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CD388 Demonstrates a High Barrier to Resistance and Retains Potent Activity against NAI^{R} Influenza A and B Variants

Simon Döhrmann, PhD

ISIRV Conference in Seattle

May 4, 2023

Disclosures

Current employee and stockholder of Cidara Therapeutics, Inc.

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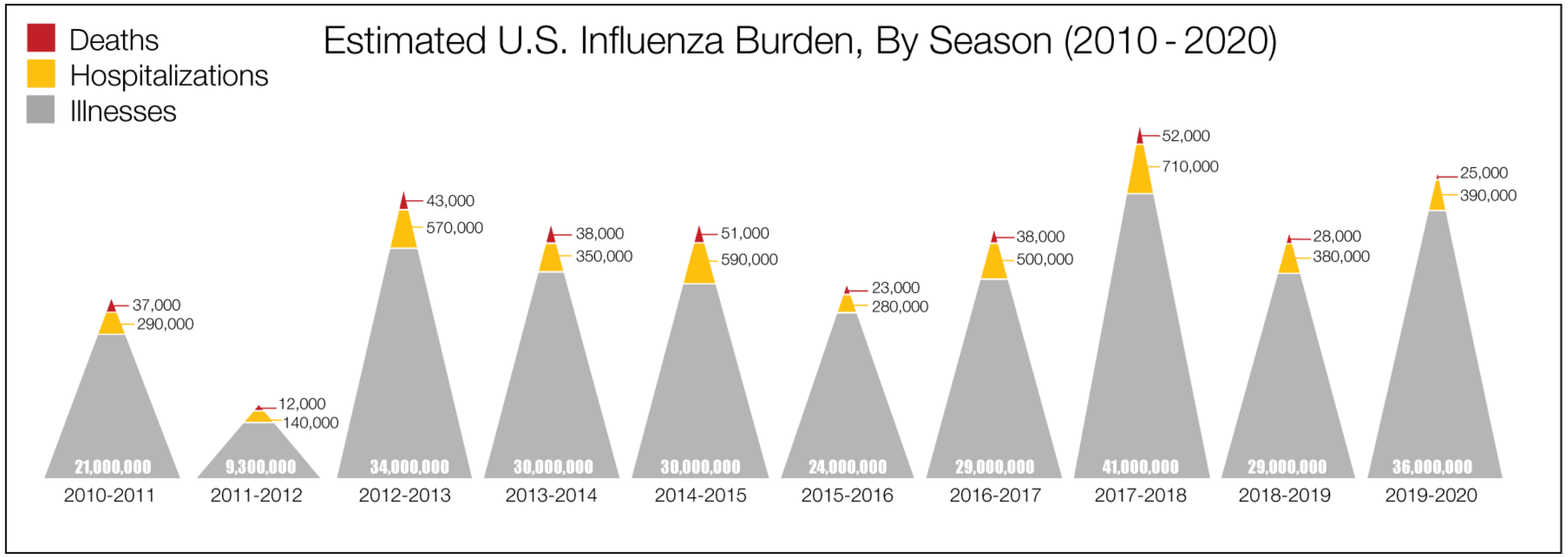
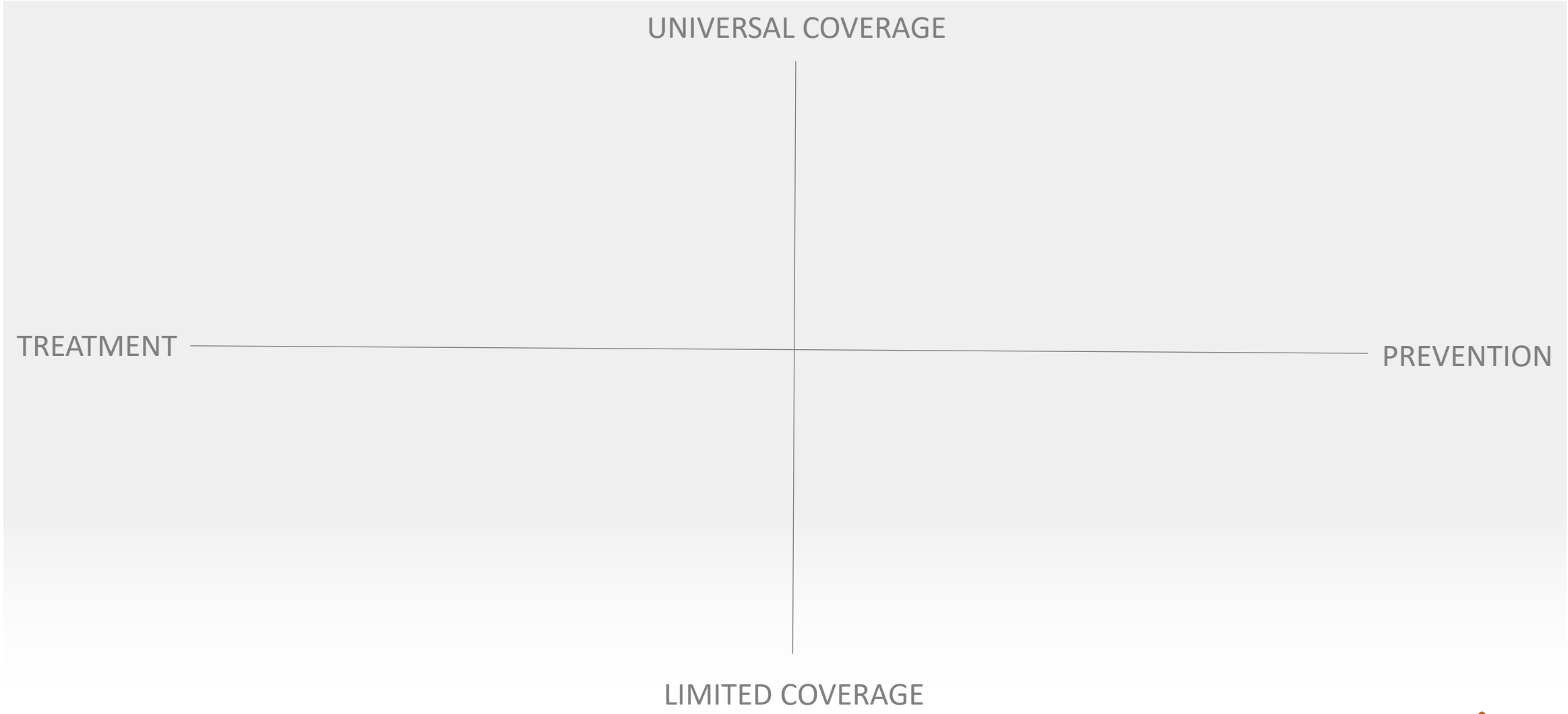
Influenza Causes Unacceptable High Levels of Disease Burden



https://www.cdc.gov/flu/about/burden/index.html

Influenza Drugs for the Treatment and Prevention of Influenza



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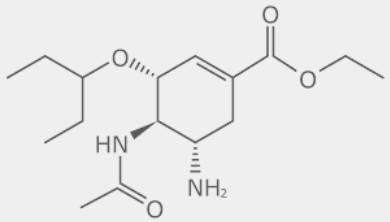
Influenza Drugs for the Treatment and Prevention of Influenza

UNIVERSAL COVERAGE



Small Molecules

TREATMENT

PREVENTION

LIMITED COVERAGE

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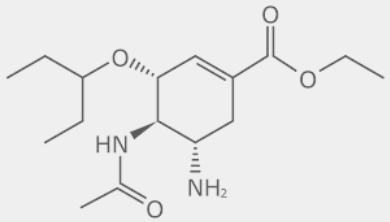
Influenza Drugs for the Treatment and Prevention of Influenza

