Targeted therapeutics at the forefront of oncology

INVESTOR PRESENTATION

January 2020
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 biopharmaceutical company developing novel small molecule therapies addressing high value targets in precision oncology

ASSETS
- Fully-owned lead asset, first-in-class CDK8 inhibitor for blood cancers and solid tumors SEL120, first patient dosed in September 2019.
- First-in-class dual PIM/FLT3 inhibitor SEL24/MEN1703 for blood cancers partnered with Menarini currently in Phase 1/2 studies.
- All clinical trials of SEL24 and SEL120 are conducted in the U.S.

TWO PROJECTS IN CLINICAL TRIALS

STRATEGY
- Self-development of SEL120
- 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)
- ~ $200M market capitalization
- ~ $20M* in cash and short-term investments
- > $25M** in grant funding secured until 2023
- >150 employees

MATURE CORPORATE GOVERNANCE

* October 2019

** Maximum non-dilutive research funding if all projects succeed according to the current research plans and grant contracts
# Clinical Projects

## Broad pipeline addressing emerging targets in oncology

### Discovery & Preclinical Projects

#### Immunooncology & Immunometabolism

<table>
<thead>
<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>
<th>Anticipated Milestones</th>
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#### Synthetic Lethality

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<th>Partner</th>
<th>Anticipated Milestones</th>
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#### Collaborations

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Differentiated internally discovered small-molecule drug candidates and new programs

**TARGETED THERAPIES**

- **SEL24**
  - Dual PIM/FLT3 inhibitor
  - Clinical
  - Partnered globally with AstraZeneca
  - 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
  - Administered independently of mutational status
  - Safe and effective combo with SoC and recent emerging agents

- **SEL120**
  - Selective CDK8 inhibitor
  - Clinical
  - 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
  - Administered independently of mutational status
  - Safe and effective combo with SoC and recent emerging agents

**IMMUNO-ONCOLOGY**

- **A2A/A2B**
  - The only dual A2A/A2B receptor antagonist known to efficiently overcome immunosuppression in the adenosine-rich tumor microenvironment
  - As efficacious in vivo in mice as the most potent disclosed STING agonists (GSK) while suitable for systemic as well as local delivery
  - 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

- **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**

- **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

- **SEL24**
  - First in class potential
  - 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

- **SEL120**
  - First in class unique mechanism: direct cytotoxicity and eradication of leukemic stem cells
  - Administered independently of mutational status
  - Safe and effective combo with SoC and recent emerging agents

- **OTHER S/L TARGETS**
  - Multiple first-in-class undisclosed targets
  - Unmet indications in solid tumors
Corporate milestones

**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

**ANTICIPATED IN THE NEXT 12 MONTHS**

- Partnering deals in the pre-clinical pipeline
- One new pre-clinical candidate from internal discovery
- SEL24 - data published by Menarini from Phase 1 Dose Escalation Study
- SEL120 – interim data from Phase 1b study
- Differentiated data from pre-clinical programs in immunooncology, immunometabolism 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

*Most common leukemia type in adults*

*Median age at diagnosis (in years)*
67

*Highest incidence in the older adults*
3-4 people/100,000 individuals

*AML patients with a ITD 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

<table>
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<tr>
<th>CDK8</th>
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<th>Dual PIM/FLT3</th>
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RYVU CLINICAL PROGRAMS FULFILL UNMET NEEDS

- overcoming resistance to single-target mutation-specific inhibitors
- efficacy in broader patient populations
- reducing chemotherapy-based treatment regimens
SEL120: Highly selective CDK8 inhibitor with broad potential in multiple indications

**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**

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

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

**ORPHAN INDICATIONS**
- DIAMOND-BLACKFAN ANEMIA
SEL120: potential role of CDK8 in AML treatment

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
- 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
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)

![Kinome Scan Image]

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)

**p-STAT5 Ser726**

p<0.018

RESPONDERS NON-RESPONDERS

**p-STAT1 Ser727**

p<0.007

RESPONDERS NON-RESPONDERS
Complete regression with SEL120 in CD34+ AML patient-derived xenografts and bone marrow recovery

