Warsaw, **April 22, 2024**
place and date

PRICE INQUIRY No. RIA/7/PR57346/2024
conducted in the market research mode

In connection with the implementation of the project entitled "Design and development of an innovative solution - a complex, three-component medicinal product targeting the treatment of hypertension" financed from the state budget by the Medical Research Agency, Zakłady Farmaceutyczne Polpharma S. A. is asking for offers to **conduct a phase IV study.**

I. NAME AND ADDRESS OF THE ORDERING PARTY

Zakłady Farmaceutyczne Polpharma S. A.
Pelplińska 19, 83-200 Starogard Gdański, Poland
Website: https://www.polpharma.pl/

II. PROCEDURE OF AWARDING THE ORDER

1. This order is not subject to the provisions of the Act of September 11, 2019, Public Procurement Law (consolidated text: Journal of Laws of 2019, item 2019).
2. The proceedings are conducted in a market research manner, in a purposeful and economical manner, in compliance with the principles of:
   1) obtaining the best results from given inputs;
   2) optimal selection of methods and means to achieve the assumed goals;
   3) transparency, fair competition and equal treatment of contractors.

III. DESCRIPTION OF THE SUBJECT OF THE PRICE INQUIRY

III.1. The subject of the price inquiry is service of conducting phase IV, prospective, non-interventional, multicenter study to evaluate efficacy and safety of triple agent combination therapy in comparison to baseline dual therapies in the management of hypertension.

III.2. CPV CODE: 73120000-9 - Research and development services
III.3. Scope of the price inquiry:

III.3.1 Investigational medicinal products are drugs currently authorized and marketed in EU for treatment of hypertension and specific names to be disclosed in study synopsis provided after confirmation of respective confidentiality agreement between ordering party and bidding party.

III.3.2 Description of the study

- **Objective:** The primary objective of the study is to evaluate the efficacy of the triple agent combination in comparison to baseline dual therapies of same agents in the treatment of hypertension in adult patients.

The secondary objective of the study is the safety and tolerability evaluation of the treatment administered to the patients

- **Primary endpoint:** Change from baseline in the average BP measurement [mm Hg] after 12 weeks of triple combined therapy in comparison to baseline dual therapies
- **Study population:** 220 adult European patients with hypertension grade 1 or 2.

III.3.3 A detailed description of the subject matter of the contract ***(Appendix No. 4*** containing the Requirements Specification - Summary of the Study) will be provided to Contractors after signing the Non-disclosure agreement ***(Appendix No. 3***). The Contractor should send the completed Non-disclosure agreement Ann editable version to the email address barbara.wendolowska@polpharma.com. Upon receipt of the NDA, signatures by the authorized person (or persons), according to the representation rules of the respective Contractor, will be collected by the DocuSign platform. The Buyer will make ***Appendix No. 4*** to this Request for Proposal available through digital channels, no later than two business days from the date of signing the Non-disclosure agreement.

III.4. The contractor will be responsible for providing the complete service of conducting the study: the clinical part (including the preparation of full documentation specified in the detailed description of the order) and statistical part of the study along with the preparation of reports, as well as data management and study management. In particular, contractor is responsible for:

- Appointing Principal Investigator
- Recruitment and screening of an appropriate number of patients for the study by identifying and directly contracting sufficient number of clinical sites and/or clinical investigators
- Overall Project Management
- Management and oversight of contracted clinical sites
- Reporting required study status/progress including safety data (Pharmacovigilance) to respective authorities if applicable, adhering to timelines outlined as per the local regulatory requirements and in the ICH Guidelines.
- Providing standardized blood pressure measurements by means of 24hrs ABPM devices
- Clinical assessment of patients during screening and during the course of the study (in accordance with local requirements, relevant European guidelines and regulations and contractor procedures),
- Preparation of full study documentation – including: study protocol and protocol amendments (if applicable), ICF, CRF, submission of a clinical trial application to the regulatory body (if applicable) and Ethics Committee (including fees), EudraCT management (if applicable), as well as data management and study management,
- Preparation of full study report eCDT format in accordance with the requirements of the European Medicines Agency (EMA), as well as archiving research documentation for 25 years

III.5. The study must be designed, conducted and documented in accordance with the principles of ICH-GCP, GLP, Directives 2001/20/EC, 2001/83/EC, 2005/28/EC, the Declaration of Helsinki and applicable European guidelines, in particular the guideline EMA/CHMP/29947/2013/Rev. 4 (to the extent feasible for non-interventional Phase IV study)

III.6. The documentation (including the Protocol, ICF, CRF and Final Study Report) must be prepared in accordance with guideline CPMP/ICH/137/95 and written in English and in the local language if required by local law; the study final report should be prepared in the eCTD format,

III.7. The Contractor will represent the Ordering Party before the relevant authorities and the Ethics Committee in the process of obtaining required approvals, as well as respond to inquiries from regulatory agencies in the procedure of marketing authorization application and potential study audits/inspections.

