REQUEST FOR PROPOSAL

RFP – 026318–PIVOTAL BIOEQUIVALENCE STUDY OF A NEW FIXED COMBINATION MEDICINAL PRODUCT FOR ORAL ADMINISTRATION

In connection with the implementation of the project no. KPOD.07.07-IW.07-0267/24 entitled "Development and clinical confirmation of bioequivalence of mono and combo products used in the treatment of type 2 diabetes" financed by the National Recovery Plan from the Medical Research Agency, Adamed Pharma S.A. invites you to submit bids for the performance of the subject of the contract defined below, Adamed Pharma S.A. invites to submit tenders for the below-defined service.

I. Subject of the Tender:

Conducting a pivotal bioequivalence study of a new fixed dose combination formulation containing known active substances used in the treatment of type 2 diabetes.

Study Sponsor (Contracting Authority): **Adamed Pharma S.A.**

The Contracting Authority stipulates that disclosure of the full details concerning the subject **(including Appendices no. 2-3 and 6-14)** will be done after signing of confidentiality agreement which is attached to this inquiry **(Appendix no. 1).** Contractors who have already signed a confidentiality agreement must provide the signed agreement before full information regarding this request for proposal is disclosed to them. The signed CDA shall be sent to: **aleksandra.stojak@adamed.com**

The order, which is expected to be carried out according to the schedule presented in point 8, includes:

1. Conducting of pivotal bioequivalence study (submitting the application along with the study documentation to obtain approvals to conduct the study, conducting the clinical, bioanalytical, pharmacokinetic (PK) and statistical parts of the study, data management, medical writing, preparing the study report and study management).

General information about the study:

Pivotal bioequivalence study	
Investigational products	• **Reference product –** two film-coated tablets containing individual active substances at specific strength, administered with water • **Test product-** one film-coated tablet containing two active substances at specific strengths, administered with water
Study design	Open-labelled, randomized, 2-period, 2-treatment, single-dose, cross-over bioequivalence study in healthy subjects under fasting conditions.

Study objectives	• Bioavailability assessment for each active substance from the immediate release solid fixed combination formulation. The study results should be evaluated against the bioequivalence acceptance criteria: 80.0%-125% • Evaluation of safety and tolerability of the test and reference formulations • Evaluation of the pharmacokinetics of the active substances in plasma after a single dose administration under fasting conditions.

2. The following activities are planned:

- to prepare the study design in accordance with applicable EU regulations and EMA guidelines, particularly EMA guidelines on bioequivalence studies and clinical development of fixed combination medicinal products,
- to prepare the essential study documentation (Protocol, ICF, CRF, and other documents required to obtain approval/permission to conduct the study),
- to prepare the redacted versions of documents for submission to CTIS (if applicable)
- to represent the Sponsor before the Competent Authorities (CA) and the Ethics Committee (EC) (if applicable),
- to submit the study documentation and obtain the required CA approval, EC opinion (if applicable) along with fees,
- to submit Amendments to study documentation at the request of CA and EC (if applicable), along with fees (if applicable),
- to translate the CA approval/EC opinion into English as well as comments on the submitted documentation (if applicable),
- to submit required notifications to Competent Authorities (CA) and Ethics Committee (EC) (if applicable), in accordance with EU Regulation 536/2014 or local law,
- to prepare a summary of clinical study results and a lay person summary of results for submission to CTIS (if applicable),
- to conduct participant recruitment and ensure remuneration for study participants,
- to conduct the clinical part of the study including necessary medical procedures and laboratory tests to ensure participant safety, PK samples collection and processing, conduct required study procedures in accordance with the approved Study protocol, ensure payment for personnel involved in conducting the study,
- to prepare the randomization list,
- IMPs labelling for individual study participants according to the randomization list and dispensing (Sponsor will provide IMPs in multi-dose packages),
- disposal of the IMPs remaining after the end of the clinical study on site (certificate or confirmation of disposal is required),
- Analytical method development and validation (in accordance with current EU guidelines, particularly with ICH guideline M10 on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022) including preparation of Validation Report – if the Tenderer does not have a validated analytical method for the investigated active substances,
- to determine the concentrations of the investigated substances in plasma samples using the analytical methods validated in accordance with current guidelines, including ICH guideline M10 on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022) (the validation report should be made available to the Sponsor),

