# CURRENT REPORT 11/2025
# April 25, 2025

## Posters on preclinical data on RVU305 and Synthetic Lethality Programs presented at the 2025 AACR Annual Meeting

The Management Board of Ryvu Therapeutics S.A., headquartered in Kraków (the "Company," "Ryvu"), in reference to current report no. 7/2025 dated March 26, 2025 informs that the Company has presented preclinical data on RVU305 program and on its; synthetic lethality platform at the 2025 AACR Annual Meeting, which takes place on April 25-30, 2025, in Chicago, United States.

**Details on poster presentations are as follows:**

**Poster Title:** "Preclinical candidate RVU305, an MTA-cooperative PRMT5 inhibitor, shows activity in MTAP-deleted tumors resistant to immune checkpoint treatment."
**Session Name:** HDAC and Methyltransferase Inhibitors
**Session date and time:** Tuesday, April 29, 9:00 AM - 12:00 PM EST
**Poster Number:** 17

RVU305, a potentially best-in-class, brain-permeable MTA-cooperative PRMT5 inhibitor, demonstrates significant potential in targeting MTAP-deleted cancers. In preclinical studies, RVU305 effectively inhibited tumor growth in MTAP-null cancer models without affecting normal cells. RVU305 also demonstrated CNS penetration with predicted efficacious exposure in the brain in cynomolgus monkeys. In CNS cell lines, RVU305 exhibited high potency and efficacy. Furthermore, co-treatment with an anti-PD-1 antibody was well tolerated and resulted in antitumor activity in an MTAP-deleted model resistant to immune checkpoint inhibitors (ICI). The efficacy of RVU305 was supported by pharmacodynamic changes observed in tumor tissue. These results position RVU305 as a promising therapeutic option for patients carrying MTAP-deleted cancers resistant to ICI.

**Poster Title:** "Discovery of novel synthetic lethal targets for effective and safe colorectal cancer therapies."
**Session Name:** Experimental and Molecular Therapeutics
**Session date and time:** Monday, April 28, 2:00 PM - 5:00 PM EST
**Poster Number:** 3

This study highlights the discovery and validation of novel therapeutic targets for colorectal cancer (CRC) through synthetic lethal (SL) interactions, addressing the urgent need for more effective and personalized treatment options. The team identified key vulnerabilities in CRC using advanced models, including genetically engineered human intestinal stem cells (hISCs) and patient-derived xenografts (PDXs) in combination with CRISPR/Cas9 technology.

Genome-wide SL screens revealed targets associated with common CRC driver mutations, particularly APC and KRAS. These findings were robustly validated. Notably, knock-out of the identified target

selectively killed mutant patient-derived cells while sparing healthy intestinal stem cells, demonstrating a favorable therapeutic window.

Furthermore, we identified small-molecule inhibitors that block the activity of the newly discovered target. These compounds modulate downstream biomarkers and phenocopy the differential effects observed in our genetic studies, supporting this approach's translational potential.

Together, these results lay the groundwork for developing targeted therapies tailored to the genetic makeup of CRC tumors.

All posters are now available online and can be obtained from the conference site: https://www.aacr.org/

*Disclaimer: This English language translation has been prepared solely for the convenience of English-speaking readers. Despite all the efforts devoted to this translation, certain discrepancies, omissions or approximations may exist. In case of any differences between the Polish and the English versions, the Polish version shall prevail. Ryvu Therapeutics S.A., its representatives and employees decline all responsibility in this regard.*

**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