RYVU THERAPEUTICS

Developing therapeutics
at the forefront of oncology

Corporate Presentation

June 2024

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Ryvu at a glance

FIRST-IN-CLASS CLINICAL PIPELINE

RVU120

- First-in-class, selective, oral CDK8/19 inhibitor
- Fully-owned by Ryvu
- Two Ph II studies ongoing in AML/HR-MDS (mono and combo)
- Two additional Ph II studies planned in LR-MDS and MF

MEN1703

- First-in-class dual PIM/FLT3 kinase inhibitor in Phase II; DLBCL study to initiate
- Potential across hematology
- Partnered with Menarini Group

SMALL MOLECULE DISCOVERY PLATFORM: NOVEL SYNTHETIC LETHALITY TARGETS & IO PARTNERSHIPS

Developing small molecule therapies to address high-value emerging targets and pathways in oncology

SYNTHETIC LETHALITY

- PRMT5
- WRN
- Novel SL targets

IMMUNO-ONCOLOGY

- BioNTech: STING standalone license and multi-target research collaboration
- Exelixis: STING ADC collaboration

FULLY INTEGRATED RESEARCH & DEVELOPMENT ORGANIZATION

- **LISTING:** WSE:RVU (mWIG40 index); cash runway to Q1 2026
- **TEAM:** >320 employees, including ~185 scientists (with ~100 PhDs)
- **SITE:** Fully-owned, state-of-the-art 108,000 sq ft facility

Team with a strong track record of clinical development and shareholder value creation

Pawel Przewiezlikowski, MSc, MBA
CEO and Founder

Krzysztof Brzozka, PhD, MBA
CSO

Hendrik Nogai, MD
CMO

Kamil Sitarz, PhD, MBA
COO

Vatnak Vat-Ho, MBA
CBO

Miika Ahdesmäki, PhD, MBA
CIO

Jakub Janowski, MSc
General Counsel

Bartlomiej Konicki, MSc
Financial Director

Tomasz Rzymski, PhD, MBA
Director of Translational Medicine

Justyna Zoltek, MSc
Director of HR

SUPERVISORY BOARD

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RAFAL CHWAST, *MSc*	
AXEL GLASMACHER, *M.D.*	
TADEUSZ WESOLOWSKI, *Ph.D*	

Broad pipeline addressing emerging targets in oncology

PROGRAM	INDICATION	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PARTNER	EXPECTED MILESTONES
CLINICAL PROJECTS							
RVU120 (CDK8/19)	R/R AML/HR-MDS (RIVER-52) (monotheraphy)					LEUKEMIA & LYMPHOMA SOCIETY	Initial Ph II data in 4Q24
	R/R AML (RIVER-81) (combination therapy)						Initial Ph II data in 4Q24
	Other Hematology (LR-MDS, MF)						Initiation of Ph II in mid-2024
	Solid Tumors						Complete Ph I data & Translational Studies in 2024
MEN1703 (SEL24) (PIM/FLT3)	DLBCL					MENARINI	Initiation of Ph II in mid-2024
DISCOVERY AND PRECLINICAL PROJECTS							
SYNTHETIC LETHALITY							
PRMT5	SOLID TUMORS						IND-enabling Studies in 2024
WRN	SOLID TUMORS						Lead to Development Candidate in 2024/5
NOVEL TARGETS	ONCOLOGY						
IMMUNO-ONCOLOGY							
STING & MULTI-TARGET IMMUNE MODULATION COLLABORATION	ONCOLOGY					BIONTECH	
STING ADC	ONCOLOGY					EXELIXIS	

Study start-up

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RVU120:
First-in-Class CDK8/19 Inhibitor in Hematologic and Solid Tumor Malignancies

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RVU120 is a fully-owned CDK8/19 inhibitor currently in Phase II

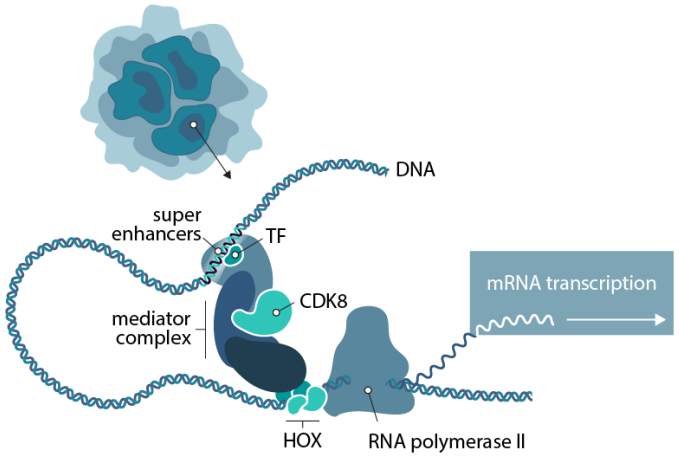
- First-in-class
- High potency

- High selectivity
- Low risk of DDI

- Easy to formulate
- Orally available

CDK8/19 mediator promotes AML growth

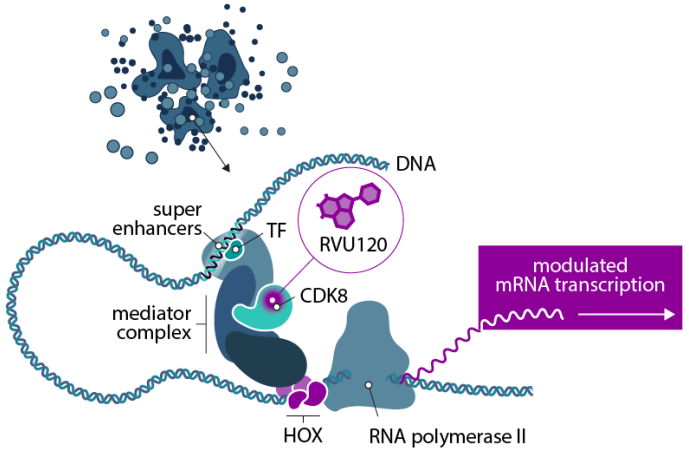
Viability of tumor cells



Maintenance of malignant stem cells
Suppression of differentiation

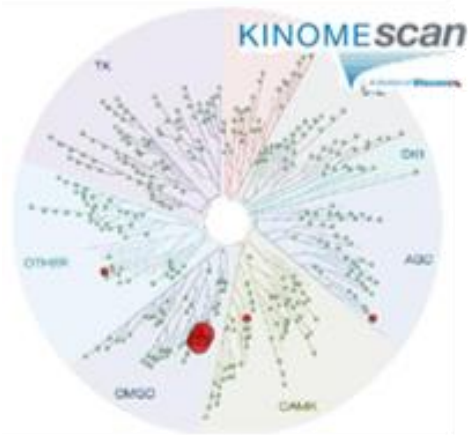
CDK8/19 inhibition by RVU120 triggers differentiation and apoptosis

Apoptosis of tumor cells



Apoptosis of malignant stem cells, incl. stem cells
Lineage Commitment

RVU120 is highly selective for CDK8/19



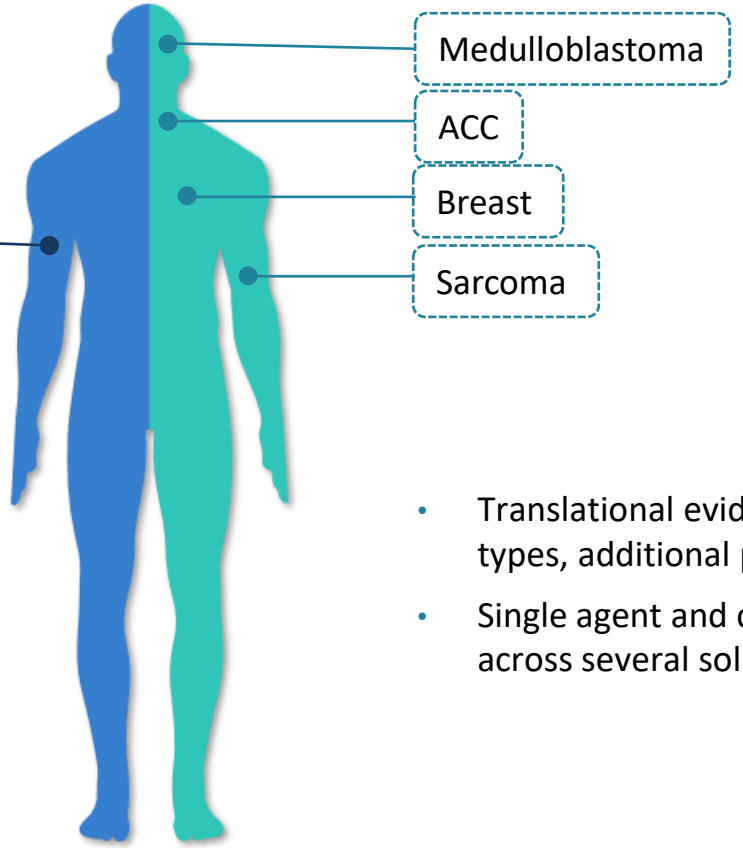
Current RVU120 development plan could lead to three accelerated approvals in 2026-2027

RVU120: opportunities across a broad range of cancers

Blood Cancers & Disorders

AML
High-risk MDS
Low-risk MDS
Myelofibrosis (MF)
MDS/MPN overlap syndrome
NHL
Diamond-Blackfan Anemia

Solid Tumors



- **Signs of clinical activity in AML/HR-MDS**
- Broad potential across hematologic disorders
- Responder hypothesis in AML
  – unmet need with no approved therapies
- Synergy with standard-of-care in AML and MF
- **Next expected clinical data release – Q2 2024**

