

REQUEST FOR THE PROPOSAL No 35/2021 - DUBs**I. ORDERING PARTY**

OncoArendi Therapeutics S. A. ul. Żwirki i Wigury 101 02-089 Warsaw VAT ID: 728 27 89 248	Contact person: Tomasz Rejczak e-mail: t.rejczak@oncoarendi.com Tel No. (+48) 690 204 434
---	--

II. OBJECT FOR THE REQUEST

ADME (Absorption, Distribution, Metabolism and Excretion) studies for small molecule compounds within 4 months from the signing of the agreement.

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

— **DUBs:** „RESEARCH AND DEVELOPMENT OF DEUBIQUITINASE INHIBITORS IN ANTITUMOR IMMUNOTHERAPY” (POIR.01.01.01-00-0615/19)

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 Act of 11 September 2019 - Public Procurement Law (Journal of laws of 2019, item 2019 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 Competitiveness 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 (also referred to in the text as "Request for the proposal") 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.
- III.8 For the avoidance of doubt, the selection of an offer as the best in the procedure does not constitute a

contract or an order to perform any services or perform any deliveries. The contract will be concluded in writing or in a documentary form, at the Ordering Parties' choice.

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 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 Submitting 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 – Research laboratory services

The research services that are the subject of this request are listed in the table below:

No.	Assay	Assay description	Amount of assays
1	Determination of Caco-2 bidirectional permeability (pH 6.5/7.4)	1 compound, 1 concentration	10
2	Determination of MDCKII-MDR1 bidirectional permeability	1 compound, 1 concentration	3
3	Determination of PAMPA permeability	1 compound, 1 concentration	10
4	Determination of intrinsic clearance (CL _{int}) using liver microsomes (Human, Rat, Mouse)	1 compound, 1 concentration	3
5	Determination of intrinsic clearance (CL _{int}) using liver microsomes (Monkey, Dog, Minipig)	1 compound, 1 concentration	3
6	Determination of intrinsic clearance (CL _{int}) using intestinal microsomes (Human, Rat, Mouse)	1 compound, 1 concentration	3
7	Determination of intrinsic clearance (CL _{int}) using intestinal microsomes (Monkey, Dog)	1 compound, 1 concentration	3
8	Determination of intrinsic clearance (CL _{int}) using cryopreserved hepatocytes (Human, Dog, Rat, Mouse)	1 compound, 1 concentration	3
9	Determination of intrinsic clearance (CL _{int}) using cryopreserved hepatocytes (Monkey, Minipig)	1 compound, 1 concentration	3
10	Determination of plasma stability (Human, Rat, Mouse)	1 compound, 1 concentration	3
11	Determination of plasma stability (Monkey, Dog)	1 compound, 1 concentration	3
12	Determination of plasma protein binding (Human, Rat, Mouse)	1 compound, 1 concentration	3
13	Determination of plasma protein binding (Monkey, Dog, Minipig)	1 compound, 1 concentration	3
14	Microsomal protein binding (Human, Minipig, Rat, Mouse)	1 compound, 1 concentration	3
15	Microsomal protein binding (Monkey, Dog)	1 compound, 1 concentration	3
16	Tissue homogenate protein binding (mice or rat; e.g. brain)	1 compound, 1 concentration	5
17	Blood to plasma ratio (Human, Rat, Mouse)	1 compound, 1 concentration	3
18	Blood to plasma ratio (Monkey, Dog, Minipig)	1 compound, 1 concentration	3
19	Metabolite identification <i>in vitro</i> (liver microsomes) cold compound; Human, Monkey, Dog, Minipig, Rat, Mouse)	1 compound, 1 concentration	2
20	Metabolite identification <i>in vitro</i> (cryopreserved hepatocytes); cold compound; Human, Monkey, Dog, Minipig, Rat, Mouse)	1 compound, 1 concentration	2
21	Reactive metabolite assessment (glutathione trapping) (1 compound, HLM in the presence and absence of NADPH)	1 compound, 1 concentration	3
22	CYP reaction phenotyping (CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A4; recombinant enzymes)	1 compound, 1 concentration	5
23	UGT reaction phenotyping (UGT2B7, UGT1A1, UGT1A3, UGT1A6, UGT1A9, UGT2B15, UGT1A4) (recombinant enzymes)	1 compound, 1 concentration	3

24	Evaluation of cytochromes inhibition including: CYP1A, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A (midazolam and testosterone as probe substrates) (HLM, 1 TA concentration), package of 8 assays	1 compound, 1 concentration	15
25	Evaluation of cytochromes inhibition for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A (midazolam and testosterone as probe substrates) (HLM, IC ₅₀ determination), non-package	1 compound, 8 concentrations	10
26	Evaluation of cytochromes inhibition for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A (midazolam and testosterone as probe substrates) (HLM, time-dependent inhibition (IC ₅₀ shift))	1 compound, 5 concentrations	5
27	Evaluation of cytochromes induction (CYP1A2, CYP2B6, CYP3A4; 3 donors; 3 concentrations; mRNA endpoint)	1 compound, 3 concentrations	5
28	Inhibition of drug transporters including: P-gp, BCRP, BSEP, MRP2, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, MATE1, MATE2-K (1 concentration)	1 compound, 1 concentration	5
29	Inhibition of drug transporters for P-gp, BCRP, BSEP, MRP2, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, MATE1 or MATE2-K (IC ₅₀ determination)	1 compound, 5 concentrations	3

Each commissioned study should end with a report containing the results of the analysis. The data obtained during the test should be available or sent upon request till 31.03.2023. The Ordering Party plans to send a maximum 20 compounds for testing during the contract period. Research will be commissioned and compounds will be sent successively depending on the research plans. All commissioned studies should be completed by the end of March 2022. The Ordering Party reserves the right not to provide the services in the specified quantities.

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:

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

P_c – points received in the price criterion

C_{min} – the smallest Net price out of the submitted offers that are not subject to rejection

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

VI.2 Payment deadline– weight: 20% (20 pts.)

The number of points for the criterion payment deadline will be awarded according to the following scheme:

20 points – when the payment deadline is >= 30 days from the date of delivery of a correctly issued invoice

10 points - when the payment deadline is set between 20-29 days from the date of delivery of a correctly issued invoice

0 points – when the payment deadline is 19 days or less from the date of delivery of a correctly issued invoice

- 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. For any of the evaluation criteria, the additional offer may not be less favorable than the one submitted in response to the Request for offers (i.e. in the first offer).

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: **03/11/2021 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 via email to: p.chmielewska@oncoarendi.com
- VII.6 The receipt of the offer via electronic means indicated in point VII.5 shall be considered as a date of submitting the offer.
- VII.7 Offers that do not meet the deadline, are incomplete (despite a request for supplementation, if such a request was possible and in accordance with the regulations) 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 t.rejczak@oncoarendi.com (+48 690 204 434) no later than 21/10/2021 15:00 (CET). Contact person is: Tomasz Rejczak.
- VII.9 Any questions concerning the formal issues of the tender should be addressed to k.kazimierczak@oncoarendi.com no later than 21/10/2021 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 Art. 106e section 11 of the Act of 11 March 2004 on Goods and Services Tax (Journal of Laws of 2021, item 685, 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 2021 item. 685 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 Competitiveness 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 contract value.

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

X. APPENDENCIES TO REQUEST FOR PROPOSAL

- 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