The AMR Accelerator: from individual organizations to efficient antibiotic development partnerships

Fernow J, Olliver M, Couet W, et al. The AMR Accelerator: from individual organizations to efficient antibiotic development partnerships. Nature Reviews Drug Discovery **24**, 1-2 (2025) First online September 23, 2024. doi:10.1038/d41573-024-00138-9

Josepine Fernow* (*Uppsala University*, COMBINE), Marie Olliver* (*Uppsala University*, COMBINE), William Couet (*University of Poitiers*, AB-Direct), Sophie Lagrange (*Evotec*, COMBINE, GNA NOW and ERA4TB), Meindert H. Lamers (*Leiden University Medical Center*, RespiriNTM and RespiriTB), Ole F. Olesen (*European Vaccine Initiative*, PrIMAVeRa), Kristina Orrling (*Lygature*, GNA NOW), Michel Pieren (*BioVersys*, TRIC-TB), Derek Sloan (*Radbouducm & University of St Andrews*, UNITE4TB), Juan José Vaquero (*Universidad Carlos III de Madrid*, ERA4TB), Tim Miles** (*GSK*, COMBINE and GNA NOW) and Anders Karlén** (*Uppsala University*, COMBINE)
*, ** These two authors contributed equally to this work.

The AMR Accelerator is an Innovative Medicines Initiative programme integrating nine projects with the shared goal of progressing the development of new antibiotics and building antimicrobial resistance research capability. Five years in, we reflect on the programme's value, results and key challenge: ensuring the sustainability of assets, infrastructures and expertise.

Introduction

Antimicrobial resistance (AMR) is a major global challenge, with an estimated 4.95 million deaths associated with bacterial AMR in 2019. It is a complex problem that involves a multitude of bacteria, and the process is exacerbated by the misuse and overuse of antibiotics. Although available treatments are becoming less effective, the rate of development of new antibiotics is declining2. One reason for this is the low return on investment, limiting the profit potential. As a result, many large pharmaceutical companies have scaled down or abandoned their antibiotic development programmes, resulting in a loss of expertise in the field.

In the past decade, several collaborative push incentives have been initiated to address challenges in antibiotic research and development (R&D). In 2012, the Innovative Medicines Initiative (IMI) launched New Drugs for Bad Bugs: eight projects addressing scientific, regulatory and business challenges hampering antibiotics development. The AMR Accelerator followed in 2019, representing a strategic European investment to address unmet medical needs for patients suffering from infections with drug-resistant *Mycobacterium tuberculosis*, nontuberculous mycobacteria (NTM), and Gram-negative bacteria. This public–private partnership programme comprises nine projects (AB-Direct, COMBINE, ERA4TB, GNA NOW, PriMAVeRa, RespiriNTM, RespiriTB, TRIC-TB, and UNITE4TB; Supplementary Table 1), linking key stakeholders from academia, industry, small- and medium-sized enterprises, patient organizations, regulators, and health technology

assessment; with the joint mission of accelerating antibiotic development and building capability for research on treatment and prevention of resistant infections. With a total budget of €479 million, it represents a substantial investment from the European Commission and industry. In this article, we discuss the value and key challenges of the partnership.

The value of the AMR Accelerator

Strengthening the antibiotic pipeline. Similar to other initiatives, such as CARB-X, GARDP, PAN-TB and TBDA, the AMR Accelerator is addressing the pipeline issue for antibiotics with a large portfolio of assets ranging from discovery to phase II trials. Antibiotic development has a high failure rate, but the public–private partnership model allows organizations to share the risks and costs. To date, the AMR Accelerator has progressed 44 antibacterial programmes, of which 15 have been discontinued. It is advancing well towards its overall goal — to deliver 10 preclinical or clinical candidates and 5 phase II or phase III-ready assets — with the identification of 16 preclinical and clinical candidates, 2 completed phase I studies and 5 ongoing phase I and II studies.

Developing research infrastructures. Unlike most other antibiotics R&D funding programmes, the AMR Accelerator has an overall mission of developing research infrastructures to build capability for future anti-infective R&D globally (Supplementary Table 2). For example, projects provide innovative in vitro and in vivo models, standardized in vivo models, bacterial strain repositories, physiologically based pharmacokinetic (PBPK) models and bioassays, as well as software, tools and infrastructures for FAIR data management. Moreover, the legacy includes a European preclinical and phase I platform to accelerate the development of new tuberculosis (TB) treatment regimens, and mathematical models to predict the impact of vaccines and monoclonal antibodies on the reduction of AMR, which can help prioritize products.

Building critical mass and efficient cross-project networks. Together, the AMR Accelerator projects achieve the necessary critical mass to tackle the AMR challenge. With 98 organizations engaged, the partnerships create opportunities to extend networks and access new knowledge and technologies. As a research community with a common goal, it has become a global forum for sharing know-how and best practices. Within the AMR Accelerator, the COMBINE project supports the other projects with overall coordination, data management, communication, and stakeholder engagement (Supplementary Table 3). Cross-project scientific interest groups centred around topics such as machine learning, animal models and science communication promote networking and knowledge sharing across projects, sparking new ideas for collaboration that can progress into sustainable scientific networks.

Challenges and lessons

Collaboration. Complex, multi-party collaborations inevitably involve an intricate interplay of different interests, perspectives and approaches. Some differences in culture, particularly between academia and industry, require proactive risk management strategies. For example, developing research aims that are independent of the continuation of a drug development programme helps minimize the risk for academic partners that have responsibilities to deliver publications. Sharing data between partners also requires proactive solutions to ensure that projects can manage intellectual property and data confidentiality issues. By identifying robust data security measures from the outset, projects can enable access to data that might be required to generate models.

