RYVU THERAPEUTICS S.A.

ANNUAL REPORT

2022

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1 ECONOMIC AND FINANCIAL HIGHLIGHTS

1.1 Financial Results Obtained in the Reporting Period

Financial Statements of Ryvu Therapeutics S.A. ("Company", "Issuer", "Ryvu") for the period from January 1, 2022 to December 31, 2022 are prepared in accordance with the International Financial Reporting Standards.

Selected balance sheet data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand		Data in EUR thousand	
Item	**31.12.2022**	31.12.2021	**31.12.2022**	31.12.2021
Total assets	**474,977**	228,813	**101,277**	49,748
Short-term receivables	**16,931**	11,741	**3,610**	2,553
Share issue receivables	**242,962**	0	**51,805**	0
Cash and cash equivalents	**101,917**	83,236	**21,731**	18,097
Other financial assets	**528**	4,994	**113**	1,086
Total liabilities	**131,586**	67,512	**28,057**	14,678
Long-term liabilities	**86,772**	31,312	**18,502**	6,808
Short-term liabilities	**44,814**	36,200	**9,555**	7,871
Total equity	**343,390**	161,302	**73,219**	35,070
Share capital	**7,342**	7,342	**1,565**	1,596

Selected income statement data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
Item	**From 01.01.2022 to 31.12.2022**	From 01.01.2021 to 31.12.2021	**From 01.10.2022 to 31.12.2022**	From 01.10.2021 to 31.12.2021	**From 01.01.2022 to 31.12.2022**	From 01.01.2021 to 31.12.2021	**From 01.10.2022 to 31.12.2022**	From 01.10.2021 to 31.12.2021
Revenues from sales	**142**	828	**40**	273	**30**	181	**9**	59
Revenues from subsidies	**29,491**	24,226	**9,997**	6,033	**6,290**	5,292	**2,132**	1,302
Revenues from R&D projects	**38,804**	10,358	**24,579**	10,358	**8,277**	2,263	**5,242**	2,235
Other operating revenues	**2,054**	723	**406**	189	**438**	158	**87**	41
Revenues from operating activities	**70,490**	36,135	**35,022**	16,853	**15,036**	7,894	**7,469**	3,636
Operating expenses	**-148,913**	-114,734	**-35,706**	-35,160	**-31,763**	-25,065	**-7,615**	-7,587
Operating expenses without Incentive Scheme and valuation of Nodthera shares	**-117,800**	-92,021	**-32,335**	-26,122	**-25,126**	-20,103	**-6,896**	-5,636
Depreciation	**-12,900**	-12,561	**- 2,926**	-3,445	**-2,752**	-2,744	**-624**	-743
Valuation of Incentive Scheme	**-22,184**	-22,999	**-2,244**	-8,004	**-4,732**	-5,024	**-479**	-1,727
Profit/loss from operating activities (EBIT)	**-78,422**	-78,599	**-684**	-18,307	**-16,727**	-17,171	**-146**	-3,950
Profit/loss from operating activities (EBIT) without Incentive Scheme and valuation of Nodthera shares	**-47,309**	-55,886	**2,687**	-9,269	**-10,091**	-12,209	**573**	-2,000
Profit/loss before income tax	**-79,195**	-78,599	**-2,425**	-18,342	**-16,892**	-17,171	**-517**	-3,958
Net profit/loss	**-83,782**	-79,078	**-8,525**	-18,453	**-17,871**	-17,275	**-1,818**	-3,982
Net profit/loss without Incentive Scheme	**-61,598**	-56,079	**-6,281**	-10,449	**-13,139**	-12,251	**-1,339**	-2,255
EBITDA	**-65,522**	-66,038	**2,242**	-14,862	**-13,976**	-14,427	**478**	-3,207
EBITDA without Incentive Scheme and valuation of Nodthera shares	**-34,409**	-43,325	**5,613**	-5,824	**-7,339**	-9,465	**1,197**	-1,257
Net cash flows from operating activities	**21,319**	-58,886	**59,923**	-723	**4.547**	-12,864	**12,779**	-156
Net cash flows from investing activities	**690**	8,055	**137**	2,941	**147**	1,760	**29**	635
Net cash flows from financing activities	**-2,455**	-2,152	**-770**	-2	**-524**	-470	**-164**	0
Total net cash flow	**19,554**	-52,983	**59,290**	2,216	**4,171**	-11,575	**12,644**	478
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)	**-4.56**	-4.31	**-1.09**	-1.01	**-0.97**	-0.94	**-0.23**	-0.22
Diluted profit (loss) per share (in PLN)	**-4.56**	-4.31	**-1.09**	-1.01	**-0.97**	-0.94	**-0.23**	-0.22
Book value per share (in PLN)	**18.71**	9.23	**18.71**	9.23	**3,99**	2.01	**3,99**	2.01
Diluted book value per share (in PLN)	**18.71**	9.23	**18.71**	9.23	**3,99**	2.01	**3,99**	2.01
Declared or paid dividend per share (in PLN)	**-**	**-**	**-**	**-**	-	-	-	-

Selected financial data presented in the annual 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 – 31/12/2022: PLN 4.6883;
   - for the period from 01/01/2021 – 31/12/2021: PLN 4.5775;
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 31 December 2022: PLN 4.6899;
   - as of 31 December 2021: PLN 4.5994.

1.2 Management Board comments to the financial results

Ryvu Therapeutics S.A. has only one operating segment, i.e. innovative segment.

In 2022, Ryvu Therapeutics S.A. recognized the total operating revenue of PLN 70,490 thousand, which constitutes a 95% increase compared to the corresponding period in 2021, when the total operating revenue amounted to PLN 36,135 thousand. This results from both the increase in revenues from R&D projects (increase of PLN 28,446 thousand) and increase in revenues from subsidies (increase of PLN 5,265 thousand) compared to the corresponding period in 2021.

Revenues from R&D projects in 2022 resulted from the following transactions:

- The exclusive license agreement with Exelixis Inc. The agreement combines Ryvu's proprietary small molecule STING agonists and STING biology knowhow with Exelixis' network of expertise and resources in antibody engineering, antibody-drug conjugate (ADC) technologies, and oncology therapeutics development and commercialization experience. Under the terms of the agreement, Exelixis paid Ryvu an upfront fee of USD 3 million in July 2022.
- The exclusive research collaboration and license agreement with BioNTech SE. Under the terms of the License Agreement, BioNTech paid Ryvu an upfront fee (less withholding tax) of EUR 20 million (PLN 93.6 million converted at the average exchange rate of the NBP for November 29, 2022, EUR 1 = PLN 4.6813) in exchange for the global, exclusive license to develop and commercialize Ryvu's STING agonist portfolio as standalone small molecules, including as monotherapy and in therapeutic combinations, and for the right to license on an exclusive basis multiple small molecule programs ("BioNTech Exclusive Targets") as part of multi-target research collaboration. In accordance with the accounting policy of Ryvu and IFRS 15, in 2022 Ryvu recognized only part of the upfront revenues in the amount of EUR 5 million (PLN 23.4 million). The remaining amount of upfront payment (EUR 15 million (PLN 70.3 million)) together with the impact of the settlement of the investment agreement regarding BioNTech's participation in December's share issuance (PLN 1,1 million – the difference between the price fixed for investors during the issue and the price specified in the BioNTech's investment agreement) will be recognized equally in each period for the next 5 years.

In 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 period ended December 31, 2022, amounted to PLN 83,782 thousand in comparison to the net loss of PLN 79,078 thousand in the corresponding period of 2021. The slightly bigger loss in 2022 is related to the fact that not all of the upfront from BioNTech is recognized in revenue in 2022 (described above). Additionally bigger loss in 2022 is related to higher expenditure incurred on research and clinical projects and to negative impact on the valuation of NodThera shares in the amount of PLN 8,929 thousand.

Valuation of shares in NodThera Inc.

Valuation of shares

As of December 31, 2022, four types of shares existed in NodThera Inc.: ordinary stock and preferred stock (Junior Preferred Stock, Series A1 and A2 Preferred Stock, Series B Preferred Stock and Series C Preferred Stock). Ryvu is a holder of the Junior Preferred Stock.

Associated with the Series A, B and C Preferred Stock is the right to receive dividends in the form of cash or the issuance of shares of the same class and also the non-dilution right. The payment of dividends and execution of the anti-dilution right may be made only 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. The shares held by Ryvu, i.e. Junior Preferred Stock, do not have the aforementioned right to pay dividends or the non-dilution right.

Series C Preferred Stock was issued by NodThera Inc. on September 20, 2022. The issue comprised of 8,698,375 shares at a price of USD 2.8741 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. Ryvu did not participate in the issue.

Thanks to the receipt of funds raised from the Series C share issue, according to information obtained from NodThera Inc., 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 seek additional capital for development in 2024 and the following years.

The Management Board of Ryvu has decided to include in the valuation of the shares held by Ryvu in NodThera, a 15.23% 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 December 31, 2022.

Therefore, a share valuation of GBP 2.4363/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) should be used as a basis for the calculations. As of 31.12.2022 Ryvu held 3.18% shares in NodThera on a fully diluted basis and the total valuation of the Issuer's shares in NodThera Inc. amounts to PLN 20,475,200 (at the average NBP exchange rate of 4,4018 PLN/USD).

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

new share issue price (in USD)	2.4363
average NBP exchange rate from December 31, 2022	4.4018
new share issue price (in PLN)	10.72
number of the Company's shares in NodThera Inc.	1,910,000
value of shares in the balance sheet as of December 31, 2022	20,475,200
value of shares in the balance sheet as of December 31, 2021	29,403,922
change in valuation – gross impact on the valuation of shares	**-8,928,722**
value of shares in the balance sheet as of September 30, 2022	21,602,100
gross impact on valuation of shares	-1,126,900

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 to the Company free of charge by Mr. Paweł Przewięźlikowski – founder, President of the Management Board and Company's largest shareholder, 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 December, 2022 the Company recognized the non-cash cost of valuation of this incentive program of PLN 22,184 thousand – more details are described in note 32 to the financial statements.

Issue of Series "J" Shares

In Q4 2022, the Company also carried out a successful issue of Series "J" Shares, as a result of which the Company secured over PLN 242.5 million net. See Section 2.7.A below for more details.

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

As of December 31, 2022, the value of the Company's assets was PLN 474,977 thousand and increased by PLN 246,164 thousand compared to the end of 2021 (PLN 228,813 thousand), mainly due to the issue of series "J" shares and cash inflow from BioNTech and Exelixis license agreements, partially compensated by expenditures on R&D projects. At the end of December 2022, the largest component of the current assets are share issue receivables in the amount of PLN 242,962 thousand (at the end of 2021 it was none). Ryvu was eligible to receive the funds from the issue after the registration of the capital increase, which took place in January 2023. Therefore, as of December 31, 2022, in assets the "Share issue receivable" and in the equity "Share premium paid up but not registered as at the balance sheet date" were recognized. The second largest component of the current assets was cash which amounted to PLN 101,917 thousand (at the end of 2021 it was PLN 83,236 thousand). The increase in cash resulted from the aforementioned cash inflow from BioNTech and Exelixis license agreements, partially compensated by spending incurred on R&D projects and Polish 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 CBR and laboratory equipment and the valuation of NodThera of PLN 20,475 thousand. The value of non-current assets decreased compared to December 31, 2021, by PLN 17,518 thousand. The decrease consists mainly of the negative impact from the valuation of NodThera shares (described above) and depreciation of fixed assets partially compensated by expenditures on the new lab equipment.

The main item in Ryvu's equity and liabilities is equity, which amounted to PLN 343,390 thousand as of December 31, 2022, and increased by PLN 182,088 thousand compared to December 31, 2021. The increase in equity is mainly a result of the share's issue compensated by net loss recognized for the period. The other source of assets funding are long-term liabilities which amounted to PLN 86,772 thousand at the end of December 2022. Long-term liabilities mainly related to deferred income related mainly to the deferred revenue from 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:

	31.12.2022	31.12.2021
Current ratio current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)	8.82	3.83
Quick ratio (current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)	8.77	3.75

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

1.4 Current and Projected Financial Condition

The Company's financial position as of the report date is very good taking into account the current cash position and expected financing from the EIB. As of December 31, 2022, the value of the Company's cash amounted to PLN 101,917 thousand and as of March 17, 2023, it was PLN 320,589 thousand. The increase in cash mainly results from the receipt of funds from the issue of series "J" shares carried out in December 2022.

On August 16, 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 2.7.A 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.

1.5 Significant off-balance sheet items

Significant off-balance sheet items are described in Note 34 to the financial statements.

1.6 Financial forecasts

The issuer did not publish financial forecasts for 2022.

1.7 Principles of preparation of annual financial statement

These principles were described in Issuer's financial statement.

1.8 Unusual factors and events having impact on activities results

Coronavirus (COVID-19)

The Coronavirus (COVID-19) pandemic continued during the reporting period. Its impact on the operations and results of the Issuer is presented below in section 2.8.

1.9 Data regarding agreement with entity authorized to audit financial statements

The agreement with an entity authorized to audit financial statements, i.e. PricewaterhouseCoopers Polska spółka z ograniczoną odpowiedzialnością Audyt sp. k. to audit the financial statements of Ryvu Therapeutics S.A. was concluded on September 19, 2022 for the period of 2022-2024.

The remuneration of the entity authorized to audit financial statements together with the classification of particular types of services is described in the financial statements.

