



**RYVU THERAPEUTICS S.A.**  
ANNUAL REPORT  
**2020**



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# 1 ECONOMIC AND FINANCIAL HIGHLIGHTS

## 1.1 Financial Results Obtained in the Reporting Period

Financial Statements of Ryvu Therapeutics S.A. for the period from January 1, 2020 to December 31, 2020 are prepared in accordance with the International Financial Reporting Standards.

Pursuant to the adopted resolution of the Issuer's Extraordinary General Meeting held on June 4, 2020, about which the Company informed in current report No. 15/2020 of June 4, 2020, the Issuer began preparing financial statements based on IFRS from January 1, 2020. The decision is justified by the fact that the Company's shares are listed on the regulated market of Warsaw Stock Exchange, which gives the Company the opportunity to prepare financial statements in accordance with IFRS. In the Company's opinion, the financial statements prepared in accordance with IFRS will be more useful to investors, especially foreign investors. It will also ensure the comparability of the Company's financial data with entities operating in the biotechnology industry, which in the vast majority carry out financial reporting in accordance with IFRS.

Therefore data in this management report is presented:

- a) for the net profit or loss - for periods ended on: December 31, 2019 and December 31, 2020
- b) for the statement of financial position - as at January 1, 2019; December 31, 2019 and December 31, 2020.

Additionally, when comparing the Company's financial data for comparative periods, it should be taken into account that on October 1, 2019, the split of Ryvu Therapeutics S.A. (formerly Selvita S.A.) took place, as a result of the transfer of the organized part of the enterprise to Selvita S.A. (formerly Selvita CRO S.A.). The organized part of the enterprise consisted of:

- the tangible and intangible assets dedicated to the provision of service activities in the field of biotechnology, of the Contract Research Organization type;
- shares in the subsidiaries i.e.: Selvita Services Sp. z o.o., BioCentrum Sp. z o.o. (subsequently merged with Selvita Services sp. z o.o.), Ardigen S.A., Selvita Ltd., and Selvita Inc.

In connection with the above, the comparative data presented in the financial statements for the year ended December 31, 2019 covers three quarters of continued and separated operations and the fourth quarter of continued operations only, i.e. the innovative segment.

Selected income statement data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
	From 01.01.2020 to 31.12.2020	From 01.01.2019 to 31.12.2019	From 01.10.2020 to 31.12.2020	From 01.10.2019 to 31.12.2019	From 01.01.2020 to 31.12.2020	From 01.01.2019 to 31.12.2019	From 01.10.2020 to 31.12.2020	From 01.10.2019 to 31.12.2019
Revenues from sales	<b>1,336</b>	3,798	<b>486</b>	649	299	883	106	152
Revenues from subsidies	<b>21,300</b>	29,922	<b>6,798</b>	7,547	4,761	6,956	1,487	1,763
Revenues from R&D projects	<b>14,315</b>	-	-	-	3,199	-	-	-
Other operating revenues	<b>377</b>	419	<b>64</b>	114	84	97	14	27
Revenues from operating activities	<b>37,328</b>	34,139	<b>7,348</b>	8,310	8,343	7,936	1,608	1,941
Operating expenses	<b>-73,025</b>	-79,524	<b>-18,851</b>	-19,376	-16,322	-18,486	-4,124	-4,526
Depreciation	<b>-12,357</b>	-7,989	<b>-4,361</b>	-2,293	-2,762	-1,857	-954	-536
Profit/loss on operating activities (EBIT)	<b>-35,697</b>	-45,385	<b>-11,503</b>	-11,066	-7,978	-10,550	-2,517	-2,585
Profit/loss before income tax	<b>-30,616</b>	-44,109	<b>-10,690</b>	-9,995	-6,843	-10,254	-2,339	-2,335
Net profit/loss	<b>-31,688</b>	-44,270	<b>-10,943</b>	-10,172	-7,082	-10,291	-2,394	-2,376
EBITDA	<b>-23,340</b>	-37,396	<b>-7,142</b>	-8,773	-5,217	-8,693	-1,563	-2,049
Net cash flows from operating activities	<b>-10,636</b>	-17,401	<b>364</b>	-10,162	-2,377	-4,045	80	-2,374
Net cash flows from investing activities	<b>-55,942</b>	-2,604	<b>-27,959</b>	-2,094	-12,503	-605	-6,117	-489
Net cash flows from financing activities	<b>130,689</b>	-2,746	<b>-424</b>	-695	29,210	-638	-93	-162
Total net cash flow	<b>64,111</b>	-22,751	<b>-28,019</b>	-12,951	14,329	-5,289	-6,130	-3,025
Number of shares (weighted average)	<b>16,765,977</b>	15,971,229	<b>18,355,474</b>	15,971,229	16,765,977	15,971,229	18,355,474	15,971,229
Profit (loss) per share (in PLN)	<b>-1.89</b>	-2.77	<b>-0.60</b>	-0.69	-0.42	-0.64	-0.13	-0.16
Diluted profit (loss) per share (in PLN)	<b>-1.89</b>	-2.77	<b>-0.60</b>	-0.69	-0.42	-0.64	-0.13	-0.16
Book value per share (in PLN)	<b>13.34</b>	7.55	<b>12.19</b>	7.55	2.89	1.77	2.64	1.77
Diluted book value per share (in PLN)	<b>13.34</b>	7.55	<b>12.19</b>	7.55	2.89	1.77	2.64	1.77
Declared or paid dividend per share (in PLN)	-	-	-	-	-	-	-	-

**Selected balance sheet data are as follows:**

<b>Ryvu Therapeutics S.A.</b>	<b>Data in PLN thousand</b>		<b>Data in EUR thousand</b>	
<b>Item</b>	<b>31.12.2020</b>	<b>31.12.2019</b>	<b>31.12.2020</b>	<b>31.12.2019</b>
Total assets	<b>295,640</b>	183,630	<b>64,063</b>	43,121
Short-term receivables	<b>7,948</b>	14,681	<b>1,722</b>	3,447
Cash and cash equivalents	<b>136,218</b>	72,107	<b>29,518</b>	16,932
Other financial assets	<b>24,969</b>	-	<b>5,411</b>	-
Total liabilities	<b>71,920</b>	63,050	<b>15,585</b>	14,806
Long-term liabilities	<b>38,106</b>	32,434	<b>8,257</b>	7,616
Short-term liabilities	<b>33,813</b>	30,616	<b>7,327</b>	7,189
Total equity	<b>223,721</b>	120,580	<b>48,479</b>	28,315
Share capital	<b>7,342</b>	6,388	<b>1,591</b>	1,500

**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 01/01/2020 – 31/12/2020: PLN 4.4742;
  - for the period from 01/01/2019 – 31/12/2019: PLN 4.3018;
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 2020: PLN 4.6148;
  - as of 31 December 2019: PLN 4.2585;

## 1.2 Management Board comments to the financial results

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

From significant events that took place in the reporting period it is worth emphasizing that the phase I study of SEL24/MEN1703 (program licensed to Berlin-Chemie, belonging to Menarini group) was finished in the first quarter of 2020. This event constituted a milestone under the license agreement for which Ryvu Therapeutics S.A. received a payment in the amount of EUR 1,750 thousand.

Also, on April 15, 2020, the Company concluded a research and development cooperation agreement with Galapagos NV. The subject of cooperation is the discovery and development of innovative small molecule compounds with potential therapeutic applications in inflammatory diseases. Under the agreement, the Company received an advance payment of EUR 1,500 thousand, as well as will be entitled to receive total payments of up to EUR 53,500 thousand in case of successful development and commercialization of a potential drug that will be created based on the results of the cooperation.

In the 2020, Ryvu Therapeutics S.A. recognized total operating revenue of PLN 37,328 thousand, which constitutes an increase of 9% compared to the corresponding period in 2019, when total operating revenue amounted to PLN 34,139 thousand. The increase in revenue is due to the significant increase in revenue from sales (increase of PLN 11,853 thousand), partially compensated with the decrease in revenues from subsidies (decrease of PLN 8,622 thousand) comparing to the corresponding period in 2019.

The increase in revenues from external sales results mainly from the abovementioned end of the Phase I study of the first-in-human clinical trial using SEL24 / MEN1703 - oral dual PIM / FLT3 kinase inhibitor in patients with acute myeloid leukemia and a contract with Galapagos NV for the discovery and development of innovative small molecule compounds in inflammatory diseases.

The current decrease in subsidy revenue, while maintaining a similar level of operating costs, is primarily due to a change in the structure of expenditure. In 2020, there was less expenditure on grant projects, and more on projects not yet subsidized.

In 2020, Ryvu Therapeutics S.A. reported a net loss as well as the loss on the operational level. The above is a result of the implementation of the new Company's strategy 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 CR No. 27/2017 of August 2, 2017 (before the division of the Issuer). According to the Strategy Company focuses currently on increasing the value of the ongoing projects, that will be commercialized at later stages.

Company's net loss for period ended December 31, 2020, amounted to PLN 31,688 thousand in comparison to the net loss of PLN 44,270 thousand in the corresponding period of 2019. The smaller loss in 2020 is related to the revenue recognized from the end of the Phase I study discussed above in the project SEL24 / MEN1703 and signing a contract with Galapagos NV. as well as from the revaluation of shares in NodThera Ltd. (described below).

