Warsaw, 18/02/2021

REQUEST FOR THE PROPOSAL No 03/2021 - ARG

I. ORDERING PARTY

OncoArendi Therapeutics S. A. ul. Żwirki i Wigury 101 02-089 Warsaw VAT ID: 728 27 89 248	**Contact person:** Łukasz Mąkolski Magdalena Tyszkiewicz e-mail: l.makolski@oncoarendi.com m.tyszkiewicz@oncoarenid.com **Tel No. +48 572 572 888**

II. OBJECT FOR THE REQUEST

Development of formulation and manufacturing of investigational medicinal product (IMP) in accordance to Good Manufacturing Practice for clinical trials of phase I & II.

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

ARG: "PRE-CLINICAL AND CLINICAL DEVELOPMENT OF ARGINASE INHBITOR FOR CANCER IMMUNOTHERAPY" (POIR.01.01.01-00-0415/17)

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 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 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.

III.8 The technical conditions of the order execution (including work schedule) will be specified in the contract signed with the selected Contractor.

III.9 A quality agreement will be signed with the selected Contractor prior to the proper contract.

III.10 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.

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 appropriate technical potential capable of performing the contract described in request for the proposal 3/2021 - ARG;

B) have necessary knowledge and experience - none less than 3 years in performing of the activities described in this request for the proposal that means: development of formulations, development of analytical methods, manufacturing and storage of investigational medicinal product in GMP standard for purposes of early stage clinical trials;

C) have valid license for manufacturing of investigational medicinal products for clinical trials in human;

D) have valid GMP certificate;

E) will prove, that none of the inspections conducted within last 5 years showed any major inconsistencies and will attach to the proposal list of all inspections that were conducted by regulatory agencies in Contractor facilities (between December 2015 and December 2020) or if Contractor period of activity is shorter than 5 years, the above mentioned list applies to the entire period of Contractor's activity. Copy of the report of the last inspection issued by regulatory agency is required.

The Ordering Party reserves the right to demand additional copies of the selected reports issued by regulatory agencies after the inspection, that took place between December 2015 and December 2020. If the above mentioned copies will not be shared within 3 days since the official request, the proposal will be consider incomplete and will not be further assessed;

F) are in a good economic and financial standing, which assures proper execution of the order within the time declared;

G) 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), copy of the license for manufacturing of the investigational medicinal product for clinical trials in human, copy of the GMP certificate, list of the inspection and a copy of the report issued by regulatory agency from last inspection (as described in point E).

IV.3 The offers may be issued by Contractors who have personnel capable of performing the contract. In Human Resources the Ordering Party requires the Contractor to engage at least:

A) Project Manager that has at least 2 years of experience in managing the R&D projects carried out in the name of third parties regarding the development and manufacturing of the pharmaceutical products

B) Specialist Technologist that has proven experience in development of the solid form of medicinal products (capsules), handling of process equipment for the production and manufacturing of solid forms of the medicinal products and investigational medicinal products. The Ordering Party requires that the engaged Specialist should have been leading specialist for at least 3 years.

C) Specialist Analytic that has proven experience in realization of the analytical part of the development of the investigational medicinal products, including development, transfer and validation of the analytical methods for API and medicinal products and in stability studies of the pharmaceutical products. The Ordering Party requires that the engaged Specialist should have been a leading specialist for at least 3 years.

D) Qualified Person (QP) with permission to release investigational medicinal product.

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) and CV's of the above mentioned specialists.

IV.4 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.5 The Ordering Party does not allow the Contractor to subcontract to the third parties any of the main parts of the order, that is: polymorph screening, formulation development, manufacturing in GMP standard and tests of the quality of investigational medicinal product intended for clinical trials on humans, storage of investigational medicinal product. Minor parts of the order, that is: singular specific analytical tests, except of tests on IMP issued for release, can be subcontracted to the third parties. Contractor is responsible for qualification of the subcontractor and is fully responsible for the

commissioned works.

IV.6 Contractor must obtain written permission from the Ordering Party if the subcontracted works are covered by CDA.

IV.7 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: 73100000-3 - Research and experimental development services

73120000-9 Experimental development services

The object of this proposal is formulation development of the investigational medicinal product in form of hard capsules and manufacturing of the investigational medicinal product in GMP standard for clinical trials of phase I & II.