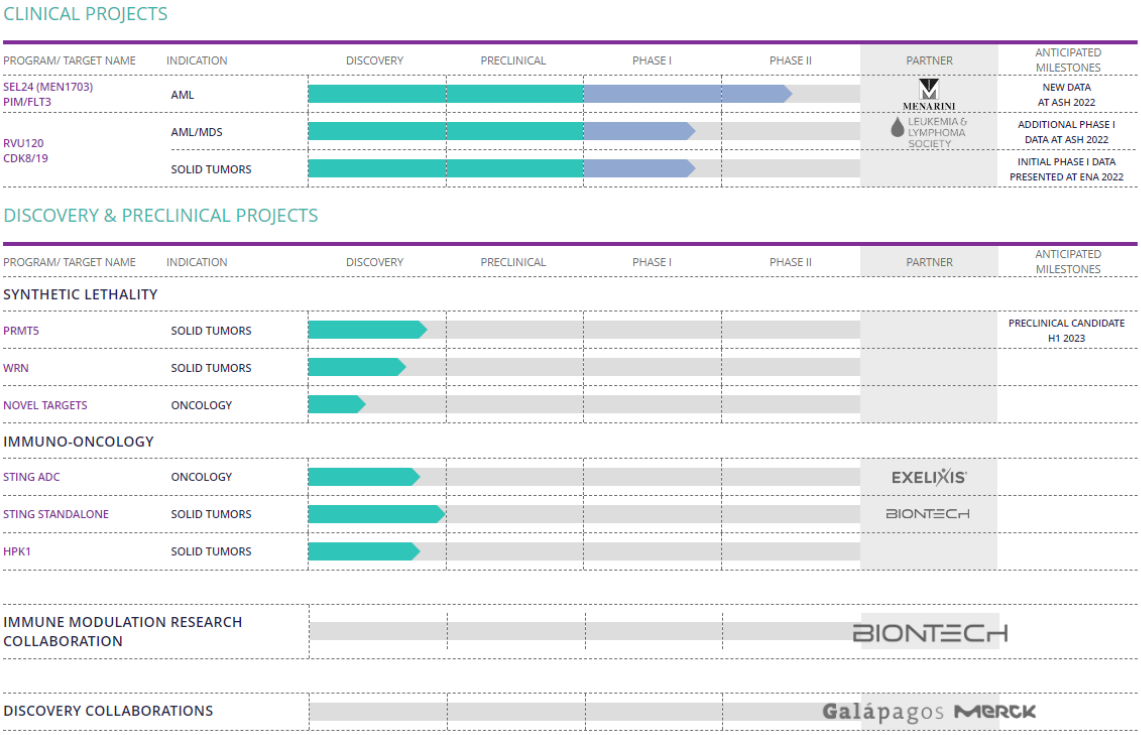
2 INFORMATION ON ISSUER'S ACTIVITIES

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 and immuno-oncology 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. Ryvu has also been assisting in translational research on the project.

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.

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.

In June 2022 during the ASCO Annual Meeting and at the EHA Hybrid Congress 2022 Menarini presented a poster 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. One patient with an IDH1 mutation achieved a CRh at cycle 3 and underwent hematopoietic stem cell transplant. 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.

During the ASH Annual Meeting & Exposition in December 2022, Menarini and its collaborators presented translational data on SEL24 (MEN1703). There were four posters on combination therapy of SEL24 (MEN1703) with gilteritinib and SEL24 (MEN1703)-induced PIM inhibition and mechanism of action demonstrated *in vitro* in multiple myeloma (MM), classical Hodgkin lymphoma-tumor-associated macrophages (cHL-TAMs), and diffuse large B-cell lymphoma (DLBCL) models showing the potential of SEL24 (MEN1703) in these malignancies.

Ryvu receives information on the study progress from Menarini during periodic technical and joint steering committee meetings. Based on information received by Ryvu in March 2023, Menarini is considering additional clinical trials in order to better explore the potential of SEL24 (MEN1703) in various disease settings, however as of the date of the report no further clinical development plans have yet been approved by the Menarini management.

RVU120 (SEL120)

RVU120 (also known as SEL120) is a clinical stage, selective, first-in-class dual inhibitor of CDK8 and CDK19 kinases. RVU120 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 CDK19 using 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 [RIVER-51], 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 RIVER-51 clinical trial was dosed in September 2019. The study is currently enrolling at seven investigational sites in the US and Poland. Ryvu presented updated data on the safety and efficacy of RVU120 at doses between 75 mg and 110 mg of this ongoing study at the ASH Annual Meeting & Exposition in December 2022. As of November 11, 2022, 19 patients have been treated with RVU120. Nine of 16 evaluable patients showed clinical benefit: one patient with AML had a complete response, four patients had hematologic improvement and four patients had blast reductions. Importantly, RVU120 demonstrated a favorable safety profile. Additionally, a dose- and exposure-dependent inhibition of pSTAT5 as a marker of target engagement has been observed in patients treated with RVU120. As of March 3, 2023,enrollment was ongoing at the dose of 135 mg EOD.

The other ongoing clinical study with RVU120 (RVU120-SOL-021 [AMNYS-51], 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. Part 2 (Phase II) is aimed both at safety and efficacy expansion. Part 2 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 study is currently enrolling at five investigational sites in Poland and Spain. Preliminary data of the dose escalation part were presented as a poster at the 34th EORTC-NCI-AACR Symposium in October 2022. After the data cut-off for that conference, a biomarker inhibition of >70% has been achieved in a patient dosed at the 135mg cohort. Based on preclinical assumptions, this threshold is sufficient to obtain high efficacy in selected patient groups with hematologic malignancies. As of March 3, 2023, enrollment was ongoing at the dose of 375 mg EOD.

Key achievements in RVU120 clinical development:

- Poster presentation at the European Hematology Association Congress in Vienna in June 2022, Ryvu presented data from RIVER-51, the ongoing Phase Ib dose-escalation study of RVU120 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.
- Poster presentation at the 34th EORTC-NCI-AACR Symposium in Barcelona in October 2022, Preliminary data from the ongoing dose escalation part of AMNYS-51 patients with relapsed/refractory metastatic or advanced solid tumors were presented. As of the cut-off date, 17 patients had been treated with RVU120 at doses between 75 mg and 175 mg. The adverse event profile was favorable with mild or moderate gastrointestinal events as the most frequent. There were no drug-related serious adverse events (SAEs), no dose-limiting toxicities (DLTs), and no adverse event was leading to drug discontinuation. A dose-dependent increase of RVU120 exposure was observed with expected variability. pSTAT5 inhibition as a marker of target engagement correlated with exposure and a more than 60% inhibition was observed at a dose of 135 mg. Disease stabilization was achieved in 4 out of 11 evaluable patients, of which 3 lasted for more than 4 months.
- Poster presentation at the ASH Annual Meeting & Exposition in December 2022, updated safety and efficacy data were presented of a total of 19 patients (16 patients with AML, 3 patients with HR-MDS). Nine of 16 evaluable patients showed clinical benefit: One patient with AML had a complete response, four patients had hematologic improvement and four patients had blast reductions. RVU120 demonstrated a favorable safety profile. A meaningful inhibition of pSTAT5 of >70% has been observed in patients treated with RVU120 in a dose- and exposure-dependent manner.

In the opinion of Ryvu's Management Board, the data warrant continuation of dose escalation and collection of additional clinical data.

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 CLI120-001 (RIVER_51) study 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

Ryvu is carrying out several discovery stage projects in the area of synthetic lethality. Ryvu's most advanced project in the field of synthetic lethality focuses on cancers with a deletion of the metabolic gene MTAP, which occurs in 10 to 15% of all human tumors. MTAP deletion results in massive accumulation of methylotioadenosine (MTA) in cells. MTA at 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 a 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 year 2022 focused on the expansion of the main chemical series into a lead series with the key aim to demonstrate in vivo proof of concept, which would then allow for the nomination of a preclinical candidate in 2023. Experimental works on improving the properties of the chemical series were continued with respect to potency, selectivity measured by the inhibition of SDMA in MTAP-deleted versus MTAP WT cells, and particularly PK parameters in rodent species (necessary for pharmacological and toxicological characterization). Ryvu compounds selectively inhibit growth of MTAP-deleted cancer cells in prolonged 3D culture, which strongly correlates with inhibition of PRMT5-dependent protein symmetric dimethylation (SDMA) in those cells. Selectivity between effects observed in MTAP-deleted and WT cells exceeds 100-fold both for SDMA and growth inhibition. This optimization allows for selection of new improved, orally bioavailable derivatives for larger scale synthesis and efficacy studies in animal models, which are planned in H1 2023.

Results on the development of MTA-cooperative PRMT5 inhibitors were presented at the two international conferences: (i) first one, the annual AACR (American Association for Cancer Research) conference in New Orleans, United States in April 2022, and (ii) a second one, with a summary of optimization progress and an early lead compound profile, together with *in vivo* results in a mouse model showing tumor growth inhibition and pharmacodynamic biomarkers in MTAP-deleted tumors at the annual ENA (EORTC-NCI-AACR) symposium in Barcelona, Spain in October 2022.

The goal of the second disclosed project from synthetic lethality portfolio is to identify and develop first-in-class, small molecule, chemical inhibitors of the Werner syndrome helicase (WRN), which plays an important role in cell proliferation, the replication stress response, and DNA repair. Loss of DNA mismatch repair is a common initiating event in cancer development and it is responsible for 10-30% of endometrial, colorectal, ovarian and gastric cancers. Scientific data reveals promising synthetic

lethal interaction between inactivation/inhibition of the WRN helicase and tumors with microsatellite instability (MSI) - a phenotype that arises from DNA mismatch repair deficiency. These studies have highlighted the therapeutic potential of WRN inhibitors and holds promise for patients bearing tumors with MSI.

Ryvu's WRN project was initiated by several high-throughput screening campaigns that provided a number of small-molecule WRN-inhibiting actives, characterized by different scaffolds. Several most promising chemotypes were selected for further development. In 2022 major research efforts were focused on optimization of key physicochemical properties and expansion around the main chemical series, as well as validation and exploration of the inhibitor mode of action.

In addition to the two disclosed projects, Ryvu is currently running a number of internal initiatives focused on identifying and validating new targets in the field of synthetic lethality, with potential for first-in-class drug discovery. Work is currently underway to validate several therapeutic targets identified so far. High-throughput screening campaigns and alternative approaches are ongoing to identify active compounds for two of the selected molecular targets. At the end of H2 2022, both targets were in the hit validation stage, where the desired biological activity and specificity are confirmed using orthogonal biochemical and biophysical methods.

Since the beginning of 2022, work has been underway to implement Ryvu's own innovative target discovery platform based on genome-wide screening in cancer cells with defined genotype. The methodology enables the detection of new biological targets that meet the definition of synthetic lethality and other candidates for targeted therapies (e.g. disease specific, actionable oncogenic drivers). These therapies will target genetically stratified patient populations in which the tumor genotype significantly increases the chances of a clinical response. The Ryvu platform enables modeling the influence of the tumor microenvironment (stress conditions and 3D culture) and the use of cells directly isolated from patients' tumors (primary cells) in high-throughput screening. The Ryvu platform is currently used for genomic alterations (mutations or deletions of genes) with the biggest unmet medical need.

Collaboration with BioNTech on Immunotherapy and STING

On November 29, 2022, BioNTech and Ryvu entered into a multi-target research collaboration for several small molecule immunotherapy programs as well as an exclusive license agreement for Ryvu's STING agonist portfolio as standalone small molecules. BioNTech received a global, exclusive license to develop and commercialize Ryvu's STING agonist portfolio as standalone small molecules, including as monotherapy and in therapeutic combinations. In addition, BioNTech and Ryvu will jointly undertake drug discovery and research projects to develop multiple small molecule programs directed at exclusive targets selected by BioNTech, primarily focused on immune modulation within oncology, with potential applications in other disease areas. BioNTech has the option to license global development and commercialization rights to these programs at the development candidate stage. Multiple research programs are underway jointly but remain confidential.

Collaboration with Exelixis on STING ADCs

On July 7, 2022, Exelixis and Ryvu entered into an exclusive license agreement focused on the development of novel targeted therapies utilizing Ryvu's STING technology. As part of the optimization of the STING agonists developed by Ryvu, the company identified active compounds with a variety of chemical groups that allow easy combination with a reactive chemical group. This modification allows

for further development of agonists in the form of antibody-drug conjugates (ADC), where the antibody enables targeted delivery of the active STING agonist. Under the terms of agreement, Exelixis will develop antibody-drug conjugates leveraging Ryvu's STING agonist portfolio.

In January 2023, the first milestone within the collaboration was achieved, which, in line with the agreement, made Ryvu entitled to a payment of USD 1 million. Further project progress remains confidential.

Collaboration with Galapagos on Inflammation

On April 16, 2020, Galapagos and Ryvu entered into a collaboration focused on the discovery and development of novel small molecule drugs in inflammation. On December 14, 2021, the companies announced that Galapagos exercised its exclusive option for the program. The joint research collaboration is focused on the discovery and development of novel small molecule drugs in inflammation. In November 2022, Galapagos announced a strategy to focus its R&D investment in the areas of immunology and oncology, and so a further update on progress and prioritization is expected with high risk of terminating the collaboration with Ryvu.

