A single prophylactic dose of CD388 provides protection against highly pathogenic bovine-origin Influenza A(H5N1) virus in the ferret model

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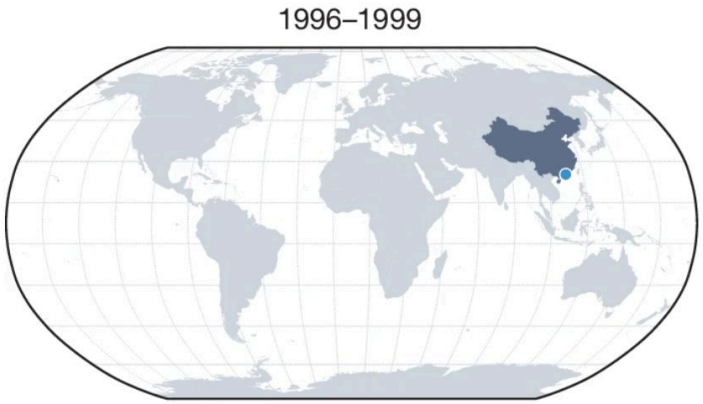
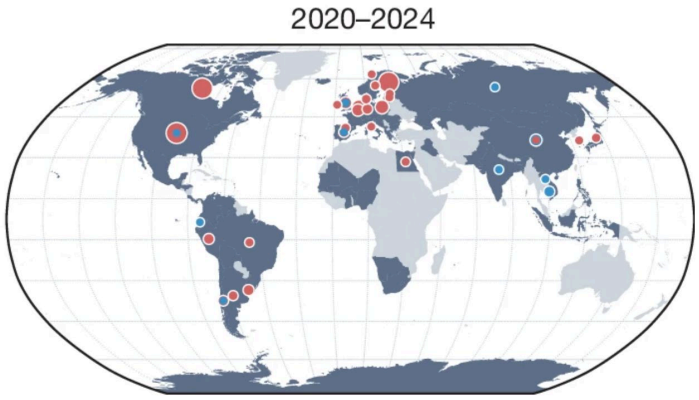
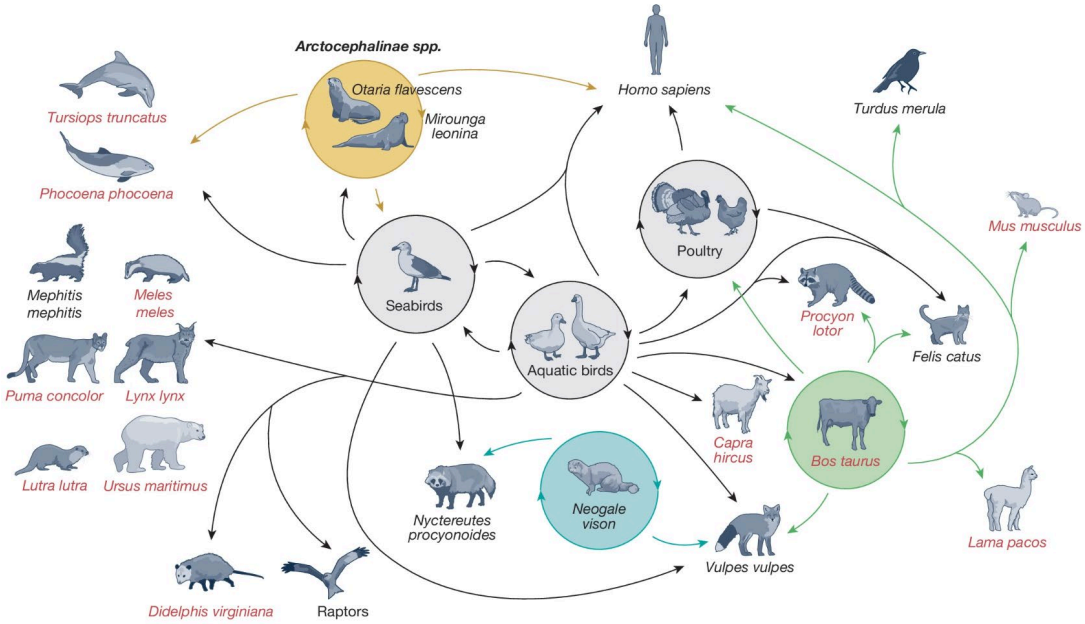
8TH ISRV-AVG MEETING & 3RD IMRP 2025
17-20 SEPTEMBER 2025 | SINGAPORE

