



Developing therapeutics
at the forefront of oncology

Corporate Presentation

March 2025



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

Clinical and Preclinical 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; DLBCL study to initiate with potential across hematology
- Partnered with Menarini Group

RVU305

- Best-in-class oral 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

- **WRN** as a novel ADC payload and multiple novel ADC payloads in development
- **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
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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			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			Initial Ph II data in 4Q25
Dapolsertib (PIM/FLT3)	DLBCL (mono and combo with glofitamab)			JASPIS-01			Phase II initiation in 1Q25
RVU305 (MTA-cooperative PRMT5)	MTAP-deleted tumors						Complete IND-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	

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



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

Medulloblastoma

ACC

Breast

Sarcoma

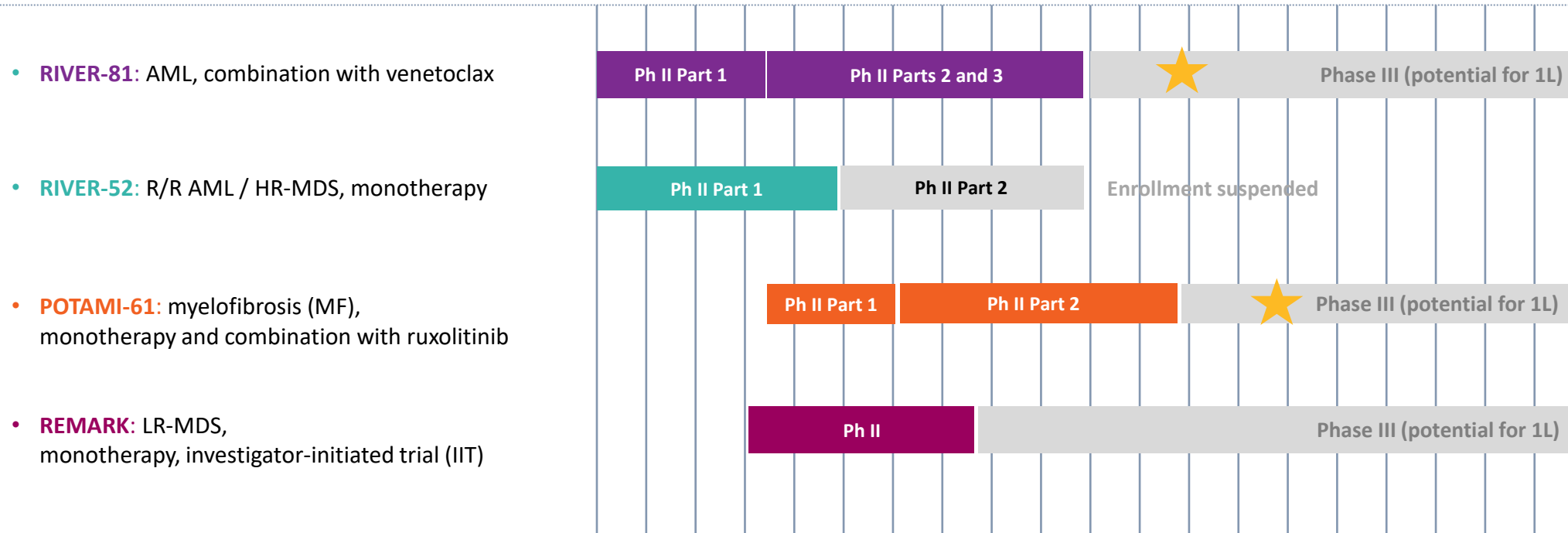
- Translational evidence in multiple tumor types, additional potential in combinations
- Single agent and combination potential across several solid tumors

RVU120 development plan is focused on hematological malignancies
Three Phase II studies are enrolling

2024				2025				2026				2027				2028			
I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV

Beyond 2028

Phase II studies in hematologic malignancies



★ Approval process in selected regions

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

15 of 30 evaluable patients showed clinical benefit across dose levels

Clinical benefits

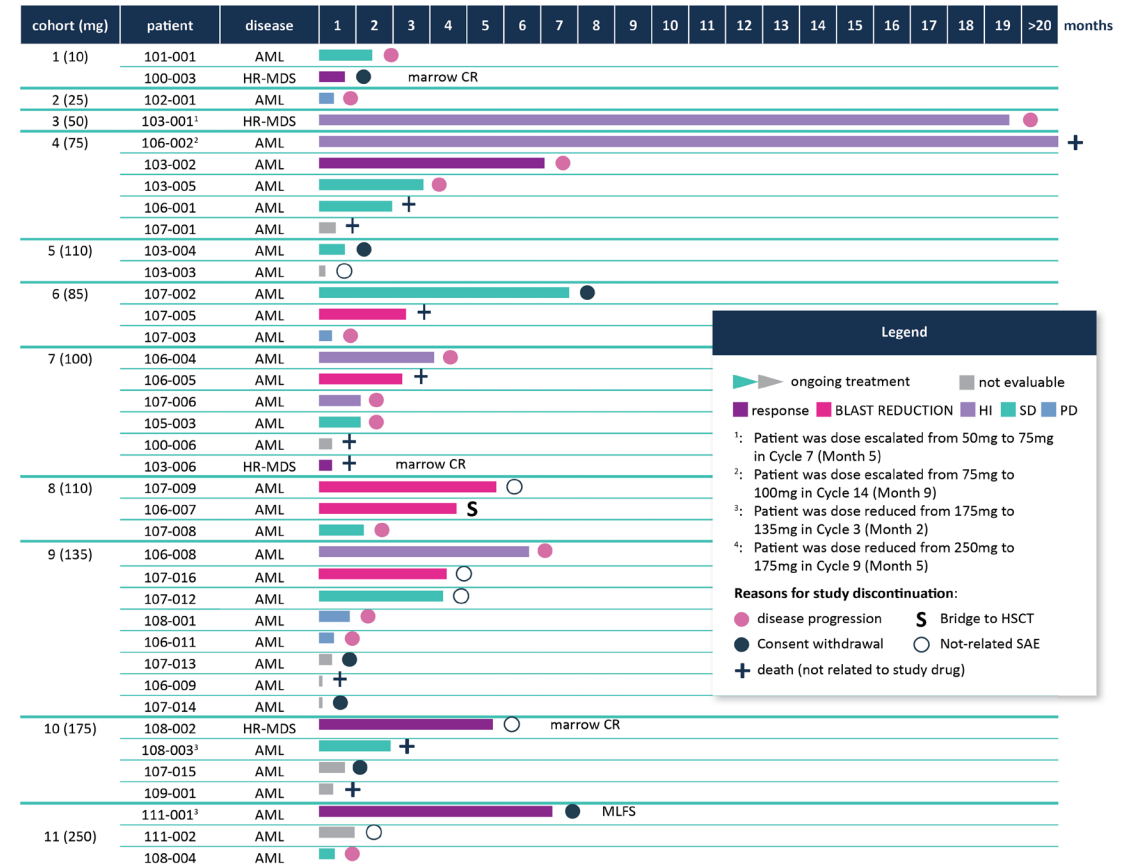
- 30 treated patients are evaluable for response (38 were treated in total)
- 9 patients achieved clinically significant BM blast reduction
 - (including 1 CR, 1 MLFS, 3 marrow CRs)
- 5 patients achieved erythroid hematological improvement (HI-E), 4 of those became transfusion-independent, of which 2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

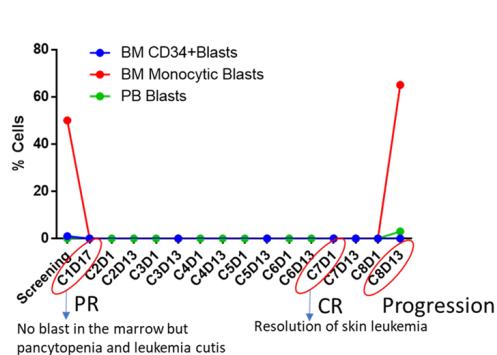
Data generated in RIVER-51 study support further development of RVU120 in AML, LR-MDS and MF