OTHER PROJECTS

Ryvu is also 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. The results of the project so far are compounds with high selectivity for HPK1 kinase, metabolic stability and in vivo activity in a mouse model for selective pharmacodynamic biomarkers. At the same time, the main chemical series and the lead compound require further improvement of the safety parameters related to the potential risk of cardiotoxicity and an increase of the therapeutic window.

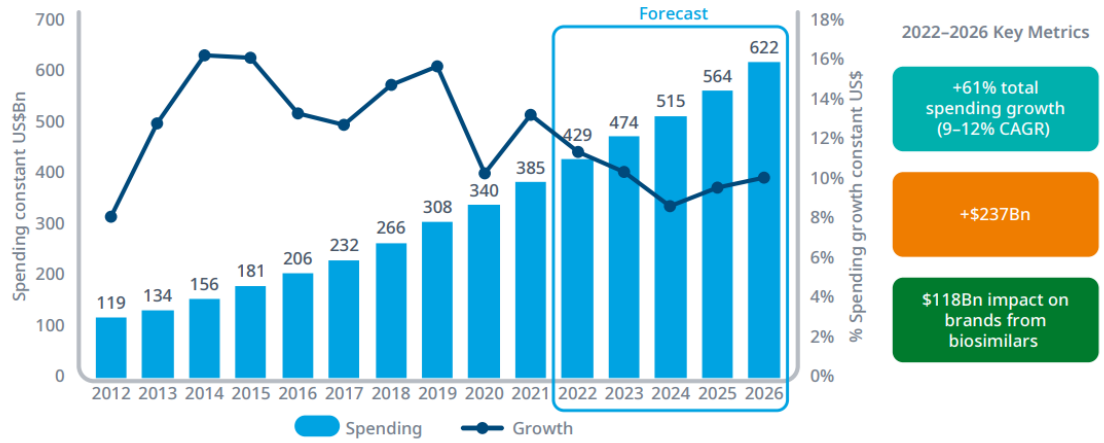
2.2 Characteristics of the biotechnology industry

The life science industry is one of the most globalized sectors of the economy. Compounds with therapeutic potential developed in one country are protected by international patents and commercialized as drugs all over the world. Their creation often involves many subcontractors operating in different countries on different continents. It is a truly global marketplace where the discovery and development of projects in one part of the world has a direct impact on the industry in other parts of the world. For this reason, the assessment of the competitive environment for innovative companies in the pharmaceutical industry makes sense only in a global context.

According to IQVIA, the global pharmaceutical market will reach $ 1.8 trillion in 2026, growing at a rate of 3-6% CAGR annually through 2026. The main growth leaders will likely be the US market and emerging markets (including China, Bangladesh, Brazil, Chile, Russia, India, Algeria and the Philippines), where the annual growth rate is up to 3% and 5-8%, respectively. IQVIA analysts predict that developed countries will see growth of 2-5% through 2026. The largest emerging market is expected to be China where revenue is estimated to exceed $205 billion in 2026 with growth of 2.5-5.5%.

The research and development portfolios of companies in the industry are constantly growing, while at the same time the success rates in drug development are at historic highs. It is expected that this will result in an increasing number of new products that will be commercialized over the next five years. Over the next five years, more than 250 new active substances are expected to launch in the U.S., with an aggregate total of more than $22 billion in new brand spending per year. Globally, product launches of new active substances launches are projected to average 54-63 launches per year, totaling 290-315 launches total in 2022-2026.

Exhibit 38: Global biotech spending and growth



Source: IQVIA Institute, Nov 2021

In addition to the above-mentioned statistical figures, a characteristic feature of the biotechnology market is also that the commercialization of the final drug product is preceded by several formal stages, which often take many years to be completed and are characterized by various degrees of probability of success.

These stages can be described as follows:

1) drug discovery stage,

2) preclinical studies (in vitro and in vivo)

3) clinical trials (which typically include three phases)

4) regulatory evaluation and approval

5) commercialization of an approved drug

A key characteristic of the biotechnology market is that only a small percentage of substances that were analyzed at the drug discovery stage will be approved by the relevant authorities and consequently commercialized as an actual drug. An important element is that at each of the above-mentioned stages, it may turn out that company will be unable to advance the project to the next phase. It is also possible that the company, despite the project's transition to the next stage, will be forced to return to an earlier stage in order to conduct additional research or development activities (for example, due to a requirement of the relevant authorities or due to new circumstances).

In connection with the above, a characteristic feature of the biotechnology market is also that projects can span many years, and the probability of success can be extremely difficult to estimate.

Oncology drugs market

According to GLOBOCAN, 19.3 million people in the world were diagnosed with cancer in 2020 (in 2012 it was 14.1 million people, so the number of cases increased by 37% compared to 2012). Furthermore 9.95 million patients died, which is 21% more than in 2012, when 8.2 million fatalities were reported (source: http://gco.iarc.fr/). The current data and forecasts for Poland show that in 2015-2024 cancer will be second in the rankings of the most common causes of mortality (comprising 20% of deaths), and this phenomenon reflects the global trend ("Strategy for Fighting Cancer" http://www.walkazrakiem.pl/).

According to estimates by Allied Market Research, the global market for oncology drugs market was worth USD 135,494 million in 2020 and is expected to reach USD 274,400 million in 2030, growing at a rate of 7.5% (CAGR) from 2021 to 2030. The key drivers of the global oncology/cancer drugs market are a surge in the geriatric population, surge in prevalence of cancer, higher rate of early screening for cancer, and higher number of R&D activities to develop cancer therapeutics. Promising drugs in late stage development in emerging economies are further expected to provide lucrative opportunities for market expansion. However, adverse effects related to cancer drugs impede the oncology drugs market growth.

In recent years, a record number of anticancer drugs have been released to the market, offering much needed new therapeutic options for cancer patients. In the US alone over the past 5 years, there were 62 unique new cancer medicines launched with many approved for more than one indication. More than half of these new therapies are for oral administration, have the status of a rare disease drug, or are for use in the presence of a specific biomarker. Of the cancer types accounting for the majority of spending in developed countries, kidney cancer, non-small cell lung cancer, chronic lymphocytic leukemia, melanoma, and multiple myeloma saw a 20% or higher increase in annual spending since 2017, reflecting new treatment options with new mechanisms, improved diagnosis rates and longer treatment durations.

Therapeutic guidelines have also changed to maximize the benefit that patients can achieve. Unfortunately, despite the high R&D activity, oncology remains the area of the greatest unmet medical needs and, at the same time, the greatest research and development challenge.

Oncology trial starts in 2020 reached historic high levels, 60% higher than started in 2015, reflecting strong momentum in this area.

According to the data provided by IQVIA, global spending on oncology drugs reached $164 billion in 2020 and has increased at a compound annual growth rate of 14.3%, driven by the surge in innovative treatments, expanded access and a strong focus across health systems to increase early-stage diagnosis and treatment of patients.

IQVIA also predicts that R&D spending in the oncology area will grow at a rate of 3% by 2024, compared to 4.2% in 2010-2018. This decrease can be attributed to drug development strategies focused on increasingly narrower therapeutic indications (i.e. biomarker driven), where the cost of clinical trials is often lower.

Oncology drugs reached record high proportions of drug development, accounting for more than 40% of early-stage and more than 30% of late-stage pipeline development. Half of the late-stage oncology pipeline is in development for rare cancers and includes a wide range of next-generation and targeted therapies. Growth in the pipeline of next-generation biotherapeutics stalled in 2020 after almost

doubling in the prior two years, but further growth may be expected in the areas of cell and gene therapy and RNA therapeutics, for example.

By therapeutic area, oncology and immuno-modulatory drugs were the most expensive to develop, coming in at a median of $2.8 billion, according to estimates published by JAMA in 2020.

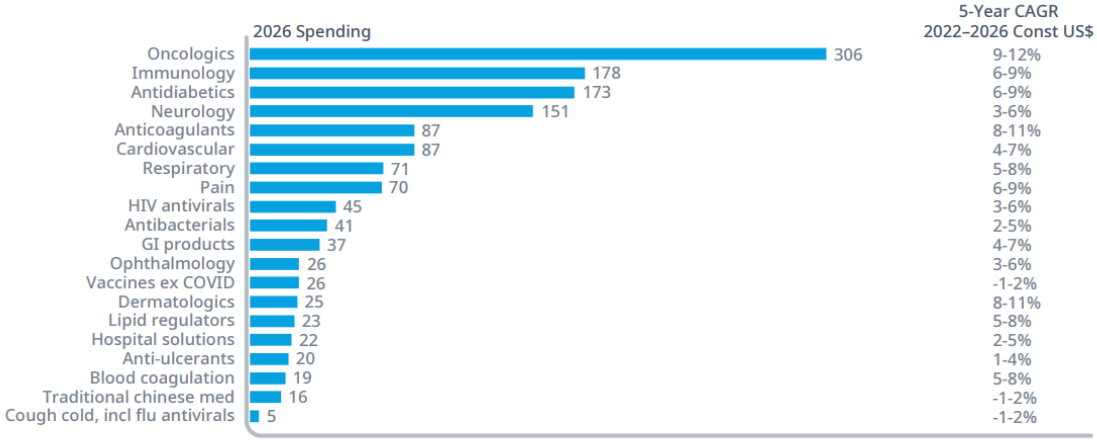
Oncology partnering

For the Issuer's innovative projects, a key strategic element is the market of partnering agreements (licensing and collaboration agreements) concluded between companies within the biotechnology and pharmaceutical industry. The growing importance of partnering is related to the prevailing model of innovation in the pharmaceutical industry where there are several key players with distinct but often overlapping focuses: 1) academic institutions, generally conducting basic research, 2) biotechnology companies, generally conducting early stage research and development, 3) and pharmaceutical companies, generally involved in advanced clinical research and global drug commercialization. Almost half of the revenues of large pharmaceutical companies are from drugs that have been developed outside their laboratories. This model creates an extensive market of projects, purchased by large pharma/biotech companies from other pharma/biotech companies across the spectrum of development from discovery through commercial stages.

Investments in oncology far exceed those in other therapeutic areas, and partnering is a key strategy for these investments. In the years 2016-2020, the cumulative value of contracts in oncology totaled $331 billion, according to Clarivate Analytics.

The two leading global therapy areas — oncology and immunology — are forecast to grow 9–12% and 6–9% CAGR through 2026, lifted by significant increases in new treatments and medicine use and offset by losses of exclusivity, including biosimilars. Oncology is projected to add 100 new treatments over five years, contributing nearly $120 billion in new spending and bringing the total market to more than $300 billion in 2026.

Exhibit 42: Top 20 therapy areas in 2026 in terms of global spending with forecast 5-year CAGRs, const $US



Source: IQVIA Institute, Nov 2021

Immuno-oncology is a significant subsegment of oncology drug development, both in terms of investment in research and development and partnering. It is estimated that by 2025 the total immuno-oncology market will be worth around USD $93 billion at a compound annual growth rate (CAGR) of 10%. This increase will also be associated with significant changes in the way cancer patients

are treated, which are expected to occur over the next decade (according to GlobalData, a research and consulting company).

2.3 Significant contractors

The Issuer's operations require the use of services necessary for R&D work. The contractors providing services to the Issuer is relatively well diversified. The share of contractors (service providers) that have reached at least 10% of total sales revenues is moderate. The key contractors shown below are not related to the Issuer.

	Financial year ended 31/12/2021 [net value] PLN
Contractor A	**7,668,042.70**
Contractor B	**4,639,317.59**

The main customers are presented in the financial statements in the Note 6.

The transactions with related companies are presented in the financial statements in the Note 29.1.

2.4 Changes in the basic principles of managing the Issuer's enterprise

There were no such changes in the 2022 financial year.

2.5 Employment data

At the end of 2022 Ryvu Therapeutics S.A. was employing 215 people.

	As of 31.12.2022	As of 31.12.2021	As of 31.12.2020
Ryvu Therapeutics S.A.	**215**	**190**	**161**

2.6 Sponsoring and charitable activities

Charitable activities are essential to Ryvu's commitment to social responsibility and community engagement. Throughout 2022, the company undertook various initiatives to support and uplift the communities it operates in.

Ryvu Therapeutics intends to build long-term relationships with charity organizations as part of its Corporate Social Responsibility. The Company supports UNICORN Charitable Association in Krakow, a charitable organization established in 1999 which supports oncology patients and their families. The association runs the first Polish psycho-oncology centre, where cancer patients receive professional psychological help to support them through the diagnosis and treatment.

Ryvu Therapeutics also participated in a Krakow charity run organized by Poland Business Run Foundation, supporting people with mobility impairment in overcoming social barriers. Also, the foundation promotes awareness of disabilities and tries to change the social perception of disabled people.

Furthermore, in 2022, Ryvu started working with “Dom Ukraiński” Foundation, a non-governmental organization located in Poland that aims to promote Ukrainian culture and integrate the Ukrainian community into Polish society. During times of war, the Foundation focuses on providing humanitarian aid and support to affected Ukrainian people.

Charitable donations by Ryvu Therapeutics in 2022 amounted to over 42 thousand PLN.

2.7 Significant events in 2022

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.

Earlier, on September 24, 2021 Ryvu 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. The total value of the Contract was PLN 68,783,585.34 including VAT.

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 its 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 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 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 disease settings.

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.