The AMR Accelerator has benefited from clear agreements for collaboration and non-disclosure, forming the basis for collaborative work across the projects. Partners are involved in decision-making through structured and open communication, formalized via a coordination committee that meets regularly to discuss strategic and operational issues. In addition, annual in-person meetings bring opportunities for cross-project discussions, with webinars and online training providing additional platforms for knowledge transfer. Finally, the partnership has created a neutral ground where competing companies can work together on a portfolio of antibiotics, including novel combinations of anti-TB drugs.

Synergies. Connecting the AMR Accelerator projects in a coordinated programme has fostered transparent processes and prevented duplication of efforts. Moreover, it has created platforms where synergies can develop, such as the cross-project scientific interest groups. The involvement of some partners in more than one project facilitates the transfer of assets, knowledge and expertise from one project to another. This is exemplified by the ERA4TB and UNITE4TB projects, which col-laborate to maximize the translational value of preclinical and clinical data through reciprocal exchange, where the exploration of different antibiotic combinations allows ERA4TB assets that complete phase I trials to be integrated into UNITE4TB phase II trials.

The inclusion of AMR in a broad sense (TB, NTM and Gram-negative bacteria) under an umbrella programme provides opportunities to consider new paths for translational R&D. By involving multiple partners from industry and academia, the practices of individual organizations are challenged, which can lead to optimization. Finally, the effort fosters synergies between stakeholders by their inclusion as project partners and through research collaborations, such as the standardized in vivo pneumonia model developed by COMBINE, which is being evaluated by CARB-X, CAIRD, iiCON and Pharmacology Discovery Services3.

Sustainability. One major challenge for the AMR Accelerator is ensuring the sustainability of assets and research infrastructures when projects end. Continued funding is needed to ensure that a robust pipeline is maintained and that the assets reach the next stage of development and, ultimately, the patients who need them. So far, TRIC-TB has managed to

secure resources for a phase IIa study from the European & Developing Countries Clinical Trials Partnership. However, long-term strategies are missing for most of the projects. Regular funding calls are also needed to sustain the infrastructures, data and networks required to develop antibiotics. Open data resources such as the TB-APEX platform developed in ERA4TB are key multipliers that provide opportunities for reuse by the AMR R&D community. However, maintaining and providing access to data from the projects needs resources for long-term curation.

The AMR Accelerator draws its strength from its networks, and, together, the projects have provided training for a new generation of AMR experts. Recently, the AMR Industry Alliance reported that the size of the antibiotics R&D workforce is declining4. Without a long-term funding strategy for antibiotics R&D, we risk losing expertise, critical knowledge and, with these, the capacity for antibiotic development.

Conclusions

Antibiotic resistance is a major public health issue, undermining modern health-care systems that rely heavily on antibiotics to prevent and treat infections. Public–private partnerships can tackle this issue by uniting interdisciplinary expertise and ensuring cooperation between key stakeholders. With critical mass and high-quality science applied across indications and development stages, the AMR Accelerator programme is a forum for public and private stakeholders to join forces to progress a pipeline of antibiotics and build capability for AMR research.

There are few researchers and organizations left with the expertise, skills and infrastructure to tackle AMR and discover new antibiotics. Long-term funding for antibiotic development partnerships will help attract young scientists to the field and keep companies in anti-infective drug development. To secure a sustainable future for efforts of this scale, we call on government leaders, the private sector and other stakeholders to invest in the development of antibiotics and AMR research.

Acknowledgements

The authors (members of the nine AMR Accelerator projects) thank all colleagues and partners involved in the AMR Accelerator and gratefully acknowledge the COMBINE Coordination and Support Office, the AMR Accelerator Coordination Committee, Science Communication Interest Group, and participants in the AMR Accelerator cross-project meetings in 2023 and 2024 for providing valuable insights. The authors wish to thank the AMR Accelerator Communications Advisory Board for critically reading the manuscript.

The projects have received support from the Innovative Medicines Initiative 2 Joint Undertaking under Grant Agreements No 853967 I 853989 I 853979 I 853932 I 853800 I 853903 I 853976 I 101007873 I 101034420. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and EFPIA. ERA4TB

receives additional support from Global Alliance for TB Drug Development, Bill & Melinda Gates Foundation and University of Dundee. UNITE4TB receives additional support from Deutsches Zentrum für Infektionsforschung e. V. (DZIF), and Ludwig-Maximilians-Universität München (LMU). EFPIA/AP contribute to 50% of funding, whereas the contribution of DZIF and the LMU University Hospital Munich has been granted by the German Federal Ministry of Education and Research. This article reflects the authors' views. Neither IMI nor the European Union, EFPIA, or any Associated Partners are responsible for any use that may be made of the information contained herein.

References

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet, 399, 629-55 (2022). DOI: https://doi.org/10.1016/S0140-6736(21)02724-0
2. OECD, Embracing a One Health Framework to Fight Antimicrobial Resistance, OECD Health Policy Studies, OECD Publishing, Paris (2023). DOI: https://doi.org/10.1787/ce44c755-en
3. Collaboration to improve the quality of in vivo antibiotics testing. EurekAlert! news release (2024). https://www.eurekalert.org/news-releases/1007971
4. AMR Industry Alliance. Leaving the Lab: Tracking the Decline in AMR R&D Professionals (2024). https://www.amrindustryalliance.org/mediaroom/leaving-the-lab-tracking-the-decline-in-amr-rd-professionals/.

Supplementary information

Supplementary Table 1 | Overview of the AMR Accelerator projects.
Supplementary Table 2 | AMR Accelerator research infrastructure and tools/resources for drug discovery and development.
Supplementary Table 3 | COMBINE coordination and support.