

Antibiotic resistance: a global health preparedness crisis



CARB-X funds and supports the development of treatment, prevention and diagnostic solutions for the most urgent drug-resistant bacteria.

CARB-X
Combating Antibiotic-Resistant Bacteria

**BOSTON
UNIVERSITY**

ANNUAL REPORT 2019-2020

CARB-X Mission

Accelerate a diverse portfolio of innovative antibacterial products towards clinical development and regulatory approval with funding, expert support and cross-project initiatives. We focus on the dangerous bacteria identified by the WHO and CDC priority lists.

Who we are

CARB-X is a global partnership created in 2016 to fund early-development antibacterial research around the world. CARB-X funders have earmarked up to US\$480 million in 2016-22 to accelerate the development of innovative products to prevent, diagnose and treat drug-resistant infections. CARB-X provides non-dilutive funding and support for therapeutics and preventatives in the early phases of preclinical development through the end of Phase 1, and for diagnostics from feasibility through the early development phases of product verification and validation. CARB-X is entirely non-profit, with headquarters at Boston University.

Why we fund antibacterial research and development

700,000 people

die each year from resistant bacterial infections, and the numbers are growing¹

1

new class of antibiotics (cefiderocol) approved for Gram-negatives since 1962

\$1.3B

to develop a new antibiotic plus \$400M more post-approval to break even²

10-15 years

to develop a new antibiotic³

¹ World Health Organization

² Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. JAMA. 2020;323(9):844-53.1

³ <https://wellcome.ac.uk/news/why-is-it-so-hard-develop-new-antibiotics>

Antibiotic resistance — bacteria's ability to rapidly evolve to avoid the effects of antibiotics — is one of the world's greatest public health threats. Since they were introduced in the 1940s, antibiotics have transformed modern medicine and saved millions of lives. But many decades after the first patients were treated with antibiotics, bacterial infections are again killing thousands and threatening modern medicine as drug resistance spreads, spurred by overuse, misuse and lack of innovation due to poor economic incentives. A more sustainable economic model is urgently needed.



“The antibiotic-resistance crisis is already upon us, threatening health security. CARB-X is funding the development of life-saving products to address this crisis.”

The CARB-X portfolio has grown in size and diversity

*Message from Kevin Outtersen,
CARB-X Executive Director and Professor of Law at Boston University*

When 2020 dawned, the public was largely unaware of the pandemic to come. While COVID-19 has impacted us all and changed the way we live and work, here at CARB-X, it has not slowed us down. To the contrary, the pandemic underscores the critical need to be prepared for global health crises today and in the future.

The 2019-20 fiscal year, which closed July 31, was CARB-X's most productive year yet, with 23 new awards to product developers around the world — more than in any year since CARB-X was launched. We added our first CRISPR/phage project, and expanded CARB-X's global reach with our first projects in Spain, Germany and Australia. We increased funding for product developers, now providing 80 to 90 percent of project costs depending on the development phase. We expanded our team of in-house experts under the leadership of R&D Chief Erin Duffy, who joined CARB-X in September 2019. Erin has brought enhanced strategic vision, scientific rigor and high-quality expertise to the portfolio and organization. We strengthened scientific and business support for projects, tapping CARB-X's Advisory Board and Global Accelerator Network to provide specialized expertise and services tailored to the needs of each product developer.

Other outstanding achievements came from progress in the projects we fund. T2 Biosystems' T2Resistance™ Panel was the first diagnostic to graduate from CARB-X's portfolio in 2019, and has since been approved in Europe and became the first granted a New Technology Add-on Payment by US Medicare. Specific Diagnostics' Reveal™ diagnostic and antibiotic susceptibility testing system graduated in 2020 and is also progressing. Other portfolio successes are highlighted in this report.

As we enter our 5th year, CARB-X's achievements and progress are solid. Thanks to the vision and leadership of CARB-X funders, Advisory Board experts and talented people behind CARB-X, novel products are receiving vital support. Since it was created in 2016, CARB-X has funded 67 projects in 10 countries, and invested \$241.9 million, plus additional funds if milestones are met. At CARB-X, actions speak louder than words.

But as we look to the future, we know that even more is needed. There is a critical need for new life-saving antibacterial products. At least 700,000 people die each year from drug-resistant bacteria, and that number is growing as resistance spreads.

Better incentives and a new economic model are required to sustain antibacterial innovation and the delivery of new approaches to patients. COVID-19 is a bitter reminder of the costs of being unprepared. Global leadership and political will are needed to win the race against drug-resistant bacteria. Now is the time to act.

Kevin Outtersen

funding & support diversity global progress strategic vision innovation

Progress in CARB-X's fourth year

Diversity and growth

CARB-X's portfolio grew significantly during the fiscal year and continues to expand in size and scientific diversity.

At year end July 31, 2020, CARB-X was supporting the development of 45 antibacterial projects. During fiscal 2019-20, CARB-X announced awards for 23 new projects. Some highlights:

- **1st phase:** Eligo Bioscience's innovative CRISPR-based bacteriophage is a new generation of highly specific antimicrobials to prevent multi-drug-resistant bacterial infections in organ transplant patients.
- **1st Australian project:** The University of Queensland Institute for Molecular Bioscience is developing a new class of last resort antibiotics to treat polymyxin-resistant Gram-negative pathogens.
- **1st from Spain:** Vaxdyn is developing a new vaccine to prevent life-threatening pneumonia.
- **1st Indian diagnostic:** Module Innovations is developing a rapid diagnostic for drug-resistant urinary tract infections (UTI), a problem globally, but particularly in low- and middle-income countries for pregnant women.
- **1st FDA Orphan Drug Designation:** Peptilogs' antibiotic peptide for prosthetic joint infections.
- **New frontiers:** Many new projects focus on ground-breaking approaches. For example, Day Zero Diagnostics and Pattern Bioscience are using machine learning to rapidly diagnose complex bacterial infections and perform antibiotic susceptibility testing. Trellis Bioscience is developing a monoclonal antibody designed to disrupt the protective biofilm that makes bacteria resistant to antibiotics.

