Q3 2021 REPORT

Ryvu Therapeutics S.A.

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1. SELECTED FINANCIAL DATA FOR Q3 YTD 2021 AND MANAGEMENT BOARD COMMENTS TO THE FINACIAL RESULTS

1.1. Results for the reporting period

Financial Results Obtained in the Reporting Period

Financial Statements of Ryvu Therapeutics S.A. (“”Company”, “Issuer”, “Ryvu”) prepared for the period from January 1, 2021 to September 30, 2021 are prepared in accordance with the International Financial Reporting Standards.

Selected balance sheet data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand		Data in EUR thousand	
Item	**30.09.2021**	31.12.2020	**30.09.2021**	31.12.2020
Total assets	**233,896**	295,640	**50,486**	64,063
Short-term receivables	**9,518**	7,948	**2,054**	1,722
Cash and cash equivalents	**81,019**	136,218	**17,488**	29,518
Other financial assets	**9,990**	24,969	**2,156**	5,411
Total liabilities	**55,568**	71,920	**11,994**	15,585
Long-term liabilities	**31,874**	38,106	**6,880**	8,257
Short-term liabilities	**23,694**	33,813	**5,114**	7,327
Total equity	**178,328**	223,721	**38,492**	48,479
Share capital	**7,342**	7,342	**1,585**	1,591

Selected income statement data are as follows:

Ryvu Therapeutics S.A.	Data in PLN thousand				Data in EUR thousand			
Item	**From 01.01.2021 to 30.09.2021**	From 01.01.2020 to 30.09.2020	**From 01.07.2021 to 30.09.2021**	From 01.07.2020 to 30.09.2020	**From 01.01.2021 to 30.09.2021**	From 01.01.2020 to 30.09.2020	**From 01.07.2021 to 30.09.2021**	From 01.07.2020 to 30.09.2020
Revenues from sales	**1,031**	850	**290**	450	**226**	191	**63**	101
Revenues from subsidies	**18,193**	14,502	**6,872**	4,897	**3,991**	3,265	**1,500**	1,102
Revenues from R&D projects	**-**	14,315	**-**	-	**-**	3,223	**-**	-
Other operating revenues	**405**	313	**245**	161	**89**	70	**53**	36
Revenues from operating activities	**19,629**	29,980	**7,407**	5,508	**4,306**	6,749	**1,617**	1,240
Operating expenses	**-81,241**	-54,174	**-30,896**	-17,865	**-17,822**	-12,196	**-6,744**	-4,020
Operating expenses without Incentive Scheme	**-66,246**	-54,174	**-22,768**	-17,865	**-14,532**	-12,196	**-4,970**	-4,020
Depreciation	**-9,116**	-7,996	**-3,191**	-3,132	**-2,000**	-1,800	**-697**	-705
Valuation of Incentive Scheme	**-14,995**	-	**-8,129**	-	**-3,289**	-	**-1,774**	-
Profit/loss on operating activities (EBIT)	**-61,612**	-24,194	**-23,489**	-12,357	**-13,516**	-5,447	**-5,127**	-2,781
Profit/loss on operating activities (EBIT) without Incentive Scheme	**-46,617**	-24,194	**-15,361**	-12,357	**-10,226**	-5,447	**-3,353**	-2,781
Profit/loss before income tax	**-60,257**	-19,926	**-22,635**	-12,092	**-13,219**	-4,486	**-4,941**	-2,721
Net profit/loss	**-60,625**	-20,745	**-22,817**	-12,136	**-13,299**	-4,670	**-4,981**	-2,731
Net profit/loss without Incentive Scheme	**-45,630**	-20,745	**-14,688**	-12,136	**-10,010**	-4,670	**-3,206**	-2,731
EBITDA	**-52,496**	-16,198	**-20,298**	-9,225	**-11,516**	-3,647	**-4,431**	-2,076
EBITDA without Incentive Scheme	**-37,501**	-16,198	**-12,170**	-9,225	**-8,227**	-3,647	**-2,657**	-2,076
Net cash flows from operating activities	**-58,163**	-11,000	**-18,522**	1,850	**-12,759**	-2,476	**-4,043**	416
Net cash flows from investing activities	**5,114**	-27,983	**16,277**	-11,212	**1,122**	-6,300	**3,553**	-2,523
Net cash flows from financing activities	**-2,150**	131,113	**-890**	135,059	**-472**	29,516	**-194**	30,394
Total net cash flow	**-55,199**	92,130	**-3,135**	125,697	**-12,109**	20,740	**-684**	28,287
Number of shares (weighted average)	**18,355,474**	16,232,278	**18,355,474**	16,748,700	**18,355,474**	16,232,278	**18,355,474**	16,748,700
Profit (loss) per share (in PLN)	**-3.30**	-1.28	**-1.24**	-0.72	**-0.72**	-0.29	**-0.27**	-0.16
Diluted profit (loss) per share (in PLN)	**-3.30**	-1.28	**-1.24**	-0.72	**-0.72**	-0.29	**-0.27**	-0.16
Book value per share (in PLN)	**9.72**	14.46	**9.72**	14.01	**2.10**	3.19	**2.10**	3.10
Diluted book value per share (in PLN)	**9.72**	14.46	**9.72**	14.01	**2.10**	3.19	**2.10**	3.10
Declared or paid dividend per share (in PLN)	**-**	-	**-**	-	-	-	-	-

Selected financial data presented in the Quarterly report were converted to Euro as follows:

1. Items relating to the profit and loss statement and the cash flow statement were converted using the exchange rate constituting the arithmetic average of the exchange rates, applicable as of the last day of every month in the given period, based on the information published by the National Bank of Poland (NBP):
    - for the period from 01/01/2021 – 30/09/2021: PLN 4.5585;
    - for the period from 01/01/2020 – 30/09/2020: PLN 4.4420;
2. Balance sheet items were converted using the average exchange rate announced by the NBP applicable as at the balance sheet date; which were:
    - as of 30 September 2021: PLN 4.6329;
    - as of 31 December 2020: PLN 4.6148.