- study and data management, Quality Control and Quality Assurance including internal audits of documentation and processes during the study (the internal audit certificate has to be a part of the Study Reports),
- to perform pharmacokinetic and statistical calculations (ANOVA) and prepare the statistical report, (if the study is conducted in groups, additional calculations including group effect assessment should be conducted,
- to provide the pharmacokinetic data in an electronic format which allows recalculation of results (e.g., Excel format or other),
- medical writing and preparing of the Clinical Study Report in accordance with ICH-E3 guideline: Note for Guidance on Structure and Content of Clinical Study Reports (CPMP/ICH/137/95, July 1996),
- to print and deliver the paper version of the Clinical Study Report along with CRFs to the Sponsor (if only electronic versions of the mentioned documents are provided, this should be noted),
- to provide the electronic version of the Clinical Study Report and CRFs,
- to prepare and submit to the Sponsor the study summary (part of module 2.7.1) as required by Appendix IV of the "Guideline on the Investigation on Bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1): Presentation of Biopharmaceutical and Bioanalytical Data in Module 2.7.1.",
- to archive the study documentation for at least 25 years after the study completion
- to store the back-up plasma samples for at least 3 months from the date of the Clinical Study Report,
- to organize the liability insurance for the Investigator and Sponsor

3. The study should be designed and conducted in accordance with:

- Good Clinical Practice (ICH GCP (R3)),
- the basic principles defined in the EU Clinical Trials Directive 2005/28/EC, 2001/83/EC and Regulation (EU) No. 536/2014 of the European Parliament and of the Council,
- Guideline on the Investigation of Bioequivalence (EMA/CHMP/ICH/953493/2022, 25 July 2024 and CPMP/EWP/QWP/1401/98 Rev.1/Corr**, 20 January 2010),
- Guideline on clinical development of fixed combination medicinal products (EMACHMP/158268/2017, 23 March 2017),
- Act of 9 March 2023 on clinical trials on medicinal products for human use (Dz.U. 2023 poz. 605) (if applicable),
- the principles enunciated in the World Medical Association Declaration of Helsinki (Helsinki, Finland, October 2024)
- the principles of GLP,
- ICH guideline M10 on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022),
- Note for Guidance on Structure and Content of Clinical Study Reports (CPMP/ICH/137/95, July 1996).

4. In **Appendix no. 2** the Contracting Authority proposed the study design, the number of blood samples and the number of study participants which should be taken into consideration while completing **Appendix no. 3**. The Ordering Party stipulates that only offers in which the bidders have priced the implementation of the study according to the scheme presented by the Ordering Party will be considered in the proceedings. It is possible to indicate an alternative study scheme along with the valuation (in a separate sheet, similar to Appendix No. 3), but only the cost

estimate that takes into account the study scheme presented by the Ordering Party will be evaluated in accordance with the criteria adopted in the proceedings. The Ordering Party does not allow for the submission of variant offers. The possibility of indicating the study scheme by the Bidder does not constitute the admissibility of submitting variant offers.

5. The Tenderer must complete information required in **Appendix no. 3** in section III. GENERAL INFORMATION ABOUT THE STUDY**.** The offer without the completed Appendix no.3 will not be considered.
6. The contract between the Contracting Authority and the Tenderer must cover the entire service specified in the Subject of the tender. Offers for part of the services will not be accepted and will be rejected.
7. The contract concerning the realization of the study will be signed under the conditions of the offer presented in the current tender procedure.
8. The offer shall take into account the following schedule:

Pivotal bioequivalence study	
Planned date of availability of simplified IMPD/certificates of analysis required for obtaining the approvals for conducting the study:	**to 07.08.2025**
Availability of the preliminary study results:	**to 15.01.2026**
Availability of draft Clinical Study Report:	**to 31.01.2026**
Clinical Study Report (final):	**to 28.02.2026**

The above indicated timeframes are presented based on the estimated availability of the IMPD/certificates of analysis. The Contracting Authority may change the timeframes for conducting the studies adopted in the request for proposal, taking into account the progress of work on the project (circumstances that were impossible to foresee at the stage of realization of tender procedure and signing the agreement), what will be the subject of an Annex to the concluded agreement.