Research performed at:

- PDX cells
- NSG mice
- Vehicle / SEL120 46mg/kg
- Leukemia burden analysis
- Reduced splenomegaly
SEL120: Broad potential in oncology beyond AML and orphan blood disease

**SEL120**

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

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

**DIAMOND-BLACKFAN ANEMIA**

**WILMS’ TUMOR**

**BREAST CANCER**

*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

<table>
<thead>
<tr>
<th>FIT PATIENTS</th>
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<tr>
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<tr>
<td>Aggressive Salvage Chemotherapy</td>
<td>Low Intensity Therapy or Targeted Therapy</td>
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<td><strong>MUTATION-DRIVEN</strong></td>
<td><strong>MUTATION-DRIVEN</strong></td>
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<td>Intensive Induction Chemotherapy + Targeted Therapy</td>
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<td>Targeted Therapy</td>
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**FIRST LINE**

**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

**PRIMARY OBJECTIVES:**
- To assess safety and tolerability of SEL120 in patients with 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

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<th>2019</th>
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- **Site activation**
- **Ph1 Dose Escalation**
- **Expansion: Sequential or Combined Treatment**
- **FIRST PATIENT DOSED**
- **SITE INITIATION VISITS**
- **INVESTIGATOR MEETING**
- **FINAL CLINICAL STUDY REPORT**
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
- SEL24/MEN1703 is in Phase 1/2 study at five major cancer centers in the U.S.
- Expansion planned to 40 sites planned in U.S. and 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

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

- Upfront payment $104M
- Total potential value of milestones & refund of R&D costs $5.6M
- Up to double digit royalties for Ryvu from Menarini

**CLINICAL RATIONALE**

- PIM and FLT3 are oncogenes involved in AML
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- Expansion planned to 40 sites planned in U.S. and Europe
Potent efficacy of oral SEL24/MEN1703 in models of multiple AML subtypes

**FLT3-ITD POSITIVE**

**FLT3-ITD NEGATIVE**

**MV-4-11**

- Tumor volume kinetics
- Control
- SEL24/MEN1703, 75 mg/kg BID
- SEL24/MEN1703, 25 mg/kg BID
- BID – twice a day

**MOLM-13**

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

**MOLM-16**

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

**KG-1**

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

*BID – twice a day, QD – once a day*
SEL24: Phase 1/2 study of SEL24/MEN1703

Study title: A Phase I/II Study of SEL24 in Patients With Acute Myeloid Leukemia

- Study was initiated in 2017 as the first clinical trial testing a dual PIM/FLT3 inhibitor in patients with AML regardless of the FLT3 status and potentially able to overcome FLT3 inhibitor resistance

 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

 STATUS: Completing the dose escalation part, 24 patients treated (November 2019)

 PLANS: Cohort expansion at the recommended Phase 2 dose (RP2D) is planned to confirm the safety profile and assess single agent activity at approximately 40 sites in the U.S. and EU.

55th ASCO Annual Meeting 2019
"CLI24-001: First-in-human study of SEL24/MEN1703, an oral dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia” (abstract #256995)

24th EHA Meeting 2019
"CLI24-001: First-in-human study of SEL24/MEN1703, an oral dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia” (abstract #PF281)

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 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

**Ryvu Strategy**

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

**Synergistic Potential**

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

**Preclinical Development** (non-GLP Tox studies)

- Dual targeting of A2A/A2B should result in enhanced immunostimulatory responses

Adenosine is a potent and widespread immunosuppressive factor in TME that hampers the antitumor activity of all types of immune cells.

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**Ryvu Approach Provides Strong Preclinical Competitive Advantage**

<table>
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<tr>
<th>High Adenosine Concentration</th>
<th>Dual A2A/A2B Antagonist</th>
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<th>Activation of Dendritic Cells</th>
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RVU330 A2A/B antagonists outperform competitors in \textit{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 (TNF\textsubscript{\alpha} production).

