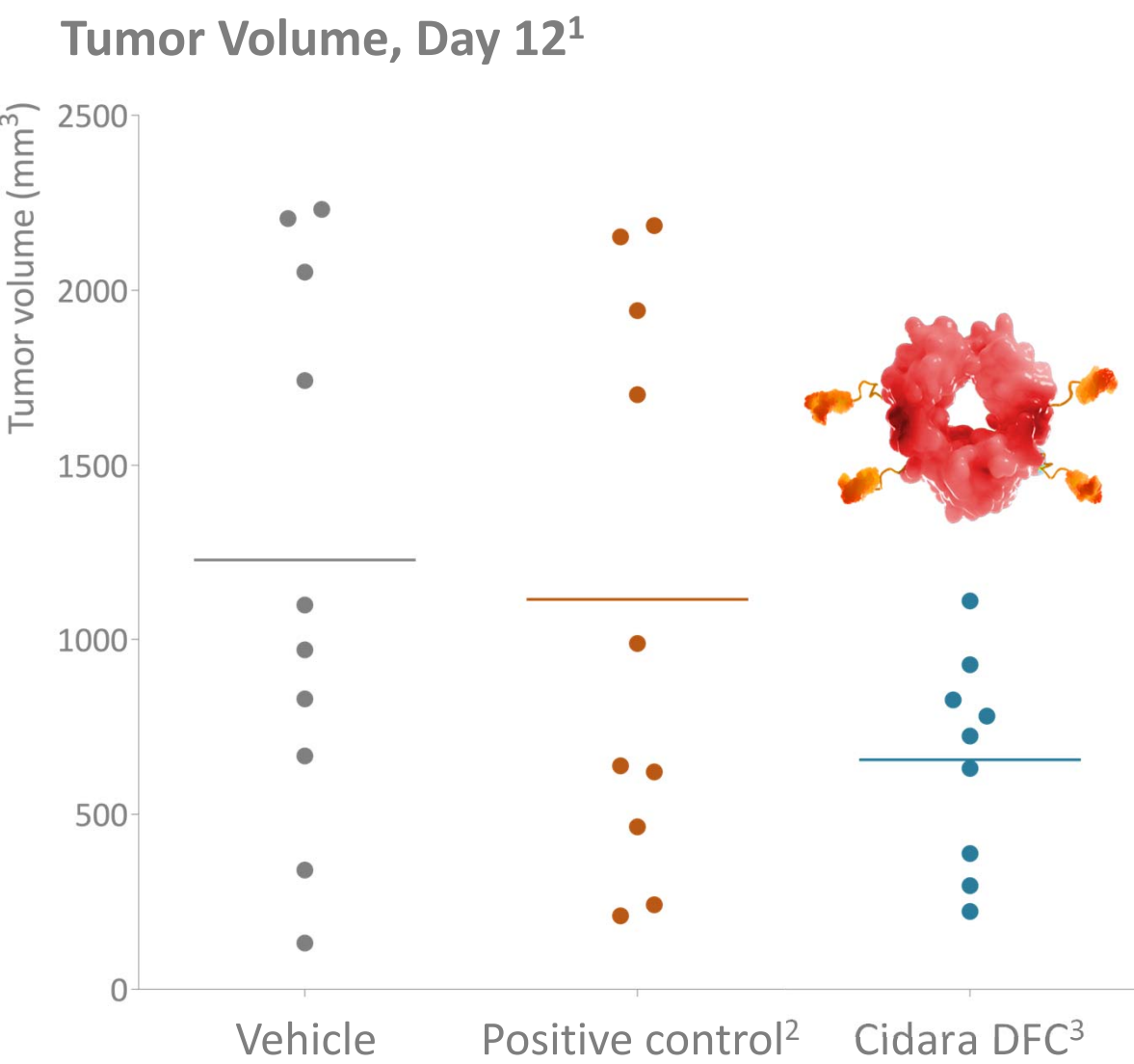
(IP Injection)	Days	0	2	4	6	8	10	12					
Positive control													
Dose (mg/kg)		30	30	30	30	30	30	30	30	30	30	30	30
Cidara DFC													
Dose (mg/kg)		20	20	20	20	20	20						