1.2. Management Board comments on the financial results

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

In the first three quarters of 2021, Ryvu Therapeutics S.A. recognized the total operating revenue of PLN 19,629 thousand, which constitutes a decrease of 35% compared to the corresponding period in 2020, when the total operating revenue amounted to PLN 29,980 thousand. This mainly results from the decrease in revenues from R&D projects (decrease of PLN 14,315 thousand), partially compensated by the slight increase in revenues from subsidies (increase of PLN 3,691 thousand) compared to the corresponding period in 2020.

The decrease in revenues from R&D projects results mainly from the fact that in current period Ryvu Therapeutics S.A. did not receive milestones from partnerships for any of its projects compared to the corresponding first nine months of 2020, when:

- the Phase I first-in-human clinical study of SEL24 / MEN1703 - oral dual PIM / FLT3 kinase inhibitor in patients with acute myeloid leukemia was completed. Accomplishment of Phase I study, in accordance with the terms of the agreement with Berlin-Chemie (the Menarini group), resulted in Ryvu Therapeutics S.A. receiving a milestone payment and recognizing the revenue in the amount of EUR 1,750 thousand (PLN 7,524 thousand),
- the Company concluded a research and development cooperation agreement with Galapagos NV. The subject of agreement is the discovery and development of innovative small molecule compounds with potential therapeutic applications in inflammatory diseases. Under the Agreement, the Company received an upfront payment of EUR 1,500 thousand (PLN 6,791 thousand), and is 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 research collaboration.

In the first nine months of 2021, Ryvu Therapeutics S.A. reported a net loss as well as an operating loss. The net and operating losses are the result of the new Company's strategy of Ryvu Therapeutics S.A. published on June 15, 2020 for the years 2020-2022, which develops and revises the assumptions of the strategy adopted by the Company for 2017-2021, published in the current report No. 27/2017 of August 2, 2017 (before the division of the Issuer). According to the Strategy, the Company focuses

currently on increasing the value of the ongoing projects, that will be commercialized at a later stage of development.

The Company's net loss for period ended September 30, 2021, amounted to PLN 60,625 thousand in comparison to the net loss of PLN 20,745 thousand in the corresponding period of 2020. The bigger loss in 2021 is related to the aforementioned lack of commercialization-related revenues, non-cash cost of valuation of incentive program for its employees of PLN 14,995 thousand (described below) partially compensated by the revaluation (positive exchange rate impact) of shares in NodThera Ltd. (described below).

Valuation of shares in NodThera Ltd.

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

Funds in the amount of GBP 20.2 million were transferred to NodThera Ltd. in accordance with the share capital increase registered on June 2, 2020. The Series B preferred Shares were acquired at an issue price of GBP 2.9702 per share. The remaining part of the funding in the amount of GBP 24.2 million was to be provided by Investors after achieving certain milestones in the development of the NodThera's research projects in accordance with the investment agreement.

Due to amendment to the above-mentioned investment agreement entered into in April 2021 (which was concluded by the Investors; the Company is not a party to this agreement), Investors decided that the first tranche of financing would be extended by an additional issuance of GBP 12.1 million (at the current issue price per share), while the original second tranche of financing will amount to GBP 12.1 million. The remaining of the financing would be provided by Investors and will be accomplished upon reaching certain milestones, no later than October 1, 2022. The issue price of the second tranche was set at GBP 3,1191 per share.

The amount of financing resulting from the extended first tranche of financing was paid to the company in September 2021 due to achievement of scientific milestones in the development of the company's research program in accordance with the amended investment agreement. After this increase, as at the date of this Report, the Issuer's share in the share capital of NodThera Ltd. amounted to 5.24%. After closing the second tranche of financing, the Issuer's share in the share capital of NodThera will drop to 4.63%.

In the opinion of the Management Board, the above-mentioned issuance of shares within extended first tranche of financing at the issue price of GBP 2,9702 per share in accordance with amended investment agreement constitutes a reasonable basis for adopting the valuation of NodThera's shares at the balance sheet date of GBP 2,9702 per share by the Management Board of the Issuer.

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

share issue price (in GBP)	2.9702
average NBP exchange rate from September 30, 2021	5.3653
share issue price (in PLN)	15.94
the number of the Company's shares in NodThera Ltd.	1,910,000
value of shares in the balance sheet as at September 30, 2021	30,437,787
value of shares in the balance sheet as at December 31, 2020	29,118,228
change due to currency exchange rates movements - impact on gross result	1,319,559
deferred tax	250,716
impact on the net result	1,068,843

Incentive Scheme

On May 17, 2021, the General Shareholders Meeting adopted the non-dilutive Stock Grant Program for 2021-2024 for all employees in the form of the right to acquire shares of the Company. Subject of the Stock Grant Program is a total of 1,247,720 ordinary shares of the Company that have been donated free of charge by Mr. Paweł Przewięźlikowski – founder, President of the Management Board and Company's largest shareholder to the Company, constituting a total of 25% of the Company's shares held by Mr. Paweł Przewięźlikowski. The Stock Grant Program provides employees with the right to acquire shares at a preferential price of PLN 0.19 per share, covering the Company's administrative costs incurred in order to accomplish the Stock Grant Program. The fair value of the shares granted is determined as at the grant date and recognized over the vesting period in remuneration costs in correspondence with the capital increase own at the time of vesting by employees during the program. For the period ended September, 2021 the Company recognized the non-cash cost of valuation of this incentive program of PLN 14,995 thousand – more details are described in note 36 to the interim financial statements.