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 retained all development and commercial rights to develop its STING agonist portfolio as standalone small molecules; these rights were subsequently licensed to BioNTech (see below). Under the terms of the Agreement, Exelixis 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 the 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 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 at 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 early-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 a 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's 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 and amendment of Articles of Association

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 can give flexibility to size 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.

The amendments to the Company's Articles of Association resulting from the increase of its authorized capital have been registered by the registry court on October 3rd.

Resolution on issuance of shares within the framework of authorized capital and conclusion of lock-up agreements

On October 5, 2022, the Company's Management Board adopted a resolution on increasing the Company's share capital within the limits of authorized capital through the issuance of series J shares, excluding the pre-emptive rights of existing shareholders in full, and amending the Company's Articles of Association. The exclusion of pre-emptive rights was made with the approval of the Company's Supervisory Board. The Management Board's resolution provides for a priority right of existing shareholders to acquire series J shares. In accordance with the Management Board's resolution, the Company's share capital was increased by no more than PLN 1,905,869.60 through the issuance of no more than 4,764,674 new series J ordinary bearer shares with a par value of PLN 0.40.

At the same time, a lock-up agreement (the "Agreement") was concluded between Mr. Paweł Przewięźlikowski, President of the Company's Management Board Mr. Krzysztof Brzózka, Vice President of the Company's Management Board ("Shareholders"), and Trigon Dom Maklerski S.A., based in Warsaw. Pursuant to the Agreement, the Shareholders agreed that for a period of 12 months from the date of allotment of the Company's series J shares (the "Lock-Up Period"), they will not make any disposition of the Company's shares held by the Shareholders as of the date of the Agreement, as well as new shares of the Company, if any, to be acquired by the Shareholders during the Lock-Up Period.

New clinical and preclinical data presented for RVU120 program at 34th AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Symposium

On October 26, 2022 Ryvu presented updated data for RVU120 project showing the clinical and preclinical activity of the Company's lead oncology drug candidate for cancer therapy, at the 34th AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Symposium.

Poster presentations included:

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

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

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

Details of the poster presentations are as follows:

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

Clinical data demonstrate a favourable safety profile of RVU120 at doses of 75 mg, 100 mg, and 125 mg in all 9 patients enrolled to date. None of the patients experienced dose- Ryvu Therapeutics S.A. www.ryvu.com limiting toxicity (DLT), drug-related serious adverse events (SAE), or drug-related AE of Grade three or higher after being dosed with RVU120. Disease stabilization was observed in two heavily pre-treated patients, one lasting 18 weeks in gastro-esophageal junction cancer, and another, ongoing after 33 weeks in adenoid cystic carcinoma. Two patients are awaiting their first assessment. The most common reason for treatment discontinuation was progressive disease (5 patients). One patient withdrew consent, and 3 patients are ongoing. In the Company's management board opinion, available data warrant continuation of dose escalation and collection of additional clinical data.

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

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

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

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

Clinical and Translational Data of RVU120 and SEL24 (MEN1703) presented at the 2022 American Society of Hematology (ASH) Annual Meeting

On December 11, 2022 Company announced new data demonstrating clinical and preclinical activity of RVU120 and SEL24 (MEN1703) at the American Society of Hematology (ASH) Annual Meeting 2022 which is being held on December 10-13, 2022 in New Orleans, USA.

Presented data included updated clinical results for RVU120, a selective CDK8/19 inhibitor being developed for the treatment of hematological malignancies and solid tumors. RVU120 demonstrated single-agent activity with a Complete Response, 4 Blast Reductions, and 4 Erythroid and/or Platelet responses in patients with Relapsed/Refractory Acute Myeloid Leukemia (AML) or High-Risk Myelodysplastic Syndrome (HR-MDS).

Moreover, Ryvu's global partner Menarini Group, which is currently developing SEL24 (MEN1703) on the basis of an exclusive licence agreement concluded with the Company, presented new data on SEL24 (MEN1703), a first-in-class, oral, dual type I PIM/FLT3 inhibitor. Preclinical antitumor activity of SEL24 (MEN1703) was demonstrated in multiple myeloma (MM), Hodgkin's lymphoma (HL), and diffuse large B-cell lymphoma (DLBCL) as well as in AML in combination with gilteritinib.

RVU120

With a data cut-off of November 11, 2022, data highlights for Phase 1b Interim Efficacy and Safety Results on RVU120 include:

- 16 relapsed/refractory (R/R) acute myeloid leukemia (AML) and 3 high-risk myelodysplastic syndrome (HR-MDS) patients with a median of 3 prior lines of therapy have been treated with RVU120 at doses between 75 and 110 mg;
- Clinical activity was demonstrated in 9 out of 16 evaluable patients, all of them with molecular markers preclinically predicted to respond to CDK8 inhibition;
- One AML patient achieved a complete response;
- 4 patients demonstrated blast reductions;
- 4 patients showed erythroid and/or platelet responses;
- RVU120 was generally well tolerated at all doses;
- Most frequent adverse events were nausea/vomiting, worsening of thrombocytopenia grade 3 to 4, and febrile neutropenia;

After the data-cut-off for the poster, dose escalation has continued, and the 110 mg dose cohort has now been fully enrolled. In total, 22 patients have been enrolled in the study through December 7, 2022.

Additionally, the on-target activity of RVU120 was evaluated in AML and HR-MDS patient samples by measuring changes in pSTAT5 levels. As of the cut-off date, the inhibition of pSTAT5 reached >50% in some patients, a threshold that may be sufficient for robust efficacy in certain groups of super-responder patients. Combined results from the ongoing dose-escalation trials (in 10-135 mg dose range) in AML/HR-MDS and solid tumor patients indicate that pSTAT5 inhibition is dose-dependent.

SEL24 (MEN1703)

Ryvu licensee, Menarini Group, and academic collaborators presented new data on SEL24 (MEN1703), a first-in-class, oral, dual type I PIM/FLT3 inhibitor. Combination therapy of SEL24 (MEN1703) with gilteritinib, a highly potent and selective oral FLT3 inhibitor, induces strong tumor regression and complete responses in vivo, demonstrating the potential of concomitant FLT3 and PIM inhibition kinases in AML.

SEL24 (MEN1703)-induced PIM inhibition, and the mechanism of action was also demonstrated in vitro in multiple myeloma (MM), classical Hodgkin lymphoma-tumor-associated macrophages (cHL-TAMs), and diffuse large B-cell lymphoma (DLBCL) models. In multiple myeloma preclinical models, SEL24 (MEN1703) induces cytotoxicity of MM cell lines, disrupts MM endothelial cell vessel formation, and decreases the activity of several pathways essential for myeloma cell survival. This study demonstrates the promising therapeutic potential of SEL24 (MEN1703) in MM and reveals the underlying mechanism of PIM inhibition. PIM-dependent oncogenic signaling pathways were also inhibited following SEL24 (MEN1703) treatment of MM cells.

Details of the poster presentations are as follows:

- **CDK8/19 Kinase Inhibitor RVU120 in Patients with AML or Higher-Risk MDS: Safety and Efficacy Results from New Dose Escalation Cohorts** (Publication Number: 2771), Camille Abboud, MD (Washington University in Saint Louis/ Washington University School of Medicine) *et. al.*
    - Session name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET
- **Multiomics Analysis Confirms Effective Target Engagement for RVU120 – a First-in-class CDK8/19 Kinase Inhibitor in AML and MR-MDS Patients and Reveals the Mechanism of Action** (Publication Number: 2642), dr Tomasz Rzymski (Ryvu Therapeutics) *et. al.*
    - Session name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET
- **PIM Inhibition By SEL24/MEN1703 Combines Synergistically with Gilteritinib in FLT3-ITD Preclinical Models of Acute Myeloid Leukemia** (Publication Number: 1333), Daniela Bellarosa (Grupa Menarini) *et. al.*
    - Session name: 604. Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET
- **Super-enhancer-driven PIM Kinase Upregulation in Multiple Myeloma Maintains the Plasma Cell-specific Oncogenic and Microenvironmental Circuits and Can Be Efficiently Targeted by the Pan-PIM Inhibitor MEN1703** (Publication Number: 1822), Filip Garbicz (Institute of Hematology and Transfusion Medicine, Warsaw, Poland) *et. al.*
    - Session name: 651. Multiple Myeloma and Plasma Cell Dyscrasias: Basic and Translational: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET
- **PIM Kinases Regulate Super-Enhancer-Dependent Gene Expression In Diffuse Large B-Cell Lymphoma** (Publication Number: 1310), Sonia Debek (nstitute of Hematology and Transfusion Medicine, Warsaw, Poland) *et. al.*
    - Session name: 603. Lymphoid Oncogenesis: Basic: Poster I
    - Date and time of the presentation: Saturday, December 10, 2022; 5:30 PM – 7:30 PM ET
- **MEN1703-mediated PIM kinases inhibition impairs protumoral and immunosuppressive phenotype and functions of macrophages in classical Hodgkin Lymphoma** (Publication Number: 2867), Maciej Szydlowski (Instytut Hematologii i Transfuzjologii w Warszawie), *et. al.*
    - Session name: 622. Lymphomas: Translational–Non-Genetic: Poster II
    - Date and time of the presentation: Sunday, December 11, 2022; 6:00 PM - 8:00 PM ET

The ASH Conference ranks among the top scientific events, bringing together the scientific community as well as potential customers and business partners - biotech and pharmaceutical companies from around the world, as well as industry investors.

Execution of an exclusive Research Collaboration Option and Exclusive License Agreement and Equity Investment Agreement with BioNTech SE

On November 29, 2022 Ryvu entered into an exclusive research collaboration and license agreement ("License Agreement") and equity investment agreement ("Investment Agreement") (together "Agreements") with BioNTech SE with its registered office in Mainz, Germany ("BioNTech"). The multi-target research collaboration will comprise several small molecule immunotherapy programs, as well as an exclusive license for Ryvu's STING agonist portfolio as standalone small molecules. The initial collaboration term is five years and can be mutually prolonged by both parties.

Under the terms of the License Agreement, BioNTech paid Ryvu an upfront fee of EUR 20 million (PLN 93.626.000 converted at the average exchange rate of the NBP for November, 29 2022, EUR 1 = PLN 4,6813) in exchange for the global, exclusive license to develop and commercialize Ryvu's STING agonist portfolio as standalone small molecules, including as monotherapy and in therapeutic combinations; and for the right to license on an exclusive basis multiple small molecule programs ("BioNTech Exclusive Targets") as part of a multi-target research collaboration. The goal of the collaboration is generation of drug candidates to be further developed in pre-clinical studies and clinical trials, and eventually with the goal of producing an approved licensed product. BioNTech Exclusive Targets will be in the field of immunomodulation, and may be relevant for the treatment of oncology, immunology, or other disorders where modulation of immune cells could be therapeutically beneficial.

Moreover, until the fifth anniversary of the effective date of this Agreement or the selection of multiple BioNTech Exclusive Targets, whichever comes first, BioNTech will have the right of the first negotiation regarding any non-partnered, immune modulation target in Ryvu's portfolio.

Under the License Agreement BioNTech will fund all discovery, research and development activities under the multi-target research collaboration. Ryvu will be eligible to receive success-based development, regulatory and commercialization milestones, as well as low single-digit royalties on the annual net sales of any products that are successfully Ryvu Therapeutics S.A. www.ryvu.com commercialized and contain a stand-alone STING compound or any compound directed to a given BioNTech Exclusive Target that is developed under the Agreement. Ryvu will be eligible to receive potential maximum milestone payments of up to EUR 876,2 million (PLN 4.101.755.060 converted at the average exchange rate of NBP for 29, November 2022, EUR 1 = PLN 4,6813). The Management Board emphasizes that the above amount is the maximum amount possible to obtain (bio-euro value), while the amount of revenues that Ryvu will actually obtain from the Licence Agreement will depend on the progress of scientific research and clinical trials, the success of the registration process and the level of revenue from sales of the potential drugs achieved by BioNTech or its licensee. Moreover, the timeline for achieving the milestones and receiving the above potential payments are unknown at this time and not in the near future.

Under the Investment Agreement BioNTech has invested EUR 20 million by subscribing for new series J ordinary shares issued by the Company under the authorised capital and offered in a public offer, at a price of PLN 48.86.

BioNTech undertook not to dispose or acquire, directly or indirectly, shares or other securities convertible into shares from 29 November 2022 until the date falling 12 months after the admission and introduction of the series J shares to trading on the regulated market of the WSE, subject to exceptions provided in the Investment Agreement, including upon the Company's written consent to a transaction or upon termination of the License Agreement.

Public offering of J series shares

In December 2022 the Issuer conducted a public offering of series J shares, which offering was envisioned in Ryvu Development Plans for 2022-2024 as a way to obtain financing necessary for achieving Ryvu's goals.

1. Subscription opening and closing date:

Subscription opening and closing date for retail investors:
- Subscription opening: 8 December 2022 r.
- Subscription closing: 15 December 2022 r.

Subscription opening and closing for institutional investors:
- Subscription opening: 16 December 2022 r.
- Subscription closing: 20 December 2022 r.

Subscription opening and closing for BioNTech SE (the "**BioNTech Tranche**"):
- Subscription opening: 16 December 2022 r.
- Subscription closing: 21 December 2022 r.

2. Date of allotment of securities:

22 December 2022.

3. Number of securities the subscription applies to:

4,764,674 Series J Shares.