UNIVERSAL COVERAGE



Small Molecules

TREATMENT

PREVENTION

Vaccines

LIMITED COVERAGE

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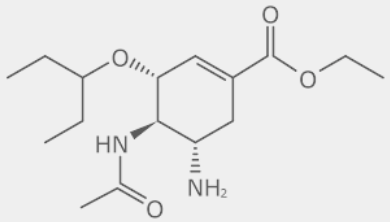
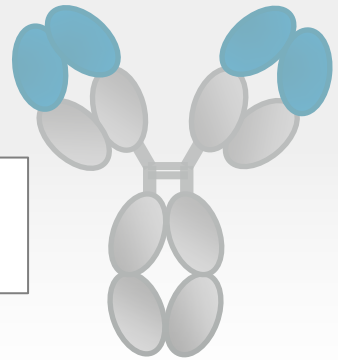


Small Molecules

TREATMENT

PREVENTION



Monoclonal antibodies

Vaccines

LIMITED COVERAGE

Anti-influenza mAbs are not FDA-approved, but currently in Clinical Development

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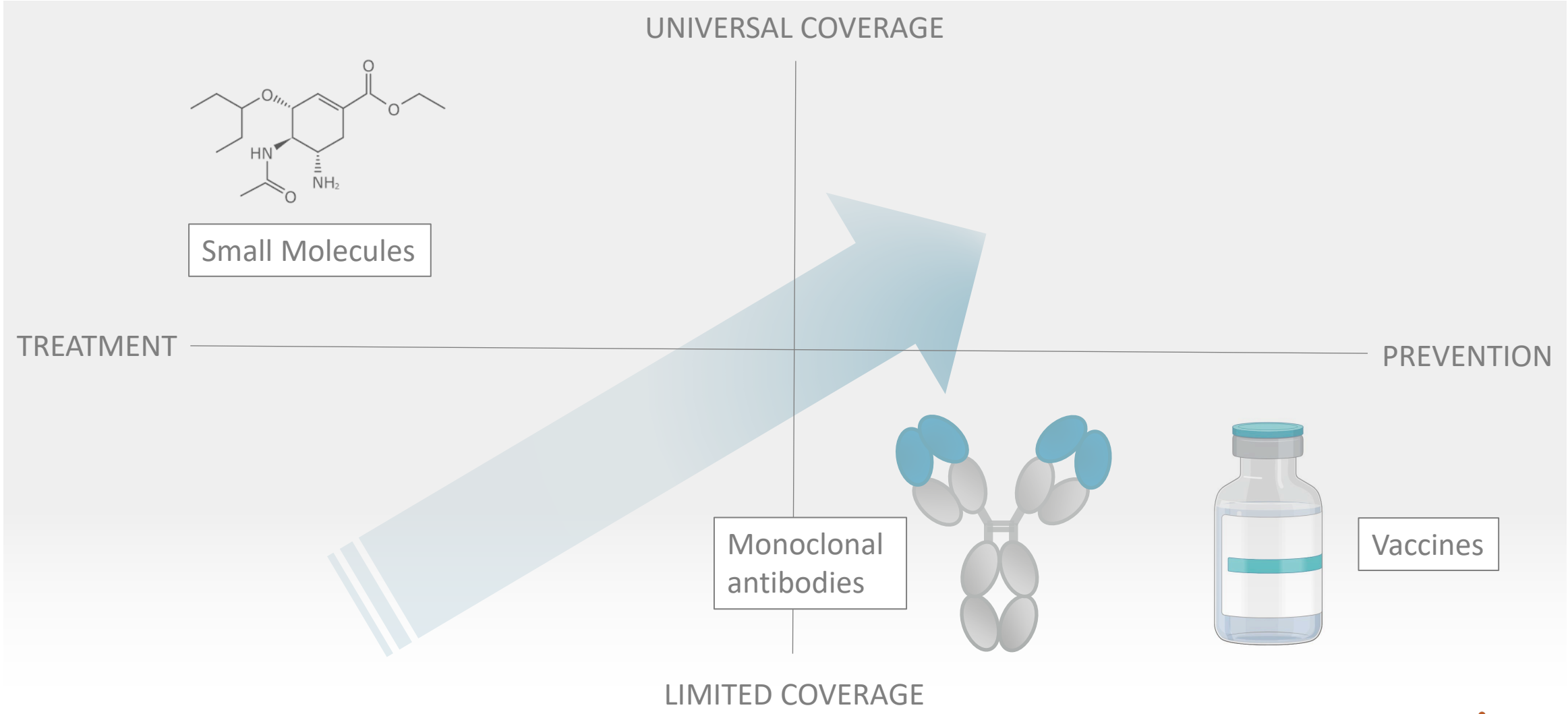
Unmet Need for Long-Acting, Universal Agent for Influenza Prevention



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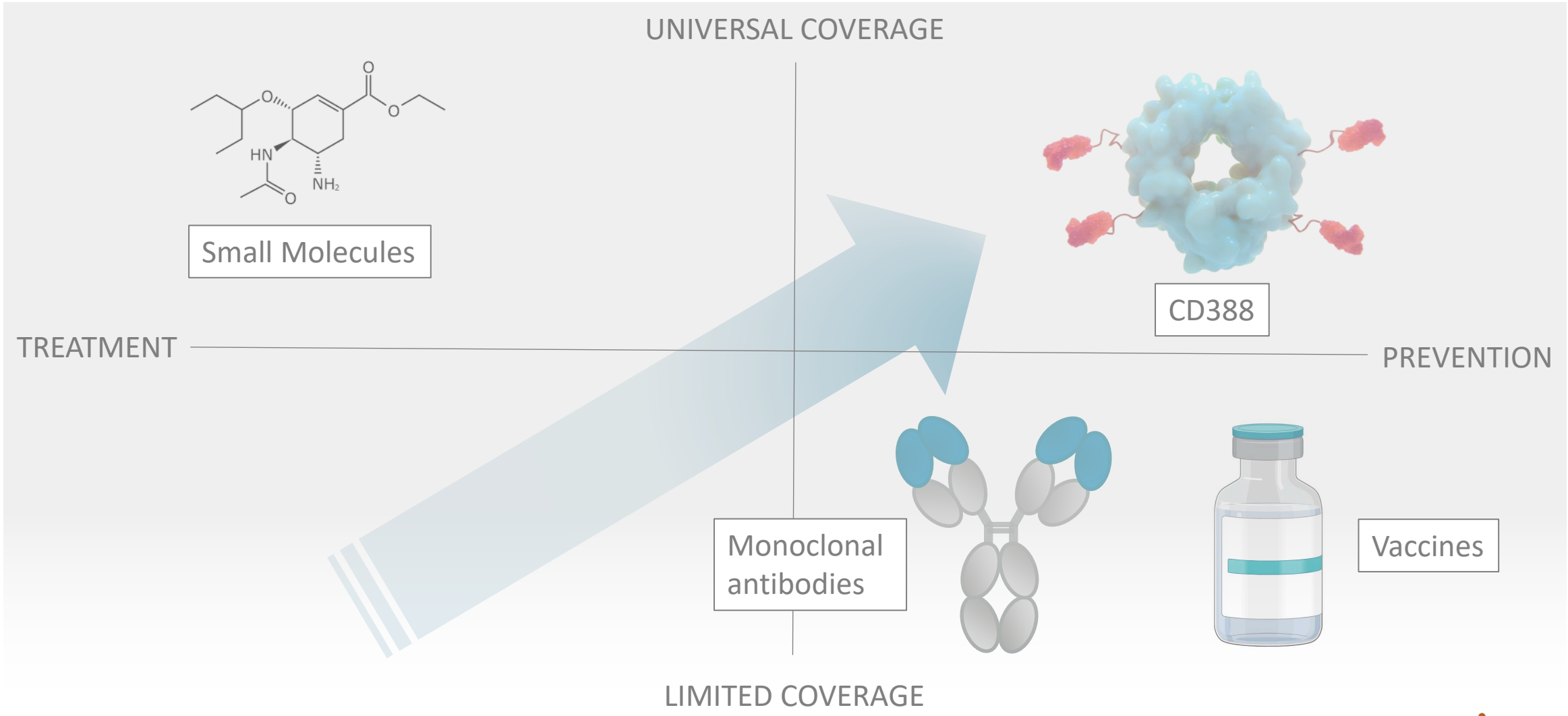
Unmet Need for Long-Acting, Universal Agent for Influenza Prevention



