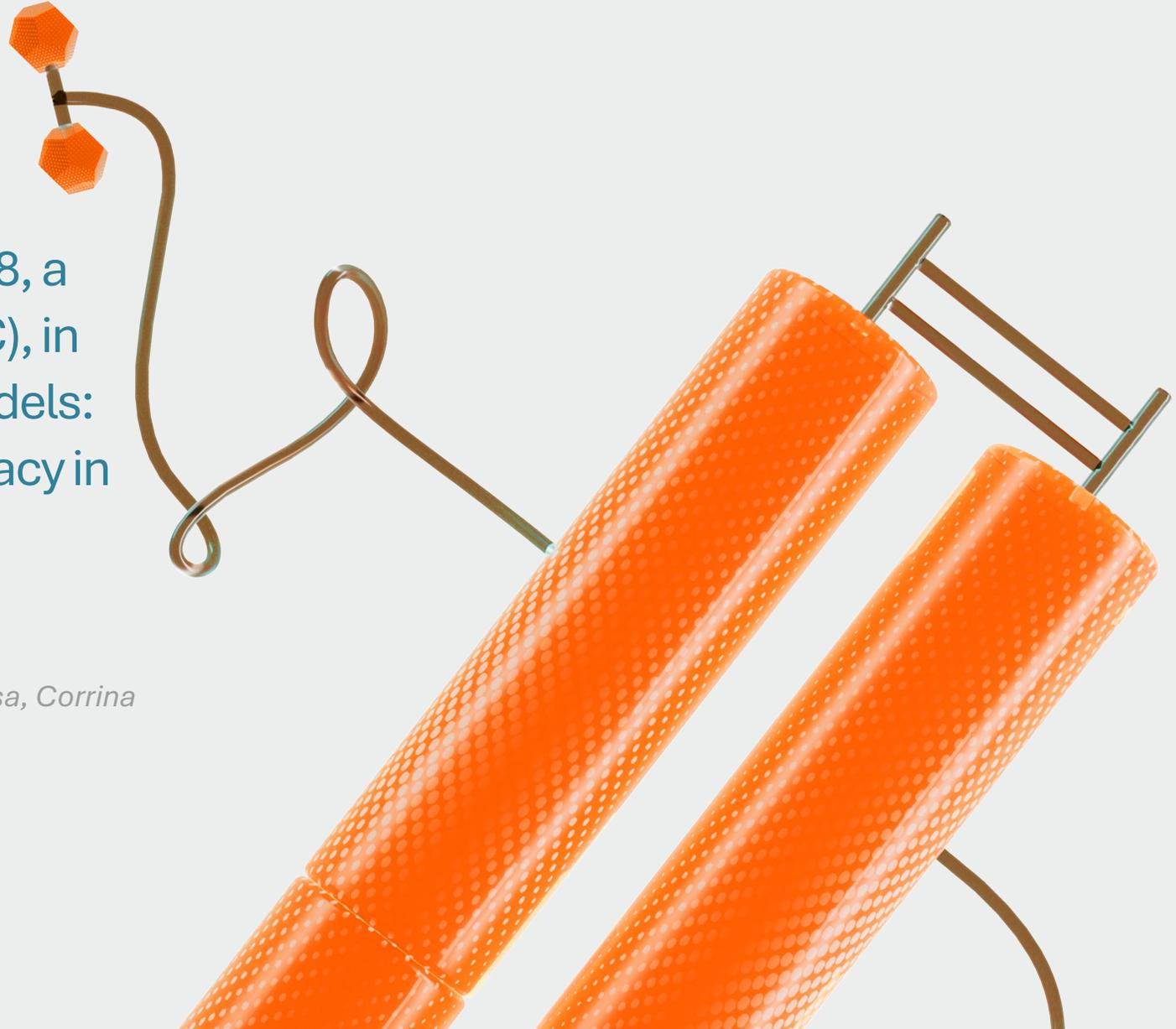