RYVU THERAPEUTICS S.A.

H1 2022 report

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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, 2022 to June 30, 2022 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 statement of financial position are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand		Data in EUR thousand	
Item	**30.06.2022**	31.12.2021	**30.06.2022**	31.12.2021
Total assets	**179,372**	228,813	**38,322**	49,748
Short-term receivables	**14,061**	11,741	**3,004**	2,553
Cash and cash equivalents	**44,626**	83,236	**9,534**	18,097
Other financial assets	**-**	4,994	**-**	1,086
Total liabilities	**57,136**	59,392	**12,207**	12,913
Long-term liabilities	**25,567**	23,192	**5,462**	5,042
Short-term liabilities	**31,570**	36,200	**6,745**	7,871
Total equity	**122,235**	169,422	**26,115**	36,836
Share capital	**7,342**	7,342	**1,569**	1,596

Selected data of statement of comprehensive income are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
Item	**From 01.01.2022 to 30.06.2022**	From 01.01.2021 to 30.06.2021	**From 01.04.2022 to 30.06.2022**	From 01.04.2021 to 30.06.2021	**From 01.01.2022 to 30.06.2022**	From 01.01.2021 to 30.06.2021	**From 01.04.2022 to 30.06.2022**	From 01.04.2021 to 30.06.2021
Revenues from sales	**491**	741	**263**	309	**106**	163	**57**	68
Revenues from subsidies	**14,027**	11,321	**7,273**	5,200	**3,021**	2,490	**1,568**	1,150
Revenues from R&D projects	**-**	-	**-**	-	**-**	-	**-**	-
Other operating revenues	**185**	160	**74**	67	**40**	35	**16**	15
Revenues from operating activities	**14,703**	12,222	**7,610**	5,576	**3,167**	2,688	**1,641**	1,233
Operating expenses	**-79,560**	-49,613	**-45,711**	-29,214	**-17,137**	-10,911	**-9,856**	-6,460
Operating expenses without Incentive Scheme and valuation of Nodthera shares	**-55,631**	-43,478	**-29,933**	-21,177	**-11,983**	-9,562	**-6,454**	-4,683
Depreciation	**-6,700**	-5,925	**-3,325**	-3,036	**-1,443**	-1,303	**-717**	-671
Valuation of Incentive Scheme	**-16,270**	-6,866	**-8,121**	-6,866	**-3,504**	-1,510	**-1,751**	-1,510
Loss from operating activities (EBIT)	**-64,857**	-37,391	**-38,101**	-23,638	**-13,970**	-8,223	**-8,215**	-5,227
Loss from operating activities (EBIT) without Incentive Scheme and valuation of Nodthera shares	**-40,928**	-31,256	**-22,323**	-15,601	**-8,816**	-6,874	**-4,813**	-3,450
Loss before income tax	**-64,921**	-37,622	**-38,338**	-24,398	**-13,984**	-8,274	**-8,266**	-5,395
Net loss	**-63,456**	-37,808	**-36,920**	-24,245	**-13,668**	-8,315	**-7,960**	-5,361
Net loss without Incentive Scheme	**-47,186**	-30,942	**-28,799**	-17,378	**-10,164**	-6,805	**-6,209**	-3,845
EBITDA	**-58,157**	-31,466	**-34,776**	-20,601	**-12,527**	-6,920	**-7,498**	-4,556
EBITDA without Incentive Scheme and valuation of Nodthera shares	**-34,228**	-25,331	**-18,998**	-12,565	**-7,372**	-5,571	**-4,096**	-2,778
Net cash flows from operating activities	**-39,183**	-39,641	**-17,376**	-28,397	**-8,440**	-8,718	**-3,746**	-6,279
Net cash flows from investing activities	**1,668**	-11,163	**-2,475**	-9,125	**359**	-2,455	**-534**	-2,018
Net cash flows from financing activities	**-1,286**	-1,260	**-518**	-527	**-277**	-277	**-112**	-117
Total net cash flow	**-38,801**	-52,064	**-20,369**	-38,049	**-8,357**	-11,450	**-4,392**	-8,414
Number of shares (weighted average)	**18,355,474**	18,355,474	**18,355,474**	18,355,474	**18,355,474**	18,355,474	**18,355,474**	18,355,474
Profit (loss) per share (in PLN)	**-3.46**	-2.06	**-2,01**	-1.32	**-0.74**	-0.45	**-0.43**	-0.29
Diluted profit (loss) per share (in PLN)	**-3.46**	-2.06	**-2,01**	-1.32	**-0.74**	-0.45	**-0.43**	-0.29
Book value per share (in PLN)	**6.66**	10.52	**6.66**	10.52	**1.42**	2.33	**1.42**	2.33
Diluted book value per share (in PLN)	**6.66**	10.52	**6.66**	10.52	**1.42**	2.33	**1.42**	2.33
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 01/01/2022 – 30/06/2022: PLN 4.6427;
   - for the period from 01/01/2021 – 30/06/2021: PLN 4.5472;
2. Balance sheet items were converted using the average exchange rate announced by the NBP applicable as at the balance sheet date; which were:
   - as of 30 June 2022: PLN 4.6806;
   - as of 31 December 2021: PLN 4.5994.

1.2 Management Board comments to the financial results

In the first half year of 2022, Ryvu Therapeutics S.A. recognized the total operating revenue of PLN 14,703 thousand, which constitutes an increase compared to the corresponding period in 2021, when the total operating revenue amounted to PLN 12,222 thousand. This results from the increase in revenues from subsidies (an increase of PLN 2,706 thousand), partially compensated by the decrease in revenues from sales (decrease of PLN 250 thousand) compared to the corresponding period in 2021.

In the first six months of 2022, Ryvu reported a net loss, as well as an operating loss. The net and operating losses are the result of 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, 2022, amounted to PLN 63,456 thousand compared to the net loss of PLN 37,808 thousand in the corresponding period of 2021. The bigger loss in 2022 is related to the non-cash cost of valuation of incentive program for its employees of PLN 16,270 thousand (described below), negative change in NodThera shares valuation of PLN 6,204 thousand (described below), as well as higher expenditure incurred on research and clinical projects.

Valuation of shares in NodThera Inc.

Valuation of shares

As of June 30, 2022, three types of shares existed in NodThera Inc.: ordinary stock and preferred stock (Junior Preferred Stock, Series A1 and A2 Preferred Stock, and Series B Preferred Stock. Ryvu is a holder of the Junior Preferred Stock.

Associated with the Series A and B Preferred Stock is the right to receive dividends in the form of cash or the issuance of shares of the same class. The payment of dividends may be made in cases specified in the investment agreement, in particular in the event of a sale of the company or the admission of its shares to trading on a stock exchange. There is no such dividend right associated with the shares held by Ryvu, i.e. Junior Preferred Stock.

As of June 30, 2022, in aggregate, shareholders of Series A and Series B preferred stock were entitled to receive 4,797,014 shares of NodThera stock as dividends. Accordingly, should this dividend be paid out, Ryvu's share in the share capital of NodThera would decrease from 4.63% to 4.15%.

Moreover, on September 20, 2022, NodThera Inc. issued Series C Preferred Stock. The issue comprised of 8,698,375 shares at a price of USD 2.8741 per share (i.e. GBP 2.367 per share). As a result of this issue, NodThera received financing in the total amount of USD 25,000,002.47. The issue was addressed only to existing investors. Series C shares are preferred in the same way as Series A and B shares.

