Kiełpin, 8th Oct 2020

Purchaser:

Celon Pharma SA
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Request for Quotation no. 3/2020/M/LINDA

In connection with Celon Pharma S.A.'s project: "Second phase clinical evaluation and response predictive markers verification for CPL500036 – a novel PDE10 inhibitor in therapy of L-DOPA induced dyskinesias in Parkinson's disease" (LINDA) within the Smart Growth Operational Programme 2014-2020 (Program Operacyjny Inteligentny Rozwój), we invite you to submit bids for:

> Development and validation of an analytical method and quantitative analysis of one analyte in human plasma samples from phase II clinical trial patients with levodopa-induced dyskinesia in Parkinson's disease.

The order includes the development and validation of an analytical method for the quantitative analysis of analyte (CPL500036) in human plasma using the LC/MS/MS method (liquid chromatography – tandem mass spectrometry) and analysis of human plasma samples phase II clinical trial patients after multiple dose administration of Investigational Medicinal Product – PG20

CPV code: 73000000-2
Research and development services and related consultancy services

A detailed description of the order:

The order consists of two parts: 1) development and validation of an analytical method for quantitative analysis of analyte in human plasma samples, 2) quantitative analysis of human plasma samples from phase II clinical trial patients after multiple dose administration in levodopa-induced dyskinesia in Parkinson's disease.

Detailed descriptions of the activities are presented in the table below.

Development and validation of an analytical method for the quantitative analysis of analyte in human plasma samples.	
Analyte	CPL500036 (molecular formula: $C_{13}H_{16}ClNO$)
Analytical method	LC/MS/MS
Matrix	Human plasma
Compliance	Good Laboratory Practice (GLP) Based on the 'Guideline on bioanalytical method validation' (July 2011; EMEA/CHMP/EWP/192217/2009) of the European Medicines Agency (EMA) and the 'Guidance for Industry. Bioanalytical Method Validation' (May 2001) of the U.S. Food and Drug Administration (FDA).
Quantitative analysis of analyte in human plasma samples from phase II clinical trial patients with levodopa-induced dyskinesia in Parkinson's disease	
Analyte	CPL500036
Analytical method	LC/MS/MS with the validated method
Matrix	Human plasma
Compliance	Good Laboratory Practice (GLP) Based on the 'Guideline on bioanalytical method validation' (July 2011; EMEA/CHMP/EWP/192217/2009) of the European Medicines Agency (EMA) and the 'Guidance for Industry. Bioanalytical Method Validation' (May 2001) of the U.S. Food and Drug Administration (FDA).
Number of samples	Samples will be delivered in the time intervals indicated by the Purchaser based on the description of procedures regarding blood samples for clinical centers that will carry out the clinical

	trial, prepared by the Bidder (mainly based on the stability of analyte in the plasma). For example, samples will be delivered to the Bidder at the end of each 3-month period in the number of samples collected by centers from recruited patients. The analysis of samples should also take place in intervals set with the selected Bidder, regardless of the number of samples that will be delivered to the Bidder during this period. Total number of samples from the study: approx. 2800
Incurred sample reanalysis (ISR)	The ISR number will depend on the number of samples analyzed for a given time interval and should be in accordance with the EMA and FDA guidelines. For the purpose of this request for quotation, a reanalysis of 10% of the total number of samples, i.e. 280 ISR, should be considered. The total number of samples re-analysis (ISR) needed will be known during the study's progress.
Internal standard	The necessity of use internal standard and its type will be determined after selection of the winning bid.
Sample handling	The Bidder is obliged to prepare the sample handling procedure for the clinical centre which will be conducting the clinical trial.
Blood volume per sample	The maximum blood volume per one sample for quantification of analyte will not exceed 5 mL.
Sample storage	The minimum sample storage time to be included in the quotation – 3 months following the delivery of the final report. This time applies both to primary and back-up samples, which will be delivered to the Bidder at specified time intervals. A possible longer storage period, if needed, will be discussed with the chosen Bidder as part of an additional order.
Documentation archiving	The minimum time for the study documentation archiving to be included in the quotation – 5 years. A possible longer archiving period, if needed, will be discussed with the chosen Bidder as part of an additional order.
Final report	The final analytical report with results of all sample analysis from study with one draft report for the Purchaser's approval.

