GARDP
Global Antibiotic Research & Development Partnership
A joint DNDi / WHO initiative

Request For Proposal

Zoliflodacin toxicology studies

Dated: July 2019

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1. PURPOSE

1.1 GARDP mission

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavoring to ensure their sustainable access.
Initiated by the World Health Organization (WHO) and the Drugs for Neglected Disease initiative (DNDi) in May 2016, GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage research and development of new antimicrobial agents and diagnostics. GARDP became its own legal entity ("The GARDP Foundation") in July 2018 and was incubated by DNDi until March 2019.

During its incubation, and through the generous support of donors and partners, GARDP has built a skilled and dedicated team with expertise from a range of sectors and backgrounds led by a Board of Directors comprising leading international experts in the global health arena.

In the last three years, GARDP has formed numerous partnerships with industry, academia and research institutions in support of its clinical programmes to develop antibiotics for drug-resistant infections for children, newborns with sepsis, and sexually-transmitted infections. These collaborations span the drug development lifecycle and include screening chemical libraries for antibacterial activity, assessing the viability of potential antibiotic candidates, and the completion of three clinical trials.

For more information, please visit GARDP website: https://www.gardp.org/

1.2 Sexually Transmitted Infections Program

GARDP R&D strategy for Sexually Transmitted Infections (STI) aims at delivering, within 7 years-time, at least one treatment that i) works against drug-sensitive and drug-resistant gonorrhea; ii) is suitable for integration into WHO-recommended STIs case management (including syndromic management); iii) works in both uro-genital and extra-genital (i.e. pharyngeal and anorectal) infections. In order to fulfill this aim GARDP has partnered with Entasis Therapeutics to accelerate the development and registration of Zoliflodacin for the treatment of uncomplicated gonorrhea. It constitutes the first and main priority of the overall STI program.
The objective of the GARDP zoliflodacin project is to accelerate the development and registration of zoliflodacin, a first-in-class oral gyrase inhibitor that has shown high efficacy in adult patients with uncomplicated urogenital gonococcal (GC) infection.

1.3 Zoliflodacin

In July 2017, Global Antibiotic Research & Development Partnership (GARDP) partnered with Entasis to develop zoliflodacin, a novel bacterial type-II topoisomerase inhibitor from the spiropyrimidinetrione class, in late-stage clinical development.
Zoliflodacin has demonstrated activity in vitro against N. gonorrhoeae, including drug-resistant strains. To date, 5 clinical studies have shown that Zoliflodacin has the potential to be a safe, effective (high cure rates level for urogenital and rectal infections) and convenient single dose oral treatment of uncomplicated gonorrhoea. Currently, a non-inferiority phase 3 study is about to start to assess the efficacy and safety of zoliflodacin against uncomplicated gonorrhoea globally.

The development strategy is to register Zoliflodacin with the US FDA and EMA first, and then roll it out to a number of priority countries.

2. RFP INSTRUCTIONS

2.1 General information

a) GARDP invites you as a Service Provider to submit one proposal covering the services described in Section 3.

b) This entire RFP and all the related discussions, meetings, information exchanges and subsequent negotiations that may occur are subject to the confidentiality terms and conditions of the Intent to Participate attached as Annex 1.

c) All bidders are required to complete and return the Intent to Participate letter.

d) The issuance of this Request for Proposal in no way commits GARDP to make an award. GARDP is under no obligation to justify the reasons of its choice of service provider following the competitive bidding. GARDP may choose not to justify its business decision to the participants of the RFP.

e) GARDP reserves the right to:

- Reject any proposal without any obligation or liability to the potential service provider.
- Withdraw this RFP at any time before or after the submission of bids without any advance notice, explanation or reasons.
- Modify the evaluation procedure described in this RFP
- Accept a proposal other than the one containing the lowest financial offer

- Award a contract on the basis of initial proposals received without discussion of best and final offers
- Award all services to only one supplier or allocate parts of them to different suppliers according to the needs of GARDP

f) Proposals submitted after the deadline are subject to rejection.

