CARB-X Portfolio: Accelerating Innovation in Antibacterial Drug Development

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FDA Workshop: Advancing Animal Models for Antibacterial Drug Development
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CARB-X

Combating Antibiotic Resistant Bacteria

A global non-profit partnership accelerating science to fight drug resistant bacteria. CARB-X supports R&D from around the world to address the most serious drug-resistant bacterial infections.

FUNDERS

ASPR – Assistant Secretary for Preparedness and Response

BARDA – Biomedical Advanced Research and Development Authority

NIH – National Institute of Allergy and Infectious Diseases

wellcome

UKaid from the British people

Bundesministerium für Bildung und Forschung

ALLIANCE PARTNER

Bill & Melinda Gates foundation

HEADQUARTERS & ADMINISTRATION

Boston University

ACCELERATORS

Basel Area. Swiss

BioInnovation Institute

DZIF German Center for Infection Research

FIND Because diagnosis matters

ILSE Institute for Life Science Entrepreneurship

CLSI California Life Sciences Institute

C-CAMP Centre for Cellular and Molecular Platforms

MassBio Massachusetts Biotechnology Council

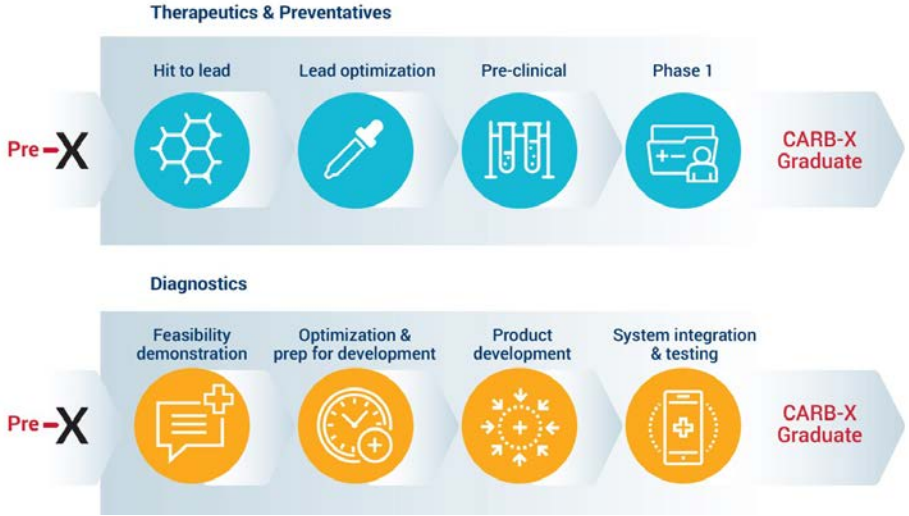
RTI International

CARB-X Funds Candidates that Address Serious Bacterial Threats

Portfolio includes

- Traditional and non-traditional therapeutics
- Preventives such as vaccines, microbiome, and antibodies
- Rapid diagnostics for pathogen ID/AST

Projects must target specific bacteria on the **Antibiotic Resistance Threats** list issued by the CDC in 2013, the **Priority Bacterial Pathogens** list published by WHO in 2017, or included in the **Vaccines to Tackle Drug Resistant Infections: An Evaluation of R&D Opportunities** joint report from The Wellcome Trust and Boston Consulting Group.



In Addition to Funding, CARB-X Provides Scientific, Regulatory and Business Expertise and Support

