RYVU THERAPEUTICS S.A.

ANNUAL REPORT

2021

TABLE OF CONTENTS

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, 2021 to December 31, 2021 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	**31.12.2021**	31.12.2020	**31.12.2021**	31.12.2020
Total assets	**228,813**	295,640	**49,748**	64,063
Short-term receivables	**11,741**	7,948	**2,553**	1,722
Cash and cash equivalents	**83,236**	136,218	**18,097**	29,518
Other financial assets	**4,994**	24,969	**1,086**	5,411
Total liabilities	**59,392**	71,920	**12,913**	15,585
Long-term liabilities	**23,192**	38,106	**5,042**	8,257
Short-term liabilities	**36,200**	33,813	**7,871**	7,327
Total equity	**169,422**	223,721	**36,836**	48,479
Share capital	**7,342**	7,342	**1,596**	1,591

Selected income statement data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
Item	**From 01.01.2021 to 31.12.2021**	From 01.01.2020 to 31.12.2020	**From 01.10.2021 to 31.12.2021**	From 01.10.2020 to 31.12.2020	**From 01.01.2021 to 31.12.2021**	From 01.01.2020 to 31.12.2020	**From 01.10.2021 to 31.12.2021**	From 01.10.2020 to 31.12.2020
Revenues from sales	**1,478**	1,336	**447**	486	**323**	299	**96**	106
Revenues from subsidies	**25,244**	21,300	**7,051**	6,798	**5,515**	4,761	**1,521**	1,487
Revenues from R&D projects	**10,358**	14,315	**10,358**	-	**2,263**	3,199	**2,235**	-
Other operating revenues	**430**	377	**25**	64	**94**	84	**5**	14
Revenues from operating activities	**37,510**	37,328	**17,881**	7,348	**8,194**	8,343	**3,858**	1,608
Operating expenses	**-115,377**	-73,025	**-34,136**	-18,851	**-25,205**	-16,322	**-7,366**	-4,124
Operating expenses without Incentive Scheme	**-84,691**	-73,025	**-18,445**	-18,851	**-18,502**	-16,322	**-3,980**	-4,124
Depreciation	**-12,561**	-12,357	**-3,445**	-4,361	**-2,744**	-2,762	**-743**	-954
Valuation of Incentive Scheme	**-22,999**	-	**-8,004**	-	**-5,024**	-	**-1,727**	-
Profit/loss from operating activities (EBIT)	**-77,867**	-35,697	**-16,255**	-11,503	**-17,011**	-7,978	**-3,507**	-2,517
Profit/loss from operating activities (EBIT) without Incentive Scheme	**-54,868**	-35,697	**-8,251**	-11,503	**-11,986**	-7,978	**-1,780**	-2,517
Profit/loss before income tax	**-77,419**	-30,616	**-17,162**	-10,690	**-16,913**	-6,843	**-3,703**	-2,339
Net profit/loss	**-77,535**	-31,688	**-16,910**	-10,943	**-16,938**	-7,082	**-3,649**	-2,394
Net profit/loss without Incentive Scheme	**-54,536**	-31,688	**-8,906**	-10,943	**-11,914**	-7,082	**-1,922**	-2,394
EBITDA	**-65,306**	-23,340	**-12,810**	-7,142	**-14,267**	-5,217	**-2,764**	-1,563
EBITDA without Incentive Scheme	**-42,307**	-23,340	**-4,806**	-7,142	**-9,242**	-5,217	**-1,037**	-1,563
Net cash flows from operating activities	**-57,868**	-10,636	**295**	364	**-12,642**	-2,377	**64**	80
Net cash flows from investing activities	**8,055**	-55,942	**2,941**	-27,959	**1,760**	-12,503	**635**	-6,117
Net cash flows from financing activities	**-3,170**	130,689	**-1,020**	-424	**-693**	29,210	**-220**	-93
Total net cash flow	**-52,983**	64,111	**2,216**	-28,019	**-11,575**	14,329	**478**	-6,130
Number of shares (weighted average)	**18,355,474**	16,765,977	**18,355,474**	18,355,474	**18,355,474**	16,765,977	**18,355,474**	18,355,474
Profit (loss) per share (in PLN)	**-4.22**	-1.89	**-0.92**	-0.60	**-0.92**	-0.42	**-0.20**	-0.13
Diluted profit (loss) per share (in PLN)	**-4.22**	-1.89	**-0.92**	-0.60	**-0.92**	-0.42	**-0.20**	-0.13
Book value per share (in PLN)	**9.23**	13.34	**9.23**	12.19	**2.01**	2.89	**2.01**	2.64
Diluted book value per share (in PLN)	**9.23**	13.34	**9.23**	12.19	**2.01**	2.89	**2.01**	2.64
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 01/01/2021 – 31/12/2021: PLN 4.5775;
   - for the period from 01/01/2020 – 31/12/2020: PLN 4.4742;
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 2021: PLN 4.5994;
   - as of 31 December 2020: PLN 4.6148;

1.2 Management Board comments to the financial results

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

In 2021, Ryvu Therapeutics S.A. recognized the total operating revenue of PLN 37,510 thousand, which constitutes a slight increase compared to the corresponding period in 2020, when the total operating revenue amounted to PLN 37,328 thousand. This mainly results from the increase in revenues from subsidies (increase of PLN 3,944 thousand), partially compensated by the decrease in revenues from R&D projects (decrease of PLN 3,957 thousand) compared to the corresponding period in 2020.

Revenues from R&D projects in 2021 resulted mainly from the following transactions:

- Galapagos NV exercised its exclusive option to license program with therapeutic potential in inflammatory diseases based on compounds discovered and developed by Ryvu. Upon execution of the option Ryvu was eligible to receive an option exercise fee in the amount of EUR 1,250 thousand and is eligible to receive research and development milestone payments, as well as royalties on future sales.
- Ryvu received from Menarini Group a development milestone in the amount of EUR 1.000 thousand based on the successful achievement of an efficacy signal in IDH-mutated AML patients in the initial Dose Escalation Study and all-comers AML Expansion Cohort Study of SEL24 (MEN1703).

In 2021, Ryvu reported a net loss as well as an operating loss. The net and operating losses are the result of the new Company's strategy of Ryvu published on June 15, 2020 for the years 2020-2022, which develops and revises the assumptions of the strategy adopted by the Company for 2017-2021, published in the current report No. 27/2017 of August 2, 2017 (before the corporate split of the Issuer). According to the Strategy, the Company focuses currently 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, 2021, amounted to PLN 77,535 thousand in comparison to the net loss of PLN 31,688 thousand in the corresponding period of 2020. The bigger loss in 2021 is related to non-cash cost of valuation of incentive program for its employees of PLN 22,999 thousand (described below) as well as higher expenditure incurred on research and clinical projects.

Valuation of shares in NodThera Ltd. (currently shares in NodThera Inc.)

Introduction

In June 2020, NodThera Ltd. announced the information that it had obtained financing in connection with the issuance of new series B preferred shares with a total value of GBP 44.5 million, which were acquired by global biotechnology funds, the so-called blue chip investors, including new investors: Novo Holdings A / S (investment part of the pharmaceutical concern Novo Nordisk), Cowen Healthcare Investments and Sanofi Ventures (fund of the pharmaceutical concern Sanofi), as well as its current shareholders 5AM Ventures, F-Prime Capital Partners, Sofinnova Partners and Epidarex Capital ("Investors"). The financing was divided into two tranches.

Funds in the amount of GBP 20.2 million were transferred to NodThera Ltd. in accordance with the share capital increase registered on June 2, 2020. The Series B preferred Shares were acquired at an issue price of GBP 2.9702 per share. The remaining part of the funding in the amount of GBP 24.2

million was to be provided by Investors after achieving certain milestones in the development of the NodThera's research projects in accordance with the investment agreement.

Due to an amendment to the above-mentioned investment agreement entered into in April 2021 (which was concluded by the Investors; the Issuer is not a party to this agreement), Investors decided that the first tranche of financing would be extended by an additional issuance of GBP 12.1 million (at the current issue price per share), while the original second tranche of financing will be decreased from GBP 24.2 million to GBP 12.1 million. The funds related to the extended first tranche were received by NodThera Ltd. in September 2021, in view of the achievement of the scientific milestones of the development of the company's research program in accordance with the amended investment agreement, i.e. after the submission of the application to commence clinical trials (CTA) for the NT-0796 molecule. The capital increase was carried out at the existing price of the first series B tranche, i.e. GBP 2.9702/share. As a result of the capital increase, Issuer's share in the share capital of NodThera Ltd. at the time amounted to 5.24%.

The decreased second tranche in the amount of GBP 12.1 million was provided to the company as a capital increase in December 2021. Investors subscribed for 3,895,328 shares at the price initially set in May 2020, i.e. GBP 3.1191/share. As a result of the above, the share capital of NodThera has been further diluted and in consequence Issuer's share in the share capital of NodThera amounted to 4.73% as of 31 December 2021.

With the receipt of the second tranche of proceeds raised from the Series B share issue, NodThera anticipates it has the necessary financial resources to operate smoothly throughout 2022 and fund ongoing projects through 2022.

NodThera redomiciliation to the U.S.

