RYVU THERAPEUTICS

Developing therapeutics
at the forefront of oncology

Corporate Presentation

May 7, 2025

Note on the presentation and forward-looking statements

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Ryvu is developing novel therapies to address high-value emerging targets in oncology

Clinical and Prelinical Candidate Pipeline

RVU120

- First-in-class, oral **CDK8/19** inhibitor
- Four Ph II studies ongoing: mono and combo in AML, MF, and LR-MDS

Dapolsertib
(MEN1703, SEL24)

- First-in-class dual **PIM/FLT3** kinase inhibitor in Phase II in DLBCL with potential across hematology
- Partnered with Menarini Group

RVU305

- Best-in-class, oral, brain-penetrant, MTA-cooperative **PRMT5** inhibitor in IND/CTA-enabling studies

Novel Multi-Target Discovery

ONCO Prime Platform

- Multiple novel precision oncology targets, including synthetic lethality

Novel ADC Payloads

- Multiple novel ADC payloads, including immunocytotoxic and synthetic lethal MOAs
- **Exelixis**: STING ADC collaboration

Immuno-oncology

- **BioNTech**: multi-target research collaboration

FULLY INTEGRATED RESEARCH & DEVELOPMENT ORGANIZATION

- **LISTING:** WSE:RVU; cash runway to H2 2026
- **TEAM:** ~200 employees, including ~100 scientists (with ~60 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 Przewięźlikowski, MSc, MBA
CEO and Founder

Krzysztof Brzózka, PhD, MBA
CSO

Hendrik Nogai, MD
CMO

Kamil Sitarz, PhD, MBA
COO

Vatnak Vat-Ho, MBA
CBO

Justyna Żółtek, MSc
CPO

Jakub Janowski, MSc
General Counsel

Bartłomiej Konicki, MSc
Financial Director

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Broad pipeline addressing emerging targets in oncology

PROGRAM	INDICATION	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PARTNER	EXPECTED MILESTONES
RVU120 (CDK8/19)	R/R AML (combo with venetoclax)				**RIVER-81**	LEUKEMIA & LYMPHOMA SOCIETY	Updated Ph II data in 2Q25
	R/R AML/HR-MDS (monotherapy)				**RIVER-52** (enrollment suspended)		Updated Ph II data in 2Q25
	Myelofibrosis (mono and combo with ruxolitinib)				**POTAMI-61**		Initial Ph II data in 2Q25
	LR-MDS (monotherapy)				**REMARK**	EMSCO MYELODYSPLASTIC SYNDROMES	Initial Ph II data in 4Q25
Dapolsertib (PIM/FLT3)	DLBCL (mono and combo with glofitamab)				**JASPIS-01**	MENARINI	Ph II data in 2026
RVU305 (MTA-cooperative PRMT5)	MTAP-deleted tumors						Complete IND/CTA-enabling studies in 2H25
RYVU TECHNOLOGY							
ADCs – Novel Payloads	Oncology	Multiple Targets/Payloads					
ONCO Prime – Novel Small Molecule Precision Oncology	Oncology	Multiple Targets					
PLATFORM COLLABORATIONS							
Immune Modulation	Oncology					BIONTECH	
STING ADCs	Oncology					EXELIXIS	

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

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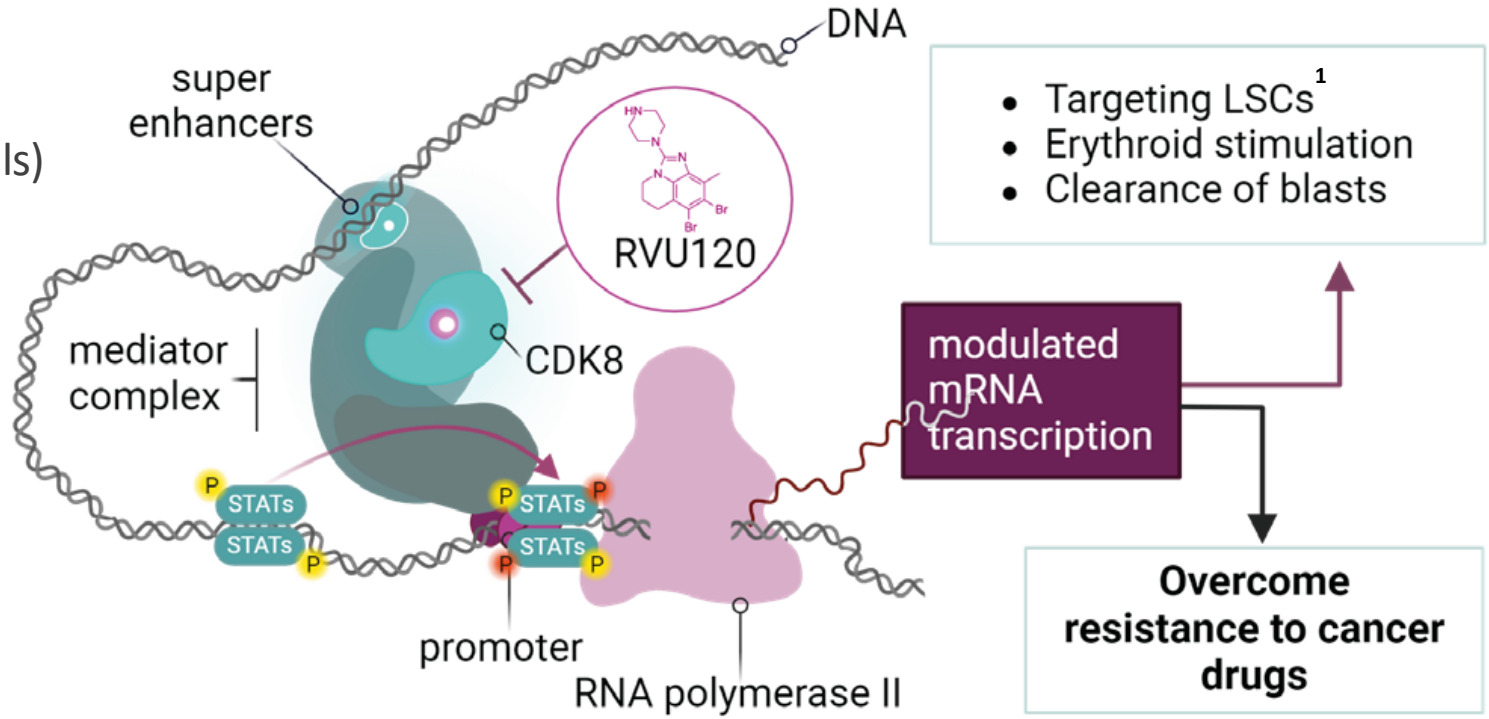
RVU120 is a clinical-stage, first-in-class, small molecule CDK8/19 kinase inhibitor developed and fully-owned by Ryvu

- high selectivity
- low risk of DDI (esp antifungals)
- easy to formulate
- orally bioavailable
- favorable safety profile



RVU120 is an innovative dual CDK8/19 inhibitor designed to target the expression of genes crucial for cancer cell survival and differentiation

[1] leukemic stem cells

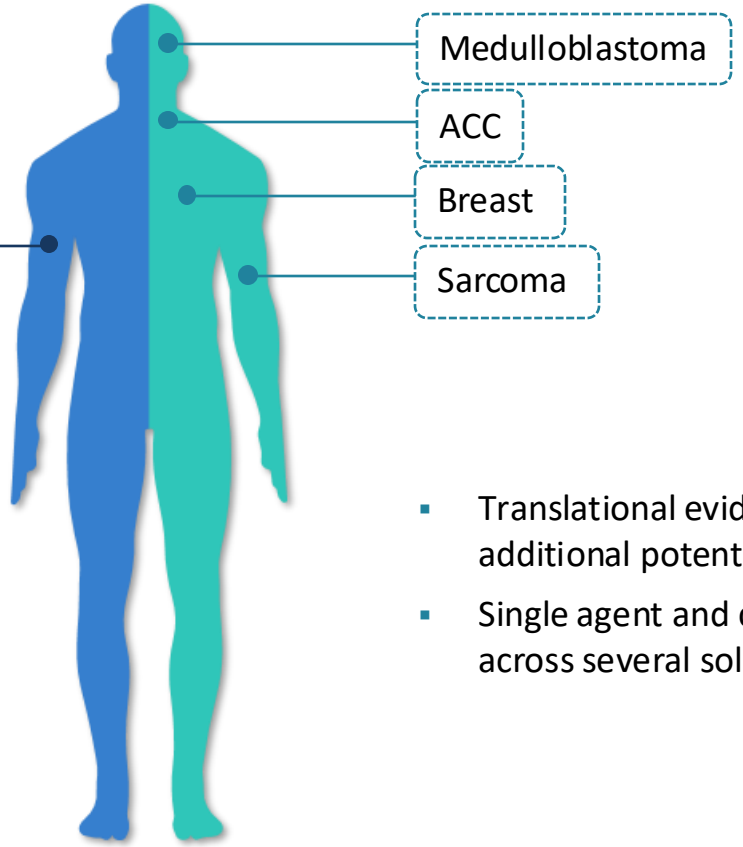
RVU120: opportunities across a broad range of cancers

Blood Cancers & Disorders

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

- **Signs of clinical activity in AML**
- Broad potential across hematologic disorders
- Synergy with standard-of-care in AML and MF
- **Next expected clinical data release – Q2 2025**

