

INCATE: a partnership to boost the antibiotic pipeline

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INCATE, the INCubator for Antibacterial Therapies in Europe, aims to boost the antibiotic pipeline by accelerating the translation of academic innovation into industrial R&D projects to tackle antimicrobial resistance. Founded in 2021 as a partnership of research institutions and pharma companies, INCATE provides advice, community and non-dilutive funding to start-up companies.

10 Effective antibiotics remain the cornerstone of modern medicine, and novel therapies are urgently needed to fight the threat of antimicrobial resistance (AMR). According to the recently published “Global
15 Research on AntiMicrobial Resistance Project (GRAM)” paper, there were an estimated 4.95 million deaths associated with bacterial AMR in 2019, including 1.27 million deaths directly attributable to bacterial AMR¹.

20 However, the global antibiotic pipeline is meagre. Incentives for large pharmaceutical companies to invest in developing novel antibiotics have been limited for decades by the low potential for return on investment because of cheap pricing regimes, the rapid
25 development of resistance to newly launched drugs, and more recently also by stewardship principles aimed at reserving novel antibiotics as last-resort treatments to minimize the emergence and spread of resistance. The traditional business model for antibiotic research and development (R&D) is broken, and the scientific, technical and economic challenges in
30 discovering and developing novel antibiotics exacerbate the situation further. Consequently, many of the pharmaceutical companies with sufficient size and expertise to bring novel antibiotics to market have
35 abandoned R&D in the field².

Recognizing this crisis, multiple initiatives have been started in the past few years in an attempt to encourage industry to re-engage in antimicrobial
40 R&D. ‘Push’ initiatives include CARB-X, a global non-profit partnership focused on promoting the progression of innovative antibacterial candidates into clinical trials. It has received over US\$500 million from funders including the US government and the Well-
45 come Trust, who have recently committed up to an additional US\$370 million over the next ten years. So far, CARB-X has invested US\$361 million of non-dilutive funding to support the advancement of 92 pro-

jects. Another promising push initiative for the clinical development phase is the AMR Action Fund, which aims to bring two to four new antibiotics to patients by 2030. To achieve this, the fund is expecting to invest more than US\$1 billion in biotech companies, and it announced the first investments earlier
50 this year.

On the ‘pull’ side, the UK will soon become the first country to introduce a subscription model involving the payment of a fixed fee up to £10 million per year to pharmaceutical companies for supplying novel antibiotics to the National Health Service³. Several other countries are evaluating this subscription model and other reward-based pull incentives such as patent extensions. Beyond these measures, a report by the World Bank indicates that putting resources into
65 AMR containment is now one of the highest-yield investments countries can make⁴.

Despite the growth in funding and other advances in re-establishing a viable business model for antibiotic R&D, the early-stage pipeline of novel drug candidates remains insufficient and without signs of improvement in the short term. With market entry potentially becoming more commercially attractive in a few years’ time, a sustained flow of innovative candidates must now be ensured. Although funding is one
75 key need to support this flow, there are others. The current landscape for antimicrobial R&D lacks fertile ecosystems for entrepreneurs in the field. Furthermore, what is often missing in academia and emerging start-ups is not scientific innovation, but expert support and advice during the translational phase.
80 The need for this input includes scientific and early development aspects, such as understanding about which preclinical studies are necessary from a regulatory perspective and in which activities to invest to most efficiently reach the clinical phase. Understanding of commercial aspects such as engagement with

investors, technology transfer and intellectual property protection is also needed.

The mission of **INCATE** is thus to address these needs and strengthen the early-stage antibiotic pipeline, which ultimately will help to increase the quality and quantity of promising candidates to fight AMR.

INCATE's structure, scope and strategy

INCATE was founded in 2021 as a partnership of research institutions, pharmaceutical companies and other non-governmental organizations. It provides three key elements to bridge the gap between academic research on AMR and the next stage of funding and support: advice, community and non-dilutive funding (Supplementary Figure 1). INCATE is driven by leading academic institutions in Germany and Switzerland, represented by the German Center for Infection Research (DZIF), InfectControl (associated with the Leibniz Institute for Natural Product Research and Infection Biology), and the Swiss National Centre of Competence in Research (NCCR) "AntiResist", in collaboration with, and legally hosted by the Innovation Office at the University of Basel. Industry partners with an interest in antimicrobial R&D, including Roche, Boehringer Ingelheim Venture Fund, MSD Germany and Shionogi, provide non-dilutive funding, and importantly, insights on market demand and R&D advice. Other supporting partners help to add crucial competencies and link INCATE to a broader community (Supplementary Table 1).

