Warsaw, 24.11.2023

PRICE INQUIRY NO. NETLA/9A/PR34372/2023

In connection with the project: *"Design and development of an innovative solution – a complex, two-component medicinal product in the form of eye drops in a multi-dose package without preservatives, aimed at the treatment of open-angle glaucoma.*", funded from the state budget by the Medical Research Agency, WZF Polfa S.A. kindly requests you to submit a bid **for the purchase of service associated with synthesis and characterisation of selected aminoisoquinoline amide-derivative salts, their stability testing, in accordance with the ICH Q1A guidelines, and the delivery of the selected salts.**

I. NAME AND ADDRESS OF THE BUYER

Warszawskie Zakłady Farmaceutyczne Polfa Spółka Akcyjna

ul. Karolkowa 22/24

01-207 Warszawa

II. PRICE INQUIRY PROCEDURE

1. This Price Inquiry is not subject to the provisions of the Public Procurement Law of 11 September 2019 (consolidated text: Journal of Laws of 2019, item 2019).

2. The procedure is being conducted as an intentional and cost-efficient market assessment study while respecting the following rules:

1) achieving the best possible outcomes using the available measures;
2) choosing the best possible means and methods to meet the pre-defined objectives;
3) ensuring transparency, fair competition and equal treatment of contractors.

III. DESCRIPTION OF THE SUBJECT OF THE PRICE INQUIRY

3.1. The subject of the Price Inquiry is the purchase of service associated with synthesis and characterisation of selected aminoisoquinoline amide-derivative salts, their stability testing, in accordance with the ICH Q1 guidelines, and the purchase of the selected salts. The service consists of five stages.

3.2. Stages and scope of service:

3.2.1. **Synthesis of selected aminoisoquinoline amide-derivative salts** (detailed information will be presented after signature of the Confidential Disclosure Agreement with the Bidder). The final list of salts to be synthetised will be consulted and approved by the Buyer, and the amount of salts ultimately qualified for synthesis shall not be less than four.
Product: providing a description of the synthesis method in English.

3.2.2. **Identification, purity testing and enantiomeric purity testing** of the obtained salts using the HPLC technique and the salt characterisation using the ^{1}H and ^{13}C NMR, PXRD and IR techniques. Determination of the counterion content. Investigation of the solubility of the obtained salts in different pH buffers with a pH value in the range of 4 to 7.
Product: providing results of the NMR, PXRD and IR testing and analytical certificates in English along with a report on the conducted work in English.

3.2.3. **Stability testing of the obtained aminoisoquinoline amide-derivative salts** in accordance with the ICH guidelines, and at 25°C/60%RH and 40°C/75%RH for a minimum 1 month (timepoints: week 1, week 2, week 3, week 4). Parameters monitored during the stability

testing: appearance, assay (HPLC), related substances (HPLC), water content, PXRD, enantiomeric purity and counterion content.
Product: providing results of the NMR, PXRD and IR testing and analytical certificates in English along with a report on the conducted work in English.

3.2.4. **Synthesis of 25g of the selected aminoisoquinoline amide-derivative A salt** demonstrating the highest stability. The required active substance assay: 95.0% – 105.0% (per anhydrous substance free from solvents).
Product: providing 25g of the substance and analytical certificates in English.

3.2.5. **Synthesis of 10g of the selected aminoisoquinoline amide-derivative B salt**. The required active substance assay: 95.0% – 105.0% (per anhydrous substance free from solvents).
Product: providing 10g of the substance and analytical certificates in English.

3.3. The Customer does not accept partial or variant bids, since the synthesis of the selected aminoisoquinoline amide-derivative salts, their characterisation, stability testing, as well as the synthesis and delivery of stable salts must be performed by one Bidder.

3.4. A detailed description of the subject matter of the contract **(Attachment No. 4**) will be provided to bidders after signing the Non-Disclosure Agreement **(Attachment No. 3**). The bidder should send the completed agreement to the email address barbara.wendolowska@polpharma.com Upon receipt of the Non-Disclosure Agreement, signatures by the authorized person (or persons), according to the representation rules of the respective Bidder, will be collected by the DocuSign platform. The Procuring Entity will make Exhibit No. 4 to this Request for Proposal available through digital channels, no later than two business days after the date of signing the confidentiality agreement.