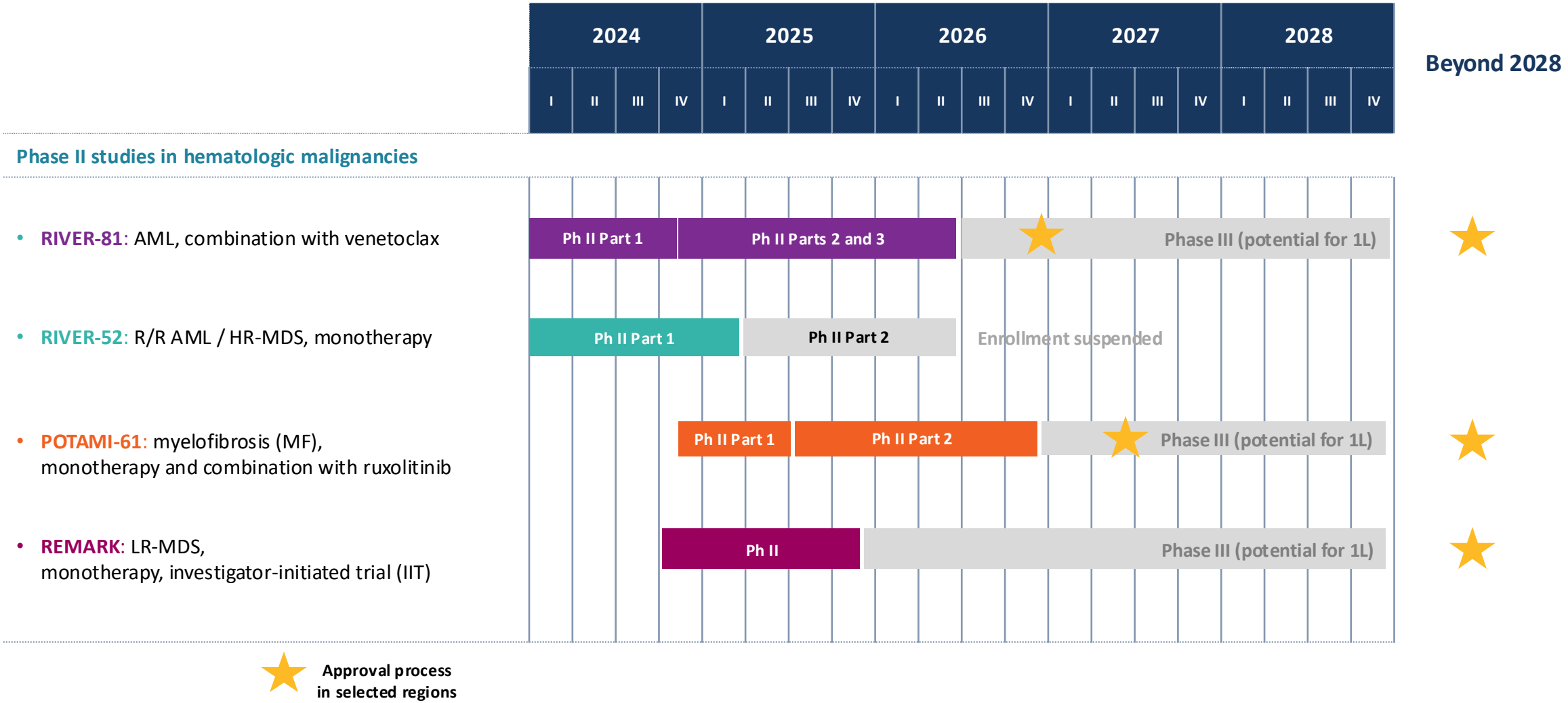
Solid Tumors



- 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
Three Phase II studies are enrolling

RVU120 Diversified clinical program with high commercial potential



RVU120 Phase II development plan rationale: RIVER-51 clinical data

15 of 30 evaluable patients showed clinical benefit across dose levels

Clinical benefits

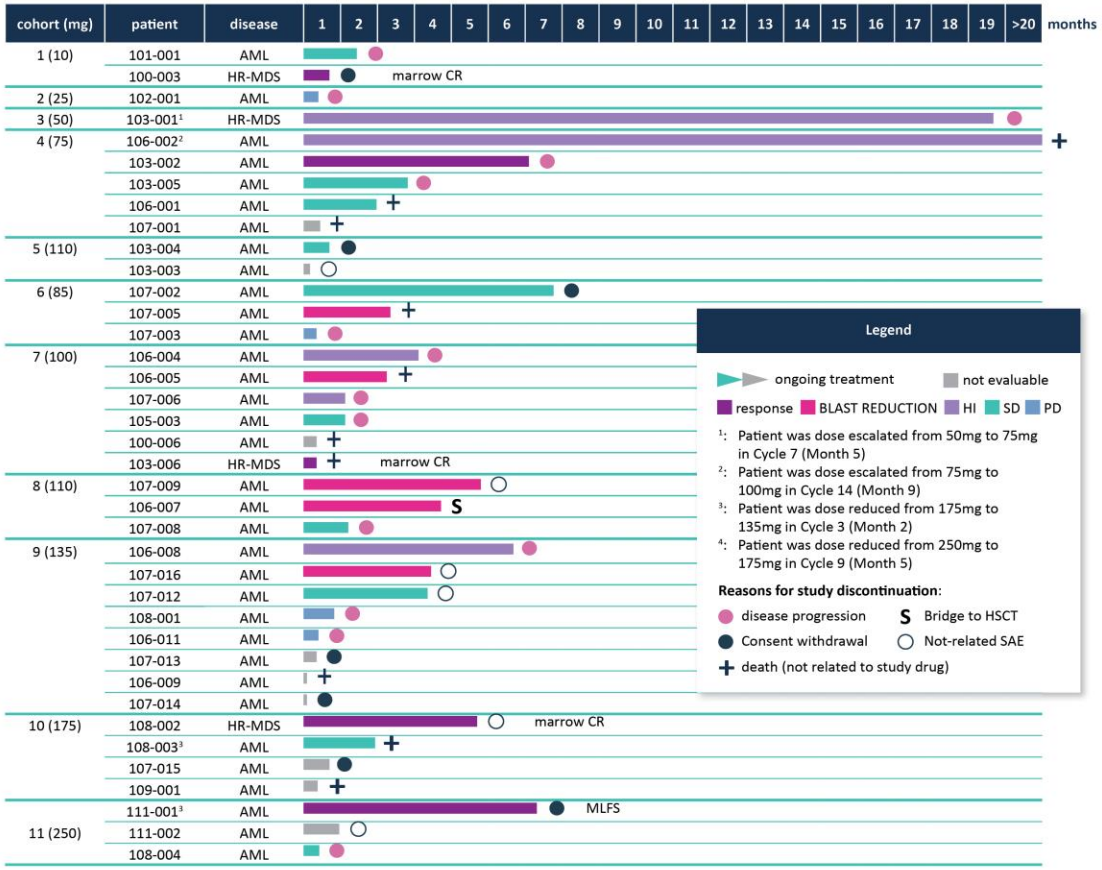
- **30 treated patients are evaluable for response (38 were treated in total)**
- **9 patients achieved clinically significant BM blast reduction**
- (including 1 CR, 1 MLFS, 3 marrow CRs)
- **5 patients achieved erythroid hematological improvement (HI-E),**
  4 of those became transfusion-independent,
  of which 2 normalized also their Grade 3 thrombocytopenia

NPM1 and DNMT3A mutations

- An **NPM1 mutation** was identified in 2 pts – **one patient achieved a CR**, the other experienced an unrelated SAE in cycle 2 and progressed
- Three additional patients had a **DNMT3A mutation** without NPM1 mutation and 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
- **3 of these pts had >10 % blasts at baseline, all of them met the Cheson criterion of marrow CR during treatment with RVU120**



Favorable safety profile

Target engagement levels between 50-70% at a dose of 250 mg QOD – selected for Phase II development

Data generated in RIVER-51 study support further development of RVU120 in AML, LR-MDS and MF

Significant blast reductions

- Confirmed CR in a patient with AML
- Several patients with significant blast reduction

Transfusion independence

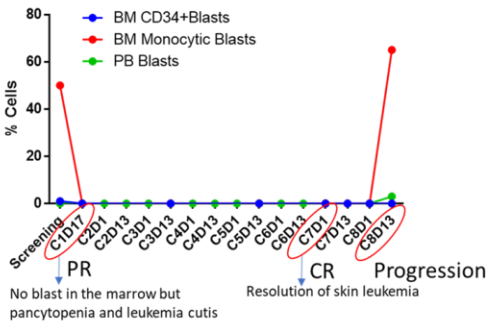
- >20% patients, (all with AML-MR or HR-MDS), showed hematological improvement, meeting Cheson criteria for erythroid response

Improvement of BM architecture

- Signs of activity in secondary AML
  - reduction of fibrosis and hematologic impr.
- Supported by non-clinical data in MF/MDS models

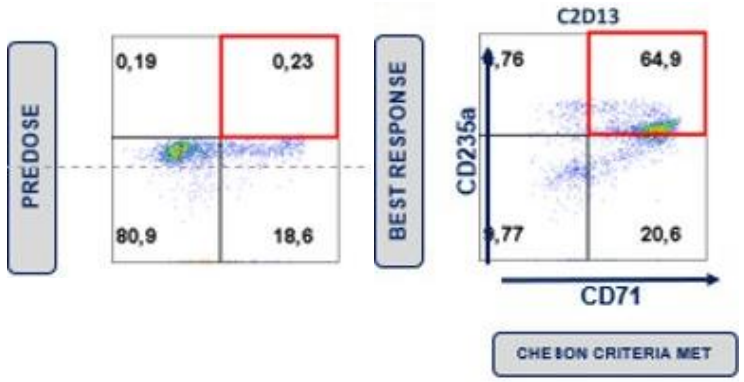
P103-002 AML

- NPM1, DNMT3A, FLT3-ITD.,NRAS
- 46,XX, 3 prior treatment lines
- 6U RBC/3 weeks and 6U Plts/4 weeks



P106-004 AML -MR

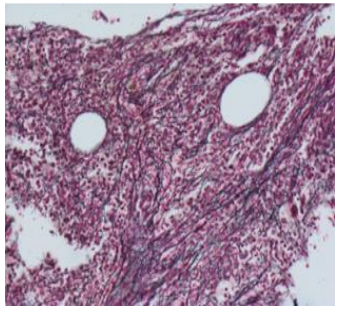
- Mutations: GATA2, RUNX1, SF3B1,TET2, WT1
- Karyotype: 47,XY,+21; 3 prior treatment lines
- 9U RBC/8 weeks; grade 4 Thrombocytopenia



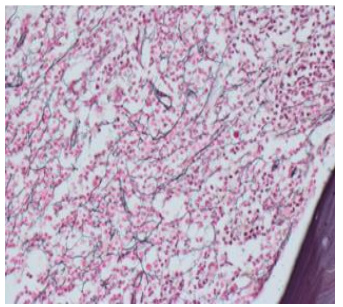
P108-002 HR-MDS

- Mutations: MPL, DNMT3A, U2AF1
- Karyotype: 46XY, add (4)(q21); 1 prior treatment line
- Best response: marrow CR

C2D13 fibrosis grade 3



C6D1 fibrosis grade 2

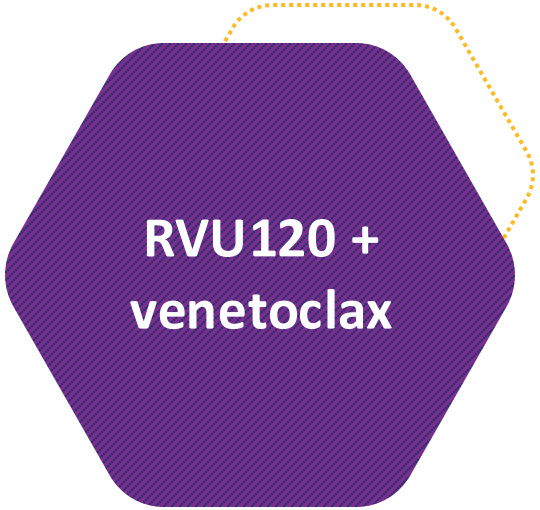


CR achieved end of C1 with persistent skin leukemia, resolved in C5

RBC-TI and Plt-TI on RVU120 treatment

Reduction of fibrosis grade and marrow CR

RIVER-81 Phase II study testing RVU120 in combination with venetoclax in ven-refractory patients with AML



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
- Estimated enrollment: **~35-97 patients**(1)
- Up to **50 clinical sites** planned globally

MEDICAL RESEARCH AGENCY

RIVER-81 is supported in part by a PLN 62 milion grant from the Polish Medical Research Agency (ABM)

PART 1 (N = 17 pts)

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

PART 2 (N = ~39 pts)

Expansion Cohort at selected doses of RVU120 and venetoclax
(Simon 2-stage design + optional enrichment cohort)

PART 3 (N = ~41 pts)

Confirmatory Cohort at doses of RVU120 and venetoclax as in Part 2

(1) 35 patients for: Part 1 (N=17 pts) and Stage 1 of Part 2 (N=18 pts); 97 patients for: complete planned enrollment into Parts 1, 2 and 3, including optional additional enrichment cohort.

