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Dosing of the first patient in the RIVER-81 Phase II study of RVU120 in combination with venetoclax

The Management Board of Ryvu Therapeutics S.A., with its registered office in Krakow, Poland (the "Issuer", “Ryvu”), announces that the first patient has been dosed with the study drugs in a Phase II clinical trial investigating RVU120 in combination with venetoclax for the treatment of patients with relapsed/refractory acute myeloid leukemia (r/r AML) – the RIVER-81 study (NCT06191263) (the "Study").

The primary goal of the RIVER-81 study will be to evaluate safety and efficacy of RVU120 in combination with venetoclax in a population of r/r AML patients who have failed prior venetoclax treatment. The RIVER-81 study is initially launching at clinical sites in Poland and Italy. Ultimately, the study will expand to other EU and non-EU countries, covering up to 50 clinical sites globally. The planned overall enrollment for the Study is up to approximately 98 patients. The Study is part of the RVU120 development plan outlined in the current report 45/2023 dated October 23, 2023, and aligns with Ryvu cash runway to Q1 2026. Execution of the Study is supported with a PLN 62.3 mln grant from the Polish Medical Research Agency (ABM).

RIVER-81 is a multicenter, open-label clinical trial that aims to assess the safety, tolerability, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) of RVU120 when administered in combination with venetoclax to adult patients with AML who are relapsed or refractory to prior therapy with venetoclax and a hypomethylating agent.

The study is divided into two parts. Part 1 aims to identify safe and tolerated doses of RVU120 and venetoclax when used in combination, through dose escalation of both study drugs. In Part 2, the selected doses will be evaluated for both safety and efficacy in a larger group of patients.

In H1 2024, Ryvu plans to launch four Phase II RVU120 clinical studies and enroll over 100 patients across them by the end of the year. Ryvu aims to prioritize further development options in Q1 2025, based on the study outcomes. Clinical trials conducted in various hematological indications and treatment regimens (monotherapy and combination therapy) will contribute to the global RVU120 safety database, which would support potential future regulatory approvals.

The study has received approval from the Competent Authorities in Poland and Italy following a clinical trial application in accordance with the European Union Clinical Trial Regulation (EU-CTR) 536/2014, as well as positive opinions from the respective Ethics Committees, enabling patient enrollment in both

countries. At the same time, start-up activities in other EU and non-EU countries are currently in progress.

RIVER-81 marks the commencement of the first of four planned RVU120 Phase II clinical studies, scheduled to launch in H1 2024. Following RIVER-81, Ryvu intends to initiate the RIVER-52 study (evaluating RVU120 as a monotherapy in patients with genetically defined subtypes of AML and in patients with HR-MDS). Upcoming plans also include the initiation of the REMARK study (conducted as an investigator-initiated trial, exploring RVU120 as a monotherapy for the treatment of patients with low-risk myelodysplastic syndromes; LR-MDS) and the POTAMI-61 study (evaluating both monotherapy and combination therapy for the treatment of patients with myelofibrosis; MF).

Disclaimer: This English language translation has been prepared solely for the convenience of English-speaking readers. Despite all the efforts devoted to this translation, certain discrepancies, omissions or approximations may exist. In case of any differences between the Polish and the English versions, the Polish version shall prevail. Ryvu Therapeutics S.A., its representatives and employees decline all responsibility in this regard.

Legal basis: Article 17.1 of MAR
Representatives of the Issuer:

- Hendrik Nogai – Member of the Management Board
- Kamil Sitarz – Member of the Management Board