BARDA INDUSTRY DAY

CARB-X

Global Accelerator for Revitalizing Antibiotic Clinical Pipeline

Tina Guina, PhD
CARB-X Program Manager, BARDA

BARDA Industry Day
Addressing AMR: CARB-X and Other Models

October 29-30, 2018 | Grand Hyatt • Washington, D.C.
Antibiotic Resistance is an Urgent Health Security Threat. How Do We Repopulate the Clinical Pipeline?

<table>
<thead>
<tr>
<th>Hit-to-Lead &amp; Lead Optimization</th>
<th>Preclinical</th>
<th>Phase 1</th>
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<th>Phase 3</th>
<th>Registration</th>
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<tbody>
<tr>
<td>CARB-X</td>
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<td>BARDA BAA</td>
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<table>
<thead>
<tr>
<th>Probability of success</th>
<th>Time</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>.02 - 2.5%</td>
<td>3-7 yrs</td>
<td>$100-130M</td>
</tr>
<tr>
<td>3-5%</td>
<td>1/2 - 2 yrs</td>
<td>$60-70M</td>
</tr>
<tr>
<td>6-14%</td>
<td>1-2 yrs</td>
<td>$70-100M</td>
</tr>
<tr>
<td>25-30%</td>
<td>2 - 3.5 yrs</td>
<td>$130-160M</td>
</tr>
<tr>
<td>50-64%</td>
<td>2.5 - 4 yrs</td>
<td>$190-220M</td>
</tr>
<tr>
<td>75-90%</td>
<td>1-2 yrs</td>
<td>$18-20M</td>
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Licensed product
CARB-X Accelerates R&D To Combat Antibiotic Resistant Bacterial Infections

Global nonprofit partnership provides non-dilutive funding for antibacterial innovation around the world. CARB-X’s network of accelerators provides science & business support to product developers. Investments are leveraged (cost share).
CARB-X Accelerator Provides Push Incentives in The High-Risk Space

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- **Probability of success**
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  - **2.5 - 4 yrs**
  - **1-2 yrs**

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  - **$60-70M**
  - **$70-100M**
  - **$130-160M**
  - **$190-220M**
  - **$18-20M**
CARB-X Funds Products that Target Antibiotic Resistant Bacteria

• Products that address serious bacterial threats
  ▪ antibiotics and other therapeutics
  ▪ rapid diagnostics
  ▪ prevention such as vaccines

• Projects must target infections caused by bacteria on the Antibiotic Resistance Threats list issued by the Centers for Disease Control and Prevention (CDC) in 2013 or on the Priority Bacterial Pathogens list published by the World Health Organization (WHO) in 2017
CARB-X Supports Programs in Early Development
CARB-X Welcomes Applications from Around The World

Projects are selected through a competitive process by panels of experts. Funded projects are supported by a network of world-class accelerators.

Funding & Alliance Partners ($500 million+ 2016-2021)

Other Partners & Accelerators (Scientific & Business)

CARB-X

Scientific Review: Advisory Board reviews applications & makes recommendations

Governance: Joint Oversight Committee makes funding decisions

Administration: Boston University hosts CARB-X

Applications for funding

Received from companies around the world

Selected projects

Receive funding & accelerator support
End of Year 2 Results By The Numbers

- 33 projects in the pipeline
- $91.1M invested, plus an additional $96.5 million committed if project milestones are met
- 7 countries
- 10 new classes of antibiotics
- 11 new molecular targets
- 11 non-traditional candidates
- 5 diagnostics
- 3 microbiome programs
- 1 vaccine
- 5 candidates advanced into clinic*

*Spero Therapeutics SPR741 completed Phase 1, not shown in current pipeline
Benefits of being *Powered by CARB-X*

- Non-dilutive funding
- CARB-X Support Team established for each company
  - CARB-X Support Team Lead
  - Accelerator support aligned to company profile and needs – business mentoring and scientific expertise
  - Streamlined access to NIAID preclinical services
- Benefits of CARB-X ecosystem
Every $1 that CARB-X invested in Powered by CARB-X projects was followed by $8.7 in private funding.

* As of June 30, 2018

** Total CARB-X investment announced to June 30, 2018. Does not include obligations to be paid in future periods.
### Saving Lives. Protecting Americans.

