Łomianki, 20.03.2017r.

Purchaser:

Celon Pharma S.A.
Mokra 41A
05-092 Łomianki / Kiełpin
tel.: +48 22 751 74 78
fax: +48 22 751 74 77
KRS: 0000437778
NIP: 118 - 16 - 42 - 061
e-mail: dominika.kasprowiak@celonpharma.com

REQUEST FOR QUOTATION (RfQ)no. 04/2017/M/AMDBP

In relation to the planned initiation of the project: *AMDBP* – aiming to develop the innovative production technology and evaluation of novel Fab biosimilar dedicated for ADM therapy by Celon Pharma S.A. as part of the contest in the sectoral program dedicated to support to R&D endeavours in the pharmaceutical sector and increase research results commercialisation in neuromedicine and pharmacy sector – INNONEUROPHARM (hereinafter "the Project"), we hereby request your quotation for:

Conducting the following subcontracted tasks aiming to develop of scalable up and downstream process together with production and release of non-GMP\GMP bathes for TOX and clinical studies of Fab fragment in CHO expression system, necessary to complete the Project:

A. Process scale-up:
- Feasibility study of the existing laboratory scale up and downstream process,
- Fermentation process scale up to small bioreactors (1 – 10 L);
- Fermentation process optimisation (clone/ feeding regimen/ bioprocess conditions-combination);
- Purification (DSP)-development optimization;

B. WCB\MCB manufacturing and characterization:
- Generation and characterisation of WCB\MCB in accordance with: CPMP/ICH/139/95; CPMP/ICH/294/95;CPMP/ICH/295/95 and EMEA/CHMP/BWP/398498/2005 guidelines,
- Manufacture up to 250 vials on bank,
- MCB full characterization, compatible with EU and US regulatory requirements;
- Generation of all related documentation for the bank;
- Delivery of characterization protocols and final reports;
- Stability data delivery;
- Certificate of analysis delivery,

C. Analytical methods development, validation and qualification:
- Development and validation of in process control methods,

- Validation and qualification od the final DS and DP release and stability indicating methods, fulfilling EMA guidelines for biosimilar : HIC-HPLC; clEF; SDS-PAGE (reduced); SDS-PAGE (non-reduced); Binding Assay; SEC-HPLC; N-terminal sequence; Western; Disulfide Bond w/ Free thiol; Intact Mass Spec; Peptide Map; HCP Assay (process impurities); HC-DNA Assay (process impurities); Endotoxins; Bioburden; Sterility;

D. DP Pre-formulation development:

- Preparation of 3 formulation buffers feasible for the intraocular or ocular administration;

E. DS short-term stability screening (3 months); 24 months stability studies (DS and DP):

- execute a short-term (up to 3 months) stability study;
- execute a short-term (up to 3 months) stability study including accelerated conditions;
- studies should be performed for the DS in its final elution buffer;

F. Scale-up and engineering run\ GMP run:

- Preparation of BPRs, SOPs and other production related documentation;
- Perusing of the bio fermentation process in single use 250 L scale bioreactor, generation of the full reports;
- Production and release of the non-GMP DS material for TOX studies, generation of the full process report;
- Analysis of the material, stability studies and issue of the Certificate of Analysis;

G. DP manufacturing, fill and finish and product release for clinical studies,

- Manufacturing of the Drug Substance for Phase I clinical studies – GMP,
- Preparation of all supporting GMP documentation – required by EMA according to: guidelines;
- Analysis of the material, stability studies and issue of the Certificate of Analysis;
- Preparation of DP (300-400 syringes\injectors) required for clinical studies;
- Preparation of DP (syringes\injectors) required for QC-testing and stability-studies;
- Generation and preparation of all GMP manufacturing supporting documentation including complete batch production records and analytical protocols;
- Delivery of DP specification in accordance to ICH, EMA guidelines;
- Issue of bath certificate;

Additional information:

- The planned studies program will be conducted in accordance with both Good Manufacturing Practices (GMP) and Good Laboratory Practice (GLP).
- The planned studies program will be conducted in accordance with The European Medicines Agency's scientific guidelines on the non-clinical testing of medicines.
- The English language must be used for all purposes in preparing documents and reporting.
- Further details of the request for quotation will be presented to the Bidder once the confidentiality clause is signed.

