CARB-X
Combating Antibiotic-Resistant Bacteria

BOSTON UNIVERSITY

The crucial role of the GLG on AMR to support antibacterial innovation

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Governments should close the funding gap for early-stage product development

Five Joint Recommendations to the GLG on R&D and Access

1. WHO should formalize a numerical target of “highly-impactful” antibacterial treatments (including innovative products as well as paediatric formulations and combinations of new and existing and antibiotics) for the next decade so that governments and philanthropic organizations, with the support of the Global AMR R&D Hub, can compare needed and expected investments to guide their long-term funding
2. **Governments should close the funding gap for early-stage product development in order to replenish the clinical pipeline with much-needed innovative and “highly-impactful” projects**
3. Governments should close the funding gap for clinical development, registration, manufacturing, post-approval trials and sustainable access in high-burden LMICs
4. Government should implement pull incentives that bring private investors back into antibacterial R&D while ensuring equitable and sustainable access globally
5. Provided there are adequate funding and financing mechanisms in place, pharmaceutical companies should align their R&D programs to address unmet needs defined under the WHO Priority Pathogen List, and assure equitable and sustainable access to new and existing antibiotics

Funding early-stage R&D is urgent and indispensable

- **Without a healthy early-stage development pipeline, there will be no R&D projects to develop clinically and no treatments to make accessible.**
- **Early-stage R&D is where the most promising but most vulnerable projects are.**
  - The AMR Action Fund has struggled to find investment opportunities, with Henry Skinner saying the clinical pipeline is "much thinner" than he had originally realized (Jan 2023)
  - WHO agrees that "the ***clinical*** pipeline and recently approved antibiotics are insufficient to tackle the challenge of increasing emergence and spread of AMR." In contrast, "[t]he ***preclinical*** pipeline is innovative and includes a large number of non-traditional approaches" (May 2022)
  - Yet, "[t]he ***preclinical*** antibacterial pipeline continues to rely on micro (< 10 employees) and small (< 50 employees) companies and academic institutions," and the "analysis of groups with programmes in the ***preclinical*** antibacterial pipeline clearly indicates significant volatility and turnover in the R&D ecosystem" (May 2022)

6+ innovative high-impact treatments are needed per decade

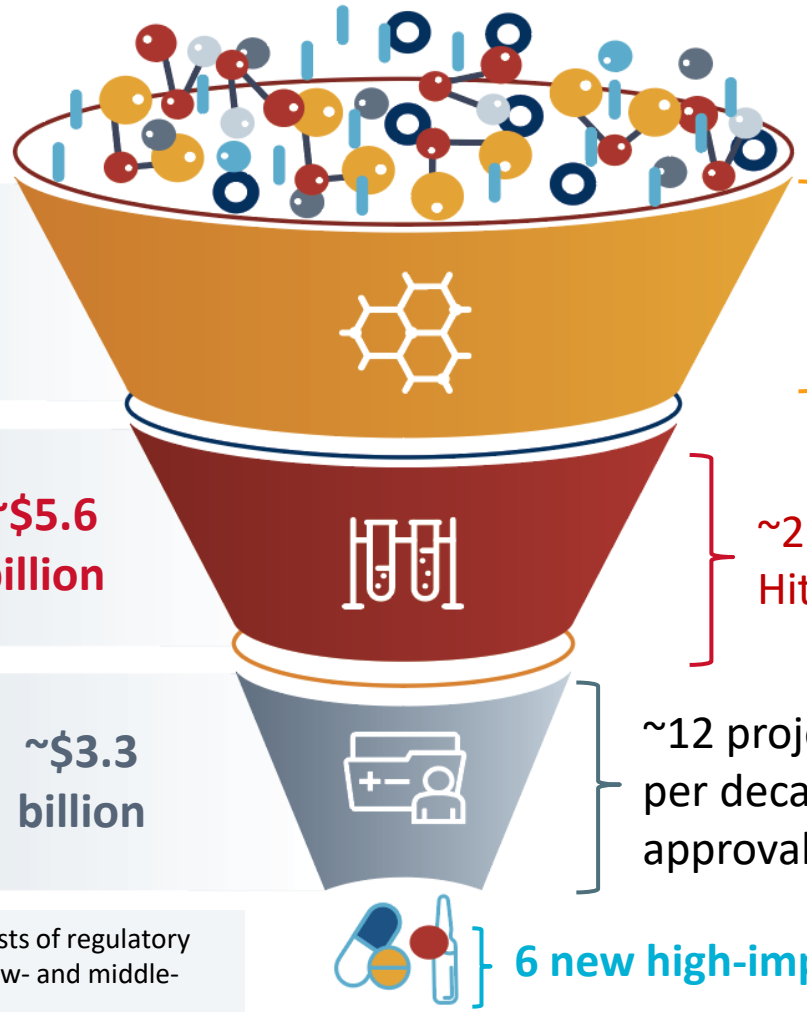
Report/strategy	Target (therapeutics)	Extrapolation for 10 years
IDSA 10x20	10 “new systemic” over 10 years	10
AMR Review	15 “new”, of which at least 4 “breakthrough”, over a decade	15 (of which 4 breakthrough)
GUARD	One additional “high-need” per year	10
DRIVE-AB	16-20 “truly innovative” over 30 years	5-7
U.S. NAP 2020-2025	Three “new” by 2025	6
BARDA Strategic Plan 2022-2026	Three “novel” by 2026	6