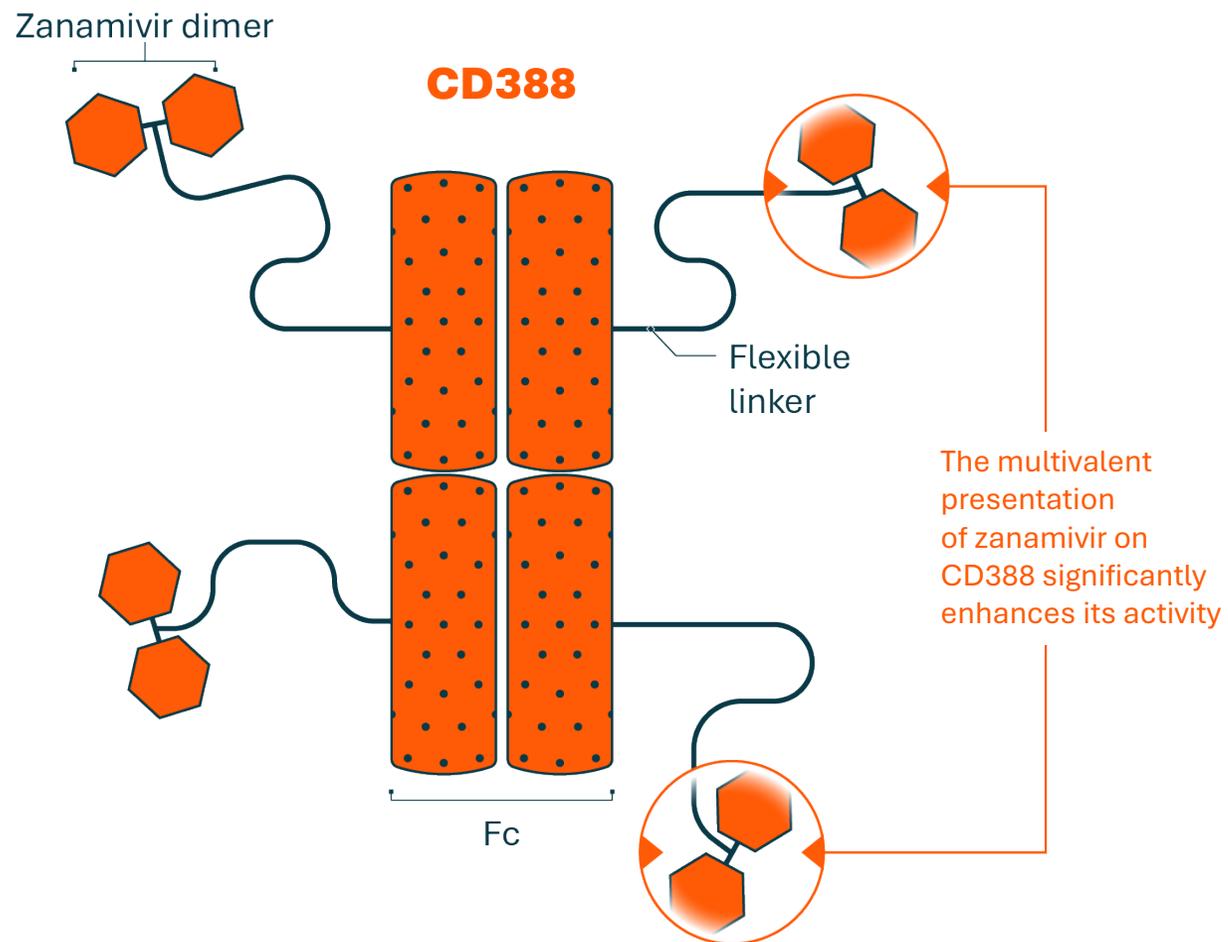# CIDARA THERAPEUTICS