Ryvu did not participate in the issue, and as a result, Ryvu's share in the fully diliuted share capital of NodThera decreased to 3.2% as of the date of this report.

Thanks to the receipt of funds raised from the Series C share issue, NodThera has the necessary financial resources to fully implement the projects currently underway. In addition, the proceeds will provide enough cash for the company to operate smoothly until the end of 2023 and to safely raise further capital for development.

The Management Board of Ryvu has decided to include in the valuation of the shares held by Ryvu in NodThera, a **11.63% discount** (reflecting no right to dividend) **to the price at which they were subscribed under the last share capital increase, i.e. issuance of series C on 20 September 2022** and the above approach was also applied as of June 30, 2022.

Therefore, a share valuation of GBP 2.0917/share (share price from last financing round from 20 September 2022 including a discount corresponding to the class of shares held by the Issuer) should be used as a basis for the calculations. As of 30.06.2022 Ryvu held 4.15% shares in NodThera on a fully diluted basis and the total valuation of Issuer's shares in NodThera Inc. amounts to PLN 21,745,186 (at the average NBP exchange rate of 5.4429 PLN/GBP).

The change in the valuation of NodThera shares compared to the valuation reported by the Company in the periodic report for the Q1 2022 results mainly from the issue price of series C shares, lower than the price of the previous issue.

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

new share issue price (in GBP)	2.0917
average NBP exchange rate from June 30, 2022	5.4429
new share issue price (in PLN)	11.38
the number of the Company's shares in NodThera Inc.	1,910,000
value of shares in the balance sheet as of June 30, 2022	21,745,186
value of shares in the balance sheet as of December 31, 2021	29,403,922
change in valuation – gross impact on valuation of shares	-7,658,736
deferred tax	1,455,160
net impact on valuation of shares	-6,203,576

Incentive Scheme

On May 17, 2021, the General Shareholders Meeting adopted the non-dilutive Stock Grant Program for 2021-2024 for all employees in the form of the right to acquire shares of the Company. The Stock

Grant Program is comprised of 1,247,720 ordinary shares of the Company that have been donated free of charge by Mr. Paweł Przewięźlikowski – founder, President of the Management Board, and Company's largest shareholder to the Company, constituting a total of 25% of the Company's shares held by Mr. Paweł Przewięźlikowski. The Stock Grant Program provides employees with the right to acquire shares at a preferential price of PLN 0.19 per share, covering the Company's administrative costs incurred to execute the Stock Grant Program. The fair value of the shares granted is determined as of the grant date and recognized over the vesting period in remuneration costs in correspondence with the capital increase at the time of vesting by employees during the program. For the period ending June 30, 2022 the Company recognized the non-cash cost of valuation of this incentive program of PLN 16,270 thousand – more details are described in note 36 to the financial statements.

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

As of June 30, 2022, the value of the Company's assets was PLN 179,372 thousand and decreased by PLN 49,441 thousand compared to the end of 2021 (PLN 228,813 thousand), mainly due to expenditures on R&D projects. At the end of June 2022, the highest value of current assets is cash which amounted to PLN 44,626 thousand (at the end of 2021 it was PLN 83,236 thousand). The decrease in cash resulted from the aforementioned spending incurred on R&D projects and corporate income tax payment for converting shares held in NodThera Ltd. into NodThera Inc. in the amount of PLN 5,458 thousand. Fixed assets are mainly Research and Development Centre for Innovative Drugs (named 'CBR') and laboratory equipment and the valuation of NodThera of PLN 21,745 thousand. The value of non-current assets decreased in comparison to December 31, 2021, by PLN 9,248 thousand. The decrease consists mainly of the negative impact from the new valuation of NodThera shares (described above) and depreciation of fixed assets partially compensated by expenditures on new lab equipment.

The main item in Ryvu's equity and liabilities is equity, which amounted to PLN 122,235 thousand as of June 30, 2022, and decreased by PLN 47,187 thousand compared to December 31, 2021. The decrease in equity is mainly a result of the net loss recognized for the period. The other source of assets' funding is long-term liabilities which amounted to PLN 25,567 thousand at the end of June 2022. Long-term liabilities mainly related to the deferred income related mainly to the infrastructure subsidy for CBR.

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

	30.06.2022	31.12.2021
Current ratio current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)	2.68	3.83
Quick ratio (current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)	2.61	3.75

Cash surpluses, not used in the operating activities, are deposited in the low-risk financial instruments like short term bank deposits, Pekao Leasing S.A.'s bonds.

1.4 Current and Projected Financial Condition

The Company's financial position as of the report date is good taking into account the current cash position, European Investment Bank's ("EIB") financing and expected share capital issuance (please refer to Section 2.2.B of this Report). As of June 30, 2022, the value of the Company's cash amounted to PLN 44,626 thousand, and as of September 21, 2022, it was PLN 46,584 thousand. The increase in cash is the net result of mainly the received payment resulting from the signed contract with Exelixis (more in section 2.2.B of this Report) and the expenditure on R&D projects.

On 16 August 2022 the Company signed a financing agreement with EIB for a loan of EUR 22 million to support the development of the Company's pipeline. For more information please refer to Section 2.2.B of this Report.

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 EU funds supporting R&D projects and cash generated from the commercialization of projects allow the Company to execute its planned investments, in particular, the development of the ongoing and new innovative projects and expansion of laboratory infrastructure. Future Company's revenue depends strongly on the ability to commercialize the research projects.

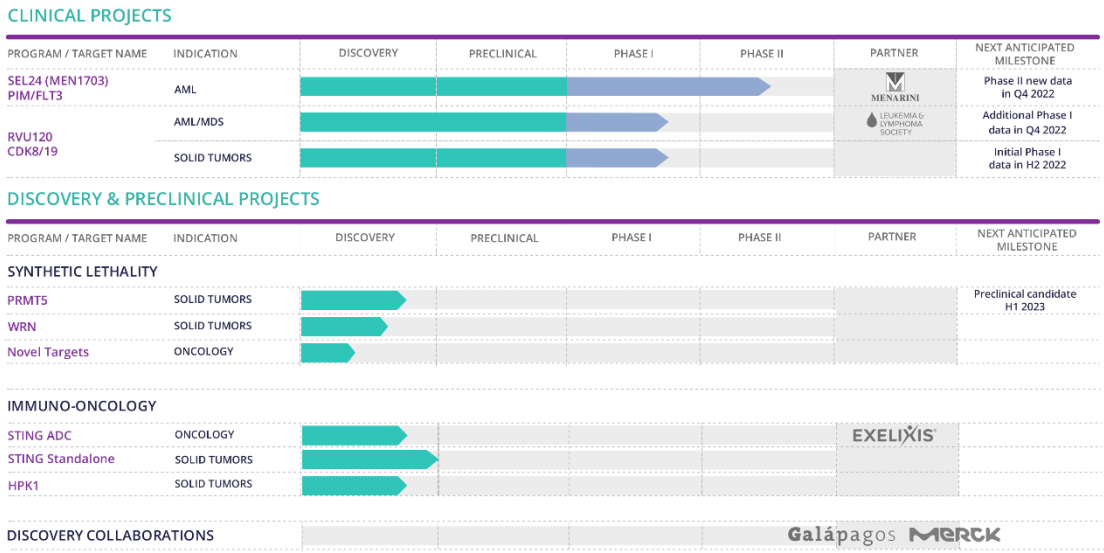
2 MANAGEMENT BOARD INFORMATION ON ACTIVITES

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 kinase, synthetic lethality, immuno-oncology and immunometabolism pathways.

