Targeted therapeutics at the forefront of oncology

CORPORATE PRESENTATION

April 2020
Note on the presentation and forward looking statements

The presentation describes the business of Ryvu Therapeutics, biotechnology company publicly listed on the Warsaw Stock Exchange ("Company") and a focused oncology drug discovery and development company.

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Clinical stage company developing novel small molecule therapies addressing high value targets in oncology

**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 immuno-oncology
- 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

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* 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
### CLINICAL PROJECTS

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<tr>
<th>PROGRAM / TARGET NAME</th>
<th>INDICATION</th>
<th>DISCOVERY &amp; PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>PARTNER</th>
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<td>SEL24/MEN1703</td>
<td>AML</td>
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<td>Phase I data (2021)</td>
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### DISCOVERY & PRECLINICAL PROJECTS

#### IMMUNOONCOLOGY & IMMUNOMETABOLISM

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#### SYNTHETIC LETHALITY

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#### COLLABORATIONS

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Differentiated internally discovered small-molecule drug candidates and new programs

**TARGETED THERAPIES**

- **SEL24/MEN1703**
  - Dual PIM/FLT3 Inhibitor
  - Clinical
  - Partnered globally with Menarini
  - Dual targeting for broader efficacy and durable responses in AML
  - Potential for patients who relapse or are unresponsive to FLT3-selective inhibitors
  - First-in-class unique mechanism: direct cytotoxicity and eradication of leukemic stem cells as a single-agent
  - Administered independently of mutational status
  - Safe and effective combo with SoC and recent emerging agents

- **SEL120**
  - Selective CDK8 Inhibitor
  - Clinical
  - The only dual A2A/A2B receptor antagonist known to efficiently overcome immunosuppression in the adenosine-rich tumor microenvironment
  - Orders of magnitude more potent than known adenosine receptor antagonists in development, including AstraZeneca, Corvus
  - As efficacious in vivo in mice as the most potent disclosed STING agonists (GSK) while suitable for systemic as well as local delivery
  - Induces long-term immunological memory
  - Strong, direct binder to heterogenous STING alleles
  - Novel, emerging kinase target with unique dual potential in oncology: boosting immune response and making T cells more resistant to immunosuppressive tumor microenvironment
  - First-in-class potential

**IMMUNO-ONCOLOGY**

- **SEL24**
  - DUAL ADENOSINE A2A/A2B ANTAGONIST
  - Non-GLP Toxicology
  - Late Lead Optimization
  - Lead Optimization
  - A2A/A2B
    - As efficacious in vivo in mice as the most potent disclosed STING agonists (GSK) while suitable for systemic as well as local delivery
    - Orders of magnitude more potent than known adenosine receptor antagonists in development, including AstraZeneca, Corvus
    - The only dual A2A/A2B receptor antagonist known to efficiently overcome immunosuppression in the adenosine-rich tumor microenvironment
    - Strong, direct binder to heterogenous STING alleles
    - Novel, emerging kinase target with unique dual potential in oncology: boosting immune response and making T cells more resistant to immunosuppressive tumor microenvironment
    - First-in-class potential

- **SEL120**
  - SMALL MOLECULE SYSTEMIC STING AGONIST
  - Late Lead Optimization
  - Lead Optimization
  - SMARCA2
    - Targets SWI/SNF chromatin remodeling complex implicated in multiple cancers, including NSCLC
    - First-in-class potential
    - Most selective disclosed SMARCA2 with confirmed synthetically lethal phenotype
    - Unique allosteric ATPase inhibitors with PROTAC approach
  - STING
    - As efficacious in vivo in mice as the most potent disclosed STING agonists (GSK) while suitable for systemic as well as local delivery
    - Induces long-term immunological memory
    - Strong, direct binder to heterogenous STING alleles
  - HPK1
    - Novel, emerging kinase target with unique dual potential in oncology: boosting immune response and making T cells more resistant to immunosuppressive tumor microenvironment
    - First-in-class potential

**SYNTHETIC LETHALITY**

- **SMARCA4-SELECTIVE SMARCA2 DEGRADER**
- **SEL120**
  - Potentially targets SWI/SNF chromatin remodeling complex implicated in multiple cancers, including NSCLC
  - First-in-class potential
  - Most selective disclosed SMARCA2 with confirmed synthetically lethal phenotype
  - Unique allosteric ATPase inhibitors with PROTAC approach

**OTHER S/L TARGETS**

- **MTAP, WRN and multiple other undisclosed targets**
- **Unmet indications in solid tumors**
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
First therapeutic area of focus: acute myeloid leukemia

AML: Lowest survival among all blood cancers
26% of patients surviving 5 years after the diagnosis

- **2nd Most common leukemia type in adults**
- **67** Median age at diagnosis (in years)
- **30%** Highest incidence in the older adults
  - 3-4 people/100,000 individuals
- AML patients with a TTD mutation in the FMS-like tyrosine kinase 3 (FLT3) gene linked to a less favorable prognosis

Source: Leukemia & Lymphoma Society, 2018
Clinical landscape: small molecule targeted therapies for acute myeloid leukemia