Translational efficacy of CD388, a novel Drug Fc-Conjugate (DFC), in mouse influenza infection models: application to prevention efficacy in the recently completed Ph2b NAVIGATE clinical study

Voon Ong, *Julie Passarell, Les Tari, Joaquin Sosa, Corrina Pavetto, Nicole Davarpanah*
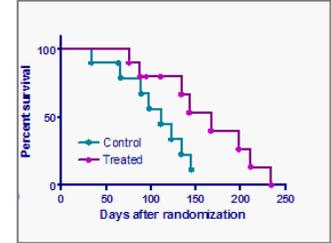
DFCs: A Novel Drug Class (that is stable, unlike ADCs)

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

Zanamivir dimer

CD388

Flexible linker

The multivalent presentation of zanamivir on CD388 significantly enhances its activity

Fc

Mouse lethal infection model

Mouse lethal (3x LD$_{95}$) infection model: ultimate challenge

Infection (3x LD$_{95}$)
(T+0d)

**Health checks
Body weight**
(T+21d)

**Kaplan-Meier
Survival
curves**

Prophylaxis
(T-7d)

OR

Treatment
(T+2h)
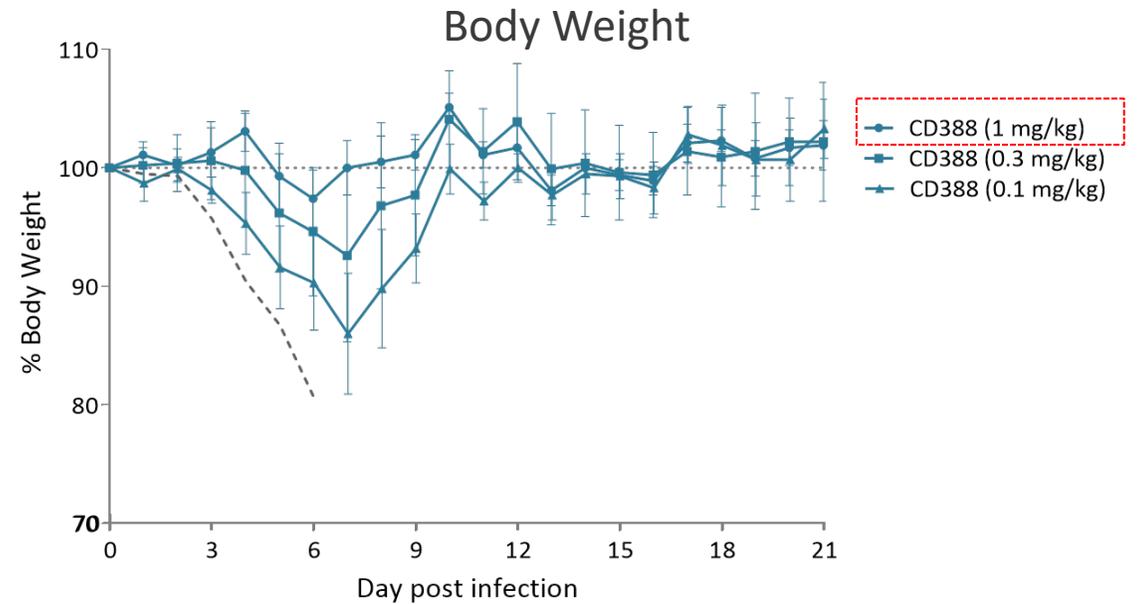
Preventive efficacy in mouse lethal challenge models

Model: T-7d prophylaxis against H1N1

100% survival across broad dose range

Survival[1]

Legend:
- CD388 (1 mg/kg)
- CD388 (0.3 mg/kg)
- CD388 (0.1 mg/kg)
- CD388 (0.03 mg/kg)
- Vehicle (PBS)
- hIgG1 Fc (1 mg/kg)

X-axis: Day post infection
Y-axis: % Survival

Protection against body weight loss

Body Weight

Legend:
- CD388 (1 mg/kg)
- CD388 (0.3 mg/kg)
- CD388 (0.1 mg/kg)

