



**RYVU THERAPEUTICS S.A.
Q3 2024 Report**

TABLE OF CONTENTS

1. ECONOMIC AND FINANCIAL HIGHLIGHTS	2
1.1 Financial Results Obtained in the Reporting Period	2
1.2 Management Board comments to the financial results	Błąd! Nie zdefiniowano zakładki.
1.3 The Company’s Assets and the Structure of Assets and Liabilities.....	6
1.4 Current and Projected Financial Condition	7
2 MANAGEMENT BOARD INFORMATION ON ACTIVITES	8
2.1 The pipeline	8
2.2 Significant events in Q3 2023	14
2.3 Unusual events occurring in the reporting period	24
3. THE ISSUER’S CORPORATE BODIES	25
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	26
5. STATEMENT OF THE MANAGEMENT BOARD REGARDING APPLICABLE ACCOUNTING PRINCIPLES.....	28
6. ADDITIONAL INFORMATION	29

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, 2024 to September 30, 2024 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	30.09.2024	31.12.2023	30.09.2024	31.12.2023
Total assets	403,178	403,202	94,220	92,733
Short-term receivables	33,243	32,837	7,769	7,552
Cash and cash equivalents	176,467	57,939	41,239	13,325
Other current and non-current financial assets	72,995	193,213	17,058	44,437
Total liabilities	225,428	143,610	52,681	33,029
Long-term liabilities	127,906	73,907	29,891	16,998
Short-term liabilities	97,522	69,703	22,790	16,031
Total equity	177,750	259,592	41,539	59,704
Share capital	9,248	9,248	2,161	2,127

Selected data of statement of comprehensive income are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
	From 01.01.2024 to 30.09.2024	From 01.01.2023 to 30.09.2023	From 01.07.2024 to 30.09.2024	From 01.07.2023 to 30.09.2023	From 01.01.2024 to 30.09.2024	From 01.01.2023 to 30.09.2023	From 01.07.2024 to 30.09.2024	From 01.07.2023 to 30.09.2023
Revenues from sales	33,954	20,788	11,559	8,531	7,892	4,542	2,698	1,893
Revenues from subsidiaries	21,049	13,924	9,959	4,194	4,893	3,042	2,324	931
Revenues from R&D projects	18,469	14,877	3,513	3,514	4,293	3,250	820	780
Other operating revenues	83	614	2	156	19	134	1	35
Revenues from operating activities	73,555	50,203	25,032	16,395	17,097	10,968	5,842	3,639
Operating expenses	-155,135	-124,236	-51,360	-40,683	-36,060	-27,142	-11,987	-9,029
Operating expenses without Incentive Scheme and valuation of Nodthera shares	-151,215	-115,995	-49,512	-40,462	-35,148	-25,341	-11,555	-8,980
Depreciation	-7,973	-8,342	-2,503	-2,773	-1,853	-1,822	-584	-615
Valuation of Incentive Scheme	-2,951	-7,267	-710	-1,272	-686	-1,588	-166	-282
Loss from operating activities (EBIT)	-81,580	-74,033	-26,327	-24,288	-18,962	-16,174	-6,144	-5,390
Loss from operating activities (EBIT) without Incentive Scheme and valuation of Nodthera shares	-77,659	-65,792	-24,478	-24,067	-18,051	-14,374	-5,713	-5,341
Loss before income tax	-76,242	-64,358	-26,552	-18,254	-17,722	-14,060	-6,197	-4,051
Net loss	-76,383	-64,358	-26,565	-18,254	-17,755	-14,060	-6,200	-4,051
Net loss without Incentive Scheme	-73,433	-57,091	-25,856	-16,982	-17,069	-12,473	-6,034	-3,769
EBITDA	-73,607	-65,691	-23,824	-21,515	-17,109	-14,351	-5,560	-4,775
EBITDA without Incentive Scheme and valuation of Nodthera shares	-69,686	-57,450	-21,975	-21,294	-16,198	-12,551	-5,129	-4,726
Net cash flows from operating activities	-101,544	-65,067	-36,256	-7,171	-23,603	-14,215	-8,462	-1,591
Net cash flows from investing activities	128,022	-197,658	76,507	-5,460	29,758	-43,182	17,856	-1,212
Net cash flows from financing activities	92,044	241,200	23,590	-360	21,395	52,695	5,506	-80
Total net cash flow	118,522	-21,525	63,841	-12,991	27,549	-4,703	14,900	-2,883
Number of shares (weighted average)	23,120,148	22,823,447	23,120,148	23,120,148	23,120,148	22,823,447	23,120,148	23,120,148
Profit (loss) per share (in PLN)	-3.30	-2.82	-1.15	-0.79	-0.77	-0.62	-0.27	-0.18
Diluted profit (loss) per share (in PLN)	-3.30	-2.82	-1.15	-0.79	-0.77	-0.62	-0.27	-0.18
Book value per share (in PLN)	7.69	12.54	7.69	12.38	1.80	2.71	1.80	2.67
Diluted book value per share (in PLN)	7.69	12.54	7.69	12.38	1.80	2.71	1.80	2.67

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 01/01/2024 – 30/09/2024: PLN 4.3022;
 - for the period from 01/01/2023 – 30/09/2023: PLN 4.5773;
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 September 2024: PLN 4.2791;
 - as of 31 December 2023: PLN 4.3480.

1.2. Management Board comments to the financial results

In the first three quarters of 2024, Ryvu Therapeutics S.A. recognized a total operating revenue of PLN 73,555 thousand, which constitutes an increase compared to the corresponding period in 2023, when the total operating revenue amounted to PLN 50,203 thousand. This results from an increase in revenues from sales (an increase of PLN 13,166 thousand), an increase in revenues from R&D projects (an increase of PLN 3,592 thousand) and an increase in revenues from subsidies (an increase of PLN 7,125 thousand) compared to the corresponding period in 2023.

The increase in revenues from sales resulted mostly from research collaboration with BioNTech SE. Under the Research Collaboration and Exclusive License Agreement, Ryvu provides appropriately qualified employees and BioNTech funds all discovery, research and development activities under the multi-target research collaboration.