In December 2021, theBoard of Directors of NodThera Ltd., after receiving a consent from its shareholders began a process of relocating company’s corporate seat from Scotland to the U.S. Due to the nature of the industry in which NodThera operates, in the eyes of its management, securing future financing for NodThera projects would be easier for a company registered in the United States.

For this process a new company registered under the laws of the State of Delaware, US was formed, which on 31 December 2021 acquired 100% of shares in NodThera Ltd. from its previous shareholders (including Ryvu) by issuing stocks and exchanging stocks in the NewCo (NodThera Inc.), replicating 1:1 Nodthera Ltd's ownership structure. As a result, each shareholder's interest in NodThera Inc. is proportionately identical to its preexisting interest in NodThera Ltd.

As a result of this process, as of December 31, 2021, the Issuer holds 1,910,000 Junior Preferred stocks in NodThera Inc.

NodThera continues to operate from its offices in Cambridge, UK, Lexington, MA (US) and Seattle, WA (US).

Valuation of shares

Three types of shares existed in NodThera Ltd: ordinary shares and preferred shares (Junior Preferred Shares and Series A and B Shares). Ryvu was a holder of Junior Preferred Shares. An analogous division by share type has been used at NodThera Inc. where ordinary (stock) and preferred stock were issued (Junior Preferred Stock, Series A1 and A2 Preferred Stock and Series B Preferred Stock). Ryvu is a holder of the Junior Preferred Stock.

Associated with the Series A and B Preferred Stock is the right to receive dividends in the form of cash or the issuance of shares of the same class. The payment of dividends may be made in cases specified in the investment agreement, in particular in the event of a sale of the company or the admission of its shares to trading on a stock exchange. As of December 31, 2021, in aggregate, shareholders of Series A and Series B preferred stock were entitled to receive 4,041,698 shares of NodThera stock as dividends. Accordingly, if the dividend is paid in the form of a share issue, Ryvu share in the share capital of NodThera would decrease from 4.73% to 4.30%. In light of the above, the Management Board of Ryvu has decided to include in the valuation of the shares held by Ryvu in NodThera, a 10.01% discount to the price at which they were subscribed under the last share capital increase, i.e. series B2.

Therefore, a share valuation of GBP 2.8069/share (share price including a discount corresponding to the class of shares held by the Issuer) should be used as a basis for the calculations and as of 31.12.2021 the total valuation of Issuer's shares in NodThera Inc. amounts to PLN 29,403,922 (at the average NBP exchange rate of 5.4846 PLN/GBP).

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

new share issue price (in GBP)	2.8069
average NBP exchange rate from December 31, 2021	5.4846
new share issue price (in PLN)	15.39
the number of the Company's shares in NodThera Inc.	1,910,000
value of shares in the balance sheet as of December 31, 2021	29,403,922
value of shares in the balance sheet as of December 31, 2020	29,118,228
change in valuation – gross impact on valuation of shares	285,694
deferred tax	54,282
net impact on valuation of shares	231,412

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. Subject of The Stock Grant Program is comprised of 1,247,720 ordinary shares of the Company that have been donated free of charge by Mr. Paweł Przewięźlikowski – founder, President of the Management Board and Company's largest shareholder to the Company, constituting a total of 25% of the Company's shares held by Mr. Paweł Przewięźlikowski. The Stock Grant Program provides employees with the right to acquire shares at a preferential price of PLN 0.19 per share, covering the Company's administrative costs incurred to execute the Stock Grant Program. The fair value of the shares granted is determined as of the grant date and recognized over the vesting period in remuneration costs in correspondence with the capital increase at the time of vesting by employees during the program. For the period ending December, 2021 the Company recognized the non-cash cost of valuation of this incentive program of PLN 22,999 thousand – more details are described in note 36 to the financial statements.

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

As of December 31, 2021, the value of the Company's assets was PLN 228,813 thousand and decreased by PLN 66,827 thousand compared to the end of 2020 (PLN 295,640 thousand), mainly due to expenditures on R&D projects. At the end of December 2021, the highest value of current assets is cash which amounted to PLN 83,236 thousand (at the end of 2020 it was PLN 136,218 thousand) and other financial assets of PLN 4,994 thousand (at the end of 2020 it was PLN 24,969 thousand). The decrease in cash and other financial assets resulted from the aforementioned spending incurred on R&D projects and equipping the Research and Development Centre for Innovative Drugs (named 'CBR'). Fixed assets are mainly CBR and laboratory equipment and the valuation of NodThera of PLN 29,404 and deferred tax assets of PLN 331 thousand. The value of non-current assets increased in comparison to December 31, 2020, by PLN 1,288 thousand. The increase consists mainly of the aforementioned expenditures on equipping CBR.

The main item in Ryvu's equity and liabilities is equity, which amounted to PLN 169,422 thousand as of December 31, 2021, and decreased by PLN 54,299 thousand compared to December 31, 2020. The decrease in equity is mainly a result of the net loss recognized for the period. The other source of assets' funding is long-term liabilities which amounted to PLN 23,192 thousand at the end of December 2021. Long-term liabilities mainly related to deferred income related mainly to the infrastructure subsidy for CBR.

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

	31.12.2021	31.12.2020
Current ratio current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)	3.83	8.95
Quick ratio (current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)	3.75	8.86

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

1.4 Current and Projected Financial Condition

The Company's financial position as of the report date is good. As of December 31, 2021, the value of the Company's cash amounted to PLN 88,230 thousand (PLN 83,236 thousand in cash at the banks and PLN 4,994 thousand in bonds), and as of March, 10 2022, it was PLN 68,269 thousand. The decrease in cash has resulted from expenditure on R&D projects and payment of the tax in the amount of PLN 5,458 thousand in January 2022 related to the U.S. flip on NodThera, which, in accordance with Polish tax law, constitutes a tax moment.

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 38 to the financial statements.

1.6 Financial forecasts

The issuer did not publish financial forecasts for 2021.

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

Agreement with an entity authorized to audit financial statements, i.e. Ernst & Young Audyt Polska sp. z o.o. to audit the financial statements of Ryvu Therapeutics S.A. was concluded on June 24, 2020 for a period of three years.

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.

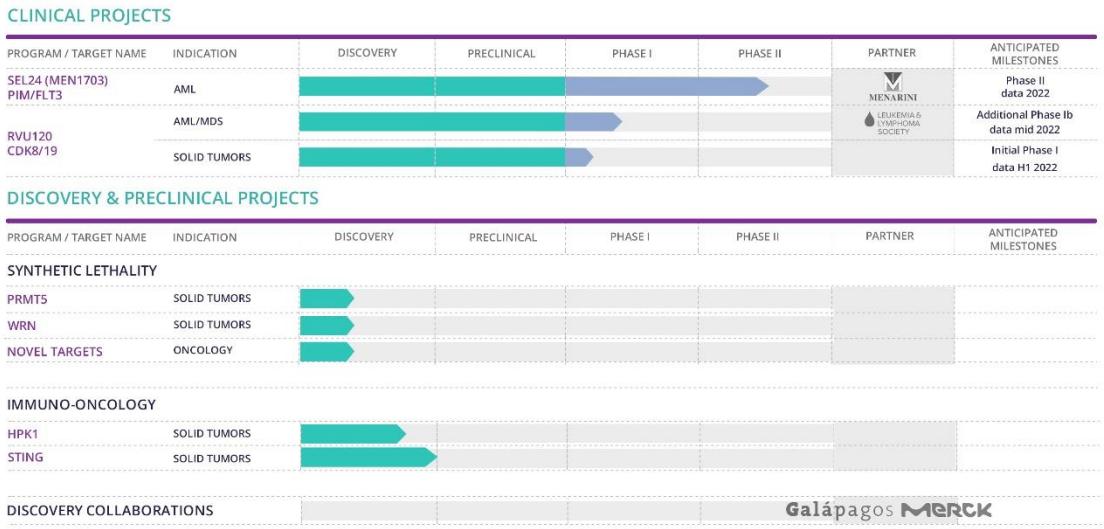
2 INFORMATION ON ISSUER'S ACTIVITIES

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, immuno-oncology and immunometabolism pathways.

These research and development projects are represented below.



Source: Company's own data.

SEL24/MEN1703

SEL24/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 (https://clinicaltrials.gov/ct2/show/NCT03008187).

The successful completion of a Phase I clinical study of SEL24/MEN1703 in AML was announced by Menarini in March 2020 and the results were presented at the 25th Annual Meeting of the European Hematology Association (EHA) 2020. Subsequently a Cohort Expansion study in relapsed/refractory AML patients has been initiated in the United States and Europe. The aim of the Phase II study is to further investigate the single agent activity and expanding safety profile of SEL24/MEN1703.

The data that have been generated in the SEL24/MEN1703 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/MEN1703 in AML, with a potential to focus in the IDH mutated subset. A subsequent study in this patient population started in July 2021.

Moreover, on November 4, 2021 Menarini announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation (ODD) to SEL24/MEN1703 for the treatment of AML.

At the 63rd ASH Annual Meeting & Exposition, held on December 11 – December 14, 2021, in Atlanta, US, Menarini presented pharmacodynamic and genomic profiling data from the First-in-Human trial. Modulation of ribosomal protein S6 phosphorylation was used as a marker for target engagement. Meaningful target engagement was achieved in 50% of patients and inhibition was maintained even at later cycles of treatment.