4. Rate of reduction in particular tranches:

The reduction rate of subscriptions submitted by retail investors without use of the priority right was 55,51 %. The reduction rate of subscriptions submitted by retail investors with the use of the priority right – none. The reduction rate for the institutional investors – none. The reduction rate in the BioNTech Tranche - none.

5. Number of securities for which subscriptions were submitted:

4,791,361 Series J Shares.

6. Number of securities allotted in the subscription:

4,764,674 Series J Shares.

7. Price at which securities were acquired (subscribed for):

Issue price of one Series J Share for retail and institutional investors: PLN 55.00.
Issue price of one Series J Share in the BioNTech Tranche: PLN 48.86.

8. The number of persons who subscribed for securities in particular tranches:

In the subscription for retail investors, 133 persons submitted subscriptions.
In the subscription for institutional investors, 93 investors submitted subscriptions.
In the BioNTech Tranche, 1 entity submitted a subscription.

9. **Number of persons to whom securities were allotted in the subscription in particular tranches**

As part of the allotment to individual and institutional investors, the Series J Shares were allotted to 226 persons.
In the BioNTech Tranche, the Series J Shares were allotted to 1 person.

10. **Name(s) of the underwriters who have taken up securities in the performance of underwriting agreements, stating the number of securities they have taken up, together with the actual price per unit of the security, being the issue or sale price, after deduction of the consideration for taking up a unit of the security, in the performance of the underwriting agreement, acquired by the underwriter:**

No underwriting agreements were concluded;

11. **The value of the conducted subscription, understood as the product of the number of securities covered by the offer and the issue price:**

The value of the conducted subscription amounted to PLN 250,284,006.82.

12. **The amount of the total costs which have been included in the costs of the issue, indicating the amount of the costs by their titles, divided at least into costs of:**

    a) preparation and conducting of the offering - PLN 352,628.97

    b) remuneration of the underwriters, for each separately - not applicable;

    c) preparation of a prospectus, including costs of advisory services - PLN 7,340,464.80

    d) promoting the offering - none

    The costs of issuing series J shares will reduce the Company's supplementary capital arising from the excess of the issue value of the issued shares over their par value. These costs will be recognized in the financial statements under the reserve capital item.

13. **Average cost of conducting the subscription per security unit being the subject of the subscription -** PLN 1.61
14. **The method of payment for the securities subscribed (acquired):**

All Series J Shares were paid in full in cash.

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

Registration of amendment of the Company's Articles of Association concerning share capital

On January 17, 2023 the District Court for Kraków-Śródmieście in Kraków, XI Commercial Division of the National Court Register, registered an amendment to the Company's Articles of Association concerning increasing the Company's share capital from the amount of PLN 7,342,189.60 PLN (seven million three hundred forty-two thousand one hundred eighty-nine zlotys and sixty groszy) to the amount of 9,248,059.20 PLN (nine million two hundred forty-eight thousand fifty-nine zlotys and

twenty groszy), by way of issue of 4,764,674 (four million seven hundred sixty-four thousand six hundred seventy-four) new series J ordinary bearer shares with a nominal value of PLN 0.40 (forty groszy) each ("Series J Shares") within the authorised capital, made pursuant to Resolution No 1 of the Company's Management Board of 5 October 2022 on increasing the Company's share capital within the limits of the authorised capital through the issue of series J shares, excluding the pre-emptive rights of the existing shareholders in full and amending the Company's Articles of Association (the "Issue Resolution"), of which the Issuer informed in a current report No 22/2022 of 5 October 2022 (the " Registration of Amendments").

After the Registration of Amendments, the share capital of the Company equals PLN 9,248,059.20 and is divided into 23,120,148 shares with a nominal value of PLN 0.40 (forty groszy) each.

Admission and introduction of the series J shares of the Company to trading on the regulated market of the WSE

On January 20th, 2023 the Management Board of the Warsaw Stock Exchange S.A. adopted Resolution No. 51/2023 on the admission and the introduction to exchange trading on the main market of the WSE of series J ordinary bearer shares of the Company, pursuant to which the Management Board of the Warsaw Stock Exchange S.A. stated that 4,764,674 series J ordinary bearer shares of the Issuer with a nominal value of PLN 0.40 each with ISIN code PLSELVT00013 ("Series J Shares") are admitted to exchange trading on the main market. The WSE Management Board decided to introduce on January 25th, 2023 the Series J Shares to exchange trading on the main market, subject to the registration of the Series J Shares by the National Depository for Securities S.A. with the ISIN code PLSELVT00013 on January 25th, 2023.

2.8 Unusual events occurring in the reporting period

COVID-19

COVID-19 pandemic continued in the beginning of the reported period, and from May 16, 2022, the epidemic state was abolished by the authorities and the state of epidemic threat came into force. The Issuer has 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 the stationary employees. 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 was 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 further 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 being 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) RIVER-51 study and (ii) AMNYS-51 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, 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 clinical studies. This has applied primarily to the 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 coronavirus 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 operated in 2022 with close to normal capacity. Only a small proportion of the Issuer's office staff still worked remotely, which could however have had an adverse effect on the speed of the carried out projects. As of Q1 2023, 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 described in Note 29 to the financial statements, 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 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.

2.9 Planned development of the Issuer, including information about adopted development strategy

Issuer's development strategy and new initiatives

On August 19, 2022 the Issuer published its Development Plans for 2022-2024, with the aim to accelerate its mission.

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 total budget for 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) to 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) 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) planned to cover G&A costs.

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 RVU120 program.

3 RISK FACTORS ASSOCIATED WITH ISSUER'S ACTIVITIES

The activities of the Issuer, its financial situation and operating results have been subject to and may be subject to negative changes in the future as a result of the occurrence of any of the risk factors described below. The occurrence of even some of the following risk factors may have a material adverse effect on the business, financial condition and financial results and may result in the loss of some or all of the invested capital. Risk factors and uncertainties other than those described below, including those which the Issuer is not aware of at present or which it considers to be insignificant, may also have a significant negative impact on the Issuer's operations, financial condition and results of operations and may result in the loss of some or all of invested capital.

3.1 Risk factors associated with the environment in which the Issuer operates

Risk associated with the access to financing and the possibility of loss of financial liquidity

The type of research and development activities carried out by the Issuer, incurs significant expenses. During research and development, Issuer's projects and activities do not generate sales revenues, and its potential value grows only with the progress of work and planned commercialization. Therefore, in the initial period of project implementation, the Company must rely on its own funds, obtained from grants or shares issuance. Despite the fact that the Company follows a disciplined cost policy, any extension of R&D works or studies including preclinical and clinical trials, may lead to the necessity of obtaining further financing rounds, which may turn out to be limited or impossible. Failure to obtain additional funds may, in such a situation, lead to the loss of financial liquidity by the Company. Due to the fact that the scale of the Issuer's financial needs is significant, and the time needed for signing and commercializing the conducted R&D works or implementing partnering agreements is estimated to be at least several years long, there is a risk that the Issuer will not be able to obtain the assumed level of financing for its activities, which would result in a reduction or, in extreme case, full cessation of the activity. The intention of the Company is to conduct a transparent information policy and maintain good relations with investors in order to reduce the risk associated with access to financing.

Risk associated with the receiving and settling of obtained subsidies

Co-financing of selected areas of the Issuer's activities or projects from public funds (EU, Polish Agency for Enterprise Development, Ministry of Science and Higher Education, etc.) is associated with the obligation of strict compliance with contracts and administrative, as well as legal regulations. The Issuer performs contracts with the utmost diligence, however, the risk of different interpretations of contract provisions by the funding institutions cannot be ruled out.

In addition, in the event of failure to meet the conditions set in the abovementioned regulations, improper implementation of projects or use of co-financing in a manner inconsistent with the intended use, there is a risk of the obligation to return some or all of the sum received by the Issuer together with interest. Such an event may adversely affect the economic situation of the Issuer. The company minimizes the risk in question through consultations with funding institutions and advisors specializing in the implementation of co-financed projects and the settlement of subsidy programs. The Issuer takes the utmost care to properly fulfill all of its obligations under the subsidy agreements.

Moreover, it should be pointed out that failure to obtain the planned further subsidies may result in the necessity to increase the involvement of Issuer's own equity, which may also have a negative impact on the operations, financial situation and strategy of the Issuer.

Risk associated with competition

The Issuer operates in the market of innovative therapeutic products and research services, which is competitive and significantly dispersed. Despite the fact that, in comparison to the entire pharmaceutical market, the market of innovative therapeutic products is characterized by relatively less competition, all of the commercial and academic activities in this area are dynamically developing, especially in the United States, the EU and Asian countries. Today, it is exactly this field of science that receives a lot of attention and large funding, especially in the areas of oncology and immunology, so those ones in which the Issuer is particularly involved in. The Issuer is not able to predict the strength and number of competitors, however, the emergence of greater competition is inevitable. Such situation creates the risk of limiting the ability to achieve the planned market share, e.g. the ability to obtain interesting molecules and the ability to sign partnering contracts.

Risk associated with the loss of managerial staff and key employees

The Issuer's activities and prospects for its further development largely depend on the competences, commitment, loyalty and experience of employees, including key managerial staff. Due to the fact that the biotechnology industry is competitive, there is a great demand on the market for experienced employees who constitute one of the Issuer's basic resources. On the one hand, this means the possible difficulties in recruitment of new employees, and on the other hand, the loss of existing employees through recruitment activities of the competition. Nevertheless. above-mentioned situation to the high extent does not apply to the Polish market, where the supply of jobs in the biotechnology industry is still relatively small. But surely it is clearly visible at the international level and in the case of employees with the highest qualifications.

Moreover, the competitiveness of the Issuer's labor market may pose a risk that in order to maintain attractive working conditions for its employees, it will be forced to increase labor costs above the previously planned level. Or, it may not be able to attract new or retain key employees in conditions that are economically acceptable.

This risk has been mitigated to a significant extent by the introduction of the Issuer's employee incentive program in 2021, which is designed to create incentives that will encourage, retain and motivate qualified individuals, key to the execution of the Company's strategy, to act in the interest of the Company and its shareholders by enabling such individuals to acquire shares in the Company.

3.2 Risk factors associated with the operational activity of the Issuer

Risk associated with the research process conducted by the Company

The development of a new molecule is a process involving several lengthy and costly stages with an uncertain end result, with the goal of demonstrating, among other things, safety of use and therapeutic benefit. Given that currently two of the molecules developed by the Issuer, i.e. SEL24 (MEN1703) and RVU120 (SEL120), are at the clinical trials stage, there may be risks characteristic of these stages. For example, there is a risk that the Issuer will encounter difficulties in concluding appropriate agreements with clinical centers, and thus it will be difficult to recruit the required number

of patients for clinical trials. Because patient recruitment is affected by factors often beyond the Issuer's control, such as the exodus of qualified personnel from clinical academic centers, the ability to prevent such risks may be limited. To minimize the above risks, the Issuer plans to significantly outsource the contracting and management of clinical centers to a clinical CRO (Contract Research Organization) experienced in this area, with ongoing monitoring of the effectiveness and quality of patient recruitment at all activated centers. In addition, the Issuer may not be able to demonstrate, for example, good tolerability, absence of side effects or efficacy of one or more of its molecules. Any failure in any of the phases of a molecule's design, manufacturing and testing could delay its commercialization and, in extreme cases, lead to the discontinuation of the project. As the SEL24 molecule (MEN1703) is being developed by the Issuer's licensee, the Menarini group, there is an additional risk of discontinuation associated with the potential periodic prioritization of Menarini's project portfolio. The Issuer cannot guarantee that the process of designing, manufacturing and testing of the molecule will proceed smoothly, on schedule in line with market needs. Any, even insignificant, errors or delays in the development of molecules may adversely affect the Issuer's business, market position, sales, financial results and growth prospects. Materialization of the risk may also lead to an increase in the necessary financial expenditures related to the research process. In such a situation, this will result in the need for prioritization within the Issuer's R&D projects, including postponement of some processes, as well as the need to obtain additional financing.

The Issuer assesses the significance of the above risk as high, because in case of its materialization the scale of the negative impact on the Issuer's financial situation could be significant. The Issuer assesses the probability of materialization of the above risk as medium in the case of RVU120, due to the specifics of the biotechnology industry, elevated in the case of SEL24, due to the lack of approval of plans for further clinical trials by Menarini's management board to date, and high in the case of cooperation with Galapagos, due to the partner's focus on the oncology area announced in 2022.

Risk associated with intellectual property rights

The issuer operates on the global biotechnology market, one of the most innovative sectors of the economy. Operating on such a market is inextricably linked to the imperfections of legal regulations and the lack of established practice in applying the law. This applies in particular to issues related to copyright and industrial property law, which are supposed to protect a number of solutions and works used by the Issuer. Such a situation creates a risk for the Issuer of issuance of unfavorable decisions by the authorities applying the law (in particular courts and tax authorities).

The risk associated with the breach of trade secrets and other confidential business information

The implementation of the Issuer's plans largely depends on the unique (including partially unpatented) technology, trade secrets, know-how and other data which are regarded by the Issuer as secrets. Their protection should be ensured by non-disclosure agreements concluded between the Issuer and its key employees, consultants, customers, suppliers, stipulating the need to maintain confidentiality. However, the Issuer cannot guarantee that these agreements will be followed. This could lead to a situation in which Issuers' competitors might come into possession of such data. On the other hand, there is also a possibility that some legal claims related to unauthorized disclosure or use of third party's trade secrets by the Issuer or its employees might be filed against the Issuer.

