CIDARA THERAPEUTICS

CD377, a Novel Antiviral Fc-conjugate, Demonstrates Potent Viral Burden Reduction Against Influenza A (H1N1) in Mouse and Ferret Models

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San Diego, CA

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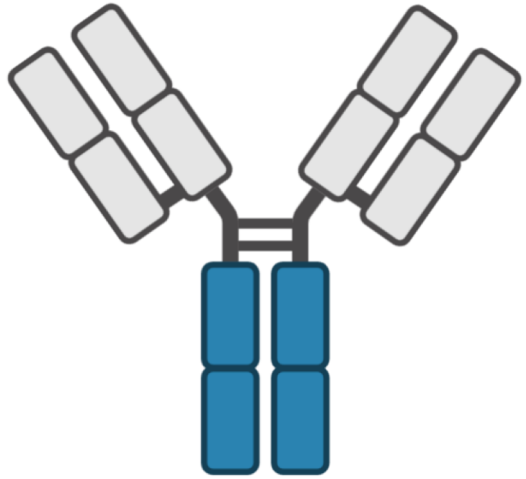
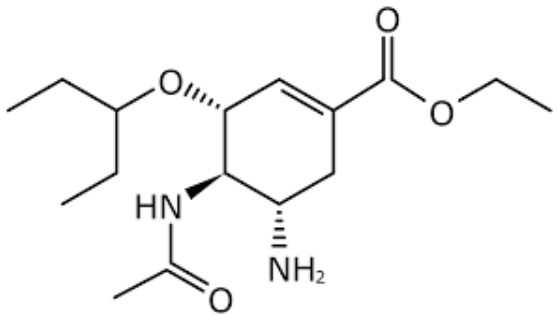
Abstract 162

Disclosures

All authors are employees and stockholder of Cidara Therapeutics, Inc.

Conventional approaches to prevent and treat influenza

Prevention → Treatment

Vaccine	Monoclonal Antibody	Small Molecule
		
Limited VE	Limited to Influenza A	Limited to Treatment

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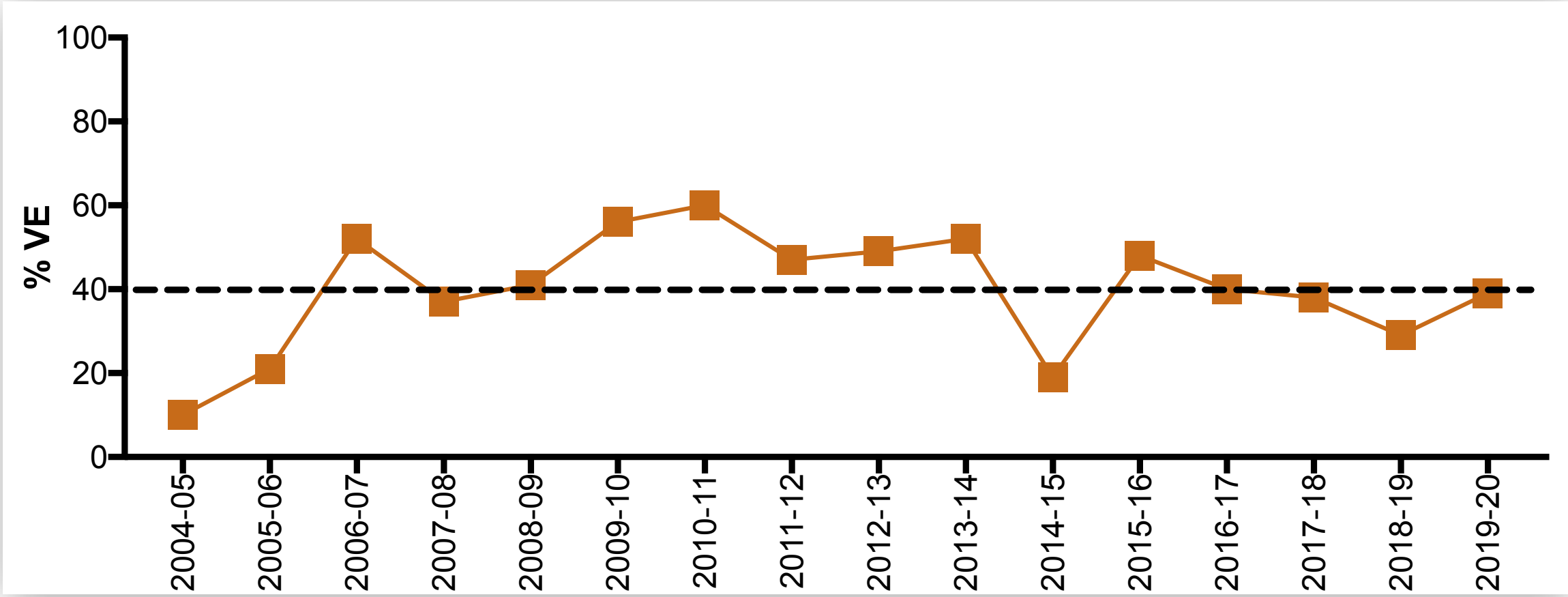
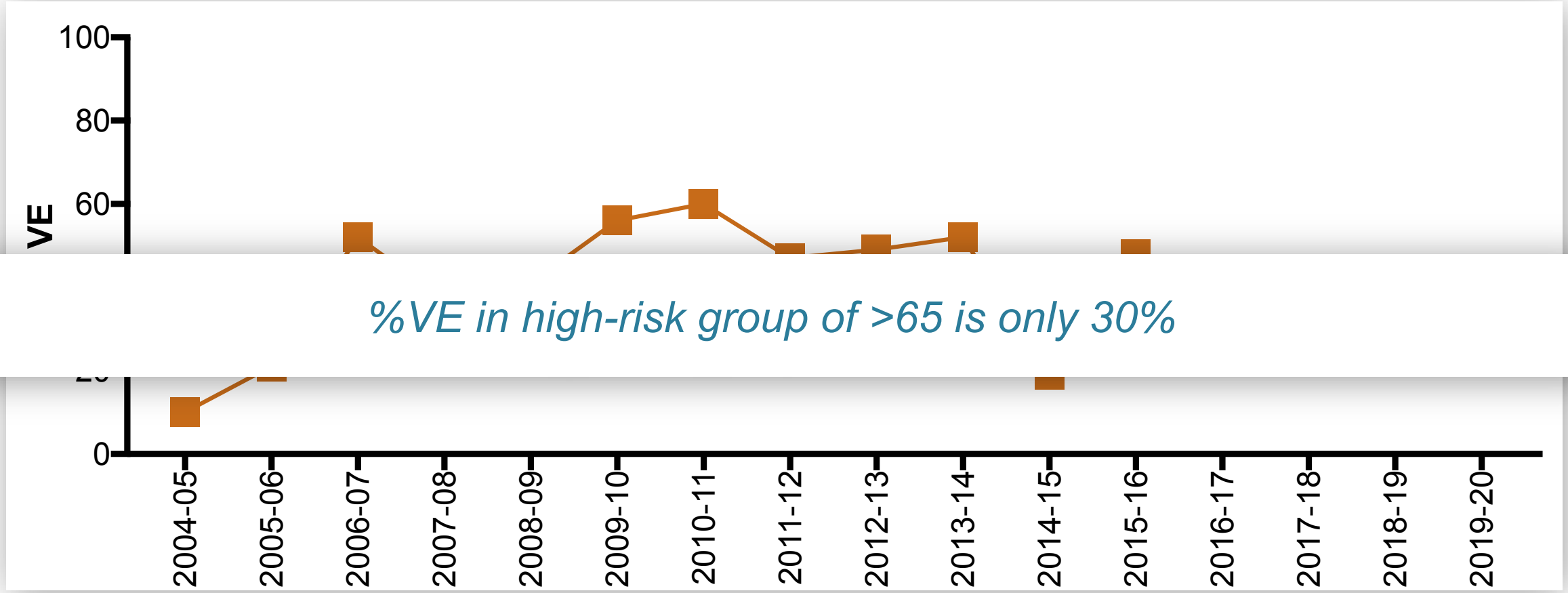
Vaccines have limited vaccine effectiveness (VE) against influenza



Source: CDC

Vaccines have limited vaccine effectiveness (VE) - especially in the elderly - against influenza



%VE in high-risk group of >65 is only 30%

Source: CDC

Annual disease burden by influenza in the US (2019-20)

