



United States Department of

Health & Human Services

Office of the Assistant Secretary for Preparedness and Response



Advancing the Development Pipeline for the Treatment of Influenza

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Roadmap

- What is our goal?
- Where have we been?
- Where are we going?
- Why now?
- What strategies we are pursuing to achieve the goal?





Program Goal

“Reduce morbidity and mortality in all patient populations during an influenza pandemic by supporting advanced development, evaluation, and approval of new influenza antiviral drugs”

- Mission established in the 2005 *National Strategy for Pandemic Influenza*, *HHS Pandemic Influenza Plan* and the 2006 *Implementation Plan for the National Strategy for Pandemic Influenza*
- Initial stockpiling goal and advanced development projects
 - Stockpile total of 81M treatment courses of influenza antiviral drugs
 - Advanced development of new antiviral drugs
- New BARDA advanced development projects are focused on developing drugs to address critical unmet needs in treating severely ill, hospitalized patients and in pediatric populations
 - Novel mechanisms of action
 - Combination therapy

Our total reliance on monotherapy with NAI's has placed us at risk of no treatment options to address a potential NAI-resistant pandemic



BARDA Influenza Therapeutics Program Line-Up



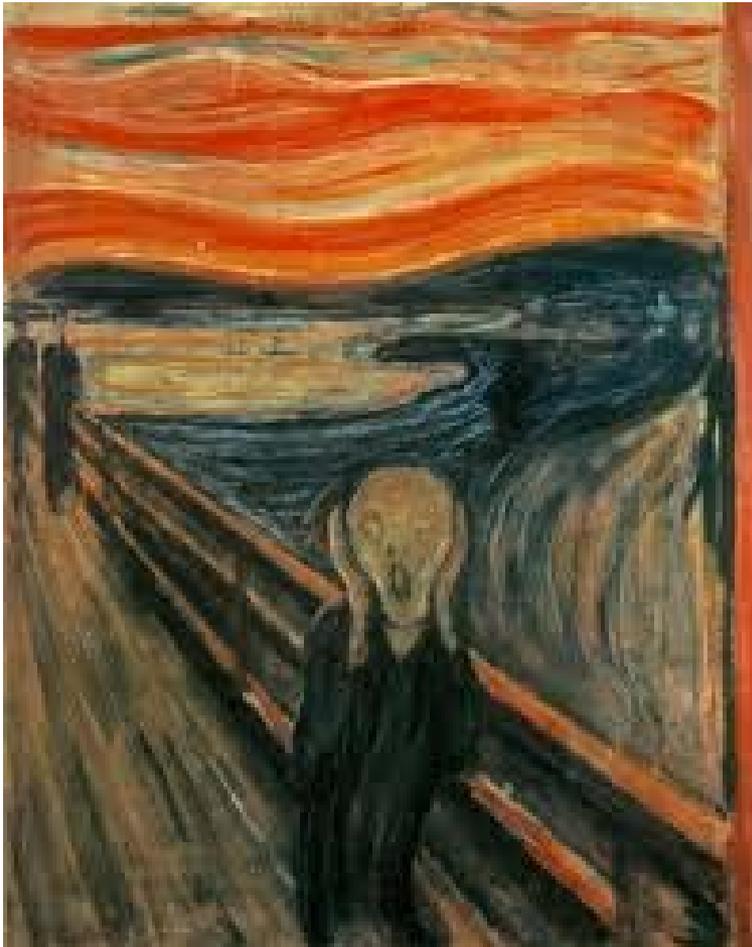
- Two large, full development programs for neuraminidase inhibitors
 - BioCryst—treatment of severely ill, hospitalized patients
 - During 2009 pandemic, IV peramivir received the 1st EUA for an unapproved drug
 - Biota—long acting, single dose treatment
- Two smaller, targeted development programs for compounds with novel mechanisms of action
 - Ansun—recombinant sialidase prevents viral attachment to cells
 - Romark—Broad spectrum antiviral targeting host pathways

FY07	FY08	FY09	FY10	FY11	FY12	FY13	FY14	FY15	FY16	FY17
			BioCryst			★				
					Biota					
						Ansun				
							Romark			