Influenza **A(H5N1)** viruses:
Host Range and Geography



Multiple transatlantic incursion in North America in 2021-2022





- Wild aquatic birds are natural reservoirs
- **Spillover** into mammals (terrestrial and aquatic mesocarnivores, peridomesticated species)
  - Outbreaks in dairy cow (2024-ongoing)

Peacock et al. Nature. 2025

Influenza **Pandemic Risk Assessment**

- 130 human infections worldwide (2020- September 2025)
  - Novel D1.1 genotype responsible for severe and lethal cases
  - Mammalian host adaptive signatures present
  - A single mutation in H5 hemagglutinin is sufficient to switch specificity from avian to human receptors (Lin et al. Science 2024)

CDC
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

Influenza **R**isk **A**ssessment **T**ool (**IRAT**)

- Limited **cross-clade reactivity** of available vaccines
  - *Sanofi Pasteur*: A/Vietnam/1194/2004 **(clade 1**)
  - *GSK*: A/Indonesia/05/2005 (**clade 2.1**)
  - *CSL Seqirus*: A/Turkey/1/2005 (**clade 2.2.1**)

World Health Organization

Tool for **I**nfluenza **P**andemic **R**isk **A**ssessment (**TIPRA**)

- **Antivirals**: last line of defense and countermeasures

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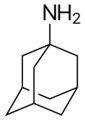
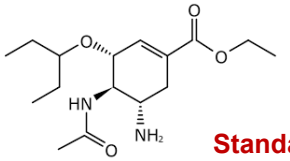
Direct-acting Antivirals: limitations against A(H5N1) infection in mice

M2 ion channel inhibitors



Amantadine
Gocovri®

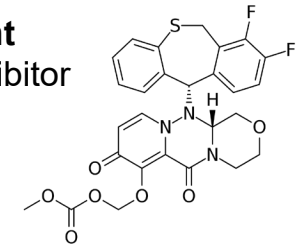
Neuraminidase inhibitors



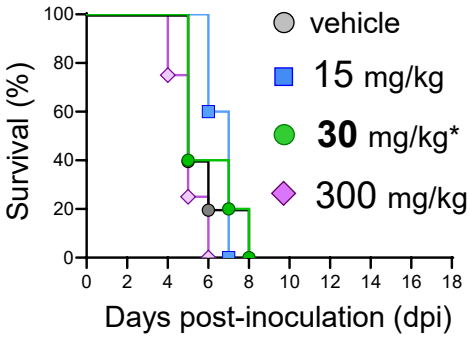
Oseltamivir
Tamiflu®

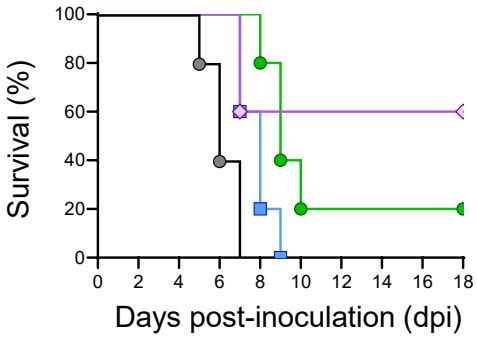
Standard of care for influenza treatment.

