



Xccelerating global antibacterial innovation

CARB-X injects up to \$48 million to accelerate first *Powered by CARB-X* portfolio of drug discovery and development projects to tackle antibiotic resistance

3 potential new classes of antibiotics, 4 innovative non-traditional products and 7 new molecular targets against the most urgent deadliest 'superbugs'

(WASHINGTON, D.C./ LONDON, U.K.) – The Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X (www.carb-x.org), announced today it is investing US\$24 million immediately and up to \$24 million in milestone-based additional payments over three years to help 11 biotech companies and research teams in the U.S. and U.K. accelerate the development of new life-saving antibacterials and diagnostics aimed at treating infections caused by the world's deadliest antibiotic-resistant bacteria. Together with private funds from the companies, today's announcement could lead to an investment of more than \$75 million in successful projects.

The funded projects are exciting early stage research programs and include 3 potential new classes of small molecule antibiotics. The last new antibiotic class approved was discovered in 1984. Also in the pipeline are 4 innovative non-traditional products, which could offer alternate approaches to targeting and killing bacteria. Further distinguishing the pipeline's focus on drug resistance, these projects target 7 new bacterial targets. All these potential new medicines target Gram-negative bacteria prioritized by the U.S. Centers for Disease Control (CDC) and the United Nation's World Health Organization (WHO).

Public health officials have warned for years that we are facing an urgent global public-health threat from antibiotic-resistant bacteria and that the pipeline of novel therapies to treat 'superbugs' is precariously thin. There are an estimated 700,000 deaths each year around the world from drug-resistant infections. In the U.S. alone, the CDC estimates that 23,000 people die each year from antibiotic resistant infections.

"CARB-X is a bold new approach to developing life-saving treatments for antibiotic-resistant infections. By accelerating promising research, it is our hope that we can speed up the delivery of new effective antibacterials, vaccines, devices and rapid diagnostics to patients who need them," said Kevin Outterson, Executive Director of CARB-X and Professor of Law at Boston University, in announcing the funding at a special event at The Pew Charitable Trusts in Washington. "The projects in the new *Powered by CARB-X* portfolio are in the early stages of research, and there is always a high risk of failure. But if successful, these projects hold exciting potential in the fight against the deadliest antibiotic-resistant bacteria."

This is the first phase of funding by CARB-X, launched July 28, 2016 as one of the world's largest public-private partnership to accelerate global antibacterial innovation, including drugs,

vaccines, rapid diagnostics and devices. CARB-X aims to invest up to \$450 million over five years with the goal of accelerating the preclinical discovery and development of at least 20 new antibacterial products and progressing at least two new products into human trials during that time. If successful, the projects will be supported through early preclinical and early clinical development to a stage where they can be positioned to be taken forward by private investors.

CARB-X was launched by the U.S. Department of Health and Human Services (HHS), Biomedical Advanced Research and Development Authority (BARDA) and the National Institute of Allergy and Infectious Diseases (NIAID). CARB-X is funded by BARDA and the Wellcome Trust, a global charitable foundation based in London. Wellcome announced today its funding share will amount to \$US155.5 million dollars over five years. NIAID is providing support in the form of preclinical services. CARB-X is a non-profit effort headquartered at the Boston University School of Law. Other partners include the Broad Institute of MIT and Harvard, the Massachusetts Biotechnology Council (MassBio), the California Life Sciences Institute (CLSI), and RTI International. CARB-X was created in response to the U.S. government's 2015 Combating Antibiotic Resistant Bacteria (CARB) initiative and the U.K. government's call in 2016 for a concerted global effort to tackle antibiotic resistance.

Tim Jinks, Head of Drug Resistant Infection at Wellcome Trust, said: "Drug-resistant infection is already a huge global health challenge – and it is getting worse. Without effective drugs, doctors cannot treat patients. We need global powers to work together on a number of fronts – from the beginning to the end of the drug and diagnostic development pipeline. Years of insufficient investment means this pipeline is all but dried up. Through CARB-X we are filling the void for early discovery support. And with this first portfolio we have taken bold decisions to ensure a broad range of approaches for finding new ways to treat and diagnose resistant infection. We hope others will now follow and add their support to CARB-X."