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<th>CPI-444</th>
<th>AB928</th>
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<tr>
<td>TNF\textalpha{} moDCS - EC\textsubscript{50} [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>
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<tr>
<td>IL-2 CD4^{+} CELLS - EC\textsubscript{50} [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>
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**RVU330 - best-in-class dual A2A/A2B antagonist**

### KEY SUCCESS FACTORS

- **COMPETITIVE ADVANTAGE**
  - 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 has 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)
Ryvu is developing next-generation direct STING agonists for immunotherapy of resistant tumors

STING agonists mobilize immune system sensitizing resistant tumors to therapy

**RYVU STRATEGY**

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

**RYVU STRATEGY**

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

**COLD, RESISTANT TUMORS**

- AIM: ACTIVATION OF IMMUNE RESPONSE

**HOT, INFLAMED TUMORS**

- AIM: OVERCOME IMMUNOSUPPRESSION

**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 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 Aduro ADU-S100 agonist (IT)
- Standalone agonists or antibody-drug conjugates (ADC)
- Wide range of patients may benefit: active in multiple STING haplotypes

**VALUE INFLECTION POINTS**

**MILESTONES**

1. Preclinical candidate nomination for IND-enabling studies: 2020
2. Clinical development: 2021
3. Immunostimulatory activity on antigen presenting cells) in nanomolar concentration range
4. In vitro and in vivo reactivation of immunosuppressive macrophages
5. Stable remissions and immunological memory in a CT26 mouse colorectal carcinoma model
Ryvu STING agonists lead to elimination of established tumors after systemic administration

Ryvu STING agonist leads to dose-dependent tumor regression in CT26 mouse model after intravenous administration on par with the most potent reference STING agonist (GSK) in clinical trials
Ryvu STING agonist outperforms antitumor efficacy of Aduro agonist and provides immunological memory in mouse CT26 colorectal carcinoma model.
Ryu develops selective SMARCA2 inhibitors 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 Ryuvi series

**RYVU STRATEGY SUCCESS FACTORS**

- 5-10% NSCLC with inactivating (LOF) and truncating mutations SMARCA4 (BRG1)
- Other SMARCA4 MUT CANCERS (GI, Skin, Cervical, Bladder, Colorectal)

**WELL DEFINED PATIENTS POPULATION**

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

**COMPETITIVE ADVANTAGE**

Optimized lead with in vivo PoC in relevant mouse models carrying mutation in SMARCA4: 2020

**UPCOMING VALUE INFLECTION POINT**

**RYVU SMARCA2 PROTACs SELECTIVELY DEGRADE SMARCA2**

SMARCA2/SMARCA4 selectivity is critical for a therapeutic window

**BINDING TO SMARCA2 (RECOMBINANT PROTEIN)**

<table>
<thead>
<tr>
<th>RVU311-5363</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MST - DNA Kd (µM)</td>
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**DEGRADATION**

<table>
<thead>
<tr>
<th>Remaining SMARCA2 after 24h</th>
<th>Remaining SMARCA4 after 24h</th>
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<tbody>
<tr>
<td>RVU311-5363</td>
<td>10%</td>
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<tr>
<td>REFERENCE</td>
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**BOEHRINGER REFERENCE**

**RVU311-5363**

<table>
<thead>
<tr>
<th>SMARCA2</th>
<th>SMARCA4</th>
<th>GAPDH</th>
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<td>3.17</td>
<td>3.33</td>
</tr>
<tr>
<td>10.0</td>
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<td>1.11</td>
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<table>
<thead>
<tr>
<th>BOEHRINGER REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.03</td>
</tr>
<tr>
<td>1.0</td>
</tr>
<tr>
<td>0.33</td>
</tr>
<tr>
<td>3.0</td>
</tr>
<tr>
<td>TO DMSO</td>
</tr>
</tbody>
</table>
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

SEL24/MEN1703
Phase 1 data (2020)

SEL120
Phase 1 interim data (2020)

IND-enabling studies for new preclinical candidates

Data from early programs

Partnering deals in the early pipeline
Management team with strong clinical and shareholder value creation track record

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
Supervisory Board assembling industry veterans and financing experts

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.
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
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.

