Warsaw, 30/06/2021

REQUEST FOR PROPOSAL No 19/2021- ARG

I. ORDERING PARTY (SPONSOR)

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II. OBJECT FOR THE REQUEST

Organization and comprehensive execution of the phase I, First-in-Human type, clinical trial for a OATD-02 compound.

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.01.01.01-00-415/17)

co-financed by the European Union Funds and carried out on the basis 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 winning 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 knowledge and experience to perform the contract:

(i) have experience in providing services in the field of organization and conduct of clinical trials of medicinal products, including early phases clinical trials (including FIH trials);

(ii) have experience in organizing and conducting oncological or haemato-oncological clinical trials (they have organized and carried out or are in the process of implementing at least 4 such studies);

(iii) they have carried out (or are in process of implementing) at least 7 projects consisting in organizing and conducting a clinical trial of a medicinal product for third parties;

(iv) have experience in conducting, managing and coordinating official matters (related to the organization and implementation of clinical trials of medicinal products) at the regulatory agency in Poland (Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, hereinafter also referred to as URLP) and bioethics committee, they have submitted so far, on behalf of sponsors (entities ordering the organization and conduct of clinical trials), at least 4 Clinical Trial Applications (CTAs) to the above-mentioned units

(v) have experience in the preparation of key clinical trial documentation, including: clinical study protocol, protocol amendments, Case Report Form (CRF), Clinical Study Report (CSR);

(vi) have experience in selecting, contracting and cooperating with subcontractors (in particular the central laboratory) in the implementation of clinical trials;

B) They have the appropriate human resources capable of performing the contract. The Ordering Party requires that the project team, that will be involved in the performance of the contract on behalf of the Contractor has documented experience and professional knowledge (including current certificates confirming training on Good Clinical Practice, in accordance with the requirements for a given position) necessary to perform the contract in strict accordance with applicable regulations, bioethical standards and guidelines of market regulators, as well as robust market practices. Moreover, the Ordering Party requires that the team knows the current polish national and Community regulations, including the European Medicines Agency (EMA) guidelines governing clinical trials. The Ordering Party requires the Contractor to have and employ (acceptable subcontracting) an appropriate team for the performance of the order, in particular:

(i) **Regulatory specialist** with a minimum of five years of experience in the preparation,

submission of regulatory documentation and contacts with regulatory authorities (including URPL), as well as bioethical committees (including committees located in Poland);

(ii) **Project Manager (PM)** who will be responsible for the comprehensive management and supervision of the implementation of the clinical trial as well as communication with potential subcontractors and the Ordering Party, who has at least five years of documented experience in organizing and managing projects in the area of clinical trials, including oncological or hemato-oncological early-stage trials, carried out on behalf of third parties;

(iii) **Qualified Person Responsible For Pharmacovigilance (QPPV)** with a minimum of three years' experience in pharmacovigilance monitoring; authorized to use the EudraVigilance database;

(iv) **Clinical Research Associate (CRA)** who has a total of at least five years of professional experience in the field of monitoring, management or auditing of clinical trials, including at least two years of experience in monitoring oncology or hemato-oncology trials, including the early phases;

(v) **Bioanalytical specialist** (who will be responsible for overseeing the part of the contract performed by the central bioanalytical laboratory) with experience in the development and validation of bioanalytical methods for clinical trials, carried out in accordance with the recommendations of the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), requirements of the EMA as well as experience in creating regulatory documentation in the field of bioanalytics. The Ordering Party requires this specialist to carry out at least 7 similar projects, within which he/she performed in particular the following tasks: (i)bioanalytical service covering the development of the bioanalytical method, (ii) full validation of the bioanalytical method in human biological material listed in the clinical trial synopsis in the section "Schedule of Assessments" and "Pharmacokinetic and Pharmacodynamic Assessments" constituting the Appendix 5 to the Request, (iii) analysis of samples taken from study participants for the purposes of clinical trials in accordance with the requirements set out in Appendix No. 5. The Ordering Party requires that a person holding the position of a bioanalytical specialist was a leading specialist for at least the last 3 years

(vi) **Data Management Team Lead** with at least three years of experience in working with data obtained from clinical trials and providing the services listed in Table 1 (points 46-48 and 51-62). The data management team leader should participate in at least 5 similar projects (involving early phases clinical trials data management) in his/her career. Participation in a project should be understood as performing tasks in the field of data management in a given project.

(vii) **Head of the biostatistical team** with at least three years of experience in biostatistical analysis of clinical trials results and in providing the services listed in Table 1 (points 49-51 and 61-62). The head of a biostatistics team should participate in at least 5 similar projects (consisting in the analysis of data including early phases clinical trials) in his career. Participation in a project should be understood as performing tasks in the field of biostatistical analysis.