Strategic vision and focus

The expanded CARB-X R&D team has renewed and enhanced our strategic vision for portfolio management and project support. Under the leadership of CARB-X R&D Chief Erin Duffy, who joined CARB-X in September 2019, our team of specialized Alliance Directors and Alliance Managers is working closely with product developers to maximize resources and tap into expertise vital to the success of their projects. The team facilitates contact with global experts on the CARB-X Advisory Board and in CARB-X's Global Accelerator Network. This support is provided free of charge to product developers.



Erin Duffy, CARB-X R&D Chief

The R&D team also helps CARB-X identify gaps in the portfolio, shape funding priorities and identify opportunities for cross-project initiatives that advance the field. Under these initiatives, the team identifies common challenges/themes across the portfolio, designs a set of hypotheses and experiments, executes the work (within portfolio or with CROs) and makes the results available for all. As an example of this, University of Queensland researchers are conducting nephrotoxicity studies, the results of which will be made public, to identify molecules that can be used to de-risk peptides (like polymyxin and colistin).

Financial and expert support

In the 2019-20 fiscal year, CARB-X rolled out a more generous cost-share formula for new and existing projects. The goal is to increase financial support for projects during difficult economic times. For therapeutic and prevention product development, CARB-X now funds 90% of costs for the Hit-to-lead, Lead Optimization and Pre-clinical (IND-enabling) stages, and 80% for the Phase 1 stage. For diagnostics, CARB-X funds 90% of the Feasibility, Optimization, and Development stages, and 80% of the Verification and Validation stage.

In addition to non-dilutive funding and expert support, CARB-X also hosts educational events, including Boot-camps for product developers. In June 2020, CARB-X hosted a webinar on Preparing for an FDA Pre-IND Meeting, attended by more than 200 people around the world.

First approval

T2 Biosystem's T2Resistance™ Panel rapid diagnostic received CE-mark regulatory approval in the fall of 2019 for use in European hospitals. T2's diagnostic is the first of hopefully many CARB-X-funded projects to graduate from the portfolio and go on to achieve regulatory approval.

T2 is one of seven graduates since CARB-X was established in 2016. Specific Diagnostics' Reveal AST System diagnostic graduated in early 2020 and is well on its way to regulatory approval. At the end of the fiscal year, Vedanta Bioscience's microbiome therapeutic was in Phase 2 trials for treatment of *C. difficile* infections. Projects led by Spero Therapeutics, Tetraphase Pharmaceuticals, Iterum Therapeutics and Oppilotech had previously graduated after completing milestones identified by CARB-X.

Progress in the pipeline

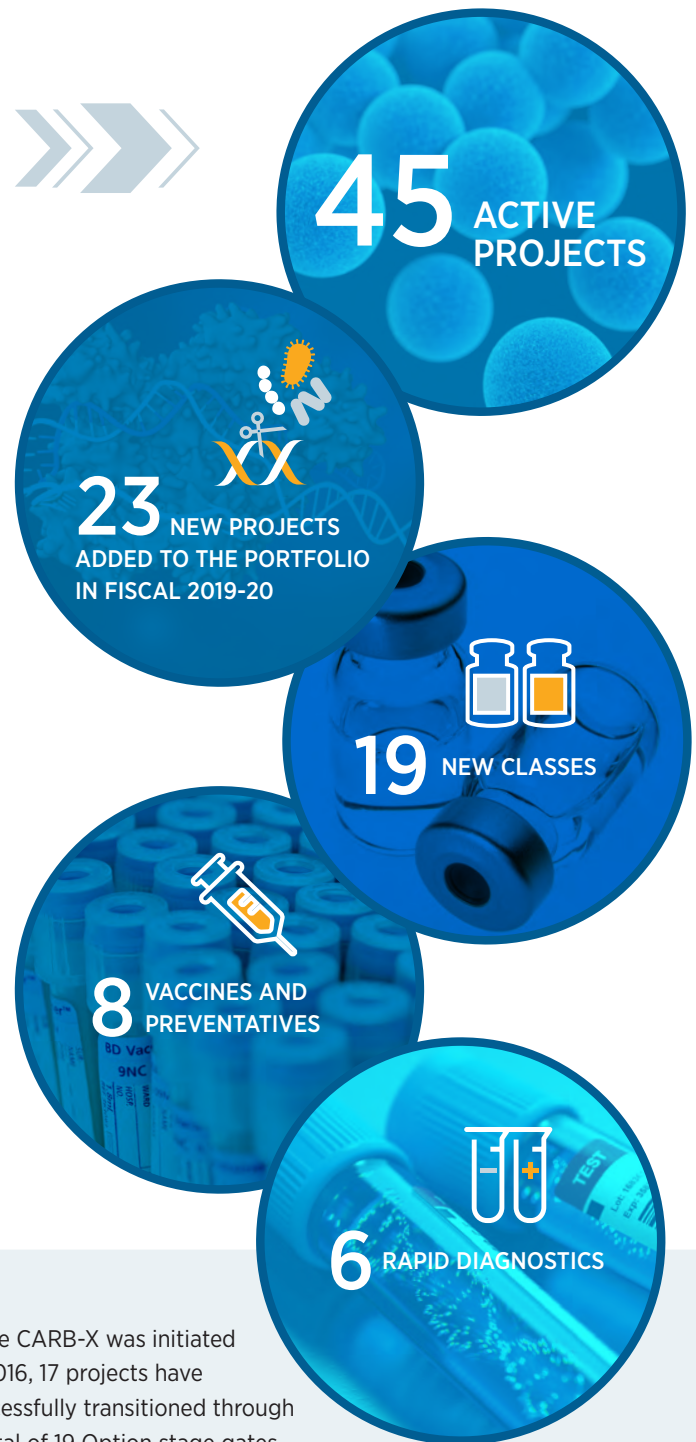
CARB-X funds projects in milestone-driven contractual Option stages. To progress through Option stage gates into the next funding stage, a project must meet or surpass milestones in the agreed development plan. These milestones may be scientific or business related.