IV. PRICE INQUIRY DELIVERY SITE AND DATE

4.1. Deadline for delivery of the subject of contract:

4.1.1. the subject of contract described in sections 3.2.1 and 3.2.2 will be delivered within up to 24 weeks from the date of agreement signature;

4.1.2. the subject of contract described in section 3.2.3 will be delivered within up to 32 weeks from the date of agreement signature;

4.1.3. the subject of contract described in sections 3.2.4 and 3.2.5 will be delivered within up to 44 weeks from the date of agreement signature.

4.2. The subject of contract is as follows:

4.2.1. For sections 3.2.1 and 3.2.2: description of the salt synthesis method and providing results of the NMR, PXRD and IR testing and analytical certificates in English.

4.2.2. For section 3.2.3: providing results of the NMR, PXRD and IR testing and analytical certificates in English for samples during stability testing.

4.2.3. For sections 3.2.4 and 3.2.5: delivery of the finished material to the Buyer along with analytical certificates in English.

4.3 The subject of contract described in sections 3.2.4 and 3.25 must be delivered to the Buyer's offices at: Warszawskie Zakłady Farmaceutyczne Polfa Spółka Akcyjna, ul. Barska 31, 02-315 Warszawa.

4.4 The Contractor shall transport the subject of contract described in sections 3.2.4 and 3.2.5 in conditions ensuring the maintenance of product stability.

V. REQUIREMENTS FOR CONTRACTORS

5.1. The contract award procedure is open to any Contractors who meet the following requirements:

5.1.1. have knowledge and experience (of at least 3 years) in synthesis of active substances of GMP-compliant quality

5.1.2. have a method developed for the synthesis of the aminoisoquinoline amide derivative or its dimesylate salt

5.1.3. have experience in the qualitative analysis of aminoisoquinoline amide derivative or its dimesylate salt

5.1.4. declare the ability to synthesise a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality

5.1.5. declare the ability to manufacture a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality, in a quantity of not less than 500 g, for the purposes of the clinical trials of a medicinal product containing this salt, within 18 months from the date of salt selection

5.1.6. declare the ability to prepare documentation for a selected aminoisoquinoline amide-derivative salt for the purposes of initiation of the clinical trials of a medicinal product containing this salt, within 24 months from the date of salt selection. The documentation must comply with the requirements of EMA/CHMP/QWP/545525/2017 Rev. 2, Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials

5.1.7. sign the Confidential Disclosure Agreement prior to the commencement of works *(**Appendix 3 to the Price Inquiry**)*

Assessment procedure:

*The Customer will consider the Contractor as meeting the above conditions if the Contractor submits a declaration of compliance with the conditions for participation in the procedure (**Appendix 2 to the Price Inquiry**).*

The Customer reserves the right to verify the fulfilment of the conditions at the Bidder's site or to call for relevant documentation to be submitted. Verification will be based on confirmation of a minimum 3-year experience in synthesis of active substances of GMP-compliant quality.

5.2. Bids submitted by Contractors who demonstrate that they meet the specified requirements will be taken forward to the bid examination and assessment stage. The compliance with the above requirements will be assessed based on a 'meet – does not meet' basis. Bids submitted by Contractors who fail to meet any of the above requirements will be rejected.

5.3. Entities for which the following circumstances occur are also excluded from the tender:

a) as described in Article 7(1) of the Act of 13 April 2022 on Special Measures to Counteract Support for the Aggression against Ukraine and to Protect National Security;

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

Method of verification of grounds/lack of grounds for exclusion:
The verification shall take place on the basis of the Bidder's declaration.

VI. METHOD OF PRICE CALCULATION

6.1. Bid price calculation: the price should be calculated as a net and a gross amount.

6.2. Bids with the price given in a currency other than PLN will be converted to PLN at the average exchange rate of the National Bank of Poland (https://www.nbp.pl/) as at the final date for the submission of bids.

6.3. The price should include all the costs related to the preparation and performance of the subject of the Price Inquiry.