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 Obwock, Poland

ALWIN KRAEMER M.D.
University of Heidelberg

PRZEMYSLAW JUSZCZYNSKI M.D., Ph.D.
Warsaw Institute of Hematology & Transfusion

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Roche

morphosys

Genentech

AMGEN

Baxalta

Pfizer

gsk

Incyte

Bristol-Myers Squibb

MERCK

GILEAD

COLGENE

Novartis

Astellas

Dana-Farber Cancer Institute

AACR
SEL120 specifically targets STAT5+/CD34+ AML cells and induces differentiation in leukemic stem cells.

**STAT5 AND LSC GENE SIGNATURES DISCRIMINATE RESPONDER/NON-RESPONDERS**

**EFFICACY AND LINEAGE COMMITMENT IN CD34+ AML LSC**

AML LSC model (CD34+, CD96+, CD123+, CD38−)

- Control
- SEL120 0.5uM
- SEL120 0.05uM

![Graph showing cell number over time for different treatments](image)
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***
In vitro synergy of SEL120 in combination with Venetoclax (ABT-199)

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.
**In vivo synergy of SEL120 in combination with Venetoclax (ABT-199)**

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

### COMPLETE REGRESSION

<table>
<thead>
<tr>
<th>MV-411 cells</th>
<th>IV</th>
<th>NSG mice</th>
<th>Latency</th>
<th>SEL120+Venetoclax Daily, PO, 21 days</th>
<th>Leukemia burden analysis</th>
</tr>
</thead>
</table>

### HEMATOLOGIC RECOVERY (BONE MARROW)

<table>
<thead>
<tr>
<th>MV-411 cells</th>
<th>SC</th>
<th>Latency</th>
<th>SEL120+Venetoclax Daily, PO, 21 days</th>
<th>Leukemia burden analysis</th>
</tr>
</thead>
</table>

### TUMOR GROWTH INHIBITION AND COMPLETE REGRESSIONS

- **Bone Marrow**
  - % hCD45+ cells
  - Number of murine BM cells

- **Tumor volume kinetics**
  - Control
  - ABT 100mg/kg PO, QD
  - SEL 100mg/kg PO, QD
  - ABT+SEL 100mg/kg PO, QD
  - Complete regressions 3/10

- **Tumor volume, day 21**
  - Control
  - ABT 100mg/kg PO, QD
  - SEL 100mg/kg PO, QD
  - ABT+SEL 100mg/kg PO, QD
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)**

- **SEL24/MEN1703**: Dual PIM/FLT3 inhibitor
- **AZD1208**: Selective PIM inhibitor
- **Quizartinib**: Selective FLT3 inhibitor
- **Cytarabine**: dual inhibitor

**GI50(µM)**

- **SEL24/MEN1703**: 0.875
- **AZD1208**: 0.7
- **Quizartinib**: 0.35
- **Cytarabine**: 0.175

**MOLM-16 (FLT3-ITD negative)**

- **SEL24/MEN1703**: 0.875
- **AZD1208**: 0.7
- **Quizartinib**: 0.35
- **Cytarabine**: 0.175
RVU330 efficiently modulates pCREB (main PD clinical biomarker used by competitors) in *in vitro* human whole blood assay.
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*

1. Ryvus 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

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

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

4. - 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

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

~8.6% OWNED BY RYVU
## Financial results – Ryvu (Selvita Oncology segment, exc. NodThera) 2018 and Q1-3 2019

<table>
<thead>
<tr>
<th>$ million</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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<tr>
<td>Grants</td>
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<tr>
<td>Costs</td>
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</tr>
<tr>
<td>EBIT</td>
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</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

> 80 PhDs

> 150 employees
What sets Ryvu apart

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