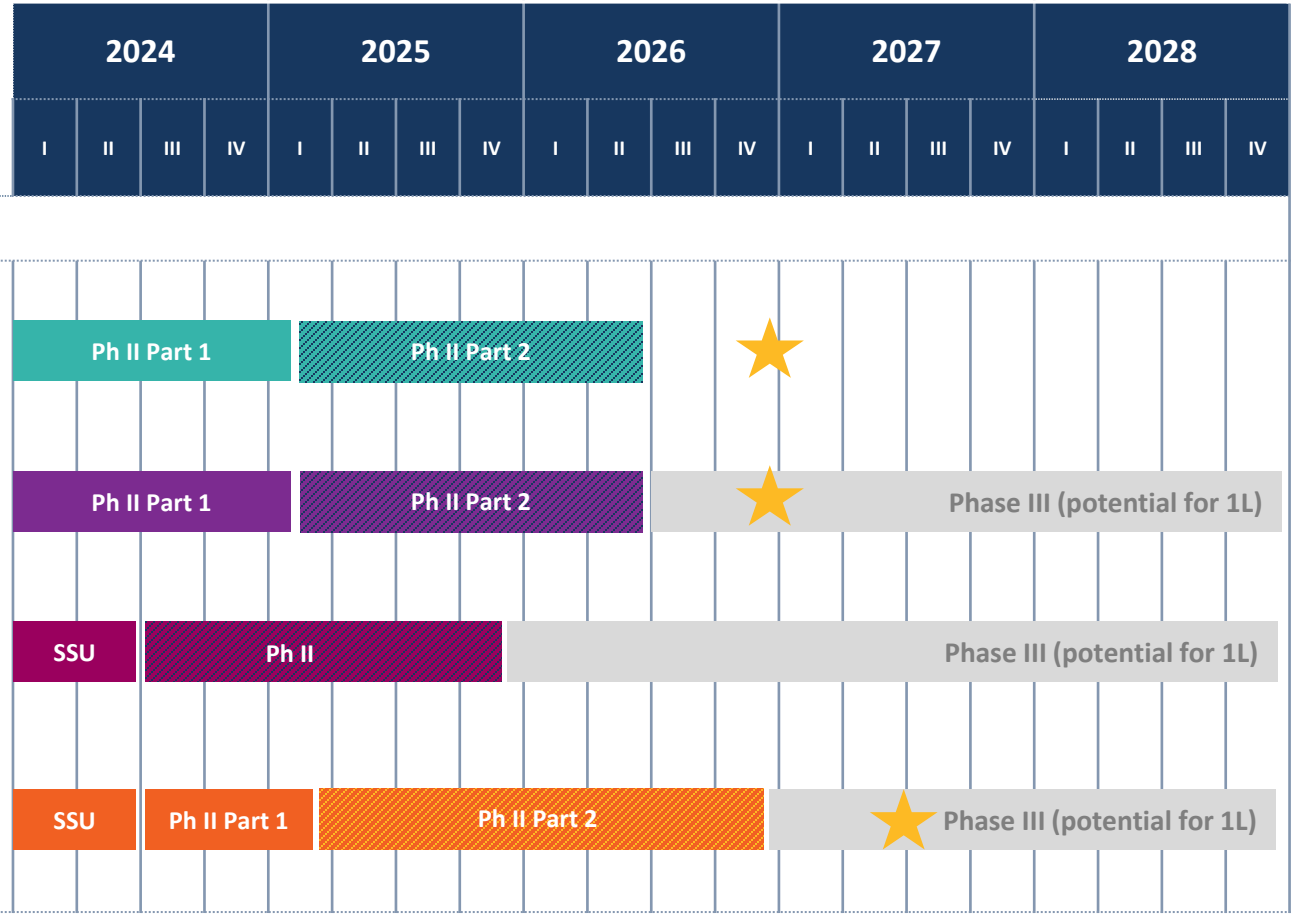
- Translational evidence in multiple tumor types, additional potential in combinations
- Single agent and combination potential across several solid tumors

RVU120 development plan is focused on hematological malignancies
Phase II studies ongoing

Clinical development of RVU120 focuses on hematologic malignancies, while translational research explores additional opportunities

Planned Ph II studies in hematologic malignancies

- **RIVER-52**: AML/HR-MDS, monotherapy
- **RIVER-81**: AML, combination with venetoclax
- **REMARK**: LR-MDS, monotherapy, investigator-initiated trial (IIT)
- **POTAMI-61**: myelofibrosis, monotherapy/combination



Approval in selected regions

Fully budgeted

Partially budgeted*

Currently not budgeted

Translational research is ongoing to support current clinical trials and to explore additional indications, including: medulloblastoma, sarcoma, TNBC, and other (undisclosed) indications

SSU = Study start-up

* budget allocation will prioritize RVU120 development scenarios based on the exploratory data from part 1.

RVU120 for potential treatment of Acute Myeloid Leukemia (AML)

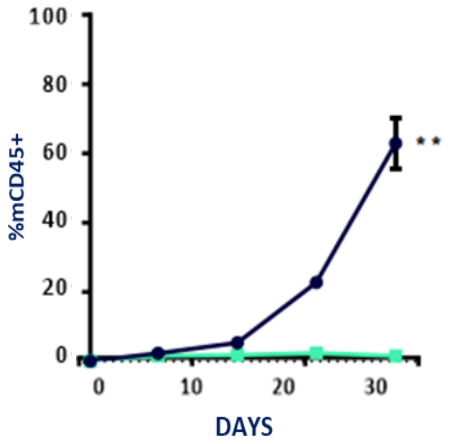
Acute Myeloid Leukemia

- Most common, highly aggressive type of acute leukemia in adults
- Poor outcomes in most patients[1]
- Annual US incidence ~20,500[2]; 11,300 deaths in the US in 2023[2]

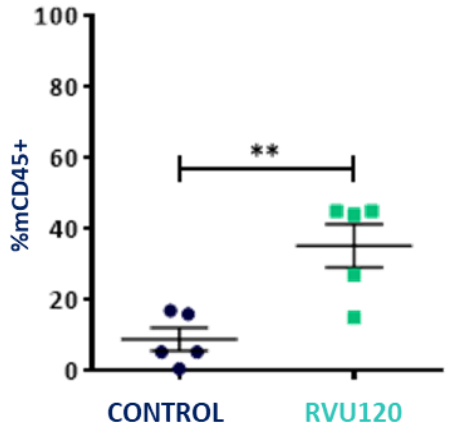
Preclinical Evidence: AML

CD34+ AML patient-derived xenografts:

Complete regression (peripheral blood)



Hematologic recovery (bone marrow)



1. Mayo Clinic; 2. Cancer.net

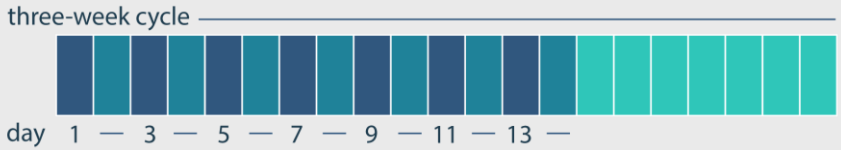
RVU120: Phase I AML/MDS study – RIVER-51

STUDY POPULATION

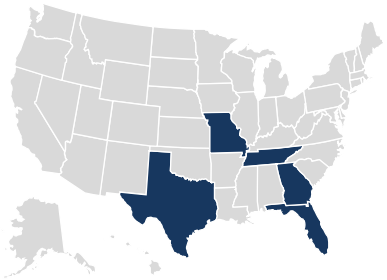
- Patients with relapsed/refractory AML or high-risk MDS
- No upfront patient stratification

TREATMENT

Three-week cycle: Single oral dose of RVU120 every other day for a total of 7 doses/cycle followed by one week off



5 SITES IN THE U.S.



The University of Texas MD Anderson Cancer Center
Washington University in St. Louis School of Medicine
Northside Hospital
Sarah Cannon Fighting Cancer Together
Sylvester Comprehensive Cancer Center, University of Miami Health System

5 SITES IN POLAND

Medical University of Gdańsk
DCO Dolnośląskie Centrum Onkologii we Wrocławiu
Medicover Integrated Clinical Services
IHiT Instytut Hematologii i Transfuzjologii
ŚCO Świętokrzyskie Centrum Onkologii

PHASE I: ESTABLISHING RECOMMENDED PHASE II DOSE (RP2D)

3 + 3 design

RP2D

SAFETY, EFFICACY, PK, PD

PHASE II
in patients with
R/R AML and HR-MDS

Data from RIVER-51 study were updated at EHA 2024

Phase II RIVER-52 study is currently enrolling

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RIVER-51 clinical update – EHA 2024:
15 of 30 evaluable patients showed clinical benefit

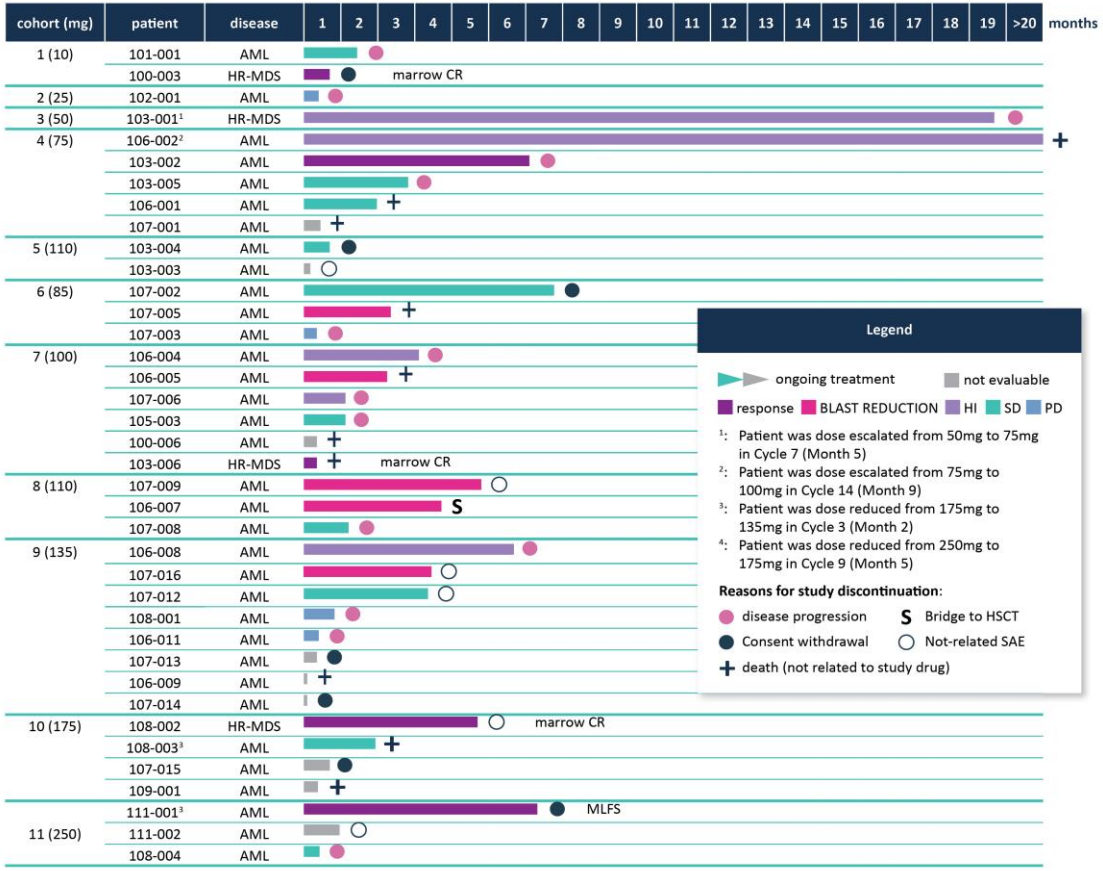
Data cut-off: May 17, 2024

30 treated patients are evaluable for response (38 were treated in total)