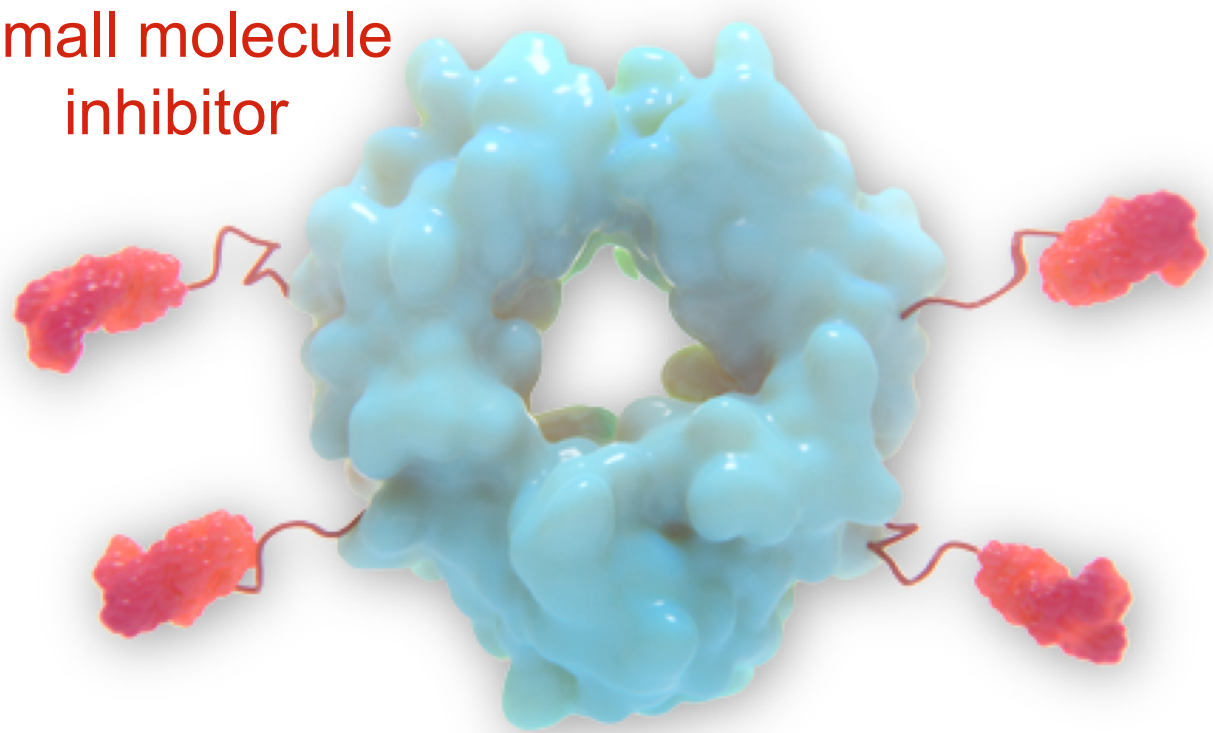
39-56M
flu illnesses

410-740K
hospitalizations

24-62K
deaths

Source: CDC

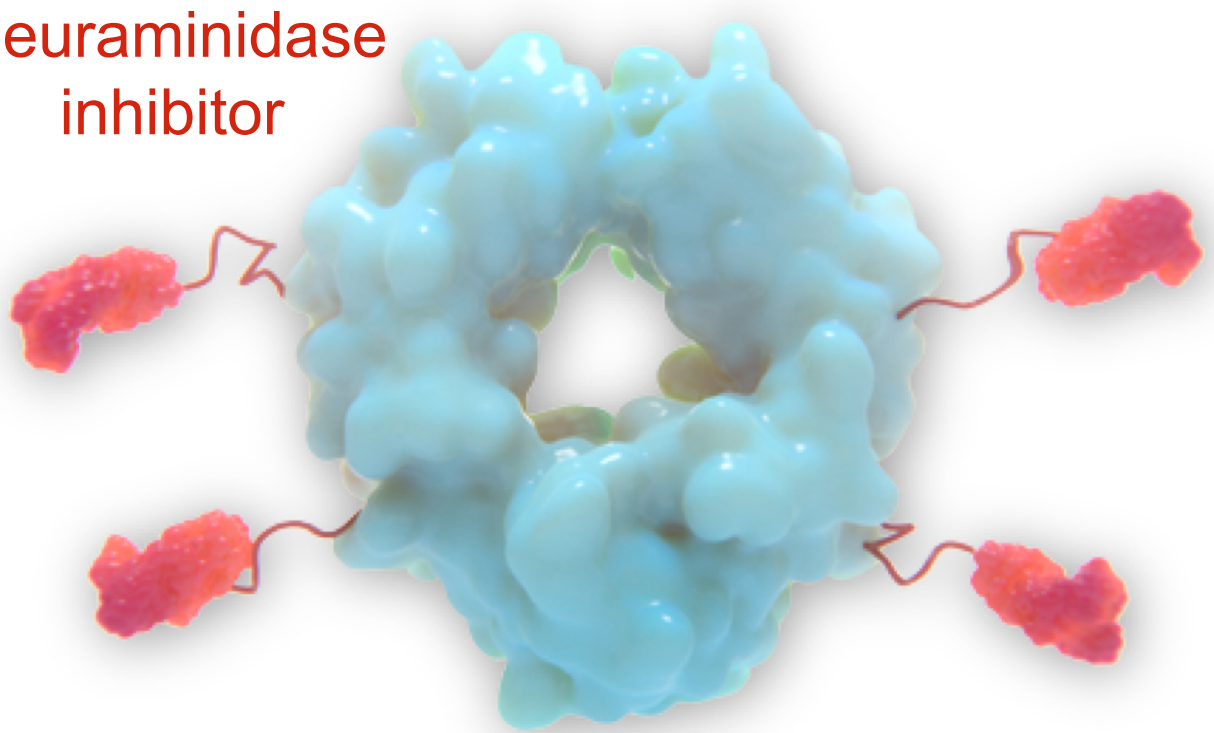
Antiviral Fc-conjugate (AVC) are a novel approach for prevention and treatment of influenza



CD377, the first development candidate of the Cloudbreak® AVC platform, for prevention and treatment of influenza

Antiviral activity

Potent, universal activity against influenza A and B

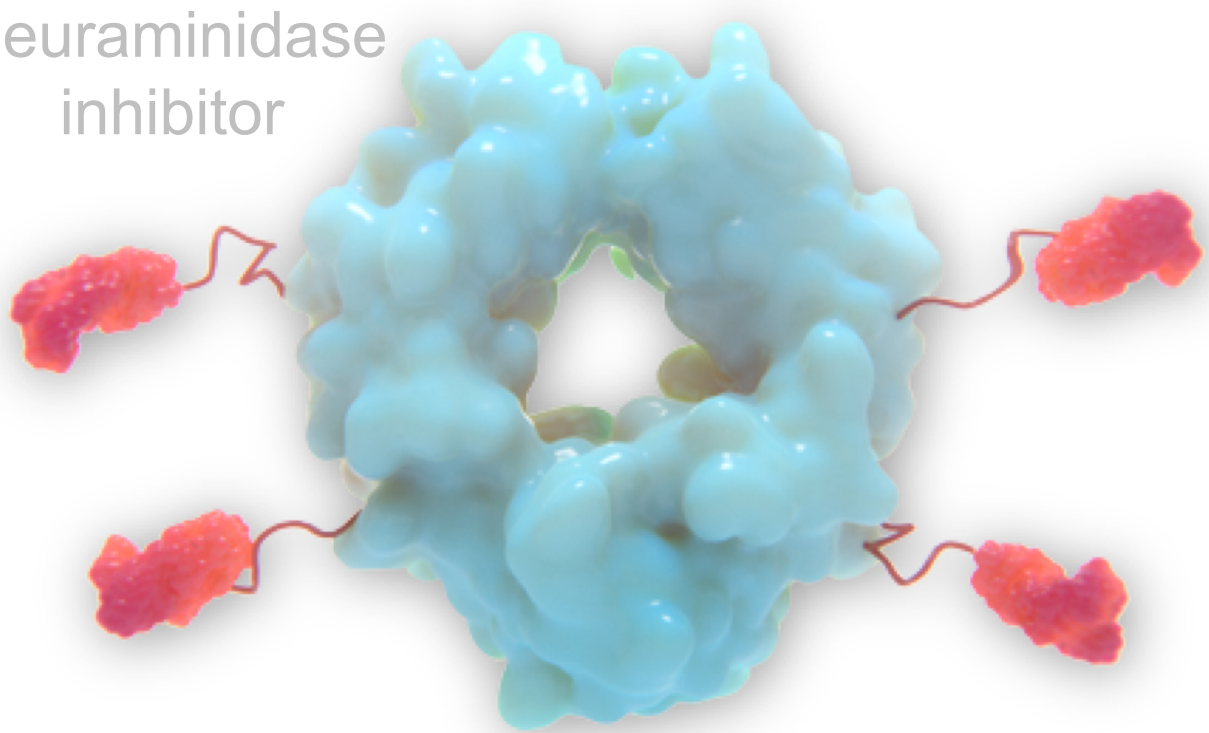


CD377, the first development candidate of the Cloudbreak® AVC platform, for prevention and treatment of influenza

Fc-mediated functions

Allows for engagement of immune effector cells

Long $T_{1/2}$



Fc domain of human IgG1

CD377 has ideal attributes for prevention and treatment of influenza

- Broad-spectrum, universal coverage
- Superior resistance profile
- Protection for High-Risk Populations
- Expanded efficacy window
- Long duration of action
- Rapid onset of activity
- Flexible administration

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CD377 has universal activity against influenza A and B *in vitro*

Neuraminidase inhibition assay (median IC_{50} nM)

Influenza subtype	CD377	Oseltamivir	Zanamivir
A (H1N1, n=9)	1.5	1.5	0.6
A (H3N2, n=6)	4.5	0.4	1
B (n=7)	3.1	28.5	5.9

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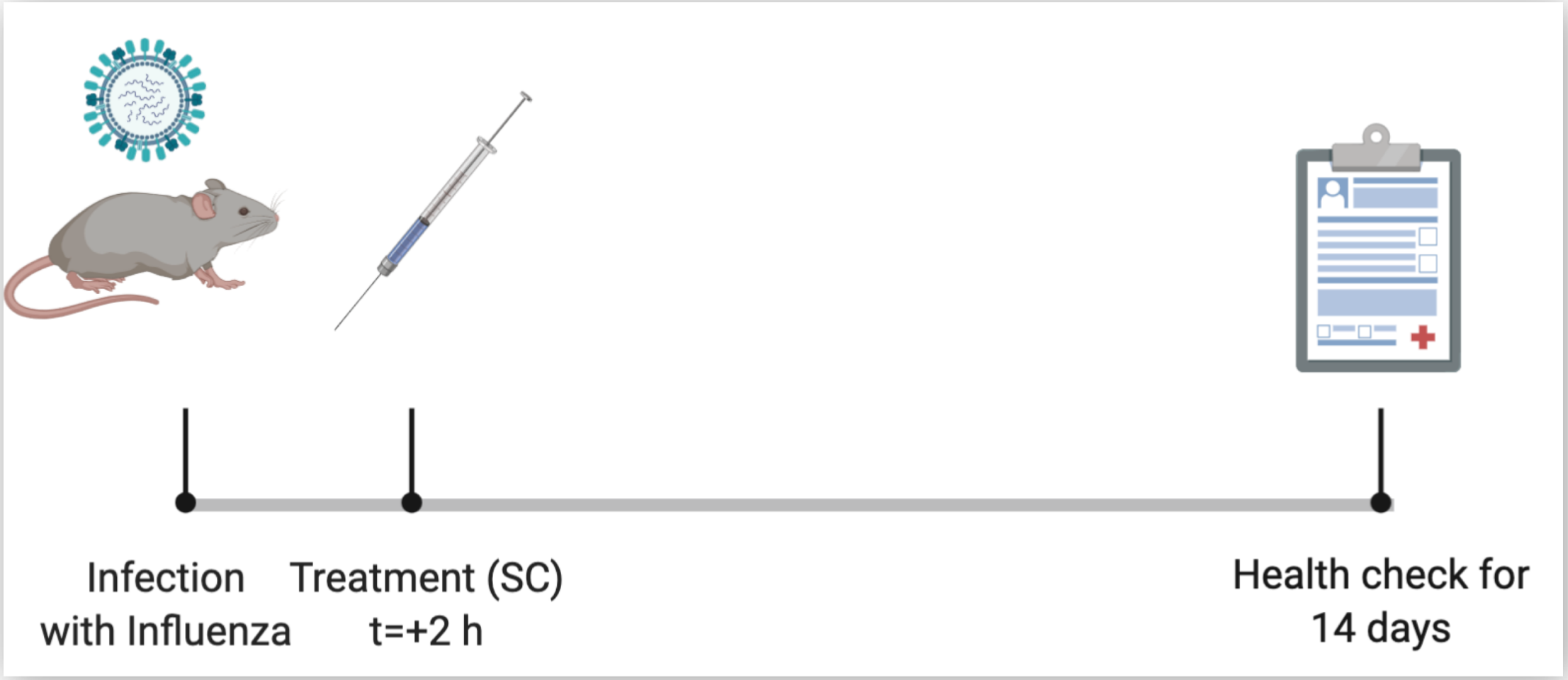
Cell-based cytopathic effect assay (median EC_{50} nM)