"NIAID welcomes the opportunity to lend its preclinical research expertise to the new CARB-X awardees and work with our partners to find and develop a new generation of safe and effective antibiotics," said NIAID Director Anthony S. Fauci, M.D.

BARDA Director Rick Bright, Ph.D said: "With CARB-X, we built on our track record of innovative partnerships to enhance national security preparedness for chemical, biological, radiological and nuclear threats, and today CARB-X began accelerating novel antibacterial products and technologies from early stage development toward the clinic. This portfolio will ensure that the United States and the world are better prepared to treat drug resistant bacterial infections."

Today's announcement represents the first projects selected for the *Powered by CARB-X* portfolio. The designation signifies that these projects have been vetted by the CARB-X Advisory Board, comprised of leading antibiotic experts. The projects were selected through a competitive process from among 168 applications from around the world and the awards were based on the merit of the company research proposals, as evaluated by the CARB-X Advisory Board and the CARB-X team. To be considered, the project must target one of the deadly antibiotic-resistant bacteria on the Serious or Urgent Threat List prepared by the CDC or appear

on the Priority Pathogens list published by the WHO. In the first year, the CARB-X portfolio priorities are weighted towards Gram-negative bacteria, which are resistant to multiple drugs and can cause infections including pneumonia, surgical site infections and meningitis in healthcare settings, and towards non-traditional approaches.

The biotechs and research teams – 8 based in the U.S. and 3 in the U.K. – could receive up to \$24 million in further funding over the next three years if milestones are hit. The projects will receive wrap-around business and drug development support services including drug development and regulatory services through our partners NIAID and RTI, and business strategy and operational mentoring from our accelerator partners in the dense, talent-rich biotech hubs of Cambridge, Mass (MassBio), the San Francisco Bay Area (CLSI) and London (the Wellcome Trust).

CARB-X is expected to announce further funding decisions with additional projects added to the *Powered by CARB-X* portfolio later this year. CARB-X aims to deliver a growing portfolio of promising new antibiotics, diagnostics, devices and vaccines, to tackle the threat posed by drug-resistant bacterial infections.

See below for details of the *Powered by CARB-X* portfolio

Media Contacts:

CARB-X:

Ann Comer-Woods +1 (617) 353-3097, anncomer@bu.edu
Kevin Outterson, mko@bu.edu

ASPR/BARDA :

Elleen Kane +1 (202) 205-8117, elleen.kane@hhs.gov

NIAID:

Kathy Stover +1 (301) 402-1663, kathy.stover@nih.gov

Wellcome Trust:

Maggie Stratton +44 (0) 207 611 8609, m.stratton@wellcome.ac.uk

Powered by **CARB-X**

The *Powered by CARB-X* Portfolio is comprised of 11 exciting early stage antibacterial and rapid diagnostics projects that, if successful, could be potential new weapons in the battle against the antibiotic-resistant bacteria. The portfolio contains a diverse mix of products including oral and intravenous candidate therapies that range in structure from classical small molecules to non-

traditional candidates based on entirely new approaches. All projects in this first round of funding projects target Gram-negative bacteria prioritized by the CDC and WHO.

The projects are in the early stages of discovery and development, and as such, there is normally a high risk of failure. Three of the projects focus on new classes of antibiotics (Forge, Oppilotech, RedX), which is significant because the last new class of antibiotic approved for acute infections was discovered prior to 1984. Antibiotics target one or more essential pathways to kill or inhibit the growth of bacteria. Four of the projects focus on new non-traditional products (Cidara, ContraFect, Microbiotix, Visterra). Nontraditional therapeutics work differently than traditional antibiotics and include such approaches as enhancing the human immune response to fight bacteria and developing drugs that incapacitate the pathogen's ability to grow. Further distinguishing the portfolio as significant is that most of these projects involve new bacterial targets.