- 34 patients had AML and 4 had HR-MDS
- Patients relapsed or were refractory to a median of 3 prior lines of therapy

Clinical benefits

- **9 clinically significant BM blast reduction**
  (1 CR, 1 MLFS, 3 marrow CRs, and 4 other clinically relevant BM blast reductions)
  - 1 patient with double leukemic clones and BM blast reduction received a transplant after nearly 4 months of treatment
- **5 patients with erythroid hematological improvement (HI-E),**
  4 of those became transfusion-independent,
  of which 2 normalized also their Grade 3 thrombocytopenia



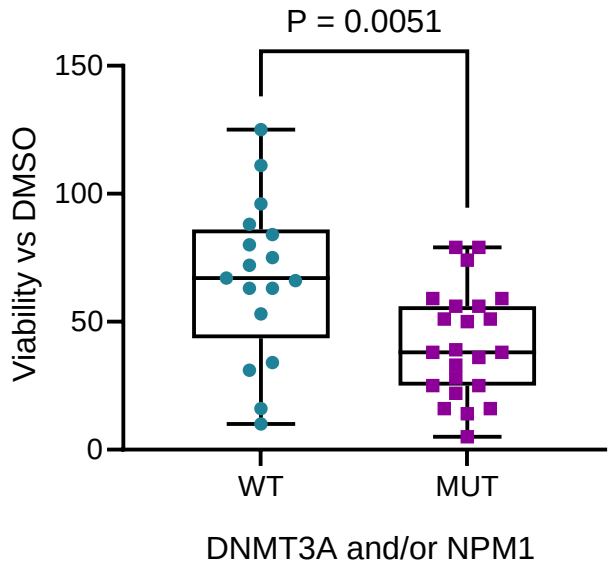
Favorable safety profile
Target engagement levels between 50-70% at a dose of 250 mg - selected for Phase II development

DNMT3A and NPM1 are potential patient selection markers in AML

DNMT3A/NPM1 mutated AML is dependent on dysregulation of HOX genes

- **Low nM activity on CDK8/19**: RVU120 reduces the viability of AML PDCs, in particular those bearing recurrent DNMT3A and NPM1 mutations
- Open chromatin status of DNMT3A and NPM1 mutants makes cells more sensitive to transcriptional changes induced by RVU120
- DNMT3A and NPM1 mutants are dependent on high expression of MEIS1 and homeobox (HOX) genes that can be regulated by RVU120
- Currently no approved therapies targeting DNMT3A or NPM1 mutations in AML

Loss of viability with RVU120 treatment



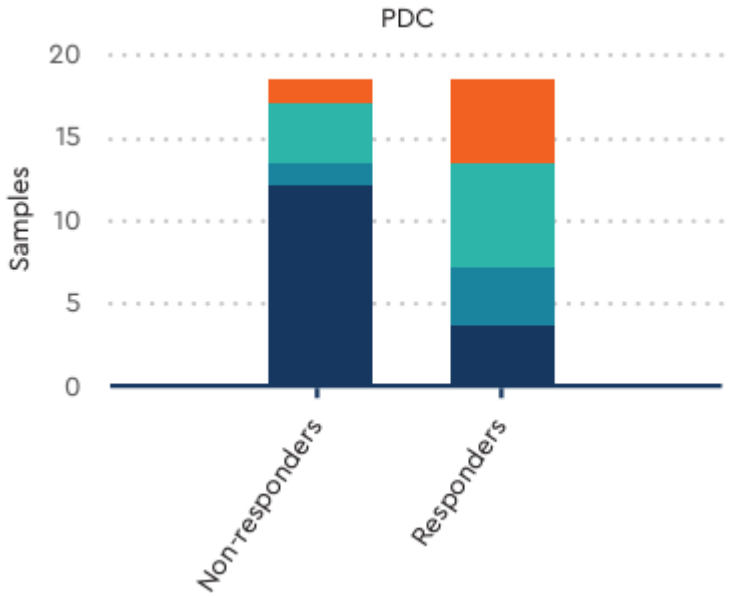
Clinical activity for RVU120 was observed in multiple populations

NPM1 and DNMT3A mutations

- **An NPM1 mutation was identified in 2 pts who received RVU120 – one patient achieved a CR, the other suffered and unrelated SAE n C2 and progressed**
- **Three additional patients had a DNMT3A mutation without NPM1 mutation achieved significant blast reductions, long-term disease control or hematologic improvement**

HR-MDS

- 4 pts with HR-MDS treated were failing 1-5 prior lines of treatment, incl. hypomethylating agents, and were heavily transfused prior to study entry
- **3 of these pts had >10 % blasts at baseline, all of them met the Cheson criterion of marrow CR during treatment with RVU120**



RIVER-52 : Phase II study with RVU120 as a single agent

Based on convincing translational rationale and clinical data, patients will be selected based on the disease features and genetic background

STUDY DESIGN

- Primary endpoints:
  - Rate of CR, CRh, CRi, with and without MRD, and DoR
- Secondary endpoints:
  - Transfusion independence, Progression-free survival, Relapse-free survival (RFS), Overall survival
- For Part 2: including PRO and HRQoL change from baseline
- Population: AML or HR-MDS with >10% blasts in BM and no alternative treatment
- Estimated enrolment: **134 patients in total**

PART 1

Genetically defined and disease specific cohorts:

- Pts with NPM1-mutated AML
- Pts with DNMT3a-mutated AML
- Pts with HR-MDS

Clinical Benefit
(CR/CRh/CRi/HI)
in any of the cohorts

PART 2

Confirmatory Cohort
Simon 2-stage design
Pts selected based on Part 1 outcome

Ongoing assessment of Part 1 will drive selection of population for Part 2

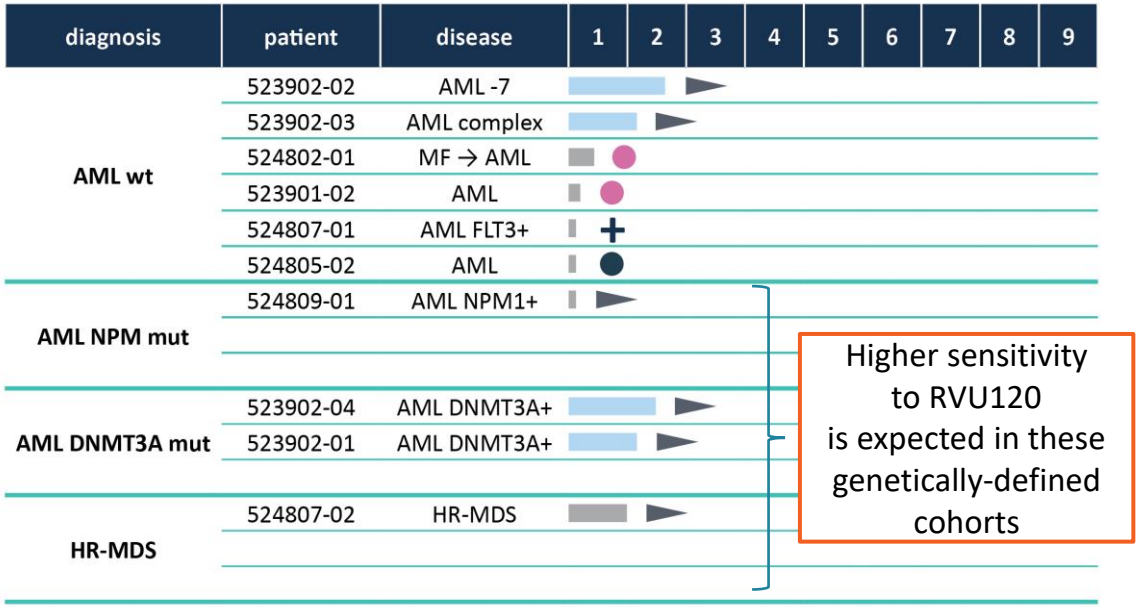
RIVER-52 – initial Phase II results

Data cut-off: May 17, 2023

- A total of 10 pts received RVU120 at 250 mg
- 6 pts are ongoing
- 4 pts were withdrawn (2 for PD, 1 for SAE unrelated to RVU120, 1 for withdrawal of consent)

Outcomes

- 1 pt with AML harboring a DNMT3A mutation, showed a peripheral blast reduction on C1D13 and an increase of the hemoglobin level of 1 g/dl average in the first month of RVU120 treatment compared to the month prior to study entry.
- 2 ongoing pts, including a patient with AML harboring an NPM1 mutation and a patient with HR-MDS, were not yet assessed for response.



Enrollment and dynamic activation of additional sites are ongoing

RIVER-51/52 – Confirmed safety at 250 mg dose

Data cut-off: May 17, 2023

- 13 pts from the Phase I/II received RVU120 at 250 mg EOD
- Gastrointestinal events are the most frequent
- Infectious complications are expected in this patient population
- The majority of AEs are of grade 1 or 2

Treatment Emergent Adverse Events (TEAE)	RVU120 (250 mg) from CLI120-001 and RIVER-52 trials Total number of pts dosed at 250 mg = 13	
	Any grade n of pts (%)	Grade 3-5 n of pts (%)
Nausea	3 (23)	1 (7)
Abdominal pain	3 (23)	1 (7)
Febrile neutropenia	2 (15)	2 (15)
Asthenia	2 (15)	1 (7)
Vomiting	1 (7)	-
Thrombocytopenia	1 (7)	1 (7)
Pneumonia	1 (7)	1 (7)
Hypokalemia	1 (7)	1 (7)

RVU120 is well tolerated at 250 mg dose
GI events are manageable with proper antiemetic premedication

RIVER-51/52 – Conclusions

1. Based on the data in the Phase I study, 250 mg was selected as the recommended Phase II dose. No DLTs were observed at the 250 mg dose level, and sufficient target inhibition was observed

2. **RVU120 as a single agent showed clinical benefit in a heavily pretreated population with AML and HR-MDS in the Phase 1 trial. The strongest evidence of benefit was observed in patients with NPM1 and DNMT3A mutation, and in patients with HR-MDS**

