CARB-X Funding Rounds for 2018
Supporting innovation to fight drug-resistant bacteria

Kevin Outterson
29 March 2018
A non-profit partnership accelerating the best science from around the world to fight drug resistant infections
CARB-X funds R&D to combat the rising threat of serious drug-resistant bacteria

Urgent public health need
Antibiotic resistance kills an estimated 700,000 people each year world-wide. No new antibiotic classes for drug-resistant Gram-negative bacteria have been approved in decades.

Turning science into products
CARB-X provides non-dilutive funding and accelerator support for projects that target Gram-negative resistant bacteria on the WHO and CDC priority lists.

Investing globally
CARB-X is a non-profit public-private partnership investing $455M in 2016-2021 to accelerate the early development of life-saving antibiotics, vaccines and rapid diagnostics.

Partnering for results
CARB-X is funded by BARDA and the Wellcome Trust. NIAID provides pre-clinical services. Partners include the Broad Institute of MIT and Harvard, Massachusetts Biotechnology Council (MassBio), California Life Sciences Institute (CLSI) and RTI International. CARB-X is led by Boston University.
Combating antibiotic resistant bacteria

Better stewardship for existing antibiotics

Eliminate inappropriate use of these lifesaving drugs in both humans and animals.

Reduce the need for antibiotics by using alternative and nontraditional approaches to disease treatment and prevention.

Ensure that antibiotics are accessible and available to the people who need them.

Innovation to find new types of antibiotics

Support targeted research initiatives to overcome scientific challenges impeding the discovery of new antibiotics.

Address the complex barriers hindering the development of new treatment options for patients.

Drug-resistant bacteria
Centers for Disease Control and Prevention
Global Reach: CARB-X Funds 28 Projects in 7 Countries*

North America

Forge Therapeutics
San Diego, CA

Cidara Therapeutics
San Diego, CA

Inhibrx
La Jolla CA

Amicrobe Inc.
Calsbad, CA

Curza
Salt Lake City, UT

Helixbind
Marlborough, MA

Macrolide Pharmaceuticals
Watertown, MA

VenatoRx Pharmaceuticals
Malvern, PA

Integrated Biotherapeutics
Rockville, MD

Contrafect Corporation
Yonkers, NY

Seres Therapeutics
Cambridge, MA

Vedanta Biosciences
Cambridge, MA

T2 Biosystems
Lexington, MA

MicuRx Pharmaceuticals
Hayward, CA

Spero Therapeutics
Cambridge, MA

Visterra Inc.
Cambridge, MA

Tetraphase Pharmaceuticals Inc.
Watertown, MA

Entasis Therapeutics (2)
Waltham, MA

Microbiotix Inc.
Worcester, MA

Europe and Asia

Iterum Therapeutics Ltd.
Dublin, Ireland

Proteus IRC
Edinburgh, Scotland

Oppilotech Ltd.
London, UK

Eligochem Ltd.
Sandwich, UK

Antabio
Labège, France

Debiopharm International S.A.
Lausanne, Switzerland

Bugworks Research India Pvt Ltd.
Bangalore, India

Shionogi & Co., Ltd
Osaka, Japan

Great science knows no boundaries

* As of 29 March, 2018
• 23 early development projects targeting serious drug resistant bacteria
• 8 new classes of antibiotics
• 10 non-traditional antibiotics
• 11 new molecular targets and a rapid diagnostic
CARB-X has announced more than $62 million in awards, plus an additional $77 million if project milestones are met.

Many more awards to come in 2018, including a significant number of additional diagnostics.
What CARB-X Funds

- Early development projects that address serious bacterial threats
  - antibiotics and therapeutics of all types
  - rapid diagnostics
  - prevention such as vaccines, microbiome, devices

- Projects must target specific 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 Funds Projects in Early Development

**Therapeutics & Preventatives**
- Hit to lead
- Lead optimization
- Pre-clinical
- Phase 1

**Diagnostics & Devices**
- Feasibility demonstration
- Optimization & prep for development
- Product development
- System integration & testing

CARB-X Graduate
CARB-X 2018 Funding Round 1

• Scope of Round 1
  – **New classes** of direct-acting small molecule and direct-acting large molecule antibiotics that target certain Gram-negative bacteria
• Expressions of Interest (EOI) accepted on-line only [www.carb-x.org/application](http://www.carb-x.org/application)
• EOI must be submitted March 22 through March 29, 2018, 5 pm EST

Applying for Round 1? Mark your calendar March 22 – 29, 2018
CARB-X 2018 Funding Round 1 – Scope

