

CURRENT STOCK REPORT 18/2020 JUNE, 15 2020

Ryvu Therapeutics Strategy for 2020-2022

The Management Board of Ryvu Therapeutics S.A. with its registered office in Krakow, Poland ("Company") has announced Company's new Strategy for 2020-2022 ("Strategy"), adopted on June, 15 2020, which further develops and revises goals set forth in the strategy document adopted by the Company in 2017 and published in a form of a current stock report no. 27/2017 of August 2, 2017 (document was prepared before Company's corporate split).

According to the Strategy, by the end of 2022, Company plans to:

- Complete Phase I clinical development of our lead fully-owned asset, SEL120 in AML/MDS;
- Expand therapeutic potential for SEL120 in solid tumors and launch a new Phase I study in selected indications in parallel to the ongoing hemato-oncology studies;
- Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in AML;
- Complete preclinical programs for A2A/A2B and STING candidates and advance at least one program into the Phase I of clinical trials;
- Strengthen our position in novel target discovery for synthetic lethality and immune-oncology and in developing novel, proprietary drug candidates;
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources, with at least one new partnering agreement in 2020.

For the execution of the Strategy by the end of 2021, Company intends to execute investments worth up to \$57.7m, including \$8.5m expenditure for advancement of SEL120 in AML/MDS, including completion of Phase 1 of Clinical Study, \$8.7m for development of SEL120 in solid tumors, including launch of a new Phase I study, \$8.2m for pre-clinical development, including conduct of IND-enabling preclinical studies and completion of IND submissions for A2A/A2B antagonist and STING agonist I/O programs, \$19.1m for advancement of early discovery synthetic lethality and I/O programs, \$4.2m for equipping of Ryvu R&D Centre and replacement Capex and \$9.0m to finance G&A costs.

The Company's Management Board considers the adoption of the Strategy for 2020-2022 as a significant corporate event, due to the fact that the Strategy sets out the Company's main goals, the achievement of which will affect the future financial situation of the Company and its further development.

The full content of the Strategy is attached to this report.

Legal basis: Article 17.1 of the Market Abuse Regulation

Representatives of the Company:

- Paweł Przewięźlikowski – President of the Management Board
- Krzysztof Brzózka – Vice President of the Management Board

Ryvu Therapeutics Strategy for 2020-2022

Executive Summary

The Management Board of Ryvu Therapeutics S.A. (“Ryvu Therapeutics” or “Ryvu”) hereby presents to the shareholders and other stakeholders the development strategy for 2020-2022. We will continue to focus on executing our mission to discover and develop drugs that will improve the lives of cancer patients and their families. According to the development plan, by the end of 2022, we plan to:

- Complete Phase I clinical development of our lead fully-owned asset, SEL120 in AML/MDS;
- Expand therapeutic potential for SEL120 in solid tumors and launch a new Phase I study in selected indications in parallel to the ongoing hemato-oncology studies;
- Support Phase II development by Menarini for lead partnered candidate, SEL24/MEN1703 in AML;
- Complete preclinical programs for A2A/A2B and STING candidates and advance at least one program into the Phase I of clinical trials;
- Strengthen our position in novel target discovery for synthetic lethality and immune-oncology and in developing novel, proprietary drug candidates;
- Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources, with at least one new partnering agreement in 2020.