These research and development projects are represented below.



Source: Company's own data.

SEL24 (MEN1703)

SEL24 (also known as MEN1703) is a selective, small molecule, dual inhibitor of PIM and FLT3 kinases, two enzymes that are strongly implicated in malignant transformation of hematopoietic cells. The compound has been discovered by Ryvu and is currently in development in collaboration with Menarini Group as a therapeutic option for cancers including acute myeloid leukemia (AML). The licensing contract with Menarini was executed in March 2017, and currently, Menarini is the sole sponsor of the ongoing phase I/II clinical study. Details of this study can be found at ClinicalTrials.gov under the identifier NCT03008187.

The data that have been generated in the SEL24 Cohort Expansion part of the study were presented in June 2021 during the American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) Virtual Congresses. Data reported in the posters confirmed the manageable safety profile of the drug at the recommended dose and showed preliminary single agent efficacy

in relapsed/refractory AML, particularly in patients with IDH mutant disease either naïve or previously exposed to IDH inhibitors.

In the above-mentioned posters, a total of four objective responses across the dose escalation (n=25) and cohort expansion (n=23) in patients with AML were reported, with 3 of those 4 responders harboring an IDH mutation. Notably, three out of five patients with IDH mutations treated at doses of 75-125 mg achieved a CR/CRi, including a patient that previously relapsed on the IDH-inhibitor enasidenib. Furthermore, one patient with an IDH1 mutation achieved a CRi and underwent allogeneic-HSCT.

Menarini stated that these results warrant further investigation of SEL24 in AML, with a potential to focus on the IDH-subset. A subsequent study in this patient population started in July 2021. Currently, the study is still active (not recruiting) with the estimated study completion date in September 2022.

On November 4, 2021, Menarini announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation (ODD) to SEL24 for the treatment of AML.

The most recent project updates were presented in June 2022 during the ASCO Annual Meeting and at the EHA Hybrid Congress 2022. Menarini's poster was entitled: "Phase 1/2 study of SEL24/MEN1703, a first-in-class dual PIM/FLT3 kinase inhibitor, in patients with IDH1/2-mutated acute myeloid leukemia: The DIAMOND-01 trial".

As of 21 April 2022 (cut-off date), 25 patients were enrolled in the IDHm cohort.

Fourteen patients had IDH2, 1 had IDH1/2, and 9 had IDH1 mutations. Concomitant mutations in FLT3-ITD were detected in 4 patients.

The median duration of treatment was 2 cycles. In total, 15 patients completed ≥1 treatment cycle and were efficacy evaluable. The ORR was 13%. One patient with IDH2 and NPM1 mutations had a partial remission at cycle 4 and achieved a CR at cycle 13. Treatment was ongoing at the cut-off date in this patient and the duration of response (DOR) was 177 days. One patient with an IDH1 mutation achieved a CRh at cycle 3 and underwent hematopoietic stem cell transplant. Treatment was ongoing in this patient, with a DOR of 133 days.

These preliminary results in the IDHm cohort confirm that SEL24/MEN1703, has a manageable safety profile and single-agent activity in patients with R/R IDHm AML.

Menarini disclosed that additional clinical trials are planned in order to better explore the potential of SEL24/MEN1703 in combination with standard-of-care therapies in different AML patient populations.

Ryvu receives information on the study progress from Menarini during periodic technical and joint steering committee meetings. Ryvu has also been assisting directly in translational research on the program funded by Menarini.

RVU120 (SEL120)

RVU120 (also known as SEL120) is a clinical stage, selective, first-in-class dual inhibitor of CDK8/CDK19 kinases. RVU120 (SEL120) has demonstrated efficacy in a number of 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; 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 AML. CDK8 and CDK19 are preclinically validated novel targets for the treatment of breast and prostate cancers. Targeting CDK8 and its paralog CDK19 using the potent and selective CDK8/19 inhibitor RVU120, may be an effective treatment for both hematologic malignancies and solid tumors with deregulated transcription.

RVU120 has been 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 an orphan drug designation (ODD) to RVU120, for the treatment of patients with AML.
At present, Ryvu is conducting two clinical studies with RVU120: (i) Phase Ib in patients with AML/HR-MDS (NCT04021368) and (ii) Phase I/II in relapsed/refractory metastatic or advanced solid tumors (NCT05052255). Additionally, multiple translational research activities are underway, aimed at further confirmation of RVU120 mechanism of action, defining the target patient population and potential combination partners as well as validating RVU120 in other hemato-oncology as well as solid tumor indications.

The primary aim of the ongoing first-in-human (FIH) Phase Ib study with RVU120 in relapsed or refractory AML or high-risk MDS (CLI120-001, NCT04021368) is to evaluate the safety and tolerability of RVU120 as well as to determine the recommended dose for Phase II (RP2D). The secondary endpoints include measurements of pharmacokinetic (PK) properties and an assessment of signs of clinical activity. Response to RVU120 will be evaluated by individual response criteria per each disease predefined in the study protocol. In addition, the exploratory objective of the study is the investigation of the relevant pharmacodynamic (PD) response by studying biomarkers of target engagement in patient samples, such as STAT5 phosphorylation, and identification of molecular markers that might point to a better response to treatment with RVU120.

The first patient in the CLI120-001 clinical trial was dosed in September 2019. The study is currently enrolling at seven investigational sites in the US and in Poland. Ryvu is planning to present updated data of this ongoing study at the ASH Annual Meeting & Exposition in December 2022. The transition into Phase II development is planned for the first half of 2023.

The other ongoing clinical study with RVU120 (RVU120-SOL-021, NCT05052255) is a Phase I/II study aiming to investigate the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors. The study is designed in two parts. Part 1 of the study (Phase I) is a dose escalation part according to a standard 3+3 design and is aimed at the enrollment of adult patients with solid malignancies who have failed available standard therapies. The primary objective of the Phase I part is to determine safety, tolerability and the RP2D. The secondary objectives include the determination of the pharmacokinetic (PK), pharmacodynamic (PD), and preliminary anti-tumor activity of RVU120 as a single agent. Phase II part is aimed both at safety and efficacy expansion. Part

2 (Phase II) will enroll patients with specific tumor types, either as a single agent or in combination with standard anticancer medicinal agents. Additional translational and biomarker studies are currently ongoing to confirm which target patient populations will be selected.

The first patient was dosed on August 25th, 2021 at the 75 mg dose. The study is currently enrolling at five investigational sites in Poland and Spain. Preliminary data of the dose escalation part will be presented as a poster at the 34th EORTC-NCI-AACR Symposium in October 2022. Transition into Part 2 is planned for the first half of 2023.

Key achievements in RVU120 clinical development:

- **Data disclosure at the 63rd ASH Annual Meeting & Exposition**, held on December 11 – December 14, 2021, in Atlanta, US. Data of the first treated patients in the ongoing Phase Ib clinical trial in AML/HR-MDS were presented. In a difficult-to-treat population with a median of three prior lines of therapy, RVU120 showed a tolerable safety profile and preliminary signs of efficacy. No DLTs and no study drug-related SAEs were reported. An 82-year-old patient with HR-MDS achieved a hematologic improvement of the erythroid lineage at the 50 mg dose level. At the 75 mg dose level, a 62-year-old patient with AML achieved complete remission. Four patients were still ongoing at the time of data cut-off.

