CURRENT REPORT 24/2022

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Ryvu Therapeutics presents new clinical and preclinical data for RVU120 program at 34th AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Symposium

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company", "Ryvu") informs, with reference to Current Report No. 23 dated October 12, 2022, about having presented updated data for RVU120 project showing the clinical and preclinical activity of the Company's lead oncology drug candidate for cancer therapy, at the 34th AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Symposium.

Poster presentations included:

- Updated clinical data for RVU120 program in relapsed/refractory metastatic or advanced solid tumors,
- preclinical data indicating RVU120's potential to enhance antibody-driven NK cells-mediated cytotoxicity,
- most recent results from the MTA-cooperative PRMT5 inhibitors program.

The most important conclusions, in the opinion of the Company's management board, from the presented posters are as follows:

- Updated data from the dose escalation phase of the phase I/II RVU120 study indicate disease stabilization in four patients with advanced solid tumors;
- RVU120's good tolerability was confirmed at all doses tested;
- Preclinical data indicate the potential of RVU120 in combination therapy with multiple therapeutic antibodies;
- Preclinical data for the MTA-co-operative PRMT5 inhibitor program indicate the compound's anti-tumor efficacy and target engagement in cancer cells with MTAP gene deletion.

Details of the poster presentations are as follows:

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

Clinical data demonstrate a favorable safety profile of RVU120 at doses of 75 mg, 100 mg, and 125 mg in all 9 patients enrolled to date. None of the patients experienced dose-

limiting toxicity (DLT), drug-related serious adverse events (SAE), or drug-related AE of Grade three or higher after being dosed with RVU120. Disease stabilization was observed in two heavily pretreated patients, one lasting 18 weeks in gastro-esophageal junction cancer, and another, ongoing after 33 weeks in adenoid cystic carcinoma. Two patients are awaiting their first assessment. The most common reason for treatment discontinuation was progressive disease (5 patients). One patient withdrew consent, and 3 patients are ongoing. In the Company's management board opinion, available data warrant continuation of dose escalation and collection of additional clinical data.

Abstract Title: *"RVU120, a small molecule inhibitor of CDK8/19 kinases, enhances rituximab-driven NK cells-mediated cytotoxicity both in vitro and in vivo"*

Preclinical data demonstrate that treatment with RVU120 in combination with an anti-CD20 antibody (rituximab) increases NK cell cytotoxicity against CD20-positive positive diffuse large B-cell lymphoma (DLBCL) cell lines in vitro and in vivo. The combined therapy of RVU120 with rituximab was well tolerated and resulted in complete tumor regressions in vivo. This study, in the opinion of the Company's management board, shows the potential of RVU120 in enhancing antibody-mediated ADCC and reinforces the rationale for the development of RVU120 combination therapies in blood cancer and solid tumors.

Abstract Title: *"Discovery of novel MTA-cooperative PRMT5 inhibitors as targeted therapeutics for MTAP deleted cancers"*

Ryvu has identified a series of MTA-cooperative PRMT5 inhibitors with drug-like physicochemical properties that block methyltransferase activity with nanomolar IC50 values. Structurally enabled hit generation and optimization allowed for a rapid expansion and delivery of several generations of compounds with novel IP, high target engagement in cells, and selective potency in MTAP-deleted cell lines. Ryvu compounds selectively inhibit the growth of MTAP-deleted cancer cells in prolonged 3D culture, and efficacy studies with the lead compound resulted in tumor growth inhibition in MTAP -/- model, accompanied by significant inhibition of target proximal PD biomarker.

The Company informs that all posters are now available for download from Ryvu corporate website: https://ryvu.com/investors-media/publications/

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