CD388 Demonstrates a High Barrier to Resistance and Retains Potent Activity against NAIR Influenza A and B Variants

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Disclosures

Current employee and stockholder of Cidara Therapeutics, Inc.
Influenza Causes Unacceptable High Levels of Disease Burden

Estimated U.S. Influenza Burden, By Season (2010 - 2020)

- Deaths
- Hospitalizations
- Illnesses

https://www.cdc.gov/flu/about/burden/index.html
Influenza Drugs for the Treatment and Prevention of Influenza

TREATMENT

PREVENTION

UNIVERSAL COVERAGE

LIMITED COVERAGE
Influenza Drugs for the Treatment and Prevention of Influenza

Small Molecules

UNIVERSAL COVERAGE

LIMITED COVERAGE

TREATMENT

PREVENTION
Influenza Drugs for the Treatment and Prevention of Influenza

**TREATMENT**

- **UNIVERSAL COVERAGE**
  - Small Molecules

- **LIMITED COVERAGE**

**PREVENTION**

- Vaccines
Anti-influenza mAbs are not FDA-approved, but currently in Clinical Development
Unmet Need for Long-Acting, Universal Agent for Influenza Prevention

Anti-influenza mAbs are not FDA-approved, but currently in Clinical Development.
Unmet Need for Long-Acting, Universal Agent for Influenza Prevention

Anti-influenza mAbs are not FDA-approved, but currently in Clinical Development
CD388 is in Clinical Development* for the Prevention of Influenza

CD388 development under exclusive, worldwide license with Janssen Pharmaceutical

Multivalent presentation of a novel, dimeric NAI

Fc fragment is engineered for PK extension

* Phase 1: NCT05285137 and Phase 2a: NCT05523089
Why Was a NAI Selected for the Design of CD388?

- NA is essential for viral replication cycle
- Positive correlation of anti-NA titers with protection against influenza\(^1\)
- Low frequency of NAI\(^R\) variants observed clinically (<1%)\(^2\)
- NA has a highly conserved active-site across influenza A and B that Small molecule NAIs specifically target (‘universal coverage’)

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1 Maier et al. Pre-existing Ant-ineuraminidase Antibodies Are Associated With Shortened Duration of Influenza A(H1N1)pdm Virus Shedding and Illness in Naturally Infected Adults. Clin Infect Dis. 2020 May 23;70(11):2290-2297. PMID: 31300819; PMCID: PMC7245146; Memoli et al. Evaluation of Antihemagglutinin and anti-NA Antibodies as Correlates of Protection in an Influenza A/H1N1 Virus Healthy Human Challenge Model PMID: 27094330

CD388 is Differentiated from Small Molecule NAIs and Demonstrates Universal Activity against Influenza A and B

Cell-Based Cytopathic Effect Assays
CD388 is Differentiated from Small Molecule NAIs and Demonstrates Universal Activity against Influenza A and B

Cell-Based Cytopathic Effect Assays

CD388 administered as a single dose at 1 mg/kg or lower conferred full protection against numerous NAI-sensitive influenza A and B viruses in lethal mouse models.
What is the Resistance Potential of CD388?

CD388 Serial Passage Methodologies: Static, sub-inhibitory and dose-escalating
CD388-Selected Variants Were Identified at Position 246 in NA

*ZAN interaction with NA from A/H1N1*
CD388-Selected Variants Remain Susceptible to CD388

Cross-resistance in Cell-Based Plaque Reduction Assays

<table>
<thead>
<tr>
<th>Influenza virus</th>
<th>NA genotype</th>
<th>CD388</th>
<th>OST</th>
<th>ZAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/WSN/1933 (H1N1), p0</td>
<td>S246¹</td>
<td>0.09</td>
<td>---</td>
<td>80.1</td>
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<tr>
<td>A/WSN/1933 (H1N1), p10</td>
<td>S246R</td>
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<tr>
<td>A/Victoria/3/75 (H3N2), p10</td>
<td>A246V</td>
<td>4.58</td>
<td>2.8</td>
<td>9.02</td>
</tr>
</tbody>
</table>

¹AA numbering based on N2
Is CD388 Active against NAI<sup>R</sup> Variants?