The Ordering Party does not allow the same person to perform more than one of the functions listed above during the performance of the contract.

The Ordering Party requires the Contractor to provide, if necessary during the execution of the contract, consultation services of a Qualified Person (QP), in particular in the scope described in point 33 in Table 1.

C) They have the technical potential to perform the order and the certificates and authorizations required by law. In the case of teams involved in conducting a clinical trial on behalf of clinical sites, the Ordering Party requires that members of the team involved in the execution of the contract, have documented experience and professional knowledge (including valid certificates confirming completion of training on Good Clinical Practice, GCP) necessary to perform the contract strictly with applicable regulations, bioethical standards and guidelines of market regulators (including URPL), as well as well-established market practices. The Contractor is also obliged to make available to the Sponsor, along with the offer, the key list of Standard Operating Procedures in order to confirm the possession of the quality system.
The Ordering Party requires the Contractor to engage in the performance of the contract:
- **central Bioanalytical Laboratory,** which will be properly equipped to complete the order on time and to guarantee the continuity of work in the event of equipment failure, having a valid certificate of Good Laboratory Practice (GLP) and appropriate, controlled storage conditions for samples for analysis (it is necessary to guarantee sufficient storage space and the way of marking the samples that enables easy identification). The laboratory must ensure that the documentation prepared and provided by the laboratory during and after the analysis is in compliance with regulatory requirements.
- **a pharmaceutical wholesaler or a central pharmacy** to which the investigated medicinal product will be delivered and where the investigated medicinal product will be stored, with a validated temperature and humidity monitoring system, controlled storage conditions at room temperature (the temperature range will be provided after the tender procedure has been resolved) and strict supervision of warehouse inventories in the premises with access control.

In addition, the Ordering Party requires the Contractor to have validated software for calculating pharmacokinetic parameters.

D) They will be able to constantly supervise the study at the sites in Poland where the clinical trial will be conducted (travel costs will be covered by the Ordering Party only in Poland, thus the Ordering Party requires that the valuation of the scope of the contract described in Table 1 (points concerning the supervision of the sites' work) takes into account the costs related to travel only in Poland);
E) They will ensure the possibility of performing the second stage of the release of the investigational medicinal product referred to in the EMA guidelines (EMA /202679/2018)
F) Guarantee the protection of the personal data of the study participants and the intellectual property of the Sponsor by at least: controlling access to confidential data and the security system operating in the building where the above data will be stored
G) Are in a good economic and financial standing, which assures proper execution of the project;

H) 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 No.2 to this request for proposal. **The Contractor is obliged to attach the CV of the persons (listed in point B) planned to be involved, that meets the requirements indicated above. The Ordering Party allows at this stage the submission of anonymous CVs and delivery of the CVs with the names and surnames of experts before signing the contract. In addition, the Ordering Party requires a copy of certificates confirming completion of training on Good Clinical Practice (referred to in points B and C) and a copy of the GLP certificate, after selecting the best offer, but before signing the contract. The Ordering Party requires the Contractor to submit a list of key Standard Operating Procedures (SOP) together with the tender documents. After contracting, the Contractor is obliged to provide to the Ordering Party the above-mentioned SOPs.**

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 No. 3 to this request for proposal.

IV4. 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: 73000000-2 (Research and development services and related consultancy services)

Order description:

The order includes the organization and execution by a specialized CRO company, the phase I clinical trial with increasing doses of the arginase inhibitor - OATD-02. The aim of the clinical trial, during which the IMP will be administered to a human for the first time (the 'First in Human' study), will be to investigate the safety, tolerability and antineoplastic activity of OATD-02 in patients with cancer diseases (both sexes). Details are described in

Appendixes No. 5 and 6. Due to the need to protect business secrets, in the event of questions regarding this request requiring the disclosure of confidential data, the Ordering Party (hereinafter also referred to as the "Sponsor") reserves the right to provide explanations after handwritten signing and sending by e-mail by the Contractor a scan of the Confidential Disclosure Agreement (CDA). The CDA document will be made available at the request of the Contractor by e-mail. The scan of the completed and signed CDA should be sent to the both indicated e-mail addresses : k.wozniak@oncoarendi.com and k.kazimierczak@oncoarendi.com. **The handwritten original of the confidentiality agreement should be sent to the following address: OncoArendi Therapeutics S.A., ul. Żwirki i Wigury 101, 02-089 Warsaw**. The Protocol synopsis, in the draft version constituting Appendix No. 5 and Appendix No. 6 to this Request will be made available to Contractors who express their interest in participating in the procedure and send a scan of the signed confidentiality agreement. The Sponsor reserves that the initial design of the clinical trial may be changed. The final study plan will be approved after reviewing all preclinical study data and following the recommendations of the regulator's scientific advice procedure. The work schedule will be agreed with the selected Contractor during a 'kick off meeting'. The description of the milestones with the planned timelines is presented in Table 1 in Appendix No. 6. The Sponsor plans to conduct a study in Poland in 3- 4 centers* that are treatment entities that routinely diagnose and treat adult oncological patients, and adult hemato-oncological patients, simultaneously adapted to early phases clinical trials of medicinal products (with possibility of 24h hospitalization of patients) and having experience in conducting such trials.

