



BARDA INDUSTRY DAY

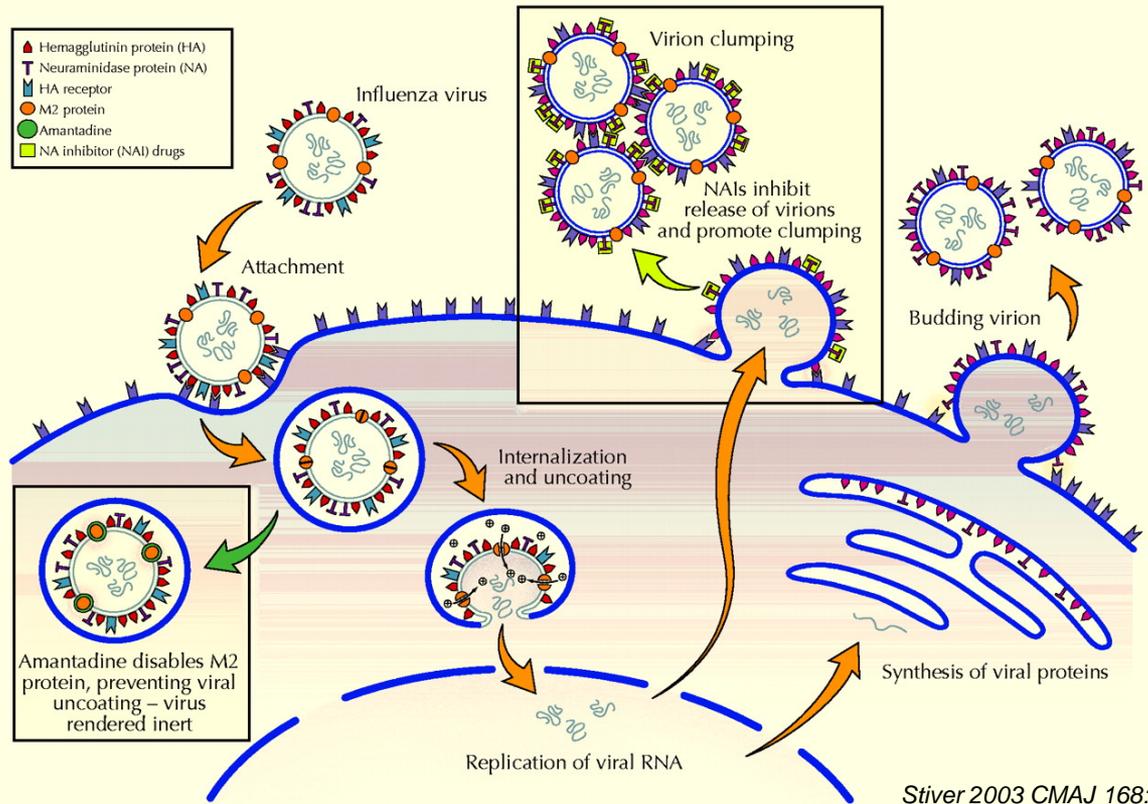
Influenza Therapeutics

Kimberly Armstrong, PhD, MT(ASCP)
Branch Chief (Acting), Therapeutics
October 29, 2018

October 29-30, 2018 | Grand Hyatt • Washington, D.C.