Revenues from R&D projects in the three quarters of 2024 resulted from the following transactions:

- achievement of a milestone and payment in the amount of USD 2 million based on the exclusive license agreement with Exelixis Inc. The agreement combines Ryvu's proprietary small molecule STING agonists and STING biology know-how with Exelixis' network of expertise and resources in antibody engineering, antibody-drug conjugate (ADC) technologies, and oncology therapeutics development and commercialization experience.
- recognition of a portion of the upfront payment in the amount of PLN 10,541 thousand from the exclusive Research Collaboration and Exclusive License Agreement with BioNTech SE. In accordance with the accounting policy of Ryvu and IFRS 15, in 2022 Ryvu recognized only a part of the upfront revenues. The remaining amount is recognized equally in each period for 5 years.

In the first nine months of 2024, Ryvu reported a net loss and an operating loss. The net and operating losses result from the Company's focus on increasing the value of ongoing projects that will be commercialized at a later stage of development.

The Company's net loss for the period ended September 30, 2024, amounted to PLN 76,383 thousand compared to the net loss of PLN 64,358 thousand in the corresponding period of 2023. The higher loss in the three quarters of 2024, in comparison to the corresponding period in 2023, is related to higher expenditures incurred on discovery and clinical development projects, partially compensated by a higher total operating revenue (described above).

Valuation of shares in NodThera Inc.

Valuation of shares

The Management Board of Ryvu has decided to include in the valuation of the shares held by Ryvu in NodThera, a 24.00% discount (reflecting no right to dividend and non-dilution right) to the price at which they were subscribed under the last share capital increase, i.e. issuance of series C on September 20, 2022, and the above approach was applied as of September 30, 2024.

Therefore, a share valuation of USD 2.1842 share (share price from the last financing round from September 20, 2022, including a discount corresponding to the class of shares held by the Issuer and last convertible notes and warrants financing) should be used as a basis for the calculations. As of September 30, 2024, Ryvu held 2.41% shares in NodThera on a fully diluted basis, and the total valuation of the Issuer's shares in NodThera Inc. amounts to PLN 15,933,575 (at the average NBP exchange rate of 3.8193 PLN/USD).

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

new share issue price (in USD)	2.1842
average NBP exchange rate from September 30, 2024	3.8193
new share issue price (in PLN)	8.3421
number of the Company's shares in NodThera Inc.	1,910,000
value of shares in the balance sheet as of September 30, 2024	15,933,575
value of shares in the balance sheet as of December 31, 2023	16,903,500
change in valuation – gross impact on the valuation of shares	-969,925

Disbursement of Tranches of financing from the European Investment Bank

On March 13, June 25, and September 5, 2024 respectively, the European Investment Bank (EIB) made a payment of Tranche A, B and C of financing in the amount of EUR 22.0 million. The funding from the disbursed tranches is recorded in the Company's financial statement as a financial liability (under bank loans) measured at amortized cost. On each reporting date, the Company determines the carrying amount (amortized cost) of the liability by applying the effective interest rate method, according to which the interest cost for the period is calculated.

The subscription warrants issued by the Company in connection with the financing obtained under Tranche A (215,575 warrants), B (215,575 warrants) and C (161,675 warrants) were recognized in

equity at the time of the disbursement of these tranches, as the difference between the amount of funds received from the European Investment Bank (EIB) by the Company and the initial fair value of the financial liability. The transaction costs directly related to the issuance of the warrants have been recognized in equity.

Additionally, because the put option issued by the Company creates a contractual obligation to repurchase its own equity instruments (warrants), on the day of the disbursement of Tranches, the Company recognized a liability for the amount required to settle the option in accordance with IAS 32, offset against equity. 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. If the put option expires without being exercised by the holder (European Investment Bank), the Company will reclassify the carrying value of the liability to equity.

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

As of September 30, 2024, the value of the Company's assets was PLN 403,178 thousand and decreased by PLN 24 thousand compared to the end of 2023 (PLN 403,202 thousand), mainly due to expenditures on R&D projects compensated by the disbursement of tranches from the European Investment Bank of EUR 22.0 million (described above). At the end of September 2024, the highest value of assets was cash, which amounted to PLN 176,467 thousand (at the end of 2023, it was PLN 57,939 thousand) and other financial assets of PLN 72,955 thousand (at the end of 2023, it was PLN 193,213 thousand). The slight decrease in cash and other financial assets resulted mainly from expenditures incurred on discovery and clinical development projects compensated by the above-mentioned tranche disbursements. 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 15,934 thousand.

The main item in Ryvu's equity and liabilities is equity, which amounted to PLN 177,750 thousand as of September 30, 2024 and decreased by PLN 81,842 thousand compared to December 31, 2023. The decrease in equity is primarily attributable to the above-mentioned recognition of the put option and warrants issued, as well as the net loss recorded for the period. The other source of asset funding are long-term liabilities, which amounted to PLN 127,906 thousand at the end of September 2024. The long-term liabilities are mainly related to the loan received from the European Investment Bank. Additionally, long-term liabilities include deferred income, largely related to deferred revenue from the BioNTech agreement and the infrastructure subsidy for CBR.

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

	30.09.2024	31.12.2023
Current ratio		
current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)	3.15	4.39
Quick ratio		
(current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)	3.12	4.35

Cash surpluses not used in 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 very good, considering the current cash position and the financing received from the European Investment Bank. As of September 30, 2024, the value of the Company's cash amounted to PLN 248,913 thousand (PLN 242,083 thousand in cash at the banks and PLN 6,830 thousand in bonds), and as of November 4, 2024, it was PLN 231,677 thousand (PLN 224,680 thousand in cash at the banks and PLN 6,997 thousand in bonds). 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 subsidies from the EU, financing received from EIB, funds supporting R&D projects and cash generated from the commercialization of projects allow the Company to execute its planned investments, particularly the development of ongoing and new innovative projects and 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.