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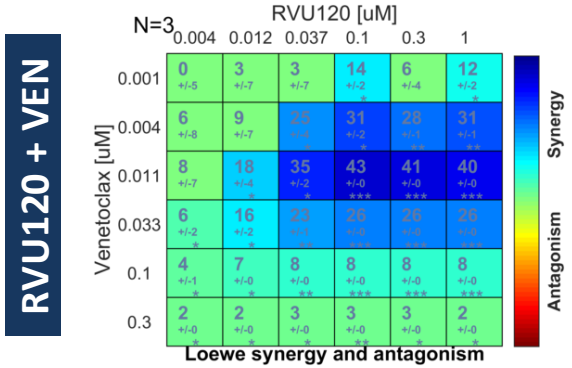
RIVER-81 Strong nonclinical evidence for synergy between RVU120 and venetoclax providing rationale for a Phase II study in venetoclax refractory patients

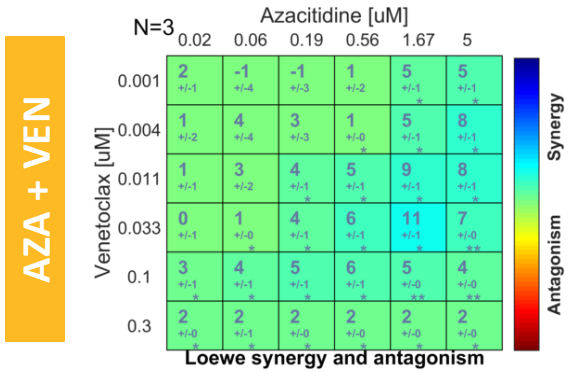
- **True Synergy and Superiority:**
  - RVU120 + ven demonstrates synergy across multiple AML cell lines and superiority over ven + aza
- **Remissions in Animal Studies:**
  - RVU120 + ven achieves remissions in animal models at doses that allow hematological recovery
- **Mechanism of Synergy:**
  - MCL-1 is a known mediator of ven resistance. RVU120 induces caspase-dependent degradation of MCL-1
  - MCL-1 inhibitors were tested in this setting, but prohibitive cardiotoxicity prevented further development
  - The safety profile of RVU120 allows exploration of this concept
  - Effectiveness on Leukemic Stem Cells (LSCs)

MV4-11

RVU120 + VEN

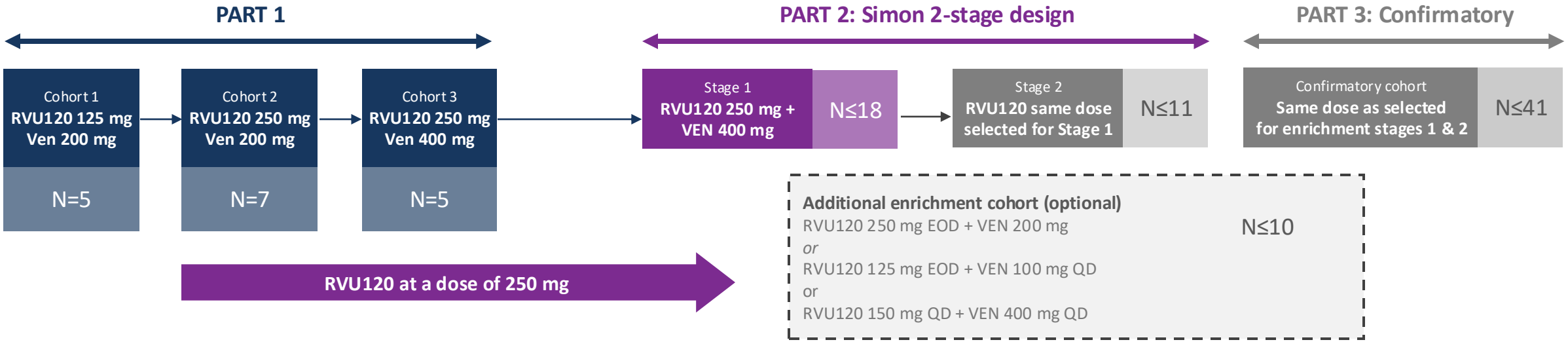


AZA + VEN



RIVER-81 Part 1 (dose escalation) has been completed; Part 2 is enrolling

STUDY PLAN

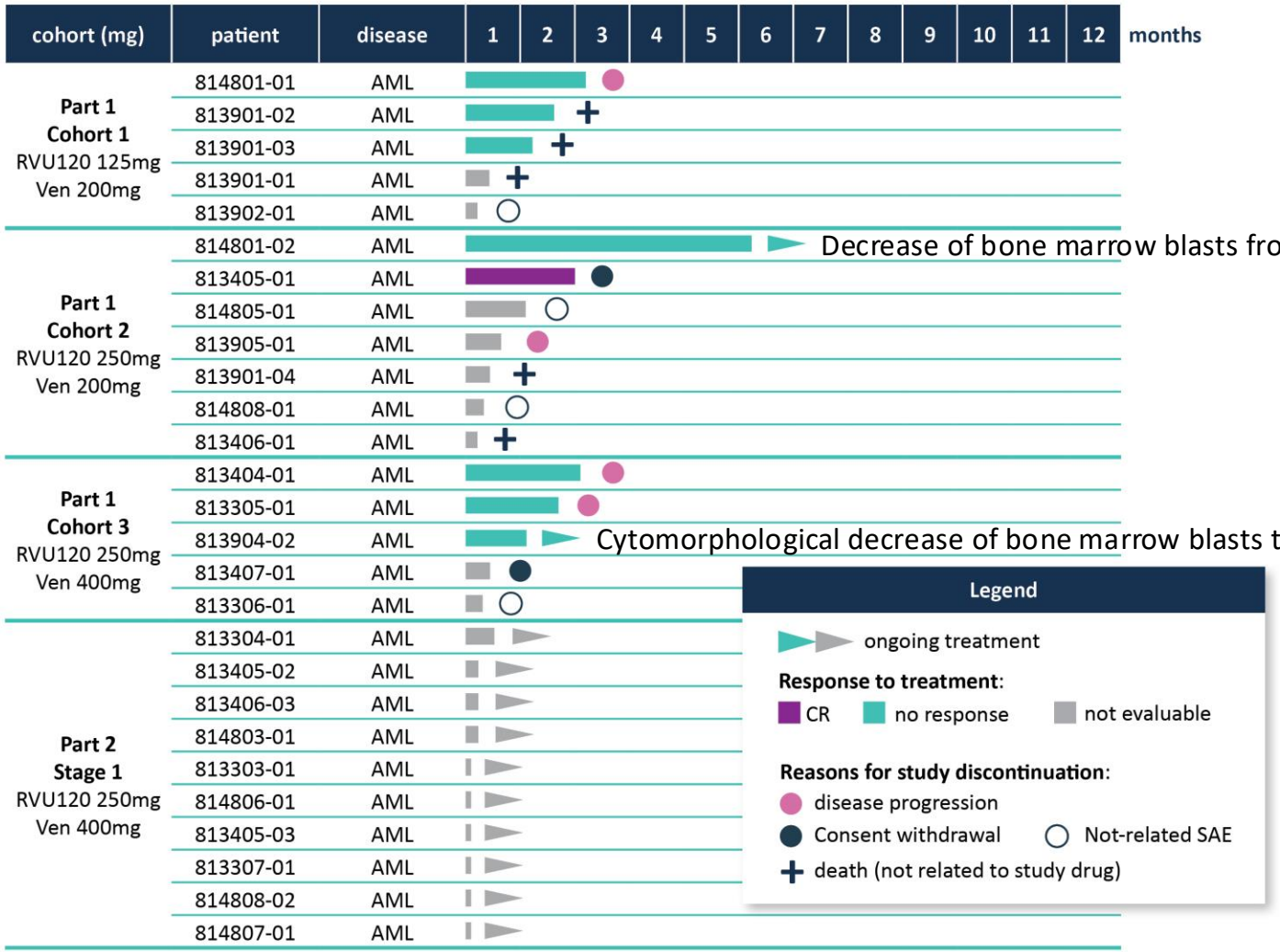


- Dose escalation successfully completed, no DLT was observed
- No altered exposure when dosed in combination with venetoclax
- Maximal anticipated RVU120 + ven combination dose (250 mg + 400 mg) achieved
- Confirmed potential for RVU120 + ven doublet and possible triplet combinations in the future

Enrollment in Part 2 was initiated based on the observed safety and early signs of efficacy of the combination.

Status as of February 24, 2025: 36 patients treated, 35 sites activated

RIVER-81 One patient achieved a CR in a difficult to treat ven-refractory population



Decrease of bone marrow blasts from 20% to 9% in flow cytometry on C2D13

Cytomorphological decrease of bone marrow blasts to < 5% on C1D13

Next data update in June 2025

Data Cut-off: December 10, 2024
Preliminary data

POTAMI-61 Phase II study of RVU120 in myelofibrosis (MF) as mono and combo – first patient was dosed in December 2024

STUDY DESIGN

- **Population:**
  - Primary or secondary MF; intermediate or high-risk MF per DIPSS;
    Cohort 1) previously treated with or ineligible for JAK inhibitor and Cohort 2) suboptimal response to RUX
  - Important: patients with thrombocytopenia can be included in Cohort 1
- **Primary endpoints:** spleen volume reduction at 24 weeks
- **Secondary endpoints**: duration of response, leukemic transformation, hematologic improvement, BM fibrosis reduction, PFS, and OS
- Estimated enrollment: **~20-230 patients**(1)
- Up to **50 clinical sites** planned globally
- Status as of February 24, 2025: **12 patients treated; 17 sites activated**

First data update (12 weeks of treatment) in June 2025

Part A (N = ~20 pts)

- **Cohort 1** (Mono RUX-ineligible or RUX-failed)
- **Cohort 2** (RUX add-on)

Part B (N = ~210 pts)

- **Expansion of Cohort 1 or 2**
- **Cohort 3** (Frontline)

Initial opportunity in second line treatment with potential to move into frontline therapy