- 1. Complete the Phase I clinical development of our lead fully-owned asset, SEL120 in AML/MDS. Expand the potential of SEL120 in solid tumors, and launching a new Phase I study in selected indications in parallel to the ongoing hemato-oncology studies.** SEL120, a highly selective first-in-class CDK8/19 inhibitor with broad potential in multiple indications, including blood cancers and solid tumors, is Ryvu’s fully owned lead clinical asset. In 2020-2022 the Company plans to continue to advance SEL120 through Phase I trials for AML/MDS and expand the potential of SEL120 in solid tumors, including breast cancers to achieve the following key milestones and value inflection points: final SEL120 Phase I data in AML/MDS in 2021; the entry of SEL120 to Phase I in solid tumors in 2021.
- 2. Support Phase II development for lead partnered candidate, SEL24, by Menarini in AML.** Ryvu’s pipeline includes also additional clinical-stage program: SEL24/MEN1703, a first-in-class PIM/FLT3 dual kinase inhibitor in oncology, globally partnered with Menarini. The program is currently advancing into Phase II trials in AML. Final Phase II readout for SEL24/MEN1703 is planned in 2022. Data publication timelines will depend on decisions of Joint Steering Committee of Menarini and Ryvu.
- 3. Complete preclinical programs for A2A/A2B and STING candidates and advance at least one program into the Phase I of clinical trials.** Ryvu plans to introduce to clinical development two other highly promising candidates from its early pipeline. As of the date of this document, two programs are planned to enter IND-enabling studies in 2020 - dual adenosine A2A/A2B antagonist

and small molecule STING agonist which should lead to the commencement of IND filings in H2 2021 and further advancement of at least one candidate into Phase I studies in 2022.

- 4. Strengthen our position in novel target discovery for synthetic lethality and immuno-oncology and in developing novel, proprietary drug candidates.** By the end of 2022, Ryvu intends to introduce to advanced lead stage or preclinical studies up to three projects from its current early pipeline, including targets in immuno-oncology (HPK1 inhibitor and novel targets) and synthetic lethality (SMARCA2 inhibitor and novel targets). Promising candidates within the early pipeline are expected to effectively reinforce the future growth potential of the Company and become promising value-drivers for Ryvu in the future.
- 5. Partner selected early pipeline programs with biotech and pharma companies providing synergistic competences and resources.** In our business development we will focus on partners providing additional expertise in solid tumors, experienced in running large clinical studies, especially in combinations and orphan drug developers. They will also provide financial resources which will allow smart and resolute development of Ryvu programs as well as additionally finance the unpartnered Ryvu pipeline to complement funding from grants and capital markets. In our partnering we will seek to retain an increasing part of deal economics including regional commercialization rights. Ryvu intends to sign at least one additional partnering agreement in 2020.

R&D budget and financing in H2 2020-2021. In the current total budget over the H2 2020-2021 period the Company plans to spend approx. \$57.7m, out of which \$8.5m will be dedicated to the SEL120 in AML/MDS, around \$8.7m to SEL120 in solid tumors, around \$8.2m for pre-clinical development of A2A/A2B antagonist and STING agonist and approx. \$19.1m on early discovery pipeline. In H2 2020-2021 the Company is planning to spend approx. \$4.2m for equipping of Ryvu R&D Center and replacement CapEx and approx. \$9.0m to finance G&A costs.

The company's Management Board assumes that the above investment expenditures will be financed from its own resources, partnering milestones, currently secured and future grants, as well as from funds raised in the form of a new capital increase (less than 20% of total number of shares that are currently listed on the main market of the Warsaw Stock Exchange, i.e. up to 2 384 245 shares, constituting 14.93% of the total number of shares). The Management Board is targeting to raise approx. \$38m from such a share issue depending on market conditions.

1. Ryvu – company overview

Ryvu was founded in 2007 by Paweł Przewięźlikowski (currently CEO of Ryvu Therapeutics) and Bogusław Sieczkowski (currently CEO of CRO Selvita). Until September 2019, Ryvu had operated under the business name “Selvita” in a hybrid structure of two independent segments - Innovations (proprietary drug discovery and clinical development projects) and the Services segment (CRO services to external clients). Selvita was listed on the Warsaw Stock Exchange in 2014. In September 2019, as a result of the corporate spin-off, CRO part of the business was spun off and the Company’s business name was changed to “Ryvu Therapeutics” (CRO business took over the business name “Selvita”).