The risk of identifying serious or unacceptable side effects resulting from the use of therapies developed by the Issuer and the possibility of identifying the limited effectiveness of the selected

clinical candidates, what can lead to resignation from or limitation of further development works related to the development of one or more potential clinical candidates

Potential clinical candidates of the Issuer are currently at the pre-clinical stage. Thus, the risk of their failure is high. It is impossible to predict when or if any of the potential clinical candidates will prove to be effective and safe for human use or will be approved for commercialization. Therefore, if the Issuer's potential clinical candidates will be proven to have undesirable side effects or have features that are unexpected and difficult to predict, the Issuer may have to discontinue their development or limit it to specific applications or using them in particular subgroups of patients to whom the adverse effects or other features will be less widespread, milder, or more acceptable in terms of risk and benefit.

As a result of the occurrence of undesirable side effects which may be observed by the Issuer during its research, the Issuer, either directly or in cooperation with a strategic partner, may not be allowed to introduce any of the current potential clinical candidates to the market. Such situation may make obtaining of expected revenues from the sale of drugs (revenues from royalty title) impossible. The Issuer's research results may reveal unacceptably high severity and frequency of side effects. In such a case, the Issuer's research may be suspended or terminated. Moreover, the Office for Registration of Medicinal Products or its foreign equivalents may order the Company to stop further development or refuse to approve potential clinical candidates for one or all indications. Many compounds which are initially promising in early stage cancer or other disease treatment trials eventually cause side effects that prevent these compounds from being developed further.

Side effects may also affect patient recruitment, the ability of patients to complete studies, or result in potential compensation claims filed against Issuer. Moreover, the Issuer's reputation may be tattered.

The risk associated with failure to identify or discover additional potential clinical candidates

One of the key elements of the Issuer's strategy is the usage of the technology platform to develop innovative drugs. Discovery of new drugs (using Issuer's knowledge and know-how) may not be effective in identifying compounds that are useful in the treatment of cancer or other diseases. The Issuer's research programs may be initially promising in identifying potential clinical candidates but ultimately fail for a number of reasons, including:

- the methodology of the research used, which may not be effective in identifying potential clinical candidates;
- Potential clinical candidates may, in a further stage of the research, show adverse side effects or other characteristics that indicate that the drugs are unlikely to be approved by the regulator or achieve market recognition; or
- potential clinical candidates may not be effective in treating diseases, which were initially intended to be treated by potential clinical candidates

Research programs in identifying new clinical candidates require significant financial, technical and human resources. The issuer may focus its efforts and resources on the wrong potential clinical candidate that may ultimately be proven to be ineffective.

If the Issuer is not able to identify the appropriate compounds for pre-clinical and clinical development, then it will not be able to obtain revenues from the sale of drugs in future periods, which will probably worsen the financial situation of the Issuer and adversely affect the valuation of its shares.

Risk associated with Covid-19

Risk associated with Covid-19 was described in section 2.8: ”Unusual events occurring in the reporting period”.

Other risks

Risks related to price, credit, equity, financial, market, currency, interest rate and liquidity risks are described in note 26.

4 STATEMENT REGARDING IMPLEMENTATION OF CORPORATE GOVERNENCE PRINCIPLES

4.1 Principles of corporate governance applying to the Issuer

The Issuer's Management Board hereby informs that in 2022 the Company complied with all the rules and recommendations of corporate governance contained in the document: "Best Practice for GPW Listed Companies 2021" (GPW – Warsaw Stock Exchange), with the exceptions described and appropriately justified below:

1.3. Companies integrate ESG factors in their business strategy, including in particular:

1.3.1. environmental factors, including measures and risks relating to climate change and sustainable development;

Explanation of the Issuer:

The Company is not subject to non-financial reporting on ESG. If an obligation to publish such information arises, the Company will implement an ESG strategy.

1.4. To ensure quality communications with stakeholders, as a part of the business strategy, companies publish on their website information concerning the framework of the strategy, measurable goals, including in particular long-term goals, planned activities and their status, defined by measures, both financial and non-financial. ESG information concerning the strategy should among others:

Explanation of the Issuer:

The Company is not subject to non-financial reporting on ESG. If an obligation to publish such information arises, the Company will implement an ESG strategy.

1.4.1. explain how the decision-making processes of the company and its group members integrate climate change, including the resulting risks;

Explanation of the Issuer:

The Company is not subject to non-financial reporting on ESG. If an obligation to publish such information arises, the Company will implement an ESG strategy.

1.4.2. present the equal pay index for employees, defined as the percentage difference between the average monthly pay (including bonuses, awards and other benefits) of women and men in the last year, and present information about actions taken to eliminate any pay gaps, including a presentation of related risks and the time horizon of the equality target.

Explanation of the Issuer:

The Company operates in a highly competitive industry. The diversity in Company's employees' remuneration results from the specific nature and type of positions held and the general dynamics of salary fluctuation in individual specializations. The Company follows the principle of equal remuneration for men and women employed in comparable positions/functions, and gender issues are not a factor affecting the terms and conditions of employment at the Company.

2.1. Companies should have in place a diversity policy applicable to the management board and the supervisory board, approved by the supervisory board and the general meeting, respectively. The diversity policy defines diversity goals and criteria, among others including gender, education, expertise, age, professional experience, and specifies the target dates and the monitoring systems for such goals. With regard to gender diversity of corporate bodies, the participation of the minority group in each body should be at least 30%.

Explanation of the Issuer:

The company has not established a formal diversity policy which covers the scope indicated in rule 2.1 and which is subsequently approved by the general meeting of shareholders. However, the Company seeks to select members of its corporate bodies based on experience and knowledge, and also considers gender diversity as a secondary factor. The company promotes equal opportunities for all employees and gender equality at all levels of the Company, and over the past several years has undertaken initiatives to promote equality and diversity.

2.2. Decisions to elect members of the management board or the supervisory board of companies should ensure that the composition of those bodies is diverse by appointing persons ensuring diversity, among others in order to achieve the target minimum participation of the minority group of at least 30% according to the goals of the established diversity policy referred to in principle 2.1.

Explanation of the Issuer:

Personal decisions on appointing members of the Company's Management Board or Supervisory Board are made by the Supervisory Board and the General Meeting of Shareholders, respectively, taking into account their qualifications to perform specific functions and their professional experience. Factors such as gender or age are not determinants justifying appointments to the Company's bodies.

2.11. In addition to its responsibilities laid down in the legislation, the supervisory board prepares and presents an annual report to the annual general meeting once per year. Such report includes at least the following:

2.11.5 assessment of the rationality of expenses referred to in rule 1.5;

Explanation of the Issuer:

The Board is informed annually of the expenditures referred to in Rule 1.5, but does not formally assess the rationality of such expenditures.

2.11.6. information regarding the degree of implementation of the diversity policy applicable to the management board and the supervisory board, including the achievement of goals referred to in principle 2.1

Explanation of the Issuer:

The Company has not implemented a formal diversity policy applicable to the Management and Supervisory Board.

3.3. Companies participating in the WIG20, mWIG40 or sWIG80 index appoint an internal auditor to head the internal audit function in compliance with generally accepted international standards for the professional practice of internal auditing. In other companies which do not appoint an internal auditor who meets such requirements, the audit committee (or the supervisory board if it

performs the functions of the audit committee) assesses on an annual basis whether such person should be appointed.

Explanation of the Issuer:

The Company has not appointed an internal auditor to head the internal audit function; however functions related to the internal audit are performed by the Company's employees within the finance and controlling department of the Shared Services Center (Centrum Usług Wspólnych) in a dispersed format.

4.1. Companies should enable their shareholders to participate in a general meeting by means of electronic communication (e-meeting) if justified by the expectations of shareholders notified to the company, provided that the company is in a position to provide the technical infrastructure necessary for such general meeting to proceed.

Explanation of the Issuer:

Currently, the Company does not enable shareholders to participate in a general meeting by means of electronic communication (e-meeting), due to the lack of interest in such a solution among the Company's shareholders and to avoid potential legal issues connected with such means of participation. If the Company's shareholders express their wish to participate in the general meeting by means of electronic communication (e-meeting) in the future, the Company will consider implementing such a solution and provide the necessary technical infrastructure.

4.3 Companies provide a public real-life broadcast of the general meeting.

Explanation of the Issuer:

The Issuer's shareholding structure does not justify broadcasting the General Meeting and real-time two-way communication and exercising the voting right by means of electronic communication.

4.7. The supervisory board issues opinions on draft resolutions put by the management board on the agenda of the general meeting.

Explanation of the Issuer:

The Supervisory Board issues opinions on draft resolutions put by the Management Board on the agenda of the General Meeting, at least with respect to resolutions of strategic importance for the Company.

4.2 Internal control and risk management systems

Internal control and risk management with regard to the process of preparing the Issuer's financial statements are carried out in accordance with the applicable internal procedures for the preparation and approval of financial statements. The Company maintains appropriate documentation describing the accounting principles adopted by it, which includes, inter alia, information on the method of valuation of assets and liabilities and determination of the financial result, the method of keeping accounting books, data and their collections protection system. Accounting of all economic occurrences is made using the eNova computerized accounting system, which is protected against unauthorized access and has functional access restrictions.

Financial statements are prepared by accounting department employees with the support of the controlling department, under the control of the Chief Accountant and the Financial Director, as part of providing shared services under the agreement for providing support services within the shared services centre with Selvita S.A. The financial statements are audited by an independent statutory auditor selected by the Supervisory Board of the Company (currently PwC). Semi-annual statements are also reviewed by an independent statutory auditor.

4.3 Managerial and supervisory 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

During the reporting period, effective August 1, 2022 Mr. Vatnak Vat-Ho and Mr. Hendrik Nogai were appointed to the Management Board by the Supervisory 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) Colin Goddard – Supervisory Board Member*

**During the reporting period, effective December 31, 2022 Mr. Colin Goddard resigned from the position of a member of the Supervisory Board.*

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) Axel Glasmacher – Member of the Remuneration Committee
3) Colin Goddard* - Member of the Remuneration Committee
4) Thomas Turalski – Member of the Remuneration Committee

*Mr. Colin Goddard resigned from the position of a member of the Supervisory Board effective December 31st, 2022.

Members of the Audit Committee in the indicated composition met the independence criteria and other requirements specified in Art. 129 sec. 1, 3, 5 and 6 of the Act of 11 May 2017 on statutory auditors, audit firms and public supervision.

Moreover, the Management Board of the Company indicates that in the scope of the Audit Committee operating within the Company:

1. Persons who meet the statutory criteria of independence are: Mr. Rafał Chwast, Mr. Piotr Romanowski and Mr. Jarl Jungnelius.
2. A person with knowledge and skills in accounting or auditing of financial statements is Mr. Rafał Chwast.
3. All Audit Committee's Members are persons with knowledge and skills in the industry in which the Issuer operates.

Main provisions of Issuer's policy for selecting an audit company which will the statutory audit of financial statements

1. The audit company which will carry out the statutory audit of the company's financial statements is selected by the Supervisory Board of the Company.
2. When selecting the entity authorized to audit, the Supervisory Board of the Company will get acquainted with the recommendations submitted by the Company's Audit Committee.
3. The Supervisory Board of the Company is in no way bound by the recommendations of the Company's Audit Committee indicated in par. 2 above. In particular, it may select an entity other than that proposed by the Audit Committee in its recommendations. Any contractual clauses in the agreements concluded by the Company that is limiting the possibility of selecting an audit company for the purpose of carrying out the statutory audit of financial statements by the Supervisory Board for example to the specific lists of audit companies or specific categories of such companies shall be deemed illegal and invalid.
4. When selecting an audit company which will conduct the audit of the Company, the following principles should be observed (in particular):
    a. the impartiality and independence of the audit company;
    b. the quality of the audit work performed;
    c. knowledge of the industry in which the Company operates;
    d. the previous experience of the audit company in auditing reports of public interest entities;
    e. professional qualifications and experience of persons directly providing services in the scope of the conducted research;
    f. the ability to provide the required scope of services;
    g. the territorial scope of the audit company and the international nature of the network in which it operates (operating in most countries in which the Company operates);
    h. the proposed price of the service provided.
5. The Audit Committee of the Company may request information, explanations and documents necessary to perform its tasks related to the selection of the audit company.
6. The Company's Audit Committee may submit recommendations aimed at ensuring the reliability of the audit company selection process.

The main goals of Issuer's policy on the permitted non-audit services provided by the audit company which conducts the statutory audit of the Company's financial statements or by the entities associated with this company and by a member of the audit company's network

1. Neither the statutory auditor or an audit company which carries out the statutory audit of the Issuer or an entity affiliated with this audit company, nor any of the members of the network to which the statutory auditor or the audit company belongs, shall not provide, directly or

indirectly, any prohibited non-audit services or financial audit activities to the Company or its affiliated entities (if any).

2. A detailed catalogue of prohibited services is specified in Article 5 of the Regulation of the European Parliament and of the Council (EU) No 537/2014 of 16 April 2014 on specific requirements regarding statutory audit of public-interest entities and repealing Commission Decision 2005/909/
3. The prohibited services referred to in point 2 above are not the services indicated in art. 136 sec. 2 of the Act on statutory auditors and their self-government, entities authorized to audit financial statements and on public supervision ("Permitted non-audit services").
4. Providing of Permitted non-audit services is possible only to the extent unrelated to the tax policy of the Company, after the Audit Committee will assesses the threats and safeguards to auditors' independence.
5. Providing of services other than audit will be carried out in accordance with the independence requirements specified for such services in the rules of professional ethics and standards for performing such services.