PROGRAM	INDICATION	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PARTNER	EXPECTED MILESTONES
RVU120 (CDK8/19)	R/R AML/HR-MDS (RIVER-52) (monotherapy)	██████████		██████████		LEUKEMIA & LYMPHOMA SOCIETY	Initial Ph II data in 4Q24
	R/R AML (RIVER-81) (combination with venetoclax)	██████████		██████████			Initial Ph II data in 4Q24
	LR-MDS (REMARK) (monotherapy)	██████████		██████████		EMSCO	Initial Ph II data in 2Q25
	Myelofibrosis (POTAMI-61) (monotherapy and combo)	██████████		██████████			Initial Ph II data in 2Q25
	Solid Tumors (AMNYS-51)	██████████		██████████			Complete Ph I data & translational studies in 2024
MEN1703 [SEL24] (PIM/FLT3)	DLBCL	██████████		██████████		MENARINI	Initiation of Ph II in 4Q24
SYNTHETIC LETHALITY							
RVU305 (PRMT5)	SOLID TUMORS	██████████					IND/CTA submission in 2H25
WRN	SOLID TUMORS	██████████					In lead optimization
NOVEL TARGETS	ONCOLOGY	██████████					
IMMUNO-ONCOLOGY							
STING & MULTI-TARGET IMMUNE MODULATION COLLABORATION	ONCOLOGY	██████████				BIONTECH	
STING ADC	ONCOLOGY	██████████				EXELIXIS	

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, having central roles in the maintenance of cancer cell viability and undifferentiated state for a variety of tumor types (Dannappel et al. 2019; Rzymiski 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.

The latest data of Part 2 of AMNYS-51 were presented at the EORTC-NCI-AACR Symposium in October 2024. Part 2 of the trial assessed the safety and tolerability of RVU120 at doses of 100 mg and 150 mg given every day for 21 days in a 21-day cycle. The findings confirmed the favorable safety profile of RVU120 in a heavily pretreated, unselected patient population. No dose-limiting toxicities or other relevant safety signals were observed. Low-grade nausea and vomiting were the most frequently reported adverse events in both parts of the study. While systemic exposure at 100 mg and 150 mg every day is similar to the equivalent dose when administered every other day, 150 mg every day may improve the tolerability of RVU120 compared to 250 mg every other day. Six out of 8 patients with adenoid cystic carcinoma achieved a longer duration of treatment on RVU120 compared with their most recent prior line of therapy. A reduction of more than 10% of target lesions was observed in 3 patients with adenoid cystic carcinoma.

The latest update of the CLI120-001 (RIVER-51) study clinical study was presented at the 29th European Hematology Association Congress (EHA) in June 2024 in Madrid. Data showed that doses up to 250 mg have been tolerated in patients with AML or HR-MDS, with the 250 mg dose demonstrating a target engagement level of 50%-70%. Based on the preclinical data, this level is predicted to produce robust antileukemic efficacy in selected populations and combinations. Identifying a therapeutic window confirms CDK8/19 inhibition as a viable approach for cancer therapies. In the CLI120-001 (RIVER-51) study, RVU120, as a single agent, demonstrated signs of clinical activity in 15 out of 30 evaluable patients (50%). This includes a complete response, a morphologic leukemia-free state, and several patients with blast reductions, hematologic improvement, or reduction of bone marrow fibrosis. In particular, early signs of efficacy were observed in patients with NPM1 mutation, DNMT3a mutation, and in patients with HR-MDS.

Considering the currently available translational and clinical data, Ryvu is executing a Clinical Development Plan (CDP) for RVU120 that includes four Phase II studies: RIVER-81, RIVER-52, REMARK and POTAMI-61. The focus of RVU120 CDP is on hematologic malignancies. While translational research is ongoing to determine the opportunities for RVU120 in solid tumors, a clinical study in patients with specific solid tumors is not yet planned.

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. The first update of this study was presented at the 29th European Hematology Association (EHA) Congress in June 2024 in Madrid. Dose level 1 (125 mg of RVU120 and 200 mg of venetoclax) was completed, and the dose of RVU120 was escalated to 250 mg, corresponding to the RP2D of RVU120 as a single agent. At dose level 1, no new safety signals were observed with RVU120 when

combined with venetoclax. Enrollment into dose level 2 (250 mg of RVU120 and 200 mg of venetoclax) had been initiated at the time of the EHA disclosure. On September 2, 2024, the Data and Safety Monitoring Board (DSMB) reviewed the data from dose level 2 and recommended escalation to dose level 3 (250 mg of RVU120 and 400 mg of venetoclax). The enrollment in this cohort is now complete, and the next DSMB meeting to perform a safety evaluation and to recommend the next steps of the trial is planned to be held shortly.

The RIVER-81 study was initially launched at the clinical sites in Poland and Italy, followed by the activation of additional sites in Spain and France. As of October 31, 2024, there had been 33 sites activated out of a total of 34 sites that the Company plans to activate in the aforementioned four countries by the end of the year. Ultimately, the study will expand to other EU and non-EU countries, covering up to 50 clinical sites globally. The planned overall enrollment for the study 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).

RIVER-52 Phase II study

On February 14, 2024, Ryvu announced the dosing of the first patient in the RIVER-52 Phase II study of RVU120 as a single agent (NCT06268574). 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. At the 29th European Hematology Association Congress in June 2024 in Madrid, data from the first 10 patients across four cohorts were presented. The safety profile was confirmed with gastrointestinal events being the most frequent adverse events, mainly grade 1 or 2. The data were immature for efficacy evaluation. Four patients discontinued treatment without achieving a response. Six patients were ongoing at the data cut-off. One of those, a patient with AML harboring a DNMT3A mutation, showed a peripheral blast reduction in the first cycle and an increase of the hemoglobin level of 1 g/dl average in the first month of RVU120 treatment compared to the month before study entry.

The RIVER-52 study was initially launched at clinical sites in Poland and Italy. Starting in September 2024, the study expanded to Spain, France and Canada. During the summer, the site activation process was slower than expected, primarily due to the limited availability of the site staff. This, along with the presence of competing clinical studies at several sites negatively impacted the enrollment rate vs. the original expectations. Increased site activation efforts, as well as additional actions taken to maximize enrollment, resulted in a return to expected patient enrollment levels starting from September 2024. As of October 31, 2024, 33 sites had been activated for enrollment, more than doubling the number of active sites since the status reported on August 31, 2024, when 16 sites were active. Ryvu aims to activate a total of 46 sites by the end of Q4 2024. Subsequently, the study will also expand to other EU and non-EU countries, reaching up to 80 clinical sites globally. The planned overall enrollment for the study is approximately 140 patients.