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

RVU120 (SEL120)

RVU120 (also known as SEL120) is a clinical stage, highly specific and orally bioavailable dual inhibitor of CDK8/CDK19 kinases. CDK8 and its paralog CDK19 have 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). 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 target patient population and potential combination partners as well as validating RVU120 in other hemato-oncology as well as solid tumor indications. As such, results of translational research are aimed at supporting the clinical development plan for RVU120.

Key achievements in 2021:

- **FDA lifted the partial clinical hold on Phase Ib clinical trial of RVU120 in AML/HR-MDS.** The partial clinical hold was issued in April 2021, following the report to the FDA of a Serious Adverse Event (SAE) involving a patient death due to pancreatitis. Study enrollment was suspended but patients who had already been on treatment could have

continued the treatment. As reported on July 14th, based on the recommendations from FDA, the study was allowed to resume enrollment at a 75mg dose EOD in a standard 3+3 design, according to a revised protocol intended to ensure patients' safety. The protocol amendment covered modified exclusion criteria, scope of monitoring and frequency of laboratory testing. Following the completion of the 75mg cohort, the data generated were reviewed by the Agency and a further dose escalation to doses of 85mg and 100mg was endorsed.

- **Phase Ib clinical trial of RVU120 in AML/HR-MDS expanded to Poland.** In Q3, two Polish clinical sites were activated for enrollment in the RVU120 AML/HR-MDS study: (i) University Clinical Centre in Gdansk and (ii) Institute of Hematology and Blood Transfusion in Warsaw. Together with the five US sites, there are currently seven clinical sites participating in the Phase Ib clinical trial of RVU120 AML/HR-MDS.

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

- **First patient dosed in Phase I/II study of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors.** On August 25th, the first patient in a single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120, received the first dose of the study drug. The clinical study had previously been approved by the Competent Authority in Poland and obtained a positive Ethics Committee opinion, enabling enrollment of patients in Poland. In Q3, two Polish clinical sites were activated for enrollment: (i) Medical University Early Phase Research Center in Gdansk, and (ii) Maria Sklodowska-Curie National Research Institute of Oncology in Warsaw. In Spain, the Vall d'Hebron Institute of Oncology was activated in February 2022. It is expected that additional sites in Spain will be activated in Q2 2022.

- The first 5 patients treated at the 75 mg and the 100 mg dose level completed the first cycle of treatment without dose-limiting toxicity, further supporting RVU120's manageable safety profile.

ABOUT RVU120 (SEL120) MOLECULE

RVU120 (SEL120) is a selective first-in-class CDK8/CDK19 inhibitor, which has demonstrated efficacy in a number of solid tumor in vitro and in vivo models as well as in hematologic malignancies. CDK8 is a kinase submodule of the mediator complex, involved in both transcriptional activation and repression. CDK8-mediator complex integrates basal transcriptional machinery with the activity of oncogenic transcriptional and epigenetic factors. Inhibition of CDK8 can repress key oncogenic transcriptional programs and induce lineage commitment genes in AML. CDK8 and CDK19 are also preclinically validated novel targets for the treatment of breast and prostate cancers. Targeting CDK8 and its paralog CDK19 using potent and selective CDK8/19 inhibitor RVU120, may be an effective treatment

for both hematological malignancies and solid tumors with deregulated transcription. According to information available to the Company, there are currently no competitive selective CDK8/19 inhibitors actively tested in clinical trials.

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.

ABOUT RVU120 AML/HR-MDS study (CLI120-001)

The primary aim of CLI120-001, first-in-human (FIH) Phase I study with RVU120 in relapsed or refractory AML or high-risk MDS, is to evaluate the safety and tolerability of RVU120 as well as establish the recommended dose for Phase II (RP2D). 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 investigates the relevant pharmacodynamic (PD) response by studying biomarkers of target engagement in patient samples, such as STAT5 phosphorylation, and identification of molecular markers that might point to a better response to treatment with RVU120.

The first patient in the CLI120-001 clinical trial was dosed on September 4th , 2019, and the study was enrolling patients in the US until April 8th , 2021, when the Food and Drug Administration (FDA) put study under a partial clinical hold, triggered by a fatal outcome of pancreatitis. Following the lift of partial clinical hold by FDA in July 2021, based on the recommendations from the Agency, the study resumed enrollment at a 75mg dose (Every Other Day – EOD) in a standard 3+3 design, according to the revised protocol. The protocol amendment covered modified exclusion criteria, scope of monitoring and frequency of laboratory testing. In addition to the five investigational sites in the US, Ryvu activated in September 2021 two new sites in Poland. Following completion of the 75mg cohort, data generated from this dose level were reviewed by the FDA and dose escalation to doses of 85mg and 100mg was endorsed, with further dose escalation to be preceded by additional data review by the FDA. The final results of the dose escalation part of the study are expected in 2022.

The CLI120-001 study is registered at ClinicalTrials.gov under the identifier NCT04021368 (https://clinicaltrials.gov/ct2/show/NCT04021368).

ABOUT RVU120 solid tumor study (RVU120-SOL-021)

The aim of the RVU120-SOL-021 Phase I/II clinical study, is 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 enrollment of adult patients with solid malignancies who have failed the available standard therapies. The primary objective of the Phase I part is to determine safety, tolerability and an RP2D. The secondary objectives include determination of the pharmacokinetic (PK), pharmacodynamic (PD) and preliminary anti-tumor activity of RVU120 as a single agent. The Phase II part is aimed both at safety and efficacy expansion. The Phase II will use an adaptive, Simon 2-stage

design and enroll patients with R/R specific tumor types, either as a single agent or in combination with standard anticancer medicinal agents, in 2 or 4 groups. The enrollment into these Phase II study groups, will be done simultaneously, therefore completion of one arm, would not affect completion of the other arms. Each study group is planned to enroll up to 24 patients. Additional translational and biomarker studies are currently ongoing to confirm which target patient populations will be selected.

The first patient was dosed on August 25th, 2021 at the 75 mg dose and the dose was escalated to the next dose level of 100 mg. The study is actively enrolling at three investigational sites in Poland and Spain. Activation of additional sites is expected in Q2 2022. Preliminary part 1 (phase I) disease assessment results are expected in 2022.

The RVU120-SOL-021 study is registered at ClinicalTrials.gov under the identifier NCT05052255

(https://clinicaltrials.gov/ct2/show/NCT05052255?term=RVU120&draw=1&rank=1).

PRECLINICAL AND DISCOVERY STAGE PROJECTS

Synthetic lethality projects

Ryvu is carrying out several research 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 in high concentrations is a very selective inhibitor of PRMT5 methyltransferase, competitive for the substrate: S-adenosylmethionine (SAM). Accumulation of MTA in cells with MTAP deletion causes a partial inhibition of the methylation activity of PRMT5, which in turn reduces the level of symmetric arginine 15emethylation of the whole proteome, and thus an increased sensitivity of cells to modulation of methylosome activity. The Company's strategy is to develop MTA-cooperative PRMT5 inhibitors, which will selectively inhibit the growth of MTAP-deleted cancer cells. The work carried out in H1 2021 focused on the identification and validation of unique chemical matter and led to the identification of new chemical series with the desired properties (confirmed synthetic lethality in *in vitro* cellular models). Identified chemical matter is currently being developed towards in vivo proof of concept and the preclinical candidate stage. The newly developed compounds are characterized for biochemical activity, differential synthetic lethality in MTAP +/- models and ADME parameters. PK experiments were performed for inhibitors characterized by the highest selectivity in terms of MTAP status and activity, which enabled the nomination of compounds for in vivo studies. Validation of the molecules in the mouse MTAP deletion xenograft model is planned for H1 2022.

Ryvu's second project focuses on development of first-in-class small molecule inhibitors of the Werner Syndrome helicase (WRN). The protein is a member of the RecQ helicase family and plays an important role in controlling DNA repair mechanisms and maintaining integrity of the genome. WRN helicase has been identified to be indispensable in tumor cells with microsatellite instability (MSI), where inhibition of the protein's helicase/ATPase activity leads to impairment of cellular viability. This therapeutic strategy holds promise for patients with MSI-high tumors across multiple indications, such as colorectal, ovarian, endometrial and gastric cancers. Ryvu carried out a high throughput screening campaign which led to the identification of a number of small-molecule WRN-inhibiting compounds. For the most promising chemotypes, further expansion and profiling were performed and are ongoing to explore the mode of action and improve necessary properties. Additionally, in 2021 a range of

alternative hit identification approaches were initiated to expand the portfolio of active chemotypes. In Q4 2021 the major focus was further validation, expansion and improvement of key properties of the active chemical series, which continues into H1 2022.

In addition to the two disclosed projects, Ryvu is currently leading multiple internal initiatives focused on identification and validation of new targets and respective hit matter in the synthetic lethality space. One of the key assumptions for the selected targets is first-in-class potential. So far, several new targets have been identified which potentially meet this criterion. Following positive target validation studies for one of the targets, the company has initiated a hit finding campaign aiming at identification of pharmacologically active compounds for this potentially first in class target. At the same time, work is underway on the selection and experimental validation of further molecular targets with first-in-class drug potential. Therapeutic targets for which active molecules can be identified and validated will be included in the company's project pipeline as they progress from target validation to successful hit stage.

