

# Cloudbreak Antiviral Conjugate (AVC) Platform

June 2020



# Forward-looking statements

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Certain statements regarding our Cloudbreak platform are also forward-looking including statements regarding whether Cidara can develop single-dose, long acting AVC for respiratory disease; whether Cidara's Cloudbreak platform can identify product candidates with intrinsic antimicrobial activity and immune engagement that will increase efficacy or represent an improvement over existing anti-infective agents; whether Cloudbreak influenza candidates, including CD377, will achieve the major attributes believed to be needed in flu such as broad spectrum, superior resistance profile, protection for high-risk populations, expanded efficacy window, long duration of action and rapid onset of activity, or flexible administration; whether results observed in preclinical studies with Cloudbreak influenza candidates, including CD377, will be observed in human use or represent an improvement over existing therapies, including potency and potency against highly resistant influenza strains, lower resistance, protection in immune compromised hosts, the ability to extend the treatment window, efficacy in multiple dosing routes, potential for long-term single dose protection, and a broad safety margin; and whether Cidara's Cloudbreak platform will identify coronavirus AVCs resulting in therapies that are fast acting and long acting; whether Cidara's HIV AVC approach will yield similar results in its coronavirus AVCs, and whether Cidara can successfully identify AVCs to inhibit viral fusion in coronavirus. This presentation also contains estimates and other statistical data made by independent parties and by Cidara relating to market size and growth and other data about Cidara's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

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# Cidara investment thesis

*Leading science on long-acting antifungal and antiviral prevention and treatment*

Rezafungin

1<sup>st</sup> antifungal in 13 years for 1<sup>st</sup> line treatment and prophylaxis

Treatment – Phase 3

ReSTORE: treatment of *candidemia* and *invasive candidiasis*

Prophylaxis – Phase 3

ReSPECT: prevention in high risk hematology (BMT) setting

Validation

Significant ex-US/ex-Japan partnership with Mundipharma

Cloudbreak AVCs

Modular antiviral platform for prevention & treatment



COVID-19 & Pan CoV

Cloudbreak: Pre-clin testing new molecules against COVID-19

# Leading the science on *antifungal* & *antiviral* prevention & treatment

Program	Proposed Indication	Discov.	<i>in-vitro</i>	<i>in-vivo</i>	IND- enable	Ph 1	Ph 2	Ph 3
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## ANTIFUNGAL: Long acting treatment and prevention

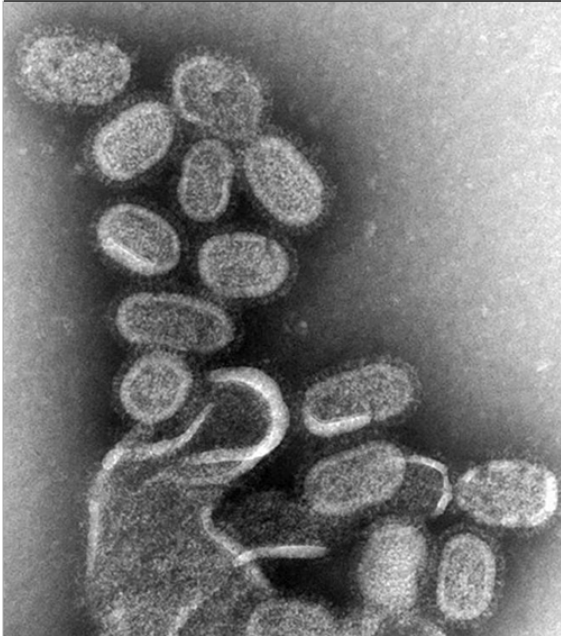
Rezafungin	Treatment of Candidemia & Invasive Candidiasis						STRIVE	ReSTORE 
Rezafungin	Prophylaxis of IFD in Blood & Marrow Transplant Patients							ReSPECT 

## ANTIVIRAL: Cloudbreak® Antiviral Conjugates (AVCs) for rapid treatment and long-term prevention

CD377	Influenza Single-dose/3months Prevention & Treatment							
AVC108	Influenza Single-dose/6months Prevention & Treatment							
RSV AVC	RSV Prevention & Treatment							
HIV AVC	HIV PEP, PrEP, Maintenance							
CoV AVC	COVID-19 & Pan CoV Prevention & Treatment							

# Vision for Antiviral Conjugates for respiratory disease: Single-dose treatment and long-acting protection

Against all strains...



In all people...



# Cloudbreak antiviral platform: a whole new class of antiviral

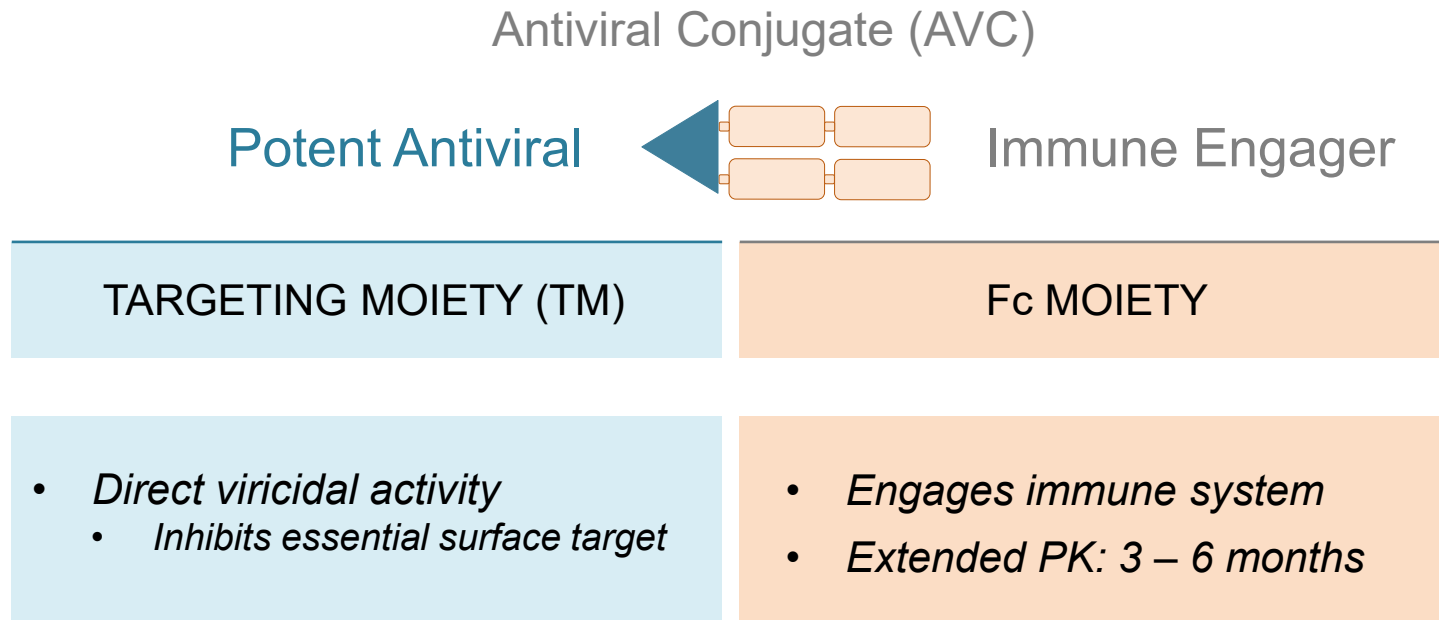
*Long acting antiviral activity and immune engagement*