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.

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). 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. The most recent translational research update was presented at the 29th European Hematology Association (EHA) Congress in June 2024 in Madrid. It was shown that RVU120 successfully attenuates myelofibrosis phenotypes when used as a single agent or combined 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 initially launched at clinical sites in Poland and Italy. As of October 31, 2024, five clinical sites have been activated for enrollment, with a total of 18 sites planned to be activated across these two countries by the end of 2024. Treatment of the first patients is expected to commence shortly.

The four 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 Q1 2026.

Ryvu aims to provide the next data update and progress report during a webinar on December 12, 2024.

Based on the study outcomes from all the RVU120 Phase II studies within the current Clinical Development Plan, Ryvu aims to prioritize further development options in Q1 2025. Clinical trials conducted in various hematological indications and treatment regimens (monotherapy and combination therapy) will contribute to RVU120's safety database, supporting potential future regulatory approvals.

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

MEN1703 (SEL24)

MEN1703 (also known as 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 in 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, MEN1703 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 was 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 MEN1703 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 has increased its involvement in the program by becoming 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 MEN1703 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 is scheduled to be initiated in Q4 2024, and start-up activities are already underway. The study will initially commence at clinical sites in Poland, with the plan to expand to additional EU and non-EU countries still within Part 1. The study is registered on ClinicalTrials.gov under NCT06534437.

Additionally, in April 2024, at the AACR Annual Meeting in San Diego, California, Menarini presented preclinical data for the MEN1703 project, which shows cytotoxic activity in myelofibrosis cell lines as monotherapy and synergistically in combination with ruxolitinib.

PRECLINICAL AND DISCOVERY STAGE PROJECTS

Synthetic lethality projects

RVU305 - PRMT5

Ryvu is actively involved in multiple early-stage projects in synthetic lethality. The lead project in this area is the PRMT5 program, which targets cancers characterized by the deletion of the MTAP metabolic gene, a phenomenon observed in approximately 10 to 15% of all human tumors. This deletion leads to a substantial methylthioadenosine (MTA) build-up 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 methylome activity. Ryvu's strategic approach involves developing MTA-cooperative PRMT5 inhibitors that selectively impede the growth of cancer cells with MTAP deletions.

On September 9, 2024, the Management Board of the Company decided to advance Ryvu's potentially best-in-class, MTA-cooperative, PRMT5 inhibitor RVU305 to further steps of preclinical development, including toxicology and API/IMP manufacturing, targeting IND/CTA filing in H2 2025. RVU305 exhibits robust antiproliferative activity in MTAP-null cancer models, including over 100% tumor growth

inhibition (TGI) and multiple complete remissions (CRs) at several dose levels in a lymphoma MTAP-deleted tumor model. Tolerability and selectivity towards MTAP-deleted cells were also demonstrated in in vitro and in vivo preclinical models. Data on RVU305, including a summary of the optimization progress and in vivo results in a mouse model showing tumor growth inhibition in several models, were presented at the annual EORTC-NCI-AACR conference in Barcelona, Spain, in October 2024. Poster presentation is available on the company website under the following link: <https://ryvu.com/investors-media/publications/>

WRN

In the second project under our synthetic lethality portfolio, we aim to discover and develop best-in-class inhibitors targeting Werner's helicase (WRN). WRN helicase plays a pivotal role in essential cellular processes, including cell proliferation, response to replicative stress, and DNA repair. Impaired DNA repair mechanisms, particularly the loss of function in unpaired DNA fragments, are frequently observed in the early stages of cancer development and contribute to 10-30% of cases in endometrial, colorectal, ovarian, and gastric cancers. WRN inhibitors induce double-strand DNA breaks (DSBs), triggering apoptosis and cell cycle arrest in microsatellite instability-high (MSI-H) cancer cell lines. This selectivity highlights the therapeutic potential of WRN helicase inhibitors, as they effectively target MSI-H cancers while sparing microsatellite-stable (MSS) cells, minimizing toxicity in non-cancerous tissues.

During Q3 2024, we focused on the selection and characterization of optimized lead compounds with enhanced potency and favorable pharmacokinetic (PK) profiles. Several promising candidates were selected and evaluated in efficacy studies and PK assessments in higher animal species, including dogs and monkeys which revealed very favorable PK profile. In vivo efficacy studies for the top compound demonstrated superior tumor growth inhibition compared to both the previous lead candidate and the standard reference compound. Furthermore, the correlation between efficacy, biomarker data, and exposure enabled us to project human efficacious doses with greater accuracy. No safety liabilities were observed in vitro, including assays for hERG inhibition, mutagenicity, and CYP inhibition. Strategies and future plans have been established to accelerate the progress and differentiation of our WRN project and advanced molecules in this highly competitive space. Data on the Company's WRN inhibitor project and optimized lead molecule data were presented at the annual EORTC-NCI-AACR conference in Barcelona, Spain, in October 2024. Poster presentation is available on the company website under the following link: <https://ryvu.com/investors-media/publications/>

New, undisclosed targets and target discovery

In addition to our disclosed projects, Ryvu is accelerating internal initiatives aimed at identifying and validating novel synthetic lethal targets for first-in-class drug discovery and new small molecules suitable for anticancer therapies. We have made significant strides in validating innovative therapeutic targets and new therapeutic approaches. Through the ONCO Prime platform, we have successfully identified promising new synthetic lethal targets in colorectal cancer and initiated efforts to develop new treatment options for patients with unmet medical needs. Ryvu disclosed advancements in the ONCO Prime platform at the RAS-targeted Drug Development Summit in Boston in September and at the annual EORTC-NCI-AACR conference in Barcelona, Spain in October 2024. Poster presentation from the conference is available on the company website under the following link: <https://ryvu.com/investors-media/publications/>

Collaboration with BioNTech on Cancer Immunotherapy and STING

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.