As projects approach the Option stage gates, product developers present their progress to the CARB-X Advisory Board. Funding of the next stage is decided by the Joint Oversight Committee (JOC), taking into account recommendations from the Advisory Board and CARB-X team.

Since CARB-X was initiated in 2016, 17 projects have successfully transitioned through a total of 19 Option stage gates.

ContraFect and Integrated Biotherapeutics each progressed through two successive Option stage gates. Product developers that transitioned through a single gate are Antabio, Bugworks, Debiopharm, Entasis (2 projects), Forge, Helixbind, Microbiotix, MicuRx, Proteus, Seres, Spero, Specific Diagnostics, T2 Biosystems, and Zikani.

Many projects funded by CARB-X are recent additions to the pipeline and are progressing toward their first Option stage review.



CARB-X quick glance

- **\$241.9 million**
invested since CARB-X was launched July 28, 2016, plus \$62.2 million in additional funds if milestones are met
- **1100+ applications**
received from around the world
- **67 projects**
in 10 countries funded so far
- **45 active projects**
in the pipeline
- **19 milestone**
progression options granted
- **7 graduates**
(1 with regulatory approval to date)

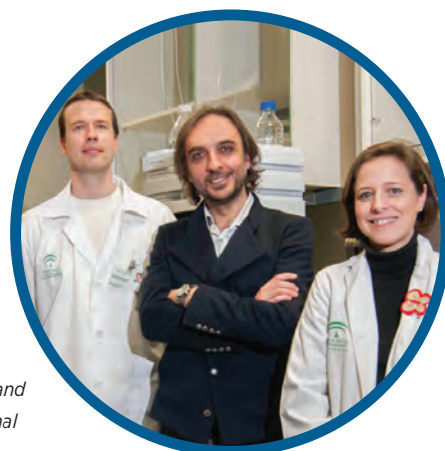
Portfolio highlights

Innovative projects in the CARB-X portfolio are in the early stages of development for the prevention, diagnosis or treatment of the most serious drug-resistant bacterial infections. CARB-X supports projects from around the world. Some examples of exciting research are highlighted on the next six pages.

Full portfolio details can be found at carb-x.org/portfolio/



L-r: Dr. Michael McConnell, Vaxdyn CSO and founder, and bacteriologist and principal investigator (PI) at the National Center of Microbiology in Madrid, Spain; Dr. Juanjo Infante, Vaxdyn CEO and co-inventor of Vaxdyn's technology platform; Dr. Pilar Pérez, Vaxdyn founder and advisor, and virologist and PI at the National Center of Microbiology.

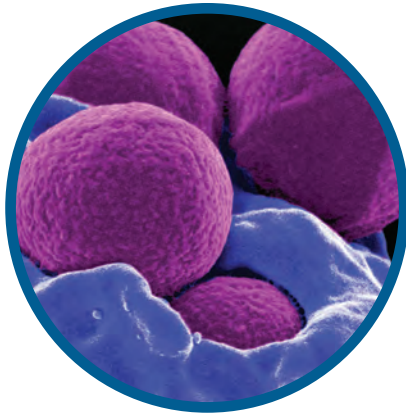


Putting an end to drug-resistant pneumonia in at-risk patients

Vaxdyn is developing multi-antigen vaccines based on detoxified bacterial cells that present key antigens in their native conformation. KapaVax, the Vaxdyn project funded by CARB-X, is under development for the prevention of infections caused by drug-resistant Gram-negative pathogens including *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* in at-risk populations, for example those with chronic lung-disease or diabetes, or patients undergoing cancer treatment.

"We are determined to develop a vaccine that will prevent life-threatening infections caused by drug-resistant bacteria, providing safe and effective immunity to patients at risk and populations around the world. CARB-X support for the KapaVax project is vital to move this ground-breaking research forward."

— Juan J. Infante, CEO, Vaxdyn, Seville, Spain



Vaccine to prevent deadly MRSA infections

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes serious infections in hospitals and the community. Integrated Biotherapeutics is developing a vaccine (IBT-V02) to prevent recurrent *S. aureus* acute infections. IBT-V02 represents a new approach by targeting the toxins that disable the immune system, destroy tissue and help bacteria spread in the body.