The order includes:

1) API characterization
2) Polymorph screening
3) Transfer of analytical methods
4) Development of analytical methods for purposes of quality control of the medicinal product
5) Validation of analytical methods
6) Drug - excipient compatibility studies
7) Formulation development
8) Scale-up manufacturing process and stability studies of the optimization series (non-GMP).
9) Procurement, testing and release of the raw materials and packaging materials necessary to manufacture the investigational medicinal product
10) Storage of the API, raw materials and packaging materials in GMP standard
11) Release of the API, raw materials and packing materials for manufacturing
12) Manufacturing, packaging and labelling of the investigational medicinal product in GMP standard:
    a. Hard capsules 2.5mg, ca. 20 000 capsules
    b. Hard capsules 10 mg, ca 20 000 capsules
13) Release of the investigational medicinal product by Qualified Person
14) Stability tests of investigational medicinal product performed in accordance with recommendation of the ICH Q1A (R2) guideline
15) Storage of the investigational medicinal product in GMP standard for at least 12 months
16) Shipment of the investigational medicinal product to two sites in Europe designated by the Ordering Party

Integral part of the Order is providing reports and protocols (in English) from every stage of the project such as: API characterization report, polymorphism study report, formulation development report, scale-up manufacturing report, stability protocol and stability studies report of non-GMP batches and IMP, methods validation/ verification

protocols and reports, GMP campaign report, Certificates of Analysis and Certificate of GMP compliance of investigated medicinal products.

The proposal should cover all costs of the contract including: cost of materials necessary for analytical methods development, procurement of the raw materials and packing materials; cost of manufacturing, packing and labelling of the investigational medicinal product in GMP standard, cost of the stability studies of non-GMP batches and IMP, cost of storage of API, raw materials and IMP, cost of shipment (temperature controlled and logged shipment) of the Investigational Medicinal Products to two sites in Europe designated by Ordering Party and cost of preparing necessary documentation related to manufacturing process.

Technical Information Package is attached as Appendix no 6.

Detailed Project Plan is attached as Appendix no 7.

MSDS for OATD-02 is attached as Appendix no 8.

PDE report for OATD-02 is attached as Appendix no 9.

Appendices 6 – 9 containing confidential data will be shared upon request of the Contractor after receiving by the Ordering Party copy of the hand-signed confidential disclosure agreement (CDA, Appendix no 5). Copy of the signed CDA should be send on l.makolski@oncoarendi.com. Original, hand-signed, document should be send at:

OncoArendi Therapeutics S.A., ul. Żwirki i Wigury 101, 02-089 Warsaw, Poland

The Contractor is required to:

1) Deliver the Site Master File.
2) Organize teleconferences to report project progress.
3) Prepare reports from project progress (in English). Reports should be issued every week or as needed.
4) Organize project meetings at Contractors site upon request of the Ordering Party
5) Develop specification of the raw materials, packing materials and investigational medicinal product
6) Being consent to conduct an audit at the manufacturing site by the Ordering Party or representative of the Ordering Party.
7) Manufacture, pack and label investigational medicinal product; release API, raw materials, packing materials and investigational medicinal product and perform stability studies in the GMP laboratory of the Contractor in accordance with current ICH guidelines and Annex 13 of Manufacturing of Investigational Medicinal Products (ENTR/F/2/AM/an D(2010) 3374)
8) Carry out operations related to receipt, storage and shipment of the investigational medicinal product in accordance with CPMP/QWP/609/96/Rev 2 „Guideline on Declaration of Storage Conditions".
9) Validate analytical methods necessary to release investigational medicinal product in accordance with recommendation of the ICH Q1A (R2) guideline.
10) Release investigational medicinal product by GMP laboratory of the Contractor.
11) Perform stability studies of medicinal investigational product (including storage of IMP) in GMP laboratory of the Contractor in accordance with recommendation of the ICH Q1A (R2) and Q1B guideline. Product will be routed to fast and long-term studies in conditions 40°C/ 75% RH and 25°C/ 60% RH. Product will

be tested at specified time points by validated analytical methods. Tested parameters will be: appearance, identity, assay, purity and related substances content, dissolution, water content, content uniformity, microbiological purity. Timetable is presented in Appendix no 7.