III.8. Conducting all required internal audits of study documentation and processes by the contractor

III.9. The contractor will conduct all required internal audits of study documentation and processes.

III.10. The order does not include study monitoring.

III.11. The Ordering Party does not allow the submission of partial or variant offers.

IV. PLACE AND DATE FOR COMPLETION OF THE PRICE INQUIRY

Deadline for completing the subject of the order:

IV.1 Estimated date of signing the contract: June 2024.

IV.2 The study has to be completed (i.e. study final report has to be available) no later than 12 months from the date signing the contract.

IV.3 Study report and other necessary documents (in electronic form or paper if required) obtained in connection with the provision of the service must be delivered at the Contractor's expense to the Ordering Party's headquarters.

IV.4 Completion time is a criterion for evaluating the offer and will be counted as the time from the signing the contract to study final report availability

V. REQUIREMENTS FROM CONTRACTORS

V.1. Contractors who meet the following conditions may apply for the contract:

V.1.1. The contractor is in an economic and financial situation ensuring timely and consistent performance of the order in question, is not in bankruptcy and is not subject to liquidation or restructuring proceedings.

How to evaluate the condition:

*The Ordering Party will consider that the Contractor meets this condition if the Contractor submits a declaration of meeting the conditions for participation in the procedure (**Appendix No. 2** to the Request for Quotation).*

V.1.2. The contractor will demonstrate that it has the appropriate potential to perform the contract:

The contractor has the ability to carry out the clinical, and statistical part, in accordance with the principles of ICH-GCP, GLP, Directive 2001/20/EC, 2001/83/EC, 2005/28/EC, the Declaration of Helsinki and applicable European guidelines, in particular with the guideline on EMA/CHMP/29947/2013/Rev. 4

How to evaluate the condition:

*Condition verification will be based on a declaration of meeting the conditions for participation in the procedure (**Appendix No. 2** to the Request for Quotation).*

The Ordering Party reserves the right to verify the compliance of the content of the Contractor's declaration with the actual situation and to conduct an audit of the Contractor.

V.1.3. The Contractor will demonstrate that it has appropriate staff, including qualified medical and nursing staff (with secondary or higher medical education), as well as key personnel necessary to perform the order, including at least one person in the position of: Principal Investigator, Statistician, Study Manager, Project Manager, Study Administrator or in an equivalent position.

Each of the above-mentioned persons, depending on their function, must:

a) have experience in conducting clinical trials (for the Principal Investigator, at least 5 years of experience and at least 10 years of experience as a physician, for a Statistician, at least 5 years of experience)
b) have specialized education (for the Principal Investigator: medicine – cardiologist; for the Statistician: medicine, biotechnology, pharmacy, biology, chemistry, mathematics, physics or related),
c) have the ability to analyze the results obtained in a clinical trial and correctly report trial data in accordance with appropriate procedures and standards.

The qualification criteria for key personnel should be included in the Contractor's appropriate procedures in accordance with the principles of ICH GCP.

How to evaluate the condition:
*The contractor must meet all conditions together. Verification of a-c points will be based on the declaration of fulfillment of the conditions for participation in the procedure (**Appendix No. 2** to the Request for Quotation).*

V.1.4. The contractor will demonstrate that he has experience and appropriate potential to perform the contract:

a) The contractor has experience in conducting prospective observational clinical studies

*The Ordering Party will consider the condition to be met based on the Contractor's declaration (**Appendix 2**) that it has performed at least 5 prospective efficacy and safety clinical studies, including at least 2 in field of hypertension over the last 10 years (if the Contractor's period of operation is shorter, during its period of operation) **and provide a list of these studies indicating pharmacological class of investigated products, study population (indication of interest), phase of the study (II/III/IV), blinding (yes/no), randomization (yes/no) and sample size.***

b) The contractor of the clinical and statistical parts will present a list of inspections for the last 10 years (if the period of the Contractor's operation is shorter - during the period of its operation) with a summary of the inspection results. At least 1 inspection must be carried out by an appropriate office of one of the European Union countries in the field of GCP (Good Clinical Practice), and the results of all inspections during the given period cannot contain critical non-compliances. Inspections of tests carried out by the Contractor before 2014 will not be taken into account.