- **Data presentation at the American Association of Cancer Research (AACR) Annual Meeting 2022**, held on April 8 – April 13, 2022, in New Orleans, US. A Trials-in-Progress poster for a Phase I/II clinical trial of RVU120 in patients with metastatic or advanced solid tumors (NCT05052255), currently ongoing in Poland and Spain, was presented. The study is designed in 2 parts: Part 1 follows a 3+3 dose escalation design, and the primary objectives are to characterize the safety and tolerability of RVU120 as a single agent in patients with different tumors types and determine the RP2D. Part 2 will primarily explore the anti-tumor activity of RVU120 as a single agent in different patient populations. As of the cut-off date of Feb 11, 2022, five patients have been enrolled in part 1 at the 75 mg and the 100 mg dose levels, and have completed their first cycles of treatment without dose-limiting toxicities (DLTs) – which further supports a manageable safety profile of RVU120. Apart from the clinical poster, translational research data on RVU120's efficacy against hormone-independent breast cancer cells in vitro and in vivo were presented.

- **Poster presentation at the European Hematology Association Congress in Vienna in June 2022**, Ryvu presented data from the ongoing Phase 1b dose-escalation study of RVU120 (SEL120) in patients with AML or high-risk myelodysplastic syndromes (HR-MDS). At the cut-off date of May 26th, 16 patients had been dosed in 7 cohorts. Preliminary data demonstrated a favorable safety profile of RVU120. No DLT and no drug-related SAE have occurred. Meaningful pharmacodynamic changes of STAT5 phosphorylation have been observed with a maximum of approximately 50% target inhibition. Clinically meaningful benefit of RVU120 monotherapy has been observed, with one CR and disease stabilizations with blast reductions in several ongoing patients who failed multiple prior lines of therapy. Dose escalation will continue.

Further translational research showed that patient-derived AML cells with DNMT3A and NPM1 mutations are more sensitive to RVU120 treatment both *in vitro* and *in vivo*. This observation is consistent with the clinical responses to RVU120 in study CLI120-001 in two patients that

harbored DNMT3A and NPM1 mutations. Anti-cancer efficacy of RVU120 was associated with transcriptomic reprogramming and lineage commitment.

PRECLINICAL AND DISCOVERY STAGE PROJECTS

Synthetic lethality projects

MTA-cooperative PRMT5 inhibitor program

Ryvu is carrying out several research stage projects in the area of synthetic lethality. The most advanced project in the field of synthetic lethality is focusing on cancers with a deletion of the metabolic gene MTAP, which occurs in 10 to 15% of all human tumors.

MTAP deletion results in a massive accumulation of methylotioadenosine (MTA) in cells. MTA in high concentrations is a very selective inhibitor of PRMT5 methyltransferase, competitive for the substrate: S-adenosylmethionine (SAM). Accumulation of MTA in cells with MTAP deletion causes partial inhibition of the methylation activity of PRMT5, which in turn reduces the level of symmetric arginine dimethylation of the whole proteome, and thus an increased sensitivity of cells to modulation of methylosome activity. The Company's strategy is to develop MTA-cooperative PRMT5 inhibitors, which will selectively inhibit the growth of MTAP-deleted cancer cells. The work carried out in H1 2022 focused on the expansion of the main chemical series into a lead series with the main aim to demonstrate in vivo proof of concept, which would then allow for the nomination of a preclinical candidate in the first half of 2023. Pilot efficacy studies with lead compound showed tumor growth inhibition in MTAP -/- model that is accompanied by ~60% of target proximal PD biomarker inhibition. In Q2 2022 properties of the chemical series were improved with respect to potency and selectivity measured by the inhibition of SDMA in MTAP-deleted versus MTAP WT cells. In addition, Ryvu PRMT5 MTA-cooperative inhibitors show improved selectivity towards MTAP-deleted cancer cells in the internal cell line panel. In Q2 2022 lead compound was also selected for external assessment of cytotoxicity in a broader cancer cell line panel (~100 cell lines with different MTAP statuses). Results of this experiment are expected in H2 2022. Currently, the optimization of chemical series focuses on the improvement of ADME properties that would drive stronger responses in vivo.

New results on the development of MTA-cooperative PRMT5 inhibitors were presented at the annual AACR (American Association for Cancer Research) conference in New Orleans, United States in April 2022. The publication can be found under following link:

WRN inhibitor program

Efforts of the second disclosed project are focusing on discovery and development of first-in-class small molecule inhibitors of the Werner Syndrome RecQ like helicase (WRN), an enzyme which is involved in genome maintenance by playing important role in DNA replication, recombination, and damage repair. WRN was identified as a strong vulnerability of microsatellite unstable (MSI) cancers, making this helicase a promising drug target. Inhibition of the protein’s helicase/ATPase activity leads to impairment of viability of cells. This therapeutic strategy holds promise for patients bearing tumors with MSI, such as colorectal, ovarian, endometrial, and gastric cancers.

Since the WRN project was revealed in Ryvu's pipeline several high throughput screening campaigns have been performed and provided multiple small-molecule WRN-inhibiting compounds characterized by different scaffolds. Several most promising chemotypes were selected for further expansion and profiling. In the first half of 2022 main focus was put on the validation and exploration of the inhibitor mode of action and improvement of key properties of the selected chemical series.

Undisclosed novel targets

In addition to the two disclosed projects, Ryvu is currently leading multiple internal initiatives focused on the identification and validation of new targets and respective hit matter in the synthetic lethality space. One of the key assumptions for the selected targets is first-in-class potential. So far, several new targets have been identified that potentially meet these criteria. Following the positive target validation studies for two targets, the company has initiated a hit finding campaign aiming at the identification of pharmacologically active compounds for these potentially first-in-class targets. As of the end of Q2, both campaigns were at the hit validation stage, where the target-specific activity of hit molecules detected in primary screening is being confirmed using multiple complementary biochemical and biophysical methods. At the same time, work is underway on the selection and experimental validation of further molecular targets with first-in-class drug potential. Therapeutic targets for which active molecules can be identified and validated will be included in the company's project pipeline as they progress from target validation to successful hit stage.

Target discovery

On top of ongoing target validation and hit identification efforts, Ryvu is implementing an innovative platform for the discovery of novel biological targets for oncology drugs based on genome-wide knockout screens in cancer cells with defined phenotype. The planned work includes modeling the impact of the microenvironment (cellular stress conditions, 3D cell culture) and utilization of primary cells during the screening. By systematically analyzing the frequency of genomic alterations in clinical databases, the platform is being applied to genomic alterations with potentially the greatest unmet medical need allowing the introduction of unique molecular targets in the area of synthetic lethality to Ryvu project portfolio. These efforts are aimed at building a robust portfolio of projects differentiated from competitor approaches by predictive biomarkers for sensitivity to target modulation and patient stratification opportunities in mid-term.

Immuno-oncology projects

STING agonist program

Currently, the Company conducts research two projects in the immunooncology space: immunoactivation by STING agonists and HPK1 inhibitors, which have the dual potential of both activating the immune response and protecting cells of the immune system against immunosuppression.

The most advanced project within the immune-oncology portfolio focuses on development of small-molecule agonists of STING (Stimulator of Interferon Genes), the protein that plays the central role in activating the immune response to cytosolic pathogen-derived or self-DNA. Stimulation of STING pathway induces type I interferons production, that promotes antigen presentation and maturation of dendritic cells, which in turn enhances antitumor T cell response.

