CURRENT REPORT 15/2024
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Posters on preclinical data on RVU120 and Synthetic Lethality Programs presented at the 2024 AACR Annual Meeting

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu"), in reference to current report 11/2024 dated March 6, 2024 on presentation of preclinical data on RVU120 and Synthetic Lethality Programs at the 2024 AACR Annual Meeting, Sand Diego, California USA ("Conference") informs that on April 9, 2024, during the Conference, the Company has presented updated preclinical data from its synthetic lethality pipeline and RVU120. Moreover, on April 7, 2024, preclinical data on MEN1703 (SEL24), was presented by Company's partner Menarini Group.

An updated information in relation to poster presentations about which the Company informed in the current report 11/2024 dated March 6, 2024 concerns:

- Company's PRMT5 program in MTAP-Deficient cancers showing that Ryvu PRMT5 inhibitors show potential best-in-class profiles, including a strong antiproliferative effect on MTAP-deleted cell lines and a good safety window versus MTAP WT cells.
- Ryvu's WRN inhibitors program that has demonstrated target engagement and selective potency with a synthetic lethal effect; *in vivo* efficacy studies exhibited pronounced tumor growth inhibition in an MSI-H colorectal cancer xenograft model.
- Ryvu's proprietary ONCO Prime discovery platform, which recently has been recommended for funding of PLN 26 million (approx. USD 6.6 million) by the Polish Agency for Enterprise Development as announced by the Company in the current report 14/2024 on March 27, 2024, has identified novel drug targets in KRAS-mutant patient-derived cells (PDCs) with therapeutic potential in colorectal cancer; the ONCO Prime platform has broad potential across multiple tumor types.
- MEN1703 (SEL24), presented by Company's partner Menarini Group, shows cytotoxic activity in myelofibrosis cell lines as a monotherapy and synergistically in combination with ruxolitinib.

Details on the updated poster presentations are as follows:

Abstract Title: "Discovery of novel MTA-cooperative PRMT5 inhibitors as targeted therapeutics for MTAP-deleted cancers."
Session Name: HDAC and Methyltransferase Inhibitors
Session date and time: Tuesday, April 9, 9:00 AM - 12:30 PM PST
Poster Number: 4598

- Ryvu has developed potentially best-in-class MTA-cooperative PRMT5 inhibitors showing favorable drug-like properties and effective PRMT5 inhibition dependent on MTA binding.
- Ryvu PRMT5 inhibitor has a robust antiproliferative effect on MTAP-deleted cell lines and provides a good safety window for MTAP WT cells, as shown in a wide cell line panel.
- Novel Ryvu compounds are characterized by significantly improved PK profile that allow for oral administration.
- *In vitro* safety evaluations did not reveal any significant liabilities of the tested compounds.
- The correlation between compound exposure and on-target effect was confirmed in PK/PD and efficacy studies in MTAP-deleted tumor models.

Abstract Title: "Discovery of WRN inhibitors as targeted therapy in the treatment of microsatellite unstable (MSI-H) tumors."
Session Name: Novel Antitumor Agents 4
Session date and time: Tuesday, April 9, 1:30 PM – 05:00 PM PST
Poster Number: 5942

- Structure-based optimization performed at Ryvu facilitated the rapid expansion and delivery of a compound library with novel intellectual property (IP), demonstrating target engagement in cells and selective potency over other RecQ family members.
- The pharmacokinetic properties of these compounds were favorable, allowing progress to in vivo studies, which confirmed the efficacy of Ryvu's WRN inhibitors in xenograft MSI-H cancer models.
- Data on Ryvu's WRN inhibitors provide pharmacological proof-of-concept with synthetic lethal effect and support WRN inhibition as a new, targeted oncological therapy in MSI-high tumors.

Abstract Title: "A comprehensive platform for identification of KRAS-specific synthetic lethal targets using patient-derived cells."

Session Name: New Targets, Technologies, and Drug Delivery Systems
Session date and time: Tuesday, April 9, 9:00 AM - 12:30 PM PST
Poster Number: 4684

- Ryvu's cutting-edge drug discovery platform uniquely combines high throughput capabilities with the precision and translational impact traditionally associated with later, lower throughput stages.
- By leveraging human stem cell-derived model cells (PDC), patient-derived xenografts (PDXs) and clinical samples, we have created a groundbreaking approach to identifying synthetic lethal (SL) targets specific to oncogenic pathways.
- In conjunction with our novel ranking algorithm, these models have successfully identified potential drug targets in KRAS-mutant cells—targets that remained undetected in immortalized CRC cell lines, likely due to genetic and epigenetic alterations accumulated over years of cell culture.
- Chemical compound screening has produced promising results that have been further validated through comparison with a varied collection of patient-derived CRC cultures, ensuring the findings' reliability and clinical relevance.
- These data position Ryvu's primary model platform as an invaluable resource for target discovery research with broad applicability across a variety of tumors.

Abstract Title: "MEN1703/SEL24 exhibits promising antitumoral activity in preclinical models of myelofibrosis both as a single agent and combined with ruxolitinib."
Session Name: Novel Antitumor Agents 2
Session date and time: Sunday, April 7, 01:30 AM – 05:00 PM PST
Poster Number: 665

- MEN1703 (SEL24) demonstrates efficacy both as a monotherapy and in combination with the JAK inhibitor ruxolitinib (RUX) in preclinical models of myelofibrosis (MF).
- MEN1703 demonstrated anti-tumoral efficacy in MF preclinical models, exhibiting *in vitro* activity at clinically relevant concentrations. Notably, the combination of MEN1703 with the standard of care, RUX, exhibited synergistic effects and molecular analyses confirmed the inhibition of downstream targets of PIM.
- The results support the therapeutic potential and relevance of MEN1703 in treating myelofibrosis.

Moreover, the Management Board of Ryvu informs that as it was previously announced in current report 11/2024 on March 6 2024, the poster highlighting synergistic effects of RVU120 in combination with ruxolitinib in myeloproliferative neoplasms will be presented today i.e. April 10, 2024.

Abstract Title: "Combination JAK1/2 and CDK8/19 inhibition demonstrates enhanced efficacy in myeloproliferative neoplasms."
Session Name: Targeted, Combination, and Differentiation Therapies
Session date and time: Wednesday, April 10, 9:00 AM - 12:30 PM PST
Poster Number: 7225

- RVU120, a highly selective and potent CDK8/19 inhibitor, shows potential efficacy as both monotherapy and in combination with ruxolitinib (RUX), a JAK1/2 inhibitor, for the treatment of myeloproliferative neoplasms (MPN) and polycythemia vera (PV).
- In vivo treatment with RVU120/RUX+RVU120 significantly reduced disease manifestation (splenomegaly, WBC, fibrosis scoring, hematopoiesis) compared to VEH/RUX.
- These data suggest that inhibition of JAK1/2 and CDK8/19 could be a novel therapeutic strategy in MPNs.

All posters are available on https://ryvu.com/our-research/

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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