EBOLA UPDATE

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October 2016
The Worst Ebola Outbreak On Record

<table>
<thead>
<tr>
<th>Total Cases</th>
<th>Confirmed Cases</th>
<th>Deaths</th>
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<td>28,652</td>
<td>15,261</td>
<td>11,325</td>
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Table above includes 513 deaths of healthcare and frontline workers.
Ebola is both an EID and a material threat to the United States.
Development and Evaluation of Ebola MCMs Has Been a Coordinated Effort

- Development
  - NIH
  - DoD
  - BARDA
  - FDA
  - PHAC
  - Industry partners

- Evaluation
  - NIH
  - DoD
  - CDC/OID/NCIRD
  - FDA
  - BARDA
  - WHO
  - NGOs
  - Industry partners
  - Liberia, Sierra Leone, and Guinea regulatory authorities
Three, Large, Phase II/III Vaccine Trials and One Therapeutic Trial

- NIH Sponsored and Supported
- MSF, WHO, and Guinea Govt. Sponsored
  WHO, WT, MSF, RC of Norway, PHAC Supported
- CDC Supported
  CDC/BARDA Supported

- Prevail II
  NIH Sponsored and Supported

- Campagne Ebola Ça Suffit
  MSF, WHO, and Guinea Govt. Sponsored
  WHO, WT, MSF, RC of Norway, PHAC Supported

- STRIVE
  CDC Sponsored
  CDC/BARDA Supported

- The Liberia-US Joint Clinical Research Partnership
  NIH Sponsored and Supported
Ebola Vaccines

- **Profectus BioSciences**
  - Recombinant vesicular stomatitis virus (rVSV) vectored monovalent vaccine against Ebola-Zaire
    - Currently in Phase I and program will transition to DoD

- **NewLink/Merck**
  - Recombinant vesicular stomatitis virus vectored monovalent vaccine against Ebola
    - Has been evaluated in Phase II/III studies in Liberia, Sierra Leone and Guinea

- **GlaxoSmithKline**
  - Chimp Ad3 vectored monovalent vaccine against Ebola
    - One of the first Ebola vaccines to enter clinical trials
    - Has been evaluated in a Phase II/III study in Liberia

- **Crucell/Bavarian Nordic**
  - HuAd26 prime with MVA trivalent, heterologous boost
    - Has been evaluated in Phase I study – Oxford
    - Multiple Phase II studies
Ebola Therapeutics

- Mapp Bio
  - Developing a cocktail of chimeric monoclonal antibodies (ZMapp)
    - Has been evaluated in a Phase II/III efficacy trial (PREVAIL II)
    - Trial was halted – trend toward efficacy but failed to meet endpoints

- Regeneron
  - Developing a cocktail of fully human monoclonal antibodies
    - Currently in Phase I

- BioCryst
  - Developing a small molecule drug (BCX4430) – potential broad spectrum
    - Currently in Phase I

- Genentech/Emergent (CIADM)
  - Developing a cocktail of humanized ZMapp clones in CHO cells
    - Currently being evaluated in non-clinical studies

- BARDA supported small-scale efforts with Medicago and Fraunhofer
Expanded Access Protocol

- BARDA is working with Mapp Bio and our International partners to maintain access to ZMapp
- Mapp Bio has established an EAP in Guinea, Sierra Leone, and Liberia
  - Provides continued access to ZMapp, supply chain and storage control of the product, and additional safety and effectiveness data collection
  - Provides a clinical site, potential mobile units, and potential air transportation for 3 years
- The EAP has also been established at the 10 Ebola treatment centers in the US and the NIH hospital
Ebola Diagnostics

- Several diagnostics have received EUA
- BARDA is supporting OraSure for the development of a rapid, POC, diagnostic
  - Has EUA status
  - Utilizes blood or oral fluid
  - Quick – point of care, lateral flow
  - BARDA will support
    - Assay design/improvement
    - Process and product validation
    - Analytical and functional testing
    - Clinical trial to support 510(k) clearance

OraSure Technologies
BARDA’s National Countermeasure Response Infrastructure

Ebola Vaccines

2006
Regulatory & Quality Affairs

2009
ADS Modeling Hub

2013
Clinical Studies Network

2012
CIADMs

2013
Nonclinical Development Network

2013
Fill Finish Mfg. Network

Ebola Therapeutics

2011

Assistant Secretary for Preparedness and Response

Department of Health & Human Services

Biomedical Advanced Research and Development Authority

2009

2011
What’s Next?

- Potential efficacy of one vaccine candidate
  - Data still needs to be reviewed by regulatory agencies
- Trend in benefit for ZMapp
- How will regulatory authorities license vaccines and therapeutics in the absence of definitive or sufficient efficacy data?
  - Animal rule
  - Accelerated approval pathway
- BARDA will continue to support development of vaccines and therapeutics
  - Need to finish the job and support licensure and approval
- Remaining questions:
  - How many vaccines and therapeutics to support?
  - What data is necessary to support potential procurement under PBS for EUA?
  - What is the regulatory path for the products?