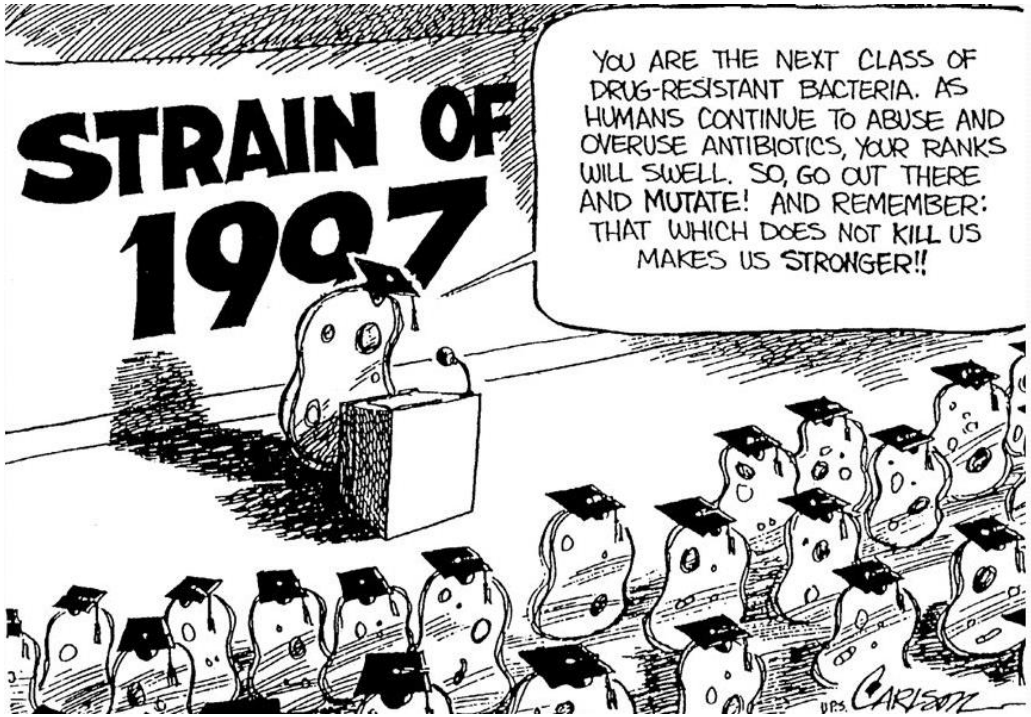
GNA NOW Open Call

A unique opportunity for the antibiotic community

The GNA NOW Consortium is looking for a novel antibiotic programme to progress to Investigational New Drug

This is a **unique opportunity** for interested candidates to join IMI's GNA NOW project & **gain access** to some of Europe's best laboratories and antibiotic drug research experts



The GNA NOW project at a glance

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Kristina Orrling, Lygature
GNA NOW Coordinator

GNA NOW project at glance

Gram(-) **Antibiotics** Now

11 partners
1 EFPIA = Evotec

>31 M€
IMI 12.3 M€
Evotec 19 M€

Part of IMI's **AMR Accelerator**

3 **+1** Programmes
×
8 Platforms

6 years
1 July 2019
-
30 June 2024

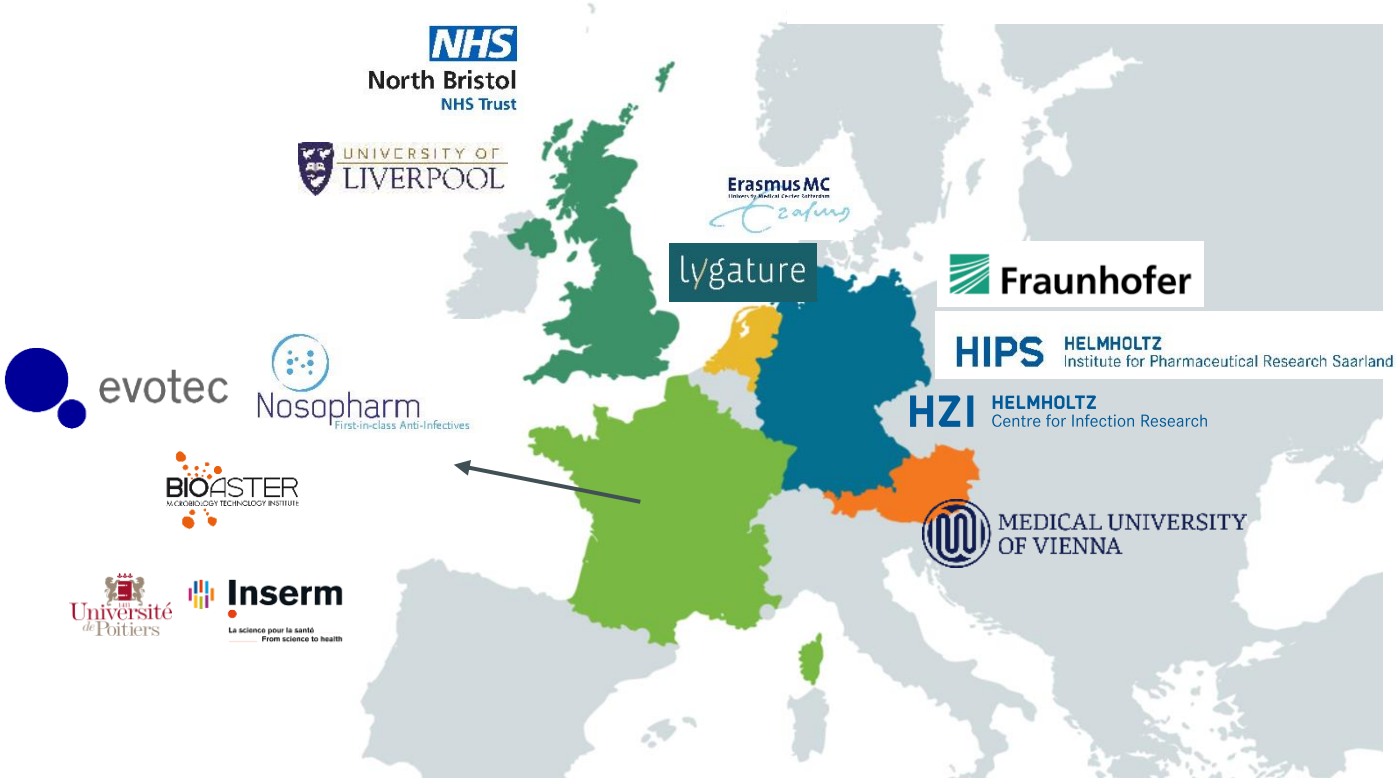
Objectives:

One Phase II ready drug

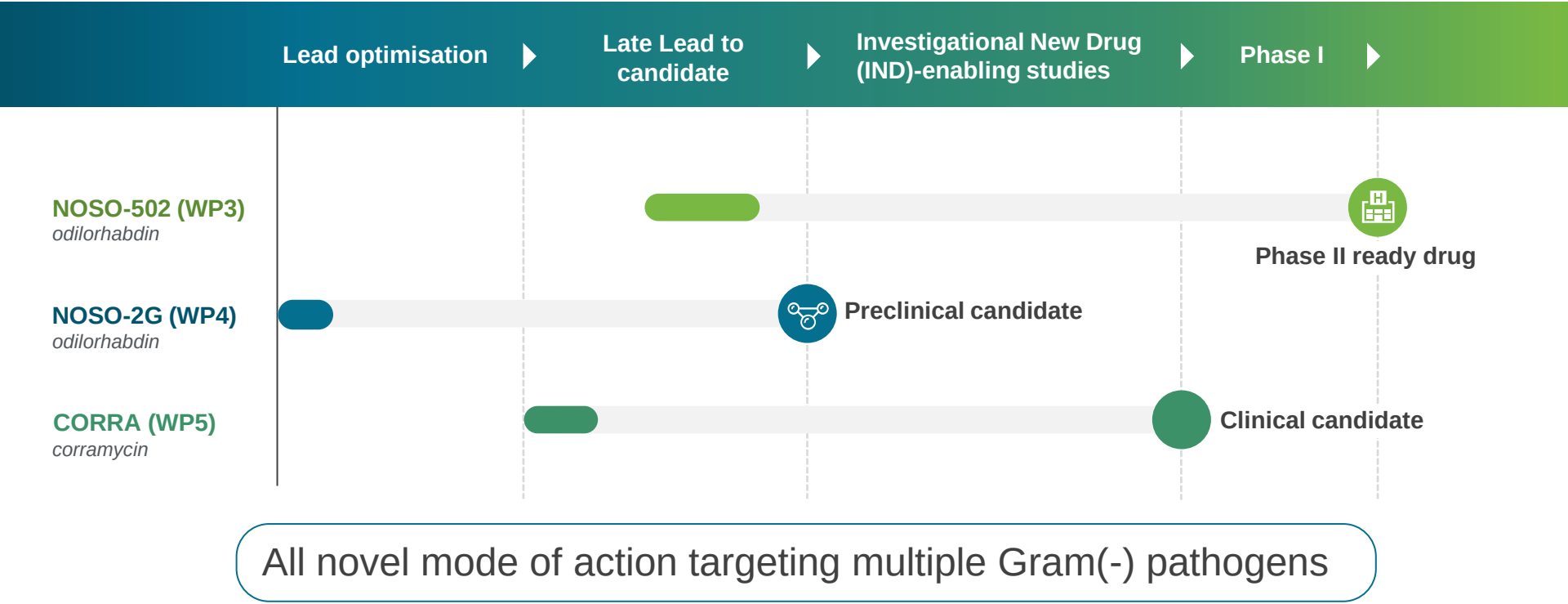
One Phase I ready candidate drug

One preclinical candidate drug

Consortium: 11 partners



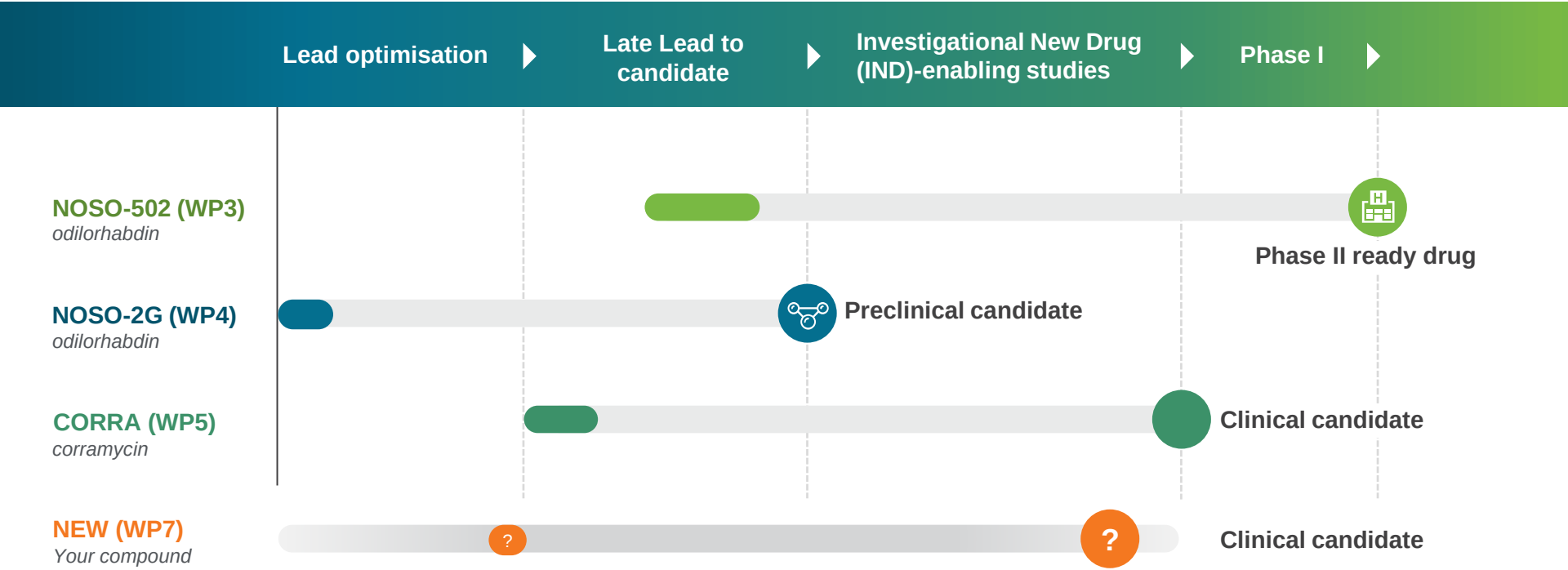
Programmes in the pipeline



All novel mode of action targeting multiple Gram(-) pathogens

Programmes in the pipeline

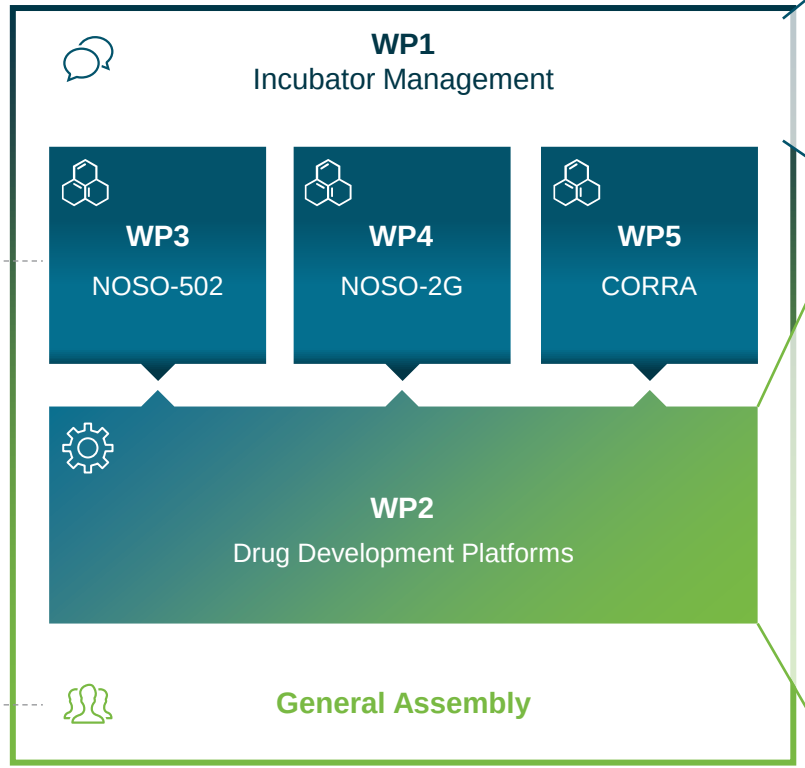
Room for one more to de-risk project goals



Structure: 3 programmes x 8 enabling platforms

External experts

Scientific Board



- Partnership Management (Lygature & Evotec)
- Communication (Lygature)
- Data Infrastructure (Fraunhofer)
- Public-Patient Involvement (Bristol NHS Trust)

WP2: Drug Development Platforms

1. Mode of Action profiling
2. Medicinal chemistry and design
3. Microbiological efficacy and resistance *in vitro*
4. Microbiological efficacy and resistance *in vivo*
5. PK/PD profiling
6. PK, Safety and ADME
7. CMC and fermentation
8. Clinical studies & modelling

How to join GNA NOW?

