AGENCJA BADAŃ MEDYCZNYCH

REQUEST FOR PROPOSAL – 02/PLX/2025
CONTRACTING AUTHORITY:
POLFARMEX S.A.
ul. Józefów 9, 99-300 Kutno, Poland
VAT No.: 7750001711

I. Background of the procedure

The procedure is conducted in connection with the implementation of the commercial project entitled: **"Development and advancement of an innovative drug combination with beneficial application in the treatment of arterial hypertension"**, co-financed by state budget funds under competitions organized by the Medical Research Agency.

II. DESCRIPTION OF THE SUBJECT OF THE CONTRACT

CPV Code: 73100000-3
The Contracting Authority invites **complete technical and commercial offers for two bioequivalence studies**:

- **Study A (Fasted)** – single-dose BE after administration in the fasted state; and
- **Study B (Fed)** – single-dose BE after administration following a high-fat, high-calorie meal.

The details of the above study and the scope of services will be provided to the Bidder after signing a **Confidentiality and Non-Disclosure Agreement (NDA)**. A Bidder interested in participating in the procedure should send, by e-mail to j.walczak@polfarmex.pl or k.rozycka@polfarmex.pl , a request to receive the NDA and return a signed scan of this agreement to the same e-mail address.
The details of the study, constituting **Annex 1A_Fasting and Annex 1B_Fed (Synopsis)**, will be made available no later than 24 business hours after the signed scan has been received. Bidders who already possess an agreement with content analogous to the template attached to this procedure may submit a scan of such a document (in this case, a signature date earlier than the publication date of this RFP is acceptable).
Annex 1A&1B contains a concise preliminary description of clinical study. In Annex 1, the Contracting Authority proposed the study design, the number and timing of blood sampling following administration of the study products, the scope of laboratory tests, and the minimum number of study participants.
When preparing the offer, the Bidder should refer directly to the assumptions set out in Annex 1.

The study must be conducted in accordance with the requirements applicable to studies used in the marketing authorization process of medicinal products in the European Union, including in particular:

a. International Council for Harmonisation – Good Clinical Practice (ICH E6(R3) GCP),
b. the principles of the Declaration of Helsinki (Fortaleza, 2013),
c. the requirements of European law on clinical trials (Directive 2001/83/EC, Directive 2005/28/EC, and Regulation (EU) 536/2014, where applicable),
d. EMA Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr, 2010),
e. principles of Good Laboratory Practice, where applicable to bioanalytical testing of biological samples (EMA/INS/GCP/532137/2010),
f. ICH M10 Guideline on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 2022),

g. ICH E3 Guideline on the structure and content of clinical study reports (CPMP/ICH/137/95, 1996).

Scope of the contract

1. **Execution of the bioequivalence study** (submission of the application with study documentation in order to obtain approvals to conduct the study, conduct of the clinical, bioanalytical, pharmacokinetic-statistical parts, data management, preparation of study documents, preparation of the study report).

2. The following activities are envisaged:
   - preparation of the basic study documentation (Protocol, ICF, CRF) (conceptual version of the protocol provided by the Sponsor),
   - preparation of documentation required to obtain approval from the local Ethics Committee (EC) and the Competent Authority (CA) to conduct the study (Investigator's Brochure provided by the Sponsor, IMPD provided by the Sponsor – if applicable),
   - submission of documentation and obtaining the required approval from the Competent Authority (CA) and the opinion of the Ethics Committee (EC), including related fees,
   - representation of the Sponsor before the authority issuing approval for the clinical trial and before the Ethics Committee (EC),
   - submission of relevant amendments to the study documentation at the request of the Competent Authority and Ethics Committee, including related fees,
   - preparation of the randomization list,
   - conduct of the clinical part of the study, medical procedures, procedures ensuring the safety of study participants and laboratory assessments, pharmacokinetic sampling, and remuneration for study participants and staff,
   - labeling of investigational medicinal products for individual study participants according to the randomization list and preparation of investigational products for administration (products will be supplied by the Sponsor in multidose packs),
   - provision of an independent study monitor (submission of a monitoring report to the Sponsor after each monitoring visit),
   - return of investigational products to the Sponsor or destruction of investigational products at the clinical site (certificate or confirmation of destruction required),
   - shipment of pharmacokinetic samples to the bioanalytical laboratory,
   - development and validation of the analytical method (in accordance with current EU guidelines, in particular ICH M10 Guideline on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022), together with preparation of a Validation Report – if the Bidder does not already have a validated analytical method for the investigated substances),
   - determination of analyte concentrations in blood samples using analytical methods validated in accordance with current guidelines, including ICH M10 Guideline on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022),
   - study and data management, quality control and quality assurance, including internal audits of documentation and processes during the study (an audit certificate must be attached to the study report),
   - performance of pharmacokinetic and statistical calculations, including preparation of a statistical analysis plan and preparation of the pharmacokinetic-statistical report,
   - delivery of pharmacokinetic data in electronic form (Excel format),
   - preparation of the clinical study report (all study documentation must be prepared in English),
   - preparation of the bioanalytical report, including the bioanalytical method validation report (all bioanalytical documentation must be prepared in English),