"We are making great progress towards a preventive solution for MRSA. We are currently conducting cGMP manufacturing and IND-enabling studies and anticipate starting the clinical trial of IBT-V02 in early 2022. This is a major undertaking in the fight against AMR that would not have been possible without the support of CARB-X."

— M. Javad Aman, President and CSO
Integrated BioTherapeutics, Rockville, MD, USA



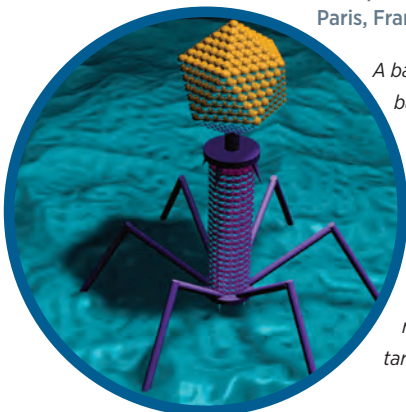
Bacteriophage-derived vectors deliver CRISPR-Cas system to disarm bacteria

Many patients enter hospitals pre-colonized by drug-resistant bacteria, but are asymptomatic. Transplant patients colonized by these superbugs have up to a 40% chance of developing post-operative infections due to transplant surgery itself, and up to 70% of such infections can be fatal.

Eligo Bioscience is developing a new generation of highly-specific antimicrobials to prevent multi-drug-resistant bacterial infections in organ transplant patients. Eligo's bacteriophage- and CRISPR-based therapeutics are designed to selectively eliminate extended-spectrum beta-lactamase-producing (ESBL) and Carbapenem-resistant *E. coli* and *K. pneumoniae* (CRE) from the microbiome of transplant patients before their procedure, thereby preventing these often-fatal infections.

"Our collaboration with CARB-X will bring our platform technology one step closer to addressing the critical problem of antibiotic resistance, starting with organ transplant patients, a population at extremely high risk of developing multi-resistant infections,"

— Xavier Duportet, CEO, Eligo Bioscience,
Paris, France



A bacteriophage is a virus that infects bacteria with its DNA or RNA. Eligo's technology transforms phages into delivery vectors that carry a synthetic DNA construct that enables the expression of a CRISPR-Cas system that creates precise double strand DNA breaks in antibiotic resistance genes carried by the targeted bacteria.

Preventing infection by modulating the gut microbiome

Bacterial infections and graft versus host disease (GvHD) can be serious complications of organ or stem cell transplantation, for example in cancer patients, particularly where drug-resistant pathogens are involved. Seres Therapeutics is advancing SER-155, a consortium of bacterial species designed to prevent mortality in transplant recipients by preventing translocation of bacteria from the gut into the blood stream. A Phase 1b study of SER-155 is planned to begin in late 2020 in collaboration with Memorial Sloan Kettering Cancer Center.



"Studies at MSKCC indicate that the gut microbiome strongly affects a person's susceptibility to infections and GvHD following a transplant. With the support of CARB-X, Seres has advanced the development of SER-155 and will launch a first-in-human

trial of our novel microbiome therapeutic approach to address this important unmet need. Success in this program may have broad implications for combating bacterial infections."

— Matthew Henn, EVP and Chief Scientific Officer
Seres Therapeutics, Cambridge, MA, USA





Debiopharm™ Taking aim at drug-resistant gonorrhea



Debiopharm's Debio 1453 development program involves a new antibiotic class for the treatment of resistant gonorrhea, a sexually transmitted bacterial infection that can cause infertility, septic arthritis, pelvic inflammatory disease as well as health problems in babies of mothers with the infection. *Neisseria gonorrhoeae* has progressively developed resistance to all but one class of antibiotics, raising concerns about the likelihood of untreatable gonococcal infections. Debio 1453 molecules tested so far are active against all existing *N. gonorrhoeae* resistant strains by inhibiting a novel target FabI, essential for the growth of this bacterium. Debiopharm is progressing toward selection of a drug development candidate among advanced optimized leads. The most suitable compound will enter preclinical studies.

*"As a growing variety of superbugs, including *N. gonorrhoeae*, are showing resistance to existing antibiotics, we must anticipate research now. This will help avoid a future epidemic of highly resistant *N. gonorrhoeae* for which there is currently no satisfactory treatment."*

— Bertrand Ducrey, CEO of Debiopharm, Lausanne, Switzerland

New hope for Cystic Fibrosis patients

Cystic fibrosis (CF) is a life-threatening genetic disease, affecting thousands world-wide. Most CF patients will develop chronic *Pseudomonas aeruginosa* lung infections which cause progressive lung damage and are resistant to conventional antibiotics. Antabio is developing a novel non-antibiotic approach targeting a key virulence mechanism (*Pseudomonas* elastase), with the goal of reducing the severity of or eradicating *Pseudomonas* infections.



*"With the help of CARB-X we have identified a pre-clinical candidate which targets the *Pseudomonas* elastase enzyme, and are now undertaking key preclinical studies to investigate its safety and effectiveness and to define a roadmap for further development. CARB-X's funding and expertise is essential to support innovative ways to tackle AMR, however new pull incentives are urgently needed to make the AMR ecosystem sustainable."*

— Martin Everett, CSO, Antabio, Labège, France



Anti-virulence drug project boosts the power of antibiotics to save lives

Microbiotix's anti-virulence project is focused on enhancing the effect of existing antibiotics to treat multi-drug resistant *Pseudomonas aeruginosa* infections. The type III secretion system (T3SS) of *P. aeruginosa* injects protein toxins into host neutrophils and macrophages to block the host innate immune defenses and facilitate infection and dissemination. CARB-X is supporting the lead optimization through to preclinical candidate selection of a novel series of inhibitors that block the bacteria's ability to defend itself against antibiotics.



