

REQUEST FOR PROPOSAL No 4/2020-IPF**I. ORDERING PARTY**

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II. OBJECT FOR THE REQUEST

In vivo study on therapeutic efficacy of two chitinase inhibitors and reference compound Elafibranor in mouse model of non-alcoholic steatohepatitis (NASH).

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

— **IPF:** DEVELOPMENT OF A FIRST-IN-CLASS SMALL MOLECULE DRUG CANDIDATE FOR TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS THROUGH CHITOTRIOSIDASE INHIBITION (POIR.01.01.01-00-0551/15)

co-financed by the 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 2019, item 1843 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 In justified cases, at any time, before the deadline for the submission of tenders, OncoArendi Therapeutics SA reserves the right to change the content of this request. If the changes can affect the content of tenders, the Ordering Party shall extend the tender submission deadline. The Ordering Party shall inform potential Contractors about any changes by publishing relevant information on its website. 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 AND A DESCRIPTION OF THE MANNER OF ASSESSING THE FULFILMENT OF THOSE CONDITIONS

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 (the Submitter should have at least 3 years of experience in mouse models of NASH) and have the appropriate technical potential and personnel capable of performing the contract.
- 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.

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.3 Excluded from the proceedings shall be those contractors who are personally or equity related to the Ordering Party 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 concerning personal and capital relations with 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: 73111000-3 – Laboratory research services

Order description:

The contract research service testing the therapeutic effect of two chitinases inhibitors ("OAT-A" and "OAT-B"), in comparison to reference compound Elafibranor, in mouse model of non-alcoholic steatohepatitis (NASH), following study protocol described below.

Service covers the efficacy study in high fat diet and sugar water-induced NASH model in DIAMOND mice with 16-week-long treatment with compounds (or equivalent model, used in research on metabolic diseases in

human). The Submitter should prove equivalence in respect to similarity of mouse model (dynamics and characteristics of pathologies development) and applicability of proposed model for efficacy testing of potential pharmaceuticals.

Study protocol:

Mouse model:

Proposed model of NASH should utilize susceptible strain of mice and specific diet that leads to development of disease (minimum high fat diet). Animals should develop pathologies with high similarity to human NASH (including metabolic dysregulation, inflammation, hepatocyte ballooning and fibrosis).

Experience and compliance with ethics regulations:

The Submitter should have at least 3 years of experience in mouse models of NASH and should perform proposed study according to appropriate regulations concerning studies on animals, study protocol must be approved by appropriate ethics committee for experimentation on animals. All required related administrative procedures should be conducted by the Supplier.

Model induction and treatment scheme:

NASH disease in mice should be induced with diet prior to treatment with compounds, for a period that (from the Submitter experience) ensures development of pathologies. Duration of treatment with tested compounds and reference compound should be determined by the Submitter and OncoArendi Therapeutics, with consideration of possible anti-inflammatory and anti-fibrotic properties of provided compounds (preferably, but not necessary, treatment for at least 10 weeks, but not longer than 18 weeks).

Suggested groups – 10 mice per group (together 50 animals):

- control (normal chow)
- diet + vehicle
- diet + compound OAT-A - 100 mg/kg, po, qd
- diet + compound OAT-B - 100 mg/kg, po, qd
- diet + reference compound Elafibranor - 15 mg/kg, po, qd

Dosing:

Once a day at defined dose.

Formulation:

Compounds suspension in 0.5% carboxymethylcellulose (CMC) in H₂O (OncoArendi Therapeutics SA will provide tested compounds, reference compound Elafibranor, and CMC, together with instruction for formulation preparation).

Samples collection:

At the conclusion of in-life part of the study, the Submitter should collect, in non-fasting condition, at least: liver (preserved in fixator for histology), liver (frozen), liver (preserved in RNAlater, then frozen), serum (for blood biochemistry analyses).

