BARDA’s Division of Chemical, Biological, Radiological and Nuclear Medical Countermeasures

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BARDA Industry Day
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ASPR: Saving Lives…Protecting America
CBRN Preparedness

Preparedness Gaps

VESICANTS
ANTHRAX
SMALLPOX
PLAGUE
TULAREMIA
BOTULISM
RADIOLOGICAL
NUCLEAR
NERVE AGENTS
MELIOIDOSIS
GLANDERS
EBOLA
MARBURG
SUDAN
PHARMACEUTICAL-BASED AGENT
CHLORINE
CYANIDE
BARDA CBRN Goals

1. Have at least one stockpiled countermeasure by 2023 for 80% of threats that have Material Threat Determinations

2. Make significant advances in all programmatic objectives by 2023
   • Reach a point where the law of diminishing returns applies

3. Continue to fill operational gaps in our MCM response
PBS Successes – 27 Products

Antitoxins
Vaccines
Botulism
Chemical

Anthrax
Smallpox

Burn Products – Nuclear, Radiation, Chem

Nuclear/Radiation
Ebola

Vaccines
High Throughput

ASPR: Saving lives...Protecting America.
Advanced Research and Development (ARD) Priorities

- Highest: addressing chemical and viral hemorrhagic fever threats
- Repurposing products to treat injuries from radiological and nuclear threats
- Sustained investment in new antibacterial agents, vaccines
- Continual re-evaluation: seeking more effective, sustainable solutions to address dire threats
• August 2017, Rempex Pharmaceuticals received FDA approval for Vabomere to treat complicated urinary tract infections

• This is the first BARDA-supported antibiotic to be FDA approved.
# CARB-X Portfolio

The CARB-X portfolio comprises 18 early stage R&D projects investigating 8 new classes of antibiotics, 5 non-traditional antibiotics, 10 new molecular targets and a rapid diagnostic test to determine the type of drug-resistant bacteria that is causing an infection.

<table>
<thead>
<tr>
<th>Company/Research Team</th>
<th>Project</th>
<th>Novelty*</th>
<th>New Class</th>
<th>New Target</th>
<th>Project Description</th>
<th>Urgency/Priority**</th>
<th>Bacteria Targeted / Stage of Early Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achaogen</td>
<td>AKAO-LpxC</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>LpxC Inhibitor</td>
<td>✓</td>
<td>Pseudomonas aeruginosa</td>
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<tr>
<td>Antbio</td>
<td>PEI</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Pseudomonas Elastase inhibitor</td>
<td>✓</td>
<td>Pseudomonas aeruginosa</td>
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<tr>
<td>Bugworks Research</td>
<td>Gyrox</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Glyrase-topoisomerase inhibitor</td>
<td>✓</td>
<td>Gram-negative activity</td>
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<tr>
<td>Cidara Therapeutics</td>
<td>CD201</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Bifunctional immunotherapy</td>
<td>✓</td>
<td>Acinetobacter + P. aeruginosa + Enterobacteriaceae</td>
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<tr>
<td>ContraFact</td>
<td>Gram-negative lysins</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Recombinant l craprotein</td>
<td>✓</td>
<td>P. aeruginosa</td>
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<td>Debiotherm</td>
<td>Debio 1453</td>
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<td>✓</td>
<td></td>
<td>Narrow-spectrum inhibitor of FabI</td>
<td>✓</td>
<td>Neisseria Gonorrea</td>
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<tr>
<td>Eligochem</td>
<td>Helical AMP</td>
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<td>✓</td>
<td></td>
<td>Helical Antimicrobial Peptide</td>
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<tr>
<td>Entasis Therapeutics</td>
<td>ETX000</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Oral Gram-negative combination</td>
<td>✓</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Forge Therapeutics</td>
<td>FG-LpxC</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>LpxC Inhibitor</td>
<td>✓</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Itera</td>
<td>Sulopenem</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Oral and N penem</td>
<td>✓</td>
<td>Gram-negative activity</td>
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<tr>
<td>Microbix</td>
<td>T3SS Inhibitor</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Virulence modifier</td>
<td>✓</td>
<td>Pseudomonas aeruginosa</td>
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<td>Oppiotech</td>
<td>LPS</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Targets synthesis of LPS</td>
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<td>Gram-negative activity</td>
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<tr>
<td>Reck Pharma</td>
<td>NBT1</td>
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<td>✓</td>
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<td>Dual-enterotoxins inhibitor</td>
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<td>Acin. + P. aeruginosa + Enterobacteriaceae</td>
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<tr>
<td>Spero Therapeutics</td>
<td>SPR741</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Potentiator</td>
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<td>Gram-negative activity</td>
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<tr>
<td>Tetraphase Pharm</td>
<td>TP-6076</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Next-generation tetracycline</td>
<td>✓</td>
<td>Acinetobacter + Enterobacteriaceae</td>
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<td>VenatoRx</td>
<td>VNRR-PBP</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>ß-lactamase Resistant PBP Inhibitor</td>
<td>✓</td>
<td>Enterobacteriaceae</td>
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<tr>
<td>Veterna</td>
<td>V5705</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Antibody-drug conjugate</td>
<td>✓</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>

