

REQUEST FOR PROPOSALS 50/2017-IBD**I. ORDERING PARTY:**

OncoArendi Therapeutics SA ul. Żwirki i Wigury 101 02-089 Warszawa VAT No. 728 27 89 248	Contact person: Karolina Czyżewska k.czyzewska@oncoarendi.com tel. 798 352 548
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II. OBJECT OF THE REQUEST / PROPOSAL:**Translational studies in vivo – deciphering the role of acidic mammalian chitinase (AMCase) in asthma and the mechanisms of action of AMCase inhibitors using transgenic mouse models**

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

- **IBD:** Preclinical and Clinical Development of a New Chemical Entity for Asthma and Inflammatory Bowel Disease (POIR.01.01.01 00-0168/15)

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 The Public Procurement Law (29/01/2004 i.e. Dz. U. z 2013 r., poz. 907 z późn. zm.).
- 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 winning 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 tenderers 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 an offer for a part of an 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:
 - have the necessary qualifications to carry out the described activity and have the appropriate technical potential and personnel capable of performing the contract,
 - are in a good economic and financial standing, which assures proper execution of the project in the declared time,
 - are licensed to carry out the activity in question, if this is required by law,

- have research facility necessary to conduct in vivo studies (e.g. animal facility experienced in breeding knockout mice) and biochemical and histochemical analysis of collected biological material,
- have proven experience in generating lung cell-specific knockout mice,
- have proven experience in in vivo studies in HDM-induced asthma model confirmed with at least 5 articles in peer-reviewed scientific journals and/or with documented collaboration with other companies/research units

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. The model statement is attached as Appendix 2 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: 73111000-3

The contract research service aims in performing translational studies in vivo studying the role of acidic mammalian chitinase (AMCase) in the lung allergic inflammation and in the maintenance of lung immune homeostasis. The aim of the studies is to verify molecular mechanisms of anti-inflammatory effects of AMCase inhibitors developed by OncoArendi.

The study should be divided in 3 stages:

1. Generation of mouse strains with cell-specific deletion of AMCase by crossing conditional-ready AMCase deficient mice with lung epithelial or macrophage-specific Cre lines, to generate mice lacking AMCase in lung epithelial cells or alveolar macrophages.
Outcome measures:
 - The cell-specific AMCase-deficiency should be confirmed by molecular biology methods e.g. qPCR.
 - Serum and BAL samples from generated mice will be collected and stored for subsequent analyses.
2. Studying the role of cell-specific expression of AMCase in HDM driven asthma
Outcome measures:
 - FACS analysis on BAL fluid cells
 - Measurement of serum HDM-specific IgE and IgG1, IgG2a by ELISA
 - Histological assessment of the degree of goblet cell metaplasia (GCM) and eosinophil influx (Siglec F immunostaining), and airway remodelling (collagen staining)
3. Studying the role of cell-specific expression of AMCase in resolution of immune responses to HDM in the lungs using mice lacking AMCase completely or specifically in epithelial cells or macrophages exposed to a HDM-driven model of asthma and treated with cytokines' blocking antibodies
Outcome measures::
 - FACS analysis on BAL fluid cells
 - BAL and lungs will be collected for subsequent analysis

The detailed study plan and study timelines will be agreed with the Ordering Party before signing an agreement.

VI. EVALUATION OF THE OFFERS:

VI.1 Price – weight: 90% (90 pts.)

In this criterion point will be calculated according to the formula below:

$$\text{Points received} = P_c = \frac{C_{\min}}{C_{\text{evaluated}}} \times 90$$

where:

P_c – 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 Payment deadline – weight: 10% (10 pts.)

up to 7 days - 0 pts.

8 – 14 days – 3 pts.

15 – 21 days – 5 pts.

22 – 30 days – 7 pts.

more than 30 days – 10 pts.

VI.3 In 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 into consideration (eg. ISO).

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 those 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. The Contractor should make the offer in Polish or English.

VII.4. The costs of the offer preparation shall be incurred by the offering party.

VII.5. Offers must be submitted no later than: 22/09/2017, 23:59 CET and must be written on the form as in Appendix 1 to the request for proposals

VII.6. Offers shall be issued via email to: k.czyzewska@oncoarendi.com

VII.7. Offers that do not meet the deadline will not be taken into consideration.

VII.8. Any questions concerning the Object of the tender should be addressed to Barbara Dymek no later than 20/09/2017, 15:00 CET. Contact person is: b.dymek@oncoarendi.com

VII.9. The offer should be valid for at least 30 days from its submission.

VII.10. The price should be set in both Net and Gross.

VII.11. The offer shall not be presented in price variants.

VIII. TENDER RESULTS

The winner will be informed via e-mail address, Formal results will be also published on the Ordering Party's website (www.oncoarendi.com) and on public domain called Baza Konkurencyjności.

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.
- 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 economic or technical reasons, in particular concerning the interchangeability and interoperability of equipment, services or installations, ordered as part of the 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 a change in the nature of the contract 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 a change in the nature of the contract and the total value of 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.

IX.3 Information regarding contractual penalties:

- a) If the offered project execution time extends for at least 90 days for reasons attributable to the Service Provider's fault (which includes only gross negligence and willful misconduct), the Service Provider shall pay the Ordering Party a contractual penalty of 5% of the net offer price for exceeding the time limit, and then another 5% of net offer price for each additional 90 days of delay. Moreover, the Ordering Party will gain a right to withdraw from the contract if the project execution time is exceeded by at least 180 days.
- b) Due to the termination or withdrawal from the Agreement by either Party for reasons attributable to the Service Provider's fault (which includes only gross negligence and willful misconduct), the Ordering Party will charge a contractual penalty of 25% of net offer price. The right of the withdrawal from the Agreement may be executed by the Ordering Party before December 31, 2018.
- c) The formal basis for charging contractual penalties will be a debit note the Ordering Party delivers to the Service Provider. The Ordering Party shall be entitled to deduct contractual penalties from payments due to the Service Provider.
- d) The Ordering Party has the right to claim damages in the amount exceeding contractual penalties based on general principles.
- e) Contractual penalties will be paid within 7 days from the debit note receipt date.

Appendices:

1. The offer form
2. Statement concerning fulfillment of all the requirements set out in part IV of the Request for offers
3. Statement concerning personal or/and capital connections between the Service Provider and the Ordering Party