
# RYVU THERAPEUTICS S.A.
# H1 2025 Report

# TABLE OF CONTENTS

# 1. ECONOMIC AND FINANCIAL HIGHLIGHTS

## 1.1 Financial Results Obtained in the Reporting Period

Condensed Interim Financial Statements of Ryvu Therapeutics S.A. (“Company”, “Issuer”, “Ryvu”) for the period from January 1, 2025, to June 30, 2025, are prepared in accordance with the requirements of the International Accounting Standard No. 34 "Interim Financial Reporting" endorsed by the EU ("IAS 34").

**Selected data of the statement of financial position are as follows:**

| Ryvu Therapeutics S.A. | Data in PLN thousand | | Data in EUR thousand | |
|---|---|---|---|---|
| Item | **30.06.2025** | 31.12.2024 restated | **30.06.2025** | 31.12.2024 restated |
| Total assets | **281,186** | 378,777 | **66,288** | 88,644 |
| Short-term receivables | **21,736** | 35,776 | **5,124** | 8,373 |
| Cash and cash equivalents | **107,167** | 160,073 | **25,264** | 37,462 |
| Other current and non-current financial assets | **48,907** | 65,876 | **11,529** | 15,417 |
| Total liabilities | **185,944** | 226,484 | **43,835** | 53,004 |
| Long-term liabilities | **116,187** | 118,556 | **27,390** | 27,745 |
| Short-term liabilities | **69,757** | 107,928 | **16,445** | 25,258 |
| Total equity | **95,242** | 152,293 | **22,453** | 35,641 |
| Share capital | **9,248** | 9,248 | **2,180** | 2,164 |

## Selected data of the statement of comprehensive income are as follows:

| Ryvu Therapeutics S.A. | Data in PLN thousand | | | | Data in EUR thousand | | | |
|---|---|---|---|---|---|---|---|---|
| Item | **From 01.01.2025 to 30.06.2025** | From 01.01.2024 to 30.06.2024 | **From 01.04.2025 to 30.06.2025** | From 01.04.2024 to 30.06.2024 | **From 01.01.2025 to 30.06.2025** | From 01.01.2024 to 30.06.2024 | **From 01.04.2025 to 30.06.2025** | From 01.04.2024 to 30.06.2024 |
| Revenues from sales | **22,912** | 22,395 | **9,493** | 12,231 | **5,428** | 5,195 | **2,230** | 2,844 |
| Revenues from subsidies | **13,090** | 11,090 | **8,989** | 7,270 | **3,101** | 2,573 | **2,112** | 1,690 |
| Revenues from R&D projects | **6,424** | 14,956 | **2,910** | 3,514 | **1,522** | 3,469 | **684** | 817 |
| Other operating revenues | **5** | 81 | **3** | 4 | **1** | 19 | **1** | 1 |
| Revenues from operating activities | **42,432** | 48,522 | **21,395** | 23,019 | **10,053** | 11,256 | **5,026** | 5,352 |
| Operating expenses | **-107,796** | -103,775 | **-49,068** | -55,801 | **-25,539** | -24,073 | **-11,527** | -12,975 |
| Operating expenses without Incentive Scheme and valuation of Nodthera shares | **-95,542** | -101,703 | **-47,742** | -54,953 | **-22,636** | -23,592 | **-11,215** | -12,778 |
| Depreciation | **-4,718** | -5,470 | **-2,295** | -2,708 | **-1,118** | -1,269 | **-539** | -630 |
| Valuation of Incentive Scheme | **-1,882** | -2,241 | **-887** | 0 | **-446** | -520 | **-208** | 0 |
| Loss from operating activities (EBIT) | **-65,364** | -55,253 | **-27,674** | -32,782 | **-15,486** | -12,817 | **-6,501** | -7,622 |
| Loss from operating activities (EBIT) without Incentive Scheme and valuation of Nodthera shares | **-53,111** | -53,181 | **-26,348** | -31,934 | **-12,583** | -12,336 | **-6,190** | -7,425 |
| Loss before income tax | **-58,917** | -49,690 | **-33,655** | -30,313 | **-13,959** | -11,527 | **-7,906** | -7,049 |
| Net loss | **-58,934** | -49,818 | **-33,658** | -30,419 | **-13,963** | -11,556 | **-7,907** | -7,073 |
| Net loss without Incentive Scheme | **-57,052** | -47,577 | **-32,771** | -29,385 | **-13,517** | -11,036 | **-7,256** | -6,833 |
| EBITDA | **-60,646** | -49,783 | **-25,378** | -30,074 | **-14,368** | -11,548 | **-5,820** | -6,993 |
| EBITDA without Incentive Scheme and valuation of Nodthera shares | **-48,392** | -47,711 | **-24,052** | -29,226 | **-11,465** | -11,068 | **-5,509** | -6,796 |
| Net cash flows from operating activities | **-68,590** | -65,288 | **-24,407** | -22,053 | **-16,251** | -15,145 | **-5,734** | -5,128 |
| Net cash flows from investing activities | **18,185** | 51,515 | **-18,979** | -25,459 | **4,308** | 11,950 | **-4,459** | -5,920 |
| Net cash flows from financing activities | **-2,170** | 68,454 | **-852** | 34,553 | **-514** | 15,879 | **-200** | 8,034 |
| Total net cash flow | **-52,576** | 54,681 | **-44,239** | -12,959 | **-12,456** | 12,684 | **-10,393** | -3,013 |
| Number of shares (weighted average) | **23,120,148** | 23,120,148 | **23,120,148** | 23,120,148 | **23,120,148** | 23,120,148 | **23,120,148** | 23,120,148 |
| Profit (loss) per share (in PLN) | **-2.55** | -2.15 | **-1.46** | -1.32 | **-0.60** | -0.50 | **-0.34** | -0.31 |
| Diluted profit (loss) per share (in PLN) | **-2.55** | -2.15 | **-1.46** | -1.32 | **-0.60** | -0.50 | **-0.34** | -0.31 |
| Book value per share (in PLN) | **4.12** | 8.88 | **4.12** | 9.17 | **0.97** | 2.13 | **0.97** | 2.13 |
| Diluted book value per share (in PLN) | **4.12** | 8.88 | **4.12** | 9.17 | **0.97** | 2.13 | **0.97** | 2.13 |
| Declared or paid dividend per share (in PLN) | **-** | - | - | - | - | - | - | |

**Selected financial data presented in the Quarterly report were converted to Euro as follows:**

1. Items relating to the profit and loss statement and the cash flow statement were converted using the exchange rate constituting the arithmetic average of the exchange rates, applicable as of the last day of every month in the given period, based on the information published by the National Bank of Poland (NBP):
   - for the period from 01/01/2025 – 30/06/2025: PLN 4.2208
   - for the period from 01/01/2024 – 30/06/2024: PLN 4.3109;
2. Balance sheet items were converted using the average exchange rate announced by the NBP applicable as of the balance sheet date, which were:
   - as of 30 June 2025: PLN 4.2419;
   - as of 31 December 2024: PLN 4.2730.

## 1.2 Management Board comments on the financial results

In the first half of 2025, Ryvu Therapeutics S.A. recognized total operating revenue of PLN 42,432 thousand, which constitutes a decrease compared to the corresponding period in 2024, when total operating revenue amounted to PLN 48,522 thousand. This results from a decrease in revenues from R&D projects (a decrease of PLN 8,532 thousand), partially compensated by an increase in revenues from sales (an increase of PLN 517 thousand), and an increase in revenues from subsidies (an increase of PLN 2,000 thousand) compared to the corresponding period in 2024.

The lower revenues from R&D projects in the first half of 2025 were due to a milestone payment of USD 2 million received under the exclusive license agreement with Exelixis Inc. in the first half of 2024.

The increase in sales revenues resulted from collaboration with Berlin-Chemie AG (Menarini Group). Under the Agreement, Ryvu assumed responsibility from Menarini for conducting the Phase II clinical trial MEN1703 in relapsed/refractory DLBCL, which Menarini had previously implemented. The increase in sales revenue was partially offset by lower revenue from cooperation with BioNTech due to BioNTech's decision to exercise its right to terminate the STING program covering Ryvu's STING agonist portfolio as standalone small molecules (RVU312) along with two other of several previously undisclosed programs.

In the first half of 2025, Ryvu reported a net loss, as well as an operating loss. The net and operating losses result from the fact that the Company focuses on increasing the value of the ongoing projects that will be commercialized at a later stage of development.

The Company's net loss for the period ended June 30, 2025, amounted to PLN 58,934 thousand compared to the net loss of PLN 49,818 thousand in the corresponding period of 2024. The higher loss in first half of 2025 in comparison to corresponding period in 2024, is related to lower operating revenues (described above) and higher negative impact in NodThera shares valuation of PLN 10,372 thousand (described below), partially compensated by positive impact of the put option issued by the Company to European Investment Bank to repurchase its equity instruments (described below). As a result of the cost discipline and the strategic reorganization announced in February 2025, the Company's operating loss in Q2 2025 decreased by PLN 5,109 thousand compared to the corresponding period of 2024.