### **Valuation of shares in NodThera Ltd.**

On June 3, 2020, the Management Board of the Company received information that NodThera Ltd. obtained financing in connection with the issue of new series B shares with a total value of GBP 44.5 million, divided into two tranches, which will be acquired by leading biotechnology investors, including new investors such as: Novo Holdings A / S (investment arm 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. One of the shareholders in Epidarex Capital is Eli Lilly, a global pharmaceutical company that is also a direct shareholder of NodThera. First tranche of Series B funding in the amount of GBP 20.2 million at an issue price of GBP 2.9702 per share was paid to the Company in June 2020. Second tranche shall be paid until 30 June 2021. In the opinion of the Management Board, the above share issue sets the grounds for the valuation as at the balance sheet date adopted at the price of 1 share for GBP 2.9702 / share. In connection with the above, the carrying amount of the shares of Ryvu S.A. in NodThera Ltd. increased from PLN 23,754 thousand as of December 31, 2019 up to the amount of PLN 29,118 thousand as of December 31, 2020.

#### Valuation of shares in NodThera Ltd. according to fair value:

new share issue price (in GBP)	2.9702
average NBP exchange rate from December 31, 2020	5.1327
new share issue price (in PLN)	15.25
the number of the Company's shares in NodThera Ltd.	1,910,000
value of shares in the balance sheet as at December 31, 2020	29,118,228
value of shares in the balance sheet as at December 31, 2019	23,754,255
change in valuation - impact on gross result	5,363,973
Deferred tax	1,019,155
impact on the net result	4,344,818

#### Issue of Series I Shares

In Q3 2020, the Issuer also carried out a successful issue of Series I Shares, as a result of which the Company secured over PLN 134 million net. See Section 2.1 below for more details.

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

As of December 31, 2020, the value of the Company's assets was PLN 295,640 thousand and increased by PLN 112,010 thousand compared to the end of 2019 (PLN 183,630 thousand), mainly due to the successful issue of Series I Shares, compensated with expenditures on R&D projects. At the end of December 2020, the highest value of current assets is cash which amounted to PLN 136,218 thousand (at the end of 2019 it was PLN 72,107 thousand) and other financial assets in the value of PLN 24,969 thousand (at the end of 2019 it was none). The increase in cash and other financial assets results from the mentioned above issue of Series I Shares, compensated with the spending incurred on research projects and the construction of the Research and Development Centre for Innovative Drugs (named 'CBR'). Fixed assets are mainly aforementioned expenditures on CBR and laboratory equipment, valuation of NodThera of PLN 29,118 and deferred tax assets of PLN 594 thousand. The value of non-current assets increased in comparison to December 31, 2019, by PLN 29,624 thousand. The increase consists mainly of the above-mentioned expenditures on CBR.

The main item in the Ryvu Therapeutics S.A.'s equity and liabilities is equity, which amounted to PLN 223,721 thousand as of December 31, 2020, and increased by PLN 103,141 thousand compared to

December 31, 2019. The increase in equity is mainly a result of issue of Series I Shares compensated with the net loss recognized for the period. The second largest source of assets' funding is long-term liabilities which amounted to PLN 38,106 thousand at the end of December 2020. 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:**

	31.12.2020	31.12.2019
<b>Current ratio</b>		
<b>current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)</b>	8.95	3.18
<b>Quick ratio</b>		
<b>(current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)</b>	8.86	3.12

Cash surpluses, not used in the operating activities, are deposited in the low-risk financial instruments like short term bank deposits, PKO Leasing'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, 2020, the value of the Company's cash amounted to PLN 161,187 thousand (PLN 136,218 thousand in cash at the banks and PLN 24,969 thousand in bonds), and as of March 10, 2021, it was PLN 151,339 thousand (PLN 126,339 thousand in cash at the banks and PLN 25,000 thousand in bonds).

The Company meets its obligations timely and maintains sustainable cash levels ensuring its financial liquidity. Cash inflow from the share issue from Q1 2018, share issue in Q3 2020, funds obtained from subsidies from EU funds supporting R&D projects and cash generated from the commercialization of projects allows the Company to execute its planned investments, in particular, the development of the ongoing and new innovative projects. Future Company's revenue depends strongly on the ability to commercialize the research projects.

#### 1.5 Significant off-balance sheet items<sup>2</sup>

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 2020.

## **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 2.9.

## **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. 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.

Our pipeline includes candidates with differentiated therapeutic mechanisms, including programs directed at kinase, synthetic lethality, immuno-oncology and immunometabolism pathways.

The pipeline of Issuer's research and development projects is 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>).

SEL24/MEN1703 has completed Phase I dose escalation study in AML. The results were presented at the 25th Annual Meeting of the European Hematology Association (EHA) 2020. Throughout the dose escalation part, SEL24/MEN1703 showed an acceptable safety profile up to the recommended dose

established at 125 mg/day. Initial evidence of single agent efficacy was observed with 1 CR and 1 CRI in elderly patients who had exhausted standard therapeutic options.

On December 1<sup>st</sup>, 2020 Ryvu announced that the poster entitled “SEL24/MEN1703 provides PIM/FLT3 Downstream Pathway Inhibition in Acute Myeloid Leukemia (AML) Blast Cells: Results of the Pharmacodynamic (PD) Assay in the Dose Escalation Part of First-in-Human DIAMOND Trial” would be presented by Menarini at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, which took place virtually on December 5-8. The poster includes positive results of the pharmacodynamic assay demonstrating target engagement in the dose escalation part of the DIAMOND-01 trial.

The Cohort Expansion study in relapsed/refractory AML patients has been initiated in the United States and Europe (including Poland, where two sites are planned to be activated). The aim of Ph II study is to further investigate the single agent activity and expanding safety profile of SEL24/MEN1703. Following Menarini’s communication on 16<sup>th</sup> September 2020, Ryvu reported that the cohort expansion has started in USA with the first patient being treated as of July 21, 2020. In Europe the first patient was dosed on 16<sup>th</sup> September 2020. For the ongoing Phase II study Menarini has increased the number of involved clinical sites to eighteen (ten in the US and eight European sites in Italy, Spain and Poland). The anticipated date for the ongoing study completion is 2H 2021.

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.

### **SEL120 (RVU120)**

RVU120 (also known as SEL120) is a highly selective, orally administered small molecule, dual inhibitor of CDK8/CDK19 kinases which are key targets involved in transcription modulation in multiple cancer types. Preclinical studies have indicated a crucial role for CDK8 (cyclin dependent kinase 8) in the regulation of oncogenic gene expression which is important in the disease biology of a number of malignancies. Inhibition of CDK8 results in enhanced direct cytotoxicity towards cancer cells over healthy cells, and additionally reverses the faulty cell differentiation in malignant cells. By targeting the population of leukemic stem cells in Acute Myeloid Leukemia (AML), CDK8 inhibition offers the potential to improve upon efficacy and safety of the existing marketed treatments. RVU120 activity has also been explored in preclinical studies of a number of other hematological malignancies, such as lymphomas, and solid tumors (eg. breast cancer or colorectal cancer), either as a single agent or in combination with currently approved anticancer treatments including chemotherapy, immunotherapy or targeted therapeutics.

The first patient, in the first in human (FIH) Phase 1b clinical trial of RVU120 in adult patients with AML or high-risk myelodysplastic syndrome (HR-MDS) CLI120-001, who have relapsed or are refractory to the available standard therapies, was dosed on 4th September 2019, and the study, called CLI120-001, is currently enrolling patients at six active investigational sites in USA. Due to COVID-19 pandemic induced limitations, all of the RVU120 clinical sites have significantly reduced their activity for about 4 months in early 2020 which has resulted in a serious slowdown of enrollment. Subsequently all sites are taking many months to regain full capacity,

The primary aim of the CLI120-001 study, is to evaluate the safety and tolerability of RVU120 as well as establish the recommended dose for phase 2 (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 biomarkers of target engagement and response to treatment with RVU120, such as STAT5 phosphorylation and identification of molecular markers who might point to a better response, in patient samples .

The CLI120-001 study is registered at ClinicalTrials.gov under the identifier NCT04021368 (<https://clinicaltrials.gov/ct2/show/NCT04021368>).The first annual safety report of RVU120 compound in clinical development was submitted to the United States Food and Drug Administration (FDA) FDA, on May 20 2020.

On March 28, 2020, FDA granted an orphan drug designation (ODD) to RVU120 for the treatment of patients with AML. It allows Ryvu to be eligible for requesting an access to FDA scientific advice during further stages of the clinical trial process and also associated with potential tax advantages with respect to the costs of clinical trials, as well as a simplified drug evaluation and registration procedure. Since 2018, RVU120 program development in hematological malignancies has been supported scientifically and financially by the Leukemia and Lymphoma Society's (LLS) Therapy Acceleration Program (TAP).