X-axis: Day post infection
Y-axis: % Body Weight

1. Single dose initiated 7 days prior to viral challenge. A/Puerto Rico/8/1934(H1N1)

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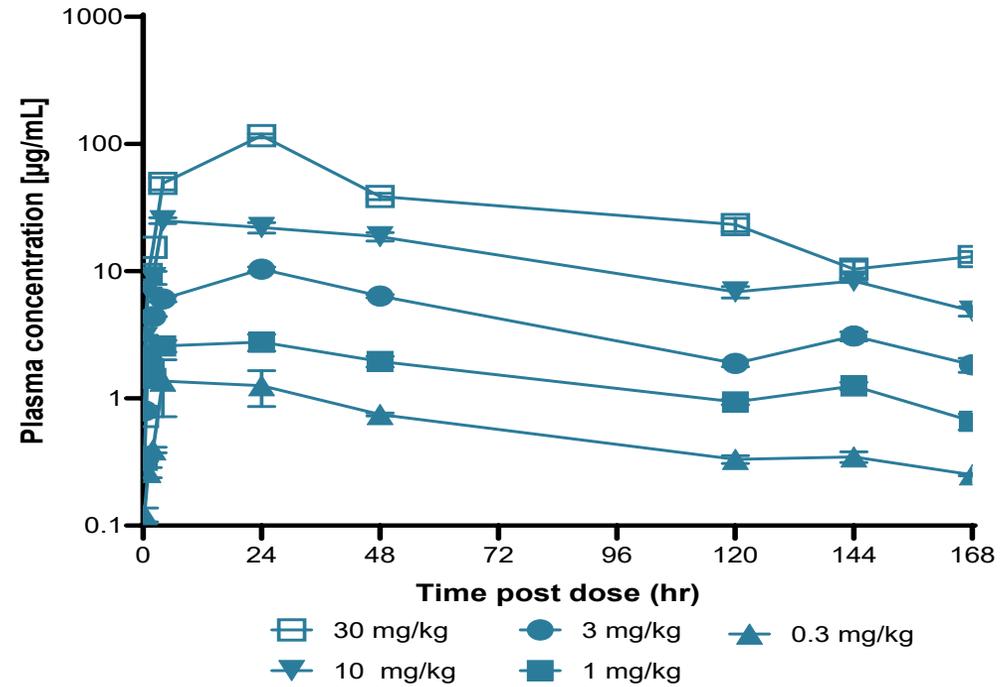# CD388 is a potent in both prevention and treatment models

Prevention (T-7d)

Subtype	Number of isolates tested	Fully protective dose required for subtype coverage (mg/kg)
A (H1N1)	7	**1**
A (H3N2)	1	**0.3**
B (Victoria)	2	**1**
B (Yamagata)	1	**0.3**

Treatment (T+2h)

Subtype	Number of isolates tested	Fully protective dose required for subtype coverage (mg/kg)
A (H1N1)	8	**1**
A (H3N2)	1	**0.3**
B (Victoria)	2	**0.3**
B (Yamagata)	1	**0.3**

- *A single dose of CD388 at 1 mg/kg in the mouse was fully protective against lethal challenge by different seasonal isolates*

6

Mouse PK Profiles: Targeting >1 µg/mL Plasma Conc

Dose (mg/kg)	AUC_{last} (µg.hr/mL)	T_{max} (hr)	C_{max} (µg/mL)	C_{ave} (µg/mL)	C_{7d} (µg/mL)
0.3	107	4	1	1	0.3
1	*270*	*24*	*3*	*2*	*1*
3	796	24	10	5	2

NAVIGATE
Phase 2b Study

Human PK Profiles: 150, 300, and 450 mg

All doses selected to remain >1 µg/mL plasma concentration through 24 weeks…i.e. >3 µg/mL for 450 mg dose

Day 197 PK subset

Dose (mg)	150	300	450
Mean conc (µg/mL)	0.98	2.07	3.13

CIDARA

CD388 Ph2b NAVIGATE Trial Design
(NCT06609460)