Influenza Antivirals as of September 2018



Adamantanes: M2 blockers

- Rimantadine
- Amantadine

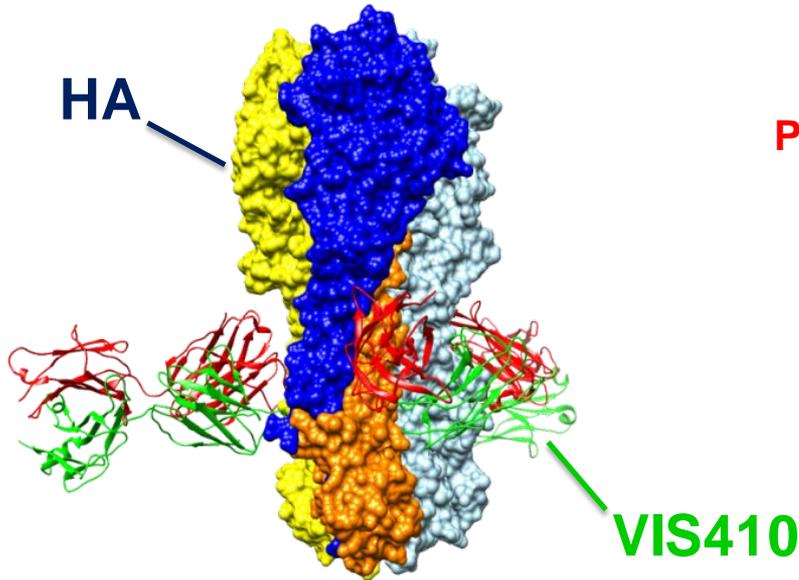
Neuraminidase inhibitors

- Oseltamivir
- Zanamivir
- Peramivir

Stiver 2003 CMAJ 168:49

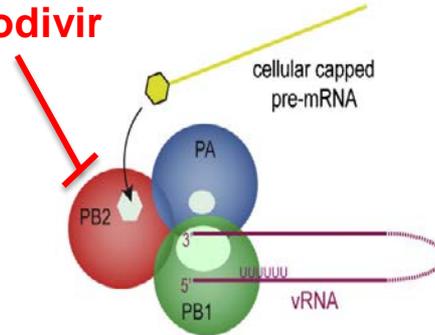
Current Portfolio Focused on Direct-Acting Antivirals

Stem-binding Monoclonal Antibodies



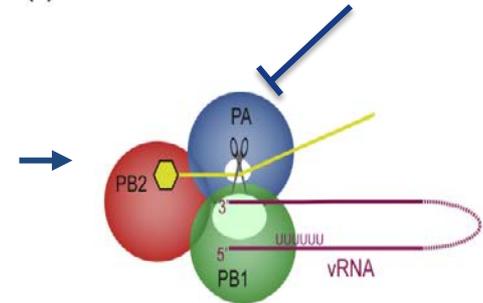
Endonuclease Inhibitors

Pimodivir



(b)

Baloxavir



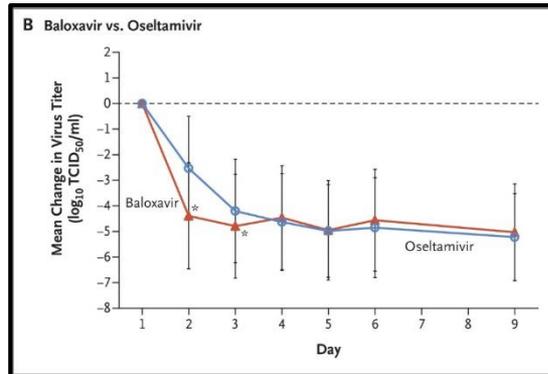
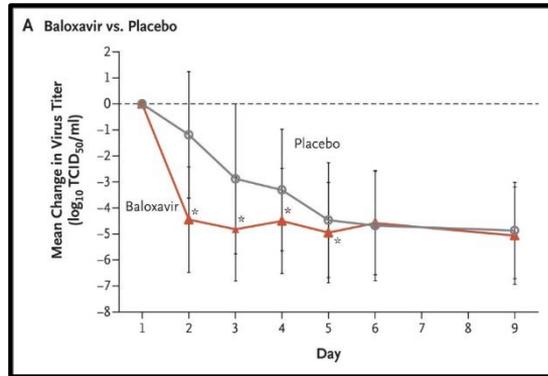
Adapted from Ruigrok. 2010. *Current Opinion in Structural Biology*. 20:104

Influenza Therapeutic Developments: Baloxavir

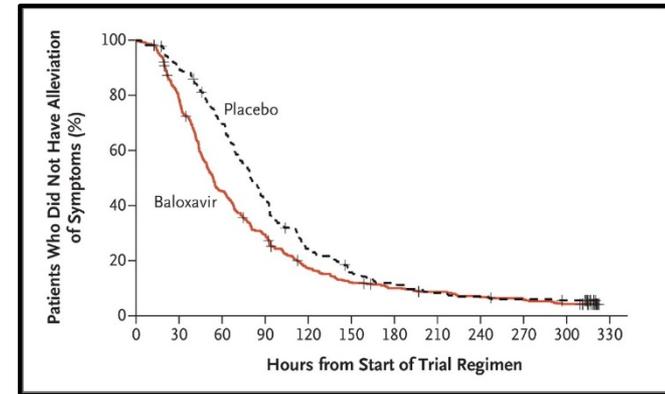
Infectious virus shedding was shorter in the baloxavir treated group

- 72 hours less shedding compared to placebo
- 24 hours less shedding compared to oseltamivir

Genentech
A Member of the Roche Group



Baloxavir significantly improves symptom alleviation compared to placebo



Hayden. 2018 NEJM
379:913

But not oseltamivir, why?



ASPR
ASSISTANT SECRETARY FOR
PREPAREDNESS AND RESPONSE



Saving Lives. Protecting Americans.