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

Immuno-oncology projects

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

The most advanced project within the immuno-oncology portfolio focuses on development of small-molecule agonists of Stimulator of Interferon Genes, known as STING. The protein is one of the intracellular sensors of nucleic acids and activation of the STING signaling pathway leads to production of type I interferons, mobilizing the immune system response and promoting cancer neoantigen presentation by dendritic cells which in turn enhances antitumor T cell response.

The proprietary chemical series developed by Ryvu are potent STING activators with robust in vitro cellular activity, which translates to in vivo antitumor efficacy leading to inhibition of tumor growth and regression in mouse syngeneic tumor models. In 2021 advanced profiling led to a shortlist of front-runner molecules which have been optimized to reach superior agonist activity in human immune cells while at the same time maintaining a good overall safety profile. In Q4 2021 Ryvu continued in vivo characterization of a pre-selected front-runner compound. In particular the antitumor effect in a mouse syngeneic model was shown to translate into development of lasting immune memory against the treated cancer. Furthermore, advanced PK/PD and preliminary toxicology studies were performed in rats to facilitate the design of IND studies. As a result of the collected data in Q4 Ryvu selected the

frontrunner agonist molecule as the preclinical candidate. Further planned work focuses on completion of additional safety profiling to support further toxicology assessment.

The second project carried out in the area of immuno-oncology aims to develop innovative, orally available, small-molecule inhibitors of HPK1 kinase (MAPK4). Hematopoietic progenitor kinase 1 (HPK1) is a negative T-cell receptor (TCR) signaling regulator. By using HPK1 inhibitors, the natural mechanisms of the anti-tumor response are stimulated, leading to the effective elimination of cancer cells. In the fourth quarter of 2021, the focus was on activities aimed at improving the safety profile, i.e., increasing the therapeutic window for the most advanced compounds. Molecules characterized by high selectivity, metabolic stability and, importantly, no toxicicity at the cellular level were progressed further. In addition, the solubility of the series was significantly improved, which had a positive effect on the permeability through cell membranes and, in the long term, may result in a more favorable PK profile and thus expand the therapeutic window. In H1 of 2022, PK/PD experiments using the most advanced molecules are planned, which will allow studying the inhibitor's activity *in vivo*, and in the next phase, to test their efficacy in a murine syngeneic tumor model.

OTHER PROJECTS

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

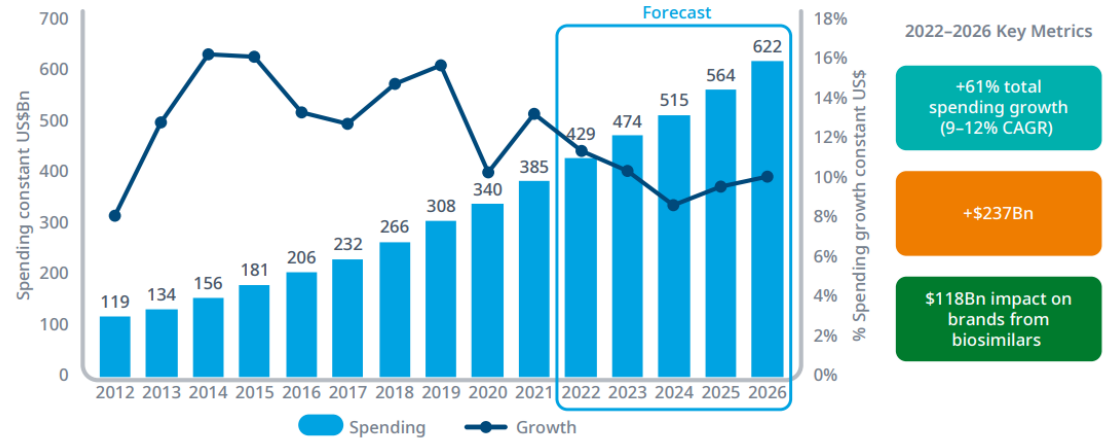
2.2 Characteristics of the biotechnology industry

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 at one end 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 from the pharmaceutical industry makes sense only when conducted on a global basis.

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 invariably 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. For China, the largest emerging market expected to exceed$205 billion in 2026, growth will be 2.5-5.5%.

The research and development portfolios of companies in the industry are constantly growing, while at the same time the success rate (in drug development) remains at historic highs. It is expected that this will result in an increasing number of new products, which 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 (or rather a specific molecule with potential therapeutic effect) discovery stage,

2) preclinical studies (in vitro and in vivo)

3) clinical trials (which typically include three phases)

4) the process of registration and approval by the relevant authorities

5) commercialization of an approved drug

6) monitoring the performance of the drug, once introduced to the market

A characteristic feature 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 successfully carry out the project to the next phase, so it will have to decide to end the project and focus its resources on other projects. It is also possible that the company, despite the project's transition to the next stage will be forced to return to the earlier stage in order to conduct additional research (by decision of the relevant authorities or due to new circumstances).

In connection with the above, a characteristic feature of the biotechnology market is also that the projects carried out by the companies last many years, and the probability of predicting the final success is 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 millions 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 higherincrease 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 phase oncology pipeline is 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.

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.

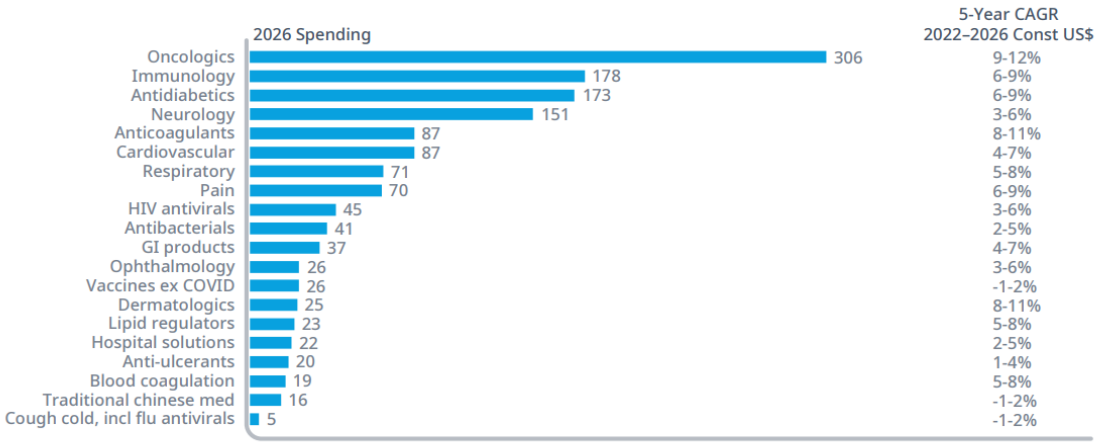
Oncology – partnering market

For the Issuer's innovative projects, a key market is the market of partnering agreements (license agreements) concluded between companies from the biotechnology and pharmaceutical industry. Its growing importance is related to the model of innovation in the pharmaceutical industry that has been present for several years now, 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 is from drugs that have been developed outside their laboratories. This creates an extensive market of projects, purchased by large pharma/biotech companies from other pharma/biotech companies, not only at the stage of clinical trials (which was characteristic in previous years), but also at the pre-clinical stage.

Investments in oncology far exceed those in other therapeutic areas, and partnering is a key strategy for these investments. In the years 2016-2020 alone, the cumulative value of contracts in oncology has reached $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 very significant area of oncology, both in terms of investment in research and development and molecule partnering. Immuno-oncology is also an area where Ryvu is active, with two early stage projects.

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 is a significant increase, especially it was estimated in 2019 that this market was supposed to be worth "only" USD $14 billion). 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 activities conducted by the Issuer require the purchase of services necessary to conduct work in the field of R&D and in last two years the Company also incurred expenses related to the new R&D Centre that was completed in July, 2020. The base of suppliers providing services for the Issuer is relatively well diversified. Due to the business model of the Company, the Issuer focuses on increasing the value of the ongoing projects, that will be commercialized at later stages and therefore the base of suppliers that reached the level of 10% of total sales revenues is significant. The key suppliers presented below are not affiliated with the Issuer.

	Financial year ended 31/12/2021 [net value] PLN
Supplier A	7 188 477,72
Supplier B	3 339 247,55
Supplier C	1 836 422,20
Supplier D	1 722 243,70
Supplier E	1 613 659,54
Supplier F	1 563 745,15
Supplier G	1 498 799,19
Supplier H	1 366 273,23
Supplier I	1 130 578,18

The main customers are presented in the financial statements in the Note 6.5.

The transactions with related companies are presented in the financial statements in the Note 33.1.

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

There were no such changes in the 2021 financial year.

2.5 Employment data

At the end of 2021 Ryvu Therapeutics S.A. was employing 190 people.

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

2.6 Sponsoring and charitable activities

As part of its Corporate Social Responsibility, Ryvu Therapeutics intends to build long-term relationships with charity organizations based mainly in Krakow and, making an impact on both local and national communities.

