RYVU THERAPEUTICS S.A.

Annual Report (Summary)

2019

RYVU THERAPEUTICS

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1 BASIC INFORMATION ON THE COMPANY

Business name of the Company	Ryvu Therapeutics S.A.
Registered office	ul. Bobrzynskiego 14, 30-348 Krakow
Company ID (REGON)	0000367359
Tax ID (NIP)	6792942955
Legal form	Joint-Stock Company
Website	www.ryvu.com

ASSETS

- Fully-owned lead asset, first-in-class CDK8 inhibitor for blood cancers and solid tumors SEL120, first patient dosed in AML/MDS in September 2019.
- First-in-class dual PIM/FLT3 inhibitor SEL24/MEN1703 for blood cancers partnered globally with Menarini entered Phase 2 studies in March 2020
- All clinical trials of SEL24/MEN1703 and SEL120 are conducted in the U.S.

TWO PROJECTS IN CLINICAL TRIALS

STRATEGY

- Development of SEL120 in multiple hemato-oncology and solid tumor indications
- All Ryvu programs have been discovered internally - robust discovery engine addressing targeted cancer therapies and immunooncology
- Expected one new pre-clinical candidate per year for self development or partnering

HIGH VALUE UPSIDE

CORPORATE

- Listed on the Warsaw Stock Exchange (WSE:RVU)
- ~ $162M market capitalization
- ~ $20M* in cash and short-term investments
- > $25M** in grant funding secured until 2023
- >150 employees

MATURE CORPORATE GOVERNANCE

* October 2019, Q3 2019 report. Data for Q4 2019 will be released on April 9, 2020.
** Maximum non-dilutive research funding if all projects succeed according to the current research plans and grant contracts

BROAD, DIVERSIFIED PIPELINE IN SMALL MOLECULE ONCOLOGY

- Mix of wholly-owned and partnered programs
- Potential first-in-class, clinical stage candidates
- Diverse kinase, synthetic lethality, immuno-oncology and immunometabolism programs
- Strong early data relative to competitors

HIGH THROUGHPUT DISCOVERY ENGINE

- 80 Ph.D.- level scientists
- History of identifying molecules with differentiated properties
- Plan to generate one new clinical candidate per year
- Platforms, by design, address key challenges of current treatments
- Focus on internal development and partnering

SCIENTIFIC AND ORGANIZATIONAL EXPERTISE

- Driven by breakthrough science
- Global partnerships with Menarini and Merck KGaA
- Research validated by Leukemia & Lymphoma Society
- Efficient R&D organization
- Secured non-dilutive financing with follow-on opportunities

Ryvu spin out company, NodThera Ltd.

Business name of the Company	NodThera Ltd.
Registered office	Aberdeen, Scotland
Company ID (REGON)	SC540381
Legal form	Joint-Stock Company
Website	www.nodthera.com
Shareholders	8,6%* shares held Ryvu Therapeutics S.A.

NodThera Ltd. was launched in 2016 by Epidarex Capital, based on research conducted at Ryvu since 2012. The company focuses on the treatment of diseases driven by chronic inflammation and develops effective medicinal chemistry platform addressing inflammation and fibrosis that drive NASH. In June 2018 NodThera announced closing of $40M Series A. The financing was co-led by Sofinnova and 5AM Ventures, with further participation from Epidarex Capital and F Prime Capital Partners. In October 2019 Series A was extended by $11M. 8,6% of Nodthera's shares are held by Ryvu.

2 THE MANAGEMENT TEAM AND SUPERVISORY BOARD

The Management Team

PAWEL PRZEWIEZLIKOWSKI, MSc, MBA
CEO and Founder

SETAREH SHAMSILI M.D., Ph.D.
CMO

KRZYSZTOF BRZOZKA Ph.D., MBA
CSO

PETER LITTLEWOOD Ph.D.
Director of DMPK

LUIGI STASI Ph.D.
Director of Chemistry

MONIKA DOBRZANSKA Ph.D.
Portfolio Management Director

MATEUSZ NOWAK Ph.D., MBA
Director of Early
Discovery & Innovation

TOMASZ RZYMSKI Ph.D., MBA
Director of Biology

KAMIL SITARZ Ph.D.
Director of R&D Operations

TOMASZ NOCUN, MSc, MBA
Director of Research Financing

The Supervisory Board

RAFAL CHWAST
MSc

Board Member and CFO at the New Style group.

Past: VP and CFO at Comarch, responsible for financial supervision of group's subsidiaries, raising capital through the stock exchange. CEO of the Association of Stock Exchange Issuers, and member of the Capital Market Council.

AXEL GLASMACHER
M.D.

