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
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Krakow, 7th June 2023

REQUEST FOR PROPOSAL No. ABM-07062023C

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 proposals for the execution of the following defined description of the order.

I. ORDERING PARTY/SPONSOR

Ryvu Therapeutics S.A.
Sternbacha 2, 30-394 Krakow, Poland
EU VAT PL6792942955
in the further content of the RFP, hereinafter referred to as the 'Ordering Party' or 'Sponsor'.

II. DESCRIPTION OF THE ORDER

This order concerns the EDC build and hosting, Data Management and Biostatistics in the concerned clinical study.

Sponsor's study assumptions

The Sponsor's assumptions on the studies are provided below. The below may be a subject of a change based on the study progress.

Table 01.

Number of Subjects (evaluable):	98
Number of sites:	Up to 35 sites in all locations
Sponsor`s desired study start (first patient dosed):	1st September 2023
Targeted enrollment completed:	1st September 2025

General task description

Table 02.

Activities	

1	**EDC build and hosting**
	• Database design (CRF design, Edict check specification and testing)
	• Database build and testing (single instance tenant EDC hosting site reserved for Ryvu studies)
	  • EDC system configuration
	  • Creation of CRF library

	• UAT • Unique and repetitive CRF pages programming and validation • Edit checks programming and validation • SAE reporting via EDC • Users (sites, sponsor and designee) set-up and administration • EDC monthly hosting (license inclusive) • EDC updates (major and minor ones due to Protocol Amendments etc.) The EDC system proposed for the study has to be a tool with global footprint, commonly used and accepted by global CROs. EDC system has to support CRF library development. EDC must be provided by a vendor independent from the service provider (EDC provider to be sub-contracted by a service provider). EDC Developers must be certified by the EDC provider and Bidder has to be accredited to perform the build (**proof of certification/authorization must be attached to the proposal form**).
2	**Data Management** • Data Management Plan development and finalization (periodic reviews inclusive e.g. per PA and/or per sponsor request) • Development, delivery and implementation of Database QC Plan, Data Validation Plan and Data Management Report • CRF Completion Guideline development (periodic reviews inclusive) ; User training platform delivery • Data Cleaning/Query Management • Medical Coding – coding of AEs, Annual dictionaries updates (coding to be done within the EDC system) • SAE reconciliation • Data transfers including external vendors and reconciliation (if used) • Interim Analysis and Lock • Database Lock • DSMB meetings – preparation and support (if used) • DM oversight – start-up, maintenance and closing phase • CRF archive
3	**Biostatistics** • Statistical Analysis Plan (SAP) development (periodic reviews inclusive e.g. per PA and/or per sponsor request) • Statistician project oversight - start-up, maintenance and closing phase • SDTM package generation • ADaM package generation • Pinnacle 21 CDISC validation report of final deliverables • Programming of unique TFLs (interim, annual, final) • Programming of repeat TFLs (interim, annual, final) • Interim analysis and reporting • Statistical Dry Run • Quarterly transfers to sponsor of analysis datasets • Statistical section of CSR development

III. CONDITIONS FOR PARTICIPATION IN THE PROCEEDINGS

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

- Bidders with operational readiness for first patient data entries to be feasible by 1st September 2023 (available slot).
- Bidders with DC programming, data management, biostatistical programming and analysis experienced staff, which have permanent employees capable of carrying out the order:
  - Oversight Director with at least 5 years of professional experience in leading data science projects in early phases clinical studies;
  - Data Manager with at least 5 years of professional experience;
  - Biostatistician with at least 5 years of professional experience.

The period of professional experience required in this section should be counted up to the date of publication of this RFP. Bidders are obliged to submit resumes (CVs) of the above-mentioned persons.

The assessment of the conditions for participation in the proceedings will be made by the system meets – does not meet.

IV. PLACE, DATE AND PROCEDURE OF SUBMISSION OF PROPOSALS

IV.1. The proposal must be submitted by: **14th June 2023 at 23.59 CET**.

IV.2. The proposal must be sent via e-mail to the following address: tenders@ryvu.com. The message with the offer should refer to the RFP number indicated on the first page: **ABM-07062023C**

IV.3. The proposal and its attachments should be prepared in English.

IV.4. The proposal should be prepared in an accordance with the form constituting Appendix 01 to this RFP and should include the following information:

- detailed description of the work given in the CRO budget grid as a unitized budget.
  Units` composition should be provided (number of hours and resource allocation per unit); provided in an MS Excel file, prices given in EUR, cost has to be grouped with functional areas in accordance with Table 02 of this RFP. Any cost not covered is to be added as an additional cost group 'Other necessary to perform' (Time and Material costing is acceptable for units not listed). A final list of deliverables, roles and responsibilities and project timelines will be agreed in the course of signing the agreement and described in the assigned Work Order (or equivalent). As an alternative scenario a fix price budget may be provided in addition to a unitized one.
- current reporting (frequency and way of updates/meetings, data format, documentation, etc.) during the course of the service, a list of all study manuals, plans, guidelines and trackers that will be generated for this study, a description of team structure (i.e. in a form of an organizational chart), project management, process overview, and communication/escalation plan, metrics used by a CRO and provided to the study sponsor on performance and compliance verification.
- if the services offered are provided by direct employees of the CRO, freelance contractors, or other form of sub-vendor(s). Details to be provided if freelance contractors or sub-vendors are used.
- all other relevant background information and strategic approaches presenting CRO's eligibility to execute the studies.