The proprietary chemical series developed by Ryvu are strong STING activators with proven cellular activity. Their potential was confirmed in *in vivo* efficacy studies, where tumor growth inhibition and regression were observed in a mouse syngeneic tumor model. As a result of advanced profiling, a shortlist of compounds was narrowed down and finally, the lead molecule was selected and nominated as the preclinical candidate, which has been optimized to reach superior agonist activity in human immune cells while at the same time maintaining a good overall safety profile.

In the first half of 2022 Ryvu continued focus on advanced PK/PD evaluation of compound administration strategies to facilitate the design and progress into further toxicology assessment.

Collaboration with Exelixis on STING

The optimization of the most advanced Ryvu STING agonists allowed for development of a chemical subseries, functionalized with additional chemical groups ("handles"), amenable to easy linking with a separate reactive moiety. This approach yielded potent agonist molecules suitable for further development as antibody-drug conjugates (ADC). The attractiveness of the ADC technology allowing for localized delivery of the compound payload after systemic administration and a high potential for Ryvu agonists led to establishing an exclusive license agreement with Exelixis. Under the terms of the agreement, Exelixis will expand its biotherapeutics portfolio by combining Ryvu's proprietary small molecule STING agonists and STING biology know-how with Exelixis' network of expertise and resources in antibody engineering, ADC technologies, oncology therapeutics development, and commercialization experience.

HPK1 inhibitor program

The second project in the field of immuno-oncology focuses on developing small molecule modulators of HPK1 (MAP4K1), a hematopoietic cell-restricted member of Ste 20 serine/threonine kinases. HPK1 is known as a negative regulator of TCR signaling. Inhibition of HPK1 leads to TCR-induced phosphorylation of SLP-76, which undergoes phosphorylation-dependent ubiquitination and results in its degradation, thereby blocking signal transduction - required for immune system activation and elimination of cancer cells. In the first half of 2022, optimization of chemical series was continued, with particular focus on improving the safety profile, i.e., increasing the therapeutic window and reducing the potential risk of cardiotoxicity. For lead molecule characterized by high selectivity, metabolic stability and good solubility PK/PD experiments were performed. Received results confirmed in vivo target engagement with dose-dependent pSLP76 modulation. These favorable outcomes allowed us to design and perform MTD experiments that demonstrated tolerability, dose-depended compound concentration in plasma and associated with it target engagement.

OTHER PROJECTS

Ryvu also carries out other research and development projects, details and status of which are currently confidential due to the intensive competitive environment and company obligations.

2.2 Significant events in H1 2022

A) DURING THE REPORTING PERIOD

Delivery of a lawsuit for payment in connection with the construction of the Research and Development Center

On January 19, 2022 Issuer informed about having been served with a lawsuit for payment filed to the Regional Court in Kraków by the Contractor in connection with the performance of the general contractor 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 the prolonged performance of the Contract, 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 from the Company a total amount of PLN 7.671.285.

The Company disputes the validity of the claims indicated in the Contractor's statement of claim both in principle and in amount. The Company will take appropriate legal steps in order to protect its interests in connection with the claims made by the Contractor.

Appointment of the new Chief Medical Officer

Effective February 1st, 2022 Mr. Hendrik Nogai, M.D. has been appointed to the role of Chief Medical Officer. Dr. Nogai will lead medical, clinical, and regulatory functions to support and guide the development of the company's pipeline. Dr. Nogai is a board-certified medical doctor in Hematology/Oncology and Internal Medicine, with almost 10 years of experience in patient care and basic research in different academic settings, including Charité – University Medicine Berlin, University Hospital Grosshadern in Munich, and Zentralklinikum Augsburg. Besides his clinical expertise, Dr. Nogai brings 17 years of industry experience including business consulting at Mercer Management Consulting/ Oliver Wyman, Medical Advisor role at Nordic Biotech Capital ApS, and positions of increasing responsibility at Bayer AG, with his most recent role of Vice President, Global Development Leader NTRK program.

AACR 2022 ANNUAL MEETING

During the American Association of Cancer Research (AACR) Annual Meeting 2022, April 8-13 2022, Company presented the latest data of its oncology projects: RVU120 (SEL120), a program developing a selective CDK8/19 kinase inhibitor as an effective therapy for the treatment of hematologic malignancies and solid tumors, as well as a project developing MTA - cooperative inhibitors of PRMT5 - as a synthetically lethal therapy for the treatment of tumors with MTAP gene deletion.

Poster details:

• **Title**: *RVU120, a selective CDK8/CDK19 inhibitor, demonstrates efficacy against hormone independent breast cancer cells in vitro and in vivo*
Abstract number: 2647

• **Title**: *Discovery of novel MTA-cooperative PRMT5 inhibitors as a targeted therapeutic for MTAP deleted cancers*
Abstract number: 1117

• **Title**: *Trials in Progress – RVU120 SOL-021: An open-label, single agent, Phase I/II trial of RVU120 (SEL120) in patients with relapsed/refractory metastatic or advanced solid tumors*
Abstract number: 8023

ASCO 2022 Annual Meeting

During the American Association of Clinical Oncology Research (ASCO) Annual Meeting 2022, June 3-7 2022, Company featured its oncology projects: RVU120 (SEL120), a program developing a selective CDK8/19 kinase inhibitor as an effective therapy for the treatment of hematologic malignancies and solid tumors (abstract book), as well as a selective PIM/FLT3 inhibitor SEL24 (MEN1703), currently under development by Menarini Group (poster presentation).

Details of abstracts:

• **Title**: *Phase 1/2 study of SEL24/MEN1703, a first-in-class dual PIM/FLT3 kinase inhibitor, in patients with IDH1/2-mutated acute myeloid leukemia: The DIAMOND-01 trial*
Session Title: Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant
Abstract number: 7024

• **Title:** *Phase I/II trial of RVU120 (SEL120), a CDK8/CDK19 inhibitor in patients with relapsed/refractory metastatic or advanced solid tumors*
Abstract Number (online publication only): e15091

NodThera announces clinical progress for lead NLRP3 Inflammasome inhibitors and candidate selection of novel brain-penetrant compound

On May 10th, 2022, NodThera announced several key advancements across the portfolio. NodThera's lead candidate, NT-0796, demonstrated positive interim results from its Phase 1 single-ascending dose (SAD) study. Additionally, the company has commenced first-in-human dosing in the Phase 1 study of its second lead candidate, NT-0249, and announced the selection of its third pipeline candidate, NT-0527 – a brain-penetrant NLRP3 inflammasome inhibitor from a novel chemotype.

The positive interim results from the SAD portion of the Phase 1 trial with NT-0796 represent early clinical proof of mechanism for NT-0796 as a potent NLRP3 inflammasome inhibitor. Across all dosing cohorts, NT-0796 was safe and well tolerated and shown to be orally bioavailable with a dose-proportional pharmacokinetic (PK) profile. This portion of the study also showed a dose-dependent pharmacodynamic (PD) effect through the ability to lower IL-1β and IL-18 levels in an ex vivo NLRP3-stimulation assay. These results confirm the criteria to advance NT-0796 further in development and continue the ongoing multiple-ascending dose (MAD) portion of the Phase 1 study to assess brain exposure through cerebrospinal fluid (CSF) sampling.

New data from RVU120 and SEL24 (MEN1703) programs presented at the EHA Hybrid Congress 2022

On June 10th the Company presented three abstracts demonstrating data from the Phase 1b dose-escalation study of RVU120 (SEL120) in patients with AML or high-risk myelodysplastic syndromes (HR-MDS) and the Phase 1/2 study of SEL24(MEN1703) in Patients with IDH1/2-Mutated AML at the Annual European Hematology Association (EHA) 2022 Hybrid Congress in Vienna, Austria and on-line.