Significant blast reductions

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

P103-002 AML

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



SCREENING



RVU120 C5D1

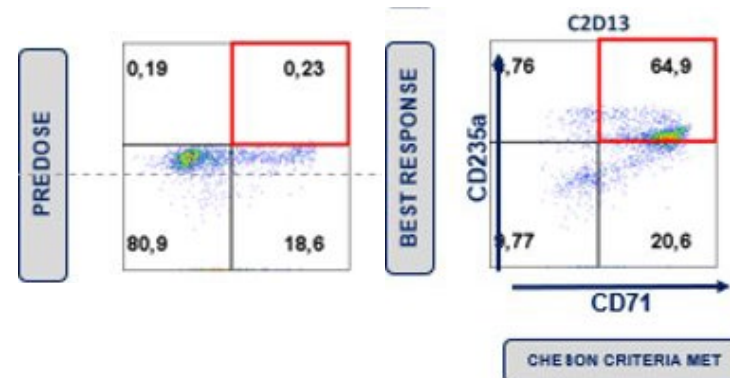


Transfusion independence

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

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



RBC-TI and Plt-TI on RVU120 treatment

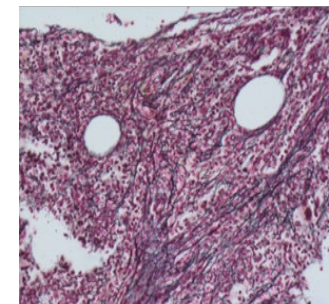
Improvement of BM architecture

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

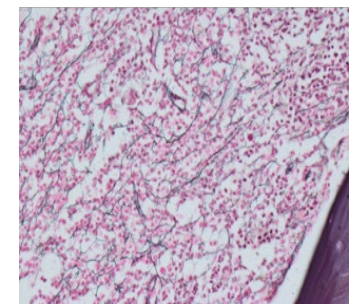
P108-002 HR-MDS

- 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

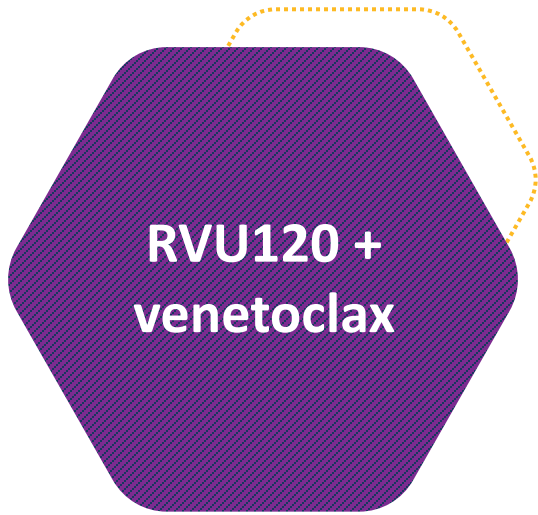


CR achieved end of C1 with persistent skin leukemia, resolved in C5

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



RIVER-81 is supported in part by a PLN 62 million 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.

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

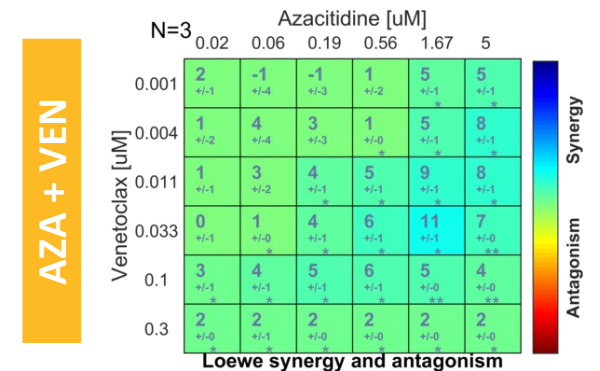
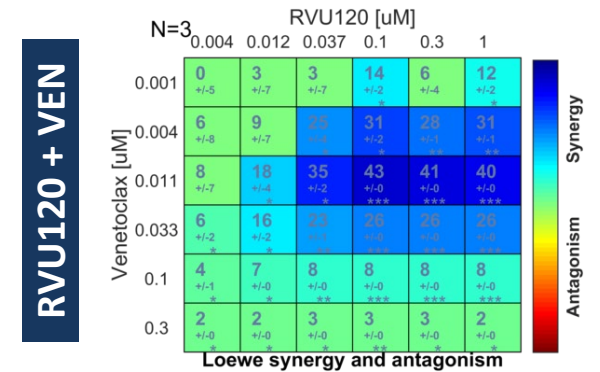
- **Remissions in Animal Studies:**

- RVU120 + ven achieves remissions in animal models at doses that allow hematological recovery

- **Mechanism of Synergy:**

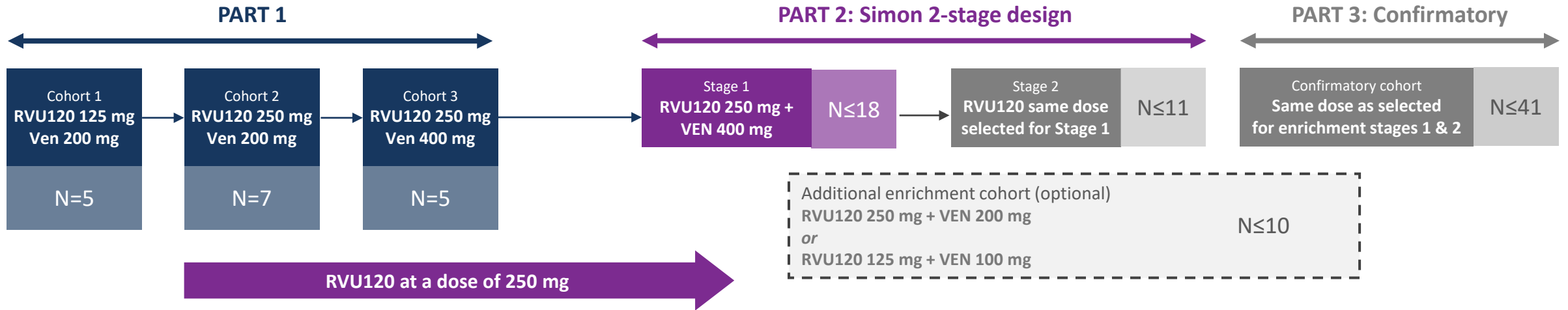
- MCL-1 is a known mediator of ven resistance. RVU120 induces caspase-dependent degradation of MCL-1
- MCL-1 inhibitors were tested in this setting, but prohibitive cardiotoxicity prevented further development
- The safety profile of RVU120 allows exploration of this concept
- Effectiveness on Leukemic Stem Cells (LSCs)

MV4-11



RIVER-81

Part 1 (dose escalation) has been completed;
currently enrolling into Part 2 at the highest dose from Part 1