*Please quote the study taking into account 4 clinical sites. Sponsor reserves the right to resign from one clinical site.

Table 1. Scope of the contract

Tasks	
Preparation of the trial and submission (application) of documents to the regulatory authority and the bioethics committee	
1.	Development (in collaboration with the Sponsor) of the final clinical trial plan (Project Plan).
2.	Preparation of a feasibility questionnaire, obtaining signed Confidential Disclosure Agreement (CDA) forms from people involved in the feasibility process on behalf of the centers also called as sites, verification the feasibility of conducting the study in selected (together with the Sponsor) sites (whose profile and experience are described in Appendix No 6), preparation of a feasibility study report and qualification of the sites to participate in the study (in cooperation with the Sponsor), in Poland.
3.	Planning and conducting a pre-study visit (PSV) by a qualified Clinical Research Associate (CRA) in 4 selected centers (with the possible participation of the representative(s) of the Sponsor *), in Poland. During the visit, the following tasks should be done: determining the composition of the study teams, discussing the assumptions of the project, verifying the feasibility of the project by the planned team, verifying the equipment and premises, collecting relevant certificates, collecting the data necessary to prepare financial contracts with Investigators and centers; preparation of a detailed report on each pre-study visit. **The Sponsor also reserves the right to participate in subsequent monitoring visits referred in point 27.*
4.	Preparation of the budget, negotiation of the budget and terms of the clinical trial agreement with the centers and Investigators selected by the Sponsor (based on the feasibility study report). Preparation of a tripartite agreement* (between the CRO, center and the Principal Investigator), conducting and finalization of the contract signing process. Preparation of annexes to agreements for centers and investigators (if necessary).**

	**The template of a trilateral agreement must be approved by the Sponsor.* ***Please include in the valuation one annex for each contract. The number of annexes might change.*
5.	Selection and contracting of a central laboratory, which will meet the requirements described in section IV.2 C
6.	Development of a clinical trial protocol based on the protocol synopsis prepared by the Sponsor. The protocol must be approved by the Sponsor. Protocol synopsis is attached as Appendix No. 5. The Sponsor informs that the initial plan of the clinical trial is subject to change.
7.	Preparation and updating of clinical trial documentation created before and during the trial and also preparation of documentation after completion or discontinuation of the trial. The clinical trial documentation must contain all required documents, including, among the other things: • Patient Information and Informed Consent Form* and Document (template) intended for the participant of the study, aimed at implementing the applicable provisions on the protection of personal data; • Pre-screening Informed Consent Form • Case report form (CRF) with an explanation and specifications adapted to the CRO format (electronic CRF)*; • Monitoring plan; • Manual for a laboratory diagnostician and study personnel collecting biological material (Laboratory Manual, for both central and local laboratories); • Management plan in case of any deviations from the Study Protocol; • Study instructions for Investigators and other members of the study team; • Instructions for collecting biological materials for biobanking • Patient diaries and other documents specific to the country in which the study will be conducted (Poland). Sponsor expects all documents to be prepared in English, and selected documents also to be prepared in polish in accordance with applicable national and community law. ** Please quote including a double update of the ICF and a triple of CRF. Number of amendments might be changed.*
8.	Preparation and submission (on behalf of the Sponsor and for the Sponsor) of application (and its possible amendments) for a clinical trial authorization and other applications* that may be necessary during the clinical trial and after its completion, to the URPL, along with the payment of official fees, in accordance with domestic requirements (fees should be included in the offer price). ** Please quote including 4 substantial amendments and 2 non substantial amendments to the protocol.* *Number of amendments might be changed.* *If, at the time of submitting the application, the Clinical Trial Information System (CTiS) which will enable the submission of one application for both the registration office and the bioethics committee, will be in use, this point will apply to one application to the above mentioned units.*
9.	Entry in the EudraCT database, application for assignment of an EudraCT number; current updating of the information (if this requirement will still apply after the entry into force of Regulation 536/2014).
10.	Registering the study on the website clinicaltrials.gov and updating the information on the website (if this requirement will still apply after the entry into force of Regulation 536/2014).
11.	Preparation and submission of an application to appropriate bioethics committee (on behalf of the Sponsor and for the Sponsor) to request an opinion on a clinical trial* and other applications that may be necessary during the clinical trial and after its completion along with the payment of the fee (fees should be included in the offer price).