## Valuation of shares in NodThera Inc.

### Valuation of shares

The Company holds shares in NodThera Inc., a biotechnology company developing NALP3 inhibitors for the treatment of inflammatory and neuroinflammatory diseases.

As of June 30, 2025, four types of shares existed in NodThera Inc.: ordinary stock and preferred stock (Junior Preferred Stock, Series A1 and A2 Preferred Stock, Series B Preferred Stock, and Series C Preferred Stock). Ryvu is the holder of the Junior Preferred Stock.

On April 4, 2025, the Series D Preferred Stock was issued. The issuance included:

- 12,666,663 Series D1 shares at a price of USD 1.50 per share,
- 41,050,852 Series D2 shares at a price of USD 0.75 per share,
- 30,048,510 Series D3 shares (constituting a conversion of debt financing) at a price of USD 0.7407 per share.

As a result, the issuance generated total funding of USD 49,788,133.50 (from Series D1 and D2) for NodThera Inc. The offering was limited to existing investors only. Series D shares carry the same preferential rights as Series A, B, and C shares. Ryvu did not participate in this issuance.

Therefore, the valuation was based on a share price of USD 0.9269 per share, which represents the weighted average price of Series D1 and D2 shares from the most recent financing round on April 4, 2025.

As of June 30, 2025, Ryvu held 1.2% shares in NodThera. Following the Series D issuance, Ryvu's shareholding decreased to 1.2%, and the total valuation of its stake amounts to PLN 6,402,399 (based on the NBP's average exchange rate of 3.3520 PLN/USD).

**Valuation of shares in NodThera Inc. according to fair value:**

| | |
|---|---|
| New share issue price (in USD) | 0.9269 |
| Average NBP exchange rate from June 30, 2025 | 3.6164 |
| New share issue price (in PLN) | 3.3520 |
| Number of the Company's shares in NodThera Inc. | 1,910,000 |
| **Value of shares in the balance sheet as of June 30, 2025** | **6,402,399** |
| Value of shares in the balance sheet as of December 31, 2024 | 16,773,742 |
| **Change in valuation – gross impact on the valuation of shares** | **-10,371,601** |

## Financing from the European Investment Bank

On August 16, 2022, the Company concluded a financing agreement with the European Investment Bank ("EIB"). Under the agreement, the EIB agreed to grant the Company a loan in the maximum amount of EUR 22,000,000. The purpose of the agreement is to support the development of the RVU120 molecule. The majority of the funding is allocated to cover expenses related to clinical trials,

necessary regulatory approval activities, internal research and development for drug discovery, and costs associated with intellectual property protection.

The financing was paid in three tranches: Tranche A and Tranche B, each in the amount of EUR 8,000,000, and Tranche C, in the amount of EUR 6,000,000. The Company is obliged to repay each of the paid tranches in one installment, 5 years after its launch. The interest rate for Tranche A is 3% per annum, for Tranche B 2.7% per annum, and for Tranche C 2.4% per annum.

Additional consideration for Tranche A, Tranche B and Tranche C, are subscription warrants corresponding in total to 2.5% of the fully issued share capital of the Company. The validity period of the Warrants is 10 years, and EIB will have the right to exercise the Warrants upon the maturity of Tranche or a voluntary or mandatory prepayment event. Under the Warrant Agreement, the Company committed to issue 592,825 subscription warrants to the EIB, entitling the holder to acquire a total of 592,825 shares in the Company with a total nominal value of PLN 237,130.

Additionally, put option issued by the Company creates a contractual obligation to repurchase its equity instruments (warrants). On each reporting date after the initial recognition, the Company updates the amount of the liability for the put option, taking into account changes in the settlement price of this option, with the effects of the valuation reflected in the statement of comprehensive income. As of June 30, 2025, Ryvu recognized a positive impact of the put option in the amount of PLN 7,775 thousand.

## 1.3 The Company's Assets and the Structure of Assets and Liabilities

As of June 30, 2025, the value of the Company's assets was PLN 281,186 thousand and decreased by PLN 97,591 thousand compared to the end of 2024 (PLN 378,777 thousand), mainly due to expenditures incurred on discovery and clinical projects. At the end of June 2025, the highest value of assets was cash, which amounted to PLN 107,167 thousand (at the end of 2024, it was PLN 160,073 thousand), and other financial assets of PLN 48,907 thousand (at the end of 2024, it was PLN 65,876 thousand). Fixed assets are mainly the Research and Development Centre for Innovative Drugs (named 'CBR') and laboratory equipment, as well as the valuation of NodThera shares of PLN 6,402 thousand.

The main item in Ryvu's equity and liabilities is equity, which amounted to PLN 95,242 thousand as of June 30, 2025, and decreased by PLN 57,051 thousand compared to December 31, 2024. The decrease in equity is primarily attributable to the net loss recorded for the period. The other source of funding for assets is long-term liabilities, which amounted to PLN 116,187 thousand as of the end of June 2025. The long-term liabilities are mainly related to the loan received from the European Investment Bank. Additionally, long-term liabilities include deferred income, primarily related to deferred revenue from the BioNTech agreement, as well as the infrastructure subsidy for CBR.

**The asset structure demonstrates the Company's high financial liquidity, which is confirmed by the following ratios:**

| | 30.06.2025 | 31.12.2024 |
|---|---|---|
| **Current ratio current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)** | 2.74 | 2.67 |

| | | |
|---|---|---|
| **Quick ratio (current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)** | 2.73 | 2.66 |

Cash surpluses, not used in the operating activities, are deposited in low-risk financial instruments like short- and long-term bank deposits and bonds.

## 1.4 Current and Projected Financial Condition

The Company's financial position as of the report date is strong, considering its current cash position and the financing received from the European Investment Bank. As of June 30, 2025, the value of the Company's cash amounted to PLN 155,541 thousand (PLN 107,233 thousand in cash at the banks, PLN 46,510 thousand in investment funds, and PLN 1,798 thousand in bonds), and as of September 8, 2025, it was PLN 131,110 thousand (PLN 84,000 thousand in cash at the banks and PLN 47,110 thousand in investment funds). The decrease in cash resulted from expenditure incurred on early pipeline and clinical development projects.

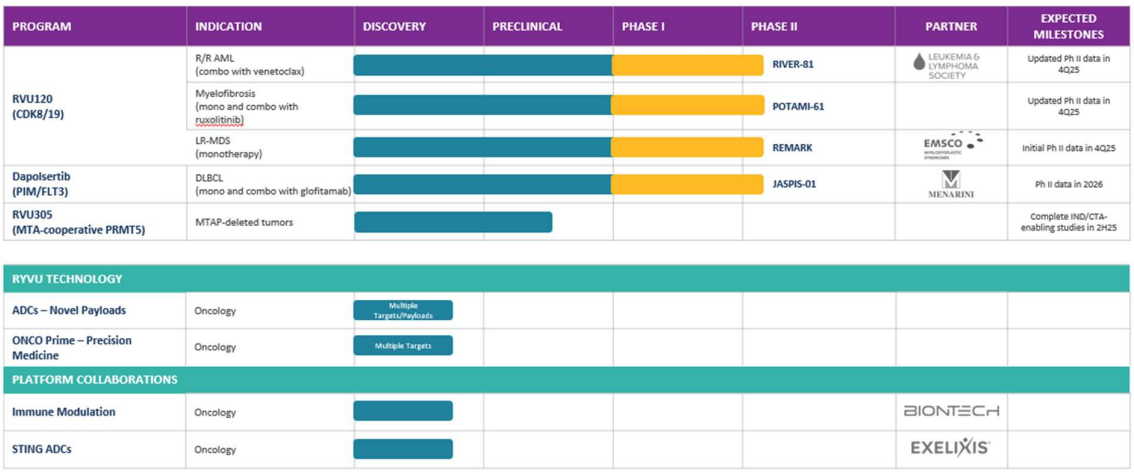
The Company meets its obligations in a timely manner and maintains sustainable cash levels, ensuring its financial liquidity. Cash inflow from previous share issues, funds obtained from EU subsidies, financing received from the EIB, funds supporting R&D projects, and cash generated from the commercialization of projects enable the Company to execute its planned investments, particularly the development of ongoing and new innovative projects and the expansion of laboratory infrastructure. The Company's future revenues will strongly depend on the ability to commercialize its R&D projects.

# 2. MANAGEMENT BOARD INFORMATION ON ACTIVITES

## 2.1 The pipeline

Ryvu Therapeutics is advancing a broad pipeline addressing emerging targets in oncology.

Ryvu's pipeline includes candidates with differentiated therapeutic mechanisms, including programs directed at kinases, synthetic lethality, immuno-oncology and immunometabolism pathways. These research and development projects are represented below.