(1) ~20 patients in Part A, ~210 patients in Parts B

POTAMI-61 RVU120 validated preclinically as a drug candidate in MF

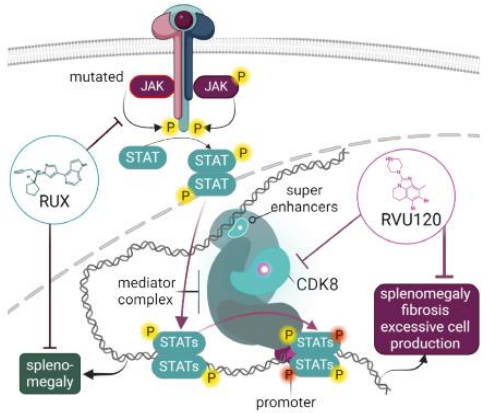
Opportunity in myelofibrosis

- 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 cytopenias

RVU120 in myelofibrosis

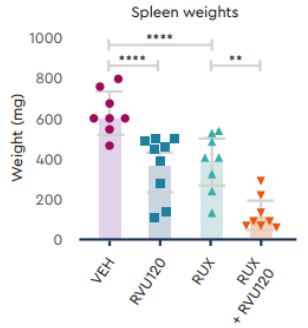
- CDK8 kinase is an important player in MPN pathogenesis, and RVU120 disrupts the downstream signaling events, mitigating MPN symptoms
- In preclinical studies, RVU120 effectively reduced splenomegaly, bone marrow fibrosis, and abnormal blood cell production. RVU120 has also demonstrated synergy in combination with JAK inhibitors
- RVU120 has erythroid stimulating activity and demonstrated a favorable safety profile on normal hematopoiesis, making it a potential candidate for broad clinical use in treating MPNs

Mechanism of RVU120 in MF



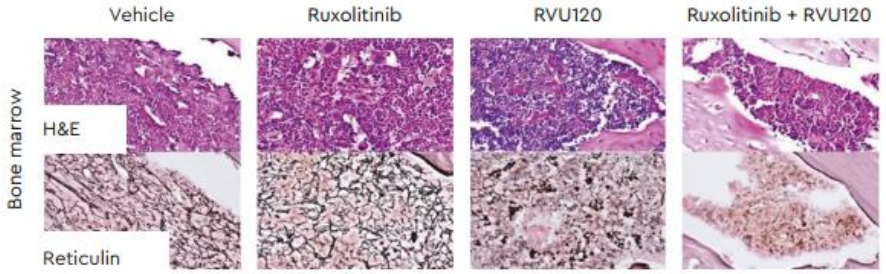
RVU120 reduces splenomegaly

RVU120 as a monotherapy and in combination with ruxolitinib reduces splenomegaly in a MPLW515L mouse model of MPN



RVU120 reduces bone marrow fibrosis

RVU120 as a monotherapy and in combination with ruxolitinib reduces bone marrow fibrosis while also increasing trilineage hematopoiesis in a MPLW515L mouse model



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

STUDY DESIGN

- Population:
  - Patients with relapsed/refractory LR-MDS
- Primary endpoint:
  - Erythroid response (HI-E) according to IWG 2018 criteria after 8 cycles of treatment
- 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 ~40 patients planned
Ongoing assessment of Phase II data will drive further development

First data update in December 2025

IIT

- **First patient dosed in September 2024;**
- **High enrollment rate, above initial expectations**
- Study conducted as an Investigator Initiated Trial with **Prof. Uwe Platzbecker within EMSCO** (European Myelodysplastic Neoplasms Cooperative Group)

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

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REMARK RVU120 validated preclinically as a drug candidate in LR-MDS

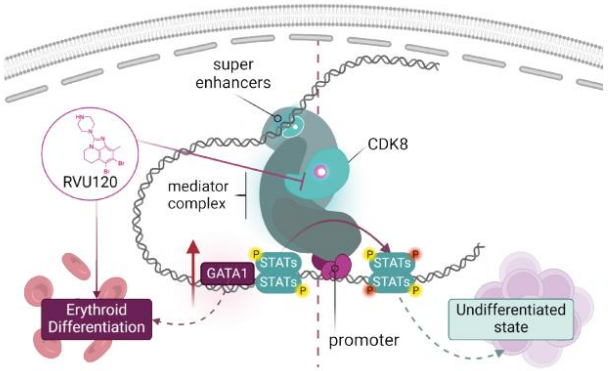
Opportunity in LR-MDS

- A high unmet medical need remains in low-risk MDS (LR-MDS) after failure of available therapies
- Transfusion burden remains high for patients with LR-MDS, resulting a poor quality of life

RVU120 in LR-MDS

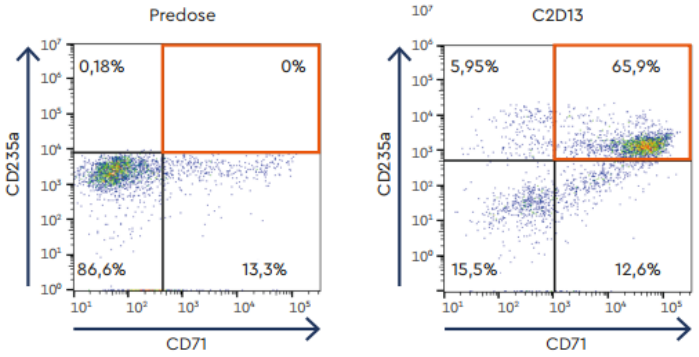
- MDS pathogenesis is influenced by gene expression alterations that hinder the maturation of hematopoietic cells.
- When aberrant stem cells from MDS patients are treated with RVU120, it triggers erythroid gene expression programs orchestrated by STAT5 and GATA1.
- Importantly, RVU120's activity does not lead to significant toxicity in the hematopoietic system. As a result, RVU120 emerges as a promising drug candidate for treating transfusion-dependent MDS patients.

Mechanism of RVU120 in LR-MDS



Clinical evidence of erythropoiesis demonstrated with RVU120

Several patients with AML and HR-MDS showed signs of hematological improvement, including an erythroid response in the RIVER-51 study. Induction of erythropoiesis was confirmed by flow cytometry.



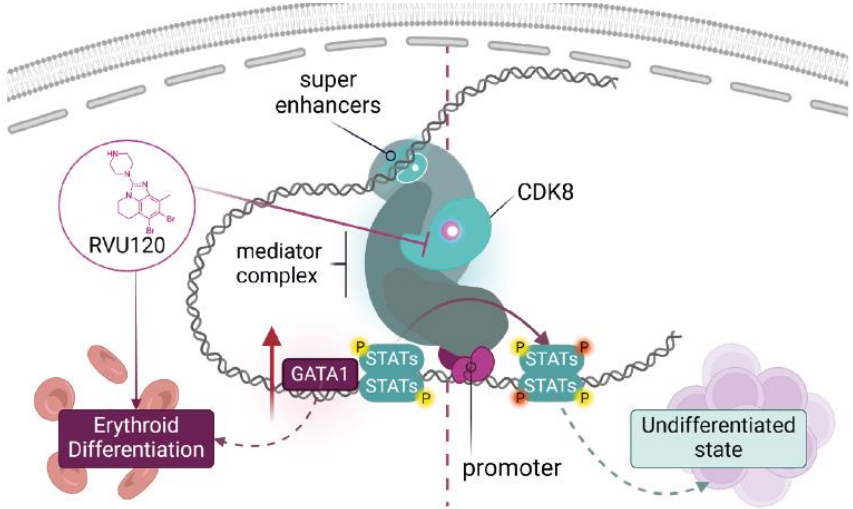
REMARK RVU120 has strong erythroid-stimulating activity in nonclinical anemia models and selected patients with AML/HR-MDS in Phase I (RIVER-51), providing the rationale for the Phase II clinical study in patients with LR-MDS

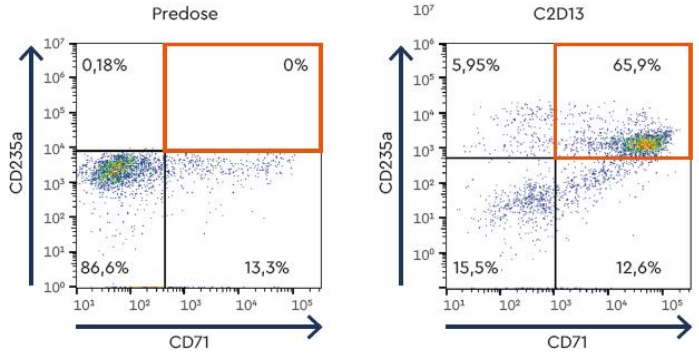
Nonclinical rationale

- Treatment of transformed CD34+ cells with RVU120 results in erythroid lineage commitment
- Isolated CD34+ cells derived from MDS and Diamond-Blackfan anemia patients differentiate into erythrocytes in the presence of RVU120
- Increased red blood cell count and hemoglobin levels were observed in animal studies
- Transcriptomic and chromatin studies identified that RVU120 can enhance GATA1-dependent transcription and reduce the expression of pro-inflammatory genes in MDS cells

Related clinical observations

- 4 AML/HR-MDS patients treated with RVU120 in Phase I showed hematological improvement
- An increase in reticulocytes was also observed in patients with solid tumors





RIVER-52 Phase II study with RVU120 as a single agent in AML/HR-MDS

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: relapsed/refractory AML or HR-MDS with no alternative treatment

PART 1 (N = ~40 pts)

Genetically defined and disease specific cohorts:

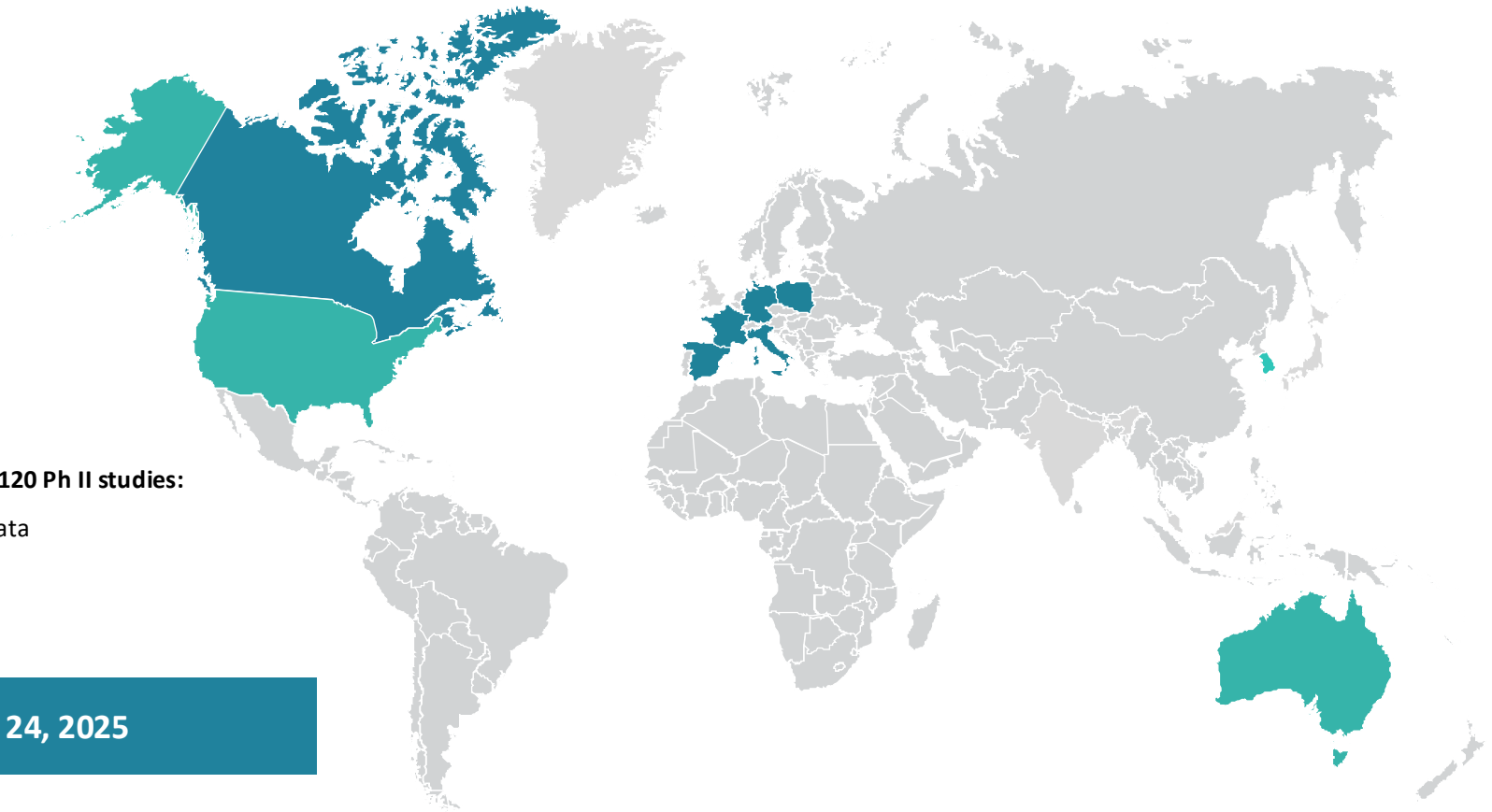
- Pts with NPM1-mutated AML
- Pts with DNMT3a-mutated AML
- Pts with HR-MDS

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

Part 2: Enrollment Suspended

- In February 2025, Ryvu decided not to enroll new patients in the RIVER-52 study. This decision was made to focus investment on other RVU120 development paths, following the initial data review.
- Patients currently enrolled will continue to receive treatment according to the protocol.
- The data collected will be used to support the safety and efficacy database.
- The next data update is planned in Q2 2025.

RVU120 Phase II clinical development 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

Status as of February 24, 2025

Number of Ph II clinical trials initiated in 2024	**Number of countries** across studies	**Number of activated clinical sites** globally	**Number of patients** enrolled	**Number of clinical vendors** managed	**Number of internal Ryvu team members** in Clinical Development and Translational teams
4	6	110+	~120	20+	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 est. 11,220 deaths in the US in 2024[2]
- **Venclexta (venetoclax) sales estimated to exceed USD 3.5 bn in 2025[3]**
- **Kura licensed rights to ziftomenib to Kyowa Kirin for USD 330M upfront and USD 1.2 bn total milestones in Nov 2024**
  - Phase III asset
  - Part of a global collaboration

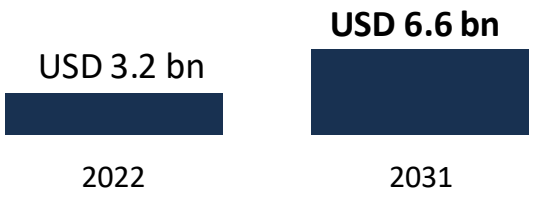
MDS (Myelodysplastic Syndrome)

- 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)

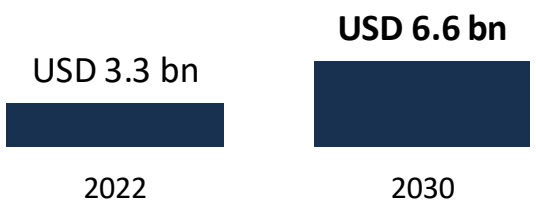
- MF is a bone marrow disease characterized by JAK mutations; often leads to severe anemia
- Chronic disease with long duration of therapy; US prevalence is est. to be ~13,000 patients[7]
- **Jakafi (ruxolitinib) sales in 2023 – USD 2.6 bn**
- **Morphosys acquired by Novartis for EUR 2.7 bn in Feb 2024**
  – primary asset is Phase III MF drug pelabresib

Global AML Market[4]



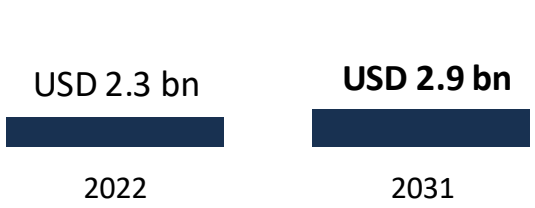
8.5% CAGR (2022-2031)

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

RVU120 Program on track with next efficacy readouts in June 2025

Approx. 120 patients have already been dosed across all RVU120 Phase II studies (as of Feb. 24, 2025)

RVU120 program summary

RIVER-81 **Next data in June 2025**

- Part 1 (combo dose escalation) completed – safety confirmed; Part 2 initiated
- One patient in Part 1 achieved a CR (as of Dec 10, 2024)
- 36 patients enrolled in Part 1 and Part 2

POTAMI-61 **Enrollment ongoing; initial data in June 2025**

- First patient dosed in December 2024
- 12 patients enrolled
- Initial efficacy data expected in Q2 2025

REMARK **Enrollment ongoing; initial data in December 2025**

- First patient dosed in September 2024
- Enrollment rate above the initial expectations
- Initial efficacy data expected by Ryvu in Q2 2025, publication in Q4 2025

Accelerating enrollment across Phase II program

- 3 Phase II studies in progress as planned: RIVER-81, POTAMI-61, REMARK
- Given emerging data, RIVER-52 deprioritized to focus on other RVU120 development paths
- Global clinical program with accelerating enrollment
- Strong interest from the investigator community

Safety and efficacy as expected early in Phase II

- Safety profile potentially better than in most drugs used in AML
- Encouraging early signs of efficacy in Phase II

On track in 2025 for key data

- Numerous data readouts expected in 2025
- No budget overruns with cash runway to H2 2026

RYVU THERAPEUTICS

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

Dapolsertib (MEN1703, SEL24) JASPIS-01 Phase II clinical study in DLBCL

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 funds all research and development costs

PROVEN SAFETY AND CLINICAL ACTIVITY

- Manageable safety profile
- Orphan drug designation (ODD) granted by FDA
- Phase II clinical data in AML indicated single-agent efficacy, but not competitive enough

DLBCL

- Development continues 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

Partnership

- As of September 2023, Ryvu has become Menarini's operational partner for Phase II execution

First patient in DLBCL dosed on March 26, 2025

Phase II in DLBCL

DAPOLSERTIB 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 consists of two parts:
  Part 1 pilot cohorts to establish combination dose and monotherapy efficacy followed by Part 2 cohort expansion
- Study locations: Poland, Spain, France, UK

RVU305: MTA-cooperative PRMT5 inhibitor

- Best-in-class potency and selectivity
- Brain-penetrant

RVU305: Best-in-class PRMT5 MTA-cooperative inhibitor in IND-enabling studies

RVU305/PRMT5i

KEY RATIONALE and MOA	PRMT5 MTA-cooperative inhibitors exert synthetic lethal phenotype in MTAP deleted cells
NOVELTY	Best-in-class potential: selectivity, potency, brain penetration and safety
TOP TUMOR INDICATIONS	MTAP deletions, up to 15% of all cancers, one of the largest genetically-defined population: GBM, lung, pancreatic, DLBCL, bladder, esophageal
STATUS	Complete IND-enabling studies in H2 2025

RVU305 has best-in-class potential based on robust multiparameter optimization

RVU305 demonstrates superior preclinical properties vs. competitors

- **Antiproliferative activity:** demonstrated in MTAP-deleted cells *in vitro;* high potency and efficacy in large cell line panel
- **Antitumor efficacy:** achieved *in vivo* in responder CDX models
- **Brain-penetrant**: observed in cyno
- **Favorable PK profile:** demonstrated in multiple species

Leading to a differentiated clinical strategy

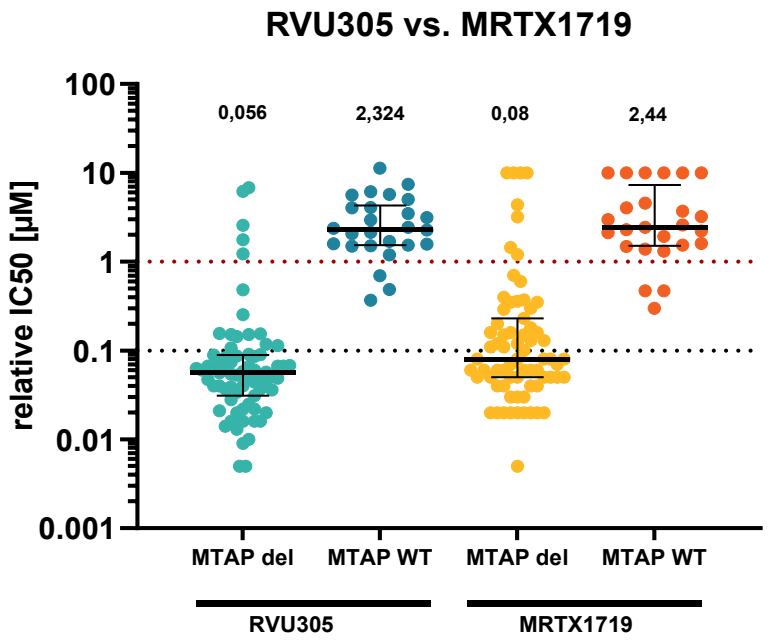
Ongoing translational work will support the selection of

- Indications/tumors
- Drug combination partners
- Patient sub-populations

RVU305 shows superiority in multiple cell lines

Analysis of pancreatic, lung and bladder cancer origin cell lines shows RVU305 superiority over MRTX1719

