GARD P
Global Antibiotic Research & Development Partnership

Instructions for Due Diligence Information Document:

Commercial Partner Selection - Zoliflodacin

Date: 31 October 2023

Subject: Request for Due Diligence Information for selection of commercial partner(s) for Zoliflodacin

1. Summary

This Due Diligence Information Document is to solicit information for selection of partner(s) for commercialization of a first-in-class antibiotic - Zoliflodacin Powder for Oral Suspension - the only drug being developed specifically to treat resistant strains of gonorrhea ("Product").

The partner must have a demonstrably viable plan as well as prior experience in successful commercialization of oral / injectable antibiotic, antiviral & anti-HIV products, preferably for Sexually Transmitted Diseases targeting the community-care settings.

The goal of this due diligence information is to identify a commercial partner ("Distributor") to market & distribute the Product initially in South Africa & Thailand, the ("Territory") in alignment with GARDP's Market Access Plan.

2. BACKGROUND & PARTNERS

In 2017, GARDP partnered with Entasis Therapeutics Limited, now a subsidiary of Innoviva, to carry out the phase 3 trial at 16 sites across 5 countries (Belgium, the Netherlands, South Africa, Thailand and the US), comparing zoliflodacin to a globally recognized regimen (500mg ceftriaxone plus 1g azithromycin) for the treatment of uncomplicated gonorrhoea. A total of 958 patients were recruited, making it the largest clinical trial ever conducted for a new treatment against gonorrhoea infection.

The top-line results of the phase 3 registrational trial are expected in Q4 2023.

The CMC development of the product is currently in progress & the product is expected to be ready for registration in South Africa & Thailand by H1 2025.

- **GARDP:**

The Global Antibiotic Research & Development Partnership (GARDP) is a Swiss not-for-profit organization developing new treatments for drug-resistant infections that pose the greatest threat to health. GARDP was created by the World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi) in 2016 and legally founded in 2018 to ensure that everyone who needs antibiotics receives effective and affordable treatment. GARDP is funded by the governments of Australia, Germany, Japan, Monaco, the Netherlands, the Public Health Agency of Canada, South Africa, Switzerland, the United Kingdom, the Canton of Geneva, as well as the European Union, Wellcome Trust and private foundations. GARDP is registered under the legal name GARDP Foundation. (www.GARDP.org)

- **Innoviva Specialty Therapeutics:**

Innoviva Specialty Therapeutics, a subsidiary of Innoviva, Inc., is focused on delivering innovative therapies in critical care and infectious disease. Innoviva Specialty Therapeutics' products, through its affiliate, La Jolla Pharmaceutical Company, include GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock, and XERAVA® (eravacycline) for the treatment of complicated intra-abdominal infections in adults. Innoviva Specialty Therapeutics' products, through its affiliate, Entasis Therapeutics Inc., include XACDURO® (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use approved for the treatment of adults with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible strains of Acinetobacter baumannii-calcoaceticus complex (Acinetobacter). For more information about Innoviva Specialty Therapeutics, please visit here.

3. Summary of Product

The target product for this Due Diligence Information Document is Zoliflodacin powder for oral suspension in a sachet form.

Zoliflodacin is under development for the treatment of drug-resistant uncomplicated urogenital gonorrhea. It is administered through oral route as an antimicrobial amorphous nonsterile powder disolved in water.. It is a benzisoxazole derivative and it acts by targeting ATP pocket of DNA gyrase and topoisomerase IV.[1]

Gonorrhea and AMR:
Anti-microbial resistance (AMR) is a growing public health threat globally, leading to more than 700,000 deaths each year. The World Health Organization (WHO) has identified AMR as a leading risk to health and economic development and a barrier to reaching sustainable development goals.[2]In 2021, G7 Health Ministers committed to making AMR a key strategic area for action.[3]

Unlike COVID-19, which raised alarm as it swiftly moved across the globe, AMR is a silent pandemic that has gained ground in countries and hospitals with little public notice.[4] While the risk from AMR infections continues to increase, only a small number of new antibiotics have been developed in recent years. Barriers to access, including lack of awareness of novel treatments and their applicability in specific settings, economic and regulatory challenges, or medication shortages, can impact use in countries at all levels of development. However, these challenges are particularly acute in low- and middle-income countries.

Gonorrhoea is among the three most common sexually transmitted infections, affecting men and women worldwide. Global infection rates of gonorrhoea are increasing, with 82 million new cases estimated each year and limited treatment options due to antimicrobial resistance.[5]

[1] https://www.pharmaceutical-technology.com/data-insights/zoliflodacin-entasis-therapeutics-uncomplicated-cervical-and-urethral-gonorrhea-likelihood-of-approval/
[2] https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

[3] https://www.who.int/news/item/09-06-2021-record-response-to-who-s-call-for-antimicrobial-resistance-surveillance-reports-in-2020

[4] https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

[5] https://gardp.org/gardp-and-innoviva-specialty-therapeutics-announce-completion-of-patient-recruitment-for-registrational-phase-3-gonorrhoea-treatment-trial/

4. Scope of Work

This scope of work includes the following activities:

GARDP desires Distributor to ensure access of the Product (on a non-exclusive basis) through carrying out activities, including but not limited to, regulatory filings, regulatory agency interactions, WHO Pre-Qualification submission, local distribution and logistic support in the territory, as described in the Market Access Plan and the Country Business plans which shall be agreed upon with GARDP

i) Public Health Activities:

The commercialization of the Product should be a part of the Distributor's current or future initiatives towards public health. The distribution activities for the Product must be aligned with the GARDP Stewardship & Access Principles , mainly to: a) Avoid the misuse &/or overuse of the Product b) limit the emergence &/or increase of bacterial resistance to the Product.

ii) Regulatory:

- To update and implement the regulatory strategy and liaison with regulatory authorities on regulatory matters, at an international (WHO PQ), regional and country level
- To submit regulatory dossiers to selected countries within Territory (South-Africa and Thailand as a first instance), and in these countries provide continued regulatory support.

iii) Pharmacovigilance:

- To provide an efficient pharmacovigilance (PV) program, with reporting back to GARDP and Innoviva as will be detailed in a separate pharmacovigilance agreement, including call centers and ability to monitor product complaints and recalls if needed, PV systems that enable monitoring and reporting of product use as required by local regulations.
- To manage the PV database and reporting to GARDP and Innoviva for the Product distributed by other entities (International Procurement Agency etc.) within Territory.

Iv) Distribution and logistics:

To implement an import, distribution and logistics strategy in the Territory, supported by an effective ordering and forecasting process, to ensure cost effective, affordable, timely and uninterrupted availability of the Product to patients in priority countries, as well as an ad-hoc early access plan for non-prioritized countries.

In addition to the distribution of the Product through own distribution network, distributor to facilitate the supply of Product, within the Sub-Licensed Territory, to International Procurement Agency in order to ensure distribution of the Product by such agency, using distributor label.

v) **Country Business plans:**

To develop a country specific Business Plans to be approved by GARDP, for each selected country within the Territory, which shall include:

- Registration requirements and timing,
- Identification of local stakeholders and partners,
- In-country efficient logistics structure to ensure timely and uninterrupted availability of the Product to patients post-launch, and medical information support systems
- Pricing considerations: distribution margins, differentiation between private & public market.

iv) **Market Intelligence generation:** To generate market intelligence within the Territory (South Africa & Thailand).

5. Instructions to interested parties

GARDP will manage the Due Diligence process for and on behalf of its partners.

a. Responses

i. All responses should be submitted in English and signed by an authorized representative of the Respondent (Form A in Annex 1).
ii. Responses should be submitted via email with the subject line Due Diligence_ZOLI to: kprabhakar@gardp.org .
iii. Responses received after the stipulated closing date will be deemed invalid.

b. Timeline The timeline for the publishing of the Due Diligence Information Document & Receipt of responses is described below. Responses received after the deadline will not be considered.

Due Diligence Document Publication on GARDP Web site	October 31 , 2023
Last date for receipt of responses	November 14 , 2023, 6pm CET

c. Costs of preparing documents

All costs associated with preparing and submitting the responses will be borne by the Respondent.

d. Confidentiality

Information which the Respondent considers to be proprietary should be clearly marked as such. All such information will be treated as confidential and used by Partners for assessment purposes only.

e. Disclosure

Information relating to the examination, clarification, and evaluation of responses shall not be disclosed to Respondents or any other persons not officially concerned with such process.

f. Terms and Conditions

All terms and conditions for the development contract will be finalized during the negotiation process after final distributor(s) have been selected. A formal agreement including these terms will be executed by GARDP and the selected Distributor.

6. Additional Information

GARDP reserves the right to request additional information, arrange interviews with the Respondent, visit the Respondent's premises and facilities, and conduct an audit to verify the information provided.

7. Evaluation

GARDP will assess each eligible response based on selection criteria that includes the overall quality of the commercialization plan provided, timelines, corporate capabilities and demonstrated expertise with similar products. GARDP anticipates that several companies will be identified for further discussions to refine project plans, timelines, and cost estimates.

GARDP may engage with a third party to perform a quality audit of the selected supplier. GARDP anticipates making a contract award post completion of evaluation & audits (if required). GARDP reserves the right to keep the final evaluation results & award information confidential.

Annex 1 Form to be Completed by Respondents

FORM A: Response to Due Diligence Information Document - Zoliflodacin

This form must be completed, signed, and returned to GARDP at kprabhakar@gardp.org .

DECLARATION

We, the undersigned, having read the Due Diligence Instructions Document for Zoliflodacin Powder for oral Suspension, submit our response, which includes the information requested in Section 6. We confirm that all the information provided is correct.

We confirm that we are interested in entering into discussions for a possible collaboration with GARDP on the Statement of Work as described in section 4.

We understand that Partners' issue of the Due Diligence Information Document and the response we submit is not a commitment by either party to enter into such discussions or collaboration. We further understand that Partners reserve the right to discuss and collaborate with one or multiple parties, no parties, or to cancel the Due Diligence at their discretion.

This Due Diligence Information Document and any response thereto shall be the property of GARDP.

Name of authorized representative:

Title:

Signature:

Date:

Company name:

Postal Address:

Telephone No.:

Email Address:
