Request for Proposal

Monitoring Services in Argentina to support the conduction of a phase 2 trial in Chagas disease

Dated: 29 June 2015
**TABLE OF CONTENTS**

1. PURPOSE .................................................................................................................. 3
2. RFP INSTRUCTIONS ................................................................................................. 3
3. DNDi OVERVIEW .................................................................................................... 6
4. SCOPE OF WORK .................................................................................................... 8
5. CRITERIA FOR SELECTING SERVICE PROVIDERS ......................................... 11
6. PROPOSAL REQUIREMENTS, DELIVERABLES & TIMELINES . 11
7. ANNEXES ................................................................................................................ 12
1. PURPOSE

DNDi plans to conduct a phase 2 study to evaluate different Oral Regimens for the Treatment of Adult Subjects with Chronic Indeterminate Chagas Disease (CD). This study is aimed to provide safety and efficacy data in order to develop new therapeutic approaches for CD to improve treatment response and tolerability and reduce the potential for development of resistance.

2. RFP INSTRUCTIONS

2.1. General information

a. DNDi invites you as a Service Provider to submit a proposal in regards of this RFP for Clinical Monitoring Services in Argentina in support for the conduction of the phase 2 trial.

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 current 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 other 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 about details of their proposal during the RFP process

h. All offers should be submitted in an electronic format

i. A proposed time plan set out below indicates the process DNDi intends to follow. If there are changes to this timelines, DNDi will notify you in writing.

2.2. Timelines

<table>
<thead>
<tr>
<th>Process steps</th>
<th>Responsible party</th>
<th>Timelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Launch RFP</td>
<td>DNDi</td>
<td>29 June 2015</td>
</tr>
<tr>
<td>Send back the Intent to Participate letter</td>
<td>Service Provider</td>
<td>3 July 2015</td>
</tr>
<tr>
<td>Q&amp;A sent to DNDi</td>
<td>Service Provider</td>
<td>3 July 2015</td>
</tr>
<tr>
<td>DNDi responses to Q&amp;A</td>
<td>DNDi</td>
<td>10 July 2015</td>
</tr>
<tr>
<td>Reception of proposals</td>
<td>DNDi</td>
<td>17 July 2015</td>
</tr>
<tr>
<td>Notification to pre-selected bidders</td>
<td>DNDi</td>
<td>22 July 2015</td>
</tr>
<tr>
<td>Bid Defense Meeting</td>
<td>DNDi</td>
<td>27 July 2015</td>
</tr>
<tr>
<td>Bidder selection</td>
<td>DNDi</td>
<td>1 August 2015</td>
</tr>
<tr>
<td>Project Start</td>
<td>Service Provider</td>
<td>Upon contract signature</td>
</tr>
</tbody>
</table>

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 its 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 on the substance 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)

<table>
<thead>
<tr>
<th>Questions types</th>
<th>Contact person</th>
<th>Title</th>
<th>Contact information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contractual &amp;</td>
<td>Christophine</td>
<td>15 Chemin Louis</td>
<td>1202 Geneva Switzerland</td>
</tr>
<tr>
<td>Technical aspects</td>
<td>MARTY MOREAU</td>
<td>Procurement</td>
<td>Phone:+41 22 906 92 61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manager</td>
<td>Email: <a href="mailto:cmarty@dndi.org">cmarty@dndi.org</a></td>
</tr>
</tbody>
</table>

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
  - Acceptance of DNDi agreement template: Clinical Trial Agreement attached as Annex 3.

- A technical proposal
  - Detailed proposal explaining how your company’s approach will enable DNDi team to meet project timelines and ensure quality results.

- A financial proposal
  - Budget template to be completed

- 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
  o 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

3.1. Mission & objectives

Neglected tropical diseases continue to cause significant morbidity and mortality in the developing world. Yet, of the 1,556 new drugs approved between 1975 and 2004, only 21 (1.3%) were specifically developed for tropical diseases and tuberculosis, even though these diseases account for 11.4% of the global disease burden.

Founded in 2003 to address the needs of patients with the most neglected diseases, DNDi is a collaborative, patient’s needs driven, not for profit drug R&D organization.

Acting in the public interest, DNDi bridges existing R&D gaps in essential drugs for these diseases by initiating and coordinating drug R&D projects in collaboration with the international research community, the public sector, the pharmaceutical industry, and other relevant partners.

