



United States Department of

Health & Human Services

Office of the Assistant Secretary for Preparedness and Response (ASPR)



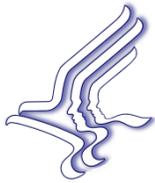
Advanced Development of New Influenza Antivirals

Biomedical Advanced Research and Development Authority (BARDA)

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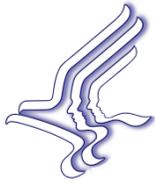
HHS/ASPR/BARDA



Integrated Portfolio Approach: Pandemic Influenza



	Vaccines	Antivirals	Diagnostics/ Respiratory Devices
Advanced Development	Cell-based, Antigen-sparing, Recombinant, Manufacturing Initiative	New Antiviral Drugs RFP I & II	<u>Diagnostics</u> Point of Care; Clinical Lab Next Generation <u>Ventilators</u>
Stockpiling & Acquisitions	H5N1 Pre-Pandemic Vaccine, Adjuvants, & H1N1 Response	Federal & State Stockpiles IV Antivirals: EUA	Masks & Respirators
Infrastructure Building	Egg-based Supply Retrofit Mfg Facilities New Mfg Facilities International Mfg Facilities		

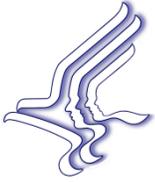


Antiviral Drugs in Pandemic Preparedness



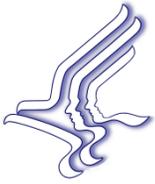
Antiviral drugs are an essential element in pandemic influenza preparedness:

- Can be deployed immediately
- Can have broad spectrum benefit against virus strains
- Can be used for treatment as well as prophylaxis
- Can be used in prophylactic fashion to help to safeguard health of first responders and critical workforce
- Can be used in cases where vaccination is not possible or is likely to be ineffective



Influenza Antiviral Drugs

- Current approved antiviral drugs
 - Oseltamivir (Tamiflu®) – available only as an oral formulation (capsules or suspension). Adult and pediatric dosing.
 - IV advanced development currently in Phase 2
 - No IV treatment courses available
 - Zanamivir (Relenza®) – available only as a powder for inhalation
 - IV advanced development currently in Phase 2
 - Laninamivir (Inavir) and IV peramivir (Rapiacta) - Japan
 - Adamantanes (resistance widespread)
- IV antiviral drug in advanced development (BARDA-supported)
 - Peramivir – currently in Phase 3 trial in the US at 600 mg dose
 - Approved in Japan by Shionogi at 600 mg dose (single-dose)
 - 11K 5-day treatment courses purchased by USG in 2009 for use under EUA



Components of Antiviral Program

- Federal stockpile – Tamiflu®, Relenza®, IV peramivir
- State stockpile – Tamiflu®, Relenza®
- Advanced development
 - BioCryst – intravenous peramivir (NA inhibitor)
 - Biota – inhaled laninamivir (NA inhibitor)

Implementation of goal 6.1.17.2 in *National Strategy for Pandemic Influenza* “HHS shall collaborate with the pharmaceutical, medical device and diagnostics industry to accelerate development evaluation, and licensure of new antiviral drugs...”

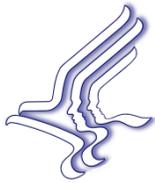


Goals of Antiviral AD Program



Identify and support advanced development of new antivirals that:

- Address currently unmet medical needs
 - Treatment of severely ill, hospitalized patients
 - Treatment of special subpopulations/age groups
 - Simplify the dosing/administration to increase use and compliance
- Target novel mechanisms of action
- Can be used in combination with treatments
- Address issues of drug resistance
- Address FDA guidance requirements for efficacy

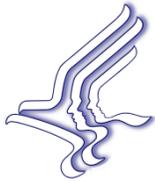


BioCryst Pharmaceuticals- IV Peramivir



Project for advanced development of antivirals to treat severely ill, hospitalized patients

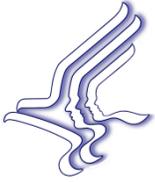
- Peramivir is a neuraminidase inhibitor in advanced development for treatment of acute, complicated cases of influenza in hospitalized settings
- Initial contract awarded in Jan 2007 for \$102.6M for advanced development of peramivir (Additional funds awarded in 2009 and 2011). Total financial support \$245M.
- Planned completion of pivotal Phase 3 clinical trial during 2012-13 Northern Hemisphere influenza season
- Submission of NDA anticipated in 4Q2013 to support indication approved for treatment of hospitalized patients with influenza
- Emergency Use Authorization (EUA)
 - Interagency collaboration to facilitate the EUA issuance and use of IV peramivir for 2009 H1N1 pandemic



Biota – CS8958



- **Project for advanced development of antivirals with single dose, long-lasting effectiveness**
- CS8958 (Laninamivir) is a neuraminidase inhibitor in advanced development for treatment of acute, uncomplicated cases of influenza
- Long duration of action (“one and done” dosing)
- Simple to use delivery device, improves compliance
- Effective against oseltamivir-resistant influenza strains
- Excellent clinical safety profile
- Approved in Japan for single-dose treatment of influenza in adults and children
- Contract awarded in 2011 for advanced development (\$231M)