Requirements to be met by bidders:

1. The Bidder must sign the Mutual Confidentiality and Nondisclosure Agreement with the Purchaser to get details enabling to create a required bid.
2. The Bidder should demonstrate the ability to conduct the study referred to in this RfQ in the shortest possible term. *Submission of Bidder's experimental time schedule (time plan) is required.* This is to include the estimated commencement date of the first study to the estimated primary completion date of the studies program. The signing of the contract is planned after receiving the funding form INNONEUROPHARM program – contract signature with the funding agency NCBiR.
3. The Bidder should hold all licences required by law to deliver the subject of the order.
4. The Bidder should have the necessary experience and potential to deliver the subject of the order. Submission of the confirmed references form 3 pharmaceutical companies concerning the experience in similar studies are highly recommended.
5. The Bidder should have the necessary technical and laboratory infrastructure to conduct the studies referred to in this RfQ and be able to conduct the selected studies in accordance with GLP.
6. The Bidder should demonstrate it has scientific personnel specialised in areas related to the subject of this RfQ. *Submission of Bidder's folder, presentation or monograph is allowed*.
7. Furthermore, the Bidder should demonstrate experience in the form of research and development projects implemented over the last 5 years. *Submission of Bidder's folder, presentation or monograph is allowed.*
8. "The Statement on absence of personal or capital ties with the Purchaser" should be submitted along with the bid.
9. Unless otherwise stated, all invoices will be payable within 30 days of the date of issuance of the invoice.
10. Finally, the Bidder's financial and economic position should ensure successful implementation of the order.

Address and date for submitting the bids:

11. Bids must be submitted to the purchaser's office at ul. Mokra 41a, 05-092 Kiełpin, if sent by traditional mail or by currier, or to dominika.kasprowiak@celonpharma.com if sent by electronic mail.
12. Bid must be submitted by 30.03.2017 at the latest. If sent by traditional mail or courier, the bid is deemed to be submitted on the day of its delivery to the purchaser's office.
13. Bids submitted after the aforementioned date will not be considered.
14. Bids will be evaluated at the Purchaser's office by 03.04.2017.
15. The final decision will be communicated to all Bidders by electronic mail and published on the website: http://celonpharma.com/category/zapof/, on 03.04.2017.

16. For further information on the Project, please contact dr Jerzy Pieczykolan, email: jerzy.pieczykolan@celonpharma.com.
17. This request for quotation is available at: http://celonpharma.com/category/zapof/

Presentation of the bids:

18. Each Bidder may submit only one bid.
19. The bid must be in English.
20. The bid must show the date of preparation, the Bidder's address, telephone number, email address, tax ID number NIP (if available).
21. The bid must include the RfQ no. in the title. The RfQ no. must also appear in the titles of electronic, traditional and courier mail.
22. The bid must remain valid for at least 3 months counted from the submission deadline.
23. The bid must contain:
    a. The price:
        i. should be presented for each single planned study including total price for this study excluding procedures specified in the section "Additional procedures to the above outline", which are to be priced separately (according to the Detailed Studies Scope – available after signing the confidentiality clause),
        ii. if submitted by a Bidder operating in Poland, the gross and net bid price and due VAT bided for delivery of the subject of the order on accordance with the requirements set forth herein,
        iii. if submitted by a Bidder operating outside Poland, the net bid price and information that not VAT or other taxes have been included in the price quotation.
    b. Iinformation about the proposed study program in accordance with a *Detailed scope of the studies*, available only after the signature of confidentiality clause.
    c. Declaration that the Bidder has scientific experience and personnel specialised in areas related to the subject of this RfQ. *Submission of Bidder's folder, presentation or monograph is allowed*.
    d. Declaration that the Bidder has the ability to conduct the studies referred to in this RfQ in 2017. *Submission of Bidder's experimental time schedule (time plan) is required.*
    e. The Statement on absence of personal or capital ties with the Purchaser should be submitted along with the bid.
24. Costs of preparing the bid shall be borne by the Bidder.

