Data from Phase 1 and Phase 2a Studies of CD388, a Drug Fc-conjugate for Seasonal Pan-Influenza Prophylaxis

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ACKNOWLEDGMENTS

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*At the time when the study was conducted.

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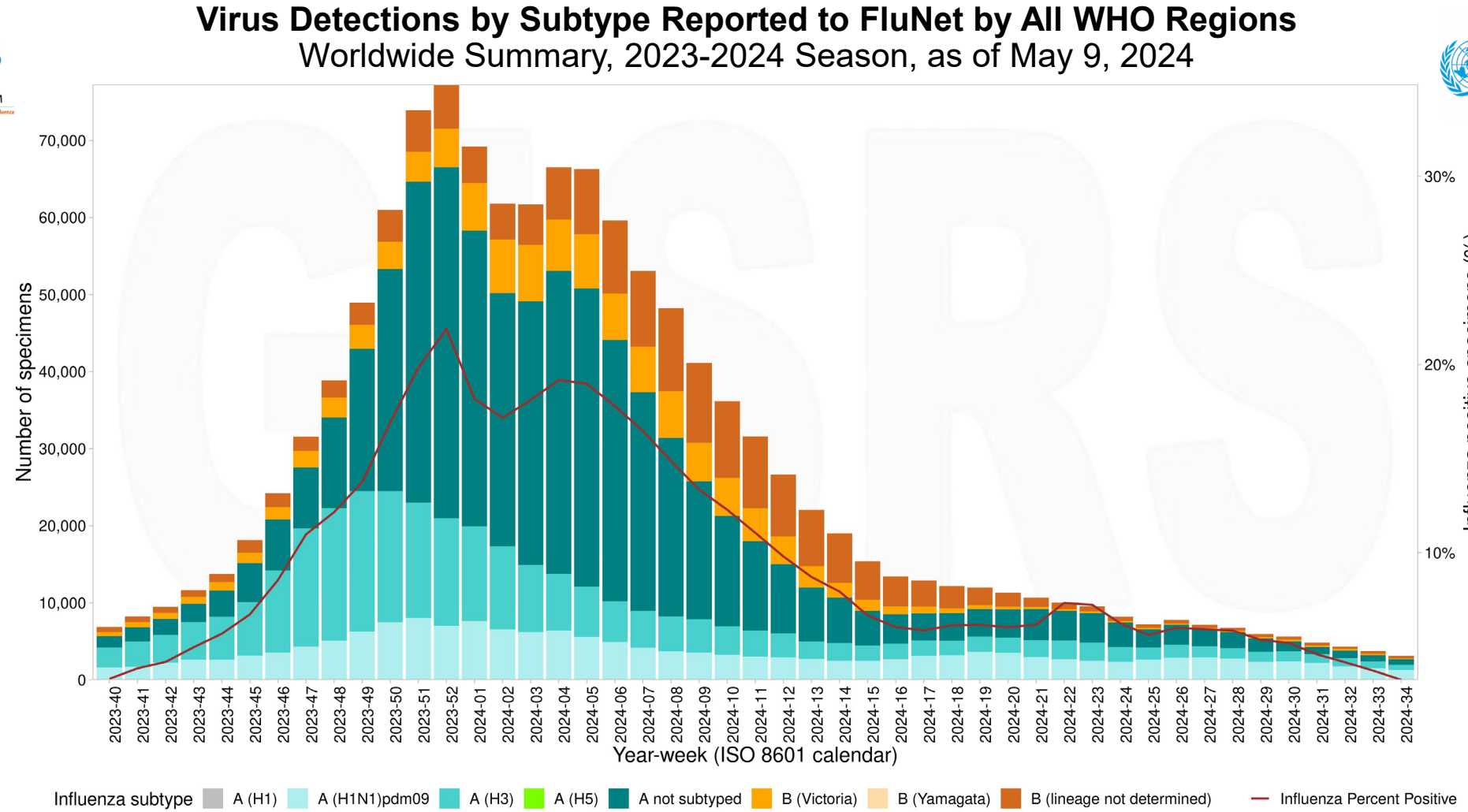
WHAT WILL THE 2024-2025 US INFLUENZA SEASON LOOK LIKE?

