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Clinical and preclinical data on RVU120, RVU305, WRN and synthetic lethality platform presented at the 2024 EORTC-NCI-AACR Symposium

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") informs that the Company has presented four posters with clinical and preclinical data from RVU120 (CDK8/19 inhibitor), RVU305 (MTA-cooperative PRMT5 inhibitor), WRN and synthetic lethality platform at the 2024 EORTC-NCI-AACR Symposium (ENA), October 23-25, 2024 Barcelona, Spain.

Details on the poster presentations are as follows:

Poster Title: Discovery of novel MTA-cooperative PRMT5 preclinical candidate as targeted therapeutics for MTAP-deleted cancers

Poster Number: 32

Session date and time: Wednesday, October 23 (12:00-19:00 CEST)

Ryvu has developed a potentially best-in-class MTA-cooperative PRMT5 inhibitor, RVU305, demonstrating favorable drug-like properties and effective PRMT5 inhibition dependent on MTA binding.

- RVU305 exhibits robust antiproliferative activity in MTAP-null cancer models, including over 100% tumor growth inhibition (TGI) at several dose levels and multiple complete remissions (CRs) at several dose levels in a DoHH2 MTAP-deleted model.
- Tolerability and selectivity towards MTAP-deleted cells was also demonstrated in *in vitro* and *in vivo* preclinical models.
- Overall, the findings highlight the potential of RVU305 preclinical candidate as a promising therapeutic option for patients with MTAP-deleted cancers.

Poster Title: Exploring synthetic lethality and novel drug combinations in patient-derived cells

Poster Number: 417

Session date and time: Friday, October 25 (09:00-15:00 CEST)

Ryvu has developed a proprietary platform, ONCO Prime, to discover novel synthetic lethal (SL) inhibitors targeting key oncogenic drivers such as KRAS and other mutations.

- Initial data are presented in colorectal cancer (CRC), but the platform has the potential to discover novel SL targets across all tumor types. ONCO Prime uses human intestinal stem cell (hISC)-derived cancer model cells, patient-derived xenografts (PDXs), and clinical samples to conduct genomic and functional analyses.
- Ryvu generated isogenic cancer models and validated them through transcriptomic profiling of patient-derived xenografts (PDXs) and patient-derived cell cultures to ensure clinical relevance.
- The data presented in this poster highlights the outcomes of chemical compound and CRISPR/Cas9 screenings, confirming the reliability and relevance of our model for identifying new therapeutic targets in oncology.

Poster Title: Discovery of WRN inhibitors as targeted therapy in the treatment of microsatellite unstable (MSI-H) tumors

Poster number: 107

Session date and time: Wednesday, October 23 (12:00-19:00 CEST)

Ryvu is developing a series of potent and selective WRN helicase inhibitors that demonstrate pronounced efficacy in tumors with high microsatellite instability (MSI-H).

- Ryvu WRN inhibitors show nanomolar potency in viability assays in MSI-H cell lines, with excellent selectivity over microsatellite-stable (MSS) cells.
- In *in vivo* studies, Ryvu inhibitor strongly suppressed tumor growth in an MSI-H model (SW48) while not impacting the MSS model (SW620).
- The compounds exhibit favorable pharmacokinetics, achieving optimal exposure and target engagement, further enhancing their therapeutic potential in MSI-H cancers.

Poster Title: Phase I/II trial of RVU120, a CDK8/CDK19 inhibitor in patients with relapsed/refractory metastatic or advanced solid tumors

Poster Number: 34

Session date and time: Wednesday, October 23 (12:00-19:00 CEST)

RVU120 is being tested in patients with solid tumors in an ongoing Phase I/II clinical trial, AMNYS-51. RVU120 has demonstrated a manageable safety profile across multiple dose levels and dosing schedules in patients with advanced or metastatic solid tumors.

- No dose-limiting toxicities (DLTs) were observed, and most treatment-emergent adverse events (TEAEs) were mild to moderate, with nausea and vomiting being the most common.
- 6/8 patients with adenoid cystic carcinoma achieve a longer duration of treatment on RVU120 compared with their most recent prior line of therapy. A reduction of 20% of target lesions was observed in 2 patients with adenoid cystic carcinoma.
- The recommended phase 2 dose (RP2D) for the QOD schedule was identified as 250 mg and remains the primary dosing schedule in clinical studies, but a continuous dosing schedule was explored and could offer an alternative to patients: continuous every day administration (QD) of RVU120 at doses of 100 mg and 150 mg is considered safe and may improve tolerability of RVU120 compared with 250 mg every other day.

Links to the presented posters can be found here: https://ryvu.com/investors-media/publications/

Upcoming Events

- R&D Update at ENA 2024: webinar on Friday, October 25 at 11:00 AM CET to discuss the data presented at the ENA Symposium. To join the webcast, please register here: https://ryvu.clickmeeting.com/ryvu-ena-2024-results/register
- RVU120 Program Progress and Data Update: webinar on Thursday, December 12, 10:00 AM CET to discuss the ongoing RVU120 Phase II studies.

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Legal basis: Article 17.1 of MAR

Representatives of the Issuer:

- Krzysztof Brzózka – Vice-president of the Management Board
- Hendrik Nogai – Member of the Management Board