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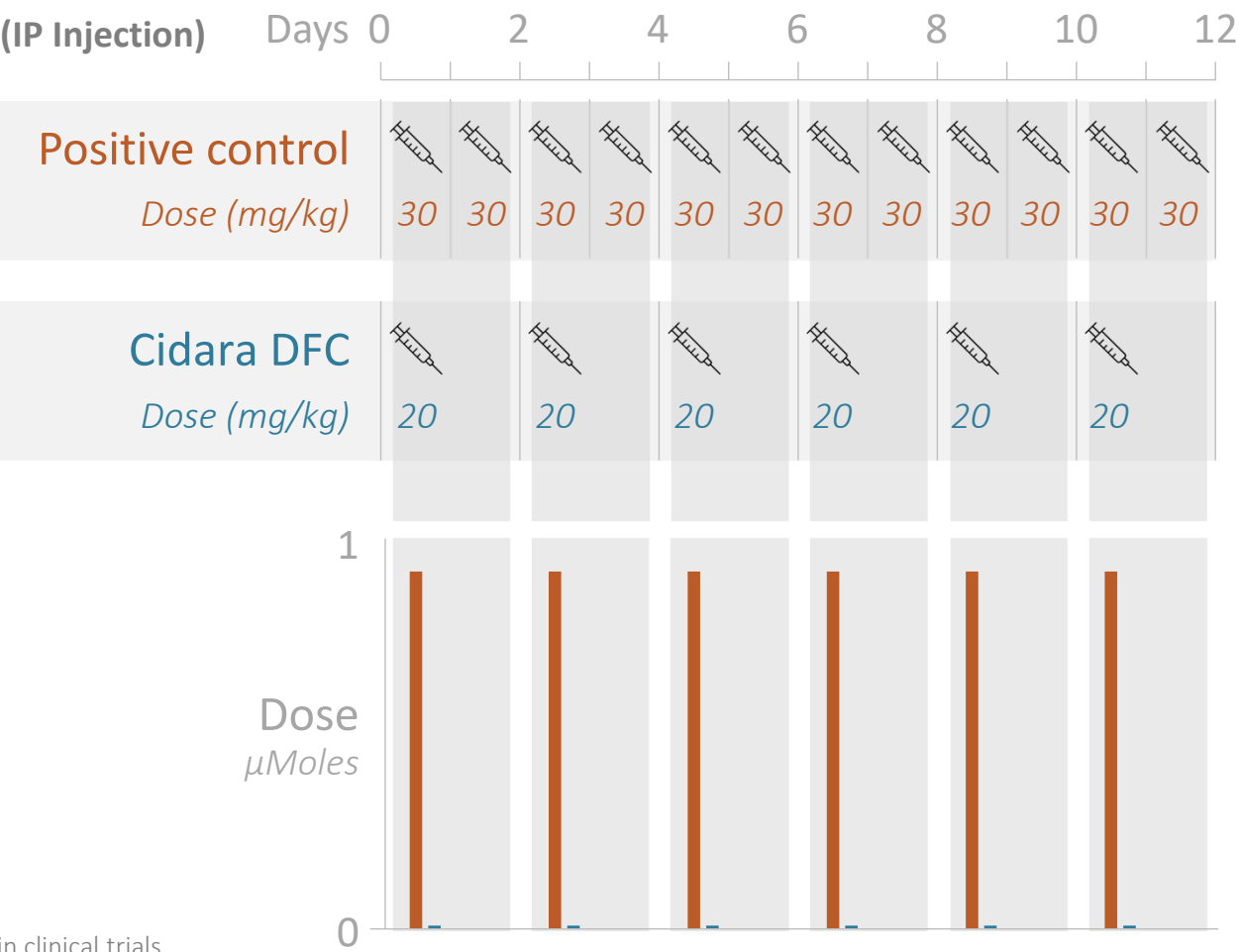
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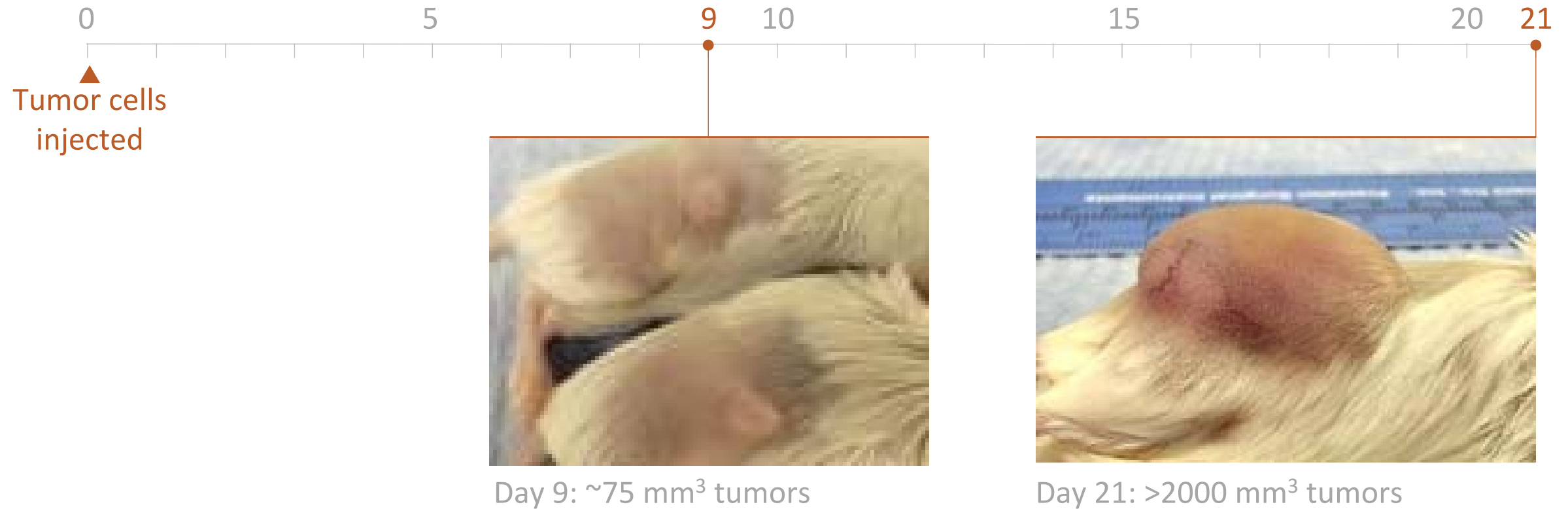
DOSING