g) GARDP reserves the right to request additional data, information, discussions or presentations to support each proposal. All bidders must be available to discuss details of their proposal during the RFP process.

h) All offers should be submitted in an electronic format.

i) Service providers are responsible for ensuring the accuracy of information provided in support of their proposal. GARDP reserves the right to reject an awardee in the event of failure to disclose any material information, or material changes or errors in any information on which the award decision was based.

j) The proposed timelines below indicate the process GARDP intends to follow. If there are changes to these timelines, GARDP will notify you in writing.

2.2 Timelines

Process steps	**Responsible party**	**Timelines**
Launch RFP	GARDP	July 19th 2019
Send back the Intent to Participate letter	Service Provider	July 26th 2019
Send the technical package to Service Provider	GARDP	July 29th 2019
Q&A sent to GARDP	Service Provider	August 7th 2019
GARDP responses to Q&A	GARDP	August 16th 2019
Reception of proposals	GARDP	August 28th 2019
Notification to preselected bidders	GARDP	September 4th 2019
Bid Defence Meetings	GARDP / Service Provider	September 12th 2019
Project award	GARDP	September 19th 2019

2.3 RFP processes and contact information

2.3.1 Instructions

All bidders may request further clarifications in regards of this current RFP, by addressing questions in writing to the dedicated key contacts identified below. These questions should be submitted to GARDP at the date mentioned in the section 0 of the RFP.

In order to keep a fair bidding process, questions on the drugs to be assessed will only be answered in a document shared with all the bidders on the date indicated in section 0 of the RFP.

To submit your questions, please use the form attached as Annex 2.

2.3.2 Confirmation of Intent

Please transmit your intent to participate by using and signing the document attached in Annex 1.
Each bidder is required to provide GARDP with a written confirmation of intent or decline to participate by the date as indicated in the section 2.2.

Please, note that the "intent to participate letter" is a standard document which GARDP cannot afford negotiating due to project priorities, time and resources dedication. This template is based on several years of experience working with suppliers and contains widely acceptable terms in RFPs.

Confirmations of intent should be sent by email to Christophine Marty-Moreau and Anthony Simon (contacts details below).

Questions types	Contact person	Title	Contact information
Contractual & Financial aspects	Christophine MARTY MOREAU	Senior Procurement Manager	15 Chemin Louis Dunant, 1202 Geneva, Switzerland Phone: +41 22 906 92 61 Email: cmarty@dndi.org
Technical aspects	Anthony SIMON	Pharmaceutical Development Manager	Email: asimon@dndi.org

2.4 Format and content of the proposal

Responses to this RFP must be in English and should contain the following information:

- **A cover letter including:**
  - Name and address of the service provider
  - Name, title, phone number and email address of the person authorized to commit contractually the service provider
  - Name, title, phone number and email address of the person to be contacted in regards of the content of the proposal, if different from above
  - Signature of this letter done by a duly authorized representative of the company
  - Acceptance of the consultation principles as detailed in section 2.1
  - Acceptance of GARDP agreement template: Clinical Trial Agreement will be provided at a later stage of the process.
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- **A technical proposal**
  - Detailed proposal explaining how your company approach will enable GARDP team to meet project timelines and insure quality results.

- **A financial proposal**
  - Detailed cost breakdown split for each activity described in section 3.

- **Administrative information**
  - Business Company information: directors and officers, creation date, corporate headquarters, locations, business turnover of the past 3 years (global and in the field of service provided), headcounts (global and in the field of service provided), general services provided, customer's reference, pricing strategy for NGOs.
  - Any other relevant information enabling GARDP to assess the opportunity of contracting with your company.

2.5 Conflict of Interest

The Company shall disclose any actual or potential conflicts of interest in the Intent to Participate letter.