The other projects in the portfolio are unique in their own right. Entasis is developing an oral antibiotic to treat Gram-negative infections, which are currently treated intravenously. Proteus is developing a rapid diagnostic imaging tool that aims to identify the type of bacteria causing a lung infection within 60 seconds, which would help speed diagnosis and effective treatment. Tetrphase is focused on producing next-generation synthetic tetracyclines. Spero is developing combination therapies that could boost the potency of existing antibiotics.

Cidara Therapeutics Inc.: Cloudbreak™ immunotherapy platform and CD201 offer new hope to treat serious multi-drug resistant bacterial infections

Awarded \$3.9M over 13 months, and potentially up to \$3M in the following 11 months

Cidara has created a proprietary immunotherapy discovery platform, Cloudbreak™, designed specifically to create compounds that direct a patient's immune cells to attack and eliminate bacterial, fungal or viral pathogens. CD201, a bispecific antimicrobial immunotherapy, is Cidara's first Cloudbreak™ drug candidate being developed for the treatment of multi-drug resistant Gram-negative bacterial infections. Cloudbreak™ has the potential to transform infectious disease similar to the way immunotherapy has transformed cancer with the intent to produce new classes of antibacterials, antifungals and antivirals. Cidara (NASDAQ: CDTX) is a clinical stage biotechnology company headquartered in San Diego, CA. For more information: www.cidara.com. Media contact: Christy Curran at christycurran@sambrown.com.

ContraFect Corporation: Antimicrobial lysins could potentially be a new weapon in the treatment of drug-resistant *Pseudomonas aeruginosa* infections

Awarded \$1.1M over 15 months, and potentially up to \$1.1M in the following 9 months

ContraFect has recently discovered 48 novel Gram-negative lysins. Lysins are bacteriophage-derived enzymes with potent antibacterial activity against antibiotic-resistant pathogens, robust anti-biofilm activity, a low propensity for resistance development, and pronounced synergy when used in combination with conventional antibiotics in pre-clinical studies. The

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CARB-X award will support development of a potential treatment for invasive infections caused by *P. aeruginosa*. These studies will allow ContraFect to proceed with further IND enabling work and the identification of lysins active against other Gram-negative pathogens. ContraFect (NASDAQ:CFRX) is a Yonkers, N.Y.-based biotechnology company. For more information: www.contrafect.com. Media contact: Paul Boni at PBoni@contrafect.com.

Entasis Therapeutics Inc.: A novel oral antibiotic to treat patients with serious drug-resistant bacterial infections

Awarded \$2.1M over 9 months, and potentially up to \$4.2M in the following 12 months

Entasis' anti-infective discovery platform has produced a pipeline of innovative preclinical and clinical programs which target Gram-negative bacterial infections. Entasis, in partnership with CARB-X, is addressing a significant unmet medical need: the lack of an oral therapy to treat multi-drug resistant Gram-negative bacterial infections, including those caused by carbapenem-resistant Enterobacteriaceae (CRE). Currently, many patients with CRE infections require hospitalization for intravenous therapy because antimicrobial resistance has rendered all available oral therapies ineffective. Entasis's novel oral agent has the potential to reduce or eliminate the need for hospitalization. Entasis is based in Waltham, MA. For information: www.entasistx.com. Media contact: kyle.dow@entasistx.com

Forge Therapeutics Inc.: Pioneering chemistry platform for first novel class of 'superbug' antibiotics in decades

Awarded \$4.8M over 15 months, and potentially up to \$4M in the following 18 months

Forge Therapeutics is a privately-held biopharmaceutical company in San Diego, CA, developing novel antibiotics to treat multi-drug resistant bacteria, or 'superbugs,' that have ignited a global health epidemic. With its proprietary chemistry approach, Forge develops small molecule inhibitors targeting metalloenzymes. 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. Forge has discovered novel small molecule inhibitors of LpxC that are potent in vitro, efficacious in vivo, and effective against drug resistant Gram-negative bacteria 'superbugs'. Learn more at www.ForgeTherapeutics.com. Media contact: Amy Conrad at amy@juniper-point.com