6.4. The price given in the bid cannot change during contract performance.

VII. CONTRACT AWARD CRITERIA

7.1. The bids will be evaluated based on the following criteria:

- Price – as a total of prices for all order delivery stages – 40%,
- - Time required for the synthesis, characterization, and 1-month stability testing of aminoisoquinoline amide-derivative salt – 30%,
- Declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials – 30%,

7.2. The scoring of the bid will be calculated according to the following formula:

$$\boldsymbol{O_P = P_C + P_W + P_K}$$

where:

O_P	-	the bid score
P_C	-	score for the criterion 'price'
P_w	-	score for the criterion 'the execution time of synthesis, characterisation and 1-month stability testing of aminoisoquinoline amide-derivative salts'
P_K	-	number of points awarded for the criterion "declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials"

7.3. The score (P_C) for the criterion 'price' will be calculated as follows:

$$P_C = \frac{C_N}{C_B} * 40 \text{ points}$$

where:

P_C - score for the criterion 'price'
C_N - the lowest total net price based on non-rejected bids
C_B - total net price of the bid under evaluation

Bids with the price given in a currency other than PLN will be converted to PLN at the average exchange rate of the National Bank of Poland as at the final date for the submission of bids.

7.4. The score (P_w) for the criterion 'the execution time of synthesis, characterisation and 1-month stability testing of aminoisoquinoline amide-derivative salts' will be calculated as follows:

$$P_w = \frac{W_N}{W_B} * 30 \text{ points}$$

where:

Pw - score for the criterion 'the execution time of synthesis, characterisation and 1-month stability testing of aminoisoquinoline amide-derivative salts'

W_N - the shortest time of delivery based on non-rejected bids
W_B - time of delivery of the subject of the Price Inquiry:

7.4.1. The Buyer understands the time of delivery as time calculated in weeks from the agreement signature.

The bid will be rejected if the execution time of synthesis, characterisation and 1-month stability testing of aminoisoquinoline amide-derivative salts is longer than 32 weeks from the agreement signature. For evaluation, the delivery time is calculated as a sum of weeks necessary to perform the subject of contract described in detail in section III, subsections 3.2.1, 3.2.2, 3.2.3.
The bid will be rejected if the time of delivery of the object of contract described in detail in section III, subsections 3.2.4 and 3.2.5 is longer than 44 weeks from the date of agreement signature.
The time of delivery of the subject of contract described in detail in section III, subsections 3.2.4 and 3.2.5 is not subject to scoring.

7.5 The score (P_K) for the criterion "declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials" will be calculated as follows**:**

$$P_K = \frac{K_N}{K_B} * 30 \text{ points}$$

where:

P_K - score for the criterion "declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials"

K_N - the shortest declared time of delivery of non-rejected bids

K_B - declared time of delivery of the subject of the Price Inquiry:

7.5.1 By the term "declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials" the Buyer understands the period of time (in months) counted from the date of salt selection.

Bids will be rejected if the declared time required for manufacturing a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality for the purposes of clinical trials exceeds 18 months from the date of salt selection.

7.6. The bid with the highest score out of all the non-rejected bids will be considered the best bid. The maximum score that can be awarded is 100 points. Calculations will be made to two decimal places.

VIII. PLACE AND DATES FOR SUBMITTING AND OPENING BIDS

8.1. The **final deadline** for submitting bids is **04th December 2023.**

- bids can be sent in electronic format as signed electronically or scanned documents to the following address: barbara.wendolowska@polpharma.com.

8.2. The date and the time when the bid is received by the Buyer determines whether the submission deadline has been complied with.

8.3. No bids submitted past the submission deadline will be considered.

8.4. The Buyer is not planning to hold a public opening of the bids.

8.5. Bids may be modified or withdrawn prior to the end of the time limit for the submission of bids.

IX. PREPARATION OF BIDS

9.1. The Seller must draw up a single price bid using the form attached as Appendix 1 hereto. Submitting more than one bid for a particular part will result in all bids submitted by the Seller being rejected.

9.2. The bid must be prepared in Polish or English language version.

9.3. The bid with appendices must be signed by persons authorised to represent the Bidder in accordance with the representation resulting from the relevant register or pursuant to a power of attorney granted. If the person(s) signing the bid (representing the Bidder) is(are) acting under a power of attorney, the power of attorney must be attached to the bid.

9.4. Bidders are required to carefully read the information contained in the Price Inquiry.

9.5. Any costs and expenses incurred in connection with the preparation and submission of bids are to be paid by the respective Bidders.

9.6. Until the end of the time limit for the submission of bids, the Buyer reserves the right to amend or add new information to this Price Inquiry.

9.7. The Bidder submitting the bid remains bound by it for 90 calendar days from the end date of the time limit for the submission of bids.

9.8. The invoice shall be due minimum 30 days from the invoice date. Bids with payment terms shorter than 30 days will be rejected.