Less Emphasis on Hospitalized Studies

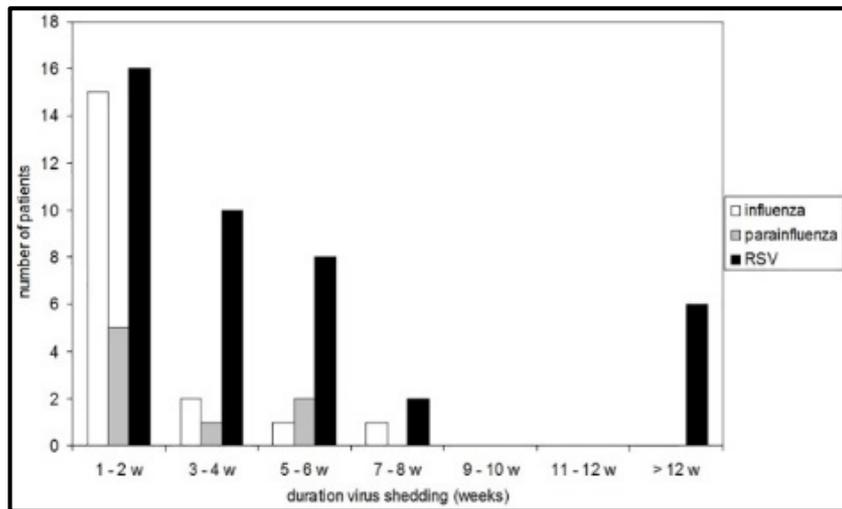
Drug	Seasons	Clinical Sites	Numbers Enrolled	Patients/Site /Season
Peramivir	3 NH, 3 SH	196	405	0.69
IV zanamivir	5 NH, 4 SH	110	626	1.26
MHAA4549A	3 NH, 2 SH	172	127	0.30
IRC002 Immune Plasma	5 NH	35	98	0.56

Beigel 2017 Lancet Respir Med. 5:500, de Jong 2014 Clin Infect Dis. 59:e172, Marty 2017 Lancet Respir Med. 5:135, Nilsson 2018 ECCMID presentation

- 1 Inefficient
- 2 Take a long time to enroll
- 3 Expensive
- 4 Global sites have variable standards of clinical care
- 5 No clinical endpoint for this population
- 6 Mostly unsuccessful

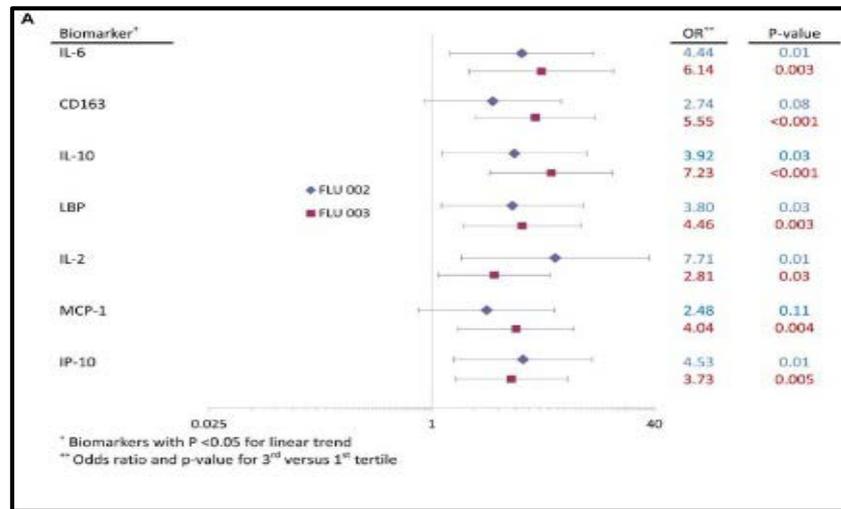
New Focus: Immune Modulators for Severe Influenza Infections

Immune compromised patients can shed virus for 7-8 weeks without excess morbidity



Lehners. 2016 PLoS ONE.
11:e0148258

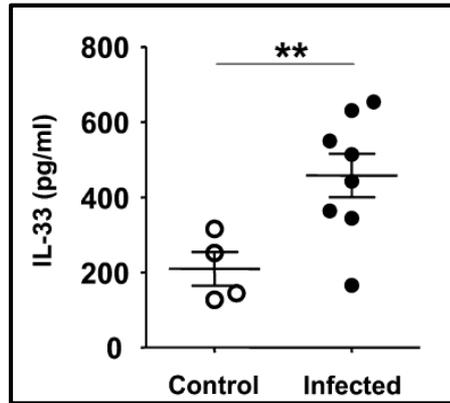
Biomarkers of inflammation associated with poor outcomes in influenza infected patients



Davey. 2013. PLoS ONE.
8:e57121

Where are the Immune Modulator Submissions?