Note:

25. The Purchaser will place the order with the bidder whose bid meets all the requirements set forth in this RfQ and is deemed the best relative to the selection criteria set forth herein.
26. When substantiated, the purchaser reserves the right to cancel the bidding process.

27. The Purchaser reserves the right to close the bidding process without selecting the successful Bidder. The Ordering party is not bound to give the reason for closing the procedure.
28. In the course of evaluation and assessment of the bids, the Purchaser may request that the bidders provide clarifications regarding their bids. In such a case, the Ordering party reserves the right to postpone the final evaluation and notification about the evaluation of quotes.
29. The Bidder may alter or withdraw its bid before the submission deadline.
30. Bids submitted past the submission deadline will not be considered.
31. Bids that do not meet the formal requirements set forth herein will not be considered.
32. The Purchaser accept variant bids. The proposed studies program shall be conducted in accordance with the guidelines of the European Medicines Agency.
    The Provider, offering a method of testing the TI which is equivalent to the testing method described in the request for quotation, is obligated to prove, on the basis of available experimental data and a written declaration, that the study it offers (each study individually) is equivalent to the study described in the request for quotations and fulfils the requirements to obtain the necessary results in accordance with the guidelines of the European Medicines Agency without requiring additional steps, including, for example, bridging studies.
33. The Purchaser accept partial bids. Information on partial bids:
    a. In this tender procedure, the Ordering Party accepts partial bids.
    b. The Contractor may submit a bid for a selected part of the order, any selected parts of the order or all parts of the order.
    c. Each part of the order is autonomous. In each single procedure, the Ordering Party will apply the above said provisions separately to each respective part, i.e. actions regarding, but not limited to, exclusion from the procedure, rejection of a bid, selection of the most advantageous bid and invalidation of the procedure shall be made separately for each respective part.
    d. The Ordering Party shall sign a contract with the Contractor that has submitted the most advantageous bid for a respective part of the tendering procedure.
34. The Purchaser permits rejecting bids whose essential content clearly raises reasonable doubts.
35. The absence of submission of the experimental time schedule (time plan) both with the estimated commencement date of the first study and the estimated primary completion date of the studies program is the base to reject the application and grant 0 points for the subsequent evaluation criteria.

The successful bid will be selected on the basis of the following criteria:

No.	CRITERIA	WEIGHT IN %
1.	Price	50
2.	Time	50

Points scoring systems during selection process will be as follows:

No.	CRITERIA	Points scoring system
1.	Price	**Price "P" – 100 pkt (weight of criterion 50%)** Scoring in the price criterion will be as follows: the lowest price for conducting all studies proposed by the Tenderer will be considered 100%, which is the maximum number of points. The points will be given based on the formula: $$\frac{Price_{lowest}}{Price_{service}} \times 100\ pkt$$ Where: $Price_{lowest}$ – the lowest price among quotes. $Price_{service}$ – price for the given tenderer. ***Criterion "P" = number of points x 50% (weight of criterion)***
2.	Time	**Time "T" – 100 pkt (weight of criterion 50%)** 100 pkt - will be given to the Bidder who will provide the earliest estimated primary completion date of the studies program. The next Bidders will receive 100 pkt with subtracted 3 pkt for every week of delay in completion date of the studies program compared to the earliest one. If the estimated primary completion date of the studies program will be later than 34 weeks compared to the earliest one, the Bidder will receive 0 pkt. ***Criterion "T" = number of points x 50% (weight of criterion)***

The final score will be calculated by substituting the data obtained above to the following formula:

Total points = *Criterion "P" + Criterion "T" + Criterion "R"*