- SEL120 is the only CDK8 inhibitor actively developed in the clinic
- MEN1703/SEL24 is an unique, clinical dual PIM/FLT3 inhibitor

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<tr>
<th>CDK8</th>
<th>FLT3</th>
<th>Dual PIM/FLT3</th>
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<td>FUJIFILM</td>
<td>MENARINI</td>
<td>Novartis</td>
<td>FORMA</td>
<td>BerGenBio</td>
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RYVU CLINICAL PROGRAMS FULLFIL UNMET NEEDS

- overcoming resistance to single-target mutation-specific inhibitors
- efficacy in broader patient populations
- reducing chemotherapy-based treatment regimens
- all oral regimen

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<thead>
<tr>
<th>Phase 1/2</th>
<th>Phase 3</th>
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SEL120: Highly selective first-in-class CDK8 inhibitor with broad potential in multiple indications

**SEL120**

- **BLOOD CANCERS**
  - AML
  - HR-MDS
  - ALL
  - LYMPHOMA

- **SOLID TUMORS**
  - COLORECTAL CANCER
  - BREAST CANCER

- **ORPHAN INDICATIONS**
  - DIAMOND-BLACKFAN ANEMIA

**Biology of CDK8 different from other CDKs**
- Different tumors responding to inhibitors
- Different toxicity profile
- Different stratification of responders and biomarkers of response

**Therapeutic potential via two mechanisms of action**
- Direct cytotoxicity (induction of apoptosis)
- Eradication of Leukemic Stem Cells (LSC) known to be responsible for tumor relapse in AML

**Different features compared to current treatments**
- Can be given to patients independently of mutational status
- Can be safely and effectively combined with standard-of-care chemo (e.g. Ara-C), as well as with recent emerging compounds (e.g. venetoclax)

SEL120 has received $3.25 M from Leukemia & Lymphoma Society Therapy Acceleration Program (TAP)
SEL120: potential role of CDK8 in AML treatment

- Selectively targets leukemic cells, sparing normal blood cells (unaffected normal hematopoiesis)
- Promotes cell death (differential cytotoxicity on STAT5+ AML)
- Represses increased levels of anti-apoptotic proteins and induces lineage commitment genes in undifferentiated AML cells

Rationale for CDK8 inhibitors in AML
- Transcriptional deregulation is a hallmark of AML
- CDK8 is a kinase subunit of the Mediator module serving as a bridge between basal transcription and regulatory elements involved in:
  - Deregulation of super enhancers (SE)
  - Affected differentiation and pro/anti-apoptotic genes

Efficacy of SEL120 - CDK8 inhibitor - in AML
Excellent on-target activity of SEL120 in pSTAT positive AML cell models

SEL120 is a potent and selective CDK8 inhibitor

Low nM activity on CDK8/CDK19 and excellent kinase selectivity (broad kinome)

Spares CDK2, CDK4, CDK6, CDK7, CDK9, etc.

U.S. patent granted in 2017

pSTAT1/pSTAT5 levels discriminate responder/non-responder

protein phosphorylation quantification (Western Blotting)
Complete regression with SEL120 in CD34+ AML patient-derived xenografts and bone marrow recovery

Research performed at: RY2U THERAPEUTICS

PDX cells

NSG mice

Vehicle / SEL120 46mg/kg

Leukemia burden analysis

17 days latency

Daily treatment 29/30 days

** COMPLETE REGRESSION (PERIPHERAL BLOOD) **

** HEMATOLOGIC RECOVERY (BONE MARROW) **

** REDUCED SPLENOMEGALY **
SEL120: Broad potential in oncology beyond AML and orphan blood disease

**SEL120**

- **BLOOD CANCER**
  - AML
  - HR-MDS
  - ALL
- **SOLID TUMORS**
  - COLORECTAL CANCER
- **ORPHAN DISEASES**
  - DIAMOND-BLACKFAN ANEMIA

**QUICK FACTS**

- SEL120 treatment results in on-target efficacy in preclinical models of AML and solid tumors
- Emerging therapeutic opportunities in solid cancers (breast and prostate cancer) and orphan hematological disorders

**MANTLE CELL LYMPHOMA**

- Z-138 xenograft (SCID/beige)
- Control
- SEL120 30 mg/kg BID

**DIAMOND BLACKFAN ANEMIA**

**WILMS’ TUMOR**

- Tumor volume kinetics SK-NEP1
- Control
- SEL120 30 mg/kg BID

**BREAST CANCER**

- Tumor volume kinetics MDA-MB-468
- Control, Cisplatin 20%, QD, PO
- Cisplatin, 8 mg/kg, E2W, IP
- SEL120 40 mg/kg, QD, PO

* Small Molecule Screens Identify CDK8-Inhibitors as Candidate Diamond-Blackfan Anemia Drugs – Lund University, Jun Chen, MD, PhD – Presentation at ASH 2018
Potential medical need for SEL120 in AML patients

