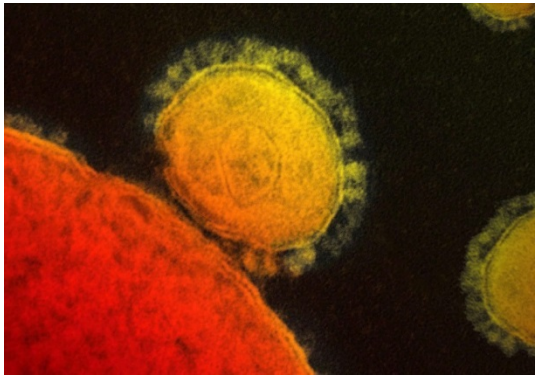
EMERGING INFECTIOUS DISEASES OVERVIEW



Rick Bright, PhD

Director
Influenza and Emerging Diseases
Biomedical Advanced Research and Development Authority
Assistant Secretary for Preparedness and Response
US Department of Health and Human Services

BARDA INDUSTRY DAY 2016
Ronald Reagan Building and International Trade Center
Washington, DC • Oct 18-20, 2016

Resilient People. Healthy Communities. A Nation Prepared.

Emerging Infectious Diseases Program Overview

- Infinite number of known and unknown emerging infectious diseases (EIDs); most zoonoses and vector-borne diseases remain localized and/or of limited medical impact
- No reliable algorithm/model for predicting which EIDs will result in severe pandemics
- The large number of known and unknown EIDs with pandemic potential and uncertainty inherent in pathogen emergence and evolution makes highly-targeted advanced countermeasure development impractical

Viruses

Andes
Australian bat lyssavirus
B19
Bagaza
Banna
Barmah Forest
Caliciviruses
California encephalitis
Cercopithecine herpes
Chikungunya
Crimean-Congo hemorrhagic fever
Dengue
Eastern equine encephalitis
Ebola sp. (Zaire, Reston)
Guama
Guanarito
Hantaviruses
Hendra
Hepatitis A
Hepatitis B
Hepatitis C
Hepatitis E
Hepatitis G
Human astrovirus
Human enterovirus A (71)
Human enterovirus B
Human herpesvirus 1
Human herpesvirus 2
Human herpesvirus 3
Human herpesvirus 5
Human herpesvirus 8
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Human papillomavirus
Human T-lymphotropic virus 1
Human T-lymphotropic virus 2
Influenza (A)
Japanese encephalitis
Junin
Kyasanur Forest disease
Laguna Negra

LaCrosse
Lassa
LCM
Machupo
Marburg virus
Mayaro
Measles
Menangle
Monkeypox
Mumps
Murray Valley encephalitis
Nipah
Norwalk
O'nyong-nyong
Oropocho
Picobirnavirus
Poliovirus
Puumala
Rabies
Rift Valley fever
Ross River
Rotavirus A
Rotavirus B
Rotavirus C
Sabia
Sandfly fever Naples
SARS
Sequoia
Sin Nombre
Sindbis
St. Louis encephalitis
Tick-borne encephalitis virus
Variola major related poxviruses
Venezuelan equine encephalitis
Wesselsbron
West Nile
Western equine encephalitis
Yellow fever
Zika

Bacteria

Aeromonas caviae
A. hydrophila
A. veronii (var. sobria)
Anaplasma phagocytophila
Bacillus anthracis (+ MDR anthrax)
Bartonella henselae
Bordetella pertussis
Borrelia burgdorferi
Brucella sp. (Brucella melitensis)
Burkholderia communis
B. mallei
B. pseudomallei
Campylobacter fetus
C. jejuni
Chlamydia psittaci
C. trachomatis
Clostridium botulinum
C. difficile
C. perfringens
Corynebacterium amycolatum
C. diphtheriae
Coxiella burnetti
Ehrlichia (chaffeensis)
E. ewingii
Enterococcus faecalis
E. faecium
Escherichia coli (O157:H7)
Francisella tularensis
Haemophilus ducreyi
H. influenzae
Helicobacter pylori
Klebsiella pneumoniae
Legionella pneumophila
Leptospira interrogans
Listeria monocytogenes
Mycobacterium avium
M. bovis
M. fortuitum
M. haemophilum
M. leprae

M. marinum
M. tuberculosis (MDR/XDR)
M. ulcerans
Neisseria gonorrhoeae
N. meningitidae
Pseudomonas aeruginosa
Ricinus communis
Rickettsia monazensi
Rickettsia sp. (rickettsii)
Salmonella sp. (Salmonella enteritidis)
S. typhi
S. typhimurium
Serratia marcescens
Shigella sp. (dysenteriae)
Staphylococcus aureus
S. epidermidis
Streptococcus (group A, pneumoniae)
S. pyogenes
Treponema pallidum
Vibrio cholerae
Vibrio sp. (parahaemolyticus, vulnificus)
Yersinia enterocolitica
Y. Pestis

Protozoa

Acanthamebiasis sp.
Babesia microti (atypical)
Cryptosporidium hominis
C. parvum
Cyclospora cayetanensis
†Entamoeba histolytica
Giardia lamblia
Giardia duodenalis
Isospora belli
Leishmania donovani
L. infantum
Plasmodium falciparum
P. vivax
Toxoplasma (gondii)
Trichomonas vaginalis
Trypanosoma brucei
T. cruzi