Furthermore, as part of this collaboration, under the signed agreement, BioNTech was granted exclusive rights for of a range of small-molecule STING agonists originally discovered and developed by Ryvu. The progress of the project is confidential.

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. During the optimization work, opportunities were discovered for molecular structure modifications that enable the combination with reactive chemical groups, allowing the formation of antibody-drug conjugates (ADCs). The appropriately selected antibody will be a carrier for the STING protein agonist. Ryvu has received two milestones in this collaboration so far, in Q1 2023 and Q1 2024, and further progress on the project remains confidential.

2.2. Significant events in Q3 2023

A) DURING THE REPORTING PERIOD

Resignation of a member of the Company's Supervisory Board from his position

On January 3, 2024, the Company received a statement of resignation of Mr. Jarl Ulf Jungnelius from his position as a member of the Company's Supervisory Board, effective immediately, without stating the reason thereof.

Take-up of series K subscription warrants by the European Investment Bank

On January 17, 2024, the Company entered into an agreement with the European Investment Bank with its seat in Luxembourg ("EIB") for the subscription of series K subscription warrants ("Warrants"), under which the EIB subscribed for 592,825 (five hundred and ninety-two thousand eight hundred and twenty-five) Warrants, each of which entitles to subscribe for one series K share of the Company. The Warrants were taken up by the EIB free of charge. The National Depository for Securities (in Polish: Krajowy Depozyt Papierów Wartościowych S.A.) stated registration on February 1, 2024, in the securities depository of 592,825 (five hundred and ninety-two thousand eight hundred and twenty-five) series K subscription warrants under ISIN code PLSELVT00088.

Dosing of the first patient in the RIVER-81 Phase II study of RVU120 in combination with venetoclax

On January 31, 2024, the Company announced that the first patient had been dosed with the study drugs in a Phase II clinical trial investigating RVU120 in combination with venetoclax for the treatment of patients with relapsed/refractory acute myeloid leukemia (r/r AML)—the RIVER-81 study (NCT06191263). The Study is part of the RVU120 development plan (as reported above). Execution of the Study is supported with a PLN 62.3 million grant from the Polish Medical Research Agency (ABM).

Achievement of the second milestone under license agreement with Exelixis Inc.

On February 3, 2024, the Company has received a notice that the second milestone has been achieved in the research collaboration with Exelixis Inc. with its registered office in Alameda, California ("Exelixis") under the license agreement dated July 6, 2022 (the "Agreement"). The Agreement aims to develop novel targeted therapies using the STING (STimulator of INterferon Genes) technology developed by Ryvu. Based on the achievement of the milestone, Ryvu is entitled to receive a payment of USD 2 million (PLN 7 928 200 converted at the average exchange rate of the National Bank of Poland on February 2, 2024, 1 USD = 3.9641 PLN).

Dosing of the first patient in the RIVER-52 Phase II Study of RVU 120 as a monotherapy for the treatment of patients with relapsed/refractory AML and HR-MDS

On February 14, 2024, the Company announced that the first patient had been dosed with the study drug in a Phase II clinical trial investigating RVU120 as a monotherapy for the treatment of patients with relapsed/refractory acute myeloid leukemia (r/r AML) and high-risk myelodysplastic syndromes (HRMDS)—the RIVER-52 study. The Study is part of the RVU120 development plan (as reported above).

Fulfillment of conditions for the disbursement of the Tranche A of financing from the European Investment Bank

On March 5, 2024, the Company received from the European Investment Bank ("EBI") confirmation that the Company has fulfilled all conditions for the disbursement of the first tranche of financing ("Tranche A") under the financing agreement concluded on 16 August 2022. As a result, the Company expects to receive on March 13, 2024, an amount of EUR 8,000,000.00 (34,582,400.00 PLN converted at the average exchange rate of the National Bank of Poland on March 5, 2024, 1 EUR = 4.3228 PLN). The Company is obliged to repay Tranche A by March 13, 2029. After the disbursement of Tranche A, EBI will be entitled to (i) convert 215.575 subscription warrants (constituting 36,364% of all the 592.825 subscription warrants held by EBI) into 215.575 ordinary bearer shares of series K of the Company, (ii) dispose of the subscription warrants, (iii) require from the Company the purchase of the subscription warrants for their cancellation, all under the terms specified in the subscription warrant issuance agreement concluded on 4 May 2023.

Conclusion of an agreement in the area of operational execution of RVU120 Phase II clinical trial in myelofibrosis

On March 28, 2024, the Company informed about the conclusion of an agreement with Fortrea Inc., headquartered in North Carolina, US ("Fortrea"), covering the operational execution of the POTAMI-61 clinical study ("Agreement"). The conclusion of the Agreement marks another step in the implementation of the RVU120 development plan ("Development Plan"), as announced by the Company in the current report 45/2023 on October 23, 2023.

The subject of the Agreement is the operational execution of the POTAMI-61 clinical study – a global, multicenter, Phase II study investigating RVU120 as a monotherapy and in combination with ruxolitinib for the treatment of patients with intermediate or high-risk, primary or secondary myelofibrosis. Services provided under the Agreement will encompass various aspects of clinical study execution,

including clinical project management, medical and safety monitoring, as well as clinical site management and monitoring.

The POTAMI-61 study consists of two parts. Part A is designed to evaluate the safety and anti-tumor activity of RVU120 as a monotherapy and in combination with ruxolitinib in a group of approximately 20 patients. Based on the outcomes of Part A, Part B will further assess safety, tolerability, and anti-tumor activity in a larger cohort, totalling up to approx. 230 patients for both Part A and Part B combined.

Following the RVU120 Development Plan, the Management Board intends to proceed with the execution of Part A of the POTAMI-61 study, as described above. The estimated cost for all study start-up activities and the execution of Part A under the Agreement is approx. EUR 3 million. This includes all relevant services, as well as fees for investigators and clinical site-related procedures.

If the Management Board decides to proceed with Part B of the study (enrolling up to approximately 230 patients), the total value of the Agreement will amount to approximately EUR 16.4 million. Further decisions regarding prioritizations within the RVU120 Development Plan, including a decision on the potential initiation of Part B of the POTAMI-61 study, are scheduled to be made in Q1 2025.