DNDi’s primary focus has been the development of drugs for the most neglected diseases, such as Human African Trypanosomiasis (HAT, or sleeping sickness), visceral leishmaniasis (kala-azar), and Chagas disease, while considering engagement in R&D projects for other neglected diseases to address unmet needs that others are unable or unwilling to address.

The primary objective of DNDi is to deliver a total of 11 to 13 new treatments by 2018 for leishmaniasis, sleeping sickness, Chagas disease, malaria, paediatric HIV, and specific helminth infections and to establish a strong R&D portfolio that addresses patient needs. Expanding upon R&D networks built on South-South and North-South collaborations, DNDi aims to bring medical innovation to neglected patients by developing field-adapted treatments.

In doing this, DNDi has two further objectives:
  • Use and strengthen existing capacities in disease-endemic countries via project implementation
• Raise awareness about the need to develop new drugs for neglected diseases and advocate for increased public responsibility.

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

3.2. Project background

Chagas disease (CD), caused by Trypanosoma cruzi (T. cruzi), ranks among the world’s most neglected diseases. In Latin America, 21 countries are endemic for CD with an estimated 70 million people at risk of contracting the disease.

The current treatment for Chagas disease has significant limitations, including long treatment durations, safety and tolerability concerns.

This proof-of-concept evaluation aims to provide further information to develop new therapeutic approaches for CD using different doses and duration of existing drugs, as well as combinations directed at multiple therapeutic targets to improve treatment response and tolerability and reduce the potential for development of resistance.

3.3. Chagas phase 2 clinical trial: Key data

• Indication: Chronic Indeterminate Chagas Disease
• Study design: Double-blind, double-dummy, randomised, prospective, comparative, placebo-controlled, pharmacokinetic-pharmacodynamic and proof-of-concept study design, with nine-parallel groups
• Nb of participating countries 3 countries - 6 sites
• Participating countries: Argentina, Bolivia and Spain
• Nb of subjects planned per site: A competitive recruitment is planned, Sponsor expects three sites high recruiters, around 70 patients each and three low recruiters, 20 patients each
• Recruitment Plan:
  ✔ Nb of subjects to be screened: 1215
  ✔ Nb of subjects to be randomized: 270
  ✔ Nb of subjects completed: 243 -10% of drop-out rate
  ✔ Nb of screen failures: 945
4. SCOPE OF WORK

The scope of this proposal refers only to clinical monitoring activities and services for the participating sites in Argentina within the context of the development of the phase 2 Chagas Trial.

Monitoring activities and services for the other participating countries (sites not located in Argentina) are not part of the scope of this RFP.

4.1. Clinical Monitoring Activities and Services:

4.1.1. General Information

DNDi would like to quote the service of clinical monitoring for the participating sites in Argentina. Three sites are planned, two in the city of Buenos Aires and one in the city of Santiago del Estero (northern of Argentina). All sites have previous experience in clinical trials, a long partnership with DNDi as well as a huge expertise in Chagas Disease.

DNDi expects the sites of Buenos Aires to be lower recruiters than the one in Santiago del Estero. A total of around 110 patients are planned to be enrolled in Argentina (recruitment is competitive, this is an estimate).

Based on these assumptions, DNDi would like to allocate one FTE CRA dedicated for the country. The CRA should be identified based upon therapeutic expertise, experience and geographic location to optimize cost and operational efficiency.

The initial monitoring plan is to conduct 100% source document verification (SDV) in all variables related to primary and secondary endpoints, including pharmacokinetic (PK) sampling timelines, laboratory results and also related to AE/SAE in all visits for the first 10 patients screened in each site. Then, 100% SDV will be performed for all remaining patients enrolled per site and only in regards to: informed consent form, inclusion/exclusion criteria, primary efficacy endpoint, AE and SAE.

4.1.2. Responsibilities

The CRA will be responsible for the clinical monitoring of the project in Argentina in accordance with study specific procedures, applicable SOPs and regulations and will act as DNDi’s direct contact with the assigned clinical sites. Other responsibilities include (but not limited to) source data verification, drug accountability, data collection and regulatory documentation.
The CRA shall report to the DNDi study manager and interact with other study CRAs as part of the sponsor study team. Accompanying visits (co-monitoring visits) by the sponsor personnel are foreseen to follow both site and monitor quality and progress.

