CD388, a Novel Drug-Fc Conjugate (DFC), Demonstrates Prophylactic Activity in an Influenza Human Challenge Model

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IDWeek – Los Angeles Paper #573 October 19, 2024

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ACKNOWLEDGMENTS

We thank the study participants of the CD388 clinical trials for their contribution to this important field of research and development.

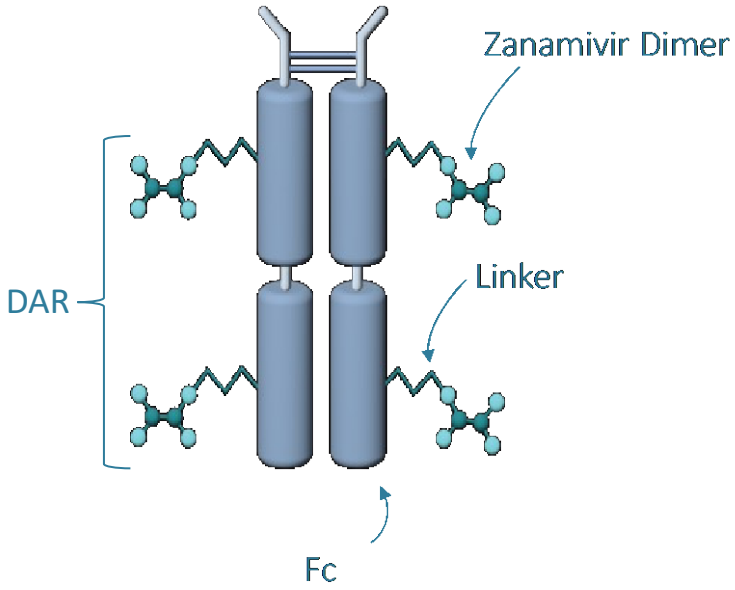
CONFLICTS OF INTEREST

All relevant financial disclosure have been mitigated.

[a]At the time when the study was conducted.

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

DAR=drug antibody ratio; 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 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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CD388 HUMAN CHALLENGE STUDY

METHODS

- Healthy participants (ages 18 to 55 years) randomized to receive SQ CD388 or placebo
- CD388 administered 5 days before intranasal challenge with A/Perth/16/2009 (H3N2)
- HAI assay performed at onset of quarantine, on Day 0 (prior to inoculation), and on Day 28
  - Confirmation of influenza infection by 4-fold increase in HAI titer (from Day 0 to Day 28)
- Participants completed a graded symptom scoring system 3x daily
  - Symptomatic influenza infection was defined as qRT-PCR-confirmed (2 quantifiable measurements on ≥2 independent samples over 2 days) or culture-confirmed (1 quantifiable TCID50 measurement) influenza infection from Day 1 (pm) to Day 8 (am) AND fever or ≥2 symptoms or any symptom of grade ≥2 at a single time point.
- Prophylactic efficacy was assessed among participants who experienced a 4-fold increase in HAI titer on Day 28

HAI=hemagglutinin inhibition assay; RT-PCR=quantitative reverse transcriptase-polymerase chain reaction; SQ=subcutaneous; TCID50=tissue culture infective dose (50%).