Blinded, randomized, controlled trial of CD388 in 3 doses vs placebo as a single SQ administration to assess efficacy and safety of CD388 in prevention of influenza in subjects not at risk for influenza complications

A Double-blind RCT of CD388 for Influenza Prophylaxis

Study Population

Generally healthy, unvaccinated adults aged 18-64 not at risk for complications of influenza
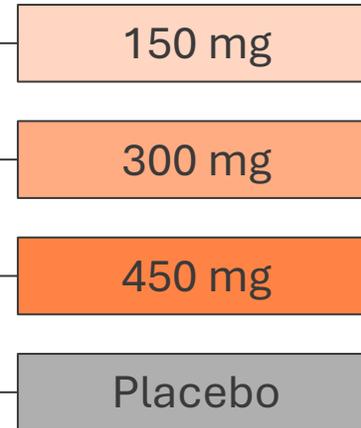
Study Size

n=5000 across CD388 and placebo groups

Sites, N=58
- US, n=57
- UK, n=1

R 1:1:1:1

| 150 mg |
| 300 mg |
| 450 mg |
| Placebo |

First/Last Dosed

Sep 2024/Dec 2024

Primary Endpoint

Prevention Efficacy (PE) of Influenza-like illness (ILI)

defined by all 3 criteria up to 24 weeks:

- Central lab-confirmed PCR+ influenza
- ≥2 respiratory or 1 respiratory and 1 systemic sign/symptom
- Body temp ≥38°C

Prevention Efficacy: Percentage by which a prevention method reduced the chance of getting sick compared to not using it

Ph2b NAVIGATE Study Successfully Met Primary Endpoint

	CD388			
Primary Endpoint**	**150 mg** N=1,175* n (%)	**300 mg** N=1,192* n (%)	**450 mg** N=1,187* n (%)	**Placebo** N=1172* n (%)
Number of Participants Protocol-Defined ILI ≥38.0 Temp[1]	14 (1.2)	13 (1.1)	8 (0.7)	33 (2.8)
Prevention Efficacy (PE) (%)	57.7	61.3	76.1	–
95% CI (%)	21.1, 78.9	27.0, 81.2	49.3, 89.9	–
P-value	0.0050	0.0024	<0.0001	–

*Sample size (N) indicates evaluable population at time of primary analysis data cut (Apr 30, 2025).

**Statistical significance for grouped 300mg + 450mg dose groups was met (PE=68.6%, p<0.0001), enabling pair-wise testing of individual dose groups versus placebo.

Abbreviations: ILI, influenza like illness; CI, confidence interval
1. ILI event defined as central laboratory-confirmed RT-PCR+ influenza infection (nasopharyngeal swab), new onset of fever (oral temperature ≥38.0°C), and new onset of ≥2 respiratory symptoms (nasal congestion, sore throat, cough) or ≥1 respiratory symptom and ≥1 systemic symptom (headache, feeling feverish, body aches/pains, fatigue).

Key Secondary Endpoints Demonstrated Statistical Significance at All Specified Temperatures