Anti-influenza mAbs are not FDA-approved, but currently in Clinical Development

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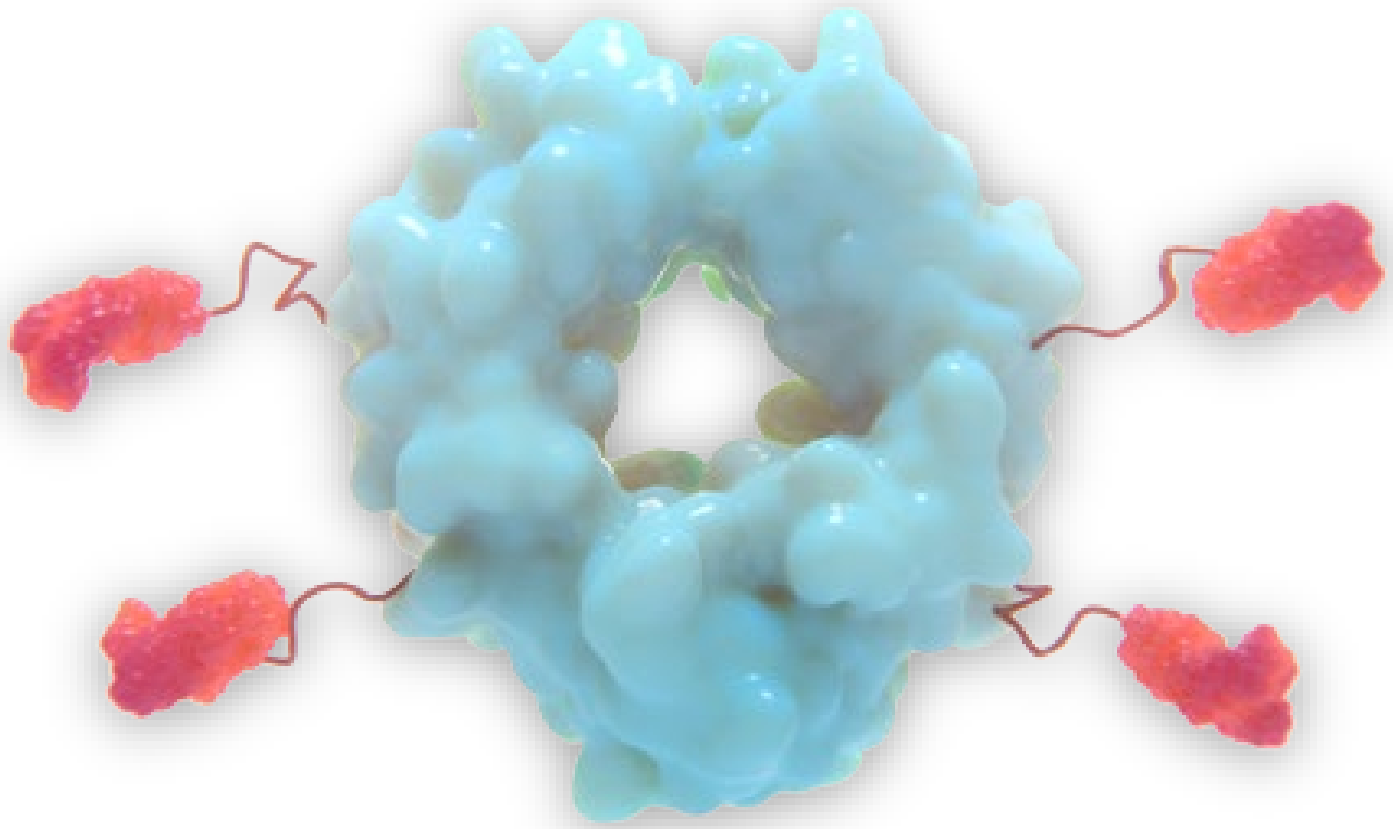
CD388 is in Clinical Development* for the Prevention of Influenza

CD388 development under exclusive, worldwide license with Janssen Pharmaceutical

Multivalent presentation of a novel, dimeric NAI



Fc fragment is engineered for PK extension

* Phase 1: NCT05285137 and Phase 2a: NCT05523089

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Why Was a NAI Selected for the Design of CD388?

- NA is essential for viral replication cycle
- Positive correlation of anti-NA titers with protection against influenza[1]
- Low frequency of NAI^R variants observed clinically (<1%)[2]
- NA has a highly conserved active-site across influenza A and B that Small molecule NAIs specifically target (‘universal coverage’)

1 Maier et al. Pre-existing Ant-ineuraminidase Antibodies Are Associated With Shortened Duration of Influenza A(H1N1)pdm Virus Shedding and Illness in Naturally Infected Adults. Clin Infect Dis. 2020 May 23;70(11):2290-2297. PMID: 31300819; PMCID: PMC7245146; Memoli et al. Evaluation of Antihemagglutinin and anti-NA Antibodies as Correlates of Protection in an Influenza A/H1N1 Virus Healthy Human Challenge Model PMID: 27094330
2 Govorkova et al. Global update on the susceptibilities of human influenza viruses to neuraminidase inhibitors and the cap-dependent endonuclease inhibitor baloxavir, 2018-2020. Antiviral Res. 2022 Apr;200:105281. Epub 2022 Mar 12. PMID: 35292289; PMCID: PMC9254721.