Independent consultant.
Past: Senior VP and Head of the Clinical R&D Hematology Oncology at Celgene. Worked on: Revlimid®, Idhifa® and Vidaza®.

Research and teaching at University Hospital in Bonn.

BOD: 4D Pharma. Medical advisory: Oncopeptides.

COLIN GODDARD
Ph.D.

Chairman and CEO of BlinkBio.
Past: CEO of OSI Pharmaceuticals for 12 years: Tarceva ® development & launch, through to $4 billion acquisition by Astellas.

BOD: Mission Therapeutics and Endocyte.

PhD in cancer chemotherapy and post-doc at the NCI, Bethesda, MD.

JARL ULF JUNGNELIUS
M.D.

CMO at NOXXON Pharma.
Past: VP of Clinical Research and Development, Solid Tumors at Celgene. Contributed to Abraxane®, Alimta®, Gemzar® and Revlimid®.

BOD: Isofol Medical, Biovica, Oncopeptides, Monocl.
M.D. from Karolinska Institutet.

PIOTR ROMANOWSKI
M.D. Ph.D., CHAIRMAN

Partner at PwC

Past; Partner at McKinsey & Company and Board Member in the banking sector

MD, PhD (cancer genetics) from Medical Academy of Gdansk, Poland; PhD (cell cycle regulation) from University of Cambridge, UK.

THOMAS TURALSKI

Portfolio Manager leading investment team at Revidea Ventures.

Past: 11yrs at Perceptive Advisors responsible e.g. for investment in Myogen, Morphosys and Pharmacyclics and Acerta Pharma, where he was a member of the founding team as well as BOD.

Graduate of Columbia University.

TADEUSZ WESOLOWSKI
Ph.D.

Highly experienced investor and manager.

Past: Founder and CEO of PROSPER, for more than 17 years one of the leading pharmaceutical distributors in Poland.

BOD: Neuca, wholesale distributor of pharmaceuticals.

3 ECONOMIC AND FINANCIAL HIGHLIGHTS

3.1. Financial Results Obtained in the Reporting Period

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., Ardigen S.A., Selvita Ltd., and Selvita Inc.

As a result of the split, Ryvu continues to focus on development of small molecule therapeutics in oncology and Selvita provides contract research services for third parties. Acquiring company (Selvita) has assumed Selvita name and brand and Ryvu has adopted a new name and brand following October 1, 2019.

In connection with the above, the data presented in the financial statements for 2019 prepared in accordance with Polish accounting principles includes three quarters of continued and spin-off (discontinued) operations, and the fourth quarter of only continued operations, i.e. the innovation segment. In case of the data for 2018, it includes both continued and spin-off operations throughout the period.

The differences in the values of disclosed data between the financial statements prepared in accordance with Polish accounting principles and the financial statements that would have been prepared in accordance with IAS were presented and explained in the financial statements in Note No. 1.

Selected income statement data are as follows:

Ryvu Therapeutics S.A. (formerly Selvita S.A.)	Data in PLN thousand				Data in EUR thousand			
Item	From 01.01.2019 to 31.12.2019	From 01.01.2018 to 31.12.2018	From 01.10.2019 to 31.12.2019	From 01.10.2018 to 31.12.2018	From 01.01.2019 to 31.12.2019	From 01.01.2018 to 31.12.2018	From 01.10.2019 to 31.12.2019	From 01.10.2018 to 31.12.2018
Revenues from sales	**42 567**	51 680	**649**	12 911	9 895	12 112	152	2 998
Revenues from subsidies	**31 187**	27 440	**7 506**	10 489	7 250	6 431	1 753	2 435
Revenues from R&D projects	**-**	-	**-**	-	-	-	-	-
Other operating revenues	**790**	611	**112**	324	184	143	26	75
Revenues on operating activities	**74 544**	79 731	**8 267**	23 724	17 329	18 686	1 931	5 508
Operating expenses	**-119 683**	-104 074	**-19 443**	-37 193	-27 822	-24 391	-4 541	-8 635
Depreciation	**-9 109**	-7 086	**-1 904**	-2 166	-2 118	-1 661	-445	-503
Profit/loss on operating activities (EBIT)	**-45 139**	-24 343	**-11 176**	-13 469	-10 493	-5 705	-2 610	-3 127
Profit/loss before income tax	**-36 029**	-22 981	**-11 090**	-13 153	-8 375	-5 386	-2 590	-3 054
Net profit/loss	**-35 999**	-23 056	**-11 083**	-13 184	-8 368	-5 403	-2 589	-3 061
EBITDA	**-36 030**	-17 257	**-9 272**	-11 303	-8 376	-4 044	-2 166	-2 624
Net cash flow from operating activities	**-17 401**	-26 046	**-12 812**	-1 273	-4 045	-6 104	-2 993	-296
Net cash flows from investing activities	**-7 936**	-31 571	**-1 031**	20 860	-1 845	-7 399	-241	4 843
Net cash flows from financing activities	**2 586**	127 870	**-3 109**	-16 617	601	29 968	-726	-3 858
Total net cash flow	**-22 751**	70 253	**-16 952**	2 970	-5 289	16 465	-3 960	690
Number of shares	**15 971 229**	15 522 744	**15 971 229**	15 971 229	15 971 229	15 522 744	15 971 229	15 971 229
Profit (loss) per share (in PLN) – continued operations	**-2,25**	-1,49	**-0,69**	-0,83	-0,52	-0,35	-0,16	-0,19
Diluted profit (loss) per share (in PLN) – continued	**-2,25**	-1,49	**-0,69**	-0,83	-0,52	-0,35	-0,16	-0,19
Book value per share (in PLN) – continued operations	**6,33**	9,76	**6,33**	9,49	1,49	2,27	1,49	2,21
Diluted book value per share (in PLN) – continued	**6,33**	9,76	**6,33**	9,49	1,49	2,27	1,49	2,21
Declared or paid dividend per share (in PLN)	-	-	-	-	-	-	-	-