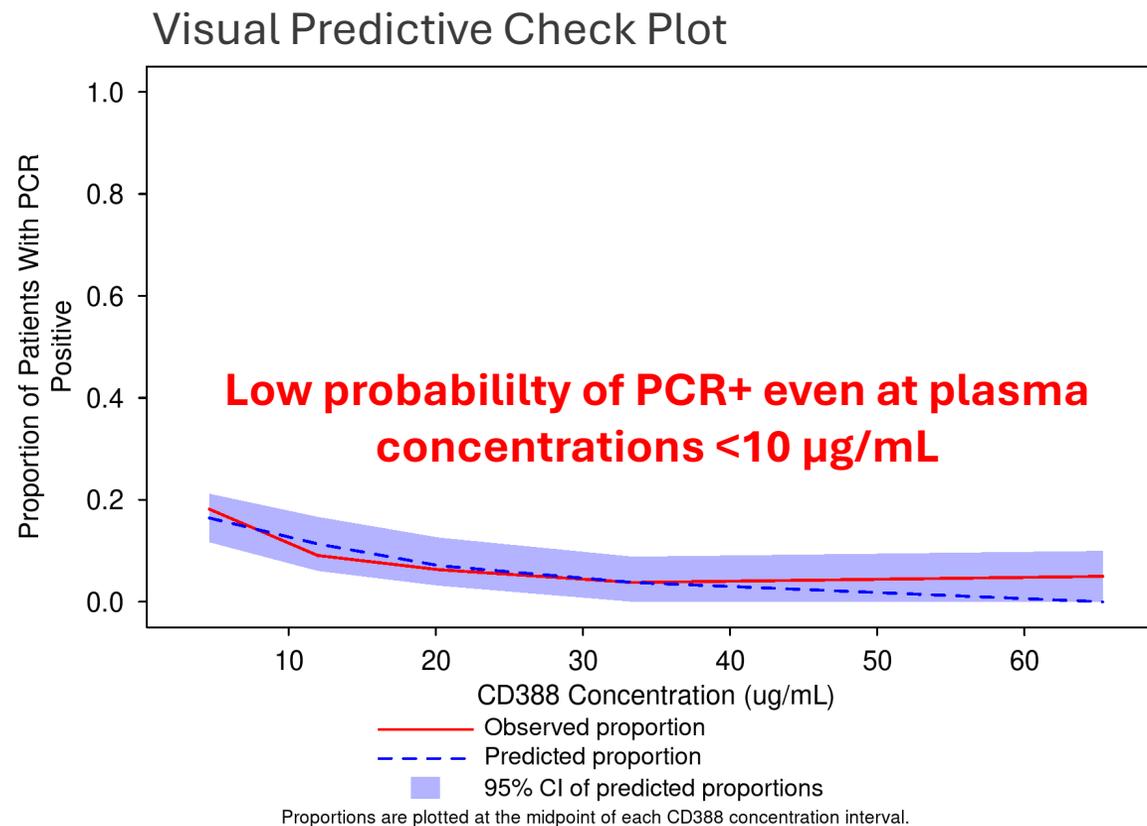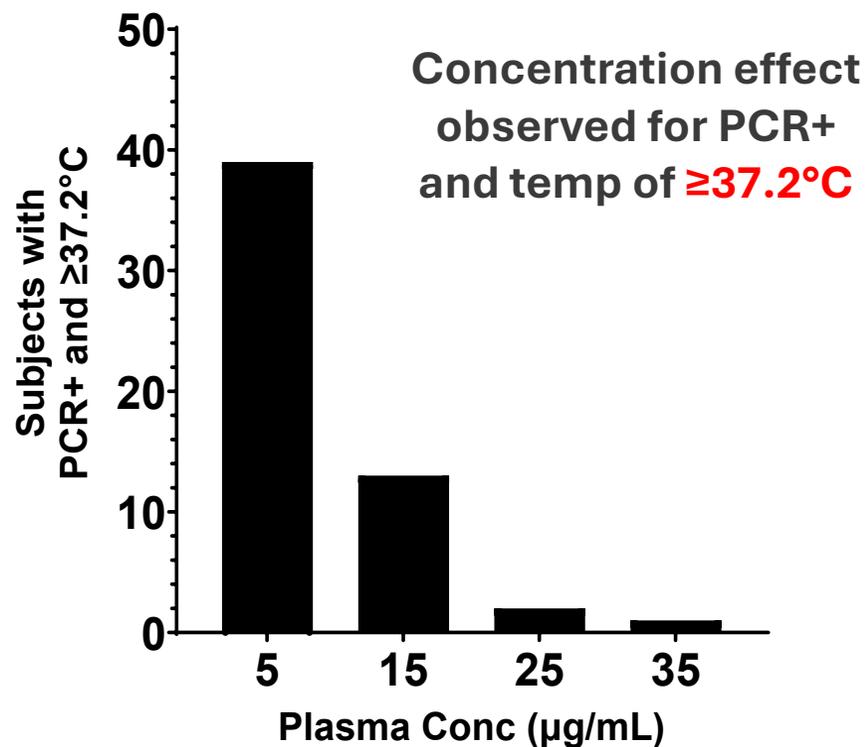|	CD388			
Secondary Endpoints	**150 mg** N=1,175* n (%)	**300 mg** N=1,192* n (%)	**450 mg** N=1,1187* n (%)	**Placebo** N=1,172* n (%)
Number of Participants with ≥37.8 Temp[1]	15 (1.3)	15 (1.3)	8 (0.7)	33 (2.8)
Prevention Efficacy (PE) (%)	54.7	55.3	76.1	–
95% CI (%)	16.7, 77.4	18.0, 77.8	49.3, 89.9	–
P-value	0.0084	0.0073	<0.0001	–
Number of Participants with ≥37.2 Temp[2]	22 (1.9)	21 (1.8)	12 (1.0)	41 (3.5)
PE (%)	46.5	49.6	71.1	–
95% CI (%)	10.2, 69.3	14.8, 71.9	45.8, 86.1	–
P-value	0.0148	0.0083	<0.0001	–