In 2017, the Company published its development strategy for 2017-2021, focused on generating greater added value by independently financing the early phases of clinical trials, following the out-licensing of Ryvu’s most advanced project SEL24 to the Menarini Group in 2017 (following Phase I entry). The main goal of the 2017-2021 strategy was the clinical development of SEL120, our wholly-owned lead asset, a first-in-class CDK8/19 inhibitor for blood cancers and solid tumors. SEL120 entered the Phase I clinical trials in 2019. Ryvu’s other main recent achievements include the completion of Phase 1 in SEL24/MEN1703, a significant advancement of the early pipeline portfolio, progressing adenosine and STING programs, and completion of the Ryvu R&D Center. Moreover, the Company’s scientific and commercial capacity was further endorsed through the discovery partnership signed with Galapagos in April 2020, and successful progress at NodThera, a Ryvu spin-off, which successfully secured \$55m for further drug development and discovery in inflammation in June 2020.

Following on from the Company’s strategy published in 2017, this document presents Ryvu’s revised mid-term strategy, and our clinical goals and drug discovery development plans for 2020-2022.

2. Ryvu’s pipeline overview and 2020-2022 development perspectives

Program/ target name	Indication	Discovery and preclinical	Phase 1	Phase 2	Partners / Collaborators	2020	2021	2022+
SEL24 / MEN1703 PIM / FLT3	AML					<ul style="list-style-type: none"> ✓ Ph. I data • Ph. II initiation 	<ul style="list-style-type: none"> • Ph. II interim data 	<ul style="list-style-type: none"> • Ph. II complete
SEL120 CDK8	AML / MDS Solid tumors					<ul style="list-style-type: none"> • Ph. I dose escalation • Ph. I preparations 	<ul style="list-style-type: none"> • Initial Ph. Ib data • Final Ph. Ib data • Ph I top line results 	<ul style="list-style-type: none"> • Ph. II initiation • Interim data • Interim data
A2A / B	Solid tumors					<ul style="list-style-type: none"> • IND enabling studies 	<ul style="list-style-type: none"> • IND filing 	<ul style="list-style-type: none"> • Ph. I dose escalation
STING	Solid tumors					<ul style="list-style-type: none"> • IND enabling studies 	<ul style="list-style-type: none"> • IND filing 	<ul style="list-style-type: none"> • Ph. I dose escalation
HPK1	Solid tumors					<ul style="list-style-type: none"> • Lead optimization 	<ul style="list-style-type: none"> • Non-GLP tox 	<ul style="list-style-type: none"> • IND enabling studies
SMARCA2	Solid tumors					<ul style="list-style-type: none"> • <i>In vivo</i> PoC 	<ul style="list-style-type: none"> • Lead optimization 	<ul style="list-style-type: none"> • IND enabling studies
WRN	Solid tumors					<ul style="list-style-type: none"> • Hit ID 	<ul style="list-style-type: none"> • Hit-to-lead 	<ul style="list-style-type: none"> • Lead optimization • IND
MTAP	Solid tumors					<ul style="list-style-type: none"> • Hit ID 	<ul style="list-style-type: none"> • Hit-to-lead 	<ul style="list-style-type: none"> • Lead optimization • IND

Ryvu Therapeutics is a clinical stage biopharmaceutical company developing novel small molecule therapeutics addressing high value emerging targets and pathways, and limitations of current

treatments in oncology. Ryvu broad pipeline includes candidates with differentiated therapeutic mechanisms of action, including programs directed at kinases, synthetic lethality and immuno-oncology.

As at the date of this document, Ryvu has projects in multiple stages of development – 2 clinical assets, 2 in advanced discovery or preclinical, and several programs in discovery. All Ryvu programs have been discovered internally. All programs at an advanced stage have strong intellectual property rights and are protected by patent applications. Clinical projects are first-in-class kinase inhibitors with novel MoA to provide treatment benefits in multiple hematological and solid cancers.

3. Clinical stage projects

Ryvu Therapeutics is developing a broad pipeline addressing targets in oncology. As mentioned above, the Company's portfolio includes two first-in-class clinical stage projects - fully-owned SEL120 in AML/MDS, and SEL24/MEN1703 in AML partnered globally with Menarini. According to Datamonitor Healthcare, AML is the most common type of acute leukemia in adults, primarily diagnosed in late adulthood (median age of around 67 years) and more commonly in males. In 2018, around 158,400 new AML incident cases were reported worldwide, and this number is expected to increase to around 169,000 in 2027, as Datamonitor Healthcare noted. According to Evaluate Pharma data, the value of the AML market is \$1.2bn and could rise to \$8.0bn in 2025.