- **5 May** — Launch of call for additional programme
- **18 June** — Deadline for submission of Expression of Interest (EoI)
- **7 July** — Top 3 EoIs invited submit a full Programme Dossier (CDA needed)
- **25 Aug** — Deadline for submission of full Programme Dossier

What are we looking for?

What's in it for you?

Eric Bacqué, Evotec
GNA NOW Lead

What GNA NOW is looking for ? (1)

- A **lead-to-candidate program or a development candidate** under or ready for preclinical development

- TPP-consistent spectrum, acceptable resistance risk, satisfactory ADME/PK properties, demonstrated *in vivo* efficacy, established IP position and suitable safety profile

- **Addressing severe hospital infections** (HAP/VAP, cUTI, cIAI and BSI) caused by Gram(-)
  - Enterobacteriaceae, *Pseudomonas* or *Acinetobacter*
  - broad spectrum TPPs or single-pathogen, non-fermenter TPPs possible

- **Novel mode of action**
  - no cross-resistance with marketed classes of antibacterials
  - possibly via modulation of a new/underexplored target or via binding to a new site of a known target

- **Directly-acting antibacterial effect or potentiators**

What GNA NOW is looking for ? (2)

- **Small molecules**
  - including also natural products and derivatives, small peptides but no biologics

- **Potential for intravenous administration** (mandatory)
  - potential for oral administration required in case of an enterobacteriaceae-only TPP

- **Technically feasible**
  - matching with available GNA NOW resources, capabilities and expertise
  - potential to benefit from industrial discovery and development expertise and capabilities

- Priority might be given to an organization eligible to IMI provisions for beneficiaries or EFPIA

What’s in it for you?

- Resources equivalent to **several million €** (to be defined according to project needs).
- Access to some of the **best laboratories and experts** in antibiotic drug research in Europe today.
- Access to **all the components needed** to progress your compound to the Phase I-ready stage.
- **Partnering contract** with Evotec, a pharmaceutical company with the experience, expertise and resources to bring a drug to the clinical development stage.
- **Continued control** of the development of your project, as a member of the Compound Steering Committee.
- Option to contribute to the GNA NOW project either as a so-called Contributing Third Party, or as a full member* of the consortium

* Limited to organisations eligible to the IMI provisions for beneficiaries, *ie* academia & SMEs in EU or associated countries, and EFPIA members

Evaluation

Proposals will be scored on a scale of 1-5 in the following four categories:

- **Scope, Innovation and Novelty**
  - Defines the *minimal criteria* for the call
  - Indication, Target Product Profile, development stage, competitor analysis, *etc*
- **Excellence**
  - Technical data of the compound/series
  - Defined with respect to the Lead and Preclinical Candidate criteria
- **Feasibility**
  - How well the programme matches the GNA NOW resources, expertise, and timelines?
  - What can the Compound Owner contribute with?
- **Implementation**
  - How mature and realistic are the project plans and timelines?

Lead criteria, *main thresholds*

- MIC_{90} ≤4 µg/ml for the targeted enterobacteriaceae and ≤ 8 µg/ml for the targeted non-fermenters
- Specific/on-target antibacterial activities demonstrated
- Manageable resistance risk for key TPP pathogens
- Phys-Chem, ADME and eTox properties documented for the lead compound and analogues
  - no more than 3-4 alerts overall.
- PK properties in mice compatible with TPP indications/routes of administration
- *In vivo* efficacy demonstrated in TPP-relevant infection models with concomitant tolerability
- Tractable and scalable chemistry allowing further optimization of the series
- Acceptable IP position
- L2C optimization strategy and flow chart defined, taking into account the liabilities of the series

The proposed lead criteria are indicative meaning that the Lead compound may not satisfy exactly all the listed quantitative criteria, or a few properties may not be properly documented. The lead dossier will be evaluated as a whole and with respect to the distance with the ideal Lead profile.