6+ innovative high-impact treatments require a pipeline

Basic Research ~$3 billion

Early-stage product development ~$5.6 billion

Advanced development and post-approval ~$3.3 billion



>6000 basic research projects per decade

~215 projects per decade, from Hit-to-Lead to First-in-Human studies

~12 projects beginning clinical efficacy studies per decade, including regulatory and post-approval costs in HICs only

6 new high-impact treatments per decade

3+ years

6 years

6.5 years

Approved

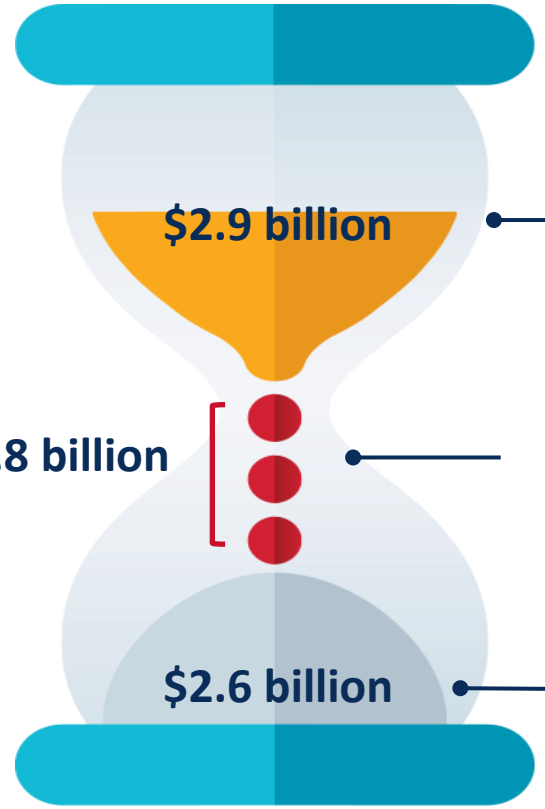
IMPORTANT: These estimates do not account for the costs of regulatory submissions, post approval and access in high-burden low- and middle-income countries. Also, TB is not included.

A comparison between what is expected and what is needed

How much public and private funding can be EXPECTED for AMR R&D therapeutics in the coming 10 years

How much funding is NEEDED to obtain 6 innovative high-impact treatments in the coming 10 years

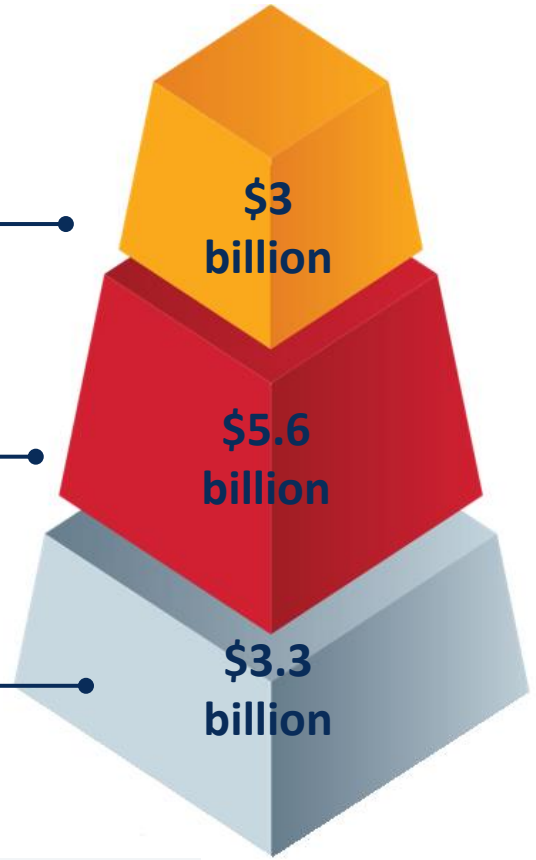
The largest funding gap is in early-stage product development



