CURRENT REPORT 25/2022

November 3rd, 2022

Clinical and Translational Data of RVU120 and SEL24 (MEN1703) to be presented at the 2022 American Society of Hematology (ASH) Annual Meeting

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") informs that it will present the latest data demonstrating the clinical and preclinical activity of RVU120, a selective CDK8/19 kinase inhibitor, and SEL24 (MEN1703), a selective PIM/FLT3 kinase inhibitor, at the upcoming American Society of Hematology (ASH) Annual Meeting 2022, to be held December 10-13, 2022 in New Orleans, USA.

As part of the poster presentations, the Company will present updated data from the Phase Ib RVU120 clinical trial in patients with relapsed/refractory acute myeloid leukemia (R/R AML) or high-risk myelodysplastic syndrome (HR-MDS). The data presentation will include efficacy and safety data for RVU120 therapy at doses between 75 mg and 110 mg. As of July 25, 2022, 17 patients were being treated with RVU120.

One patient achieved a complete response and 10 patients achieved disease stabilization. RVU120 demonstrated a manageable safety profile.

Additionally, the on-target activity of RVU120 was evaluated in AML and HR-MDS patient samples by measuring changes in the direct biomarker - pSTAT5 - levels. During dose escalation, inhibition of pSTAT5 reached >50%, a threshold that based on preclinical predictions is sufficient for robust efficacy in certain groups of super-responder patients.

Ryvu licensee, Menarini Group, and our academic collaborators will present data on SEL24 (MEN1703), a first-in-class, oral, dual type I PIM/FMS-like tyrosine kinase 3 (FLT3) inhibitor. Combination therapy of SEL24 (MEN1703) with gilteritinib (Xospata), a highly potent and selective oral FLT3 inhibitor, induces strong tumor regression and complete responses in-vivo, demonstrating the potential of concomitant FLT3 and PIM inhibition kinases in AML.

SEL24 (MEN1703)-induced PIM inhibition and mechanism of action will also be demonstrated in-vitro in multiple myeloma (MM), classical Hodgkin lymphoma-tumor-associated macrophages (cHL-TAMs), and diffuse large B-cell lymphoma (DLBCL) models. In multiple myeloma preclinical models, SEL24 (MEN1703) induces cytotoxicity of MM cell lines, disrupts MM endothelial cell vessel formation, and decreases the activity of several pathways essential for myeloma cell survival. In the Management Board's opinion, this study

demonstrates the promising therapeutic potential of SEL24 (MEN1703) in MM and reveals the underlying mechanism of PIM inhibition.

Abstracts accepted for poster presentation at the 64th ASH Annual Meeting & Exposition:

- **CDK8/19 Kinase Inhibitor RVU120 in Patients with AML or Higher-Risk MDS: Safety and Efficacy Results from New Dose Escalation Cohorts** (Publication Number: 2771), Camille Abboud, MD (Washington University in Saint Louis/ Washington University School of Medicine) *et. al.*
    - Session name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET

- **Multiomics Analysis Confirms Effective Target Engagement for RVU120 – a First-in-class CDK8/19 Kinase Inhibitor in AML and MR-MDS Patients and Reveals the Mechanism of Action** (Publication Number: 2642), dr Tomasz Rzymski (Ryvu Therapeutics) *et. al.*
    - Session name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET

- **PIM Inhibition By SEL24/MEN1703 Combines Synergistically with Gilteritinib in FLT3-ITD Preclinical Models of Acute Myeloid Leukemia** (Publication Number: 1333), Daniela Bellarosa (Grupa Menarini) *et. al.*
    - Session name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET

- **Super-enhancer-driven PIM Kinase Upregulation in Multiple Myeloma Maintains the Plasma Cell-specific Oncogenic and Microenvironmental Circuits and Can Be Efficiently Targeted by the Pan-PIM Inhibitor MEN1703** (Publication Number: 1822), Filip Garbicz (Institute of Hematology and Transfusion Medicine, Warsaw, Poland) *et. al.*
    - Session name: 651. Multiple Myeloma and Plasma Cell Dyscrasias: Basic and Translational: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET

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- **PIM Kinases Regulate Super-Enhancer-Dependent Gene Expression In Diffuse Large B-Cell Lymphoma** (Publication Number: 1310), Sonia Debek (nstitute of Hematology and Transfusion Medicine, Warsaw, Poland) *et. al.*
    - Session name: 603. Lymphoid Oncogenesis: Basic: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET

- **MEN1703-mediated PIM kinases inhibition impairs protumoral and immunosuppressive phenotype and functions of macrophages in classical Hodgkin Lymphoma** (Publication Number: 2867), Maciej Szydlowski (Instytut Hematologii i Transfuzjologii w Warszawie), *et. al.*
    - Session name: 622. Lymphomas: Translational–Non-Genetic: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET

The ASH Conference ranks among the top scientific events, bringing together the scientific community as well as potential customers and business partners - biotech and pharmaceutical companies from around the world, as well as industry investors.

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