- 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

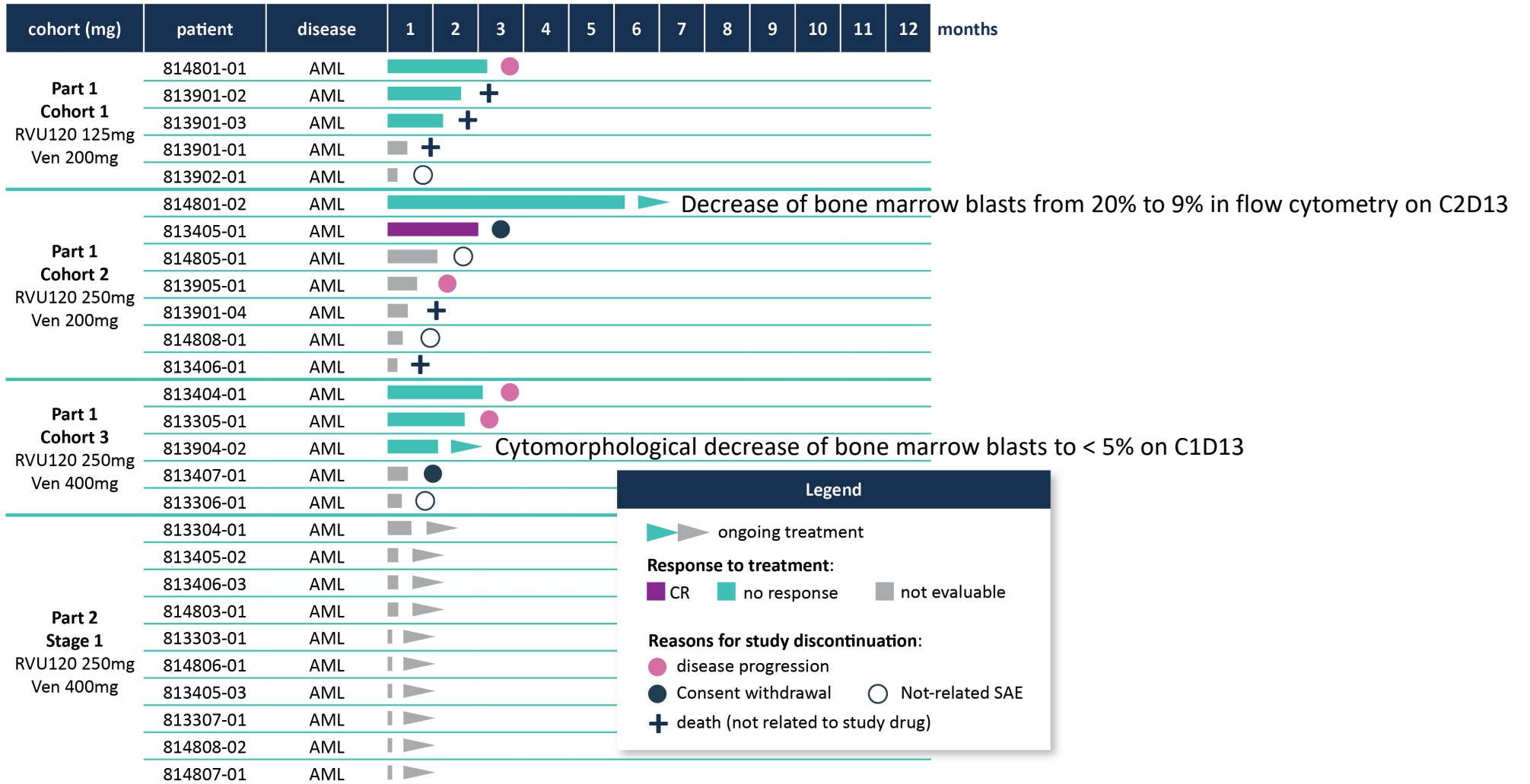
Enrollment in Part 2 was initiated based on the observed safety and early signs of efficacy of the combination.

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

Data Cut-off: December 10,
Preliminary data

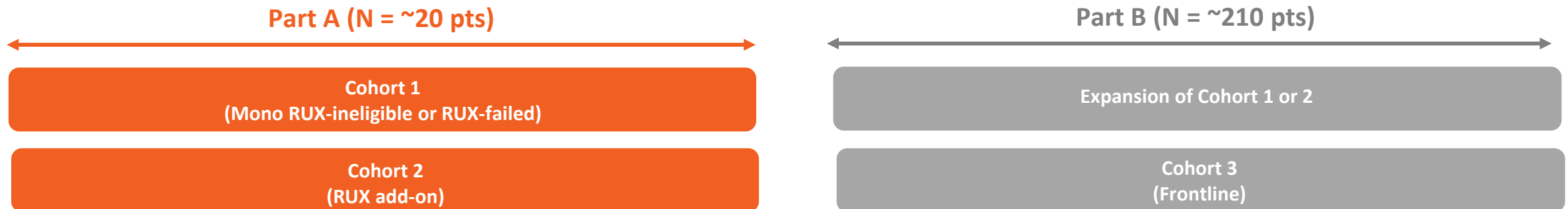


POTAMI-61

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:** DoR, 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**



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

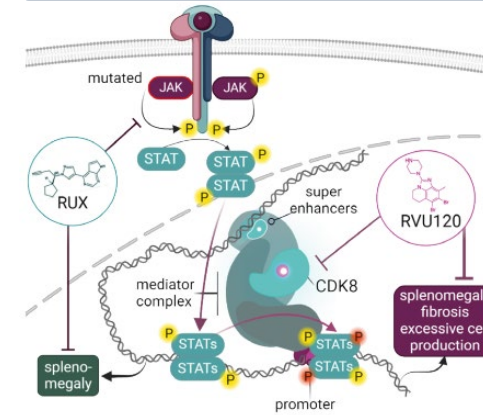
Opportunity in myelofibrosis

- 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

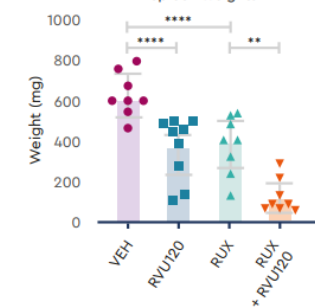
- CDK8 kinase is an important player in MPN pathogenesis, and RVU120 disrupts the downstream signaling events, mitigating MPN symptoms
- In preclinical studies, RVU120 effectively reduced splenomegaly, bone marrow fibrosis, and abnormal blood cell production. RVU120 has also demonstrated synergy in combination 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



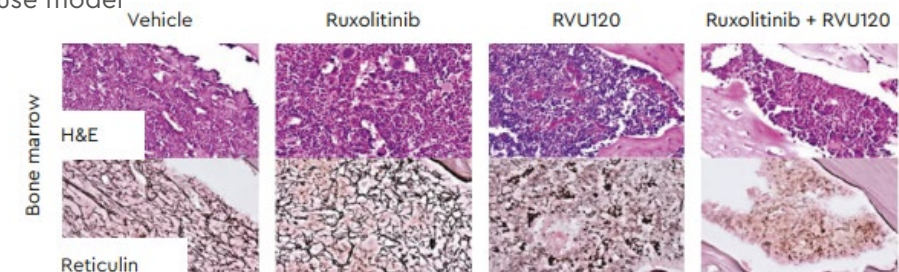
RVU120 reduces splenomegaly

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

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)



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

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

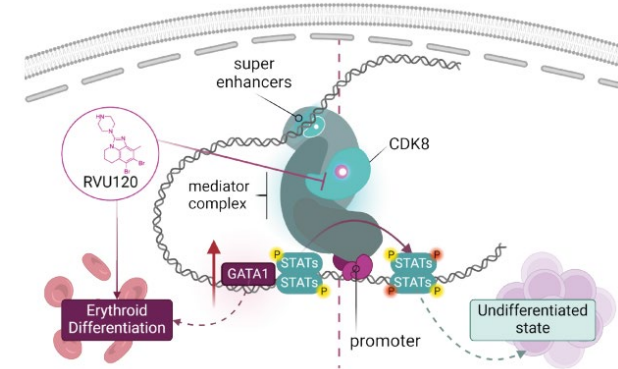
Opportunity in LR-MDS

- 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

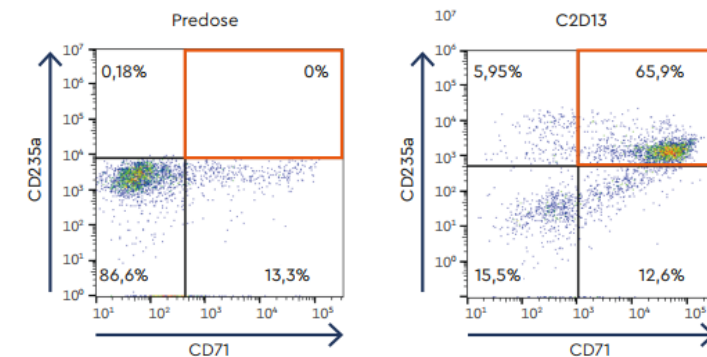
- MDS pathogenesis is influenced by gene expression alterations that hinder the maturation of hematopoietic cells.
- When aberrant stem cells from MDS patients are treated with RVU120, it triggers erythroid gene expression programs orchestrated by STAT5 and GATA1.
- Importantly, RVU120's activity does 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