Cap-dependent endonuclease inhibitor

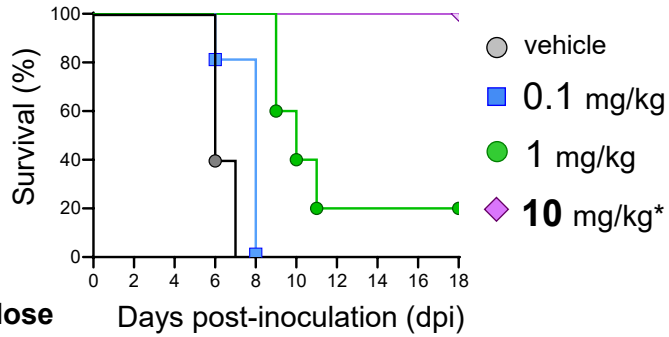


Baloxavir
Xofluza®

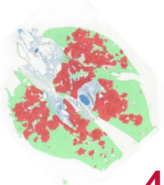




* approx. **human eq. dose**

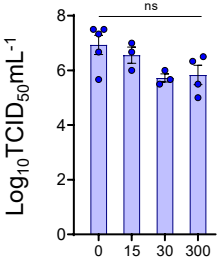


HISTOLOGY



47%
infection area

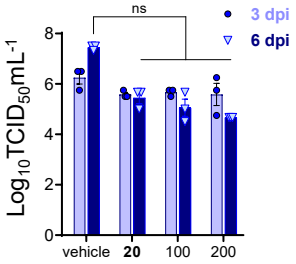
LUNG TITERS



HISTOLOGY

19%
active infection area

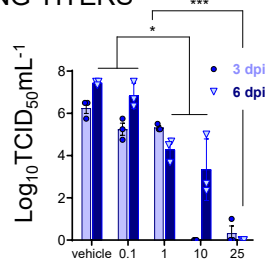
LUNG TITERS



HISTOLOGY

2%
active infection area

LUNG TITERS



Available **antivirals** except baloxavir **fail to control lethal A(H5N1) infection**

Andreev et al. (data unpublished)

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Antiviral protection of mice exposed to **A(H5N1)**-contaminated **bovine milk**

Route of infection: Oral Intranasal

Model exposure conditions to be encountered by humans

INTRANASAL route:

- only high dose Tamiflu® saved 40% of animals
- baloxavir increased survival to 50-80%,
  - reduced virus titers in respiratory and neural tissues

ORAL route:

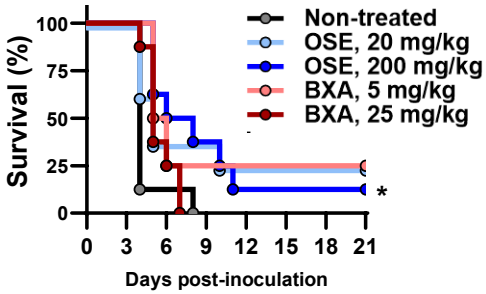
- both antivirals failed to protect
  - (≤25% survival rates)
  - did not prevent virus replication

