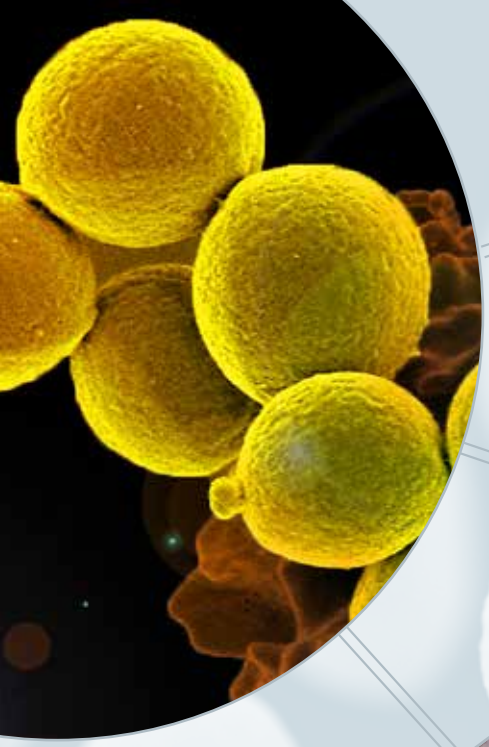


ANNUAL REPORT 2020-2021

Preparing the World Against Antibiotic-resistant Bacteria

CARB-X

Combating Antibiotic-Resistant Bacteria

Celebrating 5 years of global antibacterial innovation

BOSTON UNIVERSITY

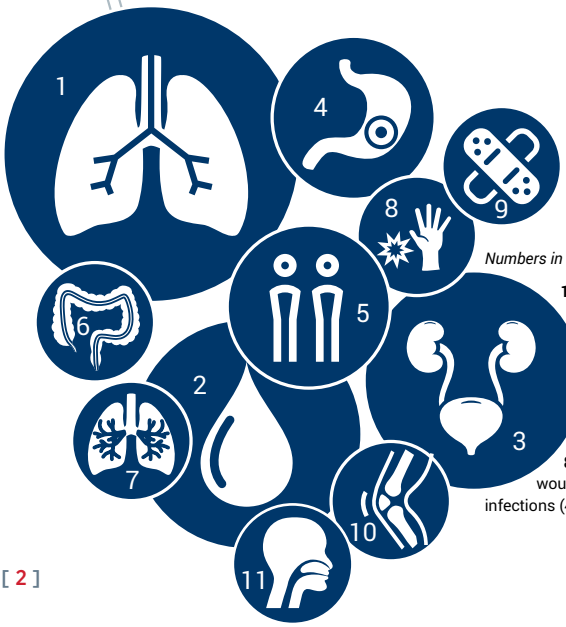
The antibiotic resistance crisis

Beginning with penicillin in 1942, antibiotics have transformed modern medicine and saved millions of lives. Antibiotic resistance — bacteria's ability to overcome the effects of the drugs designed to kill or disarm them — is one of the world's greatest public health threats. Today, over 700,000 deaths worldwide are attributed to resistant bacterial infections per year and this number is growing[1]. Resistance is spurred by overuse and misuse of antibiotics and worsened by the lack of scientific innovation due to poor economic incentives. 10-15 years of drug development is needed to produce one new antibiotic with little opportunity for commercial returns[2]. A more sustainable economic model is urgently needed.

[1] World Health Organization
[2] https://wellcome.org/news/why-is-it-so-hard-develop-new-antibiotics

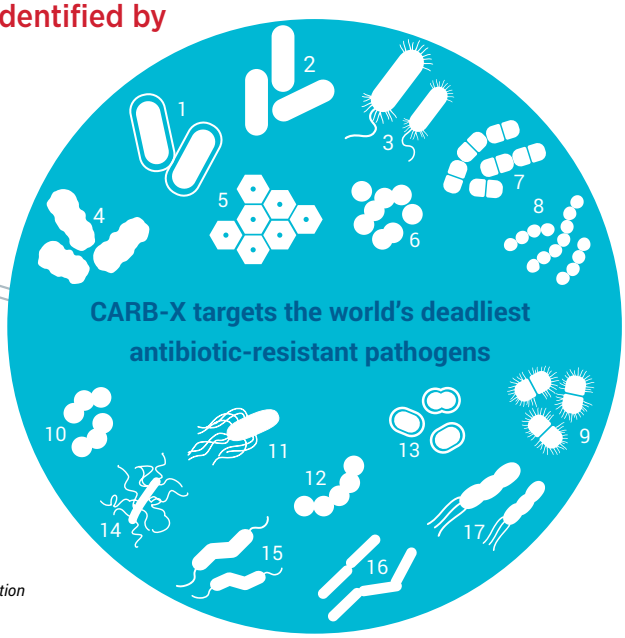
CARB-X mission

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 infections caused by the dangerous bacteria identified by the WHO and CDC priority lists.