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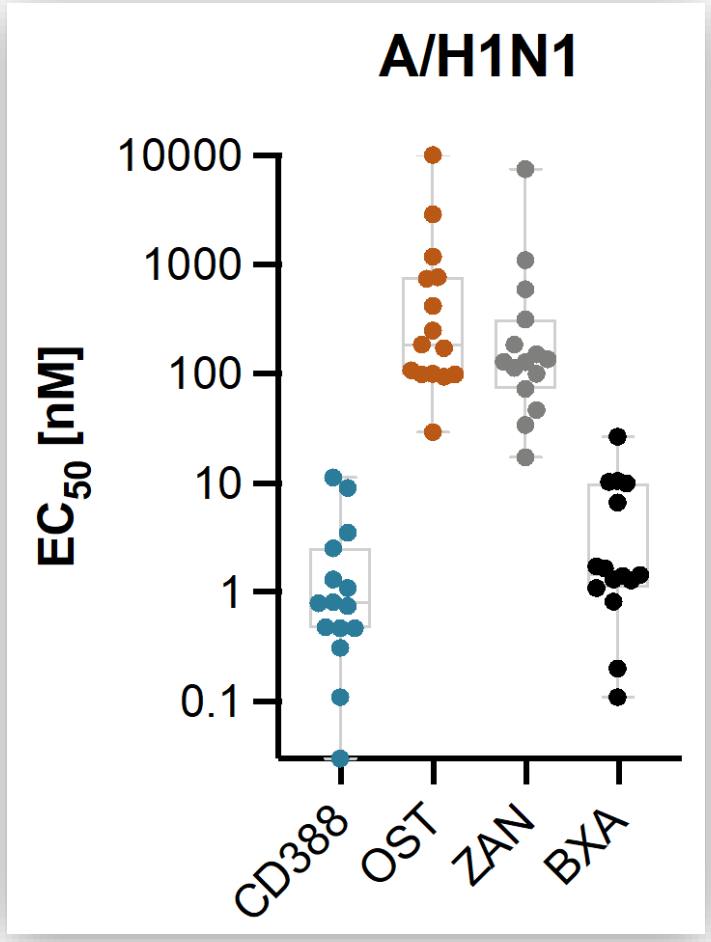
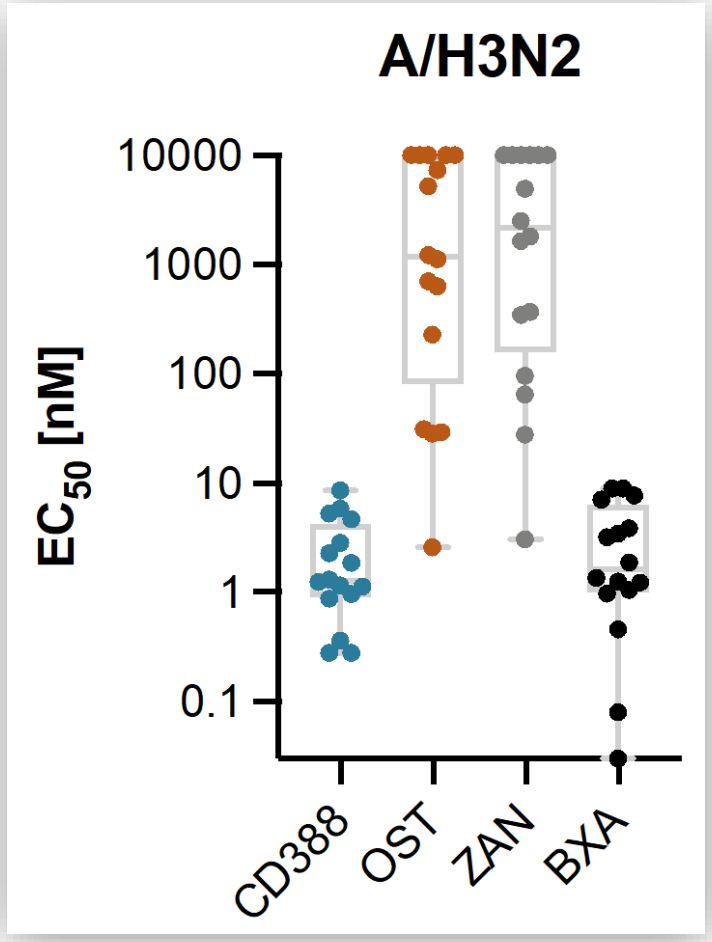
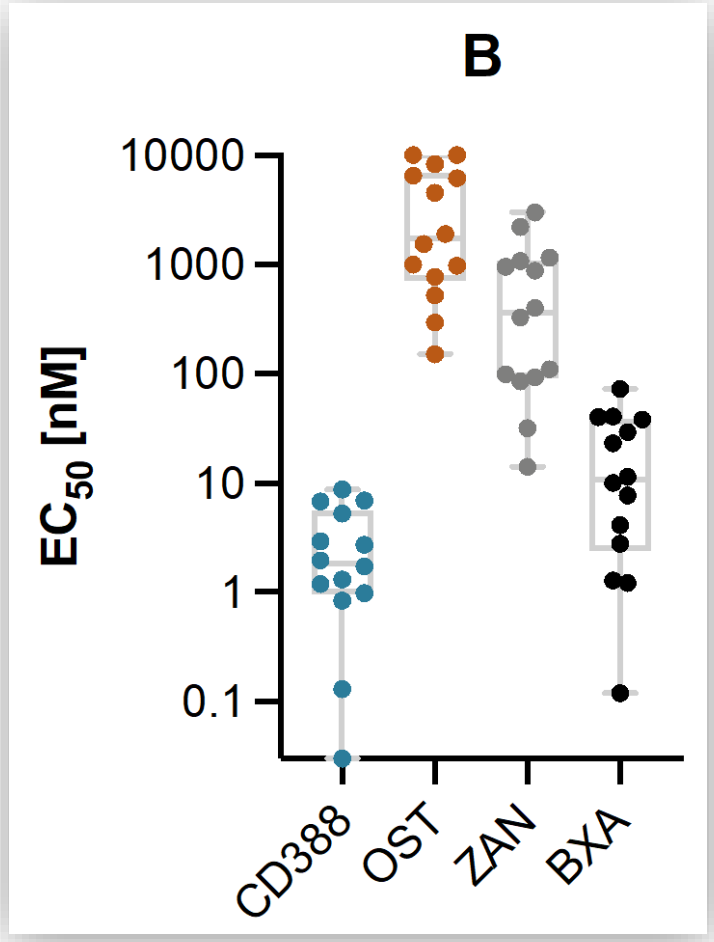
CD388 is Differentiated from Small Molecule NAIs and Demonstrates Universal Activity against Influenza A and B

Cell-Based Cytopathic Effect Assays







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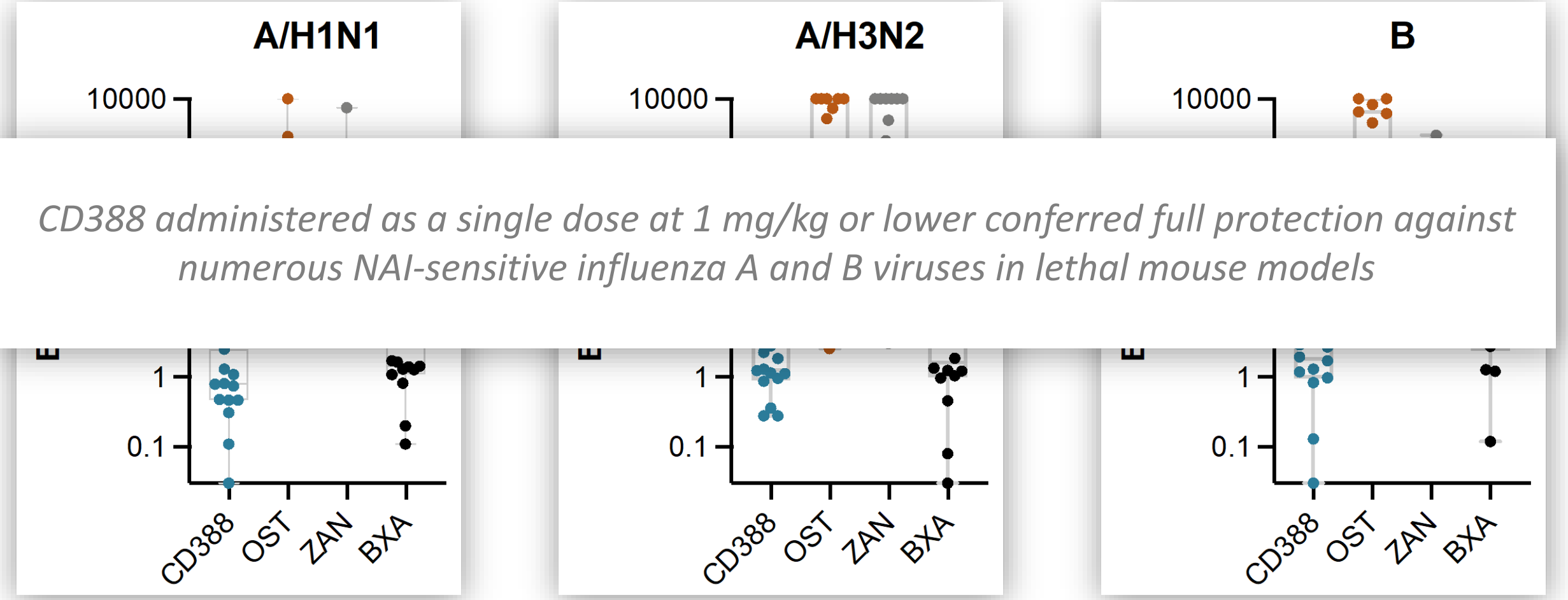
CD388 is Differentiated from Small Molecule NAIs and Demonstrates Universal Activity against Influenza A and B

Cell-Based Cytopathic Effect Assays



CD388 administered as a single dose at 1 mg/kg or lower conferred full protection against numerous NAI-sensitive influenza A and B viruses in lethal mouse models

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What is the Resistance Potential of CD388?