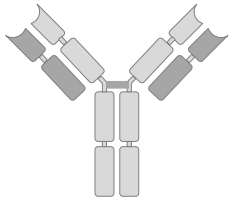
LIKE 2023-2024?



https://worldhealthorg.shinyapps.io/flunetchart/

LIMITATIONS OF CURRENTLY AVAILABLE INFLUENZA PROPHYLAXIS

- **Genetic diversity complicates prophylaxis**
  Vaccines unable to offer complete protection due to diversity between and within influenza types A and B
- **Animal-to-Human threats**
  Increasing concern that highly pathogenic avian strains (H7N9 and H5N1) may be transmitted to humans
- **High risk groups are growing and lack effective options**
  Immunocompromised (IC) individuals at risk for influenza-related complications, for example
  - Low/no vaccine efficacy against symptomatic influenza infection in IC[1,2]
  - Suboptimal antibody responses to influenza vaccines in IC
  - Immune responses to vaccine may not directly relate to vaccine effectiveness



Needs	Vaccines	Monoclonal Antibodies
Universal Protection	No	No
Potential to protect all high-risk groups	Low	High
Potential for dual prevention	Now	Limited

1.Kramer KH, et al. Human Vaccines & Immunotherapeutics. 2024 https://doi.org/10.1080/21645515.2024.2354013
2.Hughes K, et al. Clinical Infectious Diseases. 2021; 73: e4353.

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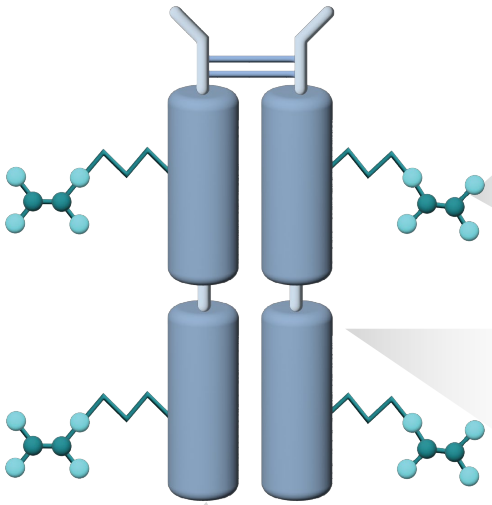
CIDARA'S RESPONSE TO THE CHALLENGES OF INFLUENZA

CLOUDBREAK DRUG-Fc CONJUGATEs (DFCs) – FUNDAMENTALLY DIFFERENT FROM ADCs AND mAbs

DRUG Fc CONJUGATE (DFC)



Small molecule Targeting Moiety (TM)

The strengths of mAbs with potential advantages

- *Efficient targeting of cryptic sites and small molecule receptors*
- *Tunable valency to exploit avidity for improved potency*
- *Multiple routes to low molecular weight multispecific agents*

Non-cleavable linker

No intracellular exposure → improved safety compared with small molecules

- *Greater freedom to optimize TMs for target potency*
- *Potential to inhibit "undruggable" targets*

Proprietary hIgG1 CH1-Fc hybrid domain

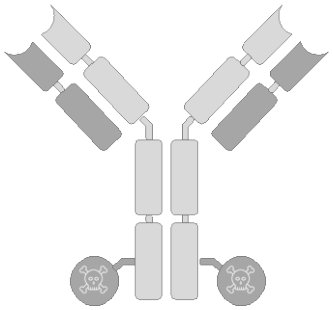
Multiple tunable attributes

- *Immune effector function*
- *Half-life extension*

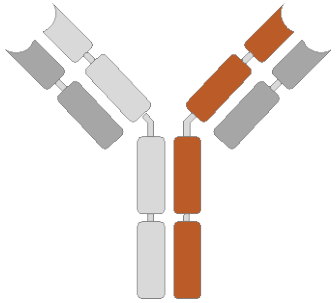
2.5x smaller than mAbs

- *Superior tissue/tumor penetration*

ADC



Bispecific mAb



ADC=antibody drug conjugate; DFC=drug Fc conjugate; mAb=monoclonal antibody.