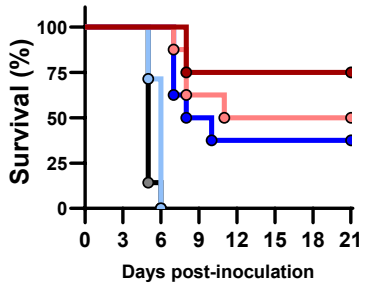
Oseltamivir phosphate

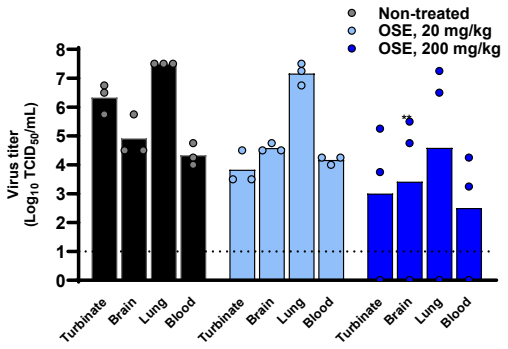
Oral, BID
5 days

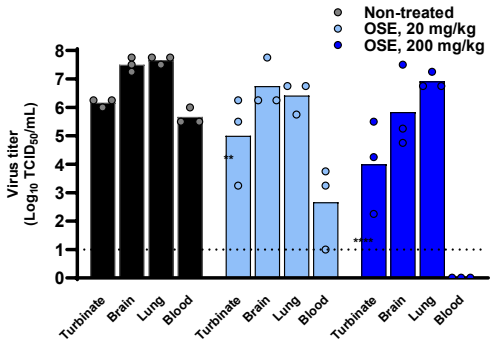
Baloxavir acid

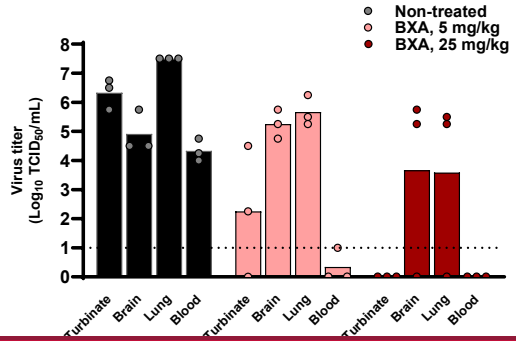
Subcutaneous
1 Dose

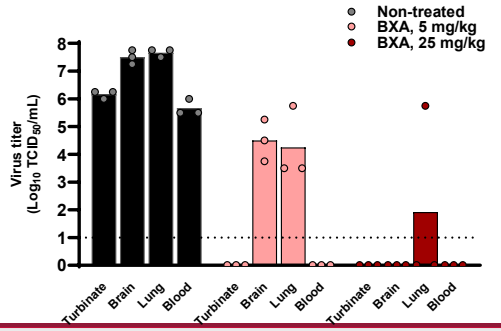












CD388: Novel Dual-Targeting Antiviral

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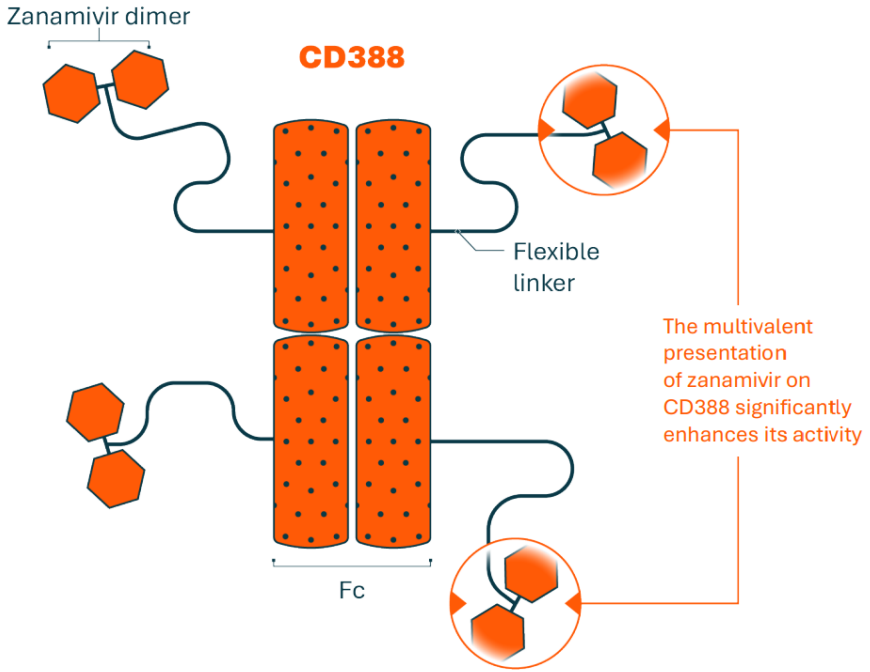
NASDAQ: CDTX

CD388 is a Drug-Fc-Conjugate (DFC) that arrays multiple copies of zanamivir, the active ingredient of FDA-approved influenza drug Relenza®, on a clinically validated human antibody fragment engineered for extended half-life



CD388: Non-Vaccine Preventative of seasonal influenza infections

- Successfully completed Phase 2b NAVIGATE Trial
- 76% efficacy at the highest dose (450 mg)

Goals and Objectives:

To evaluate in vivo efficacy of CD388 pre-exposure prophylaxis against highly pathogenic A(H5N1) infection

Preclinical **Study Design**

n = 3

tissue titers

Necropsy

5 dpi

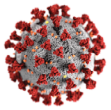
Challenge virus:
A/**bovine**/Ohio/BSU24-439/2024 (**H5N1**)

Pre-Exposure Prophylaxis regimens:

- CD388: **1**, **3**, **10**, **30** mg/kg
- Baloxavir acid (BXA):4 mg/kg

CD388/BXA single-dose (subcutaneous)

Inoculation 10^4 $TCID_{50}$ / ferret IN



Nasal washes (q.o.d.)