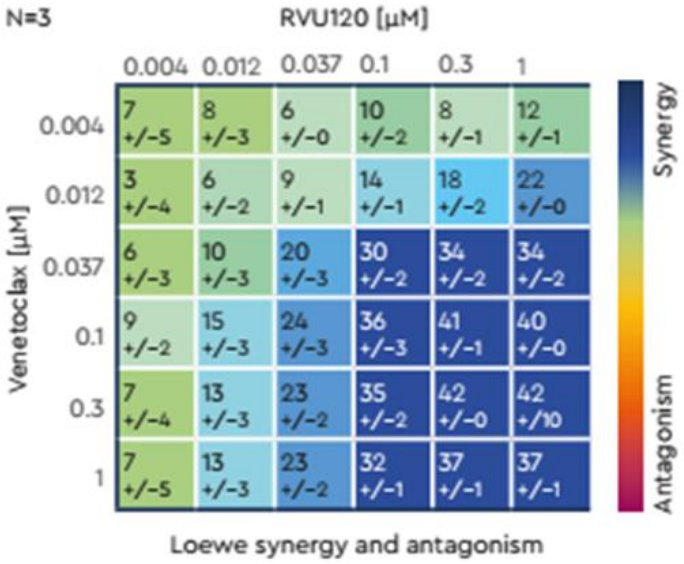
3. In RIVER-52, initial data confirm the safety and tolerability of RVU120, with gastrointestinal events as the most frequently reported

4. Data in **RIVER-52** are immature for efficacy assessment in the target population.
Preliminary signs of clinical benefit have been observed in ongoing patients

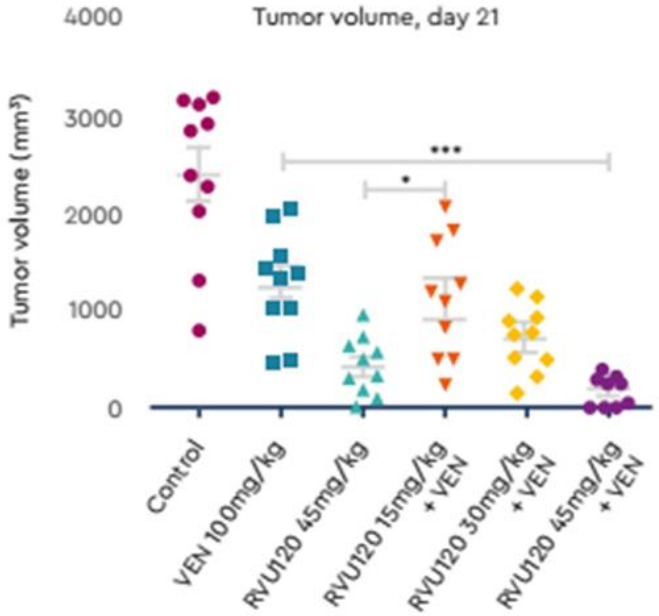
CDK8 inhibition by RVU120 synergizes with venetoclax in nonclinical AML models

Preclinical studies of RVU120 demonstrate robust anti-leukemic activity and synergy with VEN *in vitro* and *in vivo*

Loewe synergy matrix for KG-1 TP53mut AML cell line treated RVU120+VEN



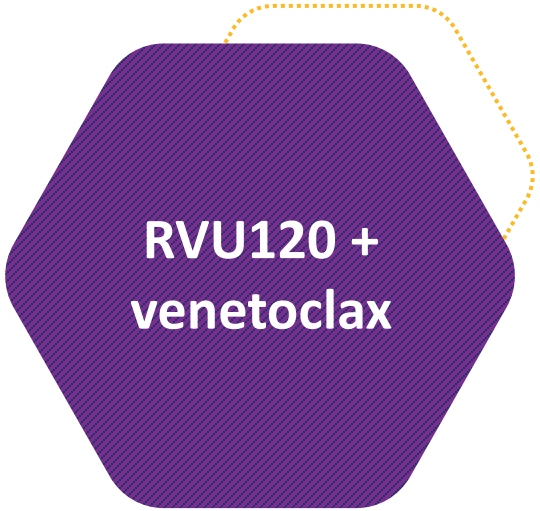
MV4-11 MLL fusion AML xenografts model treated with RVU120 +VEN



RVU120 OPPORTUNITY

Fast-to-market strategy as monotherapy in a potentially selected population and broad opportunity in early lines of treatment in combination

RIVER-81 : Phase II study testing RVU120 in combination with venetoclax



STUDY DESIGN

- Primary endpoints:
  - Rate of CR, CRh, CRi, with and without MRD, and DoR
- Secondary endpoints: Transfusion independence, PFS, RFS, OS
- For Part 2: including PRO and HRQoL change from baseline
- Population: r/r Ven-failed AML, no alternative treatments
- Approx. **57-98 patients** planned
- Up to **50 clinical sites** planned globally

MEDICAL RESEARCH AGENCY

RIVER-81 is supported in part by a €13.3M grant from the Polish Medical Research Agency (ABM)

PART 1

Dose finding in patients with relapsed/refractory AML after failing a venetoclax-based regimen

Clinical Benefit
CR/CRh/CRi, with and without MRD, and DoR

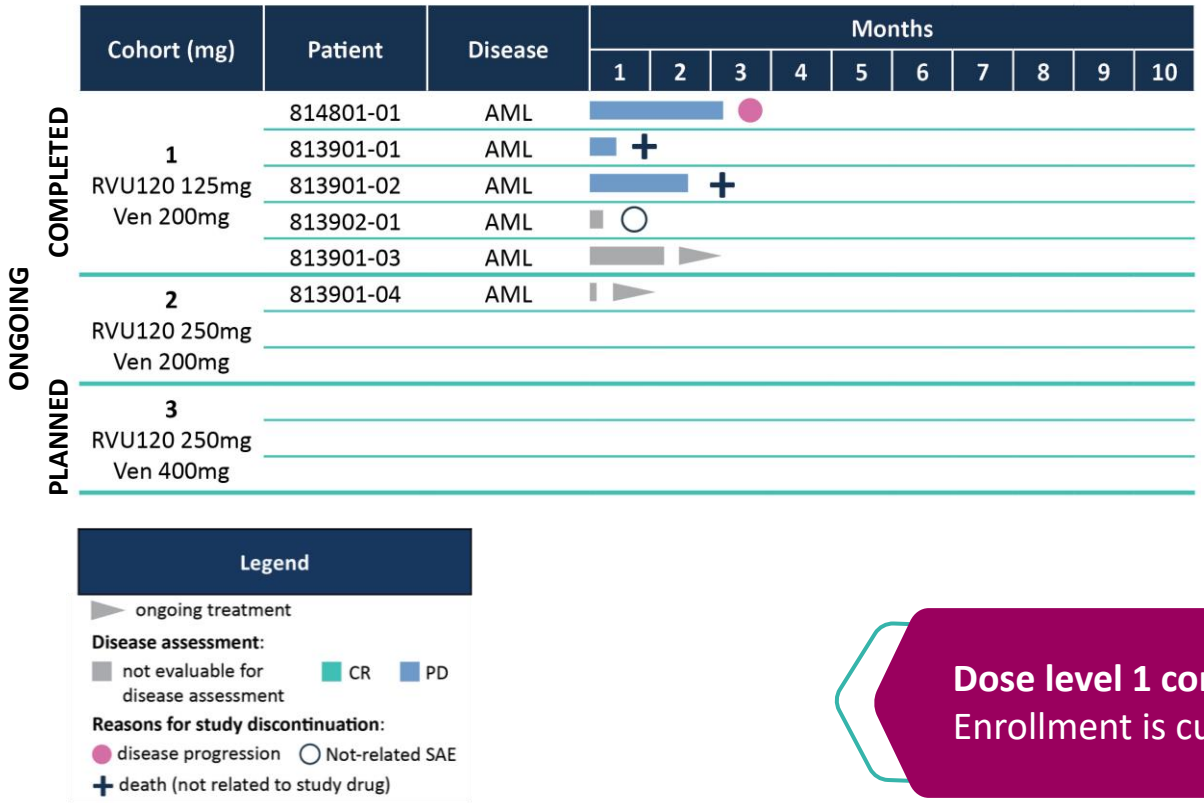
PART 2

Expansion Cohort at selected dose of RVU120 and venetoclax
Simon 2-stage design

RIVER-81: Initial clinical safety of RVU120 with venetoclax

Dose level 1 (RVU120 125 mg + VEN 200 mg) completed

Initial clinical safety confirmed



Treatment Emergent Adverse Events (TEAEs) that occurred in more than 1 patient	RVU120 125 mg + Ven 200mg (Cohort 1)	
	Any grade n (%)	Grade 3-5 n (%)
Asthenia	3 (60)	1 (20)
Febrile neutropenia	2 (40)	2 (40)
Pneumonia	2 (40)	2 (40)

Dose level 1 completed
Enrollment is currently open for Cohort 2 (RVU120 250 mg + VEN 200 mg)

RIVER-81 – Conclusions

1. Mechanistically, the combination of VEN and RVU120 leads to caspase-dependent degradation of MCL-1 protein in AML cells

2. Combining both drugs represses inflammatory and AML oncogenic pathways at the transcriptomic level

3. RVU120 with VEN exerts cytotoxic and differentiating effects on LSC from a hierarchical AML model superior to VEN alone

4. Overall, the preclinical results support RVU120 as a candidate in a venetoclax relapsed/refractory and frontline AML therapy in combination with VEN, countering therapeutic failure caused by persistent LSCs and MCL-1-mediated VEN resistance

5. **Initial data of the currently ongoing Phase II study RIVER-81 support the safety of the combination in patients with relapsed/refractory AML. RIVER-81 is currently enrolling in Cohort 2**

6. **The anti-leukemic efficacy in patients will be assessed at higher doses**

RVU120 validated preclinically as a drug candidate in myelofibrosis (MF)

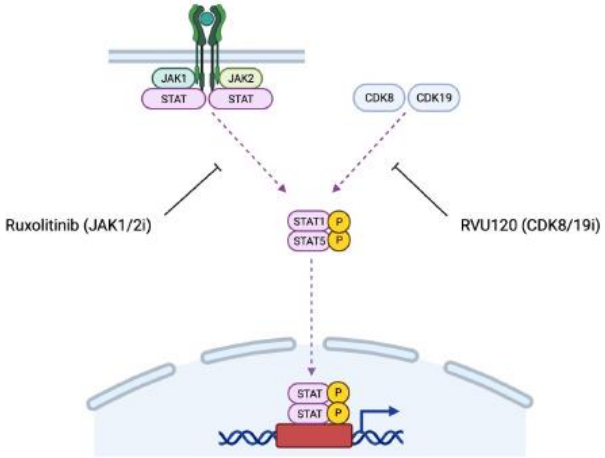
Opportunity in myelofibrosis

- Growing market with many patients undiagnosed or not treated due to lack of treatment options
- Long durations of therapy and unmet medical need, for example in patients with severe anemia