Döhrmann S, et al. bioRxiv 2024.06.04.597465; doi: https://doi.org/10.1101/2024.06.04.597465.

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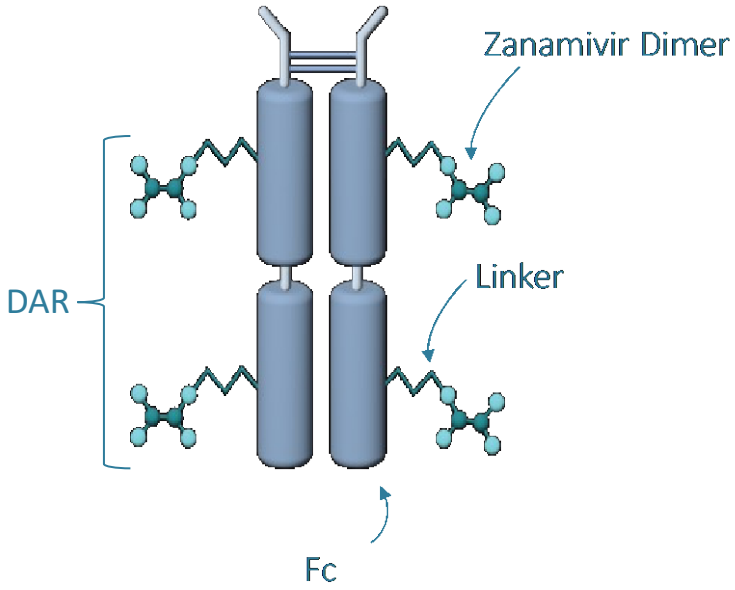
CD388: A DRUG-Fc CONJUGATE AGAINST INFLUENZA

CD388 is a multivalent conjugate of a dimeric zanamivir stably linked to a proprietary human IgG1 Fc fragment engineered for extended half-life



Nonclinical Efficacy and PK

- Potent in vitro and in vivo activity against all tested seasonal and pandemic strains of influenza A and B
- Maintains potency against NAI-resistant strains
- Similar exposure and protection via IV, SQ, or IM
- Equivalent protection in immune-competent and –compromised mouse models

Nonclinical Safety

- Doses up to 500 mg/kg in chronic toxicology studies
- No concerning findings in reproductive or genotoxicity studies

IM=intramuscular; IV=intravenous; NAI=neuraminidase inhibitor; SQ=subcutaneous.

Döhrmann S, et al. bioRxiv 2024.06.04.597465; doi: https://doi.org/10.1101/2024.06.04.597465.

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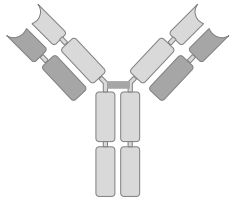
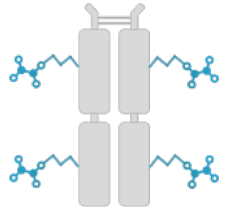
CD388: A DRUG-Fc CONJUGATE AGAINST INFLUENZA

IN DEVELOPMENT FOR SINGLE-DOSE, SEASONAL, BROAD INFLUENZA PROPHYLAXIS





Needs	Vaccines	Monoclonal Antibodies	CD388 DFC
Universal Protection	No	No	Yes
Potential to protect all high-risk groups	Low	High	High
Potential for dual prevention and treatment	Now	Limited	Yes

CD388 has the potential[1] for

- Universal protection
- Protection for immune-compromised individuals and other high-risk groups
- Dual prevention and treatment

DFC=drug-Fc conjugate.

1. Döhrmann S, et al. bioRxiv 2024.06.04.597465; doi: https://doi.org/10.1101/2024.06.04.597465.

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CD388 CLINICAL PROGRAM

Completed Phase 1 and Phase 2 Clinical Trials

	First in Human Study	Japanese Bridging Study	Human-Challenge Study
Phase	Phase 1	Phase 1	Phase 2a
Total Randomized	77 (56 active; 21 placebo)	28 (22 active; 6 placebo)	59 (30 active; 29 placebo)
Design	Randomized, double-blind, single-dose and repeat single dose, dose-escalation To determine safety, tolerability, and PK of CD388 IM or SQ administration in healthy subjects	Randomized, double-blind, single ascending dose study To determine safety, tolerability, and PK of CD388 SQ administration in healthy Japanese subjects	POC, randomized, double-blind, placebo-controlled To assess prophylactic activity against influenza, safety, tolerability, and PK of CD388 via human viral challenge model
Safety Evaluation	Double-blind assessment for injection site and systemic AEs, ECGs, vital signs, physical exam, laboratory evaluations (hematology, coagulation, chemistry, cardiac enzymes, urinalysis) Safety and respiratory tract infection surveillance in outpatient phase		Same as in Phase 1 studies, plus spirometry

AE=adverse event; US CDC=United States Centers for Disease Control and Prevention; ECG=electrocardiogram; IM=intramuscular; PK=pharmacokinetics; POC=proof-of-concept; SQ=subcutaneous.

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SAFETY POPULATIONS AND DURATION OF ASSESSMENT

Completed Phase 1 and Phase 2 Clinical Trials

STUDY	CD388 Study Dose and Route of Administration							Total CD388-Exposed Safety Population	Duration of Safety Assessment*
	50 mg		150 mg		450 mg		900 mg		
	SQ	IM	SQ	IM	SQ	IM	SQ		
First in Human	8	8	8	8†	8	8†	8	**56**	Inpatient discharge (Day 28), outpatient follow-up to Day 120 (50-mg cohort) OR Day 205±10 days following last dose† (150-mg, 450-mg, and 900-mg cohorts)
Japanese Bridging	7	–	8	–	7	–	–	**22**	Inpatient discharge (Day 28), outpatient follow-up to Day 120 (50-mg cohort) OR Day 165 (150-mg and 450-mg cohorts)
Human-Challenge	2	–	28	–	–	–	–	**30**	Started as inpatient at Day -5, H3N2 virus inoculation was on Day 0, discharge from quarantine on Day 8±1 day, final outpatient visit on Day 28±3 days, and final follow-up visit on Day 180±14 days

"–" dose/route of administration not part of the study.

*From signing of informed consent to end of study.

†150-mg and 450-mg SQ and IM cohorts received a second single dose approximately 5 half-lives after the 1st dose.

IM=intramuscular; PK=pharmacokinetics; SQ=subcutaneous.

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TREATMENT-EMERGENT ADVERSE EVENT DATA

First in Human Phase 1 Clinical Trial of CD388

TEAEs by Severity and Relatedness		Number of Unsolicited TEAEs (%)*		
			CD388	Placebo
Severity	Mild (Grade 1)		29 (52)	17 (41)
	Moderate (Grade 2)		4 (7)	3 (7)
	Severe (Grade 3)		0 (0)	1 (2)
Relatedness	Related IM 1st dose	50 mg	2 (25)	5 (56)
		150 mg	4 (50)	
		450 mg	3 (38)	
	Related IM 2nd dose	150 mg	0 (0)	2 (22)
		450 mg	2 (25)	
	Related SQ 1st dose	50mg	5 (63)	4 (33)
		150 mg	1 (13)	
		450 mg	0 (0)	
		900 mg	2 (25)	
	Related SQ 2nd dose	50mg	5 (63)	1 (8)
		150 mg	1 (13)	
		450 mg	0 (0)	
		900 mg	2 (25)	

*For severity, % = percent of all subjects in the given cohort

For relatedness % = percent of all TEAEs in the given cohort

IM=intramuscular; SQ=subcutaneous; TEAE=treatment-emergent adverse event.