*Source: Company's own data.*

### RVU120

RVU120 is a clinical-stage, selective, first-in-class dual inhibitor of CDK8 and CDK19 kinases. RVU120 has demonstrated efficacy in several solid tumors and hematologic malignancies in *in vitro* and *in vivo* models. CDK8 and its paralog, CDK19, are kinase submodules of the mediator complex, involved in both transcriptional activation and repression, playing central roles in maintaining the viability of cancer cells and their undifferentiated state across various tumor types (Dannappel et al., 2019; Rzymski et al., 2015; Philip et al., 2018). CDK8/19 mediator complex integrates basal transcriptional machinery with the activity of oncogenic transcriptional and epigenetic factors. Inhibition of CDK8/19 can repress key oncogenic transcriptional programs and induce lineage commitment genes in acute myeloid leukemia (AML).

RVU120 was internally discovered by Ryvu and has received support from the Leukemia & Lymphoma Society Therapy Acceleration Program® (TAP), a strategic initiative to partner directly with innovative biotechnology companies and leading research institutions to accelerate the development of promising new therapies for blood cancers.

On March 25, 2020, the U.S. Food and Drug Administration (FDA) granted RVU120 an orphan drug designation (ODD) for the treatment of patients with AML.

Two clinical Phase I studies with RVU120 are ongoing: (i) Phase Ib in patients with AML/HR-MDS (NCT04021368; CLI120-001, RIVER-51) and (ii) Phase I/II in patients with relapsed/refractory metastatic or advanced solid tumors (NCT05052255; RVU120-SOL-021, AMNYS-51). Enrollment is completed in both studies.

Based on the available translational and clinical data, Ryvu initiated a Clinical Development Plan (CDP) for RVU120, which includes four Phase II studies: RIVER-81, POTAMI-61, RIVER-52, and REMARK. Ryvu's focus of RVU120 CDP is on hematologic malignancies. Translational research is ongoing to determine the opportunities for RVU120 in solid tumors, and an investigator-initiated Phase I study to evaluate RVU120 in combination with everolimus in pediatric patients with medulloblastoma was announced in September 2025. The MEDWAY project will be executed by the Children's Memorial Health Institute (IPCZD) as a sponsor of the study under a PLN 40 million grant awarded by the Medical Research Agency.

**RIVER-81 Phase II study**

On January 31, 2024, Ryvu announced the dosing of the first patient in the RIVER-81 Phase II study of RVU120 in combination with venetoclax (NCT06191263). RIVER-81 is a multicenter, open-label clinical trial that aims to assess the safety, tolerability, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) of RVU120 when administered in combination with venetoclax to patients with AML who are relapsed or refractory to prior therapy with venetoclax and a hypomethylating agent.

During the European Hematology Association (EHA) meeting in June 2025, in Milan, a data update was provided. As of May 14, 43 patients had been treated across various dose levels. After an initial expansion of 250 mg RVU120 administered every other day in combination with 400 mg venetoclax in a 2-week on 1-week off schedule (Part 2), dose optimization included another cohort of 150 mg RVU120 administered every day in combination with 400 mg venetoclax in a 2-week on 1-week off schedule (Cohort 4). In Part 2, 19 patients were treated, and 13 were evaluable for response at the time of data cut-off. Out of those, 3 achieved a CRx (23%, 2 CRi, 1 CRh). In Cohort 4, 7 patients were treated, and 6 patients were evaluable for response. The CR rate in the efficacy evaluable population was 50% (3/6, 2 CRi, 1 CR). All 3 patients were ongoing at the time of data presentation. At the moment of data disclosure, the study was ongoing at 200 mg RVU120 in the same schedule as Cohort 4. Updated data are expected to be presented at the end of 2025.

In an additional presentation for the same conference, translational data were presented further to support the scientific rationale of the RIVER-81 study. It could be demonstrated that RVU120, in combination with venetoclax, has a strong capacity to overcome resistance to venetoclax. The underlying mechanism involves the downregulation of key resistance pathways, including the IL-6/JAK/STAT3, TGF-β, PI3K/AKT/mTOR, and inflammatory signaling pathways.

The planned overall enrollment for RIVER-81 is approximately 98 patients. The execution of the RIVER-81 study is supported by a PLN 62.3 million grant from the Polish Medical Research Agency (ABM).

**POTAMI-61 Phase II study**

The Phase II POTAMI-61 study investigates RVU120 as both a monotherapy and a combination therapy for treating patients with myelofibrosis (MF). In Part A, Cohort 1 assesses RVU120 as a monotherapy in patients who have been previously treated with or are ineligible for treatment with a JAK inhibitor, and Cohort 2 assesses RVU120 in combination with ruxolitinib in patients experiencing a suboptimal

response to JAK inhibitor therapy. Depending on results from Part A, cohorts 1 and/or 2 could be expanded in Part B, which will further assess safety, tolerability, and antitumor activity in a larger cohort, totaling up to approximately 230 patients for both Part A and Part B combined.

RVU120's potential in myelofibrosis is supported by its effect on bone marrow and hematopoietic cells observed in the clinical trial setting, as well as in translational data generated with Prof. Rajit Rampal at the Memorial Sloan Kettering Cancer Centre as part of a collaboration with Ryvu established in 2021. It was demonstrated that RVU120 successfully attenuates myelofibrosis phenotypes when used as a single agent or in combination with ruxolitinib in murine models of myelofibrosis, furthermore, RVU120 was shown to act synergistically with a whole class of JAK inhibitors and the BET inhibitor pelabresib.

The POTAMI-61 study was launched at clinical sites in Poland and Italy, and on December 5, 2024, the first patient received treatment.

An update of early study data was presented at the EHA Congress in June 2025. As of May 14, 21 patients had been treated across both cohorts. There were no new safety findings, and RVU120, when used as a single agent or in combination with ruxolitinib, was tolerated by patients with MF. While the primary endpoint of spleen size reduction will be assessed after 24 weeks of treatment, the first response assessment is performed after 12 weeks of treatment. At the time of data cutoff, 8 patients (3 in Cohort 1 and 5 in Cohort 2) had undergone an assessment of spleen size. Four of these patients (2 in Cohort 1, 2 in Cohort 2) had a spleen size reduction of more than 10%. Data to assess the impact on the total symptom score, which is a secondary endpoint, was available in 4 patients (1 in Cohort 1, 3 in Cohort 2). One patient in Cohort 2 exceeded the 50% reduction, and another patient in Cohort 1 had a reduction of more than 45%. Notably, in one patient with a spleen size reduction of more than 35%, a reduction of the grade of bone marrow fibrosis was detected after 12 weeks of treatment.

The study is ongoing, and more mature data will be presented at the end of 2025.

**REMARK Phase II study**

The Phase II REMARK study (NCT06243458) is being conducted as an investigator-initiated trial within the European Myelodysplastic Neoplasms Cooperative Group (EMSCO), with Prof. Uwe Platzbecker serving as the Coordinating Principal Investigator. This study explores RVU120 as a monotherapy for the treatment of patients with low-risk myelodysplastic syndromes (LR-MDS). The REMARK study has commenced enrollment of patients across five countries: Poland, Germany, France, Spain and Italy. Up to approximately 25 clinical sites will be activated across these countries, with a planned overall enrollment of approximately 40 patients. The first patient in the REMARK study was treated on September 19, 2024, and enrollment was completed in May 2025.

An oral presentation providing the scientific rationale for this study was presented at the EHA Congress in June 2025. It could be shown that RVU120 significantly enhances erythropoiesis in MDS primary cells at clinically relevant and lower doses, supporting its potential as a therapeutic strategy in this indication. The presence of ASXL1 mutations in RVU120-sensitive samples may provide a patient stratification approach to enrich for responders.

**RIVER-52 Phase II study**

RIVER-52 is a multicenter, open-label clinical trial designed to assess the safety, tolerability, anti-tumor activity (efficacy), pharmacokinetics (PK), and pharmacodynamics (PD) of RVU120 as a monotherapy in patients with genetically defined subtypes of AML (including NPM1 and DNMT3a mutations), as well

as with HR-MDS, without alternative treatment options. The latest data update was presented at the EHA Congress in June 2025. RVU120 showed an acceptable safety profile at the dose of 250 mg QOD in patients with relapsed or refractory AML. Nausea, vomiting, and infectious complications were among the most frequent events, consistent with prior findings from Phase 1 and with the risk profile of the patient population under investigation. Despite relevant blast reductions in some patients, no durable complete responses were observed in the investigated patient populations. Although single agent activity of RVU120 in patients with AML cannot be excluded, the Company announced on February 25, 2025, that the study would not recruit new patients. The results of this study will however be included in the RVU120 safety database, supporting potential future regulatory approvals.