Numbers in ( ) indicate number of projects targeting indication

1. LRTI: lower respiratory tract infections eg pneumonia (25) **2. BSI:** bloodstream infections (sepsis) (19) **3. cUTI:** urinary tract infections (18) **4. cIAI:** intra-abdominal infections (8) **5. STI:** sexually transmitted infections (gonorrhea +/- chlamydia) (7) **6. GI:** intestinal microbiome modifying (transplant, cancer, *C.difficile* infection patients) (5) **7. CF:** cystic fibrosis (5) **8. ABSSSI:** serious skin infections (4) **9. Wounds:** wound infections - surgery (4) **10. PJI:** prosthetic joint infections (4) **11. URTI:** upper respiratory tract infections (3)



Numbers in ( ) indicate the number of projects that focus on the pathogen. Some projects focus on more than one pathogen

1. *K. pneumoniae* (37) **2.** *E. coli* (35)
3. *P. aeruginosa* (28) **4.** *E. cloacae* (28)
5. *A. baumannii* (23) **6.** *S. aureus* (20) **7.** *E. faecium* (16) **8.** *S. pneumoniae* (14) **9.** *N. gonorrhoeae* (7)
10. *S. pyogenes* (group A) (4) **11.** *Salmonella sp* (4)
12. *S. agalactiae* (group B) (2) **13.** *H. influenzae* (2)
14. *C. difficile* (1) **15.** *Campylobacter sp* (1)
16. *Shigella sp* (1) **17.** *H. pylori* (1)

"Over the course of five extraordinary years, CARB-X has surpassed all goals"

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

To keep ahead of bacterial resistance, the world needs at least a couple highly innovative antibacterials every decade. Antibacterials developed over the past few decades have been extensions of well-known classes, but CARB-X is aiming higher, pursuing radically innovative classes, targets, and non-traditional approaches. Since this is risky early-stage work, success requires operating at scale, with dozens of projects at any given time to support an eventual approval. Only CARB-X is operating at global scale, with 92 projects since inception and 60 operational today.

One measure of success is the number of products we have supported into First-in-Human trials: 8 is an extraordinary achievement in 5 years. The future holds even more promise, as over 50 patents and invention disclosures have been filed for products in our portfolio.

We are the only team in the world that integrates therapeutics, diagnostics and prevention products into a coherent portfolio strategy, focusing investments where the the human need is the most dire.

We also recognize that the initial wave of antibiotics starting from the 1940s failed to reach people in need, so we have set a new global standard for antibacterial stewardship and access. These standards apply to every CARB-X-supported project for years to come and have been endorsed and extended by key stakeholders around the globe.

Low- and middle-income countries (LMICs) bear the greatest disease burden of many deadly pathogens. Of our active projects, many are targeting syndromes which disproportionately impact LMICs, including diarrheal disease, neonatal sepsis, gonorrhea and urinary tract infections. As we have seen with the COVID-19 pandemic, our lives depend on anticipating global health problems and preparing global health solutions.

Finally, we cannot do this alone. We work in partnership with many organizations, including the funders who make this possible. We are actively seeking additional funding from G7/G20 members to bring solutions to patients everywhere, protecting all of us from bacterial threats.

Kevin Outterson

Timeline: 5 years of global antibacte

February 2016 | United States HHS, ASPR and BARDA issue Funding Opportunity Announcement

April 2016 | Application submitted by Boston University in response to US HHS, ASPR and BARDA Funding Opportunity

February 2017 | First Joint Oversight Committee product developer investment decisions taken

March 2017 | Portfolio launched with 11 awards

July 2017 | Closed **first Fiscal Year** with **$42M** awarded to **18** projects — including 8 novel class antibiotics — in 6 countries across North America, Europe & Asia

December 2017 | First microbiome-modifying First-in-Human trial initiation announced (Vedanta Biosciences)

May 2018 | UK government's Global Antimicrobial Resistance Innovation Fund (GAMRIF) and the Bill & Melinda Gates Foundation joined partnership

July 2019 | Closed **third FY** with **$187M** awarded and added **10** new projects.

Now — 48 projects in 7 countries and 5 graduates total

August 2019 | First Official Development Assistance from the UK GAMRIF program for expansion of an existing program (Integrated BioTherapeutics)

March 2020 | First product developer entered collaboration with large pharma company in relation to CARB-X funded program (Forge Therapeutics)

September 2020 | First CARB-X funded project received FDA Orphan Drug Designation (Peptilogics). First CARB-X funded microbiome project received BARDA advanced development contract (Vedanta Biosciences)

October 2020 | Second CARB-X supported diagnostic product obtained CE-mark (Specific Diagnostics)

July 2021 | Closed **fifth FY** with **$361M** awarded to **25** projects.

Now — 92 projects in 12 countries and 9 graduates total

erial innovation

July 2016 | Cooperative Agreement signed. Wellcome Trust joined partnership, and CARB-X officially launched

CARB-X

August 2016 | First funding round opened

January 2017 | First Scientific Advisory Board meeting

October 2017 | First vaccine project entered portfolio (Integrated BioTherapeutics)

November 2017 | First microbiome-modifying program entered portfolio (Vedanta Biosciences)

July 2018 | Closed **second FY** with **$101M** awarded and added **20** new projects.

Now — 38 projects in 7 countries and 2 graduates total

February 2019 | Global Accelerator Network expanded (including accelerators in Switzerland, Germany and India)

March 2019 | First CARB-X-funded project received breakthrough devices designation (T2 Biosystems). Germany's Federal Ministry of Education and Research (BMBF) joined partnership

Federal Ministry of Education and Research

June 2020 | First CRISPR-phage project entered portfolio (Eligo Bioscience)

July 2020 | Strategic review and implementation of new investment priorities. Closed **fourth FY** with **$304M** awarded and added **19** new projects.