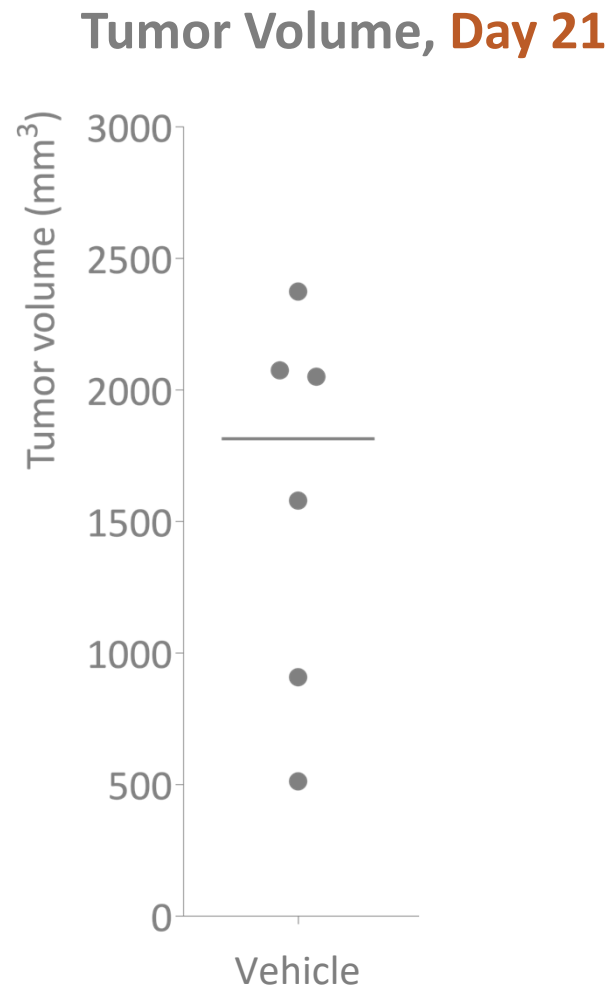
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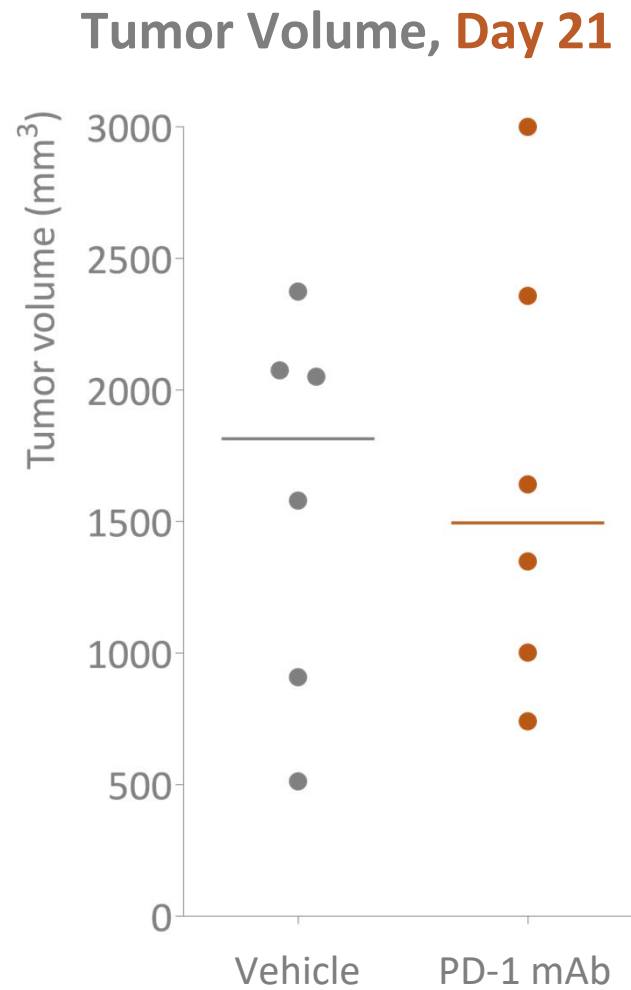
CD73 inhibitors augment PD-1 inhibitor activity