After little success for 40 years, the AML therapeutic landscape has seen rapid changes recently, with the approval of 8 new drugs by the Food and Drug Administration (FDA), providing both new opportunities and new challenges. These include FLT3 inhibitors midostaurin and gilteritinib, CPX-351 (liposomal cytarabine and daunorubicin), gemtuzumab ozogamicin (GO, anti-CD33 monoclonal antibody conjugated with calicheamicin), IDH1/IDH2 inhibitors ivosidenib and enasidenib, Hedgehog inhibitor glasdegib, and BCL-2 inhibitor venetoclax.

Despite marketing authorizations by the FDA for a number of new drugs, AML relapse is frequent and survival rates remain poor - the typical benefit of newly approved therapies on overall survival is several months and many of them rely on chemotherapy combinations with significant toxicity. Deepening the response to initial treatments in younger AML/MDS patients, and increasing the number of responders in elderly and unfit patients, also remains an unmet medical need.

It is expected that targeted therapies and immunotherapies will come to dominate the market, thus Ryvu recognized the high potential from targeting most resistant AML/MDS patients with CDK8/19 inhibitors. As at the date of this document, SEL120 is the only CDK8/19 inhibitor actively developed in the clinic.

3.1. SEL120 – lead asset, first in class CDK8/19 inhibitor

Therapeutic area. Ryvu's most important fully owned asset in clinical trials is SEL120, a first-in-class, orally administered small molecule, selective CDK8/19 inhibitor, addressing the transcription deregulation present in malignant cells. Robust efficacy in vitro and in vivo, identified stratification markers and well understood mechanism of action indicate the potential of SEL120 for a fully

personalized approach in the treatment of hematological malignancies, including AML/MDS. SEL120 has also demonstrated high potential in other hematopoietic, lymphoid malignancies and solid tumors, as a single agent and or in combination with SoC or new emerging agents, as shown preclinically. It potentially creates additional value driver for this project. 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.

Scientific rationale, preclinical results and validations. Inhibition of epigenetic and transcriptional regulators has emerged as a promising strategy in AML/MDS. Published results established CDK8 and CDK19 as targets in the treatment AML/MDS which addresses deregulated transcription present in multiple tumor types and identified as one of cancer hallmarks. Ryvu's SEL120 is a selective novel small molecule inhibitor of CDK8/19 for the treatment of AML/MDS to be administered orally in an outpatient basis.

SEL120 is particularly effective on undifferentiated AML/MDS STAT5-positive cancer cells with a stem cell characteristic. Importantly, efficacy of SEL120 in AML/MDS has been corroborated in models with a high translational potential, including activity demonstrated on primary AML cells *in vitro* and patient derived xenografts *in vivo*. Primary CD34+ AML/MDS cells treated with SEL120 showed reduced viability, induction of apoptotic cell death and lineage commitment. Furthermore, administration of the SEL120 inhibitor in mice bearing orthotopic AML patient-derived xenograft reduced tumor burden to the level undetectable by a flow cytometry leading to eradication of cancer cells. Efficacy was observed at well tolerated doses and was associated with recovery of bone marrow cells. Studies using established AML/MDS cell lines and primary cells derived from AML/MDS patients revealed strong proapoptotic activity of SEL120. Combinations of SEL120 with other agents indicates potential for a novel curative strategy in AML/MDS treatment. Ryvu showed that combination with Venetoclax is synergistic *in vitro* and leads to complete tumor regressions *in vivo*.

Competitive advantages. SEL120 has strong first-in-class potential with unique and differentiated mode of action. The competitive advantages of the drug include oral regimen, targeting leukemia stem cells responsible for resistance, promotion of cancer cells death (differential cytotoxicity on STAT5+ AML/MDS) and potentially safer treatment options (selectively targets leukemic cells sparing normal blood cells).