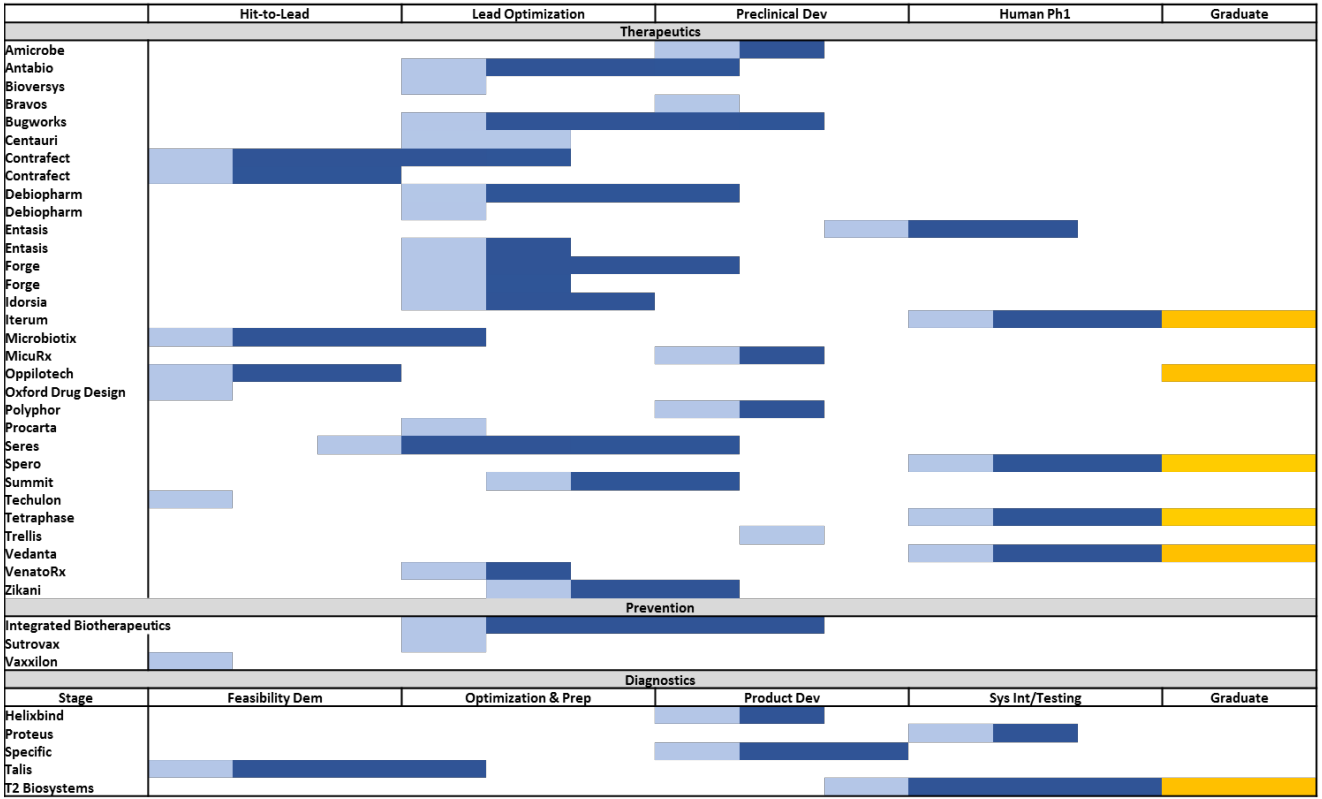
Support

- Company Support Teams and accelerators tailored to each program's needs
- Specialized know-how in antibacterial drug development, diagnostics, vaccines, business and legal strategy, regulatory affairs, and other areas essential to product development
- No cost to product developers
- Streamlined access to NIAID preclinical services
- Benefits of CARB-X ecosystem

CARB-X
Global Accelerator Network

9 world-class accelerators in 5 countries supporting the development of new antibiotics and other life-saving products to fight drug-resistant bacteria

CARB-X Program Progress Since Initiation*



*Portfolio as of Feb 1, 2020:
55 awards made since 2016
35 programs 'active'
6 programs 'graduated'

One Dx program graduate received BARDA award for support of advanced R&D through regulatory approval

Status at initiation
Program progress
CARB-X 'Graduates'

CARB-X Direct-Acting Therapeutics, Target Pathogens and Stages of Development*

Cell-wall synthesis

PBPi – next-generation
- Iterum Ph1 — ESKAPE

Novel PBPi
- Entasis LO — ESKAPE
- Venatorx HtL — Ng

BL/BLI
- Entasis Ph1 — ESKAPE

LpxC
- $Forge_{UTI}$ LO→PC — ESKAPE
- $Forge_{RTI}$ LO — ESKAPE

OMPTA
- Oppilotech HtL — ESKAPE
- Polyphor PC — ESKAPE

DNA synthesis

NBTI
- Bugworks LO→PC — ESKAPE
- Idorsia PC — ESKAPE

RNA synthesis

Protein synthesis

30S – next-generation
- Tetraphase Ph1 — ESKAPE

50S– next-generation
- Zikani LO→PC — ESKAPE

tRNA synthetase I
- Oxford D.D. HtL — ESKAPE

Fatty-acid biosynthesis

- Debiopharm LO→PC — Ng
- Debiopharm LO — ESKAPE

Other

- Summit PC — Ng

*CARB-X portfolio as of 2/1/2020

ESKAPE, nosocomial virulent drug-resistant pathogens: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* spp.
HtL, Hit-to-Lead. **LO**, Lead Optimization. **PC**, preclinical, IND-enabling, **Ph1**, Phase 1.