Selected balance sheet data are as follows:

Ryvu Therapeutics S.A. (formerly Selvita S.A.)	Data in PLN thousand		Data in EUR thousand	
Item	31.12.2019	31.12.2018	31.12.2019	31.12.2018
Total assets	157 624	197 613	37 014	45 957
Short-term receivables	9 475	18 577	2 225	4 320
Cash and cash equivalents	72 107	94 858	16 932	22 060
Other financial assets	-	15 046	-	3 499
Total liabilities	56 464	46 036	13 259	10 706
Long-term liabilities	5 290	5 896	1 242	1 371
Short-term liabilities	25 159	22 554	5 908	5 245
Total equity	101 160	151 577	23 755	35 250
Share capital	6 388	6 388	1 500	1 486

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 01/01/2019 – 31/12/2019: PLN 4.3018;
   - for the period from 01/01/2018 – 31/12/2018: PLN 4.2669.
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 2019: PLN 4.2585;
   - as of 31 December 2018: PLN 4.3000.

3.2. Management Board's comments on factors and events affecting the financial results

During the reporting period, the Company is still in the phase of very intensive investment spending, started in the previous year, as part of the implementation of the strategy for years 2017-2021. Over PLN 130 million obtained in the successful offering of shares in 2018 has enabled the increase of expenditures on the research and development projects, which will be commercialized at later stages, what in the assessment of Management Board, will secure better financial conditions of the commercialization.

After the above-mentioned split of the company, the Ryvu Therapeutics S.A. has only one operational segment, i.e. innovative segment.

In 2019, Ryvu Therapeutics S.A. recognised total operating revenue of PLN 74,544 thousand, which constitutes an decrease of 7% compared to the corresponding period in 2018, when total operating revenue amounted to PLN 79,731 thousand. The decrease in revenue is due to the significant decrease in revenue from sales (decrease of PLN 9,113 thousand, partially compensated with the increase in revenues from subsidy (increase of PLN 3,747 thousand) comparing to the corresponding period in 2018. The decrease in revenues from sales is mainly due to the lack of revenues from service activities in the fourth quarter of 2019 (this activity was transferred to Selvita S.A.) and, additionally, the reduction in the involvement of employees of Ryvu Therapeutics S.A. in the sales of external projects in favor of internal projects (including subsidized projects). The increase of subsidy revenue, compared to the corresponding period of 2018, is primarily a result of the increase in the costs incurred for new innovative projects implemented under Ryvu's strategy for years 2017-2021.

In the fourth quarter of 2019, Ryvu Therapeutics S.A. reported operating revenue of PLN 8,267 thousand, which means a decrease by PLN 15,457 thousand compared to the fourth quarter of 2018, when revenues amounted to PLN 23,724 thousand. The decrease is mainly due to the split of the organized part of the enterprise discussed above and its transfer to Selvita S.A., and the lack of these revenues in the fourth quarter of 2019.

In 2019, Ryvu Therapeutics S.A. reported a net loss as well as the loss on the operational level. This is a result of the implementation of Company's strategy adopted in 2017, according to which the innovation segment 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, 2019, amounted to PLN 35,999 thousand in comparison to the net loss of PLN 23,056 thousand in the corresponding period of 2018. The higher loss in 2019 is the result of the higher spending on the research projects, in particular, those related to the launch of SEL120 clinical trials, and the fact that the Company is strongly focused on the development of own research projects and preparing them for commercialization at a later stage of development.