Development candidate criteria, *main thresholds*

- MIC_{90} ≤ 2 µg/ml for the targeted enterobacteriaceae and ≤ 4 µg/ml for the targeted non-fermenters
- Manageable resistance risk for all key TPP pathogens and mechanism(s) of resistance documented
- No major in vitro ADMET warnings
- In vivo efficacy demonstrated for multiple strains and in multiple infection models, representative of the targeted clinical indications.
- PK data available for several species by the intended route(s) of administration
- Acceptable in vivo tox profile and safety margins in rats
- Efficacy driver determined based on first PK/PD studies
- Reasonable projected active doses in human
- Demonstrated capacity to deliver large batches of the candidate
- IP position compatible with future FTO

The proposed candidate criteria are indicative meaning that the candidate may not satisfy exactly all the listed quantitative criteria, or a few properties may not be properly documented. The dossier will be evaluated as a whole and with respect to the distance with the ideal candidate profile.

Selection Criteria – Feasibility & Implementation

Feasibility

- **Resources**
  - Your contribution, including funding
  - Expected support from GNA NOW
  - Additional resources and expertise that are assumed not to be supported by the GNA NOW consortium, including subcontracting

  Contributions from GNA NOW partners are expected to be:
  - MoA and target elucidation (Helmholtz & BioAster)
  - In vitro & in vivo microbiology (NBT, INSERM)
  - In vivo microbiology & PKPD, allometric scaling, human dose prediction (Erasmus MC & University of Liverpool)
  - Medicinal and computational chemistry, structural biology, protein production, ADME, Phys-Chem, CMC, *in vitro*/*in vivo* toxicology, pharmaceutical sciences (Evotec)
- **Budget**
  - Estimated budget for the GNA NOW activities in line with Consortium capacities

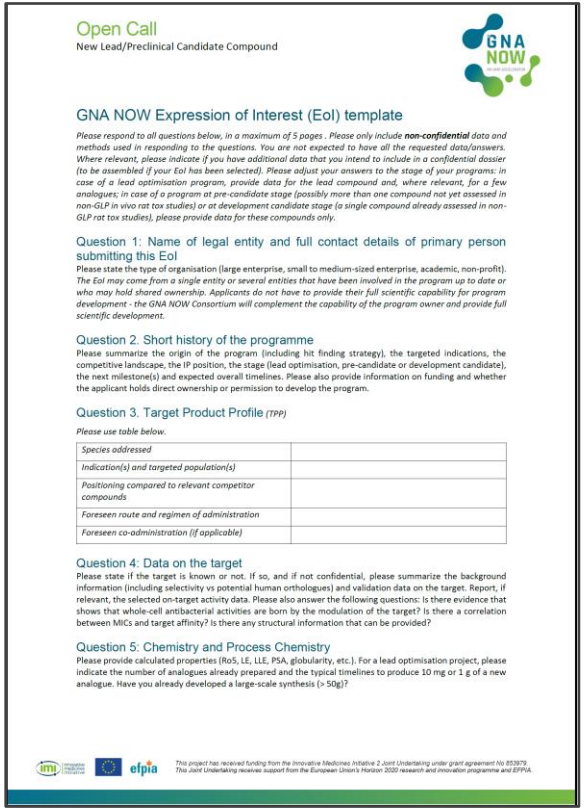
Implementation

Proposed plan (to be refined together with GNA NOW partners)

- **Action plan** to reach the next milestone
- **Timelines** (indicative)
- **Assay Cascade**
- **Tasks, deliverables and responsibilities**

Expression of Interest template

Template available at www.lygature.org/sites/lygature/files/2021-05/GNA-NOW%20EoI_final.docx



Open Call

New Lead/Preclinical Candidate Compound

GNA NOW Expression of Interest (EoI) template

Please respond to all questions below, in a maximum of 5 pages . Please only include ***non-confidential*** *data and methods used in responding to the questions. You are not expected to have all the requested data/answers. Where relevant, please indicate if you have additional data that you intend to include in a confidential dossier (to be assembled if your EoI has been selected). Please adjust your answers to the stage of your programs: in case of a lead optimisation program, provide data for the lead compound and, where relevant, for a few analogues; in case of a program at pre-candidate stage (possibly more than one compound not yet assessed in non-GLP in vivo rat tox studies) or at development candidate stage (a single compound already assessed in non-GLP rat tox studies), please provide data for these compounds only.*

Question 1: Name of legal entity and full contact details of primary person submitting this EoI

Please state the type of organisation (large enterprise, small to medium-sized enterprise, academic, non-profit). *The EoI may come from a single entity or several entities that have been involved in the program up to date or who may hold shared ownership. Applicants do not have to provide their full scientific capability for program development - the GNA NOW Consortium will complement the capability of the program owner and provide full scientific development.*

Question 2. Short history of the programme

Please summarize the origin of the program (including hit finding strategy), the targeted indications, the competitive landscape, the IP position, the stage (lead optimisation, pre-candidate or development candidate), the next milestone(s) and expected overall timelines. Please also provide information on funding and whether the applicant holds direct ownership or permission to develop the program.

Question 3. Target Product Profile *(TPP)*

Please use table below.