**FIT PATIENTS**

- **NO RELEVANT MUTATIONS**
  - Intensive Induction Chemotherapy

- **MUTATION-DRIVEN**
  - Intensive Induction Chemotherapy + Targeted Therapy

**UNFIT PATIENTS**

- **NO RELEVANT MUTATIONS**
  - Low Intensity Therapy

- **MUTATION-DRIVEN**
  - Low Intensity Therapy or Targeted Therapy

**FIRST LINE**

- Aggressive Salvage Chemotherapy

**RELAPSED/REFRACTORY**

- SEL120 MONOTHERAPY

- SEL120 + TARGETED THERAPY

- SEL120 + LOW INTENSITY THERAPY

- SEL120 + TARGETED THERAPY
SEL120: Phase 1b study – first patient dosed in September 2019

Study title: A Phase 1b Study of SEL120 in Patients with Acute Myeloid Leukemia or High-Risk Myelodysplastic Syndrome

**STUDY POPULATION:**
- Patients with relapsed/refractory AML or high risk MDS
- No upfront patient stratification

**PRIMARY OBJECTIVES:**
- To assess safety and tolerability of SEL120 in patients with relapsed/refractory AML or HR-MDS
- To determine the recommended dose of SEL120 in patients with AML or HR-MDS

**SECONDARY OBJECTIVES:**
- To evaluate the pharmacokinetics of SEL120 in patients with AML or HR-MDS
- To evaluate the preliminary anti-leukemic activity of SEL120 in patients with AML or HR-MDS

**EXPLORATORY OBJECTIVE:**
- To evaluate the pharmacodynamics of SEL120 in patients with AML or HR-MDS

Orphan Drug Designation received from the FDA on March 27, 2020
Interim data from Phase 1b study in 2020. Final data in 2021
SEL24/MEN1703 is a differentiated, first-in-class PIM/FLT3 dual kinase inhibitor

**CLINICAL RATIONALE**

- PIM and FLT3 are oncogenes involved in AML
- Dual targeting creates potential for broader activity, more durable responses than selective FLT3 inhibitors such as gilteritinib
- Potential for treating patients that have relapsed on selective FLT3 inhibitors - PIM kinases are largely responsible for the development of resistance to FLT3 inhibitors
- On 5th of March 2020 Menarini informed Ryvu of the successful completion of Phase 1 dose escalation study for SEL24/MEN1703 and establishing of the recommended dose for Phase 2 studies of the drug, triggering a milestone payment for Ryvu
- Phase 2 dose expansion started in USA and planned in Europe

**VALUE THROUGH GLOBAL DEAL WITH MENARINI**

**DEVELOPED BY RYVU UP TO INITIATION OF CLINICAL STUDIES AND OUT-LICENSING**

- Partnered globally with Menarini (37th largest pharma company in the world, based in Italy) in 2017
- Menarini is fully responsible for clinical development and funds translational research at Ryvu

- **Upfront payment** $104M
- **Total potential value of milestones & refund of R&D costs** $5.6M
- **Up to double-digit royalties for Ryvu from Menarini**
**SEL24: Phase 1/2 study of SEL24/MEN1703**

**Study title:** A Phase 1/2 Study of SEL24 in Patients With Acute Myeloid Leukemia

- Study was initiated as the first clinical trial testing a dual PIM/FLT3 inhibitor in patients with AML regardless of the FLT3 status and potentially overcome resistance to FLT3 inhibitor treatment.

**AIM OF THE STUDY:** determine the recommended Phase 2 dose (RP2D), the PK profile and the single agent activity in R/R or newly diagnosed AML patients

**PLANS:**
- Menarini will publish study results at an upcoming scientific conference
- Cohort expansion at the recommended Phase 2 dose (RP2D) to confirm the safety profile and assess drug efficacy starting at multiple clinical sites in the U.S. in Q2
- Expansion in Europe in 2020

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**RECENT CONFERENCE UPDATES**

- **55th ASCO Annual Meeting 2019**

- **24th EHA Meeting 2019**

- **61ST ASH Congress 2019**
  “CLI24-001 (DIAMOND-01): First in Human Study of SEL24/MEN1703, First in Class, Orally Available Dual PIM/FLT3 Kinase Inhibitor, in Patients with Acute Myeloid Leukemia (Poster III #3920)”
Broad early discovery pipeline addressing major cancer-related molecular pathways

**FOCUS ON NOVEL TARGETS THAT LEVERAGE IN-HOUSE EXPERTISE**

- Synthetic lethality: potential pre-clinical candidates in 2021
- Immunoncology & immunometabolism: two potential initiation of IND-enabling studies in 2020
- Novel targets

- Novel targets and attractive fast follower programs
- Deep expertise focused on novel immunokinases, helicases, ATPases
- Challenging scaffold proteins
- Excellent know how from hit ID to clinical candidate
- Strong medicinal chemistry division
- Discovery engine to generate one new clinical candidate per year
Ryvu develops dual A2A/A2B adenosine receptor antagonists

**STATUS**
- Best-in-class dual antagonist of two adenosine receptors (A2A/B) capable to restore adenosine suppressed function at high adenosine concentrations

