CURRENT REPORT 08/2022

June 10th, 2022

Publication of the updated phase 1b clinical and preclinical data for RVU120 and phase 1/2 SEL24 (MEN1703)

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") hereby announced, in connection with the current report no 06/2022 published on May 12, 2022, updated data from the ongoing Phase 1b dose-escalation study of RVU120 in patients with acute myeloid leukemia (AML) or high-risk myelodysplastic syndromes (HR-MDS) at the Annual European Hematology Association (EHA) 2022. In addition, Ryvu's partner, Menarini Group, presented a clinical update on the Phase 1/2 study of SEL24 (MEN1703) in patients with IDH1/2-mutated AML.

In the opinion of the Ryvu Management Board the clinical data achieved presented at EHA 2022 confirm the single drug efficacy of RVU120 and durable benefits for patients with very few treatment options as well as the responder hypothesis in a molecularly defined subset of patients with DNMT3A and NPM1 mutations. Based on the encouraging data, the Company is planning to continue dose escalation and further advance the clinical development of RVU120 in both biomarker-selected AML patients and the unselected broader AML population.

The data presented by Menarini on SEL24 (MEN1703) and the additional communication received from Menarini in project meetings has confirmed the single-agent activity of SEL24 and its potential for further development in different AML populations.

Ryvu will discuss data on RVU120 from EHA2022 at a dedicated webinar: "A First-in-Class CDK8/19i in Phase I Studies for Hematological Malignancies and Solid Tumors". The webinar will feature a presentation from Key Opinion Leader (KOL) Dr. Michael Savona, MD (Vanderbilt University School of Medicine) who will discuss the current treatment landscape and unmet medical needs in treating patients with acute myeloid leukemia (AML) and high-risk myelodysplastic syndromes (MDS). A live Q&A session will follow.

The event will start on Monday, June 13th at 20:30 CET. Register here: https://lifesci.events/RVU

Poster presentations featured at the Congress:

RVU120: orally available CDK8/19 inhibitor

Abstract Title*: "CLI120-001 Phase1b Dose Escalation Study of RVU120 in Patients with AML or High-Risk MDS Safety and Efficacy Data Update",* Abstract Number: #P501

Preliminary results were presented from the first seven cohorts, demonstrating a favorable safety and a predictable pharmacokinetic (PK) profile for RVU120.

As of the data cutoff date of May 26, 2022, 16 patients with AML or HR-MDS have been dosed (5 ongoing) with a median of three prior lines of therapy.

Clinically meaningful benefit of RVU120 monotherapy has been observed at doses that resulted in less than complete target engagement, with one complete remission (CR) and stable diseases with blast reductions in several ongoing patients who failed multiple prior lines of therapy and presented with a very poor prognosis:

- Complete remission in an AML patient with FLT3/DNMT3A/NPM1 mutations
- Stable disease with a duration of therapy of more than 18 months in a high-risk MDS patient with DNMT3A mutations; significant reductions in red blood cells (RBC) transfusions at various timepoints
- Three additional patients ongoing with stable disease and blast count reductions

Dose escalation is ongoing, with active enrollment in the 100 mg dose cohort (NCT04021368).

Abstract Title: "*Preclinical and Clinical Signs of RVU120 Efficacy, a Specific CDK8/19 Inhibitor in DNMT3A Mutation Positive AML and HR-MDS",* Abstract Number: #P450

Preclinical data demonstrate that treatment with RVU120 demonstrated a pronounced anti-cancer effect in AML patient-derived cells with DNMT3A and NPM1 mutations.

Preliminary evidence of clinical response to RVU120 has been shown in a r/r AML patient with DNMT3A and NPM1 mutations, who achieved a complete remission. Anti-cancer efficacy of RVU120 was associated with transcriptomic reprogramming involving lineage commitment and inhibition of homeobox genes. Repression of homeobox genes in the responder patient confirms the on-target activity of RVU120.

Further molecular studies in a larger number of patients under RVU120 treatment are ongoing and are expected to provide additional evidence for predictive markers of response to RVU120 in AML.

SEL24/MEN1703: orally available dual PIM/FLT3 inhibitor

Abstract Title: "*Phase 1/2 Study of SEL24/MEN1703, a First-In-Class Dual PIM/FLT3 Kinase Inhibitor, in Patients with IDH1/2-Mutated Acute Myeloid Leukemia: The DIAMOND-01 Trial"***,** Abstract Number: #P520

Ryvu's partner Menarini Group reported the updated safety and efficacy results from an additional expansion cohort of the DIAMOND-01 trial, which enrolled patients with relapsed or refractory (R/R) IDHm AML, treated with the dual PIM/FLT3 inhibitor, SEL24 (MEN1703).

As of a data cutoff of April 21, 2022, 25 patients were enrolled in the IDHm AML expansion cohort. SEL24 (MEN1703) was well tolerated, with no drug discontinuations or deaths due to treatment-related adverse events (TRAEs). Promising efficacy was observed, with overall response rates (ORR)

and complete remission (CR) / CR with incomplete hematologic recovery (CRi) / CR with partial hematologic recovery (CRh) of 13% for the IDHm cohort, which is similar to monotherapy activity of other drugs in R/R AML.

Based on these data, SEL24/MEN1703 may be a feasible therapy in this difficult-to-treat population of patients with R/R AML who harbor IDH mutations. Clinical trials are planned in order to better explore the potential of SEL24/MEN1703 in different AML populations.

All posters are now available for download from Ryvu corporate website: https://ryvu.com/investors-media/publications/

Legal basis: Article 17.1 of MAR

Representatives of the Issuer:

- Paweł Przewięźlikowski – President of the Management Board
- Krzysztof Brzózka – Vice President of the Management Board