IV.5. The proposal should 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.

IV.6. **The Bidders must provide the total price for the execution of the order (total fees including direct, indirect and pass throughs costs) consisted with the subject of the request. The proposal must include prices given in EUR.**

V. ADDITIONAL INFORMATION

VI.1. When pricing the service, it should be taken into account that the following changes may occur during the service:

i. the term of completion – The targeted enrollment completion date was set on 1st September 2025. Sponsor reserves the right to change the expected date of completion following changes in the scope of the signed contract for co-financing Project (extension of the duration of the Project, extension of appropriate stages of the Project, change of research plans),

ii. the number of individual units/components of the clinical trial may be changed or introduction of new units not covered by the basic order may occur, if the changes are necessary to achieve the intended overarching objective of the trial, and the necessity for their introduction is directly related to the results obtained during the conduct of the trial and were impossible to foresee at an earlier stage,

iii. the number of patients, number and types of countries and sites – which is directly related to the conduct of a particular type of study involving oncology patients and the fact that special circumstances/ events may arise during the course of the study that could not have been foreseen earlier; Sponsor reserves the right to change the number of patients and number and types of countries and sites.

iv. The Sponsor allows the possibility of awarding to the contractor supplementary orders, in an amount not exceeding 50% of the value of the final offer when such orders are consistent with the description of the order.

VI.2. 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 11th June 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.

VI.3. 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), 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.

VI.4. 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.

VI.5. 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.

VI.6. The Ordering Party reserves the right to enter into negotiations with Bidders who have submitted an offer and meets the conditions for participating in the proceedings. Arrangements regarding the date of negotiations will be carried out by e-mail. The modified offer may not contain conditions less favorable than the original quotation.

VI.7. This RFP does not oblige the Ordering Party to conclude a contract.

VI.8. For more information, please contact Aleksandra Mazgała or Anna Dziedzicka at the following email address: tenders@ryvu.com.

ATTACHMENTS

Appendix 01 - THE PROPOSAL FORM

APPENDIX 01 TO ABM-07062023C
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 'EDC build and hosting, Data Management and Biostatistics in the concerned clinical study' is consistent with the description of order of the RFP no. ABM-07062023C.

The EDC system proposed for the study is a tool with global footprint, commonly used and accepted by global CROs. EDC system support CRF library development. We are certified by the EDC provider and we are accredited to perform the build. **The proof of certification/authorization has been attached to the proposal form**.

2. We declare operational readiness (available slot) for first patient data entries to be feasible by 1st of September 2023.

3. We have EDC programming, data management, biostatistical programming and analysis experienced staff and we designate the following permanent employees capable of carrying out the order:

Ordinal number	Employee	Name and surname
1	Oversight Director with at least 5 years of professional experience in leading data science projects in early phases clinical studies	
2	Data Manager with at least 5 years of professional experience;	
3	Biostatistician with at least 5 years of professional experience.	

The period of professional experience required in this section is counted up to the date of publication of this RFP.
Resumes (CVs) of the above-mentioned persons are attached.

4. According to the section IV point 4 of the RFP we indicate:

Ordinal number	Required information	Indication or place (page/section) of indication in the offer
1	detailed description of the work given in the CRO budget grid as a unitized budget. Units` composition should be provided (number of hours and resource allocation per unit); provided in an MS Excel file, prices given in EUR, cost has to be grouped with functional areas in accordance with Table 02 of this RFP. Any cost not covered is to be added as an additional cost group 'Other necessary to perform' (Time and Material costing is acceptable for units not listed). A final list of deliverables, roles and responsibilities and project timelines will be agreed in the course of signing the agreement and	

	described in the assigned Work Order (or equivalent). As an alternative scenario a fix price budget may be provided in addition to a unitized one.	
2	current reporting (frequency and way of updates/meetings, data format, documentation, etc.) during the course of the service	
3	a list of all study manuals, plans, guidelines and trackers that will be generated for this study	
4	a description of team structure (organizational chart), project management, process overview	
5	communication/escalation plan, metrics used by a CRO and provided to the study sponsor on performance and compliance verification	
6	if the services offered are provided by direct employees of the CRO, freelance contractors, or other form of sub-vendor(s). Details to be provided if freelance contractors or sub-vendors are used.	
7	all other relevant background information and strategic approaches presenting CRO's eligibility to execute the studies.	

5. **We declare the execution of the subject of contract for the amount of …… EUR (total fees including direct, indirect and pass throughs costs).**
6. We declare that we consider ourselves bound by this offer for the time of …… calendar days after the date set for the submission of offers (minimum 30 calendar days after the date set for the submission of offers).
7. We acknowledge that in the event of false statements, the offer shall be rejected.

APPENDICES TO THE QUOTATION FORM

- Proof of certification/authorization by the EDC provider;
- Resumes (CVs) of the persons indicated for the performance of the order.
- Budget grid
- …..

…….. .....

Place and date Signature of the authorized person