Now — 67 projects in 9 countries and 7 graduates total

December 2020 | CARB-X recognized with Global Health Technologies Coalition's *Innovating for Impact Award* for progress made in accelerating research to combat antibiotic-resistant bacteria

March 2021 | Launched Stewardship and Access Plan Development Guide

May 2021 | CARB-X demonstrates a portfolio approach to targeting drug-resistant gonorrhea with 1 vaccine, 3 diagnostics and 3 novel class oral antibiotics

5 years and counting

92 PROJECTS FUNDED

60 ACTIVE PROJECTS TODAY

9 PROJECTS SUPPORTED THROUGH INVESTIGATIONAL NEW DRUG/ IND-EQUIVALENT APPROVALS

1163 APPLICATIONS REVIEWED FROM **39** COUNTRIES IN 8 FUNDING ROUNDS

USD **$361** MILLION AWARDED

9 GRADUATES

2 SECURED REGULATORY APPROVAL

1 IN PHASE 2

1 AWARDED ADVANCED DEVELOPMENT CONTRACT WITH BARDA

3 CROSS PROJECT INITIATIVES

10 PROJECTS SUPPORTED IN PHASE 1, OF WHICH **8** INCLUDED FIRST-IN-HUMAN ACTIVITIES

120 SUBJECT MATTER EXPERTS GLOBALLY

7 ACCELERATORS IN GLOBAL ACCELERATOR NETWORK

54 INVENTION DISCLOSURES

36 THERAPEUTICS **6** PREVENTATIVES

12 DIAGNOSTICS

"Infectious diseases and drug-resistance are shaking the very foundations of modern medicine. To get ahead of this crisis, we need rapid innovation. CARB-X has been incredibly successful in fostering innovation in the early stages R&D of antibiotics, vaccines, and diagnostics. This is a vital step forward in tackling drug-resistant infections and will help ensure promising products can make it to the patients who need them."

— Tim Jinks,
Head of Interventions, Infectious Diseases Health Challenge
Wellcome Trust

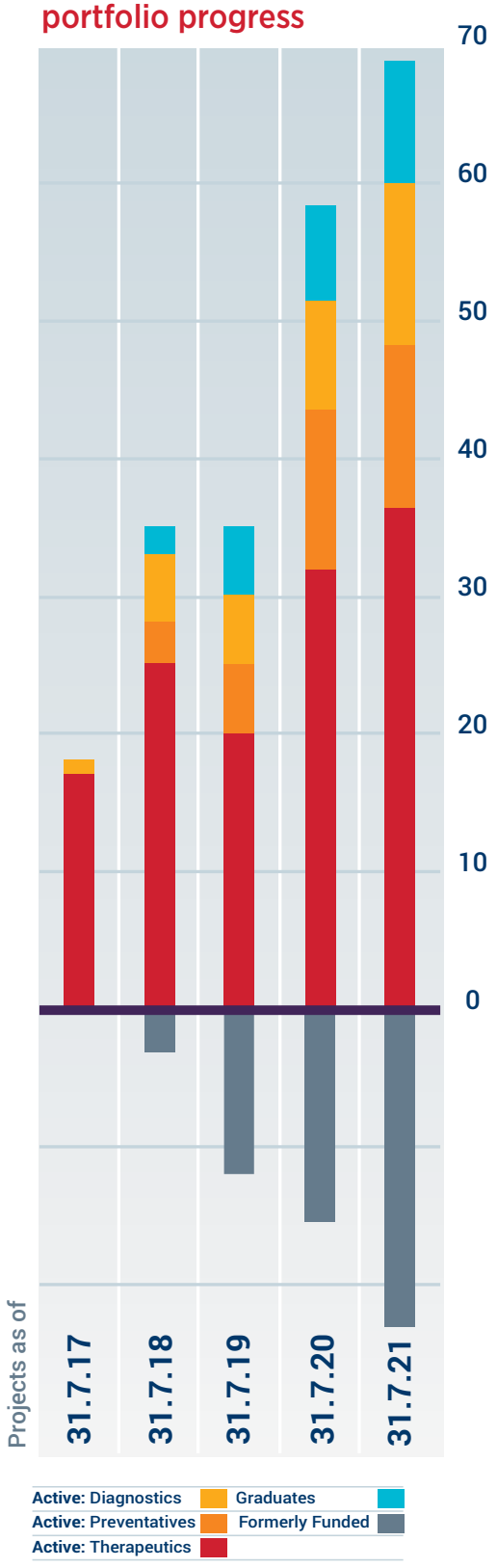
"Combatting resistant pathogens takes joint international collaborative actions, such as CARB-X. This is why the German Federal Ministry of Education and Research joined the CARB-X partnership in 2019 with a commitment of 40 million euros over four years. Over the last years CARB-X has been building a robust and diverse portfolio of new antibiotics, diagnostics and vaccines, thus becoming a valuable part of our AMR funding strategy."