-24 hpi

-1 0 1 3 5 7 9 11 . . . 21

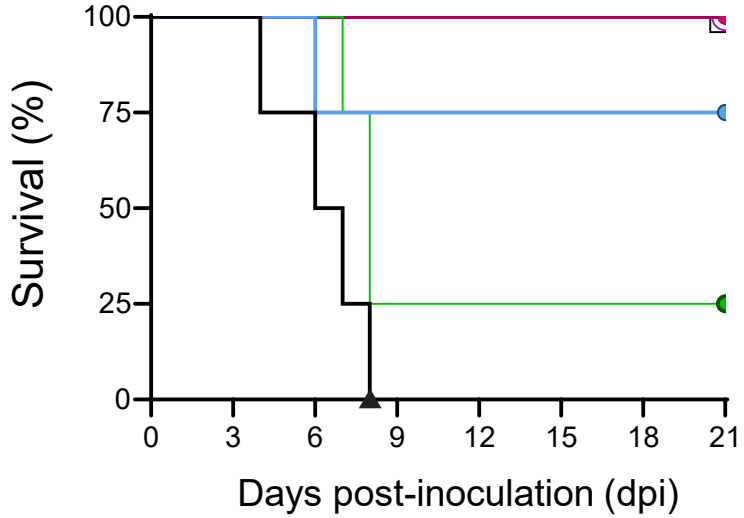
days post-inoculation (dpi)