The Phase II studies mentioned above are part of RVU120's Clinical Development Plan, presented in October 2023, and align with the Company's cash runway to H2 2026.

Additionally, multiple translational research activities are underway, aimed at further confirming RVU120's mechanism of action, defining the target patient population, identifying potential combination partners, and validating RVU120 in other hematological and solid tumor indications, including combination studies and academic collaborations on medulloblastoma and sarcoma.

## Dapolsertib (MEN1703, SEL24)

Dapolsertib (also known as MEN1703 or SEL24) is a selective, small-molecule dual inhibitor of PIM and FLT3 kinases, two enzymes strongly implicated in the malignant transformation of hematopoietic cells and lymphomagenesis. The compound has been discovered by Ryvu and is currently in clinical development in collaboration with Menarini Group as a therapeutic option for various cancers. The licensing agreement with Menarini was executed in March 2017. Initially, dapolsertib was developed as a potential treatment for patients with relapsed/refractory acute myeloid leukemia (AML). More details of the completed Phase I/II clinical study can be found at ClinicalTrials.gov under the identifier NCT03008187. Data from this part of the study were presented at multiple scientific conferences and symposia. Ryvu has been supporting this project with translational research.

Based on a decision announced in September 2023, Menarini continues the development of dapolsertib by initiating a new Phase II study in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) – JASPIS-01 study. Menarini fully funds all study activities, while Ryvu acts as the operational partner to execute JASPIS-01 study on behalf of Menarini. Translational work in other hematologic indications also continues. The licensing partnership with Menarini, including the total milestones and royalties due to Ryvu upon achieving certain events, remains unchanged.

The JASPIS-01 study is an open-label, Phase II clinical trial investigating dapolsertib as a monotherapy and in combination with glofitamab for patients with relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL). It comprises three parts: Part 1 focuses on evaluating safety and preliminary anti-lymphoma activity in approximately 18 patients; Part 2, based on Part 1 results, will assess anti-tumor activity as a primary objective in a larger group of patients, as well as safety and tolerability; and Part 3 will offer an optional randomized comparison.

The JASPIS-01 study was initiated in Q4 2024. On March 26, 2025, Ryvu announced dosing of the first patient. The study was initiated at clinical sites in Poland. Currently, it is also recruiting in France, Spain, and the United Kingdom. The study is registered on ClinicalTrials.gov under NCT06534437.

## PRECLINICAL AND DISCOVERY STAGE PROJECTS

### Synthetic lethality projects
### RVU305 Oral, brain-penetrant, MTA-cooperative PRMT5 inhibitor in IND/CTA-enabling studies

RVU305 is a potentially best-in-class oral, brain-penetrant, MTA-cooperative PRMT5 inhibitor in IND/CTA-enabling studies. It targets cancers characterized by the deletion of the MTAP metabolic gene, found in approximately 10 to 15% of all human tumors. This deletion leads to a substantial accumulation of methylthioadenosine (MTA) within cells. At high concentrations, MTA acts as a highly selective inhibitor of the PRMT5 methyltransferase, specifically competing with its substrate, S-adenosylmethionine (SAM). In cells affected by MTAP deletion, the accumulation of MTA results in a partial inhibition of PRMT5's methylation function. This inhibition consequently reduces the level of symmetric dimethylation of arginine across the proteome, heightening the cells' susceptibility to alterations in methylosome activity. RVU305 is an MTA-cooperative PRMT5 inhibitor that selectively impedes the growth of cancer cells with MTAP deletions.

In the reporting period, RVU305 has advanced to the next steps of preclinical development, including toxicology and API/IMP manufacturing, with the goal of completing these studies in H2 2025. Specifically, the repeated-dose toxicity studies of RVU305 were conducted and the starting dose range was defined for GLP toxicity studies. These preclinical safety data will be important in calculation of the first-in-human (FIH) starting dose. During the reporting period, the chemical synthesis route for the preclinical candidate RVU305 was developed and the process was scaled up from gram to kilogram scale. In addition, a GMP-compliant process for manufacturing the compound into the final drug product was established, and synthesis of a GMP batch was initiated to prepare the clinical-trial drug product.

Data on the Company's MTA-cooperative PRMT5 inhibitors, and specifically RVU305 preclinical candidate, were presented at the annual AACR American Association for Cancer Research conference in Chicago, United States, in April 2025. Ryvu will present further progress at the AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics in Boston. Poster presentations are available on the company website under the following link: https://ryvu.com/investors-media/publications/

### Novel Multi-Target Discovery
### ONCO Prime –Novel Small Molecule Precision Oncology

In addition to our disclosed projects, Ryvu is accelerating internal initiatives aimed at identifying and validating novel synthetic lethal and precision oncology targets for first-in-class small-molecule drug discovery projects. In June 2024, Ryvu concluded a funding agreement with the Polish Agency for Enterprise Development (PARP) and expects to receive approximately $6.6M (PLN 26.3 million) in grant funding over five years to support the proprietary ONCO Prime discovery platform. Ryvu has already begun utilizing the secured grant funding to accelerate the development of the ONCO Prime platform, including the expansion of its primary biobank and target discovery efforts across several cancer indications, such as lung adenocarcinoma and triple-negative breast cancer (TNBC).

Through the ONCO Prime platform, we have successfully identified new precision oncology targets in colorectal cancer and are developing small-molecule programmes in this space. Ryvu disclosed advancements in the ONCO Prime platform at the AACR Annual Meeting in April 2025 in Chicago. Ryvu's research was published in *Nature Scientific Reports* in an article entitled *Integrated transcriptomic and functional modeling reveals AKT and mTOR synergy in colorectal cancer* (Sci Rep. 2025 Jul 31;15(1):26643. doi: 10.1038/s41598-025-08649-0)
Poster presentations from the conferences are available on the company website under the following link: https://ryvu.com/investors-media/publications/.

In H2 of 2025, the updates and new results were presented at the Maria Skłodowska-Curie symposium in Warsaw with more presentations planned at the "Discovery on Target" & "AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics" in Boston (September and October), as well as the oral presentation at the Target Identification and Validation in Drug Discovery conference in Cambridge, UK, in October.

### ADC – Novel ADC payloads

In addition to our ONCO Prime Platform, Ryvu has sought ways to exploit our existing capabilities in small-molecule discovery and target selection to drive projects and capabilities in the small-molecule payload/ADC space. Building on the success of the Company's collaboration with Exelixis, Ryvu is actively developing additional payload projects and ADCs to provide alternative approaches that ultimately enhance the efficacy and safety of ADCs compared to conventional chemotherapy-based payloads. Specifically, Ryvu has been focusing on synthetic lethal, immunocytotoxic and other payloads. Ryvu is pursuing novel payload projects within our focus areas, but has disclosed only the WRN payload project. Ryvu presented data and strategy in those projects at ADC Payload Summit in Boston in May, "Exploring Next-Generation Payload Diversity Beyond Cytotoxics to Diversify Immune-Oncology MOAs."

### STING agonist ADC collaboration with Exelixis

In July 2022, Ryvu signed a licensing agreement with Exelixis to collaborate on novel targeted therapies based on the advanced STING agonist technology developed at Ryvu. To date, under the terms of the collaboration, Ryvu has received a total of $3 million in milestone payments from Exelixis. The partnership has developed highly potent STING-activating antibody-drug conjugates that demonstrate picomolar in vitro activity and antigen-specific activation of the STING pathway; further development of these compounds is currently ongoing. Further progress on the project remains confidential.

### BioNTech: Multi-target research collaboration

In November 2022, BioNTech and Ryvu initiated a comprehensive, multi-target research collaboration to advance small-molecule programs focused on immune modulation in cancer and potentially other disease areas. Under this partnership, BioNTech has the right to acquire global development and commercialization rights for these programs. While multiple research initiatives are underway as part of this collaboration, detailed information about these programs remains confidential.

## 2.2 Significant events in H1 2025

### 2.2.1 During the reporting period

#### Termination of STING program under Research Collaboration Option and Exclusive License Agreement with BioNTech SE

On January 29, 2025, BioNTech SE, with its registered office in Mainz, Germany ("BioNTech"), notified the Company that for reasons relating to change of BioNTech's portfolio strategy, the collaborator has decided to exercise its right to terminate the STING program covering Ryvu's STING agonist portfolio as standalone small molecules ("STING Program"; RVU312) along with two other of several previously undisclosed programs, which were implemented under the research collaboration and exclusive license agreement dated November 29, 2022 ("License Agreement"). The Company disclosed the conclusion of the License Agreement in its Current Report No. 26/2022, dated November 30, 2022.

As a result of the abovementioned termination, upon the expiration of the 3-month notice period, all licenses covering the terminated programs granted by the Company to BioNTech under the License Agreement will expire. Ryvu will regain full rights to the STING Program as standalone small molecules.