The auditing company auditing the Issuer's financial statements, that is PwC, did not provide the Issuer with permitted non-audit services, review, other assurance service in the period covered by this report and in the period after the balance sheet date (statement made as of the date of this Report).

Shares held by members of the Management and Supervisory Board of Ryvu Therapeutics S.A. as of Annual report publication date*

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	639 544	**4 139 544**	17,90%	**7 639 544**	28,12%
Krzysztof Brzózka		250 076	**267 321**	1,16%	**267 321**	0,98%
Kamil Sitarz		21 365	**21 365**	0,09%	**21 365**	0,08%
Vatnak Vat-Ho		18 500	**18 500**	0,08%	**18 500**	0,07%
Hendrik Nogai		9 000	**9 000**	0,04%	**9 000**	0,03%
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%
Piotr Romanowski		174 000	**174 000**	0,75%	**174 000**	0,64%
Rafał Chwast		121 115	**121 115**	0,52%	**121 115**	0,45%
Thomas Turalski		20 100	**20 100**	0,09%	**20 100**	0,07%

**After the reporting period, series J shares emission took place, which changed the total number of shares and votes in the Company. For more information, please refer to p. 31-33.*
***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 members of the Management and Supervisory Board of Ryvu Therapeutics S.A. as of December 31st, 2022

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	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		21 365	**21 365**	0.12%	**21 365**	0.10%
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)		92 975	**92 975**	0,51%	**92 975**	0.41%
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.*

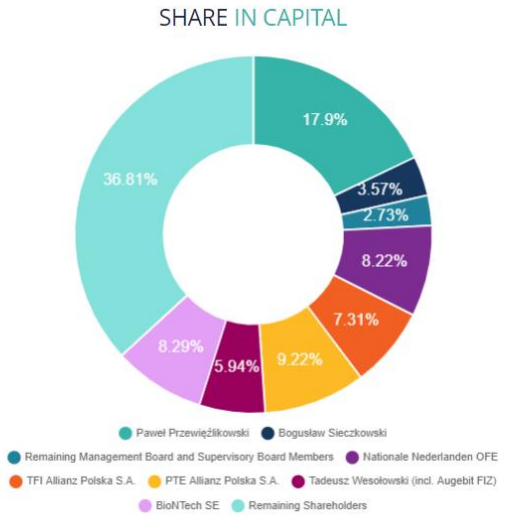
The Issuer is not aware of any contracts that could affect the proportions of the shares held by the existing shareholders. There are no other restrictions on the transfer of ownership of the Issuer's securities.

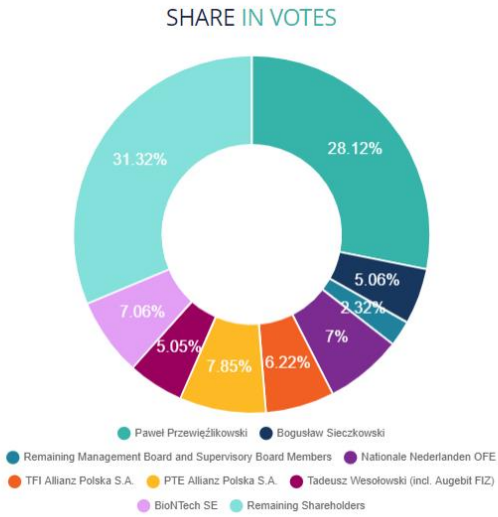
Shares held by significant shareholders of the Company

Shares held by significant shareholders of the Company as of Annual report publication date

Shareholder	Shares	% [Shares]	Votes	% [Votes]
Paweł Przewięźlikowski	4 139 544	17.90%	7 638 544	28.12%
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	1 900 980	8.22%	1 900 980	7.00%
PTE Allianz Polska S.A.	2 132 540	9.22%	2 132 540	7.85%
BioNTech SE	1 917 437	8.29%	1 917 437	7.06%

**The beneficiary of Augebit FIZ is Tadeusz Wesołowski - Vice-Chairman of the Issuer's Supervisory Board.*





Shares held by significant shareholders of the Company as of December 31st, 2022

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%
Tadeusz Wesołowski (with Augebit FIZ*)	1 132 713	6.17%	1 132 713	5.06%
Nationale Nederlanden OFE	1 530 980	8.34%	1 530 980	6.83%
Aviva OFE Santander	1 532 000	8.35%	1 532 000	6.84%

**The beneficiary of Augebit FIZ is Tadeusz Wesołowski - Vice-Chairman of the Issuer's Supervisory Board.*

Restrictions on the exercise of voting rights

Not applicable.

Restrictions on the transfer of ownership of the issuer's securities

Not applicable.

Description of the rules concerning the appointment and dismissal of managing persons and their rights, in particular the right to decide on the issue or buyback of shares

Pursuant to § 24 sec. 1 of Company's Articles of Association and § 2 sec.1. of Bylaws of the Management Board, Members of the Management Board are appointed and dismissed by Supervisory Board.

Pursuant to § 27 sec. 1 and 2 of Company's Articles of Association the Management Board manages the Company's business and represents the Company. The scope of activities of the Management Board comprises in particular all of the Company's matters that are not clearly reserved for the competencies of the General Meeting or the Supervisory Board. According to §3 of Bylaws of the Management Board, Management Board's responsibilities include in particular:

1. The Management Board manages the Company's activities, handles the Company's matters, manages the Company's property and represents the Company.
2. The Management Board looks after the transparency and effectiveness of the management system in the Company and handles its matters in accordance with the law and good practices.
3. The Management Board's responsibilities include all Company matters which are not reserved for the competence of the General Shareholders' Meeting or Supervisory Board, including, in particular:
    a) defining business goals and financial assumptions for the Company's activities;
    b) defining the Company's development strategy;
    c) handling the Company's matters;
    d) concluding contracts;
    e) shaping the Company's employment policy;
    f) compliance with information obligations of a public company;
    g) convening General Shareholders' Meetings within deadlines stipulated by the law or resulting from the Company's needs;
    h) preparing financial statements and written reports on the Company's operations (Directors' Reports) and providing them to the General Shareholders' Meeting and Supervisory Board;
    i) implementing and complying with corporate governance rules;
    j) reporting changes relating to the Company to the Register of Entrepreneurs of the National Court Register;
    k) ensuring the correct maintenance of the Company's documentation, including in particular the share register, book of resolutions of the Management Board, book of minutes of the General Shareholders' Meetings.

Description of the rules for changing the Issuer's Articles of Association

Pursuant to § 19 sec. 1 letter h of Company's Articles of Association, amendment of Company's Articles of Association is an exclusive competency of General Meeting.

The manner of operation of the general meeting and its basic competencies

Competencies of General Meeting are described in Company's Articles of Association

„General Meeting of Shareholders

§ 14

1. The General Meeting of Shareholders will be convened as an ordinary or extraordinary meeting.
2. The Ordinary General Shareholders Meeting will be convened by the Company's Management Board, at least once a year, but no later than six months after the end of each financial year.
3. The Extraordinary General Meeting of Shareholders will be convened by the Company's Management Board on its own initiative or at the written request of the Supervisory Board or of the shareholders representing at least one-twentieth of the share capital, no later than within two weeks of the date of submitting the respective application to the Management Board in writing or in electronic form.
4. The Supervisory Board may convene the Ordinary General Meeting of Shareholders if the Management Board does not convene it in the regulatory period referred to in section 2 and an Extraordinary General Meeting of Shareholders, if it considers it advisable.

§ 15

The General Meeting of Shareholders may be held in the Company's registered office, in Łódź, Katowice or in Warsaw.

§ 16

Resolutions of the General Meeting of Shareholders are passed by an absolute majority of votes, unless the Commercial Companies Code or these articles of Association stipulate otherwise.

§ 17

1. Voting at the General Meeting of Shareholders is by open ballot.
2. A secret ballot will be ordered in elections and in voting motions to dismiss members of the Company's bodies or liquidators, or to call them to account for their acts, and in personal matters.

§ 18

1. The General Meeting will be opened by the Chairman of the Supervisory Board or the Deputy Chairman, and subsequently, the Chairman will be elected from among the persons authorized to participate in the General Meeting. In the event of the absence of those persons, the General Meeting will be opened by the Chairman of the Management Board or a person appointed by the Management Board.
2. The General Meeting of Shareholders passes its rules that determine in detail the procedures for conducting the Meeting.

§ 19

1. Apart from the issues described in the legal regulations and in other provisions of the Articles of Association the General Meeting's competencies comprise:

a) purchasing and disposing of real estate, permanent usufruct or share in real estate or permanent usufruct;
b) reviewing and approving the Directors' Report and the financial statements for the prior financial year;
c) passing a resolution on profit appropriation or offset of loss;
d) discharging the members of the Company's bodies from liability;
e) taking decisions relating to claims to remedy any damage caused in the course of forming the Company or its management or supervision;
f) disposing of and leasing the enterprise or its organized part and placing restricted property rights upon them;
g) passing a resolution, in accordance with Article 394 of the Commercial Companies Code related to the conclusion of an agreement on the acquisition of any assets for the Company and for a subsidiary or cooperative subordinated to the Company for a price exceeding one-tenth of the paid-up share capital, from the Company's founder or shareholder, or for a company or cooperative subordinated to the Company's founder or shareholder, if the agreement is to be concluded before two years have passed since the date of the Company's registration;
h) amending the Company's Articles of Association;
i) increasing or reducing the share capital;
j) appointing and dismissing members of the Supervisory Board, in recognition of § 20 section 3;
k) approving the Rules of the Supervisory Board;
l) determining the principles for remunerating members of the Supervisory Board and the amount of the remuneration;
m) determining the amount of remuneration of members of the Supervisory Board delegated to perform constant individual supervisory functions;
n) setting up and reversing reserves;
o) merging the Company with other companies, transforming or demerging the Company;
p) dissolving the Company.

Description of the operation of the Issuer's management, supervisory or administrative bodies and their committees

Management Board

Manner of operation of Issuer's Management Board is described in Bylaws of the Management Board and Company's Articles of Association.

Bylaws of the Management Board

§ 2

Composition of the Management Board

1. Members of the Management Board are appointed and dismissed by the Supervisory Board.
2. The Management Board consists of 1 (one) to 7 (seven) people, including the President of the Management Board. In the case of the Management Board consisting of several people, a Vice President or Vice Presidents and Members of the Management Board can be appointed.

3. Both shareholders and non-shareholders may be appointed to the Management Board.
4. The term of office of the Management Board is five years. Members of the Management Board are appointed for a common term of office. The mandate of a Member of the Management Board appointed before the end of a given term of the Management Board expires upon the expiry of the mandates of the other members of the Management Board.
5. Any Member of the Management Board can be dismissed at any time.
6. Dismissal of a Member of the Management Board does not prejudice his/her claims under an employment agreement or another legal relationship related to his/her function as a Member of the Management Board.

Articles of the Association, §24 sec. 3

The number of members of the Management Board in each term of office will be determined by the Supervisory Board.

Bylaws of the Management Board

§ 5

Meetings of the Management Board

1. Meetings of the Management Board are convened and chaired by the President of the Management Board, and in the President's absence – by the Vice President of the Management Board or other Member of Management Board chosen by the President of the Management Board.
2. The President of the Management Board, and in the President's absence – the Vice President of the Management Board or other Member of Management Board chosen by the President of the Management Board – calls meetings of the Management Board on his/her initiative, at the request of a Member of the Management Board, or at the request of the Supervisory Board.
3. Meetings of the Management Board may be attended by people invited from outside the Management Board, after prior arrangement with the person convening the meeting. The invited people may not vote at the meetings.
4. The date and time of a meeting of the Management Board is notified to Members of the Management Board in writing, by fax, e-mail or in another agreed way, at least 1 (one) day before the date of the meeting.

§ 6

Adopting of the resolutions

1. Resolutions of the Management Board are adopted at meetings of the Management Board
2. Resolutions of the Management Board are passed by an absolute majority of votes. If voting results in a tie, the President has the casting vote.
3. Resolutions may be adopted if all members of the Management Board have been correctly notified of the meeting.
4. The appointment of a proxy requires the consent of all members of the Management Board. A proxy can be dismissed by any Member of the Management Board.

§ 7

Minutes of the meetings

1. Minutes are drawn up of all meetings of the Management Board.
2. The minutes of the meeting are taken by one of the members of the Management Board or a person from outside the Management Board appointed for this function.
3. The minutes should specify at least:
    a) the date of the meeting;
    b) names of Members of the Management Board and other people attending the meeting;
    c) agenda of the meeting;
    d) texts of resolutions passed and information about other matters which were not subject to resolutions;
    e) the number of votes cast for specific resolutions and dissenting opinions
4. The minutes are signed by Members of the Management Board present at the meeting and the person who took the minutes.