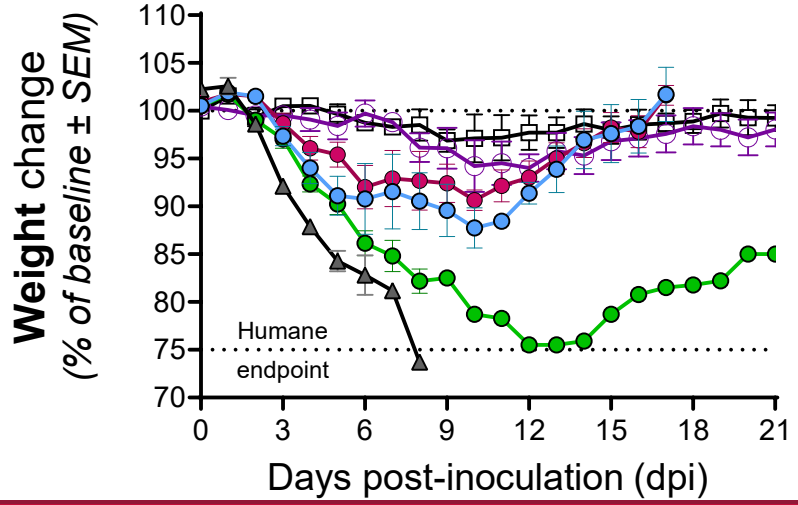
n = 4

survival, weight, clinical signs, nasal wash

Serology

CD388 **Protects 100%** Ferrets from Lethal A(H5N1) challenge

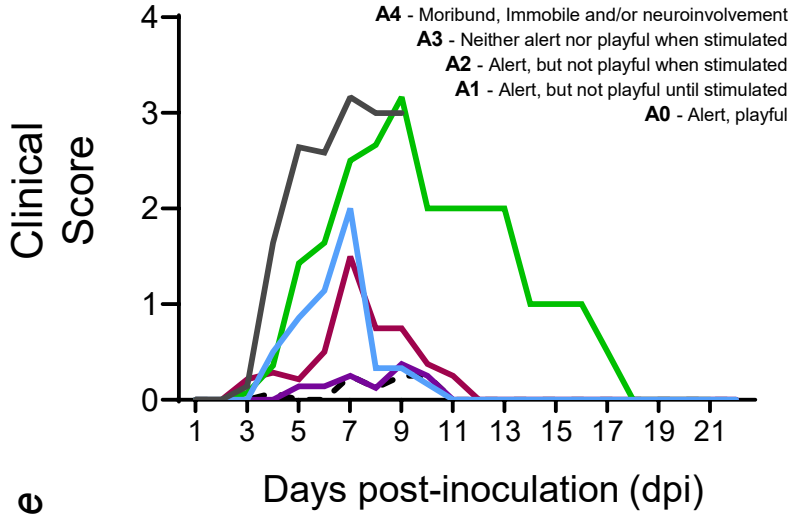


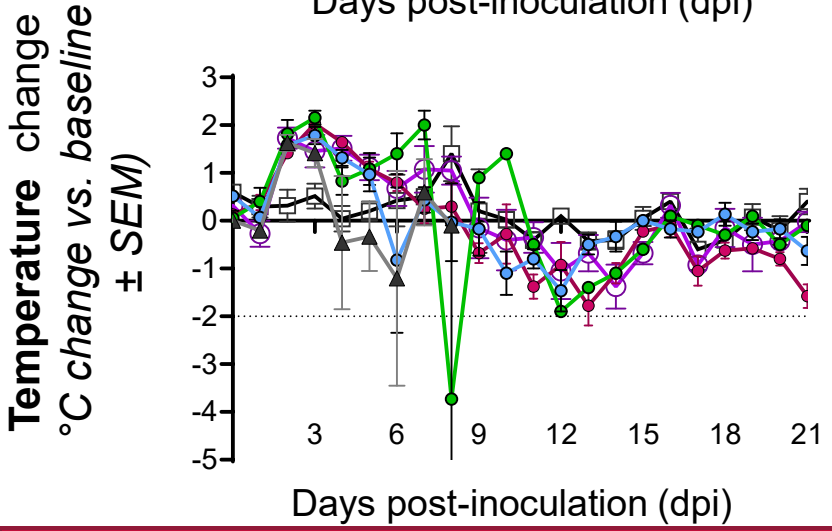


- Control (non-treated, infected) animals:
  - exhibited rapid weight loss
  - reached humane endpoints by **4-8** dpi
- CD388 at:
  - **1**mg/kg protected **25**% of ferrets;
  - **3** mg/kg protected **75**% of ferrets
  - **≥10** mg/kg protected **100**% of ferrets
- CD388-treated animals exhibited less weight loss vs. Control

Vehicle
CD388 **1** mg/kg
CD388 **3** mg/kg
CD388 **10** mg/kg
CD388 **30** mg/kg
BXA **4** mg/kg