3.3. The Company's Assets and the Structure of Assets and Liabilities

As of December 31, 2019, the value of the Company's assets was PLN 157,624 thousand and decreased by PLN 39,989 thousand compared to the end of 2018 (PLN 197,613 thousand), mainly due to above-mentioned split of Ryvu Therapeutics S.A. At the end of 2019, the highest value of current assets is the cash which amounted to PLN 72,107 thousand (at the end of 2018 it was PLN 94,858 thousand). The decrease in cash and other financial assets results, in addition to the fact of the split of the Issuer, from the spending incurred on research projects and the construction of the Research and Development Centre for Innovative Medicines (named 'CBR'). Fixed assets are mainly aforementioned expenditures on CBR and laboratory equipment, deferred tax assets of PLN 350 thousand and other long-term financial assets of PLN 679 thousand. The value of non-current assets increased in comparison to December 31, 2018, by PLN 18,106 thousand. The increase consists mainly of the above-mentioned expenditures on CBR.

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

	31/12/2019	31/12/2018
Current ratio **current assets/current liabilities including short-term provisions and accruals (excl. deferred revenues)**	3.58	5.57
Quick ratio **current assets-inventory)/current liabilities including short-term provisions and accruals (excl. deferred revenues)**	3.52	6.50

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.

The main item in the Ryvu Therapeutics S.A.'s equity and liabilities is equity, which amounted to PLN 101,160 thousand as of December 31, 2019, and decreased by PLN 50,417 thousand compared to 31 December 2018. The decrease in equity is mainly a result of the settlement of the split of the Company and the net loss for the period. The second largest source of assets' funding is long-term liabilities which amounted to PLN 5,290 thousand at the end of 2019.

3.4. Current and Projected Financial Condition

The Company's financial position as of the report date is good. As of December 31, 2019, the value of the Company's cash amounted to PLN 72,107 thousand, and as of the April 6, 2020, it was PLN 58,975 thousand.

The Company meets its obligations timely and maintains sustainable cash levels ensuring its financial liquidity. Cash inflow from the share issue from Q1 2018 and cash generated from the commercialization of their projects allows the Company to execute its planned investments, in particular, the development of the ongoing and new innovative projects and expansion of laboratory infrastructure. Future Company's revenue depends strongly on the ability to commercialize the research projects.

3.5. Significant off-balance sheet items

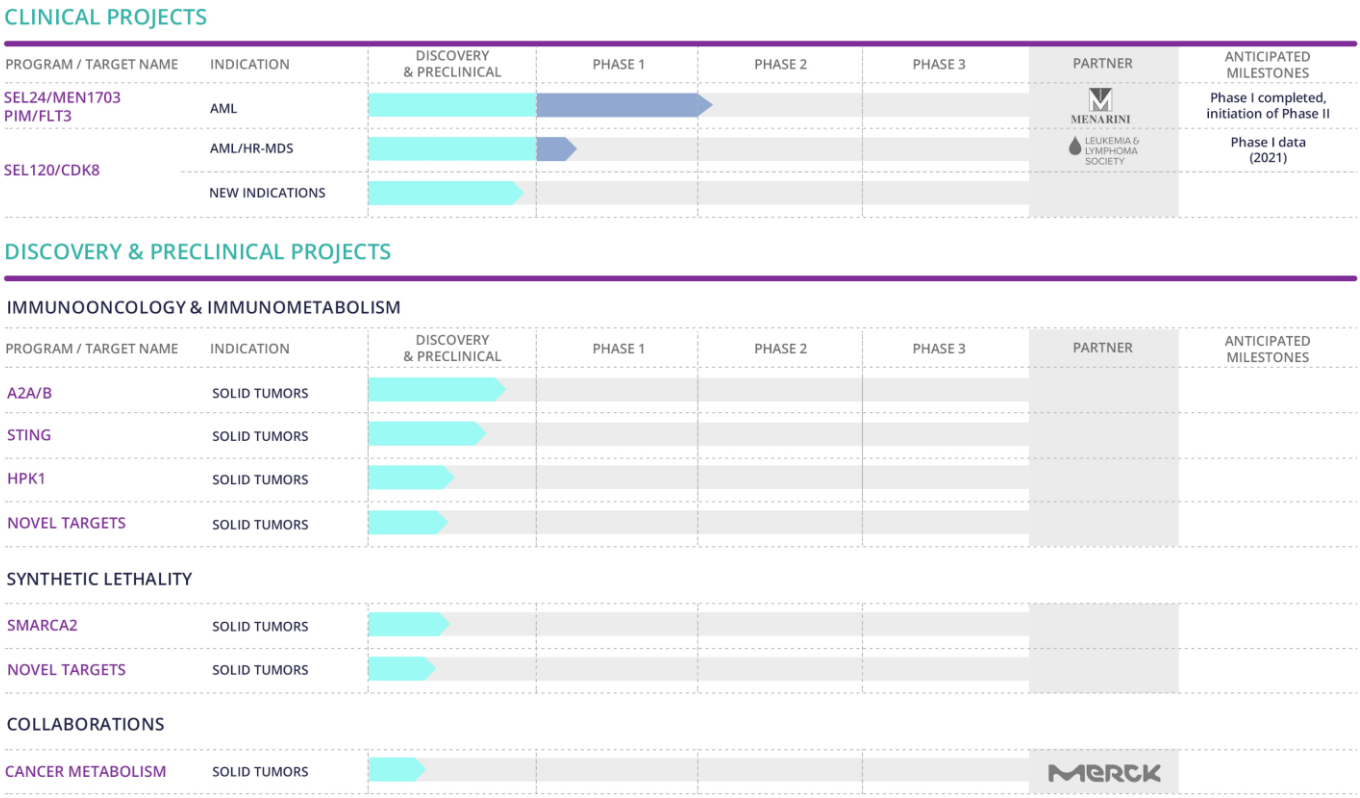
Significant off-balance sheet items are described in Note 51 to the financial statements.