*sample size (N) indicates evaluable population at time of primary analysis data cut-off (Apr 30, 2025).

Abbreviations: ILI, influenza like illness; CI, confidence interval: PCR, polymerase chain reaction.
1. CDC definition: ILI event defined as central laboratory-confirmed RT-PCR+ influenza infection (nasopharyngeal swab), new onset of fever (oral temperature ≥37.8°C), and new onset of ≥2 respiratory symptoms (nasal congestion, sore throat, cough).
2. ILI event defined as central laboratory-confirmed RT-PCR+ influenza infection (nasopharyngeal swab), new onset of fever (oral temperature ≥37.2°C), and new onset of ≥2 respiratory symptoms (nasal congestion, sore throat, cough) or ≥1 respiratory symptom and ≥1 systemic symptom (headache, feeling feverish, body aches/pains, fatigue).
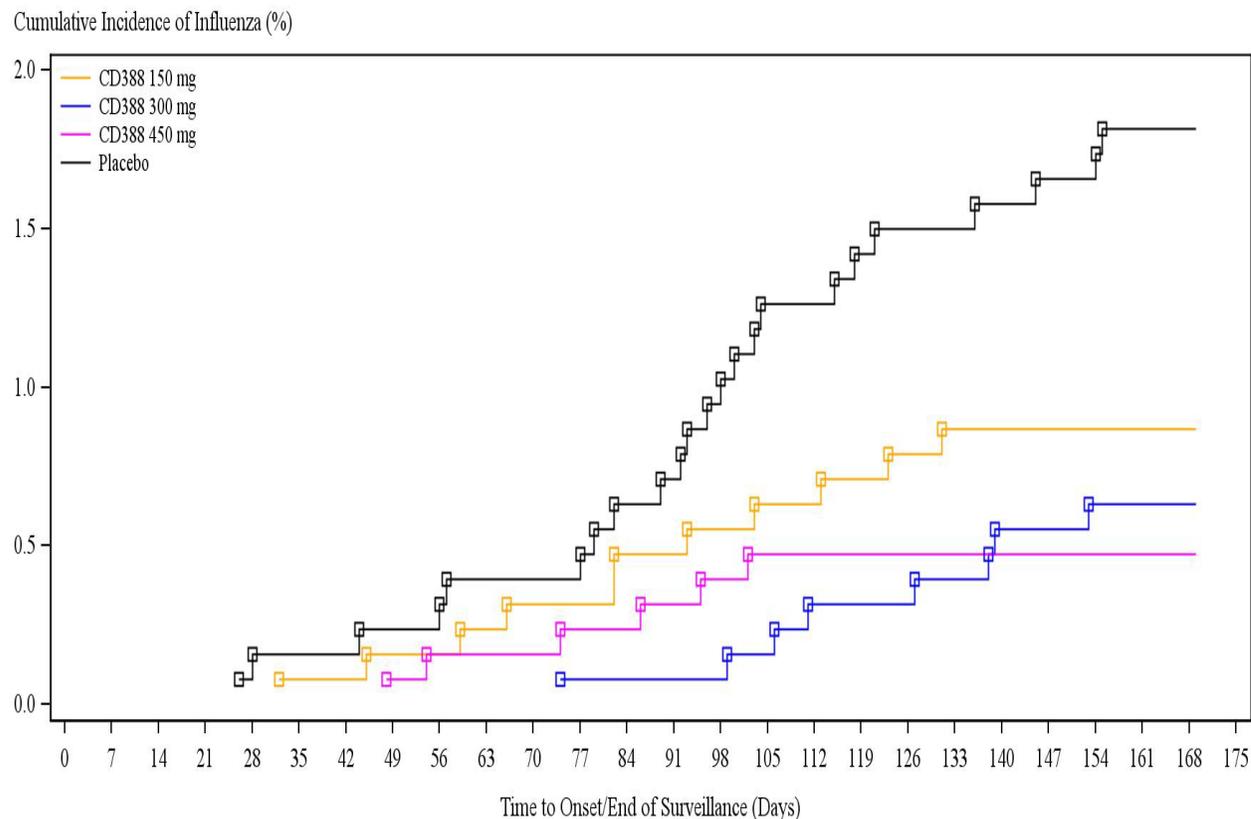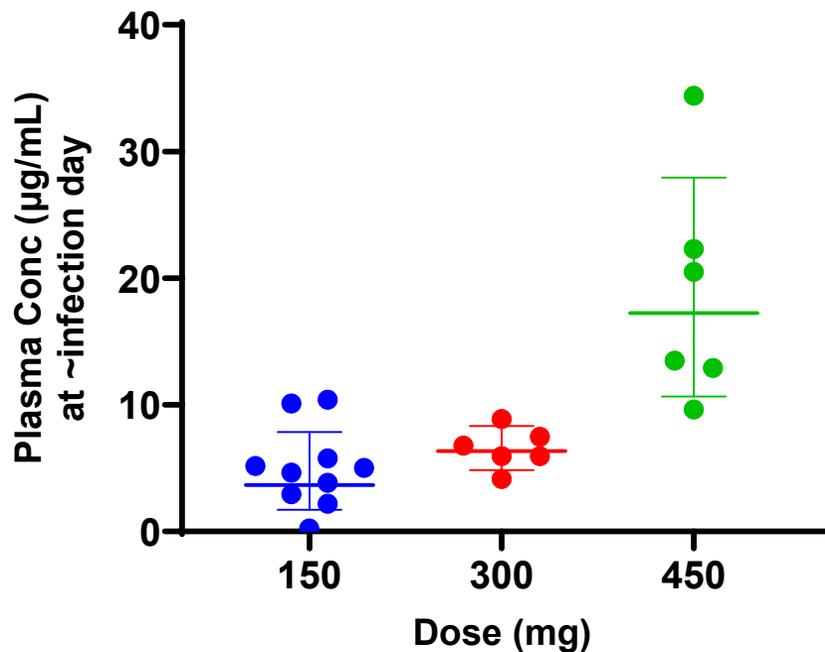
Exposure-Response (E-R) Model based on Logistic Regression

Clear E-R relationship for PCR+ and CD388 concentrations, i.e. lower CD388 concentrations are associated with higher # of ILI

Concentration effect observed for PCR+ and temp of **≥37.2°C**

Visual Predictive Check Plot

Low probabililty of PCR+ even at plasma concentrations <10 µg/mL

Proportions are plotted at the midpoint of each CD388 concentration interval.

Cumulative ILI for Primary Endpoint: Compelling 450 mg Profile

- Higher plasma conc at breakthrough infection for 450 mg vs lower doses
- No new infection beyond~100 days
- Could max preventive efficacy be limited to ~80%?

Thank You!