Ryvu Therapeutics S.A.
2 Sternbacha Street, 30-394 Krakow, Poland
registered in the District Court for the Krakow-Srodmiescie
in Krakow XI Division of the National Court Register
KRS number: 0000367359
VAT ID: PL6792942955

Krakow, 11th May 2023

REQUEST FOR PROPOSAL No. ABM-11052023M

In connection with the planned implementation by Ryvu Therapeutics S.A. of the project 'The conduct of a phase II, multicentre, open-label clinical trial (RIVER-81) evaluating the safety and efficacy of RVU120 in combination with venetoclax in patients with relapsed/refractory acute myeloid leukemia who have failed prior therapy with venetoclax and a hypomethylating agent' (the 'Project') under the Competition: Development of targeted or personalized medicine based on therapeutic products based on nucleic acids and small-molecule compounds ABM/2022/6 organized by the Medical Research Agency, Ryvu Therapeutics S.A. invites quotes for the execution of the following defined order description.

I. ORDERING PARTY

Ryvu Therapeutics S.A.
Sternbacha 2, 30-394 Krakow, Poland
EU VAT PL6792942955

II. ORDER DESRIPTION

The order description concerns developing the RVU120 monohydrochloride manufacturing process compliant with the cGMP requirements for clinical phase 2.

Due to the need to protect business secrets the order description (Appendix 01 to this RFP) will be sent upon request to all Bidders whom the Ordering Party have executed Confidential Disclosure Agreement or to who sign and send to tenders@ryvu.com the electronically signed CDA. The CDA template will be made available upon request to tenders@ryvu.com. The title of the message must contain the reference number of the RFP, which is RFP no. ABM-11052023M.

III. CONDITIONS FOR PARTICIPATION IN THE PROCEEDINGS

III.1. Bidders that fulfill the following are invited to submit a proposal:

- Bidders with operational readiness to start work in July 2023,
- Bidders with possibility of the delivery of the GMP batch by the end of Feb 2024.

These conditions will be confirmed by the statement in Appendix 02 – The proposal form. The assessment of the condition will be made using the system: meet/do not meet.

IV. PLACE, DATE AND PROCEDURE OF SUBMISSION OF PROPOSALS

IV.1. The proposal must be submitted by: **22nd May 2023 at 23.59 CET**.

IV.2. The proposal must be sent via e-mail to the following address: tenders@ryvu.com.

IV.3. The proposal must refer to the RFP number indicated on the first page: ABM-11052023M.

IV.4. The proposal and its attachments must be prepared in Polish or English.

IV.5. The proposal must be prepared in an accordance with the form constituting Appendix 02 to this RFP and must include the following proposed work details:

- a budget and a timeline to cover process and analytical methods transfer/optimization and API manufacture, including stability testing;

- selection of the starting materials and reagents, development of analytical methods for synthesis steps requiring optimization and validation/verification of the transferred batch release methods to be used during GMP manufacture and in the formal stability studies, setting up new specification if required, complete API characterization as per the revised release specification;
- process safety evaluation in order to prepare for HAZOP analysis, securing the scale-up activities;
- process transfer and optimization of indicated steps with the release of demonstration batch followed by GMP (clinical) batches manufacture (including safety assessment, raw materials sourcing and purchase, main impurities re-synthesis or isolation and characterization, standards synthesis, quality control, and batch release and storage, and any outsourced activities as applicable) using processes and methods developed as mentioned above followed by formal stability studies, as well as an outline of the anticipated work/tasks.

IV.6. The Bidders must provide the total price for the execution of the order (total fees including direct, indirect and pass throughs costs). The quote must include prices given in PLN or EUR.

IV.7. The proposal must include the validity period (minimum 30 calendar days from the date of submission). The Ordering Party may require Bidders to agree to an extension of the quote validity period for the period of up to next 30 calendar days.

V. CRITERIA FOR EVALUATION OF PROPOSALS:

V.1. Offers that comply with the order description (set out in section II.) and with conditions for participation in the proceedings (set out in section III.) will be accepted for the evaluation of offers. Offers that do not meet the requirements will be rejected.

V.2. Criterion: Net price ("C") – weight: 100% (10 points)

V.3. Net price ("C") considered as the total price for the execution of the order (total fees including direct, indirect and pass throughs costs). The quote must include prices given in PLN or EUR.

V.4. As regards prices quoted in foreign currencies, in order to compare the offers they shall be converted into PLN at the average exchange rate of the National Bank of Poland (NBP) prevailing on the day of closing the tender procedure indicated in section IV.1.

V.5. In the Net Price criterion, points will be awarded (to two decimal places) according to the formula:

$$\text{Criterion Net price "C"} = \frac{\text{the lowest net price offered among the bids submitted}}{\text{net price of the examined offer}} \times 10 \text{ points}$$

V.6. The Ordering Party will select as the most advantageous the offer that obtains the highest number of points.

V.7. Having to choose between quotation scored in the same number of points, the Ordering Party will call Bidders to re-present the prices.

VI. PROVISIONS OF THE AGREEMENT:

VI.1. The procedures will be concluded with the signing of a conditional agreement with the CRO selected in the proceedings. The conditional agreement with the selected CRO will come into effect upon the signing of a co-financing agreement for the project submitted to the Competition: Development of Targeted or Personalized Medicine Based on Nucleic Acids and Small Molecule Compounds ABM/2022/6 organized by the Medical Research Agency.

VI.2. Deadline of the implementation of the agreement (completion date): The implementation of the service in the period from the agreement conclusion with the selected Bidder to the date of 31st March 2024. The Ordering Party reserves the right to change the expected date of the contract in the case of unforeseen circumstances on the part of the Contractor for example but not exclusively in the case of technical problems, delay in obtaining launch materials, failure to scale the process, unexpected deviation from specification.

