Request for Proposal

Electronic Data capture and Data Management activities to support the conduction of a phase 2 trial in Chagas Disease

Dated: 29 June 2015
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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 Electronic Data Capture (EDC) and Data Management Services 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 an 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>
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<tr>
<td>Q&amp;A sent to DNDi</td>
<td>Service Provider</td>
<td>3 July 2015</td>
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<tr>
<td>DNDi responses to Q&amp;A</td>
<td>DNDi</td>
<td>10 July 2015</td>
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<tr>
<td>Reception of proposals</td>
<td>DNDi</td>
<td>17 July 2015</td>
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<tr>
<td>Notification to Pre-selected Bidders</td>
<td>DNDi</td>
<td>22 July 2015</td>
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<tr>
<td>Bid Defense Meetings</td>
<td>DNDi</td>
<td>29 July 2015</td>
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<tr>
<td>Bidder selection</td>
<td>DNDi</td>
<td>1 August 2015</td>
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<tr>
<td>Project Start</td>
<td>Service Provider</td>
<td>Upon contract signature</td>
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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>
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<tbody>
<tr>
<td>Contractual &amp; Technical</td>
<td>Christophine</td>
<td>Procurement</td>
<td>15 Chemin Louis Dunant</td>
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<tr>
<td>Technical aspects</td>
<td>MARTY MOREAU</td>
<td>Manager</td>
<td>1202 Geneva Switzerland</td>
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<td></td>
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<td>Phone:+41 22 906 92 61</td>
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<td></td>
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<td></td>
<td>Email: <a href="mailto:cmarty@dndi.org">cmarty@dndi.org</a></td>
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</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 Service 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 and attached as Annex 4

- 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 purpose of this Request for Proposals (RFP) refers to Electronic Data Capture services within the context of the development of the phase 2 Chagas Trial.

4.1. Electronic Data Capture Services

4.1.1. General Information

DNDi would like to quote the service for the development of a robust electronic CRF (eCRF) for electronic data capture (EDC).

The vendor shall provide EDC study set-up (database, edit checks, testing and review), site set-up (network connectivity and account management), ongoing Help Desk support, system maintenance, as detailed below.

4.1.2. Main activities

- A quote for e-CRF system development in English and a quote for the development in Spanish is required – as the participating countries are Spanish speaking, the preferred language should be Spanish
- e-CRF Completion Guidelines
- User acceptance test
- e-CRF training: in additional to the completion guideline, training of Sponsor and Sites personnel via web-based / investigators meeting is required
- Hot line (helpdesk) for users support required (Spanish is preferred, if not possible - English)

4.1.3. CRF Design

- Total nb of CRFs pages per patient: 7891 pages
- Nb of schedule CRF pages/screen failure patient: 16 pages
- Nb of schedule CRF pages/discontinued patient: 44 pages
- Nb of schedule CRF pages/completed patient: 91 pages
- Nb of queries* per patient: 1.5 per e-CRF visit ( 34 per patient)
(*Any discrepancy that requires interaction with the investigator’s site including those raised for confirmation of data values)
- Expected Terms Requiring Medical Coding per Enrolled Patient: 20
- Edit checks (automatic queries) are required: expected number: 300
- e-CRF reports and e-CRF queries:
To support the study management and follow-up
- Reports can be suggested by the vendor, according to current practice
- It is preferred that the reports can be generated and exported by the sponsor study team (as many times as needed)
- Example of reports: center recruitment, study enrollment, adverse events, SAE, cleaning status, patient status.
- Reports should be ready for implementation since e-CRF set-up in order to follow the study progress
- e-CRF Queries reports: e-CRF report for queries status and progress required

4.1.4. Additional Information
- Please specify the number of licenses provided and value for additional licenses
- The different levels of access to database (eCRF), i.e, investigator, site coordinator, data entry, CRA, medical reviewer, data manager
- Is a training database available before the study set-up and during the entire study?
- Does the system support for partial SDV and for blind review (interim data base lock)? If positive, how does it work?

4.2. Data Management Services

4.2.1. General Information

Data management systems must be compliant with 21 CFR Part 11. Data capture will be conducted electronically using Electronic Data Capture.

4.2.2. Main activities

A summary of the main activities is detailed above (list not exhaustive):
- Data Cleaning
- Data validation
- Preparation and review of data prior to the database lock
- Coding of adverse events, concomitant medications and medical history (latest versions of MedDRA and WHODrug)
- SAE Reconciliation
- Data Imports from External Vendors / Data Transfers
- Data Management Plan
- Data Validation Plan
- Data Monitoring Committee (DMC):
  - Charter development
  - Schedule and coordinate DMC meetings (3 meetings planned):
To coordinate meeting logistics (travel, hotel, catering etc.) as needed
To prepare tables and listings to incorporate into the DMC review packets and to prepare electronic meeting review packets (blinded and unblinded) for DMC members
To prepare the meeting minutes (open and closed session) and to distribute the meeting minutes and recommendations in accordance to Charter requirements

DNDi will be responsible for DMC member selection and payment management and this is not part of the scope of the DM activity.
Although safety services and medical monitoring are not under the scope of this RFP, two reconciliations between Safety Database and Clinical Database are planned and must be considered.

4.2.3. Additional Information:
DNDi would like to have additional information, as follows:
• Detailed steps and timeframes to allow DNDi to understand the DM services offered
• It is not mandatory that the designs and development of the eCRF platform and the DM services are offered by the same provider. Therefore, DNDi would like to confirm if those services can be provided in separate (as a standalone service) or not
• How long is required before first patient in to conduct EDC setup?
• After the last patient last visit how long does it take to lock the study database?

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
  o Project approach, methodology and planning
  o Experiences/skills, level of company representatives assigned to this project
  o Quality and applicability of proposal presentation
  o Customer references / Experience in related therapeutic area and country
• Capacity to deliver
  o Reasonable timelines
  o Project management capabilities
  o Past experience with similar work
  o Profile of staff involved (CVs)
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

- Project management plan
  - Proposed timelines and organizational structure
  - Deliverables (tools & reports that you intend to supply)
  - Associated services (maintenance, support, helpdesk, etc.)
  - Proposed method and communication plan

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

- Risk Management Plan to mitigate risks

- 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). We recommend the use of DNDi template inserted as Annex 4

- Project team involved

- List of tasks and responsibilities
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 EDC services, 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: Budget template
Annex 5: Schedule of Events