In June 2020, Ryvu presented a poster with details of the RVU120 phase Ib clinical trial design during the European Hematology Association (EHA) Virtual Congress. Also, in June 2020, during AACR Virtual Annual Meeting II, Ryvu presented its translational preclinical results providing a strong rationale for combination of RVU120 and a BCL-2-selective inhibitor, venetoclax, in AML as a synergistic concomitant treatment, with both agents strongly increased apoptotic cell death in established AML cell lines. Apoptosis is induced via mechanism involving phosphorylation of pro-survival MCL-1, that targets it for proteasomal degradation and increased expression of pro-apoptotic BIM. Importantly, synergistic interaction between RVU120 and Venetoclax are observed in AML cells which are relatively resistant to either single agent treatment and have been corroborated in patient derived cells. In addition with using murine models of AML, Ryvu found complete remissions of AML and associated recovery of normal cells in bone marrow of animals treated with both RVU120 and Venetoclax. Taken together, these data provide a rationale for a novel clinical strategy that may lead to durable responses in AML patients.

Ryvu also continues translational research studies supporting targeted approach in solid tumors and other hemato-oncology indications which are planned as part of a novel expanded clinical strategy which is further mentioned at this report.

Due to the onset of Covid-19 pandemic, all RVU120 clinical sites have introduced additional safety measures and risk management processes which in general have strongly impacted the possibilities for patients to participate in clinical studies. This includes also R/R AML patients who are frequently immunocompromised. Also, many patients themselves decided to limit their contacts with various healthcare facilities to minimize the possibility of Covid-19 exposure. In effect enrollment at some sites were temporarily suspended and in other sites visible slowed-down. The current delay in the planned study enrollment is approximately 6 months. As a consequence, Ryvu has decided to move the anticipated timelines for the first results of the CLI120-001 study from Q4 2020 to H1 2021. Ryvu has taken actions as part of Risk Management for COVID specific risk on clinical trial.

In the original plan of the study Ryvu intended to open the enrollment in the dose escalation part at three additional sites in the US (nine sites in total). Because of the pandemic situation in the US, Ryvu has decided to start the European arm of the study earlier than originally expected and include additional sites in Poland and other European countries. The first in Europe Clinical Trial Application (CTA) was submitted on August 11, 2020. The effect of the actions taken was that at the beginning of January 2021 the Issuer received approval from the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL) and the Independent Bioethics Committee to commence the First in Human (FIH) Phase I trial investigation RVU120 in patients with Acute Myeloid Leukemia (AML) and High-Risk Myelodysplastic Syndrome (HRMDS) in clinical centers Poland. Currently two investigational sites in Poland have been selected, however none of them are fully activated for enrollment at the time of this report.

Based on the scientific rationale and preclinical positive data of anti-tumor efficacy of RVU120 in multiple solid tumor types, Ryvu submitted a CTA for seeking approval to commence a new phase I/II study in Solid Tumors, to the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products and to the study Central Ethics Committee on 30 Dec 2020, and the full approval can be expected in H1 2021. The aim of this new clinical trial of RVU120, is to investigate the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumours. Following the approval of the CTA the Company will be able to activate the selected clinical sites in Poland and start enrolling patients.

This solid tumor study is designed in 2 parts. Part 1 serves as the phase 1 part of the study, the dose-escalation part, and will enroll 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 a recommended Phase 2 dose (RP2D). The secondary objectives include determination of the pharmacokinetic (PK), pharmacodynamic (PD) and preliminary anti-tumor activity of RVU120 as a single agent. Phase 1 part will enroll to about 24 patients, evaluable for determination of dose limiting toxicities (DLT). Part 2, serves as the phase 2 part with both safety and efficacy expansion. The phase II part of the study, uses an adoptive, Simon 2-stage design and will enroll patients with R/R specific tumor types, either as single agent or in combination with standard anticancer medicinal agents, in 2 or 4 groups. The enrollment into these phase 2 separate 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. Currently, one of this group of patient population is disclosed as R/R metastatic or advanced triple negative breast cancer (TNBC). Additional translational and biomarker studies are ongoing to confirm which additional target patient population would be selected.

## **Preclinical and discovery stage projects**

### **Immuno-oncology projects**

The main focus of projects in IO space is on discovery and development of innovative immunotherapeutics based on solutions that overcome the limitations of current therapies. Ryvu approach offers a differentiated, personalized treatment options for patients with aggressive, refractory tumors.

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

The most advanced project within immune-oncology portfolio focuses on development of small-molecule agonists of Stimulator of Interferon Genes, known as STING. The protein acts as an intracellular sensor of nucleic acids and has been identified to play a pivotal role in activating the immune response to pathogen-derived or self-DNA. Activation of the STING signaling pathway leads to production of type I interferons, mobilizing immune system and promoting cancer neoantigen presentation by dendritic cells which in turn enhances antitumor T cell response.

The proprietary compounds developed by Ryvu are potent STING activators which maintain their activity on immune cells across species and irrespectively of the different STING haplotypes naturally occurring in the human population. Additionally the in vitro activity of the developed compounds has been proven to translate into in vivo proinflammatory response ultimately leading to potent antitumor efficacy after systemic administration in syngeneic mouse tumor models.

The advanced stage of the project allowed to preselect a shortlist of most promising compounds. In Q4 2020 the focus was primarily put on advanced profiling of the top compounds with respect to their in vitro and in vivo safety properties. The obtained results allowed to further narrow down the shortlist of potential preclinical candidates and to initiate optimization of the compound manufacturing process allowing to deliver sufficient quantities of material necessary for toxicology studies. Additionally, Ryvu continued evaluation of in vivo efficacy and advanced PK/PD characterization of the shortlisted compounds in order to further optimize the administration methodology and allow to identify a suitable biomarker with clinical applicability.

Currently, the studies are primarily focused on completing in vitro and in vivo profiling of the preselected compounds which will enable final selection of the preclinical candidate molecule and lead to initiation of toxicology studies.

The second project carried out by the Company in that area is development of HPK1 kinase inhibitors, which is one of the major proteins involved in the signaling cascade triggered by TCR activation. HPK1 also known as MAPK1 is a negative regulator of lymphocyte activity. Thus, inhibition of its activity will increase T cell activity resulting in a pronounced antitumor response. Proprietary HPK1 inhibitors developed by the Company inhibit kinase activity at the low nanomolar to picomolar concentration range being one of the most potent inhibitors disclosed publicly. In Q4 2020 optimization of several chemical series was continued, with particular focus on improving PK parameters, on-target activity and selectivity. Broad expansion of in vivo profiling based on the established PK/PD protocols is planned in the upcoming quarters.

In 2020 Ryvu completed non-GLP toxicology studies, in order to confirm the safety profile in rodents and higher species of the RVU330 clinical candidate, a dual adenosine A2A and A2B antagonist. At the end of Q3 the management and supervisory boards assessed the situation of the project in context of competitive positioning, efficacy signals reported by competitive programs and the obtained safety profile from non-GLP toxicological studies as well as the analysis of scientific, process, medical and patent protection challenges in the process of preclinical studies and clinical development. Both boards came into conclusion that the overall positioning of the project in Ryvu pipeline and in partnering market has diminished significantly over recent quarters. As a result of periodical pipeline restructuring the decision has been made to discontinue SEL330 program.

## Synthetic lethality projects

The Company conducts currently several projects in this area which are focused on solid tumors with defined molecular background by inhibition of identified genetic vulnerabilities present in cancer cells.

The first disclosed project focuses on the development of first in class small-molecule inhibitors of the Werner Syndrome helicase (WRN). The protein is a member of RecQ helicase family and plays an important role in maintaining the integrity of the genome and DNA repair mechanisms. 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 tumors with microsatellite instability (MSI-high) across multiple indications, such as colorectal, ovarian, endometrial and gastric cancers.

Ryvu concluded a high throughput screening campaign which led to identification of small-molecule WRN inhibitors. In Q4 the studies performed by the Company focused on initiation of medicinal chemistry optimization of the identified hit series with the goal of improving pharmacological and physico-chemical properties. Simultaneously substantial efforts were carried out to optimize additional methodologies allowing to explore pharmacology of the identified compounds as well provide structural guidance for their further development.

Currently the work focuses on deeper profiling of the selected chemical series as well as identifying key optimization strategies. Additionally, efforts are being carried out in order to generate orthogonal hit matter in order to diversify the portfolio of WRN-inhibiting chemotypes.

The second project in the field of synthetic lethality is work focusing on cancers with a deletion of the metabolic gene MTAP. Works carried out in H2 focused on the identification and validation of unique chemical matter and on validation of new therapeutic targets in the area of synthetic lethality.

The third project which was being developed in 2020 in the field of synthetic lethality were inhibitors of ATPase activity or the degradation of the SMARCA2 protein in cells with SMARCA4 mutations. The developed compounds, despite their high in vitro activity, did not show the expected activity in the in vivo model due to limitations in physicochemical properties and PK profile. In connection with the significant progress of the competing programs and the foreseen difficulties in the further development of the project, related to the quality of the identified inhibitors, it was decided to terminate the research and development activities on SMARCA2 target.

## Other projects

Ryvu also carried out other research and development programs within the therapeutic areas presented above. Details and the current progress on other research initiatives are currently confidential due to intensive competitive environment.