	** Please quote including 4 substantial amendments and 2 non substantial amendments to the protocol. Number of amendments might be changed.* If, at the time of submitting the application, the Clinical Trial Information System (CTiS) which will enable the submission of one application for both the registration office and the bioethics committee, will be in use, this point will not apply.
12.	Correspondence with regulatory authority (URPL) and appropriate bioethics committee on behalf of and for the Sponsor - in agreement with the Sponsor. In addition, the Sponsor requires all correspondence with regulatory authority and the bioethics committee to be translated into English.
13.	Preparation and submission of periodic reports required by law, e.g. annual progress reports, etc. to the regulatory authorities and/or the appropriate bioethics committee.
14.	Arranging trial insurance in accordance with applicable regulations; along with the payment of the insurance fee.
15.	Preparation, printing and delivery to the centers of a set of documents necessary to conduct the trial (Investigator's Site Folders), including among the other things, logs regarding the status of patients in the center and the accountability of the Investigational Medicinal Products, Study protocol, template of the Patient Information and Informed Consent Form*, template of a pre-screening Informed Consent Form, a template of a document intended for a participant in the study aimed at implementing the applicable provisions on the protection of personal data*, and a template of the patient's diary* , instructions for investigators, printouts of the insurance policy, consent of the relevant regulatory authority (URPL) / bioethics committee along with correspondence. **in an amount sufficient for the planned number of patients (40)*
16.	Organization of on-line Investigator's meeting, preparation of a presentation, active participation of the CRO team in the meeting.
17.	Training of the CRO project team along with obtaining confirmation of training completion.
Project management	
18.	Coordination of all work related to the organization and conduct of a clinical trial, communication with the Sponsor and all potential subcontractors, preparation of monthly reports (at Sponsor's request), control of the project budget, organizing meetings with the Sponsor (also at the Contractor's HQ) at the Sponsor's request, etc.
19.	Supervising the status of the trial and reporting to the Sponsor including organizing teleconferences * (during which the progress of the project will be discussed) and the preparation of notes from the meeting) * please quote the weekly teleconferences. The frequency of teleconferences is subject to change.
20.	Cooperation with the Sponsor, experts and subcontractors implementing individual parts of the project, including those acting on behalf of the Sponsor e.g. the company responsible for the preparation of the Investigational Medicinal Product Dossier (IMPD) and the Investigator's Brochure (IB), as well as for the preparation of answers to the questions posed by the Regulatory Authorities during the verification of the application for permission to start a clinical trial and the documents attached to it regarding the quality, production and control of the investigational medicinal product, preclinical toxicological and pharmacological studies.
21.	Establishing the communication path with the Sponsor.
22.	Providing scans of the documentation (at the Sponsor's request).
23.	Coordinating the work of all subcontractors (e.g. central laboratory, warehouse, etc.)

24.	Preparation, delivery and presentation of all necessary data (including preliminary PK and PD reports (if applicable)) at the Safety Review Committee (SRC) meetings * Participation in SRC meetings and preparation of the meetings reports/summaries **Details regarding SRC can be found in Appendix No 5.*
25.	Providing all necessary data to the Sponsor in order to make a decision on the dose escalation / de-escalation / expansion.
Monitoring of the centers	
26.	Conducting Site Initiation Visits, including collection of the required signatures, conducting training for people who were not participating in the Investigator's meeting and supplementary training with obtaining confirmation of training completion, preparation of the initiation visits reports and follow up letters.
27.	Monitoring of the clinical trial (visits adjusted to the recruitment rate*), preparation of visits reports and follow up letters; documented telephone contacts with the sites in the form of e.g. a note containing the date of the conversation and its subject; correspondence with the Centers; drug control and accountability; training through teleconferences if necessary. ** Please quote 8 monitoring visits at each site. Number of visits might be changed.*
28.	Maintaining supervision over the Centers between visits throughout the whole recruitment and clinical observation period - remote visits by phone/Internet*, completed with the report and follow up letter. ** Please quote 4 remote visits at each site. Number of visits might be changed.*
29.	Conducting Close Out Visits at all of the sites participating in the project - preparation of the visits reports and follow up letters, collecting the required documents and verification of completeness of documents; preparation of documentation for archiving; final drug accountability.
Activities related to distribution and supervision of Investigational Medicinal Product (IMP)	
30.	Release of the IMP to a clinical trial (stage II of the release).
31.	IMP management*: receipt and storage of the IMP in conditions compliant with the requirements, delivery of the IMP to the centers, control and accountability of the IMP. ** Please quote 3 transports for each of the sites. Number of transports might be changed.*
32.	Destruction of the IMP (together with delivery of the certificate of destruction).
33.	Decision making (in agreement with the Sponsor) when deviation related to IMP occurs (e.g. medicinal product storage temperature deviations).
Conduct of Clinical trial	
34.	Organization and conduct of a clinical trial in compliance with ICH* Good Clinical Practice guidelines (*International Council on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use), Declaration of Helsinki and all other applicable international, national and community regulations.
35.	Conducting a clinical trial in accordance with the study protocol, supervision of the diagnostic tests and procedures appropriate for the each visit indicated in the study protocol.
36.	Supervision over the recruitment of study participants.
37.	Reimbursement of travel and accommodation expenses for study participants.
38.	Managing the study teams involved in the study.
39.	Management of clinical trial documentation during the project.
40.	Development of amendments to the clinical trial protocol* (if necessary) *Please quote 4 substantial and 2 non substantial amendments. Number of amendments might be changed.
41.	Preparation of annexes to financial contracts for all subcontractors* (if necessary) *Please quote 1 annex with each of the subcontractors. Number of annexes might be changed.