CD388 Serial Passage Methodologies: Static, sub-inhibitory and dose-escalating

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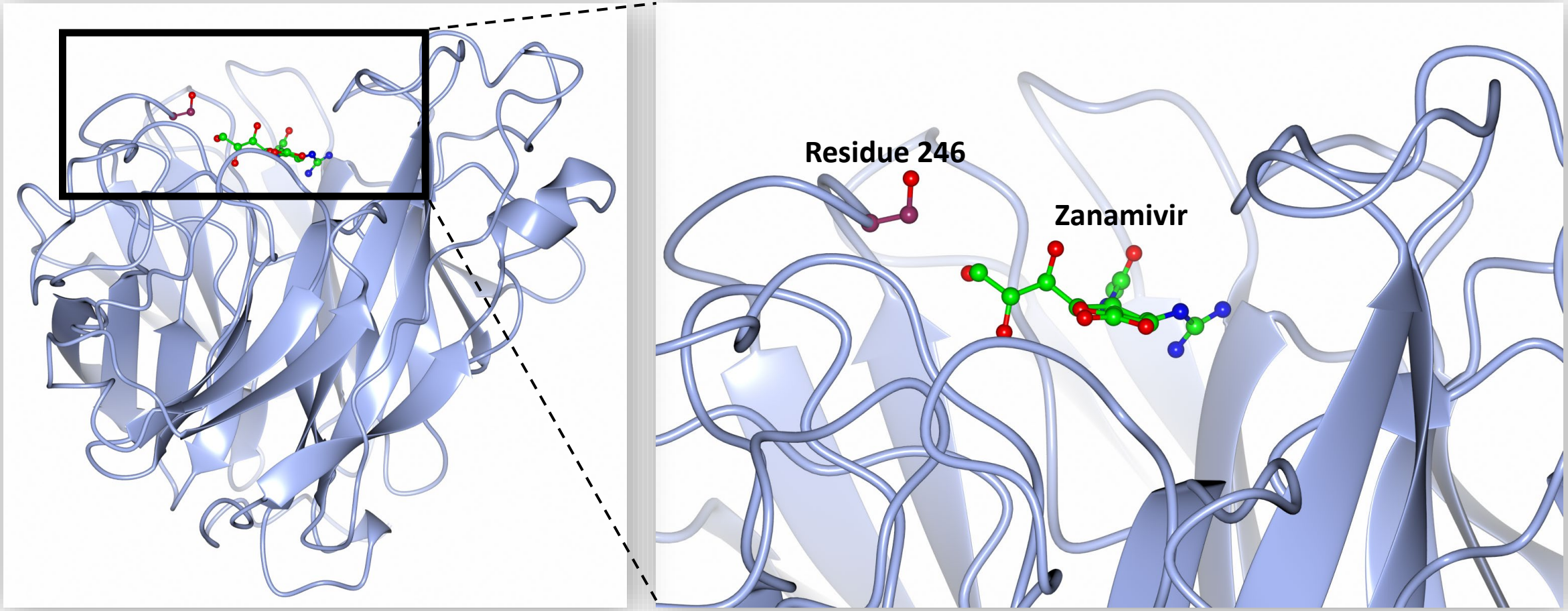
CD388-Selected Variants Were Identified at Position 246 in NA

ZAN interaction with NA from A/H1N1



NA monomer with ZAN PDB:3TI5

CD388-Selected Variants Remain Susceptible to CD388

Cross-resistance in Cell-Based Plaque Reduction Assays

Influenza virus	NA geno-type	CD388		OST		ZAN	
		EC_{50} [nM]	Fold-change	**EC_{50} [nM]**	Fold-change	**EC_{50} [nM]**	Fold-change
A/WSN/1933 (H1N1), p0	S246[1]	**0.09**	---	**80.1**	---	**6.88**	---
A/WSN/1933 (H1N1), p10	S246R	**0.23**	2.6	**50.0**	0.6	**9.77**	1.5
A/Victoria/3/75 (H3N2), p0	A246	**1.65**	---	**1.80**	---	**6.09**	---
A/Victoria/3/75 (H3N2), p10	A246V	**4.58**	2.8	**9.02**	5	**58.7**	11

[1]AA numbering based on N2

Is CD388 Active against NAI^{R} Variants?

NA inhibition Assays

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CD388 Retains Potency against NAI^{R} Variants

NA Inhibition Assays

Influenza virus	NA geno-type	CD388		OST		ZAN	
		IC_{50} [nM]	Fold-change	**IC_{50} [nM]**	Fold-change	**IC_{50} [nM]**	Fold-change
A/Illinois/45/2019 (H1N1)	H275	**1.30**	---	**0.33**	---	**0.19**	---
A/Alabama/03/2020 (H1N1)	H275Y	**0.98**	1	**426.8**	1304	**0.16**	1
B/Laos/0080/2016	H134	**7.44**	---	**33.35**	---	**2.61**	---
B/Laos/0654/2016	H134N	**4.66**	1	**171.8**	5	**310.8**	119

Source: IRR, Cat#FR-1755 CoA 70037427 NI=Normal inhibition (<10-fold vs influenza A virus (IAV)/<5-fold vs influenza B virus (IBV) above NI), RI = reduced inhibition (10 - 100-fold vs IAV/5 - 50-fold vs IBV above NI), HRI = highly reduced inhibition (>100-fold vs IAV/>50-fold vs IBV above NI)