NA inhibition Assays
## CD388 Retains Potency against NAI<sup>R</sup> Variants

### NA Inhibition Assays

<table>
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<tr>
<th>Influenza virus</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IC&lt;sub&gt;50&lt;/sub&gt; [nM]</td>
<td>Fold-change</td>
<td>IC&lt;sub&gt;50&lt;/sub&gt; [nM]</td>
</tr>
<tr>
<td>A/Illinois/45/2019 (H1N1)</td>
<td>H275</td>
<td>1.30</td>
<td>---</td>
<td>0.33</td>
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<tr>
<td>A/Alabama/03/2020 (H1N1)</td>
<td>H275Y</td>
<td>0.98</td>
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<td>B/Laos/0080/2016</td>
<td>H134</td>
<td>7.44</td>
<td>---</td>
<td>33.35</td>
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<tr>
<td>B/Laos/0654/2016</td>
<td>H134N</td>
<td>4.66</td>
<td>1</td>
<td>171.8</td>
</tr>
</tbody>
</table>

Source: IRR, Cat#FR-1755 CoA 70037427 NI=Normal inhibition (<10-fold vs influenza A virus (IAV)/<5-fold vs influenza B virus (IBV) above NI), RI = reduced inhibition (10 - 100-fold vs IAV/5 - 50-fold vs IBV above NI), HRI = highly reduced inhibition (>100-fold vs IAV/>50-fold vs IBV above NI)
ZAN is Protective against ZAN$^S$ Strain in Lethal Mouse Model

ZAN dosed IN starting t+2h post-infection (QD x 5)
ZAN has 10x Reduced Efficacy against a ZAN\textsuperscript{R} Variant in Lethal Mouse Model

ZAN dosed IN starting t+2h post-infection (QD x 5)
CD388 Demonstrates Efficacy with Single, Low Dose against ZAN\textsuperscript{S} Strain in Lethal Mouse Model

*Single IM dose at t+2h post-infection*
CD388 Demonstrates Unchanged Efficacy against a ZAN\textsuperscript{R} Variant in Lethal Mouse Model

Single IM dose at t+2h post-infection
CD388 Demonstrates Unchanged Efficacy against ZAN$^R$ Variant in Lethal Mouse Model

*Single IM dose at t+2h post-infection*

CD388 Retains Activity against Multiple H275Y Variants in A/H1N1 background in Lethal Mouse Models (not shown)
Summary

- CD388 demonstrates universal activity against influenza A and B
- CD388 demonstrates a high-barrier to resistance in serial passage experiments and retains potency against CD388-selected variants
- CD388 retains potent activity against the CDC panel of NAI^R influenza variants
- CD388 protective doses in lethal mouse models are identical against NAI^S and NAI^R influenza variants
CIDARA THERAPEUTICS ANNOUNCES PROMISING INTERIM PHASE 2A DATA ASSESSING THE SAFETY AND EFFICACY OF A SINGLE DOSE OF CD388 IN AN INFLUENZA CHALLENGE MODEL

March 1, 2023

- A single dose of CD388 decreased influenza viral replication in the upper respiratory tract and lowered influenza incidence rate in a human challenge model when compared to placebo.
- CD388 was generally safe and well tolerated with no adverse events related to study drug reported as of the February 13, 2023 data cut-off.
- Ongoing study being conducted in collaboration with Janssen.

SAN DIEGO, March 01, 2023 — Cidara Therapeutics, Inc. (NASDAQ: CDTX), a biotechnology company developing long-acting therapeutics designed to help improve the standard of care for patients facing serious diseases, today announced promising efficacy and safety data from a planned interim analysis of the ongoing Phase 2a trial evaluating...
Acknowledgements

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