— Veronika von Messling
Director-General for Life Sciences, German Federal Ministry of Education and Research

"This global partnership demonstrates the powerful positive impact that government, international partners, and the private sector can have when we work together toward a common goal. Through this partnership, we are revitalizing the antibacterial product pipeline, driving new, innovative products into clinical development with the potential to turn the tide on antibiotic-resistant infections and save lives."

—Gary Disbrow, Ph.D.
Director, BARDA

CARB-X 5-year portfolio progress



Year 5 portfolio highlights

ENTASIS THERAPEUTICS

Urinary tract infections (UTIs) are one of the most common bacterial infections. They occur when bacteria from the skin or periurethral area enter the urethra and infect the urinary tract and bladder. Most UTIs, while uncomfortable, are relatively easy to treat; however, the bacteria that cause them have become resistant to many of the antibiotics used for treatment, thereby rendering them ineffective. Entasis Therapeutics is developing a differentiated oral combination of a novel broad-spectrum inhibitor of Class A and C beta-lactamases (ETX0282) with cefpodoxime to treat complicated UTIs including carbapenem resistant Enterobacteriaceae (CRE). This combination restores the utility of a formerly-effective antibiotic, cefpodoxime, by inhibiting the enzymes that degrade it. Additionally, the oral form is considered an additional differentiating feature since the product has the potential to be used in the community and as stepdown therapy as patients are discharged from the hospital. After progressing from preclinical through a First-in-Human study supported by CARB-X, Entasis graduated in April 2021.

SERES THERAPEUTICS™

The human microbiome – the collective bacteria that live inside and on the human body – plays many roles in keeping us healthy, including protection against colonization by bad bacteria, regulation of immune function and contributing to energy metabolism. When the microbiome is disrupted by antibiotic use, inflammation or other forces, we become more vulnerable to disease and infection. Seres Therapeutics' SER-155 is an oral, rationally-designed microbiome consortium for the prevention of breakthrough antibiotic-resistant bacterial infections and graft-versus-host disease in patients following solid organ and allogeneic stem cell transplantation. This program graduated from the CARB-X portfolio in June, 2021 after successfully progressing from hit-to-lead through preclinical studies, filing an IND application with, and receiving a safe-to-proceed to First-in-Human studies from, the US Food and Drug Administration (FDA). Seres is CARB-X's ninth graduate since inception.

As of 31 July 2021 CARB-X had an active portfolio of 60 projects

19 ANTIBIOTICS WITH NOVEL CLASSES

16 NON-TRADITIONAL THERAPEUTICS

12 VACCINES & PREVENTATIVES

12 RAPID DIAGNOSTICS

1 UNIQUE ENHANCEMENT TO EXISTING CLASS

25 NEW AWARDS IN FY 21

This year's First-in-Human programs:

Bugworks is developing a novel class broad-spectrum antibiotic to target multi-drug resistant Gram-negative bacteria. The lead compound, BWC0977, is a Novel Bacterial Topoisomerase Inhibitor and is the product of an aggressive lead-optimization campaign supported by CARB-X. BWC0977 was designed to offer oral and intravenous presentations that — combined with the broad-spectrum activity — have the potential to treat many of the infections for which we lack robust therapies today. Also with our support, BWC0977 progressed through preclinical studies and in 2021 gained approval from the Australian regulatory authorities to commence human clinical trials. Bugworks intends to commence a First-in-Human study later this year.

Escherichia coli is a key causative pathogen resulting in UTIs. **GSK**'s orally bioavailable small-molecule drug, GSK3882347, targets an adhesion protein found on the surface of *E. coli* bacteria called FimH. By binding to FimH, GSK3882347 prevents *E. coli* from attaching to the bladder wall, thereby preventing infection. It is also antibiotic-sparing, which should help slow antibiotic resistance. Given the non-traditional mechanism of action, GSK3882347 could be beneficial in helping to combat the problem of increasing antibiotic resistance. With CARB-X support, GSK is exploring the safety, tolerability and pharmacokinetics of GSK3882347 in healthy volunteers in a First-in-Human study expected to complete in 2021.

No novel systemic antimicrobial peptide for the treatment of Gram-negative infections has been approved in over 60 years. Such antibiotics, including the older polymyxin drugs colistin and polymyxin B, exhibit excellent efficacy against Gram-negative pathogens but carry a high risk for adverse effects, mainly due to toxicity affecting the kidneys. MRX-8, an innovative 'soft drug' polymyxin antibiotic designed by **MicuRx Pharmaceuticals**, targets clinically important therapy of multidrug-resistant infections including *E. coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii.* With support from CARB-X, MicuRx has successfully completed the preclinical development of MRX-8, and in 2020, gained FDA permission to proceed into human clinical studies. MicuRx is presently conducting a First-in-Human Phase 1 study with MRX-8 that is expected to be completed early next year.

NIH research found that roughly 75% of clinically significant infections are refractory to antibiotics due to the biofilm that protects bacteria. **Trellis Bioscience**'s TRL1068 is a native human monoclonal antibody that targets and disintegrates bacterial biofilm by extracting a key scaffolding protein. This renders the bacteria more susceptible to attack by the immune system and more sensitive to conventional antibiotics. TRL1068 has been shown to enhance antibiotic activity against antibiotic-resistant strains of Gram-positive and Gram-negative bacteria. With CARB-X support, Trellis Bioscience completed preclinical development of TRL1068 and in 2020 received approval from the FDA to commence human clinical trials. Trellis has commenced a First-in-Human study in patients with prosthetic joint infections.

