CBRN Antivirals & Antitoxins Program

David Boucher, PhD
Branch Chief (Acting)
October 16, 2019
Antivirals & Antitoxins Program

GOAL
Protect the population by developing and maintaining safe and effective therapeutics for anthrax, botulism, smallpox and filoviruses

FOCUS AREAS
• Maintain/enhance preparedness and pursue licensure for Smallpox, Anthrax, Ebola, Botulism therapeutics
• Advance early stage efforts for Sudan & Marburg viruses

STRATEGY
• Sustainability: New technology to reduce life cycle costs and utilize flexible stockpiling strategy
• Improve operational logistics with better formulation
• Reduce risk with diverse portfolios
Antivirals & Antitoxins Portfolio

Discovery

Preclinical

Phase I

Phase II

Phase III

Licensure

Production & Delivery

Filovirus Antivirals

Smallpox Antiviral

Smallpox Antiviral

Anthrax Antitoxin

Botulism Antitoxin

Smallpox Antiviral

Filovirus Antivirals

CHIMERIX

BioCryst Pharmaceuticals, Inc.

ReGENERON

RIDGEBACK BIO

UNCLASSIFIED

Anthrax Antitoxin Program

OBJECTIVE

Protect the population by developing safe and effective anthrax antitoxins to treat patients with inhalational anthrax

Approved Products:

- Raxibacumab
- AIG IV (Anthraxil)
- Obiltoxaximab (Anthim®)

All three products are in the Strategic National Stockpile and available for deployment
Anthrax Antitoxins: Program Strategy and Opportunities

Continuing Efforts
- Coordinate with industry and ASPR/SNS to ensure medical countermeasure preparedness
- Extend shelf-life and improve CONOPs of existing products
- Support completion of post-marketing commitments

Program Objectives
- Further diversify the portfolio and, in turn, our response capabilities

Opportunities
- BARDA BAA, AOI #2.1, ≥TRL-6 and at least one of the following:
  - Peptides, small molecules or novel compounds
  - Unique Mechanism
  - Transformational change in operational use and/or Life Cycle Costs
Smallpox Antiviral Program

OBJECTIVE
Protect the population by developing safe and effective antivirals to treat patients with smallpox disease

Approved Product

ST-246/TPOXX (SIGA)
• Available for deployment from the SNS

Ongoing Programs

CHIMERIX

2019 Starts
Smallpox Antivirals: Program Strategy and Opportunities

Continuing Efforts
- Coordinate with industry and ASPR/SNS to ensure medical countermeasure preparedness
- Extend shelf-life and improve CONOPs of existing products
- Support completion of post-marketing commitments

Program Objectives
- Further diversify the portfolio and, in turn, our response capabilities

Opportunities
- BARDA BAA, AOI #2.3, candidates with evidence of activity against orthopoxviruses
- Candidates ≥TRL-5 are preferred; however, earlier candidates can be considered based on program impact
Botulinum Antitoxin Program

**OBJECTIVE**

Protect the population by developing safe and effective botulism antitoxins to treat patients with botulism intoxication caused by serotypes A-G

**Approved Product:**

hBAT

hBAT is in the Strategic National Stockpile and available for deployment
Botulinum Antitoxins: Program Strategy and Opportunities

Continuing Efforts
- Coordinate with industry and ASPR/SNS to ensure medical countermeasure preparedness
- Support completion of post-marketing commitments

Program Objectives
- Diversify the portfolio and, in turn, our response capabilities

Opportunities
- BARDA BAA, AOI #2.2, candidates that meet at least one of the following:
  - mAbs, peptides, small molecules or novel compounds
  - Unique Mechanism
  - Transformational change in operational use and/or Life Cycle Costs
Filovirus Antiviral Program
Ebola Zaire, Ebola Sudan, Marburg

OBJECTIVE
Protect the population by developing safe and effective antivirals to treat patients infected with Ebola, Sudan or Marburg viruses

ARD Programs
mAb114 (Ebola)
Galidesivir (Marburg)
MBP091 (Marburg)
MBP134 (Sudan)

PBS Programs
ZMapp (Ebola)
REGN-EB3 (Ebola)
Filovirus Antivirals: Program Strategy and Opportunities

**Continuing Efforts**
- Advance products to licensure
- Continue to support field use of REGN-EB3 & mAb114 while maintaining domestic preparedness