Fungi

Aspergillus fumigatus
Blastomyces dermatitidis
Candida albicans
Candida glabrata
C. krusei
Coccidioides immitis
Coccidioides posadasii
Cryptococcus neoformans
Fusarium moniliforme
F. oxysporum
F. solani
Histoplasma capsulatum
Malassezia pachydermatis
Penicillium marneffei
Pneumocystis carinii
Scedosporium prolificans
Trichosporon beigelii
Encephalitozoon cuniculi
E. hellem
E. intestinalis
Enterocytozoon bieneusi
Nosema connori
Trachipleistophora hominis
Microsporidia (pollum)
genera

Helminths

Ancylostoma simplex
Echinococcus granulosus
Loa loa
Metorchis conjunctus
Onchocerca volvulus
Schistosoma mansoni
Strongyloides stercoralis
Taenia solium
Trichinella spiralis
Wuchereria bancrofti

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ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Emerging Infectious Disease: Charge to BARDA

- The Pandemic and All-Hazards Preparedness Act- Title IV, sec. 401 calls for the Secretary to "**integrate … emerging infectious disease requirements with the advanced research and development strategic initiatives for innovation, and the procurement of qualified countermeasures and qualified pandemic and epidemic products**"

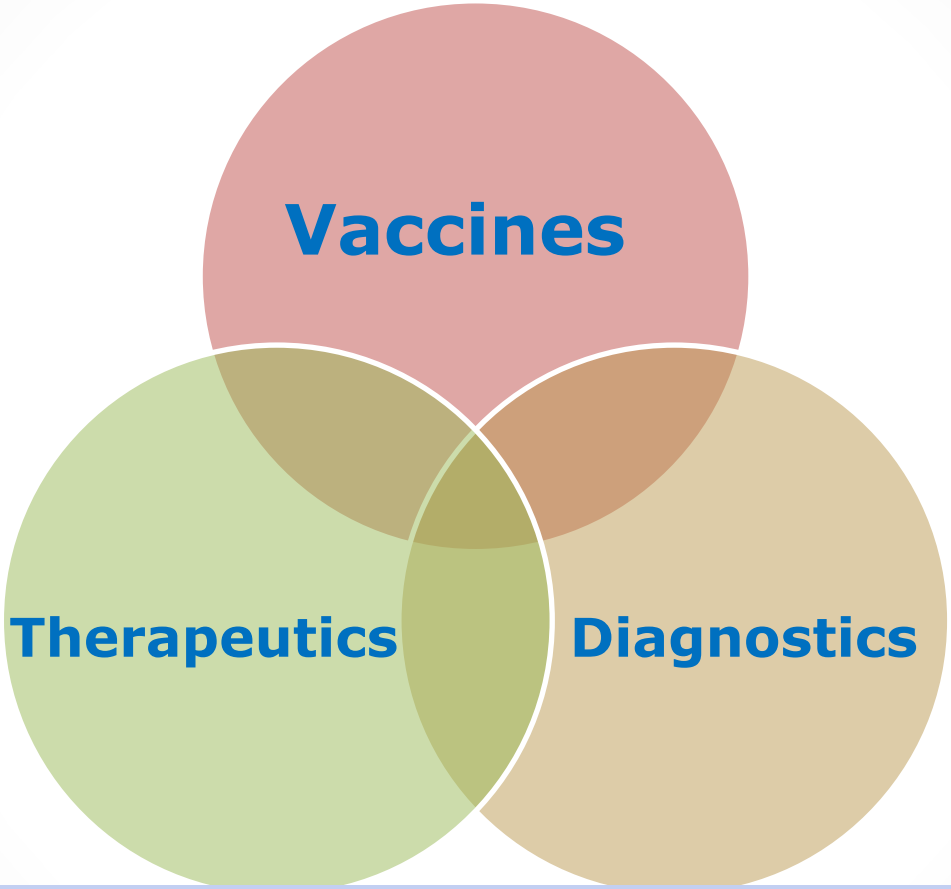
- Emerging infectious diseases fall within the charge of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)

- BARDA has assembled the staff, gathered the expertise, and built the program structure for dealing with Pan Flu and CBRN threat preparedness, and is well-positioned to apply this knowledge base to EID threat preparedness