**RYVU STRATEGY**
- Synergistic potential in combination with immunotherapies (anti-PD1/PDL1, CAR-T), targeted therapies and chemotherapy

**SYNERGISTIC POTENTIAL**
- Current stage: non-GLP Tox studies

**UPCOMING VALUE INFLECTION POINTS**
- IND-enabling studies in 2020

**RYVU APPROACH PROVIDES STRONG PRECLINICAL COMPETITIVE ADVANTAGE**

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Adenosine is a potent and widespread immunosuppressive factor in TME that hampers the antitumor activity of all types of immune cells.
Ryvu has small molecule, direct, systemic STING agonists with confirmed antitumor efficacy in a mouse model

**KEY SUCCESS FACTORS**  
**COMPETITIVE EDGE**
- Small molecule, direct STING agonists with multiple routes of administration (intravenous, subcutaneous, intratumoral)
- Antitumor efficacy after systemic administration comparable to the best clinical small molecule agonist (GSK) and outperforming the intratumoral agents (Aduro)
- Standalone agonists or antibody-drug conjugates (ADC)
- Wide range of patients may benefit: active in multiple STING haplotypes

**VALUE INFLECTION POINTS**  
**MILESTONES**
- Preclinical candidate nomination for IND-enabling studies: 2020
- Clinical development: 2021

- Ryvu has unique, direct small-molecule STING agonists, with a chemotype distinct from any other known agonists with secured intellectual property
  - Immunostimulatory activity on antigen presenting cells) in nanomolar concentration range
  - *In vitro* and *in vivo* reactivation of immunosuppressive macrophages
  - Stable remissions and immunological memory in a CT26 mouse colorectal carcinoma model
Ryvu STING agonists lead to elimination of established tumors after systemic administration on par with the most potent disclosed STING agonist (GSK)

Ryvu STING agonist leads to dose-dependent tumor regression and complete remissions (CRs) in CT26 mouse model after intravenous administration on par with reference STING agonist diABZI (GSK) currently in Phase 1 clinical trials

CONTROL GROUP

REFERENCE GSK diABZI

1.5 mg/kg, E3Dx3, IV

CR 4/10

1 mg/kg, E3Dx3, IV

CR 0/10

2 mg/kg, E3Dx3, IV

CR 4/10

3 mg/kg, E3Dx3, IV

CR 5/10

RYVU STING AGONIST, INTRAVENOUS ADMINISTRATION
Ryvu develops selective SMARCA2 inhibitors and degraders targeting SMARCA4 loss of function tumors based on synthetic lethality mechanism

**Ryvu Approach**

**Status**
- Unique mechanism of action: Allosteric small molecule inhibitors of SMARCA2 ATPase activity with PROTACs probe based on proprietary Ryvu series

**Ryvu Strategy Success Factors**
- WELL DEFINED PATIENTS POPULATION
  - 5-10% NSCLC with inactivating (LOF) and truncating mutations SMARCA4 (BRG1)
  - Other SMARCA4 mut cancers (GI, Skin, Cervical, Bladder, Colorectal)

**Competitive Advantage**
- First-in-class potential
  - The only disclosed, most selective SMARCA2 over SMARCA4 ATPase PROTAC inhibitors known with confirmed synthetic lethal phenotype in vitro, competitors series based on bromodomain ligands

**Upcoming Value Inflection Point**
- Optimized lead with in vivo PoC in relevant mouse models carrying mutation in SMARCA4: 2020

**Ryvu SMARCA2 PROTACs Selectively Degradate SMARCA2**
- SMARCA2/SMARCA4 selectivity is critical for a therapeutic window

**Ryvu SMARCA2 Protac**

<table>
<thead>
<tr>
<th>Reference</th>
<th>MW/ logP/ PSA</th>
<th>Binding to SMARCA2 (Recombinant Protein)</th>
<th>Degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVU311-5363</td>
<td>&lt;1400/5.1/292</td>
<td>MST - DNA Kd (µM)</td>
<td>Remaining SMARCA2 after 24h</td>
</tr>
<tr>
<td></td>
<td>&lt;1000/3.7/209</td>
<td>0.7</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no binding (BRD domain)</td>
<td>Remaining SMARCA4 after 24h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>46%</td>
</tr>
<tr>
<td></td>
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<td>9%</td>
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**Boehringer Reference**

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<tr>
<td>RVU</td>
<td>0.12</td>
<td>0.37</td>
<td>1.11</td>
<td>3.33</td>
</tr>
<tr>
<td>SMARCA2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMARCA4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAPDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Covid-19 impact on Ryvu Therapeutics

Clinical trials:
- Industry risk: Clinical trials in locations impacted by Covid-19 such as the US may 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 and hrMDS with potential new therapeutic options – risk/benefit management policies will mainly dependent on site decisions
- As of March 30, 2020 five SEL120 sites confirmed continued patient enrollment, one site suspended enrollment

Laboratory operations:
- Ryvu introduced the first risk Covid-19 management steps already in February and reduced laboratory operations to critical experiments from March 30
- Most non-lab associates work from home
- Planned full restart of laboratory activities on April 12 depending on the situation in Krakow/Poland
- Thanks to the early government intervention (March 12) Poland is so far one of the countries least impacted by Covid-19 in Europe (as of March 30 <300 cases and <10 deaths per day, 16% average daily case dynamic between March 24 and March 31, trending lower)
- Outsourcing – limited capacity at some European CROs. Key providers less impacted. Risk-management with Asian CROs.

