Warsaw, 26.08.2024

PRICE INQUIRY NO. No. JODO/15/PR68772/2024
conducted by means of market discernment

In connection with the implementation of the project entitled "**Development and introduction to the market of the first non-antibiotic product for the treatment of infectious eye diseases with an innovative ophthalmological composition in the form of eye drops, containing an active substance - povidone iodine**" funded by **the** state budget from the Agency for Medical Research, Polpharma Pharmaceutical Works S.A, is requesting bids for **to conduct a non-clinical study of pharmacodynamics and safety after repeated administration in an animal model of adenoviral eye infection (adaptive design).**

I. NAME AND ADDRESS OF THE ORDERING PARTY

Zakłady Farmaceutyczne POLPHARMA S.A.
19 Pelplińska Street, 83-200 Starogard Gdański

II. PRICE INQUIRY PROCEDURE

II.1. This order is not subject to the provisions of the Act of September 11, 2019. Public Procurement Law (i.e. Journal of Laws of 2019, item 2019)

II.2. Proceedings conducted by market discernment, in an expedient and economical manner in compliance with the rules:

a) Getting the best results from given inputs;
b) Optimal selection of methods and means to achieve the set goals;
c) 3) openness, fair competition and equal treatment of contractors.

III. DESCRIPTION OF THE SUBJECT OF THE PRICE INQUIRY

III.1. The subject of the inquiry is **service** to **conduct a non-clinical pharmacodynamics and safety study after repeated administration in an model of adenoviral eye infection (adaptive design)**

III.2. CPV CODE: 73120000-9 - Research and development services

III.3. Scope of inquiry:

III.3.1. **Conducting a study aimed at:**

a. Primary objective: to find the optimal concentration and frequency of administration of investigational product (eye drops) in an animal model of ocular infection relevant to adenoviral conjunctivitis
b. Secondary objective: to check the safety, including local tolerance of the tested eye drops after multiple doses

III.3.2. **Nature of the study:** the study is adaptive in nature and will consist of two phases:

a. Phase I (pilot - viral model testing)
b. Phase II (pivotal, on a revised/improved test plan) - attempt to reduce concentration/frequency of use)

III.3.3. **The result of the study:** Final report of the study. Required to provide draft report for comment. Final report available no later than 3 weeks after submission of comments on draft report.

III.3.4. Activities under the ongoing service to conduct a non-clinical study of pharmacodynamics and safety after repeated administration in an adaptive model of adenoviral eye infection:

III.3.5. Planning and conducting the study, including:

a) Providing adequate number of animals and their proper allocation into test groups,
b) Preparation of full study documentation - including the study plan with amendments (if applicable), submission of the application for non-clinical studies to the regulatory body and bioethics committee (including fees), as well as data management and study management,
c) Management of tested products (including their destruction and reconciliation),
d) Administering test products to animals,
e) Assessment of animal health at screening and during the study and clinical-statistical analysis (in accordance with local requirements, relevant European guidelines and regulations, and contractor procedures),

III.3.6. Preparation of a final report on the study (including photographic documentation).

III.3.7. A detailed description of the subject matter of the contract (**Appendix 4** containing the Requirements Specification - Summary of the Study) will be provided to the Contractors after signing the Confidentiality Agreement (**Appendix 5**). The Contractor should send the completed Confidentiality Agreement in an editable version to the email address dominika.radzanowska@polpharma.com Upon receipt of the Confidentiality Agreement, signatures by the authorized person (or persons), in accordance with the representation rules of the respective Contractor, will be collected by the DocuSign platform. The Buyer shall make Exhibit No. 4 to this Request for Proposal available through digital channels, no later than two business days from the date of signing the confidentiality agreement.

III.4. The Contractor shall be responsible for performing the complete service of conducting the study, including providing expert support to the Employer at the stage of planning and conducting the study, preparing full documentation as specified in the description of the subject matter of the contract, in the experimental scope, as well as in the scope concerning the clinical and statistical analysis of the study results with the preparation of the report, as well as data management and management of the study.

The Contractor shall also be obliged to undertake any necessary additional activities in connection with the performance of the service that could not have been foreseen at the time of the announcement of the request for proposal and that were not mentioned in the body of the request for proposal (including Exhibit 4), if required by the Contractor's internal regulations or local laws in its area of operation, and which are necessary for the performance of the service.