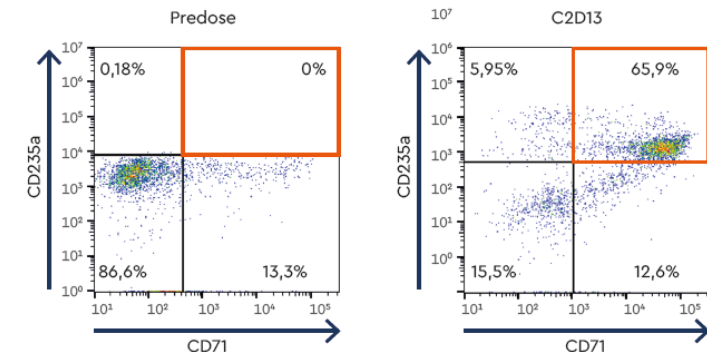
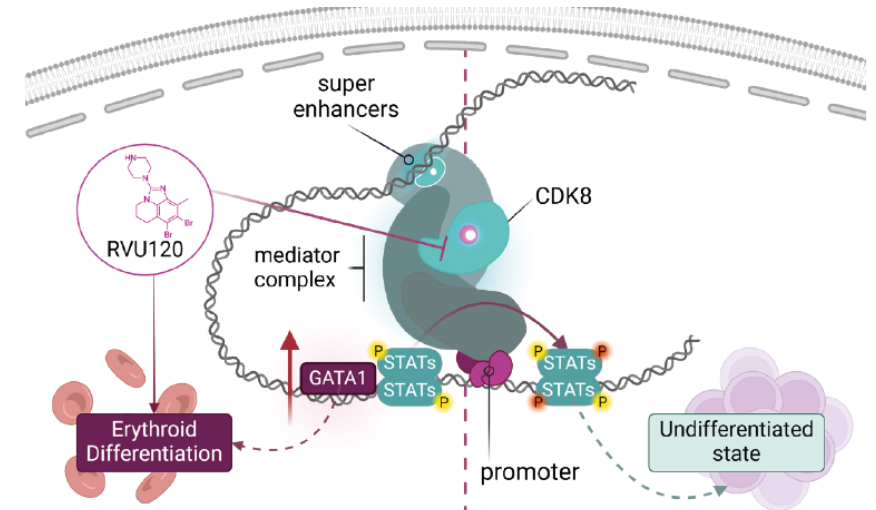
RVU120 has strong erythroid-stimulating activity in nonclinical anemia models and selected patients with AML/HR-MDS in Phase I (RIVER-51), providing the rationale for the Phase II clinical study in patients with LR-MDS

Nonclinical rationale

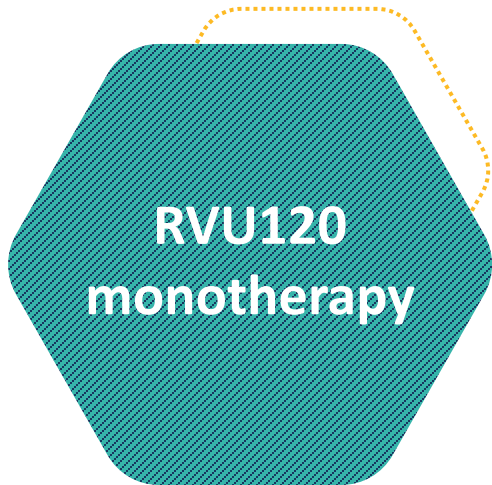
- Treatment of transformed CD34+ cells with RVU120 results in erythroid lineage commitment
- Isolated CD34+ cells derived from MDS and Diamond-Blackfan anemia patients differentiate into erythrocytes in the presence of RVU120
- Increased red blood cell count and hemoglobin levels were observed in animal 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

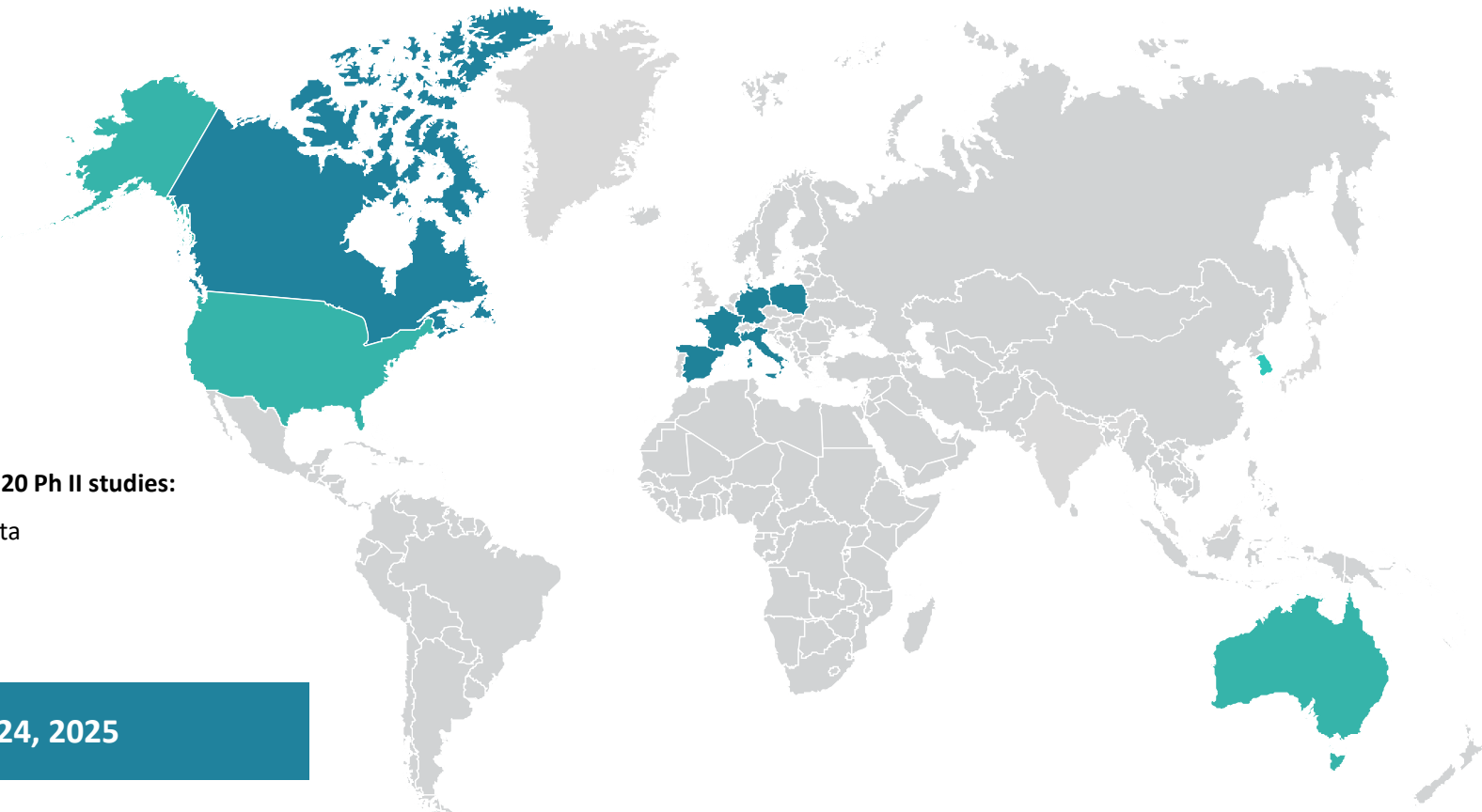


Part 2: Enrollment Suspended

- 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



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

4

Number of countries across studies

6

Number of activated clinical sites globally

110+

Number of patients enrolled

~120

Number of clinical vendors managed

20+

Number of internal Ryvu team members in Clinical Development and Translational teams

70+

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

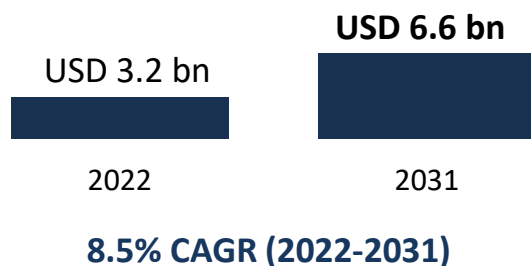
MDS (Myelodysplastic Syndrome)

