RYVU THERAPEUTICS

Developing therapeutics
at the forefront of oncology

Corporate Presentation

February 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

FIRST-IN-CLASS CLINICAL PIPELINE

RVU120
Fully-owned

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

MEN1703
Partnered

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

DISCOVERY PLATFORM

SYNTHETIC LETHALITY
Fully-owned

- **RVU305**: best-in-class oral MTA-cooperative **PRMT5** inhibitor in IND/CTA-enabling studies
- **WRN** program
- **Novel SL** targets

IMMUNO-ONCOLOGY
Partnered

- **BioNTech**: multi-target research collaboration
- **Exelixis**: STING ADC collaboration

FULLY INTEGRATED RESEARCH & DEVELOPMENT ORGANIZATION

- **LISTING:** WSE:RVU (mWIG40 index); cash runway to Q1 2026
- **TEAM:** >300 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 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

Miika Ahdesmäki, PhD, MBA
CIO

Jakub Janowski, MSc
General Counsel

Bartłomiej Konicki, MSc
Financial Director

Tomasz Rzymski, PhD, MBA
Director of Translational Medicine

Justyna Żółtek, MSc
Director of HR

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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/HR-MDS (RIVER-52) (monotheraphy)					LEUKEMIA & LYMPHOMA SOCIETY	Updated Ph II data in 2Q25
	R/R AML (RIVER-81) (combo with venetoclax)						Updated Ph II data in 2Q25
	LR-MDS (REMARK) (monotherapy)					EMSCO MYELODYSPLASTIC SYNDROMES	Initial Ph II data in 2Q25
	Myelofibrosis (POTAMI-61) (mono and combo with ruxolitinib)						Initial Ph II data in 2Q25
	Solid Tumors (AMNYS-51)						
MEN1703 (SEL24) (PIM/FLT3)	DLBCL (mono and combo with glofitamab)					MENARINI	
SYNTHETIC LETHALITY							
RVU305 (PRMT5)	SOLID TUMORS						IND/CTA submission in 2H25
WRN	SOLID TUMORS						In lead optimization
NOVEL TARGETS	ONCOLOGY						
IMMUNO-ONCOLOGY							
MULTI-TARGET IMMUNE MODULATION COLLABORATION	ONCOLOGY					BIONTECH	
STING ADC	ONCOLOGY					EXELIXIS	