II. Conditions for participation in the proceedings:

1. The order cannot be awarded to entities affiliated personally or financially with the Contracting Authority. Personal or financial relationships are understood as mutual connections between the Contracting Authority and the Supplier or persons authorized to enter into commitments on behalf of the Contracting Authority or persons performing on behalf of the Contracting Authority activities associated with the preparation and conduct of the Supplier selection procedure, consisting in particular of:
    a. participating in a company as a partner in a civil or personal company, holding at least 10% of shares or stocks (unless a lower threshold results from legal regulations), serving as a member of the supervisory or management board, proxy, attorney,
    b. being in a marital relationship, in a direct line of kinship or affinity, in a collateral line of kinship or affinity up to the second degree, or being related by adoption, guardianship, or custody, or being in cohabitation with the contractor, their legal representative, or members of the contractor's management or supervisory bodies,
    c. being in such a legal or factual relationship that there is a justified doubt about their impartiality or independence in connection with the procurement procedure.

To meet this condition a Tenderer is required to submit a signed statement along with the offer about the lack of connections (**Appendix 4** to this RFP).

2. Orders cannot be awarded to:
    a. a Contractor referred to art. 7 sec. 1 indicated in lists specified in Regulation no 765/2006 and Regulation no 269/2014 or entered in list on basis of a decision on entry in the list deciding on application of measure referred to article 1 point 3 of the Act of April 13, 2022 on special solutions in field of counteracting supporting aggression against Ukraine (Polish Journal of Laws no 835).
    b. a Contractor whose beneficial owner within meaning of the Act of 1 March 2018 on counteracting money laundering and financing terrorism (Polish Journal of Laws no 593 and 655) is a person indicated in lists specified in Regulation 765/2006 and the Regulation 269/2014 or entered on list or being such a beneficial owner from February 24, 2022, provided that it was entered on list on the basis of a decision on entry in the list determining application of measure referred to in art. 1 point 3 of the Act of April 13, 2022 on special solutions in field of counteracting supporting aggression against Ukraine (Polish Journal of Laws no 835);
    c. a Contractor whose parent undertaking or subsidiary entity within the meaning of Art. 3 sec. 1 point 37 and 39 of the Accounting Act of 29 September 1994 (Polish Journal of Laws no 217, 2105 and 2106) is an entity indicated in the lists specified in Regulation 765/2006 and Regulation 269/2014 or entered on the list or being such a parent undertaking from February 24, 2022, provided that it was entered on list on the basis of a decision on entry in list determining application of measure referred to in art. 1 point 3 of the Act of April 13, 2022 on special solutions in field of counteracting supporting aggression against Ukraine (Polish Journal of Laws no 835).

    In order to fulfill this condition a Tenderer is obliged to send with the offer signed statement (**Appendix 5** to this RFP).

3. This offer is addressed to entities:
    a. Declaring the conduct of the offered study in accordance with current European Law and EMA guidelines. The Tenderer is required to submit a signed relevant statement **(Appendix no. 6).**
    b. Having the ability to recruit male and female participants (not pregnant), capable of using one of contraceptive methods, to the offered pivotal bioequivalence study. The Tenderer is required to submit a signed relevant statement (**Appendix no. 7)**.
    c. Having certificates confirming compliance of the provided services with GCP/GLP principles or presenting a history of inspections by Regulatory Authorities in the scope of GCP/GLP with a brief summary of the outcome (number of the findings and their categories). **Certificates or the list of inspections** should be submitted along with the offer.
    d. Having a history of inspection from European Regulatory Authorities, with no critical findings in the last **3 years**. **The list of the inspections** with a brief summary of the outcome (number of the findings and their categories) should be submitted with the offer.
    e. Having the required knowledge and at least **3 years** of experience in conducting bioavailability studies (including bioequivalence studies) and conducted **at least 3 bioequivalence/bioavailability** studies in 2024. The Tenderer is required to submit a signed relevant statement **(Appendix no.8)**

f. Having experienced staff competent for conducting the study.
   - The **CV** of the **Principal Investigator** and the **CV** of **Pharmacokineticist/Statistician** should be submitted, including experience and a list of trainings they have attended in the last **3 years**.
   - For the **Principal Investigator** and **Pharmacokineticist/Statistician** experience in conducting at least **6 bioavailability studies** in the last **3 years** is required. The Tenderer is required to submit a signed relevant statement **(Appendix no.9)**
   - The Principal Investigator must have GCP training (not older than 3 years) which should be documented in the current CV or GCP training certificate.

