

Krakow, 24<sup>th</sup> January 2024

### REQUEST FOR PROPOSAL No. ABM-24012024A

In connection with the 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" no. 2022/ABM/06/00002/P/02 (hereinafter: "Project") co-financed from the state budget by the Medical Research Agency under the Competition: Development of targeted or personalized medicine based on therapeutic products based on nucleic acids and small-molecule compounds no. ABM/2022/6, 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

#### II. DESCRIPTION OF THE ORDER

This order concerns the execution of the **sequencing service** in the phase II clinical study of a study drug in combination with a market drug in patients with AML.

##### II.1. Description of the order

###### (1) DNA isolation from starting material – frozen cell pellet

###### (2) Sequencing of samples in a panel of 749 genes (list of genes below); research (Ordering Party does not need diagnostic/clinical grade):

- a. Quality control,
- b. Library preparation,
- c. Sequencing (read length 2x100bp, output 10Gb per sample),
- d. Bioinformatic analysis consisting of:
  - i. Demultiplexing and adapter trimming of the sequencing data (FASTQ format), metrics (CSV format), multiQC report (HTML format),
  - ii. Mapping of the sequencing data (BAM format), metrics (CSV format). Reference genome: hg19,
  - iii. Calling of single nucleotide variants (SNVs) and small insertions and deletions (indels) (VCF format), metrics (CSV format),
  - iv. Annotation of the SNVs and indels (JSON and TSV format),
- e. Report preparation.

The minimum number of experiments to be performed during the contract period (number of samples to be tested) is 2.

The estimated number of experiments to be performed during the contract period (number of samples to be tested) is 40.

**Partial orders are possible. The cost of sample delivery is the responsibility of the Ordering Party.**

**If the sample fails the quality control, the Ordering party will to pay only for part of the service i.e. (1) DNA isolation from starting material and (2)a. Quality control.**

##### **Gene list (749 genes) for DNA-based analysis**

AAK1, ABCB1, ABCG2, ABL1, ABL2, ABRAXAS1, ACD, ACVR1, ADGRA2, ADRB1, ADRB2, AIP, AIRE, AJUBA, AKT1, AKT2, AKT3, ALK, ALOX12B, AMER1, ANKRD26, APC, APLNR, APOBEC3A, APOBEC3B, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKB, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BAX, BCHE, BCL10, BCL11A, BCL11B, BCL2, BCL3, BCL6, BCL9, BCL9L, BCOR, BCORL1, BCR, BIRC2, BIRC3, BIRC5, BLM, BMI1, BMPR1A, BRAF, BRCA1, BRCA2, BRD3, BRD4, BRD7, BRIP1, BTK, BUB1B, CALR, CAMK2G, CARD11, CASP8, CBFEB, CBL, CBLB, CBLG, CCDC6, CCND1, CCND2, CCND3, CCNE1, CD274, CD79A, CD79B, CD82, CDC73, CDH1, CDH11, CDH2, CDH5, CDK1, CDK12, CDK4, CDK5, CDK6, CDK8, CDKN1A, CDKN1B, CDKN1C, CDKN2A, CDKN2B, CDKN2C, CEBPA, CENPA, CEP57, CFTR, CHD1, CHD2, CHD4, CHEK1, CHEK2, CIC, CIITA, CKS1B, CNKSR1, COL1A1, COMT, COQ2, CREB1, CREBBP, CRKL, CRLF2, CRTCL1, CSF1R, CSF3R, CSMD1, CSNK1A1, CTCF, CTLA4, CTNNA1, CTNNA1, CTNNA1, CTNNA1, CTR9, CTRC, CUX1, CXCR4, CYLD, CYP1A2, CYP2A7, CYP2B6, CYP2C19,