Multi-hazard advanced development strategies

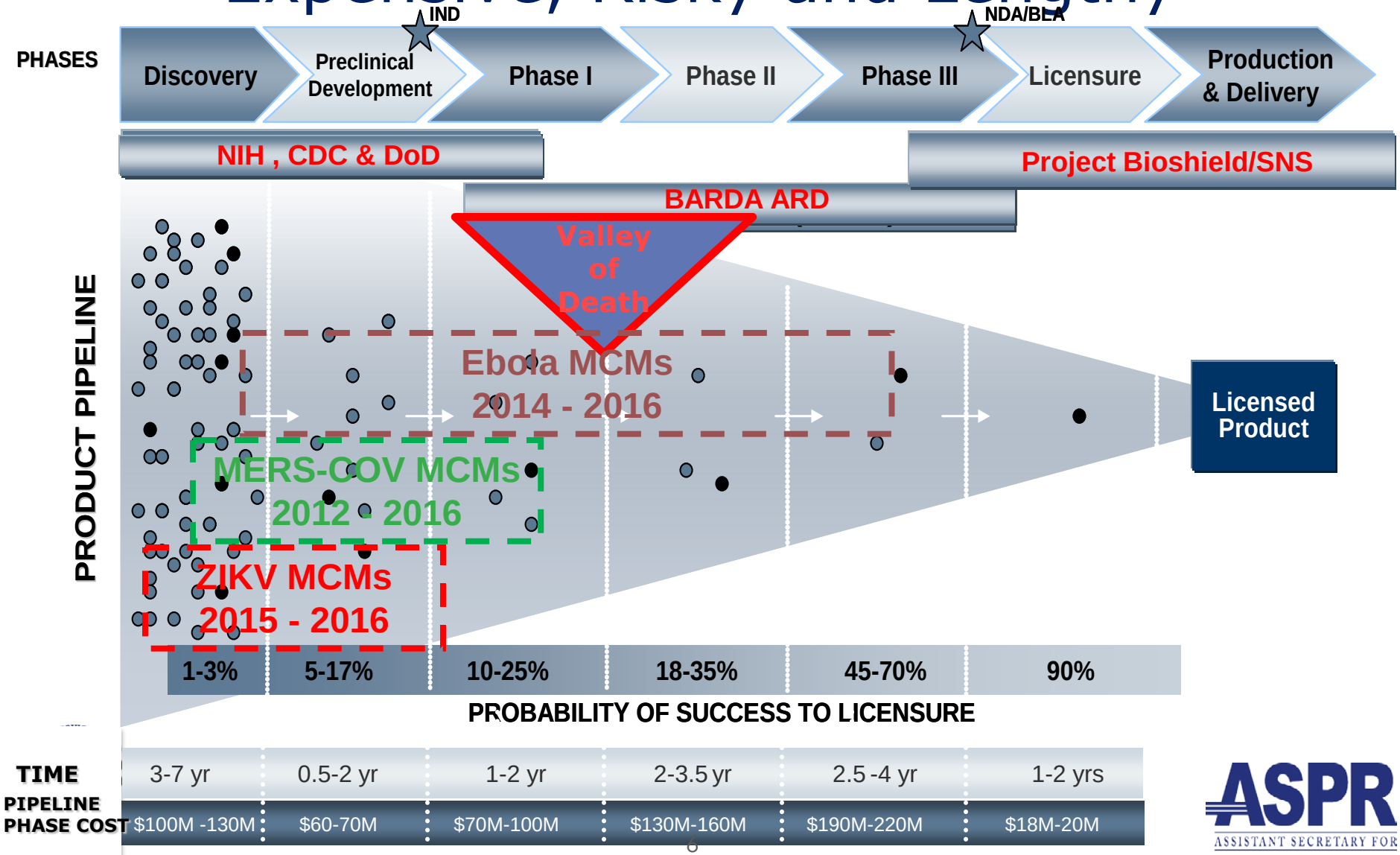
- Approach preparedness against unpredictable disease threats through multi-hazard strategies
- Within multi-hazard strategies, particular focus can be given to pathogens which currently pose a high threat (quantifiable assessment)
- Complements and strengthens current BARDA programs, initiatives, and capabilities

Emerging Threats Require An Integrated Response



Early Detection → Early Response → Saving Lives

Vaccine & Drug Development is Expensive, Risky and Lengthy



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BARDA EID Consideration Framework

Threat-Based Criteria:

Is the pathogen/ pathogen group capable of being a *public health threat* to the U.S.?
-documented threat of emergence
-highly transmissible
-rapid and uncontrollable spread
-high morbidity/mortality rates

Yes

Countermeasure-Based Criteria:

No or few developed, licensed, and highly effective MCMs already on the market?

Need for additional incentive for Industry to rapidly develop MCMs?

Need for advanced development MCM support (BARDA/CBRN, Global Health NGOs,?)

Yes

CONTINUAL RE-ASSESSMENT OF THREATS, COUNTERMEASURES, AND STATE OF THE SCIENCE

Scientific criteria:

Is the level of basic MCM research, proof of concept, and basic development sufficient to progress to advanced development?

Public Health need for BARDA expertise, resources, and capabilities?