What is in the **Powered by CARB-X Pipeline?**
Ten New Classes of Antibiotics

- Gyrase-topoisomerase Inhibitor: GYROX
- Direct-Acting Small Molecule Therapeutic: CZ-02
- Narrow-spectrum Inhibitors of FabI: Debio1453
- Helical AMPS: Helical AMP
- Direct-Acting Small Molecule Therapeutic: Non-BL PBPI
- Direct-Acting Small Molecule Therapeutic: TOPESKAPE
- LpxC Inhibitor: FG-LpxC
- Direct-Acting Small Molecule Therapeutic: Pyrrolocytosines
- Direct-acting Small Molecule Therapeutic: SMT-571 Series
- β-lactamase Resistant PBP Inhibitor: VNRX-PBP

Powered by CARB-X
## Eleven Candidates with New Molecular Targets

<table>
<thead>
<tr>
<th>Company</th>
<th>Target/Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANTABIO</td>
<td>Developing tomorrow's antibacterials</td>
</tr>
<tr>
<td>CIDARA Therapeutics</td>
<td>Bifunctional immunotherapy</td>
</tr>
<tr>
<td>ContraFect</td>
<td>Recombinant lysozyme protein</td>
</tr>
<tr>
<td>CURZA</td>
<td>Direct-Acting Small Molecule Therapeutic</td>
</tr>
<tr>
<td>DebiopharmGroup</td>
<td>Narrow-spectrum inhibitors of FabI</td>
</tr>
<tr>
<td>FORGE Therapeutics</td>
<td>LpxC Inhibitor</td>
</tr>
<tr>
<td>PEI</td>
<td></td>
</tr>
<tr>
<td>CD201</td>
<td></td>
</tr>
<tr>
<td>Lysins</td>
<td></td>
</tr>
<tr>
<td>CZ-02</td>
<td></td>
</tr>
<tr>
<td>Debio1453</td>
<td></td>
</tr>
<tr>
<td>FG-LpxC</td>
<td></td>
</tr>
<tr>
<td>INHIBRx</td>
<td>Indirect therapeutic - multi-specific antibody</td>
</tr>
<tr>
<td>Melinta</td>
<td>Direct-Acting Small Molecule Therapeutic</td>
</tr>
<tr>
<td>MICROBIOTIX Inc.</td>
<td>Indirect therapeutic - virulence modifier</td>
</tr>
<tr>
<td>Summit Therapeutics</td>
<td>Direct-acting Small Molecule Therapeutic</td>
</tr>
<tr>
<td>Visterra</td>
<td>Antibody-drug conjugate</td>
</tr>
<tr>
<td>INBRX-111</td>
<td></td>
</tr>
<tr>
<td>Pyrrolocytosines</td>
<td></td>
</tr>
<tr>
<td>T3SS</td>
<td></td>
</tr>
<tr>
<td>SMT-571</td>
<td></td>
</tr>
<tr>
<td>VIS-705</td>
<td></td>
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</table>
Twenty Small Molecules

- Achaogen: Direct-Acting Small Molecule Therapeutic
- Antabio: Pseudomonas Elastase Inhibitor
- Bugworks: Gyrase-topoisomerase Inhibitor
- CIDARA Therapeutics: Bifunctional immunotherapy
- Curza: Direct-Acting Small Molecule Therapeutic
- Debiopharm Group: Narrow-spectrum Inhibitors of FabI
- Eligochem: Helical AMPS
- Entasis Therapeutics: Oral Gram-negative combination
- Entasis Therapeutics: Direct-Acting Small Molecule Therapeutic
- Forge Therapeutics: LpxC Inhibitor
- Idorsia: Direct-Acting Small Molecule Therapeutic
- Iterum Therapeutics: Oral and IV penem
- Macrolide Pharmaceuticals: Direct-Acting Small Molecule Therapeutic
- Melinta Therapeutics: Direct-Acting Small Molecule Therapeutic
- Microbiotix Inc.: Indirect therapeutic - virulence modifier
- MicuRx Pharmaceuticals: Direct-Acting Small Molecule Therapeutic
- Shionogi: Direct-Acting Small Molecule Therapeutic
- Summit Therapeutics: Direct-acting Small Molecule Therapeutic
- Tetrophage Pharmaceuticals: Next-generation tetracycline
- Venator Pharmaceuticals: β-lactamase Resistant PBP Inhibitor