- preparation of the integrated study report in accordance with ICH E3 Note for Guidance on Structure and Content of Clinical Study Reports (CPMP/ICH/137/95, July 1996), including appendices (integrated report in English),
- printing and delivery to the Sponsor of a paper version of the clinical study report together with CRFs,
- preparation and delivery to the Sponsor of a study summary in accordance with Appendix IV of the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1): Presentation of Biopharmaceutical and Bioanalytical Data in Module 2.7.1,
- archiving of study documentation (in accordance with national legal requirements or until the Sponsor informs that the documentation is no longer needed, whichever is longer),
- storage of backup plasma samples for at least 3 months from the date of the final study report,
- support for the Sponsor in preparing responses to queries from regulatory authorities in the product registration process, relating to the conducted study, if such arise.

The Contracting Authority does not allow partial offers.

III. CONTRACTING AUTHORITY (STUDY SPONSOR)

POLFARMEX S.A.
ul. Józefów 9, 99-300 Kutno, Poland

IV. TIMELINE FOR CONTRACT EXECUTION

- First subject enrollment is planned for the period **01 June – 01 September 2026** (understood as the signing of the informed consent form for participation in the study).
- The schedule has been prepared based on the estimated availability date of the IMPD – **30 March 2026**.
- According to the study schedule. Details are provided in **Annex 1A&1B**.

V. CONDITIONS FOR PARTICIPATION IN THE PROCEDURE

1. Bidders invited to submit offers must meet the following requirements:

Regulatory compliance

- declare compliance of the study with ICH E6(R3) GCP, the Declaration of Helsinki, EMA Guideline on the Investigation of Bioequivalence, ICH M10 (bioanalysis), ICH E3 (reporting), and applicable EU regulations.

Experience and competencies

- have documented experience in conducting bioavailability/bioequivalence studies: at least 3 studies within the last 3 years, including at least one that resulted in marketing authorization in the EU,
- have experience in obtaining opinions from Ethics Committees and approvals from Competent Authorities,
- have the capacity to recruit healthy participants of both sexes, in line with the study protocol criteria.

Personnel

- Bidder can confirm on the day of submitting the offer that it will*:
    - employ a Principal Investigator with valid GCP training (documented with a certificate),
    - have a pharmacokinetics/statistics specialist with relevant experience,
    - employ staff competent in preparing integrated clinical study reports (CSR) compliant with ICH E3.

*We accept both contracts and letters of intent/other commitments.

Bioanalysis

- possess validated bioanalytical methods or the ability to validate them before initiation of the clinical part of the study, in line with ICH M10 (LLOQ < 0.01 × Cmax),

- possess infrastructure, equipment, and experience in analyzing biological samples (determination of analyte concentrations in blood/plasma).

Quality system and inspections

- hold valid GCP/GLP certificates or have a positive history of regulatory inspections in this area,
- have not received critical findings during inspections by European agencies in the last 4 years,
- maintain a quality assurance system compliant with GCP and up-to-date SOPs.

Participant safety

- possess infrastructure and procedures ensuring immediate treatment of participants in case of adverse events,
- maintain AE/SAE reporting procedures compliant with GCP and EMA requirements (SAEs reported to the Sponsor within 24 hours).