4 INFORMATION ON THE COMPANY'S ACTIVITY IN 2019

4.1 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.



4.1.1 Clinical stage projects

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 was discovered by Ryvu (previously: Selvita) 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 study. Details of the study can be found at ClinicalTrials.gov under the identifier NCT03008187 (https://clinicaltrials.gov/ct2/show/NCT03008187).

On March 5, 2020 Ryvu Therapeutics received information from the Menarini Group about the successful completion of Phase I dose escalation study and establishing of the recommended dose for Phase II studies of the drug. The second part of the study – the expansion cohort at the recommended dose level is planned to confirm the safety profile of the compound and assess its activity. As indicated in the abstracts and posters published by Menarini at American Society of Clinical Oncology Conference in May and European Hematology Association in June, as well as during American Society of Hematology, ASH in December, the phase II of the study, will be extended in the US and Europe. Ryvu receives information from Menarini on the study progress during periodic technical meetings and steering committee meetings. Ryvu is also involved in translational research on the program funded by Menarini.

SEL120

SEL120 is a highly selective, orally administered small molecule CDK8 kinase inhibitor. Preclinical studies have indicated a crucial role for CDK8 in the regulation of oncogenic gene expression, which is important in the disease biology of a number of malignancies. In preclinical studies, inhibition of CDK8 results in enhanced cytotoxicity towards cancer cells over healthy cells, and induces cell differentiation. By targeting the population of leukemic stem cells in Acute Myeloid Leukemia (AML), CDK8 inhibition offers the potential to improve upon existing marketed treatments. SEL120 activity has also been explored in preclinical studies of a number of other hematological malignancies, such as lymphomas and solid tumors (eg. Breast cancer), either as single agent or in combination with currently approved anticancer agents such as chemotherapy, immunotherapy or targeted therapeutic medicines. Results of the collaboration with scientists from the Lund University validated SEL120 as a promising agent in the treatment of ribosomopathies, such as Diamond-Blackfan anemia, a rare hematological disease in both pediatric and adult patient population, with a critical unmet medical need.

Phase 1b clinical trial of SEL120 in adult patients with relapsed or refractory AML or high-risk myelodysplastic syndrome (HR-MDS) is enrolling since September 2019, and currently is ongoing in six investigational sites in USA. The primary aim of this study is to evaluate the safety and tolerability of SEL120 as well as establish its recommended dose for phase 2 part of the study (RP2D) and further development. Secondary endpoints include measurements of pharmacokinetic properties and an assessment of signs of clinical activity. Response to SEL120 will be evaluated by the study protocol predefined state of art response criteria per each disease. In addition, the exploratory objective of the study investigates the relevant biomarkers of response to treatment with SEL120, such as STAT5 phosphorylation in patients samples. The study is registered at ClinicalTrials.gov under the identifier NCT04021368 (https://clinicaltrials.gov/ct2/show/NCT04021368).

The SEL120 program development in hematological malignancies is supported scientifically and financially by the Leukemia and Lymphoma Society's (LLS) Therapy Acceleration Program (TAP).