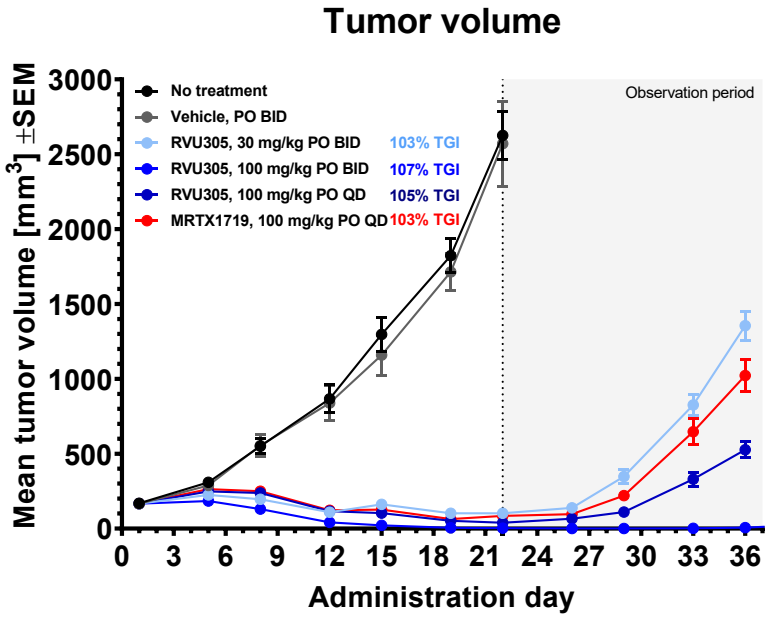
- Panel of MTAP-deleted and MTAP-wt cells was profiled with RVU305 in a 5-day CellTiter-Glo assay
- A differential response to Ryvu PRMT5 MTA-cooperative inhibitor is seen between cells with different MTAP status
- RVU305 shows higher potency than MRTX1719 (comparing to results published by Engstrom et al., 2023)



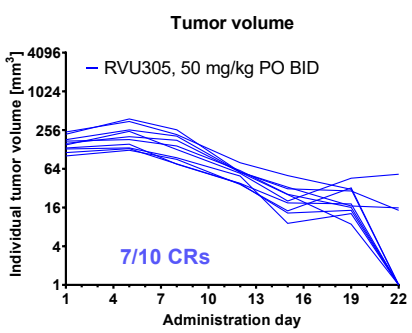
RVU305 shows significant antitumor efficacy *in vivo*

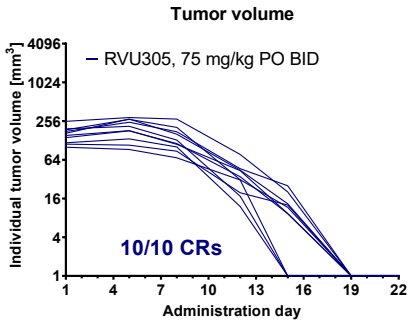
Strong antitumor efficacy

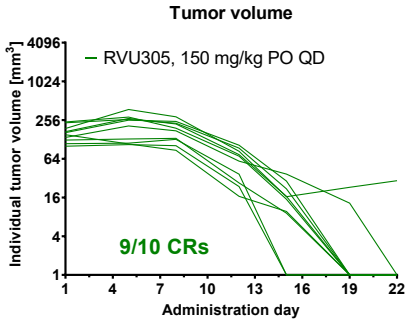
DoHH2 MTAP-deleted model (DLBCL)

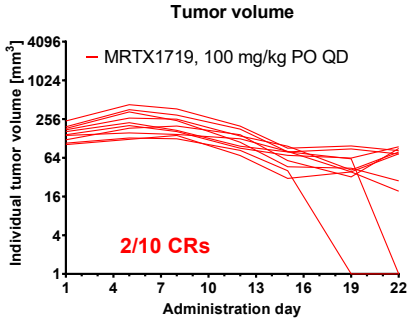


Complete responses demonstrated in vivo: favorable vs. MRTX1719







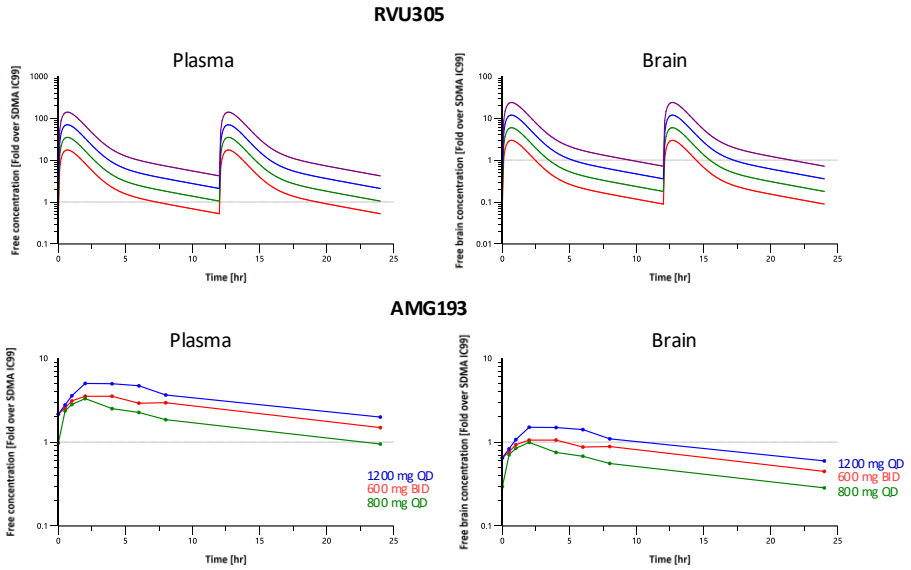


DoHH2 MTAP-deleted model. Individual tumor volumes in a log2 scale from efficacy study in which RVU305 was administered orally (PO) once (QD) or twice (BID) daily, and MRTX1719 was administered PO QD to SCID mice bearing DoHH2 (DLBCL carcinoma) tumors (n=10 animals/group). Either no tumor growth (10 mg/kg BID) or tumor volume regression (other BID dose levels and QD administration) were present after RVU305 treatment.

RVU305 is CNS-penetrant PRMT5 inhibitor with predicted efficacious exposure in the brain

RVU305 shows optimal systemic target coverage and excellent brain penetration

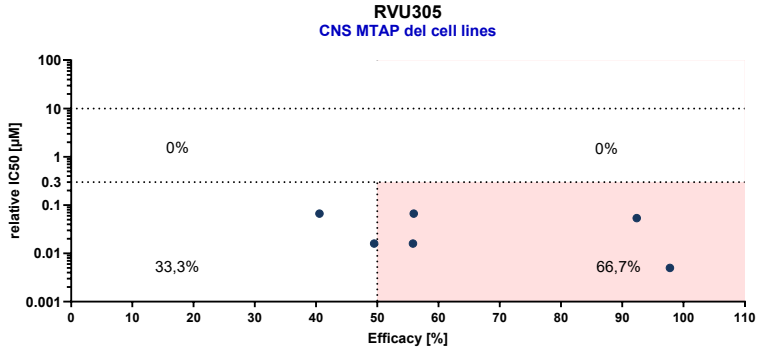
Predicted free RVU305 exposure in projected human escalation phases



Systemic exposure measurements of AMG193 indicate only partial coverage of the target in the brain at clinical doses

Human PK data from: DOI: 10.1016/j.annonc.2024.08.2339

RVU305 exhibits high potency and efficacy against CNS cell lines



RVU305 demonstrated IC50 < 300nM and EC50 > 50% for 67% of the cell lines tested

Brain penetration enables potential efficacy in glioblastoma and tumors with high brain mets, such as lung cancer

RVU305 has a potentially best-in-class profile

	MRTX1719/ BMS-986504	TNG462	TNG456	AMG193	RVU305
Potency*	+++	+++	++	++	+++
Brain penetration	-	-	Yes	Yes (+)^	Yes (++)^
Viability fold shift MTAP KO/MTAP WT	+++	++	++	++	++++
Residence Time	+++	ND	ND	ND	+++
% of sensitive MTAP deleted cell lines in Omniscreen	36% #	ND	ND	ND	63% #

- RVU305 is **brain-penetrant** and shows **better target coverage in brain** compared to AMG193
- RVU305 has **better selectivity** in MTAP-deleted vs WT cells compared to MRTX1719/ BMS-986504, and may have exposure benefits
- RVU305 shows approximately **10-fold better cellular potency** in MTAP-deleted cells compared to AMG193
- RVU305 has **2x better potency shift** between MTAP-deleted vs WT cells when compared to TNG462 (29-fold vs 66-fold)

* Viability in vitro in MTAP-del cell line model
^ Based on head-to-head comparison in cynomolgus brain PK experiment and simulations
# Based on Mirati data and Omniscreen panel, where 0.3uM (the level of response WT cells) was used as a cutoff for sensitivity

Early pipeline

Dual-pronged strategy with potential to generate multiple oncology medicines

Novel precision oncology drug discovery platform

ONCO Prime

ADCs

Next-generation novel ADC payloads

Broad potential to discover novel precision oncology targets, including synthetic lethal targets across a variety of tumor types – initial case study data presented in colorectal cancer

Several novel targets for **KRAS-driven tumors identified**

Approach that allows exploring **novel treatment strategies via phenotypic screening**

Potential to improve efficacy, safety and combinability in next generation ADCs

Newer/innovative approach to development of immunomodulatory, synthetically lethal and immunocytotoxic ADC payloads **(including WRN)**

Leveraging Ryvu's internal competences and ADC collaboration with Exelixis

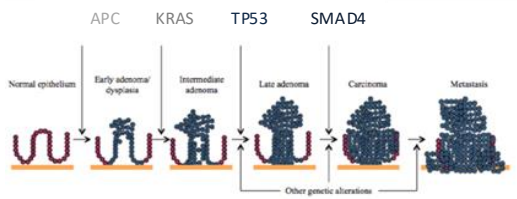
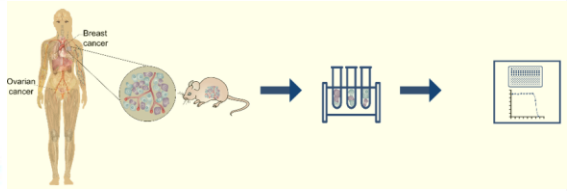
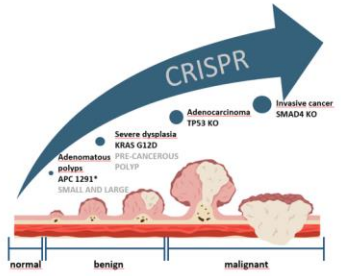
ONCO Prime:
Novel Precision Oncology