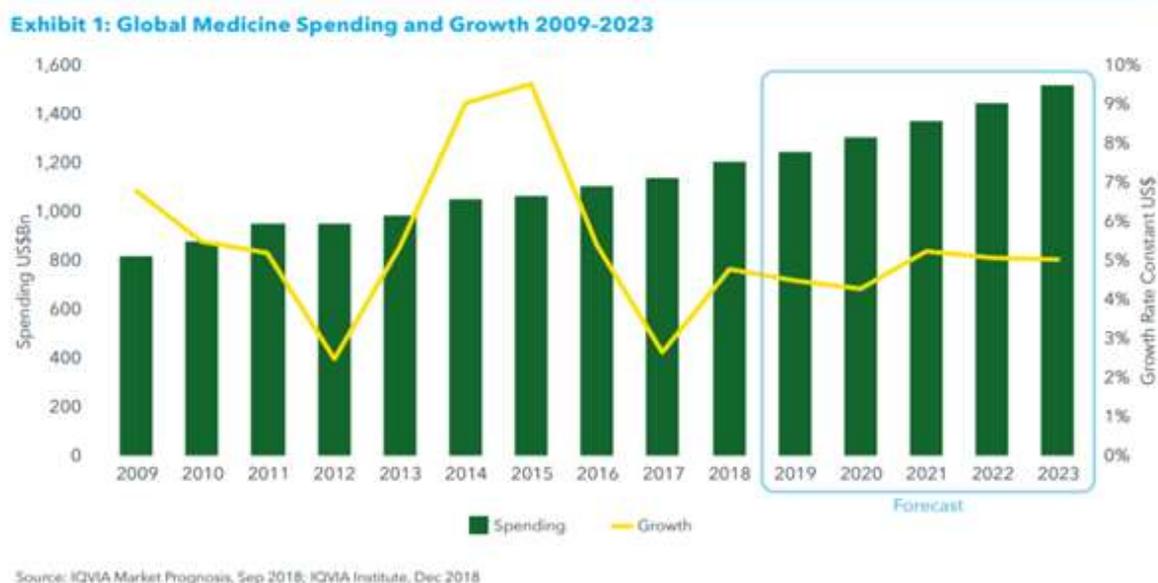
## 2.2 Characteristics of biotechnology industry

The life science industry is one of the most globalized sectors of the economy in the world. 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 and subproviders 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 global basis.

According to IQVIA, the global pharmaceutical market will reach \$ 1.5 trillion in 2023, growing at a rate of 3-6% annually over 2020-2023. 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 4-7% and 5-8%, respectively. IQVIA analysts predict that developed countries will see a slight slowdown in growth to 1-4% compared to 3.8% in the previous five years. For China, the largest emerging market expected to hit \$ 140-170 billion in 2023, growth will also slow to down 3-6%.

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 released on the market over the next five years. On average, 54 new active substances per year are expected to be released to the market in the period 2020-2023. This is an increase comparing to the average of 46 per year over the previous five years.



In addition to the above-mentioned statistical figures, a characteristic feature of the biotechnology market is also the fact that the commercialization of the final product, which is a drug, 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) discovering stage,
- 2) preclinical studies (in vitro and in vivo)
- 3) clinical trials (which include two 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, which was introduced to the market

A characteristic feature of the biotechnology market is that only a small percentage of substances that were analysed 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 research. 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 the fact 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 got cancer in 2020 (in 2012 it was 14.1 million people, so the number of cases increased by 37% compared to 2012). 9.95 millions of 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 on the second place in the ranking of the most common causes of mortality (20% of deaths), and this phenomenon reflects the global trend ("Strategy for Fighting Cancer" <http://www.walkazrakciem.pl/>).

According to estimates by Allied Market Research, the global oncology drugs market was worth USD 97.4 million in 2017 and is expected to reach USD 176.5 million in 2025, growing at a rate of 7.6% (CAGR) over 2018- 2025. Biological drugs based on monoclonal antibodies have emerged as the preferred therapeutic option for many types of cancer, especially for hematological cancers such as leukemia. The increase in cancer incidence, the increase in the popularity of technologically advanced therapies and a significant increase in the elderly population worldwide are the main factors driving the growth of the global cancer drug market. Moreover, increasing awareness and the availability of anti-cancer therapies are factors that can fuel this growth even more.

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 2018, 15 new oncological therapies were approved for 17 indications. More than half of the new therapies are available for oral administration, have the status of a rare disease drug, or for use in the presence of a specific biomarker. Drugs approved for commercial sale in 2014-2018 currently have 89 indications in 23 types of cancer. As many as 31% of the approved indications in the last five years are for hematological cancers such as leukemia, lymphomas and multiple myeloma, while lung cancer is the leader in the category of solid tumors with 12 indications, breast cancer with seven, and melanoma with six indications.

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

The number of clinical trials in the field of oncology which were initiated in 2018, is 27% higher than in the previous year, and at the same time it has increased by as much as 68% over the last five years.

Oncology is also an area where the largest proportion of expenses is spent on clinical trials. In 2024 clinical trials consisted as much as 40% of the development value of the entire oncology portfolio and nearly 20% of the value of drug sales in this area.

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 observed mainly because of the fact that companies are increasingly focusing on narrower therapeutic indications, where the cost of clinical trials is often lower.

Oncology continues to be the main area of research and development for the biopharmaceutical industry. According to EvaluatePharma, this is the area where - as already mentioned - the largest expenses related to the clinical development of drugs are incurred. This is somewhat surprising given the risk of successful drug development in this area; also in oncology, the highest number of FDA-approved drugs of any therapeutic area is predicted.

At an expense of \$ 0.7 billion per approved drug, oncology is one of the most expensive areas for new drug development, but this cost is projected to translate to \$ 78.2 million in Net Present Value (NPV), or \$ 30.6% of the total Net Present Value (NPV) of the current portfolio of cancer drugs under development.

### **Oncology – partnering market**

For the Issuer's innovative projects the most important market is the market of partnering agreements (license agreements) concluded between companies from the biotechnology / pharmaceutical industry. Its growing importance is related to the model of innovation in the pharmaceutical industry that has been present on the market for several years now, where there is an increasingly strong division into academic institutions - conducting basic research, biotechnology companies – conducting early stage of research and development, and pharmaceutical companies – involved in advanced clinical research and global drug commercialization. Almost half of the revenues of large pharmaceutical concerns comes from drugs that have been developed outside their laboratories. This creates an extensive market of projects, purchased by large concerns from biotechnology companies, not only at the stage of clinical trials (which was characteristic in previous years), but also at the pre-clinical stage.

Therefore, smaller biotechnology companies, which, compared to large pharmaceutical concerns, do not carry out several dozens of projects at the same time, but rather focus on a few specialized research, are able to "commercialize" the molecule they have developed at a much earlier stage of research than the commercialization of the drug itself. As a result, such companies obtain capital that they can further use in new research areas. A typical partnering agreement consists of three types of payments: the so-called upfront payment (payable upon signing the contract or shortly after), milestones payments (payments for achieving individual stages in the process of research and registration of a drug) and royalties (usually as a percentage of the selling price of a drug on a given market after it is launched for sale and starts to earn revenues). Thanks to this, through the implementation of individual stages, a smaller biotechnology company can count on a constant inflow of capital and reduction of financial risk in the event of a project failure.

The investments which the industry is making in oncology far exceed those in other therapeutic areas, and partnering is at the heart of the strategy for these investments. In the last four years alone, the cumulative value of contracts in oncology has reached \$ 331 billion, according to Clarivate Analytics.

The area of oncological diseases is responsible for as much as 42% of the partnering activity of companies in 2018, according to Clarivate Analytics. The value of all partnering agreements concluded in 2018 reached the level of over USD 111 billion, and in Q4 2018 alone, 12 agreements referred to as "mega deals" were concluded, with a minimum value of at least USD 1 billion.

Oncology remains an extremely attractive area of research, development and partnering. Partnering activity for projects in the early stages of development is more and more noticeable. This may be due to the fact that there is a lack of interesting projects at more advanced stages, perhaps companies are more likely to risk more and invest earlier, counting on breakthrough therapies and exclusive access to them, and perhaps also because they believe that the investment at an early stage is less risky. Regardless of the motives, in the oncology itself in Q4 2018 - Q1 2020, most contracts were concluded for molecules at the stage of early development and pre-clinical development. Contracts for molecules at this stage totalled \$ 600 million for early development (30 contracts), and \$ 550 million for pre-clinical (27 contracts) (Clarivate Analytics).

Immunooncology is a very significant area of oncology, both in terms of investment in research and development and molecule partnering. It definitely dominates in terms of partnering contracts concluded in the area of oncology.

Immunooncology is also an area where Ryvu is active, developing its early-stage project. In 2018 it reached its all-time high, with approximately 140 IO license agreements totaling over \$ 1 billion.