Species addressed	
Indication(s) and targeted population(s)	
Positioning compared to relevant competitor compounds	
Foreseen route and regimen of administration	
Foreseen co-administration (if applicable)	

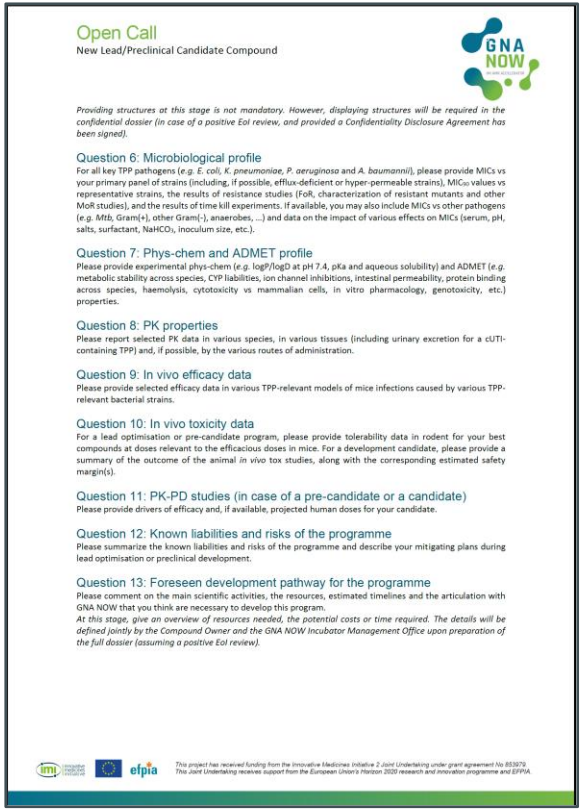
Question 4: Data on the target

Please state if the target is known or not. If so, and if not confidential, please summarize the background information (including selectivity vs potential human orthologues) and validation data on the target. Report, if relevant, the selected on-target activity data. Please also answer the following questions: Is there evidence that shows that whole-cell antibacterial activities are born by the modulation of the target? Is there a correlation between MICs and target affinity? Is there any structural information that can be provided?

Question 5: Chemistry and Process Chemistry

Please provide calculated properties (Ro5, LE, LLE, PSA, globularity, etc.). For a lead optimisation project, please indicate the number of analogues already prepared and the typical timelines to produce 10 mg or 1 g of a new analogue. Have you already developed a large-scale synthesis (> 50g)?

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 853979. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.



Open Call

New Lead/Preclinical Candidate Compound

Providing structures at this stage is not mandatory. However, displaying structures will be required in the confidential dossier (in case of a positive EoI review, and provided a Confidentiality Disclosure Agreement has been signed).

Question 6: Microbiological profile

For all key TPP pathogens (*e.g. E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii*), please provide MICs vs your primary panel of strains (including, if possible, efflux-deficient or hyper-permeable strains), MIC_{50} values vs representative strains, the results of resistance studies (FoR, characterization of resistant mutants and other MoR studies), and the results of time kill experiments. If available, you may also include MICs vs other pathogens (*e.g. Mtb*, Gram(+), other Gram(-), anaerobes, ...) and data on the impact of various effects on MICs (serum, pH, salts, surfactant, $NaHCO_3$, inoculum size, etc.).

Question 7: Phys-chem and ADMET profile

Please provide experimental phys-chem (*e.g.* logP/logD at pH 7.4, pKa and aqueous solubility) and ADMET (*e.g.* metabolic stability across species, CYP liabilities, ion channel inhibitions, intestinal permeability, protein binding across species, haemolysis, cytotoxicity vs mammalian cells, in vitro pharmacology, genotoxicity, etc.) properties.

Question 8: PK properties

Please report selected PK data in various species, in various tissues (including urinary excretion for a cUTI-containing TPP) and, if possible, by the various routes of administration.

Question 9: In vivo efficacy data

Please provide selected efficacy data in various TPP-relevant models of mice infections caused by various TPP-relevant bacterial strains.

Question 10: In vivo toxicity data

For a lead optimisation or pre-candidate program, please provide tolerability data in rodent for your best compounds at doses relevant to the efficacious doses in mice. For a development candidate, please provide a summary of the outcome of the animal *in vivo* tox studies, along with the corresponding estimated safety margin(s).

Question 11: PK-PD studies (in case of a pre-candidate or a candidate)

Please provide drivers of efficacy and, if available, projected human doses for your candidate.

Question 12: Known liabilities and risks of the programme

Please summarize the known liabilities and risks of the programme and describe your mitigating plans during lead optimisation or preclinical development.

Question 13: Foreseen development pathway for the programme

Please comment on the main scientific activities, the resources, estimated timelines and the articulation with GNA NOW that you think are necessary to develop this program.

At this stage, give an overview of resources needed, the potential costs or time required. The details will be defined jointly by the Compound Owner and the GNA NOW Incubator Management Office upon preparation of the full dossier (assuming a positive EoI review).

