

REQUEST FOR THE PROPOSAL No 54/2020 - YKL-40**I. ORDERING PARTY**

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II. OBJECT FOR THE REQUEST

Ex-vivo study on therapeutic efficacy of three YKL40 inhibitors and reference compound on cell and tissue IPF models.

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

- YKL-40: "DEVELOPMENT OF A FIRST-IN-CLASS SMALL MOLECULE DRUG CANDIDATE FOR CANCER TREATMENT THROUGH YKL 40 INHIBITION" (POIR.01.01.01-00-0552/16)

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 the changes made by publishing relevant information on its website, on Concurrency database website and by e-mail to all Contractors to which the request was sent or to all Contractors who submitted bids.
- 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 Contractors who:

- A) have the necessary qualifications (5 years of experience in research of the mechanisms leading to pulmonary diseases, including fibrotic changes) to carry out the described activity 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 order;
- 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. Equity or personal relationship is understood as relations between the Ordering Party or individuals authorized to take commitments on behalf of the Ordering Party or those acting on behalf of the Ordering Party in order to prepare and implement the Contractor selection procedure and the Contractor, including 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 and in particular the essential terms of the contract.

V. DETAILED DESCRIPTION OF THE OBJECT OF THE REQUEST

CPV Code: 73111000-3 – Laboratory research services

Order description:

Research service to test the therapeutic effect of three YKL40 inhibitors ("OAT-A", "OAT-B" OAt-3), compared to the reference compound Nintedanib, in an ex vivo idiopathic model pulmonary fibrosis (IPF) using **finely-sectioned lung sections precision cut lung slices (PCLS) cut with a machine dedicated to cutting live lung fragments (~300µm) without destroying the lung structure** and other materials such as fibroblasts from donors with IPF according to the testing protocol described below.

Study details:

The study will be divided into the following parts:

1) Assessment of YKL40 target protein concentration in:

- a) Frozen tissue samples: from 10 healthy donors and 10 donors with IPF. The material will be digested, RNA and protein isolated and the concentration of YKL40 will be assessed by qPCR and ELISA.
- b) Isolated parenchymal fibroblasts: from 6 healthy donors and 6 donors with IPF. The material will be digested, RNA and protein isolated, and the concentration of YKL40 will be assessed by qPCR and ELISA. The protein concentration will also be assessed in the supernatant.
- c) TGF-β stimulated donor fibroblasts for 24 hours (4 healthy donors) and 48 hours (4 healthy donors). Gene analysis (YKL40, Pal1, Col1a1) and protein analysis (YKL40, Col1a1).
- d) TGF-b stimulated IPF fibroblasts for 24 hours (4 donors with IPF) and 48 hours (4 donors with IPF). Gene analysis (YKL40, Pal1, Col1a1) and protein analysis (YKL40, Col1a1).

2) Assessment of the anti-fibrotic effect of small molecule inhibitors in:

- a) isolated parenchymal fibroblasts from 4 healthy donors and 4 donors with IPF. 3 inhibitors will be tested at 3 concentrations. Half of the plates will be additionally stimulated with TGF-β for 24h. Suggested configuration for one donor:

vehicle vehicle	vehicle TGF-beta	IFNgamma TGF-beta
Inhibitor 1 (low) TGF-beta	Inhibitor 1 (middle) TGF-beta	Inhibitor 1 (high) TGF-beta
Inhibitor 2 (low) TGF-beta	Inhibitor 2 (middle) TGF-beta	Inhibitor 2 (high) TGF-beta
Inhibitor 3 (low) TGF-beta	Inhibitor 3 (middle) TGF-beta	Inhibitor 3 (high) TGF-beta

Suggested test readings: RNA: PAI1, COL1a1, Col3a1, SMA, fibronectin 1, TIMP1, MMP1, protein: COL1a1, SMA

b) precision cut lung slices (PCLS) from donors with IPF. Material from a minimum of 3 donors and a maximum of 5 donors. The 3 inhibitors will be tested at the single best concentration obtained from the results of 2a, the inhibitor will be added daily. The experiment will last up to 7 days. Suggested configuration:

untreated	Inhibitor 1	Inhibitor 2	Inhibitor 3	IFNg	
untreated	Inhibitor 1	Inhibitor 2	Inhibitor 3	IFNg	
untreated	Inhibitor 1	Inhibitor 2	Inhibitor 3	IFNg	
untreated	Inhibitor 1	Inhibitor 2	Inhibitor 3	IFNg	