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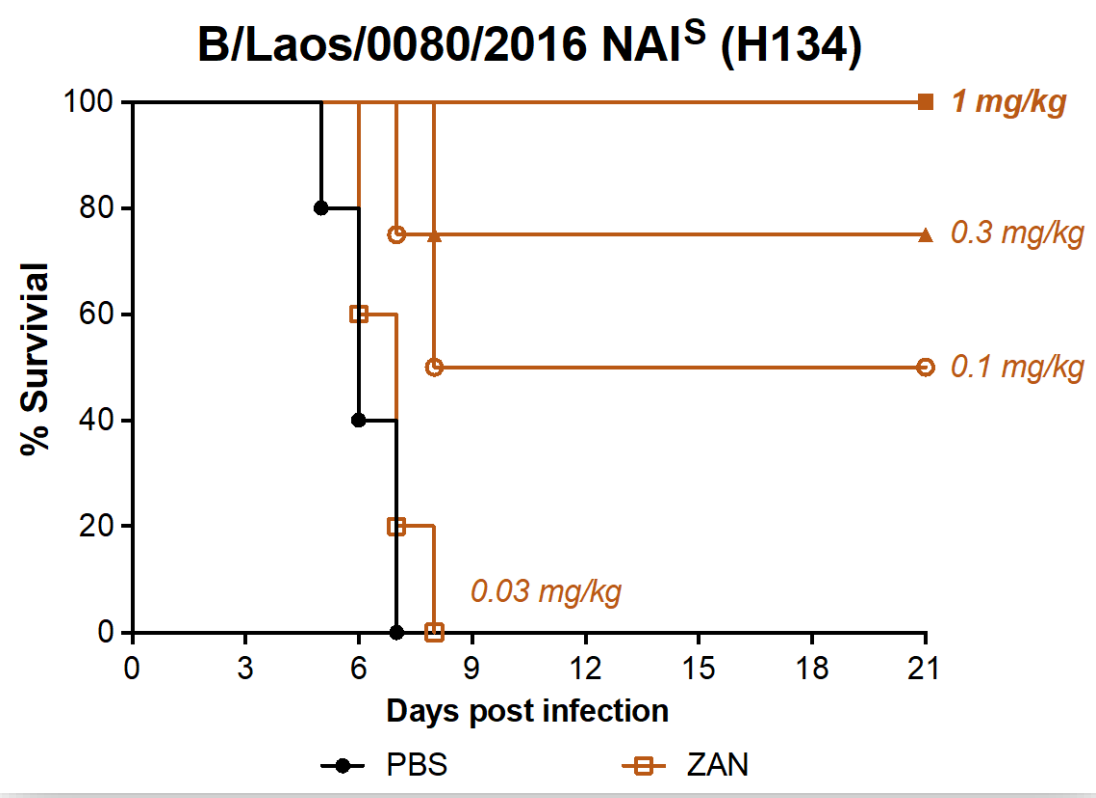
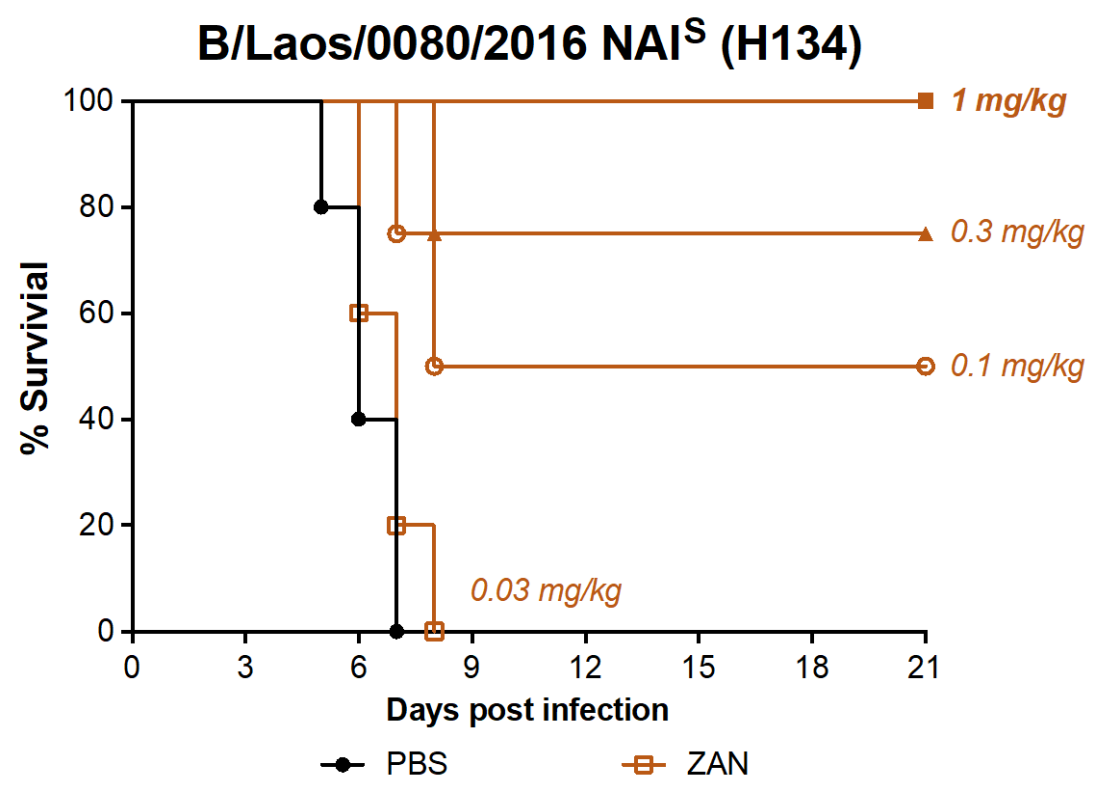
ZAN is Protective against ZAN^{S} Strain in Lethal Mouse Model

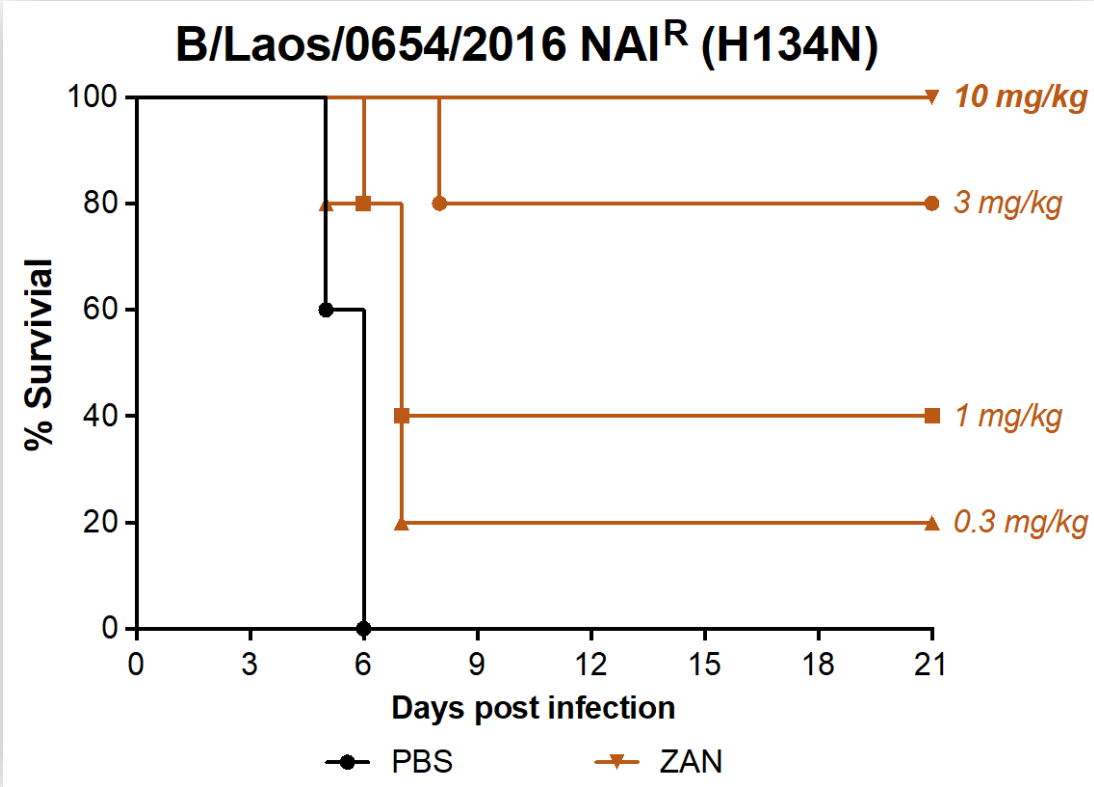
ZAN dosed IN starting t+2h post-infection (QD x 5)



