

Warsaw, 12/02/2018

REQUEST FOR PROPOSAL 11/2018 - STRATEGMED/ARG

I. ZAMAWIAJACY

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II. OBJECT FOR THE REQUEST:

Manufacturing of the Active Pharmaceutical Ingredient – OATD-02 in compliance with Good Manufacturing Practice (cGMP)

The order carried out as a part of the projects titled:

- **STRATEGMED:** DEVELOPMENT OF NEW THERAPIES BASED ON THE STIMULATION OF ANTI-CANCER ACTIONS OF THE IMMUNE SYSTEM (STRATEGMED2/265503/3/NCBR/15)
- **ARG:** „PRE-CLINICAL AND CLINICAL DEVELOPMENT OF ARGINASE INHIBITOR FOR APPLICATION OF ANTI-CANCER IMMUNOTHERAPY” (POIR.01.01.01-00-415/17)

co-financed by the National and European Union Funds and because of the competitiveness principle

III. THE FORM OF THE ORDER:

- III.1 The request is not made under The Public Procurement Law (Journal of laws of 2013, item 907 as mentioned).
- III.2 This order is carried out in accordance with the principle of competitiveness, openness, transparency and equal access.
- III.3 The Ordering Party reserves the right to cancel this procedure without providing reasons and also to complete the procedure without choosing the winner tender.
- III.4 In the course of examination and evaluation of the offers the Ordering Party may require Contractors to present explanations concerning the content of submitted bids.
- III.5 The Ordering Party reserves the right to change the content of this request. If the changes can affect the content of tenders submitted in the procedure, the Ordering Party shall extend the tender submission deadline. Any changes made shall be provided promptly to all tenders to which the request was sent and shall be binding on them.
- III.6 This procedure does not set the obligation for OncoArendi Therapeutics SA to sign any formal contracts.
- III.7 It is not possible to make and offer for part of order.

IV. CONDITIONS FOR PARTICIPATION IN THE PROCEEDINGS:

IV.1 The Request for offers relates to potential Contractors whose scope of business activity is in full compliance with the subject of this Request.

IV.2 The offers may be issued by parties who:

A) Have the necessary qualifications to carry out the described activity and have the appropriate technical potential and personnel capable of performing the contract.

- In terms of knowledge and experience, the Ordering Party requires that the Contractor:

has documented experience in providing services related to the synthesis of low-molecular organic compounds under the GMP standard, intended for the phase I of clinical trials at the request of third parties. The Ordering Party requires that the Contractor has experience in conducting multi-stage syntheses of organic compounds, optimizing reactions and increasing their scale.

- In terms of human resources, the Ordering Party requires that the Contractor should have and engage for the implementation of the Contract:

1. Project Manager, who will be responsible for coordinating all activities related to the implementation of the project and effective communication with the Ordering Party. The Ordering Party requires that the manager planned to be involved has several years of experience in coordinating projects carried out on behalf of third parties.

2. Experienced Organic Chemist, who will be responsible for the implementation of the contract, including among others for planning experiments and analyzing obtained results. The Ordering Party requires that the specialist planned to be involved should have a doctorate in chemical sciences and documented experience in conducting and optimizing the synthesis of organic compounds on a kilogram scale.

3. Experienced Analytical Chemist, who will be responsible for the implementation of the contract, including, among others for transferring of the analytical methods received from the Ordering Party and their implementation and validation. The Ordering Party requires that the specialist planned to be involved has documented experience in the development and validation of methods of analysis of organic compounds.

4. A qualified person (QP) with the authority to release an active substance in accordance with ICH guidelines.

- In terms of equipment, the Ordering Party requires that the Contractor should have:

1. Glass reactor with a volume of min. 10 L with a double heating and cooling jacket enabling the reaction to be carried out at a temperature of $\leq -70^{\circ}$ C.

2. Glass reactor with a volume of min. 30 L with a heating and cooling jacket enabling the process to be carried out in the temperature range from -20° C to 100° C.

3. Apparatus enabling continuous extraction for liquids with a density lower than water for a total water phase volume of at least 2.5 L.