III.5. The study must be designed, conducted and documented in accordance with Directives 2010/63/EU and 2001/83/EC and applicable guidelines (European and international), including:

- ICH Guidelines M3 (R2) on non-clinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals (EMA/CPMP/ICH/286/1995),
- ICH Topic S 7 A Safety Pharmacology Studies for Human Pharmaceuticals Step 5, Note for Guidance on Safety Pharmacology Studies for Human Pharmaceuticals (CPMP/ICH/539/00).
- EMA/CHMP/SWP/2145/2000 Rev. 1, Corr. 1* Guideline on non-clinical topical tolerance testing of medicinal products

- ISO 10993-23:2021 Biological evaluation of medical devices - Part 2: Tests for irritation.

III.6. The study must be conducted by a facility operating under the principles of Good Laboratory Practice, including:

- By GLP-qualified and GLP-trained personnel,
- In GLP-certified facilities,
- using GLP-controlled and calibrated apparatus,
- in a manner that manages samples and data in accordance with GLP,
- According to the documentation and reporting process in accordance with GLP.

Documentation (including the protocol and final report of the study) must be in English and in the local language, if required by local law. The final report should contain all relevant data in the form of text, charts, photos, summary tables and related reports. The final report should be sent in the form of pdf files, searchable text, with hyperlinks and bookmarks.

III.7. As part of the service, the Contractor will represent the Employer before the relevant authorities and the bioethics committee in the process of obtaining approval to conduct the study, as well as respond to inquiries from registration agencies in the drug product approval procedure and potential auditors of the dossier.

III.8. The scope of the contract also includes internal audits of documentation and processes by the contractor during and after the study. Audit reports will be made available to the Contracting Authority each time it is requested.

III.9. The contracting authority does not allow partial or variant bids.

IV. PLACE AND DATE OF EXECUTION OF THE SUBJECT OF THE INQUIRY

IV.1. Deadline for completion of the subject of the contract:

IV.1.1. **Planned contract signing date: September-October 2024.**

IV.1.2. **Planned start of the study (understood as the first administration of the investigational product): no later than 90 days from the signing of the contract**

IV.1.3. The study deadline must be completed no later than 90 calendar days, counted from the date of the start of the study (understood as the first dosage) to the receipt of the final report of the study.

IV.1.4. **The term of the contract, calculated from the date of signing the contract to the receipt of the final report, must not exceed 180 days.**

IV.1.5. The results of the study and the necessary documents (in electronic and paper form) obtained in connection with the service must be delivered at the Contractor's expense to the Employer's premises.

IV.1.6. The deadline is a criterion for bid evaluation and will be counted as the time from the first dosage until the final audit report and all final audit reports are submitted to the Contracting Authority.

V. REQUIREMENTS FROM CONTRACTORS

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

V.1.1. The contractor has the ability to carry out the experimental part, as well as statistical analysis of test results in accordance with Directives 2010/63/EU and 2001/83/EC, as well as applicable guidelines (European and international), including:

- ICH Guidelines M3 (R2) on non-clinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals (EMA/CPMP/ICH/286/1995),
- ICH Topic S 7 A Safety Pharmacology Studies for Human Pharmaceuticals Step 5, Note for Guidance on Safety Pharmacology Studies for Human Pharmaceuticals (CPMP/ICH/539/00),
- EMA/CHMP/SWP/2145/2000 Rev. 1, Corr. 1* Guideline on non-clinical topical tolerance testing of medicinal products
- ISO 10993-23:2021 Biological evaluation of medical devices - Part 2: Tests for irritation.

How to evaluate the condition:
*The Contracting Authority will consider that the Contractor meets this condition if the Contractor submits a statement of compliance with the conditions for participation in the proceedings (**Appendix No. 2 to the Request for Proposal)**.*

V.1.2. The Contractor has experience in conducting non-clinical animal studies, including for ophthalmic products. (Has performed at least 10 non-clinical animal studies, including at least 5 studies for an ophthalmic product in the last 5 years (if the Contractor's period of operation is shorter).

V.1.3. The Contractor of the study shall submit a list of inspections for the last 5 years (if the Contractor's period of activity is shorter - during the period of its activity) with a summary of the result of the inspection. At least 1 inspection must have been conducted by a relevant GLP (Good Laboratory Practice) body of one of the European Union countries, and the results of all inspections during the period must not contain critical discrepancies. Test inspections conducted by the Contractor before 2019 will not be considered.