The scope includes innovative treatments and interventions that could help reduce the prevalence and impact of AMR, such as new antibiotic classes, phage therapies, antisense platforms and antibiotic-resistance breakers. In future, INCATE will also support tools such as artificial intelligence platforms and molecular diagnostics for better, faster and more selective pathogen detection and antibiotic sensitivity profiling. With regard to development stage, INCATE considers projects from technology readiness levels (TRLs) 1 to 4. For therapeutic development, TRL 1 covers the scientific concept stage or platform technologies. At TRL 2, initial data (usually in vitro) are generated. TRL 3 provides initial mode-of-action and in vivo proof-of-concept data (lead generation/optimization), and at TRL 4, proof-of-concept in multiple animal models is expected. The focus of the selection is on start-up companies or academic groups with the ambition to become entrepreneurs, with innovation being key regardless of the modality.

On a quarterly basis, applications are evaluated and selected by the INCATE selection committee, which is composed of the pharma industry partners and complemented by individuals with experience from the **BEAM Alliance**, the Global Antibiotic Research and Development Partnership (GARDP) and the Paul-Ehrlich-Institute (the German Federal Institute for Vaccines and Biomedicines). For successful applicants, non-dilutive funding is available in two stages (stage I up to €10,000; stage II up to €250,000) to answer critical questions to advance

projects into the next development stage, so as to become more attractive for follow-up funding or venture capital investors. Beyond funding, INCATE provides advice to applicants on building a high-quality translational plan and target product profile to align with medical and market needs.

These activities are based on a strong and active start-up community hosted by the Innovation Office at the University of Basel, which is located in a leading innovation and start-up hub in Europe. Initiatives such as the virtual AMR Entrepreneurs Club aim to boost the entrepreneurial spirit, connect scientists to supporters of entrepreneurship and revitalize the AMR community in Europe.

INCATE has been fully operational since August 2021 and has reviewed more than 100 applications as of July 2022. So far, 12 ventures across Europe have received awards and entered **the INCATE portfolio**. The selected ventures are working on innovative phage therapy approaches, virulence inhibition, antisense technologies and novel direct-acting antibacterial small molecules. INCATE aims to provide at least 50 ventures with stage I funding and at least five with stage II funding between 2022–2024. INCATE will continue to support their growth until seed or series A funding.

Outlook

After successfully establishing itself and proving its functionality in the first funding rounds, INCATE plans to expand the operational team to other European countries. Experience over the last three funding rounds has shown that most applications were received from countries where active scouting was performed. In order to expand scouting activities, to guarantee the continuing ability to provide sufficient individual R&D advice, and to ensure a solid and sustainable flow of ventures, more partners are welcome to join INCATE. Due to the semi-virtual set-up of the incubator, INCATE expects that collaborations with other countries will be possible, enabling the establishment of international cooperation focused on early-stage support to address the global threat of AMR. The biggest goals of INCATE are still to facilitate the urgently needed entry of innovations into the development pipeline, and to build on a network of researchers and companies to inspire and connect the next generation of innovators fighting the "stealthy and silent pandemic" of drug-resistant microbial infections⁵.

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Competing interests

The authors declare no competing interests.

Supplementary information

Supplementary information is available for this paper at
220 <https://doi.org/10.1038/s415XX-XXX-XXXX-X>

RELATED LINKS

WHO: 2021 Antibacterial agents in clinical and preclinical development: an overview and analysis: <https://www.who.int/publications/i/item/9789240047655>

CARB-X: <http://www.carb-x.org>

225 AMR Action Fund: <http://www.amractionfund.com>

INCATE: <https://www.incate.net/>

BEAM Alliance: <https://beam-alliance.eu/>

230 Addresses

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