- 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⁾**

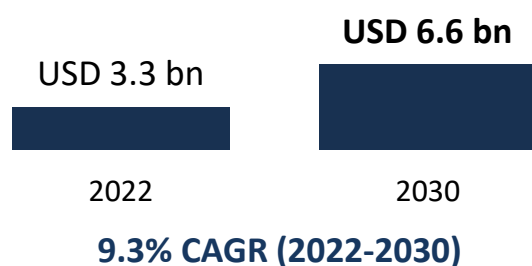
MF (Myelofibrosis)

- 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

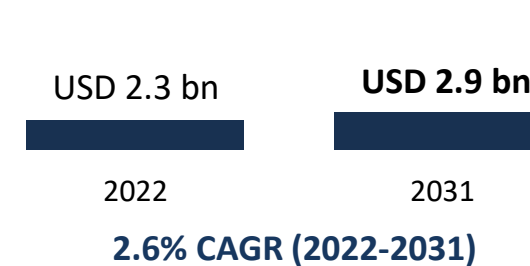
Global AML Market ⁽⁴⁾



Global MDS Market ⁽⁴⁾



Global MF Market ⁽⁷⁾



RVU120 program summary

RIVER-81

Next data in Q2 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 (as of Feb 24, 2025)

POTAMI-61

Enrollment ongoing; initial data in Q2 2025

- First patient dosed in December 2024
- 12 patients enrolled (as of Feb 24, 2025)
- Initial efficacy data expected in Q2 2025

REMARK

Enrollment ongoing; initial data in Q4 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

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



PARTNERSHIP AGREEMENT WITH MENARINI GROUP (2017)

PROVEN SAFETY AND CLINICAL ACTIVITY

- 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

- 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 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

Partnership

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

Phase II clinical study in DLBCL to be launched in Q1 2025

Initiating Phase II in DLBCL



DAPOLCERTIB 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: Europe

RVU305: Differentiated PRMT5 inhibitor



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

RVU305/PRMT5i

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

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: pancreatic, lung, DLBCL, bladder, esophageal

STATUS

Complete IND-enabling studies in H2 2025

RVU305 demonstrates superior preclinical properties vs. competitors

Leading to a differentiated clinical strategy

- **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-penetration:** observed in cyno
- **Favorable PK profile:** demonstrated in multiple species

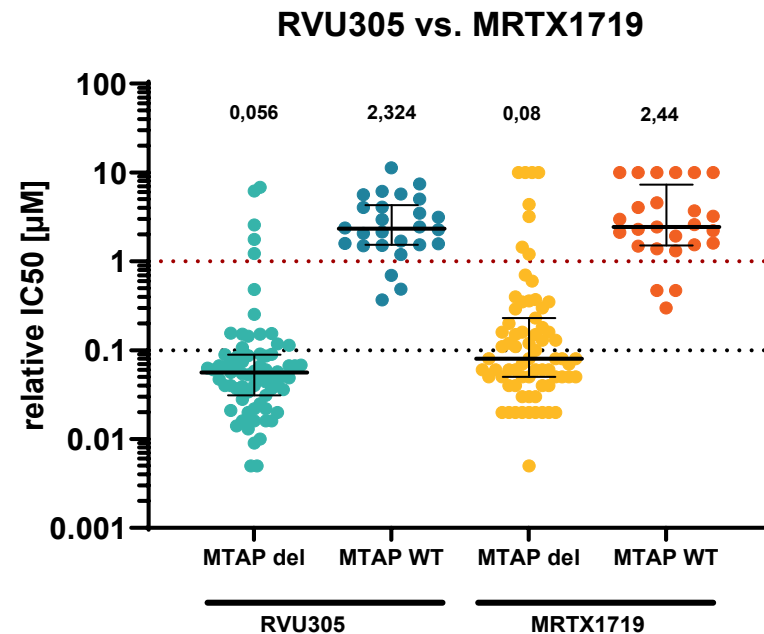
Ongoing translational work will support the selection of

- 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

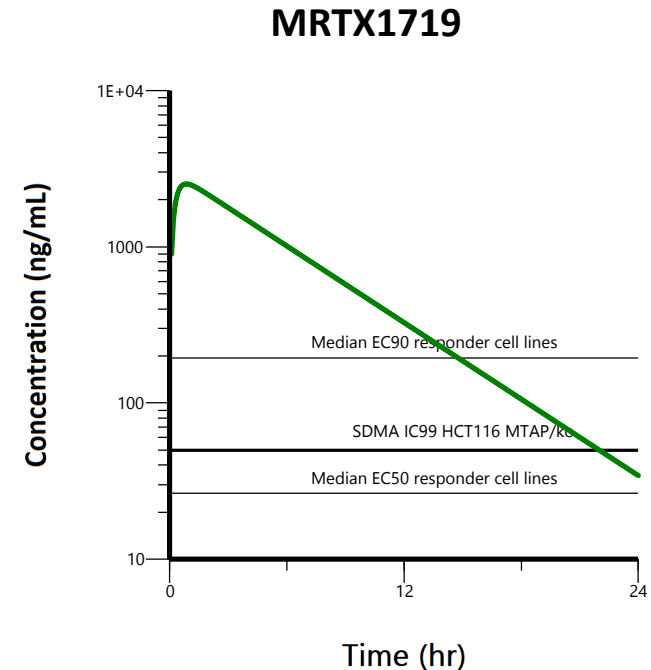
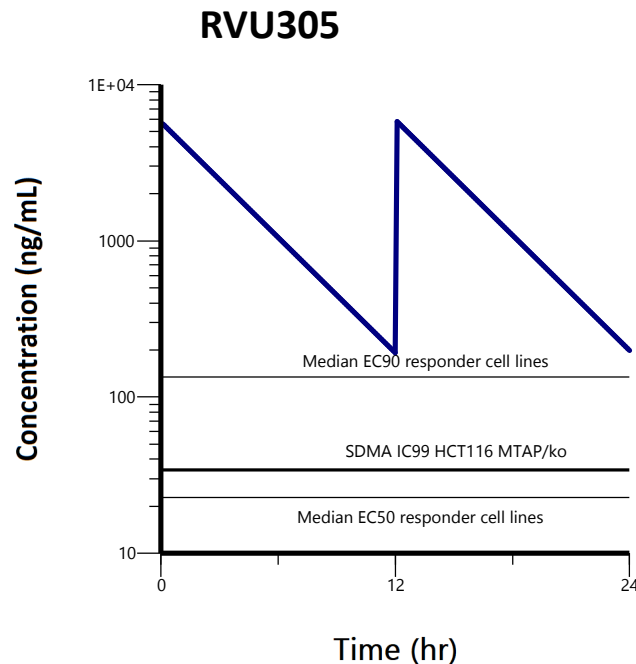
- Panel of MTAP-deleted and MTAP-wt cells was profiled with RVU305 in a 5-day CellTiter-Glo assay
- A differential response to Ryvu PRMT5 MTA-cooperative inhibitor is seen between cells with different MTAP status
- RVU305 shows higher potency than MRTX1719 (comparing to results published by Engstrom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



Favorable PK profile for RVU305 is promising for clinical development

RVU305 shows improved exposure and target coverage compared to MRTX1719.

The murine pharmacokinetic profile and exposure at pharmacologically relevant doses—75 mg/kg BID for RVU305 and 100 mg/kg QD for MRTX1719 – indicates that RVU305 achieves higher exposure, target engagement, and target coverage

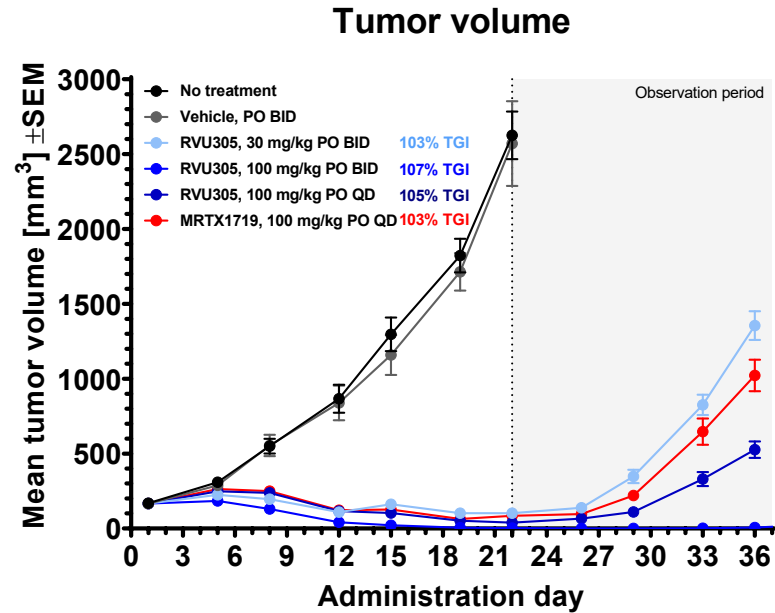


SDMA EC99 (measured via ELISA assay in HCT116 MTAP knockout cells) was used as a target engagement marker. The 2D viability assay median EC50/90 values were derived from panel of multiple MTAP/del cell lines (BXPC3, Lu99, HUPT4, MiaPaca2, A549, DoHH2, HCT116-MTAP-DEL).