Multi-asset platform generating first-in-class therapeutics

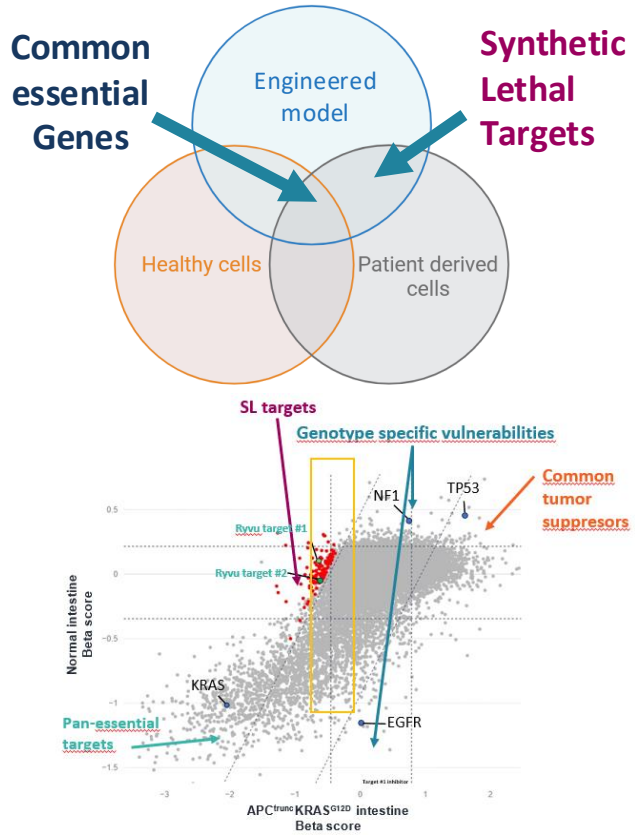
RYUU THERAPEUTICS

Driving novel precision oncology drug discovery with Ryvu's ONCO Prime platform

Ryvu's CRISPR-based target Discovery Platform

Engineered Model	Patient-Derived Cells (PDCs)
	
Isogenic Primary Cells Recreating the stages of tumor development	Tumor heterogeneity & relevant transcriptomic profile
	**Awarded USD 6.6M grant** Polish Agency for Enterprise Development[1]

Discovering Novel Precision Oncology Targets, including Synthetic Lethal Targets



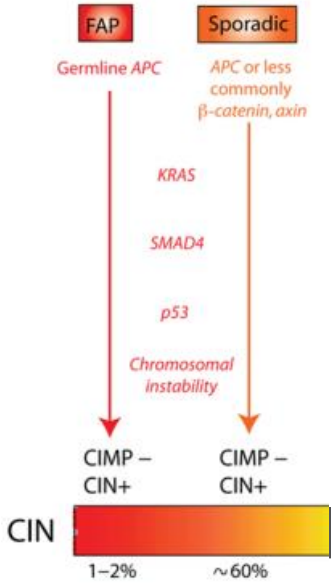
1) ONCO Prime is co-financed by the European Union under the Operational Programme European Funds for Modern Economy 2021-2027. Project title: "ONCO Prime: new possibilities for personalised anti-cancer therapy based on patient-derived primary cell cultures, omics characterisation, and functional assays". Grant Agreement no: FENG.01.01-IP.02-0095/23.

Initial ONCO Prime data presented in CRC; broad applicability across oncology

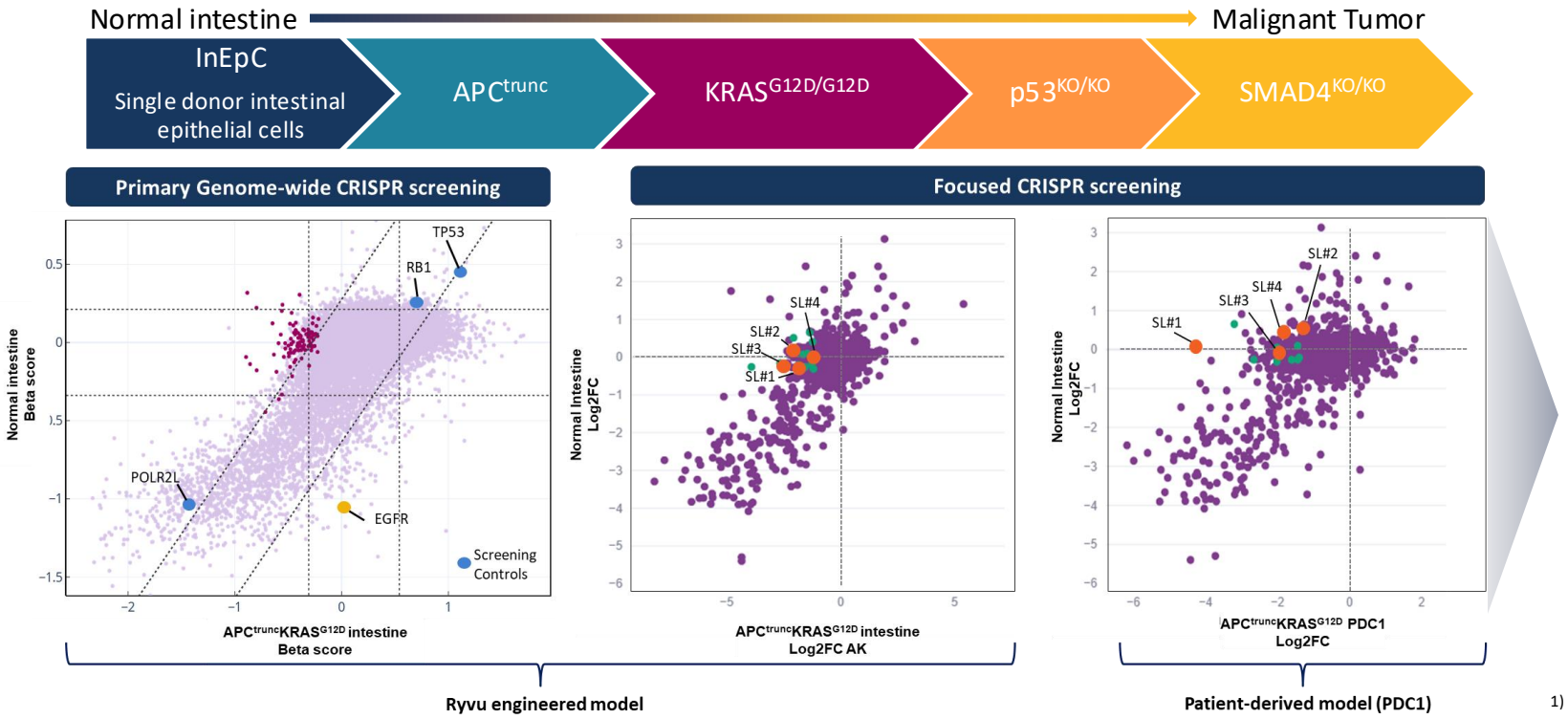
CRC

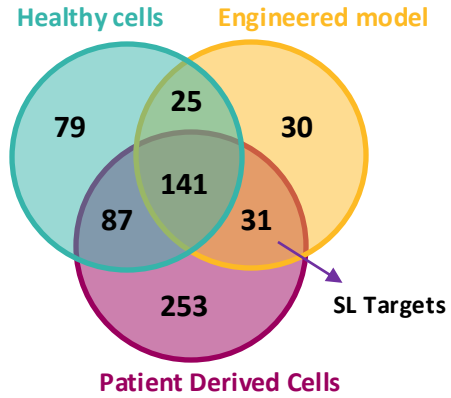
- **The third most prevalent cancer worldwide**
- Estimated number of colorectal cancers in the US for 2024 are 153,000 new cases[1]
- Diagnosed usually at an advanced stage. Mortality still remains high.
  Five-year survival shown by SEER database is **around 65%**, the survival drops to **13%** at stage 4.
- **Lack of targeted therapies** (except KRAS G12C which showed moderate PFS)

Conventional adenomas progress through the sequential accumulation of genetic mutations and chromosomal instability



Based on East et al. 2017

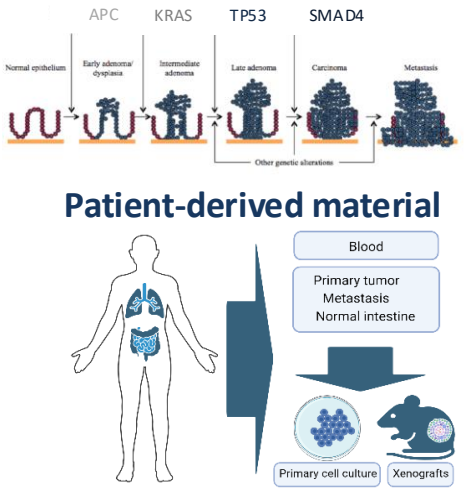




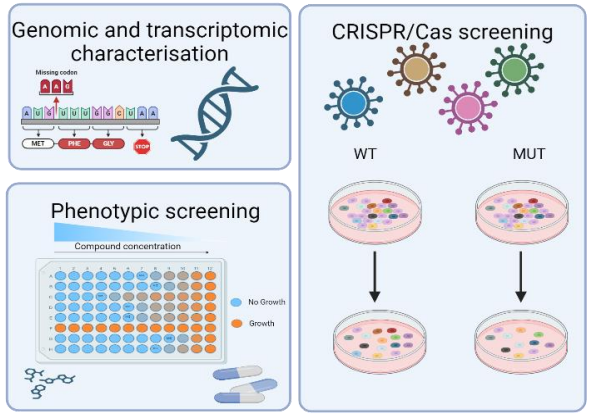
1) American Cancer Society

ONCO Prime is accelerating the development of novel precision medicine targets, including synthetic lethal targets

Modeling cancer progression



High Throughput Screenings



Novel Targets & Treatments

- Ryvu's OncoPrime platform has **broad potential to discover novel precision oncology targets, including synthetic lethal targets** across a variety of tumor types – initial case study data presented in colorectal cancer
- Ryvu Target Discovery platform has identified **several novel targets** for **KRAS-driven tumors**
- Our approach allows exploring novel treatment strategies via phenotypic screening

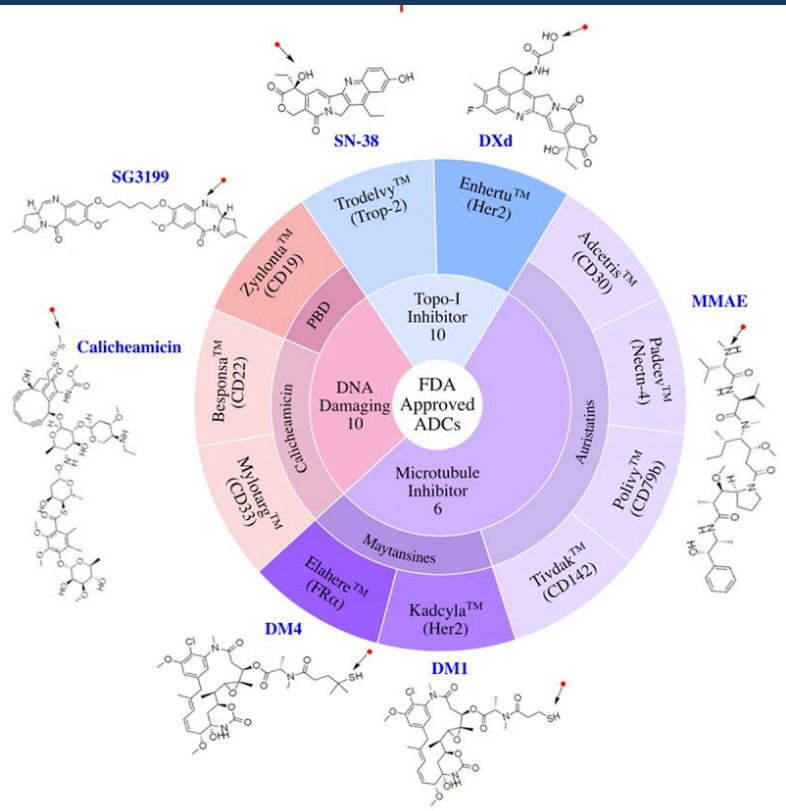
ADCs with Novel Payloads

Generating multiple first-in-class therapeutics

RYUU THERAPEUTICS

Novel payloads have the potential to improve efficacy and safety in next generation ADCs

Approved ADCs use three main types of payloads



Maecker et al., MAbs, 2023.