*"Mortality from *P. aeruginosa* ventilator-associated pneumonia ranges from 40% to nearly 70% and recurs in over 30% of patients, even with standard-of-care antibiotic therapy. These novel anti-virulence inhibitors aim to address this critical medical need, and CARB-X support has enabled us to advance this program toward clinical development."*

— Terry Bowlin, President and CEO, Microbiotix Inc., Worcester, MA, USA



A new class of PBP Inhibitors with optimized resistance profile

Entasis Therapeutics' candidate, ETX0462, seeks to tackle multidrug-resistant *Pseudomonas* infections. Designed from the same chemical scaffold as Entasis' β -lactamase inhibitors, durlobactam and ETX0282, ETX0462 was engineered to target and kill bacteria rather than resurrect β -lactam antibiotic activity. The result is a novel class of highly potent antibacterial agents, leveraging the same target as β -lactam antibiotics, penicillin binding proteins (or PBPs), but impervious to all β -lactamases tested to date.

"CARB-X's collaboration and support has allowed us to identify ETX0462, the first candidate of a novel class of antibiotics. Due to its novel mode of inhibition, ETX0462 is not readily de-activated by β -lactamases thus overcoming the main cause of resistance to β -lactams. CARB-X's continued support enables our advancement of ETX0462 through IND-enabling toxicology and Phase 1 studies."

— Manos Perros, CEO, Entasis Therapeutics, Waltham, MA, USA



Lytic agents eradicate bacteria through novel extracellular mechanisms

ContraFect



ContraFect's platform of direct lytic agents (DLAs) aims for superior clinical outcomes in treating serious infections. CARB-X supports two separate proprietary programs at ContraFect — lysins and amurins. CF-370, an engineered lysin

targeting *P. aeruginosa*, was brought forward as a lead candidate at the end of 2019. This milestone is emblematic of the rapid progress made since CARB-X began funding ContraFect's discovery stage lysin program in 2017.

Amurins are a new class of lytic agents that exhibit broad-spectrum activity against Gram-negative ESKAPE pathogens and have potent ability to clear biofilms and synergize with existing antibiotics. ContraFect's DLAs targeting Gram-negative pathogens are in development for pulmonary exacerbations of cystic fibrosis and hospital-acquired and ventilator-associated bacterial pneumonia.

"Pseudomonas presents as one of the most lethal and highly-resistant bacterial pathogens. The support from CARB-X allowed us to quickly move from the initiation of a discovery program to the identification of CF-370, an investigational therapy with potent in vivo activity against Pseudomonas, in less than three years."

— Cara Cassino, MD, Executive Vice President of Research & Development and Chief Medical Officer of ContraFect, Yonkers, NY, USA



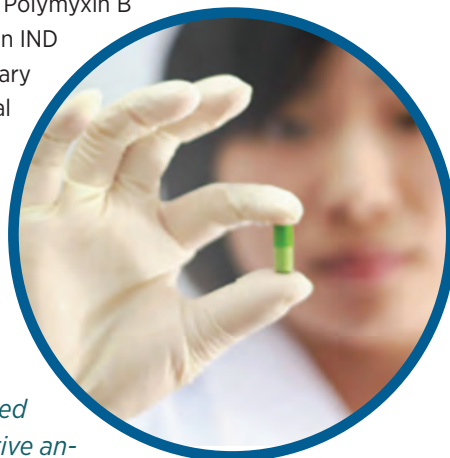
MicRx PHARMACEUTICALS

New polymyxin aims to be less toxic, more effective

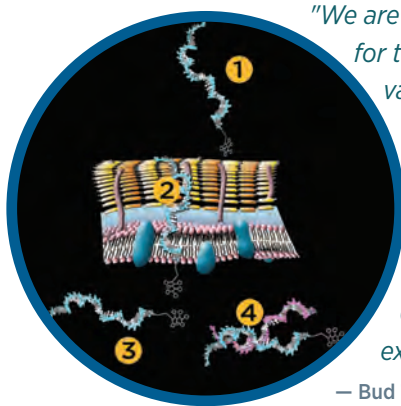
Funded and supported by CARB-X since 2018, MicRx is developing MRX-8, a novel polymyxin active against infections caused by multidrug-resistant Gram-negative pathogens, including Enterobacteriaceae, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. MRX-8 is differentiated by its minimized renal and neurological toxicities compared to current polymyxins, and has exhibited superior efficacy to Polymyxin B in certain nonclinical models in IND enabling studies, such as urinary tract and lung infection animal models. MRX-8 has recently received clearance from US FDA for Phase I clinical trials to proceed.

"We are very grateful for an opportunity to collaborate with CARB-X in addressing the global need for safer and more effective antibiotics, and appreciate the generous financial and technical support."

— Zhengyu Yuan, President and CEO, MicRx Pharmaceuticals, Foster City, CA, USA



Techulon is using antisense compounds to develop a new class of antimicrobials. These compounds selectively target specific genes that are critical to bacterial survival and "turns them off" thereby killing the targeted bacteria. Since the compounds selectively target specific bacteria, these are narrow spectrum drugs. This will enhance antibiotic stewardship programs and will benefit patients by preserving their beneficial bacteria.