Other industry specific risks
- Slowed-down business development (pharma demand)
- Market volatility and more difficult access to capital

Currency risk
- $ (US. dollar) has gained 8% vs PLN (Polish zloty) since January 1, 2020
Ryvu investment highlights and near term milestones

- Developing **novel small molecule therapies** that address **emerging targets in oncology**
- Targeting **kinases, synthetic lethality, immune response and immuno-metabolism** pathways
- Validation from strategic **collaborations**
- **Partnership options** for early stage candidates
- **Limited cash burn** thanks to non-dilutive grants and cost-efficient discovery platform, significant resources located in Poland
- **Potential milestone payments** and royalties from partnered programs
- Steady **generation of differentiated candidates**

### Near Term Milestones:

- **SEL24/MEN1703**
  - Phase 1 data (2020)
- **SEL120**
  - Phase 1 interim data (2020)
- IND enabling studies for new pre-clinical candidates
- Data from early programs
- Partnering deals in the early pipeline
Contact data

Pawel Przewiezlikowski
Chief Executive Officer
pawel.przewiezlikowski@ryvu.com

Ryvu Therapeutics S.A.
www.ryvu.com
ryvu@ryvu.com
Management team with strong clinical and shareholder value creation track record

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAWEL PRZEWIEZLIKOWSKI, MSc, MBA</td>
<td>CEO and Founder</td>
</tr>
<tr>
<td>SETAREH SHAMSILI M.D., Ph.D.</td>
<td>CMO</td>
</tr>
<tr>
<td>KRZYSZTOF BRZOZKA Ph.D., MBA</td>
<td>CSO</td>
</tr>
<tr>
<td>PETER LITTLEWOOD Ph.D.</td>
<td>Director of DMPK</td>
</tr>
<tr>
<td>LUIGI STASI Ph.D.</td>
<td>Director of Chemistry</td>
</tr>
<tr>
<td>MONIKA DOBRZANSKA Ph.D.</td>
<td>Portfolio Management Director</td>
</tr>
<tr>
<td>MATEUSZ NOWAK Ph.D., MBA</td>
<td>Director of Early Discovery &amp; Innovation</td>
</tr>
<tr>
<td>TOMASZ RZYMSKI Ph.D., MBA</td>
<td>Director of Biology</td>
</tr>
<tr>
<td>KAMIL SITARZ Ph.D.</td>
<td>Director of R&amp;D Operations</td>
</tr>
<tr>
<td>TOMASZ NOCUN, MSc, MBA</td>
<td>Director of Research Financing</td>
</tr>
</tbody>
</table>
Supervisory Board assembling industry veterans and financing experts

RAFAŁ 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®, Ixifi® 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, Bivoca, Oncopeptides, Monoc. 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 Pharmacys and Acerta Pharma, where he was a member of the founding team as well as BOD.
Graduate of Columbia University.

TADEUSZ WESOŁOWSKI 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.
Scientific advisory board assembles expertise across hematology, oncology and precision medicine

GREG NOWAKOWSKI M.D.
Mayo Clinic

HEINZ-JOSEF LENZ M.D.
University of Southern California

RALF-DIETER HOFHEINZ M.D.
Mannheim University Hospital

MICHAEL SAVONA M.D.
Vanderbilt University

CEZARY SZCZYLIK M.D., Ph.D.
ECZ Otwock, Poland

ALWIN KRAEMER M.D.
University of Heidelberg

PRZEMYSŁAW JUSZCZYŃSKI M.D., Ph.D.
Warsaw Institute of Hematology & Transfusion

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Roche
EMD Serono
Genentech
AMGEN
Baxalta
Incyte
Gilead
Pfizer
Merck
Novartis
Astellas
Roche

Dana-Farber Cancer Institute

Danish Cancer Society

AACR

Bristol-Myers Squibb
SEL120 specifically targets STAT5+/CD34+ AML cells and induces differentiation in leukemic stem cells.
Single agent efficacy of SEL120 *in vivo*

- Favorable PK enables once daily oral administration or less frequently
- Efficacy *in vivo* correlates with inhibition of specific CDK8 biomarkers pSTAT1/STAT5

**SINGLE AGENT EFFICACY**
**IN CD34+ AND pSTAT5+ AML MODELS *IN VIVO***

**SINGLE AGENT EFFICACY**
**IN CD34- AND pSTAT5+ AML MODELS *IN VIVO***

---

![Graph A: Tumor volume kinetic, KG-1](image1)
![Graph B: Tumor volume kinetic, MV-4-11](image2)