Microbiotix Inc.: Type III secretion inhibitors could boost the body's ability to fight bacteria and potentiate host defenses against resistant *P. aeruginosa* in pneumonia patients

Awarded \$1.6M over 12 months, and potentially up to \$1.6M in the following 12 month

Microbiotix's unique approach to targeting drug-resistant Gram-negative bacteria focuses on bacterial virulence, specifically the type III secretion system of *Pseudomonas aeruginosa*. The novel inhibitors, discovered by Microbiotix scientists, have been shown to reverse the pathogen's disruption of the host innate immune response to infection and are not subject to efflux or existing antibiotic resistance mechanisms. Microbiotix's lead program, MBX-400, is a

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novel potent nucleoside dual DNA polymerase/kinase inhibitor for the management of cytomegalovirus disease in transplant patients and is Phase 2 ready. Microbiotix is based in Worcester, MA. For information: www.microbiotix.com. Media contact: Terry Bowlin, President & CEO, at tbowlin@microbiotix.com +1-508-757-2800

Oppilotech Ltd: Using computational modeling to develop potentiators, which weaken the bacterial membrane and break antibiotic resistance

Awarded \$0.12M over 6 months

Oppilotech is focused on the development of safe antibacterial compounds against drug resistant organisms. This approach entails developing potentiators – agents that can permeabilize the cell envelope allowing the use of established antibacterial compounds. To develop potentiators, Oppilotech has built the most detailed, accurate, computational network model of bacterial cell envelope (LPS, peptidoglycan & phospholipids components) biogenesis that has ever been assembled. The model has allowed Oppilotech to identify a protein involved in the synthesis of LPS found in Gram-negative bacteria that has unique features making it an excellent viable target for drug development. The CARB-X funding allows Oppilotech to undertake early stage experimental analysis of agents that can modulate this target to disrupt the envelope. Oppilotech is based in London, UK. For more information, visit www.oppilotech.com. Media contact: Ajay Mistry at Ajay.Mistry@oppilotech.com.

Proteus IRC: New optical imaging technology could allow rapid and accurate diagnosis of bacterial infection in the lungs, and help speed up access to life-saving treatment

Awarded \$0.64M over 21 months, and potentially up to \$0.48M in the following 20 months

The multidisciplinary Proteus team is developing technology to visualise bacteria and the host response in the deepest parts of human lungs in just 60 seconds, using bacteria-specific Smartprobes and fibre-based imaging. This potentially game-changing optical molecular technology will be used in critical care units, which are the largest consumer of antibiotics and an epicentre of antimicrobial resistance development in hospitals. Used at the bedside of patients who are mechanically ventilated and critically unwell, it will enable precision in diagnosing and prescribing, and has widespread applicability elsewhere in the human body for point-of-care bacterial detection and host-response monitoring. Proteus is based in Edinburgh, Scotland. For more information, see: www.proteus.ac.uk. Media contact: Amy.tyndall@ed.ac.uk or Jen.Middleton@ed.ac.uk

Redx Pharma Plc: Novel bacterial inhibitors target multi-drug resistant bacteria and hold potential for the treatment of serious hospital-acquired infections

Awarded \$1M over 18 months

Redx has developed novel bacterial topoisomerase inhibitors which combine efficacy with an excellent safety profile against some of the most difficult-to-treat gram negative pathogens. Redx compounds from this series have demonstrated activity against a range of resistant bacterial species and have shown efficacy against a multi-drug resistant strain of A.

baumannii in an animal model. With support from CARB-X, Redx aims to rapidly progress these compounds into clinical development with the goal of delivering to patients a new treatment for serious infections such as hospital-acquired pneumonia. Redx (LON: REDX) is headquartered in Alderley Park, UK, and is focused on the discovery and development of proprietary small molecule therapeutics to address areas of unmet medical need, principally in cancer, immunology and infection. By improving the characteristics of existing drug classes to create highly differentiated novel best-in-class drugs, Redx has already established a broad portfolio of proprietary drug programs. For more information: www.redxpharma.com. Media contact: Karl Hård at K.Hard@redxpharma.com.