1.3. The Company's assets and the structure of assets, liabilities and equity

As of September 30, 2021, the value of the Company's assets was PLN 233,896 thousand and decreased by PLN 61,744 thousand compared to the end of 2020 (PLN 295,640 thousand), mainly due to expenditure on R&D projects. At the end of September 2021, the highest value of current assets is the cash which amounted to PLN 81,019 thousand (at the end of 2020 it was PLN 136,218 thousand) and other financial assets in the value of PLN 9,990 thousand (at the end of 2020 it was PLN 24,969 thousand). The decrease in cash and other financial assets results from the aforementioned spending incurred on research projects and continuation of equipping the Research and Development Centre for Innovative Medicines (named 'CBR'). Fixed assets are mainly CBR and laboratory equipment and the valuation of NodThera shares of PLN 30,438 thousand. The value of non-current assets increased in comparison to December 31, 2020, by PLN 4,052 thousand. The increase consists mainly of the aforementioned expenditures on equipping of CBR.

The main item in the Company's equity and liabilities is equity, which amounted to PLN 178,328 thousand as of September 30, 2021, and decreased by PLN 45,393 thousand compared

to 31 December 2020. The decrease in equity is mainly a result of the net loss recognized for the period. The second largest source of assets' funding is long-term liabilities which amounted to PLN 31,874 thousand at the end of September 2021. Long-term liabilities mainly related to deferred income related mainly to the infrastructure subsidy for CBR.

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

	30.09.2021	31.12.2020
Current ratio **current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)**	5.61	8.95
Quick ratio **(current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)**	5.44	8.86

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

1.4. Current and anticipated financial standing and evaluation of the management of financial resources

The Company's financial position as of the report date is good. As of September 30, 2021, the value of the Company's cash amounted to PLN 91,009 thousand (PLN 81,019 thousand in cash in bank deposits and PLN 9,990 thousand in bonds), and as of October 31, 2021, it was PLN 84,876 thousand (PLN 74,886 thousand in cash in bank deposits and PLN 9,990 thousand in bonds). The decrease in cash from the end of September to end of October is mainly due to expenditure on R&D projects.

The Company meets its obligations in a timely manner and maintains sustainable cash levels ensuring its financial liquidity. Cash inflow from previous share issuances, funds obtained from subsidies from EU funds supporting R&D projects and cash generated from the commercialization of projects allow the Company to execute its planned investments, in particular, the development of ongoing and new innovative projects and expansion of laboratory infrastructure. Future Company's revenue depends strongly on the ability to commercialize and partner research projects.

2. SIGNIFICANT EVENTS IN Q1-Q3 2021

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

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

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

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

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

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

Conclusion of an agreement concerning operational execution of Phase I clinical trial of RVU120 (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 contract research organization (CRO) with 25-years of experience in running clinical trials. The company has a long track record of global clinical experience in executing oncology trials, with solid tumors being amongst the top indications in terms of Covance's expertise. In the past five years, Covance has run over 1,000 clinical studies in Oncology, with Phase I studies being the most often executed ones.

Covance will be responsible for operational execution of a Phase I clinical study (dose escalation). The estimated cost of the Agreement is EUR 2,223,529 (PLN 10,206,665 converted at the average exchange rate of the National Bank of Poland of March 8, 2021, EUR 1 = PLN 4.5903) and will be co-

financed by the European Regional Development Fund and the Government of Poland as part of the project titled "Clinical development of an innovative drug candidate in solid tumors" within the Smart Growth Operational Program 2014-2020, measure 1.1.1. "Fast Track". The value of the contract may change in the event of extending the scope of the order.

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

On 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 presented data from multiple oncology programs: RVU120, a CDK8/CDK19 inhibitor program, as well as data from small-molecule STING agonists and HPK1 inhibitors. Details of the e-poster presentations are as follows:

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

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

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

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

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

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

The Company announced on April, 8 2021 that the U.S. Food and Drug Administration, FDA, placed a partial clinical hold on the first in human phase Ib, dose escalation clinical trial of RVU120 (also known as SEL120) in patients with relapsed/refractory (R/R) AML and high-risk MDS, being conducted in the United States. Patients who were taking RVU120 could continue treatment in the study but no new patients could have been enrolled in the study. FDA subsequently lifted the partial clinical hold, which the Company disclosed in the current report no. 25/2021 dated July, 14 2021. Enrollment in the Phase Ib study has resumed.

Non-dilutive Stock Grant Program (2021-2024)

On April 20, 2021 the Company announced that it had received a letter of intent from Mr. Paweł Przewięźlikowski - the main shareholder and President of the Management Board of the Company

regarding declaration of donation of part of the shares held by the Shareholder for the purpose of establishing an incentive program for employees and associates of the Company ("Program"). On May 17, 2021 the General Shareholders Meeting adopted a resolution regarding adoption of the Program for the years 2021-2024.

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

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

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

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

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

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

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

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

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

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

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

Ryvu Therapeutics received full approval to conduct Phase I/II study of RVU120 (SEL120) in patients with relapsed/refractory metastatic or advanced solid tumors in Poland

On May, 28 2021 the Company has announced that its Clinical Trial Application (CTA) to commence a single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120 (SEL120) in patients with relapsed/refractory metastatic or advanced solid tumors in Poland, was fully approved by the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, and the respective Central Ethics Committee.

The study is designed in two parts. Phase I part has the key objectives of assessing safety and tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary anti-tumor activity of RVU120 (SEL120) during dose escalation cohorts, and determination of the recommended phase II dose (RP2D). Phase II part will include patients with specific tumor indications, enrolled at distinct study groups.

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

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

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

The ASCO Annual Meeting 2021 is considered one of the most important scientific events, gathering researchers, as well as potential clients and business partners - biotechnology and pharmaceutical companies and industry investors.

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

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

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

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

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

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

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

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

Clinical data on SEL24 (MEN1703) including patients enrolled in the Phase II, cohort expansion (CE) phase of the study, confirmed a manageable safety profile at the recommended dose (RD) and preliminary single agent efficacy in R/R AML. These results warrant further investigation of SEL24(MEN1703) in AML.

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

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

The partial clinical hold was issued following Ryvu's report to the FDA of a serious adverse event involving a patient death that might have possibly been related to RVU120. Study enrollment was

suspended but patients already on treatment could continue treatment. As of the current report publication date (September 6, 2021) one patient still remains on RVU120 treatment.