It is estimated that by 2024 the total immuno-oncology market will be worth around US \$ 34 billion (this is a significant increase in the value comparing to current state, especially taking into account that few years ago it was estimated that in 2019 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 has been accomplished in July, 2020. The base of suppliers providing services for the Issuer is relatively well diversified. Due to 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 31/12/2020
	PLN
Supplier A	28,424,990
Supplier B	3,595,432
Supplier C	3,576,368
Supplier D	2,726,064
Supplier E	2,292,646
Supplier F	1,946,694
Supplier G	1,898,685
Supplier H	1,854,506
Supplier I	1,694,172

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 2020 financial year.

## 2.5 Employment data

At the end of 2020 Ryvu Therapeutics S.A. was employing 161 people.

	As of 31.12.2020	As of 31.12.2019
Ryvu Therapeutics S.A.	161	173

## 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' lives.

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 – a place where patients get professional psychological help to support them getting through the oncology diagnosis and treatment.

Ryvu Therapeutics took also 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 the awareness about 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 "PRO CHEMIA"

Foundation at the Faculty of Chemistry at Jagiellonian University. The foundation aims to support the Faculty to renew its material base, mostly state-of-the-art laboratory equipment for research and development.

Charitable trust in Ryvu Therapeutics in 2020 amounted to over 31 thousand PLN.

## **2.7 Use by the Issuer of capital raised through the issuance of shares**

In 2020, the Company carried out the issuance of „Series I“ shares. As a result of the above-mentioned issuance, the Company raised over PLN 134 million net (the issuance price of „Series I“ shares was set at PLN 60 per share, therefore the total capital gain from the issuance reached the sum of PLN 143,054,700, and the final costs of carried offer were established at PLN 8,212,623, reduced by PLN 51,052 compared to the information provided in the current report No. 28/2020 of August 5, 2020).

## **2.8 Significant events in 2020**

### **A) During the reporting period**

#### **Successful completion of the 1st phase of the clinical trial with the use of SEL24/MEN1703**

On 5 March 2020 the Issuer was informed by the company Berlin-Chemie, a member of the Menarini Group (“Menarini”), which is the sole sponsor of the SEL24/MEN1703 clinical trial under the global license agreement signed by the companies on 28 March 2017, about the successful completion of the 1st phase of the first-in-human clinical trial using SEL24/MEN1703 – a dual PIM/FLT3 kinase inhibitor administered orally in patients with acute myeloid leukemia. The purpose of the 1st phase clinical trial (dose escalation stage) was to determine the recommended dose to be used in the 2nd phase. In accordance with the information obtained, Menarini plans to continue the trial in the 2nd phase – cohort expansion, using the recommended dose. In accordance with the Agreement, which was mentioned by the Issuer in the current report 4/2017 dated 27 March 2017, the completion of the 1st phase constitutes the milestone for which a payment of EUR 1,750,000 is due to the Issuer.

#### **The RVU120 program has a chance of being recognized by the FDA as an orphan drug**

On 27 March 2020, the Issuer was informed by the US regulator – the Food and Drug Administration (“FDA”) about the possibility of RVU120 receiving the status of orphan drug designation (“ODD”) as an independently developed, first in its class, small-molecule CDK8 inhibitor with a potential in the treatment of acute myeloid leukemia.

If the RVU120 program obtains ODD status, it will have access to FDA scientific advice during further stages of the clinical trial process and the subsequent stages may be significantly shorter. It is also associated with potential tax reliefs at the level of 25% with respect to the costs of clinical trials, as well as a simplified drug evaluation and registration procedure. If RVU120 is marketed in the USA, the orphan drug status will make it possible to extend the exclusive right to sell the drug in the US territory to 7 years. Not all of the benefits mentioned above will directly affect the Issuer’s operations, however, they may increase the project’s value from the perspective of potential partners, if the project is commercialized.

### **Signing a research and development cooperation agreement with Galapagos NV**

On 15 April 2020, the Company signed a research and development cooperation agreement with Galapagos NV, a company with its registered office in Mechelen, Belgium. The companies will cooperate in the area of discovery and development of innovative small molecule compounds with a potential therapeutic effect in inflammatory diseases. The cooperation will be developed based on a new protein objective identified by the Company and the Company's research platform.

As part of this cooperation, the Issuer will be responsible for the discovery phase, and Galapagos NV will be responsible for further development of the compound. In accordance with the agreement, Galapagos NV has the exclusive right to obtain the exclusive global license for all intellectual property rights generated under the agreement and those generated by the Issuer in the course of its research on the protein objective conducted to date.

In accordance with the agreement, the Company has received an upfront payment of EUR 1,500,000.00 and will be entitled to receive a total of EUR 53,500,000.00 in the case of successful development and commercialization of the potential drug created on the basis of the results of this cooperation. The above-mentioned amount is the maximum amount receivable (bio-dollar value), and the actual revenue generated by the Company under the agreement will depend on the progress of scientific research and clinical trials, success of the registration process and the level of sales of the potential drug generated by Galapagos NV. The Company will also receive one-digit royalties from the sales of products developed as a result of the cooperation.

### **Completion of the construction of the Issuer's Research and Development Centre**

On 2 June 2020, the Issuer was informed that the District Construction Supervision Inspector issued a certificate of no objection concerning the commencement of use of the Research and Development Centre for Innovative Drugs ("RDC"). Thus, the Company completed the construction of the RDC, which was a significant element of the Issuer's strategy for the years 2017–2021. The new facility will ultimately allow the integration of all scientific and research projects of the Issuer, helping to improve the opportunities for the exploration of new drug candidates and maximize the efficiency of research and development work.

### **Increase in the share capital of NodThera Ltd.**

On 3 June 2020, the Company reported that it had been informed that NodThera Ltd., a company in which the Issuer currently holds 6.07% of the shares, obtained financing in connection with the issue of new B series shares with a total value of GBP 44.5 million (PLN 219.8 million), which will be taken up by biotechnological investors, including the following new investors: Novo Holdings A/S (the investment branch of the pharmaceutical company Novo Nordisk), Cowen Healthcare Investments and Sanofi Ventures (a fund which is a part of the pharmaceutical Sanofi Group), as well as the existing shareholders: 5AM Ventures, F-Prime Capital Partners, Sofinnova Partners and Epidarex Capital.

The financing will be granted in two tranches. The amount of GBP 20,249,965.22 was contributed to the company in connection with the acquisition of 6,817,711 new B series preference shares, as part of the first tranche of the financing, in accordance with the NodThera share capital increase registered on 2 June 2020. B series shares were acquired at the issue price of GBP 2.9702 per share. In accordance

with the investment agreement signed by NodThera, the shareholders and external investors, after certain milestones in the development of the company's research projects are reached, the share capital of NodThera will be increased by an additional amount of GBP 24,299,835 by issuing the second tranche of 7,790,656 B Series shares at the issue price of GBP 3.1191 per share. In accordance with the investment agreement, the above-mentioned share capital increase will take place not later than on 30 June 2021. After the share capital increases resulting from both tranches, the Issuer's interest in the share capital of NodThera will amount to 4.8%.

### **Extraordinary General Shareholders' Meeting of the Issuer**

The Extraordinary General Shareholders' Meeting of the Issuer held on 4 June 2020 passed, among others, a resolution on commencing the preparation of the Issuer's financial statements in accordance with the International Accounting Standards from 1 January 2020.

### **Conclusion of an agreement for co-financing of the Issuer's project by the National Centre for Research and Development ("NCBiR")**

On 17 April 2020, the Issuer was informed that its project entitled "New small-molecule immunomodulatory drugs in the treatment of resistant cancers" was placed on the list of projects selected for co-financing under the Smart Growth Operational Program 2014-2020 measure 1.1/sub-measure 1.1.1 "Fast Track". The agreement for co-financing was signed with the NCBiR on 4 June 2020. The project objective is to implement the drug candidate characterized in the 1st clinical phase – a small molecule modulator of the patient's immunological response to cancer cells – in the Issuer's operations. The key assumption is to develop a strictly personalized treatment with a potential to overcome the limitations of the present immunotherapies, giving a chance for effective and safe treatment of patients with aggressive and resistant forms of cancer. The total net value of the project is PLN 35,849,341.25 and the recommended financing is PLN 22,396,399. The project would be executed in the period from January 2020 to December 2023.

### **Participation in EHA conference**

The Issuer participated in the European Hematology Association (EHA) Congress, which took place on 11–14 June. The Issuer presented posters with details of the 1st/2nd phase of the RVU120 clinical trial of the CDK8 selective inhibitor, which is currently under way (the poster entitled "A First-in-human study of SEL120, a novel oral selective CDK8/19 inhibitor, in patients with acute myeloid leukemia and high-risk myelodysplastic syndrome", abstract EP636) and the SEL24/MEN1703 dual PIM/FLT3 inhibitor (the poster entitled "Results of the dose escalation part of DIAMOND trial (CL124-001): First-in-human study of SEL24/MEN1703, a dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia").

### **Participation in AACR conference**

At the AACR Annual Meeting, which took place on 22–24 June 2020, the Issuer presented the latest results of oncological projects in the following areas: i) immune-oncology and cancer immunometabolism, including small molecule direct STING antagonists, a dual A2A/A2B antagonist

and small molecule HPK1 inhibitors; ii) synthetic lethality – SMARCA2 (BRM) protein degraders, in cancer cells with SMARCA4 mutations.

