Poster 361

NAVIGATE: A Phase 2b, Randomized, Double-blind, Placebo-controlled, Multicenter Dose-ranging Study to Evaluate the Efficacy and Safety of CD388, a Novel Long-acting Antiviral Conjugate, for Prevention of Influenza in Participants not at Risk for Influenza Complications

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INTRODUCTION

CD388 is a novel drug-Fc-conjugate (DFC) which arrays multiple copies of a novel dimeric presentation of zanamivir, the active ingredient of the FDA-approved drug Relenza®, on a proprietary human antibody fragment engineered for extended half-life (1).

CD388 has the potential to provide long-acting protection against influenza A and B following a single dose which would benefit high risk individuals known to have poor vaccine responsiveness (2,3), because the activity of CD388 does not rely on the human immune system as is the case with vaccines.

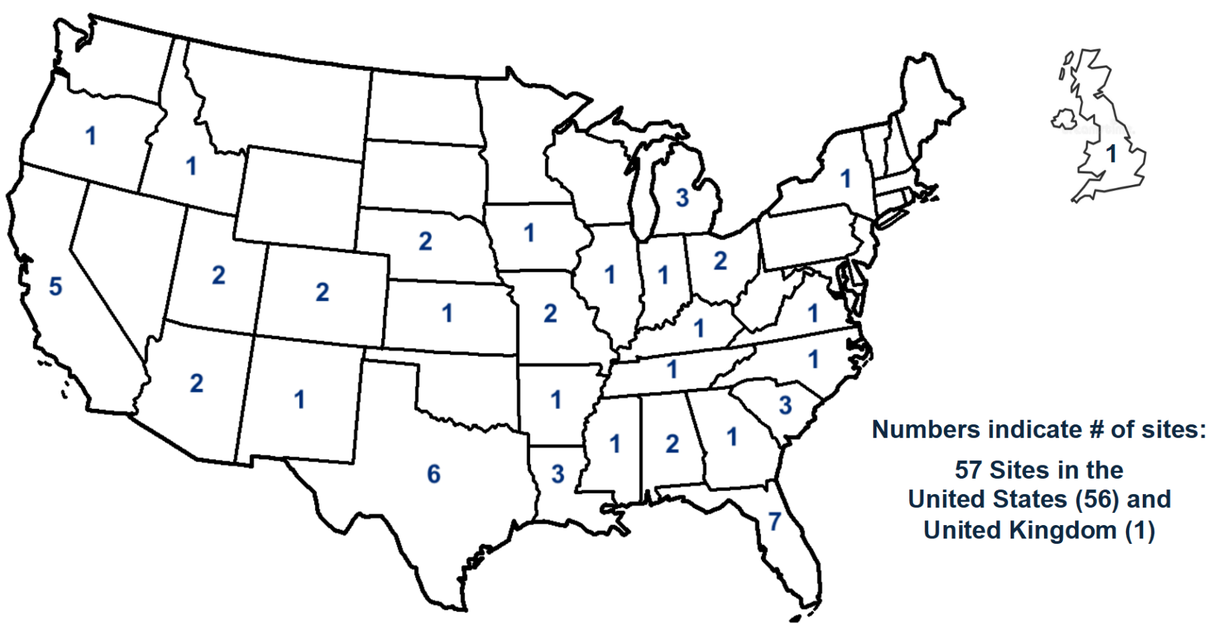
Assays for inhibition of viral neuraminidase (NA) determined that the median IC50s for CD388 was 1.29 nM against subtype A/H1N1 (n=17), 2.24 nM against subtype A/H3N2 (n=18), and 2.37 nM against influenza B (n=13). Activity of CD388 against recombinant NA from highly pathogenic avian influenza demonstrated an IC50 of 3.73 nM for A/H5N1 (n=1) and a median IC50 of 1.23 nM for A/H7N9 (n=2) (1).

Following completion of two Phase 1 studies and one Phase 2a human challenge study, the Phase 2b NAVIGATE trial of CD388 (NCT06609460) was initiated in the fall of 2024 in the Northern Hemisphere (NH) to evaluate the safety and preventive efficacy of CD388 in a target population of 5000 participants who had not received the current influenza vaccine.

METHODS

NAVIGATE is a double-blind, randomized, placebo-controlled trial of CD388 administered as a single subcutaneous (SQ) dose to participants who are followed for the entire influenza season to monitor for occurrence of symptomatic influenza infections. A total of 57 clinical sites (56 across 28 states in the US and one site in the UK) were recruited to conduct the trial (Figure 1). Healthy unvaccinated adults, aged 18 to <64 years, without identified risk factors for influenza complications, who provided informed consent, were screened and received a SQ dose of study drug on Day 1. Randomization was 1:1:1:1 to treatment with either CD388 150 mg, CD388 300 mg, CD388 450 mg, or placebo. The first participant was dosed on 20 Sep 2024 and the last participant was dosed on 06 Dec 2024. Thus, the majority of participants were dosed prior to the onset of the 2024-2025 NH influenza season.