CD388 Alleviates **Clinical Symptoms** of A(H5N1) Infection in Ferrets

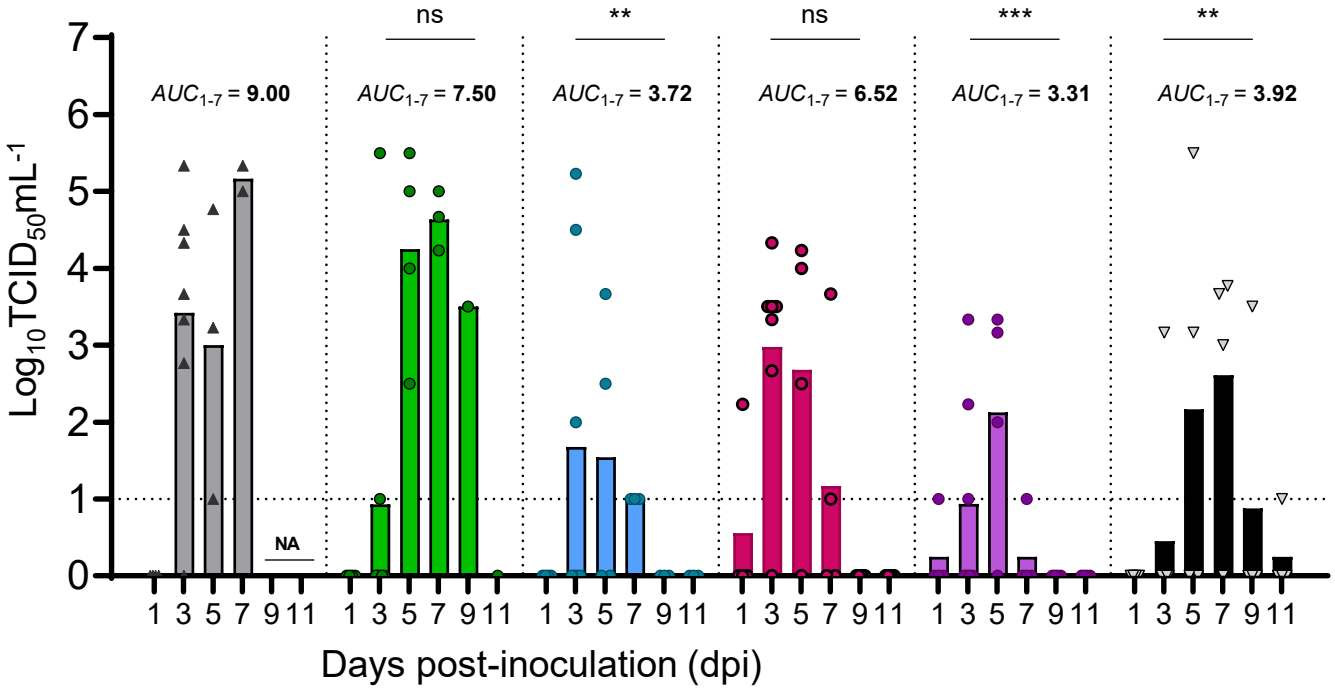


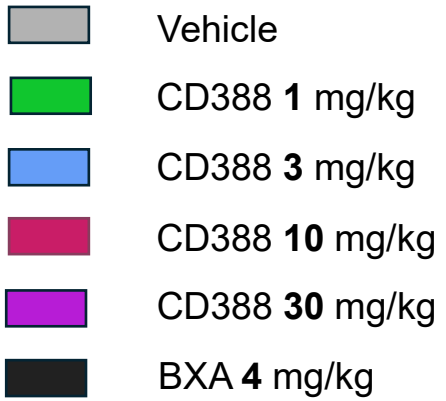


- Control animals:
  - neurological symptoms (ataxia, tremor, seizures, hind limb paresis
  - Clinical/alertness score reached ≥3 by 5-7 dpi
- CD388 at:
  - **≥3** mg/kg reduced clinical symptoms vs. Control
  - All CD388 regimens caused an increase in the body temperature (≤2°C above the baseline) 2-5 dpi

Vehicle
CD388 **1** mg/kg
CD388 **3** mg/kg
CD388 **10** mg/kg
CD388 **30** mg/kg
BXA **4** mg/kg

CD388 Reduces **Virus Shedding** in A(H5N1)-Infected Ferrets





AUC1-7: Area under the shedding curves from 1 - 7 dpi
Asterisks indicate statistical comparison vs. matched Vehicle group time point,
(ns: *p* > 0.05; ** *p* ≤ 0.01; ***: *p* ≤ 0.001)
NA - not applicable, no surviving animals at these time points

- Control animals:
  - Virus present in nasal washes (3-7 dpi, 10^3-10^5 $TCID_{50}$/mL)
- CD388 at:;
  - **≥ 3** mg/kg reduced nasal wash titers by 7 dpi
  - **≥3** mg/kg has cleared out the virus from the upper respiratory tract completely by 9 dpi

