Warsaw, 23.01.2024
place and date

INVITATION TO TENDER No. JODO/9/PR43746/2024
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 Medical Research Agency, Warszawskie Zakłady Farmaceutyczne Polfa S.A., requests bids for **to conduct a non-clinical topical tolerance study for a medicinal product in the form of eye drops.**

I. NAME AND ADDRESS OF THE ORDERING PARTY

Warszawskie Zakłady Farmaceutyczne Polfa S.A.
Karolkowa Street 22/24
01-207 Warsaw

II. MODE OF AWARDING THE CONTRACT

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)
2. Proceedings conducted by market discernment, in an expedient and economical manner in compliance with the rules:
   1) getting the best results from given inputs;
   2) optimal selection of methods and means to achieve the objectives;
   3) openness, fair competition and equal treatment of contractors.

III. DESCRIPTION OF THE SUBJECT OF THE INQUIRY

III.1. The subject of the inquiry is **service to conduct a non-clinical topical tolerance study for a medicinal product in the form of eye drops.**

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

III.3. Scope of inquiry:

III.3.1. Type: single dose, preclinical local tolerance study

- Species: white albino rabbits
- Strain: New Zealand
- Sample size: 18 animals (3 animals per test product)
- Test products: 6 products to be evaluated (i.e., 2 eye drop formulations, 3 powers for each formulation)
- Negative control: placebo carrier (applied to the contralateral eye)
- Random allocation of animals to individual test products
- Dosage:
  - Route of administration of test product and negative control: into the lower conjunctival sac
  - Test product dripped into one eye, negative control to be dripped into contralateral eye

- Frequency of administration: single dose
- Study endpoints (and frequency of assessment):
  - Ophthalmic evaluation:
    - Assessment of damage to the following tissues of the eye and surrounding areas: cornea, iris, conjunctiva, eyelids, choroid, lens, vitreous body, fundus.
    - Duration and frequency of evaluation: 1 (±0.1) h, 24 (±2) h, 48 (±2) h, and 72 (±2) h after injection, extended follow-up (up to 21 days) may be required for persistent lesions
    - Evaluation technique: using a slit lamp and an ophthalmoscope, as well as the current condition of the eyes, which should be documented with photographs before injection and at each time point.
  - General condition of animals (once a day):
    - Overall clinical assessment
    - Mortality, morbidity and clinical manifestations
    - Food consumption
    - Body weight (also on admission to the center)

- Evaluation of results: descriptive and using a scale to classify changes, for quantitative variables, provide mean, median and SD.
- Report: Provide draft report for comment. Final report available no later than 3 weeks after submitting comments on draft.

III.3.2. Activities covered:

Planning and conducting a single-dose local tolerance study, including:

- Ensuring that there are enough animals and that they are properly allocated to test groups,
- 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,
- Management of tested products (including their destruction and accounting),
- Feeding test products to animals,
- 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),
- Preparation of survey reports

III.4. The Contractor shall be responsible for performing the complete service of conducting the study (including preparation of full documentation as specified in the description of the subject of the contract), including the main experimental part, as well as clinical and statistical analysis of the results of the study with preparation of reports, as well as data management and management of the study.

III.5 The test must be designed, conducted and documented in accordance with Directives 2010/63/EU and 2001/83/EC, Good Laboratory Practice (GLP) 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.

Documentation (including test plans and final test reports) must be in English and in the local language, if required by local law. Final reports should include all relevant data in the form of text,

charts, photos, summary tables and related reports. Final reports should be uploaded as pdf files, with searchable text, hyperlinks and bookmarks.

III.6 The Contractor shall represent the Contracting Authority 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.7 Conduct internal audits of documentation and processes by the contractor during test execution,

III.8 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:

1. **Planned contract signing date: February/March 2024.**
2. **Planned study launch: March/April 2024**
3. The term of the contract must be completed no later than 120 calendar days from the start of the study.
4. Test results 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.
5. The deadline is a criterion for bid evaluation and will be counted as the time from the start of the audit until all final audit reports are submitted to the Employer.