Partial results	The Bidder will be obliged to provide partial results of the samples' analyses from a given time interval.

Additional information:

- The planned study will be conducted with the use of CPL500036, which is small molecule classified as phosphodiesterase inhibitor 10a
- Samples (primary and background) will be sent to the selected Bidder at designated time intervals (eg. in 3-month intervals regardless of the number of collected samples depending on the number of recruited patients in the period preceding the dispatch). The analysis of samples should also take place in intervals set with the selected Bidder, regardless of the number of samples that will be delivered to the Bidder during this period. The Bidder will be required to provide the results of the analysis of samples from a given time interval.
- The lower limit of quantification (LLOQ), for analyte should be low, approx. below 2 ng/mL of plasma. The method validation should be based on the 'Guideline on bioanalytical method validation' (July 2011; EMEA/CHMP/EWP/192217/2009) of the European Medicines Agency (EMA) and the 'Guidance for Industry. Bioanalytical Method Validation' (May 2001) of the U.S. Food and Drug Administration (FDA).
- Incurred sample reanalysis, in accordance with EMA and FDA guidelines, should be performed for the % of samples accordingly to their number.
- All reports, interim and final, including all study documentation must be prepared in English.
- Sample transport costs will be borne by the Purchaser.

Requirements to be met by Bidders:

1. Bids can be submitted by Bidders who meet the following requirements:
   - The Bidder must run a business with the capacity of conducting the activities which are the subject of the order and possess the current Good Laboratory Practice Certificate (GLP).
   - The Bidder must have the necessary technical and laboratory infrastructure to conduct the study referred in this RFQ and be able to conduct study in accordance with Good Laboratory Practices (GLP).
   - The Bidder must have experienced personnel specializing in areas related to the subject of this RFQ.
   - The Bidder must have at least 5 years of experience in development and validation of analytical methods, as well as in the quantitative analysis of analyte in clinical trial samples.
   - The Bidder's financial and economic situation should ensure successful implementation of the order and there cannot be any indications suggesting that this situation will change during the period covered by the agreement. The Bidder is not subject to insolvency proceedings initiated, nor his bankruptcy has not been declared, is not subject to liquidation proceedings,

and his cases are not covered by a receivership or court order. The Bidder is not behind with taxes, fees or social insurance or health insurance contributions.

2. Excluded from the proceedings shall be those Bidders who are personally or equity related to the Ordering Party. By personal or capital ties the interactions between the Purchaser or persons authorized to enter into commitments on behalf of the Purchaser, or persons performing activities related to the preparation and the procedure for selecting the Contractor on behalf of the Purchaser and the Contractor, are meant, in particular, trough:
   - Participation in the company as a shareholder or partner,
   - Possession of at least 10% of the shares, unless a lower threshold arises from the law or has been defined by the Managing Authority for Operational Programs,
   - Acting as a member of the supervisory or management board of the company or the proxy or the attorney,
   - Remaining married, in a consanguinity or affinity relationship in a straight line (parents, children, grandchildren, in-laws, son-in-law), the collateral line to the second degree (siblings, spouse relatives) or remain in the relationship of adoption, custody or guardianship.
3. The due date for each issued invoice should be at least 30 days.