## A new class of long-acting drugs

*Not* a vaccine, monoclonal antibody or traditional therapeutic

A stable conjugate of a potent antiviral with an Fc antibody fragment

Rapid onset, potent activity coupled with 3-6 months of protection

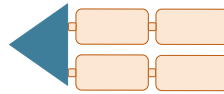




# Two mechanisms of action against the flu

*CD377: A conjugate of a neuraminidase inhibitor with human Fc domain*

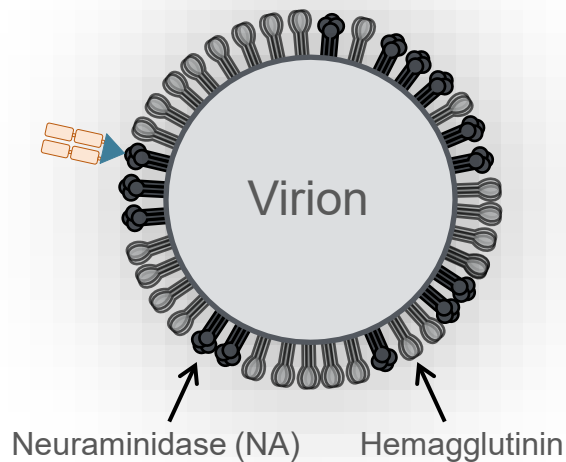
Potent antiviral



Fc immune engager

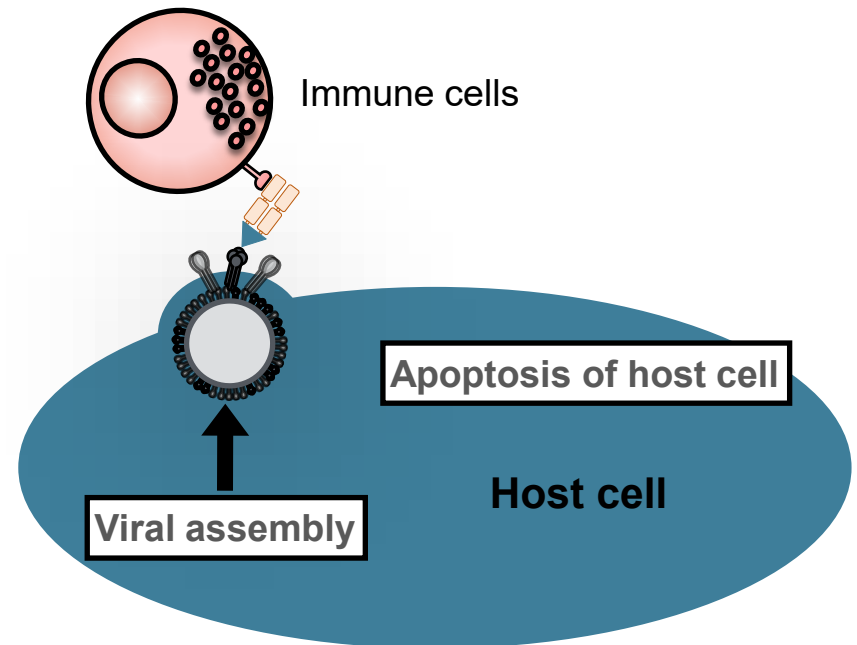
## 1. Inhibit viral proliferation

NA inhibition: Direct inhibition of viral proliferation



## 2. Immune-mediated clearance

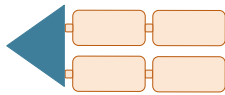
Targeted clearance of infected cells



# Cidara's Cloudbreak AVC platform

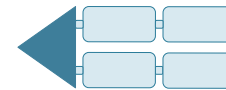
*Proprietary engineered Fc domains provide dose and immune response options*

**CD 377** (Dev. Can.)



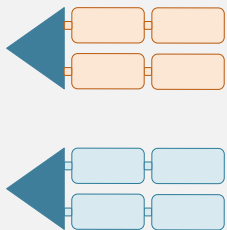
Single dose/~3 months  
Full immune engagement