*The Ordering Party will consider the condition to be met based on the Contractor's declaration (**Appendix 2**) and the **presentation of the above-mentioned inspection list**.*

How to evaluate the condition:

*The contractor must meet all required requirements together. The Ordering Party will consider the condition to be met on the basis of the Contractor's declaration (**Appendix No. 2** to the Request for Proposal, list of clinical studies referred to in **point V.1.4 a** and the inspection list referred to in **point. V.1.4 b** .*

V.1.5 The offers of Contractors who demonstrate compliance with the required conditions will be accepted for examination and evaluation. The assessment of the fulfillment of the conditions presented above will be made according to the formula: "meets - does not meet". A contractor who fails to meet any of the conditions will be rejected from the proceedings.

V.1.6 Entities in relation to which the following circumstances occur are also excluded from participation in the proceedings:

a) described in art. 7 section 1 of the Act of April 13, 2022 on special solutions for counteracting support for aggression against Ukraine and for protecting national security;
b) described in art. 5k of Council Regulation (EU) No. 833/2014 of 31 July 2014 concerning restrictive measures in connection with Russia's actions destabilizing the situation in Ukraine.

Method of verifying the grounds/lack of grounds for exclusion:

*Verification will be based on the Bidder's declaration (**Appendix No. 1** to the Request for Proposal.*

VI. PLACE AND DATE FOR SUBMITTING OFFERS

VI.1. Offers must be submitted **no later than May 17, 2024** in electronic form (in the form of electronically signed documents or a scan of a signed document) to the following address:barbara.wendolowska@polpharma.com

VI.2. The submission of an offer will be considered effective if the complete offer reaches the e-mail address provided above within the deadline specified in this point.

VI.3. Offers submitted after the deadline will not be considered.

VII. DESCRIPTION OF CRITERIA WHICH THE ORDERING AUTHORITY WILL FOLLOW WHEN SELECTING AN OFFER

VII.1 When evaluating offers, the Ordering Party will apply following scoring criteria:
- total net price for the service – 60%,
- service delivery time (months) – 40%

VII.2 The offer will be scored according to the formula:

$$O_P = P_C + P_M$$

Where:

OP	point evaluation of the offer
P_C	number of points obtained in the "Total net price" criterion
P_M	number of points obtained in the "Service implementation time" criterion

VII.3 The number of points (PC) in the "Total net price" criterion will be calculated according to the formula:

$$P_C = \frac{C_N}{C_B} * 60\ pkt$$

Where:

PC	-	number of points for the "Total net price" criterion
CN	-	among the non-rejected offers, the lowest total net price of the offer
CB	-	total net price of the examined offer

Offers submitted in a currency other than PLN will be converted into PLN at the average NBP exchange rate as of the closing date for the submission of offers.

VII.4 Number points() in the criterionP_T "Service completion time" will be calculated as follows:

$$P_M = \frac{M_N}{M_B} * 40\ pkt$$

Where:

PM	-	number of points for the "service delivery time" criterion
MN	-	among the offers that were not rejected, the shortest lead time for the subject of the price inquiry
MB	-	the time of completion of the subject of the price inquiry declared in the offer

The lead time for the subject of a price inquiry should be given in months. Offers with a lead time longer than 12 months will be rejected.

VII.5 The Bidder can obtain a maximum of 100 points. Calculations will be made with an accuracy of two decimal places.