42.	Organizing the necessary laboratory materials and delivering them to the centers. Management of logistics related to transport (to the central laboratory/laboratories and to the Sponsor's headquarter) and storage of biological material collected from patients. Details regarding material shipments are described in the Appendix No 6.
43.	Management of payments for sites and study teams.
44.	Management of payment for subcontractors.
45.	Conducting training/courses for study teams related to substantial amendments to the study protocol) * **Please quote 4 trainings. Number of trainings might be changed.*
Data management and data analysis from a clinical trial along with biostatistics (plus all other necessary activities for the proper collection, processing and analysis of data)	
46.	Development of a Data Management Plan.
47.	Data management and data processing.
48.	Database design, development and validation.
49.	Development of a Biostatistical Analysis Plan.
50.	Development of a biostatistical description of the study in the partial analysis reports and in the final analysis report (Clinical Study Report, CSR*).*
51.	Data verification and analysis.
52.	Preparation of the Data Handling Report.
53.	CRF review.
54.	Edit Check Programing.
55.	Listing Programing, including: Non-Unique Table Programming, Unique Figure Programming, Non-Unique Figure Programming, Unique Listing Programming, Patient Profile Programming.
56.	Quality control and database closure.
57.	Electronic data transfer (import).
58.	Medical terms coding.
59.	Database transfer
60.	Sponsor database transfer setup.
61.	Preparation of relevant documents / data along with preliminary PK and PD reports (if applicable) for SRC team meetings.
62.	Preparation of all necessary data for the Sponsor in order to make a key decisions in the study on the further dosing (escalation / de-escalation / dose expansion) of the product, completion of the study, creating of amendments, etc.
Bioanalytical service (central laboratory)	
63.	Bioanalytical service including the development of a bioanalytical method for the determination of the main compound and biomarkers (based on preclinical data collected by the Sponsor, LC-MS/MS)*, full validation of the bioanalytical method in human biological material, performance of all determinations / measurements (in accordance with the items listed in the protocol synopsis of clinical trial in Schedule of Assessments" and „Pharmacokinetic and Pharmacodynamic Assessments") which is Annex 5 to the Request, collected from the study participants, including the provision of laboratory materials (kits). ** in the case of determination of orotic acid, Sponsor allows to use a commercial method (available in laboratories as a standard methodology), with the subject to provisions that this method must meet the Sponsor's requirements (the following parameters will be assessed among others: range of determined concentrations, Lower Limit of Quantification - LLOQ etc).*