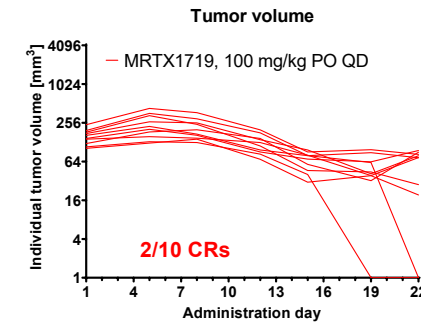
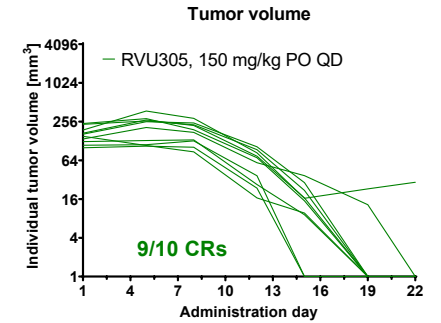
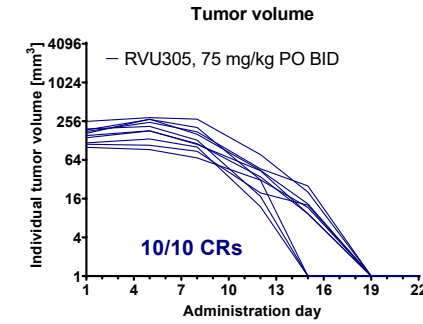
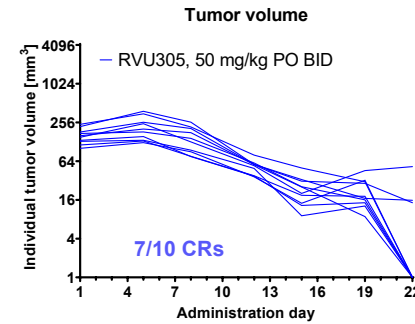
RVU305 shows significant antitumor efficacy *in vivo*

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 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