Influenza subtype	CD377	Oseltamivir	Zanamivir	Baloxavir
A (H1N1, n=10)	1	925	343	3
A (H3N2, n=6)	1	3,190	112	2
B (n=6)	3.9	654.8	67	11.5

Lethal challenge with influenza A (H1N1) in mouse model



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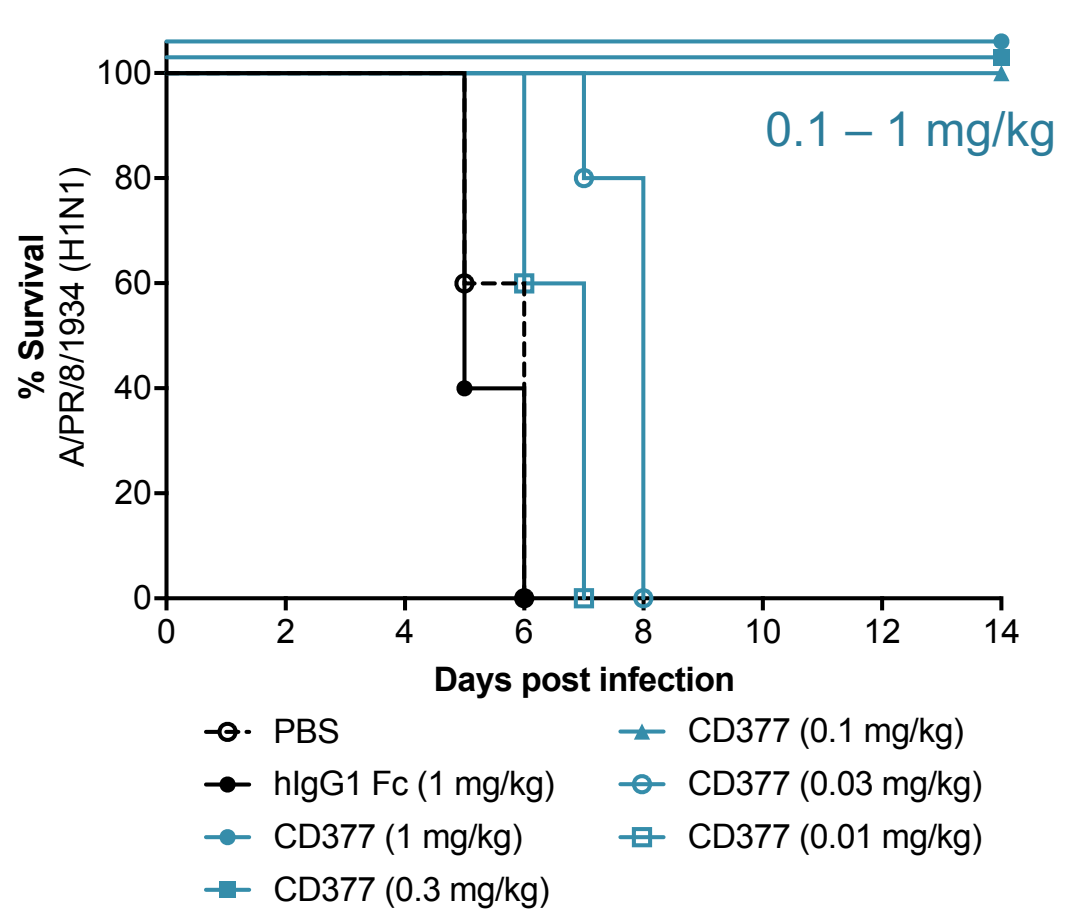
CD377 has potent efficacy against influenza A (H1N1) in mice



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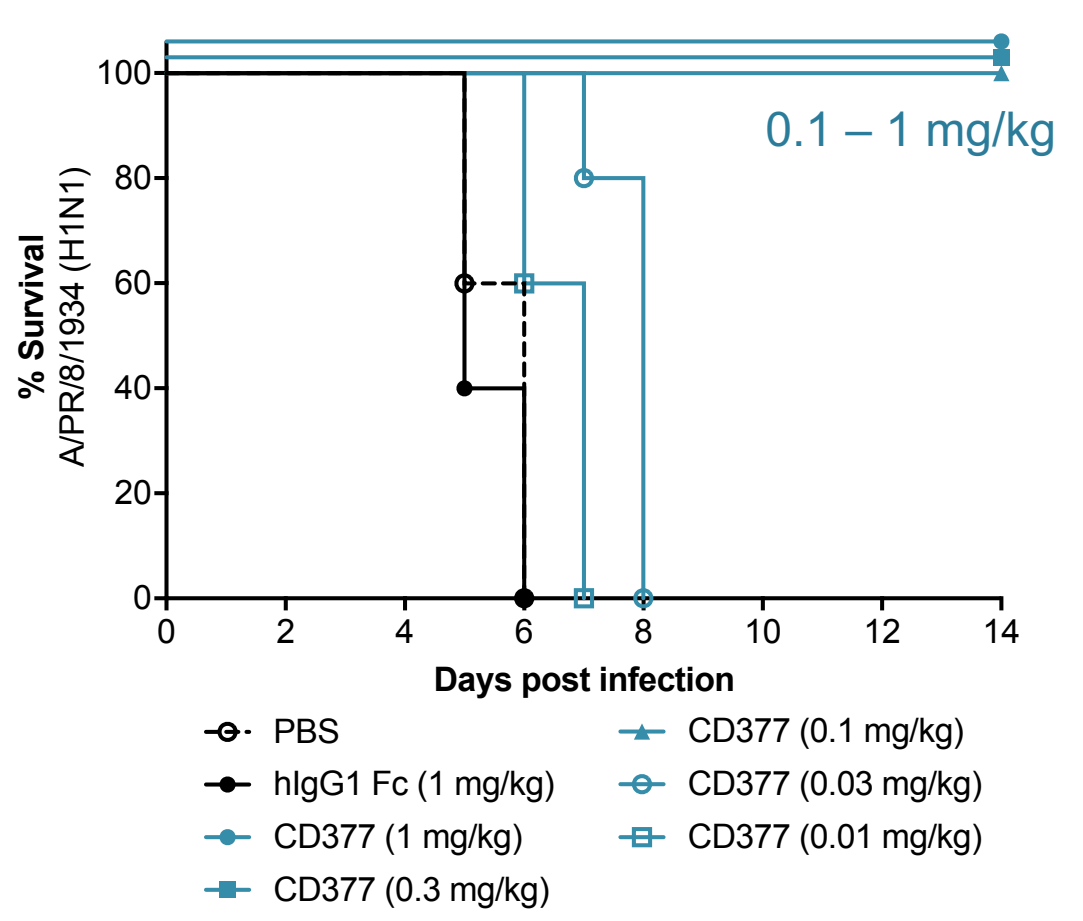