Orphan drug designation from FDA. FDA granted Ryvu Orphan Drug Designation for SEL120 in March 2020. The FDA's orphan drug designation allows the drug for the designated indication to be eligible for requesting a seven-year period of U.S. marketing exclusivity upon approval of the drug, as well as potential of other development assistance and financial incentives

Upcoming milestones and value inflection points in AML/MDS. The ongoing first-in-human (FIH), Phase Ib study in r/r AML and HR MDS for SEL120 is underway (as of the date of this document), enrolling at 6 sites in USA. Interim results are expected in 1H 2021, while final Phase I data in 2H 2021. Ryvu plans to activate 3 additional clinical sites – 2 in Poland and 1 in Europe in 2020/2021.

Cooperation with Leukemia and Lymphoma Society. The SEL120 project has been supported scientifically and financially by the Leukemia and Lymphoma Society Therapy Acceleration Program (LLS TAP) since August 2017. The Company has so far received a milestone payment from LLS TAP of \$1.75m (last payment received in September 2019 in connection with the dosing of the first patient). Overall, the Company is eligible to receive a total amount of funding from LLS TAP amounting to 3.25m.

Further clinical strategy in AML/MDS and solid tumors. Clinical strategy involves utilizing the potential of SEL120 in multiple indications. Current focus, as the fastest entry indication to market for SEL120, is on AML and MDS. The literature evidence for CDK8/19 roles in cancer together with proprietary results from Ryvu transitional research studies, also provides a strong rationale for further clinical development of SEL120 in other hematological malignancies (acute lymphoblastic leukemia (ALL), Janus kinase 2 (JAK2) mutated myelofibrosis), as well as in solid tumors, including breast, colorectal cancer and other tumor types.

Ryvu plans to expand the further clinical strategy for SEL120 in phase II studies in AML/MDS as monotherapy and in combination with chemotherapy and targeted therapeutics.

CDK8/19 as targets in breast cancer. Triple negative breast cancer accounts for approximately 14% of breast cancer, as Datamonitor noted. According to Datamonitor Healthcare, breast cancer is the second most popular cancer and the fifth cause of cancer-related deaths globally – in 2018 there were 2.1 million incident cases and 8.6 million five-year prevalent cases. Datamonitor Healthcare forecasts the former to increase to 2.3 million and the latter to increase to 9.3 million by 2027.

CDK8 and CDK19 are reported as targets in the treatment breast cancer. Robust preclinical efficacy in vitro and in vivo indicates potential of SEL120 for a personalized approach in the treatment of breast cancer, in particular estrogen and progesterone receptor negative breast cancer without overexpression of HER2 (triple negative breast cancer), where novel therapies are needed. Single agent efficacy in triple negative breast cancer mouse xenograft model suggests SEL120 may offer safer options to standard cisplatin-based therapy.

Considering all of the above options, Ryvu will continue its strategic expansion in the development of SEL120 in AML/MDS, and explore new possibilities in solid tumors, including triple negative breast cancer, as well as in other potential solid tumor indications. Ryvu intends SEL120 to enter Phase I in solid tumors in 2021.

3.2. SEL24 / MEN1703 – first-in-class dual PIM/FLT3 inhibitor

MEN1703/SEL24 is a clinical stage, first-in-class, dual PIM/FLT3 inhibitor currently progressing to Phase II studies in AML. SEL24 was discovered by Ryvu Therapeutics (at the time of discovery operating under the business name “Selvita”). The Company initiated clinical studies with this drug in 2017, and in the same year, Ryvu partnered the SEL24 program with a TOP40 Global Pharma Company, Menarini, based in Italy. The licensing deal includes a \$5.6m upfront payment, \$104m milestone payments and up to

double digit royalties. The Menarini Group is currently the sole sponsor of the SEL24/MEN1703 study - it is responsible for clinical development and funds the translational research at Ryvu.

Therapeutic area. SEL24 / MEN1703 is differentiated, selective, small molecule, first-in-class dual PIM/FLT3 kinase inhibitor. PIM and FLT3 kinases are two enzymes that are strongly implicated in malignant transformation of hematopoietic cells.