RVU120 in myelofibrosis

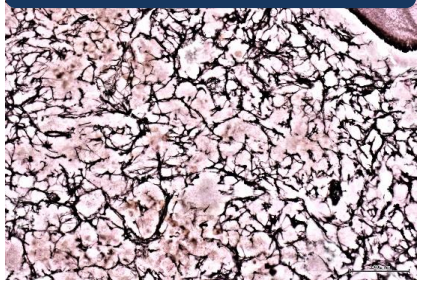
- **RVU120 alone and in combination can reduce symptoms and has disease-modifying potential in MF**
- Favorable RVU120 toxicity profile may enable targeting of patients who are not eligible for ruxolitinib treatment
- Preclinical results confirm RVU120's potential in ruxolitinib r/r MF patients
- Synergy with ruxolitinib indicates potential for combination therapy in the frontline setting and in patients with suboptimal response to JAKi

Mechanism of RVU120 activity in MF

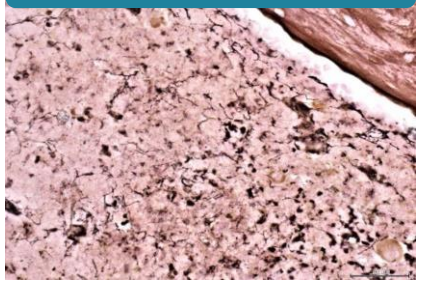


Reduction of bone marrow fibrosis

RUX



RUX + RVU120



Memorial Sloan Kettering Cancer Center

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Foundations of RVU120 POTAMI-61 study in MF

SCIENTIFIC VALIDATION

- RVU120 targets JAK2 mutant cells *in vitro*
- RVU120 stimulates erythropoiesis
- RVU120 eliminates MF symptoms *in vivo* as a single agent and shows synergy with ruxolitinib

UNMET NEED & COMMERCIAL OPPORTUNITY

- US prevalence of ~13,000 patients
- Limited activity and prohibitive toxicity of the current therapies
- Commercial opportunity validated with Sobi/CTI BioPharma deal

CLINICAL VALIDATION

- Several patients have shown induction of erythropoiesis in RIVER-51 study
- No hematologic toxicity

KOL INVOLVEMENT

- Collaboration with prof. Raajit Rampal (MSKCC)

POTAMI-61 STUDY

RVU120 in MF

Mono/Combo

- Single agent/combination (add-on) with JAKi ruxolitinib
- FPI and updates planned in H2 2024

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POTAMI-61 : MF Phase II study / RVU120 mono and combo

Study design

- **Population:**
  - Ultimate opportunity in the first line in combination with a JAK inhibitor
  - Starting point in the second line primary or secondary MF; intermediate or high-risk MF per DIPSS;
    (1) previously treated with or (2) ineligible for JAK inhibitor and patients with (3) suboptimal response to RUX
  - Important: patients with thrombocytopenia can be included in RVU120's trials
- **Primary endpoints** spleen volume reduction [SVR35] 24wks;
- **Secondary endpoints**: DoR, leukemic transformation, Hi, BM fibrosis reduction, PFS and OS
- Approx. 20-120 patients planned
- Up to 60 clinical sites planned globally

PART 1 (~20 patients)

Cohort 1
(mono RUX-ineligible)

Cohort 2
(RUX add-on)

PART 2

Expansion of Cohort 1 or 2

Cohort 3
(frontline)

REMARK: RVU120 in LR-MDS – IIT conducted by Prof. Uwe Platzbecker and the EMSCO network

STUDY DESIGN

- Population:
  - Relapsed/refractory low-risk MDS for the treatment of anemia in patients failing available options
  - Opportunity for the first line (1L) setting
- Primary endpoint:
  - Erythroid response (HI-E) according to IWG 2018 criteria
- Secondary endpoint:
  - RBC transfusion independence
  - Hb improvement
  - Quality of life (QoL)
  - Disease progression according to IWG 2018 criteria
  - Mutational pattern and burden of selected genes and their influence on response

PHASE II

EXPLORATORY
RVU120 AS A SINGLE AGENT
Patients failing available options
Enrollment of approx. 40 patients planned

ONGOING ASSESSMENT OF PHASE II WILL DRIVE FURTHER DEVELOPMENT

IIT

- Study will be conducted as an Investigator Initiated Trial with **Prof. Uwe Platzbecker within EMSCO** (European Myelodysplastic Neoplasms Cooperative Group)
- Enrollment planned in approx. 25 sites in EU

EMSCO MYELODYSPLASTIC SYNDROMES

UNIVERSITÄT LEIPZIG

Prof. Uwe Platzbecker

- Co-founder and chairman of EMSCO and co-chairman of the European Hematology Association Scientific Working Group on MDS
- Primary focus on myelodysplastic syndromes (MDS) and its treatment
- Worked on trials assessing luspatercept (Reblozyl) and imetelstat in patients with LR-MDS

RYVU THERAPEUTICS

RVU120: Phase I Solid Tumor study – AMNYS-51

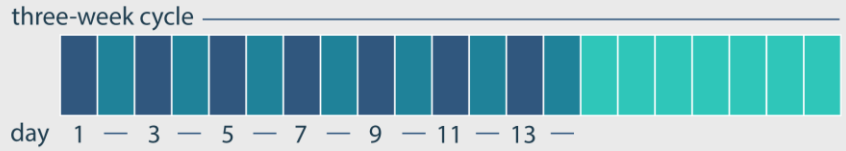
2 SITES IN POLAND + 3 SITES IN SPAIN

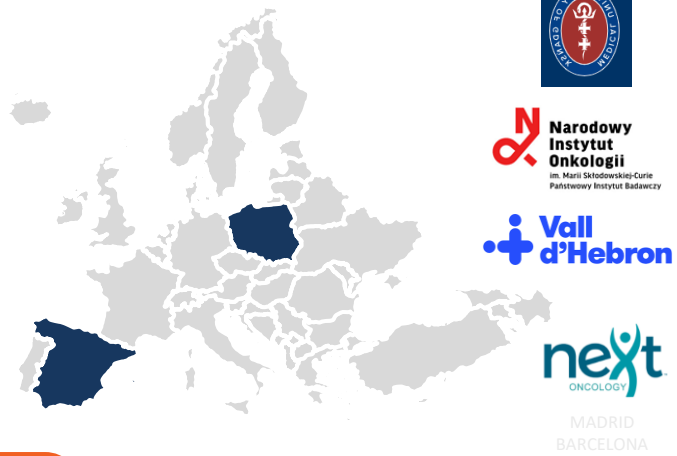
STUDY POPULATION

Patients with r/r solid tumors progressing after at least one previous line of systemic therapy

TREATMENT

Three-week cycle: Single oral dose of RVU120 every other day for a total of 7 doses/cycle followed by one week off





PHASE I: ESTABLISHING RECOMMENDED PHASE II DOSE (RP2D)

3 + 3 design

RP2D

SAFETY, EFFICACY, PK, PD

PHASE II: Efficacy and Safety Expansion

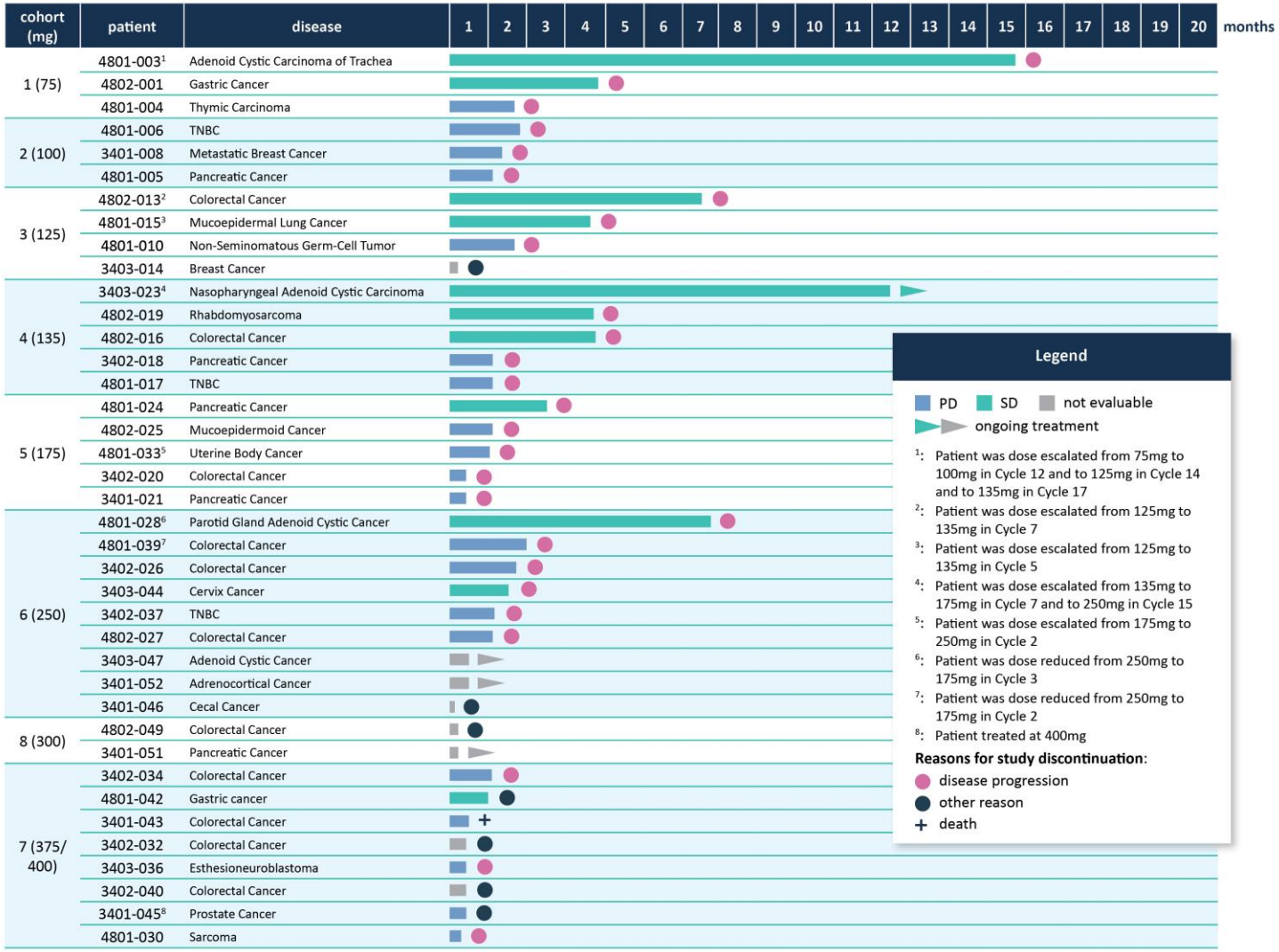
Preliminary data from the initial dose-escalation cohorts were presented at ESMO in October 2023