Based on the recommendations from the FDA, the study will resume enrollment at the 75mg dose (Every Other Day - EOD) in a standard 3+3 design, according to a revised protocol intended to increase patients' safety. Protocol amendment covers modified exclusion criteria, scope of monitoring and frequency of laboratory testing. Following the completion of the 75mg cohort, the data generated will be reviewed by the Agency and a further dose escalation strategy will be established. Additionally, Ryvu plans to use 75mg dose as the starting dose for the single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors.

The initial safety and efficacy data from the first four cohorts in the trial were presented at the Virtual EHA Congress on June 11, 2021 (Company has informed about it in the current stock no 12/2021 dated May 12, 2021). RVU120 demonstrated acceptable safety profile and two clinically relevant responses were observed in the first five AML and high risk MDS patients treated: one complete response (CR) and one erythroid response.

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

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

The single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors was approved by the Competent Authority in Poland and obtained a positive Ethics Committee opinion, enabling enrollment of patients in Poland. The CTA submission process has already been initiated in Spain as well, aiming to start enrollment in Q4 2021.

Resignation from the position in the Management Board

Dr. Setareh Shamsili, M.D., PhD resigned from her position as Executive Vice President of the Management Board and Chief Medical Officer of Ryvu for family reasons effective August 31, 2021. During the CMO transition period, Prof. Axel Glasmacher, M.D., Ryvu Supervisory Board Member since 2019, will provide additional support for the Company on a consulting basis.

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

On September 24, the Company announced that it has filed a lawsuit against Mota-Engil Central Europe S.A. in connection with construction of the Research and Development Center for the payment of PLN 13.756.717,07. With this lawsuit, the Company seeks claims related to the agreement for "Construction of the Research and Development Center of Innovative Drugs Selvita S.A." ("Contract"), the conclusion of which was announced by the Company in the current report No. 27/2018 of August 13, 2018. The total value of the Contract was PLN 68,783,585.34 including VAT. The Contractor was supposed to complete the Contract within 15 months after the execution of the Contract, which has not been done. The Parties have extended Time for Completion of the Contract until April 30, 2020 (by way of concluding two annexes) and modified the scope of works to be

performed under the Contract, including exclusion of the part of the works and performance of the substitution works.

2.1. Post balance sheet events

Establishing the Polish Association of Innovative Medical Biotechnology Companies BioInMed

On November 3, it was announced that the Polish Association of Innovative Medical Biotechnology Companies BioInMed has joined the group of industry associations present in Poland. The association was established by 11 companies such as Ardigen SA, Selvita SA, Ryvu Therapeutics SA, Captor Therapeutics SA, Celon Pharma SA, ExploRNA Therapeutics SA, OncoArendi Therapeutics SA, Polski Bank Komórek Macierzystych SA, PolTREG SA, Pure Biologics SA and WPD Pharmaceuticals Sp. z o.o. Marta Winiarska, who for the past five years has been managing public affairs and public relations activities at the Employers' Union of Innovative Pharmaceutical Companies INFARMA, has been appointed President of the Association.

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

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

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

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

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

On November 4, the Company informed that five abstracts demonstrating clinical and preclinical activity of selective CDK8/19 inhibitor RVU120 (SEL120) and selective PIM/FLT3 inhibitor SEL24 (MEN1703) have been accepted for presentation at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition, to be held on December 11 – December 14, 2021 in Atlanta (USA). A poster on the preclinical efficacy of RVU120 in breast cancer has also been accepted for presentation at the 44th Annual San Antonio Breast Cancer Symposium (SABCS) to be held on December 7 – December 10, 2021, in San Antonio (USA). Ryvu’s partner Menarini Group will be presenting SEL24/MEN1703 data from the First-in-Human, Dose Escalation (DE) and Cohort Expansion (CE) CLI24-001 trial (DIAMOND-01, ClinicalTrials.gov identifier: NCT03008187).

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

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

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

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

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

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

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

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

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

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

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

2.2. Unusual events occurring in the reporting period (Covid-19)

COVID-19

Covid-19 pandemic, which began in the first quarter of 2020, continued during the whole reported period. Because of that, already in 2020 the Issuer implemented, and during the reported period still followed, all of 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 was 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. Internal policies are constantly updated to the latest guidelines and changing conditions.

During the previous reporting periods, the pandemic significantly affected the progress of the Issuer's fully owned clinical trial - CLI120-001 (RVU120 AML/HR-MDS) study, and the impact of pandemic to some extent, has also continued in Q3 2021. Due to the onset of Covid-19 pandemic, all RVU120 clinical sites have maintained additional safety measures and risk management processes which limited possibility of in person site monitoring as well as have impacted the ability of some patients to participate in the 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 coronavirus exposure.

An additional new pandemic induced risk to cancer clinical trial enrolments was the start-up of COVID19 vaccination campaigns, which affects eligibility of the candidate patients for such trials, close to vaccination.

The Management Board of the Company analyzes the situation related to the spread of the coronavirus pandemic on an on-going basis and implements adequate safety measures. Additionally, in connection with the launch of the national vaccination program against COVID-19, Ryvu is supporting employees in taking part in the above-mentioned program.