9.9. If the supplier's income earned in association with project execution is subject to withholding tax in Poland, WZF Polfa S.A. is obliged by law to deduct the withholding tax from the supplier's remuneration and remit it to the Polish tax authorities (remuneration includes withholding tax).

9.10. Transfer to the Principal (within the agreed remuneration) of all exclusive rights and any and all transferable other rights to intangible property that arise in connection with the delivery of the subject of order (hereinafter referred to as "Intellectual Property Rights"). Accordingly, all Intellectual Property Rights arising in connection with the delivery of the order will become the sole property of the Principal. The scope of Intellectual Property Rights includes the "work", the "inventive design" and the "know-how", which will be specified in detail in the order.

X. COMMUNICATIONS BETWEEN THE BUYER AND SELLERS, PERSONS AUTHORISED FOR CONTACT

10.1. During the procedure, the Buyer and the Sellers submit all declarations, requests, notices and information in Polish.

10.2. The receipt of any notices, declarations, requests and information submitted electronically must be immediately confirmed at the request of each of the parties.

10.3. If the Seller has not confirmed the receipt of the correspondence, the Buyer will assume that the correspondence sent by the Buyer to the e-mail address provided by the Seller has been delivered in a way that enables the Seller to read it.

10.4. Any correspondence about this Price Inquiry should be sent to e-mail: barbara.wendolowska@polpharma.com

10.5. In any correspondence related to this Price Inquiry, the Seller should refer to the procedure number: Price Inquiry No. **NETLA/9A/PR34372/2023.**

10.6. The person authorised to communicate with the Seller is Ms Barbara Wendołowska.

10.7. No information, clarifications or replies to any queries submitted to the Buyer will be provided orally or by phone.

10.8. Any questions about this Price Inquiry should be sent by e-mail to the address provided above, not later than 3 days before the end of the time limit for the submission of bids.

10.9. Replies to the questions and more detailed information on the Price Inquiry following from questions asked by prospective Sellers will be sent to the entity requesting that information.

XI. BID EVALUATION PROCEDURE AND PUBLICATION OF RESULTS

11.1. During the examination and evaluation of the submitted bids, the Buyer may request the Seller to provide additional information (if it does not infringe competitiveness) and clarifications related to the submitted bids. The Buyer may also ask the Seller to correct evident mistakes and calculation errors.

11.2. The Buyer reserves the right to verify, during the bid evaluation, the documents, statements, lists, data and information provided by the Sellers.

11.3. If two or more Sellers have the same score, the bid which is best in terms of the environmental and climate impact will be selected. For this purpose, the Buyer has the right to request the Bidders with the highest final score to supplement the bid with more information indicated by the Buyer with respect to the environmental impact of the subject of the bid.

XII. ADDITIONAL INFORMATION

12.1. The Seller submitting the bid remains bound by it for 90 calendar days from the end date of the time limit for the submission of the bid. Following the procedure, the Buyer may conclude a Contract for the performance of the subject of the order with the Seller whose bid is considered the best. The selection of the best bid does not mean that the Buyer is obliged to conclude a Contract with the Contractor.

12.2. The Buyer reserves the right to place additional orders with the Seller, not covered by the Subject of the original Price Inquiry, up to 50% of the value of the Subject of the original Price Inquiry, necessary for the proper performance of the task and resulting among others from the following circumstances:

– due to technical or organisational reasons, the separation of the additional order from the Subject of the original Price Inquiry would incur excessively large costs,

– the performance of the Subject of the original Price Inquiry depends on the performance of the additional order.

12.3. The Buyer reserves the right to place a supplementary order with the Seller (consistent with the description of the subject of the original order) up to 50% of the value of the original order specified in the contract concluded with the Seller.

12.4. The Buyer makes the reservation that it has:

- the right not to choose any of the submitted Bids;
- the right to cancel the Tender Procedure at any time, without giving a reason or without prior notification of the Bidders;
- the right to change or supplement the documents making up the Price Inquiry, in which case such documents will become an integral part of the Inquiry;

- the right to extend the time limit for the submission of bids;

and the Bidders have no claims against the Buyer with respect to the above rights.

12.5. PERSONAL DATA PROTECTION.

As far as personal data contained in bids are concerned, the Buyer – as soon as the bid is submitted – will become the Data Controller as defined under Article 4(7) of Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC ("GDPR"). The Buyer will process the data for the purposes of bid evaluation, concluding an agreement with the awarded contractor and implementing the concluded agreement, i.e. under Article 6(1)(b) of the GDPR.