### **Secondary Public Offering (“SPO”) - Issue of Series I Shares**

In Q32020, the Company carried out an capital increase issuing series I ordinary bearer shares, excluding the subscription right of the existing shareholders. As a result the share capital of the Company was increased from PLN 6,388,491.60 to PLN 7,342,189.60. On August 18, 2020, the increase of the Company's share capital was registered by the District Court for Kraków-Śródmieście in Kraków, 11th Commercial Division of the National Court Register.

The Shares have been taken up in a private subscription within the meaning of art. 431 § 2 point 1 of the Commercial Companies Code, conducted as a public offering within the meaning of art. 2.d of the Prospectus Regulation carried out in Poland, exempted from the obligation to submit the prospectus or other information (offer) document ("Public Offering") and addressed only to the investors eligible for participation in the Public Offering:

- 1) qualified investors within the meaning of Art. 2 lit. e) the Prospectus Regulation, and
- 2) investors who took up Series I Shares with a total value of at least the equivalent of EUR 100,000 (one hundred thousand euro) per investor for each separate offer,

and therefore the Public Offer did not require the preparation and publication of an issue prospectus, pursuant to Art. 1 clause 4 lit. a) and d) in connection with art. 1 clause 6 of the Prospectus Regulation.

The issue price of the Series I Shares was set at PLN 60 per share, therefore the total proceeds from the issue, understood as the product of the number of shares covered by the offering and the issue price, amounted to USD 36,858,369 (PLN 143,054,700) and the total costs of the offering were USD 2,116,000 (PLN 8,212,623). Series I shares were acquired by 97 investors.

The funds obtained from the issue will allow the implementation of the Strategy for 2020-2022 adopted by the Issuer. According to the Strategy the Company plans to:

- Complete Phase I clinical development of our lead fully-owned asset, RVU120 in AML/MDS; Expand therapeutic potential for RVU120 in solid tumors and launch a new Phase I study in selected indications in parallel to the ongoing hemato-oncology studies; Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in AML;
- Complete preclinical programs for STING candidate and advance the program into the Phase I of clinical trials;
- Strengthen position in novel target discovery and in developing novel, proprietary drug candidates;
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources.

### **Annual General Shareholders Meeting**

During the Annual General Shareholders Meeting (“GSM”) that was held on August, 31 2020 the GSM:

- Approved the Financial Statement and the Management report for 2019 and approved the coverage of the loss generated in 2019 from the proceeds of the upcoming years;

- Granted votes of approval (Polish “absolutorium”) for all the members of the Management and Supervisory Boards;
- Re-appointed Supervisory Board Members (in a current composition) for the next, joint five-years term of office;
- Adopted the Remuneration Policy for the Members of the Management and Supervisory Boards of the Company (available on the Company’s website: <https://ryvu.com/investors-media/corporate-information/>);
- Confirmed the revised bylaws of the Supervisory Board adopted this year by the Supervisory Board (amendments allowing formation of the Remuneration Committee and alignment to the recent novelization of the Commercial Code regarding voting by Supervisory Board via remote means).

### **Appointment of Members of the Company's Management and Supervisory Boards for a new term of office**

In connection with the elapse of the term of the current Management and Supervisory Boards on August, 31 2020, the GSM of the Company reappointed the Company's Supervisory Board for the next, five-year term of office in the current composition, i.e. **the Supervisory Board of the Company** is composed of:

- 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

The Supervisory Board of the Company has reappointed the Company's Management Board for the next, five-year term in the current composition, i.e. **the Management Board of the Company** is composed of:

- 1) Paweł Przewięźlikowski – President of the Management Board
- 2) Krzysztof Brzózka – Vice President of the Management Board
- 3) Setareh Shamsili – Vice President of the Management Board

With respect to the abovementioned subject, the Supervisory Board also appointed 2020 Members of the Audit Committee and the Remuneration Committee for the next term of office in the current composition.

#### **The Company’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

**First patient dosed in Europe within the Expansion Cohort of Phase I/II Clinical Study of SEL24/MEN1703**

On 15th of September 2020 the Company has received a notice from Menarini Ricerche SpA, which belongs to Menarini Group (“Menarini”), who is the sole sponsor of SEL24/MEN1703 clinical trial (accordingly to the license agreement concluded between Menarini and the Issuer, about which the Issuer has informed in a current report no. 4/2017), that the first patient has been treated in Europe with SEL24/MEN1703 within the Phase II DIAMOND-01 clinical trial in Acute Myeloid Leukemia (AML).

In accordance with information received from Menarini, the patient has been dosed into the expansion cohort after the completion of the dose escalation part of the trial, which results have been recently presented by Menarini at the 25th Annual Meeting of the European Hematology Association (EHA), about which the Issuer has informed in a current report no. 11/2020.

DIAMOND-01 (CLI24-001; NCT03008187) is a First-In-Human, Phase I/II dose escalation and cohort expansion trial in AML – relapsed or refractory as well previously untreated - patients unsuitable for chemotherapy. The aim of this phase is to further evaluate the single agent activity and the safety profile of SEL24/MEN1703 at the recommended dose, as determined in the dose escalation part of the study.

In accordance with information received from Menarini the expansion cohort, will be run in major oncology centers both in the US and in Europe including clinical sites in Italy, Spain and Poland. As at the date of the report, 14 clinical centers (9 in the USA and 5 in Europe) were involved into the study.

**Change of the registered office address of the Company**

In connection with the completion of the construction of the R&D Center the Company has changed its registered address to: L. Sternbacha 2 Street, 30-394 Cracow. The statutory books of the Company have been updated with the new address at the Companies House on October 12, 2020.

**Ryvu Therapeutics abstract concerning the STING program at the SITC 2020**

The abstract regarding its STING agonists program titled *Development of improved small molecule STING agonists suitable for systemic administration* has been presented by the Company at the Society

for Immunotherapy of Cancer 35th Anniversary Annual Meeting (SITC 2020) which took place on November 9-14, 2020.

SITC 2020 provides a multidisciplinary educational and interactive environment focused on improving cancer patient outcomes by incorporating strategies based on basic and applied cancer immunotherapy.

### **The revision of the preclinical projects' pipeline of the Company**

On October 20, 2020, the Company made a decision to revise the preclinical projects' pipeline of the Company. As a consequence, the Company shall stop the development of two projects: a dual adenosine receptor antagonist (A2A/A2B) and the project in the area of synthetic lethality (SMARCA2). The above decision was made after consultation with the Supervisory Board of the Company.

When making this decision, the Management Board was guided by the analysis of the scientific results obtained during the research and development activities carried out so far, as well as the development prospects of projects in further stages. An analysis of the current and expected competitive environment, including the results of research published by competitors developing compounds targeting the above-mentioned protein targets, was also carried out.

### **Appointment of the new Management Board Member of Ryvu Therapeutics S.A.**

On November 23, 2020 Issuer's Supervisory Board adopted a resolution in which it appointed Mr. Kamil Sitarz, Ph.D., MBA for the position of a Management Board Member. At the same time Kamil Sitarz, was promoted to the Chief Operating Officer position. He will hold an executive responsibility for design, implementation, and co-ordination of day-to-day business operations, as well as financial and performance management at the Company. Moreover, he will be in charge of establishing and implementing corporate policies, procedures and processes, as well as management of administrative and operational functions at the Company.

### **Publication of three posters on SEL24/MEN1703 including Pharmacodynamic Data from the Dose Escalation Part of DIAMOND-01 Trial at American Society of Hematology (ASH) Annual Meeting**

In reporting period Issuer obtained positive results of the pharmacodynamic assay demonstrating target engagement in the dose escalation part of the DIAMOND-01 trial (CLI24-001; clinicaltrials.gov identifier NCT03008187), a study investigating SEL24/MEN1703, a first-in-class, orally available, dual PIM/FLT3 inhibitor as single agent in acute myeloid leukemia (AML), published by the Menarini Group - a global partner and sponsor of clinical trial of SEL24/MEN1703, on the basis of an exclusive license agreement concluded with the Company.

The poster entitled "*SEL24/MEN1703 provides PIM/FLT3 Downstream Pathway Inhibition in Acute Myeloid Leukemia (AML) Blast Cells: Results of the Pharmacodynamic (PD) Assay in the Dose Escalation Part of First-in-Human DIAMOND Trial*" was presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, which took place virtually on December 5-8.

Two additional posters regarding the potential therapeutic effect of PIM kinases inhibition – in both cases carried out using SEL24/MEN1703 – in other hematological cancers, namely diffuse large B-cell

lymphoma and multiple myeloma, were also published at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition:

- *"Inhibition of PIM Kinases in Diffuse Large B-Cell Lymphoma Cells Targets MYC-Dependent Transcriptional Program, Increases CD20 Expression and Augments the Efficacy of Anti-CD20 Antibodies"*;

- *"PIM Kinase Inhibition Decreases the Proangiogenic Properties of Multiple Myeloma Cells and Affects the Metabolic State of the Vascular Endothelium"*.