Only projects in scope will be considered for funding by CARB-X. Please consult the tables below carefully. To be considered, Expressions of Interest for Round 1 must be submitted online March 22, 2018 through March 29, 2018, 5 pm EST

2018 Funding Round 1 is restricted to 1) NEW classes of direct-acting small molecule therapeutics and 2) direct-acting large molecule therapeutics targeting the following Gram-negative pathogens:

- Acinetobacter baumannii, carbapenem-R
- Pseudomonas aeruginosa, carbapenem-R
- Enterobacteriaceae, carbapenem-R, 3rd-gen ceph-R (ESBL+)
- Salmonellae spp., fluoroquinolone-R
- Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R
- Shigella spp., fluoroquinolone-R

Please note

These are not considered to be NEW classes and are therefore Out-of-Scope for funding in Round 1

<table>
<thead>
<tr>
<th>Out of Scope</th>
<th>Out of Scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-lactams</td>
<td>Polymyxin</td>
</tr>
<tr>
<td>Glycopeptides (vancomycin)</td>
<td>Daptomycin</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Pleomucillin</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Oxazolidinones</td>
<td>Sulfamethoxazole</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Rifampicin</td>
</tr>
<tr>
<td>Lincosamides</td>
<td>Mupirocin</td>
</tr>
<tr>
<td>Streptogramins</td>
<td>Fosfomycin</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Fusidic acid</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Fidaxomicin</td>
</tr>
</tbody>
</table>

NEW class small molecule is defined as a core chemical structure (scaffold) that does not have an antibiotic for human use approved by the FDA or EMA as of March 1, 2018.

Beta-lactamase inhibitors and other potentiatinos are considered INDIRECT acting and therefore not in scope for Round 1

1 Applications for these pathogens should include a discussion of intended/potential routes for sourcing of funding for later stages of clinical development.

Mode of administration preference guidance

- For Enterobacteriaceae offerings: If only for ESBL (eg. lacks CRE), PO options are higher priority than IV only
- For Salmonellae spp., Shigella spp. and Neisseria gonorrhoeae offerings – oral delivery is strongly preferred
- Non-systemic modes of delivery are in-scope generally but would require well-reasoned justification for clinical utility/benefit
CARB-X 2018 Funding Round 2

• Scope of Round 2
  – **Broad scope** of therapeutics, vaccines, diagnostics and devices
• Expressions of Interest (EOI) accepted on-line only [www.carb-x.org/application](http://www.carb-x.org/application)
• EOI must be submitted June 1 through June 8, 2018, 5 pm EST

Applying for Round 2?
Mark your calendar
June 1 - 8, 2018
CARB-X 2018 Funding Round 2 – Scope

Only projects in scope will be considered for funding by CARB-X.
To be considered, Expressions of Interest for Round 2 must be submitted online June 1 through June 8, 2018, 5 pm EST.

<table>
<thead>
<tr>
<th>Pathogen Scope</th>
<th>Area Scope</th>
<th>Other requirements (if direct Tx)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diagnostics</td>
<td>Prevention</td>
</tr>
<tr>
<td>Acinetobacter baumannii, carbapenem-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, carbapenem-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Enterobacteriaceae, carbapenem-R, 3rd-gen cephr (ESBL+)</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Enterococcus faecium, vancomycin-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Staphylococcus aureus, methicillin-R, vancomycin-V/R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Helicobacter pylori, clarithromycin-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Campylobacter spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Salmonella spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae, 3rd-gen cephal-R, fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Streptococcus pneumoniae, penicillin-NS</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Haemophilus influenzae, ampicillin-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Shigella spp., fluoroquinolone-R</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Group A Streptococcus</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

1Applications for these pathogens should include a discussion of intended/potential routes for sourcing of funding for later stages of clinical development.