4.1.3. Knowledge, Skills and Abilities

- Proven clinical monitoring skills, working knowledge of Good Clinical Practices and applicable Standard Operating Procedures
- Demonstrated understanding of medical/therapeutic area knowledge and medical terminology
- Good oral and written communication skills
- Good organizational and time management skills
- Effective interpersonal skills
- Attention to detail
- Proven flexibility and adaptability
- Ability to work in a team or independently as required
- Good computer skills: good knowledge of Microsoft Office
- Fluency in English and Spanish language and grammar are mandatory. Portuguese is a plus.

4.1.4 Additional Information

The following services should also be considered within the scope of this RFP:

- Design and review of the monitoring plan including, but not limited to:
  - Monitoring visits preparation, conduction
  - Monitoring visits reports requirements and timelines
  - Close-out visits preparation, conduction
  - Close-out visits reports requirements and timelines
  - Investigator study file and Trial master file management, specific forms and logs as per DNDi SOPs
  - Flow and instructions for SAE management as per DNDi SOP and local requirements
  - IMP accountability and reconciliation
- Design and review of the recruitment plan and additional tools to follow / track the recruitment as required
- Development of the study manual in local language (Spanish) under the supervision of the sponsor study manager
- CRA should attend monitoring team meetings and / or study team meetings and investigators meetings
The scope of this RFP does not include any Project Management activity. These activities and role will be performed by DNDi study manager. All activities related to the study management as well as review and validation of the monitoring visit reports and follow-up letters will be reviewed by DNDi manager. Investigators payment and contracts will also be administered directly by DNDi.

4.1.5 Monitoring Workload

Estimate duration for the Monitoring activities: 20 – 22 months.

Estimate of the CRA workload for the country:

<table>
<thead>
<tr>
<th></th>
<th>Initiation Visits</th>
<th>Monitoring Visits (per site)</th>
<th>Close-out Visits</th>
<th>Study TC / VC (between sponsor and site personnel)</th>
<th>Study TC (with sponsor team)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of visits</td>
<td>3</td>
<td>20</td>
<td>3</td>
<td>Weekly during recruitment and then every 3 weeks</td>
<td>Weekly</td>
</tr>
<tr>
<td>Number of hours on site</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of hours Fup</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Monitoring visit interval</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Number of hours Fup</td>
<td>4</td>
<td></td>
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<td>3</td>
<td></td>
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</table>
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.

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
  - Customer references / Experience in related therapeutic area and country
- **Capacity to deliver**
  - Reasonable timelines
  - Project management capabilities
  - Past experience with similar work
  - Profile of staff involved (CVs)
- **Financial criteria**
  - Realistic costing of the proposal with NGO rates when possible

6. PROPOSAL REQUIREMENTS, DELIVERABLES & TIMELINES

6.1. RFP deliverables

Given DNDi’s requirements, describe how your approach and staff will enable your team to meet study timelines, insure quality results, and minimize expenses. Please be sure to include the following information in your proposal:

- **Overall Company profile**
  - Management Board, History, Locations, and contact
  - Key figures (Revenue, headcounts, Locations in Latin America / Bolivia and Argentina)
  - General services provided and specific expertise
  - Similar projects / experience in related area
- **Project approach for required services considering Argentinian legislation**
- **Project management plan**
  - Proposed timelines and organizational structure
  - Deliverables (tools & reports that you intend to supply)
o Associated services (maintenance, support, helpdesk, etc.)
o Proposed method and communication plan

o Proposed business terms and fee schedules to meet timelines and milestones (using the provided budget grid)

o Risk Management Plan to mitigate risks

o Budget with full details of your offer including fixed costs and Pass-Through Costs. Activities performed by subcontractors should be clearly indicated (as well as company names).

o Project team involved

o List of tasks and responsibilities

o Any other relevant information

6.2. Timelines

Beginning of services planned for Q3 2015
Completion of activities planned for Q2 2017

6.3. Additional information

Within the context of the development of the phase 2 trial for CD, DNDi is launching other RFP for the different services needed. Although this RFP refers specifically to clinical monitoring services in Argentina, candidates are allowed to apply to more than one service as long as different proposals are submitted in compliance to each of the RFP.

7. ANNEXES

Annex 1: Intent to Participate letter

Annex 2: Q & A Form

Annex 3: Clinical Service Agreement template

Annex 4: Schedule of Event