How BARDA Incentivizes Antibacterial Development from Early Development through Marketing Approval

Mark Albrecht, PhD
Chief, Antibacterials Branch
Biomedical Advanced Research and Development Authority

Enhancing the Clinical Trial Enterprise for Antibacterial Drug Development in the US
November 18-19, 2019

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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
- Non-traditional antimicrobials
- Host-directed therapeutics
- Small molecules
- Vaccines
- Diagnostics
BARDA’s Antibiotic Innovation Partners

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
Approved Product
Project BioShield
Strategic National Stockpile (SNS)

Partners in Development:
NIH
DARPA
DTRA
USAMRIID
USF
W
IMI

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CARB-X

as of 6/30/2019

43% of companies indicated not receiving prior USG funding

$74.8M
Follow-on government funding (US and other countries)

$933M
Private Investment since CARB-X Award

$180M
BARDA Investment (2016-2019)

50 Projects

38 drugs
6 diagnostics
3 microbiome
3 vaccine

7 Countries

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Antibacterials Advanced Research and Development (ARD) Program Partners
Recent Approvals to Address Unmet Medical Needs

- Approvals over the last 2 years have been a culmination of 9 years of dedication to the AMR enterprise
- Emphasis on getting drugs to market following established pathways
  - Complicated Urinary Tract Infections & Acute Pyelonephritis
  - Complicated Intra-abdominal Infections
- Operational goal has been to make antibiotics commercially available in pharmacies and hospital formularies while generating biothreat data for Emergency Use Authorization
“BARDA simply cannot continue to provide non-dilutive investment, only to have companies collapse and their newly minted antibiotics shelved or lost completely”

- Rick Bright, BARDA Director
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
**Clinical Trial Partnership**

**Global Network to Conduct the Most Challenging Antibiotic Clinical Studies**

**PROBLEM**
- Antibiotics are being approved for easier-to-get indications (e.g., cUTI, cIAI) with little product differentiation
- Priority indications (e.g., pneumonia, bloodstream infections) are challenging to pursue
- Result:
  - Investors focus on low risk, low cost, fast-to-market
  - Clinicians don’t know how these drugs will perform at alternative body sites

**SOLUTION**
- Reduce barriers (cost, risk, time) of clinical trials for critically needed indications
- Establish a global clinical trial capability committed to the AMR space
  - *How will this be done?*
    - Cost: provide funding
    - Speed: targeted enrollment for limited populations with specialized investigators
    - Reduced Risk: provide technical support, focus on high resistance rate areas

**APPROACH**
- Successful Models: Define partnership model incorporating learnings from experiences such as TB Alliance, ACTG, Mycosis Study Group, CARB-X, Oncology, and others
- Core Partners: NIAID/NIH, FDA, BARDA, Industry
- Potential Partners: Wellcome Trust, DOD, UK Government, B&M Gates Foundation, others
- Goal: Enable 4-6 label expansions
# Advantages of a Clinical Trial Partnership

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<tr>
<th>Conventional Approach</th>
<th>Clinical Trial Network Approach</th>
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<tr>
<td>Pivotal studies are complex and expensive</td>
<td>Reduce overall time and costs to completion</td>
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<td>Inefficient design: One drug = One trial</td>
<td>Optimize design: Many drugs = one trial</td>
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<td>Sponsor-led oversight: Independent decision-making for each trial, infrequent engagement with regulators, each trial protocol is unique</td>
<td>Centralize oversight: Engagement with stakeholders, e.g., FDA and NIAID throughout study planning, execution, and decision-making</td>
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<td>Each trial requires new start-up, establish CRO, identify clinical sites, initiate trial activities, and dismantle infrastructure at the end of the trial</td>
<td>Improve start-up: established contracts and data collection systems, established sites with demonstrated patient flow, trained staff reduce risk of trial failure due to conduct issues</td>
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<td>Patient accrual challenges, rare infections lead to enrollment challenges, cost increases and time delays</td>
<td>More efficient use of patients and resources, “networks could reduce trial size by up to 43%” KOL</td>
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BARDA will continue to leverage its unique authorities to provide innovative business tools that support end-to-end product development, from the earliest stages under CARB-X to commercial procurement via PBS, while at the same time exploring technical solutions to the challenges facing the commercial market.