V. REQUIREMENTS FROM CONTRACTORS

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

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**).*

2. The Contractor has experience in conducting non-clinical animal studies, including for combinations of drug substances. (Has performed at least 10 non-clinical animal studies, including at least 5 studies for an ophthalmic preparation in the last 10 years (if the Contractor's period of operation is shorter).
3. The Contractor of the main experimental and statistical part shall provide a list of inspections for the last 10 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 prior to 2013 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 provides the above-mentioned list of tests and inspections carried out.***

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.

VI. PLACE AND DEADLINE FOR SUBMITTING BIDS

VI.1. Bids must be submitted by the deadline **of 22/02/2024.**
- in electronic form (in the form of a scanned signed document) to: barbara.wendolowska@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%,

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

$$\boldsymbol{O_P = P_C + P_T}$$

Where:

O_P	offer scoring
P_C	Number of points obtained in the criterion "Total net price"
P_T	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

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 czar of the execution of the subject of the tender inquiry of the offer
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 quotation should be given in full calendar days. Bids with a lead time of more than 120 calendar days will be rejected.

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

VIII. DESCRIPTION OF BID PREPARATION

VIII.1. The bidder should prepare one bid in accordance with the model form attached as Annex 1 to the request.
VIII.2. The contracting authority does not allow partial or variant bids.
VIII.3. The bidder may amend or withdraw its bid before the deadline for submission of bids.
VIII.4. Bidders are required to carefully read the information contained in the Request for Proposal.
VIII.5. The cost of preparing and delivering the bid shall be borne by the Contractor.
VIII.6. For matters related to this inquiry, please contact the Contracting Authority, e-mail: barbara.wendolowska@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 Contract 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 laws, to the extent affecting the execution 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. to extend 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 IX.1.6 below;
IX.1.4. extension of the deadline for execution of the Agreement as a result of force majeure, with all consequences occurring in connection with the extension;
IX.1.5. changes in the parameters of the subject matter of the Agreement, not leading to changes in the nature of the Agreement - 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 of 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 Employer's assumption of the Contractor's obligations to its subcontractors.

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

IX.3. Amendments to the Agreement shall 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 shall require the fulfillment of other important bid parameters:

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

IX.5 Important terms of the contract:

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 Contracting Authority reserves the right to audit the Supplier prior to or during the execution of the contract.

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 procedure without giving any reason.

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

IX.8. withdrawal by the Contracting Authority from the conclusion of the contract in the event of notification to the contractor of the selection of its tender shall not be the basis for claims of incurred costs of participation in the procedure.

IX.9 In the course of evaluating submitted tenders, the Contracting Authority may request clarifications from contractors regarding the content of their submitted documents.

IX.10 If a 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 the Contractor whose bid has the highest number of points, 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	Model bid form
Appendix 2	Model statement on the possibility of carrying out the tests specified in the request
Appendix 3	Template of the Statement on Meeting the Conditions of Participation in the Inquiry

Appendix No. 1 to the Request for Proposal No. ***JODO/9/PR43746/2024***

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**:**

net amount: .....PLN / EUR/ USD

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

gross amount: .....PLN / EUR / USD*

*select the appropriate currency

Lead time of the order: ..... Calendar days from the date of delivery of test samples for the order.

The payment term of invoices is ..... days.

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

At the same time, we declare that:

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

Appendix No. 2 to the Request for Proposal No. ***JODO/9/PR43746/2024***

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:

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.

.....	.....
(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/9/PR43746/2024***

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 combinations of drug substances. (Has performed at least 10 non-clinical animal studies, including at least 5 studies for an ophthalmic preparation in the last 10 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 10 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 carried out 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 prior to 201 3 will not be considered.

Attachments to the statement :

1. List of ophthalmic examinations performed in the last 10 years (if the Contractor's period of activity is shorter - during the period of activity).
2. List of inspections for the last 10 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 the person(s) authorized to make a statement of intent on behalf of the Bidder)