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 853979. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Outline of EoI template

Question 1 – Legal entity & primary contact person

Question 2 – Short history of the programme

Question 3 – Target Product Profile (TPP), table provided

Question 4 – Data on target

Question 5 – Chemistry & CMC

Question 6 – Microbiological profile

Question 7 – Phys-chem and ADMET profile

Question 8 – PK properties

Question 9 – *In vivo* efficacy data

Question 10 – *In vivo* toxicity data

Question 11 – PKPD studies*

Question 12 – Known liabilities and risks

Question 13 – Foreseen development pathway

- **No** confidential information
- Max **5** pages
- Adjust the answers to the stage of your programme
- Indicate if you have relevant data that you'll include in the Dossier
- Contact the GNA NOW Office in case of questions

gnanow@lygature.org

Dossier template

Outline of template

The GNA NOW Incubator Management Office will guide you through the process

Before submitting, a CDA (Confidentiality Disclosure Agreement) has to be established

- Application summary
- Current funding & other ongoing applications
- Section 1 – Disease Background
- Section 2 – Project Background
- Section 3 – Chemistry
- Section 4 –Intellectual Property
- Section 5 – Microbiology profile of the series
- Section 6 – Phys-Chem/ADMET profile of the series
- Section 7 – Pharmacokinetics properties of best analogues
- Section 8 – In vivo tolerability and efficacy of best analogues
- Section 9 – PK-PD studies and human doses
- Section 10 – In vivo safety
- Section 11 – CMC
- Section 12 – Ongoing Activities and Project Plan
- Section 13 – Clinical translation and development plans
- Section 14 – Proposal owner information
- Scientific Advisory Board, Consultants