In 2019 Ryvu achieved several major clinical milestones for this program, including approval of IND (Investigational New Drug) application for the aforementioned first-in-human (FIH) Phase Ib clinical study (CLI120-001) by the United States Food and Drug Agency (FDA) and the relevant Institutional Review Boards (IRBs); establishing the first global Scientific Advisory Board (SAB) for SEL120 with its 1st meeting held on 22nd February 2019 in Krakow, Poland; selection and activation of five accredited investigational sites in USA; the formal start of the study with dosing the first patient (FPI) on 4th September 2019, which resulted in Ryvu receiving a milestone payment from LLS in the amount of USD 0.25 million. In addition we presented the first information of the study CLI120-001 in progress, at the international high impact congress of American Society of Hematology (ASH), in December 2019, in Orlando, USA (ASH publication:

https://ashpublications.org/blood/article/134/Supplement_1/2651/423341/SEL120-a-First-in-Class-CDK8-19-Inhibitor-As-a).

Conference materials are available at: https://ryvu.com/our-research/

4.1.2 Preclinical and discovery stage projects

Immuno-oncology and immunometabolism projects

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

Immunometabolism programs are focused on molecular targets involved in adenosine signalling pathways. Adenosine is one of the major microenvironmental immunosuppressive factors responsible for tumor immune escape. It mediates the cancer resistance mechanisms to the attack of immune system. Inhibition of both the production of adenosine by cancer cells (CD39/CD73 enzymes) and its effects on the immune cells (A2A/B receptors) is a novel therapeutic strategy. In 2019 advanced series optimization and characterization led to the selection of a preclinical candidate – a dual A2A/B receptor antagonist able to reverse the immunosuppressive effects of high adenosine concentration, which is a hallmark of multiple most resistant cancers. Ryvu has shown that the simultaneous inhibition of A2A and A2B receptors by small molecule antagonists restores the functions of several subtypes of immune cells, enhancing the effects of immune system activation *in vitro* and *in vivo*. The A2A/B antagonists promote the secretion of pro-inflammatory cytokines by T cells and dendritic cells, repolarize immunosuppressive macrophages to a proinflammatory M1-like subtype and inhibit the secretion of VEGF involved in angiogenesis. The effective *in vitro* immunoactivation in the high-adenenosine conditions has been also confirmed *in vivo* in a mouse model. The effective inhibition of both A2A/B receptors at high adenosine concentrations is unique and outperforms currently publicly disclosed antagonists in the field, constituting a strong competitive advantage of Ryvu.

A comprehensive DMPK and safety pharmacology characterization (PK and metabolite identification in higher species, off-target panels, drug-drug interaction potential, cardiac safety and human dose predictions) allowed for selection of a preclinical candidate with optimal features. Currently undergoing non-GLP toxicology studies to confirm the safety profile in rodents and higher species are planned to be completed in H1 2020. Ryvu plans to initiate IND-enabling studies required for further progression into clinical trials in H2 2020. In parallel, translational research is underway to support the development of patient stratification strategies and optimal combination therapy in clinical trials.

The latest Ryvu advances in novel A2A/A2B antagonists program were presented in November 2019 at the 34th Annual Meeting of The Society for Immunotherapy of Cancer (SITC) in the USA. The poster is available on Ryvu's website at https://ryvu.com/pl/inwestorzy-media/publikacje/.

The second most advanced project in the immune-oncology portfolio focuses on small molecule, direct STING agonists. Ryvu developed systemic STING agonists efficiently activating *in vitro* human and mouse antigen-presenting immune cells (dendritic cells and macrophages). The lead series maintains high activity in blood samples from human donors independent of STING mutations, which holds promise for therapeutic intervention in a wide patient population. Additionally, STING agonists effectively reverse *in vitro* immunosuppression in a human macrophage population, reactivating their antitumoral properties. The effect of macrophage phenotype switch and reduction of the expression of immunosuppressive

surface markers has also been confirmed *in vivo*. This mechanism could potentially uncover potential of checkpoint inhibitors in immunosuppressive tumor microenvironment, boosting therapeutic efficacy.

In 2019, Ryvu proved that proprietary STING agonists administered systemically effectively inhibit tumor growth and can lead to its complete regression in a mouse model of colorectal cancer. Cured animals were immune to the growth of re-implanted tumor cells in the re-challenge study, showing a long-lasting effect of immune memory. As a part of strategic development, an optimal *in vivo* schedule was determined for further research activities involving the design of a clinical trial protocol. Current work includes *in vitro* safety confirmation (drug-drug interaction, cardiac safety), DMPK profiling and wide selectivity panels. They aim is to select a preclinical candidate to initiate non-GLP safety studies in 2020.

The latest Ryvu advances in systemic STING agonists program were presented in November 2019 at the 34th Annual Meeting of The Society for Immunotherapy of Cancer (SITC) in the USA. The poster is available on Ryvu's website at https://ryvu.com/investors-media/publications/.