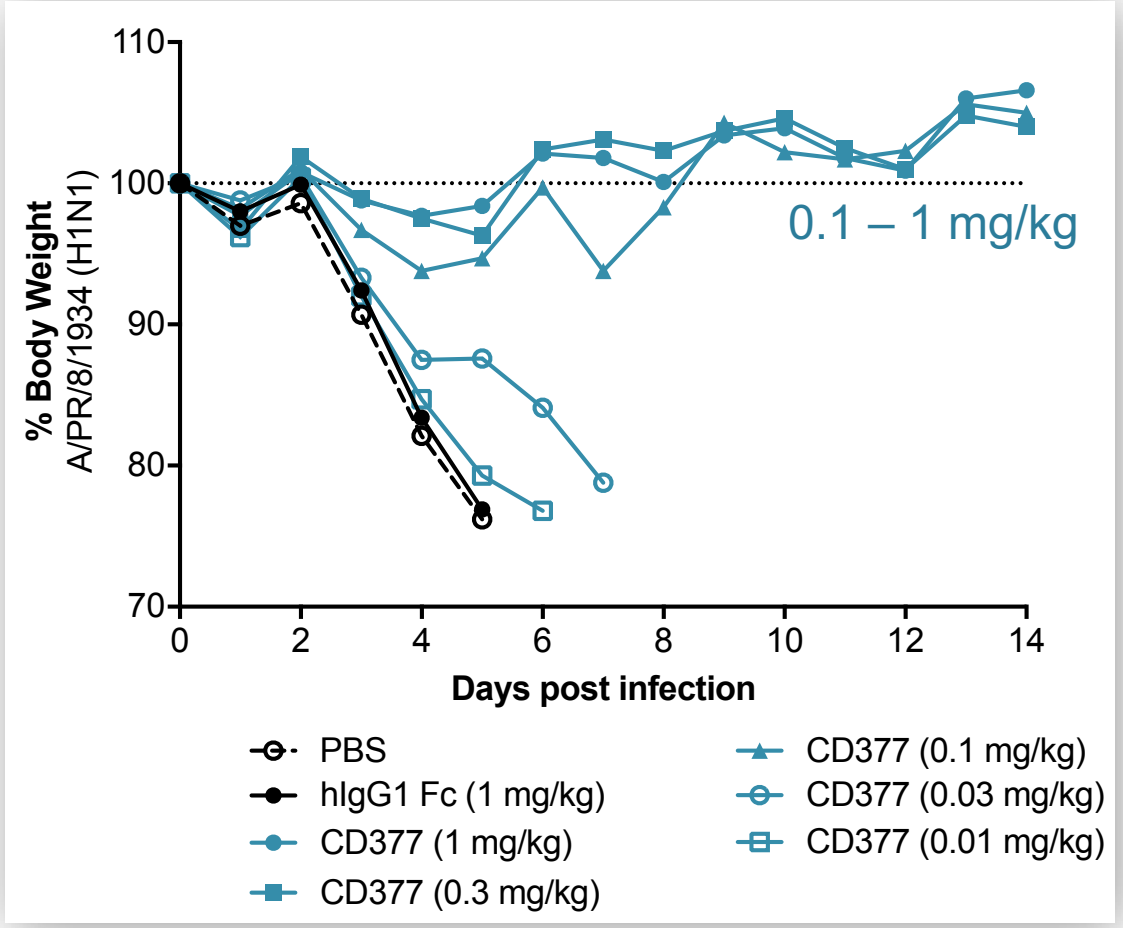

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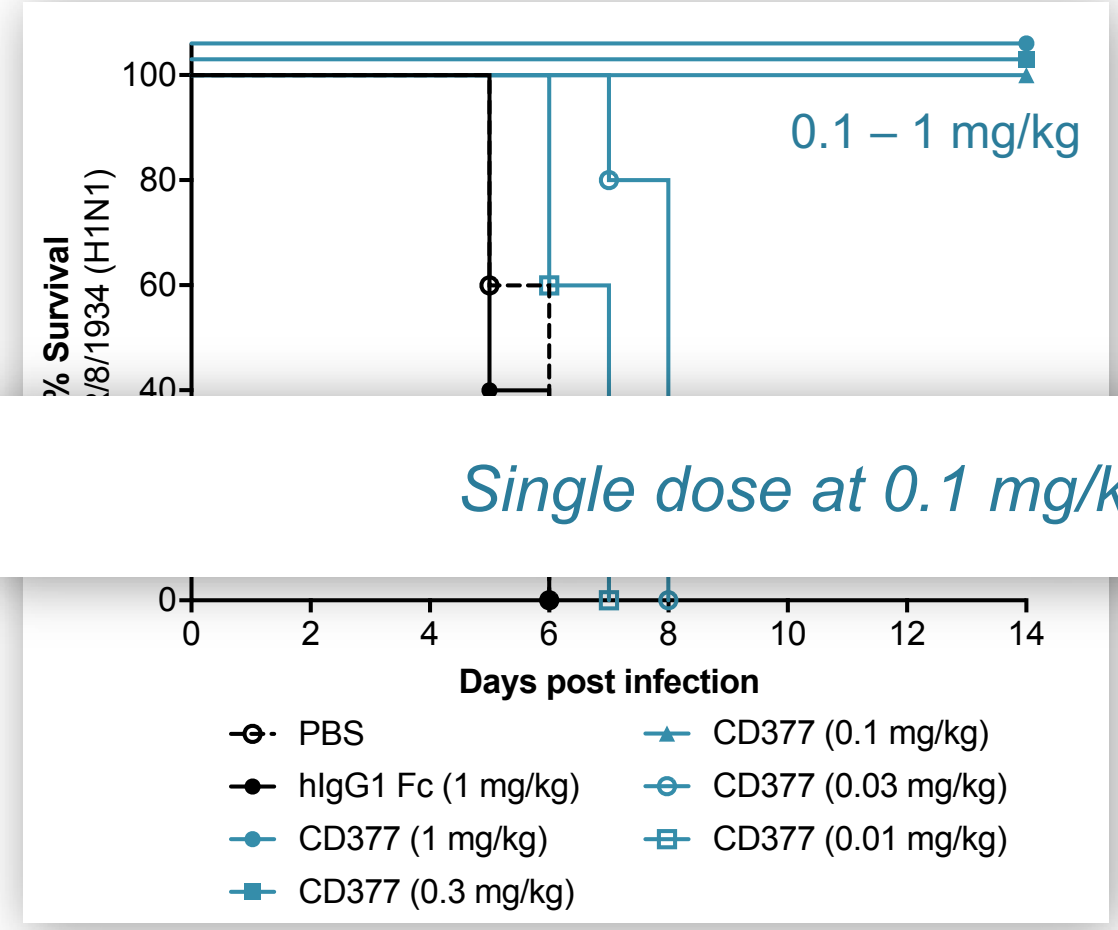
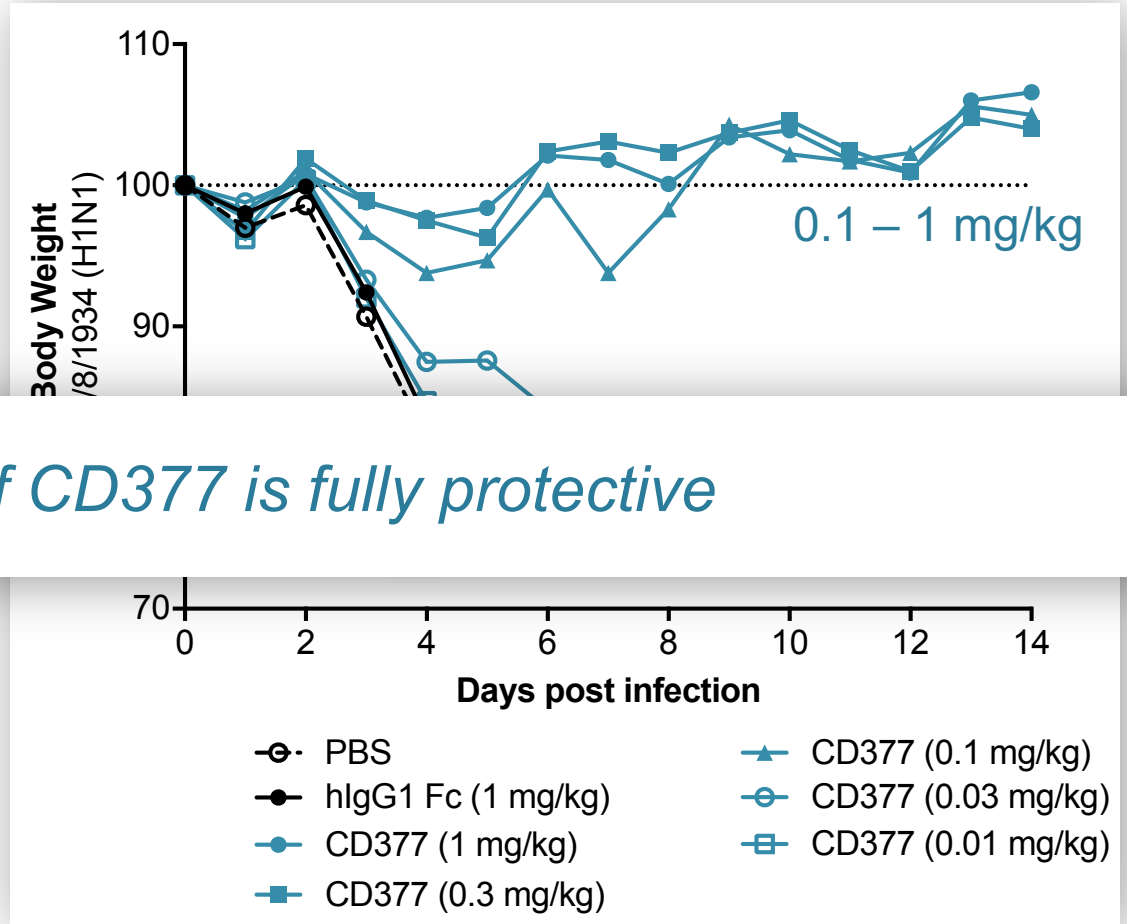
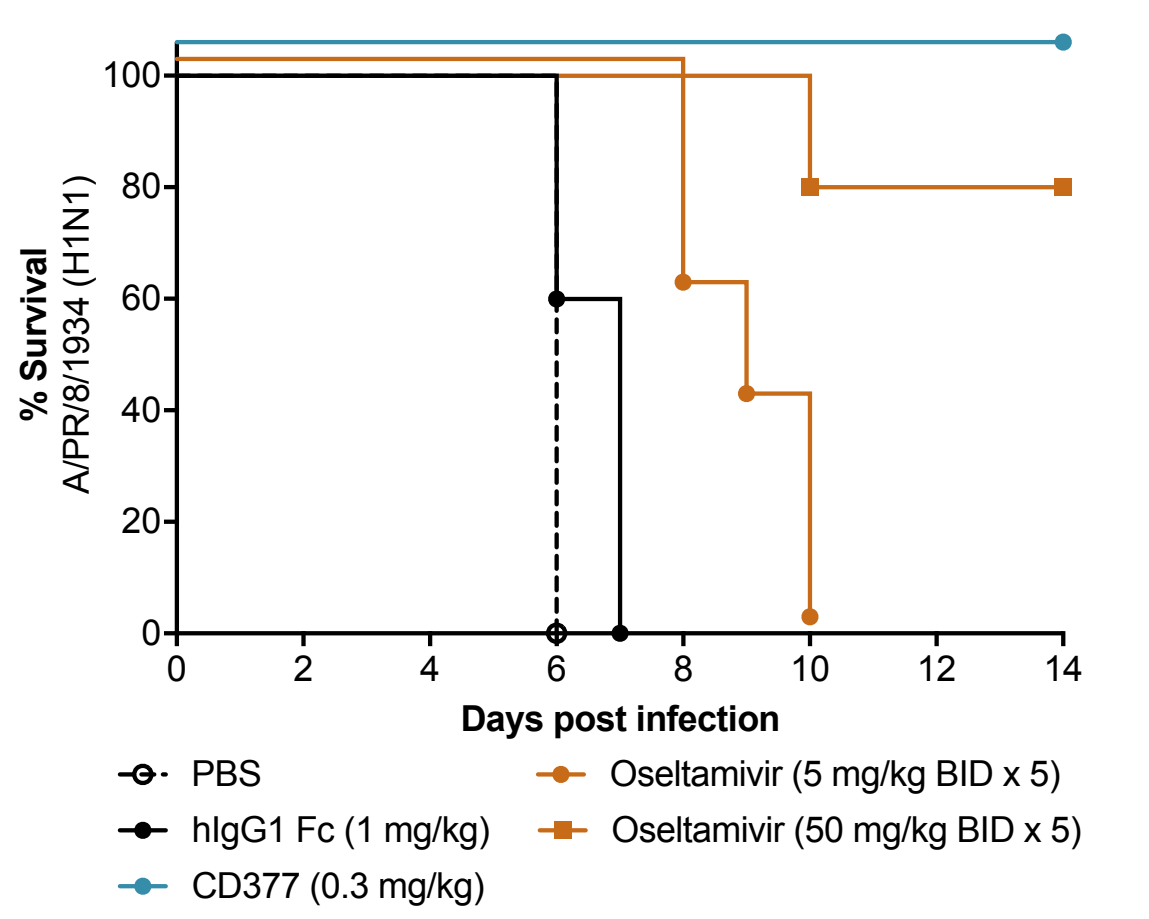