	In addition, Sponsor allows the possibility of contracting a second central laboratory for the determination of orotic acid if the first central laboratory is located outside Poland, due to the necessity to perform the analysis and deliver the results within max. 4 days from the collection of biological material. The Sponsor requires a qualifying visit at the central bioanalytical laboratory/laboratories before signing the contract with laboratory/laboratories, with the possible participation of the representative / representatives of the Sponsor. The Sponsor allows the qualification of the central laboratory by collecting the necessary documents without the need to visit the laboratory if the laboratory is located outside Poland. The decision on a possible visit to the central laboratory will be made by the Sponsor after preliminary qualification based on the supplied set of documents.
64.	Management of biological material, including its storage.
65.	Preparation of the preliminary and complete bioanalytical report.
66.	Providing the Sponsor with bioanalytical results (in the form of raw data) on an ongoing basis in line with the progress of the clinical trial.
67.	Involving, for the order execution, a team of specialists with knowledge and experience in the development and validation of bioanalytical methods for the purpose of analyzing samples of biological material collected from patients.
68.	Archiving of samples.
Medical Monitoring and Pharmacovigilance Service	
69.	Registration of persons from the Contractor's personnel authorized to the EudraVigilance database as Users in the Sponsor's Virtual Affiliate profile.
70.	Preparation of SAE forms, SUSAR forms and pregnancy forms.
71.	Maintaining supervision over pharmacovigilance in a clinical trial - full service, including: development of a safety monitoring plan and its updating, reporting of adverse events (SAE, SUSAR), pregnancy reporting, adverse events follow-up, development of safety reports and their submissions to the relevant authorities, preparation and submission of DSURs to the relevant authorities.
72.	Sending/ providing the new information regarding safety of IMP to Investigators (SUSAR Alert Letter).
73.	Reporting to regulatory authority and appropriate bioethics committee (if applicable) about new information regarding safety of IMP.
74.	Set up and maintain a safety database.
75.	Ensuring data consistency between the clinical database and the safety database (SAE reconciliation).
76.	Medical Review of SAEs.
77.	Safety assessment of study participants (relevant data set provided prior to each Dose Escalation Committee meeting).
78.	Participating in SRC meetings.
79.	Preparation of Safety Narratives.
80.	Verification of listings before database closing (per subject listings) regarding, among the others: Physical Examination, Vital Signs, Safety Lab, AEs, Concomitant Medication, Medical History, etc.)
81.	Review and analysis of subject safety profiles.
Preparation of a Clinical Study Report (CSR)	
82.	Preparation and verification of the report after conducting an interim (partial) analysis (the report must be finalized by December 2023 if the study will last longer than December 2023),

	describing the progress of works from the beginning of the project implementation until the mid November 2023* ** Partial analysis of the results for the primary endpoint will apply if the preparation of the final CSR is not possible by this date*
83.	Preparation and verification of a clinical study report (CSR).
Quality assurance	
84.	Quality assurance and quality control.
85.	Preparation for the Sponsor's audit; ensuring the presence of the Clinical Research Associate at the center during audit, participation in a teleconference regarding audit conclusions. ** Please quote audits at 2 chosen sites. The numbers of audits might change.*
86.	Quality control of all documents created before, after and during the study (among the others: study protocol, case report forms, Patient information and informed consent form, clinical study report, etc.) and continuous evaluation of the quality of data obtained from the study.
Archiving of documents	
87.	Providing the Trial Master File plan to the Sponsor. Preparation and maintenance of TMF.
88.	Delivering TMF to the Sponsor upon completion of the study.
89.	Archiving of ISF (Investigator's Site Folders) and clinical trial documentation.
Payments for the Sites and study teams for Conducting Clinical Trial	
90.	Please take into account all costs related to conducting a clinical trial in clinical centers (remuneration for study teams and the center, carrying out all procedures in accordance with the trial protocol, including biopsies and imaging, determinations in local laboratories with archiving of samples, possible 24-hour stay of patients in the centers*, storage of the medicinal product in the pharmacy, etc.) ** Please quote one-time 24-hour stay for all (40) patients. Numbers of stays might change.*
Other Charges	
91.	Please take into account all costs for subcontractors related to the conduct of a clinical trial not listed above (e.g., all license fees - if applicable, etc.). All other necessary costs, such as travel costs for team members (if necessary), accommodation costs, translation costs or other costs and expenses related to office and administrative activities (printing, scanning, copying, courier services, etc.) should also be taken into account.

The scope of the order may change as a result of circumstances that the Ordering Party could not objectively foresee at the time of concluding the contract, or circumstances resulting from the implementation and conduct of a clinical trial in accordance with the current regulations.

The Contractor is required to organize and conduct the clinical trial as a comprehensive service, the scope of which is indicated in the order description. The Sponsor allows the subcontracting of individual elements of the order. The Contractor is responsible for the qualification of the subcontractor and is responsible for the commissioned work. The selection of a subcontractor requires the consent of the Ordering Party.

The Ordering Party reserves the right to terminate the contract with the Contractor in the absence of a positive, opinion issued by the competent bioethical commission / obtaining consent to commence a clinical trial from the URPL. The Ordering Party reserves the right to terminate the contract with the Contractor also if, for scientific or business reasons, the work related to the OATD-02 molecule or the arginase program developed by the Sponsor is stopped or suspended. The contract will regulate mutual settlements between the Sponsor and the Contractor in such cases.