#### **B) Events occurred between the end of reporting period until the approval of financial statement**

##### **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) has been 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 also in 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 (SEL120) 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 (SEL120) in patients with relapsed / refractory metastatic or advanced solid tumors.

Covance Inc., is a leading global drug development service company 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 1000 clinical studies in Oncology, with Phase I studies being the most often executed ones.

Covance will be responsible for operational execution of 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 Programme 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 to present recent data from multiple oncology programs at AACR 2021 Virtual Annual Meeting**

On March, 11 2021 Issuer announced that during the American Association of Cancer Research (AACR) Virtual Annual Meeting 2021, April 10-15 and May 17-21 Company will present 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

## **2.9 Unusual events occurring in the reporting period**

### **COVID-19**

Covid-19 pandemic began in the first quarter of 2020 and continued (and still continues) during the whole reported period. Because of that the Issuer implemented the recommendations given by the Chief Sanitary Inspectorate and other government institutions in connection with the epidemiological threat, including the 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 ongoing basis and mitigate any adverse effects of the spread of the epidemic on the Issuer. The Company also developed its internal policy for preventing the spread of the coronavirus and taking actions aimed at ensuring appropriate health and safety conditions at work, in particular Company's employees are routinely tested by a third party provided using antigen tests to detect asymptomatic infections. Internal policies are constantly updated and adapted to the latest guidelines and changing conditions.

During reported period, the pandemic affected the progress of the Issuer's fully owned clinical trial , the CLI120-001 study, due to the fact that generally and globally, the First In Human (FIH) dose escalation cancer clinical trials, got impacted. This negative impact however, seems to have been stronger in the investigational sites located in the United States. Due to the onset of Covid19 pandemic all RVU120 clinical sites have introduced additional safety measures and risk management processes which have strongly impacted the possibilities for patients to participate in clinical studies. This applies also to relapsed, refractory AML patients who are frequently immunocompromised and very ill. Also, many patients themselves decided to limit their contacts with various healthcare facilities to minimize the possibility of Covid-19 exposure. In effect enrolment at some sites has been temporarily suspended for over 4 months, and in other sites we observed a visible slowed-down. The current COVID-19 induced delay in the planned study enrolment is approximately 6 months. As a consequence, Ryvu has decided to move the anticipated timelines for the first results of the study from Dec 2020 to H1 2021. An additional new pandemic induced risk to cancer clinical trial enrolments is the start-up of COVID-19 vaccination campaign, which might affect eligibility of the candidate patient for such trials, close to vaccination.

Due to the continuing pandemic, the Issuer is not able to predict further delays in the ongoing clinical trials as at the date of publication of this report, but has taken steps to minimize the risk of their negative impact on the Company's operations. In the original plan of the study Ryvu intended to open the enrolment in the dose escalation part at three additional sites in the US (nine sites in total). Because of the pandemic situation in the US, Ryvu management has decided to start the European arm of the study earlier than originally was planned, to open additional sites in Poland and other European countries. The first in Europe Clinical Trial Application (CTA) was submitted on August 11, 2020. At the beginning of January 2021 Ryvu Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, and the respective Central Ethics Committee approved Ryvu's CTA to commence RVU120 clinical trial in AML and HRMDS, in selected clinical centers in Poland.

The Issuer's research and development laboratories worked in Q2-Q4 2020 with decreased capacity. The decrease in their capacity was associated with employee absenteeism due to quarantine, the fact that some foreigners could not enter Poland and the fact that some employees had to stay home with their children, as well as due to the relocation of employees to the new R&D Center. 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 project. 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 ongoing basis and implements new solutions to limit it 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 Covid-19. Additionally, in connection with the launch of the national vaccination

program against COVID-19, Ryvu is monitoring the possibility and possible planned term of covering Ryvu's employees with 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.

## **2.10 Planned development of the Issuer, including information about adopted development strategy**

### **Issuer's development strategy and new initiatives**

The Issuer's strategy for 2020 and for the next two years was (is) following:

- Complete Phase I clinical development of our lead fully-owned asset, RVU120 in AML/MDS;
- Expand therapeutic potential for RVU120 in solid tumors;
- Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in AML;
- Complete preclinical program for STING candidate and advance this program into the Phase I of clinical trials;
- Strengthen Company's position in novel target discovery for synthetic lethality and immunology and in developing novel, proprietary drug candidates;
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources.

For the execution of the Strategy by the end of 2021, Company intends to execute investments worth up to \$57.7m, including \$8.5m expenditure for advancement of RVU120 in AML/MDS, including completion of Phase 1 of Clinical Study, \$8.7m for development of RVU120 in solid tumors, including launch of a new Phase I study, \$8.2m for pre-clinical development, including conduct of IND-enabling preclinical studies and completion of IND submissions for A2A/A2B antagonist and STING agonist I/O programs, \$19.1m for advancement of early discovery synthetic lethality and I/O programs, \$4.2m for equipping of Ryvu R&D Centre and replacement Capex and \$9.0m to finance G&A costs.

## 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 works, the invention does 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 possibility to obtain 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 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 for sure it is clearly visible at the international level and in the case of employees with the highest qualifications.

Moreover the competitiveness on , the Issuer's labour market may pose a risk that in order to maintain attractive working conditions for its employees, it will be forced to increase labour 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.

### **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, ie SEL124 and RVU120 / RVU120, 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 centres, 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 any, 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 2.9 „Unusual events occurring in the reporting period”.

## 4 STATEMENT REGARDING IMPLEMENTATION OF CORPORATE GOVERNANCE PRINCIPLES

### 4.1 Principles of corporate governance applying to the Issuer

The Issuer's Management Board hereby informs that in 2020 the Company complied with all the rules and recommendations of corporate governance contained in the document: "Best Practices for Publicly Listed Companies (listed on GPW – Warsaw Stock Exchange) 2016", including the exceptions described and appropriately justified below:

**I.Z.1.10. The company runs a corporate website and publishes there, in a legible form and in a separate place, in addition to the information required by law, financial forecasts - if the company has decided to publish them - published in the period of at least the last 5 years, along with information on the degree of their implementation.**

Explanation of the Issuer:

The company does not publish forecasts of financial results.

**I.Z.1.16. The company runs a corporate website and publishes there, in a legible form and in a separate place, in addition to information required by law, information on the scheduled broadcast of the general meeting - no later than 7 days before the date of the general meeting.**

Explanation of the Issuer:

The Issuer does not broadcast the General Meeting, at the same time, if the Issuer will decide to broadcast it, the Issuer will publish relevant information in this regard on the website.

**I.Z.1.20. The company runs a corporate website and publishes there, in a legible form and in a separate place, in addition to the information required by law, a recording of the general meeting, in the form of audio or video.**

Explanations of the Issuer:

Currently, the Issuer does not record the course of the General Meeting in audio or video form due to the lack of interest in such a solution on the side of the shareholders. If the Issuer's shareholders express their expectation in the future for the Issuer to register and provide audio / video recordings of the General Meeting, the Issuer will implement audio / video recording of the General Meeting.

**I.Z.2. A company whose shares are included in the WIG20 or mWIG40 stock exchange indexes shall also ensure that its website is available in English, at least to the extent indicated in rule I.Z.1. This rule should also be applied by companies outside the above indices if it is justified by the structure of their shareholding or the nature and scope of their business.**

Explanation of the Issuer:

The Issuer's shares are not included in the WIG20 or mWIG40 stock indexes. The Issuer's shareholding structure as well as the nature and scope of the activities conducted do not support the application of

this principle. At the same time, the Issuer will endeavour to make the website in English available to the fullest extent possible.

**IV.R.2. If it is justified by the shareholding structure or the expectations of shareholders, which were notified by them to the company, provided that the company is able to provide the technical infrastructure necessary for the efficient conduct of the general meeting by means of electronic communication, it should enable shareholders to participate in the general meeting using such means, in particular through:**

- 1) real-time transmission of the general meeting,**
- 2) real-time two-way communication, under which shareholders may take the floor during the general meeting from a location other than the place of the general meeting,**
- 3) exercising, in person or through a proxy, voting rights during the general meeting.**

Explanation of the Issuer:

The Issuer's shareholding structure does not justify broadcasting of the general meeting and real-time two-way communication, or exercising voting rights using electronic means of communication.

**IV.R.3. The company strives to ensure that when securities issued by the company are traded in different countries (or on different markets) and under different legal systems, the carrying out of corporate events related to the obtainance of rights on the part of the shareholder takes place at the same dates in all countries in which they are listed.**

Explanation of the Issuer:

Securities issued by the Issuer are traded only in Poland.

**IV.Z.2. If it is justified by the shareholding structure of the company, the company provides publicly available real-time broadcast of the general meeting.**

Explanation of the Issuer:

The Issuer's shareholding structure does not justify real-time broadcasting of the General Meeting.