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

Furthermore, the Company cooperates with the "Piekne Anioly" Association helping children and youth living in tough conditions. Ryvu Therapeutics also supports Krakow St. Lazarus Hospice, which provides palliative care and support. Also, the Company cooperates with the "Wyspy Szczesliwe" Foundation, which aims to support the treatment of children suffering from cancer by providing them with access to effective therapies.

Charitable donations by Ryvu Therapeutics in 2021 amounted to over 27 thousand PLN.

2.7 Significant events in 2021

A) DURING THE REPORTING PERIOD

The new Clinical Trial Application for the conduct of a Phase I/II study of RVU120 in patients with solid tumors submitted by Ryvu Therapeutics S.A.

In January 2021 Issuer submitted a new Clinical Trial Application (CTA), seeking approval to commence a Phase I/II trial, investigating the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors. The CTA has been submitted to the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products and to the study Central Ethics Committee.

Expansion of Phase I study of RVU120 in patients with Acute Myeloid Leukemia or High-Risk Myelodysplastic Syndrome to Poland

In January 2021 Issuer's Clinical Trial Application (CTA) to commence the First-in-Human (FIH), Phase I trial investigating RVU120, a selective CDK8/CDK19 inhibitor, in patients with Acute Myeloid Leukemia (AML) or High-Risk Myelodysplastic Syndrome (HRMDS) was fully approved by the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, and the respective Central Ethics Committee. Following these approvals, the Company can expand the clinical trial, already ongoing in the United States, to Poland.

Ryvu Therapeutics project regarding Phase I/II clinical study of RVU120 in solid tumors recommended for financing by NCBiR

On January 18, 2021 Issuer's Project titled "Clinical development of an innovative drug candidate in solid tumors" ("Project") has been approved for financing by the National Center for Research and Development (NCBiR) within the Smart Growth Operational Program 2014-2020, measure 1.1.1. " Fast Track".

Conclusion of an agreement concerning operational execution of Phase I clinical trial of RVU120 in solid tumors

On March 8, 2021, Issuer concluded an agreement with Covance Inc. based in New Jersey, USA ("Covance"), to conduct a Phase I (dose escalation) part of a Phase I / II clinical study – aimed at determining the safety and efficacy profile of RVU120 in patients with relapsed / refractory metastatic or advanced solid tumors.

Covance Inc., is a leading global contract research organization (CRO) with 25-years of experience in running clinical trials. The company has a long track record of global clinical experience in executing oncology trials, with solid tumors being amongst the top indications in terms of Covance's expertise. In the past five years, Covance has run over 1,000 clinical studies in Oncology, with Phase I studies being the most often executed ones.

Covance will be responsible for operational execution of a Phase I clinical study (dose escalation). The estimated cost of the Agreement is EUR 2,223,529 (PLN 10,206,665 converted at the average exchange rate of the National Bank of Poland of March 8, 2021, EUR 1 = PLN 4.5903) and will be co-financed by the European Regional Development Fund and the Government of Poland as part of the project titled "Clinical development of an innovative drug candidate in solid tumors" within the Smart Growth Operational Program 2014-2020, measure 1.1.1. "Fast Track". The value of the contract may change in the event of extending the scope of the order.

Ryvu Therapeutics presented data from multiple oncology programs at AACR 2021 Virtual Annual Meeting

On April 10-15 and May 17-21, during the American Association of Cancer Research (AACR) Virtual Annual Meeting 2021, Company presented data from multiple oncology programs: RVU120, a CDK8/CDK19 inhibitor program, as well as data from small-molecule STING agonists and HPK1 inhibitors. Details of the e-poster presentations are as follows:

- Title: RVU120, a CDK8/CDK19 inhibitor, possesses strong multilineage differentiation potential in AML Permanent
- Title: New generation of STING agonists - development and characterization of a novel series of systemic immunomodulators with improved potency Permanent
- Title: Development and characterization of small molecule HPK1 inhibitors Permanent

Conclusion of the grant agreement with the National Center for Research and Development

On March 17, 2021 Company obtained information about the conclusion of the grant agreement with the National Center for Research and Development (NCBiR) for the project titled "Clinical development of an innovative drug candidate in solid tumors" ("Project") within the Smart Growth Operational Program 2014-2020, measure 1.1.1. "Fast Track".

The goal of the Project is implementation into Ryvu Therapeutics S.A. business a new drug candidate – inhibitor of CDK8/19 kinases, evaluated in I/II clinical phase (until stage of dose expansion). It should overcome the limitations of current treatment options benefitting patients with most aggressive solid tumors who have exhausted therapeutic possibilities.

- Project net value: PLN 42 696 464;
- Financing granted: PLN 18 939 762.79;
- Project timeline: September 2020 - December 2023.

Partial Clinical Hold of Phase Ib Clinical Trial of RVU120 (SEL120) by the FDA in Acute Myeloid Leukemia and Myelodysplastic Syndrome, and Subsequent Lift of the Clinical Hold with Resumption of Enrollment

The Company announced on April, 8 2021 that the U.S. Food and Drug Administration, FDA, placed a partial clinical hold on the first in human phase Ib, dose escalation clinical trial of RVU120in patients with relapsed/refractory (R/R) AML and high-risk MDS, being conducted in the United States. Patients who were taking RVU120 could continue treatment in the study but no new patients could be enrolled in the study. FDA subsequently lifted the partial clinical hold, which the Company disclosed in the current report no. 25/2021 dated July 14, 2021. Enrollment in the Phase Ib study has resumed.

Non-dilutive Stock Grant Program (2021-2024)

On April 20, 2021 the Company announced that it had received a letter of intent from Mr. Paweł Przewięźlikowski - the largest shareholder and President of the Management Board of the Company regarding declaration of a donation of part of the shares held by the Shareholder for the purpose of establishing an incentive program for employees and associates of the Company ("Program"). On May 17, 2021 the General Shareholders Meeting adopted a resolution regarding adoption of the Program for the years 2021-2024.

The Program includes a total number of 1.247.720 ordinary shares of the Company ("Shares") representing 25% of the Company's shares held by the Shareholder. The program has been implemented by granting the Eligible Persons (as defined below) the right to acquire Shares at a preferential price.

Every person who has an employment or other professional relationship with the Company was entitled to participate in the Program. The list of Program participants has been prepared on the basis of the Shareholder's recommendation and approved by the Supervisory Board in relation to the Members of the Management Board of the Company and by the Management Board of the Company in relation to other persons ("Eligible Persons"). Participation in the Program is voluntary.

Shares have been donated to the Company by the Shareholder free of charge, and the Eligible Persons were granted a right to acquire Shares at a preferential price ensuring the coverage of the Program costs incurred by the Company (such as: legal advice, brokerage fees, bank fees and others), in the amount of 0,19 PLN per Share.

The Eligible Persons will be obliged to remain in an employment or other professional relationship with the Company and not to dispose the Shares granted under the Program, within a period not less than 12 months and not longer than 36 months from the date of purchase of the Shares, unless they will be relieved from that obligation, which may happen on an exceptional basis.

The purpose and goals of implementing the Stock Grant Program are as follows:
i) ensuring optimal conditions for long-term growth of the Company's value by creating a broad employee participation shareholding structure;
ii) creating an incentive that will motivate employees to act in the best interest of the Company and its shareholders and encourage them to stay in a long-term relationship with the Company;
iii) building a modern organization in which an increase in the value of the Company will translate directly into an increase in the wealth of the employees and associates of the Company.

Information concerning impact of non-dilutive incentive program on Company's financial statements

In order to assess the impact of establishing the non-dilutive incentive scheme program for the years 2021-2024, the Issuer's Management Board, together with advisers, prepared a preliminary analysis of its impact on the Company's financial statements.

Based on above-mentioned analysis, pursuant to IFRS guidelines, free of charge transaction of donation of shares listed on the Warsaw Stock Exchange, by Mr. Paweł Przewięźlikowski to the Company, by which the Company does not incur any cash expenses, cannot be recognized as a revenue. Consequently, it will not affect any item on the Company's balance sheet or profit and loss accounts.

However, granting of shares, which Company will earlier receive in a form of donation from Mr. Paweł Przewięźlikowski, during the course of the Program i.e. between years 2021 and 2024 to the employees, will be recognized, pursuant to IFRS 2, as a non-cash salary expense in Company's financial statements (therefore it will have an impact on the operating result, EBITDA and net profit) and in the equity item as its increase in the same amount as the periodic cost. The total equity of the Company will remain unchanged.

The preliminary estimation, concerning, inter alia: the participation of Eligible Persons in the Program after its adoption by the Company's General Meeting, indicates that the total non-cash expense for the Company will amount to PLN 51-62 million, which will be spread over the duration of the Program, i.e. in the years 2021-2024, same as the amount of PLN 11.2 million in 2015-2017 in connection with the previous incentive program at the Company. The current valuation is presented in the note 36 of the Financial Statements.

The cost of the Program will be included in the Company's quarterly financial statements, and its value in a given reporting period will depend, inter alia, on factors such as employee's participation in the Program, the number of shares allocated to the Eligible Persons, and the fact if the Eligible Persons remain in an employment or other professional relationship with the Company.

Ryvu Therapeutics received full approval to conduct Phase I/II study of RVU120in patients with relapsed/refractory metastatic or advanced solid tumors in Poland

On May, 28 2021 the Company announced that its Clinical Trial Application (CTA) to commence a single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120 (in patients with relapsed/refractory metastatic or advanced solid tumors in Poland, was fully approved by the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, and the respective Central Ethics Committee.