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

On April 10, 2024, the Company informed that on April 9, 2024, during the 2024 AACR Annual Meeting, Sand Diego, California, USA ("Conference"), the Company presented updated preclinical data from its synthetic lethality pipeline and RVU120. Moreover, on April 7, 2024, preclinical data on MEN1703 (SEL24) was presented by the Company's partner Menarini Group.

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

- Company's PRMT5 program in MTAP-Deficient cancers showing that Ryvu PRMT5 inhibitors show potential best-in-class profiles, including a strong antiproliferative effect on MTAP-deleted cell lines and a good safety window versus MTAP WT cells.
- Ryvu's WRN inhibitors program has demonstrated target engagement and selective potency with a synthetic lethal effect; in vivo efficacy studies exhibited pronounced tumor growth inhibition in an MSI-H colorectal cancer xenograft model.
- Ryvu's proprietary ONCO Prime discovery platform has identified novel drug targets in KRAS-mutant patient-derived cells (PDCs) with therapeutic potential in colorectal cancer; the ONCO Prime platform has broad potential across multiple tumor types.
- MEN1703 (SEL24), presented by the Company's partner Menarini Group, shows cytotoxic activity in myelofibrosis cell lines as monotherapy and synergistically in combination with ruxolitinib.

Conclusion of Funding Agreement with the National Centre for Research and Development

On May 27, 2024 a funding agreement ("Agreement") was concluded by the Company with the National Centre for Research and Development ("NCBR") for the Company's phased project titled "New targeted therapy for tumors with MTAP gene deletion - Phase II" ("Phased Project"). The Agreement

was concluded as part of the National Centre for Research and Development's SMART Pathway - Phased Projects competition, which enables obtaining funding for the implementation of Phase II of projects selected for funding based on the 2014-2020 perspective regulations under the Smart Growth Operational Programme 2014-2020 (SG OP), sub-measure 1.1.1 or measure 1.2. (research and development projects).

The Phased Project is subject to the Company's project with the funding agreement number: POIR.01.01.01-00-0638/18-00 titled: "New targeted therapy for tumors with MTAP gene deletion" ("Project"), aimed at the development and implementation of a next-generation oncology drug candidate characterized at the level of Phase I clinical trial. This candidate is a targeted therapy based on the phenomenon of synthetic lethality in tumors with MTAP deletion. As MTAP deletion is one of the most common genetic alterations found in human cancers, this gives hope for creating a targeted therapy for a significant population of cancer patients (up to 15%).

Rvvu is utilizing this mechanism in the implementation of the project for MTA-cooperative inhibitors of PRMT5 protein activity, with the selection of a preclinical candidate planned for 2024.

The Phased Project includes preclinical development and Phase I clinical study. The total funding in the form of a grant may amount to a maximum of PLN 10.28 million, which constitutes approximately 45% of the eligible costs of the Phased Project. The execution period for the Phased Project is up to 50 months, with the Agreement allowing for changes to the schedule. The funding will be disbursed in tranches, according to the schedule specified in the Agreement.

Under the Agreement, the Company has committed to implementing the results of the Project, i.e., the results of the R&D work, within 3 years of its completion, either by incorporating the results into its own business activities, granting a license to use the rights to the R&D results, or selling the rights to the results to the third party on market terms.

Obtaining the status of Associate Partner within IPCEI Med4Cure

On May 28, 2024, the Board of Directors of the Company has received information that the European Commission has approved the first Important Project of Common European Interest ("IPCEI") to support research, innovation and the first industrial deployment of healthcare products, as well as innovative production processes of pharmaceuticals. As part of the approved "IPCEI Med4Cure" project, jointly notified by six member states - Belgium, France, Spain, Slovakia, Hungary and Italy - the Company was officially announced as one of 11 and the only Associated Partner from Poland.

The Associated Partner status is the result of a successful selection at the national level in a targeted call for innovative projects in the field of health organized by the Ministry of Development and Technology. The subject of the project submitted by the Company under the working name PANACEA-NOVO to IPCEI Med4Cure is the creation of a unique platform for the discovery of new therapeutic targets with potential in the treatment of rare cancers, combined with several early discovery campaigns for innovative drugs.

The European Commission's decision to grant the Company Associate Partner status does not yet mean that the Company has been granted financing. Obtaining the above status means that the Company has been qualified for the final stage of the process, which will be participation in a dedicated

call at the national level. The results of the call will be a final decision on the terms, scope and intensity of funding. The date for the announcement of the call has not yet been set.

The Management Board expects the total costs of the project to be submitted to the call to amount to not more than PLN 142.5 million. At this stage, the Management Board of the Company expects that the majority of project activities will meet the criteria for industrial research, for which the funding intensity in similar projects is about 75-80%. The Company estimates that the project may start in 2025 and will last between 60 and 72 months.

The Company's Management Board expects that most of the work in the project will be performed by current employees and does not anticipate a significant increase in employment related to the PANACEA-NOVO project.

Conclusion of funding agreement with the Polish Agency for Enterprise Development

On June 3, 2024, the Company has concluded a funding agreement ("Agreement") with the Polish Agency for Enterprise Development ("PARP") for the Company's project titled: "ONCO Prime: new possibilities for personalised anti-cancer therapy based on patient-derived primary cell cultures, omics characterisation and functional assays" ("Project").

The Project is a significant component of the Company's plans in the area of the early pipeline. Its goal is to enable fighting cancer more effectively by creating the innovative ONCO Prime research platform, which addresses a number of current challenges and barriers in the development of new, personalized anti-cancer therapies.

The establishment of a new platform for discovering innovative therapeutic targets using unique patient-derived primary cancer cell cultures will open entirely new possibilities for identifying previously unknown targets, molecular classification of patients, and drug testing. The ONCO Prime platform will become a source of new cancer models with the highest translational potential, containing medical history, histopathological, genomic as well as transcriptomic data, enabling the correlation of clinical and molecular data.

- The total net value of the Project is: PLN 39 176 251.50;
- The maximum amount of the funding: PLN 26 339 315.38;
- The maximum Project implementation period: 56 months.