Yes

CANDIDATE EIDs FOR BARDA ADVANCED DEVELOPMENT

DEPARTMENT OF HEALTH & HUMAN SERVICES

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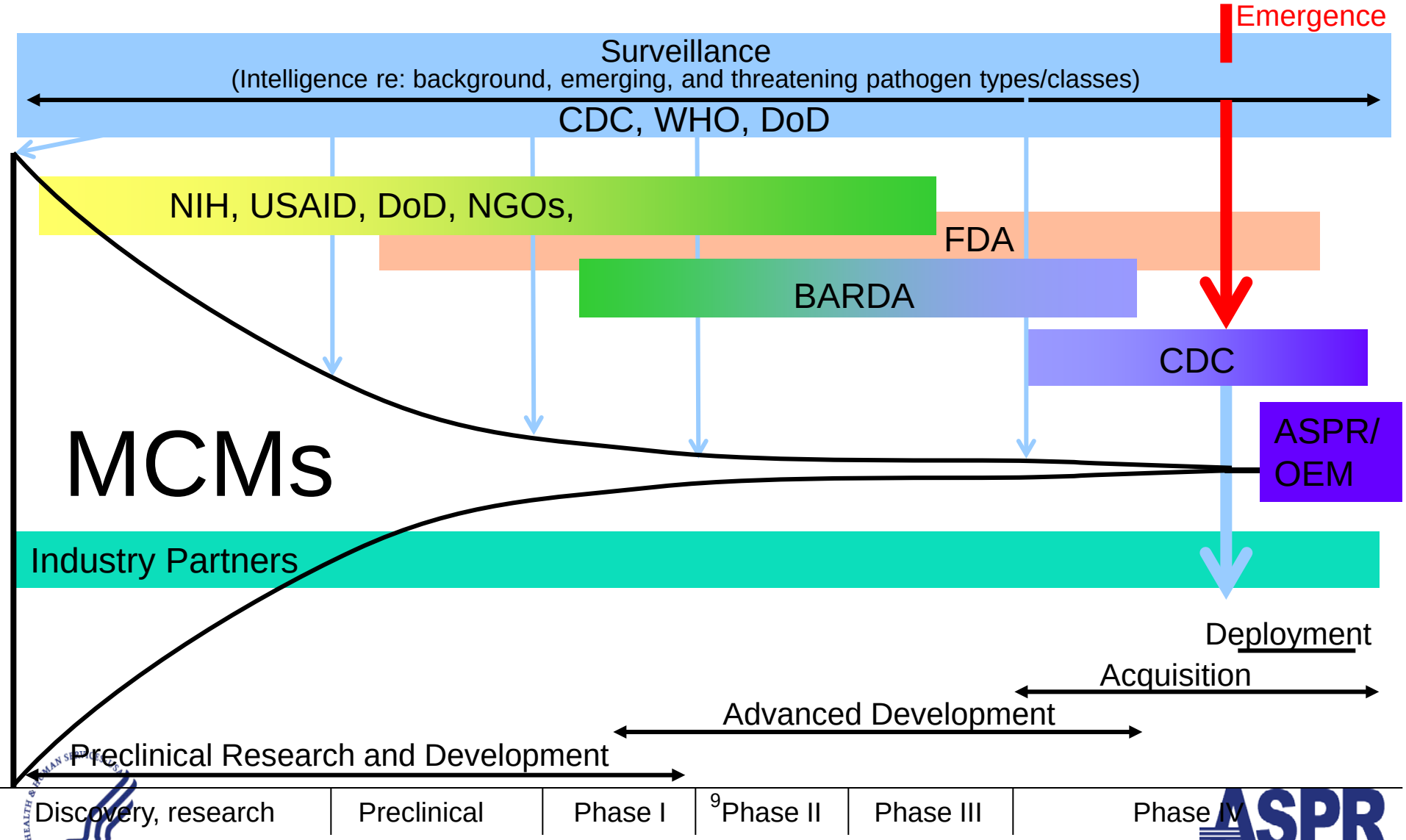
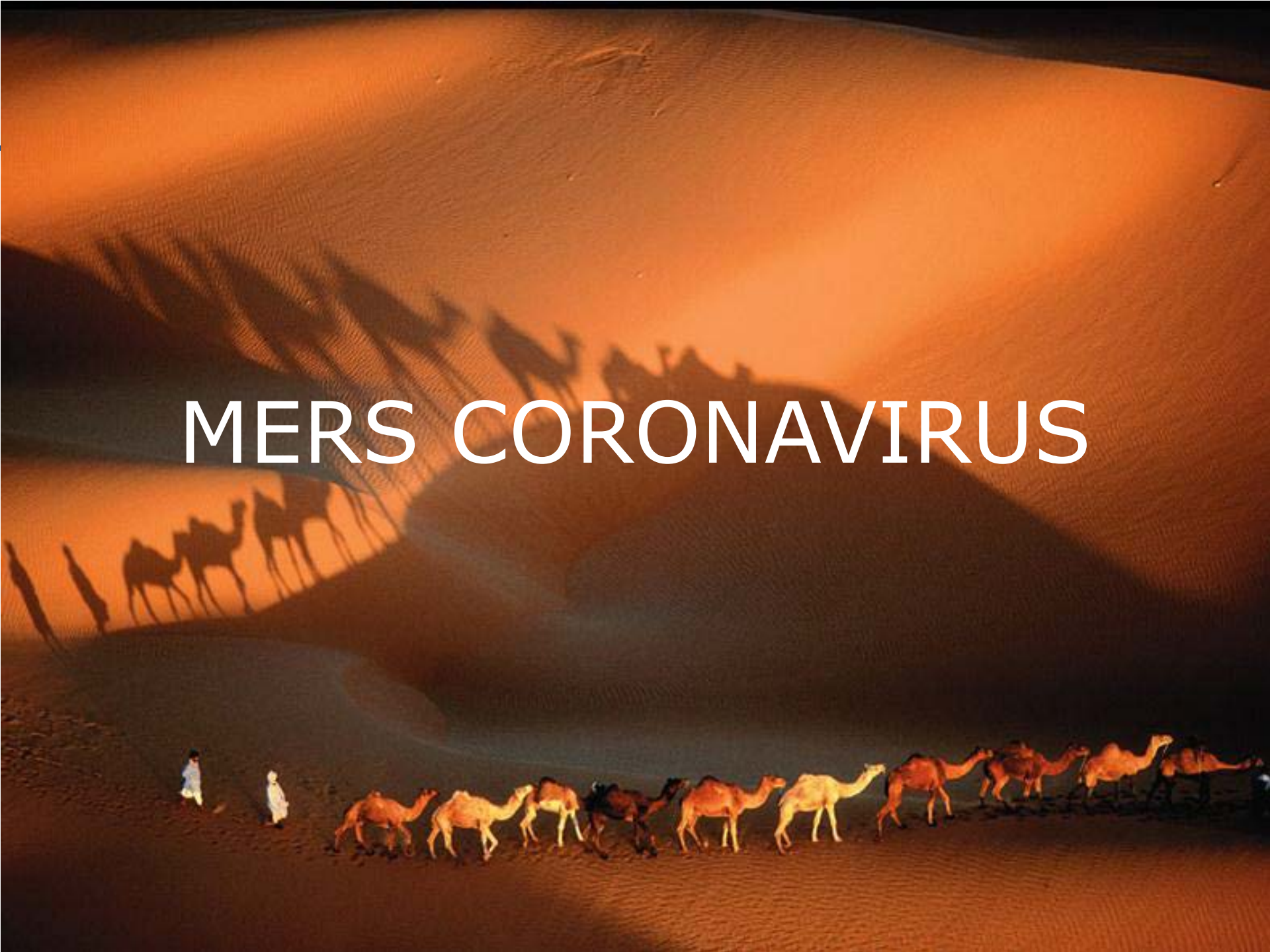
Emerging Infectious Diseases Program Align with Broad BARDA Initiatives