4. Apparatus enabling purification of the active substance by preparative liquid chromatography under reversed phase conditions.
5. Access to analytical equipment enabling the analyzes necessary to release the active substance and to conduct stability tests in accordance with the ICH guidelines. These are among others:
 - 5.1. High performance liquid chromatograph with UV detector and fluorescent detector equipped additionally with pre-installed post-column system for derivatization of samples.
 - 5.2. Gas chromatography system with FID and/or MS detector and Head Space adapter.
 - 5.3. Coulometric or conductometric Karl Fischer titrator equipped with an oven adapted for the analysis of samples reacting with Karl-Fischer reagent.
 - 5.4. IR spectrophotometer.
 - 5.5. XRPD powder diffractometer.
 - 5.6. Differential scanning calorimeter (DSC).
 - 5.7. Thermogravimeter (TGA).
 - 5.8. Stability chambers.
- B) Are in a good economic and financial standing, which assures proper execution of the project in the declared time.
- C) Will pursue the contract in a way that is beneficial to the environment by minimizing the consumption of materials, raw materials energy, etc. (with environmental certificates such as ISO 14001:2015)

As a proof of the above, the Ordering Party requires that the Contractor submit, along with the tender, a statement about fulfilling conditions for participation in the proceedings, CV's of the Specialists mentioned in IV.2. and contact details, of at least two persons, to which the Ordering Party may apply to request a reference letter. The model statement is attached as Appendix 2 to this request for proposal.

- IV.3 Excluded from the proceedings shall be those contractors who are personally or equity related to the Ordering Part by in particular:
- A) participation in the company, in a civil or limited partnership;
 - B) holding at least 10% shares or interests;
 - C) serving a function of a member of the supervisory organ, a member of the management organ or proxy;
 - D) having family ties, such as by marriage, by lineage at first or second degree, by adoption, guardianship or custody.

As a proof of the above the Ordering Party requires that the Contractor submit, along with the tender, a statement about not being related to the Ordering Party. The model statement is attached as Appendix 3 to this request for proposal.

- IV.4 Issuing the offer represent the full acceptance of the rules set in this Request.

V. DETAILED DESCRIPTION OF THE OBJECT OF THE REQUEST:

CPV code: 73111000 (Laboratory Research Services)

V.I General information:

The subject of the order is the synthesis of 1.5 kg of low molecular weight organic compound OATD-02 under cGMP standard and of 0.5 kg under non-GMP conditions. Synthesis of the OATD-02 compound, according to the procedure provided by the Ordering Party, requires 5 chemical steps, starting from the OAT-2391 substrate.

The cGMP quality OATD-02 material delivered by the Contractor will be used for the evaluation of toxicological properties of OATD-02, for the formulation development, and for the cGMP production of the investigational medicinal product for phase I clinical trials.

The procedure for the synthesis of the OATD-02 compound, a description of the analytical methods, the template of the analytical certificate and the MSDS of the active substance OATD-02 have been included in Appendix No. 5 (Technical Information Package) to this Invitation. Appendix No. 5 will be made available to Contractors who express their interest in participating in the procedure and will send an electronic scan of the signed confidentiality agreement constituting Appendix No. 4 to this Invitation. A scan of the completed and signed Appendix 4 should be sent electronically to the e-mail address: m.tyszkiewicz@oncoarendi.com. Appendix No. 5 will be made available to interested Contractors no later than within 48 hours after receipt of the scan of the completed and signed Appendix No. 4.

In the event of the Bidder having signed a confidentiality agreement at the stage of Estimating the total value of the order, the re-signing of Appendix No. 4 is not required, and Appendix No. 5 will be made available to the Bidder within 48 hours of the written application for participation in proceedings 11/2018 – STRATEGMED/ARG.

V.2 The contract includes:

1. Transfer of the process for the synthesis of OATD-02 compound.
2. Optimization, increase of the scale of the process and preparation of a technical batch of 0.5 kg OATD-02 together with a report.
3. Production of 1.5 kg of OATD-02 compound under cGMP.
4. Validation of analytical methods provided by the Ordering Party including Validation Reports.
5. Establishment and characterization of the OATD-02 standard together with a report (in English).
6. Analysis of the produced batches of OATD-02 together with the issuance of analytical reports.
7. Preparation of weekly progress reports on (the Ordering Party requires preparation of reports in English).
8. Preparation of a report from the GMP campaign (the Ordering Party requires preparation of the report in English).
9. Conducting 3-year stability studies of one GMP batch of the active substance OATD-02.
10. GMP storage of the active substance OATD-02 for a period of 1 year.

11. The Contractor agrees that the Sponsor may audit CRO prior to signing the contract. If the audit fails the Sponsor reserves the right to withdraw from signing the contract.

VI. EVALUATION OF THE OFFERS:

VI.1 Price – weight: 90% (90 pts.)

A) In this criterion points will be calculated according to the formula below:

$$Pc = \frac{C_{min}}{C_{evaluated}} \times 90$$

Pc – Points received

C_{min} – The smallest Net price

C_{evaluated} – Net price of the offer being evaluated

90 – weight of the criterion (90%)

VI.2 Delivery deadline – weight: 10% (10 pts.)