VIII. DESCRIPTION OF THE METHOD OF PREPARING THE OFFER

VIII.1 The tenderer should prepare one offer in accordance with the template form attached as Appendix 1 to the inquiry.
VIII.2 The Ordering Party does not allow the submission of partial or variant offers.
VIII.3 The bidder may change or withdraw his offer before the deadline for submitting offers.
VIII.4 Bidders are obliged to carefully read the information contained in the Request for Proposal.
VIII.5 The costs of preparing and delivering the offer are borne by the Contractor.
VIII.6 In matters related to this inquiry, please contact the Ordering Party, e-mail: barbara.wendolowska@polpharma.com

IX. GENERAL PROVISIONS AND CONDITIONS OF THE AGREEMENT

IX.1 The Ordering Party reserves the right to make significant changes to the provisions of the Agreement for the offered services in relation to the content of the offer on the basis of which the Contractor was selected, in the following scope and situations:
IX.1.1. Changes in legal provisions to the extent affecting the implementation of the Agreement (in particular changes in VAT rates);

IX.1.2. improving the technical parameters of the subject of the Agreement, resulting from updating solutions due to technological progress, without affecting the gross lump sum price

IX.1.3. extending the deadline for the implementation of the Agreement due to the need to perform additional works, the execution of which is necessary for the proper performance of the Agreement and the execution of which the Ordering Party, acting with due diligence, could not have predicted in advance, subject to subpoint. IX.1.6 below;

IX.1.4. extension of the deadline for the implementation of the Agreement as a result of force majeure, along with all the consequences arising in connection with the extension of this deadline;

IX.1.5. changes in the parameters of the subject of the Agreement, not leading to a change in the nature of the Agreement - technological changes, in particular: the need to implement the Agreement using other technical/technological and material solutions than those indicated in the Request for Quotation, in a situation where the use of the provided solutions would pose a risk of non-performance or defective performance of the Agreement, with reservation subpoint. IX.1.7. below;

IX.1.6. the changes concern the provision of additional deliveries or services of the Contractor not covered by the Agreement, provided that they have become necessary and the following conditions have been met:

- the change of the Contractor cannot be made for economic or technical reasons, in particular regarding the interchangeability or interoperability of equipment, services or installations ordered under the basic subject of the Agreement,
- a change of the Contractor would cause significant inconvenience or a significant increase in costs for the Ordering Party,
- the value of each subsequent change does not exceed 50% of the net value of the original subject of the Agreement;

IX.1.7. the change does not lead to a change in the nature of the Agreement and the following conditions have been met:

- the need to change the Agreement is caused by circumstances that the Ordering Party, acting with due diligence, could not have predicted,
- the value of the change does not exceed 50% of the net value of the original subject of the Agreement;

IX.1.8. The contractor is to be replaced by a new contractor:

- as a result of a merger, division, transformation, bankruptcy, restructuring or acquisition of the Contractor or his enterprise, provided that the new contractor meets the conditions for participation in the proceedings, there are no grounds for exclusion against him and it does not result in other significant changes to the Agreement,
- as a result of the Ordering Party taking over the Contractor's obligations towards its subcontractors.

IX.2. The Ordering Party also provides for the possibility of making insignificant changes to the provisions of the concluded Agreement in relation to the content of the offer on the basis of which the Contractor was selected.

IX.3. Changes to the Agreement will be introduced in the form of annexes signed by both Parties, and the possibility of their introduction depends on the acceptance by the Ordering Party.

IX.4. The ordering party requires other important offer parameters to be met:

- Payment term: minimum 30 days;
- Offer validity: 90 days;

IX.5. Important terms of the contract:

IX.5.1. Inconsistencies or defects - In the event of significant inconsistencies or defects in the performance of the Services due to the sole fault of the Supplier, the Supplier is obliged to perform the Services again at its own expense. Objections to the results should be reported to the Supplier by the Ordering Party within fourteen (14) business days. The Ordering Party will justify in detail significant

inconsistencies and defects. This work should be completed promptly and the date for receipt of services or materials specified in the relevant Project Order will be extended accordingly. If the Supplier is unable to resupply the Materials or perform the Services without such inconsistencies or defects, the Supplier will refund amounts paid for such services in the event of any inconsistencies or defects being detected.
IX.5.2. Audit - the Ordering Party reserves the right to conduct an audit of the Supplier before concluding the contract or during its implementation.
IX.5.3. Contractual penalties - The Supplier is obliged to pay contractual penalties for:

- postponing the order completion date for each day of delay, if the delay is not the fault of the Ordering Party;
- improper performance of the contract;
- incomplete performance of the contract.

