

Request for Proposal

Pharmaceutical Development (solid oral dosage form) for Visceral Leishmaniasis candidate DNDI-6148

Dated: 20 August 2021

Table of Contents

1. PURPOSE	3
2. RFP INSTRUCTIONS	3
3. DNDi OVERVIEW	7
4. SCOPE OF WORK	7
5. CRITERIA FOR SELECTING SERVICE PROVIDERS	9
6. PROPOSAL REQUIREMENTS, DELIVERABLES & TIMELINES	10
7. ANNEXES	11

1. PURPOSE

The evaluation is requested by DNDi (Drugs for Neglected Diseases *initiative*).

DNDI-6148 is in clinical development by DNDi for the treatment of Visceral Leishmaniasis (VL). A powder for oral suspension formulation was developed and is currently dosed to healthy volunteers in a single ascending dose First-in-Human clinical trial. In anticipation to Phase Ib (multiple ascending dose study starting in 2023) and subsequent Phase II clinical trials, DNDi is now sourcing a Contract Development and Manufacturing Organisation (CDMO) for formulation development activities leading to commercialisable tablet formulation, followed by GMP manufacturing and packaging of clinical supplies to support the Phase Ib and II trials. A pediatric formulation will also need to be developed to support inclusion of children in future clinical trials.

DNDi especially welcomes applicants from South Asia, as per our new strategic plan and its ambitions to increasingly work with partners and suppliers from low- and middle-income countries (LMICs).

2. RFP INSTRUCTIONS

2.1. General information

- a) DNDi invites you as a Service Provider to submit one proposal covering formulation development & GMP drug product manufacture of clinical supply and associated quality controls services.
- 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 send return the Intent to Participate letter.
- d) The issuance of this Request for Proposal in no way commits DNDi to make an award. DNDi is under no obligation to justify the reasons of its service provider's choice following the competitive bidding. DNDi could choose not to justify its business decision to the participants of the RFP.
- e) DNDi 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 another proposal than the lowest one.

- Award a contract on the basis of initial proposals received without discussions for best and final offers.
 - Award all services to only one supplier or allocate them to different suppliers according to what DNDi will consider necessary.
- f) Late submission proposals are subject to rejection.
- g) DNDi reserves the right to request additional data, information, discussions or presentations to support their 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) The proposed timelines below indicate the process DNDi intends to follow. If there are changes to these timelines, DNDi will notify you in writing.

2.2. Timelines

Process steps	Responsible party	Timelines
Launch RFP	DNDi	18 August 2021
Send back the Intent to Participate letter	Service Provider	27 August 2021
Full Technical Package disclosed to participants	DNDi	30 August 2021
Questions sent to DNDi	Service Provider	6 September 2021
DNDi responses to questions	DNDi	13 September 2021
Reception of proposals	Service Provider	24 September 2021
Bidder Preselection notification	DNDi	8 October 2021
Bid defense meetings	DNDi	15 October 2021
Project award	DNDi	30 October 2021
Project Start (Drug Product)	Service Provider	1 December 2021
Clinical Manufacturing completed	Service Provider	October 2022

2.3.RFP processes and contact information

2.3.1.Instructions

All bidders may request further clarifications regarding this RFP by addressing their questions in writing to the dedicated key contacts identified below. These questions should be submitted to DNDi at the date mentioned in the section 2.2 Timelines of the RFP.

In order to keep a fair bidding process, questions related to this RFP will only be answered in a document shared with all the bidders on the date indicated in section 2.2. Timelines 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 DNDi with a written confirmation of intent or decline to participate by the date as indicated in the section 2.2.

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

Please note the “intent of participate letter” is a standard document which DNDi cannot afford negotiating due to project priorities, time and resources dedication. This template is based on several years of experiences working with services providers and contains widely acceptable terms.

Questions types	Contact person	Title	Contact information
Contractual	Christophine MARTY MOREAU	Senior Procurement Manager	Phone: +41 22 906 92 61 Email: cmarty@dndi.org
Technical	Yannic PANNATIER SCHUETZ	Senior Pharmaceutical Development Officer	Phone: +41 22 555 19 24 Email: ypannatier@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
- A technical proposal
 - Detailed proposal explaining how your company approach will enable DNDi team to meet project timelines, deliverables and ensure quality results.
 - A financial proposal
 - Budget template for drug product (Annex 3) to be completed.
 - Completed Drug Product Manufacturing (IMP) and Packaging Quality Questionnaires.
 - Administrative information
 - Business Company information: directors and officers, creation date, corporate headquarters, locations, business turnover of the past three 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 DNDi 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. DNDi OVERVIEW

The Drugs for Neglected Diseases *initiative* (DNDi) is an international non-profit organization that discovers, develops and delivers safe, effective, and affordable treatments for the most neglected patients. Our research and development (R&D) partnerships have delivered eight field adapted and affordable treatments and affordable treatments for five deadly diseases, saving millions of lives.

Our new strategy charts an eight-year journey to 2028, by which time we aim to have delivered 25 new treatments in our first 25 years.

DNDi advances the best science for the most neglected by:

- o **Innovating to save lives:** Discovering and developing urgently needed treatments for neglected patients and working to ensure they're affordable, available, and adapted to the communities who need them
- o **Fostering sustainable solutions:** Working hand in hand with partners in low- and middle-income countries to power our progress and strengthen innovation ecosystems that put people's needs first
- o **Advocating for change:** Speaking out for policy change to enable more effective and equitable R&D and access to the fruits of science for all people, no matter their income or where they live.