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TREATMENT-EMERGENT ADVERSE EVENT DATA

Phase 1 Japanese Bridging and Phase 2a Human Challenge Clinical Trials

TEAEs by Severity and Relatedness		Number of Unsolicited TEAEs (%)*		
		CD388		Placebo
Japanese Bridging Study	**Severity** Mild (Grade 1)	16 (73)		2 (33)
	Related to Study Drug	50 mg	2 (29)	1 (50)
		150 mg	1 (33)	
		450 mg	0 (0)	
Human-Challenge Study	**Severity** Mild (Grade 1)	19 (63)		18 (62)
	Moderate (Grade 2)	3 (10)		2 (7)

No moderate (Grade 2), severe (Grade 3), or life-threatening (Grade 4) TEAEs

No severe (Grade 3) or life-threatening (Grade 4) TEAEs

No TEAEs related to study drug

*For severity, % = percent of all subjects in the given cohort; for relatedness % = percent of all TEAEs in the given cohort.

TEAE=treatment-emergent adverse event.

TREATMENT-EMERGENT ADVERSE EVENT DATA

From Completed Phase 1 and Phase 2 Clinical Trials of CD388

STUDY	Most Common Unsolicited TEAEs (System Organ Class)
First in Human	• Diarrhoea (Gastrointestinal Disorders) • Headache (Nervous System Disorder)
Japanese Bridging	• Constipation (Gastrointestinal Disorders) • Fatigue (General Disorders and Administration Site Conditions)
Human-Challenge	• Upper RTI (Infections and Infestations) • Headache • LFT out of range, T-wave inversion (Investigations)

LFT=liver function tests; RTI=respiratory tract infection; TEAE=treatment-emergent adverse event.

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SUMMARY OF CD388 SAFETY DATA

FROM COMPLETED PHASE 1 AND PHASE 2a TRIALS

- No treatment-emergent SAEs
- No discontinuation of study drug or withdrawals due to safety findings
- No consistent AE patterns
- No hypersensitivity reactions
- Most TEAEs Grade 1 (90%), few Grade 2 – All resolved
- Incidence of TEAE not dose dependent
- Few injection site events (pain, IM route mainly), Grade 1 – all resolved spontaneously; not considered related
- No clinically relevant ECG, vital signs or physical exam abnormalities
- No trends with abnormal hematology or chemistry findings