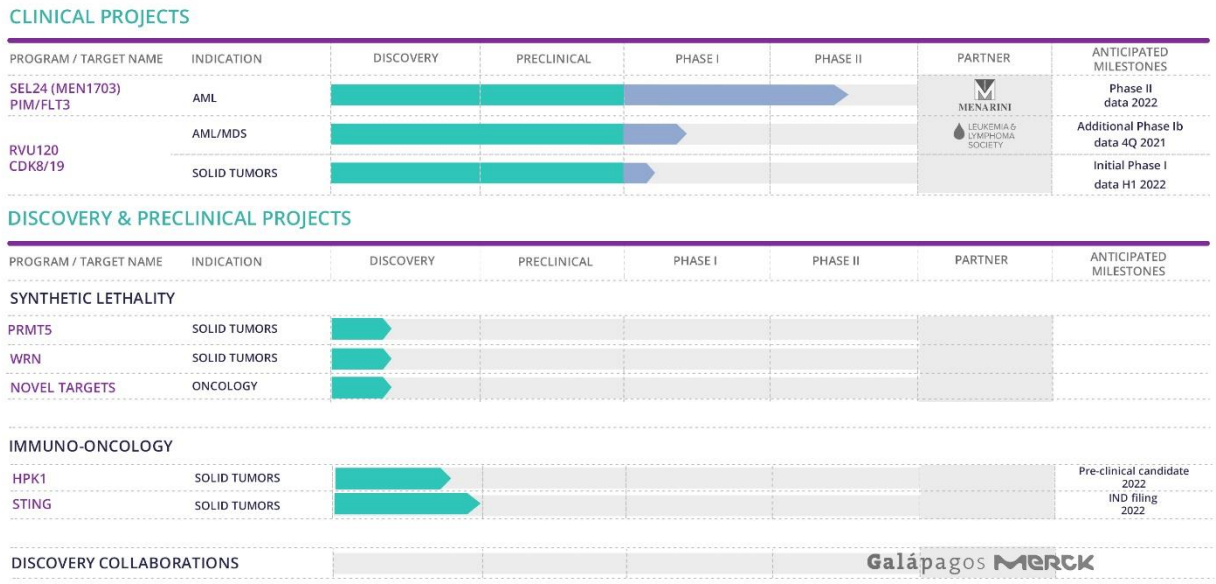
The Company's Management Board is analyzing the Issuer's situation on an on-going basis. New circumstances, if any, having a significant effect on the Issuer's financial results and business position, will be communicated promptly in the individual current reports.

3. MANAGEMENT BOARD INFORMATION ON THE ACTIVITIES

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.

Pipeline



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).

Successful completion of Phase I clinical study of SEL24/MEN1703 in AML was announced by Menarini in March 2020 and the results were presented at the 25th Annual Meeting of the European Hematology Association (EHA) 2020. Subsequently a Cohort Expansion study in relapsed/refractory

AML patients has been initiated in the United States and Europe. The aim of Ph II study was to further investigate the single agent activity and expanding safety profile of SEL24/MEN1703.

The data that have been generated in SEL24/MEN1703 Cohort Expansion part of the study was presented in June 2021 during American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) Virtual Congresses. Data reported in the posters confirmed the manageable safety profile of the drug at the RD and showed preliminary single agent efficacy in relapsed/refractory AML, particularly in patients with IDH mutant disease either naïve or previously exposed to IDH inhibitors.

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

Menarini stated that these results warrant further investigation of SEL24/MEN1703 in AML, with a potential to focus in the IDH mutated subset. A subsequent study in this patient population started in July 2021.

Additionally, on November 4th 2021 it was announced that the abstract submitted by Menarini titled: *"SEL24(MEN1703) Inhibits PIM/FLT3 Downstream Target in Acute Myeloid Leukemia (AML) Patients: Results of the Pharmacodynamics (PD) Assay and Genomic Profiling in the First-in-Human Diamond-01 Trial"* was accepted for poster presentation at the 63rd ASH Annual Meeting & Exposition, being held on December 11 – December 14, 2021, in Atlanta, US.

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

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

RVU120 (SEL120)

RVU120 (also known as SEL120) is a clinical stage highly specific and orally bioavailable dual inhibitor of CDK8/CDK19 kinases which are key targets involved in transcription modulation in multiple cancer types. At present, Ryvu is conducting two clinical studies with RVU120: (i) Phase Ib in patients with AML/HR-MDS (NCT04021368) and (ii) Phase I/II in relapsed/refractory metastatic or advanced solid tumors (NCT05052255). Additionally, multiple translational research activities are conducted, aimed at further confirmation of RVU120 mechanism of action, defining target patient population as well as validating RVU120 in other hemato-oncology as well as solid tumor indications. As such, results of translational research are aimed at support of clinical development plan for RVU120.

Key achievements in Q3:

- **FDA lifted the partial clinical hold on Phase Ib clinical trial of RVU120 (SEL120) in AML/HR-MDS.** The partial clinical hold was issued in April 2021, following the report to the FDA of a Serious Adverse Event (SAE) involving a patient death that may possibly be related to RVU120. Study enrollment was suspended but patients who had already been

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

- **First patient dosed in Phase I/II study of RVU120 (SEL120) in patients with relapsed/refractory metastatic or advanced solid tumors.** On August 25th, the first patient in a single-agent, open-label Phase I/II trial, investigating the safety and efficacy of RVU120, received the first dose of the study drug. The clinical study had previously been approved by the Competent Authority in Poland and obtained a positive Ethics Committee opinion, enabling enrollment of patients in Poland. The CTA submission process has also been initiated in Spain, aiming at starting enrollment in Q4 2021. In Q3, two Polish clinical sites were activated for enrollment: (i) Medical University Early Phase Research Center in Gdansk, and (ii) Maria Sklodowska-Curie National Research Institute of Oncology in Warsaw. The CTA submission process has also been initiated in Spain, aiming at starting enrollment in Q4 2021.

- **Phase Ib clinical trial of RVU120 (SEL120) in AML/HR-MDS expanded to Poland.** In Q3, two Polish clinical sites were activated for enrollment in RVU120 AML/HR-MDS study: (i) University Clinical Centre in Gdansk and (ii) Institute of Hematology and Blood Transfusion in Warsaw. Together with the five US sites, there are currently seven clinical sites enrolling patients in Phase Ib clinical trial of RVU120 AML/HR-MDS.