**Legend:**
- Control, water Q.D
- SEL120 30 mg/kg, Q.D
- SEL120 60 mg/kg, Q.D
**In vitro** synergy of SEL120 in combination with Venetoclax (ABT-199)

**VENETOCLAX SENSITIVE**

- **MCL-1**: NOT ENOUGH MCL-1 TO SEQUESTER ALL THE RELEASED BIM
- **BIM**: INCREASED BIM
- **BAX/BAK**: CELL DEATH

**VENETOCLAX RESISTANT**

- **MCL-1**: MCL-1 SEQUESTERS ALL THE RELEASED BIM
- **BIM**: MCL-1
- **BAX/BAK**: NO CELL DEATH

**SEL120 potentially addresses treatment resistant disease through indirect MCL-1 downregulation in cancer cells**

**Compelling potential for SEL120 in combination with Venetoclax at low concentrations**

<table>
<thead>
<tr>
<th>SEL120 (µM)</th>
<th>Venetoclax (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.004</td>
<td>0.01</td>
</tr>
<tr>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>1.0</td>
<td>3.3</td>
</tr>
<tr>
<td>3.3</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**MCL-1**
- DMSO 0.1 0.3 1 3
- SEL120 0.1 0.3 1 3
- Venetoclax 0.1 0.3 1 3
- SEL120 [µM]

**BIM**
- DMSO 0.1 0.3 1 3
- SEL120 0.1 0.3 1 3
- Venetoclax 0.1 0.3 1 3

**Bax cleaved**
- DMSO 0.1 0.3 1 3
- SEL120 0.1 0.3 1 3
- Venetoclax 0.1 0.3 1 3

**Caspase-3 cleaved**
- DMSO 0.1 0.3 1 3
- SEL120 0.1 0.3 1 3
- Venetoclax 0.1 0.3 1 3

**Actin**
- DMSO 0.1 0.3 1 3
- SEL120 0.1 0.3 1 3
- Venetoclax 0.1 0.3 1 3
**In vivo** synergy of SEL120 in combination with Venetoclax (ABT-199)

AML regression and bone marrow recovery **in vivo**

**COMPLETE REGRESSION**

**HEMATOLOGIC RECOVERY** (BONE MARROW)

**TUMOR GROWTH INHIBITION AND COMPLETE REGRESSIONS**

- MV-411 cells
- IV NSG mice
- Latency
- SEL120+Venetoclax Daily, PO, 21 days
- Leukemia burden analysis

**Bone Marrow**

- % hCD45 cells
- Number of murine BM cells

- Vehicle
- ABT-199 100mg/kg
- SEL120 20mg/kg
- SEL120 40mg/kg
- ABT+SEL120 20mg/kg
- ABT+SEL120 40mg/kg

**NSG mice**

- IV
- Latency
- SEL120+Venetoclax Daily, PO, 21 days
- Leukemia burden analysis

**Tumor volume kinetics**

- Tumor volume (mm³)
- Days

- Complete regressions 3/10
Simultaneously targeting FLT3 and PIM may provide improved efficacy and durability over narrowly targeted agents.

**SEL24/MEN1703 VS PIM INHIBITOR AZD1208 AND FLT3 INHIBITOR QUIZARTINIB IN AML CELL LINES**

**MV-4-11 (FLT3-ITD positive)**

<table>
<thead>
<tr>
<th>GI50(µM)</th>
<th>SEL24/MEN1703</th>
<th>AZD1208</th>
<th>Quizartinib</th>
<th>Cytarabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>1.6</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td>0.4</td>
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<td>0.8</td>
<td>1.6</td>
</tr>
<tr>
<td>0.8</td>
<td></td>
<td></td>
<td>1.2</td>
<td>1.6</td>
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<tr>
<td>1.2</td>
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<tr>
<td>1.6</td>
<td></td>
<td></td>
<td>1.6</td>
<td>1.6</td>
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**MOLM-16 (FLT3-ITD negative)**

<table>
<thead>
<tr>
<th>GI50(µM)</th>
<th>SEL24/MEN1703</th>
<th>AZD1208</th>
<th>Quizartinib</th>
<th>Cytarabine</th>
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<tbody>
<tr>
<td>0</td>
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<td>0.7</td>
<td>0.35</td>
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</tr>
<tr>
<td>0.175</td>
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<tr>
<td>0.35</td>
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<td>0.525</td>
<td>0.7</td>
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<tr>
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<td>0.7</td>
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<td>1.0</td>
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</table>
Potent efficacy of oral SEL24/MEN1703 in models of multiple AML subtypes

**FLT3-ITD POSITIVE**

**MV-4-11**

- Tumor volume kinetics
- Control
- SEL24/MEN1703, 75 mg/kg BID
- SEL24/MEN1703, 25 mg/kg BID

**MOLM-13**

- Tumor volume kinetics
- Control
- SEL24/MEN1703, 75 mg/kg QD
- AZD1208, 30 mg/kg QD
- Quizartinib, 10 mg/kg QD

**MOLM-16**

- Tumor volume kinetics
- Control
- SEL24/MEN1703, 25 mg/kg BID
- Quizartinib, 10 mg/kg QD