Single dose at 0.1 mg/kg of CD377 is fully protective

CD377 is superior to oseltamivir against influenza A (H1N1) in mice



Human equivalent dose of oseltamivir = 5 mg/kg BID x 5

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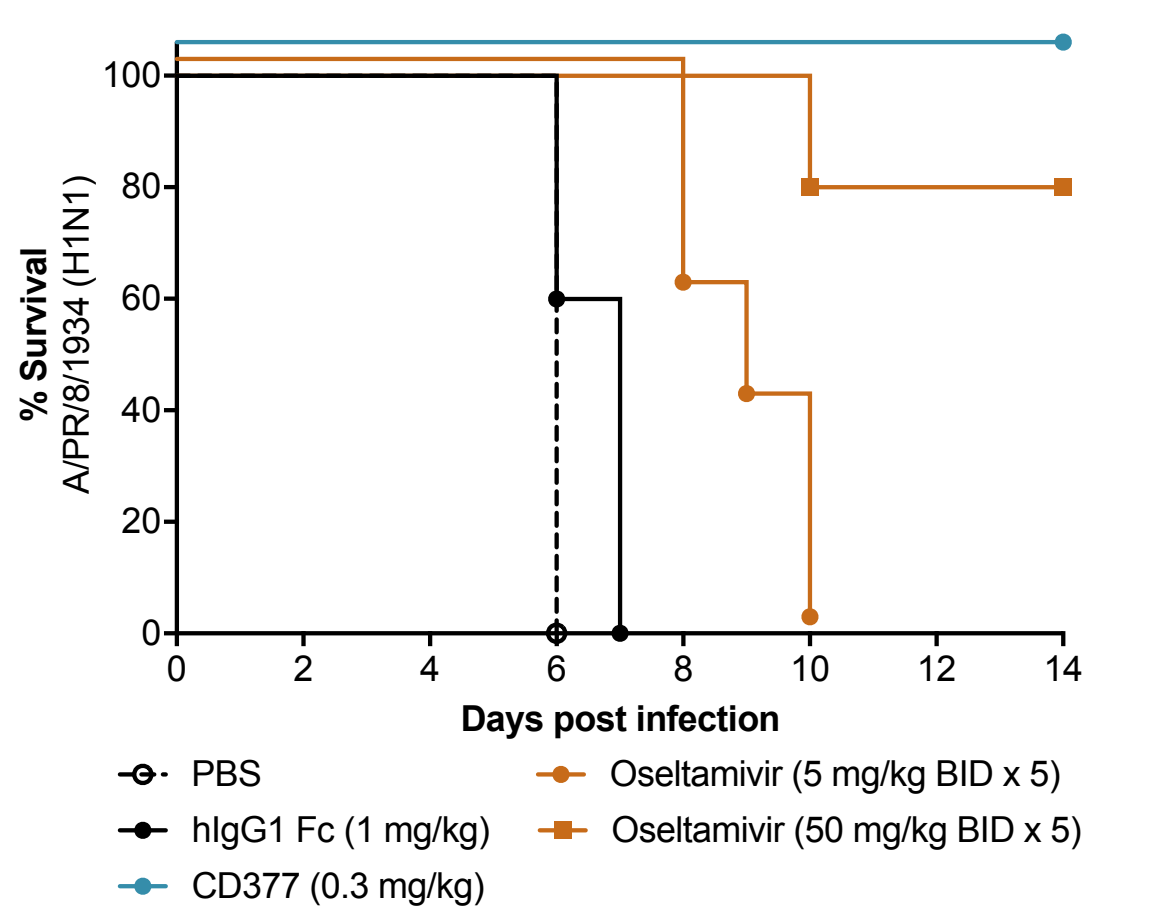