Clinical development. Menarini has successfully completed the dose-escalation part (Phase I) of the ongoing Phase I/II study with SEL24/MEN1703, triggering a €1.75m milestone payment to Ryvu. The recommended dose for the Phase II part of the study (cohort expansion) has been established. After the FDA approval received in March 2020, the trial is progressing into Phase II, which will evaluate the anti-leukemic activity of SEL24 / MEN1703, and is a potential key catalyst for Ryvu in the near term. The Company expects the initial Phase II results to be available in 2021, but the effect of the ongoing COVID-19 pandemic is not a fully determined factor at the moment. The Company looks forward to more clinical updates from Menarini on SEL24/MEN1703 as Menarini reported its plans to expand the trial to a larger number of centers in the US and Europe.

Phase I data summary (based on the EHA abstract from May 14, 2002). SEL24/MEN1703 demonstrated single agent efficacy in relapsed/refractory heavily pretreated FLT3 negative patients. As of February 11, 2020 (cut-off date), n=25 patients were treated across 6 dose levels (25, 50, 75, 100, 125, 150 mg). Objective responses were observed in 2 patients: one complete remission (CR) at 75 mg dose by Cycle 5 in an 81-y.o. patient with DNMT3A/IDH2 mutated AML progressed on enasidenib; one complete remission with incomplete hematologic recovery (CRi) at 125 mg dose by Cycle 5 in a 75-y.o. patient with prior myelodysplastic syndrome and ASXL1/EZH2 mutated AML relapsed after standard chemotherapy. SEL24/MEN1703 showed an acceptable safety profile up to the recommended dose (RD) established at 125 mg.

Upcoming milestones and value inflection points. Key expected milestones for the near future in the current Phase II include patient enrollment in 2020, initial data available in 2021 and final data in 2022. Data publication timelines will depend on decisions of Joint Steering Committee of Menarini and Ryvu.

4. Pre-clinical programs and discovery projects

Ryvu is executing two complementary strategic therapeutic approaches in early pipeline: synthetic lethality and immune-oncology. The Company has built in recent years immune-oncology capabilities to expand new opportunities in targeting patient's immune system through small molecule approaches. Moreover, Ryvu's synthetic lethality discovery engine is based on unique on a worldwide scale, proprietary synthetic lethality bioinformatic tool for robust identification of new synthetic lethal targets with SMARCA2 inhibitors as a frontrunner program.

Immunooncology

Ryvu has delivered within the last three years two differentiated pipeline candidates for preclinical development in 2020-2021: a dual A2A/A2B antagonist, potent in high adenosine concentrations and small molecule direct STING agonists for systemic delivery. Moreover, the Company's pipeline includes an HPK1 inhibitor project at lead optimization stage as at the date of this document.

4.1. Dual A2A/A2B adenosine receptor antagonists

Therapeutic area. The aim of projects in this area is the discovery and development of innovative immunotherapeutic, based on solutions that overcome the limitations of current therapies. Ryvu approach offers a differentiated treatment options for patients with aggressive, refractory tumors. Ryvu selected a preclinical candidate – a dual A2A/A2B receptor antagonist able to reverse the immunosuppressive effects of high adenosine concentration, which is a hallmark of several treatment-resistant cancers.

Pre-clinical studies. 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 elimination of immunosuppression to reinforce immune response. As at the date of this document, the undergoing non-GLP toxicology studies to confirm the safety profile in rodents and higher species are planned to be completed in H2 2020. Ryvu plans to initiate IND-enabling studies required for further progression into clinical trials in H2 2020.

Competitive advantages. Best-in-class potential. The major competitive advantage of Ryvu A2A/A2B antagonists lie in their dual mode of actions: inhibiting both A2A and A2B receptors to activate in vitro multiple subpopulations of immune system. In contrast to the majority of competitive antagonists losing activity in high adenosine concentration RVU330 has an advantage in retaining its nanomolar potency in tumor-like adenosine-rich environment. In the series of functional in vitro assays in primary immune cells, RVU330 restored release of several proinflammatory mediators that was impaired by the excessive levels of adenosine. High activity of RVU330 has been also manifested by confirmed efficacy as monotherapy in murine syngeneic model.