Suggested test readings: Trichrome - **Masson** staining and semi-automatic collagen deposition analysis (for two rows – **method for example Sircol**), the remaining 2 rows will be frozen immediately so that they can be used for protein / RNA isolation.

The cost of each of steps 1a, 1b, 1c, 2a, 2b must be estimated separately. In the event of negative results for any of the above-mentioned steps, OncoArendi Therapeutics reserves the right to discontinue testing and terminate the contract. The Contractor will be entitled to remuneration for the work performed.

The Contractor is responsible for obtaining all materials (tissues, cells) necessary to conduct the experiments.

Dosage:

Twice a day at the specified dose.

Compliance with ethical regulations:

The study protocol must be approved by the appropriate ethics committee for conducting ex vivo experiments on human tissues. All required administrative procedures related to obtaining the consent of the ethics committee should be carried out by the Contractor.

Test results delivered to the Ordering Party:

- Partial report after each step with data on all measured test parameters in steps 1a-1d and 2a-b.
- Final report
- Electronic versions of all obtained raw data
- At the request of the Ordering Party, samples of materials from the conducted experiments should be submitted to OncoArendi Therapeutics (Żwirki i Wigury 101, 02-089, Warsaw) under appropriate temperature conditions at the expense of the Contractor within 3 weeks of receiving the request from the Ordering Party (up to 2 times).

The electronic version of the interim report should be sent to OncoArendi Therapeutics no later than 2 weeks after the end of the relevant part of the study. The electronic version of the final report and all raw data must be sent to OncoArendi Therapeutics for review and approval no later than 5 weeks after completion of all studies.

The Ordering Party expects the service to be performed based on the Contractor's current version of the model.

Order due date: maximum completion date is 30.11.2021.

If the Contractor intends to entrust the performance of part of the order to a Subcontractor, the Ordering Party requires to indicate in the Appendix No. 1 to this Request the parts of the order which Contractor intends to subcontract and the name of subcontractors, if known at this stage.

VI. EVALUATION OF THE OFFERS

VI.1 Price – weight: 80% (80 pts.)

In this criterion points will be calculated (to two decimal places) according to the formula below:

$$Pc = \frac{C_{min}}{C_{evaluated}} \times 80$$

Pc – Points received

C_{min} – The smallest Net price

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

80 – weight of the criterion (80%)

VI.2 Term of the payment for invoice – weight: 20% (20 pts.)

In this criterion points will be awarded as below:

20 points – when the payment term is 23-30 days from the date of delivery of a correctly issued invoice

10 points – when the payment term is 15-22 days from the date of delivery of a correctly issued invoice

0 points – when the payment term is 14 days or less from the date of delivery of a correctly issued invoice

20 – weight of the criterion (20 %)

VI.3 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 Contractor. 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: ~~05/10/2020~~ **12/10/2020 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 a.bartoszewicz@oncoarendi.com (+48 537 161 998) no later than 01/10/2020 15:00 (CET). Contact person is: Agnieszka Bartoszewicz.
- VII.9 Any questions concerning the formal issues of the tender should be addressed to k.kazimierczak@oncoarendi.com no later than 01/10/2020 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, GBP or USD.

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 on Concurrency database website.

IX. MOST IMPORTANT PROVISIONS OF THE AGREEMENT

- IX.1 Contractor will be obligated to enter into the agreement including all conditions presented in this Request and in 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 Contractor selection, unless:
- A) The amendments concern performing additional supplies or services by the Contractor, not covered by the basic contract, provided they are necessary and the following conditions are met:
- i. The change of the Contractor cannot be made due 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 Contractor 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 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 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.

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 regarding personal and capital connections with 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