g. Having the ability to provide the services described in the RFP. To confirm this, the Tenderer should submit: the company's organigram and basic information about the facility (number of beds and a list of clinical and bioanalytical laboratory equipment). Additionally the tenderer is obliged to send the statement confirming personnel qualification **(Appendix no. 10)**.

h. In case of the need to conduct the study in groups, the cost of additional statistical analysis including the group effect should be presented in **Appendix no. 3**.

i. Having a validated analytical method or the ability to validate the analytical method (before the start of the clinical part of the study) for determination of the active substances contained in investigational medicinal products in human plasma. The validation should be conducted in accordance with the current guidelines, particularly ICH guideline M10 on bioanalytical method validation and study sample analysis (EMA/CHMP/ICH/172948/2019, 25 July 2022). The Tenderer is required to submit a signed relevant statement **(Appendix no. 11).**

j. The Tenderer is required to have an insurance policy and should submit documentation confirming the validity of the insurance.

k. Having a Quality Assurance system ensuring the conduct of studies in accordance with GCP requirements. The Tenderer is required to submit along with the offer, a signed relevant statement (**Appendix no. 12**) and a list of currently applicable Standard Operating Procedures (SOPs).

Supplementary orders may be submitted to the selected Tenderer only if they are consistent with the main purpose of this contract, with a value not exceeding 50% of the value of this contract.

The Ordering Party reserves the right to grant the Contractor additional orders, not covered by the basic order and not exceeding 50% of the value of the order being executed, necessary for its proper execution, the execution of which has become necessary as a result of a situation that could not have been foreseen earlier, if:

a. for technical or economic reasons, separating the additional order from the basic order would require incurring disproportionately high costs,
b. the execution of the basic order is dependent on the execution of the additional order.

The Ordering Party reserves that an increase or decrease in the scope of the order does not constitute a basis for the Contractor's claims. The Contractor's remuneration for the execution of supplementary orders or additional orders will be specified in a separate agreement concluded with the Ordering Party, which will cover the scope and conditions of the execution of the order.

III. Terms and methods of offer submission

1. The title of each correspondence should include the number of the procedure

RFP 026318– *Company name*

The deadline for submitting Offers is 12.05.2025 at 23:59 CET. The deadline may be changed, and all Suppliers will be informed via the Competitiveness Database website

2. Questions may be submitted on the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl.

   In exceptional cases, when asking a question on the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl involves the risk of disclosing particularly sensitive information, the Ordering Party allows the possibility of asking a question by e-mail using the sheet Attachment_13_RFP_026318_Questions_[Company Name], to the address aleksandra.stojak@adamed.com

   In such situations:

- the Contractor is obliged to justify that the publication of the question on the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl by the Contractor may expose it to the disclosure of particularly sensitive information,
- the Ordering Party reserves the right to publish the question on the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl in anonymized form.

   Answers to the questions asked will be provided until the end of the proceedings. Asking questions late in view of the deadline for completing the proceedings may result in a lack of time to provide the required answer. In order to ensure equal access to information for all Bidders participating in the procedure, questions and answers (with the author of the questions hidden) will be sent to all Bidders.

3. Each Supplier may submit only one offer.
4. Partial bids are not allowed also subcontracting parts of the order to other entities.
5. The offer should be prepared on the excel spreadsheet which constitutes Appendix to this offer: **Appendix_3 _RFP_026318_Proposal_*[CompanyName*]**. If **Appendix 3** is not filled out, the offer will not be considered.
6. All required appendices, declarations and documents must be attached to the tender - the Bidder also attaches **a completed and signed checklist** (**Appendix 14**) to the enquiry to confirm that all required documents have been provided.
7. Additionally to required, the Bidder may also prepare an offer in their own preferable format.
8. Supplier's Offer should be comprehensive in Polish or English, electronically.
9. **The offer should include at least the following information**: Supplier name, address, TAX / registry number, bid inquiry number, date of proposal, price net (PLN/EUR), payment terms, timelines).