How to evaluate the condition:
*The Contracting Authority will consider that the Contractor meets this condition if the Contractor submits a statement of compliance with the conditions for participation in the proceedings **(Appendix No. 3 to the Request for Proposal) and presents the above-mentioned list of studies and inspections. Failure to provide a list of tests performed and a list of inspections will result in rejection of the bid.***

The contracting authority reserves the right to verify the fulfillment of the conditions at the bidder's premises or to call for relevant documentation.

V.2. The bids of Contractors who demonstrate compliance with the required conditions will be admitted for examination and evaluation. Evaluation of the fulfillment of the conditions presented above will be carried out according to the formula: "meets - does

not meet". A Contractor who fails to meet any of the conditions will be rejected in the proceedings.

V.3. Also excluded from participation in the proceeding are entities with respect to which there are circumstances:

a) described in Article 7 (1) of the Law of April 13, 2022, on special solutions to prevent support for aggression against Ukraine and to protect national security;

b) described in Article 5k of Council Regulation (EU) No. 833/2014 of July 31, 2014 concerning restrictive measures in connection with Russia's destabilizing actions in Ukraine.

Method of verification of grounds/absence of grounds for exclusion:

Verification will be based on the Bidder's statement. The Contracting Authority will consider that the Bidder meets this condition, if the Bidder submits a statement of fulfillment of the conditions for participation in the proceeding found in the Bid Form ***(Appendix No. 1 to the Request for Proposal)***

VI. PLACE AND DEADLINE FOR SUBMITTING BIDS

VI.1. Bids must be submitted by the deadline of 12/09/2024.

- in electronic form (in the form of electronically signed documents or a scan of the signed document) to: dominika.radzanowska@polpharma.com

VI.2. Submission of a bid will be considered successful if a complete bid is received at the e-mail box with the above address by the deadline specified in this section.

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

VII. DESCRIPTION OF THE CRITERIA THAT THE CONTRACTING AUTHORITY WILL BE GUIDED BY WHEN SELECTING A BID

VII.1. In evaluating bids, the Contracting Authority will be guided by the criteria listed:

- Total net price for the service - 60%,
- Service delivery time - 40% The delivery time of the subject of the inquiry is understood as the time in calendar days counted from the first dosage to obtaining the final report of the study

VII.2. The scoring of the bid will be done according to the formula:

$$O_P = P_C + P_M$$

Where:

O_P	offer scoring
P_C	Number of points obtained in the criterion "Total net price"
P_M	Number of points obtained in the criterion "Service delivery time"

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

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

Where:

- P_C - Number of points for the criterion "Total net price"
- C_N - of the non-rejected bids, the lowest total net bid price
- C_B - total net price of the tested offer

For evaluation, bids submitted in a currency other than PLN will be converted into PLN at the average exchange rate of the National Bank of Poland on the closing date for submission of bids.

VII.4. The number of points (P_T) in the criterion "Service delivery time" will be awarded as follows**:**

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

Where:

- P_M - Number of points for the criterion "Service delivery time"
- M_N - from among the non-rejected bids, the shortest execution time of the subject matter of the bid inquiry
- M_B - the time declared in the offer for the execution of the subject of the tender request

The completion time of the subject of the request for proposal should be given in full calendar days. Bids with a turnaround time of more than 90 calendar days (counted from the first dosage to the final test report) will be rejected.

VII.5. The maximum the Bidder can obtain is 100 points. Calculations will be made to two decimal places.

VIII. PREPARATION OF BIDS

VIII.1. The bidder should prepare a single bid in accordance with the model form attached as Appendix 1 to the request for **proposal and a detailed schedule and price list with a description of all stages of the study, which it will attach with the bid.**

VIII.2. The bid should be signed by persons authorized to represent the Bidder on the basis of entries in the relevant registers or by power of attorney. The power of attorney should be attached to the bid.

VIII.3. The contracting authority does not allow partial or variant bids.

VIII.4. The bidder may amend or withdraw its bid before the deadline for submission of bids.

VIII.5. Bidders are required to carefully read the information contained in the Request for Proposal.

VIII.6. The cost of preparation and delivery of the bid shall be borne by the Contractor.