VI.3. Given that the requested work comprises a research and development component, the unexpected results may force the initial scope of work modification. The circumstances justifying such change are listed below, although the list is not exhaustive:

a. The original chemical route cannot be scaled-up as is,
b. Reagent replacement is beneficial for future commercial manufacturing,
c. New impurities and/or higher level of known ones will require additional control and stability testing; further analytical development may be needed,
d. Out-of-specification quality of the intermediate products or final product will require additional operations,
e. Significant change of the product specification is inevitable (triggered by the updated process outcomes)
f. Characteristics of the API will be unsuitable for compounding without additional processing.

VI.4. The Ordering Party allows for the possibility of awarding to the contractor selected in the course of this RFP supplementary orders, in an amount not exceeding 50% of the value of the contract specified in the agreement concluded with the contractor, while meeting the following conditions:

- such orders are consistent with the subject of the basic contract,
- the possibility of awarding such an order was provided for in the request for proposals and in the contract with the contractor,
- the total value of the supplementary order was taken into account when calculating the value of the basic order.

VII. ADDITIONAL INFORMATION

VII.1. The Bidders may ask the Ordering Party to clarify the content of this RFP. If the request for clarification of the content of the RFP was received later than by the end of 17th May 2023, the Ordering Party may provide explanations or leave the application unexamined. Questions must be sent to the following e-mail address: tenders@ryvu.com.

VII.2. Due to the need to protect business secrets, in the event of questions requiring the disclosure of confidential data, the Ordering Party reserves the right to provide explanations after signing and sending by e-mail by the Bidder the Confidential Disclosure Agreement (CDA). It is allowed to use an electronic signature (including a qualified electronic signature) or a trusted signature (trusted profile). The CDA document will be made available at the request of the Bidder by e-mail. The scan of the completed and signed CDA should be sent to the indicated e-mail address: tenders@ryvu.com.

VII.3. The Ordering Party reserves the right to change the content of the RFP, including changes in the terms of the procedure. Bidders will be informed.

VII.4. The Ordering Party reserves the right to ask the Bidders at any stage of the evaluation of offers for additional information, documents, additions or explanations. The Ordering Party's contact with the Bidder will take place by e-mail indicated in the content of the offer sent by the Bidder.

VII.5. The Ordering Party reserves the right to enter into negotiations with all Bidders who have submitted an offer that meets the conditions of access (i.e. admission conditions and conditions for participation in the procedure) indicated in the content of the Request for Proposal. The negotiations will be conducted according to the following principles:

a. after the deadline for submission of offers, the Ordering Party shall notify all Bidders who have submitted tenders which are not subject to rejection of the possibility of negotiations and shall invite these Bidders to negotiate, agreeing with each Bidder on individual dates of meetings,

b. arrangements regarding the date of negotiations will be carried out by e-mail,

c. only parameters that constitute criteria for the evaluation of offers are subject to negotiations,

d. the course of negotiations shall be documented in the form of a written note signed by the negotiating teams of the Ordering Party and the Bidder,

e. within the time limit specified by the Ordering Party, the Bidder submits a modified offer, taking into account the arrangements from the negotiations. The modified offer may not contain conditions less favorable than the original offer,

f. in the event that the Bidder refuses to participate in the negotiations, the negotiations do not lead to binding arrangements or the Bidder does not submit a modified offer, the Bidder's originally submitted offer shall be evaluated,

g. Ordering party by 10 calendar days from the date of submission of the last modified offer, evaluate the offers and select the Contractor whose offer is the most advantageous.

VII.6. This RFP does not oblige the Ordering Party to conclude a contract.

VII.7. For more information, please contact Aleksandra Mazgala at the following email address: tenders@ryvu.com.

ATTACHMENTS

Appendix 01 – THE ORDER DESCRIPTION

Appendix 02 – THE PROPOSAL FORM

APPENDIX 02 TO ABM-11052023M

THE PROPOSAL FORM

Data of the Bidder Name:	
Address:	
Tax ID/EU VAT:	
Person authorized to contact the Ordering Party: name and surname:	
e-mail address:	

1. We confirm that the scope of the service offered is consistent with the order description of the RFP no. ABM-11052023M.

2. We declare that we fulfill the following conditions:
We have operational readiness to start work in July 2023,
We have the possibility of the delivery of the GMP batch in Feb 2024.

3. We indicate the following proposed work details:

Ordinal number	Required information	Indication or place of indication in the offer (page, section)
1.	a budget and a timeline to cover process and analytical methods transfer/optimization and API manufacture, including stability testing	
2.	selection of the starting materials and reagents, development of analytical methods for synthesis steps requiring optimization and validation/verification of the transferred batch release methods to be used during GMP manufacture and in the formal stability studies, setting up new specification if required, complete API characterization as per the revised release specification	
3.	process safety evaluation in order to prepare for HAZOP analysis, securing the scale-up activities	
4.	process transfer and optimization of indicated steps with the release of demonstration batch followed by GMP (clinical) batches manufacture (including safety assessment, raw materials sourcing and purchase, main impurities re-synthesis or isolation and characterization, standards synthesis, quality control, and batch release and storage, and any outsourced activities as applicable) using processes and methods developed as mentioned above followed by formal stability studies, as well as an outline of the anticipated work/tasks.	

4. Deadline of the implementation of the agreement (completion date): 31st March 2024.

5. We declare the execution of the subject of request for the amount of …… PLN/EUR (the total price).

6. We consider ourselves bound by this offer for the time of …… calendar days (minimum 30 calendar days).

7. Attachments:
1 - .....

…….. .....

Place and date Signature of the authorized person*

*it is allowed use an electronic signature or to send a scan of a hand-signed proposal form.