In the delivery deadline, points will be awarded according to the formula:

10 points – when the delivery of cGMP material is less than 6 months from the date of signing of the contract.

0 points – when the delivery of cGMP material is longer than 6 months from the date of signing of the contract.

VI.3 In the case of two or more tenders with equal number of points awarded, to guarantee performance of the contract in a manner favorable to the environment, by providing minimize the consumption of materials, raw materials, energy etc. any environmental certifications will be taken onto consideration (eg. ISO 14001:2015).

If the abovementioned does not allow to choose the best offer, the Ordering Party shall call Contractors who submitted equally evaluated offers to submit, within the period specified, additional offers. Contractors cannot offer higher prices than offered in the tenders.

VII. HOW TO PREPARE AND SUBMIT THE OFFER:

VII.1 The offer should be signed by the person authorized to represent the institution.

VII.2 Each contractor may submit only one offer.

VII.3 Costs of the offer preparation shall be incurred by the offering party.

VII.4 Offers must be submitted no later than: **Mar-14-2018, 23:59 CET** and must be written on the form as in Appendix 1 to the request for proposals.

VII.5 Offers shall be issued only via email to: m.tyszkiewicz@oncoarendi.com.

VII.6 The date of receiving the email shall be considered as a date of issuing the offer.

VII.7 Offers that do not meet the deadline, are incomplete or sent to the wrong email address will not be taken into consideration.

- VII.8 Any questions concerning the Object of the tender should be addressed to m.tyszkiewicz@oncoarendi.com (+48 500 799 497) no later than Mar-05-2018, 23:59 (CET). Contact person is: Magdalena Tyszkiewicz.
- VII.9 Any questions concerning the formal issues of the tender should be addressed to m.skrzek@oncoarendi.com (+48 22 552 67 24) no later than Mar-05-2018, 23:59 (CET).
- VII.10 The offer should include the validity date (at least 30 days from the submission deadline).
- VII.11 The price should be set in both Net and Gross.
- VII.12 The values in the offer (Net and Gross) should be rounded to two decimals with the mathematical rule of rounding the numbers (according to § 5 section 6 of the regulation of Ministry of Finance of 28 November 2008 (Journal of Laws of 2008, No. 212, item 1337, as mentioned).
- VII.13 The offer price should include VAT. The correct determination of VAT is responsibility of the contractor – in accordance with the provisions of the Act of 11 March 2004 on Goods and Services Tax (Journal of Laws of 2004 No. 54 item. 535 as mentioned).
- VII.14 The offer shall not be prepared in price variants.
- VII.15 The financial settlements between the Ordering Party and the contractor may be made in PLN, EUR, USD or GBP.

VIII. TENDER RESULTS:

Bidder will be informed about choosing his offer via email. Formal results will be also published on the Ordering Party's website (www.oncoarendi.com) and concurrency database.

IX. MOST IMPORTANT PROVISIONS OF THE AGREEMENT:

- IX.1 Supplier will be obligated to enter into the agreement including all conditions presented in the Request for the Offer in the place and time specified by the Ordering Party.
- IX.2 It is not possible to introduce significant changes to the content of the agreement in relation to the content of the offer, which was the base for the Service Provider selection, unless:
- A) The amendments concern performing additional services by the Service Provider, not covered by the basic contract, provided they are necessary and the following conditions are met:
- i. The change of the Service provider cannot be made due to to the economic or technical reasons, in particular concerning the interchangeability and interoperability of equipment, services or installations, ordered as part of basic contract.
 - ii. The change of the Service Provider would cause significant inconvenience or substantial cost increase to the Ordering Party.
 - iii. The value of any subsequent changes do not exceed 50% of the basic contract value.
- B) The amendment does not lead to change in the nature of the contact and the following conditions are met:
- i. The need for the contract change is brought about by circumstances which the Ordering Party, acting with due diligence, could not foresee.
 - ii. The value of a change does not exceed 50% of the basic contract value.



- C) The amendment does not lead to change in the nature of the contract and the total value changes is less than 209 000 EUR, and at the same time is less than 10% of the basic value.

Any contract amendment must be done in writing, otherwise will not be valid.

X. APPENDENCIES:

- A) The offer form.
- B) Statement concerning fulfilment of all the requirements set out in part IV of the Request for offers.
- C) Statement concerning persona or/and capital connections between the Service Provider and the Ordering Party.
- D) Confidential Disclosure Agreement form (Appendix No. 4)
- E) Technical Information Package – available after CDA execution.