3. SCOPE OF WORK

The objective of this proposal is to complete non-clinical registration package with:

- Impurity qualification studies in rat:
  - In-vitro genotoxicity studies
  - 14 Day repeat dose oral toxicity in rat
- Pre- and postnatal (Segment III) study in rat ss per ICH guideline S5 (R3)

The details of activities are provided in the table below.

ID	Title	Species	Description/notes
1	Bioanalytical method transfer and validation for plasma Analysis (drug + main impurity)	Rat plasma	To transfer and validate a method for drug and main impurity quantification in rat plasma that will be used during GLP studies GLP
2	Analytical method development and validation for dose formulation analysis	N/A	To develop and validate a method for the formulation that will be used during GLP studies GLP
3	In-vitro Ames Assay on individual impurities (up to 4 impurities)	In-vitro	Separate study for each individual impurity to be conducted GLP
4	In vitro Chromosomal Aberration Study on individual impurities (up to 4 impurities)	In-vitro	Separate study for each individual impurity to be conducted GLP
5	7 or 14 days DRF study	Rat	Assessment of dose selection for main experiments Non-GLP
6	14 Day repeat dose oral toxicity and toxicokinetic study in Rats with 14 days recovery period	Rat	Pure drug and drug enriched with impurities will be tested for toxicity potential: – Two dose levels with pure drug – Two dose levels with enriched drug – Vehicle control group Reversibility of toxicity or delayed occurrence of toxicity will be studied for 14 days GLP

6'	Optional: Samples of bone marrow to be taken for eventual evaluation as an in vivo micronucleus test for genotoxic potential	Rat	As part of the repeat dose toxicity study using standard in vivo micronucleus protocol GLP
7	Pre- and postnatal (Segment III) study in rat	Rat	Study design per ICH guideline S5(R2) or S5(R3) Step 2 GLP
8	Drafting of nonclinical summaries for registration submissions and reports to be in SEND format	N/A	In CTD and SEND format

4. CRITERIA FOR SELECTING SERVICE PROVIDERS

The decision to award any contract as a result of this RFP process will be based on Service Providers' responses and any subsequent negotiations or discussions. The decision-making process will consider the ability of each service provider to fulfil GARDP's requirements as outlined within this RFP and the cost of the offer.

Proposals will be assessed against the main following criteria but not limited to:

- **Technical criteria**
  - Project approach, methodology and planning
  - Experiences/skills, level of company representatives assigned to this project
  - Quality and applicability of proposal presentation
  - Track records with regulatory bodies and GLP regulatory inspections outcome
  - Customer references / experience in related therapeutic area and country¨

- **Capacity to deliver**
  - Reasonable timelines fitting with our requirements
  - Project management capabilities
  - Ability to conduct all activities (avoiding as much as possible outsourcing of activities)
  - Past experience with similar work

- **Financial criteria**
  - Realistic costing of the proposal with NGO rates whenever possible

5. PROPOSAL REQUIREMENTS, DELIVERABLES & TIMELINES

5.1 Proposal requirements

Following the issuance of the RFP, all interested bidders are invited to submit a proposal that describes:

- General information of the company as described in section 2.1
- Technical and financial proposal as described in section 2.4. Budget with full details of your offer including fixed costs and Pass-Through Costs.
- Whole project timelines
- Project team involved

5.2 Deliverables

- Protocols (outlines to be provided within proposal)
- Draft study reports in SEND format for each experiment/study provided to GARDP maximum 4 weeks after the end of the experiment
- Final reports in SEND format

5.3 Timelines

Beginning of services planned for November 2019

5.4 Additional information

- After receiving their Intent to Participate letter, GARDP will provide the bidders with the documentation listed below:
    - Synopsis of studies submitted to regulatory authorities
    - Available reproductive toxicology study reports
    - Existing bioanalytical method description
- GARDP will provide in due course the API in needed quantities and internal standards

6. ANNEXES

Annex 1: Intent to Participate letter

Annex 2: Q & A Form