Basic research

Early-stage product development (from H2L to FIH)

Advanced development and post-approval in HICs



IMPORTANT: These estimates do not account for the costs of regulatory submissions, post approval and access in low- and middle-income countries. Also, TB is not included.

Preliminary results based on probabilities of success and phase costs from best available data. Validation is underway with upstream and downstream partners, including AMRAF and GARDP.

CARB-X: the global engine of antibacterial innovation

CARB-X

Combating Antibiotic-Resistant Bacteria

A **global non-profit partnership** developing antibiotics, vaccines and diagnostics to fight drug-resistant bacteria

ASPR
Administration for Strategic Preparedness and Response

BARDA
Biomedical Advanced Research and Development Authority

UKaid
from the British people

Federal Ministry of Education and Research

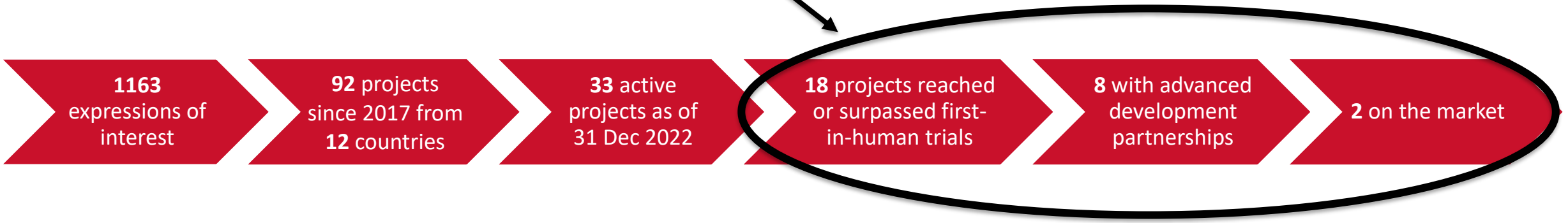
wellcome

Bill & Melinda Gates foundation

Product developers supported since 2017

CARB-X accelerates the early-stage development of innovative products against drug-resistant bacteria

- Provides non-dilutive funding **and** comprehensive business, technical and scientific support to R&D projects in early-stage product development up to First-in-Human studies (product developers assume 30-40% cost-share)
- Invested more than $400M since 2017
- Created the world's most promising discovery & early-development portfolio to address AMR, **with significant progress already**



CARB-X scope & focus

Three pillars that address serious bacterial threats:

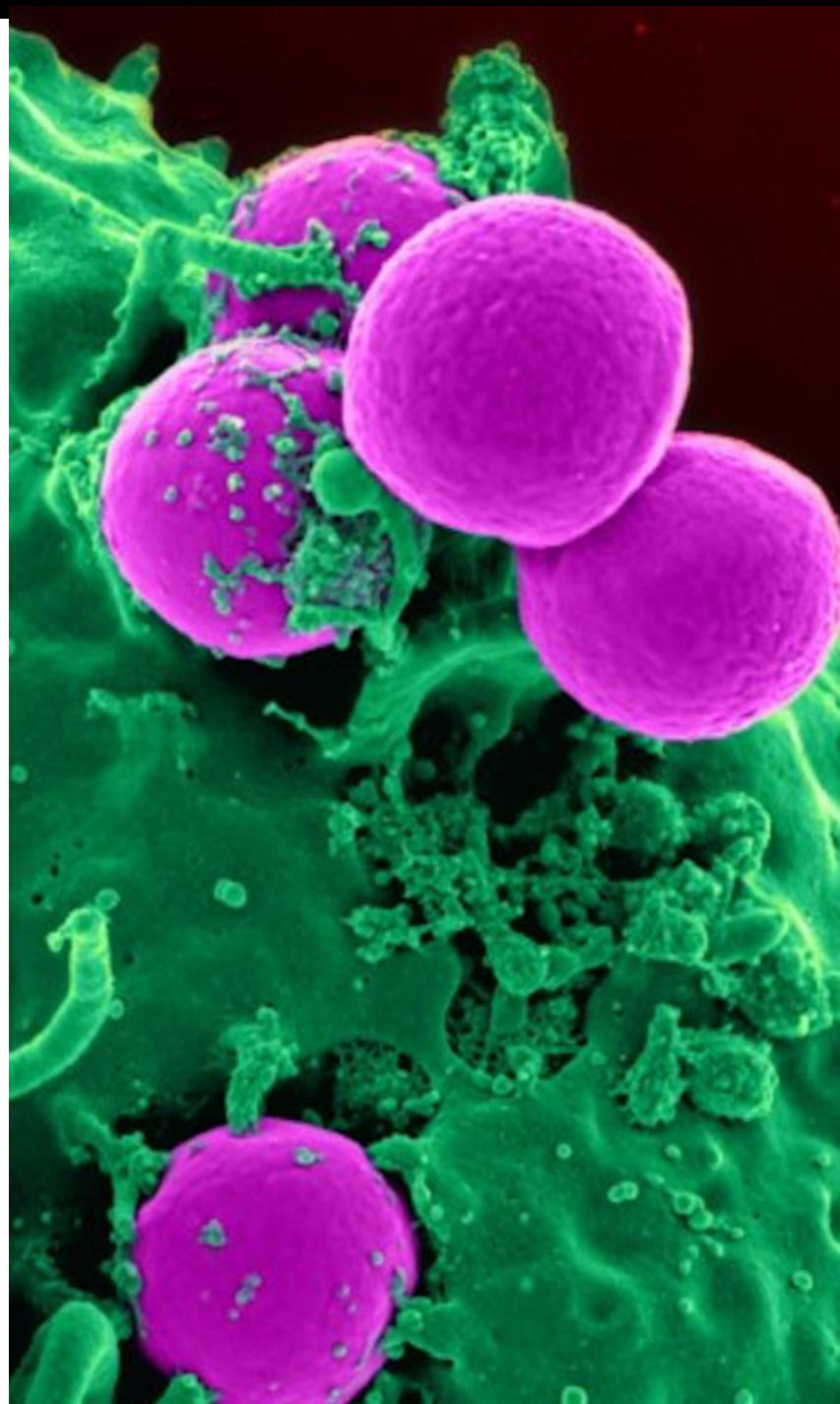
- **prevent**: e.g., vaccines, live biotherapeutics, bacteriophage and antibodies
- **diagnose**: e.g., bacterial ID and Antimicrobial Susceptibility Testing
- **treat**: e.g., antibiotics and non-traditional therapeutics such as virulence modifiers, proteins, antibodies, bacteriophage

Translational research and **early-clinical stages** of development:

- "hit-to-lead" through a demonstration of safety in healthy-human or patient populations in clinical trials, for Tx and Pv
- feasibility through validation & verification, for Dx

Focus is on the greatest bacterial threats to human health, primarily:

- syndromes where AMR is attributable to greatest mortality and morbidity, caused by
- pathogens emphasized on both the WHO/CDC bacterial threats lists



CARB-X works at scale, with a proactive portfolio strategy

*Profile of the **92** projects since inception*

- **62** therapeutics
  - 32 projects focused on new antibiotic classes; 1 enhancement to a known class
  - 23 non-traditional projects (immune-directing, proteins, peptides, anti-virulence, engineered bacteriophage)
  - 3 therapeutics in active FIH studies
- **15** preventatives
  - 8 vaccines
  - 3 live biotherapeutics
  - 3 CRISPR-phage
  - 1 monoclonal antibody
  - 1 preventative in active FIH studies
- **15** rapid diagnostics