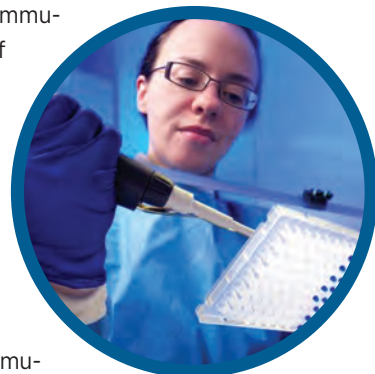


"We are deeply appreciative of CARB-X for their mission to support innovation in antibiotic development so that an enhanced pipeline of therapeutics is created to address AMR infections. The insight and guidance we have received from the CARB-X team has been extremely beneficial."

— Bud Thompson, CEO, Techulon, Blacksburg, VA, USA

1. Agent interacts with bacterial cell wall
2. Agent intercalates with cell wall and permeates it
3. Agent is intracellular
4. Agent targets and abrogates a specific essential mRNA sequence. Essential genes are targeted leading to lethal outcomes for the bacteria.

Centauri Therapeutics is developing immunotherapies as an entirely new way of fighting life-threatening infections. Centauri's Alphamer platform comprises a natural antibody-recruiting effector domain, a pathogen-targeting domain, and proprietary linker technology. Alphamers are designed to redirect a pre-existing immune response and thereby bring about immediate (within minutes) immunotherapeutic benefit to patients. Alphamers recruit polyclonal antibodies, thereby engaging multiple mechanisms of bacterial clearance. The CARB-X-funded program, CTL-ABX01, aims to provide potent antimicrobial activity against Gram-negative bacteria, and to label the bacteria for clearance by the immune system.



"At Centauri, with CARB-X's support, we are focused on finding innovative ways to boost host immunity to help fight serious infections more effectively. We must continue to drive innovation so that new effective medicines with novel mechanisms of action can be delivered to patients."

— Mike Westby, CEO, Centauri, Discovery Park, Kent, UK

With its proprietary chemistry approach to drug development, Forge's lead effort is focused on LpxC, a zinc metalloenzyme found only in Gram-negative bacteria and which is essential for bacteria to grow. CARB-X is supporting Forge's efforts to deliver a safe and effective product from this highly-sought-after target. In addition to project support, CARB-X's validation has also been helpful to Forge in attracting new research funding and partners. These include relationships with Evotec and more recently, partnerships with Basilea and Roche.

"We are employing our proprietary chemistry technology to discover novel small molecule inhibitors of bacterial metalloenzymes including LpxC. The scientists at Forge have identified lead compounds that are advancing through lead optimization activities toward clinical studies. Working with CARB-X and other funding partners,



we are developing novel classes of antibiotics that address several of the bacteria on the CDC urgent threat list including carbapenem-resistant Enterobacteriaceae, multidrug-resistant Acinetobacter, and multidrug-resistant Pseudomonas."

— Zachary A. Zimmerman, CEO, Forge Therapeutics, San Diego, CA, USA

HELIXBIND

Rapid diagnostics speed appropriate treatment of infections

Sepsis leads to over 6 million deaths per year worldwide. Identification of the underlying infection is crucial, allowing clinicians to intervene with appropriate antibiotics and avoid inappropriate drugs. Unfortunately, current diagnostics commonly require days, but prognosis for these patients deteriorates hourly. With CARB-X support, Helixbind is developing a diagnostic test, RaPID/BSI, to identify and characterize the infection directly from blood within three hours, helping clinicians improve outcomes, save lives and reduce the spread of drug-resistant bacteria. The RaPID/BSI (shown here) received Breakthrough Device Designation from the Food and Drug Administration (FDA) in August 2020.



“Combating antimicrobial resistance requires an arsenal of effective drugs and the knowledge of when to use them and when not to. With the support of CARB-X, we will provide clinicians the ability to identify infections and find the right drug when it’s most important.”

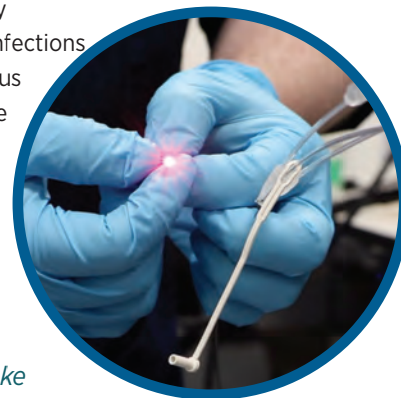
— Alon Singer, CEO, HelixBind, Marlborough, MA, USA

New imaging technology to diagnose drug-resistant lung infections

Proteus, based at the University of Edinburgh, supported by CARB-X since 2017, is developing a technology platform for diagnosis of lung infections at patients’ bedsides. The Proteus platform combines cutting-edge chemistry, physics, engineering and biology to allow real-time visualisation of bacteria in the alveolar space.



PROTEUS



“Development of new diagnostic tools that allow clinicians to rapidly make informed treatment decisions are key to reducing inappropriate antibiotic use, and essential in the fight against AMR. CARB-X support has been instrumental in helping us accelerate development of our imaging platform, demonstrating safety and efficacy in vitro and in animal models, and progressing to in-human clinical evaluation.”

— Prof. Kev Dhaliwal, Proteus, University of Edinburgh, UK

The Panoptes Medical Device (above) forms part of the Proteus lung imaging platform. Panoptes is passed down the working channel of a bronchoscope and can deliver and visualize chemical SmartProbes for imaging of bacteria or active host immune cells in a patient’s lung.