Indicative timetable: Ongoing non-GLP toxicology. IND filing in H2 2021.

4.2. Small molecule systemic STING agonist

Therapeutic area. 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. 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. Current work includes *in vitro* safety

DMPK profiling and wide selectivity panels. The aim is to select a preclinical candidate to initiate preclinical safety studies in 2H 2020.

Competitive advantages: Best-in-class potential. The therapy is based on small molecule, direct STING agonist with confirmed *in vitro* immuno-stimulatory properties on par or outperforming competitor compounds. It is worth to note that there is a high potency confirmed across multiple species and human STING haplotypes. Moreover, compounds are suitable for multiple routes of administration, including systemic intravenous dosing with confirmed *in vivo* antitumor efficacy leading to tumor eradication. Unique non-nucleotide, non-macrocyclic chemotype maintaining functional handles suitable for antibody-drug conjugates technology, allowing for targeted delivery.

Indicative timetable: Selection of a preclinical candidate – a proprietary STING agonist in 2H 2020. IND filing in H2 2021.

4.3. Selective HPK1 inhibitor

Therapeutic area. HPK1 (MAP4K1) is one of the major proteins involved in signaling 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.

Competitive advantage: The HPK1 inhibitors have the potential of best-in-class compounds. Developed HPK1 inhibitors inhibit kinase activity in the sub-nanomolar concentration range and are one of the strongest compounds of this type disclosed in the public domain. Substances developed by Ryvu have favorable selectivity towards other kinases from the MAP4K family and improved physicochemical parameters. Direct activation of T cells *in vitro* and reversal of the immunosuppression of human peripheral blood mononuclear cells (PBMCs) and T cells, restoring their ability to secrete proinflammatory cytokines was shown. In addition, *in vivo* anti-tumor efficacy was confirmed in a mouse colorectal cancer model in combination with checkpoint inhibitor (anti-mPD-1 antibody).

Indicative timetable: Ongoing lead optimization. 2H 2020 – optimized lead with combination strategy. H1 2021 - Initiation of non-GLP toxicology. IND filing 2022.

Synthetic lethality

There is a high need for novel targeted strategies in oncology. Synthetic lethality is one of the most innovative approaches for selective targeting of cancer cells with defined genetic background. SMARCA2 and SMARCA4 are two mutually exclusive helicase/ATPase catalytic subunits belonging to SWI/SNF chromatin remodeling complex. Development of SMARCA2 selective inhibitors/degraders is an attractive approach for cancer therapy with unmet medical need. The Company's pipeline includes apart from SMARCA2 inhibitor also other synthetic lethal targets such as WRN, new approaches in MTAP and confidential new targets.

4.4. Selective SMARCA2 degrader

Therapeutic area. Project is focused on resistant solid tumors with defined molecular background. Two unique approaches have been developed: innovative, first-in-class allosteric inhibitors of ATPase/helicase activity of SMARCA2 and protein-degrading compounds using Proteolysis Targeting Chimera (PROTAC) technology. 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 from NCBiR.

Competitive advantages. First in class allosteric inhibitors of SMARCA2/4 ATPase and selective degraders of SMARCA2 protein showing differential in SMARCA4 mutated cancer cells confirming synthetic lethal phenotype in vitro. Selective SMARCA2 degradation led to induction of apoptotic pathways and in consequence to a targeted cell death of SMARCA4 mutated cancers.

Indicative timetable: Ongoing hit-to-lead. 2021 – lead optimization, 2022 and beyond – non-GLP and IND enabling studies.

