

**REQUEST FOR PROPOSAL NR 28/2019 - DUBs****I. ORDERING PARTY**

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**II. OBJECT FOR THE REQUEST:**

*Research service of testing ADMET/pharmacokinetic properties of small molecule compounds*

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

**DUBs** – RESEARCH AND DEVELOPMENT OF DEUBIQUITINASE INHIBITORS IN ANTITUMOR IMMUNOTHERAPY

which would be 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 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.
- 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. 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: 73111000-3 – Laboratory research services

The subject of the service are:

No.	Service
1	Ames fluctuation assay, evaluating the mutagenic potential of chemicals
2	Cell membrane permeability test in Caco2 cell line
3	Determination of binding with plasma proteins (mouse, rat, dog, human)
4	Cell membrane permeability test (PAMPA)
5	Determination of solubility in certain pH
6	Determination of dopamine transporter inhibition (radioligand)
7	Evaluation of hERG inhibition in patch clamp assay
8	Evaluation of Nav1.5 inhibition in patch clamp assay
9	Evaluation of GABAA inhibition in patch clamp assay
10	Evaluation of GABAA1 (alpha 1,beta 2,gamma 2) binding assay (radioligand)
11	Evaluation of Cl- channel (GABA-gated) (TBOB site) binding assay (antagonist radioligand)
12	Determination of inhibition or activation of kinase panel including: Abl kinase, Akt1/PKBalpha, AurA/Aur2 kinase, CaMK2alpha

	CDC2/CDK1 (cycB), CDK2 (cycA), CHK1, CHK2, c-Met kinase EGFR kinase, EphA2 kinase, EphA3 kinase, EphB4 kinase ERK2 (P42mapk), FGFR1 kinase, FGFR2 kinase FGFR3 kinase, GSK3beta, HGK (MAP4K4), IKKalpha IRAK4, IRK (InsR), JAK3, JNK1, KDR kinase (VEGFR2) Lck kinase, MAPKAPK2, MARK1, MNK2, MST4 kinase NEK2, p38alpha kinase, PAK2, PAK4, PDK1, Pim2 kinase PKA, PKCbeta 2, PLK1, RAF-1 kinase, ROCK1, SGK1, SIK Src kinase, TAOK2 (TAO1), TRKA
13	Evaluation of metabolic stability using microsomes (human, rat, mouse, dog).
14	Evaluation of metabolic stability using hepatocytes (human, rat, mouse, dog).
15	Evaluation of cytochromes inhibition including: CYP1A, CYP2B6, CYP2C8, CYP2C9 CYP2C19, CYP2D6, CYP2E1, CYP3A CYP3A
16	Evaluation of cytochromes induction including: CYP1A, CYP2B6, CYP3A4
17	Inhibition of drug transporters including: P-gp, BCRP, MRP1, MRP2, MRP3, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, ASBT, NTCP
18	Metabolite identification <i>in vitro</i> (Liver microsomes, S9, hepatocyte)
19	Diversity panel GPCRs
20	<i>In vivo</i> pharmacokinetic profile of compound analyzed in mice or rat with renal or biliary clearance
<b>ADDITIONAL SERVICES</b>	
21	Intrinsic clearance (intestinal microsomes, human)
22	Intrinsic clearance (intestinal microsomes, rat, Sprague-Dawley)
23	Intrinsic clearance (intestinal microsomes, dog, Beagle)
24	Metabolic stability in hepatocytes – monkey
25	Metabolic stability in hepatocytes - mini-pig
26	SET Human Serotonin Transporter Binding (Antagonist Radioligand) Assay
27	5-HT3 (Non-Selective) Human Serotonin Ion Channel Binding (Antagonist Radioligand) Assay
28	5-HT1A Human Serotonin GPCR Binding (Agonist Radioligand) Assay
29	5-HT2A Human Serotonin GPCR Binding (Agonist Radioligand) Assay
30	5-HT2B Human Serotonin GPCR Binding (Antagonist Radioligand) Assay
31	5-HT2B Human Serotonin GPCR [125I] (±)DOI Binding (Agonist Radioligand) Assay
32	5-HT6 Human Serotonin GPCR Binding (Agonist Radioligand) Assay

## VI. EVALUATION OF THE OFFERS:

VI.1 Price – weight: 70% (70 pts.)

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

$$Pc = \frac{C_{min}}{C_{evaluated}} \times 70$$

Pc – Points received

C<sub>min</sub> – The smallest Net price

C<sub>evaluated</sub> – Net price of the offer being evaluated

70 – weight of the criterion (70%)

VI.2 Payment deadline– weight: 30% (30 pts.)

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

30 points – when the payment deadline is than 30 days of the invoice date

25 points – when the payment deadline is between 21-29 days of the invoice date

10 points – when the payment deadline is between 14-20 days of the invoice date

5 points – when the payment deadline is between 7-13 days of the invoice date

0 points – when the payment deadline is less than 7 days

30 – weight of the criterion (30 %)

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: **15/04/2019 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 [p.chmielewska@oncoarendi.com](mailto:p.chmielewska@oncoarendi.com) (+48 798 352 548) no later than 12/04/2019 15:00 (CET). Contact person is: Paula Chmielewska.

VII.9 Any questions concerning the formal issues of the tender should be addressed to [m.skrzek@oncoarendi.com](mailto:m.skrzek@oncoarendi.com) (+48 22 552 67 24) no later than 12/04/2019 15:00 (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](http://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.

IX.3 Information regarding contractual penalties:

- A) If the offered project execution time (as defined in the offer) extends for at least 15 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 60days. The Ordering Party may withdraw from the agreement until 31<sup>st</sup> Dec 2018.
- 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) 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) Declaration of compliance with the information obligations provided for in Article 13 or Article 14 of the GDPR (Appendix No. 4).