The Tenderer should provide in Appendix no. 3. the detailed timeframes for the execution of the study, specifying an estimated time required for obtaining of CA and EC (if applicable)

approvals, proposed dosing dates, preliminary results delivery and draft of the clinical study report delivery (including all required appendices) and delivery of final version of clinical study report. The cost as well as the timelines are important in the selection of the most advantageous offer. The documents which are required by Competent Authority and Ethics Committee for submission should be listed **in Appendix no. 3.**

10. If the prices in the offer are expressed in a currency other than PLN, they will be converted using the average NBP exchange rate on the day of publication of the tender. If on the day of publication of this procurement notice, the NBP average exchange rate table is not published; the rate from the last average exchange rate table published before the day of publication of the procurement notice will be used.
11. Prices in the offer should be expressed as net prices in Polish zloty (PLN), Euro (EUR). The offer should include the total cost of the requested study, including pass-through costs (if applicable).
12. Tenders submitted after the deadline will not be considered.
13. The Supplier before time-limit for receipt of tenders is entitled:

    1) to withdraw the offer by submitting a written notification by e-mail indicated for the submission of tenders,
    2) to change the offer – the notification of changes must be submitted according to the same rules as the submitted offer, appropriately marked with the note "CHANGING THE OFFER". The Supplier is required to resubmit all appendices and statements **with the updated date of submission of the changed offer**.

IV. Selection criteria and evaluation methods:

1. The Contracting Authority is entitled to reject the tender submitted by the Supplier who does not meet the conditions for participation in the proceedings, or if the offer is incomplete or incompatible with this request.
2. Formal compliance, the degree of compliance with the RFP requirements.
3. Possibility of providing the service within the timeframes specified in **Section I.8**.
4. Selection criteria:

    a) **Net price of the service (PLN/EUR), weight of the criterion – 80% of the total evaluation;**
    b) **Total execution time (in weeks) (weight of the criterion – 20% of the total evaluation)**. The execution time of the study is calculated in weeks as the sum: from the availability of simplified IMPD/certificates of analysis for the pivotal bioequivalence study to the availability of the draft Clinical Study Report.

5. The Contracting Authority shall evaluate offers based on the result of the accumulated number of points calculated on the basis of above criteria and scores:

Criteria	**Weight criterion [%]**	**Method of evaluation according to the formula**
Net price of the service	80%	net price of the offer with the lowest price / net price tested offer x 100 x 80 % = number of points

Total execution time (weeks)	20%	the shortest execution time (in weeks) of the offer / execution time (in weeks) of the tested offer x 100 x 20 % = number of points

6. **<u>The Contracting Authority reserves the right to negotiate the proposal with all the Bidders</u>. Negotiations may have several consecutive rounds with the possibility to invite Bidder to submit the updated quotation after each round of negotiations**
7. The amounts of points for each criterion after summing up will be the final number of points awarded to each tender. As the most advantageous offer will be considered that which obtains the highest number of points.
8. The results of the mathematical calculations carried out in the evaluation of tenders are rounded to the second decimal place. In case of equal scores for at least two offers the Contracting Authority will make the final choice of the offer more favorable when it comes to the impact on the environment i.e. treatment of wastewater and process exhaust gases and/or transfer of solid residues to specialized companies for disposal (e.g. unused drugs, biological samples, other materials). For this purpose, the Contracting Authority shall have the right to call the Suppliers, whose tenders have obtained the highest final points, to complete the offer by giving indicated by the Contracting Authority information about an impact of the offer on the environment. The deadline to complete the offer will be determined by the Contracting Authority, but it cannot be less than 3 working days from receipt of the request.