★ = NDA Filing

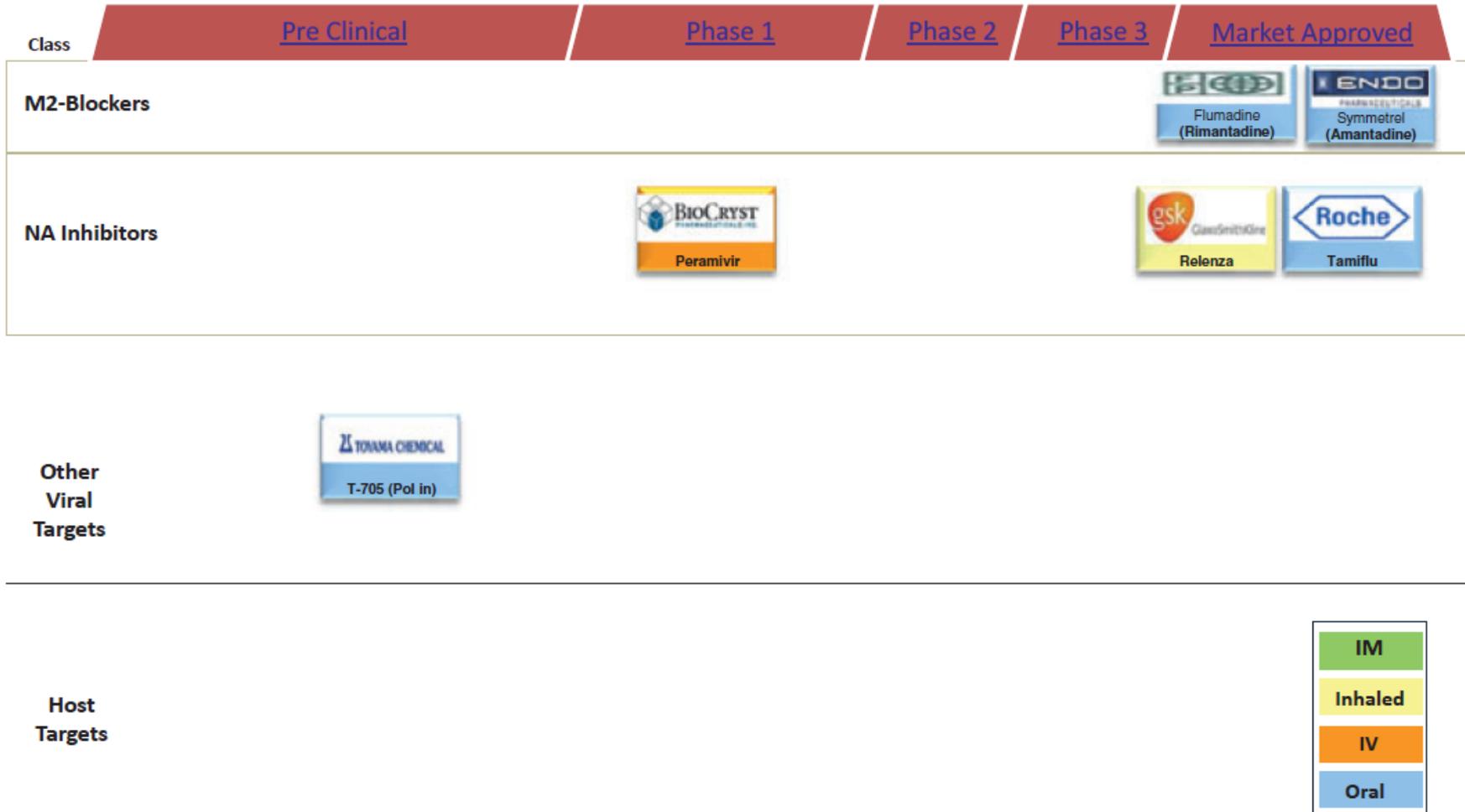
■ Existing ■ Completed/Ended

Challenges and Gaps



- Expecting a single drug or class of drugs to treat all stages of influenza infection and all populations might be a stretch
- Historically driven by a limited pipeline
- Leaves gaps in our preparedness:
 - Severely ill, hospitalized influenza patients
 - More effective treatment options, suitable for all populations including pediatrics

A



Influenza Antiviral Landscape 2014

Phase 2

M-2 Blockers

Flumadine (Rimantadine)	Symmetrel (Amantadine)

NA Inhibitors

Tamiphosphor

Laninamivir

Zanamivir

Tamiflu

Inavir

Peramivir

Relenza

RapiActa

Other Viral Targets

Virazole (ribavirin)

Cap Snatch/ Endonuclease

FluCide™

Flufirvitide-3

TCAD Combo

T-705 (Pol in)

