**REQUEST FOR PROPOSALS FOR PRE-CLINICAL TRIALS (PHYSIOCHEMICAL TESTS, ADME-TOX, GENOTOXICITY, SAFETY PHARMACOLOGY AND TOXICOLOGY) NECESSARY TO COMMENCE CLINICAL TRIALS AND PHASE FOR EC313 COMPOUND.**

Case ZO-07-2017

Commencing a job within project no, POIR.01.01.01-00-0123/16 entitled ***"Development of Selective Endometriosis Therapy Based on Mesoprogestins"*** we invite to submit a tender for making pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313.

1. **CONTRACTING ENTITY:**

Evestra Onkologia Sp. z o.o., seated in Łódź at ul. Jana Muszyńskiego 2 lok. 3. 22, 90-151 Łódź, KRS 0000544596, NIP 5311691730, REGON: 360861230, e-mail: [zamowienia@evestraonkologia.pl](mailto:mwierzbicki@evestraonkologia.pl);

1. **PROCEDURE TYPE:**

The procedure is in the form of a request for proposals according to the competitiveness rule, pursuant to art. 70¹ - 705 of the act of 23rd April 1964 – the Civil Code (i.e. Off. J. of 2014, item 121).

1. **GENERAL INFORMATION:**

The order is co-financed from the Smart Development Operating Programme 2014-2020 within the project no. POIR.01.01.01-00-0123/16 entitled ***"Development of Selective Endometriosis Therapy Based on Mesoprogestins"*** The project key objective is to validate a new active substance on in vitro and in vivo models and to perform clinical trials for further development of a new form of endometriosis therapy.

1. **DESCRIPTION OF THE SUBJECT OF THE PROCUREMENT:**
2. The subject of the procurement includes services of pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313 compound which is the subject of the project entitled: "Development of Selective Endometriosis Therapy Based on Mesoprogestins" A detailed scope of the procurement has been included in Attachment no. 4 hereto. Generated data shall be used to prepare documentation required to apply for clinical trials permit and subsequently shall be included into the so called IMPD (Investigational Medicinal Product Dossier) / IND (Investigational New Drug)
3. The procurement includes:
4. requesting a respective Ethical Commission for Tests on Animals for a permit for research works (if applicable in particular task);
5. making experiments divided into the following tasks:

Task no. 1 – Physiochemical tests

Task no. 2 – Pharmacokinetic tests

Task no. 3 – Metabolism tests (ADME-TOX)

Task n. 4 – Safety pharmacology

Task no. 5 – Genotoxicity (in vitro)

Task no. 6 – Genotoxicity (in vivo)

Task no. 7 – Toxicology (rodents)

Task no. 8 - Toxicology (primates)

1. The Contractor shall develop a time attachment for tests within each task, which shall in particular include:
2. maximum time to deliver the active substance
3. period for methods' validation (if applicable),
4. experimental part for in vitro,
5. part regarding animals' acclimatisation,
6. experimental part on animals (counted from 1st administration till necropsy of the last animal),
7. time needed to prepare a non-audited draft report;

and shall include the following data in the form of a graph for animal tests:

- first day of administration;

- end of the in vivo phase for a given test;

- draft report delivery time;

- delivery time of a draft report with audited tabular data.

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| NOTE: the time attachment should only include information of use in case of performing a given task within the procured service. **A time attachment template constitutes Attachment no. 5 hereto.** |

1. In case only one or some of the tasks are performed, before commencing the task(s), the Contractor shall be obliged to deliver to the Contracting Entity information regarding:

- a need for certain data (acquired from previous tasks) to be transferred by the Contracting Entity, providing their type and delivery date;

- a need to perform tests by the Contracting Entity or another entity which are necessary for the performance of the task, providing their type and completion date.