AMNYS-51 - ESMO 2023 data release

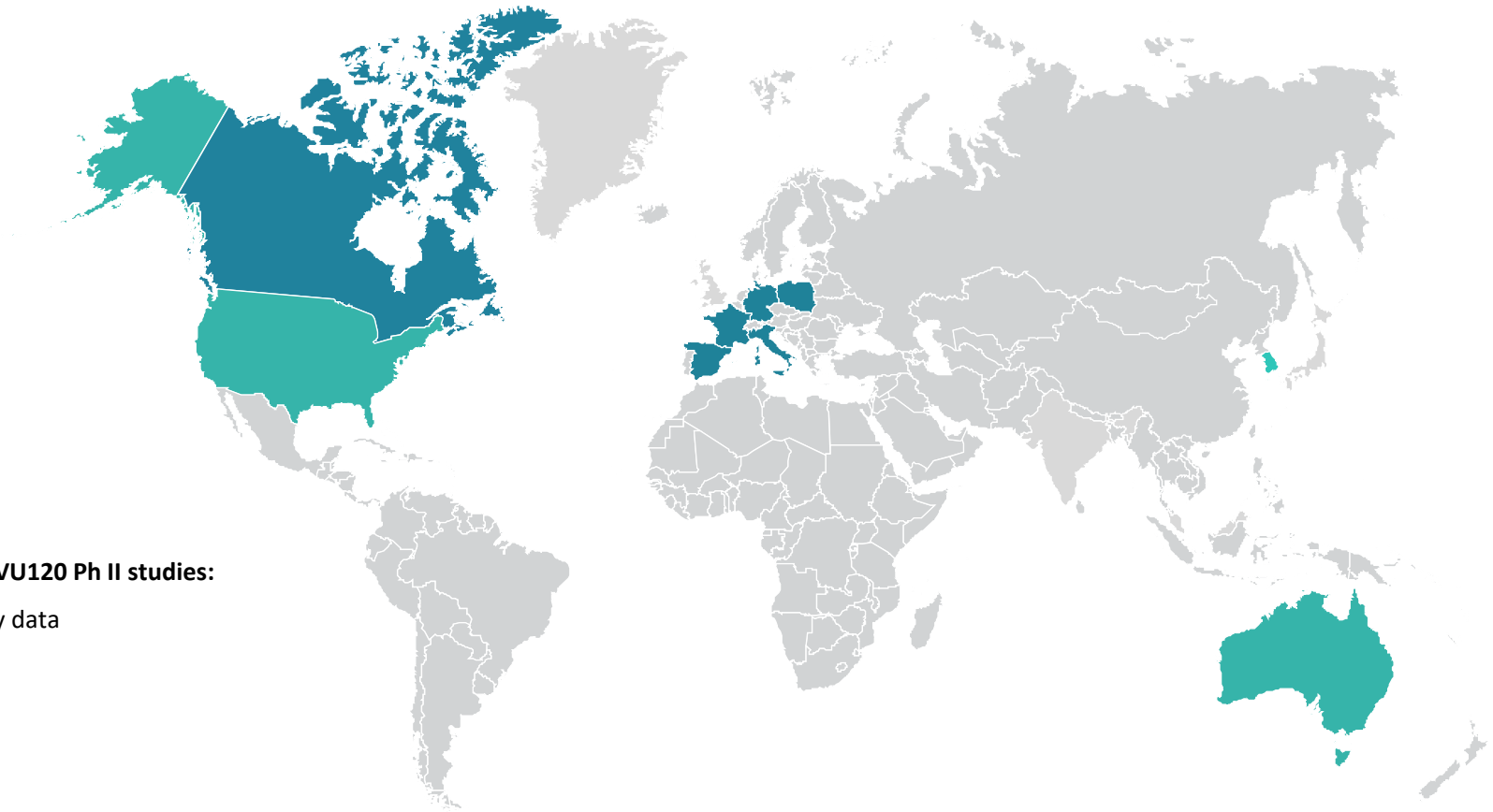
39 patients treated at doses up to 400 mg

Data cut-off: Sept 26, 2023

- A total of 39 patients have been treated in 8 cohorts
- Patients were unselected and heavily pretreated
- RVU120 demonstrates a favorable safety profile. No dose limiting toxicities (DLTs) or other safety signals were observed, confirming CDK8/19 inhibition as a viable approach for cancer therapies.
- Low grade nausea and vomiting were the most frequent AEs, contributing to suboptimal tolerability in Cohort 7
- Out of 12 patients who achieved a stable disease on RVU120, treatment in 8 patients lasted longer than on previous therapy line
- Trend to longer treatment duration was observed in patients with adenoid cystic carcinoma
- Dose schedule optimization will continue



Phase II clinical development of RVU120 with a global footprint



Planned locations for RVU120 Ph II studies:

- Part 1: exploratory data
- Part 2: expansion

Global site locations and patient population

Global CROs and clinical vendors

Regulatory authorities worldwide

Number of Ph II clinical trials initiated in H1 2024	**Number of countries** across studies	**Number of clinical sites** globally	**Number of patients** to be enrolled	**Number of clinical vendors** to be managed	**Number of internal Ryvu team members** in Clinical Development and Translational teams
4	10+	170+	270+	30+	70+

RVU120 market potential in hematological malignancies

AML (Acute Myeloid Leukemia)

- The most common, highly aggressive type of acute leukemia occurring in adults; unfavorable outcomes for most patients[1]
- Annual incidence in the US at ~20,800 with an estimated 11,220 deaths in the US in 2024[2]
- **Venclexta (venetoclax) sales estimated to exceed USD 3.5 bn in 2025[3]**

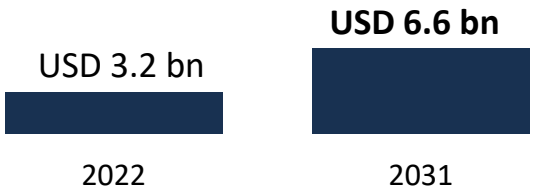
MDS (Myelodysplastic Syndrome)

- Disease leading to bone marrow damage, classified as cancer
- Growing market due to faster diagnosis of the disease and potential new therapies
- US incident cases expected to increase from 36,000 in 2018 to 46,000 in 2028[4]
- **Reblozyl (luspatercept) projected peak sales of USD 3.2 bn by 2029[5]**
- **Rytelo (imetelstat) projected peak sales of USD 1.2 bn[6]**

MF (Myelofibrosis)

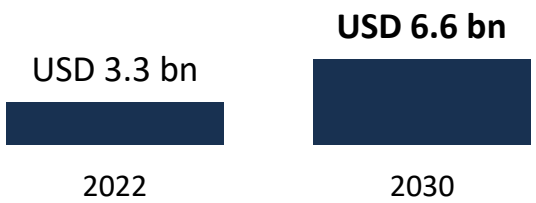
- MF is a bone marrow disease characterized by JAK mutations; often leads to severe anemia
- Chronic disease with long duration of therapy; US prevalence is estimated to be ~13,000 patients[7]
- **Morphosys acquired by Novartis for EUR 2.7 bn** in Feb 2024 – primary asset is Phase 3 MF drug pelabresib

Global AML Market[4]



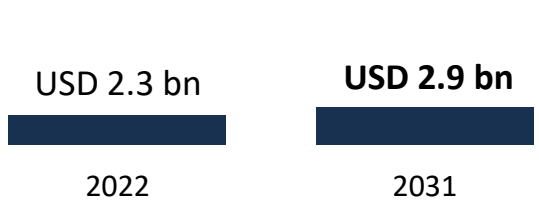
8.5% CAGR (2022-2031)

Global MDS Market[4]



9.3% CAGR (2022-2030)

Global MF Market[7]



2.6% CAGR (2022-2031)

1. Mayo Clinic 2. cancer.org January 2024 3. Biomedtracker 5 March 2023 4. GlobalData forecast 5. Goldman Sachs forecast 6. Coherent Insights

MEN1703 (SEL24): First-in-Class PIM/FLT3 Inhibitor

MEN1703 (SEL24)

Licensed to Menarini Group, currently in Phase II

PARTNERSHIP AGREEMENT WITH MENARINI GROUP (2017)

- EUR 4.8m upfront payment
- EUR 3.5m further milestone and translational research funding at Ryvu in 2017-2021
- Possible additional EUR 80m bio-dollar value + royalties
- Menarini conducts and funds all research and development costs

PROVEN SAFETY AND CLINICAL ACTIVITY

- Phase II clinical data (EHA2022) indicate efficacy in AML with IDH1/IDH2 gene mutations, similar to other drugs used as monotherapy
- Manageable safety profile
- Orphan drug designation (ODD) granted by FDA

Future directions – 2023+

DLBCL

- Development to continue with the initiation of a **new Phase II** study in relapsed/refractory diffuse large B-cell lymphoma (DLBCL)

Future Opportunities

- Ongoing translational work supports potential development in other hematologic indications
- Development in AML to be deprioritized

Partnership

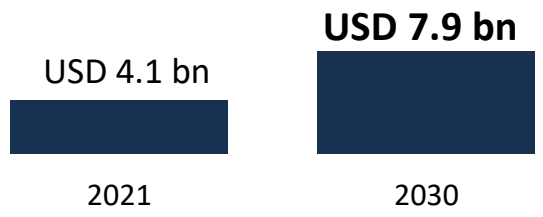
- As of September 2023, Ryvu has become Menarini's operational partner for Phase II execution
- The licensing partnership with Menarini remains unchanged, with Menarini funding all R&D. The total milestones and royalties due to Ryvu upon achievement of certain events remains unchanged

Unmet medical need and high commercial potential for MEN1703 in DLBCL

DLBCL (DIFFUSE LARGE B-CELL LYMPHOMA)

- Non-Hodgkin's lymphomas (NHL) are a heterogeneous group of lymphoproliferative disorders with DLBCL the being the most common type
- 30% to 40% of DLBCL patients will relapse during the first 2 years
- These patients often have significant comorbid conditions, which complicate the choices of often toxic treatment options and lead to decreased treatment rates in 3L+

Global DLBCL Market (1)



7.5% CAGR

COMMERCIAL POTENTIAL AND UNMET NEED

- Strong unmet medical need: estimated 23k incident DLBCL cases in North America in 2027 and 37k in the EU
- Targeted therapies have emerged as the dominant treatment options; choice of therapy is informed by type and response to prior therapies; timing of relapse; patient age, fitness, and comorbidities; disease kinetics; and product availability

RELAPSED/REFRACTORY PATIENTS INELIGIBLE FOR TRANSPLANT:

- Currently there is no optimal SOC defined for patients not candidates for transplant. Tafasitamab + lenalidomide reflect a preferred option for these patients. CAR-T cells and bispecific antibodies will move to the second line space
- The post CAR-T cell setting will require novel effective options in hard-to-treat patients that are often not eligible for clinical trial enrolment due to prolonged cytopenias