**AVC 108** (Dev. Lead)

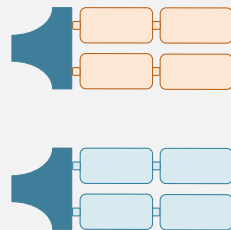


Single dose/~6 months  
Attenuated immune engagement

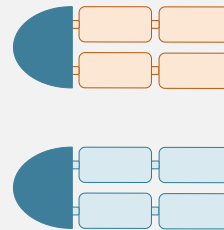
FLU



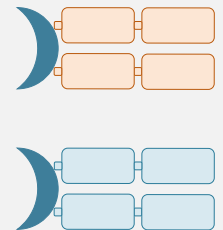
Co-V



RSV



HIV





# Flu vaccines have well known limitations...

## Viral coverage



Strain-specific,  
variable coverage

10%-60% effective  
(2004-2018)<sup>1</sup>

## Patient



Less effective in elderly &  
immune compromised

~2-week lag time to  
achieve full protection<sup>2</sup>

## Manufacturing



Challenging in a pandemic:  
long, complex production

Difficult to scale, low yields  
can limit production capacity<sup>3</sup>

1. <https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>

2. <https://www.cdc.gov/flu/protect/keyfacts.htm>

3. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>

... which place a substantial burden on the US population

**49%**

immunization rate

**40% or less**

vaccine effectiveness

**9M to 45M**

people who get the flu

**31.4M**

outpatient visits

**140K – 810K**

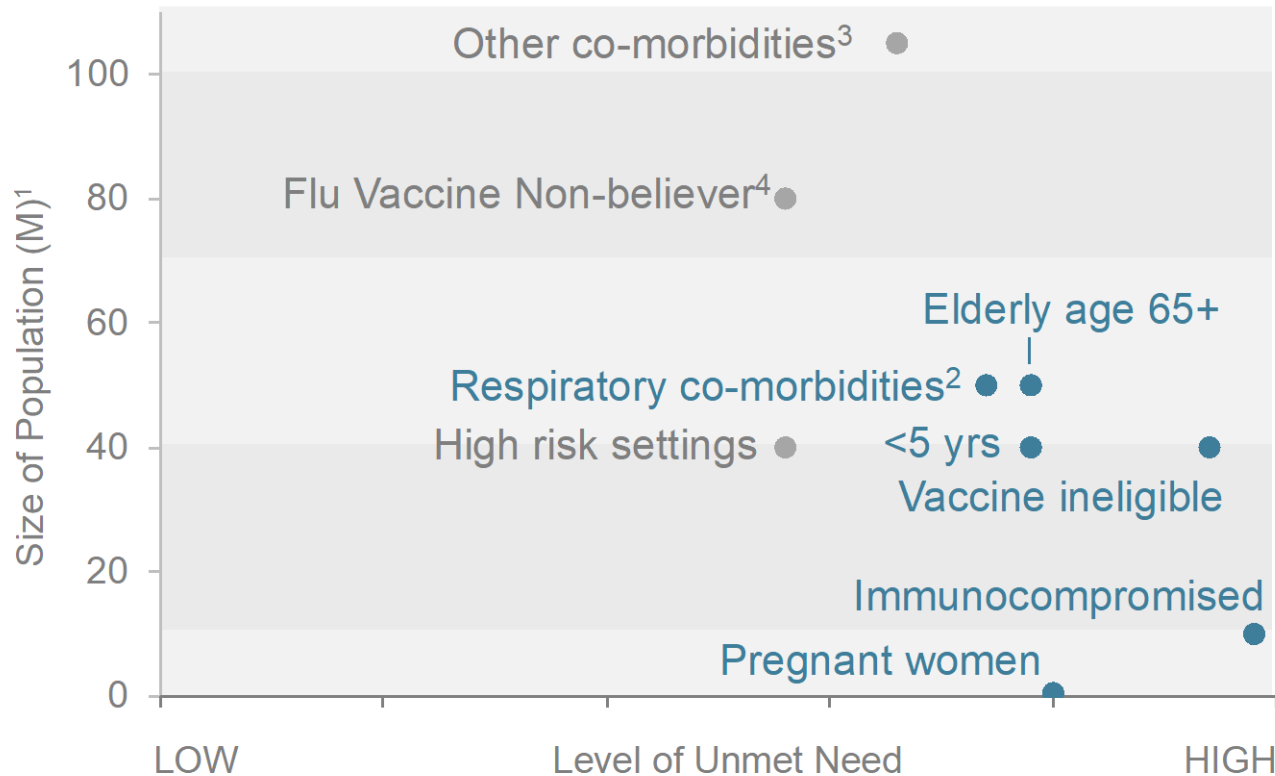
hospitalizations

**12K – 80K**

deaths

The top range of these burden estimates are from the 2017-2018 flu season

# ~320M people should be vaccinated/year in US



*~100M people in US in higher risk groups alone<sup>1</sup>*

1. CDC.gov. Census Bureau 2017. Harpaz, Open Forum Infectious Disease Vol 3 Fall 2016
2. Respiratory co-morbidities include asthma and COPD
3. Other co-morbidities, driving higher risk, include all chronic conditions, but the major ones are diabetes, CV disease, etc.
4. Based on a 2018 US national survey commissioned by Research!America and American Society for Microbiology (N=1004), 53% people didn't get flu vaccine in last year, and 48% chose "do not trust flu vaccine" as the reason for not getting flu vaccine

# CD377 for influenza: Validation of the approach in respiratory viruses

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



# CD377 development candidate profile summary

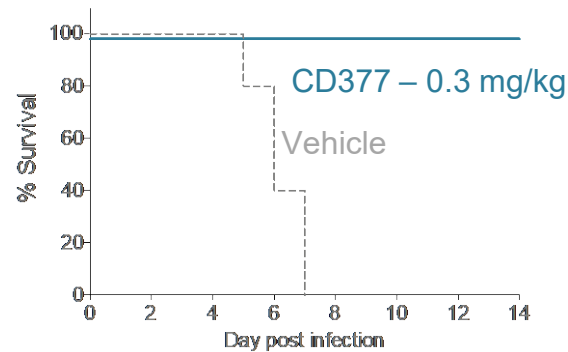
*Now in IND enabling studies*

	Target Attribute	CD377
Indication	Universal prevention and treatment	All data are supportive
Spectrum	A & B + drug resistant strains, low resistance potential	Potent <i>in-vivo</i> activity against all seasonal and pandemic strains
Safety/Tolerability	High safety margin for long term prevention	> 54x exposure margin in 14-day primate toxicity studies
Dosing Frequency	1 to 2x per flu season	Estimated 3 to 6-month coverage with single SC or IM dose
Route of Administration	SubQ, IM and IV dosing	Equivalent exposures and efficacy
Target Populations	High risk populations where vaccines are not effective	Equally effective in immune compromised & immune competent models at similar doses

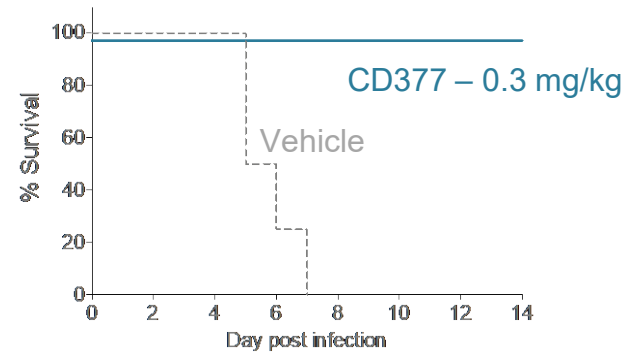
# CD377 is highly potent *in vivo* – influenza A & B

Single SC dose, lethal influenza models - BALB/c mice

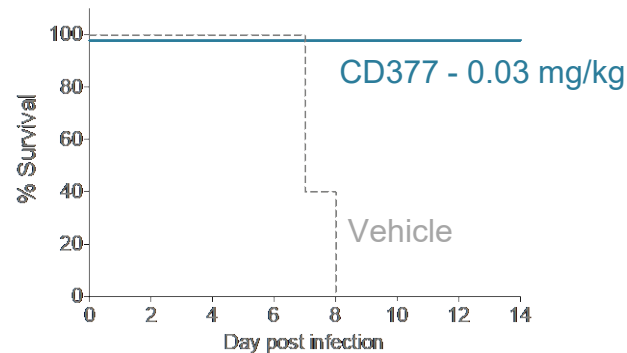
A/California/07/2009  
H1N1pdm



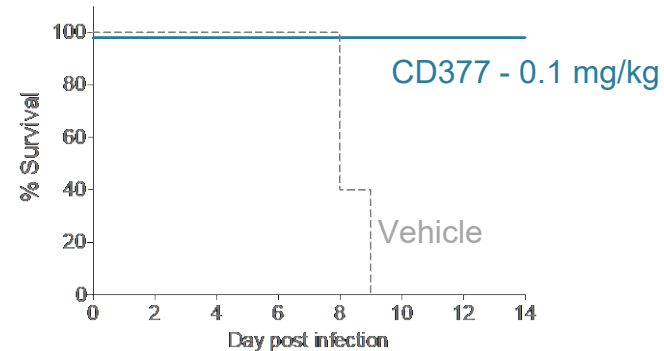
A/Hong Kong/1/68  
H3N2



B/Florida/4/2006  
(Yamagata)