*Novelty characterizations of new class and new target are established by CARB-X following the Pew Trusts pipeline analysis model. Pew defines a novel chemical class as a group of antibiotics that share a new common core molecular structure. Non-traditional products include lysins and monoclonal antibodies.

**Urgent and priority drug-resistant bacteria are determined by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).

Stage of development is approximate as of July 2017.
MCM Status: Anthrax

- Vaccine stockpiled
- Next generation vaccine under PBS-lower cost, improved CONOPs
- Multiple antibiotics
- Multiple antitoxins
- Future: Sustainment
MCM Status: Botulism

• Emergent has performed under BARDA contract since 2006 for the development of an equine heptavalent botulism antitoxin (hBAT)

• hBAT was approved to treat confirmed or suspected botulism in adults and pediatrics in March 2013

• Product is capable of treating all seven serotypes of botulism

• Future: sustainment, need to plan for next gen solution
MCM Status: Smallpox

- Stockpiled vaccine for special populations
- Stockpiled antiviral drug for the treatment of symptomatic infections
- Need for IV formulation
- Future: 2nd antiviral drug, new formulations
MCM Status: Bacterial Threats

- Multiple generic antibiotics stockpiled for bacterial threat agents
- Support development of new antibiotics to mitigate impact of resistance on our ability to respond to ALL threats
- Future: FDA approval of late stage candidates out of ARD portfolio, graduate programs out of CARB-X
MCM Status: Radiation

- Biodosimetry to triage patients
- Stockpiled cytokines to treat neutropenia
- Future: Thrombocytopenia, Coagulopathy, point-of-care Biodosimetry
MCM Status: Thermal Burns

- Stockpiling 4 products awarded under PBS
- Working towards transforming the continuum of care for burn patients
- Future: Studies in pediatric populations, Temporizing matrix, enhanced imaging devices
MCM Status: Ebola/VHF

- PBS awards for late stage development and stockpiling of Ebola Zaire vaccine(s) therapeutic(s) completed in FY2017

- Goal will be licensure/approval of those products

- Future: Transition support to Ebola Sudan and Marburg MCMs
MCM Status: Nerve Agents

- Published decontamination guidance
- In process of stockpiling midazolam as anti-seizure therapy
- Future: Therapies to treat seizures refractory to midazolam treatment
• We need MCMs for these threat agents

• Advanced Research and Development efforts focused on treating the injury

• Focus on repurposing where possible

• Future: Heavy investment, transition to PBS
MCM Status: Cyanide

• Need for improved antidotes

• Focus on more rapid delivery, ease of administration-intranasal formulations

• Future: Transition programs to PBS
Overarching Challenges

- Sustainment
- Maintaining an industry base
- Thin MCM Pipeline (chemical and radiological and nuclear)
- Limited BSL-4 space
CBRN Initiatives

- Develop animal models to support licensure of Ebola/VHF MCMs
- Develop animal models to support the FDA approval of chemical and radiological and nuclear MCMs
- Invest in technologies to enhance sustainment, improve response operations, lower life cycle costs
Summary

- BARDA has successfully developed and stockpiled MCMs against multiple threats
- Significant threats remain unaddressed
- Sustainability is a challenge
- BARDA seeks to partner with industry to address the remaining gaps with flexible, nimble public private partnerships
BARDA’s ORISE Fellowship

• BARDA initiated the ORISE fellow program at BARDA to attract early career scientists

• Anticipating hosting 3-5 fellows/per year for a 2 year fellowship

To apply:
www.zintellect.com and search BARDA

Please send questions by email to:

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