1. Data Intelligence, Aug 2023

Initiating Phase II in DLBCL

MEN1703 PROFILE

- First-in-class dual PIM/FLT3 inhibitor with a unique mechanism of action
- Differentiated activity in cellular models compared to selective PIM inhibitors (broader activity profile)

CLINICAL STUDIES TO DATE

- H1 2017- H1 2021 Phase I dose escalation and cohort expansion in R/R AML – MTD of 125 mg established
- H2 2021 – H1 2023 Phase II in IDH+ R/R AML
- 73 patients dosed so far across all studies, including 48 at R2PD
- Manageable safety profile
  - No QTc prolongation, no differentiation syndrome, no gastrointestinal tox
  - No hematologic toxicity

PHASE II in DLBCL

- Phase II study to consist of two parts: Part 1 pilot cohorts to establish combination dose and monotherapy efficacy followed by Part 2 cohort expansion
- Study locations: USA, Europe
- Phase II study to be initiated in mid-2024

Small Molecule Platform with Focus on Synthetic Lethality

Integrated Discovery Engine at Ryvu

TARGET IDENTIFICATION AND VALIDATION

- Discovery of novel synthetic lethal target pairs and actionable oncogenic drivers
- Combination of the experimental engine and bioinformatic analysis using proprietary approaches

DRUG DISCOVERY

- Integrated, multidisciplinary processes: rapid lead identification/optimization with deep translational biology support
- Platform has delivered two projects in clinical development; multiple projects in discovery/research
- Team of ~200 scientists (with ~100 PhDs) with international expertise in drug discovery and track record in delivering new clinical candidates

RESEARCH PIPELINE

- Broad portfolio of synthetic lethal and immuno-oncology targets at various stages of the cycle – clinical candidate selection to target validation and hit finding

Synthetic Lethality

PRMT5, WRN, Novel SL targets

Immuno-Oncology

Partnerships with BioNTech (STING and multi-target IO collaboration) and Exelixis (STING ADCs)

Ryvu discovers novel synthetic lethal targets through multipronged target discovery, including the proprietary ONCO Prime platform

Novel Target Discovery at Ryvu → **Novel Therapeutics**

Isogenic cell line pairs

- "Classical" approach, genome-wide screens in isogenic pairs
- Focus on unexplored genomic alterations

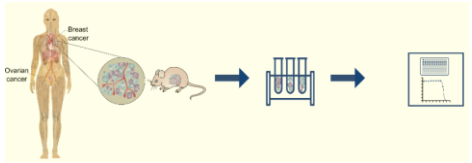
ONCO Prime

Isogenic primary cells

- Gradual transformation of healthy primary cells with mutations typical for tumor evolution of specific tissue type

Patient-derived cells (PDCs)

- Clones derived from actual primary tumor tissue with tumor heterogeneity retained
- Collaboration with Polish academic institutions



- ONCO Prime is the recipient of a **PLN 26 million (~USD 6.6M) grant** from the **Polish Agency for Enterprise Development** (PARP)

Ryvu pipeline:

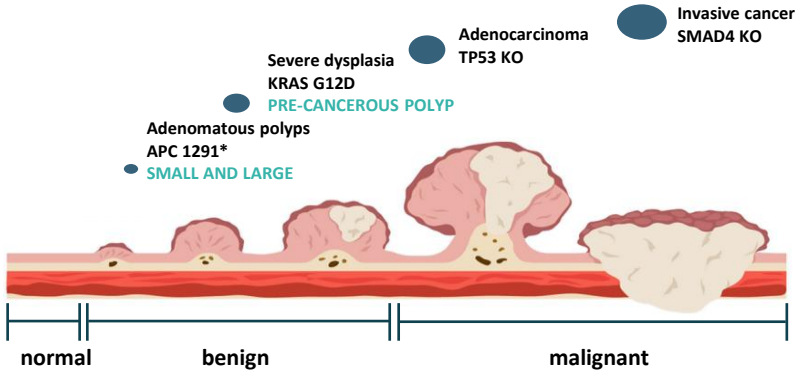
- **PRMT5** – lead optimization
- **WRN** – lead optimization
- **Novel targets in synthetic lethality**
  - 10+ novel programs in various stages of discovery/research from target validation to hit finding
  - First novel targets emerging in ONCO Prime initiative with CRC primary patient-derived cells

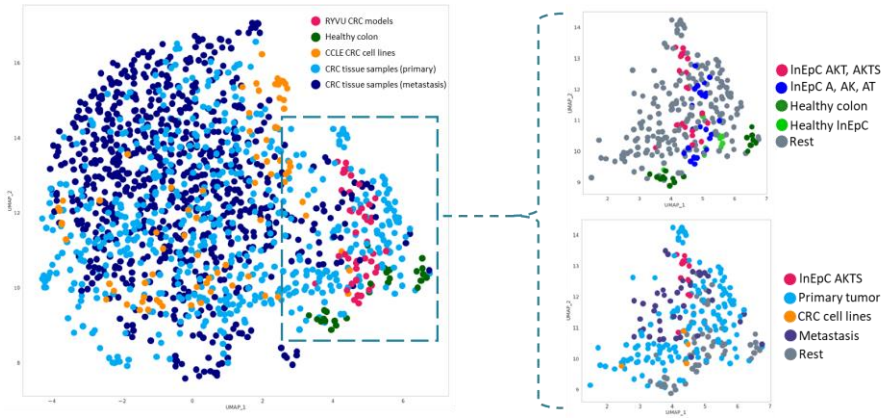
RYVU THERAPEUTICS

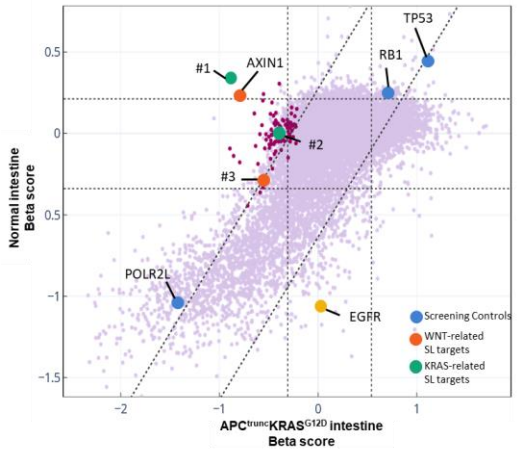
ONCO Prime: Broad potential to identify novel cancer targets – first data in KRAS-driven CRC

Ryvu's KRAS-mutated CRC tumor cells are representative of CRC patients

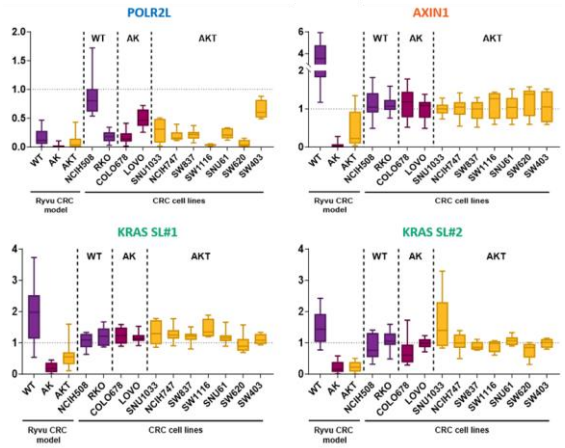
Screen of Ryvu cells yield synthetic lethal targets not seen in public data sets including DepMap







- Blue denotes internal screening controls (tumor suppresor and common essenial genes)
- Orange signifies synthetic lethal targets involved in WNT pathway regulation
- Green represents synthetic lethal targets involved in RAS pathway regulation.



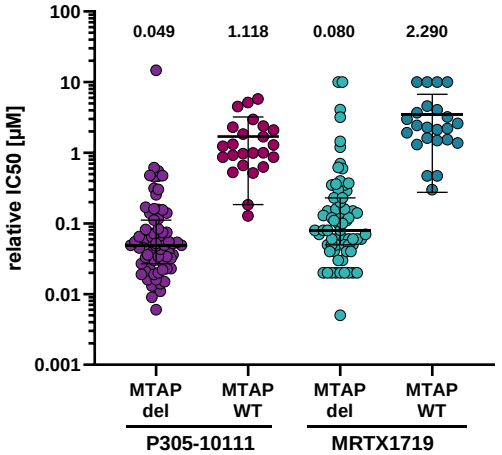
PRMT5 MTA-cooperative inhibitors

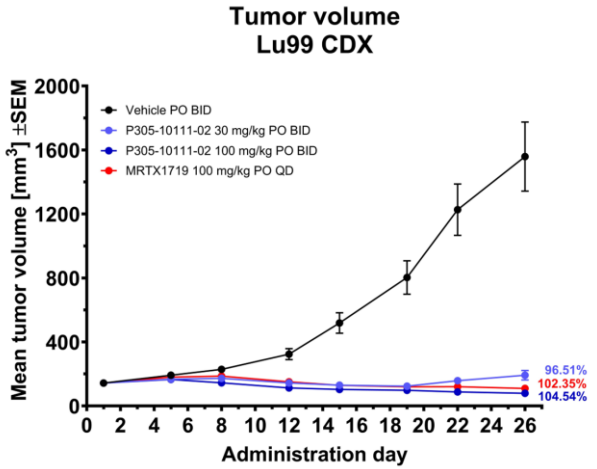
PRMT5 SL INHIBITOR PROGRAM IN RYVU

KEY RATIONALE	PRMT5 MTA-cooperative inhibitors exert synthetic lethal phenotype in MTAP deleted cells
MECHANISM OF ACTION	MTA-cooperative inhibitors
NOVELTY	Best-in-class potential (vs Mirati, Tango, Amgen)
TOP TUMOR INDICATIONS	MTAP deletions, up to 15% of all cancers, one of the largest genetically-defined population: pancreatic, lung, DLBCL, bladder, esophageal (by %: mesothelioma, GBM)
BIOMARKERS	MTAP deletion status SAM (plasma), SDMA (tissue) levels
STATUS	Lead optimization to candidate nomination is ongoing
TIMELINES	2024: IND-enabling studies initiation

RYVU HAS SL PRMT5 INHIBITORS WITH THE BEST-IN-CLASS POTENTIAL

Ryvu PRMT5 inhibitors demonstrate high cellular potency and MTA-cooperativity *in vitro* coupled with excellent in vivo activity





Multiparameter optimization of Ryvu PRMT5 inhibitors has resulted in:

- **Antiproliferative activity** for MTAP-deleted cells *in vitro:* high proportion of efficacy in large cell line panel
- **Improved PK profile** of Ryvu PRMT5 inhibitors demonstrated in different species PK studies
- **Antitumor efficacy and target engagement** achieve *in vivo* in responder DoHH-2 CDX model