VIII.7. For matters related to this inquiry, please contact the Contracting Authority, e-mail: dominika.radzanowska@polpharma.com

IX. GENERAL PROVISIONS AND TERMS AND CONDITIONS

IX.1. The Contracting Authority 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 the law, to the extent affecting the implementation of the Agreement (in particular, changes in VAT rates);

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

IX.1.3. extension of the term of the Contract as a result of the need to perform additional work, the performance of which is necessary for the proper execution of the Contract, and the performance of which the Contracting Authority, acting with due diligence, could not have foreseen earlier, subject to Section IX.1.6 below;
extension of the deadline for execution of the Agreement as a result of force majeure, together with all consequences occurring in connection with the extension;

IX.1.4. Changes in the parameters of the subject matter of the Agreement, not leading to a change in the nature of the Agreement

IX.1.5. technological changes, in particular: the need to implement the Agreement using other technical/technological, material solutions than those indicated in the Request for Proposal, in a situation where the use of the provided solutions would threaten non-performance or faulty performance of the Agreement, subject to IX.1.7. below;

IX.1.6. changes relate to the performance of additional supplies or services of the Contractor, not covered by the Contract, if they have become necessary and all the following conditions are met:

- change of the Contractor cannot be made for economic or technical reasons, in particular concerning interchangeability or interoperability of equipment, services or installations, ordered within the basic subject of the Contract,
- change of 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 net 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 together:

- the need to amend the Contract is due to circumstances that the Contracting Authority, acting with due diligence, could not foresee,
- the value of the change does not exceed 50% of the value of the original net subject of the Agreement;

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

- as a result of a merger, demerger, transformation, bankruptcy, restructuring or acquisition of the Contractor or its enterprise, provided that the new contractor meets the conditions for participation in the proceedings, there are no grounds for exclusion against it and it does not involve other material changes to the Contract,
- as a result of the Ordering Party's assumption of the Contractor's obligations to its subcontractors.

IX.1.9. The contracting authority allows for an extension of the contract due to significant changes in the design of the Phase II study, after the results of the Phase I study have been obtained.

IX.2. The Contracting Authority also provides for the possibility of making non-substantive changes to the provisions of the Agreement in relation to the content of the offer on the basis of which the Contractor was selected.

IX.3. Amendments to the Agreement will be made in the form of annexes signed by both Parties, and the possibility of their introduction is subject to approval by the Ordering Party.

IX.4. The buyer requires that other important bid parameters be met:

- Payment term: a minimum of 30 days;
- Bid validity: 90 days;

IX.5. Important terms of the agreement:

IX.5.1. Inconsistencies or Defects - In the event of material inconsistencies or defects in the performance of the Services through the sole fault of the Supplier, the Supplier shall re-perform the Services at its own expense. Objections to the results shall be notified to the Supplier by the Ordering Party within fourteen (14) working days. The Ordering Party shall justify in detail the significant inconsistencies and defects. These works should be performed immediately, and the date for acceptance of services or materials specified in the corresponding Project Order will be postponed accordingly. If the Supplier is unable to redeliver the Materials or perform the Services without such inconsistencies or defects, the Supplier shall refund the amounts paid for such services when the inconsistencies or defects are discovered.

IX.5.2. Audit - The Procuring Entity reserves the right to audit the Supplier prior to or during the execution of the contract, in particular during the experimental (in vivo) part of the study.

IX.5.3. Contractual penalties - The Supplier is obliged to pay contractual penalties for:

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

The Supplier agrees to deduct the amount of liquidated damages directly from the payment of the VAT invoice at the time of delivery.

IX.6. The contracting authority reserves the right to cancel the proceedings without giving any reason.

IX.7. In the event of cancellation of the procurement procedure, suppliers are not entitled to a claim for reimbursement of the costs of participation in the procedure.

IX.8. The Contracting Authority's withdrawal from the conclusion of the contract in the event of notification to the contractor of the selection of his bid cannot be the basis for claims of incurred costs of participation in the procedure.

IX.9. In the course of evaluating the bids submitted, the Contracting Authority may require contractors to provide explanations regarding the content of the documents submitted by them.

IX.10. If the bid does not contain all the required elements, the Contracting Authority may, in justified cases, call on the Contractor to supplement it.

IX.11. **The contracting authority reserves the right to negotiate bids** 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 successive rounds with the possibility of inviting the bidder to submit an updated bid after each round of negotiations.

X. OTHER INFORMATION

X.1. The bidder shall bear all costs associated with the preparation and submission of the bid.

X.2. Until the deadline for submission of tenders, the Procuring Entity reserves the right to amend or supplement the contents of this request for proposals.

XI. LIST OF ANNEXES

The following documents are attached to this Request for Proposal:

Annex Designation	Name of the Annex
Appendix 1	Bid form
Appendix 2	Statement on the possibility of carrying out the tests specified in the request
Appendix 3	Statement about Meeting the Conditions of Participation in the Inquiry
Appendix 4	Specification of requirements - Summary of the study
Appendix 5	Template of Confidentiality Agreement.

