



*United States Department of*

**Health & Human Services**

**Office of the Assistant Secretary for Preparedness and Response**



# **Improving the Development Pipeline for Influenza Antivirals**

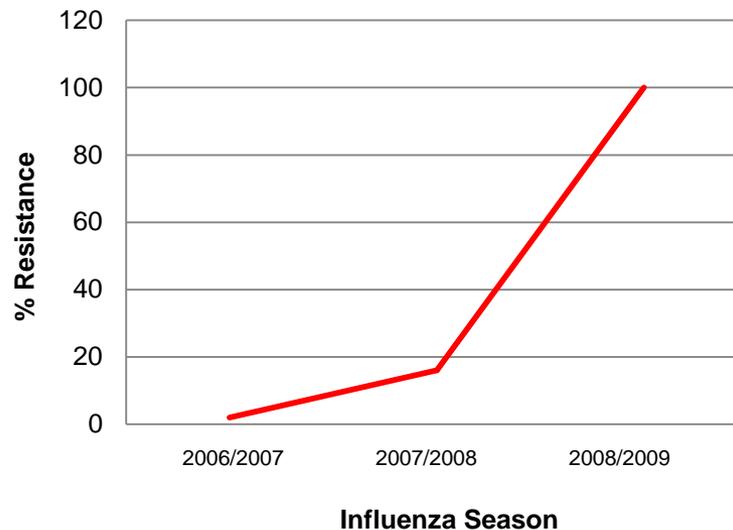
**BARDA Industry Day  
November 12, 2013**

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Chief, Antiviral Advanced Development  
BARDA**



- **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

## H1N1 Resistance to Oseltamivir



## NAI Activity Against H7N9\*

Virus	Genotype	Neuraminidase IC <sub>50</sub> (nM)			
		Oseltamivir	Peramivir	Zanamivir	Laninamivir
A/Anhui/1/2013	WT	0.17	0.06	0.33	0.46
A/Shanghai/1/2013	R292K	4987	102	23	15

\* K Sleeman *et al.* (2013) R292K Substitution and Drug Susceptibility of Influenza A (H7N9) Viruses. *Emerging Infect. Disease* **19**:1521-1524.



# Influenza Antiviral Landscape

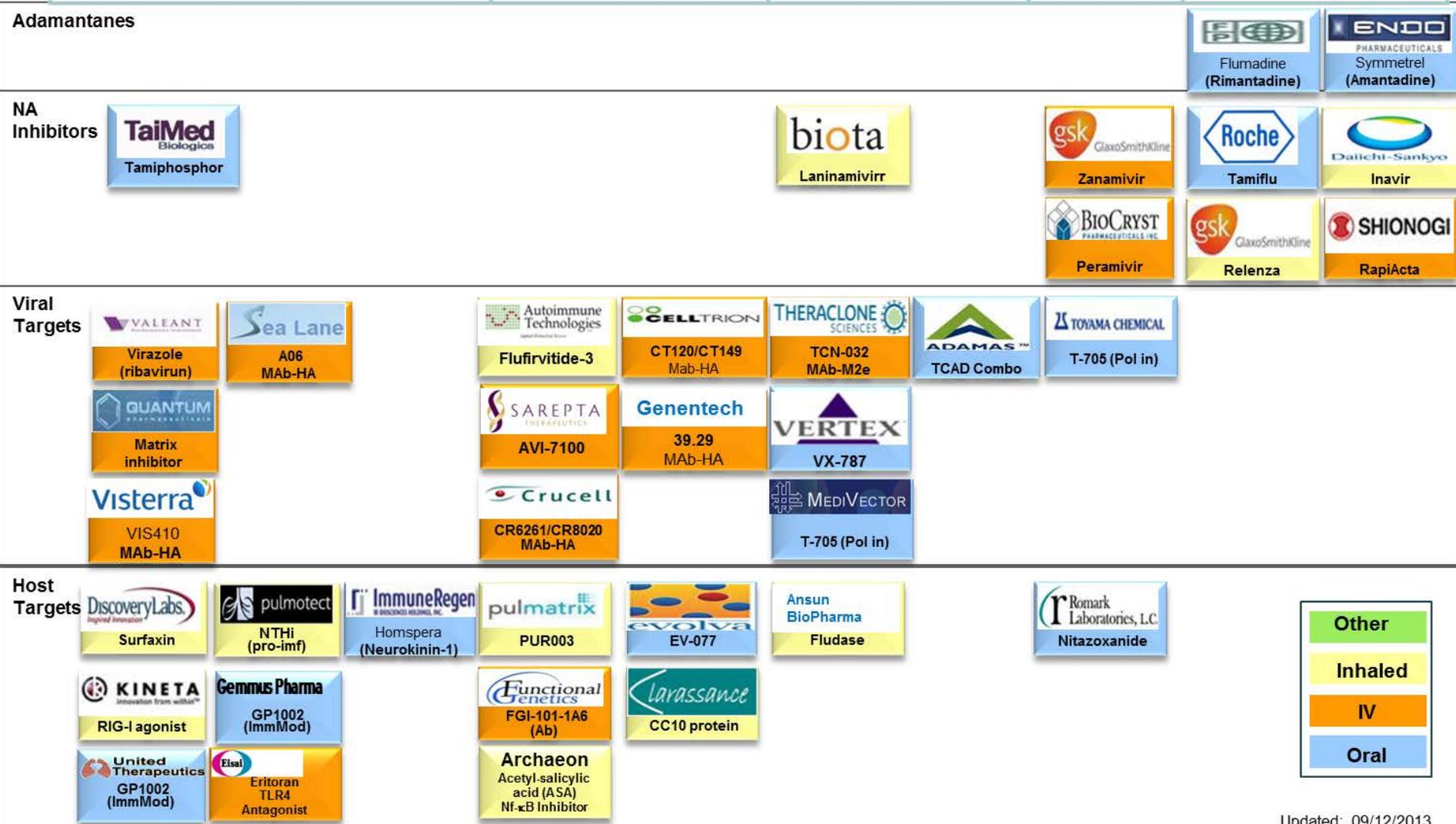
Pre Clinical

Phase 1

Phase 2

Phase 3

Market Approved



Other
Inhaled
IV
Oral



# 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



# BARDA Influenza Antiviral Program



## Questions?