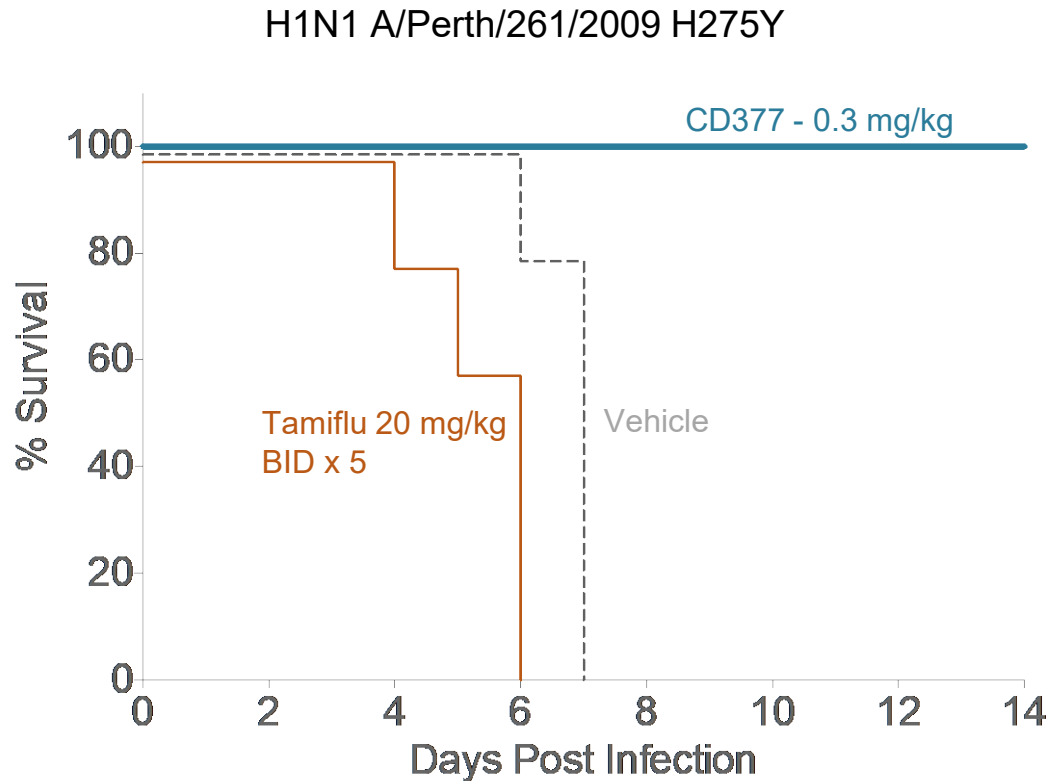


B/Malaysia  
(Victoria)



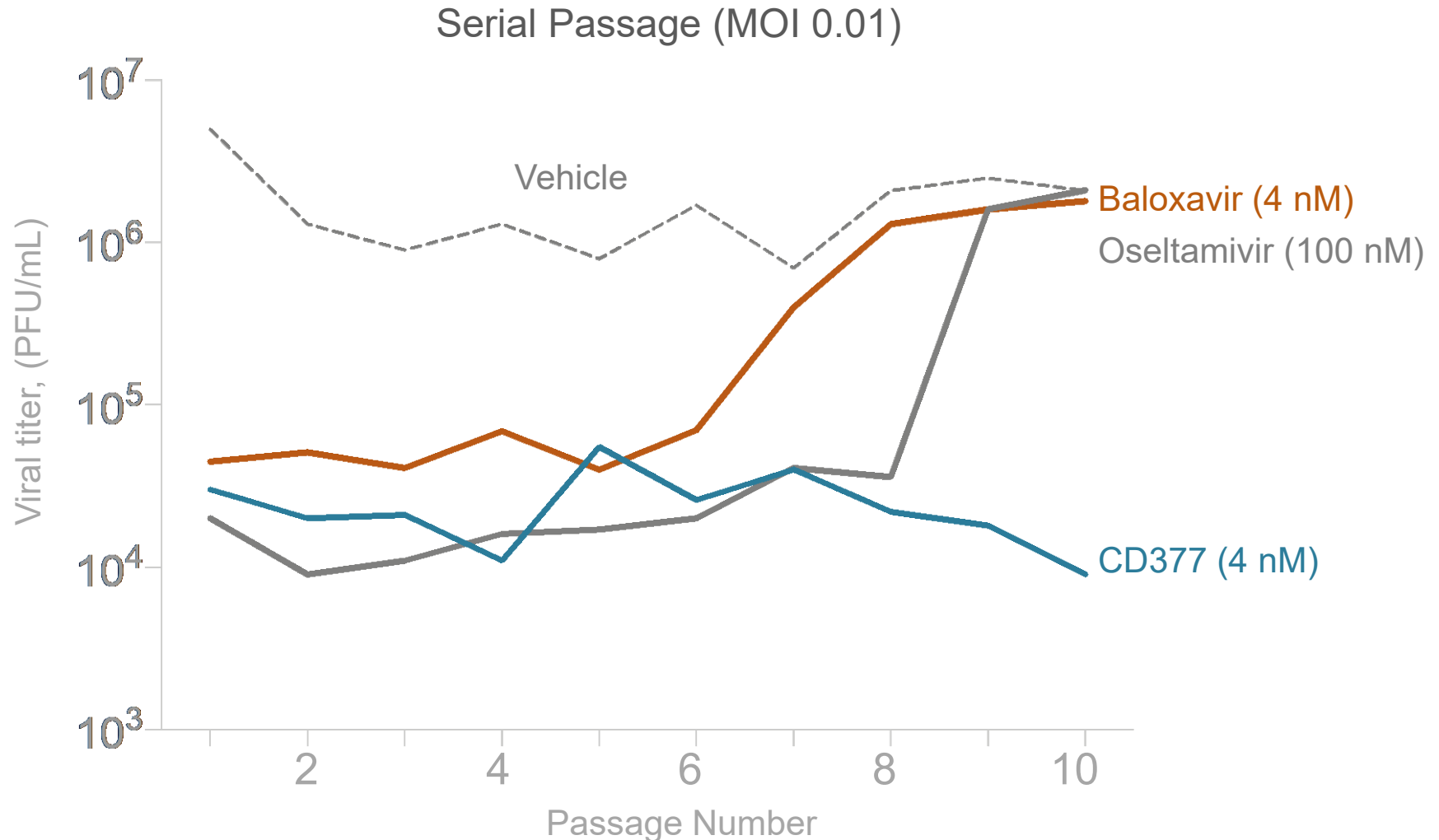
# CD377 retains potency versus Tamiflu resistant viruses