BioNTech and Ryvu will continue their multi-target research collaboration in the field of small-molecule immunotherapy under the terms and conditions concluded in the License Agreement, including the funding by BioNTech of all discovery, research, and development activities thereunder.

#### Conclusion of funding agreement with the Małopolska Centre for Entrepreneurship

On February 14, 2025, a funding agreement ("Agreement") was concluded with the Małopolska Centre for Entrepreneurship ("MCP") for the Company's project titled: "InfraADC - Research infrastructure enabling R&D activities on Antibody-Drug Conjugates (ADC) as next generation targeted therapies in oncology" ("Project"). The Company informed that the Project was recommended for funding, in the current report 35/2024 dated November 29, 2024.

The aim of the Project is to implement new technologies not previously used by the company and to adapt the DMPK (bioanalytical), biochemical, and biological laboratories accordingly. As part of the Project, the Company plans to purchase specialist research equipment and software to control and support the operation of these devices. The acquired equipment will enable work on the technology of drug-antibody conjugates (ADC). As part of the planned R&D work, the Company plans to launch new production processes, understood as a research process for the discovery and development of innovative oncological drugs, and to expand its product portfolio with ADC projects in oncology.

- the total value of the Project is: PLN 7,523,159.70;

- recommended amount of the funding: PLN 3,085,312.00;

- assumed project implementation period: 24 months.

The funding granted in connection with the conclusion of the Agreement will reduce the Company's reliance on its funds.

#### Ryvu Therapeutics announces strategic reorganization to extend the cash runway for the development of RVU120 and the preclinical pipeline

On February 25, 2025, the Management Board of the Company announced its decision to undertake strategic reorganization measures aimed at extending the Company's cash runway from Q1 to H2 2026, with a focus on driving the RVU120 clinical program and the early pipeline to key data inflection points.

As part of the strategic reorganization mentioned above, the Company has taken actions primarily in two areas:

1. Workforce reduction
2. Pipeline adjustments

**Re 1. Workforce reduction**

The Management Board of the Company informed about the completion of the consultation procedure with the representatives of the Company's employees on the intention to carry out a collective redundancy in the Company (the "Collective Redundancy") and about the adoption of the rules of the Collective Redundancy specifying the rules of conduct in matters concerning the employees affected by the intended Collective Redundancy and about the decision of the Management Board of the Company to carry out the Collective Redundancy on the terms set out in the established rules. The Collective Redundancy was carried out from February 25, 2025, to June 30, 2025, and affected approximately 30% (no more than 95) of the Company's employees. As a result of the Collective Redundancy, the Company still employed approximately 200 employees, retaining its full potential to develop the projects described below.

**Re 2. Pipeline adjustments**

The Management Board has made decisions regarding changes to the project pipeline. Current status and key project objectives in the period 2025-2026:

In case of RIVER-52 – a Phase II clinical trial of RVU120 as a monotherapy in patients with r/r AML or HR-MDS – initiated as in the Current Report No. 10/2024 dated February 14, 2024, the Management Board of Ryvu decided to suspend the enrolment of new patients to focus investment on the other RVU120 development paths. Currently enrolled patients will continue to receive treatment per protocol. Other RVU120 Phase II studies (RIVER-81, POTAMI-61, and REMARK) progress as planned. The decision to progress RIVER-81 and suspend enrolment in RIVER-52 was based on data analysis and feedback from advisory boards in February 2025.

In the RVU305 program, which the Company announced in Current Report No. 28/2024 dated September 10, 2024, IND/CTA-enabling studies are ongoing. Their completion is planned for the second half of 2025.

For preclinical discovery and research, the Company will pursue a dual-pronged strategy, each of which has the potential to generate multiple oncology medicines:

(i) **ONCO Prime – novel small molecule precision medicine**: as part of its proprietary ONCO Prime platform, Ryvu will continue to advance several novel precision oncology targets, including synthetic lethality targets.

(ii) **ADCs (antibody-drug conjugates) with novel payloads**: Ryvu will continue to develop ADCs with next-generation novel payloads, including synthetically lethal and immunomodulatory mechanisms. Ryvu will develop novel ADCs internally and through its existing collaboration with Exelixis, focusing on STING-based ADCs. The WRN

program, which was previously focused on standalone development, will be developed as a novel ADC payload program to differentiate itself in terms of efficacy, resistance profile, and safety compared to competitors.

Ryvu continues to advance three key biopharma partnerships (BioNTech, Exelixis, and Menarini), unchanged from its previous status, retaining full reimbursement for its expenses and the potential to earn financial milestones.

### Dosing of the first patient in the JASPIS-01 phase II study of dapolsertib (MEN1703, SEL24) for the treatment of patients with relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL)

On March 26, 2025, the first patient was dosed with dapolsertib (MEN1703, SEL24) in the JASPIS-01 study ("JASPIS-01 Study") for the treatment of patients with relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL). The JASPIS-01 Study is being conducted by Syneos Health, LLC, a Delaware limited liability company with principal offices located in the United States at 1030 Sync Street, Morrisville, North Carolina 27560, together with Syneos Health UK Limited, a company with principal offices located at Farnborough Business Park, 1 Pinehurst Road, Farnborough, Hampshire, GU14 7BF, England, Europe, as announced by the Company in current report no. 31/2024 dated October 18, 2024.

The JASPIS-01 Study is an open-label, Phase II clinical trial investigating dapolsertib as monotherapy and in combination with glofitamab for the treatment of patients with relapsed/refractory (r/r) DLBCL. It comprises three parts: Part 1 focuses on evaluating safety and preliminary anti-tumor activity in approximately 18 patients; Part 2 will assess, based on the results of Part 1, anti-tumor activity as a primary objective in a larger group of patients, as well as safety and tolerability; and Part 3 will offer an optional randomized comparison to show the contribution of dapolsertib and glofitamab over glofitamab alone. The JASPIS-01 Study is registered on ClinicalTrials.gov under NCT06534437. The JASPIS-01 Study was initiated at clinical sites in Poland, with plans to expand to additional EU and non-EU countries.

Dapolsertib hydrochloride is the new International Non-proprietary Name (INN) for MEN1703 (SEL24) as accepted by the World Health Organization (WHO). Dapolsertib is a selective, small-molecule, dual inhibitor of PIM and FLT3 kinases, two enzymes strongly implicated in the malignant transformation of hematopoietic cells and lymphomagenesis. The Company has discovered the compound, which is currently in clinical development in collaboration with Menarini (as defined below), as a potential therapeutic option for various cancers.

The license agreement with Berlin-Chemie AG, headquartered in Berlin, Germany, a part of the Italian Menarini Group ("Menarini"), was signed on March 28, 2017, as previously reported by the Company in current report no. 4/2017. Menarini holds global development and commercial rights to dapolsertib. Initially, dapolsertib was developed as a potential treatment for patients with relapsed/refractory (r/r) acute myeloid leukemia (AML). More details on the completed Phase I/II clinical study can be found at ClinicalTrials.gov under NCT03008187. Data from this study were presented at multiple scientific conferences and symposia.

Encouraged by promising results from translational research, Menarini decided to continue the development of dapolsertib by initiating a new Phase II study in patients with r/r DLBCL – the JASPIS-01 study. Menarini fully funds all study activities, while the Company serves as the operational partner for executing the JASPIS-01 Study on behalf of Menarini, as announced by the Issuer in the current report No. 40/2023, dated September 14, 2023.

### Decision not to enter into a Grant Agreement with the Medical Research Agency

On April 8, 2025, Management Board of the Company decided not to enter into a grant agreement with the Medical Research Agency (in Polish: Agencja Badań Medycznych, "MRA") regarding the project titled: "Identification of selection markers for patients that can benefit from the treatment with novel PRMT5 developed by Ryvu Therapeutics" (Ref. No. KPOD.07.07-IW.07-0250/24). This project had previously been recommended for funding under the Call for Proposals for Entrepreneurs to Conduct Research in the Area of Drug Safety, Innovative Therapies, and Medicines of the Future (2024/ABM/05/KPO), as reported by the Issuer in Current Report No. 3/2025 dated February 7, 2025.

The decision to withdraw from signing the agreement results from a strategic shift in the scope of the Company's translational research, which will now focus on the treatment of tumors that may benefit from the newly identified blood-brain barrier–penetrating properties of RVU305 — such as gliomas and cancers with a high propensity to metastasize to the brain.

### Conclusion of a grant agreement with the Medical Research Agency

On April 23, 2025, the Company concluded a grant agreement (the "Agreement") with the Medical Research Agency (in Polish: Agencja Badań Medycznych, "MRA") for the co-financing of the Company's project entitled: "ADCraft – next-generation small-molecule payloads for antibody-drug conjugates in oncology" (the "Project"). The Company had previously informed about the recommendation of the Project for co-financing in Current Report No. 2/2025 dated February 7, 2025.

The aim of the Project is to develop methods for discovering and testing the new generation of payloads for Antibody-Drug Conjugates (ADC), along with a portfolio of R&D activities focused on new therapeutic modalities used in oncology.