A portfolio approach to drug-resistant gonorrhea

Gonorrhea is a sexually-transmitted disease caused by the pathogen *Neisseria gonorrhoeae*. This is a global disease, impacting disproportionately those in LMICs. With female patients, the effects of gonorrhea include life-threatening ectopic pregnancy and infertility; with all patients, there is an increased risk of HIV. *N. gonorrhoeae* has progressively become resistant to every one of the many antibiotics at our disposal, leaving only one that is generally effective. As we've learned from COVID, it is critical to diagnose and prevent, but we also must have effective treatments. In this case, and because antibiotics are generally disseminated in sexually-transmitted-disease clinics, oral antibiotics are critical.

With continued exploration of novel Type II fatty acid synthesis inhibitors, **Debiopharm** has discovered Debio 1453, an orally active small molecule with activity against *N. gonorrhoeae*, including multidrug-resistant forms. This program has commenced IND-enabling studies that will support Debio 1453's progression to clinical trials in humans.

Genes associated with *trans*-translation have been found in every bacterial genome sequenced to date. Mutations in these components affect viability or virulence in a wide variety of bacteria. **Microbiotix**'s project aims to develop a series of broad-spectrum bacterial *trans*-translation inhibitors into a new class of antibiotic for use as a single-dose oral therapy to treat sexually transmitted infections caused by *N. gonorrhoeae*.

Venatorx Pharmaceuticals is developing an oral cyclic-boronate as a penicillin-binding protein (PBP) inhibitor for third-generation-cephalosporin-resistant gonorrhea. The company is aiming to offer a new therapeutic option to address growing resistance to ceftriaxone, the only remaining outpatient antibiotic for treatment of gonorrhea. CARB-X funding will help progress this novel class program from hit-to-lead through IND-enabling studies.

The Jenner Institute, based within the University of Oxford, joined the CARB-X portfolio in 2021. They are developing a novel vaccine to prevent infections caused by *N. gonorrhoeae*. The vaccine contains blebs, or fluid-filled blisters, from the outer surface of *N. gonorrhoeae*, called Native Outer Membrane Vesicles. With gonorrhea affecting an estimated 78 million people worldwide, particularly in LMICs, the vaccine is ultimately aiming to be affordable for global use.

New to the CARB-X portfolio, **Novel Microdevices** aims to offer a rapid point-of-care molecular test (<25 minutes) for the identification of sexually transmitted infections, and will detect antibiotic-resistant bacteria, including *Chlamydia trachomatis* and *N. gonorrhoeae*. The device uses an onboard innovative sample-preparation technology that is battery powered and is very portable and easy to use, making it well-suited for use across the globe, including LMICs.

Joining the CARB-X portfolio in April, 2021, **SpeeDx** has developed a rapid molecular test using polymerase chain reaction technology called InSignia™ to assist in detecting chlamydia and active infections of gonorrhea. Through susceptibility testing, the technology will identify the best antibiotic choice for gonorrhea treatment from the set of antibiotics most used in LMICs: cefixime, ciprofloxacin, and azithromycin. It will be combined with a battery-powered, easy to use device developed by QuantumDx that may be used in remote and low-resource settings around the world and deliver results in under one hour.

Talis Biomedical will deliver a high-performance, low-cost molecular diagnostic capability at the point-of-care. The clinical focus of this diagnostic platform is to enable rapid identification (<20 minutes) of chlamydia and gonorrhea.

New frontiers of innovation

CARB-X invests with the goal of delivering important antibacterial products to the patients that need them. We have placed a high value on innovation, and this includes embracing non-traditional modalities for which there is neither a well-trodden preclinical nor a well-defined clinical history, requiring us to work with the broader community to forge new ground for these novel technologies. To best achieve this, we have invested in several unique technologies focused on different chemistries, modalities, pathogens and syndromes, starting at various stages of discovery and development and executed by unique scientific teams. In conjunction, we are engaging with regulatory authorities to learn and shape requirements for entering the clinic as well as clinical trial designs. Areas where we substantially augmented our portfolio this year include bacteriophage, vaccines, peptides and anti-virulence.

Bacteriophage

Also known as 'phage', bacteriophage are viruses that infect bacteria with their DNA or RNA and replicate among bacteria. They are some of the most common structures in our ecosystem and can be found wherever bacteria exist. Typically, they are species-specific and as such are considered harmless to the gut microbiota. They have been used as an alternative to antibiotics since the late 20th century. Thanks to modern molecular biology, the field is represented by both native and engineered phage products. In the last two years, we have made four investments in projects developing engineered phage products: the following are the three that entered the portfolio in year five:

Locus Biosciences is developing LBP-KP01 to treat serious, recurrent UTIs caused by the bacterial pathogen *Klebsiella pneumoniae*. Their technology enhances the natural destructive power of bacteriophage by adding CRISPR Cas3, which degrades bacterial genomic DNA, to deliver a killing efficacy level that exceeds standard-of-care antibiotics while removing only the target bacterial species, thereby sparing the patient's microbiome. This offers physicians a novel mechanism to overcome current forms of resistance and could complement existing standard of care.

