Warsaw, 20.12.2022

PRICE INQUIRY NO. 19
being conducted as a market assessment study
- amendment to the content

Pertaining to the implementation of the project titled "Development of a universal fast-response platform, based on RNA technology, ensuring the national drug and epidemiological safety", funded from the state budget by the Medical Research Agency, WZA Polfa Warszawa S.A., you are kindly requested to submit a quotation for services involving the development, manufacture and delivery of an active substance in the form of a modified oligonucleotide – an 18-mer RNA and Technology Transfer to a designated manufacturing site.

I. NAME AND ADDRESS OF THE CONTRACTING PARTY

Warszawskie Zakłady Farmaceutyczne Polfa S.A.
ul. Karolkowa 22/24
01-207 Warszawa

II. CONTRACT AWARD PROCEDURE

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

II.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 CONTRACT

III.1. This price inquiry relates to *the provision of services involving:*
Development, manufacture and delivery of an active substance in the form of a modified oligonucleotide – an 18-mer RNA (Nusinersen sodium salt) and technology transfer to a designated manufacturing site

III.2. The subject of the contract is as follows:

III.2.1. development of the manufacturing technology of Nuisinersen sodium, incl. but not limited to:
III.2.1.1. solid-phase synthesis (production of crude Nusinersen)
III.2.1.2. purification process
III.2.1.3. ultrafiltration
III.2.1.4. final detritylation
III.2.1.5. freeze drying process
III.2.2. manufacturing technology transfer III.2.1 to ZF Polpharma S.A. as per scope defined in point IV
III.2.3. development and validation of analytical methods for Nusinersen sodium and Raw Materials testing
III.2.4. (4) transfer of analytical methods III.2.3 to ZF Polpharma S.A.

III.2.5. (5) manufacture and delivery of 2 g of Nusinersen under non-GMP conditions
III.2.6. (6) manufacture and delivery of 11 g of Nusinersen under non-GMP conditions with proved sameness based on the draft FDA guideline PSG_209531

III.3. This price inquiry includes as follows:
III.3.1. Development of a specification for the active substance based on ICH Q6 guideline, omitting assessment elements not applicable to oligonucleotides.
III.3.2. Development and transfer of analytical methods
III.3.3. Manufacture of the material under non-GMP (3 different batches in equal quantities) in quantities and conditions specified in Section III.2
III.3.4. Delivery of certiefied standards (API and impurities) in an amount not less than 200 mg in total
III.3.5. Technology transfer to ZF Polpharma SA (incl.GMP validation at ZF Polpharma premises)
III.3.6. scientific support and all required CMC documentation in preparation of registration dossier for the active substance based on GMP validation at ZF Polpharma SA. premises
III.3.7. Demonstration of sameness to the reference product Spinraza based on draft FDA guideline PSG_209531

III.4. The Contracting Party reserves exclusive rights to sell the Nusinersen drug in the following markets: PL, DE, DK, FI, NO, SE and with rights of unrestricted sales in the rest of the world

III.5. No partial or variant proposals will be accepted. The Contracting Party reserves the right to change the quantity of substances to be manufactured and delivered.

IV. TECHNOLOGY AND TECHNOLOGY TRANSFER

IV.1. Critical success factors for manufacturing technology to be transferred are as follows:
IV.1.1. Free to operate regarding IP constraints (of the patents before the effective date of the future agreement)
IV.1.2. Cost effective at the desired scale
IV.1.3. Transferable to commercial scale

IV.2. Technology Transfer scope includes but is not limited to:
IV.2.1. manufacturing technology transfer based on delivered Technical Package (detailed scope to be agreed in future agreement)
IV.2.2. scientific support for ZF Polpharma during technology transfer (incl. production documentation preparation, i.a. batch records, validation protocol) to ZF Polpharma S.A. (teleconferences, visit of the technology specialist of both parties)
IV.2.3. in person technical support during demonstration and GMP batches at ZF Polpharma premises
IV.2.4. transfer of analytical methods to Polpharma according to Polpharma's transfer procedure
IV.2.5. scientific support and all required CMC documentation in preparation of registration documentation