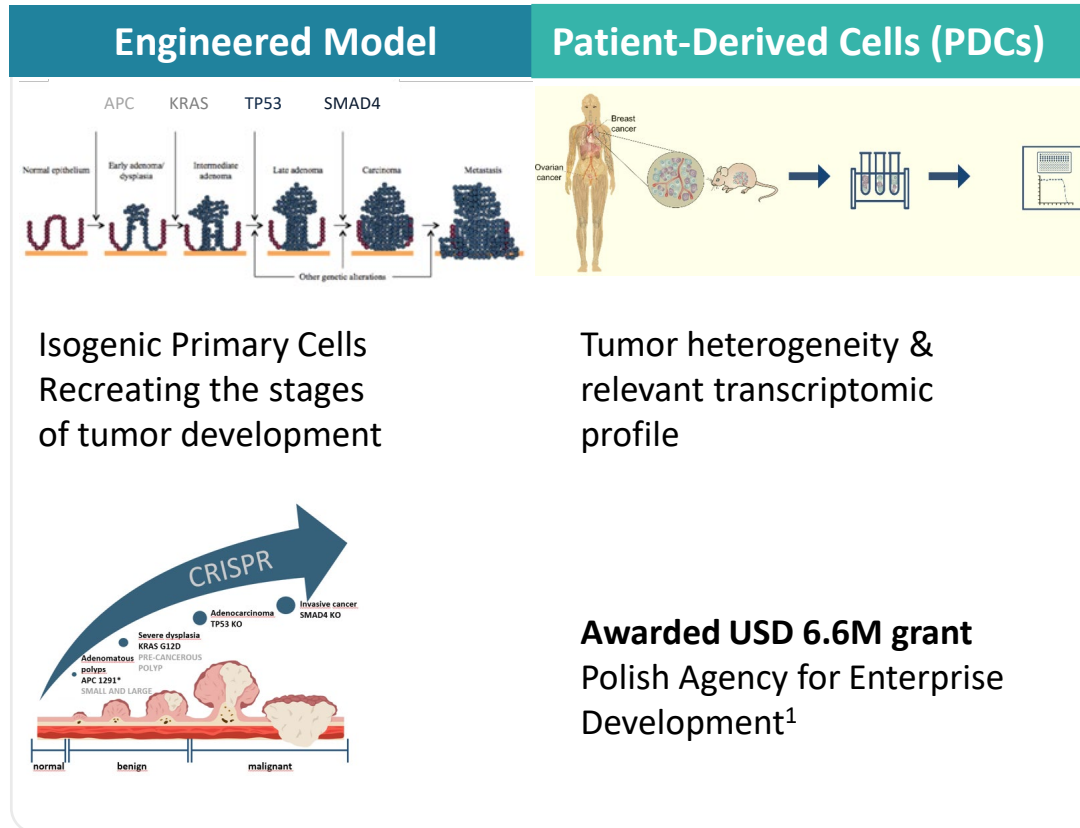
ONCO Prime: Novel Precision Oncology

Multi-asset platform generating
first-in-class therapeutics

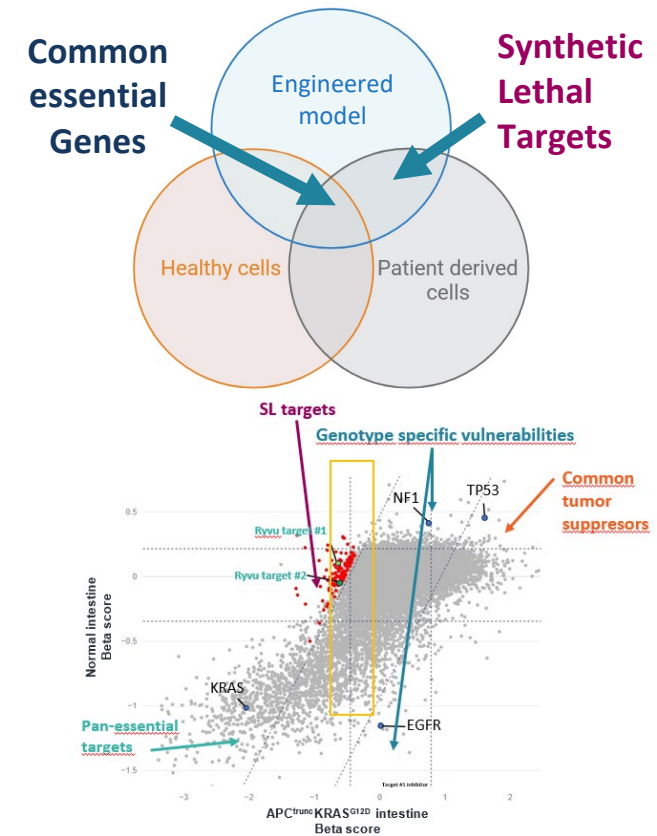


Driving novel precision oncology drug discovery with Ryvu's ONCO Prime platform

Ryvu's CRISPR-based target Discovery Platform



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

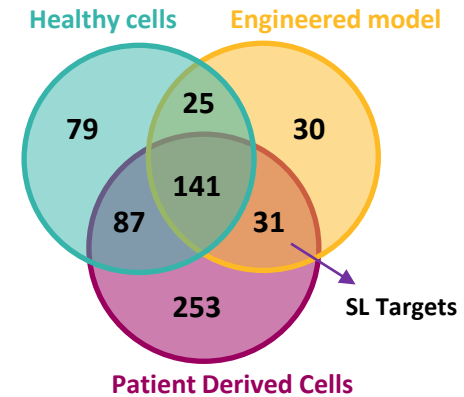
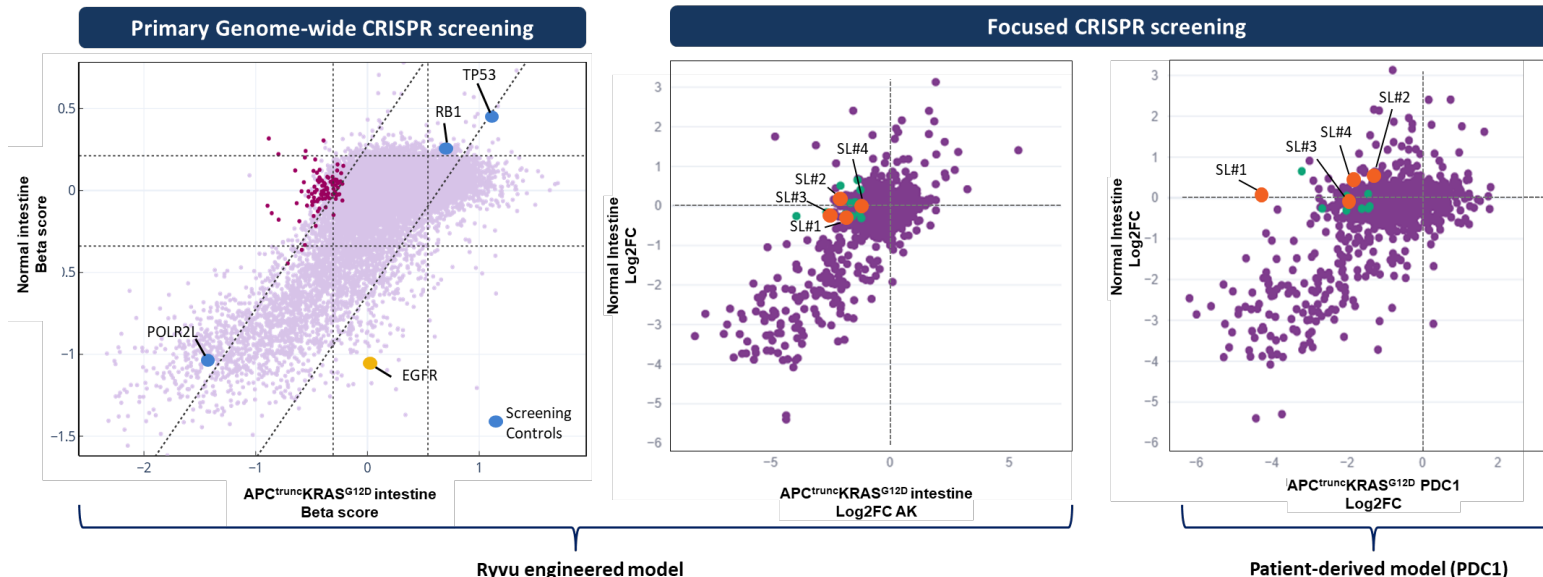
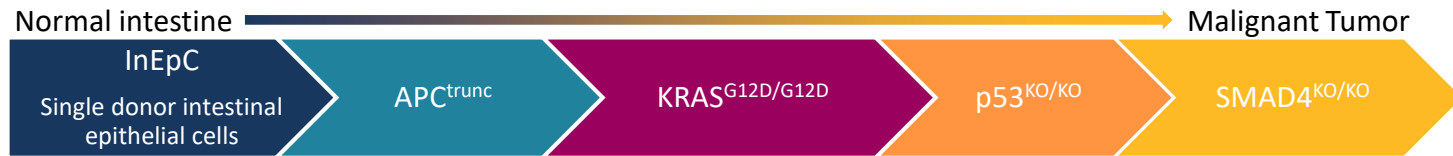


- The third most prevalent cancer worldwide
- Estimated number of colorectal cancers in the US for 2024 are 153,000 new cases¹
- Diagnosed usually at an advanced stage. Mortality still remains high. Five-year survival shown by SEER database is **around 65%**, the survival drops to **13%** at stage 4.
- **Lack of targeted therapies** (except KRAS G12C which showed moderate PFS)

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

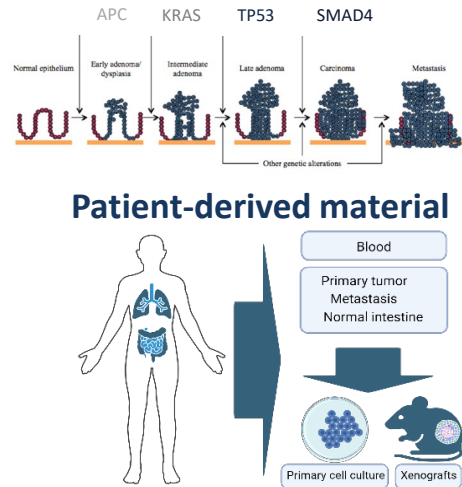


Based on East et al. 2017

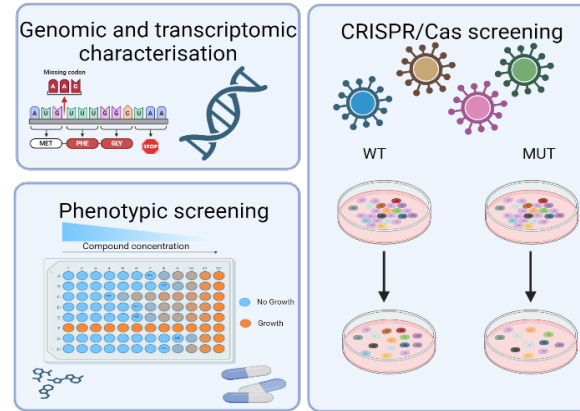


ONCO Prime is accelerating the development of novel precision medicine targets, including synthetic lethal targets