Phico Therapeutics is developing their SASPject technology using engineered bacteriophages delivering antibacterial small acid-soluble spore proteins (SASPs) as their payload. The SASPs bind to and inactivate bacterial DNA preventing the bacteria from being able to reproduce This project is laser-focused on treating ventilator-associated bacterial pneumonia caused by *Pseudomonas aeruginosa.*

SNIPR Biome is developing a new CRISPR product that aims to decolonize the gut of pathogenic *E. coli* bacteria in cancer patients with hematological malignancies, thereby reducing the opportunity for these pathogens to breach the gut barrier and cause bloodstream infections.

Vaccines

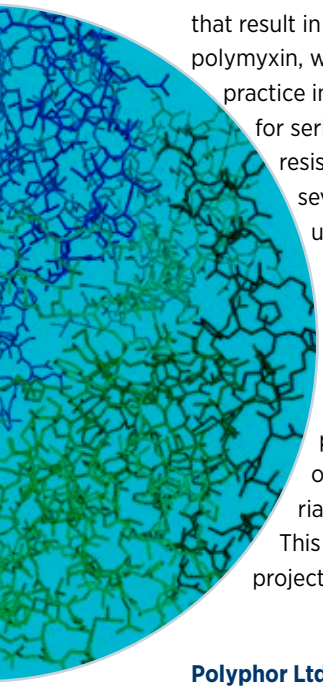
The COVID-19 pandemic certainly has taught us how critical vaccines are to tackling infectious pathogens. We lack vaccines for the vast majority of bacterial pathogens that the CDC and WHO name as posing the greatest threat. There are many reasons for this including the need for a better understanding of the underlying biology, epidemiology or transmission, the proper selection of antigens, the translatability of animal infection models to the clinical setting and the optimal design of clinical trials. In addition to the Jenner Institute vaccine mentioned earlier, we also added the following vaccines to the portfolio in year five:

Affinivax aims to develop a multivalent vaccine using its Multiple Antigen Presenting System (MAPS) technology, to prevent infections caused by *S. aureus*.

GSK Biologicals SA (GSK) with the support of its affiliate GSK Vaccines Institute for Global Health (GVGH) is developing two new vaccines: one to prevent Group A Streptococcus infections and and one to prevent invasive non-typhoidal salmonellosis and typhoid fever using a licensed Typhoid Conjugate Vaccine plus salmonella antigens. Both vaccines aim to reduce morbidity and mortality and help reduce the growing threat of resistance.

Antimicrobial peptides and polymyxins

These are naturally-occurring antibiotics that target bacteria. They have long been considered an alternative source of antibiotics, particularly in the face of antibiotic resistance, and are appreciated for their broad-spectrum coverage of Gram-negative bacteria. However, owing to their typical chemical composition, they often have off-target activities that result in toxicities to humans. Colistin, an example of a polymyxin, was discovered in 1949 and first used in clinical practice in the 1950s. It remains the last line of therapy for serious hospital infections caused by multidrug-resistant Gram-negative bacteria. However, it has several liabilities, including its inability to distribute effectively to key human tissues that may be burdened with infection and its nephrotoxicity and neurotoxicity. Furthermore, worrisome resistance to colistin has emerged. Taken together, these support the need for new peptides. In the last year, we added a new peptide program and augmented an existing one to consider both direct-acting antibacterial activity and antibiotic-potentiation activity. This brings the peptide portfolio to seven unique projects.



Polyphor Ltd. is utilizing its macrocycle discovery platform to deliver novel synthetic antimicrobial peptide-derived antibiotics, the Outer Membrane Protein Targeting Antibiotics (OMPTA), in two programs targeting the essential outer-membrane surface proteins BamA and LptA, respectively. The novelty in chemistry and in target offer the promise of avoiding cross-resistance to current therapies, including colistin, and might offer a safety advantage with respect to nephrotoxicity which remains a challenge for the cationic peptide class of molecules. While BamA-OMPTA has been in the portfolio and is a broad-spectrum agent with a focus on HAP/VAP; the more recent LptA-OMPTA program focuses on Enterobacteriaceae, including multi-drug-resistant isolates, and as such is focused on UTIs and lung infections.

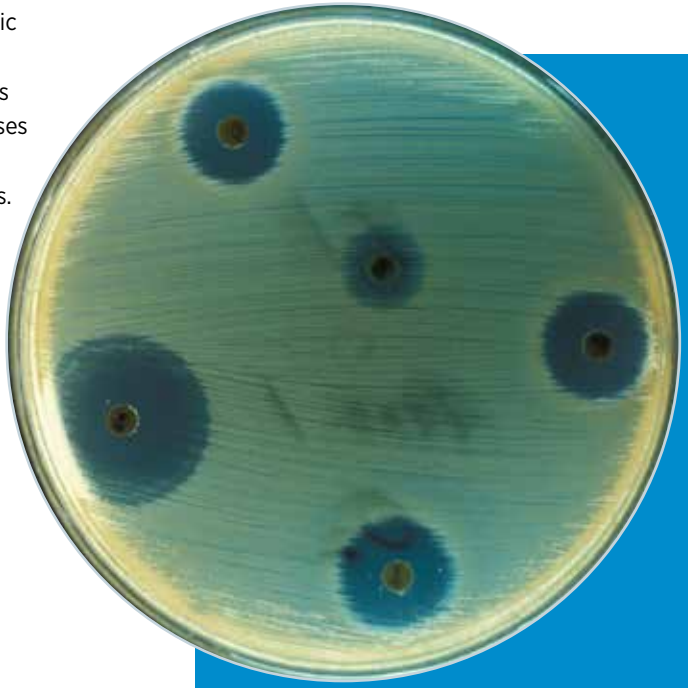
In addition to exploring the extent to which the octapeptins demonstrate broad-spectrum Gram-negative activity, including activity against colistin-resistant isolates, **The University of Queensland** will also evaluate the ability of the octapeptins to potentiate the activity of existing antibiotics. If successful, they could, for instance, broaden the spectrum of Gram-positive-only antibiotics to encompass Gram-negative activity.