- the total net value of the Project is: PLN 13,172,227.85;

- recommended amount of the funding: PLN 9,879,170.99;

- the planned duration of the Project: 18 months.

In case the grant agreement is concluded and the Project is implemented, the granted funding may limit the use of the Company's funds.

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

The Company presented preclinical data on the RVU305 program and its synthetic lethality platform at the 2025 AACR Annual Meeting, held from April 25 to 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 with MTAP-deleted cancers that are 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 for this disease. 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 identified targets associated with common CRC driver mutations, particularly those involving 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, thereby supporting the translational potential of this approach.

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

### Receipt of a notification under Article 69 of the Public Offering Act from TFI Allianz Polska S.A. regarding the decrease below the 5% threshold of the total number of votes in the Company

On May 2, 2025 Management Board of the Company received a notification from TFI Allianz Polska S.A., acting on behalf of the following funds: Allianz FIO, Allianz Inwestycje SFIO, Allianz Plan Emerytalny SFIO, and Bezpieczna Jesień SFIO (the "Funds"), prepared in accordance with Article 69(1)(1) and Article 87(1)(2)(a) of the Act of 29 July 2005 on Public Offering, Conditions Governing the Introduction of Financial Instruments to Organized Trading, and Public Companies, regarding a decrease below the 5% threshold of the total number of votes at the Company's General Meeting.

According to the content of the notification, as a result of a sale transaction of the Company's shares carried out on 28 April 2025 (settlement date: 30 April 2025), the total share of the Funds in the total number of votes at the General Meeting of the Company decreased below the 5% threshold and currently amounts to 4.96%.

### Changes in the Management Board of Ryvu Therapeutics S.A.

On May 27, 2025, the Supervisory Board of the Company, acting pursuant to Article 368 § 4 of the Polish Commercial Companies Code (k.s.h.), appointed Ms. Justyna Żółtek to the Management Board of the Company, effective as of June 1, 2025.

Ms. Justyna Żółtek joined the Company in 2021 and has served as Chief People Officer since May 2024. She is responsible for the Administration and HR functions, including all employee development processes and the Company's internal culture.

### Data on RVU120 presented at the 2025 European Hematology Association Congress

The Company has presented data on RVU120 at the 2025 European Hematology Association Congress (EHA), which took place from June 12 to June 15 in Milan, Italy.

**Details on the oral and poster presentations are described below. The presentation related to the presented posters is attached to this report.**

**# RVU120 in combination with venetoclax in AML**

**Poster PS1509:** Preliminary results from RIVER-81, a Phase II study of RVU120+VEN in patients with AML failing first-line VEN+HMA

**Session date and time:** 14 June 2025, 6:30 pm – 7:30 pm CEST

Preliminary results from the open-label RIVER-81 Phase II clinical study demonstrate that RVU120, when combined with venetoclax (VEN), shows promising anti-leukemic activity in patients with relapsed or refractory acute myeloid leukemia (r/r AML) who failed first-line VEN-based treatment. As of May 14, 2025, 43 patients had been treated, of which 27 patients were evaluable for response across exploratory Parts 1 and 2. In total, 7 out of 27 evaluable patients (26%) achieved a complete remission with or without incomplete hematologic recovery (CR/CRi). One out of three evaluable patients from Cohort 2 achieved a complete remission (CR). 3 out of 13 evaluable patients from stage 1 of Part 2 achieved a complete remission with incomplete count recovery (CRi), suggesting that RVU120 may help overcome VEN resistance. With optimized dosing in Cohort 4 (150mg of RVU120 QD + 400mg VEN), the efficacy results have further improved – the CR rate in the evaluable population in this cohort was 50% (3 out of 6 patients. As of June 6, 2025, 4 patients who have achieved a CR/CRi across all cohorts remain in remission on study treatment. The study continues enrollment in Cohort 6 at a dose of 200mg of RVU120 QD + 400mg VEN, with the potential to maximize the duration of response. The study supports further exploration of RVU120+VEN as a potential therapeutic strategy for AML with poor prognosis. The combination has been tolerated, with nausea as the most common adverse event.

**Poster PF415:** Overcoming venetoclax resistance: synergistic potential of RVU120, a CDK8/CDK19 inhibitor, in combination treatment

**Session date and time:** 13 June 2025, 6:30 pm – 7:30 pm CEST

RVU120 demonstrates strong synergy when combined with venetoclax (VEN) to overcome resistance to VEN in the treatment of AML. Preclinical studies reveal that RVU120+VEN effectively targets key VEN resistance pathways, including IL6/JAK/STAT3, TGF-β, and PI3K/AKT/mTOR. The combination also retains efficacy in models of bone marrow stroma-mediated resistance, a common mechanism of therapy failure. These findings support the ongoing Phase II RIVER-81 trial, exploring RVU120+VEN in patients with AML who have failed prior VEN-based treatments. This research underscores RVU120's potential to improve treatment outcomes by overcoming venetoclax resistance in AML.

**# RVU120 as a monotherapy and in combination with RUX in MF**

**Poster PF861:** An Open-Label Clinical Trial of RVU120 as Monotherapy and in Combination with Ruxolitinib in Patients with Intermediate or High-Risk, Primary or Secondary Myelofibrosis (POTAMI-61)

**Session date and time:** 13 June 2025, 6:30 pm – 7:30 pm CEST

The open-label POTAMI-61 Phase II clinical trial evaluates RVU120 as a monotherapy and in combination with ruxolitinib (RUX) for patients with intermediate or high-risk myelofibrosis (MF). As of May 14, 2025, 21 patients were treated, completing the enrollment in the exploratory part. The median time on treatment was 10 weeks, with 8 patients completing at least 12 weeks of treatment, but no patient had met the follow-up for the primary endpoint at 24 weeks due to insufficient time on study. The ongoing trial is assessing spleen volume reduction, symptom burden, and safety over a 24-week period. Initial signs of clinical activity were observed in selected patients: TSS improvement was noted in 3 out of 4 patients at week 12; initial changes in spleen size reduction were observed in 4 out of 8 patients. Considering the early read-out after only 12 weeks, the data are encouraging and warrant further exploration of RVU120 in patients with MF. RVU120 was found to be tolerated by patients with MF, both when used as a single agent or in combination with RUX. The full week 24 data are anticipated in Q4 2025.

**# RVU120 in MDS**

**Oral Presentation:** RVU120 enhances erythroid potential in MDS patient-derived cells: preclinical mechanistic insights into CDK8/CDK19 inhibition and potential patient stratification

**Session date and time:** 12 June 2025, 5:00pm – 6:15pm CEST

**Session title:** s450 MDS cellular and molecular therapeutic targeting

RVU120 demonstrates significant potential in enhancing erythroid differentiation in MDS patient-derived cells confirmed by transcriptomic and functional analysis. Data show that RVU120 promotes erythropoiesis in CD34+ bone marrow cells derived from MDS patients, particularly benefiting those with differentiation defects. Results from multiple patient-derived samples indicate potential patient stratification based on ASXL1 mutations. These findings support RVU120 as a promising therapeutic candidate in the REMARK Phase II clinical study in patients with low-risk myelodysplastic syndromes (LR-MDS).

**# RVU120 as a monotherapy in AML**

**Poster PF548:** RIVER-52: A Multicenter, Open-Label Clinical Trial of RVU120 in Patients with Relapsed or Refractory High-Risk Myelodysplastic Syndrome or Acute Myeloid Leukemia

**Session date and time:** 13 June 2025, 6:30 pm – 7:30 pm CEST

The open-label RIVER-52 Phase II clinical study evaluated RVU120 monotherapy in patients with acute myeloid leukemia (AML) or relapsed or refractory high-risk myelodysplastic syndrome (HR-MDS). As of May 14, 2025, 39 patients received RVU120 (27 AML and 12 HR-MDS patients). RVU120 demonstrated a manageable safety profile, with gastrointestinal and infectious adverse events being the most common. Two patients, one NPM1-mutated and one DNMT3A-mutated, showed more than 50% bone marrow blast reduction at their C2D13 disease assessment. A patient with HR-MDS achieved a CR but was lost to follow-up. Despite relevant blast reductions in some patients, no durable CRs were observed, and enrollment was suspended. The data collected will be used to support the RVU120 safety and efficacy database.

### 2.2.2. Events occurred between the end of the reporting period until the approval of financial statement

#### Conclusion of Strategic Agreement with BioNTech SE to Support Clinical Trials for BioNTech's Investigational Cancer Immunotherapies in Poland

On September 1st, 2025, Ryvu has concluded a Strategic Agreement ("Agreement") with BioNTech SE, with its registered office in Mainz, Germany ("BioNTech"). The Agreement is of a framework nature, and specific services will be performed by Ryvu under SOWs (Scope of Work) submitted by BioNTech.