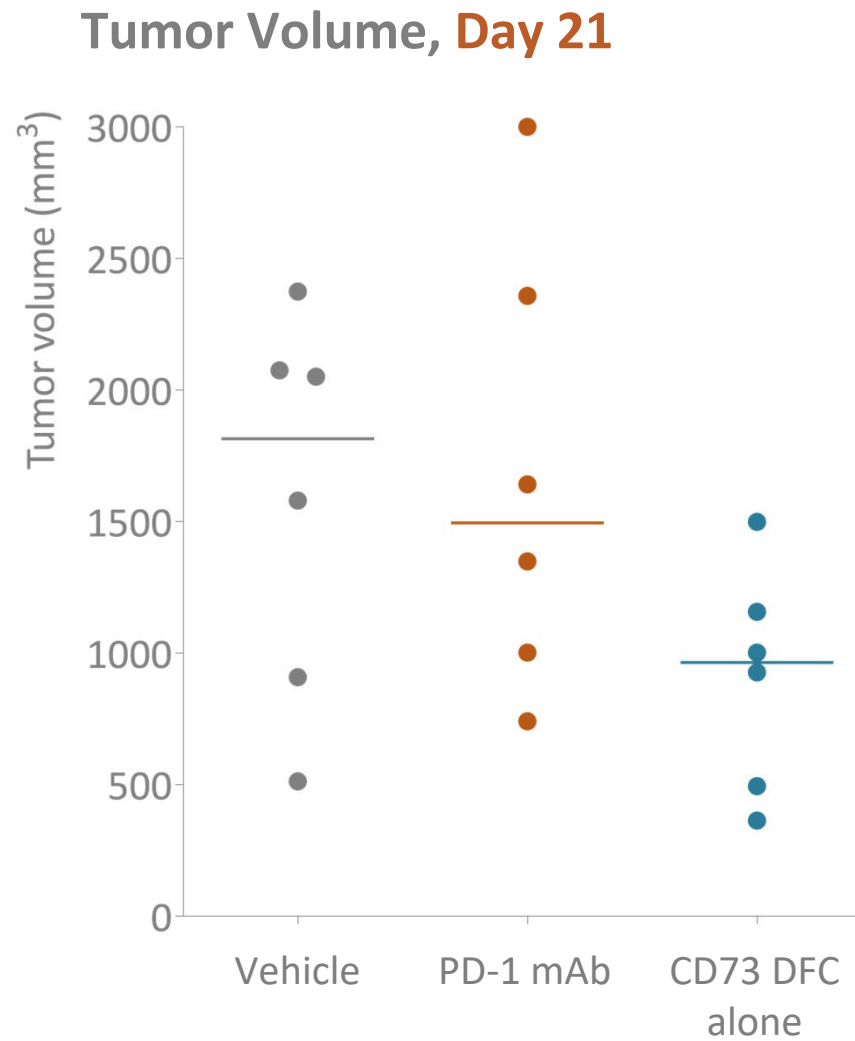
CD73 inhibitors augment PD-1 inhibitor activity