Matrix inhibitor

AVI-7100

VX-787

Antibodies

Anti-NA

2D1 mAb-HA

Fl6v3 mAb-HA Grp1+2

CT-P27 mAb-HA Grp1+2

Anti-Flu A mAb-HA Grp1+2

TCN-032 mAb-M2e Grp 1+2

Hyperimmune IVIG

Anti-HA

Fabenflu Equine pAb (H5N1)

VIS410 mAb-HA Grp1+2

CR6261 mAb-HA Grp1

CR8020 mAb-HA Grp2

CR9114 mAb-HAGrp1+2

A06 MAb-HA

CF-404

Anti Influenza IVIG

Other
Inhaled
IV
Oral



Influenza Antiviral Landscape 2014

Pre-Clinical

Phase 1

Phase 2

Phase 3 / Market Approved

Host Targets


NTHi
(pro-Imf)


GP1002


Eritoran
TLR4
Antagonist


Homspera
(Neurokinin-1)


Surfaxin


PUR003


Acetyl-salicylic
acid (ASA)
Nf-κB Inhibitor


EV-077


CC10 protein


Alferon LDO


Fludase


Nitazoxanide

Other
Inhaled
IV
Oral



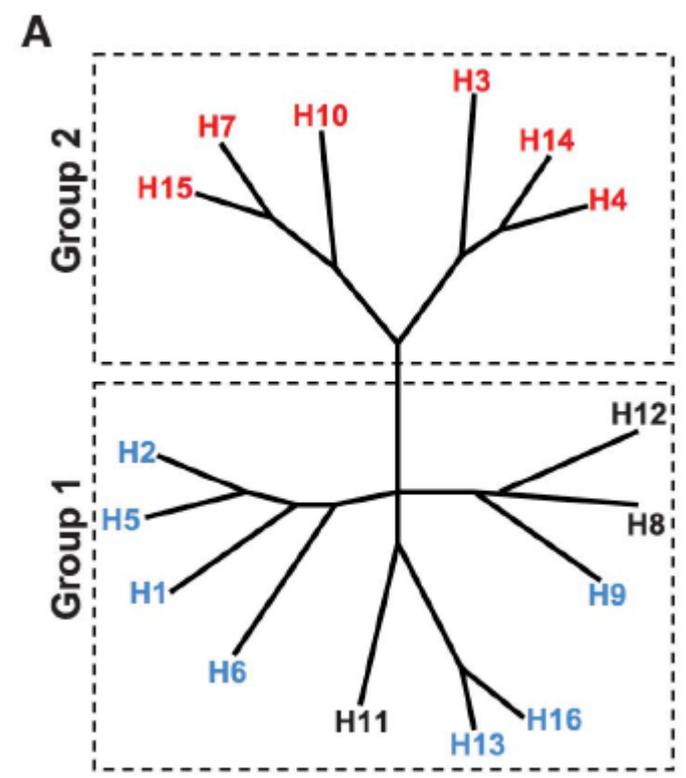
Where Are We Going?