Photo: Proteus



Rapid culture-free diagnostics for antibiotic-resistant bacteria

Day Zero Diagnostics (DZD) is on a mission to transform the way infectious disease diagnostics are performed. DZD has developed a method for ultra-high bacterial enrichment, whole genome sequencing, and machine learning to determine both the species and antibiotic resistance profile of an infection in hours rather than days. DZD’s sequencing-based approach allows for the simultaneous testing of a comprehensive set of bacterial species and resistance determinants, without the need for cultures that currently can take up to five days to provide similar information.



“CARB-X is investing in new, technologically differentiated approaches to infectious disease diagnostics. We believe that the time has come for the field to move from analog approaches like culture-based testing to digital approaches that use sequencing data and machine learning to understand drivers of resistance and spread. We hope to dramatically reduce hospital length of stay, the overuse of expensive and often ineffective antibiotics, and most importantly, excess mortality.”

— Jong Lee, CEO, Day Zero Diagnostics, Boston, MA, USA

The Power of Leadership, Vision and Partnership

CARB-X partners show outstanding leadership and vision in the global effort to accelerate the delivery of products to prevent, diagnose and treat serious drug-resistant bacterial infections. CARB-X funds and supports early development of innovative products to address drug-resistant bacteria. Through CARB-X, our partners are investing up to \$480 million in 2016-2022 to accelerate antibacterial product development. So far, we have supported 67 R&D projects around the world, with more to come.



The Biomedical Advanced Research and Development Authority (BARDA), one of CARB-X's founding US partners, and part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) in the Department of Health and Human Services, is focused on emergency preparedness and strengthening national health security. BARDA committed up to \$180 million to CARB-X from 2016-2021.



CARB-X's founding UK partner, Wellcome Trust, is one of the world's largest charitable foundations working to improve health globally. It is a leading funder of biomedical R&D, with significant experience and commitment in antibacterial R&D. Wellcome has committed up to \$155.5 million to CARB-X.



The US National Institute of Allergy and Infectious Diseases (NIAID), a US founding partner of CARB-X and part of the National Institutes of Health (NIH), is focused on research to better understand, treat, and prevent infectious, immunologic, and allergic diseases. NIAID provides pre-clinical services valued at \$50 million to CARB-X-funded projects.



Germany's Federal Ministry of Education and Research (BMBF) joined the CARB-X partnership in March 2019 as part of its strategy to support R&D that addresses drug resistance. Germany has committed €39 million to CARB-X over 4 years.



The UK Government's Global Antimicrobial Resistance Innovation Fund (GAMRIF), part of the Department of Health and Social Care (DHSC), supports innovative R&D to address the threat of antimicrobial resistance, particularly in low- and middle-income countries. GAMRIF has committed up to £20 million to CARB-X.



The Bill & Melinda Gates Foundation supports the development of new vaccines against drug-resistant bacterial infections, particularly for vulnerable populations in low- and middle-income countries. The Gates Foundation has committed \$25 million.



Boston University leads the CARB-X partnership and CARB-X is headquartered in the Boston University School of Law. Boston University supplies operational and administrative support.

Supporting Great Science and Innovation

CARB-X works with specialized experts and accelerators around the globe to provide scientific, technical and business support to the growing number of CARB-X-funded projects. Services are provided at no cost to the product developer.

CARB-X's Advisory Board experts — more than 100 industry and discipline leaders from around the world — provide outstanding counsel and strategic support on a range of scientific issues, such as translational science, tailored to the individual needs of the product developer from the application stage through to graduation from the CARB-X portfolio. The Advisory Board is comprised of leading antibiotic and diagnostic professionals, as well as experts in other modalities including vaccines, microbiome, phage and immunology. We thank each member of the Advisory Board for the high quality of their expertise and dedication to the CARB-X mission.

The Global Accelerator Network, with seven organizations in four countries (US, Germany, Switzerland and India), is a unique source of specialized know-how in antibacterial drug development, diagnostics, vaccines, business and legal strategy, regulatory affairs and other areas essential to accelerating CARB-X's growing portfolio. Network organizations also provide applicant support.

In addition, CARB-X provides educational services to product developers on such things as preparing for meetings with regulatory officials.

"The path to market is challenging with numerous obstacles, especially for the small companies. By providing business and technical support alongside funding, and working with partners from the public, private and philanthropic sectors, we believe that more companies can get their products to the patients who need them the most."

— Tim Jinks,
Head of Wellcome Trust's Drug Resistant Infections Programme

CARB-X
Global Accelerator Network



How CARB-X works

CARB-X is governed by the Joint Oversight Committee (JOC), which acts as the board of directors with full oversight for CARB-X, ensuring the highest scientific and ethical standards. The JOC is made up of representatives of CARB-X's funding organizations and management team. The JOC makes research investment decisions based on recommendations from the Advisory Board which reviews applications for funding selected through a global competitive process. Members of the JOC and the Advisory Board complete a conflict-of-interest process and are excluded in participating in any decision in which they may have a conflict. We thank them sincerely for their work.

CARB-X is a non-profit partnership led by Boston University and is headquartered at the Boston University School of Law.

BOSTON
UNIVERSITY

Physically distant — working as a team

During the COVID-19 pandemic, CARB-X has remained open for business, thanks to the dedication and professionalism of the team at CARB-X and Boston University. Working virtually, we continue to hold Advisory Board meetings to search for new projects to fund, make payments, support projects and announce new awards. It is critical that we continue to accelerate the development of innovative products to address drug-resistant bacteria.