Spero Therapeutics LLC.: Developing new combination drugs aimed at disrupting the Gram-negative bacterial membrane and allowing antibiotics to get their targets

Awarded \$1.6M over 12 months, and potentially up to \$5.4M in the following 24 months

Spero's lead program, SPR741, also called Potentiator, is a platform approach to combination therapy to treat multi-drug resistant gram negative infections, such as Enterobacteriaceae and *Acinetobacter baumannii*, including carbapenem-resistant strains. SPR741 increases the spectrum and potency of more than two dozen classes of Gram-positive antibiotics to include activity against multidrug resistant Gram-negative infections when used in combination. As a part of the CARB-X program, Spero will be screening antibiotic partners for SPR741, with the goal of identifying at least one partner to take through Phase 1 clinical trials. Spero is a clinical-stage biopharmaceutical company based in Cambridge, MA. For more information, visit www.sperotherapeutics.com. Media contact: Maia Arnold at marnold@spectrumscience.com

Tetraphase Pharmaceuticals Inc.: Clinical candidate TP-6076, a novel synthetic fluorocycline antibiotic, targets most urgent multi-drug resistant Gram-negative bacteria

Awarded \$4M over 18 months

Tetraphase Pharmaceuticals uses its proprietary chemistry technology to create novel antibiotics for bacterial infections, including those caused by multidrug-resistant bacteria. The CARB-X collaboration will support the advancement of TP-6076. This phase 1 drug candidate is a novel, synthetic, fluorocycline antibiotic being developed for the treatment of serious and life-threatening bacterial infections, including those caused by pathogens otherwise resistant to current treatment options. It is highly active against clinically important Gram-negative pathogens, including carbapenem-resistant *Acinetobacter baumannii* and Enterobacteriaceae. Tetraphase (NASDAQ:TTPH) is a clinical-stage biopharmaceutical company based in Watertown, MA. For information: www.tphase.com. Media contact: Teri Dahlman at TDahlman@tphase.com.

Visterra Inc.: Developing antibody-drug conjugate as single-dose curative therapy, engineered to kill strains of deadly *Pseudomonas* bacteria

Awarded \$3M over 12 months, and potentially up to \$4.2M in the following 12 months

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Visterra applies its novel Hierotope® platform to design and engineer precision antibody-based biological medicines directed against disease targets that are not adequately addressed with conventional approaches. These targets include viruses and bacteria – which have a high degree of diversity among strains with frequent mutations – and proteins within the body. Using our platform we have designed, engineered and are developing an antibody that attaches to the deadly Pseudomonas bacteria and facilitates its killing. We combined our antibody with a potent anti-microbial peptide that we designed, resulting in a single molecule called an antibody-drug conjugate, which delivers a one-two punch to kill the bacteria. With funding and support by CARB-X, we are developing this antibody-drug conjugate as a single-dose curative therapy, engineered to kill all strains of the deadly Pseudomonas bacteria, including multi-drug resistant strains. Visterra is a clinical-stage biopharmaceutical company based in Cambridge, MA. For more information, visit www.visterrainc.com. For media inquiries, contact Barbara Yates, barbara@theyatesnetwork.com, at +1-781-258-6153.

About CARB-X

CARB-X is the world's largest public-private partnership devoted to antibacterial preclinical R&D. Funded by BARDA and Wellcome Trust, with in-kind support from NIAID, we will spend \$450 million from 2017-2021 to support innovative products moving towards human clinical trials. CARB-X focuses on high priority drug-resistant bacteria, especially Gram-negatives. CARB-X is a charitable global public-private partnership led by Boston University School of Law. Other partners include the Broad Institute of Harvard and MIT, MassBio, the California Life Sciences Institute and RTI International. For more information, please visit www.carb-x.org and follow us on Twitter [@CARB_X](https://twitter.com/CARB_X).