The study is designed in two parts. Phase I part has the key objectives of assessing safety and tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary anti-tumor activity of RVU120 during dose escalation cohorts, and determination of the recommended phase II dose (RP2D). The Phase II part will include patients with specific tumor indications, enrolled in distinct study cohorts.

Following the above-mentioned approvals, the Company initiated the clinical study and started enrolling patients in Poland. Clinical Trial Applications in other European countries will be submitted over the coming months.

Presentation of poster on SEL24 (MEN1703) at ASCO Annual Meeting 2021

On June 4-8, 2021 during the annual American Society of Clinical Oncology ("ASCO") conference, development partner Menarini presented a poster containing data from the ongoing Phase I/II clinical trial of SEL24 (MEN1703), a first in class, orally available, dual PIM/FLT3 inhibitor titled "Updated results from DIAMOND-01 (CLI24-001) trial: a Phase I/II study of SEL24/MEN1703, a first-in-class dual PIM/FLT3 kinase inhibitor, in acute myeloid leukemia".

The ASCO Annual Meeting is considered one of the most important scientific events, gathering researchers, as well as potential clients and business partners - biotechnology and pharmaceutical companies and industry investors.

New data from RVU120 and SEL24(MEN1703) programs presented at the EHA Congress 2021

On June 9 - June 17, 2021 one oral and one poster presentation with results demonstrating clinical and pre-clinical activity of the selective CDK8/19 inhibitor RVU120 (SEL120) and one poster regarding selective PIM/FLT3 inhibitor SEL24(MEN1703) were presented during the Annual European Hematology Association (EHA) 2021 Virtual Congress:

- An oral presentation "RVU120/SEL120 CDK8/19 inhibitor - a drug candidate for the treatment of MDS can induce erythroid differentiation in transformed CD34+ hematopoietic progenitor cells"

Preclinical studies indicated strong antileukemic potential of RVU120 (SEL120) that was often associated with multilineage commitment of CD34+ AML cells. Moreover, research shows that RVU120 could improve proliferation and induce erythroid differentiation of CD34+ cells derived from Diamond-Blackfan anemia (DBA) patients. Presented results indicate strong erythroid differentiation potential of RVU120 in (Lin-) CD34+, that acquired genetic abnormalities resulting in arrested erythroid commitment, characteristic of many MDS (myelodysplastic syndromes) and AML (acute myeloid leukemia) subtypes. Observed differentiation phenotype strikingly resembles effects of RVU120 in DBA cells caused by disruption of genes encoding ribosomal proteins. Detailed transcriptomic profiling strongly associated differentiation with enrichment of genes representing regulators of erythroid commitment and hemoglobin metabolism. Further studies are warranted to investigate efficacy of RVU120 in anemias associated with bone marrow failures in AML and MDS patients.

- A poster presentation: "CLI120-001 Phase1b Study of SEL120/RVU120 in patients with AML or High Risk MDS: Preliminary clinical and PK results from initial dose escalation cohorts"

The FIH Phase Ib clinical trial with RVU120 in patients with relapsed/refractory (R/R) AML or High Risk MDS is currently open for enrollment at 6 sites in the US (NCT04021368). The poster presented the preliminary results of the first four single patient dose escalation cohorts which have shown a favorable safety and PK profile of RVU120. The first signals of single agent clinical activity have been observed at doses 50 to 75 mg.

In addition, a clinical poster regarding the FIH study of dual PIM/FLT3 inhibitor SEL24(MEN1703) conducted by Company's partner Menarini Group were also presented:

- **"Results from DIAMOND-01 (CLI24-001) trial: First In Human study of SEL24/MEN1703, a dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia"**

Clinical data on SEL24 (MEN1703) including patients enrolled in the Phase II, cohort expansion (CE) phase of the study, confirmed a manageable safety profile at the recommended dose (RD)

and preliminary single agent efficacy in R/R AML. These results warrant further investigation of SEL24(MEN1703) in AML.

FDA lifts partial clinical hold on RVU120 (SEL120) Phase Ib study in acute myeloid leukemia and myelodysplastic syndrome

On July, 14 2021 the Company announced that FDA lifted a partial clinical hold on the first-in-human Phase Ib, dose escalation clinical trial of RVU120 in patients with relapsed/refractory (R/R) AML and high-risk MDS, which is conducted in the United States.

Ryvu Announced First Patient Dosed in Phase I/II Study of RVU120 (SEL120) in Patients with Relapsed/Refractory Metastatic or Advanced Solid Tumors and CMO Transition

On August, 25 2021 the Company announced that the first patient enrolled in the Phase I/II clinical trial investigating RVU120 (SEL120) in relapsed/refractory metastatic or advanced solid tumors, received the first dose of the study drug.

The single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors was approved by the Competent Authority in Poland and obtained a positive Ethics Committee opinion, enabling enrollment of patients in Poland.

Currently the study is actively enrolling at three investigational sites in Poland and Spain. Activation of additional sites (in Spain) is expected in Q2 2022.

Resignation from the position in the Management Board

Dr. Setareh Shamsili, M.D., PhD resigned from her position as Executive Vice President of the Management Board and Chief Medical Officer of Ryvu for family reasons effective August 31, 2021. During the CMO transition period, Prof. Axel Glasmacher, M.D., Ryvu Supervisory Board Member since 2019, provided additional support for the Company on a consulting basis. Effective February 1st, 2022 Mr. Hendrik Nogai, M.D. has been appointed to the role of Chief Medical Officer.

Filing a lawsuit against Mota-Engil Central Europe S.A.

On September 24, the Company announced that it 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." ("Contract"), 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. The Contractor was supposed to complete the Contract within 15 months after the execution of the Contract, which has not been done. The Parties have extended Time for Completion of the Contract until April 30, 2020 (by way of concluding two annexes) and modified the scope of works to be performed under the Contract, including exclusion of the part of the works and performance of the substitution works.

Establishing the Polish Association of Innovative Medical Biotechnology Companies BioInMed

On November 3, it was announced that the Polish Association of Innovative Medical Biotechnology Companies BioInMed has joined the group of industry associations present in Poland. The association

was established by 11 companies such as Ardigen SA, Selvita SA, Ryvu Therapeutics SA, Captor Therapeutics SA, Celon Pharma SA, ExploRNA Therapeutics SA, OncoArendi Therapeutics SA, Polski Bank Komórek Macierzystych SA, PolTREG SA, Pure Biologics SA and WPD Pharmaceuticals Sp. z o.o. Marta Winiarska, who for the past five years has been managing public affairs and public relations activities at the Employers' Union of Innovative Pharmaceutical Companies INFARMA, has been appointed President of the Association.

The Association was established to work with all stakeholders and public administration to build an ecosystem that will allow medical biotechnology to become a hallmark of Polish innovation, and in the future, perhaps, the driving force of the economy.

Ryvu licensee Menarini Receives FDA Orphan Drug Designation for SEL24/MEN1703 for the Treatment of Acute Myeloid Leukemia

On November 4, the Company informed that the U.S. Food and Drug Administration (FDA) granted orphan drug designation (ODD) to SEL24/MEN1703 inhibitor for the treatment of Acute Myeloid Leukemia (AML). SEL24/MEN1703 is a first-in-class, orally available, dual PIM/FLT3 inhibitor, in-licensed by Menarini from the Company.

ODD is granted by the FDA to therapies intended for the treatment of conditions that impact fewer than 200,000 people in the US and provides companies with several incentives to support the development of therapeutics and diagnostics for rare diseases. ODD does not supersede the process of regulatory approval, and drugs for rare diseases are required to undergo the same rigorous scientific review process as any other drug. However, obtaining ODD status allows use of FDA's scientific advice to further the process of clinical trials and can significantly shorten the subsequent stages of studies.

Announcing Progress of NT-0796, a Novel NLRP3 Inflammasome Inhibitor, into a Phase 1 First-in-Human Study

On November 4, 2021 it was announced by NodThera that the first healthy volunteers have been dosed in a Phase 1 clinical trial of its lead investigational candidate, NT-0796. NT-0796 is a small molecule NLRP3 inflammasome inhibitor with differentiated novel chemistry that provides unprecedented potency and potential for prolonged pharmacodynamic (PD) effect, with the ability to cross the blood brain barrier in preclinical species. NT-0796 selectively inhibits NLRP3, the upstream regulator of the body's inflammation response, to reduce levels of both IL-1β and IL-18 – pro-inflammatory cytokines known to play a role in chronic inflammation underlying a wide range of chronic diseases. Pharmacokinetic (PK) and PD data from an ex vivo IL-1β/IL-18 stimulation assay and cerebrospinal fluid (CSF) sampling in the Phase 1 study will inform further clinical development.

The primary objective of this study is to assess the safety and tolerability of NT-0796, while secondary objectives include assessment of PK and PD and CSF sampling to assess NLRP3 target engagement and compound exposure after single and multiple ascending doses.