**Program Objectives**
- Expand the Sudan & Marburg virus portfolios
- Further diversify the Ebola virus portfolio

**Opportunities**
- BARDA BAA, AOI #2.4, ≥TRL-5 and, for EBOV only, one of the following:
  - Single mAbs, peptides, small molecules or novel compounds
  - Unique Mechanism
  - Transformational change in operational use and/or Life Cycle Costs

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Voice of America, 2017

UN News, 2019
Antivirals and Antitoxins TEAM

Networking Session: Today, 10:45 to 12:00
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CBRN Antibacterials Program

Brian Tse, PhD
Health Scientist, Antibacterials Program
Biomedical Advanced Research and Development Authority
Bacterial Threats in Multiple Dimensions

Key Biothreat Agents

- Plague
  - Y. pestis
- Tularemia
  - F. tularensis
- Melioidosis
  - B. pseudomallei
- Glanders
  - B. mallei
- Anthrax
  - B. anthracis

Opportunistic and Secondary Infections

- Chlorine
  - Dyspnea
  - Lung injury
- Sulfur Mustard
  - Blistering
  - Cellulitis
- Burns
  - Blistering
  - Skin sloughing
- Acute Radiation
  - Neutropenia
  - Immune ablation
- Anthrax
  - Pneumonia
  - Disruption of gut flora
- Influenza
  - Fever
  - Congestion
- Ebola
  - Fever
  - Vomiting / diarrhea
- Smallpox
  - Fever
  - Extensive rash / pustules

Opportunistic Infections

- Persistent infection + sepsis
- Systemic infection + sepsis
- Persistent infection + sepsis
- Systemic infection + sepsis
- Systemic infection + sepsis
- Systemic infection + sepsis
- Systemic infection + sepsis
- Systemic infection + sepsis

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Drug development has not kept pace with the development of antimicrobial resistance.

Antibiotic Resistance (AMR) causes 700,000 global deaths each year.

Deaths may rise to 10M annually by 2050 costing $100 trillion.

Common medical procedures are becoming too dangerous to undertake.

THE LACK OF EFFECTIVE ANTIBACTERIALS IMPEDES OUR ABILITY TO RESPOND TO ANY PUBLIC HEALTH EMERGENCY

Antibacterials Program

MISSION: Revitalize the antibacterial pipeline through innovative public-private partnerships

GOAL: Reduce the morbidity and mortality caused by antimicrobial resistant (AMR) bacterial infections following a mass casualty event or a disease outbreak

STRATEGY: Invest in new types of antimicrobials
- Novel mechanisms of action
- Host-directed therapeutics
- Small molecules
- Non-traditional antimicrobials
- Vaccines
- Diagnostics
Antibacterials – A Continuum of Support

Discovery & Hit-to-Lead

Preclinical Development

Phase I

Phase II

Phase III

Approval & Post-Marketing Commitments

Production

Delivery

IND

NDA/BLA

SNS

CARB-X

Advanced R&D

Project BioShield

Approved Product

Strategic National Stockpile (SNS)

Partners in Development:

NIH National Institute of Allergy and Infectious Diseases

DARPA

DTRA

USAMRIID

US Army Medical Research Institute of Infectious Diseases

Wellcome

IMI Innovative Medicines Initiative

ASPR

BARD
CARB-X
Combating Antibiotic Resistant Bacteria

A Biopharmaceutical Accelerator
Supporting Innovation and Early R&D

Funders

Administration

Accelerators

Alliance Partner

• 30 active projects:
  • 13 new classes of antibiotics
  • 15 new molecular targets
  • 11 non-traditional candidates
  • 4 diagnostics
  • 1 microbiome program
  • 3 vaccines

• $81.5 million in active awards
  • Additional $89.7 million available if project milestones are met

• 6 candidates advanced into clinic

(as of September 24, 2019)
BARDA’s Partners in Advanced Development

Roche
Genentech
Melinta
CUBRC
TETRAPHASE
Rempex Pharmaceuticals
The Medicines Company SD LLC
VenatorRx
S PER Therapeutics
AtoxBio
Summit Therapeutics
QPEX Biopharma
gsk
Basilea
Pfizer
Project BioShield: A First for Antibacterials

Biothreat agents may be resistant to antibiotics already in Strategic National Stockpile (SNS)

Emerging antibiotic resistance may complicate a response to any public health emergency