- the amount of API required with schedule of deliveries

1. All tests within task no. 4 (item 1, 2, 3), no. 6 (item 1), no. 7 (item 2), no. 8 (item 2) being the subject of the procurement must be conducted according to the Good Laboratory Practice.
2. Unless Attachment 4 provides to the contrary**, the Contractor shall incur all and any costs related to the Service, including the costs of: animals' supply/maintenance in good welfare, reagents and consumables needed for the experimental procedures (needles, syringes, test tubes), own use of lab equipment, access to third parties' lab equipment, including possible transfer of samples to be analysed from the Contracting Entity which shall be necessary for the full performance of the procured tasks, animal euthanasia.** NOTE: The purchase of materials/reagents for the Service should be monitored for safety certificates and confirmation that they are non-contaminable products which can be used in works following the GMP standard. Disposal of animals and waste generated during experiments after the tests have been completed shall comply with the waste procedure which involves the environmental aspect.
3. **The Contracting Entity shall deliver animals for tests described in task 2 (item 1), task 6 (item 1), task 7 (item 1 and 2). The animals shall be delivered according to procedures applicable at the Contractor's.**
4. The Contractor shall be obliged to allow Contracting Entity's representatives (upon Contracting Entity's request) participation in the tests in the capacity of observers.
5. The Contractor shall deliver full documentation on the tests in a hard copy and in an electronic format (on a medium), sent in an MS Office editable format, in the English language:
6. Interim reports – which are records of each Service in the form of a description of the methodology of preparation and execution, conditions in the laboratory, results in numeric form and registered images together with their analysis, delivered after full set of tests for each tested material is completed;
7. Final report – including a detailed description of achieved results and photographs of significant changes found during anatomopathological examination and microscopic photographs of significant changes in organs found during histopathological examination, graphs and tables in an MS Office editable format.
8. The Contractor shall prepare a final presentation (MS Power Point) presenting the course of tests, achieved results and conclusions and shall present the same during a seminar organised in the Contracting Entity's seat within two weeks from the Contracting Entity's approval of the final report.
9. As of the date of Contracting Entity's approval of each of the Interim Reports and within the fee, the Contractor shall transfer to the Contracting Entity copyright to the pieces (hereinafter referred to as the "Pieces") in the understanding of the Copyright and Related Rights Law (i.e. Off. J. of 2016, item 666, hereinafter referred to as the "Law") created within the procurement by Contractor's employees or subcontractors.
10. The assignment of the copyright and related rights to the Pieces shall be unlimited in time and territory, upon all known fields of exploitation, and in particular shall include the following exploitation fields:
11. recording on any medium, regardless of system and format standards;
12. multiplication by any technique, including for editorial and publishing purposes;
13. making publicly available in Poland and abroad;
14. using, introducing, displaying, transferring and storing in any format, system or standard;
15. entering into computer memory and a multimedia network, including the Internet;
16. placing on digital platforms;
17. making available in such a manner that anyone can access them in a place and time of their choice;
18. dissemination in the form of print, digital recording, multimedia transmission.
19. Procurement Classification according to Common Procurement Vocabulary (CPV): 73.10.00.00 – 3 Research, experiment and development services.
20. **DELIVERY DATE:**

The order shall be completed till 03st February 2019, whereby this date refers to the entire procurement. Completion dates of particular tasks can be different.

1. **PROCEDURAL INFORMATION:**
2. Contractors who meet the following criteria can apply:
3. in respect of competencies or authorisations to perform specific activities, the Contracting Entity has set no specific conditions.

This condition shall be assessed based on a submitted declaration on meeting the criteria for participation in the proceedings.

1. in respect of technical capacity, the Contracting Entity has set the following minimum criteria:
2. in respect of available resources necessary for the due performance of the procurement, the Contractor shall be obliged to show it has a dedicated laboratory with equipment which allows for the performance of the tests;

This condition shall be assessed based on a submitted declaration on having a dedicated laboratory.

1. in respect of professional capacity, the Contracting Entity has set the following minimum criteria:
2. in respect of staff capable of performing the task, the Contractor shall show that it can delegate at least two individuals to work on the procurement who have higher education, experience and qualification necessary to perform the experiments included in the submitted tender.

This condition shall be assessed based on a submitted list of individuals delegated by the Contractor to perform the order, including information on their qualifications, education, experience, scope of entrusted activities together with basis for such individuals to be at the Contractor's disposal.

1. in respect of economic or financial situation necessary for the due performance of the procurement, the Contracting Entity has set no special condition.

This condition shall be assessed based on a submitted declaration on meeting the criteria for participation in the proceedings.

1. the following shall not cause exclusion from the procedure:
2. circumstances listed in Guidelines Chapter 6 sect. 6.5.1 item 8;
3. liquidation or no bankruptcy declared, excluding contractors who after being declared bankrupt executed a composition agreement approved by a legally valid court decision, if the agreement does not provide for satisfaction of creditors by liquidation of the bankrupt's assets.

This condition shall be assessed based on documents listed in item 2 point 1).