The Supplier agrees to deduct the amount of contractual penalties directly from the payment of the VAT invoice at the time of delivery.
IX.6. The Ordering Party reserves the right to cancel the procedure without giving a reason.
IX.7. If the procurement procedure is canceled, suppliers are not entitled to a claim for reimbursement of the costs of participation in the procedure.
IX.8. The Ordering Party's withdrawal from concluding the contract in the event of notifying the contractor of the selection of its offer cannot constitute the basis for claims for the costs of participation in the proceedings.
IX.9. In the course of assessing the submitted offers, the Ordering Party may request that the contractors provide explanations regarding the content of the documents they submitted.
IX.10. If the offer does not contain all the required elements, the Ordering Party may, in justified cases, call on the Contractor to supplement it.
IX.11.The Ordering Party reserves the right to negotiate offers with all Bidders, especially when the price offered by the Contractor exceeds the budget allocated by the contracting authority for the execution of the contract. Negotiations may have several subsequent rounds, with the possibility of inviting the bidder to submit an updated offer after each round of negotiations.
IX.12 If the supplier's income obtained in connection with the implementation of the project is subject to withholding tax in Poland, then the Ordering Party (ZF Polpharma SA) is obliged by law to deduct withholding tax from the supplier's remuneration and pay it to the Polish tax **authorities (the remuneration presented in the offer includes withholding tax).**

X. OTHER INFORMATION

X.1. The bidder bears all costs related to the preparation and submission of the offer.
X.2. Until the deadline for submitting offers, the Ordering Party reserves the right to change or supplement the content of this price inquiry.

XI. LIST OF ANNEXES

The following documents are attached to this Quotation Request:

Attachment designation	Attachment name
Appendix 1	Pricing form template

Appendix No. 2	Declaration on meeting the conditions for participation in a price inquiry
Appendix No. 3	Non-Disclosure Agreement
Appendix No. 4	Detailed study design description (Requirements Specification - Summary of the Study)

Appendix No. 1 *to the Price Inquiry No.* ***RIA/7/PR57346./2024***

PRICE FORM

Bidder:

Full name (company) or name and surname	
Registered office/place of residence/address of main place of business	
E-mail address to which the Ordering Party should send correspondence	
Tax Identification Number	
Statistical numer (if aplicable)	
Telephone	
Contact person with the Ordering Party	

We offer the execution of the subject of the order in the scope of services related to **conducting a phase IV study** in accordance with the requirements of the price inquiry, for the price of:

net amount: ……PLN / EUR/ USD

VAT rate: ……%, VAT amount: PLN / EUR / USD

gross amount: ……PLN / EUR / USD* *select the appropriate currency

Study completion time: ……..months from the date of signing the contract to study final report availability

The payment deadline for invoices is ..... days.

The bidder has the status of - SME / Large Entrepreneur * (delete as appropriate)

At the same time, we declare that: :

a. we have read the Price Request with attachments and have no objections and have obtained the necessary information to prepare the offer,

b. the price includes a lump sum remuneration for all the obligations of the future Contractor necessary to complete the subject of the Quotation Request,

c. By submitting this offer, we declare that we meet the conditions for participation specified in point. V price inquiry.

d. By submitting this offer, we are bound by it for a period of 90 days from the deadline for submitting offers,

e. The following circumstances do not apply to us:

1. described in art. 7 section 1 of the Act of April 13, 2022 on special solutions for counteracting support for aggression against Ukraine and for protecting national security;
2. described in art. 5k of Council Regulation (EU) No. 833/2014 of 31 July 2014 concerning restrictive measures in connection with Russia's actions destabilizing the situation in Ukraine.

……	……
(place and date)	(signature of the person(s) authorized to submit a declaration of will on behalf of the Bidder)

Appendix No. 2 *to the Price Inquiry No.* ***RIA/7/PR57346/2024***

STATEMENT OF MEETING THE CONDITIONS OF PARTICIPATION IN THE PRICE REQUEST

…… *(name of the tenderer)*

I/we declare that we meet the conditions for participation in the proceedings specified by the Ordering Party in Part V of the Request for Quotation, regarding:

1) economic and financial situation,

2) technical or professional capacity,

3) staff capacity,

4) experience.

Attachments to the declaration:

a) a list of at least 5 clinical studies
b) inspection list for the last 10 years

…… (place and date)

…… (signature of the person(s) authorized to submit a declaration of will on behalf of the Bidder)