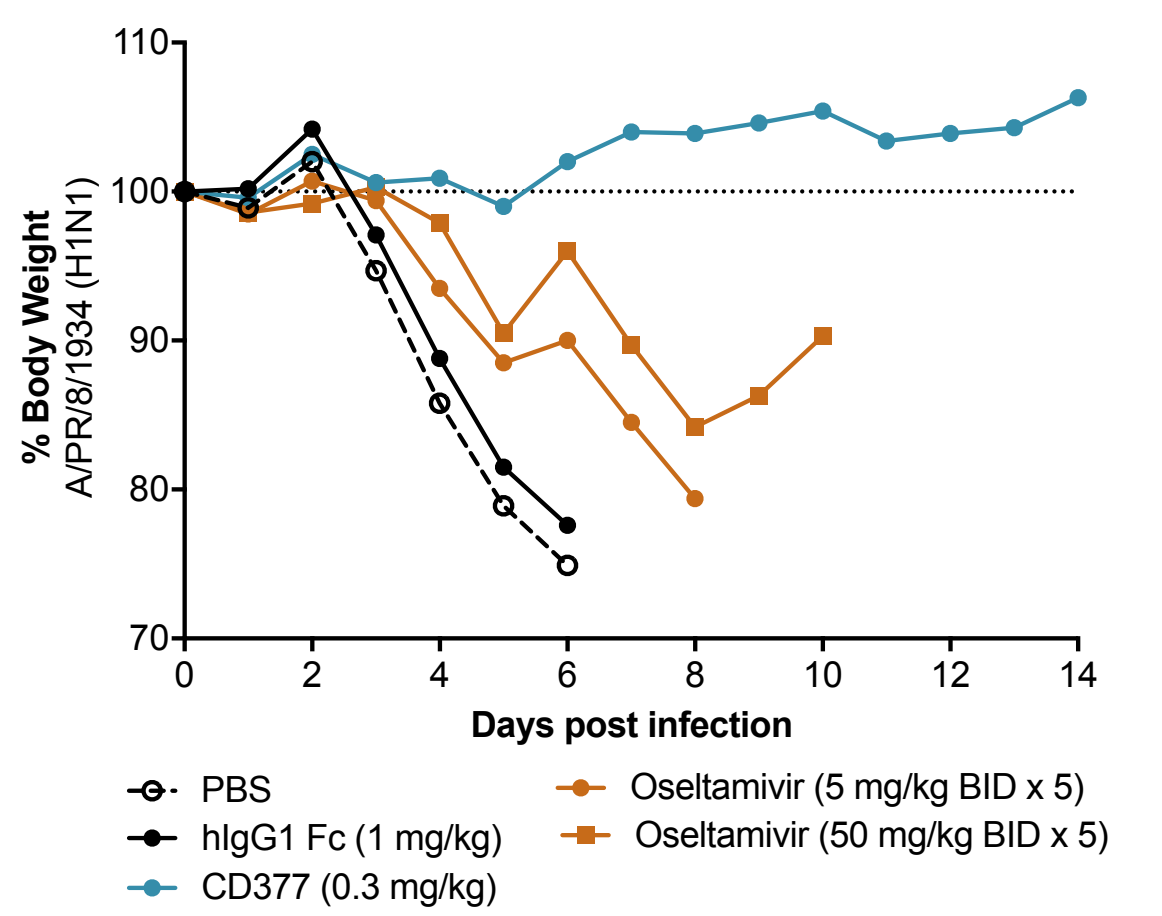

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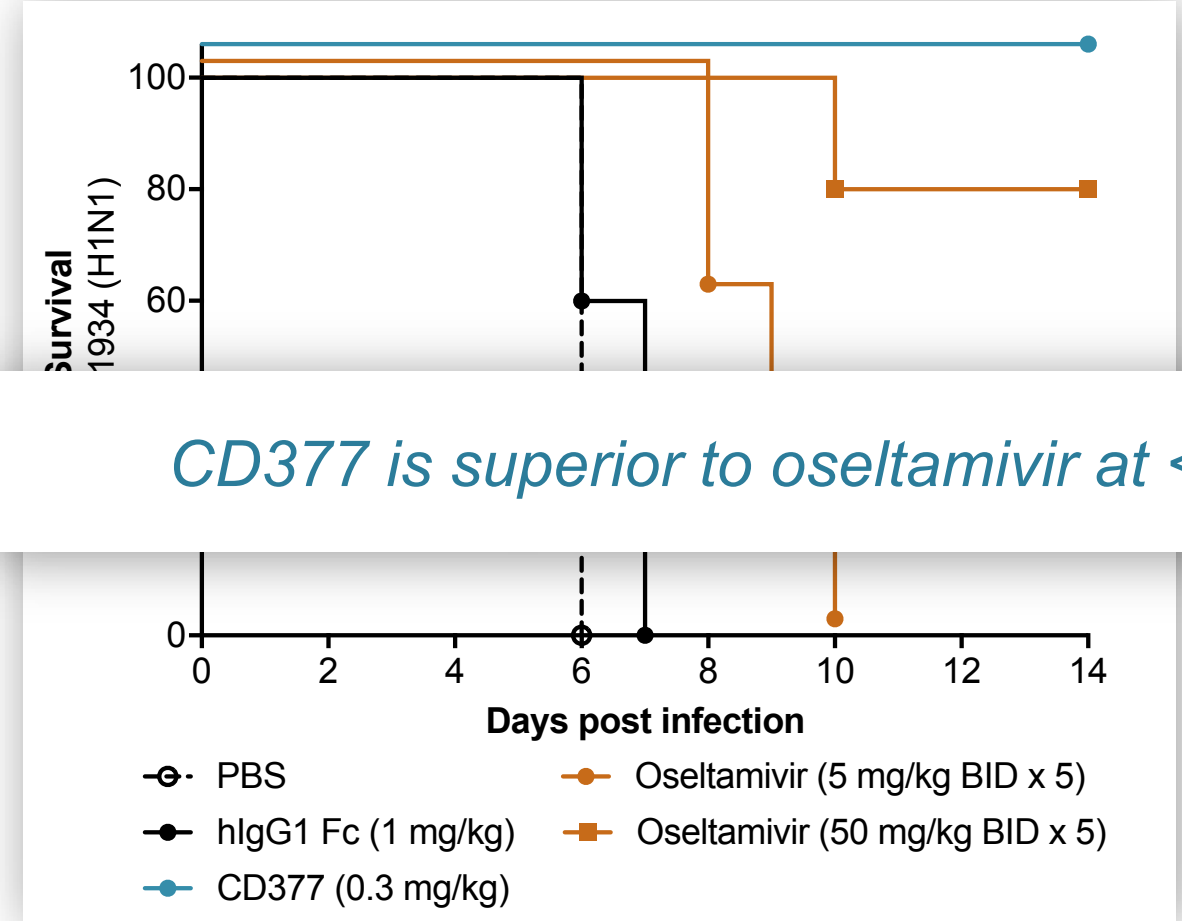
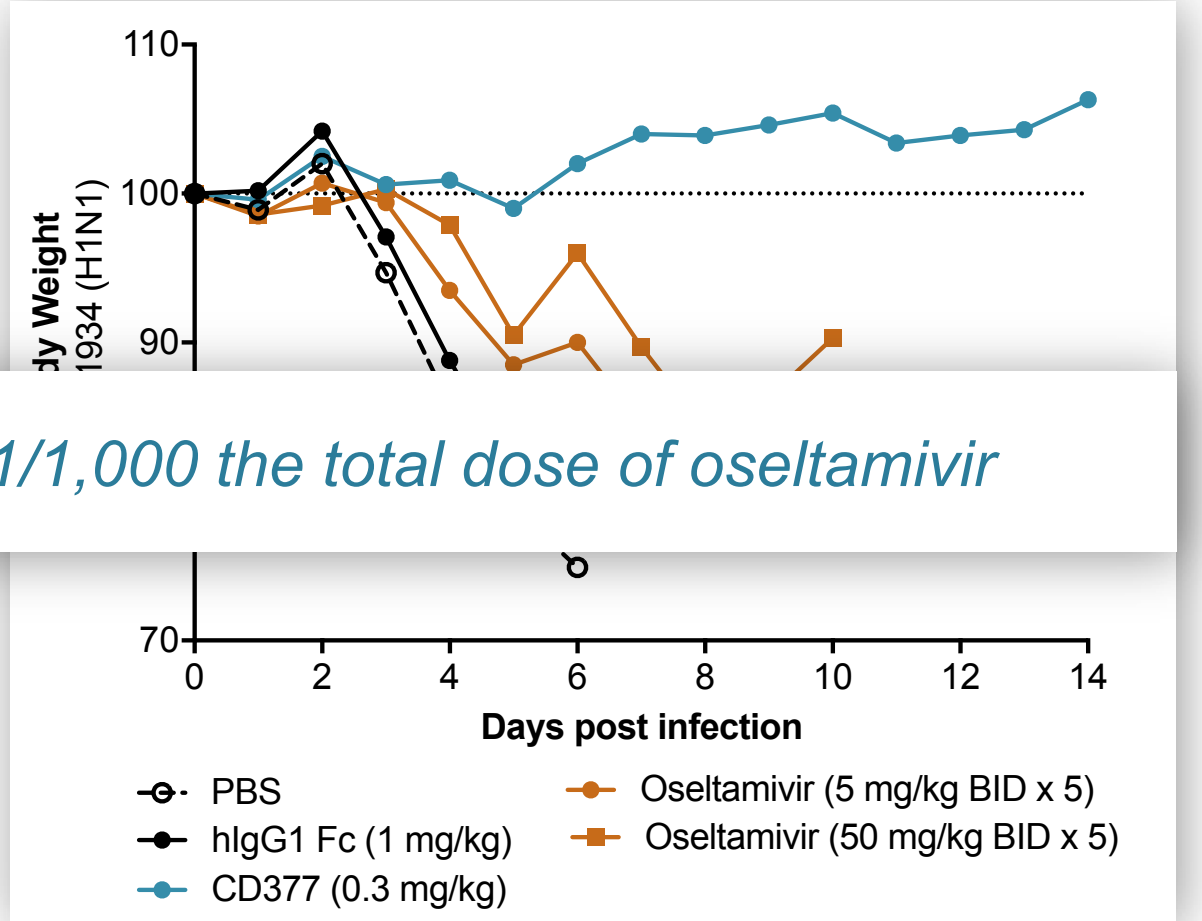
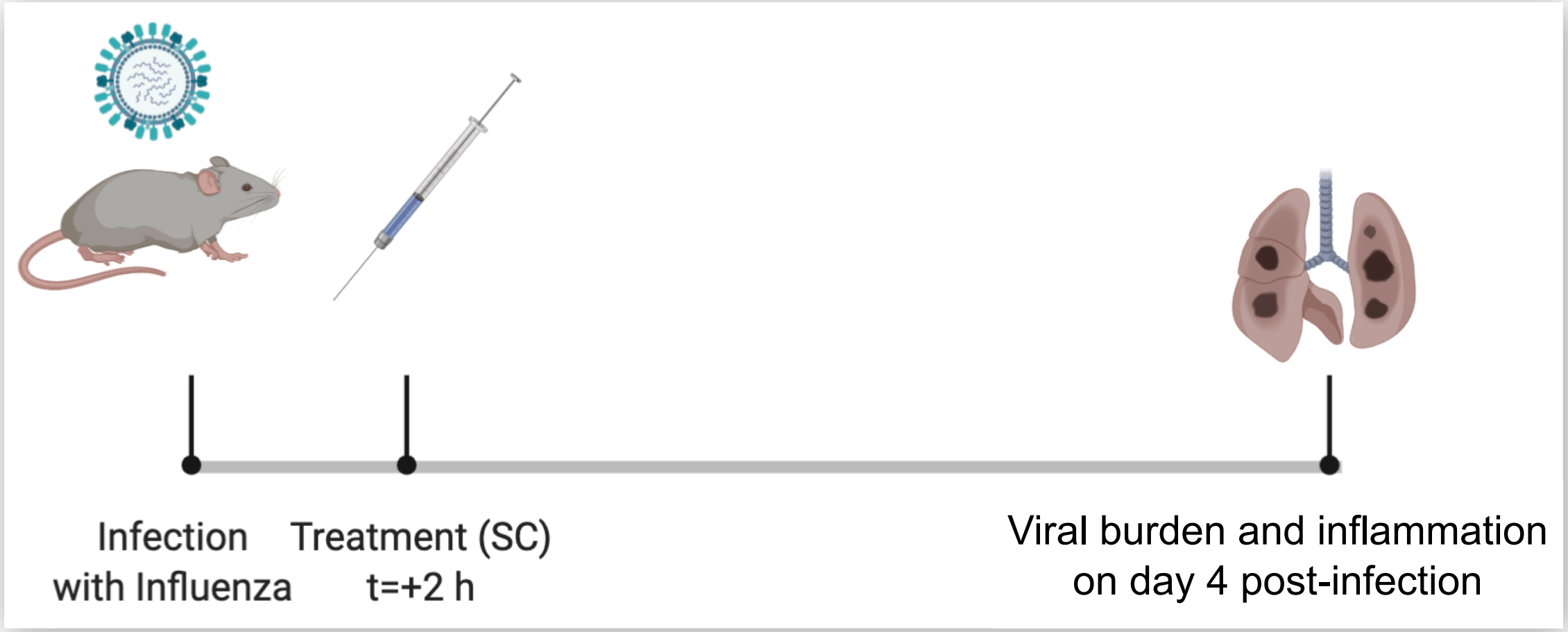




CD377 is superior to oseltamivir at < 1/1,000 the total dose of oseltamivir

Viral burden and cytokine analysis on day 4 after lethal challenge with influenza A (H1N1) in mice