1. Apart from the declaration on meeting the criteria to participate in the proceedings which constitutes Attachment no. 3 hereto, the Contractor shall submit:
2. In order to confirm no grounds to exclude from the proceedings due to a conflict of interests, the Contractor shall submit:
3. a declaration according to a specimen which constitutes Attachment no. 2 hereto – regardless of its organisational and legal status;
4. Contractors who are subject to compulsory registration in a separate register shall include a current copy from the register appropriate for them due to their organisational and legal status;
5. In order to confirm the fulfilment of the obligation laid down in item 1 point 2, the Contractor shall submit a declaration on availability of resources necessary to complete the order. A list template constitutes Attachment no. 3 hereto.
6. In order to confirm the fulfilment of the obligation laid down in item 1 point 3, the Contractor shall submit a list of individuals delegated to work on the order, including information on their education, qualifications, experience needed for the due performance of the order and the scope of delegated works together with basis for such individuals to be at the Contractor's disposal.
7. The Contractor can only place one offer for the entire subject of the procurement within a given task. The Contracting Entity has not set a maximum number of tasks a Contractor may apply for. The Contracting Entity has not set any restrictions on the number of tasks which can be granted to one contractor.
8. The tender value should include all costs related to the performance of the order, and in particular: costs of making and submitting an application and obtaining a permit from the Bioethical Commission for tests on animals, costs of making interim and final reports, costs of purchase and maintenance of animals, costs of purchase of materials and animals necessary to perform tests, costs of transferring copyright to the tests' outcomes to the Contracting Entity, unless stated otherwise in attachment no. 4

The offer should be made in the Polish or English language, in a permanent way which guarantees that the content can be read.

1. The Contracting Entity recommends the tender to be prepared using forms which constitute attachments hereto or exactly according to the Offer Form which constitutes Attachment no. 1 hereto.
2. The Contracting Entity recommends numbering all the pages in the tender and securing them against getting disassembled by stapling or binding - for offers submitted in writing.
3. The Contractor shall place the offer in a non-transparent envelope with a note:

***"Offer for pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313 compound.***

***Do not open before 1st  of September 2017"***

1. **The Contracting Entity allows Contractors to submit motions and enquire about the contents hereof.** To this end, the Contracting Entity has established the following forms of communication with Contractors: electronic, to the address: zamowienia@evestraonkologia.pl and [rkochanski@evestraonkologia.pl](mailto:rkochanski@evestraonkologia.pl). A written form shall always be acceptable.
2. Any information regarding the proceedings shall be published by the Contracting Entity on its own website and in the competitiveness base under the address: bazakonkurencyjności.funduszeeuropejskie.gov.pl
3. Individuals authorised to contact Contractors:
4. for substantive issues:

- dr Ze'ev Shaked,

e-mail: zshaked@evestraonkologia.pl;

- Prof. Klaus Nickisch

e-mail: knickisch@evestraonkologia.pl

- MD, PhD Maciej Wierzbicki,

e-mail: [mwierzbicki@evestraonkologia.pl](mailto:mwierzbicki@evestraonkologia.pl) ;

b) for formal issues:

- Robert Kochański, MA

e-mail: [rkochanski@evestraonkologia.pl](mailto:robertkochanski@evestraonkologia.pl) ;

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| **All electronic correspondence should be addressed CC: zamowienia@evestraonkologia.pl** |

1. The Contracting Entity may introduce changes in the terms and conditions of the proceedings. Provisions of point 12 shall apply respectively.
2. The Contracting Entity shall correct the offer in respect of obvious spelling errors, calculation mistakes considering calculation consequences resulting from the changes and other mistakes which make the offer incompliant with the request, provided this does not introduce essential changes in the offer.
3. The Contracting Entity shall request the contractor to remedy any deficiencies in the offer, and in particular the documents named in item 2.
4. The Contracting Entity can invalidate the proceedings without providing any reason or terminate the proceedings without an outcome during each phase.
5. **The agreement will be concluded subject to the approval of the National Centre for Research and Development and it's approval of further research.**
6. **OFFER VALIDITY TERM:**

The Contractor shall be bound by the submitted tender for a period of 90 days. The 90-day period shall commence on the elapse of the deadline for tender submission.