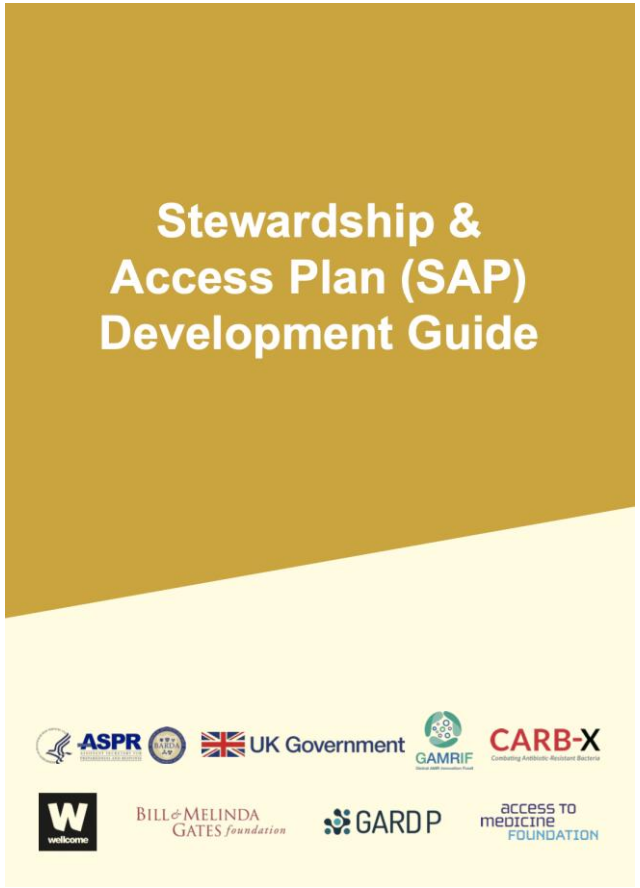
CARB-X targets the most deadly and burdensome threats

Global deaths attributable to (dark grey) and associated with (light grey) drug-resistant bacterial infections, by syndrome, 2019*

Source: Antimicrobial Resistance Collaborators, The Lancet, published online January 20, 2022
*: mostly targeted secondary indication

CARB-X funding comes with a contractual obligation for Stewardship & Access Plans (SAPs)

- Product developers prepare a non-confidential SAP when product enters pivotal clinical trials
  - Every CARB-X PD has agreed to the same terms
- SAP updated and published on CARB-X website when product is first approved by any of the FDA, EMA (or national authorities), MHRA, or PMDA
  - Updated following any significant market or product changes
- Obligations survive termination/expiration of CARB-X funding; follows the product to the expiration of Project IP Rights
- Wellcome Trust succeeds to CARB-X's rights, if need be



A central and indispensable link of the R&D chain

NIH

erc

Wellcome

UKRI Medical Research Council

CIHR IRSC

Swiss National Science Foundation

Coordination via jpiamr

CARB-X

Combating Antibiotic-Resistant Bacteria

ND4BB ENABLE (closing)

IMI AMR Accelerator (mainly TB)

repair impact fund novo holdings (paused)

BARDA

HERA

GARDP Global Antibiotic Research & Development Partnership

AMR ACTION FUND

CARB-X: Who we are

- **Non-profit**, driven by public health objectives & unmet medical need
- **Public-private partnership**, leveraging private sector expertise while funded and governed by governments and private foundations committed to global health
- **Endorsed by G7 and G20**
- **Crucial translational link of the R&D chain in between basic research and advanced development**, coordinating closely with upstream and downstream funders, including NIAID, JPIAMR, BARDA, AMR Action Fund and GARDP
- **Already working at scale (>1200 applications, >90 projects, $400m) and globally (applications from 39 countries in five continents)**, with a portfolio strategy that diversifies scientific approaches and increases the likelihood of success
- **Lean and efficient**, with 95% of funding going to product developers via non-dilutive grants and in-kind support

CARB-X: What we do

- **Target the most dangerous and burdensome drug-bug-syndrome combinations** based on WHO / CDC data & and the 2022 GRAM study
- **Translate early-stage product development**, where projects are most innovative and product developers are most vulnerable
- Accelerate products across three pillars: **treatment, prevention, and diagnosis**
- Support **breakthrough scientific advances**, including new drug classes, bacteriophages and microbiome-based approaches
- Every funding contract includes identical **stewardship & access obligations**
- **Comprehensive scientific, regulatory and business support** in addition to grants
- **Portfolio Acceleration Tools** which support multiple product developers, including the wider ecosystem not currently funded by CARB-X

Q&A

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