Joint Oversight Committee

Nick Adkin

Deputy Director, Global Health Security,
Department of Health & Social Care

Mark Albrecht

Chief, Antibacterials
Division of CBRN Medical Countermeasures, BARDA

Cameron Bess

Project Officer and Biologist, US Department of Health and Human Services, BARDA

Dennis M. Dixon

Chief, Bacteriology and Mycology Branch, NIH/NIAID

Erin Duffy

Chief of Research and Development, CARB-X

Ann Eakin

Senior Scientific Officer, NIH/NIAID

Alyson Fox

Lead Sponsor, Drug-Resistant Infection Programme, Wellcome Trust

Karen Gallant

Deputy Executive Director, CARB-X

Christopher Houchens

Director, Division of CBRN Medical Countermeasures, BARDA

Tim Jinks

Head, Drug-resistant Infections Programme, Wellcome Trust

Marit Metternich

Policy Officer, Global Health Research, Federal Ministry of Education and Research, Germany BMBF

Louise Norton-Smith

Head of AMR Strategy, Department of Health & Social Care

Kevin Outterson

Executive Director & PI, CARB-X

Andrea Spelberg

Division Head, Global Health Research, Federal Ministry of Education and Research, Germany BMBF

CARB-X Executive Team

Erin Duffy, PhD — *Chief of R&D*

Karen Gallant, PhD — *Deputy Executive Director*

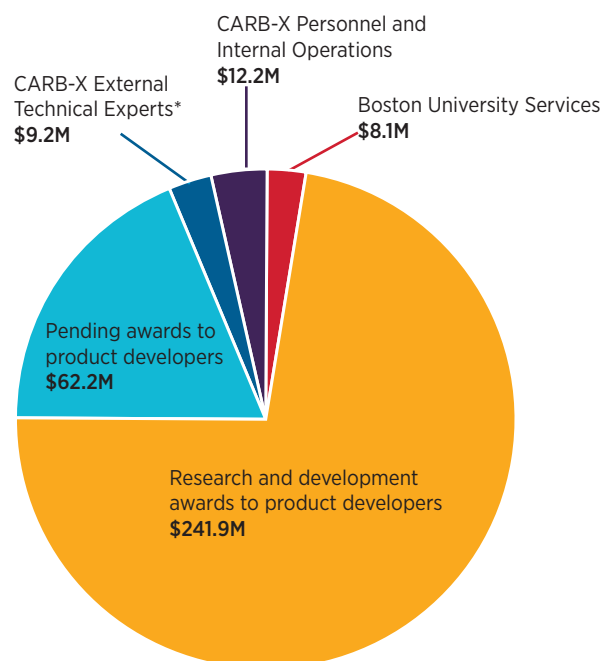
Rich Lawson, PhD — *Director of the Project Management Office*

Diane MacDonald, MPA — *Chief Operating Officer*

Kevin Outterson, JD, LL.M. — *Executive Director & PI*



4 years of support



*External Technical Experts includes Global Accelerator Network, Advisory Boards, and technical experts

More awards, more money, more progress

CARB-X accelerated its support for antibacterial R&D during the fiscal year 2019-20, its 4th year of operation, stepping up both the numbers and size of awards. During the year, CARB-X provided \$127.5M in awards, and approved new awards for 23 product developers, bringing the number of active projects in the portfolio to 45 as of July 31, 2020.

Since CARB-X was established in 2016, it has obligated a total of \$241.9M to support the early development of 67 projects, and committed \$62.2M in additional funds if projects achieve milestones. To provide scientific and business support to product developers in the portfolio, CARB-X has spent \$9.2M for services delivered through the Global Accelerator Network, Advisory Boards and external technical experts. CARB-X staff and internal operations totaled spending of \$12.2M. Boston University has provided \$8.1M in administrative and facilities support since CARB-X was launched.

“Antibiotics are a very serious health problem for us, and it is getting worse. Resistant microbes outstrip new antibiotics. It is an ongoing problem. It is not like we can fix it and it is over. We have to fight continued resistance with a continual pipeline of new antibiotics and continue with the perpetual challenge.”

— Anthony Fauci, Director, U.S. National Institute of Allergy and Infectious Diseases

“The CARB-X initiative plays an important role in BARDA’s goal to catalyze the early stage development pipeline and enhance our national health security preparedness. CARB-X allows BARDA to tap into a partnership of co-funders, accelerators, and innovators who are pushing critical novel antimicrobials from discovery to the market to address the public health and national security concerns of antibiotic resistant bacteria.”

— Gary L. Disbrow, PhD,
BARDA Acting Director

“Global collaboration is the most effective way to tackle global health threats, and it’s more important than ever that we work together to address AMR. This year, CARB-X and the product developers have made exceptional progress. I am so proud to see the development of antibacterial solutions through the UK’s Global AMR Innovation Fund’s support to CARB-X. Together, we are supporting sustainable solutions for people in low- and middle-income countries, where the impact of the AMR is highest. Collaboration is our only way forward to avert the AMR pandemic.”

— Professor Dame Sally Davies,
Master, Trinity College, Cambridge, and UK Special Envoy on Antimicrobial Resistance



Federal Ministry
of Education
and Research

BILL &
MELINDA
GATES
foundation



CARB-X

Combating Antibiotic-Resistant Bacteria

CARB-X

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