- Build Emerging Disease requirements into solicitations for general, flexible, or adaptive technologies and countermeasures, including:
  - Personal Protective Equipment
  - Broad-spectrum Therapeutics
  - Platform Technologies
    - Vaccines
    - Diagnostics
  - Enhancing Manufacturing Capacity

Emerging Infectious Disease MCM Continuum



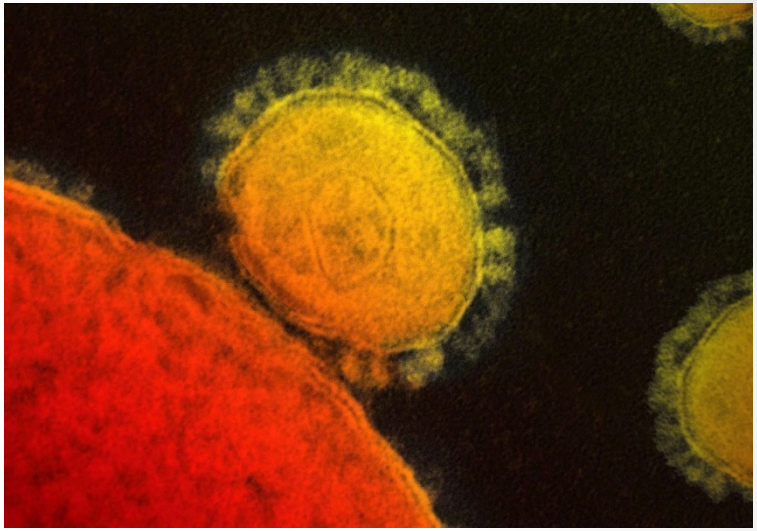


MERS CORONAVIRUS

Middle East respiratory syndrome coronavirus (MERS-CoV)

- MERS-CoV belongs to the family Coronaviridae
- Other coronaviruses include:
  - SARS-CoV
  - Human coronavirus 229E & OC43
- Enveloped viruses containing nonsegmented, positive-strand RNA genome
- Two outbreaks of novel coronaviruses causing acute respiratory distress syndrome and high death rates this century