The Buyer will transfer the personal data contained in the submitted bids, under relevant regulations, to authorised bodies and institutions entitled to audit projects co-financed from the funds of the Medical Research Agency. For more information on the processing of personal data by competent institutions, visit: https://abm.gov.pl/pl/wolnytekst/198,Polityka-dotyczaca-cookies.html

The Buyer will process the personal data throughout the period during which it is required, under relevant regulations, to store the whole documentation related to projects co-financed from the funds of the Medical Research Agency.

XIII. LIST OF APPENDICES

The following appendices are attached to this Price Inquiry:

Appendix number	Appendix title
Appendix 1	Bid Form
Appendix 2	Contractor's Declaration
Appendix 3	Confidential Disclosure Agreement
Appendix 4	Detailed description of the subject of the price inquiry

Appendix 1 to the Price Inquiry No. ***NETLA/9A/PR34372/2023***

BID FORM

Bidder:

Name / Company	
Registered office/home address/address of the principal place of business	
E-mail address for the Buyer to send information related to the Price Inquiry	
NIP [Taxpayer ID Number]	
REGON [Statistical ID Number]	
Phone number	
Contact person for the Buyer	

We offer the delivery of the subject of order **for the purchase of service associated with synthesis and characterisation of selected aminoisoquinoline amide-derivative salts, their stability testing, in accordance with the ICH Q1A guidelines**, and the delivery of the selected salts, in accordance with the terms of the Price Inquiry for the following **price**:

	Subject of the Price Inquiry	**Unit net price for testing (PLN/EUR/USD*)**	**Execution time in weeks (from agreement signature)**
1	Synthesis and characterisation of selected aminoisoquinoline amide-derivative salts, described in subsections 3.2.1, 3.2.2 and 4.1.1.		
2	Stability testing of obtained aminoisoquinoline amide-derivative salts, described in subsections 3.2.3 and 4.1.2.		
3	Synthesis and characterisation of 25g of the selected aminoisoquinoline amide-derivative A salt demonstrating the highest stability, in accordance with subsections 3.2.4 and 4.1.3.		
4	Synthesis and characterisation of 10g of the selected aminoisoquinoline amide-derivative B salt, described in subsections 3.2.5 and 4.1.3.		

***Delete as appropriate, select the appropriate currency**

We declare the ability to manufacture a batch of a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality, in a quantity of not less than 500 g, for the purposes of the clinical trials of a medicinal product containing this salt, **within …..... months** from the date of salt selection.

We declare the ability to prepare documentation for a selected aminoisoquinoline amide-derivative salt for the purpose of initiation of the clinical trials of a medicinal product containing this salt, **within ……. months** from the date of salt selection. The documentation must comply with the requirements of EMA/CHMP/QWP/545525/2017 Rev. 2, Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials.

We also declare that:

a. We have read the Price Inquiry and appendices thereto, we raise no objections and we have obtained the information necessary to prepare our bid.

b. Our bid price includes a lump sum that covers all the obligations of the future Seller as necessary to deliver the subject of this Price Inquiry.

c. Our bid will remain valid and binding for 90 calendar days from the end date of the time limit for the submission of bids.

d. The following circumstances do not occur with respect to us:

a) as described in Article 7(1) of the Act of 13 April 2022 on Special Measures to Counteract Support for the Aggression against Ukraine and to Protect National Security;

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

…… ……

(place and date) (signature(s) of person(s) authorised to submit statements of will on behalf of the Bidder)

*delete as appropriate

CONTRACTOR'S DECLARATION

By submitting the bid for the purchase of service associated with synthesis and characterisation of selected aminoisoquinoline amide-derivative salts and their stability testing, in accordance with the ICH Q1A guidelines, we hereby declare that:

1) we have knowledge and experience (of at least 3 years) in synthesis of active substances of GMP-compliant quality,
2) we have a method developed for the synthesis of the aminoisoquinoline amide derivative or its dimesylate salt,
3) we have experience in the qualitative analysis of the salts of the aminoisoquinoline amide derivative or its dimesylate salt,
4) we have the ability to synthesise a selected aminoisoquinoline amide-derivative salt of GMP-compliant quality.

……	……
(place and date)	(signature(s) of person(s) authorised to submit statements of will on behalf of the Bidder)