As of the date of execution of the Agreement, the total value of SOWs attributed to Ryvu is € 2,946,000 (PLN 12,542,300 converted at the average exchange rate of the National Bank of Poland on September 1st, 2025, 1 EUR = 4.2574 PLN). Based on the SOWs received, the Company will support BioNTech in the acceleration of site activation and patient enrolment for several of BioNTech's priority oncology clinical programs in Poland, in indications such as lung, breast, and colorectal cancers.

By entering into the Agreement, the parties expand the scope of their current cooperation carried out under the exclusive research collaboration and license agreement concluded on November 29, 2022 ("License Agreement"), which the Company announced in its current report No. 26/2022. Based on the Agreement, the parties plan to leverage Ryvu's operational excellence, expertise in oncology clinical operations and existing trial site network to streamline access of Polish patients to BioNTech's investigational immunotherapies.

#### RVU120 to be tested in an investigator-initiated Phase I study to treat pediatric patients with medulloblastoma

The Company has initiatied a collaboration with the Children's Memorial Health Institute (pl. Instytut „Pomnik – Centrum Zdrowia Dziecka", "IPCZD", "the Institute") as part of the MEDWAY project ("MEDWAY Project") – a new, non-commercial Phase I clinical study aimed to evaluate the CDK8/19 inhibitor RVU120 in combination with everolimus in children with recurrent or progressive Group 3 or 4 medulloblastoma. On September 9, 2025, IPCZD signed a funding agreement with the Polish Medical Research Agency (pl. Agencja Badań Medycznych "MDR") for the MEDWAY Project under a grant awarded in ABM's call for non-commercial clinical trials and research experiments in oncology (ABM/2024/2). The study will assess the safety and potential efficacy of RVU120 in combination with everolimus, targeting unique molecular mechanisms of the disease.

The study will be led by Prof. Bożenna Dembowska-Bagińska and the clinical team at IPCZD's Oncology Clinic, in collaboration with the research teams of Prof. Wiesława Grajkowska and Prof. Joanna Trubicka. The MEDWAY Project will be supported by the Pediatric Clinical Trials Support Center and the Pediatric Regional Center for Digital Medicine operating at IPCZD. Medulloblastoma is one of the most common and aggressive forms of childhood brain cancer, with limited treatment options, especially for recurrent or progressive cases.

The total value of the grant awarded to IPCZD under the MEDWAY Project is PLN 40,151,060.47. Of this amount, approximately PLN 2 million is allocated in the MEDWAY Project budget directly to cover the costs of manufacturing, preparing, and releasing the investigational medicinal product – RVU120 – for use in the planned clinical trial. These funds cover only the production costs, excluding

commercial markups or margins; however, the Company will not bear any costs related to the supply of RVU120 for the study. The first shipment of RVU120 is expected in Q2 2026. The MEDWAY Project is expected to run from July 1, 2025, to June 30, 2033, with the potential for earlier completion. Ryvu will work closely in collaboration with the IPCZD team throughout the study.

## 2.3 Unusual events occurring in the reporting period

### Conflict in Ukraine

Due to the Ukraine conflict outbreak, the Issuer's Management Board has analyzed the potential impact of the ongoing war on the Issuer's operations. In the opinion of the Management Board, apart from the currency risk, the Management Board did not identify any other significant risks that could affect the Issuer's operations.

In particular, it should be noted that the Issuer has no assets in Ukraine and does not conduct business and operations in Ukraine and Russia. The share of entities from Ukraine or Russia as suppliers in the Issuer's structure remains insignificant and is mostly limited to the provision of compound libraries for discovery stage projects at their early stage.

Nevertheless, the Company's Management Board analyzes the Issuer's situation on an ongoing basis. Any new circumstances that significantly impact the issuer's financial results and business situation will be communicated to investors.

## 3. THE ISSUER'S CORPORATE BODIES

### Issuer's Management Board:

1) Paweł Przewięźlikowski – President of the Management Board
2) Krzysztof Brzózka – Vice President of the Management Board
3) Kamil Sitarz – Member of the Management Board
4) Vatnak Vat-Ho – Member of the Management Board
5) Hendrik Nogai – Member of the Management Board
6) Justyna Żółtek – Member of the Management Board

### Issuer's Supervisory Board :

1) Piotr Romanowski – Chairman of the Supervisory Board
2) Tadeusz Wesołowski – Vice Chairman of the Supervisory Board
3) Rafał Chwast – Supervisory Board Member
4) Axel Glasmacher – Supervisory Board Member
5) Thomas Turalski – Supervisory Board Member
6) Scott Z. Fields – Supervisory Board Member
7) Peter Smith – Supervisory Board Member

### Issuer's Audit Committee:

1) Rafał Chwast – Chairman of the Audit Committee
2) Piotr Romanowski – Member of the Audit Committee
3) Tadeusz Wesołowski – Member of the Audit Committee

### The Company's Remuneration Committee:

1) Piotr Romanowski – Chairman of the Remuneration Committee
2) Axel Glasmacher – Member of the Remuneration Committee
3) Thomas Turalski – Member of the Remuneration Committee

## 4. INFORMATION ON THE SHAREHOLDERS HOLDING (DIRECTLY OR INDIRECTLY) AT LEAST 5% OF THE TOTAL NUMBER OF VOTES AT THE GENERAL SHAREHOLDERS' MEETING OF THE COMPANY AND ON SHARES HELD BY MEMBERS OF THE ISSUER'S MANAGEMENT BOARD AND SUPERVISORY BOARD

### Shares held by members of the Management and Supervisory Board of Ryvu Therapeutics S.A. as of June 30, 2025 and as of the date of publication of the Report

| Shareholder | Preferred shares* | Ordinary shares | Number of shares | % of Share Capital | Number of Votes | % of Votes at SM |
|---|---|---|---|---|---|---|
| **The Management Board** | | | | | | |
| **Paweł Przewięźlikowski** | 3 500 000 | 482 160 | **3 982 160** | 17,22% | **7 482 160** | 27,54% |
| **Krzysztof Brzózka** | | 267 321 | **267 321** | 1,16% | **267 321** | 0,98% |
| **Kamil Sitarz** | | 39 230 | **39 230** | 0,17% | **39 230** | 0,14% |
| **Vatnak Vat-Ho** | | 57 000 | **57 000** | 0,25% | **57 000** | 0,21% |
| **Hendrik Nogai** | | 22 500 | **22 500** | 0,10% | **22 500** | 0,08% |
| **Justyna Żółtek** | | 18 265 | **18 265** | 0,08% | **18 265** | 0.07% |
| **The Supervisory Board** | | | | | | |
| **Tadeusz Wesołowski (directly)** | | 92 975 | **92 975** | 0,40% | **92 975** | 0,34% |
| **Tadeusz Wesołowski (indirectly through Fundacja Rodzinna Rodziny Wesołowskich Fundacja Rodzinna w Krakowie**)** | | 1 279 738 | **1 279 738** | 5,54% | **1 279 738** | 4,71% |
| **Rafał Chwast** | | 121 115 | **121 115** | 0,52% | **121 115** | 0,45% |
| **Thomas Turalski** | | 20 100 | **20 100** | 0,09% | **20 100** | 0,07% |

**A single Series A share entitles to two votes at the Shareholder Meeting.*
***The beneficiary of Fundacja Rodzinna Rodziny Wesołowskich Fundacja Rodzinna w Krakowie is Mr. Tadeusz Wesołowski - Vice-Chairman of the Issuer's Supervisory Board.*

### Shares held by significant shareholders of the Company

**Shares held by significant shareholders of the Company as of June 30, 2025 and as of the date of the publication of the Report**

| Shareholder | Shares | % [Shares] | Votes | % [Votes] |
|---|---|---|---|---|
| Paweł Przewięźlikowski | 3 982 160 | 17,22% | 7 482 160 | 27,54% |
| Bogusław Sieczkowski | 825 348 | 3,57% | 1 375 348 | 5,06% |
| Tadeusz Wesołowski (with Fundacja Rodzinna Rodziny Wesołowski Fundacja Rodzinna w Krakowie*) | 1 372 713 | 5,94% | 1 372 713 | 5,05% |

| | | | | |
|---|---|---|---|---|
| Nationale Nederlanden OFE | 1 389 036 | 6,01% | 1 389 036 | 5,11% |
| Allianz Polska OFE | 2 132 540 | 9,22% | 2 132 540 | 7,85% |
| BioNTech SE | 1 917 437 | 8,29% | 1 917 437 | 7,06% |

**The beneficiary of Fundacja Rodzinna Rodziny Wesołowskich Fundacja Rodzinna w Krakowie is Mr. Tadeusz Wesołowski - Vice-Chairman of the Issuer's Supervisory Board.*