§ 8

Obligations of the Members of the Management Board

1. All members of the Management Board are obliged and entitled to handle jointly the Company's matters.
2. A Member of the Management Board in all his/her dealings is obliged to perform his/her duties with due care appropriate for the actions performed in business trading, in strict compliance with the law and the provisions of the Company's Articles of Association.
3. A Member of the Management Board may not, without the permission of the Supervisory Board, engage in competitive interests or participate in a competitive undertaking as a partner of a partnership or a member of a body of a corporate entity, or participate in another competitive legal entity as a member of its body. This ban also covers participation in a competitive company, if a Member of the Management Board holds at least 10% of shares or the right to appoint at least one Member of the Management Board.
4. In the event of a conflict of interest of the Company with the interest of a Member of the Management Board, his/her spouse, relatives or next of kin to the second degree and people with whom he/she is personally related. A Member of the Management Board should refrain from participation in the consideration of such matters and may request a respective mention in the minutes.

Supervisory Board

Manner of operation of Issuer's Management Board is described in Bylaws of the Supervisory Board and Company's Articles of Association.

Articles of Association

§ 20

1. The Supervisory Board comprises from 5 (five) to 10 (ten) persons.
2. Members of the Supervisory Board, including its Chairman, are appointed and dismissed by the General Meeting of Shareholders, in recognition of section 3.
3. (deleted)

4. Members of the Supervisory Board are appointed for a joint, five-year term of office.
5. In respect of the voting for members of the Supervisory Board in individual groups, the Chairman of the Supervisory Board is selected from among the members of a particular group.
6. If the mandate of a member of the Supervisory Board expires before the end of the term of office, the Management Board is required to immediately convene a General Meeting of Shareholders to complete the composition of the Supervisory Board.

§ 21

The Supervisory Board adopts the Rules that it submits to the General Meeting of Shareholders for approval.

§ 22

1. The Supervisory Board exercises continuous supervision over the Company's operations.
2. In particular, the competencies of the Supervisory Board comprise:
    a) assessing the Company's financial statements, the Directors' Report and the respective conclusions as to the appropriation of profit and offset of loss, and submitting the annual reports on the results of the assessments;
    b) appointing an independent statutory auditor to audit the Company's financial statements and the Group consolidated financial statements;
    c) appointing and dismissing members of the Company's Management Board;
    d) determining the principles for remunerating members of the Management Board and the amount of the remuneration;
    e) representing the Company in agreements and disputes between the Company and members of the Management Board unless the General Meeting appoints a plenipotentiary for this purpose;
    f) approving the Rules of the Management Board;
    g) approving the financial plan prepared by the Management Board;
    h) granting consent to members of the Management Board for engaging in activities competitive against the Company's or to participate in companies or ventures competitive against the Company.

§ 23

1. The Supervisory Board will hold meetings at least once a quarter.
2. The members of the Supervisory Board will exercise their rights and responsibilities in person. The Supervisory Board may delegate members to individually perform particular supervisory activities. Those members will receive separate remuneration, the amount of which will be decided by the General Meeting of Shareholders. Those members are required to meet non-competition obligations.

3. In order for the Supervisory Board's resolutions to be valid, it is necessary to invite all the Supervisory Board members to the meeting and to ensure that at least one-half of all Supervisory Board members are present at the meeting.

4. The resolutions of the Supervisory Board are passed by an absolute majority of votes of the Supervisory Board members. In the event of an equal number of votes, the Chairman of the Supervisory Board has the casting vote.

Audit Committee

Audit Committee is operating within the Supervisory Board. Description of operation of this Committee is described in Bylaws of Supervisory Board.

1. The Supervisory Board appoints members of the Audit Committee, including its Chairman.
2. Members of the Audit Committee are appointed among the members of the Supervisory Board.
3. The Audit Committee consists of at least three members.
4. Most members of the Audit Committee, including its chairman, meet the criterion of independence, in particular within the meaning of Art. 129 section 3 of the Act of 11 May 2017 on Statutory Auditors, Audit Firms and Public Oversight (Journal of Laws of 2017, item 1089), and at least one member of the Audit Committee, shall meet the knowledge and skills criteria specified in art. 129.1.5 of the abovementioned Act.
5. The tasks of the Audit Committee include in particular:
    1) monitoring of:
        a) the financial reporting process;
        b) effectiveness of internal control systems and risk management systems as well as the internal audit, also in respect of financial reporting;
        c) carrying out financial audit activities, in particular audits carried out by an audit company, taking into account all the conclusions and findings of the Audit Supervision Commission which result from an inspection carried out in the audit company;
    2) controlling and monitoring the independent status of the auditor and the audit company, in particular when other, non-audit services are provided to the public interest company by the audit firm;
    3) informing the supervisory board or another supervisory or controlling body of the public interest entity of the results of the audit and explaining how the audit contributed to the reliability of the financial reporting in the public interest entity, and the role of the audit Committee in the auditing process;
    4) reviewing the independence of the auditor and giving consent to permitted non-audit services provided by him to the public interest entity;
    5) drawing up a policy for selecting an audit company to be charged with the audit of the company;
    6) drawing up a policy for providing permitted non-audit services by the audit company which conducts the audit, its related entities, and by a member of the audit company's network;
    7) determining the procedure for the public interest entity selecting an audit company;
    8) presenting the supervisory board or another supervisory or controlling body, or the body referred to in Art. 66 (4) of the Accounting Act of 29 September 1994, the recommendations referred to in Art. 16 (2) of Regulation 537/2014, in accordance with the policies referred to in points and 6;
    9) submitting recommendations aimed at ensuring the reliability of the financial reporting process in the public interest entity.
6. The principles of the Supervisory Board's operation, i.e. in particular holding meetings and adopting resolutions by the Supervisory Board shall apply accordingly to the functioning of the

Audit Committee, unless the Audit Committee decides otherwise.

Renumeration Committee

Renumeration Committee is operating within the Supervisory Board. Description of operation of this Committee is described in Bylaws of Supervisory Board.

1. The Supervisory Board appoints and dismissed members of the Remuneration Committee, including its Chairman.
2. Members of the Remuneration Committee, including its Chairman, are appointed among the Supervisory Board Members.
3. The Remuneration Committee consists of at least three Members.
4. In particular, the competencies of the Supervisory Board comprise:
    1) Regarding the remuneration of members of the Company's Management Board:
        a) assessing the basic salary, bonuses and share-based compensation received by members of the Company's Management Board in relation to the scope of duties of members of the Company's Management Board and the manner of their performance, as well as market conditions,
        b) presenting proposals to the Supervisory Board regarding appropriate forms of contracts with members of the Company's Management Board and the amount of their remuneration,
    2) Regarding directors and senior employees' remuneration:
        a) making a general assessment of the correctness of the Company's policy regarding remuneration of the directors and senior employees,
        b) issuing general recommendations to the Company's Management Board regarding the level and of remuneration for directors and senior employees,
        c) monitoring the level and structure of remuneration for directors and senior employees based on relevant information provided by the Company's Management Board,
    3) Regarding share-based compensation that can be granted to members of the Management Board and employees of the Company:
        a) discussing the general principles for implementing equity incentive programs based on shares, share options, subscription warrants,
        b) presenting proposals to the Supervisory Board in this respect,
        c) presenting proposals to the Supervisory Board regarding equity incentive programs.
5. The principles of the Supervisory Board's operation, in particular holding of meetings and the adoption of resolutions by the Supervisory Board shall apply accordingly to the Remuneration Committee, unless the Remuneration Committee decides otherwise.

Agreements signed between the Issuer and managing persons, providing for compensation in the event of their resignation or dismissal

The Issuer has not concluded any agreements with managing persons providing for compensation in the event of their resignation or dismissal from their position without valid reason.

Remuneration of the members of management and supervisory bodies

Remuneration of the members of the Management Board of Ryvu Therapeutics S.A. for period 1.01.2022-31.12.2022 [in PLN]*

Members of the Management Board	Remuneration for performing functions in the Management Board	Remuneration for employment contracts concluded with the Issuer	Remuneration for other contracts	Total remuneration in 2022
Paweł Przewięźlikowski	164 640	176 747.77	-	**341 387.77**
Krzysztof Brzózka	322 500	273 007.40	-	**595 507.40**
Nogai Hendrik	0.00	728 009.40		**728 009.40**
Kamil Sitarz	312 000	173 541.24	-	**485 541.24**
Vat-Ho Vatnak	0.00	935 104.00*	2 880 (civil contract)	**937 984.00**

**Mr. Vat-Ho's remuneration is paid by a third-party entity with its registered office in the US and then reinvoiced to Ryvu Therapeutics S.A. on a basis of an agreement between the two companies.*

Remuneration of the members of the Supervisory Board of Ryvu Therapeutics S.A. for period 1.01.2022-31.12.2022 [in PLN]

Members of the Board	Remuneration for performing functions in the Supervisory Board
Piotr Romanowski	150 477.48
Tadeusz Wesołowski	148 254.94
Rafał Chwast	150 477.48
Axel Glasmacher	148 255
Colin Goddard	148 255
Jarl Jungnelius	148 255
Thomas Turalski	148 255

Transactions concluded by the Issuer with affiliated entities in 2022

None.

System of control of employee share scheme

The incentive program based on the Company's shares donated by Mr. Pawel Przewieźlikowski, operating from 2021 to 2024, was approved by the General Meeting on May 17, 2021. Implementation of the program is directly supervised by the Supervisory Board and the Company's Management Board.

The diversity policy implemented by the Issuer with regard to its administrative, management and supervisory bodies

The aim of the diversity policy implemented by the Company is to build awareness and organizational culture open to diversity, which leads to increased work efficiency and prevents discrimination.

When selecting the Company's governing bodies and its key managers, the Company strives to ensure versatility and diversity, especially in the area of gender, education, age and professional experience. The basis of diversity management is to provide equal opportunities in access to professional development and promotion. Currently, the Management Board and Supervisory Board of the Company consists of only men. The decisive aspects are, above all, the qualifications and substantive preparation to perform a specific function.

5 STATEMENT OF THE MANAGEMENT BOARD REGARDING APPLICABLE ACCOUNTING PRINCIPLES

Management Board of Ryvu Therapeutics S.A. confirms that, to the best of its knowledge, the annual 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, reliable and clear manner the property and financial situation of the Company and its financial result.

Report of the Management Board on the activities of Ryvu Therapeutics S.A. contains a true picture of the development and achievements as well as the Company's situation, including a description of the basic threats and risks.

6 STATEMENT OF THE MANAGEMENT BOARD TOGETHER WITH INFORMATION REGARDING CHOICE OF STATUTORY AUDITOR

Management Board of Ryvu Therapeutics S.A. declares that the entity authorized to audit financial statements auditing the annual financial statements for the financial year 2022 was selected in accordance to the provisions of law and that the entity and the statutory auditors auditing these statements met the conditions for expressing an impartial and independent opinion on the audit, pursuant to relevant provisions of national law and professional standards.

Management Board of Ryvu Therapeutics S.A. hereby informs that the selection of the audit company conducting the audit of the annual financial statements, i.e. Pricewathercooperhouse Polska spółka z ograniczoną odpowiedzialnością Audyt sp. k., was made in accordance with the applicable law, including those relating to the selection and selection procedure of an auditing company, and also:

a) the audit company and members of the team conducting the audit met the conditions for the preparation of an impartial and independent report from the audit of the annual financial statements in accordance with the applicable regulations, professional standards and professional ethics rules,
b) the Issuer complied with all of the applicable regulations regarding the rotation of the audit company and the key statutory auditor as well as the mandatory grace periods,
c) The issuer adopted a policy for the selection of an audit firm and a policy for additional non-audit services, including services conditionally exempt from prohibition of providing services by audit company, provided to the issuer by the audit company, entity affiliated to the audit company or a member of its network.

7 OTHER INFORMATION

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

The Issuer does not operate within Capital Group. As of the date of the Report, the Issuer holds 3.18% of shares, on a fully diluted basis, in NodThera Inc. with its registered office in the US.

Credits and Loans

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 at 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).

Structure of major capital deposits and investments

The structure of the main capital deposits and investments is presented in the financial statements.

Court Proceedings

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.". 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.

Despite holding several mediation sessions, the parties ultimately failed to reach an agreement. The mediation officially ended on 16.06.2022.

Both proceedings are on the stage of a pre-trial hearing.

Assurances and guarantees

Event did not occur in 2022.

Purchase of own shares

As part of the incentive program, the Company acquires its own shares temporarily - see note 21.2 for details.

Information about owned branches (plants)

Company does not own any branches.

Information on risks arising from held financial instruments

Risks affiliated with held financial instruments were described above.

The annual report of Ryvu Therapeutics S.A. for the financial year
1 January 2022 - 31 December 2022 is hereby approved.

Krakow, March 22, 2023

Dokument
podpisany przez
Paweł Tadeusz
Przewięźlikowsk
i
Data: 2023.03.22
21:17:37 CET

Paweł Przewięźlikowski
President of the Management Board

Dokument
podpisany przez
Krzysztof Daniel
Brzózka
Data: 2023.03.22
22:33:03 CET

Krzysztof Brzózka
Vice-President of the Management Board

Dokument
podpisany przez
Kamil Sitarz
Data: 2023.03.22
20:52:49 CET

Kamil Sitarz
Member of the Management Board

Signed by /
Podpisano przez:

Franz Hendrik
Nogai

Date / Data:
2023-03-22 21:05

Hendrik Nogai
Member of the Management Board

Digitally signed by
Vatnak Vat-Ho
Date: 2023.03.22
14:50:59 MDT

Vatnak Vat-Ho
Member of the Management Board

CONTACT

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GENERAL INQUIRIES

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RYVU THERAPEUTICS