

Innovations for Gram-Negative Antibiotic Discovery

Grand Challenges

Request for Proposals

Applications due no later than Mar 25, 2025, 11:30 a.m. U.S. Pacific Time

Before applying, applicants should familiarize themselves with the supporting documents for this Grand Challenge, including the terms and conditions of Wellcome, the Gates Foundation, and the Novo Nordisk Foundation, [Rules and Guidelines](#), [Application Instructions](#), and [Frequently Asked Questions](#).

Overview

In 2021, antimicrobial resistance (AMR) was associated with 4.7 million deaths, predominantly impacting low- and middle-income countries (LMICs), but the 2024 GRAM report projections indicate that development of novel antibiotics targeting Gram-negative bacteria would lead to a reduction in AMR burden. In response to this global health priority, the Novo Nordisk Foundation (NNF), Wellcome, and the Gates Foundation (GF) are jointly launching a new initiative, Gram-Negative Antibiotic Discovery Innovator (Gr-ADI), to drive innovation in early drug discovery for Gram-negative pathogens. Gr-ADI will function as a consortium, working collectively across multiple funders, research institutions, and industry partners. The consortium will be formed through this Grand Challenges request for proposals (RFP), with a focus on the discovery of direct-acting small molecule antibiotics with broad-spectrum activity against *Enterobacteriaceae*, using *Klebsiella* spp. as the pathogen to initiate a discovery program.

Background

Bacterial AMR is now the 3rd-leading cause of death globally, behind ischemic heart disease and stroke. The WHO has classified life-threatening community- and hospital-acquired infections due to Gram-negative bacteria, highlighting carbapenem-resistant *Enterobacteriaceae* (CRE) (including *K. pneumoniae* and *E. coli*) and *Acinetobacter baumannii* (CRAB) as the most critical AMR global health threats.

Recent progress in new antibiotic development has been dominated by incremental improvements in well-established drug classes, such as β -lactam antibiotics, already impacted by resistance. There are few drugs in development that target a new mode of action, which is essential for combatting the ongoing emergence of bacteria resistant to existing classes of antibiotics. While there are multiple factors that have impeded the progression of a diverse antibiotic pipeline, a key factor has been a lack of coordinated investment and collaborative effort.

This Grand Challenges RFP will be a first step to build a collaborative portfolio of Gr-ADI projects across multiple sectors, all working towards a common goal and unifying efforts

of early antibiotic discovery by fostering cooperation and synergy among researchers. Successful applicants will demonstrate a spirit of collaboration and embrace the consortium approach, with all grantees functioning within the consortium under a single data sharing agreement [See [Cooperation and Data-Sharing Principles](#)].

Acknowledging that Gr-ADI operates within a wider antibiotic R&D ecosystem, encompassing several initiatives further downstream in the development pipeline, it is anticipated that the most promising projects graduating from Gr-ADI could be supported by one of these initiatives.

The Challenge

The ultimate objective of Gr-ADI will be to enable discovery of safe and simple first-line broad-spectrum drugs for syndromic management, through:

- Development of novel and emerging biological, chemical, and AI tools that could be applied broadly for antibiotic discovery to identify new antibiotic targets.
- Application of these innovative approaches to generate chemical starting points for project-based drug discovery.
- Fostering a collective mindset to address gaps in knowledge, solve problems, and manage a portfolio of targets and hits.

This Grand Challenges RFP will identify and select the first projects within the consortium. **The focus of this RFP will be on the discovery of antibiotics with broad spectrum activity against *Enterobacteriaceae*, using *Klebsiella* spp. as the pathogen to initiate a discovery program.** This provides a common focus point on *Klebsiella* spp. for all projects in the consortium and facilitates sharing of knowledge and data for mutual benefit. As such, proposals must have a primary focus on *Klebsiella* spp. but can also include investigation of other *Enterobacteriaceae*.

Proposals must address at least one of the following themes:

1. Development of genome-scale tools or other innovative technologies to identify new chemical starting points linked to targets as well as assessment of potential drug target vulnerability, singly or in combination.
2. Development of innovative technologies to select targets and chemical leads with a very high bar to resistance.
3. Gaining a better understanding of the chemistry underlying penetration of compounds to different compartments of the bacterial cell to build a platform to rapidly test whether compounds reach and accumulate at their target.
4. Development of novel and coordinated approaches to identifying new chemical leads for clinically or *in vivo* validated drug targets, for which there is currently no agent in Phase 3.

Funding Level and Process

Projects with a duration of up to three years and a maximum requested budget of \$5,000,000 USD are eligible for funding. Exploratory projects with shorter durations or lower budgets that focus on high-risk, innovative areas are strongly encouraged and will be given priority.

Budgets should be commensurate with the proposed scope of work. Indirect costs will be considered by some funders and should be included within the total budget of up to \$5,000,000 USD. Indirect/overhead cost policies vary by funder, please refer to the application instructions document for specific details. Projects with secured co-funding are eligible to apply, provided they fully comply with the Gr-ADI collaborative ways of working and funding conditions, as if entirely funded by Gr-ADI.

Wellcome, NNF, and GF will collaborate to achieve the overall objectives of the Gr-ADI. Successful projects will receive awards either through Wellcome, NNF, or GF and will be bound by the specific terms and conditions of the individual funder (see terms for each funder linked below).