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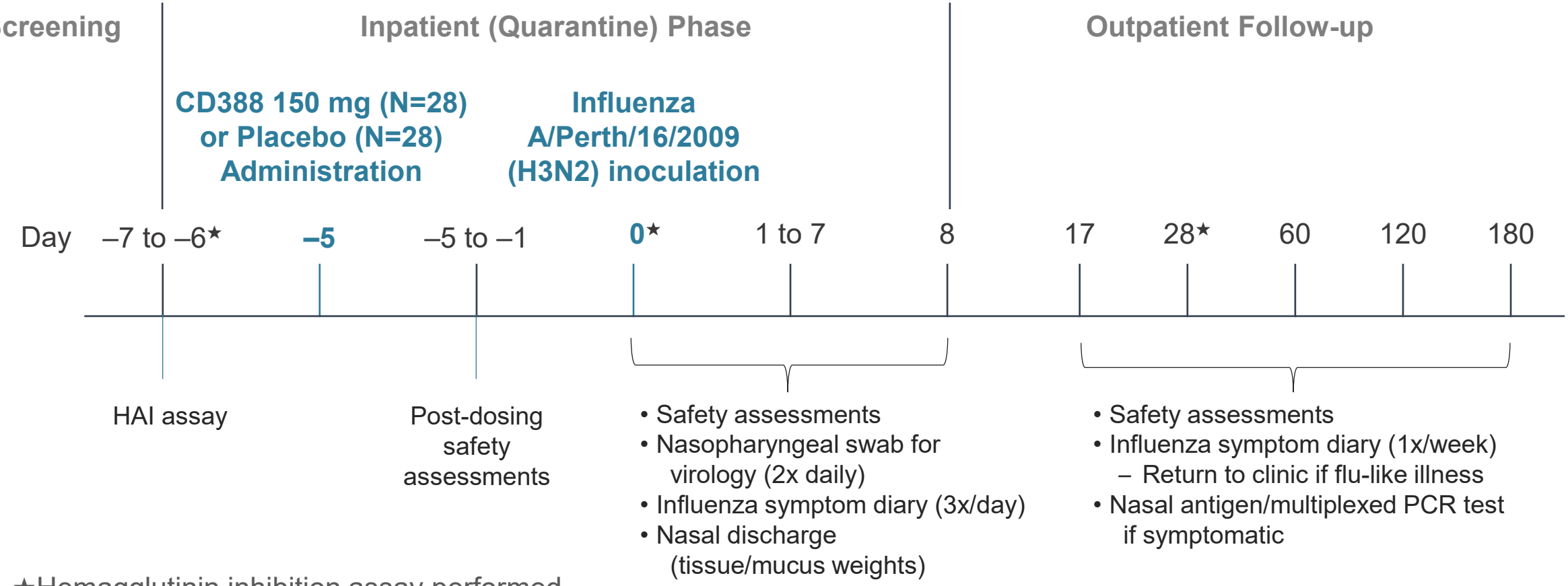
CD388 HUMAN CHALLENGE STUDY