In the opinion of the Ryvu Management Board, the clinical data achieved presented at EHA 2022 confirm the single drug efficacy of RVU120 and durable benefits for patients with very few treatment options as well as the responder hypothesis in a molecularly defined subset of patients with DNMT3A and NPM1 mutations. Based on the encouraging data, the Company plans to continue dose escalation and further advance the clinical development of RVU120 in both biomarker-selected AML patients and the unselected broader AML population. The data presented by Menarini on SEL24 (MEN1703) and the additional communication received from Menarini in project meetings has confirmed the single-agent activity of SEL24 and its potential for further development in different AML populations.

Details of abstracts:

RVU120: orally available CDK8/19 inhibitor

• Abstract Title: *Preclinical and Clinical Signs of RVU120 Efficacy, a Specific CDK8/19 Inhibitor in DNMT3A Mutation Positive AML and HR-MDS*
Abstract number: #P450

Preliminary results were presented from the first seven cohorts, demonstrating a favorable safety and a predictable pharmacokinetic (PK) profile for RVU120.
As of the data cutoff date of May 26, 2022, 16 patients with AML or HR-MDS have been dosed (5 ongoing) with a median of three prior lines of therapy.
Clinically meaningful benefit of RVU120 monotherapy has been observed at doses that resulted in less than complete target engagement, with one complete remission (CR) and stable diseases with blast reductions in several ongoing patients who failed multiple prior lines of therapy and presented with a very poor prognosis:

- Complete remission in an AML patient with FLT3/DNMT3A/NPM1 mutations
- Stable disease with a duration of therapy of more than 18 months in a high-risk MDS patient with DNMT3A mutations; significant reductions in red blood cells (RBC) transfusions at various time points
- Three additional patients ongoing with stable disease and blast count reductions Dose escalation is ongoing, with active enrollment in the 100 mg dose cohort (NCT04021368).

• Abstract Title: *CLI120-001 Phase1b Dose Escalation Study of RVU120 in Patients with AML or High-Risk MDS Safety and Efficacy Data Update*
Abstract Number: #P501

Preclinical data demonstrate that treatment with RVU120 demonstrated a pronounced anti-cancer effect in AML patient-derived cells with DNMT3A and NPM1 mutations. Preliminary evidence of clinical response to RVU120 has been shown in a r/r AML patient with DNMT3A and NPM1 mutations, who

achieved a complete remission. Anti-cancer efficacy of RVU120 was associated with transcriptomic reprogramming involving lineage commitment and inhibition of homeobox genes. Repression of homeobox genes in the responder patient confirms the on-target activity of RVU120. Further molecular studies in a larger number of patients under RVU120 treatment are ongoing and are expected to provide additional evidence for predictive markers of response to RVU120 in AML.

SEL24 (MEN1703): orally available dual PIM/FLT3 inhibitor

• Abstract Title: *Phase 1/2 Study of SEL24/MEN1703, a First-In-Class Dual PIM/FLT3 Kinase Inhibitor, in Patients with IDH1/2-Mutated Acute Myeloid Leukemia: The DIAMOND-01 Trial*
Abstract Number: #P520

Ryvu's partner Menarini Group reported the updated safety and efficacy results from an additional expansion cohort of the DIAMOND-01 trial, which enrolled patients with relapsed or refractory (R/R) IDHm AML, treated with the dual PIM/FLT3 inhibitor, SEL24 (MEN1703). As of the data cutoff of April 21, 2022, 25 patients were enrolled in the IDHm AML expansion cohort. SEL24 (MEN1703) was well tolerated, with no drug discontinuations or deaths due to treatment-related adverse events (TRAEs). Promising efficacy was observed, with overall response rates (ORR) Ryvu Therapeutics S.A. www.ryvu.com and complete remission (CR) / CR with incomplete hematologic recovery (CRi) / CR with partial hematologic recovery (CRh) of 13% for the IDHm cohort, which is similar to monotherapy activity of other drugs in R/R AML. Based on these data, SEL24/MEN1703 may be a feasible therapy in this difficult-to-treat population of patients with R/R AML who harbor IDH mutations. Clinical trials are planned in order to better explore the potential of SEL24/MEN1703 in different AML populations.

B) EVENTS OCCURRED BETWEEN THE END OF REPORTING PERIOD UNTIL THE APPROVAL OF FINANCIAL STATEMENT

Execution of an exclusive license agreement with Exelixis, Inc. to develop novel STING agonist-based targeted cancer therapies

On July 6th, 2022 the Company entered into an exclusive license agreement ("Agreement") with Exelixis, Inc. with its registered office in Alameda, California ("Exelixis"). The aim of the collaboration is to develop novel therapies utilizing Ryvu's STING (STimulator of INterferon Genes) technology. 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. Exelixis will seek to incorporate Ryvu's small molecule payloads into targeted biotherapeutics such as antibody-drug conjugates. Ryvu will also provide expert guidance and know-how during the early research phase of the collaboration, and upon selection of each development candidate, Exelixis will be responsible for all development and commercialization activities.

Ryvu will retain all development and commercial rights to develop its STING agonist portfolio as standalone small molecules. Under the terms of the Agreement, Exelixis has paid to Ryvu an upfront fee of USD 3 million (PLN 14,038,800 at the average exchange rate of the National Bank of Poland as at July 6, 2022, 1 USD = 4.6796 PLN) in exchange for certain rights to Ryvu's STING agonist small molecules. Ryvu will also be eligible to receive research funding when the parties agree on a research

plan, as well as an additional USD 3 million (PLN 14,038,800 at the average exchange rate 1 USD = 4.6796 PLN) in near-term research-based milestones, a double-digit milestone at first development candidate selection, and additional development, regulatory and commercialization milestone payments and tiered single-to-low double-digit royalties on the annual net sales of any products that will be successfully commercialized. In total, Ryvu is eligible to receive research, development, and commercial milestones of just over USD 400 million (PLN 1,871,840,000 at the average exchange rate 1 USD = 4.6796 PLN) for each potential product developed under this Agreement.

The amount of revenue the Company will actually receive under the Agreement will depend on the progress of scientific research and clinical trials, the success of the registration process, and the level of revenues from sales of the potential drug achieved by Exelixis or its partners.

Changes in Ryvu's Management Board

On July 25th, 2022 Ryvu's Supervisory Board appointed Mr. Vatnak Vat-Ho and Mr. Hendrik Nogai, M.D. to the Management Board of the Company, effective August 1st, 2022. Mr. Vatnak Vat-Ho has been Ryvu's Chief Business Officer since April, 2021. Mr. Vat-Ho has been responsible for a wide scope of corporate and business development activities at Ryvu including strategic positioning, partnering discussions, alliance management as well as investor interactions. Dr. Nogai has been appointed Ryvu's Chief Medical Officer in January 2022. Dr. Nogai has been leading medical, clinical, and regulatory functions to support and guide the development of the company's clinical pipeline.

Conclusion of a financing agreement with the European Investment Bank

On August 16th, 2022 the Company has entered into a financing agreement (the "Agreement") with the European Investment Bank ("EIB" or "Bank") under the European Fund for Strategic Investments program, launched to provide financing for projects having high societal and economic value contributing to EU policy objectives. Under the Agreement, EIB agreed to provide the Company with credit in a maximum amount of EUR 22.000.000 (PLN 103.241.600 converted at the average exchange rate of the National Bank of Poland on August 16, 2022 1 EUR = 4,6928 PLN).

