Warsaw, 09/08/2019

REQUEST FOR PROPOSAL No. 63/2019 - IBD/IPF/YKL40/ARG

I. ORDERING PARTY

OncoArendi Therapeutics SA ul. Żwirki i Wigury 101 02-089 Warszawa VAT ID: 728 27 89 248	**Contact person:** Barbara Dymek b.dymek@oncoarendi.com

II. OBJECT FOR THE REQUEST:

Research services of testing ADME/Tox properties of small molecule compounds within 24 months from the signing of the agreement.

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

- **IBD**: „PRE-CLINICAL AND CLINICAL RESEARCH OF CANDIDATE FOR INNOVATIVE DRUG IN ASTHMA AND INFLAMMATORY BOWEL DISEASES THERAPY" (POIR.01.01.01 00-0168/15)
- **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)
- **YKL-40**: DEVELOPMENT OF A FIRST-IN-CLASS SMALL MOLECULE DRUG CANDIDATE FOR CANCER TREATMENT THROUGH YKL40 INHIBITION (POIR.01.01.01-00-0552/16)
- **ARG**: „PRE-CLINICAL AND CLINICAL DEVELOPMENT OF ARGINASE INHBITOR FOR CANCER IMMUNOTHERAPY" (POIR.01.01.01-00-415/17)

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

Assay	Assay details	No. of compounds tested
Ames fluctuation assay	1 cmpd at 4 concentrations	8
Bidirectional cell membrane permeability in Caco2 cell line (pH 7.4/7.4	1 cmpd at 1 concentration	10
Determination of binding with plasma proteins (mouse)	1 cmpd at 1 concentration	10
Determination of binding with plasma proteins (rat)	1 cmpd at 1 concentration	10
Determination of binding with plasma proteins (dog)	1 cmpd at 1 concentration	10
Determination of binding with plasma proteins (human)	1 cmpd at 1 concentration	10
Determination of dopamine transporter inhibition (radioligand)	1 cmpd at 1 concentration in duplicate	30
DAT Human Dopamine Transporter Functional Antagonist Uptake Assay	1 cmpd at 1 concentration in duplicate	30
DAT Rat Dopamine Transporter Functional Antagonist Uptake Assay	1 cmpd at 1 concentration in duplicate	30
Evaluation of hERG inhibition in patch clamp assay	1 cmpd at 5 concentrations in duplicate	25
Diversity Panel [Km ATP], KinaseProfiler including: SAPK2A (p38alpha), Akt1 (PKBalpha), GSK3beta, PRAK, MAPKAPK2, CHK1, c-Raf (Raf-1), MEK1, PKA, Fyn, PKCtheta, CDK2 /CyclinA, CDK1 /CyclinB, IKKalpha, PDGFRbeta, IGF1R, CDK7 /CyclinH, PAK2, PKCalpha, p70S6K (T412E), RSK1, LYN, Aurora-A, CDK6 /CyclinD3, Abl, EGFR, TYRO3, NEK2, EphB4, ALK, PI3Kgamma (p120gamma), SRPK1, Plk3, Pim1, IRAK4, TAK1, ROCK1, PI3Kalpha, PI3Kbeta, PI3Kdelta, ASK1, MSK2, MST1, KDR (VEGFR2), EphA5, JAK2, eEF-2K, CaMK1alpha, MNK2, DRAK1, CDK9 /CyclinT1, LOK, PKG1 (alpha), CK2alpha2, MLK1, CK1gamma1, mTOR, AMPKalpha1	1 cmpd at 1 concentration in duplicate	5
Evaluation of metabolic stability using hepatocytes (human)	1 cmpd at 1 concentration in in duplicate in five time-points	5
Evaluation of metabolic stability using hepatocytes (rat)	1 cmpd at 1 concentration in in duplicate in five time-points	5

Evaluation of metabolic stability using hepatocytes (mouse)	1 cmpd at 1 concentration in in duplicate in five time-points	5
Evaluation of metabolic stability using hepatocytes (dog)	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), rat	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), dog	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), human	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), monkey	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), mouse	1 cmpd at 1 concentration in in duplicate in five time-points	5
Intrinsic clearance (liver microsomes), minipig	1 cmpd at 1 concentration in in duplicate in five time-points	5
Evaluation of cytochromes inhibition including: CYP1A, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A, CYP3A – Human liver microsome assay	1 cmpd at 1 concentration in duplicate	8
Evaluation of cytochromes induction including: CYP1A, CYP2B6, CYP3A4 – 3 donors	1 cmpd at 3 concentrations in triplicate	5
Inhibition of drug transporters including: P-gp, BCRP, MRP1, MRP2, MRP3, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, OCT2, ASBT, NTCP	1 cmpd at 1 concentration in duplicate	5
Diversity panel including: NK1 receptor, NK2 receptor, NK3 receptor, Rat Neuropeptide Y receptor, alpha2 Rat Adrenoceptor, Rat Opioid receptor, B1 Bradykinin receptor, H2 Histamine receptor, Glutamate Rat Ion Channel, Rat P2X Ion Channel, Rat P2Y receptor, H3 Histamine receptor, CRF1 receptor, ER NHR, MT1 receptor, CHT1, V1A Human Vasopressin / Oxytocin receptor, Cav1.2 (L-type) Rat Calcium Ion, TRH receptor, Cav1.2 (L-type) Rat Ion Channel, KATP Rat Ion Channel, KV rat Ion Channel, SKCa Rat Ion Channel, Rat Sodium Ion Channel, Rat GABAA Ion Channel, beta1 Adrenoceptor receptor, MAO-A, EP2 Prostanoid receptor, A1 Adenosine receptor, beta2 Adrenoceptor receptor, ATPase (Na+/K+), Brain, Pig, PDE5, HDAC3, Tyrosine Hydroxylase, CENPE, EG5 Human Kinesin, IP Human Prostanoid receptor, PR Human Progesterone NHR, AT1 receptor, HDAC4, HDAC6, Sirtuin 1, Sirtuin 2, PTP1B, AT2 receptor, HDAC11, 5-HT1, Rat GABAA Ion Channel, Adenylyl Cyclase, Guanylyl Cyclase,	1 cmpd at 1 concentration in duplicate	8