The duration of the contract:

The Ordering Party also reserves the maximum deadlines for the implementation of the following activities:

1) The term of contracting the centers by the CRO – no later than end of May 2022;
2) The deadline for submitting documents together with the application for authorization and commencing a clinical trial of a medicinal product to the regulatory authority (pl.URPL) and for the opinion of the relevant bioethics committee - 8 (calendar) days after the Ordering Party provides the last documents (details can be found in Appendix No 6);
3) The date of enrollment of the first patient - may not be longer than 4 weeks from the occurrence of the last of the following events: (i) obtaining consent to commence the clinical trial, (ii) obtaining a positive opinion from the bioethical committee about the study, (iii) delivering the IMP to the center;
4) The deadline for submission of the final CSR and TMF - 26 weeks from the end of the last visit of the last patient.

The implementation of the contract should begin immediately after signing the contract, and the planned date of receipt by the Contractor the last documents that will be a component of the package submitted to the URPL and the relevant bioethical committee is no later than end of first quarter 2022.

VI. EVALUATION OF THE OFFERS

VI.1 **Price** – weight: 50% (50 pts.)

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

$$Pc = \frac{C_{min}}{C_{evaluated}} x50$$

Pc – Points received

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 **The term of contracting the centers by the CRO -** weight: 15% (15 points)

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

15 points - when according to the declaration the centers are contracted by April 15, 2022 (inclusive)
10 points - when according to the declaration the centers are contracted by April 29, 2022 (inclusive)
0 points - when according to the declaration the centers will be contracted by May 31, 2022 (inclusive)

The maximum deadline for signing contracts with the centers may not be longer than May 31, 2022.

VI.3 **The deadline for submitting documents together with the application for authorization and commencement of the clinical trial of the medicinal product to the regulatory office (pl. URPL) and for the opinion of the relevant bioethics committee** (after the Ordering Party has provided the last documents ***) – weight: 15% (15 pts.)

In this criterion, points will be awarded (with accuracy to two decimal places) according to the formula:

$$Tz = \frac{T_{min}}{T_{evaluated}} x15$$

T_z - points in the criterion of the deadline for submitting documents together with the application for authorization and commencement of the clinical trial of the medicinal product to the regulatory office (pl.URPL) and for the opinion of the relevant bioethics committee

T_{min} - the shortest declared deadline for submitting documents along with the application for authorization and commencement of the clinical trial of the medicinal product to the regulatory office (URPL) and for the opinion of the relevant bioethical committee, counted in full days from among the submitted offers that cannot be rejected

$T_{evaluated}$ - the term declared in the evaluated offer, counted in full days

The maximum deadline for submitting the documents may not be longer than 8 (calendar) days from the delivery of the last documents by the Ordering Party.

*** The last documents provided to the Contractor, included in the package submitted to the URPL and the bioethics committee, in order to obtain consent to commence the study, will be the documents listed in Appendix No 6. The remaining documents included in the package must be prepared by the Contractor prior to the finalization of the documents mentioned above.

VI.4 **The date of enrolment of the first patient** - Weight: 15% (15 pts.)

In this criterion, points will be awarded (with accuracy to two decimal places) according to the formula:

$$Tp = \frac{T_{min}}{T_{evaluated}} x15$$

T_p - points in the criterion, the date of enrolment of the first patient

T_{min} - the shortest declared date of enrolment of the first patient counted in full weeks out of submitted offers that are not subject to rejection

$T_{evaluated}$ - the period declared in the evaluated offer, counted in full weeks

For the avoidance of doubt, in the event that an incomplete week is declared in the offer, this period will be rounded in accordance with the mathematical rules (i.e. endings less than 50 will be omitted, and endings 50 and more will be increased to whole numbers).

The maximum date of enrolment of the first patient cannot be longer than 4 weeks from the occurrence of the last of the following events: (i) obtaining consent to commence the clinical trial, (ii) obtaining a positive opinion from the bioethical committee about the study, (iii) delivering the IMP to the center.

* The possible delay in the delivery of the IMP cannot be caused by reasons attributable to the Contractor.

VI.5 **The deadline for submission of the final CSR and TMF from the end of the last visit of the last patient (LPLV)** - Weight 5% (5 pts.)

In this criterion, points will be awarded (with accuracy to two decimal places) according to the formula:

$$Td = \frac{T_{min}}{T_{evaluated}} x5$$

T_d - points in the criterion, the deadline for submission of the final CSR and TMF
T_{min} - the shortest declared deadline for the delivery of the final CSR and TMF documents counted in full weeks, out of the submitted offers that are not subject to rejection
$T_{evaluated}$ - the period declared in the evaluated offer, counted in full weeks

For the avoidance of doubt, in the event that an incomplete week is declared in the offer, this period will be rounded in accordance with the mathematical rules (i.e. endings less than 50 will be omitted, and endings 50 and more will be increased to whole numbers).