*Single SC dose, lethal influenza models - BALB/c mice*



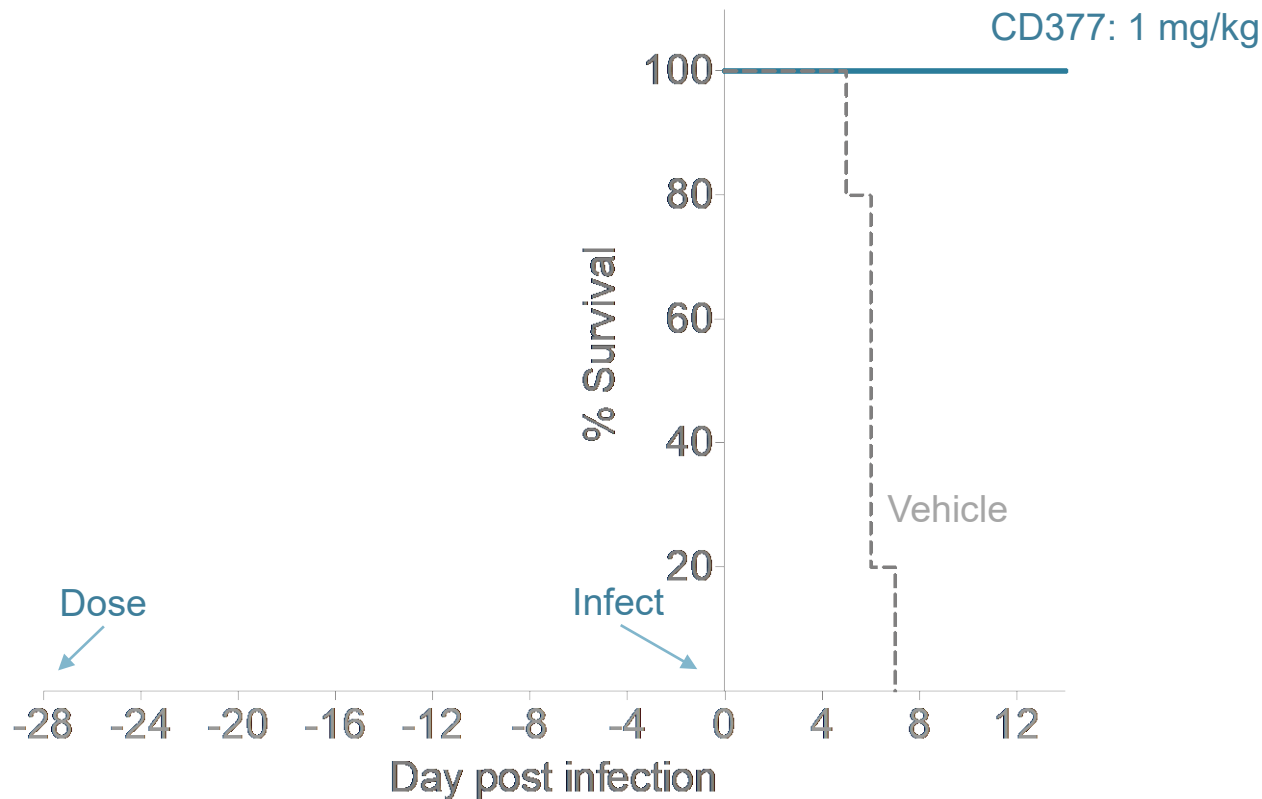


# CD377 demonstrates lower resistance potential than baloxavir and oseltamivir vs. A/CA/07/2009 H1N1pdm



# Potential for long-term single dose protection

*Single 1 mg/kg subcutaneous dose protects mice from pandemic H1N1 for a month*

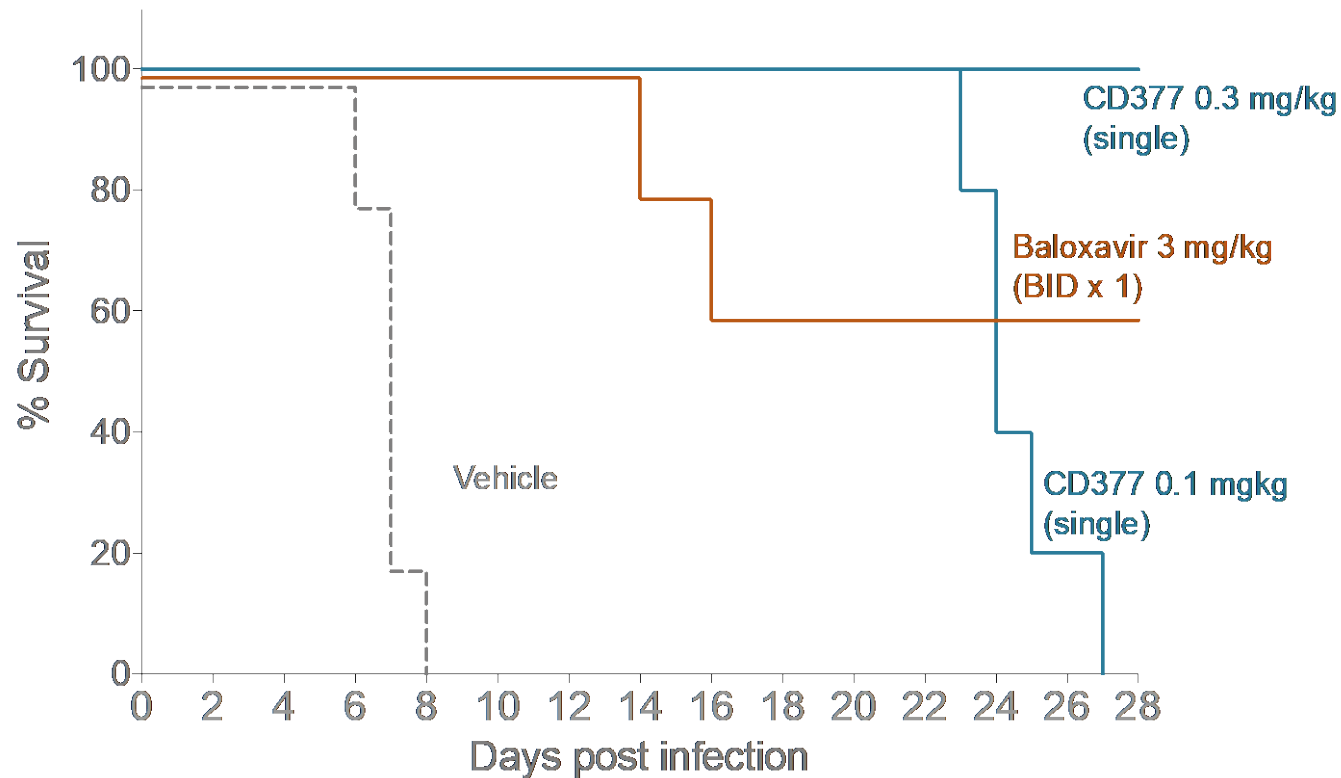


Single 1 mg/kg doses were fully protective vs H1N1 (above), A/Hong Kong/1/68 H3N2, and Influenza B (Malaysia)