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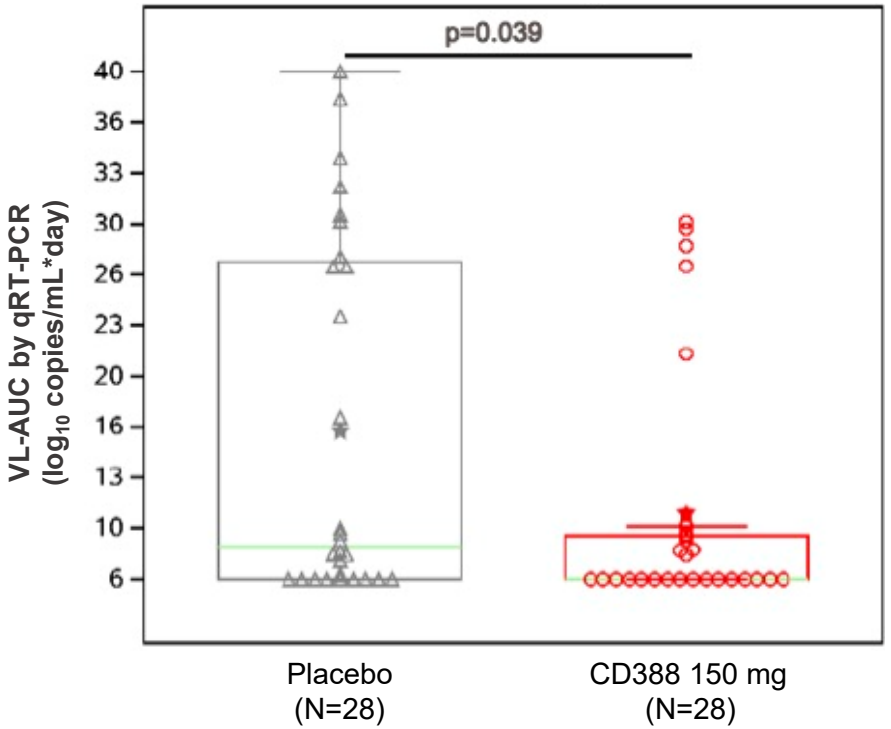
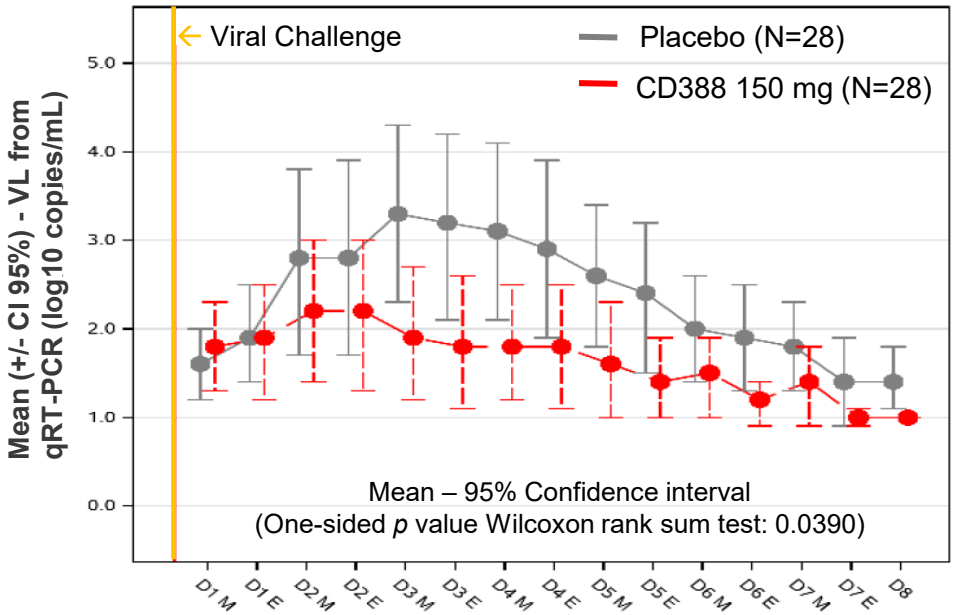
CD388 EFFICACY DATA – COMPLETED PHASE 2a TRIAL

One SQ dose of CD388 (150 mg) 5 days prior to viral challenge significantly reduced nasal viral load vs placebo

Primary Efficacy Endpoint:
Viral Load-AUC from qRT-PCR



Mean Viral Load from qRT-PCR Over Time



Rojas RE, et al. Presented at ESCMID Global 2024. Barcelona, Spain; April 27-30, 2024. Poster P0079.
Flanagan S, et al. Accepted for presentation at IDWeek 2024. Los Angeles, CA; October 16-20, 2024. Poster P-1104.

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CD388 PHASE 2b NAVIGATE CLINICAL TRIAL

A Double-Blind RCT of CD388 for Influenza Prophylaxis

Phase	2b
Design	**Blinded, randomized, controlled trial of CD388 or placebo administered as a single, SQ dose** at the beginning of the influenza season and followed for the entire influenza season to monitor for breakthrough cases of influenza, **to assess efficacy and safety of CD388 in prevention of influenza in subjects not at risk for influenza complications**
Primary Endpoint	To compare rates of laboratory-confirmed clinical influenza between different single doses of CD388 and placebo over an influenza season using CDC definition of influenza
Study Population	Generally healthy, unvaccinated adults not at risk of complications from influenza
Study Size	Target of 5000 across CD388 (150, 300, and 450 mg) and placebo group (1:1:1:1 randomization)
Study Sites	60 sites in the US; 1 site in the UK
First/Last Dosed	September 2024/November 2024

RCT=randomized controlled trial.

THANK YOU

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