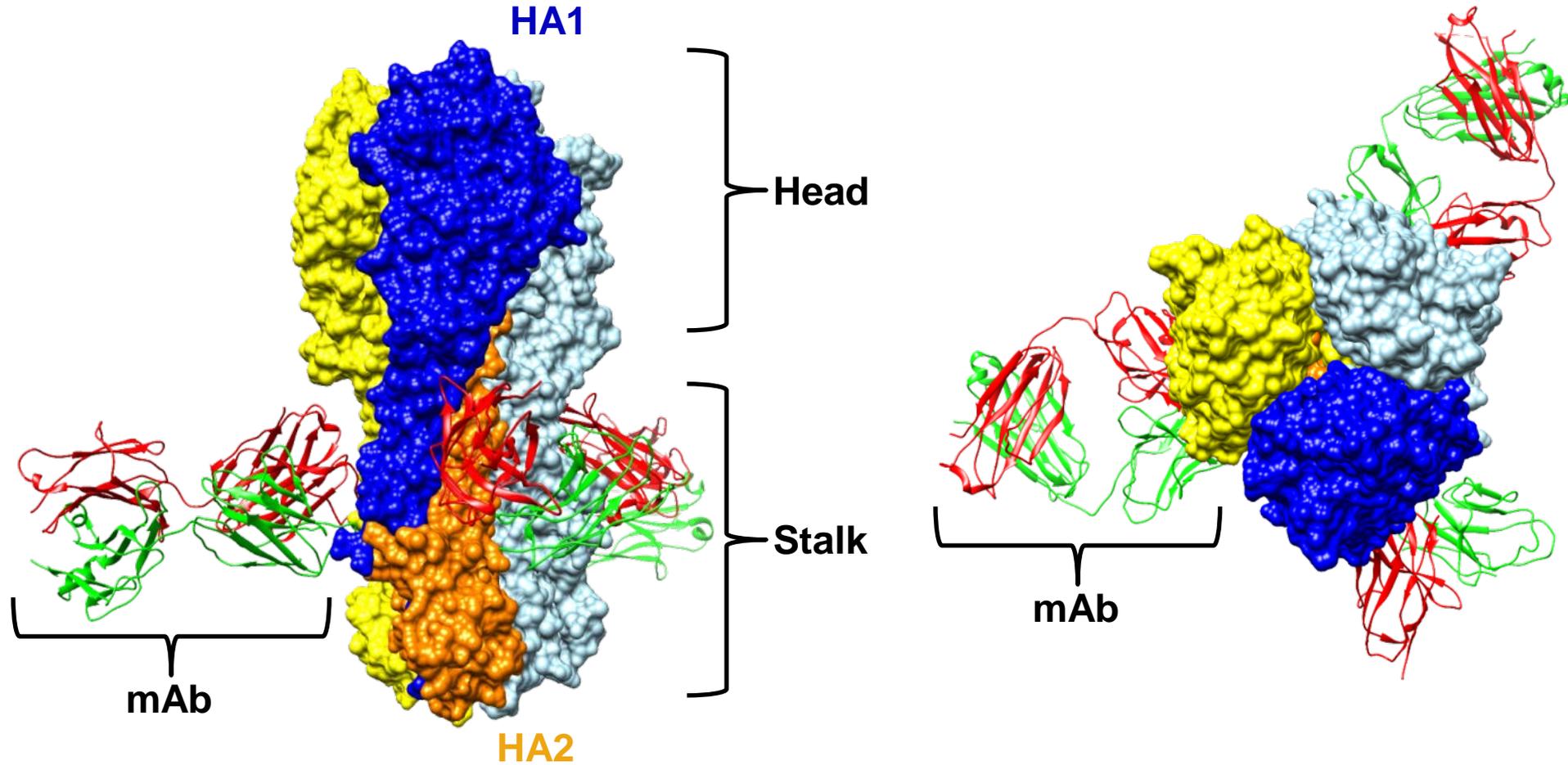
- **We need new options to address pandemic threats**
 - Therapies with a wider treatment window
 - >48h of symptom onset
 - Therapies that have a reduced threat of resistance
 - Novel MOA including host directed therapies
 - Combination therapies
 - Options for special populations
 - Alternative formulations (IV for hospitalized)
 - Approved drugs for severely ill, hospitalized patients
 - Treatment options and formulations for pediatric patients
 - Broad spectrum activity for influenza and/or other emerging diseases suitable for community use

Broad Spectrum Neutralizing Monoclonal Antibodies

- Target the HA stalk
 - Highly conserved
 - Novel target
 - Broad spectrum – Group 1 and 2, Influenza B
- Unique properties
 - Extended treatment window
 - Long half life resulting in single dose administration
 - Large binding surface reducing likelihood for resistance



Influenza HA and Stalk mAbs





Strategies to Address Unmet Needs

Critical unmet medical needs:

- **Severely ill, hospitalized influenza patients**
- **More effective treatment options, suitable for all populations**

- If the drug is a monoclonal antibody, then:
 - Broad spectrum = one or two mAbs cover all subgroups of Influenza A
 - IV formulation amenable to treatment of the severely ill
 - Expanded treatment window = must be effective more than 48 hours after symptom onset

- If the drug is a small molecule, then:
 - Needs to work better than neuraminidase inhibitors (NAIs)
 - Inhibits all Influenza A strains tested
 - Expanded treatment window beyond 48 hours
 - Suitable for combination therapy with existing NAI
 - Oral and IV formulations



Strategies to Address Unmet Needs (2)



Critical unmet medical needs:

- **Severely ill, hospitalized influenza patients**
- **More effective treatment options, suitable for all populations**
- If the drug is a host directed therapy, then:
 - Can have direct antiviral activity
 - Restore immunological homeostasis in an influenza infection
 - Demonstrate improved outcomes in the severely ill, hospitalized population when given alone or in combination with SOC antivirals
 - Expanded treatment window = must be effective more than 48 hours after symptom onset



Partnership Opportunities with BARDA



- Broad Agency Announcement (BAA)
<https://www.medicalcountermeasures.gov/newsroom/2013/now-open-broad-agency-announcements.aspx>
- Request for Proposal (RFP) FY2015
 - RFP with funding to make base awards for promising programs

Questions?

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