Novel payloads have the potential to improve on…

- **Efficacy**: overcome resistance to existing payloads and potentially improve on potency
- **Safety**: expand the safety window by leveraging targeted payloads (e.g. synthetic lethality) or immunomodulatory MOAs
- **Combinability**: emergence of bispecific and dual/multiple payload ADCs could represent a new combination approach

ADCs Ryvu's payload strategy is focused on novel and potent mechanisms

PAYLOAD CLASSES

POTENT CYTOTOXINS

Traditional approach

Established cytotoxics including calicheamicin, microtubule inhibitors and topoisomerase inhbitors

IMMUNOMODULATORY PAYLOADS

A newer approach

- Experience from STING as payload (licensed to Exelixis)
- Multi-target collaboration with BioNTech to develop immuno-modulatory small molecule candidates (press release November 30, 2022)

SYNTHETICALLY LETHAL/ PRECISION PAYLOADS

Innovative approach

- Ryvu's track record in synthetic lethality provides a jump start with advanced molecules from Ryvu's portfolio

IMMUNOCYTOTOXIC PAYLOADS

Innovative approach

- Exploring cytotoxic payloads that also exert an immunomodulatory effect
- Pan-cytotoxic mechanism of action clinically validated by classic payloads

RYVU'S STRATEGY

Ryvu has shortlisted several immunocytotoxic payloads to advance

Based on initial screens at Ryvu, several targets have been selected as promising immunocytotoxic payloads.
Some blinded examples are presented below.

Target	Drug name	Low nM inhibitors available *	Pantoxic profile	PoC as ADC payload	Type of immune response	Single agent immune mediated efficacy	IO combo efficacy
Target 1	Several clin. cand. grade	●	●	●	dsRNA and INF response ↑, immunopeptidome ↑	●	●
Target 2	Several clin. cand. grade	●	●	●	Micronuclei mediated INF response ↑, ICD	● **	● **
Target 3	Several clin. cand. grade	●	●	ND	↓ pSTAT3, INF response ↑, DC maturation, ICD	●	●
Target 4	One clin. cand. grade	●	●	ND	Systemic inflammatory disease	ND	ND

● Poor
● Medium
● Good

Common essentials

Immunomodulating and pan-cytotoxic

Cytostatic activity
* IC50 of inhibitors in **cell viability assay** in low nM range
** In ADC payload context
*** autoimmune syndrome caused by heterozygotic partially inactive target LoF mutant. If this is to be phenocopied to TME, will only result from bystander effect in tumor infiltrating immune cells

RYVU THERAPEUTICS

Ryvu has already developed a portfolio of immunostimulatory payloads: STING agonists licensed to Exelixis for ADCs

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

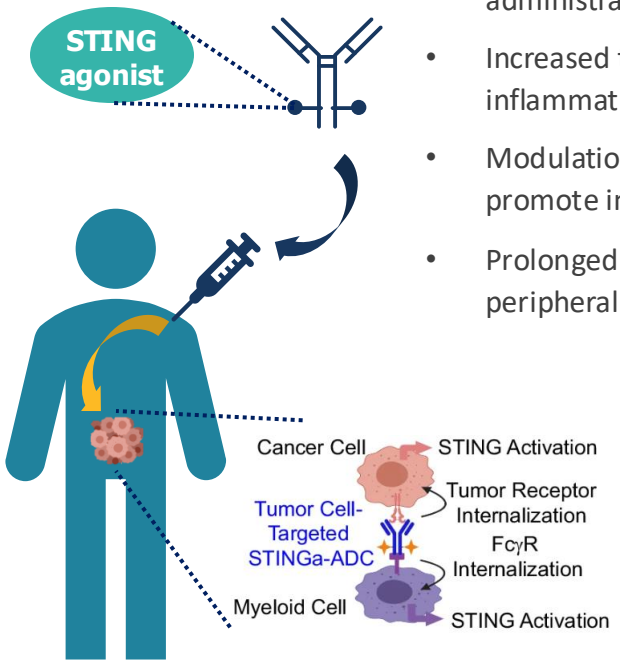
Key Financial Terms

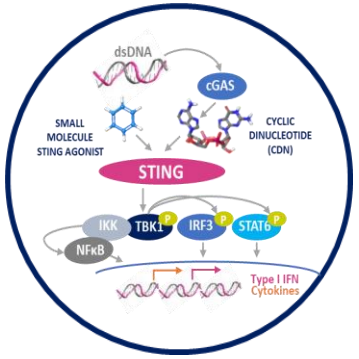
- $3M upfront cash; first milestone of $1M achieved in Q1 2023; second milestone of $2M achieved in Q1 2024
- Additionally, Ryvu is eligible to receive research funding, a double-digit milestone at first development candidate selection, and additional milestones
- In total, Ryvu is eligible to receive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

STING activating Antibody-Drug Conjugates

STING activating Antibody-Drug Conjugates

- Localised immune response after systemic administration
- Increased tolerability due to limited systemic inflammation
- Modulation of tumor microenvironement to promote immune cell infiltration
- Prolonged STING agonist exposure without peripheral effects

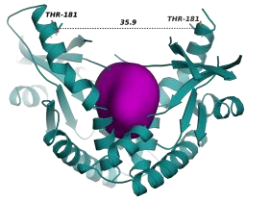




RYVU THERAPEUTICS × EXELIXIS®

- Proprietary STING agonist chemotype
- Small-molecule, non-CDN structures
- ADC-amenable
- Robust STING-specific activity in vitro and in vivo

- ADC development expertise
- Antibodies against cancer-relevant antigens
- Linker and conjugation technology



Antibody-drug conjugate

- Highly potent STING-activating antibody-drug conjugates
- Picomolar activity range *in vitro*
- Antigen-dependent STING activation
- **Ongoing development of STING-activating ADCs**

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

Largest-ever Ryvu deal: November 2022

BIONTECH

RYVU THERAPEUTICS

Partnership

- Multi-target research collaboration: Ryvu is conducting 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.
- Partnership revised in Q1 2025 to focus on earlier-stage projects

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

Corporate Progress

Full-Year Financial Results: 2024

€ million	2023*	2024*
Revenues	**15.0**	**23.7**
Partnering	*10.5*	*18.1*
Grants	*4.5*	*5.6*
Total Costs**	**34.7**	**51.0**
Clinical Pipeline	*12.0*	*25.7*
Early Pipeline	*14.7*	*16.6*
G&A	*8.0*	*8.7*
EBIT**	**-19.7**	**-27.4**
EBITDA**	**-17.2**	**-24.9**
Net Results***	**-18.5**	**-24.9**

Partnering revenues in 2024:
Exelixis (€1.9M), BioNTech (€13.6M)

Cash position March 9, 2025

€43.7M (PLN 182.3M)

In addition, the company has secured approximately €21.8M (PLN 91.0M) in non-dilutive grant funding.

Ryvu Employees

~200

Employees with PhD

~60

- **Pipeline optimization and employment reduced by 30% in Feb. 2025, extend the cash runway to H2 2026**
- Next update (2025Q1 quarterly report) – May 22, 2025

* Recalculated from PLN using 4.5284 PLN/EUR, and 4.3042 PLN/EUR – for 2023 and 2024, respectively
** Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of €1.8m and €1.0m in 2023 and 2024 respectively) and valuation of NodThera (+ €0.8m (increase of costs) in 2023, and + €0.0m in 2024, respectively)
*** Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of €1.8m and €1.0m, in 2023 and 2024 respectively)

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

2025 / KEY GOALS AND FINANCING

PIPELINE

- **RVU120 broad development (including potential fast-to-market strategy in AML/LR-MDS/MF)**
- Dapolsertib progressing in Phase II in DLBCL (with Menarini Group)
- Discovering **ADCs with novel payloads,** and novel precision medicine targets through the **ONCO Prime discovery platform**

BUSINESS

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

RVU120 PROGRESS SUMMARY

- **Accelerating enrollment across Phase II program**
  - Three Phase II studies in progress as planned: RIVER-81, POTAMI-61, REMARK
  - Given emerging data, RIVER-52 deprioritized (enrollment suspended) to focus on the other development paths
  - Global clinical program in progress
  - Strong interest from the investigator community
- **Safety and efficacy as expected early in Phase II**
  - Safety profile potentially better than in most drugs used in AML
  - Encouraging early signs of efficacy in Phase II
- **On track in 2025 for key data, no budget overruns**

2025 / KEY ANTICIPATED EVENTS

- **Multiple updates from RVU120 in June and December**
- Complete RVU305 IND-enabling studies in H2

STRONG CASH POSITION WITH MULTIPLE POTENTIAL INFLOWS

- **Secured €64 million (PLN 273 million)[1] with cash runway to H2 2026**
- **Numerous potential inflows**
  - Milestones from the ongoing partnerships
  - New grant applications in review and planned
  - New partnerships

1. €43m (PLN 182m) in cash and other marketable securities, €23m (PLN 91m) in already secured grant funding; as of Feb 23, 2025, including the €22m EIB debt (payable from 2029).

Ryvu equity summary

IPO on WSE **Corporate Split: Selvita and Ryvu**	Nov 2014 Oct 2019
Ticker: WSE	RVU
52-Week Range[1]	PLN 17.62 – 55.80
Average Daily Volume (YTD) [1]	63,749
Market cap[1]	PLN 751M (EUR 176M)
Shares outstanding	23.1 M
Cash[2]	EUR 43.7M

Top Holders[3]		
1	Paweł Przewięźlikowski	17.4%
2	Allianz OFE	9.2%
3	BioNTech SE	8.3%
4	Allianz TFI	6.9%
5	Nationale-Nederlanden OFE	6.0%
6	Tadeusz Wesolowski (incl. Augebit)	5.9%
7	PZU OFE	4.5%
8	Bogusław Sieczkowski	3.6%
9	Norges Bank	2.1%
10	Goldman Sachs TFI	1.9%
11	UNIQA OFE	1.8%
12	Generali OFE	1.5%
13	Skarbiec TFI	1.4%
14	Vienna OFE	1.2%

Analyst Coverage

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

1. As of 6 May, 2025 2. As of 09 March 2025 3. From stooq.pl as of May 6, 2025.

Thank you

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