# Ten Nontraditionals and One Vaccine

<table>
<thead>
<tr>
<th>AMICROBE</th>
<th>Pseudomonas Elastase Inhibitor</th>
<th>CIDARA THERAPEUTICS</th>
<th>ContraFect</th>
<th>INHIBRx</th>
<th>Integrated Biotherapeutics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct-Acting Large Molecule</td>
<td>Bifunctional immunotherapy</td>
<td></td>
<td>Recombinant lysin protein</td>
<td>Indirect therapeutic - multi-specific antibody</td>
<td>Vaccine</td>
</tr>
<tr>
<td>Therapeutic, Topical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amicidin-β</td>
<td>PEI</td>
<td>CD201</td>
<td>Lysins</td>
<td>INBRX-111</td>
<td>IBT-V02</td>
</tr>
</tbody>
</table>

| MICROBIOTIX Inc.              | Microbiome                      | VISTERRA            | VIS-705    |         |                           |
| SCIBAC                        | Direct-Acting Microbiome-based  | VEDANTA BIOSCIENCES | VE303      |         |                           |
| Inc.                          | Therapeutic                     |                      |            |         |                           |
| always trust your gut.        |                                | Antibody-drug conjugate |          |         |                           |
| T3SS                          | SCB-102                         | SER-155             | VE303      | VIS-705 |                           |

Immunotherapeutics, microbiome, lysin, amino acid copolymers, toxin inhibitor, protein secretion inhibitor
Five Diagnostics

- HELIXBIND: Direct-from-Specimen Diagnostic
- PROTEUS: Optical bacterial imaging Diagnostic
- SPECIFIC: Diagnostic
- T2Biosystems: Diagnostic
- TALIS: POC Diagnostic

- Rapid/BSI
- Optical Bacterial Imaging
- SPECIFAST
- T2MR
- POC DX FOR NG/CT

Powered by CARB-X

**Five Candidates Achieved Clinical Development**

<table>
<thead>
<tr>
<th>Company</th>
<th>Description</th>
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<tr>
<td>Entasis Therapeutics</td>
<td>Oral Gram-negative combination</td>
</tr>
<tr>
<td>Iterum Therapeutics</td>
<td>Oral and IV penem</td>
</tr>
<tr>
<td>Spero Therapeutics</td>
<td>Potentiator indirect Therapeutic</td>
</tr>
<tr>
<td>Tetraphase Pharmaceuticals</td>
<td>Next-generation tetracycline</td>
</tr>
<tr>
<td>Vedanta Biosciences</td>
<td>Direct-Acting Microbiome-based Therapeutic</td>
</tr>
<tr>
<td><strong>Oral BI-BLI combination</strong></td>
<td>Oral and IV penem</td>
</tr>
<tr>
<td><strong>Oral and IV penem</strong></td>
<td><em>Antibiotic potentiator</em></td>
</tr>
<tr>
<td><strong>Next generation tetracycline</strong></td>
<td>Next generation tetracycline</td>
</tr>
<tr>
<td><strong>Microbiome therapeutic</strong></td>
<td>Microbiome therapeutic</td>
</tr>
</tbody>
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*Completed Phase 1 and graduated from Powered by CARB-X portfolio in 2Q2018*
## Pathogens Targeted in Current Portfolio

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Therapeutic</th>
<th>Vaccine</th>
<th>Diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative activity</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Broad spectrum</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Acinetobacter baumanii</em></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td>✓</td>
<td></td>
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CARB-X Partnership is Growing Globally

• UK Government and Bill & Melinda Gates Foundation joined CARB-X partnership in May 2018. New partners expected soon

• CARB-X’s global Accelerator Network is expanding to support Powered by CARB-X companies. Stay tuned

• Education and training platforms developed with organizations including GARDP and Pew Charitable Trusts

• 2018 has been a year of exceptional growth – pipeline has almost doubled and is growing in size and diversity. New awards to be announced in 2019. Stay tuned
Acknowledgments

CARB-X Core (16)