IL-33 increases with influenza infection

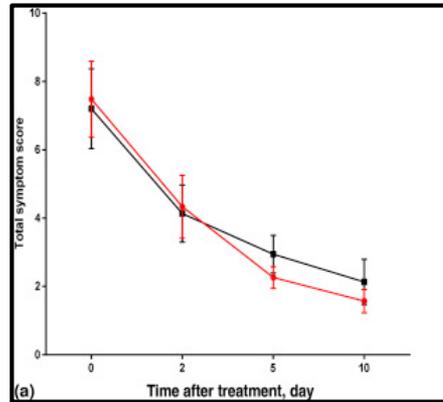


AnaptysBio Anti-IL-33 in phase 2

REGENERON Anti-IL-33 in phase 1

Le Goffic. 2011. *Am J Respir Cell Mol Biol.* 45:1125

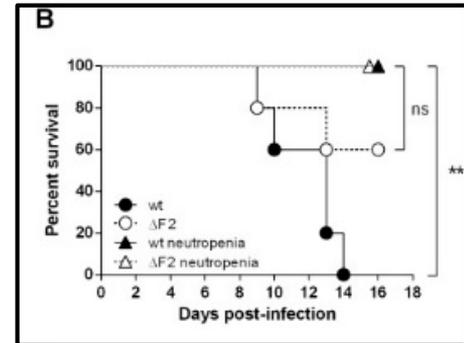
Treatment with macrolides reduces symptom scores in hospitalized patients



Pfizer Azithromycin

Lee. 2017. *Antiviral Res.* 144:48

Neutropenic mice are protected from death



gsk GlaxoSmithKline

Danirixin, selective CXCR2 antagonist, in phase 2 for COPD

MERCK

Navarixin, CXCR2 antagonist, in phase 2 for COPD

Vidy. 2016. *PLoS ONE.* 11:e0165361

Requirements for BARDA BAA Submission have not Changed



Must have an open US IND for influenza



Phase 1 data must be available for review



Drug must be safe!



Demonstrated activity against seasonal & potential pandemic influenza

If you need help conducting these early development studies, please contact **Amy Krafft** at NIAID, krafft@niaid.nih.gov or 240-627-3295

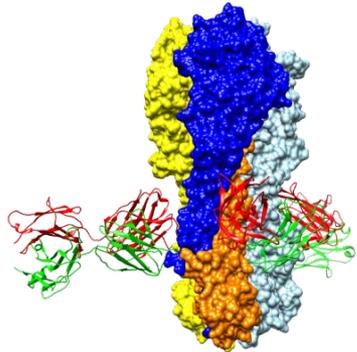
New Influenza Therapeutics Plan



Pimodivir



Baloxavir



Monoclonal antibodies

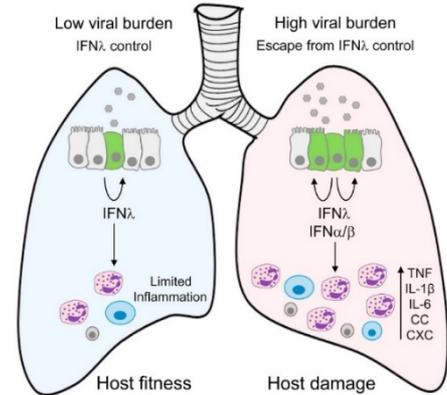


**Current strategy
new mechanisms
of action**



**Strategies
we are
interested in**

Immune modulators



One of many potential pathways to target

Galani 2017 Immunity. 46(5):875

Thank
you

Kimberly Armstrong, Branch Chief (Acting)

kimberly.armstrong@hhs.gov

202-260-0130

Karl Erlandson, Interdisciplinary Scientist

karl.erlandson@hhs.gov

202-692-4676

Peter Adams, Health Scientist

peter.adams@hhs.gov

202-260-0074



How to contact BARDA



Medical
Countermeasures.gov

[medicalcountermeasures.gov/home.aspx](https://www.mediccountermeasures.gov/home.aspx)

Portal to BARDA: **Register to request a TechWatch meeting!**



www.fbo.gov/
("FedBizOpps")

Official announcements and
info for all government
contract solicitations



<https://www.phe.gov/about/BARDA/Pages/default.aspx>

Program description, information,
news, announcements



www.drive.hhs.gov

DRIVE questions

USAJOBS[®]
"WORKING FOR AMERICA"

<https://www.usajobs.gov/>
Join the team!



ASPR
ASSISTANT SECRETARY FOR
PREPAREDNESS AND RESPONSE



Saving Lives. Protecting Americans.