Small molecule inhibitors of WRN

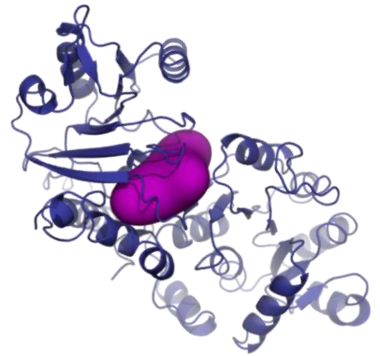
WRN INHIBITOR PROGRAM AT RYVU

KEY RATIONALE	Synthetic lethality of WRN with microsatellite instability (MSI-high)
MECHANISM OF ACTION	WRN inhibitors of ATPase activity selectively targeting tumors with microsatellite instability (MSI)
NOVELTY	First- or best-in-class potential Focus on selectivity (RecQ family)
TOP TUMOR INDICATIONS	Tumor agnostic with MSI-high vulnerability (~10-30% of colorectal, endometrial, gastric, ovarian cancers)
STATUS	Hit-to-lead generation ongoing
TIMELINES	2024/5: Lead to Development Candidate

Ryvu WRN inhibitors of ATPase activity selectively targeting tumors with microsatellite instability

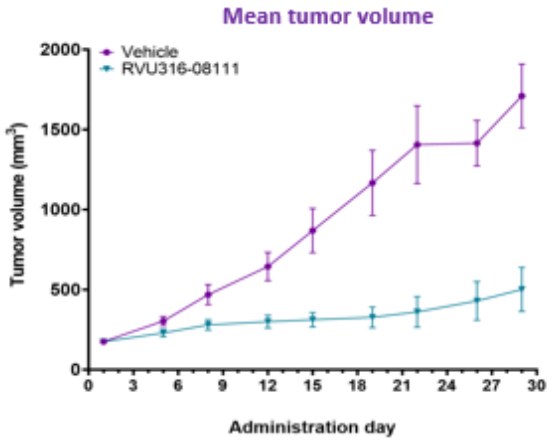
1. Helicase function validated *in vitro* as critical requirement for synthetic lethal phenotype
2. Full in-house cascade developed
3. Ryvu identified small molecule inhibitors of WRN with strong and selective activity on MSI-H cells

X-ray of WRN helicase with Ryvu ligand



In vivo efficacy study

In vivo efficacy study of the Ryvu WRN inhibitor exhibited **pronounced tumor growth inhibition (TGI)** in a microsatellite instability-high (MSI-H) colorectal cancer (CRC) xenograft model



BioNTech and Ryvu: global collaboration to develop and commercialize immune modulation small molecule candidates

Largest-ever Ryvu deal: November 2022

1. Multi-target discovery collaboration on small molecule programs in immune modulation
2. STING agonist license as a monotherapy and in combinations

Partnership

- **Multi-target research collaboration**: Ryvu will conduct discovery and research activities to develop multiple small molecule programs targeting immune modulation in cancer and potentially other disease areas based on targets selected by BioNTech; BioNTech will hold exclusive worldwide development and commercialization rights.
- **STING agonist**: BioNTech receives a global, exclusive license to develop and commercialize Ryvu's STING agonist portfolio as standalone small molecules, including as monotherapy and in therapeutic combinations.

Key Financial Terms

- Ryvu received €40 million from BioNTech, comprised of €20 million in upfront cash and a €20 million equity investment
- All R&D funded by BioNTech
- Ryvu is eligible for R&D and commercial milestones, and low single-digit royalties on product sales

Exelixis and Ryvu: exclusive license agreement to develop novel STING agonist-based targeted cancer therapies

July 2022

1. Building STING-based antibody drug conjugates (ADCs)
2. Leveraging Ryvu's STING agonist portfolio and Exelixis's ADC technology

Partnership

- Exclusive license agreement to combine Ryvu's small molecule STING agonists and STING biology know-how with Exelixis' antibody engineering, antibody-drug conjugate (ADC) technologies and drug development expertise
- Ryvu retains global rights for the development and commercialization of standalone STING agonists (licensed to BioNTech)

Key Financial Terms

- 3M upfront cash; first milestone of $1M achieved in Q1 2023; second milestone of $2M achieved in Q1 2024
- Additionally, Ryvu is eligible to receive research funding, $2M in near-term research-based milestones, and a double-digit milestone at first development candidate selection
- In total, Ryvu is eligible to receive milestones of over $400 million plus tiered single-to-low double-digit royalties on annual net sales per product developed/commercialized

Corporate Progress

Financial Results: Q1 2024

$ million	2023*	Q1YTD 2023*	Q1 YTD 2024*
Revenues, *incl.:*	**16.3**	**4.3**	**6.4**
Partnering	*11.2*	*2.9*	*5.4*
Grants	*4.9*	*1.3*	*1.0*
Total Costs**, *incl.:*	**37.6**	**7.5**	**11.7**
Clinical Pipeline	*13.0*	*1.8*	*4.2*
Early Pipeline	*15.8*	*3.7*	*5.1*
G&A	*8.8*	*2.0*	*2.4*
EBIT**	**-21.3**	**-3.3**	**-5.3**
EBITDA**	**-18.7**	**-2.6**	**-4.6**
Net Results***	**-20.0**	**-3.3**	**-4.6**

Cash position
June 14, 2024

$55.4M

Excludes an additional $8.58 expected from the EIB for Tranche B

Ryvu Employees

>320

Employees with PhD

~100

Partnering revenues in Q1 YTD 2024:
Exelixis ($2.0 million), BioNTech ($3.2 million recognized)

* recalculated from PLN using 4.1823 PLN/USD, 4. 3630 PLN/USD and 3.9941 PLN/USD – for 2022, Q1 YTD 2022 and Q1 YTD 2023, respectively
** excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of $2.0m, $0.7m and $0.3m in 2023, Q1 YTD 2023 and Q1 YTD 2024 respectively) and valuation of NodThera (+$0.9m (increase of costs), +$0.2m in 2023, and Q1 YTD 2023, respectively)
*** excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of $2.0m, $0.7m and $0.3m, in 2023, Q1 YTD 2023 and Q1 YTD 2024 respectively)

EUR 22m venture debt obtained from the European Investment Bank

European Investment Bank

LONG-TERM FINANCING FOR INNOVATIVE GROWTH COMPANIES

RYVU THERAPEUTICS

1 Instrument structure adapted to the business model

Long-term financing repaid through *bullet repayment*, and remuneration independent of interest rates, partially secured by the Company's capital

2 Non-dilutive funding

Additional financial leverage to motivate the management board and existing shareholders, as well as significantly increasing the potential ROI for equity investors

3 Backing from one of the largest funding institutions in the EU

EIB financing is seen as an instrument that strongly validates the business model and attracts additional capital investors

AMOUNT OF CREDIT

Up to **€22m (~100 mPLN)**

- Tranche A of €8m received; Tranche B of €8M expected
- €6m remains in final Tranche C

PAY-OFF DATE

Up to **5 years** for each tranche

DEBT COST

Fixed annual interest, warrants subscription

RYVU THERAPEUTICS

Ryvu's Vision: from 2026, Ryvu will improve the lives of cancer patients worldwide

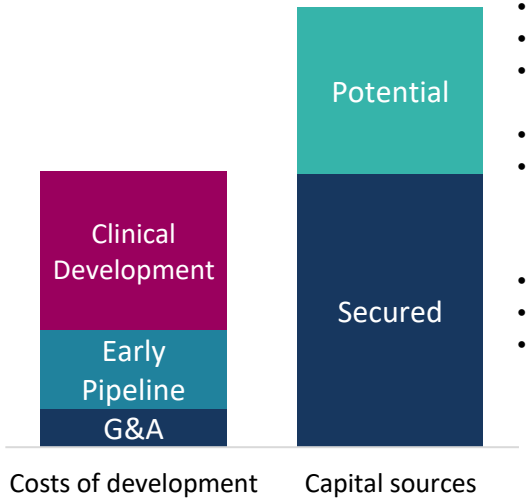
2024 KEY GOALS AND FINANCING

PIPELINE

- **RVU120 broad development (including potential fast-to-market strategy in AML/HR-MDS)**
- SEL24 (MEN1703) to start Phase II in DLBCL (with Menarini Group)
- **Advancement of one preclinical program into Phase I clinical trials**
- Strengthening of Synthetic Lethality Platform and acceleration in the early pipeline progress

BUSINESS

- **Achieving financial milestones in existing collaborations** (i.e. BioNTech, Exelixis, Menarini)
- **At least one new partnering deal per year**



- Research funding from existing R&D collaborations
- Milestones from existing R&D collaborations
- New grant funding
- New deals in the early pipeline
- RVU120 limited licensing (limited regions and/or co-development)
- NodThera exit
- Other

- Cash at hand + interest on cash
- EIB venture debt
- Existing grants

2024 – DEVELOPMENT PLAN KEY ASSUMPTIONS

- Accelerating the pipeline to deliver cancer therapeutics to patients
- Capital for development secured; potential additional non-dilutive sources
- Significant increase of the company's value
- Development strategy includes alternative, de-risking partnering scenarios

2024 – KEY ANTICIPATED EVENTS

- **Clinical data updates from RVU120 in Q2 and Q4**
- New preclinical candidate in the early pipeline

Ryvu equity summary

IPO on WSE **Corporate Split: Selvita and Ryvu**	Nov 2014 Oct 2019
Ticker: WSE	RVU
52-Week Range[1]	PLN 47.00 – 72.40
Average Daily Volume (YTD) [1]	11,303
Market cap[1]	PLN 1,202 M ($305m)
Shares outstanding	23.1 M
Cash[2]	$59.0m

Top Holders[3]		
1	Paweł Przewięźlikowski	18%
2	Allianz OFE	9.2%
3	BioNTech SE	8.3%
4	Nationale-Nederlanden OFE	7.9%
5	Tadeusz Wesolowski (incl. Augebit)	4.9%
6	PZU OFE	4.5%
7	Boguslaw Sieczkowski	4.0%
8	Allianz TFI	2.4%
9	Goldman Sachs TFI	2.1%
10	Norges Bank	2.1%
11	UNIQA OFE	1.8%
12	Generali OFE	1.5%

Analyst Coverage

ERSTE Group	mBank	NOBLE SECURITIES DOM MAKLERSKI	TRIGON DOM MAKLERSKI	ipopema	Bank Pekao Biuro Maklerskie	Santander Biuro Maklerskie
Vladimira Urbankova	Beata Szparaga-Waśniewska	Krzysztof Radojewski	Katarzyna Kosiorek	Łukasz Kosiarski	Marcin Górnik	Tomasz Krukowski

1. As of 14 May 2024 2. As of 09 May 2024 3. As of 29 Dec 2023

Thank you

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