The application process will be conducted in two stages:

1. A letter of inquiry, with a scientific proposal not to exceed five pages, should be submitted through this Grand Challenges RFP.
2. Applicants selected to provide a full proposal will be informed by the end of June 2025 and will receive further details on the submission, review, and decision timeline at that time.

Cooperation and Data Sharing

The funded projects will collectively form a consortium to catalyze and accelerate early antibiotic drug discovery. The funded organizations (including collaborators receiving Gr-ADI funding) will be required to enter into a consortium-wide data sharing agreement (before they receive their funding) to facilitate their interactions and to maximize cross-learnings and integration. Applicants should review and consider the [Gr-ADI Cooperation and Data Sharing Principles](#), which will be reflected in the formal data sharing agreement. The full data sharing agreement will be shared with applicants invited to submit a full application. These describe how the collaboration will share data (with the exception of detailed chemical structures of proprietary compounds) during the course of funded projects to support Gr-ADI's research efforts and how outputs will be shared more broadly upon completion of each project to benefit the wider research community.

Eligibility Criteria

- This initiative is open to nonprofit organizations, for-profit companies, international organizations, government agencies, and academic institutions.
- Only individuals who are applying through a legally recognized corporate entity are eligible.

- We particularly encourage applications from institutions based in LMICs and projects led by women and other groups that are historically underrepresented in the drug discovery field. All applications received will then be reviewed on their merits.
- Lead applicants must be able to demonstrate the experience needed to drive and lead a project and to deliver on the objectives.
- Applications can be from multi- and inter-disciplinary teams, and we encourage lead applicants to put together diverse teams, promoting a diverse, inclusive, and supportive research environment.
- Researchers may participate as co-applicants or collaborators on multiple proposals but may submit only one application as a lead applicant to this RFP. If researchers are co-applicants or collaborators on multiple proposals, they must be able to demonstrate that they can dedicate enough time and resources to all projects if all the projects they are involved in are funded.
- Applicants must be able to sign up to the terms and conditions of at least one of the funders to be eligible to apply.

We are looking for proposals that:

- Address one or more of the thematic areas described above.
- Focus on (direct acting) small molecule drug discovery for *Klebsiella* spp.
- Focus on the earliest phases of drug discovery up to lead optimization through a concentrated and coordinated effort addressing the specific, well-defined problems articulated above
- Provide preliminary data in support of the proposed approach; if no preliminary data exists then proposals should be limited in scope with specific Go/No Go milestones
- Request the appropriate funds and time to achieve the objectives of the proposed work. Exploratory projects of lower cost but higher risk are strongly encouraged and will be prioritized.
- Promote a diverse, inclusive, and supportive research environment.

We will not consider funding proposals that:

- Do not directly address the core objectives as outlined above. Proposals not focused on direct acting small molecules (e.g. vaccines, phages, peptides, microbiome) would not be in scope.
- Do not include *Klebsiella* spp.
- Use surrogate organisms to develop tools or identify leads that will then need to be validated in pathogens of interest.
- Are focused solely on basic exploratory scientific research without a direct connection to or impact on advancing antibiotic discovery. There must be a component of development of novel tools and technologies or methodologies.
- Focus on development of technologies that do not have a direct link to development of small molecules.
- Describe a distributed, broad approach to fixing the portfolio and/or pipeline.

- Are submitted by teams not committed to collaborating with other projects funded through this RFP.
- Are not willing to agree to sign up to the data sharing agreement between the cohort of successful projects.
- Aim to conduct clinical trials or randomized control trials.
- Cannot be accomplished within a three-year project duration or have a requested budget exceeding \$5,000,000 USD.
- Support organizations or individuals who are affiliated with the tobacco industry, or who receive (or are applying for) funding from the tobacco industry, which includes manufacturers and distributors of e-cigarettes or vaping products.

This Grand Challenge is a collaboration between the GF, NNF and Wellcome, but each funder will make independent funding decisions. Applicants successful at the preliminary stage will be invited to submit a full application via GF, NNF, or Wellcome as applicable. Note: success at the preliminary stage does not guarantee that the full application will be successful in receiving funding.

Applicants should familiarize themselves with the supporting documents for this Grand Challenge, including the rules and guidelines and application instructions, as well as the relevant terms and conditions for each funder at the following links:

Wellcome funding to universities and not for profit research institutions will be made via grants (i.e. under our [grant conditions](#) and subject to our [grant funding policies](#)).

Wellcome funding to companies will be made via grants in instances where all of the research outputs will be made freely available to the wider research community.

Wellcome funding to companies will be made via program related investments (convertible loans or revenue sharing agreements) if subsequent commercialisation of identified lead compounds is a possibility.

Gates Foundation: [sample terms & conditions](#) and [RFP terms and conditions](#)

NNF: [example terms and conditions](#).

Please note that the final terms and conditions for awards made under this RFP will have additional conditions specific to Gr-ADI and to align with the wider trilateral partnership (NNF, Wellcome, and Gates Foundation) under which the Gr-ADI initiative is being run. Further information will be provided to applicants invited to submit full applications.