ABOUT RVU120 (SEL120) MOLECULE

RVU120 (SEL120) is a selective first-in-class CDK8/CDK19 inhibitor, which has demonstrated efficacy in a number of solid tumor in vitro and in vivo models as well as in hematologic malignancies. CDK8 is a kinase submodule of the mediator complex, involved in both transcriptional activation and repression. CDK8-mediator complex integrates basal transcriptional machinery with the activity of oncogenic transcriptional and epigenetic factors. Inhibition of CDK8 can repress key oncogenic transcriptional programs and induce lineage commitment genes in AML. CDK8 and CDK19 are also preclinically validated novel targets for the treatment of breast and prostate cancers. Targeting CDK8 and its paralog CDK19 using potent and selective CDK8/19 inhibitor RVU120, may be an effective way for treatment of both hematological malignancies and solid tumors with deregulated transcription. According to information available to the Company, there are currently no competitive selective CDK8/19 inhibitors actively tested in clinical trials.

RVU120 has been internally discovered by Ryvu and has received support from the Leukemia & Lymphoma Society Therapy Acceleration Program® (TAP), a strategic initiative to partner directly with innovative biotechnology companies and leading research institutions to accelerate the development of promising new therapies for blood cancers.

On March 25, 2020, the U.S. Food and Drug Administration (FDA) granted an orphan drug designation (ODD) to RVU120, for the treatment of patients with AML.

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

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

The first patient in CLI-120 clinical trial was dosed on September 4th, 2019, and the study was enrolling patients in the US until April 8th, 2021, when the Food and Drug Administration (FDA) put study under a partial clinical hold, triggered by a SUSAR, reported by Ryvu as possibly/probably related to the study drug. Following the lift of partial clinical hold by FDA in July 2021, based on the recommendations from the Agency, the study resumed enrollment at a 75mg dose (Every Other Day – EOD) in a standard 3+3 design, according to the revised protocol. The protocol amendment covered modified exclusion criteria, scope of monitoring and frequency of laboratory testing. Additionally to the five investigational sites in the US, Ryvu activated in September two new sites in Poland. Following completion of the 75mg cohort, data generated from this cohort as well as further dose escalation strategy will be reviewed by the FDA. Conditional to the Agency's approval, dose escalation to the subsequent cohorts >75mg will be allowed. Final results of Phase Ib study are expected in 2022.

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

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

The aim of RVU120-SOL-021 Phase I/II clinical study, is to investigate the safety and efficacy of RVU120 in patients with relapsed/refractory metastatic or advanced solid tumors. The study is designed in two parts. Part 1 of the study (phase I) is a dose escalation part according to a standard 3+3 design and is aimed at enrollment of adult patients with solid malignancies who have failed the available standard therapies. The primary objective of the Phase I part is to determine safety, tolerability and a recommended Phase II 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 II part is aimed both at safety and efficacy expansion. Phase II part of the study uses an adaptive, Simon 2-stage design and will enroll patients with R/R specific tumor types, either as a single agent or in combination with standard anticancer medicinal agents, in 2 or 4 groups. The enrollment into these Phase II study groups, will be done simultaneously, therefore completion of one arm, would not affect completion of the other arms. Each study group is planned to enroll up to 24 patients. Additional translational and biomarker studies are currently ongoing to confirm which target patient populations will be selected.

The first patient was dosed on August 25th, 2021 at the 75 mg dose. The study is actively enrolling at two investigational sites in Poland, and the CTA submission process has already been initiated in Spain. Preliminary part 1 (phase I) results are expected in 2022.

The RVU120-SOL-021 study is registered at ClinicalTrials.gov under the identifier NCT05052255 (https://clinicaltrials.gov/ct2/show/NCT05052255?term=RVU120&draw=1&rank=1).

PRECLINICAL AND DISCOVERY STAGE PROJECTS

Synthetic lethality projects

The Company currently conducts 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 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 controlling DNA repair mechanisms and maintaining integrity of the genome. WRN helicase has been identified to be indispensable in tumor cells with microsatellite instability (MSI), where inhibition of the protein's helicase/ATPase activity leads to impairment of cellular viability. This therapeutic strategy holds promise for patients with MSI tumors across multiple indications, such as colorectal, ovarian, endometrial and gastric cancers.

Ryvu concluded a high throughput screening campaign which led to identification of several small-molecule WRN inhibitor series representing varying chemotypes. Subsequent profiling of the selected chemical series allowed to deselect chemotypes with potentially undesired profiles, while further generation of new data sets provided additional chemotypes for further profiling and expansion.

In Q3 2021 the project focused on further expansion and optimization of key parameters for the most promising chemotypes. Continued profiling of newly developed compounds allowed for advanced characterization of chemical series and their cellular activity. At the same time major focus was put on additional hit identification efforts in order to provide new chemical matter characterized by orthogonal modes of action. In particular additional virtual and physical focused high-throughput screenings were performed. Currently major focus in the project is put on validation of novel hit sets as well completion of additional screening approaches in order to provide a further diversified portfolio of WRN-inhibiting chemotypes. At the same time optimization of selected chemical series is continued to allow for progression into further stages of development.

The second project in the field of synthetic lethality is focusing on cancers with a deletion of the metabolic gene MTAP, which occurs in 10 to 15% of all human tumors. MTAP deletion results in massive accumulation of methylotioadenosine (MTA) in cells. MTA in high concentrations is a very selective inhibitor of PRMT5 methyltransferase, competitive for the substrate: S-adenosylmethio nine (SAM). Accumulation of MTA in cells with MTAP deletion causes a partial inhibition of the methylation activity of PRMT5, which in turn reduces the level of symmetric arginine dimethylation of the whole proteome, and thus an increased sensitivity of cells to modulation of methylosome activity. The Company's strategy is to develop MTA-cooperative PRMT5 inhibitors, which will selectively inhibit the growth of MTAP-deleted cancer cells. PRMT5 inhibitors currently tested in clinical trials do not

differentiate by MTAP status. The work carried out in reported period focused on the identification and validation of unique chemical matter and led to the identification of new chemical series with the desired properties (confirmed synthetic lethality in in vitro cellular models). Identified chemical matter is currently developed towards in vivo proof of concept and preclinical candidate stage based on established project workflow. Validation of the molecules in the mouse MTAP deletion xenograft model is planned for Q1 2022.