ZAN has 10x Reduced Efficacy against a ZAN^{R} Variant in Lethal Mouse Model

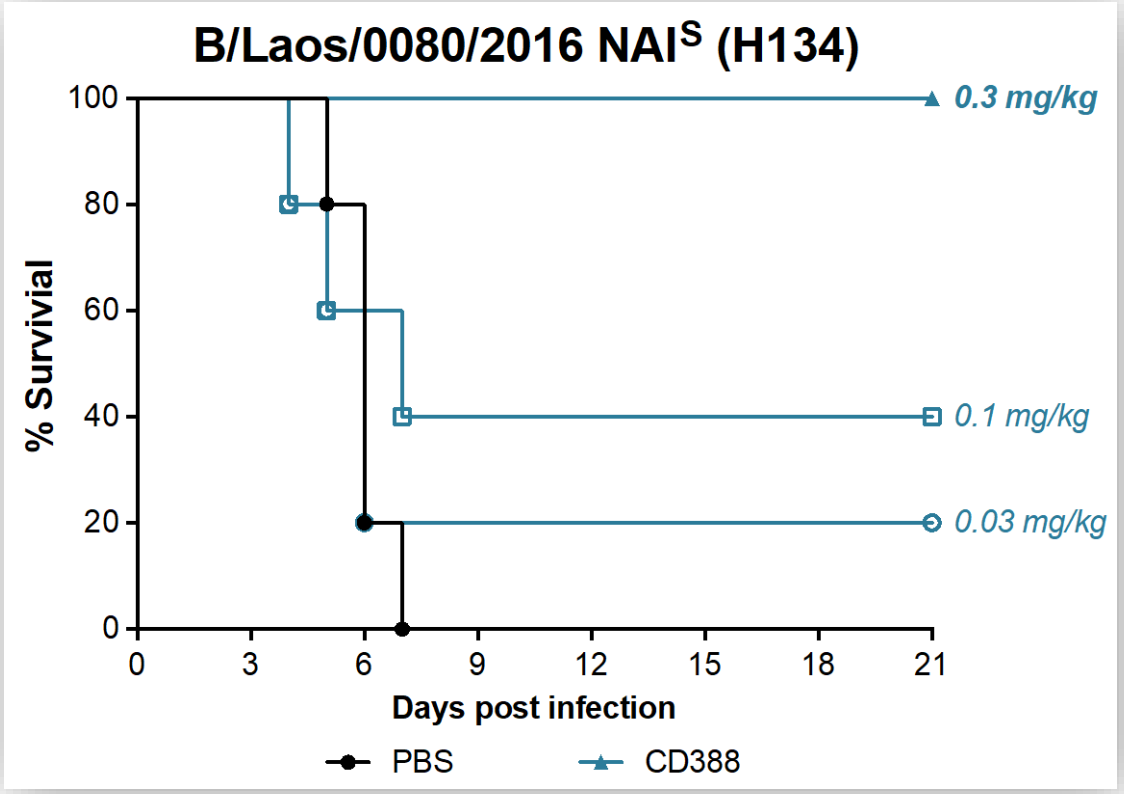
ZAN dosed IN starting t+2h post-infection (QD x 5)





CD388 Demonstrates Efficacy with Single, Low Dose against ZAN^{S} Strain in Lethal Mouse Model

Single IM dose at t+2h post-infection



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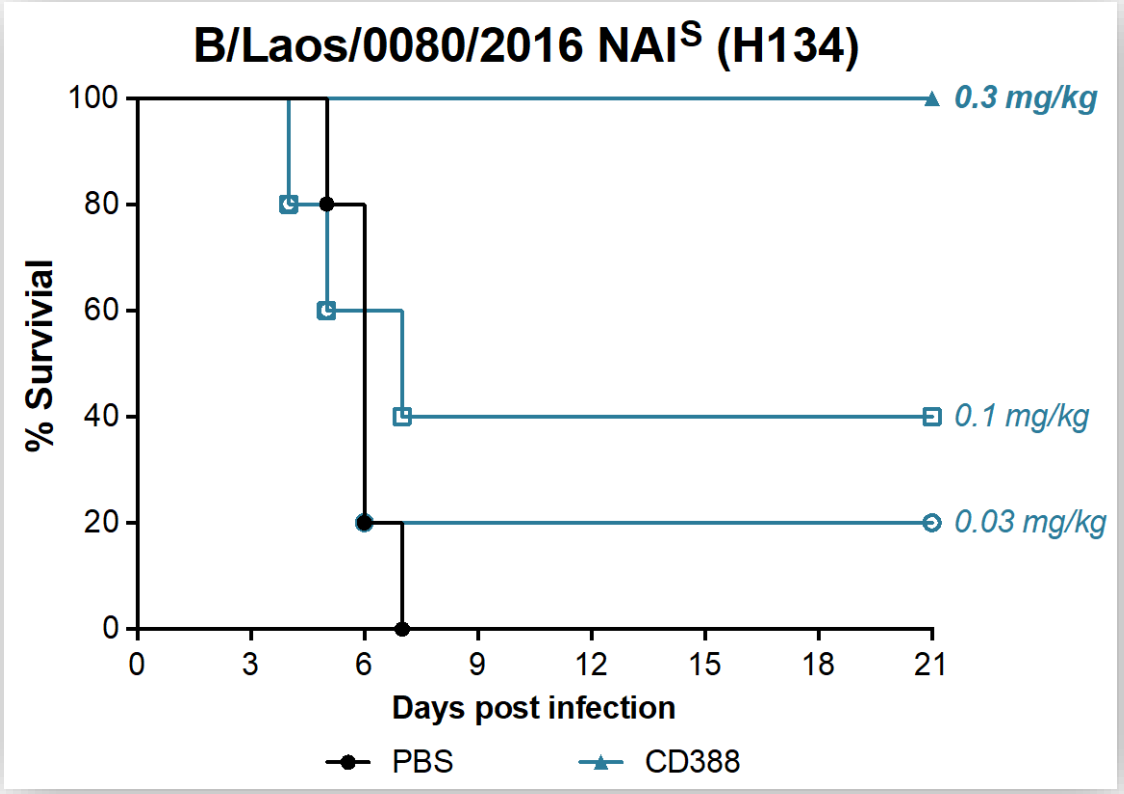
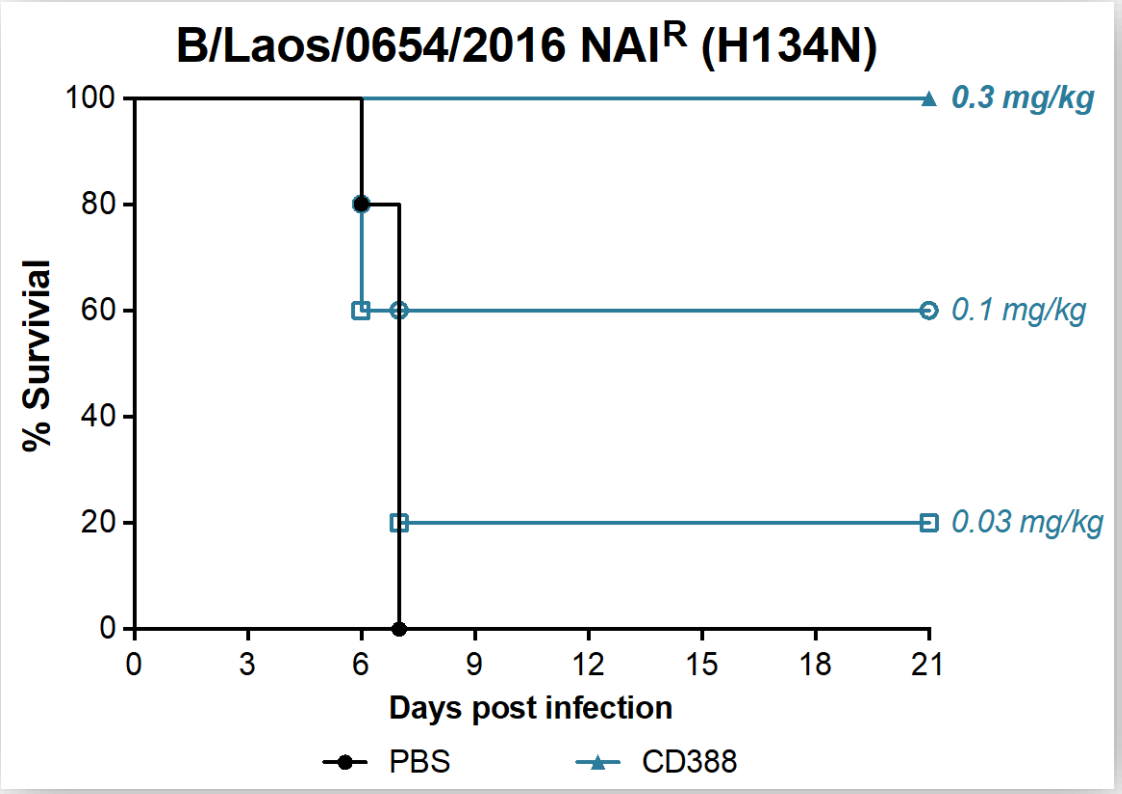
CD388 Demonstrates Unchanged Efficacy against a ZAN^{R} Variant in Lethal Mouse Model