Adding to SNS novel antibiotics that overcome resistance enhances national security, serves as additional market
Achieving Success, Looking Beyond

- 9 years of partnerships
- Over $1.2 billion invested
- 3 FDA Approvals so far

Breakout Session:
“Addressing the Failing Commercial Market for New Antimicrobial Products”

Wednesday, October 16
Room: Penn Quarter, Grand Hyatt
Time: 1:30 – 2:45 PM
Led by: Dr. Rick Bright, PhD
BARDA Director
Drug class:
- Unprecedented
  - Novel class
- Precedented
  - Priority forms of AR
- Non-traditional Tx
  - Phage
  - Host-based
- Prevention
  - Vaccines
  - Microbiome

Biothreats:
- B. pseudomallei
- B. mallei
- F. tularensis
- Y. pestis
- B. anthracis
- MDR B. anthracis
- Genetically-engineered bacteria

Antibiotic resistance:
- MDR A. baumannii
- MDR P. aeruginosa
- ESBL Enterobacteriaceae
- CR Enterobacteriaceae
- VR Enterococcus
- DR S. pneumoniae
- MR S. aureus

Utility:
- Indications:
  - HABP/VABP
  - CABP
  - BSI
- Route of Administration
  - Oral delivery

www.fbo.gov: BAA-18-100-SOL-00003
What are the Needs of the Antibacterials Program?

- Priority pathogens - especially Gram-negative, or those for which few treatment options exist
- Substantial improvements over existing products - first-in-class, differentiated spectrum, etc.
- Novel approach - novel clinical trial design, continuous manufacturing, etc.
- Late-stage development - more advanced candidates preferred
- Special populations - pediatric, older adults, pregnant, etc.
- Regulatory feedback - supportive FDA feedback
- Cost-sharing

Is the development approach fundamentally sound?
BARDA Antibacterials Team

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CBRN Vaccine Programs

Daniel Wolfe
October 16, 2019
Emergent BioSolutions Announces Exercise by BARDA of the First Contract Option, Valued at $261 Million to Procure Doses of AV7909 Anthrax Vaccine Candidate for the Strategic National Stockpile
Thank you!

Pipeline of Early Stage Vaccine Candidates

Transition of AR&D Programs to Project BioShield

Supporting Programs

- altimmune
- Public Health Vaccines LLC
- Sabin Vaccine Institute
- MERCK
- BAVARIAN NORDIC
- Janssen
- emergent biosolutions™
- Inserm
- Battelle
- UTMB
- Rho

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CBRN Vaccines Program

Pursue licensure and procure vaccines

2019: MVA

2020: V920

2021: AV7909, Ad26

Advance early stage efforts

https://www.sciencenews.org/article/fda-approves-first-smallpox-treatment-tpox

http://www.anthim.com/what-is-anthrax.html

https://www.cdc.gov/media/releases/2013/p0916-untreatable.html

http://www.ox.ac.uk/news/2014-09-08-risk-ebola-emergence-mapped
Smallpox, Anthrax, and Zaire Ebolavirus Vaccines

Program Goals

• Licensure of liquid frozen MVA vaccine, V920, Ad26/MVA, and AV7909
• Pre-Emergency Use Authorization for use in special populations
• Enhanced operational logistics/utility
Marburg and Sudan Vaccines

Program Goals

• Near-term:
  o Establish pipeline of monovalent Marburg and Sudan vaccines
  o Support nonclinical models & assays

• Long-term:
  o Enhance VHF preparedness
  o Achieve Licensure

https://www.sciencedirect.com/science/article/pii/B9780128009468000192
https://www.santafenewmexican.com
https://en.wikipedia.org/wiki/Marburg_virus
https://www.sciencedirect.com/science/article/pii/B9780128009468000192
AMR Bacterial Threat Vaccines

Program Goals

• Focus:
  o Support vaccine programs in areas with limited pipelines
  o *E. coli*, *P. aeruginosa*, *S. aureus*, *A. baumannii*

• Strategy:
  o Partner with industry to push candidates into the clinic

https://www.biocote.com/blog/five-facts-e-coli/
https://wickhamlabs.co.uk/technical-resource-centre/fact-sheet-staphylococcus-aureus/
CBRN VACCINES TEAM

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Broad Agency Announcement:
BAA-18-100-SOL-00003
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