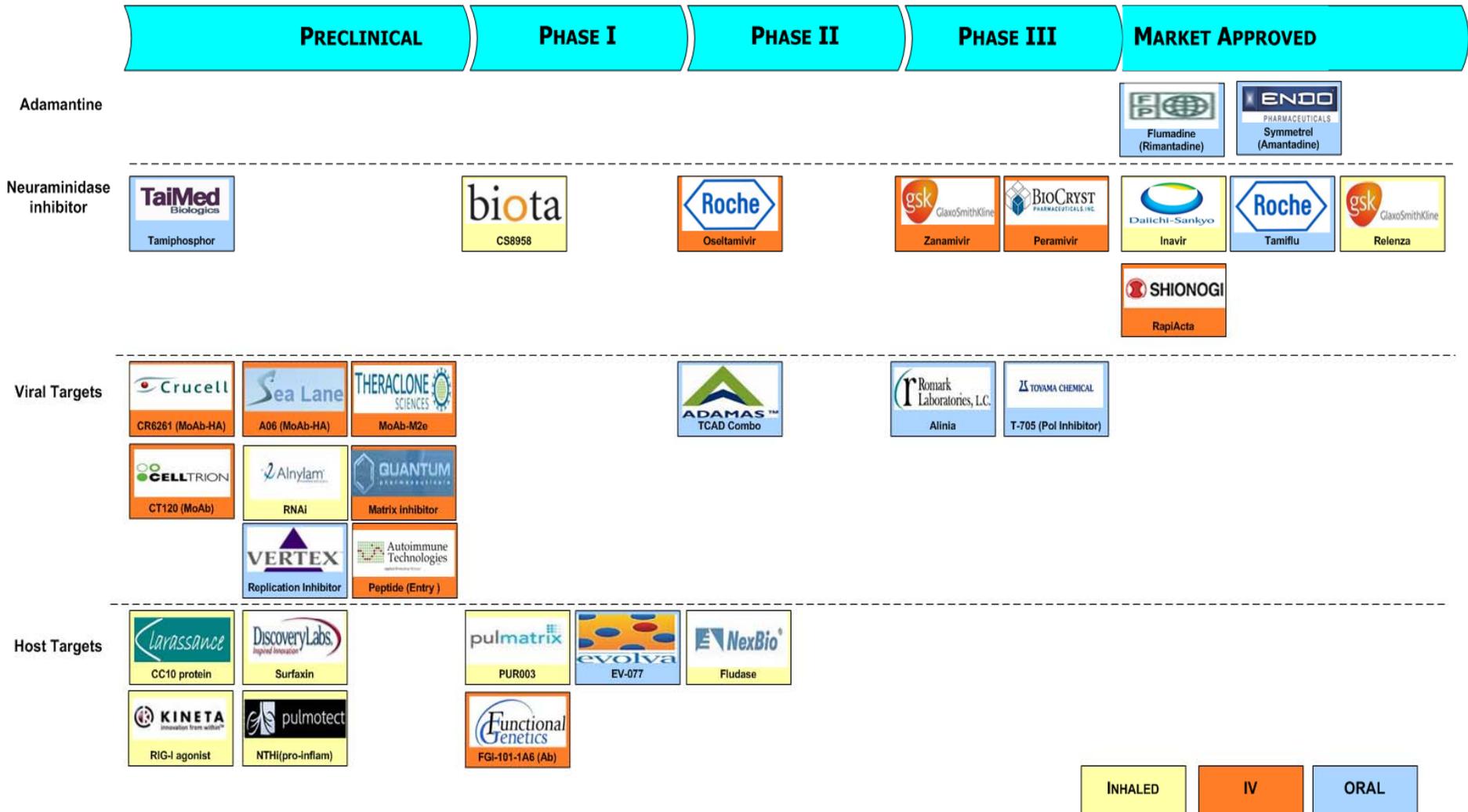
Future Directions

Support advanced development of new antivirals and approaches with improved pharmacological attributes

- Novel targets / mechanism of action
- Improved ease of administration
- Combination therapies
- Peptides, small molecule or immunomodulatory therapeutics with novel mechanisms of action, enhanced shelf life or other innovative formulations
- Ancillary activities such as animal models, surrogate endpoints, innovations in clinical studies



Influenza Antiviral Technology Landscape (05/2011)

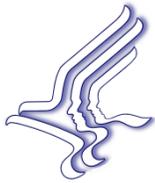




Summary



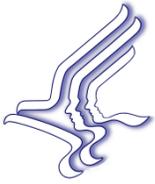
- Antiviral drugs for influenza are an essential component of pandemic preparedness
- Gaps remain in the portfolio for drugs to address unmet medical needs
- Concerns about drug resistance necessitate the development of newer, better drugs
- A number of drug candidates, including “first-in-class”, focusing on novel viral and cellular targets, are in early stages of development
- The approval of better drugs, or existing drugs that can be used in combination, will depend on clear clinical/regulatory pathways with defined endpoints



Antiviral Advanced Development Program



- BARDA's advanced development program drives innovation to address unmet medical needs and provide alternatives and improvements to currently approved antivirals
- BARDA's advanced development program leadership enabled the first EUA issued for an unapproved drug – IV peramivir
- In collaboration with the CDC, BARDA surpassed the NSPI antiviral stockpile goal to protect US population
- BARDA supports cooperation with interagency and industry partners to further USG antiviral drug strategies



Interfacing with BARDA

- www.phe.gov
 - Program description, information, news, announcements
- www.medicalcountermeasures.gov
 - Portal to BARDA
 - Register, request a meeting
 - Tech Watch
- www.fedbizopps.gov
 - Official announcements and detailed information about all government contract solicitations

