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Ryvu Therapeutics presents Clinical and Translational Data of RVU120 and SEL24 (MEN1703) 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") announced on December 11, 2022 new data demonstrating clinical and preclinical activity of RVU120 and SEL24 (MEN1703) at the American Society of Hematology (ASH) Annual Meeting 2022 which is being held on December 10-13, 2022 in New Orleans, USA.

Presented data included updated clinical results for RVU120, a selective CDK8/19 inhibitor being developed for the treatment of hematological malignancies and solid tumors. RVU120 demonstrated single-agent activity with a Complete Response, 4 Blast Reductions, and 4 Erythroid and/or Platelet responses in patients with Relapsed/Refractory Acute Myeloid Leukemia (AML) or High-Risk Myelodysplastic Syndrome (HR-MDS).

Moreover, Ryvu's global partner Menarini Group, which is currently developing SEL24 (MEN1703) on the basis of an exclusive licence agreement concluded with the Company, presented new data on SEL24 (MEN1703), a first-in-class, oral, dual type I PIM/FLT3 inhibitor. Preclinical antitumor activity of SEL24 (MEN1703) was demonstrated in multiple myeloma (MM), Hodgkin's lymphoma (HL), and diffuse large B-cell lymphoma (DLBCL) as well as in AML in combination with gilteritinib.

RVU120

With a data cut-off of November 11, 2022, data highlights for Phase 1b Interim Efficacy and Safety Results on RVU120 include:

- 16 relapsed/refractory (R/R) acute myeloid leukemia (AML) and 3 high-risk myelodysplastic syndrome (HR-MDS) patients with a median of 3 prior lines of therapy have been treated with RVU120 at doses between 75 and 110 mg;
- Clinical activity was demonstrated in 9 out of 16 evaluable patients, all of them with molecular markers preclinically predicted to respond to CDK8 inhibition;
- One AML patient achieved a complete response;
- 4 patients demonstrated blast reductions;
- 4 patients showed erythroid and/or platelet responses;
- RVU120 was generally well tolerated at all doses;

- Most frequent adverse events were nausea/vomiting, worsening of thrombocytopenia grade 3 to 4, and febrile neutropenia;

After the data-cut-off for the poster, dose escalation has continued, and the 110 mg dose cohort has now been fully enrolled. In total, 22 patients have been enrolled in the study through December 7, 2022.

Additionally, the on-target activity of RVU120 was evaluated in AML and HR-MDS patient samples by measuring changes in pSTAT5 levels. As of the cut-off date, the inhibition of pSTAT5 reached >50% in some patients, a threshold that may be sufficient for robust efficacy in certain groups of super-responder patients. Combined results from the ongoing dose-escalation trials (in 10-135 mg dose range) in AML/HR-MDS and solid tumor patients indicate that pSTAT5 inhibition is dose-dependent.

SEL24 (MEN1703)

Ryvu licensee, Menarini Group, and academic collaborators presented new data on SEL24 (MEN1703), a first-in-class, oral, dual type I PIM/FLT3 inhibitor. Combination therapy of SEL24 (MEN1703) with gilteritinib, 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 the mechanism of action was also 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. This study demonstrates the promising therapeutic potential of SEL24 (MEN1703) in MM and reveals the underlying mechanism of PIM inhibition. PIM-dependent oncogenic signaling pathways were also inhibited following SEL24 (MEN1703) treatment of MM cells.

Details of the poster presentations are as follows:

- **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
- **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