In addition to the two disclosed projects, Ryvu is currently leading multiple internal initiatives focused on identification and validation of new targets in the synthetic lethality space. One of the key assumptions for the selected targets is their first-in-class potential. So far, several new targets have been identified which potentially meet this criteria. Target validation studies are ongoing. For one of the selected molecular targets, validation was carried out in in vitro cellular models and in H2 2021 the company has initiated a hit finding campaign aiming at identification of pharmacologically active compounds for this potentially first in class target. At the same time, work is underway on the selection and experimental validation of further molecular targets with first-in-class drug potential. Therapeutic targets for which active molecules can be identified and validated will be included in the company's project pipeline as they progress from target validation to successful hit stage.

Immuno-oncology projects

The main focus of Ryvu's projects in IO space is the discovery and development of differentiated, innovative immunotherapeutics for targets that can be addressed therapeutically with small molecules. Currently, the Company conducts research on two such projects: immunoactivation by STING agonists and HPK1 inhibitors, which have the dual potential of both activating the immune response and protecting cells of the immune system against immunosuppression.

The most advanced project within 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 with confirmed *in vitro* cellular activity, which translates to in vivo antitumor efficacy in mouse syngeneic tumor models. In the course of the project Ryvu identified structural features allowing the molecules to reach superior agonist activity in human immune cells. Further characterization allowed to narrow down the selection to a shortlist of most promising compounds with the best overall activity and safety profile.

In Q3 2021 the project focused primarily on generating additional in vivo data (both efficacy and PK/PD) for a pre-selected frontrunner molecule in order to prepare a dataset necessary for progression into toxicology studies. As a result, a favorable in vivo activity of the compound was confirmed, leading to complete tumor regressions in syngeneic mouse tumor model. Furthermore, advance PK/PD studies were continued to facilitate the design of preclinical studies. Additionally, a scale-up optimization process for the pre-selected frontrunner was completed allowing to prepare the material in quantities necessary to support ongoing profiling as well as toxicology studies.

The second research program carried out in the area of immuno-oncology aims to develop small molecule inhibitors of HPK1 kinase (MAP4K1), an enzyme involved in the signaling cascade of the TCR receptor. This protein is a negative regulator of the pathway, so that inhibition of HPK1 kinase activity results in activation of T lymphocytes. Such stimulation enables the immune system to more efficiently recognize and attack cancer cells. Developed in RYVU laboratories compounds are one of the most potent inhibitors, demonstrating nanomolar activity against HPK1. Tested small molecules characterize good *in vitro* selectivity over potential anti-targets from the TCR signaling pathway, good permeability, and *in vivo* absorption. In the third quarter of 2021 lead optimization was continued, with a particular focus on improving safety, selectivity, metabolic stability, physicochemical and PK parameters. PK and PK / PD experiments were performed for the inhibitors characterized by the highest selectivity and activity. The obtained data enabled evaluation of the *in vivo* activity of selected compounds and nomination of a candidate for the efficacy study in a mouse model of triple-negative breast cancer. When dosed orally, initial activity signals for tested molecule were observed in a mammary carcinoma EMT-6-challenged syngeneic mice. Further work aiming at the improvement of safety and target engagement *in vivo* is ongoing.

OTHER PROJECTS

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

4. THE ISSUER'S CORPORATE BODIES

The Management Board:

1) Pawel Przewiezlikowski – President of the Management Board
2) Krzysztof Brzozka – Vice President of the Management Board
3) Kamil Sitarz – Member of the Management Board

The Supervisory Board:

1) Piotr Romanowski – Chairman of the Supervisory Board
2) Tadeusz Wesolowski – Vice Chairman of the Supervisory Board
3) Rafal 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 Audit Committee:

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

The 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

During reporting period, effective August 31, 2021, Dr. Setareh Shamsili, M.D., PhD resigned from the position of Executive Vice President of the Management Board and Chief Medical Officer of the Company for personal reasons. During the CMO transition period, Prof. Axel Glasmacher, M.D., Ryvu Supervisory Board Member since 2019, has been providing additional support for the Company on a consulting basis.

5. INFORMATION ON THE SHAREHOLDERS HOLDING (DIRECTLY OR INDIRECTLY) AT LEAST 5% OF THE TOTAL NUMBER OF VOTES AT THE GENERAL SHAREHOLDERS' MEETING OF THE COMPANY AND ON SHARES HELD BY MEMBERS OF THE ISSUER'S MANAGEMENT BOARD AND SUPERVISORY BOARD

Shares hold by Members of the Issuer's Management and Supervisory Board as of September, 30 2021

Shareholder	Series A*	Series B	Series C,D,E,F, G1,G2	Number of shares	% of Share Capital	Number of Votes	% of Votes at SM
The Management Board							
Paweł Przewięźlikowski	3 500 000	73 033	307 630	**3 949 517**	21,52%	**7 449 517**	33,25%
Krzysztof Brzózka		17 245	250 076	**267 321**	1,46%	**267 321**	1,19%
Kamil Sitarz		17 865		**17 865**	0,10%	**17 865**	0,08%
The Supervisory Board							
Tadeusz Wesołowski (directly)			92 975	**92 975**	0.51%	**92 975**	0.41%
Tadeusz Wesołowski (indirectly through Augebit FIZ)			1 039 738	**1 039 738**	5.66%	**1 039 738**	4.64%
Piotr Romanowski			331 000	**331 000**	1,80%	**331 000**	1,48%
Rafał Chwast			121 115	**121 115**	0.76%	**121 115**	0.60%
Thomas Turalski			20 100	**20 100**	0.11%	**20 100**	0.09%

**Series A shares are privileged (one share gives the right to two votes at the General Meeting)*

In the reporting period, since the last periodic report, there was a change resulting from the sale of 50,000 shares by Mr. Piotr Romanowski, about which the Issuer informed in the current report No. 26/2021 of July, 21 2021. Before the transaction, Mr. Piotr Romanowski owned 381,000 shares entitling to the same number of votes at the Issuer's general meeting, which constituted 2.08% of shares in the share capital and 1.69% of votes, respectively. After the transaction, Mr. Piotr Romanowski holds 331,000 shares entitling to the same number of votes (1,08% in the share capital and 1.48% of votes, respectively).