nAChR (alpha4/beta2) Ion Channel, B2 Bradykinin receptor, MAO-B, sigma, NET, NOP (ORL1) Opioid receptor, Acetylcholinesterase, CB2 receptor, CCK1 receptor, A2A Adenosine receptor, PDE1B, PDE2A1, PDE3A, PDE4D2, CCK2 receptor, COX1, MC4 receptor, SET, D1 receptor, CDC25A, D2S receptor, GABA transaminase, PKCalpha, GR, CB1 receptor, D3 receptor, D4.4 receptor, V2 Human Vasopressin / Oxytocin receptor, DAT, ETA receptor, ETB receptor, Rat GABAA Ion Channel, A3 Adenosine receptor, GABA Rat Transporter, PPARgamma, Glutamate Rat Ion Channel, 5-LOX, alpha1 (Non-Selective) Rat Adrenoceptor, Imidazoline I2, CysLT1 receptor, H1 Histamine receptor, Rat Acetylcholine receptor, AR Androgen NHR		
Safety screen 44 panel including: Delta DOP, mu MOP, H2 histamine receptor, alpha2A Adrenoceptor, 5-HT1A, D2S Dopamine, 5-HT2B, V1A Human Vasopressin/Oxytocin receptor, Cav1.2 (L-type) Rat Calcium Ion Channel, KV (Non-Selective) Rat Potassium Ion Channel, Rat Sodium Ion Channel, beta1 Adrenoceptor, beta2 Adrenoceptor, alpha1A adrenoceptor, Rat GABAA Ion Channel, Lck, nAChR (alpha4/beta2), NET, acetylcholinesterase, CB2, CCK1 (CCKA), A2A Adenosine receptor, PDE3A, PDE4D2, hERG, 5-HT3, COX1, COX2, 5-HT1B, SET, D1, MAO-A, kappa (KOP) receptor, GR, CB1 receptor, 5-HT2A, DAT, ETA receptor, NMDA Rat Ion Channel, H1 Histamine receptor, M1 Acetylcholine receptor, M2 Acetylcholine receptor	1 cmpd at 1 concentration in duplicate	8
NK2 Human Tachykinin GPCR Binding (Agonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	30
NK2 Human Tachykinin GPCR Cell Based Agonist & Antagonist Calcium Flux Assay	1 cmpd at 1 concentration in duplicate	20
Non-Selective Rat Sodium Ion Channel [3H] Batrachotoxinin Binding (Site 2) Assay	1 cmpd at 1 concentration in duplicate	30
sigma (Non-Selective) Human Binding (Agonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	20
EP2 Human Prostanoid GPCR Binding (Agonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	20
Nav1.1 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay (3 Conc.)	1 cmpd at 3 concentrations in duplicate	5
Nav1.2 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5

Nav1.3 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
Nav1.4 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
Nav1.5 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
Nav1.6 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
Nav1.7 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
Nav1.8 Human Sodium Ion Channel Cell Based Automated Patch Clamp Assay	1 cmpd at 3 concentrations in duplicate	5
D1 Human Dopamine GPCR Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D2S Human Dopamine GPCR Binding (Agonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D2L Human Dopamine GPCR Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D3 Human Dopamine GPCR Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D4.4 Human Dopamine GPCR Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D5 Human Dopamine GPCR Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	10
D1 Human Dopamine GPCR Cell Based Agonist & Antagonist cAMP Assay	1 cmpd at 1 concentration in duplicate	10
SET Human Serotonin Transporter Binding (Antagonist Radioligand) Assay	1 cmpd at 1 concentration in duplicate	30
SET Rat Serotonin Transporter Functional Antagonist Uptake Assay	1 cmpd at 1 concentration in duplicate	10
SET Human Serotonin Transporter Functional Antagonist Uptake Assay	1 cmpd at 1 concentration in duplicate	30

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:

$$Pc = \frac{C_{min}}{C_{evaluated}} x70$$

Pc – Points received

C_{min} – The smallest Net price

$C_{evaluated}$ – 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 30 or more 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 of the invoice date

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: **09/09/2019 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 b.dymek@oncoarendi.com no later than 02/09/2019 15:00 (CET). Contact person is: Barbara Dymek

VII.9 Any questions concerning the formal issues of the tender should be addressed to m.skrzek@oncoarendi.com (+48 22 552 67 24) no later than 02/09/2019 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) 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.

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).