V. The choice of Supplier and way of announcing:

1. The Contracting Authority will select the most advantageous offer on the basis of the selection criteria defined in this request for proposal.
2. The Ordering Party will inform about the results of this inquiry on the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl

VI. General provisions

1. The Contracting Authority reserves the right to cancel the procedure at any stage without giving any reason.
2. The Contracting Authority requires that the offer is valid for a minimum of 90 days.
3. In the event of cancellation of the contract the Suppliers are not entitled to claim for reimbursement of the costs of participation in the proceedings.
4. Submission of the application for registration in the process or a tender implies acceptance without reservation all the conditions of the proceedings.
5. Withdrawal by the Contracting Authority from the conclusion of the contract after the notification the Supplier about the selecting the offer, cannot be the basis for claims of incurred costs of participation in the proceedings.
6. During the evaluation of the submitted applications, the Contracting Authority may seek information from the contractors concerning the content of the documents submitted by them.
7. If the application does not contain all the required elements, the Contracting Authority may, in justified cases, call the Supplier to complete it.
8. The Contracting Authority reserves the right to audit the Tenderer before the conclusion of the contract. In case of obtaining not satisfactory results of the audit, the Contracting Authority may withdraw from signing the contract.

9. The Bidder's withdrawal from the conclusion of the contract upon notification of the contractor about the selection of their offer may serve as a basis for the Ordering Party's claims, including those related to the damages incurred (such as delays resulting from the necessity to choose another contractor). In such cases, the provisions of the Civil Code shall apply accordingly. Therefore, the Ordering Party requests that thoughtful offers be submitted, in compliance with all the expected conditions of the order, taking into account the indicated foreseeable deadlines for its execution.
10. The Ordering Party reserves the right to exclude from the procedure a Bidder who has avoided concluding a contract in another Adamed tender.
11. Terms of contract change: The contracting authority envisages the possibility of introducing significant changes to the contract concluded as a result of the conducted contract award procedure in relation to the content of the offer, on the basis of which the contractor was selected, in the event of the necessity to change the indicated scope of works specified in the offer/contract resulting from:

    a) necessary or justified changes in the project documentation resulting from unforeseeable reasons, which may be caused by, among others, amendment of legal acts, guidelines, the result of "Scientific advice" in Regulatory Agency, publication of new scientific data and for other reasons that affect the scope, type or design of clinical trials and the final sample size, the scope of analytical methods and their validation, the number of collected pharmacokinetic samples, and other aspects related to clinical development of the medicinal product;
    b) delays in the manufacturing or delivery of a medicinal product for a clinical trial resulting in the change of the clinical trial schedule due to unforeseeable reasons or circumstances beyond the control of the Contracting Authority; among others, the necessity to make changes in the formulation of the medicinal product, changes in analytical methods and their validation, changes in the product quality documentation, delays in the delivery of raw materials and packaging, production failures and downtimes, transit delays, delays in customs clearance or any other reasons;
    c) the necessity or justification for introducing changes to the clinical study design as a result of new data on the active substance or during the work on the study protocol or as a result of the Authority's recommendation at the stage of obtaining approval to start the study;
    d) delays or postponements in the clinical study schedule caused by the Authority's request to supplement the gaps in the documentation, make changes to the study protocol or correct the study documentation at the stage of the study approval;
    e) the need to increase the sample size after the exclusion of study subjects (e.g due to, voluntary withdrawal, adverse events, etc.), resulting in the need to recruit additional study subjects;
    f) perform necessary or justified additional activities in connection with the conducted clinical study to ensure the conduct of the clinical study with appropriate quality and diligence, in accordance with the principles of ICH-GCP;
    g) financial constraints on the part of the Contracting Authority or changes in legal requirements limiting the scope of work included in the offer;
    h) other necessary or justified changes in the delivery time and conditions of the contract subject arising from unforeseeable reasons.

    Any changes and additions to the contract concluded with the selected Tenderer will be made in the form of written annexes to the contract signed by both parties, under rigor of invalidity.

VII. Cooperation and communication during the tender

1. All questions should be submitted via the website https://bazakonkurencyjnosci.funduszeeuropejskie.gov.pl subject to point 2 of the Deadline and method of preparing the offer section of this Request. All answers will be provided to Contractors via the Competitiveness Database of the procedure in question.