# CD377 demonstrates durable protection in severely immune compromised hosts

*Lethal influenza model (H1N1: A/Puerto Rico/8/34 in mice)*

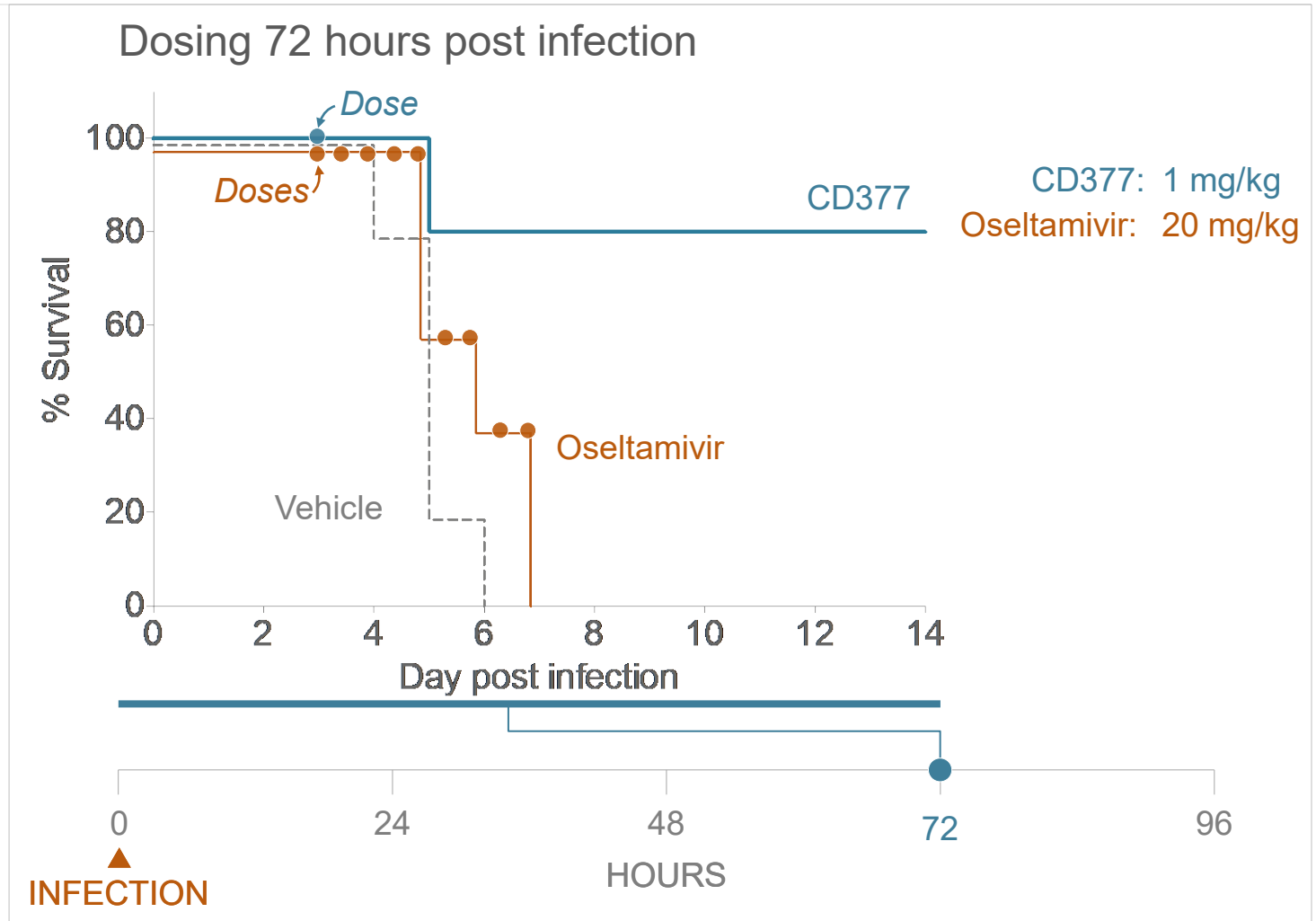
## Efficacy in BALB/c SCID mice



5 mice per cohort. CD377 (SC) and baloxavir (PO) dosing was initiated 2 hours post-infection.

# CD377 extends the treatment window

*Lethal influenza model (H1N1: TX/36/91 in mice)*



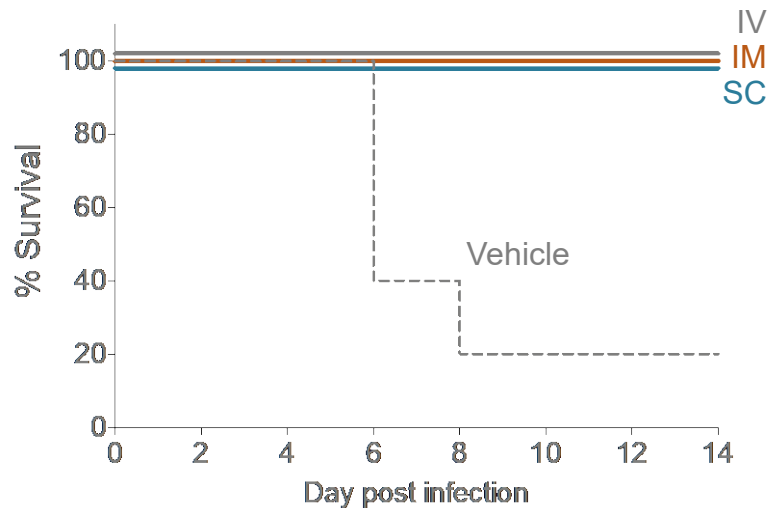
5 mice/cohort, CD377 dosed IV, Oseltamivir dosed PO