IV.3. Technology Transfer acceptance criteria includes but are not limited to:
IV.3.1. successful demonstration and GMP batches at desired scale (min. 12 gram/batch) at ZF Polpharma premises as expected (product meeting specification, desired yield obtained) planned schedule for batches manufacture – demonstration batch Q1/2024 – Q2/2024, GMP validation Q3/2024 - Q4/2024

IV.3.2. GMP validation batches sameness to the reference product Spinraza based on draft FDA guideline PSG_209531 and any other regulatory (FDA or EMA) guidelines which will be published - Q3/2024 - Q4/2024

IV.3.3. completion of registration dossier for the active substance

V. CONTRACT DELIVERY SITE AND DATE

V.1. The deadline for the completion of the subject of the inquiry in accordance with the schedule presented below in point V.2

V.2. Planned schedule for the realization of the subject of the inquiry will be as follows:

– *Supply of 2* g of the API in Q1 2023, about 11** g *(under non-GMP conditions) of the API in Q3 2023.*

*(*All quantity equivalent to anhydrous 100% Nusinersen acid)*

- *Supply of certified standards (API and impurities) in an amount not less than 200 mg in total in Q3 2023;*
- Technology Transfer – by end of 2024

V.3. Terms of delivery of active substance:

- Material (API) CIP Warsaw (Incoterms® 2020)

VI. REQUIREMENTS FROM CONTRACTORS

VI.1. The procedure is open to any Contractors who meet the following conditions:

- have knowledge and experience in the manufacture of active substances in a quality system compliant with GMP,

- have access to facilities for the synthesis, purification and freeze-drying of oligonucleotides,

– have access to analytical equipment that enables the determination of the quality of the active substance to be manufactured;

– have experience in preparing registration dossiers for active substances;

– have staff with experience in the synthesis of active substances and, in particular, in the synthesis of oligonucleotides.

- have knowledge and experience in technology transfer to the GMP area

<u>Assessment procedure</u>

The Contracting Party will consider Contractor as meeting this condition if Contractor submits a declaration of compliance with the conditions for participation in the procedure (Appendix 2 to the Price Inquiry).

The Contracting Party reserves the right to verify the fulfilment of the conditions at the Bidder's site or to request the submission of relevant documentation.

VI.2. *Entities with personal or capital ties with the Ordering Party are excluded from the tender.*

The capital or personal ties are understood to mean mutual ties between the Supplier and the Ordering Party or persons authorized to contract obligations on behalf of the Ordering Party , or persons performing, on behalf of the Ordering Party , actions involved in the preparation and conduct of the Supplier selection procedure, consisting, in particular, in:

VI.2.1. participation in a partnership in the capacity of a partner in a civil-law company or partnership;

VI.2.2. holding at least 10% of stocks or shares;

VI.2.3. holding the position of a member of a supervisory or management body, a commercial representative or an attorney;

VI.2.4. being married to or having lineal consanguinity or direct affinity, collateral consanguinity or affinity to the second degree to, or being adopted by, under the guard or custody of the parties.

Assessment procedure:
The verification will be based on the Supplier's declaration on not having the above-mentioned capital or personal links with the Ordering Party (Appendix 3 to the Price Inquiry).

VI.3. Quotations submitted by Contractors who demonstrate that they meet the specified conditions will be taken forward to the quotation evaluation stage. The compliance with the above conditions will be assessed based on a 'meet – does not meet' basis. Quotations submitted by Contractors who fail to meet any of the above conditions will be rejected.

VII. CONTRACT AWARD CRITERIA

VII.1. The quotations will be evaluated based on the following criteria:
– net contract price – 75%,
– GMP compliant quality system– 25%.

VII.2. The quotation score will be calculated according to the following formula:

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

where:
O_P the quotation score
P_C – score for the criterion "net contract price"
P_G score for "a quality system conforming to GMP requirements"

VII.3. The score (P_C) for "Total Net Price" will be calculated according to the following formula:

$$P_C = \frac{C_N}{C_B} * 75\ points$$

where:
P_C - score for the "net price"
C_N - the lowest net price from among non-rejected quotations
C_B - net price of the quotation under assessment

Quotation offering prices in currencies other than PLN will be converted to PLN using the average exchange rate published by the National Bank of Poland (NBP) as at the final date for submitting quotations.