Address and date for submitting the bids:

4. Bids must be submitted to the Purchaser's HQ office at Ogrodowa 2A Street, 05-092 Kiełpin/Łomianki if sent by traditional mail/courier, or to anna.zalecka@celonpharma.com if sent by electronic mail.
5. Bids must be submitted by **23.10.2020 till 12:00 (CET)** at the latest. If sent by traditional mail or courier, the bid is deemed to be submitted if day of its delivery to the Purchaser's HQ is no later than on day indicated as the final date for Bid submission.
6. Bids submitted after the aforementioned date will not be considered.
7. For further information on this RfQ, please contact Ms. Marta Panek, e-mail: marta.panek@celonpharma.com.

Bid results:

8. Bids will be evaluated at the Purchaser's office by **04.11.2020.**
9. The final decision will be forwarded to all Bidders via email up to and including **06.11.2020** as well as published in the Competitiveness Base: https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl/

Presentation of the bids:

10. Each Bidder may submit only one bid.
11. The bid must be prepared and presented in Polish or English.
12. The bid must contain the date of preparation, the Bidder's address, telephone number, email address, tax ID number (NIP number in Poland) (if available).
13. The bid should include the RFQ No. in the title. The RfQ No. should also appear in the titles of emails, headings of traditional mail and headings of consignments sent by courier.

14. The bid must remain valid **for at least 9 months** counted from the submission deadline.
15. Costs of preparing the bid shall be borne by the Bidder.
16. The bid should be initialled and signed by persons authorized to represent the Bidder.
17. The bid must contain:
    a. The price:
        i. Total price for the aforementioned study should be presented specifying the prices for each part: development and validation of the analytical method, analysis of human plasma samples from multiple dose administration of phase II clinical trial in levodopa-induced dyskinesia in Parkinson's disease. It is possible that circumstances independent of the Purchaser will occur and will lead to changes in the study protocol, change the number of patients. In this case, there might be a change in number of samples. Therefore, apart from the total price for the study, a unit price per sample analysis should also be presented and should be a fixed, even in case of changes in the number of samples. The price can be expressed in PLN, EUR or USD. For the purpose of comparing the submitted pricing offers, the offer prices will be converted into PLN according to the average exchange rate of the National Polish Bank applicable on the day on which this Request for Quotation is published.
        ii. If submitted by a Bidder operating in Poland, the gross and net bid price and the due VAT offered for the delivery of the subject of the order in accordance with the requirements set forth herein.
        iii. if submitted by a Bidder operating outside Poland, the net bid price and information that VAT or other taxes have not been included in the price quotation.
    b. Execution time including completion time for development and validation of the analytical method. If the Bidder already has a validated method, this time can be accepted as one.
    c. Declared low limit of quantification (LLOQ) for analyte.
    d. A copy/scan of the current Good Laboratory Practice Certificate.
    e. The statement of compliance with the requirements (Attachment 1):
        i. The Bidder runs a business with the capacity of conducting the activities which are the subject of the order.
        ii. The Bidder has the necessary technical and laboratory infrastructure and has an experienced personnel specializing in areas related to the subject of the order to conduct the study in accordance with Good Laboratory Practices (GLP).
        iii. The Bidder has at least 5 years of experience in development and validation of analytical methods as well as in the quantitative analysis of analyte in clinical trial samples.
        iv. The Bidder's financial and economic situation ensures successful implementation of the order and there are no indications suggesting that this situation will change during the period covered by the agreement. The Bidder is not subject to insolvency proceedings initiated, nor his bankruptcy has not been declared, is not subject to liquidation proceedings, and his cases are not covered by a receivership or court order. The Bidder is not behind with taxes, fees or social insurance or health insurance contributions.

f. The Statement on the absence of personal or capital ties with the Purchaser should be submitted along with the bid (Attachment 2).
g. A copy/scan of the Bidder's current Registration Document.