STUDY SCHEMATIC

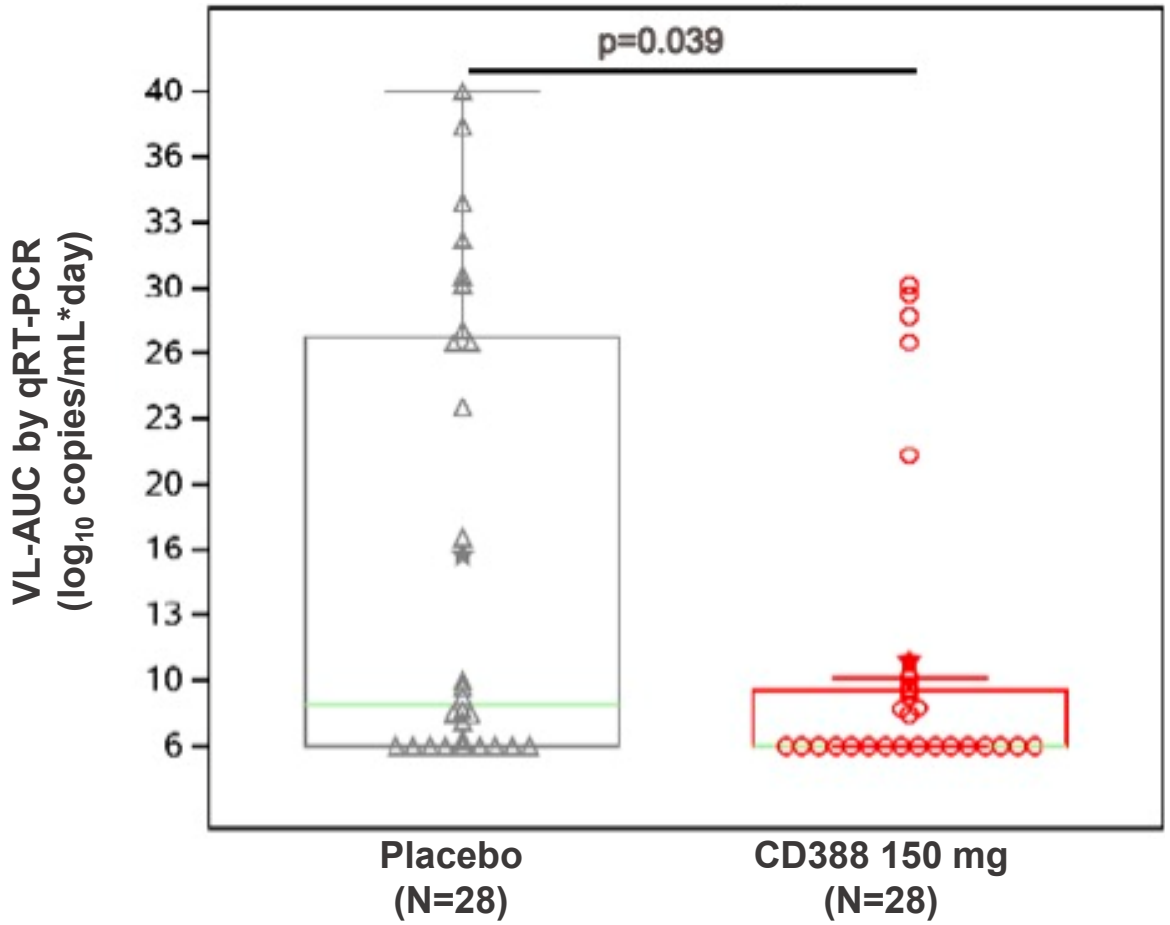


★Hemagglutinin inhibition assay performed.

HAI=hemagglutinin inhibition assay; PCR=polymerase chain reaction.

CD388 HUMAN CHALLENGE STUDY

PRIMARY EFFICACY ENDPOINT: VIRAL LOAD-AUC FROM qRT-PCR



One SQ dose of CD388 (150 mg)

5 days prior to viral challenge

significantly reduced nasal viral load vs placebo

Mean values indicated by star (★)

Median indicated by green line

AUC=area under the curve; qRT-PCR=quantitative reverse transcriptase-polymerase chain reaction.
Analyses of the Per Protocol analysis set (ie, all participants who were randomized, treated (with placebo or CD388), inoculated with virus, with valid results for at least 80% of the planned qRT-PCR in nasal samples from Day 1 to Day 8).