Insurance and audit

- hold valid liability insurance covering study participants and the entire study period, including responsibility for the payment of compensation (no-fault compensation),
- accept the possibility of Sponsor audits of the site and laboratory.

The Bidder may subcontract part or all of the services specified in this RFP. The Bidder must ensure that subcontractors meet the requirements set out in this RFP. To confirm the subcontractors' qualifications, the Bidder must provide documents demonstrating their ability to perform the assigned services. Bidder/Subcontractors must hold a valid GCP/GLP certificate or present a history of regulatory inspections in the field of GCP/GLP, including a short summary of their outcome (number and categories of findings). The Bidder is obliged to conclude relevant agreements/sign letters of intent with subcontractors.
To confirm fulfillment of the eligibility criteria, Bidders are required to complete and attach to their offer a signed **Annex 2 (confirmation of eligibility criteria)**.

2. This request for proposal is **not addressed to** (exclusion criteria):

a) Bidders related to the Contracting Authority by personal or capital ties. Personal or capital ties are understood as mutual relationships between the Contracting Authority and the Supplier, or persons authorized to incur obligations on behalf of the Contracting Authority, or persons performing activities related to the preparation and conduct of the supplier selection procedure on behalf of the Contracting Authority, consisting in particular of:

- participation in the company as a partner in a civil or personal partnership,
- holding at least 10% of shares or stock,
- serving as a member of a supervisory or management body, proxy, or attorney,
- being married, related by direct kinship, affinity up to the second degree, collateral kinship up to the second degree, or related by adoption, guardianship, or custody.

To meet this condition, the Bidder is required to submit together with the offer a signed **statement of no ties** (Annex 3 to this RFP).

b) Bidders:

- referred to in Art. 7(1) of the lists specified in Regulation 765/2006 and Regulation 269/2014, or entered into the list based on a decision regarding entry to the list determining the application of a measure referred to in Art. 1(3) of the Act of 13 April 2022 on special measures to counteract support for aggression against Ukraine (Journal of Laws, item 835);
- whose beneficial owner, within the meaning of the Act of 1 March 2018 on counteracting money laundering and financing of terrorism (Journal of Laws of 2022, items 593 and 655), is a person listed in the registers specified in Regulation 765/2006 and Regulation 269/2014, or entered into the list or being such a beneficial owner as of 24 February 2022, if entered into the list based on a decision determining the application of a measure referred to in Art. 1(3)

of the Act of 13 April 2022 on special measures to counteract support for aggression against Ukraine (Journal of Laws, item 835);

- whose parent company or subsidiary, within the meaning of Art. 3(1)(37) and (39) of the Accounting Act of 29 September 1994 (Journal of Laws of 2021, items 217, 2105, and 2106), is an entity listed in the registers specified in Regulation 765/2006 and Regulation 269/2014, or entered into the list or being such an entity as of 24 February 2022, if entered into the list based on a decision determining the application of a measure referred to in Art. 1(3) of the Act of 13 April 2022 on special measures to counteract support for aggression against Ukraine (Journal of Laws, item 835).

To meet this condition, the Bidder is required to submit together with the offer a signed **statement** (Annex 4 to this RFP).

VI. METHOD OF PRICE CALCULATION

- Prices in the offer should be quoted net of VAT.
- The offer should include all costs of conducting the study, including so-called pass-through costs (if applicable).
- Prices expressed in a currency other than PLN will be converted into PLN according to the average exchange rate of the National Bank of Poland on the date of opening of the procedure.