Kevin Outterson
Diane MacDonald
Barry Eisenstein
Karen Gallant
Rich Lawson

Johnny Sihakhamfong
Kathleen Chardavoyne
Merribeth Morin
Nadia Cohen
Raj Shetty
Rose Garson

Alexandra Regan
Alison Haight
Christina Mercado
Jason Vo
Jennifer Robinson

Sinnamon Tierney
Su Chiang
Yelena Greenberg

CARB-X Scientific Advisory Board (80+)

Partners and Accelerators (30+)

Finance and Grants (25)

Diane Baldwin
Gretchen Hartigan
Others

Others

Thank You for Your Attention!
Addressing AMR: CARB-X and Other Models
Panel Discussion

Ann Eakin, PhD  
Senior Scientific Officer  
Concept Acceleration  
NIAID/NIH

Kevin Outterson, JD  
CARB-X Exec. Director  
Professor of Law  
Boston University Law School

Lynn Marks, MD  
Advisor to BARDA  
Ex-SVP Clinical Development  
GSK

Tyler Merkeley, MS, MBA  
Interim Director  
DRIVE, BARDA
Audience Q&A

Thank you!

Tina.Guina@hhs.gov
Backup Slides
## What to Expect When You Apply for CARB-X Funding

<table>
<thead>
<tr>
<th>Month</th>
<th>Cycle begins</th>
<th>Expression of Interest</th>
<th>Review by CARB-X</th>
<th>Short Form</th>
<th>Review by CARB-X</th>
<th>Long form</th>
<th>Final Review</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CARB-X sets the scope and timing of funding cycle, and opens the application period.</td>
<td>Companies submit Expressions of Interest summarizing the product proposed as a candidate for support. EOs should not include confidential information.</td>
<td>CARB-X evaluates the application and selects qualifying projects. CARB-X invites selected applicants via email to provide more detail in a confidential Short Form.</td>
<td>Selected companies submit confidential Short Forms.</td>
<td>CARB-X evaluates the Short Form and invites selected applicants via email to provide more detail in a confidential Long Form.</td>
<td>Selected applicants submit Long Form and a detailed budget.</td>
<td>Long Form applicants are invited to present their project proposals in person to an Advisory Board panel. Applicants undergo due diligence.</td>
<td>Final funding decisions made by CARB-X’s JOC. Sub-award negotiations begin on project plan, milestones and budgets. Applicants must agree contractually to certain standards and conditions. Project support begins.</td>
</tr>
</tbody>
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Who Can Apply for CARB-X Funding?

CARB-X welcomes applications from around the world

- Projects must be in scope – CARB-X and specific round
- Applicants must have legal entity and be considered a going concern – solvent with funding in place for at least 12 months
- Applicants must own or have rights to the intellectual property and reasonable expectation of freedom to operate required to carry out the project
- Applicants must be able to contribute at least 30% of the cost of the program/project
- Applicants must have appropriate operations or capabilities in place to support product development, at least through proposed project phases
- Applicants from noncommercial drug development centers or academic institutions must meet additional requirements (next slide)
CARB-X Welcomes Applications from Academic and Non-commercial Developers

Organization must be able to demonstrate R&D/business capabilities, including

- Capabilities similar to those expected of a drug development industry partner, particularly through the development stages in scope for CARB-X.
- Access to and use of relevant experts (internal and/or external) to advance projects toward clinical investigation within the framework of a major regulatory agency, e.g. FDA, EMA, PMDA
- Active management of IP supporting the project
- Well-developed strategy for advancement to human clinical with options for ‘exit strategy’ from organization (e.g. spin out, licensure to biotech)
- Capabilities in commercial (business) development and technology transfer
- Financial commitment and stability to cover cost share of at least 30% of the total cost of the project

Please note: CARB-X does not fund basic research/drug discovery including screening for novel targets
How to contact BARDA

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

- www.fbo.gov/ ("FedBizOpps")
  Official announcements and info for all government contract solicitations

- https://www.phe.gov/about/BARDA/Pages/default.aspx
  Program description, information, news, announcements

- www.drive.hhs.gov
  DRIVE questions

- https://www.usajobs.gov/
  Join the team!
How to contact BARDA

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  - DRIVe questions

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  - Join the team!