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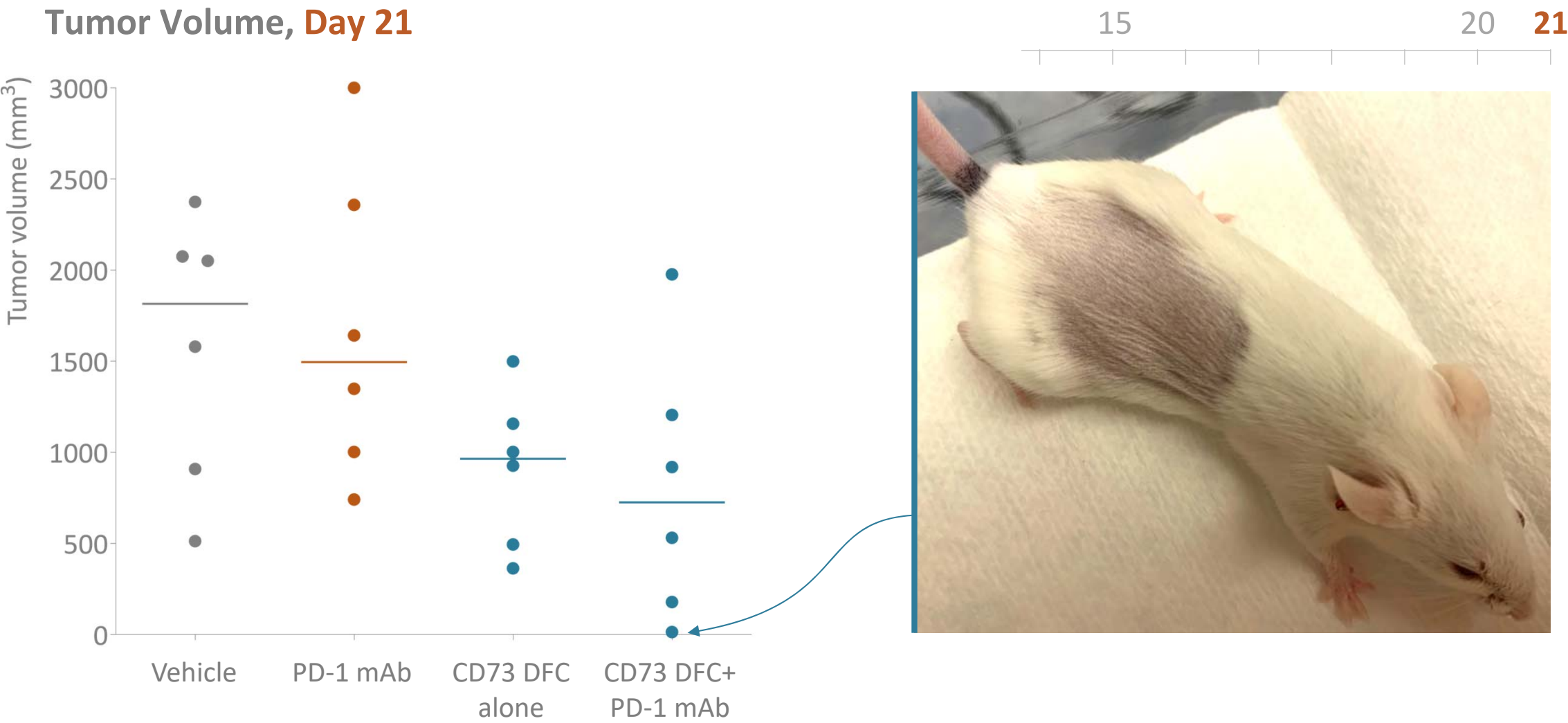