Deliverables:

- Interim report with data regarding minimum:

- In-life parameters: body weights record, measured minimum weekly
- Terminal parameters: body weights, liver weights, liver-to-body weight ratios
- Final report containing data regarding at least:
 - Standard serum biochemistry tests ("liver panel"), minimum ALAT, AspAT
 - Histopathology on blinded slides (HE and PSR stainings): assessment of severity of steatosis, fibrosis, inflammation, ballooning
- Electronic versions of all obtained raw data
- Samples should be transferred in appropriate temperature conditions to OncoArendi Therapeutics (Zwirki i Wigury 101, 02-089, Warsaw, Poland) at the Submitter costs (price can be included in final quotation for the study): frozen serum leftovers (dry ice), frozen liver samples (dry ice), frozen liver in RNAlater (dry ice), paraffin-embedded blocks and glass slides (room temperature). Packages should be sent within 2 weeks after acceptance of final report.

Electronic version of interim report should be sent to OncoArendi Therapeutics not later than 2 weeks after in-life part of the study is concluded. Electronic version of final report and all raw data should be sent to OncoArendi Therapeutics for verification and acceptance not later than 5 weeks after in-life part of the study is concluded.

Order due date: 30/06/2020

VI. EVALUATION OF THE OFFERS

VI.1 Price – weight: 75% (75 pts.)

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

$$Pc = \frac{C_{min}}{C_{evaluated}} \times 75$$

Pc – Points received

C_{min} – The smallest Net price

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

75 – weight of the criterion (75%)

VI.2 Start of the study – weight: 15 % (15 pts.)

In the start of the study, points will be awarded as below:

15 points – when the start of the study is within 7 days from acceptance of the order for the service

10 points – when the start of the study is between 8-14 days from acceptance of the order for the service

5 points - when the start of the study is between 15-21 days from acceptance of the order for the service

0 points – when the start of the study is later than 21 days from acceptance of the order for the service

15 – weight of the criterion (15 %)

VI.3 Payment deadline – weight: 10% (10 pts.)

In the payment deadline, points will be awarded as below:

10 points – when the payment deadline is over than 29 days from the invoice delivery

5 points – when the payment deadline is set between 14-29 days from the invoice delivery

0 points – when the payment deadline is less than 14 days from the invoice delivery

10 – weight of the criterion (10 %)

- VI.4 In the case of two or more tenders with equal number of points awarded 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. If the offer is signed by an attorney, a power of attorney must be attached to the offer.
- 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: **10/02/2020 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: **p.chmielewska@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.mlacki@oncoarendi.com** (+48 798 352 548) no later than 07/02/2020 15:00 (CET). Contact person is: **Michał Młacki**.
- VII.9 Any questions concerning the formal issues of the tender should be addressed to k.kazimierczak@oncoarendi.com no later than 07/02/2020 15:00 (CET). Contact person is: Kinga Kazimierczak.
- 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 214 000 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 project execution time extends for at least 30 days, the Service Provider shall pay the Ordering Party a contractual penalty of 1,5% of the net offer price for exceeding the time limit, and then another 2% of net offer price for each additional 15 days of delay. Moreover, the Ordering Party will gain a right to withdraw from the contract of the project execution time is exceeded by at least 60 days. The right of withdrawal can be exercised until December 31, 2021.
 - B) Due to the termination or withdrawal from the Agreement by either Party for reasons caused by the Service Provider, the Ordering Party will change a contractual penalty of 25% of net offer price.
 - C) The formal basis for changing 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) The Ordering Party has the right to claim damages in the amount exceeding contractual penalties based on general principles.
 - F) Contractual penalties sum up.

X. APPENDENCIES

- A) Appendix No. 1 - The offer form,
- B) Appendix No. 2 - Statement concerning fulfillment of all the requirements set out in part IV of the Request for offers,
- C) Appendix No. 3 - Statement concerning personal or/and capital connections between the Service Provider and the Ordering Party,
- D) Appendix No. 4 - Declaration of compliance with the information obligations provided for in Article 13 or Article 14 of the GDPR.