The funding granted in connection with the conclusion of the Agreement will reduce the use of the Company's own funds.

Preclinical data on RVU120 and Synthetic Lethality Programs presented at the 2024 European Hematology Association Congress

On June 14, 2024, the Company presented clinical and preclinical data from RVU120 at the 2024 European Hematology Association Congress (EHA), June 13,-16, Madrid, Spain.

Details on the poster presentations are as follows:

Poster Title: RVU120, a first-in-class CDK8 inhibitor for the treatment of relapsed/refractory AML and high-risk MDS: preliminary results from two ongoing studies.

The poster includes data on 30 evaluable patients out of 38 total dosed patients in the phase I trial (RIVER-51) and initial data from the phase II trial (RIVER-52).

- RVU120 as single agent showed clinical benefit in a heavily pretreated population with AML and HR-MDS in the phase I trial CLI120-001 (RIVER-51). The strongest evidence of benefit was observed in patients with NPM1 and/or DNMT3A mutations, and in patients with HR-MDS.
- At the poster presentation's data cut-off, RIVER-52, the phase II trial of RVU120 in monotherapy for patients with relapsed/refractory AML and HR-MDS, had immature data for efficacy assessment in the target population, even though preliminary signs of clinical benefit had been observed in ongoing patients.
- The safety and tolerability of RVU120 at the RP2D of 250 mg administered every other day was confirmed in patients treated in both trials, with mild or moderate gastrointestinal events being the most frequently reported.

Poster Title: Synergistic potential of RVU120, a first-in-class CDK8/CDK19 inhibitor, with venetoclax in AML: preclinical and initial clinical insights.

- Ryvu presents a mechanism of synergy between RVU120 and venetoclax in preclinical models of acute myeloid leukemia (AML).
- The combination of RVU120 and venetoclax leads to caspase-dependent degradation of MCL-1 protein and represses inflammatory and AML oncogenic pathways at the transcriptomic level in AML cells.
- RVU120, when combined with venetoclax, exerts cytotoxic and differentiating effects on leukemic stem cells (LSCs) from a hierarchical AML model, surpassing the efficacy of venetoclax alone.
- By countering therapeutic failure caused by persistent LSCs and MCL-1-mediated venetoclax resistance, this combination offers hope to patients with AML in the refractory and the frontline setting.
- Initial data from the ongoing Phase II study RIVER-81 demonstrate the safety of RVU120 in combination with venetoclax at the initial dose level in patients with relapsed/refractory AML. Enrollment is currently ongoing in Cohort 2.

Poster Title: CDK8/19 Inhibition: A Promising Therapeutic Strategy in Myeloproliferative Neoplasms.

- In murine models of disease, RVU120 effectively attenuates myeloproliferative neoplasms (MPN) phenotypes (single-agent or combined with ruxolitinib (RUX)) partly through downregulation of pro-inflammatory cytokines.
- RVU120 exhibits synergy with a whole class of JAK inhibitors and the BET inhibitor pelabresib. These exciting findings open new potential therapeutic options for MPN patients, including myelofibrosis.
- The combination of RVU120 and RUX acts synergistically by downregulating JAK/STAT signaling and inflammatory pathways at the transcriptomic level.

- Based on compelling preclinical results, Ryvu Therapeutics is launching the clinical study POTAMI-61 (NCT06397313). This study will evaluate RVU120 as a single agent or in combination with ruxolitinib in patients with myelofibrosis.

Fulfillment of conditions for the disbursement of the Tranche B of financing from the European Investment Bank

On June 17, 2024, the Company received confirmation from the European Investment Bank (“EIB”) that it has fulfilled all conditions for the disbursement of the second tranche of financing (“Tranche B”) under the financing agreement concluded on August 16, 2022.

As a result, the Company expects to receive on June 25, 2024, an amount of EUR 8,000,000.00 (34,864,800.00 PLN converted at the average exchange rate of the National Bank of Poland on June 14, 2024, 1 EUR = 4.3581). The Company is obligated to repay Tranche B by June 25, 2029.

Fulfillment of conditions for the disbursement of the Tranche C of financing from the European Investment Bank

On August 28, 2024 the Company received from the European Investment Bank (“EIB”) confirmation that the Company has fulfilled all conditions for the disbursement of the third tranche of financing (“Tranche C”) under the financing agreement concluded on August 16, 2022.

As a result, the Company received on September 5, 2024, an amount of EUR 6,000,000.00 (25,630,200.00 PLN converted at the average exchange rate of the National Bank of Poland on September 05, 2024, 1 EUR = 4.2717). The Company is obligated to repay Tranche C by September 5, 2029.

Continuation of the development of PRMT5 program

The Management Board on September 9, 2024, based on the results of works on MTA-cooperative PRMT5 inhibitors, which showed best-in-class potential, favorable drug-like properties and effective PRMT5 inhibition dependent on MTA binding and taking into the account that:

- Ryvu PRMT5 inhibitors showed robust antiproliferative effects on a range of MTAP-deleted cell lines, providing a good safety window for MTAP WT cells;
- Further characterization did not reveal any significant liabilities;
- Compounds showed an excellent correlation between compound exposure and on-target effect in PK/PD studies and very good efficacy in in vivo xenograft models;

has decided to advance Ryvu’s potentially best-in-class PRMT5 inhibitor RVU305 to further steps of preclinical development, including toxicology and API/IMP manufacturing, targeting IND/CTA filing in H2 2025.

Dosing of the first patient in the REMARK Phase II Study of RVU120 for the Treatment of Anemia in Patients with Lower-Risk Myelodysplastic Syndromes (LR-MDS)

On September 19, 2024 the first patient has been dosed in the REMARK study (“REMARK Study”), a Phase II clinical trial investigating RVU120 as a monotherapy for the treatment of patients with lower-risk myelodysplastic syndrome (LR-MDS).

REMARK Study is an open-label, multicenter Phase II study of RVU120, a novel small-molecule cyclin-dependent kinase (CDK) 8/19 inhibitor; the study aims to treat anemia in patients with LR-MDS. In REMARK Study, RVU120 is being explored as a single agent in patients with LR-MDS who have exhausted available treatment options.