MERS-CoV

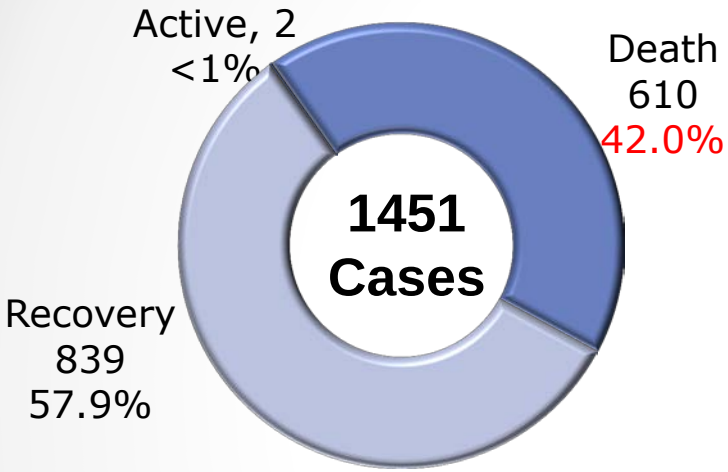


South Korea Wedding during the MERS outbreak

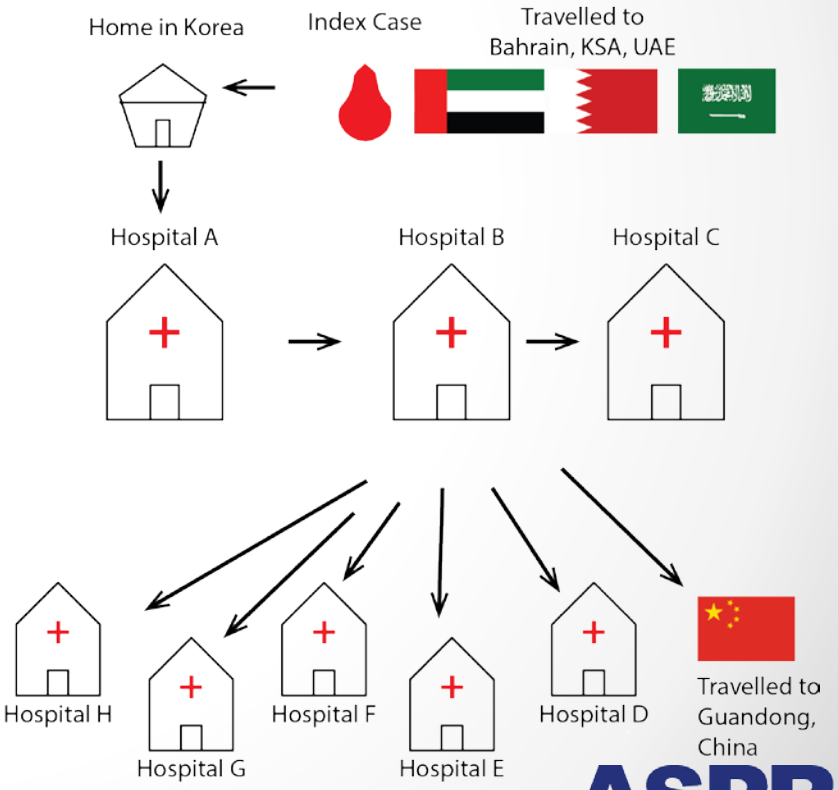
There are currently no licensed or approved vaccines or treatments for Coronaviruses

MERS-CoV outbreaks in Saudi Arabia and South Korea

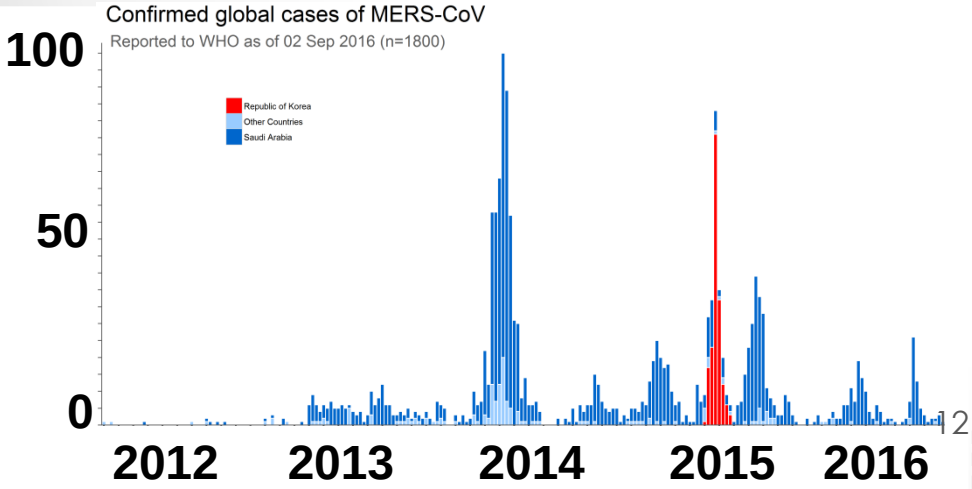
Saudi Arabia since 2012



South Korea, 2015



Global cases per week



http://www.jidc.org/index.php/journal/article/view/7278
http://www.who.int/emergencies/mers-cov/epi-2-september-2016.png?ua=1
http://www.moh.gov.sa/en/CCC/PressReleases/Pages/statistics-2016-09-11-001.aspx