Mode of administration preference guidance:
For Enterobacteriaceae offerings: If Tx is only for ESBL (eg. lacks CRE), PO options are higher priority than IV only.
For Salmonella spp., Shigella spp. and Neisseria gonorrhoeae offerings – if Tx (direct or indirect), oral delivery is strongly preferred.
Non-systemic modes of delivery are in-scope generally but would require well-reasoned justification for clinical utility/benefit.
Tx = therapeutic
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 a legal entity and be considered a going concern – solvent with funding in place for operations 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 from larger or better-resourced companies are encouraged to propose higher amounts of cost share where feasible, as this demonstrates financial commitment to the 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 (if IP is controlled by a university, is the project supported by the Technology Transfer office?)
- 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 Funding Decisions are Made

**Scientific review:** Advisory board reviews applications and makes recommendations

**Governance:** Joint Oversight Committee makes funding decisions
## What to Expect When You Apply

**About 8 months from EOI to decision**

<table>
<thead>
<tr>
<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>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>
</table>
Recap

CARB-X 2018 Funding Rounds will open for Expressions of Interest
Round 1: March 22-29, 2018
Round 2: June 1-8, 2018

• CARB-X welcomes applications from around the world
• Expressions of Interest applications must be submitted on-line at www.carb-x.org/application
• To qualify for funding and support, projects must be in scope and organizations must meet certain criteria
• The *Powered by CARB-X* portfolio is the world’s largest and most scientifically diverse portfolio of early development antibacterial products to respond to the threat of the most serious drug-resistant bacteria and we intend to continue to build the portfolio

• More information: www.carb-x.org
Discussion and questions
Back up slides
Discovery of novel antibiotics is not keeping up with emergence of new superbugs

This chart excludes bedaquiline, which is the first drug in a new class to treat tuberculosis.
Global antibiotics pipeline is precariously slim

- 48 antibiotics in the global clinical pipeline in September 2017\(^1\)
- but only 12 in development to treat superbugs on the WHO critical threat pathogen list\(^2\)
  - Enterobacteriaceae (CRE)
  - *Pseudomonas aeruginosa*
  - *Acinetobacter baumannii*

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1 Pew Charitable Trusts, Dec 2017
2 World Health Organization, “Global Priority List of Antibiotic-Resistant Bacteria to Guide Research, Discovery, and Development of New Antibiotics” 2017
Lengthy, risky, and costly

It takes on average 10-12 years and hundreds of millions of dollars to deliver a new drug to market.

<table>
<thead>
<tr>
<th>Hit-to-Lead &amp; Lead Optimization</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Valley of Death&quot;</td>
<td>IND</td>
<td></td>
<td></td>
<td>NDA/BLA</td>
<td>Prod/Delivery</td>
</tr>
<tr>
<td>0.2 - 2.5%</td>
<td>3.5%</td>
<td>6-14%</td>
<td>25-30%</td>
<td>50-64%</td>
<td>75-90%</td>
</tr>
<tr>
<td>3-7 yrs</td>
<td>1/2 - 2 yrs</td>
<td>1-2 yrs</td>
<td>2-3.5 yrs</td>
<td>2.5-4 yrs</td>
<td>1-2 yrs</td>
</tr>
<tr>
<td>$100 - 130M</td>
<td>$60-70M</td>
<td>$70-100M</td>
<td>$130 - 160M</td>
<td>$190-220M</td>
<td>$18-20M</td>
</tr>
</tbody>
</table>

Probability of success

Supporting great science

Outstanding experts make up CARB-X's Science Advisory Board (SAB). The SAB ensures the highest scientific standards in evaluating applications for CARB-X funding. Every member of the CARB-X SAB and JOC completes a conflicts of interest process and is excluded from participation in the review or approval of any application with which they have a conflict of interest. We thank them sincerely for their work.

More than 60 outstanding experts from around the world make up the CARB-X Advisory Board.

As of August 2017
# Accelerating products to fight drug resistance

With CARB-X support in the past year, 5 projects progressed into the clinic (Ph1)

## Phase 1 Progressions - CARB-X Antibacterial Treatment and Prevention Product Portfolio

<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>New Abx Class</th>
<th>New Non-traditional Product</th>
<th>New Target</th>
<th>Description</th>
<th>Development Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entasis Therapeutics</td>
<td>ETX0282CPDP</td>
<td></td>
<td></td>
<td></td>
<td>Oral Gram-negative combination</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Iterum</td>
<td>Sulopenem</td>
<td></td>
<td></td>
<td></td>
<td>Oral and IV penem</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Spero Therapeutics</td>
<td>SPR741</td>
<td></td>
<td>✓</td>
<td></td>
<td>Potentiator</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Tetraphase Pharmaceuticals</td>
<td>TP-6076</td>
<td></td>
<td></td>
<td></td>
<td>Next-generation tetracycline</td>
<td><em>Acinetobacter + Enterobacteriaceae</em></td>
</tr>
<tr>
<td>Vedanta</td>
<td>VE303</td>
<td>✓</td>
<td></td>
<td></td>
<td>Microbiome</td>
<td><em>C. difficile</em></td>
</tr>
</tbody>
</table>