The immune-oncology project portfolio focuses also on identification of therapeutic targets that could simultaneously improve T cell function, tumor antigen presentation and combat the immunosuppressive tumor microenvironment. HPK1 (MAP4K1) is one of the major proteins involved in signalling cascade triggered by TCR activation. Inhibition of HPK1 kinase activity stimulates dendritic cells for antigen presentation, T cells for maturation and increased proliferation resulting in a pronounced antitumor response. The proprietary HPK1 inhibitors have been shown to inhibit kinase activity in the low nanomolar concentration range being one of the most potent inhibitors disclosed publicly. Substances developed by Ryvu have favourable selectivity towards other kinases from the MAP4K family and improved physicochemical parameters. HPK1 inhibitors enhanced activation of human and mouse T cells providing resistance to prostanglandin-mediated immune suppression. In addition, immunostimulatory properties translated into *in vivo* antitumor efficacy in a mouse colorectal cancer model. Optimization of the chemical series is underway. In 2020 intensive *in vivo* profiling is planned in order to identify inhibitors with the greatest therapeutic potential.

Synthetic lethality projects

Synthetic lethality projects are focused on resistant solid tumors with defined molecular background and haematological malignancies by inhibition of proteins responsible for epigenetic reprogramming of cancer cells.

One of the revealed protein targets for pharmacological inhibition is BRM/SMARCA2 to benefit patients with loss of function mutations in the SMARCA4 gene observed in over 8% of lung cancers (NSCLC) and other malignancies. Two unique approaches were developed in 2019: innovative, first-in-class allosteric inhibitors of ATPase/helicase activity of SMARCA2 and protein-degrading compounds using Proteolysis Targeting Chimera (PROTAC) technology. Current best compounds show satisfactory activity in low concentration range, high specificity and selectivity *in vitro*. Cellular profiling indicated on-target mechanism of action and differential activity in cells bearing loss of function mutations of SMARCA4, outperforming SMARCA2 inhibitors published in the public domain. Intensive optimization is currently underway to select the lead molecule with improved DMPK parameters allowing to demonstrate anti-tumor activity in animal models.

In February 2020 Ryvu received funding for the development of SMARCA2 inhibitors and other innovative programs in the area of synthetic lethality until phase I clinical trials under the contract with the National Center for Research and Development (NCBiR). The grant is aims at the "Development of targeted

therapies in oncology based on the mechanism of synthetic lethality" and covers the amount of PLN 32.7 million (USD 8.3 million).

Another Ryvu project targets cancers with a deletion of the metabolic MTAP gene. Current research focuses on the identification of unique chemical matter and the optimization of *in vitro* models for identification of lead compound in 2020. Other proprietary programs cannot be revealed due to confidentiality restrictions. Ryvu received funding from the National Center for Research and Development for this project in the amount of 39,5 MPLN (the total budget amounts to 67,9 MPLN).

Other projects

Ryvu 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.

4.2 Corporate milestones 2019/2020

ACHIEVED IN 2019

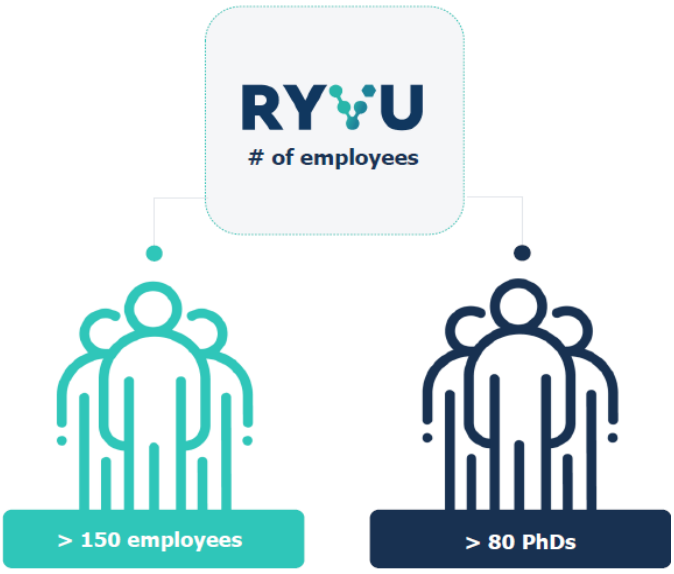
- First patient dosed with SEL120 in first indications (AML and HR-MDS) – September 2019
- Completed the regulatory process of the split of Ryvu (oncology) and Selvita (drug discovery and development services) segments
- $10.5M non-dilutive grant funding received for discovery and Phase I development of a synthetic lethality program
- Two SEL120 posters at ASH:
  - *Data from Preclinical Studies and Introduction to a Phase Ib Clinical Trial*
  - *CDK8 Inhibitors Induce Transcriptional Reprogramming of AML Cells Associated with Differentiation*
- SEL24 posters at ASCO, EHA and ASH