12) Prepare necessary documentation (in English or English/mother language) related to manufacturing process including:
    a. GMP Certificate
    b. Specification of API, raw and packing materials
    c. Specification of *in bulk* and final product. Specification for stability studies
    d. Documents accepted by the quality assurance department concerning conducting and control of the manufacturing process, packing and labelling (including technological instructions and reports) of the investigational medicinal product.
    e. Batch records of the manufacturing of the investigational medicinal product (copies of the reports)
    f. Certificates of analysis for API, raw materials and packing materials
    g. Certificates of analysis for investigational medicinal product
13) shipment (temperature controlled and logged shipment) of the Investigational Medicinal Products to two sites in Europe designated by the Ordering Party

For the purpose of the contract the Ordering Party will provide:

1) All necessary information about active ingredient OATD-02, active substance standard, impurities standards.
2) Certificates of analysis, material safety data sheet (MSDS) of API
3) Transfer of analytical methods, access to development of analytical methods reports (assay and related substances content), raw date and consultation with analytical expert.
4) API (manufactured in GMP standard) in amount required to manufacture investigational medicinal product but no more than 1,2 kg, 1 g of API standard and 0,1 g of related substances standards (impurities).
5) Report issued after audit at manufacturer of API
6) Direct address for the delivery of investigational medicinal product including contact person details (phone number and email).

Project completion date, understood as the manufacturing of the investigated medicinal product including report after 6th month of stability studies: **30.09.2022**
Deadline for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches: **52 weeks from singing the contract.**

VI. EVALUATION OF THE OFFERS

VI.1 Price – weight: 90% (90 pts.)

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

$$Pc = \frac{C_{min}}{C_{evaluated}} x90$$

Pc – Points received

C_{min} – The lowest Net price

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

90 – weight of the criterion (90%)

VI.2 **Deadline for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches – weight: 10% (10 pts.)**

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

10 points – when the deadline for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches is set at maximum of 48 weeks from singing the contract

5 points - when the deadline for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches is set at 49-50 weeks from singing the contract

0 points – when the deadline for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches is set at 51-52 weeks from singing the contract

10 – weight of the criterion (10%)

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: **22/03/2021 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 only via email to: **l.makolski@oncoarendi.com** (the total size for attachments cannot exceed 15 MB).

VII.6 The date of receiving the email 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 **l.makolski@oncoarendi.com** (+48 572 572 888) no later than 15/03/2021 15:00 (CET). Contact person is: Łukasz Mąkolski and Magdalena Tyszkiewicz.

VII.9 Any questions concerning the formal issues of the tender should be addressed to k.kazimierczak@oncoarendi.com no later than 15/03/2021 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 § 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.

IX.3 Information regarding contractual penalties:

A) If the offered execution time for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches (as declared by the Contractor in point 3 of Appendix

No. 1) extends for at least 7 days, the Contractor shall pay the Ordering Party a contractual penalty of 0,5% of the net offer price, and then another 1% of net offer price for each additional 7 days of delay. Moreover, the Ordering Party will gain a right to withdraw from the contract of the project execution when execution time for manufacturing of Investigational Medicinal Product, including 3 months of stability tests of non-GMP batches is exceeded by at least 30 days. The right of withdrawal can be exercised until December 31, 2022.

B) Due to the termination or withdrawal from the Agreement by either Party for reasons caused by the Contractor, the Ordering Party will charge a contractual penalty of 15% of net offer price.

C) The formal basis for charging contractual penalties will be a debit note the Ordering Party delivers to the Contractor. The Ordering Party shall be entitled to deduct contractual penalties from payments due to the Contractor.

D) The Ordering Party has the right to claim damages in the amount exceeding contractual penalties based on general principles.

E) Contractual penalties will be paid within 7 days from the debit note receipt date.

F) Contractual penalties sum up.

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

E) Appendix No. 5 - Confidentiality Agreement

F) Appendix No. 6 - Technical Information Package

G) Appendix No. 7 - Detailed Project Plan

H) Appendix No. 8 - MSDS for OATD-02

I) Appendix No. 9 - PDE report for OATD-02