Note:

18. The Purchaser will place an order with the Bidder whose bid meets all the requirements set forth in this RFQ and has been deemed the best with regard to the selection criteria set forth herein. The signing of the agreement is planned for the QIV of 2020. The expected order execution time – approx. 18 months from the time the Purchaser obtain the last of the two: approval for the clinical trial from the competent regulatory authority or the positive opinion of the competent Bioethical Committee.
19. The Purchaser reserves the right to prolong the expected order execution, which will be directly related to the extension of the duration of the clinical trial.
20. The Purchaser allows the possibility of negotiating with Bidders who submit offers in the bidding process before the selection of the winning bid.
21. The Purchaser reserves the right to cancel the bidding process.
22. The Bidder reserves the right to close the bidding process without selecting the winning Bidder. The Purchaser is not obliged to give the reason for closing the procedure.
23. In the course of evaluation and assessment of the bids, the Purchaser may request that the Bidders provide clarification regarding their bids. In such a case, the Purchaser reserves the right to postpone the final evaluation and notification about the evaluation of quotes.
24. The Purchaser may alter or withdraw its bid before the submission deadline.
25. Bids which do not meet the formal requirements set forth herein will not be considered.
26. The Purchaser does not accept variant bids.
27. The Purchaser does not accept partial bids.
28. The Purchaser reserves the right to reject bids the contents of which raise reasonable doubts.

Conditions for introducing changes in the agreement concluded as a result of the conducted RfQ procedure - in case it is necessary to introduce such changes:

29. The Bidder selected on the basis of conducted RfQ procedure will be obligated to enter into the agreement on terms set out in the present RfQ.
30. The Purchaser reserves the right to make changes to the provisions of the contract in relation to the content of the offer, based on which the selection of the Bidder was made when there are circumstances independent of the Purchaser, forcing such changes, like opinions of the Bioethical Committee, recommendations of the competent regulatory authority or European Medicines Agency - forcing changes in the Study protocol or changes in therapy standards or unexpected deterioration in the health of the study participants.
31. If there is a need to change the original plan of any of the clinical trial, change the number of patients (affecting the number of samples analyzed), the total number of samples may change, therefore the total price of the order. The unit price per sample and the price for the

development and validation of the analytical method should not change. Due to the need for shipment and analysis of samples at specific time intervals, the total number of sample revisions (ISR) needed will be known only when analyzing the last samples from a given study. This should also not affect the unit price per sample.

32. In the above cases the introduction of the necessary changes will be limited to:
    a. Introducing changes providing for the performance of additional services by the Bidder, not covered by the basic contract, provided they are necessary and that the following conditions are met:
        i. The change of the Bidder cannot be made due to economic or technical reasons, in particular regarding the interchangeability or interoperability of the equipment, services or installations ordered in relation to the basic contract.
        ii. The change of the Bidder would cause a significant inconvenience or a substantial cost increase to the Purchaser.
        iii. The value of any subsequent changes does not exceed 50% of the basic contract value.
    b. Introducing changes which do not lead to a change in the nature of the contract; the following conditions must be met:
        i. The necessity to introduce the change is due to circumstances which the Purchaser, acting with due diligence, could not have predicted.
        ii. The value of the change does not exceed 50% of the basic contract value.
    c. Introducing changes that do not lead to a change in the nature of the contract and the total value of changes is less than the value specified in provisions issued based on Article 11 Paragraph 8 of Public Procurement Law, and at the same time is less than 10% of the basic contract value.
    d. Changes introduced cannot lead to a change in the nature of the contract.
33. Any changes to the contract must be made in writing, otherwise being null and void.

Contractual penalties

34. If the declared time of development and validation of the analytical method is exceeded by at least 30 days, the Bidder will pay the contractual penalty for exceeding the deadline, in the amount of 5% of the net value of this part of the order, and then another 5% of net value for each subsequent 20 days of delay. In the event of non-performance and / or improper performance of the duties by the Bidder (resulting from the Bidder's fault) specified in the contract, the Bidder shall pay the Ordering Party a contractual penalty in the amount of PLN 10 thousand net for each case of infringement.
35. The Purchaser will also have the right to withdraw from the contract if the Bidder fails to comply with its terms, including in particular in the case of:
    a. not to provide services within the period specified in the contract;
    b. delivering the subject of the contract that does not comply with the requirements set out in the contract and its annexes.