Anti-virulence

Bacteria are pathogenic to humans via production of virulence factors which are molecules, cell structures, and regulatory systems that enable bacterial pathogens to colonize the human host, damage cells and tissues and evade or inhibit the immune response. Anti-virulence, therefore, blocks and disarms the bacterial pathogen's ability to cause infectious diseases. Whether anti-virulence agents can be used as standalone therapies, which would therefore be an antibiotic-sparing approach, or whether they will be given on top of an antibiotic is something we will learn. We have doubled our anti-virulence portfolio this year, now with six active programs emphasizing three pathogen/syndrome foci. In addition to the GSK program mentioned above, below are the additions in year five:

The **Helmholtz Centre for Infection Research (HZI)** and the Lead Discovery Center GmbH are developing a new small-molecule inhibitor drug to disable an important toxin (alpha-hemolysin) in *Staphylococcus aureus* and thereby prevent exacerbation of pneumonia.

The Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) is developing a small-molecule inhibitor of elastase (LasB) to disarm *Pseudomonas aeruginosa* in cystic fibrosis patients, suppressing the bacteria's disease-causing properties.



Stewardship and access

Stewardship and access principles must exist alongside the research and development of new products so that these vital products are available to patients who need them, used responsibly, and safeguarded for future generations. Companies funded by CARB-X are contractually obligated to develop Stewardship and Access Plans. This year, together with leading funders of research and development of new antibiotics and other products targeting antibiotic-resistant bacteria, we released a **Stewardship and Access Plan Development Guide** providing comprehensive guidance on strategies and activities to support stewardship and access for the research and development community, both in the CARB-X portfolio and for the larger research and development community.

"Sound Stewardship and Access Plans are key to the success of new products in the AMR space, because they ensure global accessibility to new treatments while also preventing inappropriate antimicrobial use in healthcare settings and beyond. But what does a good plan look like? This Guide will be made available to all developers, to help them articulate and formulate their own activities when they bring much-needed products to market, enabling us to achieve that goal of "access, not excess" to these essential medicines."

— Dame Sally Davies
UK Special Envoy on AMR

Thank you to our partners

CARB-X's global mission to accelerate the early development of innovative products to address antibiotic-resistant bacteria would not be possible without our partners. They are vital to our success, the success of our product developers, and, ultimately, securing the future health of humanity.

The Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) in the U.S. Department of Health and Human Services, invests in the innovation, advanced research and development, acquisition, and manufacturing of medical countermeasures – vaccines, drugs, therapeutics, diagnostic tools, and non-pharmaceutical products needed to combat health security threats. To date, BARDA has supported 61 FDA approvals of products that cut across our threat space and include vaccines, therapeutics, diagnostics and devices. BARDA co-founded the Combating Antibiotic-Resistant Bacteria Accelerator, currently managed as CARB-X by Boston University, and committed up to US$180 million from 2016-2022.

Wellcome supports science to solve the urgent health challenges facing everyone. Wellcome supports discovery research into life, health and wellbeing, and are taking on three worldwide health challenges: mental health, infectious disease and climate. Wellcome Trust was CARB-X's first international partner and committed over US$155 million from 2016-2021.

The US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. NIAID provides in-kind services such as preclinical services valued at US$50 million to CARB-X-funded projects.

Education and research are the foundations for our future. The promotion of education, science and research by the BMBF represents an important contribution to securing Germany's prosperity. Education and research are a Federal Government policy priority, which is reflected in the development of the funding it is making available to these fields. BMBF is providing up to €500 million over ten years towards research to combat antimicrobial resistance. In 2019, BMBF committed €39 million to CARB-X over four years plus an additional €1 million to DZIF directly for one of the accelerators in the CARB-X Global Accelerator Network.

This research is co-funded by the UK Department of Health and Social Care as part of the Global AMR Innovation Fund (GAMRIF). This is a UK aid programme that supports early-stage innovative research in underfunded areas of antimicrobial resistance (AMR) research and development for the benefit of those in low- and middle-income countries (LMICs), who bear the greatest burden of AMR. GAMRIF committed up to £20 million to CARB-X.

The Bill & Melinda Gates Foundation is a major funder of global health research and development. The foundation supports the development of new vaccines and novel biologics against antibiotic-resistant bacterial infections, particularly for vulnerable populations in low- and middle-income countries. They committed US$25 million to CARB-X over four years.

Boston University leads CARB-X, providing operational and administrative support. CARB-X headquarters are located at the Boston University School of Law.