CYP2C8, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DAXX, DCC, DDB2, DDR1, DDR2, DDX11, DDX3X, DDX41, DEK, DHFR, DICER1, DIS3L2, DNMT1, DNMT3A, DOT1L, DPYD, E2F3, EBP, EED, EFL1, EGFR, EGLN1, EGLN2, EIF1AX, ELAC2, ELF3, EME1, EML4, EMSY, EP300, EPAS1, EPCAM, EPHA2, EPHA3, EPHB4, EPHB6, ERBB2, ERBB3, ERBB4, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERG, ERFFI1, ESR1, ESR2, ETNK1, ETV1, ETV4, ETV5, ETV6, EWSR1, EXO1, EXT1, EXT2, EZH1, EZH2, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXO11, FBXW7, FEN1, FES, FGF10, FGF14, FGF19, FGF2, FGF23, FGF3, FGF4, FGF5, FGF6, FGF9, FGFBP1, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLI1, FLT1, FLT3, FLT4, FOXA1, FOXE1, FOXL2, FOXO1, FOXP1, FOXQ1, FRK, FRS2, FUBP1, FUS, FYN, G6PD, GALNT12, GATA1, GATA2, GATA3, GATA4, GATA6, GGT1, GLI1, GLI2, GLI3, GNA11, GNA13, GNAQ, GNAS, GNB3, GPC3, GPER1, GREM1, GRIN2A, GRM3, GSK3A, GSK3B, GSTP1, H3-3A, H3-3B, H3C2, HABP2, HCK, HDAC1, HDAC2, HDAC6, HGF, HIF1A, HLA-A, HLA-B, HLA-C, HLA-DPA1, HLA-DPB1, HLA-DQA1, HLA-DQB1, HLA-DRA, HLA-DRB1, HMGA2, HMGR, HMGN1, HNF1A, HNF1B, HOXB13, HRAS, HSD3B1, HSP90AA1, HSP90AB1, HTR2A, ID2, ID3, IDH1, IDH2, IDO1, IFNGR1, IFNGR2, IGF1R, IGF2, IGF2R, IKBKB, IKBKE, IKZF1, IKZF3, IL1B, IL1RN, ING4, INPP4A, INPP4B, INPPL1, INSR, IRF1, IRF2, IRS1, IRS2, ITPA, JAK1, JAK2, JAK3, JUN, KAT6A, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KIAA1549, KIF1B, KIT, KLF2, KLF4, KLHL6, KLLN, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, KSR1, LATS1, LATS2, LCK, LIG4, LIMK2, LRP1B, LRRK2, LTK, LYN, LZTR1, MAD2L2, MAF, MAGI1, MAGI2, MAML1, MAP2K1, MAP2K2, MAP2K3, MAP2K4, MAP2K5, MAP2K6, MAP2K7, MAP3K1, MAP3K13, MAP3K14, MAP3K3, MAP3K4, MAP3K6, MAP3K8, MAPK1, MAPK11, MAPK12, MAPK14, MAPK3, MAX, MBD1, MBD4, MC1R, MCL1, MDC1, MDH2, MDM2, MDM4, MECOM, MED12, MEF2B, MEN1, MERTK, MET, MGA, MGMT, MITF, MLH1, MLH3, MLLT10, MLLT3, MN1, MPL, MRE11, MS4A1, MSH2, MSH3, MSH4, MSH5, MSH6, MSR1, MST1R, MTAP, MTHFR, MTOR, MT-RNR1, MTRR, MUC1, MUTYH, MXI1, MYB, MYC, MYCL, MYCN, MYD88, MYH11, MYH9, NAT2, NBN, NCOA1, NCOA3, NCOR1, NF1, NF2, NFE2L2, NFKB1, NFKB2, NFKBIA, NFKBIE, NIN, NKX2-1, NLRC5, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NQO1, NR1H3, NRAS, NRG1, NSD1, NSD2, NSD3, NT5C2, NTHL1, NTRK1, NTRK2, NTRK3, NUMA1, NUP98, NUTM1, OBSCN, OPRM1, PAK1, PAK3, PAK4, PALB2, PALD, PARP1, PARP2, PARP4, PAX3, PAX5, PAX7, PBK, PBRM1, PBX1, PDCD1, PDCD1LG2, PDGFA, PDGFB, PDGFC, PDGFD, PDGFRA, PDGFRB, PDK1, PDPK1, PGR, PHF6, PHOX2B, PIAS4, PIGA, PIK3C2A, PIK3C2B, PIK3C2G, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIK3R3, PIM1, PLCG1, PLCG2, PLK1, PML, PMS1, PMS2, POLD1, POLE, POLH, POLQ, POT1, PPM1D, PPP2R1A, PPP2R2A, PREX2, PRKAR1A, PRKCA, PRKCI, PRKDC, PRKN, PRMT5, PRSS1, PSMB1, PSMB10, PSMB2, PSMB5, PSMB8, PSMB9, PSMC3IP, PSME1, PSME2, PSME3, PSPH, PTCH1, PTCH2, PTEN, PTGS2, PTK2, PTK7, PTPN11, PTPN12, PTPRC, PTPRD, PTPRS, PTPRT, RABL3, RAC1, RAC2, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD54B, RAD54L, RAF1, RALGDS, RARA, RASA1, RASAL1, RB1, RBM10, RECQL4, REST, RET, RFC2, RFWD3, RFX5, RFXANK, RFXAP, RHBDF2, RHEB, RHOA, RICTOR, RINT1, RIPK1, RIT1, RNASEH2B, RNASEL, RNF43, ROS1, RPS20, RPS6KB1, RPS6KB2, RPTOR, RSF1, RUNX1, RYR1, SAMHD1, SAV1, SBDS, SCG5, SDHA, SDHAF2, SDHB, SDHC, SDHD, SEC23B, SERPINB9, SETBP1, SETD2, SETDB1, SF3B1, SGK1, SH2B1, SH2B3, SHH, SIK2, SIN3A, SKP2, SLC19A1, SLC26A3, SLC1B1, SLIT2, SLX4, SMAD3, SMAD4, SMARCA4, SMARCB1, SMARCE1, SMC1A, SMC3, SMO, SOCS1, SOS1, SOX11, SOX2, SOX9, SPEN, SPINK1, SPOP, SPRED1, SRC, SRD5A2, SRGAP1, SRSF2, SSTR2, SSX1, STAG1, STAG2, STAT1, STAT3, STAT5A, STAT5B, STK11, SUFU, SUZ12, SYK, TAF1, TAF15, TAP1, TAP2, TAPBP, TBK1, TBL1XR1, TBX3, TCF3, TCF4, TCL1A, TEK, TERC, TERF2IP, TERT, TET1, TET2, TFE3, TGFB1, TGFB2, TMEM127, TMPRSS2, TNFAIP3, TNFRSF13B, TNFRSF14, TNFRSF8, TNFSF11, TNK2, TOP1, TOP2A, TP53, TP53BP1, TP63, TPMT, TPX2, TRAF2, TRAF3, TRAF5, TRAF6, TRAF7, TRIM28, TRRAP, TSC1, TSC2, TSHR, TTK, TYMS, U2AF1, UBE2T, UBR5, UGT1A1, UGT2B15, UGT2B7, UIMC1, UNG, USP9X, VEGFA, VEGFB, VHL, VKORC1, WRN, WT1, XIAP, XPA, XPC, XPO1, XRCC1, XRCC2, XRCC3, XRCC5, XRCC6, YAP1, YES1, ZFXH3, ZNF217, ZNF703, ZNRF3, ZRSR2