**FLT3-ITD NEGATIVE**

**KG-1**

- Tumor volume kinetics
- Control
- SEL24/MEN1703, 50 mg/kg QD
- AZD1208, 30 mg/kg QD
- Quizartinib, 10 mg/kg QD

BID – twice a day, QD – once a day
**RVU330 - best-in-class dual A2A/A2B antagonist**

### Key Success Factors

- Best-in-class potential
  - The only dual A2A/A2B antagonist efficient in high adenosine tumor environment
- Dual mode of action manifesting in activity in all immune cell types, unlike competitors compounds, providing potentially more pronounced anti-tumor effect
- May be efficacious in patients in which „1st wave“ A2A (repositioned PD drugs) do not work

### Planned Inflection Points and Milestones

- Nomination of preclinical candidate and initiation of IND enabling studies: H1 2020
- Initiation of phase I clinical trials: 2021

**Ryvu developed most potent, known A2A/A2B antagonist** with nanomolar activity *in vitro* in functional immune assays outperforming competitors

**Confirmed immunostimulatory mode of action**
- Induction of antitumor cytokine production by T cells and dendritic cells – stimulation of both innate and adaptive immunity
- Macrophages repolarization
- NK cells mobilization
- Exceptionally potent, superior to clinical competitors, blockade of CREB phosphorylation in human whole blood assay – clinical biomarker used by most of competitors (Arcus, Corvus)
RVU330 efficiently modulates pCREB (main PD clinical biomarker used by competitors) in *in vitro* human whole blood assay.

### RVU330 modulates PD biomarker in CD4+ T-cells

<table>
<thead>
<tr>
<th></th>
<th>AZD4635</th>
<th>CPI-444</th>
<th>AB928</th>
<th>Example 7</th>
<th>RVU330</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCREB WBA CD4+ T cells EC$_{50}$ [nM]</td>
<td>1186 ± 860</td>
<td>7798 ± 1734</td>
<td>182 ± 140</td>
<td>1.1 ± 0.6</td>
<td>1.6 ± 0.9</td>
</tr>
<tr>
<td>pCREB WBA CD8+ T cells EC$_{50}$ [nM]</td>
<td>&gt; 10 000</td>
<td>&gt; 10 000</td>
<td>83.7 ± 0.1</td>
<td>2.4 ± 2.3</td>
<td>2.2 ± 1.4</td>
</tr>
</tbody>
</table>
RVU330 A2A/B antagonists outperform competitors in *in vitro* activation of immune cells at high adenosine concentrations.

**RVU330 restores functional activity CD4⁺ T cells that is suppressed by high adenosine concentration (IL-2 production)**

**RVU330 reactivates dendritic cells (moDC) suppressed by high adenosine concentration (TNFα production)**

<table>
<thead>
<tr>
<th></th>
<th>AZD4635</th>
<th>CPI-444</th>
<th>AB928</th>
<th>Example 7</th>
<th>RVU330</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFα moDCS - EC₅₀ [nM]</td>
<td>&gt;10 000</td>
<td>&gt;10 000</td>
<td>699 ± 144</td>
<td>&gt;3 000</td>
<td>13 ± 5</td>
</tr>
<tr>
<td>IL-2 CD4⁺ CELLS - EC₅₀ [nM]</td>
<td>&gt;10 000</td>
<td>&gt;10 000</td>
<td>203 ± 97</td>
<td>4 ± 0.1</td>
<td>0.4 ± 0.2</td>
</tr>
</tbody>
</table>
Ryvu STING agonist outperforms antitumor efficacy of Aduro agonist and provides immunological memory in mouse CT26 colorectal carcinoma model.

**CONTROL GROUP**

**REFERENCE ADURO ADU-S100**

- 5 mg/kg (100 µg), EODx3, IT
- CR 3/10

**RYVU STING AGONIST**

- 5 mg/kg (100 µg), EODx3, IT
- CR 7/10

Subcutaneous inoculation with CT26 mouse colorectal carcinoma cells

**1. INTRATUMORAL ADMINISTRATION OF STING AGONIST**

**2. MICE WITH TUMOR REGRESSION**

**3. RE-CHALLENGE**

Subcutaneous inoculation with CT26 mouse colorectal carcinoma cells

**4. LONG-TERM IMMUNOLOGICAL MEMORY**

No tumor growth

**5. CONTROL GROUP REFERENCE**

ADURO ADU-S100

RYVU STING AGONIST
Ryvu is developing next-generation direct STING agonists for immunotherapy of resistant tumors

**RYVU STRATEGY**

**STATUS**
Best-in-class small molecule direct, systemic STING agonists active across STING haplotypes

**RYVU STRATEGY**
Malignant tumors resistant to checkpoint inhibitor monotherapy; Synergistic potential in combination with immunotherapy (anti-PD1/PDL1, CTLA4), chemotherapy and radiotherapy