Scientific, regulatory and business expertise

In addition to our Research & Development team, we have built **a curated cadre of 120 global subject matter experts (SMEs)**. Many of these experts have held senior positions at the US Food & Drug Administration, global pharmaceutical companies, emerging biotechnology companies, academia and their own consultancies.

CARB-X's Global Accelerator Network (GAN) consists of seven organizations with specialized know-how in antibacterial drug development, diagnostics, vaccines, business and legal strategy, and regulatory affairs. They include California Life Sciences Institute (CLSI), RTI International, Institute for Life Sciences Entrepreneurship (ILSE), Massachusetts Biotechnology Council (MassBio), Foundation for Innovative New Diagnostics (FIND), the German Center for Infection Research (DZIF), and the Centre for Cellular and Molecular Platforms (C-CAMP).

CARB-X Global Accelerator Network

Both our SMEs and GAN provide CARB-X with tremendous flexibility and scalability in designing acceleration plans and raise awareness about CARB-X within their regional communities.

Uniquely advancing ecosystem understanding

In CARB-X's first five years, we offered webinars and workshops to address challenges that face multiple product developers in our portfolio. Topics included fundraising, pre-Investigational New Drug application preparation, and technical issues. In 2020, CARB-X launched Cross-Project Initiatives (CPIs) to create efficiencies across multiple funded product developers, a higher-level understanding of common issues facing developers, and potentially create funding calls around focused areas of innovation and development. Outcomes generated from the CPIs are intended to benefit the larger AMR community. Examples include:

- Early evaluation of pre-existing resistance risk (therapeutics) or antigenic variability (preventatives)
- Consistent assessment of key safety risks
- Improved animal models of infection

Executive team

Erin Duffy, PhD — *Chief of Research & Development*

Karen Gallant, PhD — *Deputy Executive Director*

Genevieve Holmes — *Director of Strategic Initiatives*

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

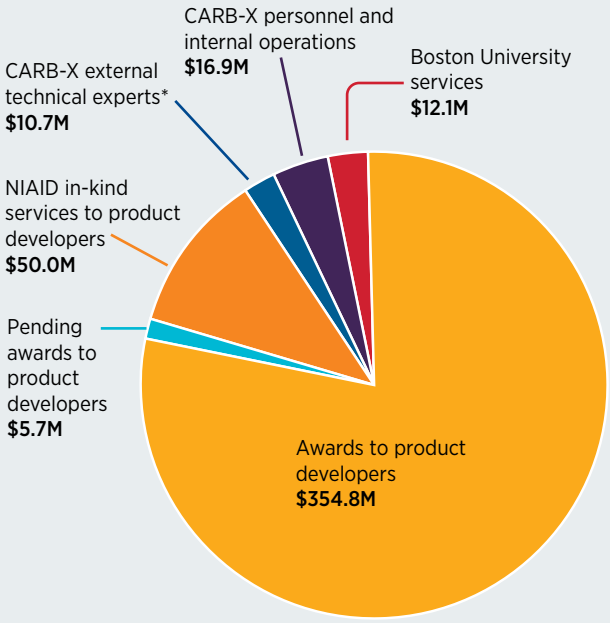
Diane MacDonald, MPA — *Chief Operating Officer*

Kevin Outterson, JD, LLM — *Executive Director & Principal Investigator*

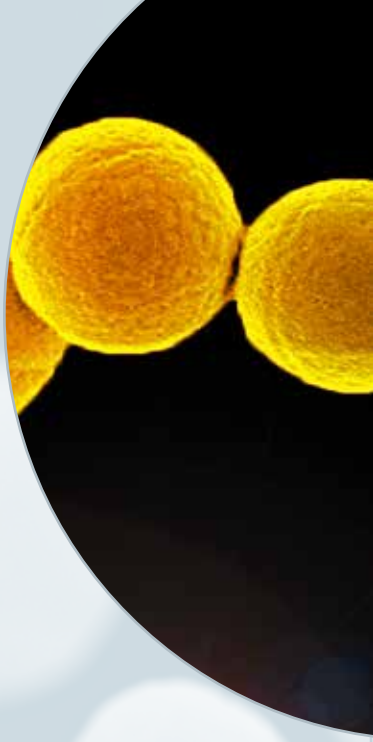
Joint oversight committee

CARB-X is governed by the Joint Oversight Committee (JOC), which serves as the board of directors, ensuring the highest scientific and ethical standards. The JOC is comprised of representatives from CARB-X's funders and members of the CARB-X executive team.

Five years of support



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



Founded in 2016, CARB-X is a global non-profit partnership dedicated to accelerating antibacterial research and development. From 2016-2022, CARB-X is investing $480 million in non-dilutive funding to develop innovative products to prevent, diagnose and treat antibiotic-resistant infections. In addition to funding, CARB-X provides scientific, regulatory and business expertise to product developers. We support diagnostics from feasibility into product verification and validation and therapeutics and preventatives from lead discovery through preclinical development and into a demonstration of safety in human clinical studies.

ASPR BARDA wellcome NIH National Institute of Allergy and Infectious Diseases UKaid from the British people Federal Ministry of Education and Research Bill & Melinda Gates foundation BOSTON UNIVERSITY

CARB-X

Combating Antibiotic-Resistant Bacteria

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