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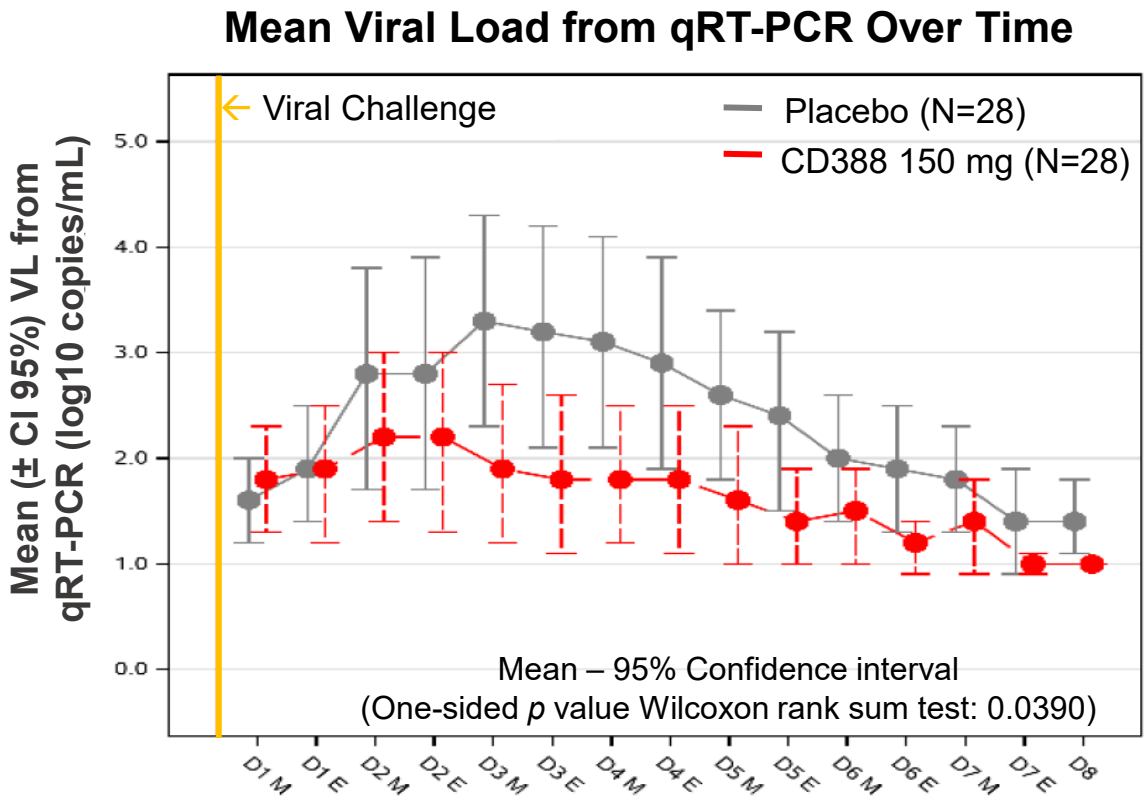
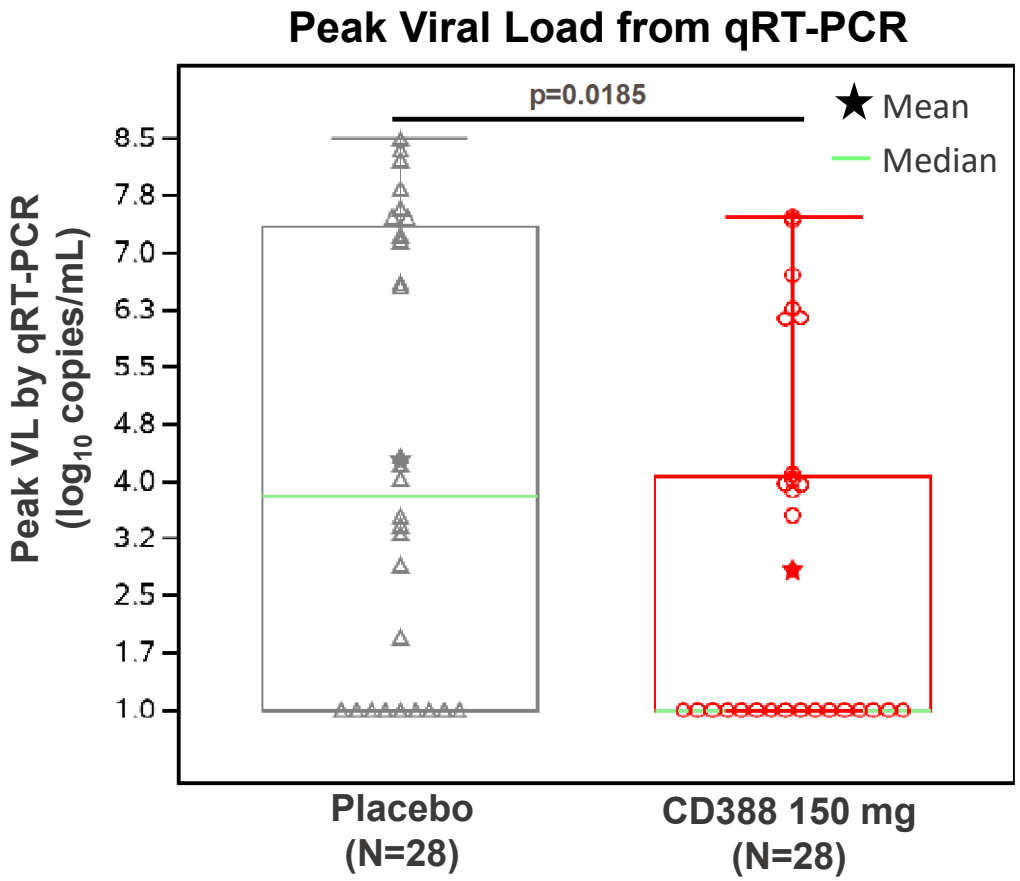
CD388 HUMAN CHALLENGE STUDY

EFFICACY RESULTS: VIRAL LOAD





qRT-PCR=quantitative reverse transcriptase-polymerase chain reaction; VL=viral load.
Analyses of the Per Protocol analysis set (ie, all participants who were randomized, treated (with placebo or CD388), inoculated with virus, with valid results for at least 80% of the planned qRT-PCR in nasal samples from Day 1 to Day 8).

CD388 HUMAN CHALLENGE STUDY

PROPHYLACTIC EFFECTIVENESS AGAINST SYMPTOMATIC INFLUENZA INFECTION

Endpoint	CD388 150 mg N=28	Placebo N=28
n/N (%) with 4-fold increase in HAI on Day 28	17/28 (60.7)	15/28 (53.6)
n/N (%) with 4-fold increase in HAI and with symptomatic influenza infection	3/17 (17.6)	9/15 (60.7)
VL-AUC in participants with 4-fold increase in HAI and symptomatic influenza infection, median TCID50 (min, max)	6.1 (3.3, 9.7)	10.8 (5.7, 17) p value=0.008

HAI=hemagglutinin inhibition assay; VL-AUC=area under the viral load–time curve; TCID50=tissue culture infectious dose 50%.