6. Summary of planned investment expenditures in H2 2020-2021 and their financing

Ryvu Therapeutics Strategy		Costs H2 2020 - 2021 [\$m]		Financing H2 2020 - 2021 [\$m]			
		Total costs [\$m]	Total costs allocation [%]	Grants and committed milestones [\$m]	Cash [\$m]	Share issue [\$m]	Share issue allocation [%]
Category							
SEL120	SEL120 - AML/MDS	8.5	15%	1.5	4.0	3.0	9%
	SEL120 - solid tumors	8.7	15%	0.0	0.0	8.7	27%
Preclinical programs	A2A/A2B and STING	8.2	14%	1.3	0.6	6.3	20%
Discovery programs	Synthetic lethality and immuno-oncology	19.1	33%	9.7	2.4	7.0	22%
G&A		9.0	16%	0.0	2.1	6.9	22%
R&D Center		4.2	7%	1.2	3.0	0.0	0%
TOTAL		57.7	100%	13.7	12.1	31.9	100%

The Company's budget over the H2 2020-2021 period assumes total costs of approximately \$57.7m, including:

- approximately \$8.5m for advancement of SEL120 in AML/MDS, including completion of Phase 1 dose escalation and safety expansion study, as well as survival follow-up;
- approximately \$8.7m for development of SEL120 in solid tumors, including conduct of Phase 1 dose escalation study with survival follow-up;
- approximately \$8.2m for pre-clinical development, including conduct of IND-enabling preclinical studies and completion of IND submissions for A2A/A2B antagonist and STING agonist I/O programs;
- approximately \$19.1m for advancement of early discovery synthetic lethality and I/O programs;
- approximately \$4.2m for equipping of Ryvu R&D Centre and replacement CapEx;
- approximately \$9.0m to finance G&A costs.

The Management Board of Ryvu assumes that the above investment expenditures will be financed from its existing cash (\$12.1m as of June 5, 2020), grants and committed milestones (\$13.7m) as well as well as from funds to be raised in the form of a capital increase through the issue of new shares (less than 20% of shares admitted to public trading, i.e. up to 2 384 245 shares, constituting 14.93% of the total share number). The company's Management Board is targeting to raise gross proceeds of approx. \$38m from a capital increase depending on market conditions.

Based on Company's current plans, the Management Board expects that the existing cash, together with available grant funding, committed milestones and net proceeds from the capital increase, will be sufficient to fund Company's operating expenses and capital expenditure requirements until H1 2022.

6. Impact of COVID-19 on the Company's operations

When analyzing the impact of COVID-19 on operations, the Company would like to highlight that its priority remains to ensure the safety and health of patients, collaborators and employees by introducing additional security procedures and measures, as well as implementing procedures securing the continuity of project execution during the pandemic. The Company indicates significant level of uncertainty regarding the development of the situation in the mid-term horizon, at the same time it emphasizes that has solid basis to expect that it will manage to achieve its planned business goals despite the unfavorable impact of the pandemic.

Clinical trials in locations impacted by Covid-19 such as the US have been and may in future be impacted by Covid-19 pandemic in multiple ways (slow or suspended enrollment, difficulties in patient monitoring, delayed DRCs, etc.). Clinical studies provide patients suffering from life threatening disorders such as AML/MDS with potential new therapeutic options – risk/benefit management policies are mainly dependent on individual investigational site decisions. In the first and second quarter of 2020, the pandemic affected the progress of the Issuer's clinical trials due to the fact that they are conducted in the centers located in the United States. Therefore, temporary problems were encountered in this period, such as suspension or slow-down in recruitment of new patients for SEL120 trials as well as restrictions

of access to the hospitals for clinical monitors. The resulting delay in SEL120 enrollment is approximately 3 months which in turn moves the first expected read-outs from this study from Q4 2020 to H1 2021. The Issuer follows the information provided by the FDA and adapts its activities to the current situation in the USA.

The pandemic had limited impact on Ryvu lab operations with additional work safety measures that needed to be implemented and transient suspension of lab activities from March 30 to April 9 during the peak of the local epidemic in Krakow. From April 12, 2020 Ryvu laboratories have been functioning without major limitations.

Due to the gradual “defrosting” of the economy commenced by the Polish government and public authorities in May / June 2020 Ryvu expects further improvement and stabilization of the situation in the near future. The Company’s Management Board will analyze the Company’s situation on an ongoing basis. New circumstances, if any, having a significant effect on the Company’s financial results and business position, will be communicated promptly in the individual current reports.

Kraków, June 15, 2020

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