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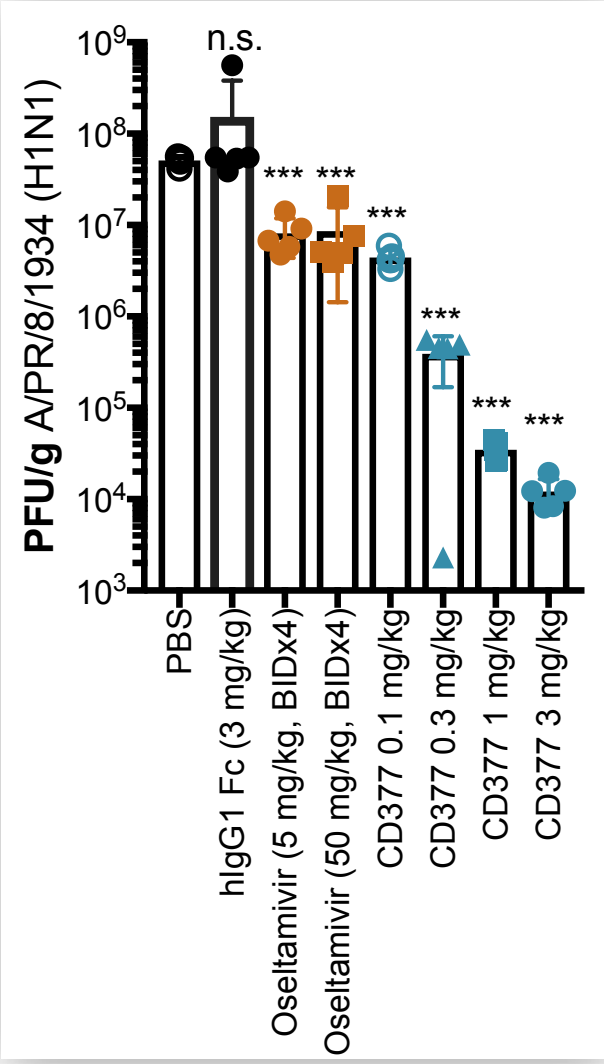
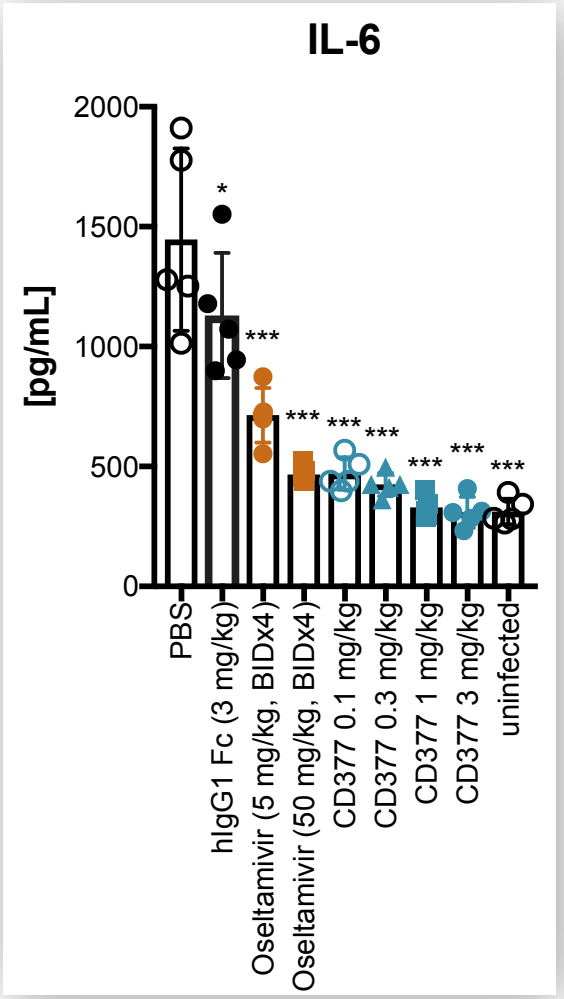
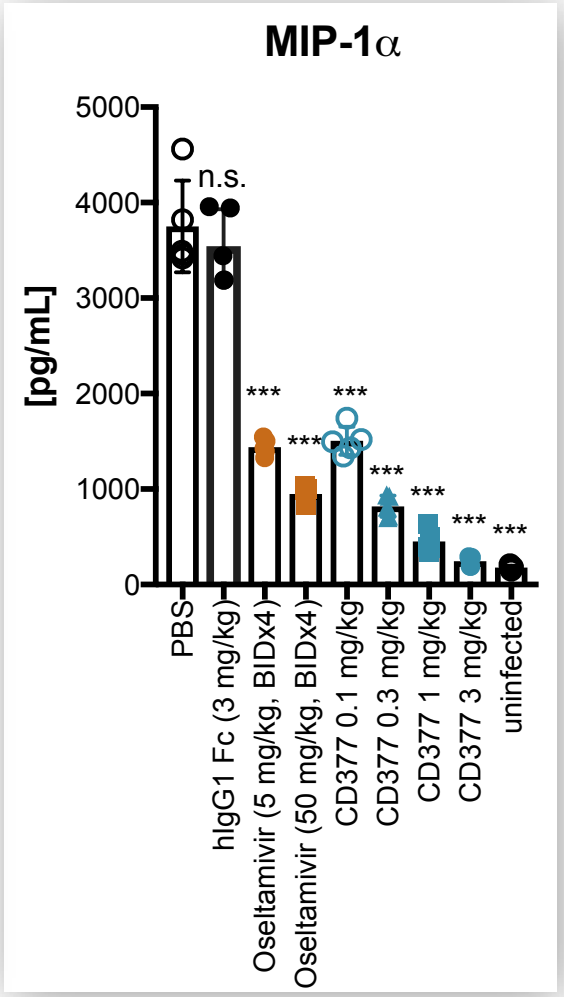
CD377 demonstrates dose-dependent viral burden reduction against influenza A (H1N1)

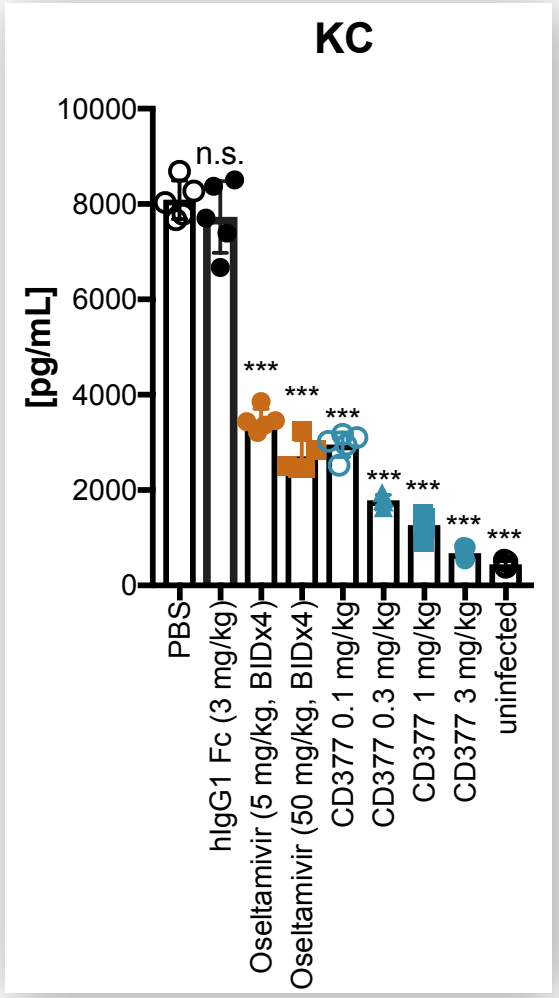


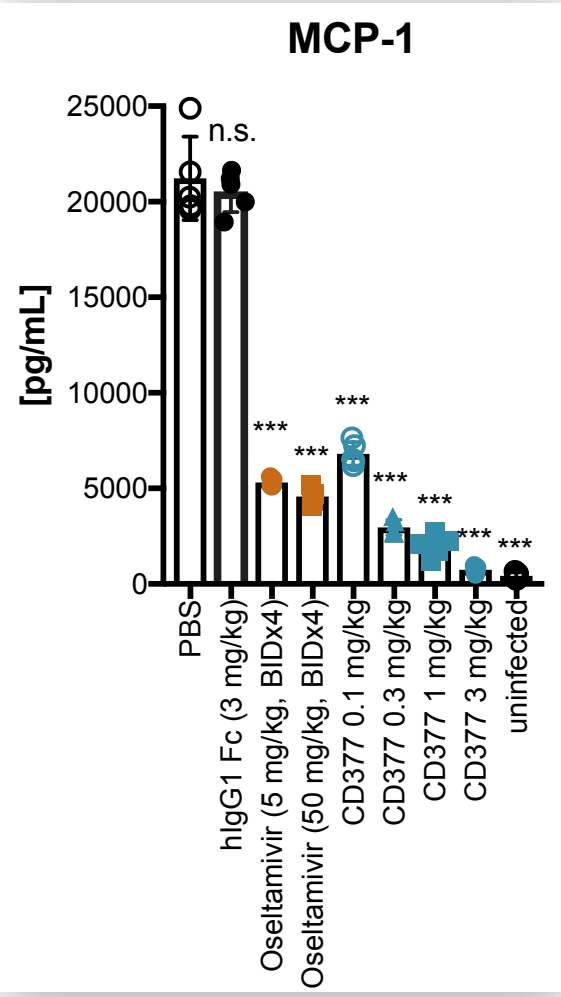
Test article [mg/kg]	Log reduction
PBS [0]	0.00
hIgG1 Fc [3]	-0.5
Oseltamivir [5]	0.8
Oseltamivir [50]	0.8
CD377 [0.1]	1.1
CD377 [0.3]	2.1
CD377 [1]	3.2
CD377 [3]	3.6

Dose-dependent reduction in inflammation by CD377 correlates with viral burden reduction

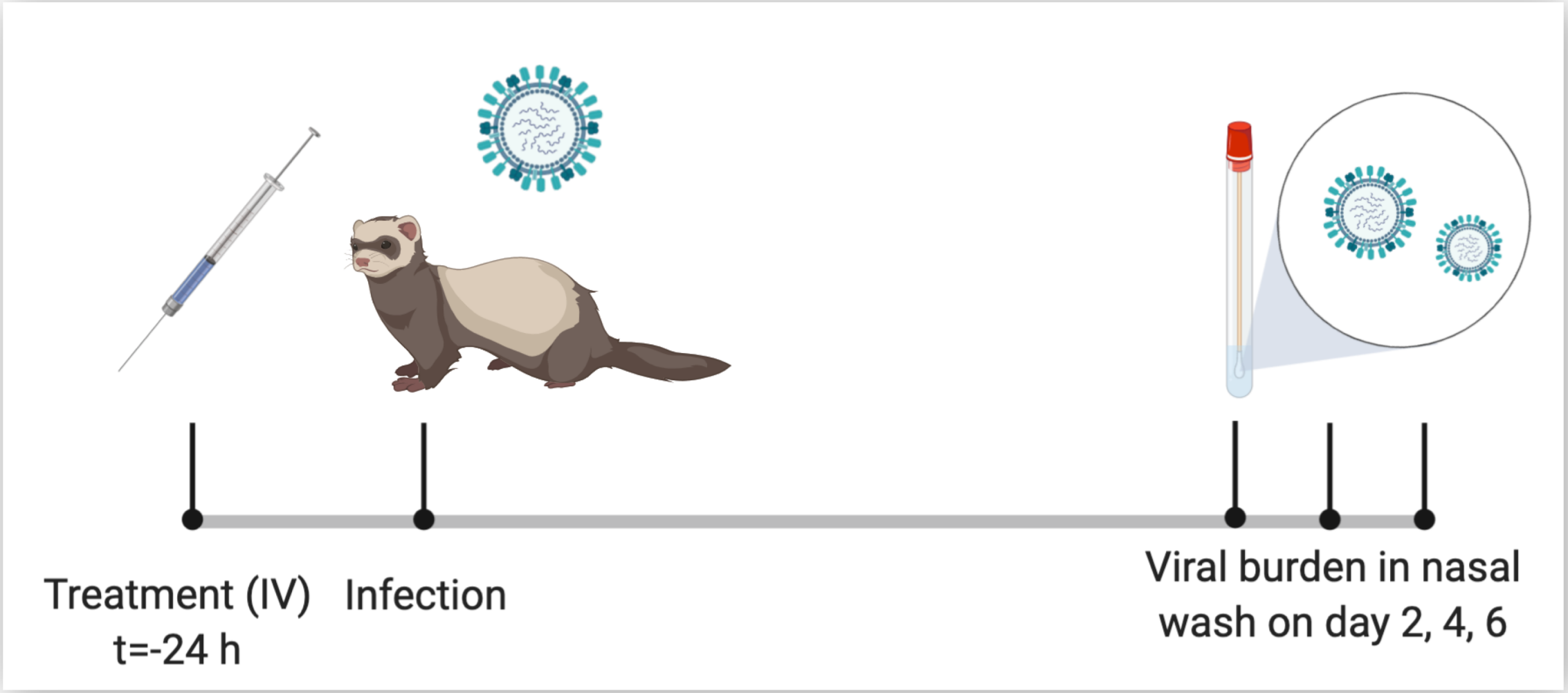








High-challenge dose, transient infection with influenza A/CA/07/2009 (H1N1)pdm in ferret model