The aim of the Agreement is to support the development of selective, orally administered small molecule RVU120, Ryvu's lead drug candidate in AML/MDS and solid tumors (clinical Phase 2/3 trials), as well as earlier stage pipeline. The investment will predominantly cover costs related to clinical trial expenses, the necessary activities to enable regulatory approvals, internal R&D related to drug discovery and intellectual property-related costs.

Funding will be disbursed in three tranches: Tranche A and B in the amount of EUR 8.000.000 each and Tranche C in the amount of EUR 6.000.000. Each tranche may be disbursed to the Company during a period of 36 months from the date of signing the Agreement. The Company is obliged to repay each tranche disbursed to it in a single installment after 5 years from its disbursement. The interest rate for Tranche A will be 3% per annum, for Tranche B 2.7% per annum and for Tranche C 2.4% per annum. Interest on each tranche will be payable annually.

The disbursement of each tranche is subject to the Company's fulfillment of the conditions set forth in the Agreement, primarily relating to the clinical development of RVU120. Disbursement of Tranche A is subject to the Company (a) providing evidence of the Phase II clinical trial approval consisting of the declaration of the recommended Phase II dose (RP2D) for RVU120 in the solid tumor study, for which

no additional approval to initiate Phase II study is needed, or a Phase II approval in the AML/MDS study; and (b) issuance of warrants to the EIB in accordance with the terms and conditions set out in the warrant agreement that will be concluded by and between EIB and the Company. The conditions for payment of Tranche B are: (a) evidence of the successful initiation of Phase II clinical trials with RVU120 in AML/MDS, including First Patient Dosed; (b) evidence of the advancement of at least one additional research project into IND-enabling studies or partnering of one of Company's research projects with a defined minimum deal value; and (c) evidence of the Company having received co-financing in readily available funds in an amount equal to the amount drawn under Tranche B, in the form of for example equity capital increase, or non-EU grants since 1 July 2022. Tranche C is contingent upon (a) progress of the Phase II clinical trials with RVU120 in AML/MDS, demonstrated by the enrolment of at least ten patients in Phase II RVU120 clinical studies, and (b) the Company obtaining additional funding of at least EUR 10 million in upfront payments, research funding and milestone payments under any current or future research collaboration or partnership agreements since 30 September 2021.

As additional remuneration for each Tranche A, Tranche B and Tranche C, the Company shall issue to the EIB subscription warrants which will be subscribed by the EIB free of charge, in total corresponding to 2.5% of the Company's fully-diluted share capital ("Warrants"). The Warrants shall have a life of 10 years and EIB will have the right to exercise the Warrants upon maturity of Tranche A, or a voluntary or mandatory prepayment event.

Ryvu Therapeutics' development plans for 2022-2024

On August 19th, 2022 Ryvu announced the adoption of the Company's development plans for 2022-2024 (the "Development Plans"). The key objectives of the Development Plans include:

- Completing the ongoing Phase I clinical studies for RVU120 in acute myeloid leukemia (AML), high-risk myelodysplastic syndrome (HR-MDS) and solid tumors;
- Advancing the clinical development of RVU120 as a monotherapy by executing Phase II studies in hematology – with the potential fast-to-market strategy in AML/HR-MDS – and selected solid tumor indications - with the primary focus on triple-negative breast cancer (TNBC);
- Expanding the therapeutic potential of RVU120 by initiating Phase I/II clinical development in combination regimens in AML/HR-MDS with synergistic drug partners and additional hematology and solid tumor indications;
- Supporting the continued clinical development of SEL24 (MEN1703) led by the Menarini Group;
- Completing preclinical development and advancing into Phase I clinical trials one program from the Company's early pipeline;
- Strengthening the Synthetic Lethality Platform to deliver first-in-class preclinical candidates and further expanding the therapeutic target discovery platform;
- Achieving financial milestones in the existing R&D collaborations and advancing selected programs by partnering with collaborators with synergistic competencies and resources, signing at least one new partnering agreement per year.

In the current total budget for the H2 2022-2024 period, the Company anticipates to spend approximately PLN 535m (USD 115m at the average exchange rate of National Bank of Poland as of August 18th, 2022 1 USD = 4,6468 PLN), out of which:

- approximately PLN 297m (USD 64m) will be dedicated to: (i) broad clinical development of RVU120 in hematology and solid tumors, as well as (ii) initiation of Phase I study for one new candidate from the early pipeline;
- approximately PLN 174m (USD 37m) is planned for: (i) execution of preclinical development for at least one candidate from Ryvu pipeline and (ii) further strengthening of the Synthetic Lethality Platform and expansion of proprietary target discovery activities;
- approximately PLN 64m (USD 14m) is planned to cover G&A costs.

The execution of the Development Plans for 2022-2024 is planned to be financed through:

- Existing cash (USD 9.6m, as of June 30, 2022),
- Venture debt from European Investment Bank (EUR 22.0m),
- Anticipated milestone payments from existing collaborations and secured grants (USD 10.6m),
- Assumed future grants (USD 6.5m),
- Other sources including proceeds from equity capital markets and new partnering deals (USD 66.1m).

The Company plans to secure funds for portfolio expansion from various sources, with the aim of reducing the risk to Shareholders and minimizing their possible dilution. At the same time, the Company has developed several alternative scenarios aimed at minimizing investment risks, for example, with regard to the broad development plan for the RVU120 program.

Extraordinary General Shareholders Meeting

On September 19, 2022, the Company's Extraordinary General Meeting was held, during which the Company's shareholders resolved to authorize the Company's Management Board to increase the Company's authorized capital by no more than PLN 3,386,246 by issuing no more than 8,465,615 ordinary shares within the authorized capital, and to exclude, with the approval of the Supervisory Board, the pre-emptive rights of the Company's existing shareholders in whole or in part.

The primary purpose of authorizing the Management Board to increase the Company's authorized capital within the framework of authorized capital is to provide the Company with a flexible instrument that enables it to obtain financing relatively quickly and efficiently through the issue of new shares. The authorized capital shall enable the Company to issue and offer shares faster than under the ordinary procedure. This shall enable the Company’s Management Board to efficiently obtain funds, which may be allocated to financing the further development of the Company, in accordance with the Ryvu Development Plans for 2022-2024.

In the opinion of the Management Board, the authorized capital adopted in the Company will serve as a tool to capitalise the Company at a convenient time, taking into account the Company's business

prospects, the current market price and demand for the Company's shares, as well as the situation on the financial markets, in particular the situation in the biotechnology industry. Authorising the Management Board to increase the share capital within the authorized capital shall allow to adjust the size of a given issue to the financial needs of the Company at a given moment and to obtain financing on terms that are optimal from the Company's and its Shareholders' perspective.

2.3 Unusual events occurring in the reporting period

COVID-19

Covid-19 pandemic continued during the whole reported period - as of May 16, 2022, the epidemic status was lifted and the epidemic emergency status took effect, which is still in effect as of the date of this report. Because of that, the Issuer implemented recommendations given by the Chief Sanitary Inspectorate and other government institutions in connection with the epidemiological threat, including implementation of remote work and ensuring safe working conditions for stationary employees. Moreover, most business trips were still suspended. The Issuer used remote communication in its business contacts. Furthermore, the Issuer appointed a working team consisting of the representatives of various organizational units, whose task is to respond to the situation on an on-going basis and mitigate any adverse effects of the spread of the pandemic on the Issuer. The Company has also developed its internal policy for preventing spread of the coronavirus and has been taking actions aimed at ensuring appropriate health and safety conditions at work, including access for Company's employees to routine antigen testing. Internal policies are constantly updated and adapted to the latest guidelines and changing conditions.