CARB-X 'Non-traditional' Therapeutics, Target Pathogens and Stages of Development*

Anti-Virulence

Antabio (elastase i) LO→PC	ESKAPE
Microbiotix (T3SSi) PC	ESKAPE
Bioversys (AgrAi) LO	ESKAPE
Trellis (biofilm) PC	ESKAPE

Potentiators

Spero Ph1	ESKAPE
Taxis HtL	ESKAPE

Phage/Lysins

Contrafect HtL→LO	ESKAPE

Membrane Disruption

Peptides	
Amicrobe (topical) PC	ESKAPE
Contrafect (amurin) HtL	ESKAPE
MicuRx (polymyxin) PC	ESKAPE

Microbiome

Vedanta Ph1	Cd
Seres PC	ESKAPE
Vedanta PC	ESKAPE

Other

Bravos PC	ESKAPE
Centauri LO	ESKAPE
Procarta LO	ESKAPE
Techulon HtL	ESKAPE

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CARB-X R&D Opportunities in Utilization of Animal Models and PK/PD to Support Clinical Development

We aim to establish best practices and guide developers in utilizing animal model data to mitigate development risk and support product clinical pharmacology dossier. For example:

- HABP/VABP, MDR pathogen studies
- Narrow spectrum indications, most candidates are ‘nontraditionals’
  - ✓ *Pseudomonas*
  - ✓ *Acinetobacter*
  - ✓ MRSA
  - ✓ *Neisseria gonorrhoeae*
  - ✓ *Clostridium difficile*
  - ✓ *Enterobacter*
- Anti-virulence candidates - regulatory pathway??
- Nephrotoxicity models and translation to clinic, etc.

Efficacy Models Considerations for CARB-X Portfolio

Product Candidate Class	Pathogens & Indications	Questions on Animal Models
Narrow spectrum direct-acting agents	*Acinetobacter* *Pseudomonas* HABP/VABP	Best models to translate in vitro activity?
Narrow spectrum indirect-acting, nontraditional agents	*Acinetobacter* *Pseudomonas* *Staphylococcus* HABP/VABP	Best models to translate in vitro activity? Are the best predictive models the same as those used for direct-acting agents?
Peptides and other nontraditional agents	ESKAPE broad spectrum HABP/VABP	If in vitro activity is higher for Pseudomonas and/or Acinetobacter, what is the best demonstration of efficacy to justify a narrow clinical focus?
Direct acting agents	*Neisseria gonorrhoeae*	Best models to translate in vitro activity?

BARDA Nonclinical Development Network

- Facilitates nonclinical model development and/or supportive reagents and assays for regulatory acceptance of BARDA MCMs and evaluates potential MCM candidates prior to BARDA investment
- Network partnerships with 19 nonclinical laboratories to support:
  - **Biological Nonclinical Program support of antibacterial studies**
    - ✓ **Development and refinement of nonclinical infection models for evaluation of antimicrobial agents**
      - **Porcine model of VABP caused by *Pseudomonas aeruginosa***
      - **Hamster model of *Clostridioides difficile* infection**
      - **Multiple models of infection with Tier 1 bacterial select agents**
  - Chemical Nonclinical Program
  - Rad/Nuc Nonclinical Program

Supported 40+ programs across BARDA divisions.
Contributed to licensure or approval of 6 MCMs under the Animal Rule.

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BOSTON UNIVERSITY

CARB-X Ecosystem Partners
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How to Contact BARDA

phe.gov/BARDA
Program description, information, news, announcements, connect to TechWatch

medicalcountermeasures.gov
Portal to BARDA: ***Register to request a TechWatch meeting!***

beta.sam.gov/
Official announcements and info for all government contract solicitations

drive.hhs.gov
Learn about DRIVe, including our Accelerator Network and EZ BAA

www.usajobs.gov
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