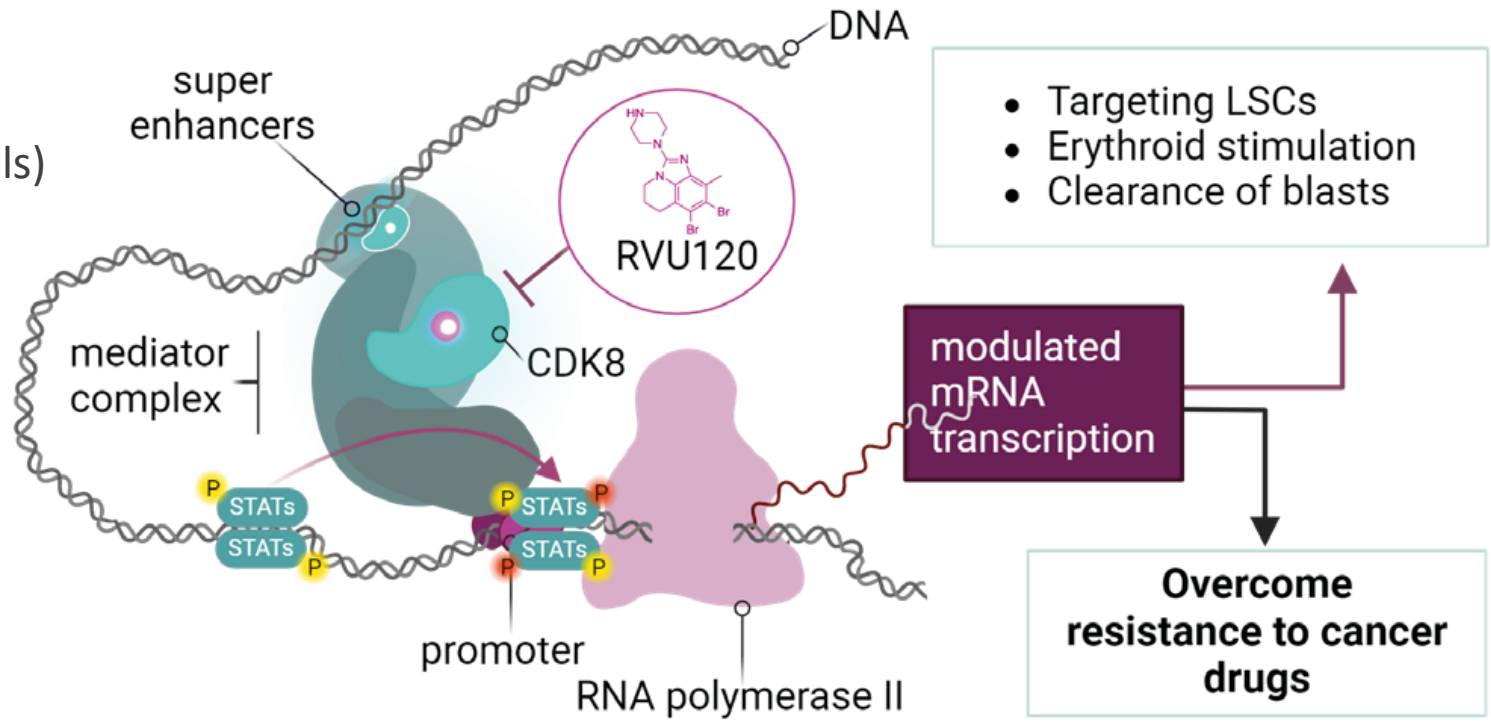
Study start-up

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

RYVU THERAPEUTICS

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



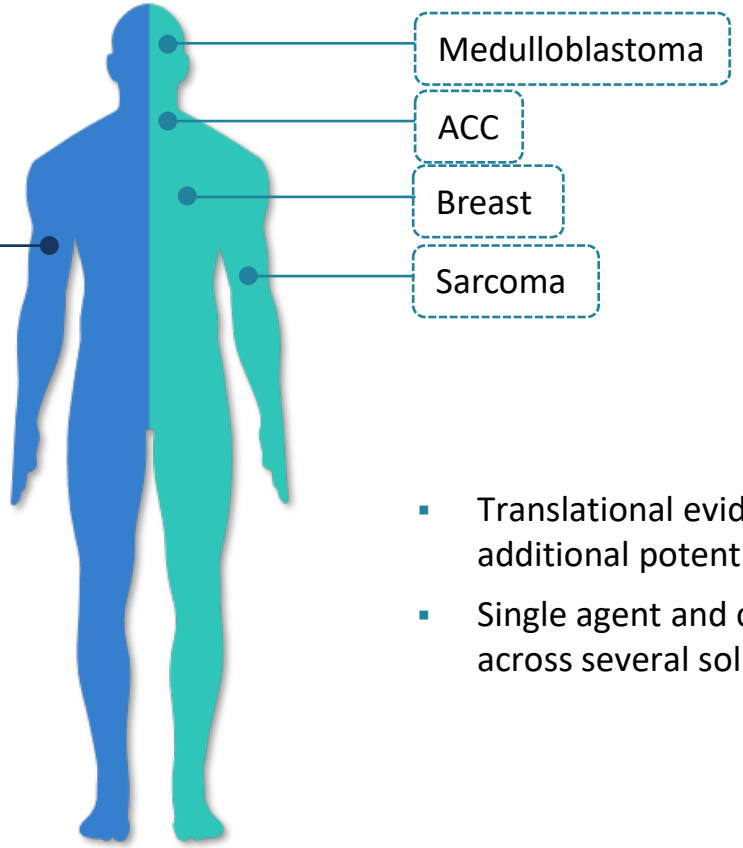
RVU120 is an innovative dual CDK8/19 inhibitor designed to target the expression of genes crucial for cancer cell survival and differentiation

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 2025**

- 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
Four Phase II studies ongoing

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

15 of 30 evaluable patients showed clinical benefit across dose levels

Clinical benefits

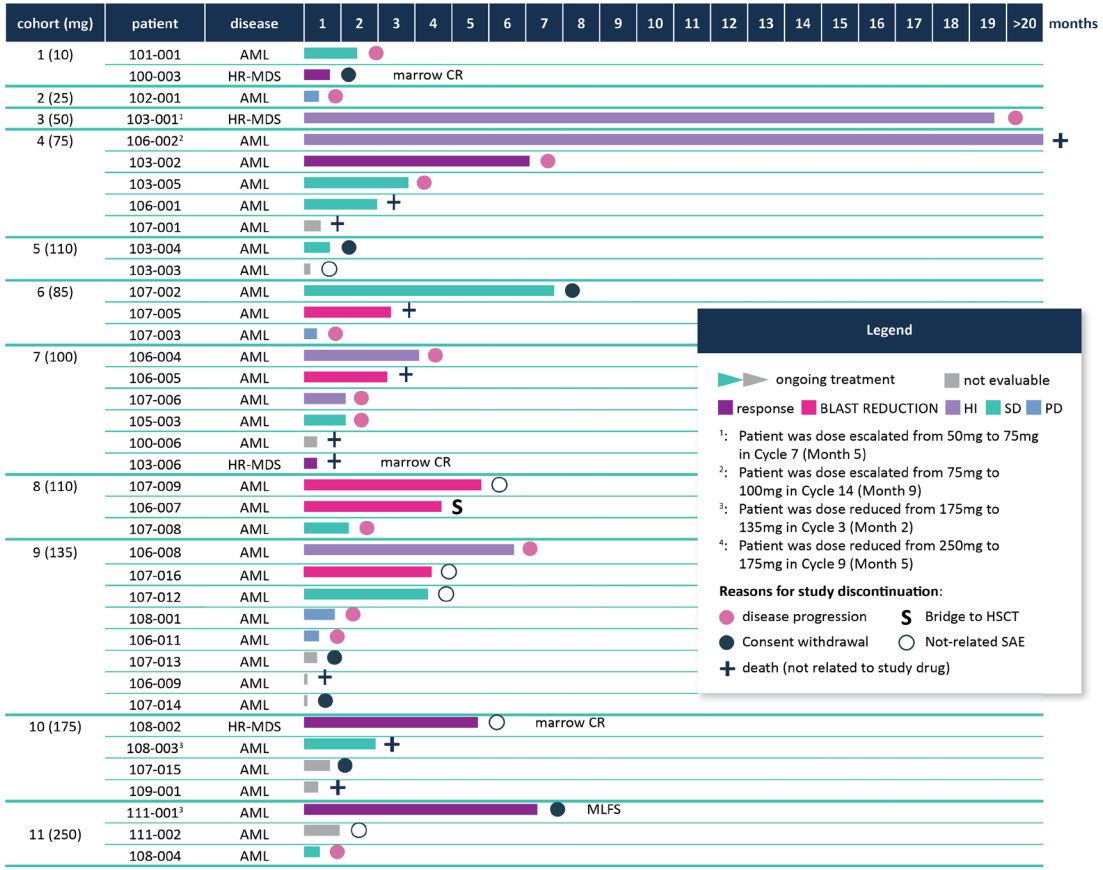
- **30 treated patients are evaluable for response (38 were treated in total)**
- **9 patients achieved clinically significant BM blast reduction**
- (including 1 CR, 1 MLFS, 3 marrow CRs)
- **5 patients achieved erythroid hematological improvement (HI-E),**
  4 of those became transfusion-independent,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