VII.4. The score (P_G) for having in place "a quality system conforming to GMP requirements" will be calculated as follows:

$$P_G = T * 25\ points$$

where:
P_G - score for "a quality system conforming to GMP requirements"
T - score awarded: "0" if the Bidder does not have a quality system conforming to GMP requirements "1" if the Contractor has a quality system conforming to GMP requirements

VII.5. The maximum score that can be awarded is 100 points. Calculations will be made to two decimal places.

VIII. PLACE AND CLOSING DATE FOR SUBMISSION OF QUOTATIONS

VIII.1. The final deadline for submitting quotations is **11.01.2023 by 11:59 p.m.**
– quotations can be sent in electronic format (in the form of a scan of the signed document or document signed with qualified signature) to the following address: **urszula.strzalinska@polpharma.com**

VIII.2. A quotation will be considered to have been properly submitted if a complete quotation is delivered to the above e-mail address within the time limit stipulated in this section.

VIII.3. No quotations submitted past the submission deadline will be taken into consideration.

IX. PREPARATION OF QUOTATIONS

IX.1. The Bidder should draw up one quotation using the template attached as Appendix 1 hereto.

IX.2. Quotations may be modified or withdrawn prior to the end of the time limit for the submission of quotations.

IX.3. Bidders are required to carefully read the information contained in the Price Inquiry.

IX.4. The costs of preparing and delivering quotations will be borne by the respective Bidder.

IX.5. For any matters related to this Price Inquiry, please contact the Contracting Party, e-mail: urszula.strzalinska@polpharma.com

X. AMENDMENTS TO THE CONTRACT

X.1. The Contracting Party reserves the right to make material amendments to the concluded Contract in relation to the quotation on the basis of which the Contractor was selected to the following extent and in the following situations:

X.1.1. changes to the European Union or national law that affect the performance of the Contract (in particular changes of the VAT rate);

X.1.2. improving technical standards of the subject of the contract resulting from new solutions brought about by technological progress, without any impact on the gross flat rate;

X.1.3. extending the deadline for the performance of the Contract due to additional work which must be completed for the proper performance of the Contract and which the Contracting Party, acting with due diligence, could not have foreseen earlier, subject to subsection IX.1.6 below;

X.1.4. extending the deadline for the performance of the Contract due to force majeure, with all the consequences of such extension;

X.1.5. **c**hanging the parameters of the subject of the Contract which does not lead to a change in the nature of the Contract – technological changes, in particular: the need to perform the Contract using technical/technological or material-related solutions other than as specified in the Price Inquiry if the application of the planned solutions could lead to a failure to perform or to improper performance of the Contract, subject to subsection IX.1.7. below;

X.1.6. changes relate to additional supplies or services from the Contractor which are not covered by the Contract, as long as they are necessary and all of the following conditions are met:

X.1.6.1. – the Contractor cannot be changed due to economic or technical reasons, in particular relating to the interchangeability or interoperability of the equipment, services or installation ordered in connection with the original subject of the Contract,

X.1.6.2. the change of the Contractor would cause significant inconvenience or a considerable increase of costs for the Contracting Party,

X.1.6.3. the value of each subsequent change does not exceed 50% of the value of the original subject of the Contract (net amount);

X.1.7. the change does not lead to a change in the nature of the Contract and all of the following conditions are met:

X.1.7.1. the Contract must be changed due to the circumstances which the Contracting Party, acting with due diligence, could not have foreseen,

X.1.7.2. the value of the change does not exceed 50% of the value of the original subject matter of the Contract (net amount);

X.1.8. The Contractor may be replaced with a new contractor:

X.1.8.1. as a result of merger, division, transformation, bankruptcy, restructuring or purchase of the Contractor or its enterprise as long as the new contractor meets the conditions for participating in the tender procedure, there are no grounds for exclusion and the change does not entail other material changes to the Contract,

X.1.8.2. as a result of the Contracting Party taking over the Contractor's obligations towards his subcontractors;

X.1.9. the amendment to the Contract does not lead to a change in the nature of the Contract and the total value of the amendments is less than EUR 215,000 and at the same time is lower than 10% of the value of the original subject of the Contract (net amount).

X.2. The Contracting Party also allows for making non-material amendments to the concluded Contract in relation to the bid on the basis of which the Contractor was selected.

X.3. Amendments to the Contract will be made in the form of an annex signed by both parties and they are subject to the Contracting Party's approval.