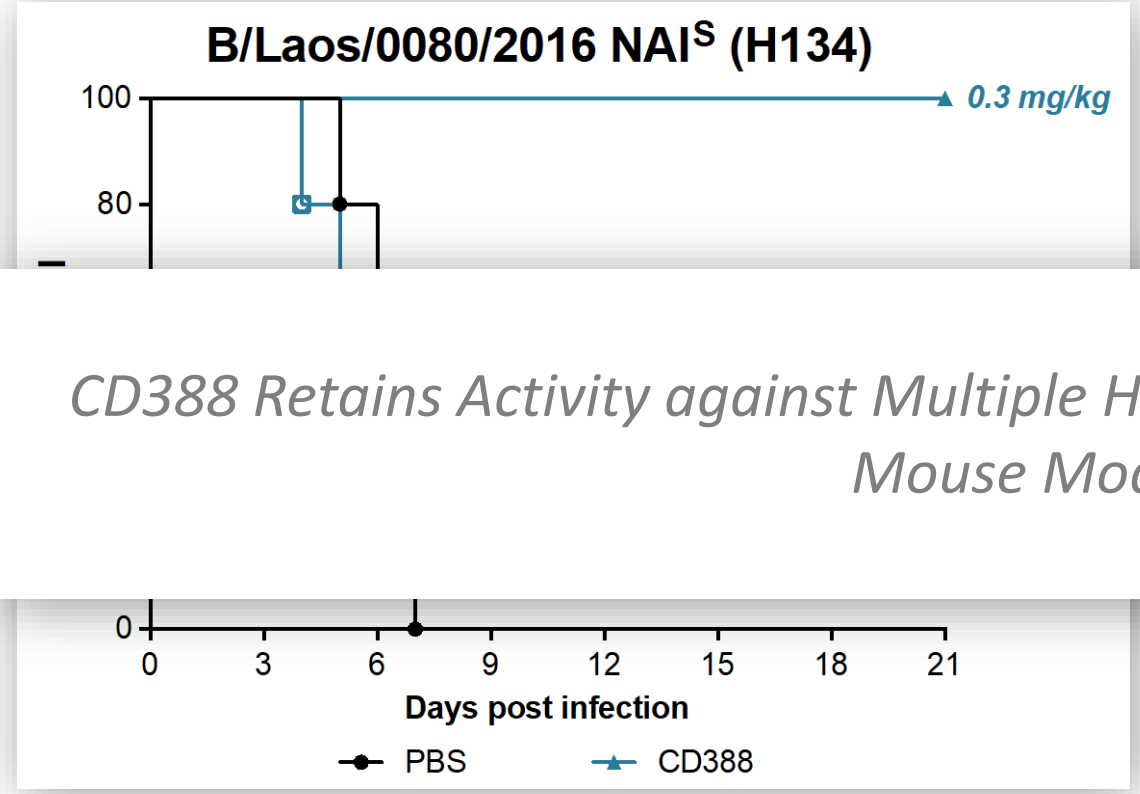
Single IM dose at t+2h post-infection

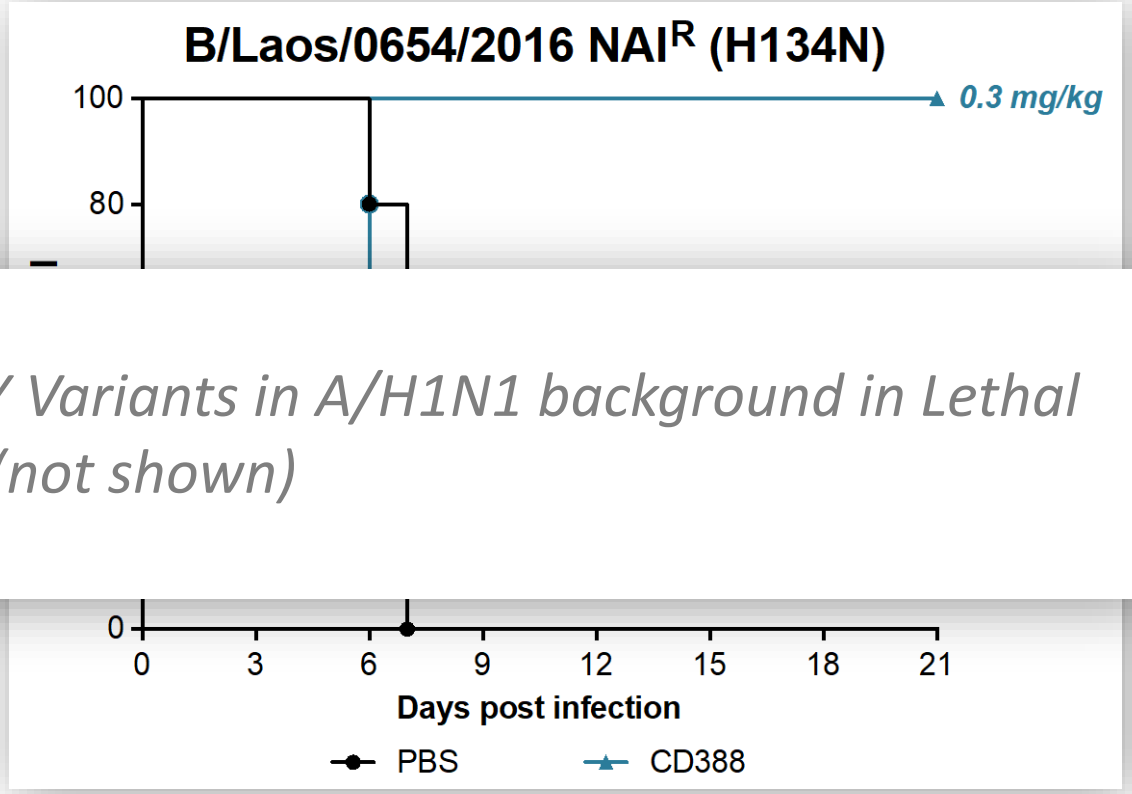




CD388 Demonstrates Unchanged Efficacy against ZAN^{R} Variant in Lethal Mouse Model

Single IM dose at t+2h post-infection





CD388 Retains Activity against Multiple H275Y Variants in A/H1N1 background in Lethal Mouse Models (not shown)

Summary

- CD388 demonstrates universal activity against influenza A and B
- CD388 demonstrates a high-barrier to resistance in serial passage experiments and retains potency against CD388-selected variants
- CD388 retains potent activity against the CDC panel of NAI^R influenza variants
- CD388 protective doses in lethal mouse models are identical against NAI^S and NAI^R influenza variants

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PRESS RELEASES

CIDARA THERAPEUTICS ANNOUNCES PROMISING INTERIM PHASE 2A DATA ASSESSING THE SAFETY AND EFFICACY OF A SINGLE DOSE OF CD388 IN AN INFLUENZA CHALLENGE MODEL

March 1, 2023

- *A single dose of CD388 decreased influenza viral replication in the upper respiratory tract and lowered influenza incidence rate in a human challenge model when compared to placebo*
- *CD388 was generally safe and well tolerated with no adverse events related to study drug reported as of the February 13, 2023 data cut-off*
- *Ongoing study being conducted in collaboration with Janssen*

SAN DIEGO, March 01, 2023 — Cidara Therapeutics, Inc. (NASDAQ: CDTX), a biotechnology company developing long-acting therapeutics designed to help improve the standard of care for patients facing serious diseases, today announced promising efficacy and safety data from a planned interim analysis of the ongoing Phase 2a trial evaluating

Phase 2a: NCT05523089

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Acknowledgements

Cidara Team:

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- **James Levin, PhD**
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- Daniel C. Bensen
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- Thomas P. Brady, PhD
- Jeffrey Locke, PhD
- Jeffrey L. Stein, PhD

Janssen Pharmaceuticals Team

External Collaborators:

- Stacey Schultz-Cherry, PhD (St. Jude's)
- Sumit Chanda, PhD (TSRI)
- Laura Martin-Sancho, PhD (Imperial College)
- Paul DeJesus (TSRI)

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