ACHIEVED/ANTICIPATED IN 2020

- SEL24
  - successful completion of Phase 1 Dose Escalation Study in AML announced on March 6, 2020
  - Phase 2 started
  - data from Phase 1 to be published by Menarini at an upcoming scientific conference
- SEL120
  - Orphan Drug Designation granted by the FDA on March 26, 2020
  - interim data from Phase 1b study by year-end
- Partnering deals in the pre-clinical pipeline
- One new pre-clinical candidate from internal discovery
- Differentiated data from pre-clinical programs in immunooncology, and synthetic lethality

5 EMPLOYMENT DETAILS

As of December, 31 2018, 553 employees were employed by Selvita Capital Group. As a result of the split, which was completed on October 1, 2019, 441 employees were transferred to Selvita S.A. (and its Affiliates) and 180 employees were employed by Ryvu Therapeutics. As of December, 31 2019 the staffing level in Ryvu Therapeutics was 173. In connection with the above and as a result of the corporate split of Ryvu Therapeutics the staffing level at Ryvu Therapeutics S.A. dropped slightly in 2019 comparing to 2018.



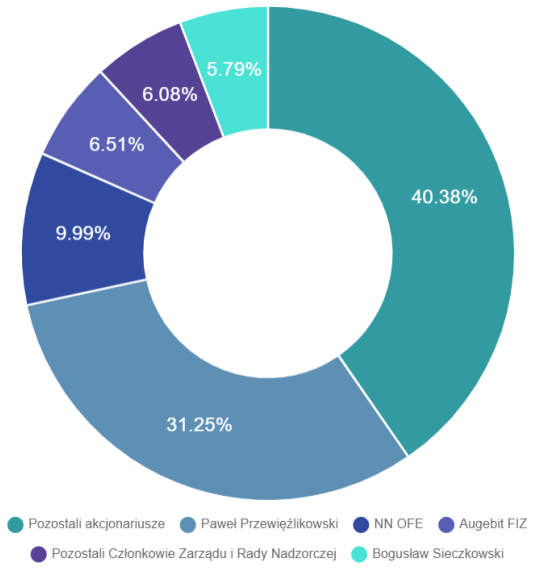
6 INFORMATION ON THE COMPANY'S SHAREHOLDING STRUCTURE

As of the date of publication of the Report, the shareholder structure of Ryvu Therapeutics S.A. including shareholders holding at least 5 % of votes at the Meeting of Shareholders, is as follows:

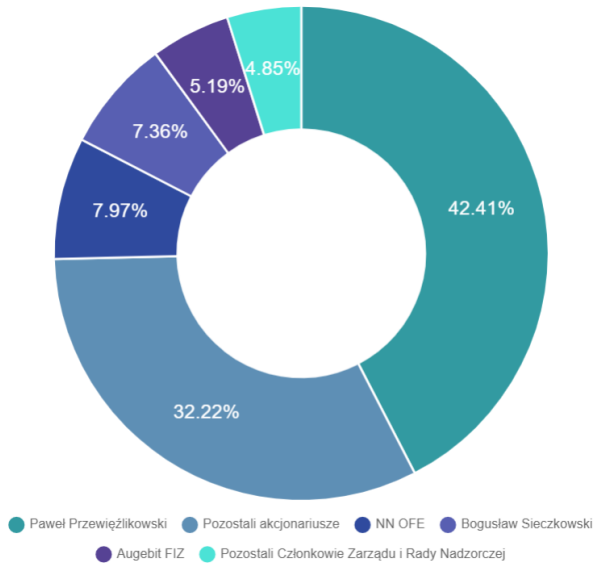
Shareholder	Shares	% of shares	Votes	% of votes
Paweł Przewięźlikowski	4 990 880	31,25%	8 490 880	42,41%
Bogusław Sieczkowski	924 384	5,79%	1 474 384	7,36%
Augebit FIZ*	1 039 738	6,51%	1 039 738	5,19%
Nationale Nederlanden OFE	1 594 749	9,99%	1 594 749	7,97%
Remaining shareholders	7 421 478	46,47%	7 421 478	37,07%
Total	**15 971 229**	**100,00%**	**20 021 229**	**100,00%**

**The beneficiary of Augebit FIZ is Tadeusz Wesołowski – Vice Chairman of Ryvu Therapeutics' Supervisory Board*

SHARE IN CAPITAL



SHARE IN VOTES



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RYVU THERAPEUTICS