Annex No. 1 to the Request for Proposal No. JODO/15/PR68772/2024

BID FORM

Bidder:

Full name (company) or first and last name	
Registered office/place of residence/address of main place of business	
The e -mail address to which the Employer should send correspondence related to the inquiry	
NIP	
REGON	
Phone	
Contact person for the Purchaser	

We offer to perform the subject of the contract ***for the service of conducting a non-clinical topical tolerance test for a medicinal product in*** the ***form of eye drops***, in accordance with the requirements of the request**:**

Scope of service	**Net price**	**Gross price**	**Currency**	**Lead time (calendar days)**
Conducting a non-clinical topical tolerance study for an eye drop medicinal product			PLN / EUR/ USD*	
TOTAL **The net amount will be taken for scoring in accordance with the provisions of paragraph. VII.**			PLN / EUR/ USD*	**Total ..... days calendar**
Invoice payment term				

Minimum 30 (days)	**..... days**	

*select the appropriate currency

Time required to prepare the appropriate number of animals, prepare the test plan, submit the test application and receive the necessary approvals ..... (maximum 90 calendar days). Bids with more than 90 calendar days will be rejected.

The bidder will provide a detailed schedule and price list with a description of all stages of the study, which will be attached with the bid.

The bidder has the status - SME (Micro, Small and Medium Enterprise) / Large Entrepreneur * (delete as appropriate)

<u>At the same time, we declare that</u>:

a. we have acquainted ourselves with the Request for Proposal and its annexes and do not raise any objections, and we have acquired the necessary information to prepare our offer,

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

c. By submitting this offer, we declare that we meet the conditions for participation specified in point. V of the request for quotation.

d. By submitting this bid, we are bound by it for a period of 90 days from the closing date for submission of bids,

e. circumstances do not apply to us:

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

..... (place and date)

..... (signature of the person(s) authorized to make a statement of intent on behalf of the Bidder)

Appendix No. 2 to the Request for Proposal No. JODO/15/PR68772/2024

A STATEMENT OF THE ABILITY TO CONDUCT THE TESTS SPECIFIED IN THE REQUEST FOR PROPOSALS

..... *(Bidder's name)* declares that it meets the conditions set forth in the request for proposals in the following scope:

The contractor has the ability to carry out the experimental part, as well as statistical analysis of test results in accordance with Directives 2010/63/EU and 2001/83/EC, as well as applicable guidelines (European and international), including:

- ICH Guidelines M3 (R2) on non-clinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals (EMA/CPMP/ICH/286/1995),
- ICH Topic S 7 A Safety Pharmacology Studies for Human Pharmaceuticals Step 5, Note for Guidance on Safety Pharmacology Studies for Human Pharmaceuticals (CPMP/ICH/539/00),
- EMA/CHMP/SWP/2145/2000 Rev. 1, Corr. 1* Guideline on non-clinical topical tolerance testing of medicinal products
- ISO 10993-23:2021 Biological evaluation of medical devices - Part 2: Tests for irritation.

.....	.....
(place and date)	(Signature of person(s) authorized to make a statement of intent on behalf of the Bidder)

Appendix No. 3 to the Request for Proposal No. JODO/15/PR68772/2024

STATEMENT ABOUT MEETING THE CONDITIONS SET OUT IN THE REQUEST FOR PROPOSALS

..... *(Bidder's name)* declares that it meets the conditions set forth in the request for proposals in the following scope:

1. The Contractor has experience in conducting non-clinical animal studies, including for ophthalmic products. (Has performed at least 10 non-clinical animal studies, including at least 5 studies for an ophthalmic product in the last 5 years (if the Contractor's period of operation is shorter).
2. The Contractor of the main experimental and statistical part shall provide a list of inspections for the last 5 years (if the Contractor's period of activity is shorter - during the period of its activity) with a summary of the inspection result. At least 1 inspection must have been conducted by a relevant GLP (Good Laboratory Practice) body of one of the European Union countries, and the results of all inspections during the period must not contain critical discrepancies. Test inspections conducted by the Contractor before 2019 will not be considered.

Attachments to the statement:

1. List of ophthalmic examinations performed in the last 5 years (if the Contractor's period of activity is shorter - during the period of activity).
2. List of inspections for the last 5 years (if the Contractor's period of activity is shorter - during the period of its activity) with a summary of the result of the inspection

.....	.....
(place and date)	(Signature of person(s) authorized to make a statement of intent on behalf of the Bidder)