During the reported period, the pandemic affected progress of the two Issuer's fully owned clinical trials: (i) CLI120-001 study and (ii) RVU120-SOL-021 study, due to the fact that generally and globally, phase I, dose escalation cancer clinical trials, got impacted. Due to the onset of COVID-19 pandemic, US and Polish clinical sites in both RVU120 studies have introduced additional safety measures and risk management processes which have impacted the possibilities for patients to participate in the clinical studies. This have applied primarily to relapsed, refractory AML patients who are frequently immunocompromised and very ill. Some patients themselves decided to limit their contacts with various healthcare facilities to minimize the possibility of COVID-19 exposure, while some were unable to enter the study due to an on-going coronavirus infection. As a result of that, enrollment in the study could have been impacted.

The Issuer's research and development laboratories worked in H1 2022 with close to normal capacity. Any decrease in their capacity was associated with employees absence due to quarantine, the fact that some foreigners could not enter Poland in time and the fact that some employees had to stay home with their children. A significant proportion of the Issuer's office staff however still worked remotely, which could also have had an adverse effect on the speed of carrying out the projects.

As of September 2022, thanks to the improving pandemic situation globally, and specifically in Poland, the residual impact of Covid-19 on Ryvu operations is very limited.

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 does not have any assets 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.

The Issuer also identifies foreign exchange risk. 90% of the Issuer’s cash is kept in PLN. The grants obtained are also denominated in PLN, whereas the costs of clinical trials and external research and development services are mostly denominated in foreign currencies. This risk is partly mitigated by guaranteed and expected revenues from the commercialization of projects, which are denominated in foreign currencies.

The Company’s Management Board is analyzing the Issuer’s situation on an on-going basis. New circumstances, if any, having a significant effect on the Issuer’s financial results and business position, will be communicated promptly in the individual current reports.

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) Colin Goddard – Supervisory Board Member
6) Jarl Ulf Jungnelius – Supervisory Board Member
7) Thomas Turalski – 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
4) Jarl Ulf Jungnelius – Member of the Audit Committee

The Company's Remuneration Committee:

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

**Mr. Vatnak Vat-Ho and Mr. Hendrik Nogai were appointed to the Management Board effective August 1st, 2022.*

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 the date of Report publication

Shareholder	Series A*	Ordinary shares	Number of shares	% of Share Capital	Number of Votes	% of Votes at SM
The Management Board						
Paweł Przewięźlikowski	3 500 000	400 544	**3 900 544**	21.25%	**7 400 544**	33.03%
Krzysztof Brzózka		267 321	**267 321**	1.46%	**267 321**	1.19%
Kamil Sitarz		17 865	**17 865**	0.10%	**17 865**	0.08%
Vatnak Vat-Ho		18 500	**18 500**	0.11%	**18 500**	0.08%
Hendrik Nogai		9 000	**9 000**	0.05%	**9 000**	0.04%
The Supervisory Board						
Tadeusz Wesołowski (directly)		75 575	**75 575**	0.41%	**75 575**	0.34%
Tadeusz Wesołowski (indirectly through Augebit FIZ)**		1 039 738	**1 039 738**	5.66%	**1 039 738**	4.64%
Piotr Romanowski		331 000	**331 000**	1.80%	**331 000**	1.48%
Rafał Chwast		121 115	**121 115**	0.66%	**121 115**	0.54%
Thomas Turalski		20 100	**20 100**	0.11%	**20 100**	0.09%

**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 the date of Report publication

Shareholder	Shares	% [Shares]	Votes	% [Votes]
Paweł Przewięźlikowski	3 900 544	21.25%	7 400 544	33.03%
Bogusław Sieczkowski	825 348	4,50%	1 375 348	6.14%
Nationale Nederlanden OFE	1 530 980	8,34%	1 530 980	6,83%
Aviva OFE Aviva Santander	1 532 000	8,35%	1 532 000	6.84%

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. ADDITIONAL INFORMATION

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

On September 24, 2021 the Company has filed a lawsuit against Mota-Engil Central Europe S.A. in connection with construction of the Research and Development Center for the payment of PLN 13.756.717,07. With this lawsuit, the Company seeks claims related to the agreement for "Construction of the Research and Development Center of Innovative Drugs Selvita S.A.", the conclusion of which was announced by the Company in the current report No. 27/2018 of August 13, 2018. The total value of the Contract was PLN 68,783,585.34 including VAT.

Mota-Engil has filed a lawsuit for payment against to the Regional Court in Kraków in connection with the performance of the general contractor agreement for the project entitled: "Construction of the Research and Development Center for Innovative Drugs Selvita S.A.". The lawsuit was delivered to the Company on January 19, 2022. In the lawsuit the Contractor is claiming damages for the costs incurred in connection with prolonged performance of the Contract, the unpaid portion of the lumpsum 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 from the Company a total amount of PLN 7,671,285.

Significant non-arm's length transactions with related entities

Not applicable.

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

As at the publication date of the report, the Issuer does not form a Capital Group. As at the date of this Report, the Issuer holds 3,20% of shares in fully diluted share capital of 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:

- Complete Phase I/II clinical development of our fully-owned lead asset RVU120 in AML/MDS;
- Expand therapeutic potential for RVU120 in solid tumors in the ongoing Phase I/II study;
- Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in IDH-mutated AML and potentially other indications;

- Strengthen position in novel target discovery and in developing novel, proprietary drug candidates in synthetic lethality;
- Complete preclinical programs for STING candidate
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources.

Description of factors and events, in particular of an unusual nature, having a significant effect on the financial performance

In the reported period, the Covid-19 pandemic occurred. The Issuer described its effect on the Company's operations under Significant events that occurred in the reporting period.

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 30 to the financial statements.

Information on deferred income tax provisions and assets

Information on deferred income tax provisions and assets is provided in note 10 to the financial statements.

Information on significant purchases or disposals of tangible fixed assets

Information on tangible fixed assets is provided in note 13 to the consolidated financial statements.

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

Information on the liabilities in respect of purchases of tangible fixed assets is provided in note 37 to the consolidated financial statements.

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

Information on events that occurred after the date for which the financial statements were prepared is provided in note 46 to the financial statements.

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 38 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 27th, 2022

Dokument podpisany przez PAWEŁ TADEUSZ PRZEWIĘŹLIKOWSKI
Data: 2022.09.27 09:41:13 CEST

Paweł Przewięźlikowski
President of the Management Board

Dokument podpisany przez Krzysztof Daniel Brzózka
Data: 2022.09.27 12:59:31 CEST

Krzysztof Brzózka
Vice-President of the Management Board

Dokument podpisany przez Kamil Sitarz
Data: 2022.09.27 00:25:32 CEST

Kamil Sitarz
Management Board Member

Signature Not Verified
Digitally signed by Vatnak Vat-Ho
Date: 2022.09.27 01:16:56 MDT

Vatnak Vat-Ho
Management Board Member

Signature Not Verified
Digitally signed by Franz Hendrik Nogai
Date: 2022.09.27 08:39:46 CEST

Hendrik Nogai
Management Board Member

CONTACT

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GENERAL INQUIRIES

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RYVU THERAPEUTICS