Figure 1. Map of NAVIGATE Study Sites in the US and UK



Participants were provided with a thermometer, rapid tests for influenza, an electronic diary (eDiary), and were instructed to record any injection site reactions during the 1-week period after dosing and to monitor for acute respiratory infection (ARI) during the entire influenza season, recording data in the eDiary twice per week. Study site visits for follow-up safety evaluations were scheduled to occur on Day 8, Day 29, Day 85, and Day 197, with remote contact on Days 15, 57 and 169. If symptoms of ARI occurred at any time during the study, the participant enters the signs and/or symptoms in their eDiary (the ARI trigger). The study site then contacts the participant to schedule an in-clinic visit for evaluation if ARI is suspected. In-clinic evaluations included collection of a mid-turbinate (MT) nasal swab specimen for molecular assay for influenza and a nasopharyngeal (NP) swab specimen for central laboratory virologic analysis. Visits at the study site confirmed suspected ARIs.

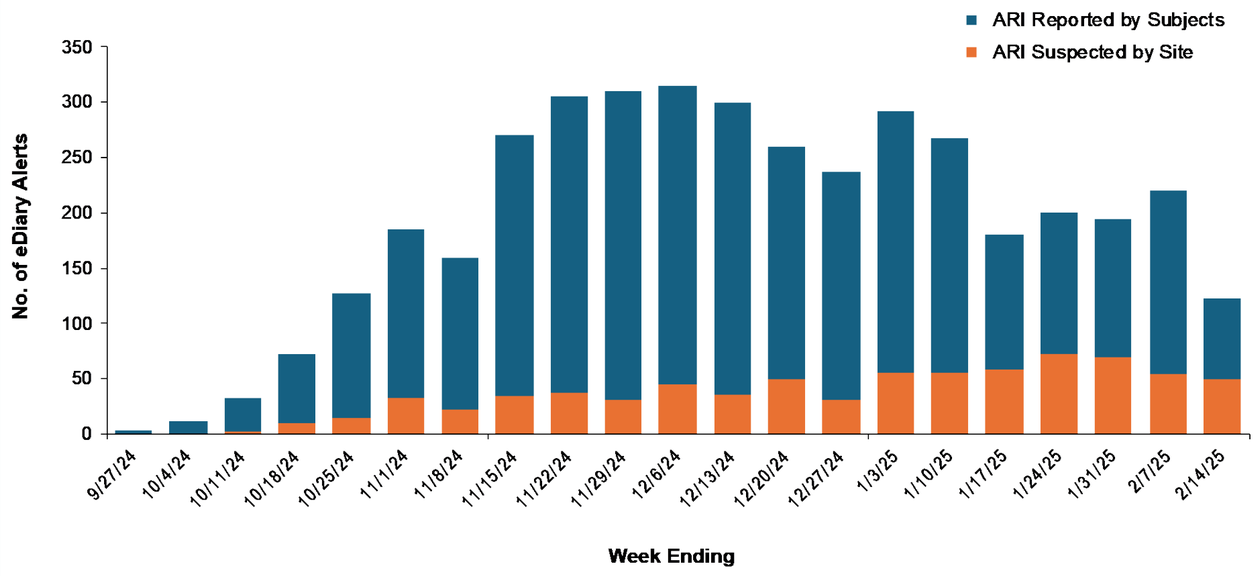
The study's primary endpoint consists of a composite of a positive RT-PCR for influenza A or B from a NP swab specimen, new onset of fever, and new onset of respiratory and/or systemic symptoms characteristic of acute influenza.

RESULTS

A total of 5040 participants received a single dose of study drug; 54% are female and 46% are male, with mean ages of 40.4 years and 38.7 years, respectively.

As of 14 February 2025, participants had triggered a total of 4066 eDiary ARI alerts. Figure 2 shows the incidence of ARI triggers by the participants and suspected ARIs (n=764) based on study site evaluations from the week ending 27 Sep 2024 through the week ending 14 Feb 2025.

Figure 2. Incidence of Acute Respiratory Infection (ARI) Alerts



Safety

Participants recorded injection site reactions (ISRs) in eDiaries during the 7 days following SQ administration of study drug. Based on preliminary data, a total of 3924 participants (77.8%) did not report any ISRs while 22.2% (1116 of 5040 participants) recorded at least one ISR. Table 1 shows the highest severity of the four types of ISRs entered by the 1116 participants who recorded ISRs.

Table 1. ISRs By Severity among the 1116 Participants with ISRs

Type of ISR (Any ISR: 1116/5040 [22.2%])	Number of Participants (%)[a]		
	Mild	Moderate	Severe
Pain	416 (8.3)	41 (0.8)	4 (0.08)
Tenderness	604 (12)	96 (1.9)	8 (0.16)
Erythema	331 (6.6)	65 (1.3)	5 (0.1)
Induration	219 (4.3)	27 (0.5)	2 (0.04)

ISR = Injection Site Reaction.
[a]Percentages are based on a denominator of 5040 participants; 480 participants reported more than one symptom.

As of 14 Feb 2025, a total of 237 participants (4.7%) have been discontinued from the study for the following reasons: lost to follow-up (n=113), participant election (n=99), other* (n=10), unable to comply (n=8), investigator decision (n=4), and adverse event (n=3). (*clarification in progress)

CONCLUSIONS

A robust 2024-2025 NH influenza season, together with the collaboration of 57 investigators in the US and UK, has provided the opportunity to critically evaluate the safety and preventive efficacy of CD388 in a real-world environment.

Preliminary data show that study drug administered by SQ injection appeared well-tolerated with 22.2% of participants reporting ISRs with the majority characterized as mild in severity.

Data outputs from this trial, available in the fall of 2025, will inform critical data points including dose selection for the planned Phase 3 development program for CD388. The target populations for this novel long-acting antiviral conjugate are individuals known to be at risk for complications of influenza.

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