VII. EVALUATION CRITERIA

- The Contracting Authority will reject offers submitted by a Bidder who does not meet the participation conditions or whose offer is inconsistent with this Request for Proposal.
- **Criteria for the selection of offers:**

Net service price – 70 points (weight 70%)
Points for this criterion will be awarded as follows: the lowest price offered by a Bidder will be considered 100%, which constitutes the maximum number of points. Points will be calculated according to the formula:
(Lowest Price / Bidder's Price) × 70 points
Total completion time (weeks) – 20 points (weight 20%)
Points for this criterion will be awarded as follows: the shortest completion time, calculated in weeks from the date of first subject enrollment to the first version of the integrated study report, will be considered 100%, which constitutes the maximum number of points. Points will be calculated according to the formula:
(Shortest Time / Bidder's Time) × 20 points
Availability of validated bioanalytical methods at the date of offer submission – 10 points (weight 10%)
Points for this criterion will be awarded as follows:

- Validated methods available for analyte determination in the presence of the other analyte (for both analytes) – 10 points
- Validated methods available for determination of individual analytes (without the presence of the other) for both analytes – 8 points
- Validated method available for at least one analyte – 5 points
- No validated analytical methods available – 0 points
- The most advantageous offer will be the one that achieves the highest total score after summing the points from all evaluation criteria. An offer may obtain a maximum of 100 points. Calculations will be made with an accuracy of two decimal places.
- If more than one offer obtains the highest score, the most advantageous among them will be the offer with the lowest price.

VIII. DEADLINE AND FORM OF SUBMISSION OF OFFERS

- Offers must be submitted no later than **15 October 2025**. Offers submitted after this deadline will not be considered.
- Offers must be submitted electronically as signed documents to the following e-mail addresses:
  - j.walczak@polfarmex.pl
  - k.rozycka@polfarmex.pl
- All correspondence must include in the subject line the number of the request for proposal.
- The offer must be submitted using the attached template or must include all information specified in the template. The offer template is provided in **Annex 5**.
- In Annex 5, the Bidder must specify the timelines for the study execution, including: waiting time for authorization from the Competent Authority to conduct the study, Ethics Committee approval (if applicable), proposed dates of drug administration, availability of preliminary results, and delivery of the draft clinical study report (with all required appendices). Annex 5 must also list the documents required for submission to the Competent Authority and the Ethics Committee.
- Questions may be submitted to the e-mail addresses j.walczak@polfarmex.pl and k.rozycka@polfarmex.pl no later than 4 business days before the deadline for the procedure. Questions submitted after this deadline will remain unanswered. To ensure equal access to information for all Bidders participating in the procedure, questions and answers (with the identity of the author hidden) will be sent to all Bidders who have signed an NDA and, where they do not concern parts covered by the NDA, will be published in the same manner as this RFP.
- Each Supplier may submit only one offer.
- The offer must include all required annexes, declarations, and documents.
- The offer must be prepared in Polish or English in a legible manner.
- Before the deadline for submission of offers, the Bidder has the right to:
  - withdraw the offer by submitting written notification through the procedure specified for submitting offers,
  - modify the offer – in such case the Bidder must resubmit all annexes and declarations with an updated date of submission of the modified offer.

IX. OTHER ESSENTIAL TERMS OF THE CONTRACT

- Completion of **Annex 2** is mandatory.
- The Contracting Authority may request clarifications/supplements and reserves the right to verify source documents (e.g., inspection reports, validation reports, SOPs) after the preliminary evaluation and before awarding the contract. Failure to confirm the declared information may result in exclusion from the procedure.
- Payment terms: bank transfer, VAT invoice, payment term to be specified in the contract.
- Contractual penalties: the amount of contractual penalty will be determined between the parties in a separate study agreement.
- Bidders **shall submit offers for both Study A and Study B**. Combined or bundled discounts may be proposed but each study must be clearly itemised.
- **Sequencing and condition precedent (Go/No-Go).** Study B (Fed) **will be initiated only after** the Sponsor reviews the **top-line BE results** of Study A (Fasted) and issues a **written Go decision**. For the avoidance of doubt:
  - A **"negative result"** is defined as **failure to meet** the predefined BE acceptance criteria for the primary PK parameters (e.g., 90% CI outside 80.00–125.00% for AUC and/or Cmax, unless otherwise specified in the Synopsis).
  - If Study A yields a **negative result** or is **terminated**, the Sponsor **will not proceed** with Study B and **has no obligation to fund** Study B work.

- **Decision-gate deliverables from Study A.** Within **[10] business days** of DBL for Study A (or earlier if feasible), the CRO shall provide a **Top-Line BE Memo** and the **PK/Stats tables & listings** sufficient to support the Sponsor's Go/No-Go decision for Study B.