XI. ADDITIONAL INFORMATION

XI.1. Until the end of the time limit for the submission of quotations, the Contracting Party reserves the right to amend or add new information to this Price Inquiry.

XI.2. Submitted quotations will remain valid and binding for 60 days from the final date for submitting quotations.

XII. LIST OF APPENDICES

The following documents are appendices to the Price Inquiry:

Appendix number	Appendix title
Appendix 1	Quotation form
Appendix 2	Declaration of compliance with the eligibility criteria for the participation in the procedure
Appendix 3	Model declaration on not having personal or capital ties with the Buyer

Appendix 1 to Price Inquiry No.19

QUOTATION FORM

Bidder:

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

We offer to perform the contract for the provision of services involving the development, manufacture and delivery of an active substance in the form of a modified oligonucleotide – an 18-mer RNA and technology transfer to a designated manufacturing site as per the requirements of the Price Inquiry for **the total price of:**

net amount: PLN/EUR* ……

applicable VAT at ……%: PLN/EUR* ……

gross amount: PLN/EUR* ……

(say: ……..……..)

Net price per gram of substance manufactured under non-GMP conditions: PLN/EUR* …….

We have a quality system conforming to GMP requirements: ……. (please say YES or NO)

**Delete as appropriate*

We also declare as follows:

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

b. Our bid price includes a lump sum that covers for all the obligations of the future Contractor as necessary to deliver the subject of the contract referred to hereunder.

c. Our quotation will remain valid and binding for 60 days from the final date for submitting quotations.

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

Appendix 2 to the Price Inquiry No. 19

Contracting Party:
WZF Polfa S.A.
ul. Karolkowa 22/24
01-207 Warszawa

Contractor's Declaration

OF COMPLIANCE WITH THE ELIGIBILITY CRITERIA FOR THE PARTICIPATION IN THE PROCEDURE

By submitting this quotation for*:* **the provision services involving the development, manufacture and delivery of an active substance in the form of a modified oligonucleotide – an 18-mer RNA and technology transfer to a designated manufacturing site,** funded from the state budget by the Medical Research Agency, I hereby declare as follows:

INFORMATION ON THE CONTRACTOR:

I represent that we meet the conditions for participation in the tender procedure as specified by the Customer in part VI of the Price Inquiry and relating to:

- we have knowledge and experience in the manufacture of active substances in a quality system compliant with GMP,
- we have access to facilities for the synthesis, purification and freeze-drying of oligonucleotides,
– we have access to analytical equipment that enables the determination of the quality of the active substance to be manufactured;
– we have experience in preparing registration dossiers for active substances;
– we have staff with experience in the synthesis of active substances and, in particular, in the synthesis of oligonucleotides;
-we have knowledge and experience in technology transfer to the GMP area

…… ……
(place and date) (signature of the Contractor's representative)

Appendix 3 to the Price Inquiry No. 19

……
(Seller's stamp)

Buyer:

Warszawskie Zakłady Farmaceutyczne Polfa Spółka Akcyjna

ul. Karolkowa 22/24

01-207 Warszawa

DECLARATION

I declare that when submitting a bid for the **the development, manufacture and delivery of an active substance in the form of a modified oligonucleotide – an 18-mer RNA and technology transfer to a designated manufacturing site** funded by the state budget from the Medical Research Agency, **I have no capital or personal ties with the Buyer**, i.e.: WZF Polfa Spółka Akcyjna.

Capital or personal ties mean mutual ties between the Bidder and the Buyer or persons authorised to contract obligations on behalf of the Buyer, or persons performing on behalf of the Buyer any actions involved in the preparation and performance of the Seller selection procedure, including in particular:

a) participation in the company in the capacity of a partner in a civil law company or partnership;
b) holding of at least 10% of stocks or shares;
c) holding the function of a member of a supervisory or management body, a commercial representative or an attorney;
d) being married to or having lineal consanguinity or direct affinity, collateral consanguinity or affinity to the second degree to or being adopted by, under the guard or custody of the beneficiary or of such persons.

I also declare that **I am not an entity designated in the Act of 13 April 2022 on Special Measures to Counteract the Support of Aggression Against Ukraine and to Protect National Security.**

…… (place and date)

…… (signature of the person(s) authorised to make a declaration of will for the Seller)