*The above information on the state of possession of the Issuer's shares by shareholders (including those being members of the Company's bodies) holding directly and indirectly at least 5% of the total number of votes at the Company's General Meeting has been prepared on the basis of information obtained from shareholders through their performance of duties imposed on shareholders of public companies by virtue of relevant legal regulations, including on the basis of the provisions of the Act of 29. July 2005 on public offering and the conditions for introducing financial instruments to the organized trading system and on public companies (art. 69 and art. 69a) and on the basis of the provisions of the Regulation (EU) No 596/2014 of the European Parliament and of the Council of 16 April 2014 on market abuse and repealing Directive 2003/6/EC of the European Parliament and of the Council and Commission Directive 2003/124/EC, 2003/125/EC and 2004/72/EC (MAR Regulation, art. 19). In addition, information on the ownership of the Company's shares is provided on the basis of publicly available data on the portfolio exposure and asset structure of investment funds or pension funds, including information on the number of shares registered at the Company's General Meeting (data available periodically, inter alia, based on information from the financial statements of investment funds and pension funds - data may be subject to change since the date of publication of the last information).*

# 5. MANAGEMENT BOARD STATEMENT ON ADOPTED ACCOUNTING PRINCIPLES

The management board of Ryvu Therapeutics S.A. confirms that, to the best of its knowledge, these interim condensed financial statements of Ryvu Therapeutics S.A. and comparative data have been prepared in accordance with the applicable accounting principles and reflect in a true, fair and clear manner the Company's property and financial position and its financial result.

The interim condensed report of the management board on the activities of Ryvu Therapeutics S.A. contains a true picture of the development, achievements and situation of the Company, including a description of the main threats and risks.

# 6. ADDITIONAL INFORMATION

**Proceedings pending at court, before an arbitration institution or a public administration authority**

The Company has filed a lawsuit against DUNA POLSKA S.A. (formerly: Mota-Engil Central Europe S.A.) ("Contractor") to the Regional Court in Kraków concerning the construction of the Research and Development Center under the agreement for "Construction of the Research and Development Center of Innovative Drugs Selvita S.A." dated August 13, 2018 ("Construction Agreement"). The claims include the payment of contractual penalties for failure to meet the final deadline and intermediate deadlines, as well as for rectification or untimely reflection of defects related to the scope of the Construction Agreement, totalling PLN 13,756,717.07. The total value of the Construction Agreement was PLN 68,783,585.34, including VAT. The proceedings are taking place before the District Court in Kraków in the first instance. On July 8, 2024, the Court concluded the oral hearings of witnesses and the Parties, simultaneously requiring the Parties to pay advances towards the expert's opinion (by July 22, 2024) and to inform the Court about the mutually agreed candidates for experts (by September 1, 2024). The Parties responded to the Court's request on the above-mentioned dates. The Parties responded to the Court's request within the above-mentioned deadlines. Subsequently, the Court requested the Parties to take a position on the offer of the expert selected by the Parties, who will prepare an opinion within the scope of the evidence outlined by the Parties. Both Parties accepted the offer. The files have been sent to an expert who will prepare an opinion based on the questions outlined by the Parties.

The Contractor has filed a lawsuit for payment against the Company to the Regional Court in Kraków in connection with the performance of the Construction Agreement for the project entitled: "Construction of the Research and Development Center for Innovative Drugs Selvita S.A." In the lawsuit, the Contractor is claiming damages for the costs incurred in connection with prolonged performance of the Construction Agreement, the unpaid portion of the lump sum fee as well as supplementary remuneration for additional, replacement and omitted works (PLN 5,391,425.63) as well as damages resulting from the Company's unauthorized - in the Contractor's opinion - application of the performance bond and removal of the defects and faults (PLN 2,063,507.56). With the statutory interests, the Contractor demands a total amount of PLN 7,671,285 from the Company. On 22 November 2023, the hearings of all witnesses and parties were completed. Subsequently, the files were forwarded to a court expert for the preparation of an opinion. On 8 April 2025, the expert's opinion was delivered to the Company, to which the Parties submitted objections in a procedural letter dated 30 May 2025. Currently, the Parties are awaiting the expert's response to the objections to the opinion submitted by the Parties.

**Significant non-arm's-length transactions with related entities**

Not applicable.

**Information on organizational or capital relations of the Issuer with other entities**

As of the report's publication date, the Issuer does not form a Capital Group. As at the date of this Report, the Issuer holds 1.2% of shares in NodThera Inc.

**Warranties for loans and borrowings and guarantees granted**

Not applicable.

**Other information significant for the assessment of the Issuer's position in the area of human resources, assets, cash flows, financial results and changes thereof and information significant for the assessment of the Issuer's ability to settle its liabilities**

Not applicable.

**Factors which, in the Issuer's opinion, will affect the results over at least the following quarter**

The results of the subsequent quarters will depend primarily on the execution of the Company's strategy, which assumes, in particular, that the following business objectives will be met:

- Expanding therapeutic potential of RVU120 by initiating and executing broad Phase II clinical development across multiple hematology indications and in diverse treatment settings (monotherapy and combination therapy);
- Supporting clinical development of our partnered candidate, SEL24 (MEN1703) by Menarini Group;
- Conducting preclinical development and advancing into Phase I clinical trials of one new program;
- Strengthening of our Synthetic Lethality Platform and accelerating progress in the early pipeline;
- Achieving financial milestones in the existing R&D collaborations (i.e. BioNTech, Exelixis, Menarini);
- Signing at least one new partnering agreement per year.

**Explanations regarding the seasonal or cyclical nature of the Issuer's operations in the reported period**

Not applicable.

**Information on inventory write-downs to the net realizable amount and reversal of such write-downs**

Not applicable.

**Information on impairment write-downs in respect of financial assets, tangible fixed assets, intangible assets or other assets and the reversal of such write-downs**

Not applicable.

**Information on the set-up, increase, utilization and reversal of provisions**

Information on the changes in provisions for holidays and bonuses is provided in note 17 to the financial statements.

**Information on deferred income tax provisions and assets**

No significant changes.

**Information on significant purchases or disposals of tangible fixed assets**

No significant changes.

**Information on significant liabilities in respect of purchases of tangible fixed assets**

No significant changes.

**Information on significant settlements resulting from court cases**

Not applicable.

**Error corrections relating to previous periods**

Information is provided in note 15 to the financial statements.

**Information on changes in the economic situation and business conditions, which have a significant effect on the fair value of the entity's financial assets and financial liabilities**

Not applicable.

**Information on the failure to repay a loan or borrowing or a breach of significant terms and conditions of a loan agreement, with respect to which no corrective action had been taken by the end of the reporting period**

Not applicable.

**Information on changes in the method of valuation of financial instruments measured at the fair value**

Not applicable.

**Information on changes in the classification of financial assets due to a change in their purpose**

Not applicable.

**Information on the issue, redemption and repayment of non-equity and equity securities**

Not applicable.

**Information on dividends paid (or declared) in the total amount and per share, divided into ordinary and preference shares**

Not applicable.

**Events that occurred after the date for which the quarterly financial statements were prepared, not disclosed in these financial statements although they may have a significant effect on the Issuer's future financial results**

Not applicable.

**Information on changes in contingent liabilities or contingent assets that occurred after the end of the last financial year**

Information on changes in contingent liabilities or contingent assets is provided in note 22 to the financial statements.

**Other disclosures which may have a material impact on the assessment of the Issuer's financial position and results of operations**

Not applicable.

**Amounts and types of items affecting the assets, liabilities, equity, net profit/ (loss) or cash flows, which are unusual in terms of type, amount or frequency**

Not applicable.

Krakow, September 16th, 2025

Dokument podpisany przez Paweł Tadeusz Przewięźlikowski
Data: 2025.09.16 12:10:59 CEST

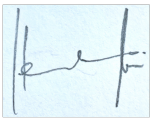
Paweł Przewięźlikowski
President of the Management Board

Dokument podpisany przez Krzysztof Daniel Brzózka
Data: 2025.09.16 09:44:03 CEST

Krzysztof Brzózka
Vice-President of the Management Board

Dokument podpisany przez Kamil Sebastian Sitarz
Data: 2025.09.16 08:43:52 CEST

Kamil Sitarz
Management Board Member



Signed by / Podpisano przez:
FRANZ HENDRIK DR. NOGAI
Date / Data: 2025-09-16 12:55

Hendrik Nogai
Management Board Member

Digitally signed by Vatnak Vat-Ho
Date: 2025.09.16 06:09:19 MDT

Vatnak Vat-Ho
Management Board Member


Elektronicznie podpisany przez Justyna Katarzyna Żółtek
Data: 2025.09.16 09:22:01 +02'00'

Justyna Żółtek
Management Board Member

# CONTACT


## RYVU THERAPEUTICS

2 Sternbacha Street

30-394 Krakow, Poland

P: +48 12 314 02 00

## GENERAL INQUIRIES

ryvu@ryvu.com


RYVU THERAPEUTICS