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

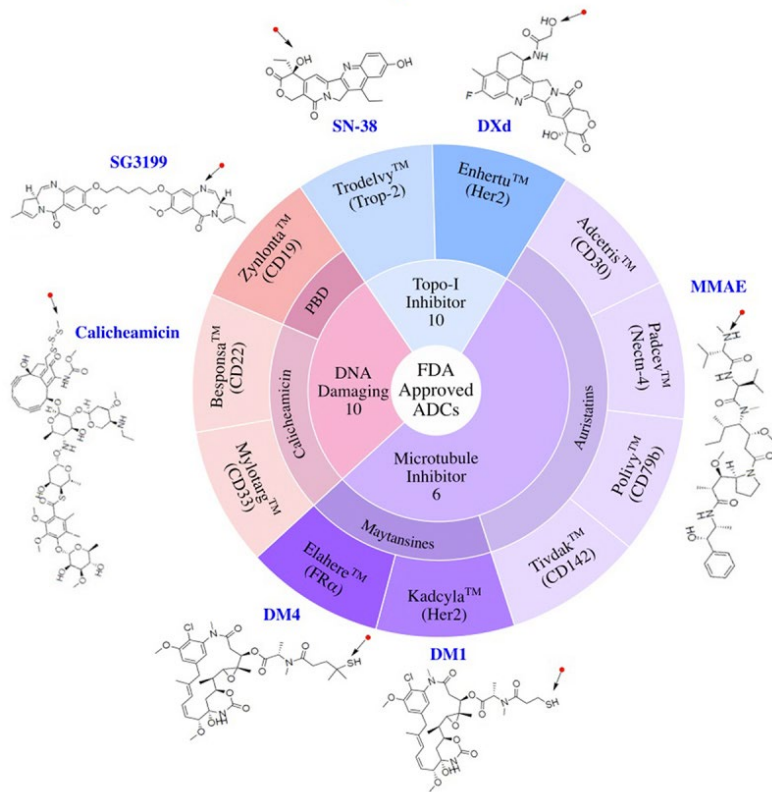
ADCs with Novel Payloads

Generating multiple first-in-class therapeutics






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

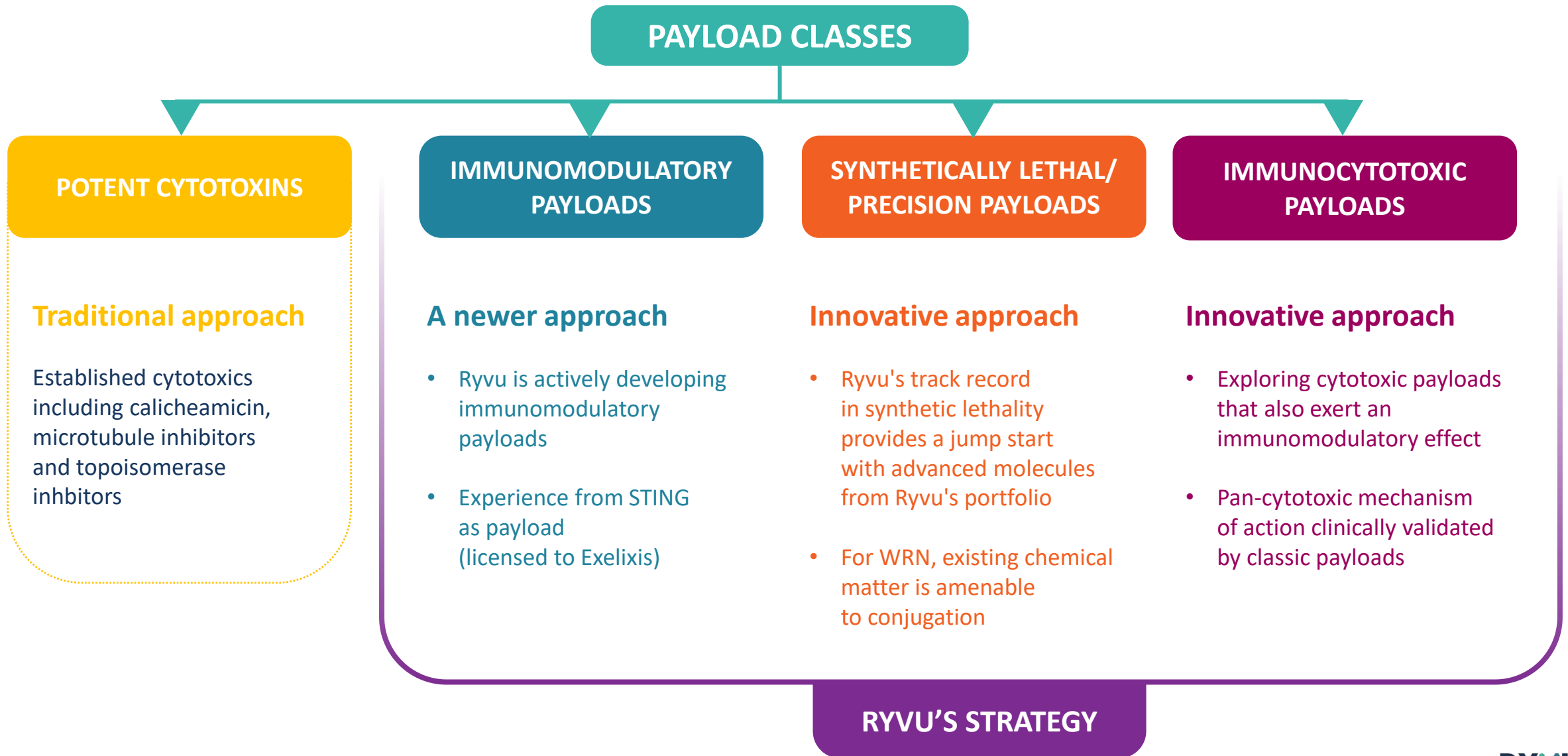
Approved ADCs use three main types of payloads



Maecker et al., MAbs, 2023.

Novel payloads have the potential to improve on...

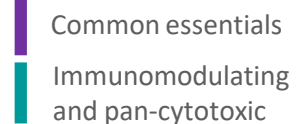
- 
Efficacy: overcome resistance to existing payloads and potentially improve on potency
- 
Safety: expand the safety window by leveraging targeted payloads (e.g. synthetic lethality) or immunomodulatory MOAs
- 
Combinability: emergence of bispecific and dual/multiple payload ADCs could represent a new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



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



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 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



Key Financial Terms

- 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
- \$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

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

Largest-ever Ryvu deal: November 2022

BIONTECH

RYVU
THERAPEUTICS



Partnership



Key Financial Terms

- **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.
- 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
<i>Partnering</i>	<i>10.5</i>	<i>18.1</i>
<i>Grants</i>	<i>4.5</i>	<i>5.6</i>
Total Costs**	34.7	51.0
<i>Clinical Pipeline</i>	<i>12.0</i>	<i>25.7</i>
<i>Early Pipeline</i>	<i>14.7</i>	<i>16.6</i>
<i>G&A</i>	<i>8.0</i>	<i>8.7</i>
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)

* 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)

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

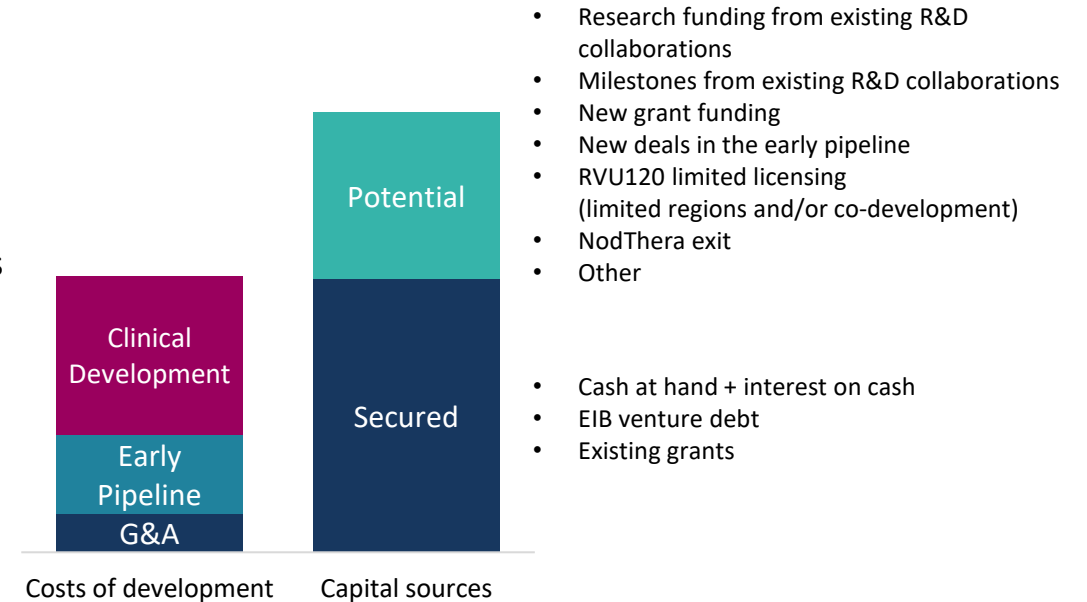
Employees
with PhD

~60

Ryvu's Vision: 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 to enroll 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**



2025 – 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

2025 – KEY ANTICIPATED EVENTS

- **Clinical data updates from RVU120 in Q2**
- Advance RVU305 from IND-enabling studies to IND/CTA filing

Ryvu equity summary

IPO on WSE	Nov 2014
Corporate Split: Selvita and Ryvu	Oct 2019
Ticker: WSE	RVU
52-Week Range¹	PLN 17.62 – 59.40
Average Daily Volume (YTD)¹	34,266
Market cap¹	PLN 446M (EUR 106M)
Shares outstanding	23.1 M
Cash²	EUR 43.7M

Top Holders ³		
1	Paweł Przewięźlikowski	17.4%
2	Allianz TFI	9.9%
3	Allianz OFE	9.2%
4	BioNTech SE	8.3%
5	Nationale-Nederlanden OFE	7.9%
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%

Analyst Coverage



Vladimira
Urbankova



Beata Szparaga-
Waśniewska



Krzysztof
Radojewski



Katarzyna
Kosiorek



Łukasz
Kosiarski



Tomasz
Krukowski

1. As of 12 March 2025 2. As of 09 March 2025 3. From stooq.pl as of 12 December 2024.

Thank you

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