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Posters to be presented at the AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Conference

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") announces that it will present the latest data from its synthetic lethality platform at the upcoming AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics International Conference, to be held October 11-15, 2023, in Boston, Massachusetts.

Poster presentations will concern:

- preclinical data from Ryvu's PRMT5 program in MTAP-Deficient cancers and its synthetic lethality platform in colorectal cancer models
- preclinical efficacy data of MEN1703 (SEL24) in Diffuse Large B-Cell Lymphoma (DLBCL), presented by Ryvu's partner Menarini Group

Details of the poster presentations are as follows:

Abstract Title: "*Discovery of Novel MTA-cooperative PRMT5 Inhibitors as Targeted Therapeutics for MTAP-deleted Cancers*"

- Poster Number: *C135*
- Session date: *Saturday, October 14, 2023, 12:30 - 4:00 p.m. EST*

Ryvu developed potentially best-in-class MTA-cooperative PRMT5 inhibitors showing favorable properties and effective PRMT5 inhibition dependent on MTA. Structure-based lead optimization enabled rapid expansion and delivery of a compound library with novel intellectual property (IP), high target engagement in cells, and selective potency in MTAP-deleted cell lines. These compounds have shown over 300-fold selectivity for MTAP-deficient cells compared to WT cells. The inhibitors can be orally administered and have demonstrated efficacy in animal tumor models, supporting their progression towards clinical trials.

Abstract Title: "*A Comprehensive Platform for Unraveling the Molecular Mechanisms and Vulnerabilities of Colorectal Cancer: A Step Forward in Target Discovery*"

- Poster Number: *A162*
- Session date: Thursday, October 12, 2023, 12:30 - 4:00 p.m. EST

Colorectal cancer (CRC) is one of the most prevalent and deadly cancers globally. However, molecular mechanisms and vulnerabilities of CRC remain still poorly understood. Ryvu has developed a comprehensive platform using CRC model cells derived from human

intestinal stem cells, patient-derived xenografts, and clinical samples. Through transcriptomic and genomic analyses using RNA-seq and whole-exome sequencing and the use of CRISPR/Cas9 system, samples were characterized, and distinct molecular signatures and pathways associated with different mutational variants were identified. Moreover, by utilizing normal intestinal stem cells from a healthy donor, it was possible to identify among the essential genes those that are critical only for the transformed cells.

This innovative platform provides a tool for target discovery and validation in CRC, with potential applicability to other cancer types and personalized medicine approaches.

Abstract Title: *"MEN1703/SEL24, A Potent PIM Inhibitor, Demonstrates Promising Anti-Tumor Activity in Activated B Cell Like DLBCL, Mantle Cell Lymphoma and Marginal Zone Lymphoma Cells"*

- Poster Number: *C144*
- Session date: *Saturday, October 14, 12:30 - 4:00 p.m. EST*

PIM kinases have been identified as potential therapeutic targets due to their overexpression and mutations in certain lymphomas. Pharmacological inhibition with MEN1703 (SEL24), a first-in-class, oral, dual type I PIM/FLT3 inhibitor was evaluated across various lymphoma cell lines. MEN1703 demonstrated anti-proliferative effects across a broad range of lymphoma cell lines. Importantly, MEN1703 was effective even in lymphoma cells resistant to other treatments and induced apoptosis in most cell lines. RNA-Seq indicated that the molecule modulates the transcriptome of highly responsive DLBCL cell lines differently from other, poorly responsive cells, providing clues to mechanisms involved in sensitivity to PIM inhibitors and supporting potential in treating B-cell lymphomas.

Company informs that it will host a webinar on Monday, October 16, at 9:30 am CEST to discuss the PRMT5 data, which will be available here: https://bit.ly/3RL1YWp.

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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