The REMARK Study is being conducted as an investigator-initiated study through the EMSCO network. Prof. Uwe Platzbecker, a globally renowned expert in the field of LR-MDS, is the Coordinating Principal Investigator.

REMARK Study represents the third of four planned RVU120 Phase II clinical studies scheduled for launch in 2024. Ryvu has already started patient treatment in the RIVER-81 (r/r AML; RVU120 in combination with venetoclax) and RIVER-52 (r/r AML and HR-MDS; RVU120 as monotherapy) studies, as reported by Ryvu in current report 5/2024 dated January 31, 2024, and current report 10/2024 dated February 14, 2024 respectively. In the near future, the Company also plans to begin patient recruitment for the POTAMI-61 study, evaluating RVU120 both as a monotherapy and in combination therapy for the treatment of patients with myelofibrosis (MF).

2.2.1. EVENTS OCCURRED BETWEEN THE END OF REPORTING PERIOD UNTIL THE APPROVAL OF FINANCIAL STATEMENT

Conclusion of an agreement in the area of operational execution of MEN1703 (SEL24) Phase II clinical trial in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL)

On October 18, 2024, the Company concluded an agreement with 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 (“Syneos”), covering the operational execution of the JASPIS-01 clinical study (“Agreement”).

The JASPIS-01 study is an open-label, Phase II clinical trial investigating MEN1703 (SEL24) 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 is scheduled to initiate in Q4 2024, and start-up activities are already underway. The study will initially commence at clinical sites in Poland, with the plan to expand to additional EU and non-EU countries still within Part 1. The study is registered on ClinicalTrials.gov under NCT06534437.

The subject of the Agreement is the operational execution of Part 1 of the JASPIS-01 study. It includes services related to clinical study execution, such as clinical project management, medical and safety monitoring and clinical site management.

The total cost of the Agreement, €3,821,572.99, includes all the relevant services, as well as fees for investigators and clinical sites-related procedures. Additionally, costs associated with the study start-up activities already performed by Syneos under the Initial Service Agreement (“ISA”) are also included in the total amount of the Agreement. All costs of the Agreement will be fully reimbursed by the Company's partner, Menarini Group (as defined below). This reimbursement is in line with an agreement concluded between the Company and Berlin-Chemie AG with its registered office in Berlin, Germany, part of the Italian Menarini Group (“Menarini Group”), as reported by the Issuer in current report no. 40/2023 dated September 14, 2023.

Syneos Health is a contract research organization (CRO) that provides comprehensive services for drug development. It supports pharmaceutical and biotechnology companies through all phases of clinical trials, offering expertise in areas like regulatory affairs, patient recruitment, and data management to facilitate the efficient delivery of new therapies.

The Agreement meets the criteria of a significant agreement due to its importance for further developing the MEN1703 clinical program. The terms of the Agreement do not deviate from the conditions customarily accepted for this type of agreement.

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

The Company has presented four posters with clinical and preclinical data from RVU120 (CDK8/19 inhibitor), RVU305 (MTA-cooperative PRMT5 inhibitor), WRN and the 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, the 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.

2.3. Unusual events occurring in the reporting period

Conflict in Ukraine

Due to the outbreak of the conflict in Ukraine, 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 Management Board of the Company analyzes the Issuer's situation on an ongoing basis. Any new circumstances having a significant impact on the financial results and business situation of the Issuer 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

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) Jarl Ulf Jungnelius – Supervisory Board Member*
- 6) Thomas Turalski – Supervisory Board Member
- 7) Scott Z. Fields – Supervisory Board Member
- 8) Peter Smith – Supervisory Board Member

** Mr. Jarl Ulf Jungnelius resigned from the position of a member of the Supervisory Board, effective January 3, 2024*

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
- 4) Jarl Ulf Jungnelius – Member of the Audit Committee

Issuer'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 Rvvu Therapeutics S.A. as of 30.09.2024 and as of the date of Report publication

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	516 985	4 016 985	17,37%	7 516 985	27,67%
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		13 500	13 500	0,06%	13 500	0,05%
The Supervisory Board						
Tadeusz Wesołowski (directly)		92 975	92 975	0,40%	92 975	0,34%
Tadeusz Wesołowski (indirectly through Augebit FIZ**)		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 Augebit FIZ is 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 30.09.2024 and as of the date of Report publication

Shareholder	Shares	% [Shares]	Votes	% [Votes]
Paweł Przewięźlikowski	4 016 985	17,37%	7 516 985	27,67%
Bogusław Sieczkowski	825 348	3,57%	1 375 348	5,06%
Tadeusz Wesołowski (with Augebit FIZ*)	1 372 713	5,94%	1 372 713	5,05%
Nationale Nederlanden OFE	1 817 324	7,86%	1 817 324	6,69%

Allianz Polska OFE	2 132 540	9,22%	2 132 540	7,85%
TFI Allianz Polska S.A.	2 277 909	9,85%	2 277 909	8,38%
BioNTech SE	1 917 437	8,29%	1 917 437	7,06%

**The beneficiary of Augebit FIZ is 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. STATEMENT OF THE MANAGEMENT BOARD REGARDING APPLICABLE ACCOUNTING PRINCIPLES

The management board of Ryvu Therapeutics S.A. confirms that, to the best of its knowledge, these quarterly 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 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 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 in relation to the scope of the Construction Agreement, totalling the amount of 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. Subsequently, the Court will appoint an expert from the candidates for experts proposed by the Parties who will prepare an opinion based on the evidentiary theses defined 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 22.11.2023, the hearings of all witnesses and parties were completed. The case files have been sent to a court-appointed expert, who will prepare an opinion based on the specified questions.

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 2.41% 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, 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

Not applicable.

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, November 6, 2024

Paweł Przewięźlikowski
President of the Management Board

Krzysztof Brzózka
Vice-President of the Management Board

Kamil Sitarz
Management Board Member

Vatnak Vat-Ho
Management Board Member

Hendrik Nogai
Management Board Member

CONTACT



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GENERAL INQUIRIES

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