# Efficacious by multiple dosing routes

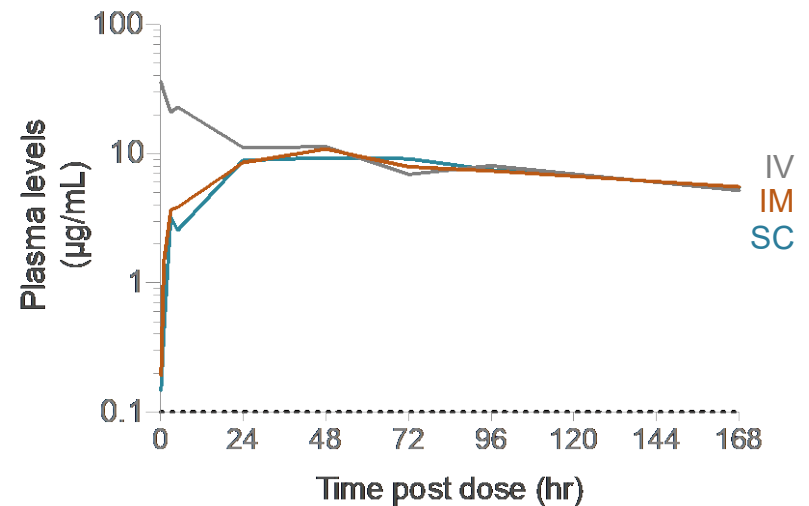
*Lethal influenza model (A/California/07/2009 H1N1pdm)*

*CD377 dosed once 2 hours after viral challenge*

Efficacy of CD377 dosed by different routes  
(BALB/c mouse) 0.1 mg/kg



PK of CD377 dosed by different routes (BALB/c mouse) 5 mg/kg

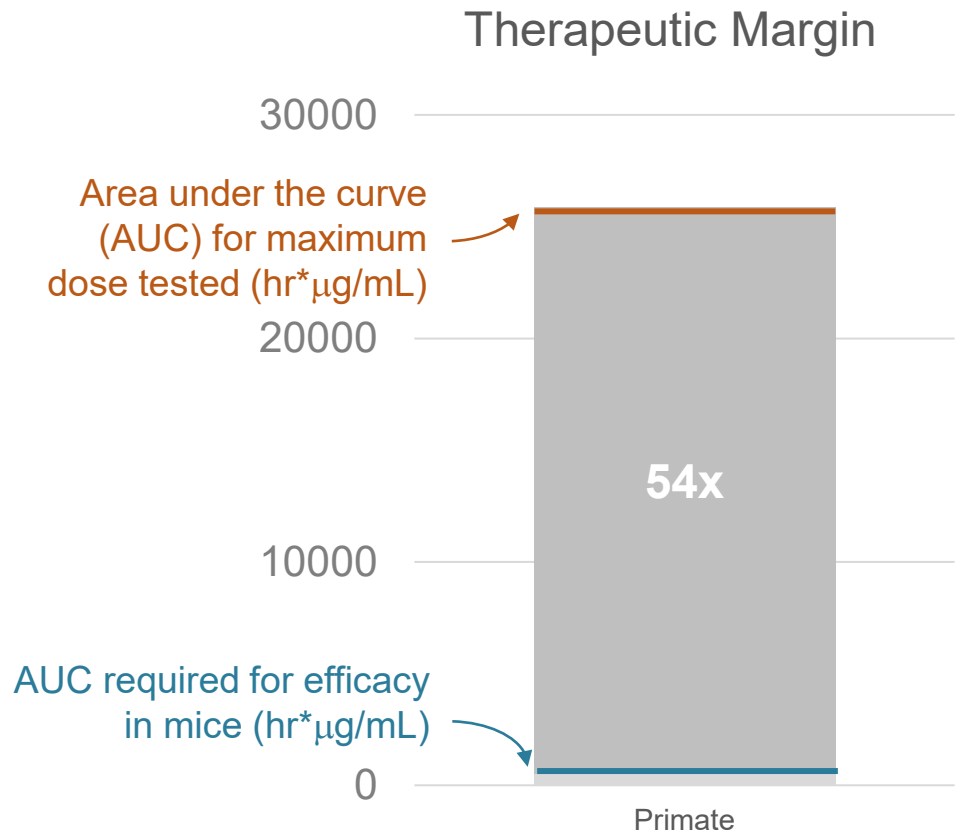


# Broad safety margin in primates (CD377)

*Results of 14-day toxicity testing*

## NO ADVERSE FINDINGS FOR:

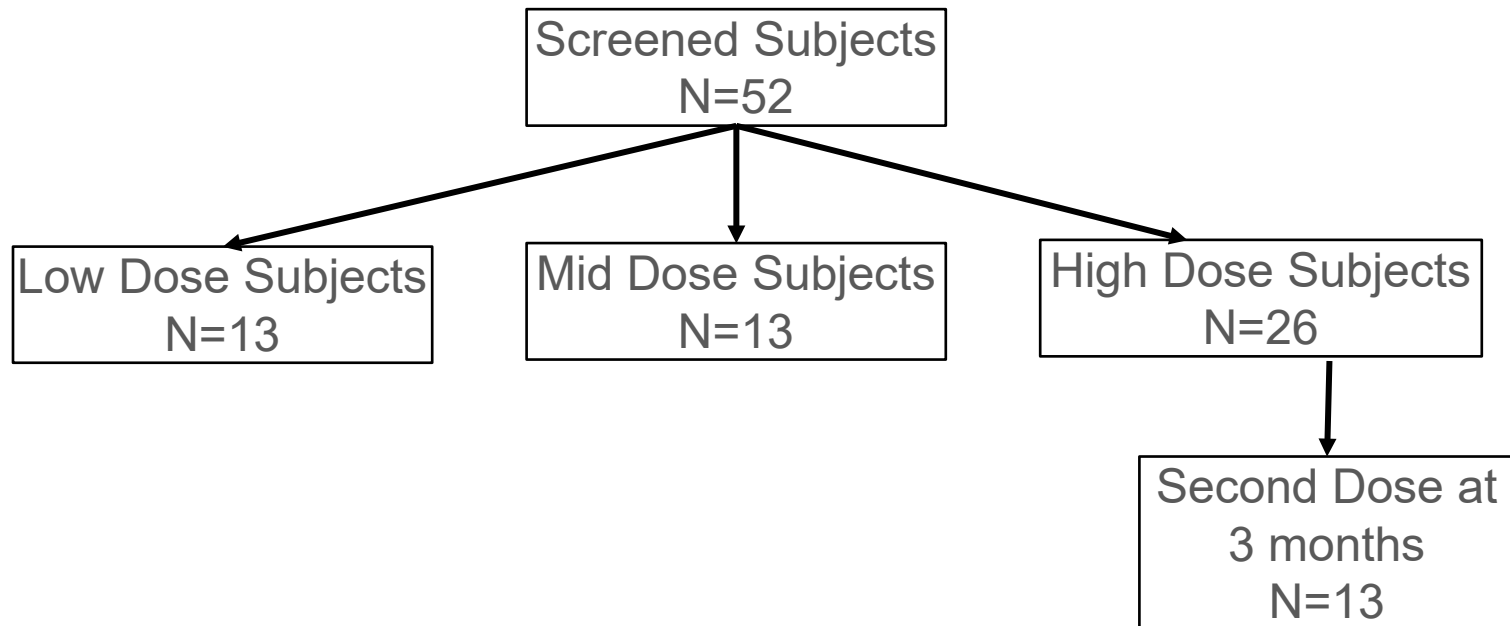
- Clinical observations
- Hematology
- Clinical Chemistry
- Coagulation
- Urinalysis
- Immunophenotyping
- Cytokines
- Histopathology