Highlighting HPK1 and STING Programs at the SITC Conference

On November 10-14, 2021 Issuer presented two research posters on its HPK1 and STING programs at the Society for Immunotherapy of Cancer 36th Annual Meeting & Pre-Conference Programs (SITC 2021) that took place in Washington, DC. The first poster concerns novel, orally administered HPK1 inhibitors which hold promising potential as a treatment in a variety of solid tumor indications. HPK1 inhibitors developed by the Company exhibit nanomolar activity in an immunosuppressive

environment. These small molecules have shown favorable PK profiles allowing for in vivo target engagement after oral administration.

The second poster highlighted a novel small-molecule STING agonist, RVU-27065. Selective STING pathway activation with RVU-27065 allows for repolarization of immunosuppressive tumor-associated macrophages into a pro-inflammatory phenotype without a negative impact on T-cell functioning. With favorable drug-like properties and good safety profile, RVU-27065 is a promising candidate for standalone treatment as well as targeted delivery as a payload for antibodies.

Clinical and Translational Data from RVU120 and SEL24(MEN1703) programs presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition and the 44th Annual San Antonio Breast Cancer Symposium (SABCS)

On December 11-14, the Company presented five abstracts demonstrating clinical and preclinical activity of selective CDK8/19 inhibitor RVU120 (SEL120) and selective PIM/FLT3 inhibitor SEL24 (MEN1703) at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition, held in Atlanta (USA). A poster on the preclinical efficacy of RVU120 in breast cancer has also been presented at the 44th Annual San Antonio Breast Cancer Symposium (SABCS) held on December 7 – 10, 2021, in San Antonio (USA). Ryvu's partner Menarini Group presented SEL24/MEN1703 data from the First-in-Human, Dose Escalation (DE) and Cohort Expansion (CE) CLI24-001 trial (DIAMOND-01, ClinicalTrials.gov identifier: NCT03008187).

RVU120 has demonstrated an acceptable safety profile and early signs of efficacy in patients harboring DNMT3A mutations, including a Complete Response, in the first five dose cohorts. Preclinical models show potential for clinical efficacy of RVU120 in breast cancer.

During the conference ASH Annual Meeting & Exposition the Company presented the following abstracts:

- CLI120-001 Phase Ib Study of RVU120(SEL120) in Patients with AML and High Risk MDS: Updated Safety/Efficacy Results from Initial Dose Escalation (Publication Number: 3418), Camille Abboud Sr., MD (Washington University in Saint Louis/ Washington University School of Medicine) et al.
- RVU120 (SEL120) CDK8/19 Inhibitor - a Drug Candidate for the Treatment of MDS Can Induce Erythroid Differentiation (Publication Number: 1518), Tomasz Rzymski, PhD (Ryvu Therapeutics) et al.
- Inhibition of Cyclin Dependent Kinase 8 (CDK8): A Novel Approach to Target the Leukemia Initiating Cells (LICs) in T-Cell Acute Lymphoblastic Leukaemia (T-ALL) (Publication Number: 2250), Sujan Piya, PhD (MD Anderson Cancer Center) et al.
- Preclinical and Clinical Signs of Efficacy of RVU120 (SEL120), a Specific CDK8/19 Inhibitor in DNMT3A-Mutated AML (Publication Number: 2371), Tomasz Rzymski, PhD (Ryvu Therapeutics) et al.
- SEL24(MEN1703) Inhibits PIM/FLT3 Downstream Target in Acute Myeloid Leukemia (AML) Patients: Results of the Pharmacodynamics (PD) Assay and Genomic Profiling in the First-in-Human Diamond-01 Trial (Publication Number: 3436), Alessandro Paoli (Menarini Group) et al.

The abstract accepted for the poster presentation at **the 2021 San Antonio Breast Cancer Symposium®**, that took place on December 7-10, 2021, at Henry B. Gonzalez Convention Centre in San Antonio, Texas:

- Selective CDK8/CDK19 inhibitor RVU120 demonstrates efficacy against hormone-independent breast cancer cells *in vitro* and *in vivo* (#1766), Tomasz Rzymski, PhD (Ryvu Therapeutics) et al.

During the poster presentations an acceptable safety profile and early signs of efficacy were presented for RVU120, a selective CDK8/19 inhibitor being developed in hematologic and solid tumors, in the first-in-human (FIH) Phase Ib dose escalation trial (CLI120-001) currently ongoing in patients with relapsed/refractory (R/R) acute myeloid leukemia (AML) or high-risk myelodysplastic syndrome (HR-MDS). The preliminary signs of efficacy for RVU120 include a Complete Response (CR) in an AML patient and an erythroid response (ER) in an HR-MDS patient, who relapsed after several lines of previous treatment.

Translational research was presented that potentially links the clinical response in an AML patient to DNMT3A-mutations via evidence in DNMT3A-mutated AML patient-derived cells (PDCs). Further translational research shows evidence that the clinical erythroid response in an MDS patient is potentially a result of strong erythroid differentiation potential of RVU120 in preclinical models. Enrollment is ongoing in cohort 4 at seven locations in the US and Europe to gather additional safety data in the study.

Both the ASH conference and the San Antonio Breast Cancer Symposium are considered to be one of the most important scientific events, gathering researchers, as well as potential clients and business partners - biotechnology and pharmaceutical companies from all over the world and industry investors.

Galapagos NV exercised its exclusive option to license program with therapeutic potential in inflammatory diseases

On December 13, 2021 Issuer received a notice from Galapagos NV with its registered office in Mechelen, Belgium, indicating that Galapagos has chosen to exercise its option under the Option, License and Research Collaboration Agreement to obtain an exclusive license to continue the research, development and commercialization of the program with therapeutic potential in inflammatory diseases based on compounds discovered and developed by Ryvu. Upon execution of the option Ryvu is eligible to receive an option exercise fee in the amount of EUR 1,250,000 (PLN 5,775,500 converted at the rate of NBP from 13th of December 2021, EUR 1 = PLN 4.6204) and is eligible to receive research and development milestone payments, as well as royalties on future sales.

Ryvu Therapeutics receives a development milestone based on an amended global License Agreement from Menarini Group

On December 30, 2021 Issuer informed about amending the global license agreement concluded with Berlin-Chemie AG under which Menarini Group has been granted an exclusive license to develop the SEL24 (MEN1703) ("Agreement"). The amendment clarifies certain milestone payments due under the Agreement. As a result, Issuer was granted a development milestone in the amount of EUR 1.000.000,00 based on the successful achievement of an efficacy signal in IDH-mutated AML patients in the initial Dose Escalation Study and all-comers AML Expansion Cohort Study in SEL24 (MEN1703) clinical trial.

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

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 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.

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

Appointment of the new Chief Medical Officer

Effective February 1st, 2022 Mr. Hendrik Nogai, M.D. has been appointed to the role of Chief Medical Officer. Dr. Nogai will lead medical, clinical, and regulatory functions to support and guide the development of the company's pipeline. Dr. Nogai is a board-certified medical doctor in Hematology/Oncology as well as in 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.

2.8 Unusual events occurring in the reporting period

COVID-19

Covid-19 pandemic began in the first quarter of 2020 and continued during the whole reported period. Because of that, the Issuer implemented recommendations given by the Chief Sanitary Inspectorate and other government institutions in connection with the epidemiological threat, including implementation of remote work and ensuring safe working conditions for stationary employees. Moreover, most business trips have been suspended. The Issuer used remote communication in its business contacts. Furthermore, the Issuer appointed a working team consisting of the representatives of various organizational units, whose task is to respond to the situation on an on-going basis and mitigate any adverse effects of the spread of the pandemic on the Issuer. The Company has also developed its internal policy for preventing spread of the coronavirus and has been taking actions

aimed at ensuring appropriate health and safety conditions at work, including access for Company's employees to routine antigen testing. Internal policies are constantly updated and adapted to the latest guidelines and changing conditions.

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

Due to the still on-going pandemic, the Issuer is not able to predict any further delays in the current clinical trials as of the date of publication of this report, but has taken steps to minimize the risk of their negative impact on the Company's operations.

The Issuer's research and development laboratories worked in 2021 with limited capacity. The decrease in their capacity was associated with employees absence due to quarantine, the fact that some foreigners could not enter Poland in time and the fact that some employees had to stay home with their children.. A significant proportion of the Issuer's office staff worked remotely, which could also have had an adverse effect on the speed of carrying out the projects. The research and development work was additionally slowed down by the procedures implemented to prevent infections, e.g. dividing teams into smaller ones, limiting personal contact, decontamination of laboratories, and shift work. The Issuer also identifies foreign exchange risk. 90% of the Issuer's cash is kept in PLN. The grants obtained are also denominated in PLN, whereas the costs of clinical trials and external research and development services are mostly denominated in foreign currencies. This risk is partly mitigated by guaranteed and expected revenues from the commercialization of projects, which are denominated in foreign currencies. The Issuer also identified risks associated with delays in administrative processes relating to granting and settling grants or VAT reimbursement and regulatory processes concerning clinical trials. The Management Board of the Company analyses the situation related to the spread of the pandemic on an on-going basis and implements new safety measures on an ongoing basis, including, in particular, increased sanitary regime, disinfection of laboratories and the entire facility of the Research and Development Center, by using masks, temperature measurements and voluntary testing of the employees for coronavirus infections. Additionally, in connection with the launch of the national vaccination program against COVID-19, Ryvu is strongly supporting the above-mentioned program.