Moreover, in the reporting period, there was a change resulting from the transfer of 1,109,277 series B shares in the implementation of the Stock Grant Program for the years 2021-2024 in the Company. The Company informed about the conclusion of the share donation agreement between the Company and Mr. Paweł Przewięźlikowski - the founder, President of the Management Board and the main shareholder of the Company in the current report No. 22/2021 of July 8, 2021 and the current report No. 27/2021 of August 13, 2021. All employees were eligible to participate in the program including Management Board Members, therefore, on July 9, 2021, Mr. Krzysztof Brzózka - Vice President of the Management Board of the Company, acquired 17,245 shares of the Company, and Mr. Kamil Sitarz - Member of the Management Board of the Company - 17,865 shares of the Company, about which the Company notified in the current report no. 24/2021 of July 13, 2021.

Mr. Przewiezlikowski has committed to donate in total 1.247.720 ordinary shares of the Company in years 2021-2024 within the framework of the Stock Grant Program.

To the best of the Issuer's knowledge there are no other contracts that may affect changes in the proportions of shares held by existing shareholders.

Shares held by significant shareholders of the Company as of September 30, 2021

Shareholder	Shares	% of shares	Votes	% of votes
Paweł Przewięźlikowski	3 949 517	21,52%	7 449 517	33,25%
Bogusław Sieczkowski	924 384	5.04%	1 474 384	6.58%
Nationale Nederlanden OFE	1 771 000	9.65%	1 771 000	7.90%
Tadeusz Wesołowski (with Augebit FIZ)	1 132 713	6.17%	1 132 713	5.06%
Aviva OFE	1 122 859	6,12%	1 122 859	5,01%

In the reporting period, Aviva OFE has informed that it has bought Company's shares and exceeded the threshold of 5% of the total number of votes at the Company's General Shareholders Meeting and currently holds 1,122,859 of the Company's shares, representing 6,12% of the Company's share capital, entitling to 1,122,859 votes at the Company's General Shareholders Meeting, which accounts for 5,01% of the total number of votes.

6. ADDITIONAL INFORMATION

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

Significant non-arm's length transactions with related entities
Not applicable.

Information on organizational or capital relations of the Issuer with other entities
As at the publication date of the report, the Issuer does not form a Capital Group. As at the date of this Report, the Issuer holds 5.24% of shares in NodThera Ltd.

Warranties for loans and borrowings and guarantees granted
Not applicable.

Other information significant for the assessment of the Issuer's position in the area of human resources, assets, cash flows, financial results and changes thereof and information significant for the assessment of the Issuer's ability to settle its liabilities
Not applicable.

Factors which, in the Issuer's opinion, will affect the results over at least the following quarter
The results of the subsequent quarters will depend primarily on the execution of the Company's strategy, which assumes in particular that the following business objectives will be met:

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

Description of factors and events, in particular of an unusual nature, having a significant effect on the financial performance
In the reported period, the Covid-19 pandemic occurred. The Issuer described its effect on the Company's operations under Significant events that occurred in the reporting period.

Explanations regarding the seasonal or cyclical nature of the Issuer's operations in the reported period
Not applicable.

Information on inventory write-downs to the net realizable amount and reversal of such write-downs
Not applicable.

Information on impairment write-downs in respect of financial assets, tangible fixed assets, intangible assets or other assets and the reversal of such write-downs
Not applicable.

Information on the set-up, increase, utilization and reversal of provisions
Information on the changes in provisions for holidays and bonuses is provided in note 30 to the financial statements.

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

Information on significant purchases or disposals of tangible fixed assets
Information on tangible fixed assets is provided in note 13 to the consolidated financial statements.

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

Information on significant settlements resulting from court cases
Not applicable.

Error corrections relating to previous periods
Not applicable.

Information on changes in the economic situation and business conditions, which have a significant effect on the fair value of the entity's financial assets and financial liabilities
Not applicable.

Information on the failure to repay a loan or borrowing or a breach of significant terms and conditions of a loan agreement, with respect to which no corrective action had been taken by the end of the reporting period
Not applicable.

Information on changes in the method of valuation of financial instruments measured at the fair value
Not applicable.

Information on changes in the classification of financial assets due to a change in their purpose
Not applicable.

Information on the issue, redemption and repayment of non-equity and equity securities
Not applicable.

Information on dividends paid (or declared) in the total amount and per share, divided into ordinary and preference shares
Not applicable.

Events that occurred after the date for which the quarterly financial statements were prepared, not disclosed in these financial statements although they may have a significant effect on the Issuer's future financial results
Information on events that occurred after the date for which the financial statements were prepared is provided in note 45 to the financial statements.

Information on changes in contingent liabilities or contingent assets that occurred after the end of the last financial year
Information on changes in contingent liabilities or contingent assets is provided in note 38 to the financial statements.

Other disclosures which may have a material impact on the assessment of the Issuer's financial position and results of operations
Not applicable.

Amounts and types of items affecting the assets, liabilities, equity, net profit/ (loss) or cash flows, which are unusual in terms of type, amount or frequency
Not applicable.

Krakow, November 9, 2021

Signature Not Verified
Dokument podpisany przez PAWEŁ TADEUSZ PRZEWIĘŹLIKOWSKI
Data: 2021.11.09 09:15:03 CET

Paweł Przewięźlikowski
President of the Management Board

Dokument podpisany przez Krzysztof Daniel Brzózka
Data: 2021.11.09 11:50:30 CET

Krzysztof Brzózka
Vice-President of the Management Board

Dokument podpisany przez Kamil Sitarz
Data: 2021.11.09 17:07:15 CET

Kamil Sitarz
Management Board Member

CONTACT

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GENERAL INQUIRIES

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RYVU THERAPEUTICS