Analyses of the Per Protocol Analysis set (ie, all participants who were randomized, treated (with placebo or CD388), inoculated with virus, with valid results for at least 80% of the planned qRT-PCR in nasal samples from Day 1 to Day 8).

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EFFICACY RESULTS: INCIDENCE OF qRT-PCR–CONFIRMED INFLUENZA INFECTION

Endpoint	Incidence of Confirmed Influenza Infection, n (%)		p value[a] (Placebo vs CD388)
	CD388 150 mg N=28	Placebo N=28	
RT-PCR–confirmed influenza infection[b]	6 (21.4)	14 (50.0)	0.0248
RT-PCR–confirmed symptomatic influenza infection[c]	4 (14.3)	9 (32.1)	0.1023
RT-PCR–confirmed moderate to severe symptomatic influenza infection[d]	3 (10.7)	7 (25.0)	0.1477

[a]One-sided Fisher's exact test.
[b]RT-PCR–confirmed influenza infection: 2 quantifiable (≥lower limit of quantification [LLOQ]) qRT-PCR measurements (reported on 2 or more independent samples over 2 days), from Day 1 (pm) up to Day 8 (am).
[c]RT-PCR–confirmed symptomatic influenza infection: RT-PCR-confirmed influenza infection[b] AND symptoms ≥2 at a single time point.
[d]RT-PCR–confirmed moderate to severe symptomatic influenza infection: RT-PCR confirmed influenza infection[b] AND any symptoms of grade ≥2 at a single time point.

VL=viral load.
Analyses of the Per Protocol Analysis set (ie, all participants who were randomized, treated (with placebo or CD388), inoculated with virus, with valid results for at least 80% of the planned qRT-PCR in nasal samples from Day 1 to Day 8).

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CD388 HUMAN CHALLENGE STUDY

SAFETY RESULTS: TREATMENT-EMERGENT ADVERSE EVENTS

Treatment-Emergent Adverse Events (TEAEs)	Number of Participants with Unsolicited TEAEs (%)	
	CD388 150 mg N=28	Placebo N=29
Any Unsolicited TEAE	21 (75.0)	19 (65.5)
By Severity		
Mild (Grade 1)	18 (64.3)	18 (62.1)
Moderate (Grade 2)	3 (10.7)	2 (6.9)
Severe (Grade 3)	0	0
Life-threatening or Disabling (Grade 4)	0	0
Any Leading to Study Discontinuation	0	0
Any Related to Study Drug	0	0
Any Serious Adverse Event	0	0
Death	0	0

% = percentage of participants in the treatment group; TEAE=treatment-emergent adverse event.

Analyses of the Safety Analysis set (ie, all participants who received study intervention (placebo or CD388).

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CD388 HUMAN CHALLENGE STUDY

SUMMARY OF SAFETY

- No TEAEs related to study drug
- No treatment-emergent SAEs
- No discontinuation of study drug or withdrawals
- No consistent AE patterns
- No hypersensitivity reactions
- No clinically relevant ECG, vital signs or physical exam abnormalities
- No trends with abnormal hematology or chemistry findings

Most Common Unsolicited TEAEs[a] (System Organ Class)

- Upper RTI (Infections and Infestations)
- Headache (Nervous System Disorders)
- LFT out of range (Investigations)

AE=adverse event; ECG=electrocardiogram; LFT=liver function test; RTI=respiratory tract infection; SAE=serious adverse event; TEAE=treatment-emergent AE..
[a]Reported by more than 2 participants during the study in the Safety Analysis set (ie, all participants who received study intervention [placebo or CD388]).

CD388 HUMAN CHALLENGE STUDY

SUMMARY

- A single subcutaneous dose of CD388 (150 mg) 5 days prior to influenza viral challenge was well tolerated and effective in preventing symptomatic disease
- CD388 also showed
  - Statistically significant lower incidence of qRT-PCR–confirmed influenza infection vs placebo
  - Reductions in the incidence of qRT-PCR-confirmed symptomatic influenza infection and incidence of qRT-PCR-confirmed moderate to severe symptomatic influenza infection (not statistically significant)
  - Significantly reduced nasal viral load compared with placebo

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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
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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