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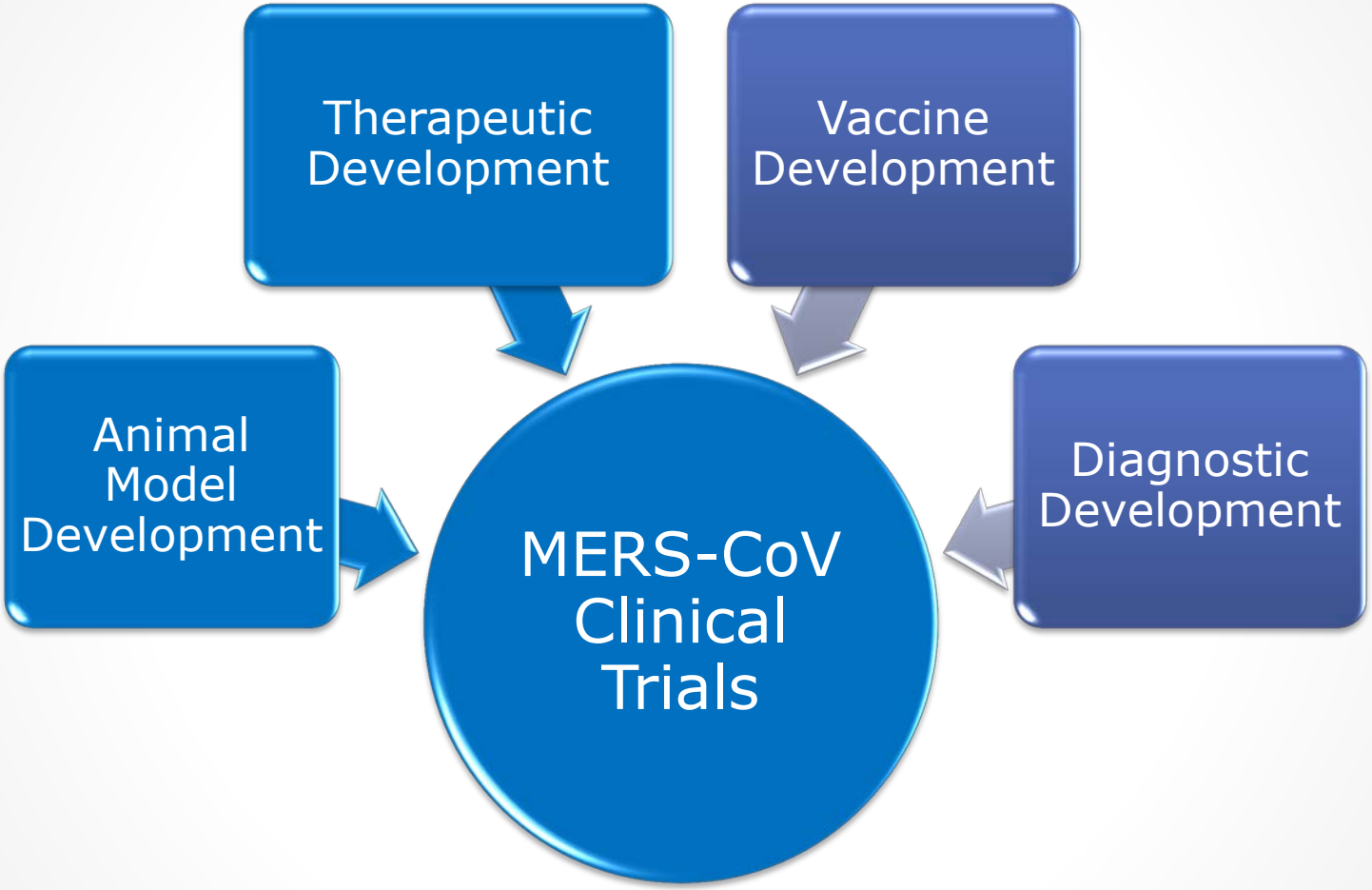
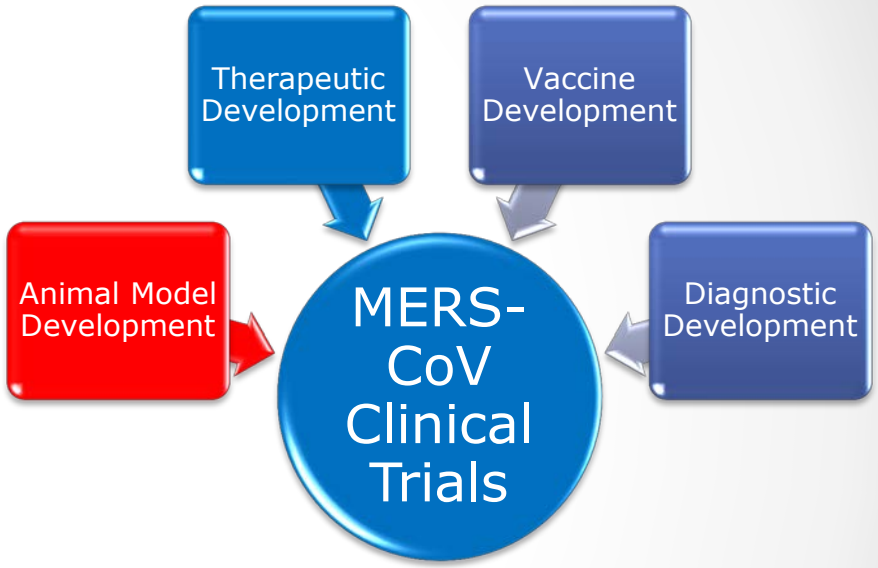
BARDA Priorities



Priorities: Animal Model Development

- Mouse studies at University of Maryland School of Medicine
- NHP studies at NIAID Rocky Mountain Laboratories
- Utilize the BARDA Nonclinical Development Network to standardize models
- NIH MERS Animal Model Standardization Workshop



