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Preclinical and clinical data on RVU120 presented at the 2023 American Society of Hematology (ASH) Annual Meeting

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") announces that clinical and preclinical data on RVU120, a selective CDK8/19 inhibitor, were presented at the 65th American Society of Hematology (ASH) Annual Meeting & Exposition, which is being held on December 9 –12, 2023, in San Diego, California.

The results from the CLI120-001 (RIVER-51) study of RVU120 in patients with r/r-AML and HR-MDS (RIVER-51) continue to improve over time. RVU120 monotherapy shows signs of clinical activity in 50% of evaluable patients, including a complete response, multiple clinically significant blast reductions, hematologic improvements, and reduction of bone marrow fibrosis. In particular, early signs of efficacy were observed in patients with NPM1 mutation, DNMT3a mutation, and in those with HR-MDS. The Company evaluates positively the 50-70% target engagement achieved at 250 mg dose, which, based on the Companie's preclinical data, is anticipated to result in robust antileukemic efficacy in selected settings.

Given the observed hematologic improvements, particularly the early signs of erythroid responses in seven patients, the Company believes that RVU120 holds the potential to be a novel erythropoiesis - stimulating agent for patients with LR-MDS and myelofibrosis. Furthermore, the preclinical study supports RVU120's development as frontline therapy in AML, as evidenced by its cytotoxic and differentiating effects on well-characterized leukemic stem cell-like populations. Based on these encouraging results, the Company plans to initiate Phase II studies in patients with AML, HR-MDS, LR-MDS, and myelofibrosis.

The Company informs, that it will host a webinar on Monday, December 11, 2023, at 8:00 AM CET to discuss the data presented at the ASH Annual Meeting. The webinar can be accessed by following this link: ryvu.clickmeeting.com/ryvu-ash-2023-results/register

Details on the poster presentations are as follows:

Abstract Title: "Safety and Efficacy Results from CLI120-001 a Phase 1 Study in RR-AML and HRMDS: Update from Higher Dose Levels"
Session Name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
Session date and time: Sunday, December 10, 2023, 6:00 PM - 8:00 PM PST
Poster Number: 2913

Updated Phase I data on RVU120 at higher dose levels in patients with relapsed/refractory (r/r) acute myeloid leukemia (AML) or high-risk myelodysplastic syndromes (HR-MDS) demonstrate clinical activity with a favorable safety profile. As of the data cut-off on November 10, 2023, 38 patients (34 with AML and four with HR-MDS) have been treated in the trial at doses up to 250 mg. Of the 28 evaluable patients, 14 showed clinically relevant benefits, including eight blast reductions to <5% in the bone marrow. Among these, there was one complete response, three marrow complete responses, and four clinically relevant BM blast reductions. Five additional patients achieved transfusion independence, and one achieved an absolute difference of >4 RBC units compared to the baseline, following Cheson 2006 criteria. One patient received a transplant after nearly four months of treatment. The first evaluable patient at 250 mg showed significant blast reduction (64%) at the end of cycle 2. Doses up to 250 mg have shown a favorable safety profile, with 50-70% target engagement achieved at a dose of 250 mg.

Abstract Title: "Preclinical and Clinical Evidence for Erythroid-Stimulating Activity of RVU120 CDK8/19 Inhibitor in AML and MDS"
Session Name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster II
Session date and time: Sunday, December 10, 2023, 6:00 PM - 8:00 PM PST
Poster Number: 2800

RVU120-induced erythroid differentiation was studied in primary malignant stem cells from MDS patients and in a stem cell model. To date, early signs of erythroid response, at the molecular level measured by increased erythroid surface markers CD71 and/or CD235a expression, were observed in seven evaluable patients in the ongoing Phase Ib. Four out of seven patients had a clinically relevant hematological response. Transcriptomic analyses of bone marrow cells in patients treated with RVU120 showed specific induction of gene expression programs leading to the maturation of erythroid cells in two out of four patients, who also exhibited clinical hematologic improvement.

These clinical and preclinical data support further development of RV120 as a novel erythroid stimulating agent. Treatment with RVU120 could be a promising treatment option for patients with lower-risk MDS who are transfusion-dependent and failing previous lines of treatment.

Abstract Title: "Novel Clinically Useful Inhibitor of Mediator Complex, RVU120, Relieves Differentiation Block in MDS/AML"
Session Name: 636. Myelodysplastic Syndromes—Basic and Translational: Poster II
Session date and time: Sunday, December 10, 2023, 6:00 PM - 8:00 PM PST
Poster Number: 3225

Data demonstrate RVU120's potential for erythroid-stimulating activity in CD34+ primary samples of myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). Treatment with RVU120 in MDS and AML models, including patient-derived sample cultures, resulted in increased erythroid differentiation, as evidenced by increased expression of erythroid surface markers. Additionally, inhibition of CKD8/19 led to transcriptional silencing in MDS-L cells. Notably, RVU120 also inhibits

phosphorylation of STAT5 and STAT1, which may represent the underlying mechanism of action. These results provide supporting rationale for further development of RVU120 for transfusion-dependent MDS/AML patients.

Additionally, the Company informs that the two posters listed below will be made public on December 11, 2023, at 6:00 PM CET:

Abstract Title: "Targeting CDK8/CDK19 to Disrupt Leukemic Stem Cell-like Population in Acute Myeloid Leukemia: Exploring RVU120 As a Promising Frontline Therapy"
Session Name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster III
Session date and time: Monday, December 11, 2023, 2023, 6:00 PM - 8:00 PM PST
Poster Number: 4175

Abstract Title: "Mediator Kinase/CDK8 Inhibition as a Strategy to Improve FLT3 Inhibitor Activity in Acute Myeloid Leukemia"
Session Name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster III
Session date and time: Monday, December 11, 2023, 6:00 PM-8:00 PM PST
Poster Number: 4173

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:

- Paweł Przewięźlikowski – President of the Management Board
- Hendrik Nogai – Member of the Management Board