1. **DEADLINE FOR THE SUBMISSION OF TENDERS:**
2. Tenders shall be submitted till 1st of September 2017 12:00 hrs – date and hour of reception by the Contracting Entity shall be binding.
3. Tenders in writing shall be submitted in the Contracting Entity's seat or sent to the following address: Evestra Onkologia Sp. z o.o., ul. Jana Muszyńskiego 2 lok. 3. 22, 90-151 Łódź, Poland.
4. The Contracting Entity allows sending the tender in an electronic format to the following address:[zamowienia@evestraonkologia.pl](mailto:zamowienia@evestraonkologia.pl) and then sending the original documents by mail or delivery in person to the Contracting Entity's seat. If the tender is sent in an electronic form, the Contractor shall safeguard the tender so that its content cannot become acquainted with before the elapse of the deadline for tender submission. In such an instance, it is recommended to give the following subject to the e-mail message: **Oferta ZO-07-2017**
5. The Contracting Entity does not provide for a public opening of tenders. According to the transparency rule of the proceedings, the Contracting Entity, upon a request from the Contractor, shall make the minutes from tenders' opening available.
6. **ASSESSMENT CRITERIA:**
7. The Contracting Entity shall evaluate the tenders according to the following tender assessment criterion:
8. Financial criterion (price) – weight 90 %;

The Contracting Entity shall score by dividing the value of the cheapest tender by the analysed offer value and then multiplying the outcome by the weight, according to the following formula: **WP= (WONC /WOB) x weight,** where WP – score value in the financial criterion, WONC – value of the cheapest tender, WOB – value of the analysed tender.

**NOTE:**

**Should the contractor provide prices in currencies other than PLN, the Contracting Entity shall use an NBP exchange rate of the date of publication of the request for proposal in the Competitiveness Base of the Ministry of Development. Exchange rate tables are available at:**  [**http://www.nbp.pl/home.aspx?f=/Kursy/kursy.htm**](http://www.nbp.pl/home.aspx?f=/Kursy/kursy.htm) **;**

**Should a tender be submitted which generates a tax obligation on the part of the Contracting Entity, according to the regulations on tax on goods and services, in order to evaluate such an offer, the Contracting Entity shall add the value added tax to the price provided therein which must be accounted for according to the said regulations. When submitting the tender, the Contractor shall advise the Contracting Entity whether its offer shall generate a tax obligation on the part of the Contracting Entity providing the name (type) of goods or services whose supply shall involve the tax and their net value. Should a tender be submitted which generates a tax obligation on the part of the Contracting Entity, according to the regulations on tax on goods and services, the price of the best or cheapest price shall be increased by the value added tax to the price provided therein which must be accounted for by the Contracting Entity according to the said regulations. Therefore, in such an instance, the price provided in the tender by such a contractor as "gross price" must not include VAT which the Contracting Entity shall be obliged to account for.**

2. Reports delivery date – weight 10%. The proposed maximum term shall be assessed for the delivery of interim reports from particular tests within a given task and final reports from the given task to the Contracting Entity. The Contracting Entity shall score the maximum delivery dates for interim reports from particular tests and final reports from the given task:

up to 10 days from the end of the experimental phase – 100 points;

up to 15 days from the end of the experimental phase – 90 points;

up to 20 days from the end of the experimental phase – 80 points;

up to 25 days from the end of the experimental phase – 50 points;

up to 30 days from the end of the experimental phase – 30 points;

up to 35 days from the end of the experimental phase – 20 points;

up to 40 days from the end of the experimental phase – 10 points;

above 40 days from the end of the experimental phase – 0 points;

the sum of all points scored for all the tests in a given task shall constitute the basis for assessment, based on the following formula: WP = (WTBO/WMAX) x weight, where: WP – point score for reports delivery criterion, WTBO – number of points scored for the proposed reports' delivery date. WMAX – maximum number of points within the completion date criterion.

1. **AMENDMENT OF THE CONTRACT:**

The Contracting Entity may amend the contract between the Contracting Entity and a Contractor, in case of:

1. changes which result from updating commonly applicable law;
2. reducing the fee amount due to limitation or exclusion of a part of the procurement by the Contracting Entity;
3. extension of the performance term of the contract, if registration or other procedures with respective authorities are extended in time;
4. change of the Contract term, in case the Project deadline varies;
5. extension of the Contract term due to organisational issues on the part of the Contracting Entity;
6. changes to the number of animals subject to tests provided for in the Contract;
7. changes in individuals in charge of contacts and supervision over the contract.
8. occurrence of any events as a result of force majeure;
9. changes in a co-financing contract the Contracting Entity shall execute with an Intermediate Body;
10. **FINAL PROVISIONS:**

The procedure shall be governed by the Polish law. In any matters not stipulated herein, provisions of the act of 23rd April 1964 – the Civil Code (i.e. Off. J. of 2014, item 121) and provisions of current Guidelines on Eligibility of Expenses within the European Regional Development Fund, European Social Fund and Cohesion Fund for the years 2014-2020.