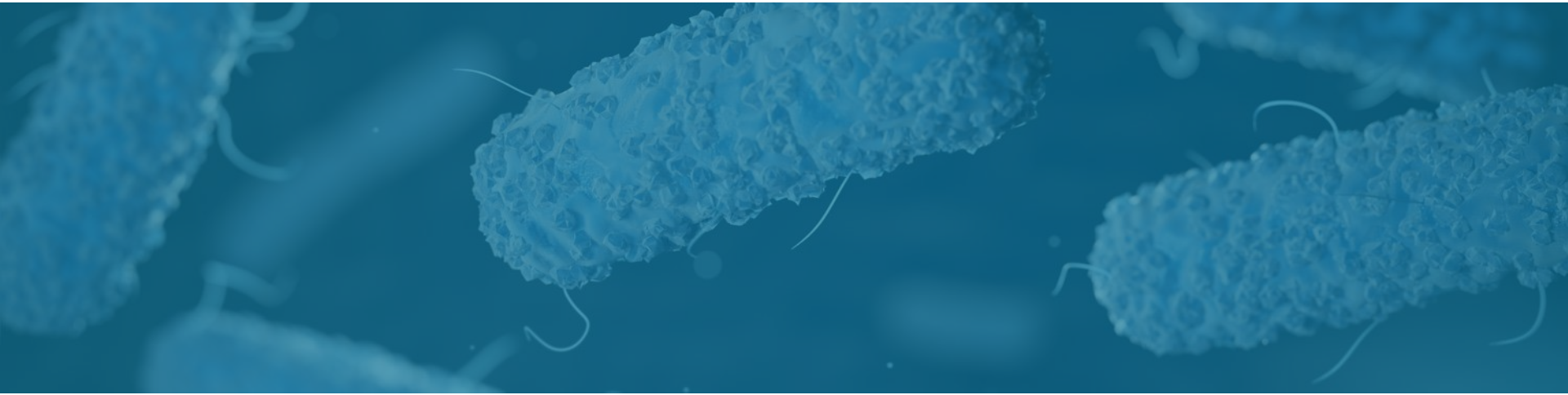
Application Process

Kristina Orrling, Lygature
GNA NOW Coordinator

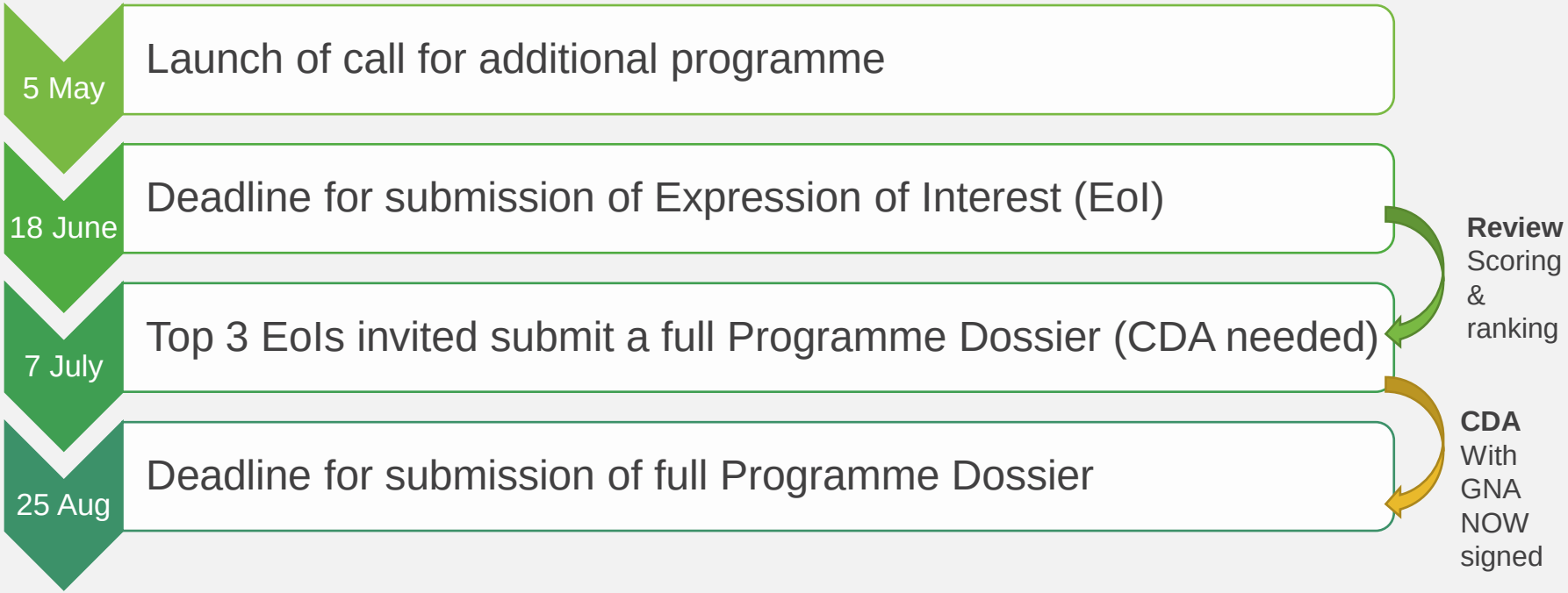
Submit your proposal (EoI) to

gnanow@lygature.org

Involve GNA NOW Office when preparing the EoI!



Process, deadlines and timelines



After submitted dossier

Review
Scoring
&
ranking

15 Sep

#1 proposal invited to sign contracts with Evotec & GNA NOW

Define new programme together with GNA NOW partners
(who will do what when?)

Establish Core Team, Steering Committee, external experts etc

Define Go/No-Go criteria

Submit revised Description of Action to IMI

How it works?

- Submission to gnanow@lygature.org of a non-confidential Expression of Interest (EoI)
  - no more than 5 pages using the provided template.
- Submission evaluated and scored by the GNA NOW Review Committee (RC)
  - RC members are a diverse set of industry, independent and academic experts in antibiotic drug discovery and development.
- Top three proposals invited to sign a CDA with GNA NOW.
- Confidential dossiers provided by selected applicants and then reviewed by the RC
  - applicants to answer to Reviewers' questions in written prior to an oral defence .
- Highest ranked dossier invited to sign partnering agreements with Evotec and with the GNA NOW Consortium.
- Project plans and deliverables (DoA) to be defined jointly between applicant and Consortium

IP – Access Rights

	Project Execution (IMI2 JU & GNA NOW)	Research Use	Direct Exploitation
Background*	• Exclusive owner • Access** (royalty free Research license)	• Access on request (license on fair & reasonable terms - non exclusive)	EVT option for direct exploitation in the field of treatment of infections caused by Gram(-) bacteria + bilateral agreement with EVOTEC
Compound Results	• Ownership transfered to cpd owner • Access** (royalty free Research license)	• Access on request (license with fair&reasonable terms- non exclusive)	EVT option for direct exploitation in the field of treatment of infections caused by Gram(-) bacteria + bilateral agreement with EVOTEC
Other results	• Ownership of beneficiaries generating results • Access** (royalty free Research license)	• Access on request for beneficiaries (Research license – royalty free-non exclusive)	• Rights/licences with a third party to be negociated

** Background:In appendix3. exclusion of background from Access Rights*

***each Beneficiary are granted Access Rights to the Results/background of any other Beneficiaries and/or CTP solely to the extent Necessary to undertake its own Allocated Work (for GNA-NOW projects execution)*

Compound Owner status

New Compound Owner status	Beneficiary	Contribution Third Party
Eligibility	Must qualify as a Beneficiary receiving IMI2 JU funding*	Any legal entity
Agreement to be signed	IMI2 GNA NOW Consortium and Grant agreements	Contributing Third Party Agreement (appendix of the CA)
Resources	GNA NOW in-kind activities Potential for funding	GNA NOW in-kind activities No funding
Governance within the consortium	Part of the governance of the entire GNA NOW project	Limited to its program
Bilateral agreement with EVT (IP, access right, exploitation)	Mandatory	Mandatory

* www.lygature.org/sites/lygature/files/2021-05/IMI2_provisions_for_participating_in_IMI2_actions.pdf

Submit your EoI
before
18 June

Thank you for your attention

You are invited to apply and to join a dynamic and skilled Consortium that will help you, in a collaborative spirit, to progress your asset to the next level!

Questions?

contact us via:
gnanow@lygature.org