If the Purchaser exercises its right to withdraw from the contract referred to above, the Bidder will be obliged to pay the Purchaser a contractual penalty of 5% of the net offer price.

36. Termination of this contract may only occur for important reasons. As an important reason justifying the termination of this contract, the parties consider in particular:
    a. lack of cooperation between the parties preventing or significantly hindering the implementation of the provisions of this contract;
    b. gross violation by a party of its basic obligations under this contract.
37. Contractual penalties will be charged on the basis of the Purchaser's encumbrance note delivered to the Bidder. The Purchaser shall be entitled to offset contractual penalties against the payments due to the Bidder.
38. The Purchaser has the right to claim damages based on general principles in the amount exceeding contractual penalties.
39. Contractual penalties will be paid within 7 days from the debit note receipt date.
40. Bidders applying jointly for the contract have joint and several liabilities for the performance of the contract and are jointly obligated to ensure its proper performance.

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

No.	Criteria	Weight in %
1.	**TOTAL PRICE**	**50**
2.	**COMPLETION TIME FOR DEVELOPMENT AND VALIDATION OF THE ANALYTICAL METHOD (1 ANALYTE)**	**30**
3.	**LOW LIMIT OF QUANTIFICATION (LLOQ)**	**20**
	TOTAL:	**100**

The scoring system in the selection process will be as follows:

No	Criteria	Points scoring system
1.	**PRICE**	**Price "P" – 50 points (weight of criterion - 50%)** Scoring rules in the price criterion will be as follows: The lowest price for conducting all study proposed by the Bidder will be considered 100%, which is the maximum number of points. The points will be given based on the following formula: $\frac{Price_{lowest}}{Price\ _{of\ the\ Bidder}} \times 50\ pts$

		Where: Price $_{lowest}$ – the lowest price among quotes. Price $_{of\ the\ Bidder}$ – total price for the given Bidder. Price "P" is considered as the total net price, meaning the sum of all costs for all parts of the order. The unit price for a single sample analysis should also be included in the offer.
2.	**COMPLETION TIME FOR DEVELOPMENT AND VALIDATION OF THE ANALYTICAL METHOD**	**"T" time – 30 points (weight of criterion - 30%)** Scoring rules in the "T" time criterion will be as follows: The shortest time for development and validation of the analytical method proposed by the Bidder is considered 100%, which is the maximum number of points. Points will be awarded based on the following formula: $$\frac{Time_{shortest}}{Time\ _{of\ the\ Bidder}} \times 30\ pts$$ Where: Time $_{shortest}$ – the shortest time among quotes. Time $_{of\ the\ Bidder}$ – time for the given Bidder. Time "T" is considered as a total time needed for the development and validation of the analytical method . If the Bidder presented time in units other than Days, for the purpose of this request for quotation, it is assumed that 1 month = 30 calendar days. If the Bidder already has a validated method, this time can be accepted as one.
3.	**LOW LIMIT OF QUANTIFICATION (LLOQ)**	**LLOQ "Q" – 20 points (weight of criterion - 20%)** Scoring rules in the LLOQ "Q" criterion will be as follows: • 20 points – if the declared LLOQ for the given analyte is ≤ 2 ng/mL of plasma, inclusive, • 10 points – if the declared LLOQ for the given analyte is 2 ng/mL < LLOQ ≤ 5 ng/mL of plasma, inclusive, • 0 points – if the declared LLOQ for the given analyte is > 5 ng/mL of plasma, inclusive.

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

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

Attachments to the Request for Quotation:

Attachment 1 - *The Statement of compliance of the Bidder with the requirements defined in the request for quotation.*
Attachment 2 - *The Statement on absence of personal or capital ties with the Purchaser.*

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Registering body: District Court for the Capital City of Warsaw,
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KRS number: 0000437778
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