About Wellcome Trust

Wellcome exists to improve health for everyone by helping great ideas to thrive. We're a global charitable foundation, both politically and financially independent. We support scientists and researchers, take on big problems, fuel imaginations and spark debate. The Wellcome Trust is a charity registered in England and Wales, no. 210183. Its sole trustee is The Wellcome Trust Limited, a company registered in England and Wales, no. 2711000 (whose registered office is at 215 Euston Road, London NW1 2BE, UK)

About HHS, ASPR and NIH

HHS is the principal federal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.

ASPR leads HHS's efforts to prepare the nation to respond to and recover from adverse health effects of emergencies, supporting communities' ability to withstand adversity, strengthening health and response systems, and enhancing national health security. Within ASPR, BARDA provides a comprehensive integrated portfolio approach to the advanced research and development, innovation, acquisition, and manufacturing of vaccines, drugs, therapeutics, diagnostic tools, and non-pharmaceutical products for public health emergency threats. These

threats include chemical, biological, radiological, and nuclear threat agents, pandemic influenza, and emerging infectious diseases.

NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. NIAID conducts and supports research — at NIH, throughout the United States, and worldwide — to study the causes of infectious and immune-mediated diseases, and to develop better means of preventing, diagnosing and treating these illnesses. For more information about NIH and its programs, visit www.nih.gov. News releases, fact sheets and other NIAID-related materials are available on the NIAID website: <http://www.niaid.nih.gov/Pages/default.aspx>.

About the California Life Sciences Institute (CLSI)

The California Life Sciences Institute (CLSI) supports the foundations of innovation that have made California home to the world's most prominent life sciences ecosystem. With a focus on the San Francisco Bay Area, CLSI's mission is to maintain California's leadership in life sciences innovation through support of entrepreneurship, education and career development. CLSI is an affiliate of the California Life Sciences Association (CLSA), which represents California's leading life sciences organization. The California Life Sciences Institute is a non-profit 501(c)(3), and was established in 1990 as the BayBio Institute. Learn more at <http://califesciencesinstitute.org>.

About RTI International

RTI International is an independent, nonprofit research institute dedicated to improving the human condition. Clients rely on us to answer questions that demand an objective and multidisciplinary approach—one that integrates expertise across the social and laboratory sciences, engineering, and international development. We believe in the promise of science, and we are inspired every day to deliver on that promise for the good of people, communities, and businesses around the world. For more information, visit www.rti.org.

About the Broad Institute of MIT and Harvard

Broad Institute of MIT and Harvard was launched in 2004 to empower this generation of creative scientists to transform medicine. The Broad Institute seeks to describe all the molecular components of life and their connections; discover the molecular basis of major human diseases; develop effective new approaches to diagnostics and therapeutics; and disseminate discoveries, tools, methods, and data openly to the entire scientific community. Founded by MIT, Harvard, Harvard-affiliated hospitals, and the visionary Los Angeles philanthropists Eli and Edythe L. Broad, the Broad Institute includes faculty, professional staff, and students from throughout the MIT and Harvard biomedical research communities and beyond, with collaborations spanning over a hundred private and public institutions in more than 40 countries worldwide. For further information about the Broad Institute, go to <http://www.broadinstitute.org>. In support of CARB-X, the Broad Institute created the Collaborative Hub for Early Antibiotic Discovery (CHEAD), which serves an interdisciplinary

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center that partners with academic investigators engaged in antibiotic development and/or resistance research to accelerate their early-stage, small molecule therapeutics toward Investigational New Drug (IND) application. For further information about CHEAD, go to <https://www.broadinstitute.org/infectious-disease-and-microbiome/carb-x-collaborative-hub-early-antibiotic-discovery>.

About MassBio

MassBio, a not-for-profit organization that represents and provides services and support for the Massachusetts biotechnology industry, is the nation's oldest biotechnology trade association. Founded in 1985, MassBio is committed to advancing the development of critical new science, technology and medicines that benefit people worldwide. Representing over 600 biotechnology companies, academic institutions, research hospitals, and service organizations involved in life sciences and health care, MassBio works to advance policy and promote education, while providing member programs and events, industry information, and services. www.massbio.org