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

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

Conflict in Ukraine

Due to the outbreak of the conflict in Ukraine, the Issuer's Management Board has analyzed the potential impact of the ongoing war on the Issuer's operations. In the opinion of the Management Board, apart from the currency risk described in Note 39 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

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

- Complete Phase I/II clinical development of our fully-owned lead asset RVU120 in AML/MDS;
- Expand therapeutic potential for RVU120 in solid tumors in the ongoing Phase I/II study;
- Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in IDH-mutated AML and potentially other indications;
- Strengthen position in novel target discovery and in developing novel, proprietary drug candidates in synthetic lethality;
- Complete preclinical programs for STING candidate and advance program into the Phase I of clinical trials or further development as an anti-body drug conjugate in a partnership;
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources.

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 above mentioned 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, immunology and the central nervous system, that is those in which the Issuer is particularly involved. 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 long-term, costly and uncertain phases aimed at demonstrating, inter alia, safety and therapeutic benefits offered for one or more indications. Taking into account the fact that currently two of the molecules developed by the Issuer, i.e. RVU120 and SEL24 (licensed to Menarini), are at the stage of clinical trials, there is an additional

possibility that particular risks characteristic for these stage may occur. For example, there is a risk that the Issuer will encounter difficulties in signing appropriate agreements with clinical centers, and thus it will be difficult to recruit the group of patients required for clinical trials. Due to the fact that the recruitment of patients is influenced by factors often beyond the Issuer's control, the possibility of preventing such risks may be limited. Furthermore, the Issuer may not be able to demonstrate, for example, good tolerance, the absence of side effects or the effectiveness of one or more of its active molecules.

Any failure in any of phases of molecule design, production or research may delay its development and commercialization, what, in extreme cases, may lead to the project being abandoned. The Issuer cannot guarantee that the process of designing, manufacturing and testing of the molecule will run smoothly and at deadlines consistent with market needs.

Moreover,even slight errors or delays in the development of molecules, may adversely affect the operations, market position, sales, financial results and development prospects of the Issuer.

Risk associated with intellectual property rights

The issuer operates on the global biotechnology market, one of the most innovative sectors of the economy. Operation 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 be sure that these agreements will be followed. This could lead to the 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 filled 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 a 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".

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 2021 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 on 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. 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 implement 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 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 E&Y). Also semi-annual statements are 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

During reporting period, effective August 31, 2021, Dr. Setareh Shamsili, M.D., PhD resigned from the position of Executive Vice President of the Management Board and Chief Medical Officer of the Company for personal reasons.

Issuer's Supervisory Board :

1) Piotr Romanowski – Chairman of the Supervisory Board
2) Tadeusz Wesołowski – Vice Chairman of the Supervisory Board
3) Rafał Chwast – Supervisory Board Member
4) Axel Glasmacher – Supervisory Board Member
5) Colin Goddard – Supervisory Board Member
6) Jarl Ulf Jungnelius – Supervisory Board Member
7) Thomas Turalski – Supervisory Board Member

Issuer's Audit Committee:

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

The Company's Remuneration Committee:

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

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 E&Y, did not provide the Issuer with permitted non-audit services 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 31.12.2021

Shareholder	Series A*	Series B	Series C,D,E,F, G1,G2	Number of shares	% of Share Capital	Number of Votes	% of Votes at SM
The Management Board							
Paweł Przewięźlikowski	3 500 000	120 411	307 630	**3 928 041**	21,40%	**7 428 041**	33,15%
Krzysztof Brzózka		17 245	250 076	**267 321**	1,46%	**267 321**	1,19%
Kamil Sitarz		17 865		**17 865**	0,10%	**17 865**	0,08%
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**	0.76%	**121 115**	0.60%
Thomas Turalski			20 100	**20 100**	0.11%	**20 100**	0.09%

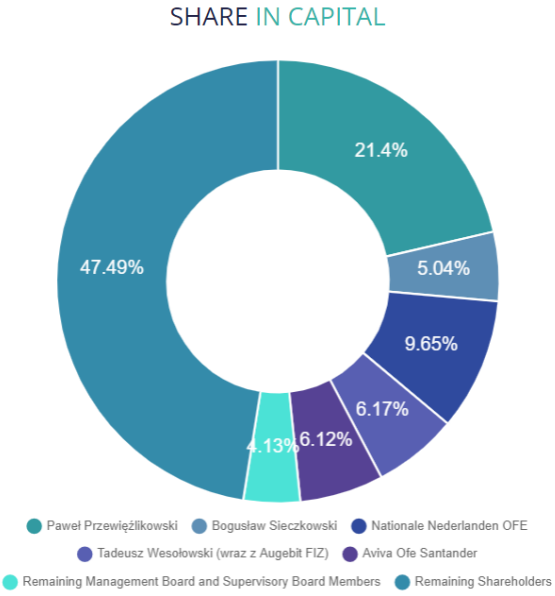
The Issuer is not aware of any contracts that could affect the proportions of the shares held by the existing shareholders. There are no other restrictions on the transfer of ownership of the Issuer's securities.

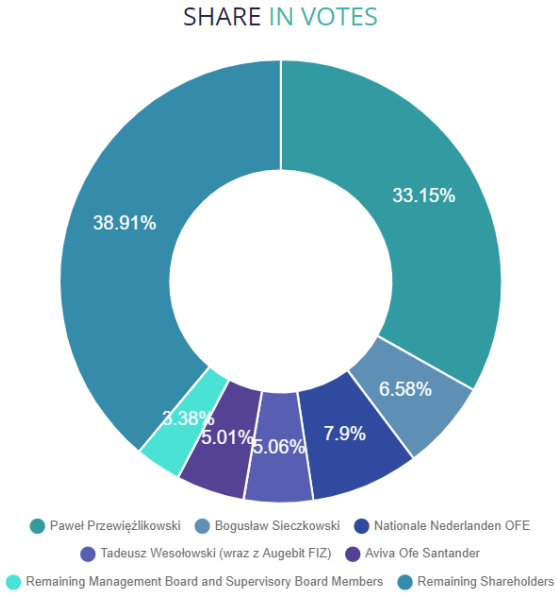
Shares held by significant shareholders of the Company

Shares held by significant shareholders of the Company as of 31.12.2021 and as of Annual Report publication date

Shareholder	Shares	% [Shares]	Votes	% [Votes]
Paweł Przewięźlikowski	3 928 041	21.40%	7 428 041	33.15%
Bogusław Sieczkowski	924 384	5.04%	1 474 384	6.58%
Nationale Nederlanden OFE	1 771 000	9,65%	1 771 000	7.90%
Aviva OFE Aviva Santander	1 122 859	6,12%	1 122 859	5,01%

**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.

Renumeration of the members of management and supervisory bodies

Renumeration of the members of the Management Board of Ryvu Therapeutics S.A. for period 1.01.2021-31.12.2021 [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 renumeration in 2021
Paweł Przewięźlikowski	988 521.00	177 028.33	-	**1,165,549.33**
Krzysztof Brzózka	1 145 143.00	272 912.02	-	**1,418,055.02**
Setareh Shamsili[1]	-	1 477 296.60	-	**1,477,296.60**
Kamil Sitarz	472 097.00	173 199.59	-	**645,296.59**

[1] *Dr. Shamsili was performing function of Member of the Management Board until August 31, 2021*

Renumeration of the members of the Supervisory Board of Ryvu Therapeutics S.A. for period 1.01.2021-31.12.2021 [in PLN]

Members of the Board	Remuneration for performing functions in the Supervisory Board
Piotr Romanowski	147,641.92
Tadeusz Wesołowski	144,740.49
Rafał Chwast	148,211.58
Axel Glasmacher	144,740.00
Colin Goddard	144,740.00
Jarl Jungnelius	144,740.00
Thomas Turalski	144,740.00

Transactions concluded by the Issuer with affiliated entities in 2021

Affiliated entity	Manner of affiliation	Transaction details	Transaction value (PLN)
ALTIUM Piotr Romanowski	Piotr Romanowski (key managerial personnel – member of Supervisory Board)	Purchase of advisory services	5,661.82

System of control of employee share scheme

There are currently no employee share schemes in the Company.

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 2021 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. Ernst & Young Audyt Polska spółka z ograniczoną odpowiedzialnością spółka komandytowa, 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 INFOMRATION

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 4.73% of shares in NodThera Inc. with its registered office in US.

Credits and Loans

No credits and/or loans has been raised.

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.

Assurances and guarantees

Event did not occur in 2021.

Purchase of own shares

Event did not occur in 2021.

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 2021 - 31 December 2021 is hereby approved.

Krakow, March 11, 2022

Dokument podpisany przez PAWEŁ TADEUSZ PRZEWIĘŹLIKOWSKI
Data: 2022.03.11 15:26:55 CET

Paweł Przewięźlikowski
President of the Management Board

Dokument podpisany przez Krzysztof Daniel Brzózka
Data: 2022.03.11 15:45:50 CET

Krzysztof Brzózka
Vice-President of the Management Board

Dokument podpisany przez Kamil Sitarz
Data: 2022.03.11 16:07:33 CET

Kamil Sitarz
Management Board Member

CONTACT

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GENERAL INQUIRIES

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RYVU THERAPEUTICS