The maximum deadline for delivering the final CSR and TMF documents cannot be longer than 26 weeks from the end of the last visit of the last patient.

VI.6 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: **30/07/2021, 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 emails to: **k.wozniak@oncoarendi.com, k.kazimierczak@oncoarendi.com** and **a.bajera@oncoarendi.com** or via the Competitiveness Database available at: **https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl/**

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: k.wozniak@oncoarendi.com, k.kazimierczak@oncoarendi.com and a.bajera@oncoarendi.com no later than 21/07/2021 15:00 (CET). Contact persons are: Kinga Woźniak, Kinga Kazimierczak and Anna Bajera.

VII.9 Any questions concerning the formal issues of the tender should be addressed to: k.kazimierczak@oncoarendi.com no later than 21/07/2021 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, 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 Competitiveness Database.

IX. MOST IMPORTANT PROVISIONS OF THE AGREEMENT

IX.1 Contractor will be obligated to enter into the agreement including all conditions presented in the 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 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 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.

IX.3 Information regarding contractual penalties:

Contractual penalties will be enforced only in the event of fault or gross negligence of the Contractor. Contractual penalties will be charged only when the breach of the obligation occurred as a result of circumstances for which the Contractor bears responsibility. In the event of failure to meet the deadlines, the Contractor is required to prove that it has taken all necessary activities to perform the obligation. For the avoidance of doubt, contractual penalties will not be charged if the extension of deadlines for the performance of the contract is made for reasons the Contractor is not liable for.

A) If the deadline for contracting the centers by the CRO (declared by the Contractor in Appendix 1 point 3.1.) extends for at least 10 days, the Contractor shall pay the Ordering Party a contractual penalty of 0.3% of the net offer price for exceeding the deadline, and then another 0.7% of the net offer price for each additional 10 days of delay. The Ordering Party will also have the right to withdraw from the contract when the offered deadline for contracting the centers by the CRO exceeds the deadline of May 31st, 2022.
B) If the deadline for submitting the documentation together with the application for authorization and commencing a clinical trial of a medicinal product to the regulatory authority (URPL) and for the opinion of the relevant bioethics committee (declared by the Contractor in Appendix No 1 point 3.2.), extends for at least 5 days, the Contractor shall pay the Ordering Party a contractual penalty of 0.2% of the net offer price for exceeding the deadline, and then another 0.5% of the net offer price for each additional 5 days of delay. The Ordering Party will also have the right to withdraw from the contract when the offered deadline for submitting the documentation together with the application for authorization and commencing a clinical trial of a medicinal product to the regulatory authority (URPL) and for the opinion of the relevant bioethics committee is exceeded by at least 20 days. In the event of submitting documentation containing formal defects resulting from the Contractor's oversight, the Ordering Party additionally reserves the right to charge a penalty of 0.4% of the net offer price.

C) If the deadline for enrolment of the first patient (declared by the Contractor in Appendix 1 point 3.3.) extends for at least 14 days, the Contractor shall pay the Ordering Party a contractual penalty of 0.2% of the net offer price for exceeding the deadline, and then another 0.5% of the net offer price for each additional 7 days of delay. The Ordering Party will also have the right to withdraw from the contract when the offered deadline for enrolment of the first patient is exceeded by at least 20 days.

D) If the delivery deadline of the final CSR and TMF documents (declared by the Contractor in Appendix 1 point 3.4.) extends for at least 14 days, the Contractor shall pay the Ordering Party a contractual penalty of 0.2% of the net offer price for exceeding the deadline, and then another 0.5% of the net offer price for each additional 14 days of delay. The Ordering Party will also have the right to withdraw from the contract if the offered delivery deadline of the final CSR and TMF documents is exceeded by at least 30 days.

E) For the termination or withdrawal from the Agreement by any of the Parties for reasons attributable to the Contractor, the Ordering Party shall charge a contractual penalty in the amount of 10% of the net offer remuneration.

F) 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.

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

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

I) The provisions on contractual penalties will be specified in the contract between the Contractor and the Ordering Party.

J) Contractual penalties sum up.

X. APPENDENCIES TO REQUEST FOR PROPOSAL

A) Appendix No. 1 - The offer form,

B) Appendix No. 2 - Statement concerning fulfilment 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 (confidential) – Protocol synopsis

E) Appendix No. 6 (confidential) - Description of milestones with the planned timelines