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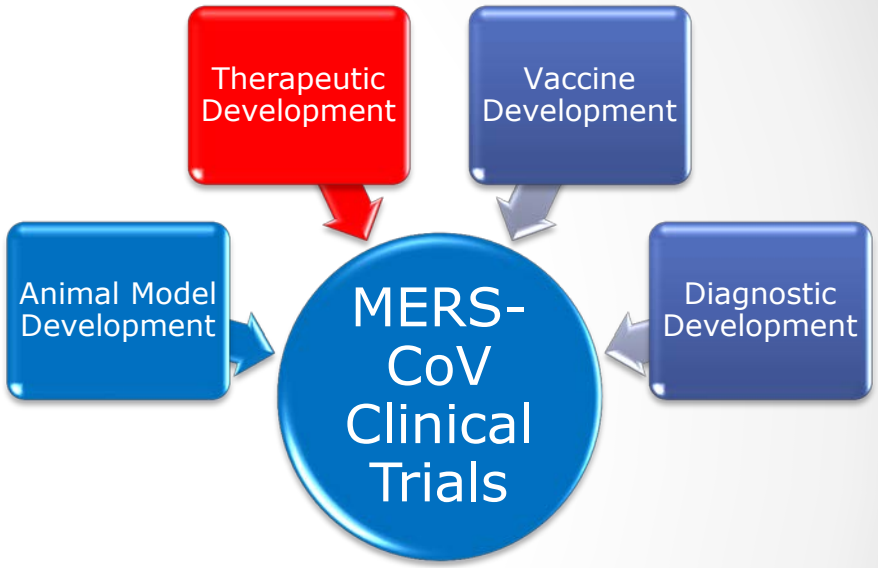
Priorities: Therapeutic Development

- Funnel all early stage drugs through the mouse models established at U. Maryland in Dr. Matt Frieman's lab
- If there is POC efficacy in the mouse, then test the drug in the NHP model established by Drs. Heinz Feldmann and Emmie DeWit at Rocky Mountain Labs
- Positive data from the NHP is the trigger for advancement into Phase 1



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DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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MERS-CoV Small Molecules Landscape

in vitro studies

- HEMISPHERX BIOPHARMA, INC. — Algeferon N (Host-directed)
- Health Care, University of Missouri Health System — Helicase Inhibitor
- Planet Biotechnology — Soluble DPP4 Decoy (binding inhibitor)
- NanoViricides Incorporated — DPP4-peptide Micelle
- LOYOLA UNIVERSITY CHICAGO, Preparing people to lead extraordinary lives — Protease Inhibitor
- MediVector — T-705 (polymerase inhibitor)
- National Institute of Allergy and Infectious Diseases — Peptide Inhibitor (fusion inhibitor)
- Autoimmune Technologies LLC, Applied Biomedical Science — CSW-1
- University of Michigan — BanLec
- Johnson & Johnson — AL-073 monophosphate (polymerase inhibitor)

Pre-Clinical

Mouse Studies

- Romark Laboratories, L.C. — Nitazoxanide In vitro-MERS (Host-directed), efficacy in Ad5 mouse under evaluation
- BioCryst Pharmaceuticals, Inc. — BCX4430 (polymerase), efficacy in Ad5 mouse under evaluation
- University of Maryland School of Medicine — FDA-Approved Drug Screen (2 hits)

NHP Studies

- Abbott — Lopinavir/ritonavir SARS Drug Screen (protease inhibitor), efficacy in marmoset
- Bayer HealthCare — Interferon B1b (Host-directed), efficacy in marmoset
- Rocky Mountain Laboratories — Ribavirin and interferon-α2b (polymerase), efficacy in Rhesus macaques
- Rocky Mountain Laboratories — PEG Interferon Alpha (Host-directed)

Clinical

- GILEAD — GS-5734 (polymerase inhibitor), testing in rhesus

NIAID Supported
BARDA Support
Other Support

ASPR — Assistant Secretary for Preparedness and Response

Updated: 12/20/2016

MERS-CoV Immunotherapeutic Landscape

in vitro studies

The University of Hong Kong

MERS-4, MERS-27

University of Minnesota

Mersmab1 – humanized

Pre-Clinical

NHP Studies

IND-Enabling

DANA-FARBER CANCER INSTITUTE | AbViro

AV-3 (3B11) – **Abviro** partner, Fully human mAbs from phage display, efficacy in Rhesus macaque

REGENERON science to medicine®

REGN3048/REGN3051 - Fully human mAbs from transgenic mice, Efficacy in transgenic Mouse and Marmoset

National Cancer Institute | Organic Vaccines

M336 – Fully human mAb from phage display, efficacy in transgenic mice, rabbits and Marmoset

HUMABS BioMed

LCA60 - mAb from human, efficacy in Ad-5 mouse and Marmoset

Clinical

وزارة الصحة Ministry of Health

Convalescent serum Clinical trial ongoing

CERUS

Convalescent serum

SAb BIOTHERAPEUTICS Personal Impact + Global Influence

SAB-301 - Fully human polyclonal antibodies from transgenic bovine, Efficacy in Ad5-Mouse, Marmoset

- NIAID Supported
- BARDA Support
- Other Support

Department of Health & Human Services · USA

ASPR Assistant Secretary for Preparedness and Response

Updated: 12/20/2016