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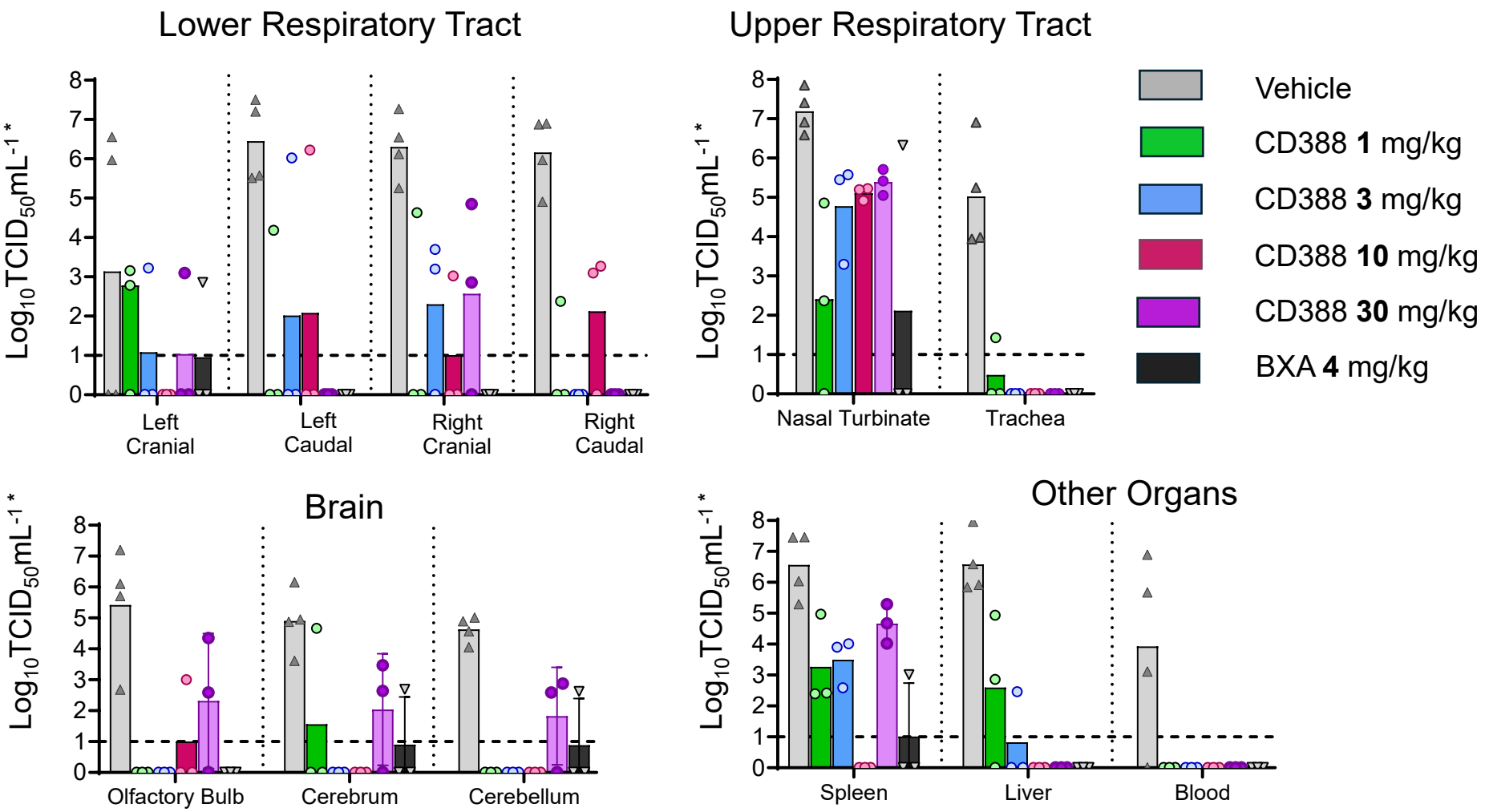
CD388 Prevents **Systemic Spread** of A(H5N1) infection in Ferrets



* per g tissue

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Conclusions

- A single prophylactic dose of CD388 at ≥3 mg/kg fully protected ferrets from lethal infection with bovine-origin influenza A(H5N1) virus.
- CD388 significantly reduced viral replication in upper and lower respiratory tracts
- CD388 prevented A(H5N1) neuroinvasion, viremia and systemic spread.

FUTURE OBJECTIVES:

- Phenotypic screening on a panel of recent D1.1-D1.3 genotypes
- Evaluate the emergence of drug-resistant variants
- Evaluate the delayed treatment of CD388 to prevented A(H5N1) infection

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