CD73 inhibitors augment PD-1 inhibitor activity



Day 21: >2000 mm³ tumors

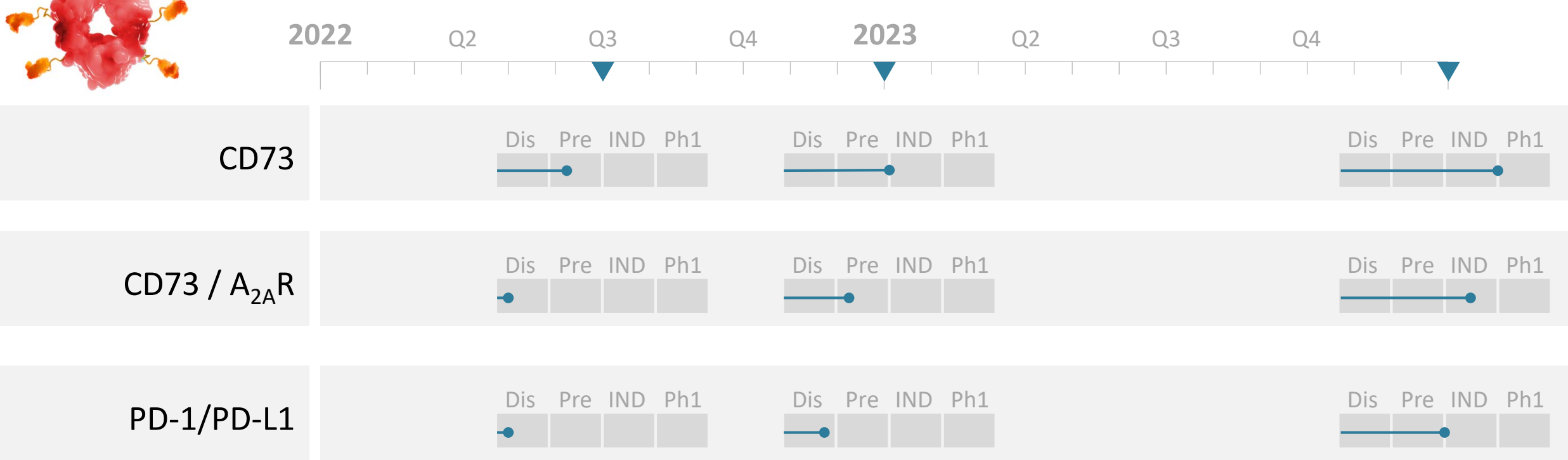
CD73 inhibitors augment PD-1 inhibitor activity



Oncology DFC programs are advancing rapidly



SOLID TUMOR PROGRAMS



Combination DFCs will be evaluated and added to the pipeline in 2022 as guided by data

Dis: Discovery
Pre: Preclinical
IND: IND enabling
Ph1: Phase one

How can Cidara succeed in the crowded space of immuno-oncology?



FOCUS: ADENOSINE PATHWAY

- Relatively limited competition
- Improve outcomes either alone or combined with existing agents
- Opportunity to create highly potent and safe “single molecule cocktails”



Discussion