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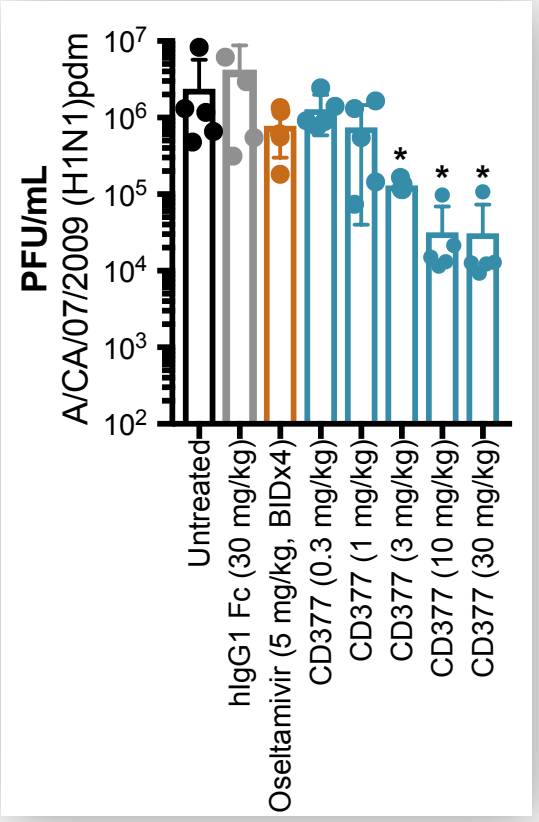
CD377 reduces viral burden in dose-dependency against influenza A (H1N1)

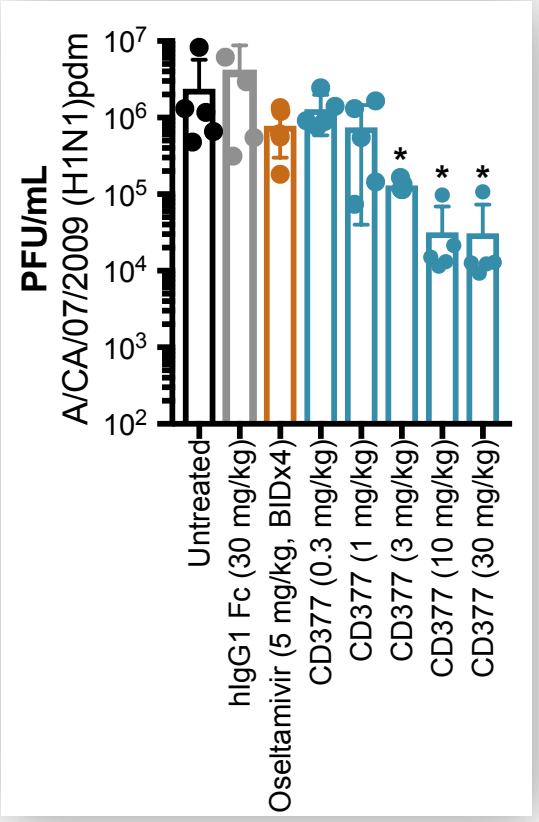
Day 2



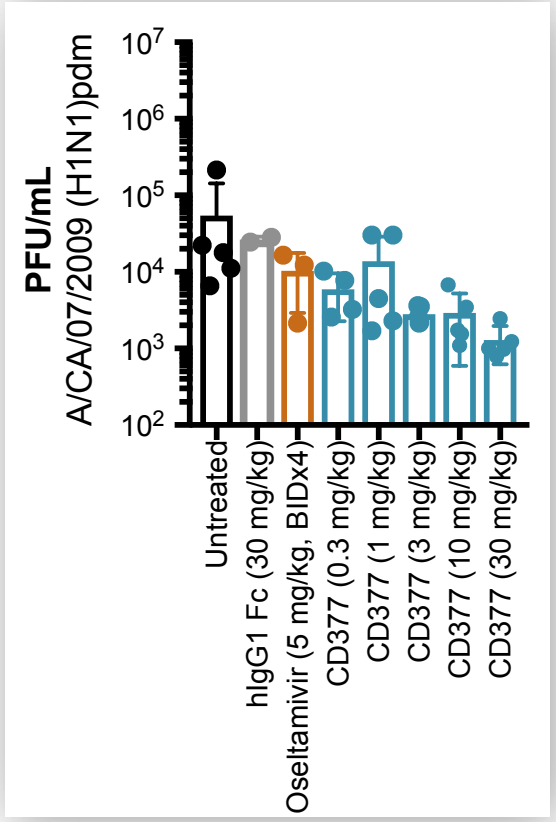
Test article [mg/kg]	Log reduction
PBS [0]	0
hIgG1 Fc [15]	-0.3
Oseltamivir [5]	0.5
CD377 [0.3]	0.3
CD377 [1]	0.5
CD377 [3]	1.3
CD377 [10]	1.9
CD377 [30]	1.9

CD377 reduces viral burden in dose-dependency against influenza A (H1N1)

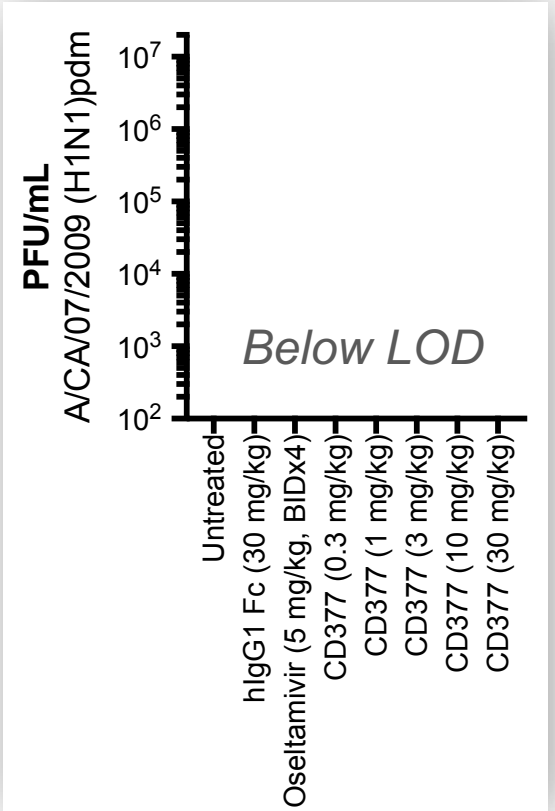
Day 2



Day 4



Day 6

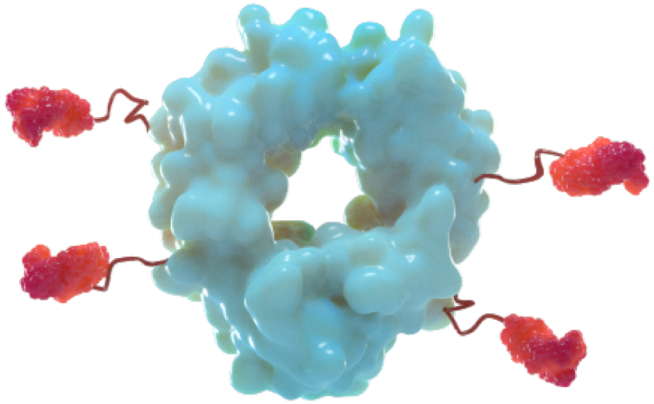


Summary of AVCs against influenza

- CD377 has universal, broad-spectrum activity against influenza A and B
- CD377 at 0.3 mg/kg or lower is protective in lethal mouse models against influenza A and B (Talk #159 presented by **James Levin, PhD**)
- CD377 has superior efficacy as compared SOC, Oseltamivir, in mice
- CD377 demonstrates dose-dependent reduction in viral burden and inflammation in mice
- CD377 demonstrates dose-dependent reduction in viral burden in ferrets

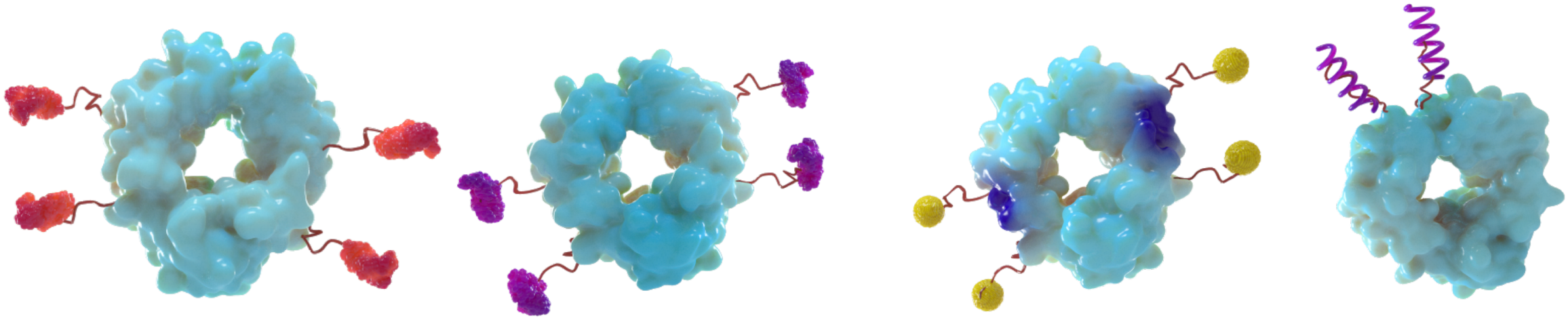
→ ***CD377 has true universal activity against influenza with potential to transform the prevention and treatment of influenza***

Cidara Cloudbreak® AVC platform: Expansion to other viruses



Influenza

Cidara Cloudbreak® AVC platform: Expansion to other viruses



Influenza **RSV** **HIV** **hCoV**

Acknowledgements

- Cidara Team
- Charles River Laboratories (Histopathology)
- IITRI (Ferret study)
- Link to Website https://www.cidara.com/cloudbreak/