Improving the Development Pipeline for Influenza Antivirals

BARDA Industry Day
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BARDA
Influenza Antivirals: The Challenge

- We need new options to address pandemic threats
  - Current therapies have a narrow treatment window
    - Treatment within 48h of symptom onset for neuraminidase inhibitors
  - Currently approved therapies under constant threat of resistance
    - Value of M-2 blockers minimized by resistance
    - Heavy reliance on neuraminidase inhibitors
    - No combination therapies available
  - Limited options in U.S. for special populations
    - No IV formulations approved
    - No drugs approved for severely ill, hospitalized patients
    - Limited treatment options for pediatric patients
  - No broad spectrum treatment options for influenza and other emerging diseases suitable for community use
The Influenza Resistance Issue

H1N1 Resistance to Oseltamivir

% Resistance

Influenza Season


NAI Activity Against H7N9*

<table>
<thead>
<tr>
<th>Virus</th>
<th>Genotype</th>
<th>Neuraminidase IC₅₀ (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Oseltamivir</td>
</tr>
<tr>
<td>A/Anhui/1/2013 WT</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>A/Shanghai/1/2013 R292K</td>
<td></td>
<td>4987</td>
</tr>
</tbody>
</table>

New Mechanisms of Action For Influenza Antivirals

Figure adapted from Neuman et al (2009) Nature 459:931

# Influenza Antiviral Landscape

<table>
<thead>
<tr>
<th>Pre Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Market Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adamantanes</strong></td>
<td><strong>Flunadine</strong> (Rimantadine)</td>
<td><strong>Symmetrel</strong> (Amantadine)</td>
<td><strong>biota</strong></td>
<td><strong>Laninamivir</strong></td>
</tr>
</tbody>
</table>

## NA Inhibitors
- **Tamiflu**
- **Inavir**

## Viral Targets
- **Sea Lane**
- **AO8**
- **MAb-HA**
- **Sea Lane**
- **CT120/CT149**
- **Mab HA**
- **TCN-032**
- **MAB-M2e**
- **TCAD Combo**
- **T-705 (Pol in)**

## Host Targets
- **Surfaxin**
- **NTHI**
- **pro-imf**
- **Neumopera (Neurokinin-1)**
- **purmatrix**
- **PUR003**
- **EVOLVA**
- **EV-077**
- **Ansun BioPharma**
- **Fludase**
- **Nitazoxanide**

Updated: 09/12/2013
BARDA Influenza Antiviral Program
Advanced Development: Status

BARDA Advanced Development Projects – Neuraminidase Inhibitor class

• BioCryst Pharmaceuticals – Development of peramivir
  • Development of IV peramivir in hospitalized patients
  • First investigational drug authorized for use under an EUA (2009 H1N1 pandemic)

• Biota Pharmaceuticals – Development of laninamivir
  • Single-dose treatment
  • Development of inhaled laninamivir for uncomplicated influenza

BARDA BAA Awards – New antiviral classes

• Ansun Biopharma - Development of Fludase (DAS-181)
  • Recombinant protein containing sialidase
  • Supported Phase 2b study in acute, uncomplicated influenza

• Romark Laboratories - Development of nitazoxanide
  • Broad-spectrum antiviral targeting host functions effecting viral replication
  • Supporting pivotal phase 3 study in acute, uncomplicated influenza
Current Broad Agency Announcement (BAA)
Area of Interest #4: Influenza Therapeutics

• Targeted Projects for Advanced Development
  — IND for Influenza indication
  — Phase I trial completed

• Antiviral Therapeutics for Treatment of Influenza Infection
  — Therapeutics with novel mechanism of action
    • Viral targets other than neuraminidase or M2
    • Host targets that reduce viral replication and ameliorate symptoms
  — Small molecules, monoclonal antibodies, therapeutic proteins, peptides, oligonucleotides, etc. would be considered
  — MOA precludes rapid emergence of resistance preferred
  — Broad-spectrum antiviral activity preferred
  — Development of combination therapeutics
    • Clinical trials combining novel and approved antivirals
What Can BARDA Offer?

In addition to funding BARDA can offer:

— Clinical trial expertise including a clinical trial network
— Manufacturing expertise and facilities
— Regulatory expertise
— Virology expertise
— Drug development expertise
— Interagency network of contacts
BARDA Influenza Antiviral Program: Vision for the Future

- A portfolio of products for treatment and prevention of influenza disease, including those:
  - Suitable for use in pediatric populations
  - Effective in hospitalized, severely ill patients
  - Effective in an expanded treatment window
  - With greater impact in changing trajectory of influenza illness
  - Effective for treatment of other viral illnesses, including those caused by emerging diseases
Questions?