## **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 Audyt Polska sp.z o.o.sp.k.). 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) Setareh Shamsili – Vice President of the Management Board
- 4) Kamil Sitarz – Member of the Management Board (since 23rd November 2020)

In 2020 the following changes have taken place in composition of the Management Board:

- on 23rd November 2020 Kamil Sitarz was appointed as a Member of Management Board

#### **Issuer's Supervisory Board :**

- 1) Piotr Romanowski – Chairman of the Supervisory Board
- 2) Tadeusz Wesółowski – 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 Wesółowski – 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. Rafat Chwast.
3. All Audit Committee's Members are the 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 Audyt Polska spółka z ograniczoną odpowiedzialnością spółka komandytowa, 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.

Shareholder	Series A*	Series B	Series C,D,E,F,G1,G2	No. of shares	% of share capital	No. of votes	% votes at GM
<b>Management Board</b>							
<b>Paweł Przewięźlikowski</b>	3 500 000	1 183 250	307 630	<b>4 990 880</b>	27.19%	<b>8 490 880</b>	37.9%
<b>Krzysztof Brzózka</b>			250 076	<b>250 076</b>	1.36%	<b>250 076</b>	1.12%
<b>Supervisory Board</b>							
<b>Tadeusz Wesołowski (directly)</b>			92 975	<b>92 975</b>	0.51%	<b>92 975</b>	0.41%
<b>Tadeusz Wesołowski (indirectly through Augebit FIZ)</b>			1 039 738	<b>1 039 738</b>	5.66%	<b>1 039 738</b>	4.64%
<b>Piotr Romanowski</b>			420 000	<b>420 000</b>	2.29%	<b>420 000</b>	1.87%
<b>Rafał Chwast</b>			121 115	<b>121 115</b>	0.66%	<b>121 115</b>	0.54%
<b>Thomas Turalski</b>			20 100	<b>20 100</b>	0.11%	<b>20 100</b>	0.09%

\* Series A Shares are privileged - one share gives the right to two votes at the General Meeting.

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.

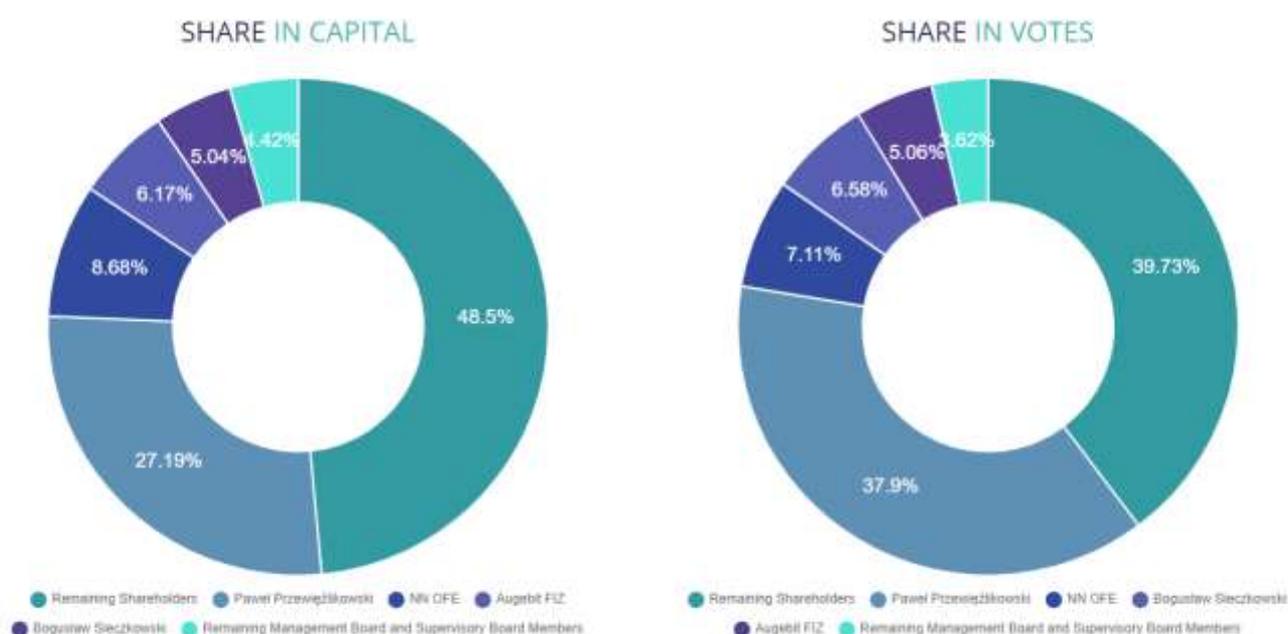
## Shares held by significant shareholders of the Company

Shares held by significant shareholders of the Company as of 31.12.2020 and as of Annual Report publication date

Shareholder	Shares	% [Shares]	Votes	% [Votes]
Paweł Przewięźlikowski	4 990 880	27.19%	8 490 880	37.9%
Bogusław Siczkowski	924 384	5.04%	1 474 384	6.58%
Nationale Nederlanden OFE	1 594 749	8.68%	1 594 749	7.11%

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

## Shareholders structure as at the date of submitting this Management Report



### **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.

### **Remuneration Committee**

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

1. The Supervisory Board appoints and dismissed members of the Remuneration Committee, including its Chairman.
2. Members of the Remuneration Committee, including its Chairman, are appointed among the Supervisory Board Members.
3. The Remuneration Committee consists of at least three Members.
4. In particular, the competencies of the Supervisory Board comprise:
  - 1) Regarding the remuneration of members of the Company's Management Board:
    - a) assessing the basic salary, bonuses and share-based compensation received by members of the Company's Management Board in relation to the scope of duties of

- members of the Company's Management Board and the manner of their performance, as well as market conditions,
- b) presenting proposals to the Supervisory Board regarding appropriate forms of contracts with members of the Company's Management Board and the amount of their remuneration,
- 2) Regarding directors and senior employees' remuneration:
    - a) making a general assessment of the correctness of the Company's policy regarding remuneration of the directors and senior employees,
    - b) issuing general recommendations to the Company's Management Board regarding the level and of remuneration for directors and senior employees,
    - c) monitoring the level and structure of remuneration for directors and senior employees based on relevant information provided by the Company's Management Board,
  - 3) Regarding share-based compensation that can be granted to members of the Management Board and employees of the Company:
    - a) discussing the general principles for implementing equity incentive programs based on shares, share options, subscription warrants,
    - b) presenting proposals to the Supervisory Board in this respect,
    - c) presenting proposals to the Supervisory Board regarding equity incentive programs.
  5. The principles of the Supervisory Board's operation, in particular holding of meetings and the adoption of resolutions by the Supervisory Board shall apply accordingly to the Remuneration Committee, unless the Remuneration Committee decides otherwise.

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

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

#### **Remuneration of the members of management and supervisory bodies**

##### **Remuneration of the members of the Management Board of Ryvu Therapeutics S.A. for period 1.01.2020-31.12.2020 [in PLN]\***

Members of the Management Board	Remuneration for performing functions in the Management Board	Remuneration for employment contracts concluded with the Issuer	Remuneration for other contracts	Total remuneration in 2020
Paweł Przewięźlikowski	407 838.00	174 249.85	-	<b>582 087.85</b>
Krzysztof Brzózka	510 474.00	270 199.01	-	<b>780 673.01</b>
Setareh Shamsili	-	1 559 080.93	-	<b>1 559 080.93</b>
Kamil Sitarz <sup>1</sup>	17 378.67	32 654.84	-	<b>50 033.51</b>

<sup>1</sup> \* Mr. Kamil Sitarz was performing function of Member of the Management Board since 23<sup>rd</sup> of November 2020

**Remuneration of the members of the Supervisory Board of Ryvu Therapeutics S.A. for period 1.01.2020-31.12.2020 [in PLN]**

Members of the Board	Remuneration for performing functions in the Supervisory Board
Piotr Romanowski	142 847.04
Tadeusz Wesołowski	140 744.72
Rafał Chwast	142 847.04
Alex Glasmacher	140 744.72
Colin Goddard	140 744.72
Jarl Jungnelius	141 403.00
Thomas Turalski	176 334.41

**Transactions concluded by the Issuer with affiliated entities in 2020**

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	20 840.99

**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 of the Company consists of one woman and three men, while the 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 2020 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 INFORMATION

### 7.1 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 6.07% of shares in NodThera Ltd. with its registered office in Great Britain.

### 7.2 Credits and Loans

No credits and/or loans has been raised.

### 7.3 Structure of major capital deposits and investments

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

### 7.4 Court Proceedings

There was no material litigation, proceedings or disputes relating to the Company in 2020.

### 7.5 Assurances and guarantees

Event did not occur in 2020.

### 7.6 Purchase of own shares

Event did not occur in 2020.

### 7.7 Information about owned branches (plants)

Company does not own any branches.

### 7.8 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 2020 - 31 December 2020 is hereby approved.

Kraków, March 12, 2020

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Paweł Przewięźlikowski  
President of the Management  
Board

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Setareh Shamsili  
Vice - President of the Management  
Board

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Krzysztof Brzózka  
Vice - President of the Management  
Board

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Kamil Sitarz  
Member of the Management  
Board

# CONTACT



## **RYVU THERAPEUTICS**

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## **GENERAL INQUIRIES**

[ryvu@ryvu.com](mailto:ryvu@ryvu.com)