# CD377 clinical development plan (Phase 1a)

*Phase 1 Safety data to enable BARDA consideration*

- Phase 1a- SAD/MAD (~1-year duration)
  - 3 dose groups (10:3 ratio of CD377 : Placebo) low, medium & high dose
  - Total follow-up of ~4 months following last dose





# CD377 for influenza development program

*Two indications – prevention and treatment*

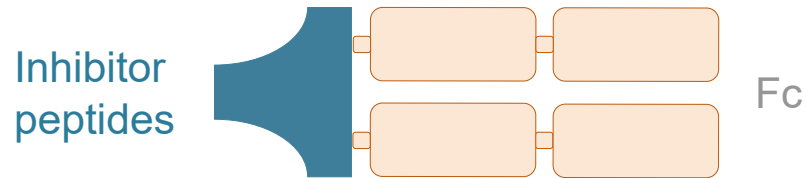
## **Prevention** – Proposed Trials

- Phase 1b: Healthy volunteer challenge study (early POC)
- Phase 2: Dose-ranging in non-vulnerable population
  - Consideration for post-exposure prophylaxis study
- Phase 3 (similar to vaccine studies in seasonal influenza): AVC vs placebo in high-risk populations as defined in Table 4 of IDSA Guidelines

## **Treatment** – Proposed Trials

- Phase 1b: Healthy volunteer challenge study (early POC)
- Phase 2: dose-ranging in uncomplicated influenza
- Phase 3: CD377 vs placebo, stratified for vaccine status
  - Focus will be on high risk outpatient or hospitalized, but could cover other influenza populations depending on regulatory interactions

# Coronavirus - Novel Cloudbreak AVC approach to treat & prevent



## Novel Fc - peptide fusion AVC inhibitors for SARS and COVID-19

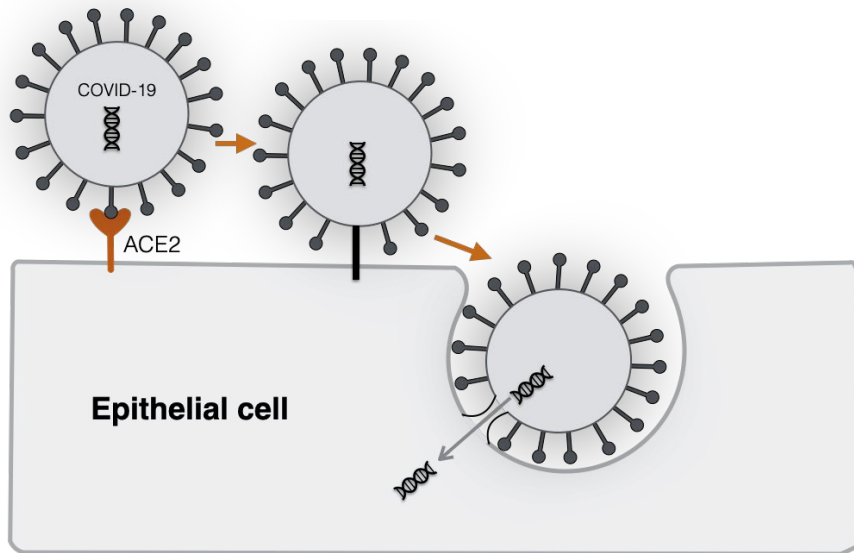
- Goal: fast-acting treatment and long-acting prevention
- 16 variants have been generated for first round of testing
- Several designs under evaluation
  - Broad spectrum activity against SARS, MERS and a-coronaviruses
  - Specific for COVID-19
- **Peptide inhibitors with a similar MOA in HIV is clinically validated<sup>1</sup>**
- **At Cidara, an analogous Fc - peptide fusion approach with HIV yielded potent (nM) *in-vitro* inhibitors of viral fusion**

1. Lalezari JP, Eron JJ, Carlson M, Cohen C, DeJesus E, Arduino RC, et al. (March 2003). "A phase II clinical study of the long-term safety and antiviral activity of enfuvirtide-based antiretroviral therapy". Aids. 17 (5): 691–8. [doi:10.1097/00002030-200303280-00007](https://doi.org/10.1097/00002030-200303280-00007)

# Coronavirus AVCs are being designed to target viral fusion

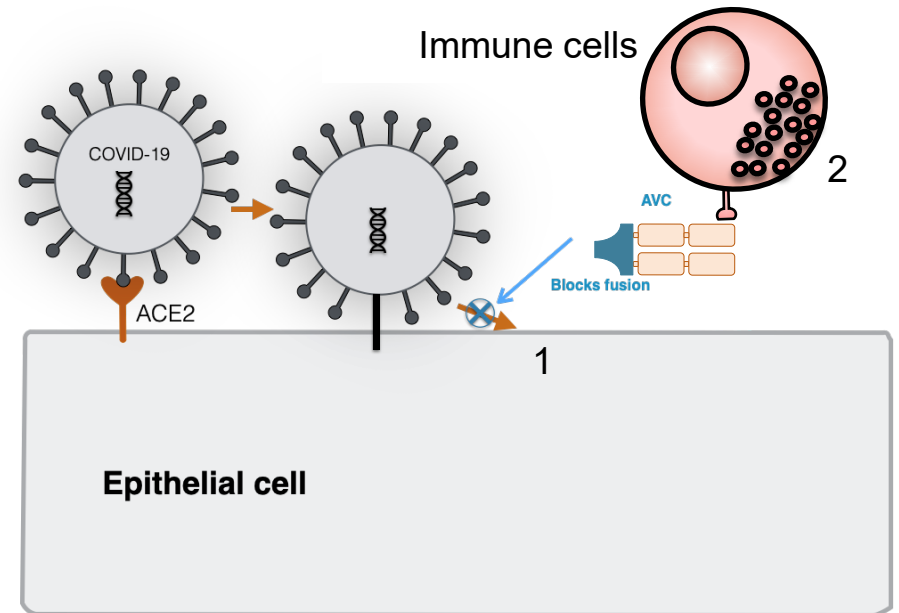
## Untreated

Virus cell fusion



## Treated

1. AVCs block key fusion step
2. Immune cell recruitment



# Cidara is much more than a typical ID company

Strategic Focus	Transformative approaches to infectious disease
Rezafungin Treatment	Enable fast clearance of infection and early discharge vs SOC
Rezafungin Prophylaxis	Transform the care of BMT patients
Cloudbreak AVC	Radically different approach to prevent and treat viral disease
Our Team	Experienced creators of shareholder value

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