Attachment no. 1 to the Request for proposal

Case ZO-07-2017

**Contracting Entity:**

**Evestra Onkologia Sp. z o.o.**

**ul. Jana Muszyńskiego 2 lok. 3.22**

**90-151 Łódź**

**TENDER FORM\***

**(copy for each task)**

Acting for and on behalf of the Contractor:

…............................................................................................................................................................

(CONTRACTOR'S NAME AND SURNAME/FULL NAME)

seated in / residence address \*\*…........................................................................................................

(RESIDENCE ADDRESS / SEAT ADDRESS)

…............................................................................................................................................................

(PHONE, FAX, E-MAIL)

in response to the request for proposal published on ………………………. 2017 at bazakonkurencyjności.funduszeeuropejskie.gov.pl and on the Contracting Entity's website, I am submitting a tender within the proceedings for **making pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313.**

, run in the form of a request for proposal.

I am offering the performance of the order within task no. …. for the price of: PLN ……………………………………………… gross (say: …………………………………………………........................................................................................)

The tender value includes all and any costs related to the performance of the order.

I declare that the order shall be completed till .............. (i.e. within ......... weeks from actual commencement).

I declare that the delivery date of reports from the end of the experimental phase for particular tests included in the task no. ... shall be ….. days.

I declare that I have experience needed for the due performance of the order.

I declare that I have infrastructure needed for the performance of the order.

I declare that I have qualified staff experienced in running tests on animals.

I declare that I shall complete the order without / with subcontractors\* (if yes, provide the scope of the order which shall be subcontracted).

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I declare that I have obtained all and any information needed for the due performance of the order.

I shall be bound by this offer for a period of 90 days from the deadline for tenders' submission.

The tender together with attachments counts ……… pages.

\* - submit a separate form for each task for which the tender is submitted

\*\* - delete not applicable

…......................................... ………………………………………………………………………

Place, date: signature and personal stamp of the authorised signatory

Attachment no. 2 to the Request for proposal

Case ZO-07-2017

**DECLARATION ON MEETING PARTICIPATION CRITERIA**

**FOR THE PROCEEDINGS AND NO GROUNDS FOR EXCLUSION**

**DUE TO A CONFLICT OF INTEREST**

On submission of the tender for pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313 compound, I declare that the Contractor:

…............................................................................................................................................................

(CONTRACTOR'S NAME AND SURNAME/FULL NAME)

seated in / residence address \*\*…........................................................................................................

(RESIDENCE ADDRESS / SEAT ADDRESS)

…............................................................................................................................................................

(PHONE, FAX, E-MAIL)

**meets / does not meet\*** the conditions for participation in respect of knowledge and experience, financial status, and technical and human potential;

**is affiliated / is not affiliated\*** to the Contracting Entity, personally or in terms of equity, by mutual relations between the beneficiary and individuals authorised to bind the beneficiary or individuals performing on behalf of the beneficiary actions related to preparation and running the proceedings for choosing a contractor and the contractor, which in particular includes:

1. being a partner to a civil partnership or another partnership
2. holding at least 10% of shares,
3. acting as member of a supervisory or management board, proxy, attorney
4. being married, in consanguinity or affinity in a straight line, in second degree of kinship or affinity of the second degree in collateral line or by adoption, guardianship or custody

….....................................................................................

signature and personal stamp of the authorised signatory

\* - delete inappropriate

Attachment no. 3 to the Request for proposal

Case ZO-07-2017

**LIST OF INDIVIDUALS DELEGATED TO WORK ON THE ORDER**

On submission of the tender for pre-clinical tests (physiochemical, ADME-tox, genotoxicity, safety pharmacology and toxicological tests) necessary to commence 1st phase clinical trials for EC313 compound, I declare that the Contractor:

…............................................................................................................................................................

(CONTRACTOR'S NAME AND SURNAME/FULL NAME)

seated in / residence address \*\*…........................................................................................................

(RESIDENCE ADDRESS / SEAT ADDRESS)

…............................................................................................................................................................

(PHONE, FAX, E-MAIL)

shall delegate the following individuals to work on the order:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No.** | **Name and surname** | **EDUCATION / EXPERIENCE / QUALIFICATIONS** | **SCOPE OF DELEGATED WORKS** | **LEGAL BASIS FOR DELEGATION** |
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signature and personal stamp of the authorised signatory