**SYNERGISTIC POTENTIAL**

**COLD, RESISTANT TUMORS**

AIM: ACTIVATION OF IMMUNE RESPONSE

**HOT, INFLAMED TUMORS**

AIM: OVERCOME IMMUNOSUPPRESSION

STING agonists mobilize immune system sensitizing resistant tumors to therapy

STING agonists are immune boosters inducing long-term immunological memory

STING agonists are developing next-generation direct STING agonists for immunotherapy of resistant tumors

STING agonists are immune boosters inducing long-term immunological memory

STING agonists mobilize immune system sensitizing resistant tumors to therapy

STING agonists are immune boosters inducing long-term immunological memory

STING agonists stimulate immune system facilitating tumor neoantigen presentation by dendritic cells, activation of CD8+ T cells and release of proinflammatory cytokines

STING agonists are immune boosters inducing long-term immunological memory

STING agonists stimulate immune system facilitating tumor neoantigen presentation by dendritic cells, activation of CD8+ T cells and release of proinflammatory cytokines
Ryvu STING agonists lead to elimination of established tumors after systemic administration

Ryvu STING agonist leads to dose-dependent tumor regression and complete remissions (CRs) in CT26 mouse model after intravenous administration on par with the most potent disclosed reference STING agonist (GSK) currently in Phase 1 clinical trials.
Ryvu is developing SMARCA2 inhibitors with first-in-class potential

**TOP SUCCESS FACTORS, COMPETITIVE ADVANTAGE**

- **First in class potential:**
  Most selective SMARCA2 over SMARCA4 inhibitors known with confirmed synthetic lethal phenotype *in vitro*

- **Unique mechanism of action:**
  Allosteric small molecule inhibitors of SMARCA2 ATPase activity
  Selective PROTACs based on proprietary Ryvu series

- **Well defined patient population**

**UPCOMING VALUE INFLECTION POINTS**

- **In vivo PoC in relevant mouse models carrying mutation in SMARCA4: 2020**

- Ryvu has the only disclosed program of small molecule allosteric inhibitors of ATPase activity and PROTAC series selectively degrading SMARCA2 showing synthetic lethal phenotype *in vitro*, competitor series based on bromodomain ligands

- **Strong responder hypothesis – validated panel of cancer cell lines carrying SMARCA4 LOF mutations; clearly defined patient population**

  - Confirmed targeted cell death in SMARCA4 mutated cancer cell lines (synthetic lethal phenotype) and strong differentiation factors from known competitors

  - Powerful Synthetic Lethality Platform consisting of unique bioinformatic tools and cellular models allowing identification and validation of novel synthetic lethal targets in oncology
Successful Ryvu spin-out company, NodThera

Discovery and development of next generation NLRP3 inflammasome inhibitors

~8.6% OWNED BY RYVU

First Ryvu deal in the immunology area

NodThera Ltd. was launched in 2016 by Epidarex Capital, based on research conducted at Ryvu since 2012

Focused on the treatment of diseases driven by chronic inflammation

Productive 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
Financial results – Ryvu (Selvita Oncology segment, exc. NodThera) 2018 and Q1-3 2019

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>Q1-3 2019</th>
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<tbody>
<tr>
<td>Revenues</td>
<td>9.7</td>
<td>6.7</td>
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<tr>
<td>Partnering</td>
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<td>0.9</td>
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<tr>
<td>Grants</td>
<td>7.1</td>
<td>5.8</td>
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<tr>
<td>Costs</td>
<td>16.6</td>
<td>15.7</td>
</tr>
<tr>
<td>EBIT</td>
<td>-6.9</td>
<td>-9.0</td>
</tr>
<tr>
<td>EBITDA (without impact of MSSF 16)</td>
<td>-5.8</td>
<td>-7.8</td>
</tr>
<tr>
<td>CAPEX</td>
<td>-4.3</td>
<td>-6.0</td>
</tr>
</tbody>
</table>

Cash position October 2019: $20M
### What sets Ryvu apart

<table>
<thead>
<tr>
<th>BROAD, DIVERSIFIED PIPELINE IN SMALL MOLECULE ONCOLOGY</th>
<th>HIGH THROUGHPUT DISCOVERY ENGINE</th>
<th>SCIENTIFIC AND ORGANIZATIONAL EXPERTISE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mix of wholly-owned and partnered programs</td>
<td>• 80 Ph.D.-level scientists</td>
<td>• Driven by breakthrough science</td>
</tr>
<tr>
<td>• Potential first-in-class, clinical stage candidates</td>
<td>• History of identifying molecules with differentiated properties</td>
<td>• Global partnerships with Menarini and Merck KGaA</td>
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<tr>
<td>• Diverse kinase, synthetic lethality, immuno-oncology and immunometabolism programs</td>
<td>• Plan to generate one new clinical candidate per year</td>
<td>• Research validated by Leukemia &amp; Lymphoma Society</td>
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<tr>
<td>• Strong early data relative to competitors</td>
<td>• Platforms, by design, address key challenges of current treatments</td>
<td>• Efficient R&amp;D organization</td>
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<tr>
<td></td>
<td>• Focus on internal development and partnering</td>
<td>• Secured non-dilutive financing with follow-on opportunities</td>
</tr>
</tbody>
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