During this Strategic Plan period, we will expand our footprint in low- and middle-income countries (LMICs) to foster sustainable solutions- growing our partnerships and industry networks to power innovation ecosystems that put people's need first, accelerate test and treat approaches, and ensure equitable access to medical care.

For more information, please visit DNDi website: www.dndi.org.

4. SCOPE OF WORK

DNDi is requesting the CDMO to carry out formulation development, GMP manufacturing, packaging, labelling, release and ICH stability studies for the Phase Ib/II clinical supplies. A solid oral dosage form (immediate release tablet) with two dose strengths is considered, along with matching placebo.

The compound is characterised by a very poor solubility (0.38 mg/mL in water), though showing good oral bioavailability in animal species so far. The formulation development activities for Phase Ib/II should focus on immediate release tablets.

A non-GMP batch of API (representative of the API manufacturing process, currently being manufactured) will be used for formulation development activities, while the cGMP API batch will be provided for clinical supplies manufacturing.

The list of activities to be performed are the following:

Work Package 1: Solid oral formulation development for Phase Ib/II

- 1.1. Formulation screening: chemical stability/compatibility for API alone, excipient alone (control), API/excipient combinations and up to four solid oral dosage form prototypes (if excipients are used, preferably on the highest dose strength)
- 1.2. Formulation development of a solid oral dosage form for Phase Ib/II: a lead formulation will be selected.
Optional - Relative bioavailability study in relevant animal species on the most promising prototype(s) (up to two)
- 1.3. Manufacture of development batch (max. 2000 units) from the lead formulation, two dose strengths
- 1.4. Formal stability study on development batch: five years, three storage conditions (one month: 50°C/75% RH, six months/accelerated: 40°C/75% RH, long term: 30°C/75% RH)

Work Package 2: Analytical support for Phase Ib/II drug product

- 2.1. Assay and related substances method development and validation
- 2.2. Dissolution method development and validation

Work Package 3: Phase Ib/II drug product manufacture and clinical supply

- 3.1. Manufacturing of clinical batches (two strengths) plus matching placebo (max. 2000 units each)
- 3.2. Clinical packaging for Phase Ib/II
- 3.3. Release
- 3.4. Shipment to clinical site
- 3.5. Clinical stability studies for each dose strengths of drug product and matching placebo: five years, two storage conditions (six months/accelerated: 40°C/75% RH, long term: 30°C/75% RH)

Work Package 4: Oral formulation development for pediatrics (*optional*)

- 4.1. Development of a suitable pediatric formulation (e.g. mini-tablets or granules in sachet, ideally from common granule used in the adult formulation). Taste-masking should also be considered.
A lead formulation will be selected.
- 4.2. Manufacture of development batch from the lead formulation
- 4.3. Formal stability study on development batch: five years, three storage conditions (one month: 50°C/75% RH, six months/accelerated: 40°C/75% RH, long term: 30°C/75% RH)

5. 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 DNDi's requirements as outlined within this RFP and the cost of the offer.

For medium and long term development, DNDi will need to identify an industrial partner able and willing to:

- Scale-up the product for registration and commercialisation (CMC full development)
- Prepare registration dossier and successfully register the New Chemical Entity
- Manufacture at low cost
- Commercialise at reasonable margins

CDMOs having expertise and interest to collaborate (risk-sharing) with DNDi on the above will be prioritised during our CDMO selection.

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

5.1. Technical criteria

- Facilities and license to perform the GMP manufacture
- Regulatory Inspection outcome
- Drug Product Manufacturing (IMP) Quality Questionnaire and Packaging Questionnaire
- Formulation and analytical development abilities

5.2. Capacity to deliver

- Reasonable timelines
- Project management capabilities
- Past experience with similar work
- Profile of staff involved (CVs)

5.3. Financial criteria

- Realistic costing of the proposal with NGO rates when possible

6. PROPOSAL REQUIREMENTS, DELIVERABLES & TIMELINES

6.1. Proposal requirements

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

- General information of the company as described in section 2.4
- Technical information (CMC, Regulatory, Quality) for each part of the project. European guidelines to be followed.
- Budget with full details of your offer including fixed costs and Pass-Through Costs. We recommend the use of DNDi template inserted as Annex 3.
- Project team involved
- List of tasks and responsibilities
- Project Gantt Chart

6.2. Major deliverables

- Clinical batches supply
- Certificate of analysis and statement of cGMP compliance (per batch manufactured)
- TSE statements for excipients
- Formulation development reports
- Executed batch records for DP manufacturing
- Analytical development reports
- Analytical test procedures, methods validation protocols and reports
- Specifications for DP release
- ICH stability protocol, interim and final reports
- Biweekly updates on project progress
- Documentation suitable for IMPD submission

6.3. Terms and Timelines

- All GMP services will be performed under a Quality Agreement
- Beginning of Services planned in December 2021
- Completion of the service (excluding ICH stability) by October 2022
- Clinical trial start in January 2023

6.4. Additional information

After receiving their Intent to Participate letter, DNDi will provide the bidders with the documentation listed below on Drug Product:

- Physical and chemical properties of the API
- Certificate of analysis of API
- Drug Product Manufacturing (IMP) Quality and Packaging questionnaires

7. ANNEXES

Annex 1: Intent to Participate letter

Annex 2: Q & A Form

Annex 3: Budget template