#### DNA-based detection of selected structural variations in these genes

ALK, BCL2, BCR, BRAF, BRD4, EGFR, ERG, ETV4, ETV6, EWSR1, FGFR1, FGFR2, FGFR3, FUS, MET, MYB, MYC, NOTCH2, NTRK1, NTRK2, NTRK3, PAX3, PDGFB, RAF1, RARA, RET, ROS1, SSX1, SUZ12, TAF15, TCF3, TFE3, TMPRSS2

#### II.2. Rules of order execution

- **CONTRACT TERM:** Deadline for performance of the contract: 31<sup>st</sup> May 2024.  
Orders will be executed from the date of signing of the contract until the date of completion of the relevant stages of the Projects, i.e. as at the date of publication of the RFQ up to 31<sup>st</sup> May 2024. In the event of prolonging the completion date of the Project stage, the agreement may be extended following changes in the Project co-financing agreement.
- **OFFER VALIDITY PERIOD:** at least until 31<sup>st</sup> March 2024.
- **ORDER COMPLETION DATE (TURNAROUND TIME):** up to 30 calendar days after the order submission (from receiving the sample for testing to returning the report).  
The execution of orders under the contract must take place within max. period given below. The turnaround time is an admission condition, proposal indicating a longer deadline for performance will be rejected.

#### III. PLACE, DATE PLACE, DATE AND PROCEDURE OF SUBMISSION OF QUOTES

- III.1. The proposal must be submitted by: **31<sup>st</sup> January 2024**.
- III.2. The proposal must be sent via e-mail to the following address: [tenders@ryvu.com](mailto:tenders@ryvu.com). The message with the proposal should refer to the RFP number indicated on the first page: **ABM-24012024A**.
- III.3. The proposal and its attachments must be prepared in English or Polish.

- III.4.** The proposal should be prepared in an accordance with the form constituting Appendix 01 to this RFP.  
**The Bidders must provide the price for the service for 1 sample and the price the execution of the scope of the contract (total price for service for 40 samples).**
- IV. ADDITIONAL INFORMATION**
- IV.1.** The Ordering Party allows for the possibility of awarding to the Contractor supplementary orders, in an amount not exceeding 50% of the value of the contract specified in the agreement concluded with the contractor, while such orders are consistent with the subject of the basic contract.
- IV.2.** The terms and conditions of the agreement may change during the course of the agreement (Ordering Party reserves the right to amend the agreement):
- in terms of the timelines and term of the agreement – following changes in the scope of the study and Project (extension of the duration of the Project, extension of appropriate stages of the Project, change of research plans);
  - in the event of force majeure as an event which is externally impossible to foresee and which could not have been prevented and whose consequences and effects could not have been prevented.
- IV.3.** The Bidders may ask the Ordering Party to clarify the content of the RFP. If the request for clarification of the content of the RFP was received later than by the end of 29<sup>th</sup> January 2024, the Ordering Party may provide explanations or leave the application unexamined. Questions must be sent to the following e-mail address: [tenders@ryvu.com](mailto:tenders@ryvu.com).
- IV.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.
- IV.5.** The Ordering Party reserves the right to ask the Bidders at any stage of the evaluation of proposals 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 proposal sent by the Bidder.
- IV.6.** This RFP serves to estimate the market price of the contract (of 40 samples to be entirely tested). The Ordering Party reserves the right to enter into negotiations with Bidders who have submitted a proposal and meets the conditions for participating in the proceedings. Arrangements regarding the date of negotiations will be carried out by e-mail. The modified proposal may not contain conditions less favorable than the original proposal.
- IV.7.** This RFP does not oblige the Ordering Party to conclude a contract.
- IV.8.** For more information, please contact Anna Dziejzicka at the following email address: [tenders@ryvu.com](mailto:tenders@ryvu.com).

#### **ATTACHMENTS**

Appendix 01 – Proposal Form

**APPENDIX 01 TO RFP no. ABM-24012024A**

**THE PROPOSAL FORM**

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

	<b>Answer / confirmation of compliance</b> *- delete inappropriate	<b>Comments, if any</b>
<p>Compliance of the offered service with the description of the subject of the order given in RFP:</p> <p>(1) DNA isolation from starting material – frozen cell pellet                      (2) Sequencing of samples in a panel of 749 genes (list of genes below); research (we do not need and do not want diagnostic/clinical grade)</p> <ul style="list-style-type: none"> <li>a. Quality control</li> <li>b. Library preparation</li> <li>c. Sequencing (NovaSeq6000; read length 2x100bp, output 10Gb per sample)</li> <li>d. Bioinformatic analysis consisting of:                             <ul style="list-style-type: none"> <li>i. Demultiplexing and adapter trimming of the sequencing data (FASTQ format), metrics (CSV format), multiQC report (HTML format)</li> <li>ii. Mapping of the sequencing data (BAM format), metrics (CSV format). Reference genome: hg19</li> <li>iii. Calling of single nucleotide variants (SNVs) and small insertions and deletions (indels) (VCF format), metrics (CSV format)</li> <li>iv. Annotation of the SNVs and indels (JSON and TSV format)</li> </ul> </li> <li>e. Report preparation</li> </ul>	<b>YES/NO*</b>	
<p><b>CONTRACT TERM:</b> Deadline for performance of the contract: 31<sup>st</sup> May 2024. Orders under the contract will be executed from the date of signing of the contract until the date of completion of the relevant stages of the Project, i.e. as at the date of publication of the RFQ up to 31<sup>st</sup> May 2024.</p> <p>In the event of prolonging the completion date of the Project stage, the agreement may be extended following changes in the Project co-financing agreement.</p>	<b>YES/NO*</b>	
<p><b>OFFER VALIDITY PERIOD:</b> at least until 31<sup>st</sup> March 2024.</p>	<b>YES/NO*</b>	
<p>Turnaround time (from receiving the sample for testing to returning the report) – max. 30 calendar days</p>	<b>YES/NO*</b>	
<p align="right"><b>NET PRICE</b></p> <p>of performing <u>one experiment</u> including all costs (points 1. and 2. from Description of the order)</p>		

<b>NET PRICE</b> of performing <u>one experiment</u> for sample which fails QC <b>(sum of 1. and 2 a. form Description of the order)</b>	
<b>TOTAL NET PRICE</b> of performing 40 experiments including all costs (points 1. and 2. from Description of the order) = max. value of the contract that serves to estimate the market price	

We confirm that the scope of the service offered is consistent with the subject of the request of the RFP no. ABM-24012024A.

.....  
Place and date

.....  
Signature of the authorized person