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

Significant blast reductions

- Confirmed CR in NPM1/DNMT3A AML patient
- Several patients with significant blast reduction

Transfusion independence

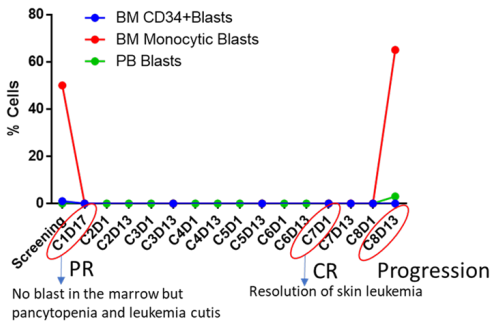
- >20% patients, (all with AML-MR or HR-MDS), showed hematological improvement, meeting Cheson criteria for erythroid response

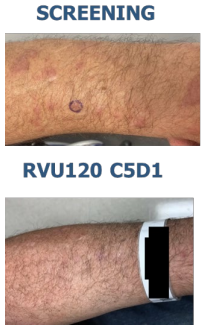
Improvement of BM architecture

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

P103-002 AML

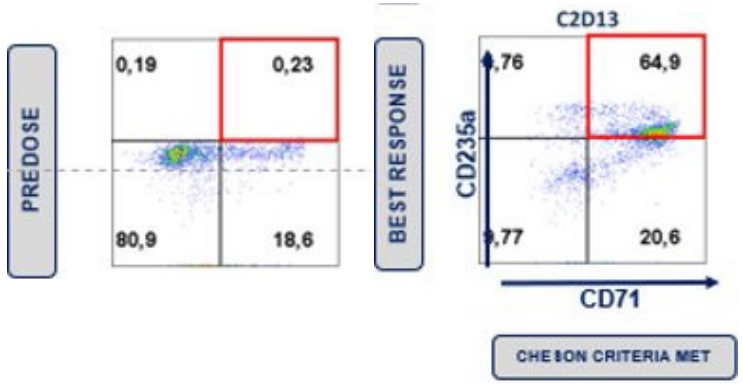
- NPM1, DNMT3A, FLT3-ITD.,NRAS
- 46,XX, 3 prior treatment lines
- 6U RBC/3 weeks and 6U Plts/4 weeks





P106-004 AML -MR

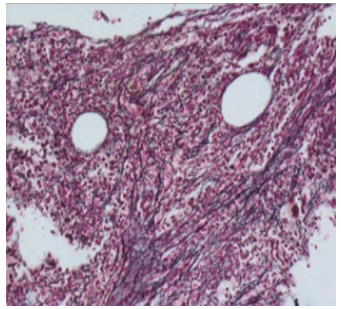
- Mutations: GATA2, RUNX1, SF3B1,TET2, WT1
- Karyotype: 47,XY,+21; 3 prior treatment lines
- 9U RBC/8 weeks; grade 4 Thrombocytopenia



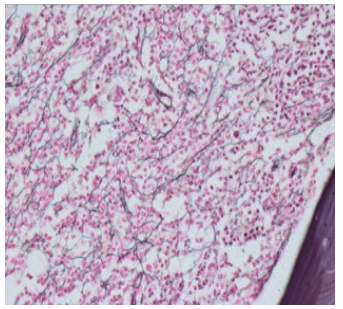
P108-002 HR-MDS

- 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

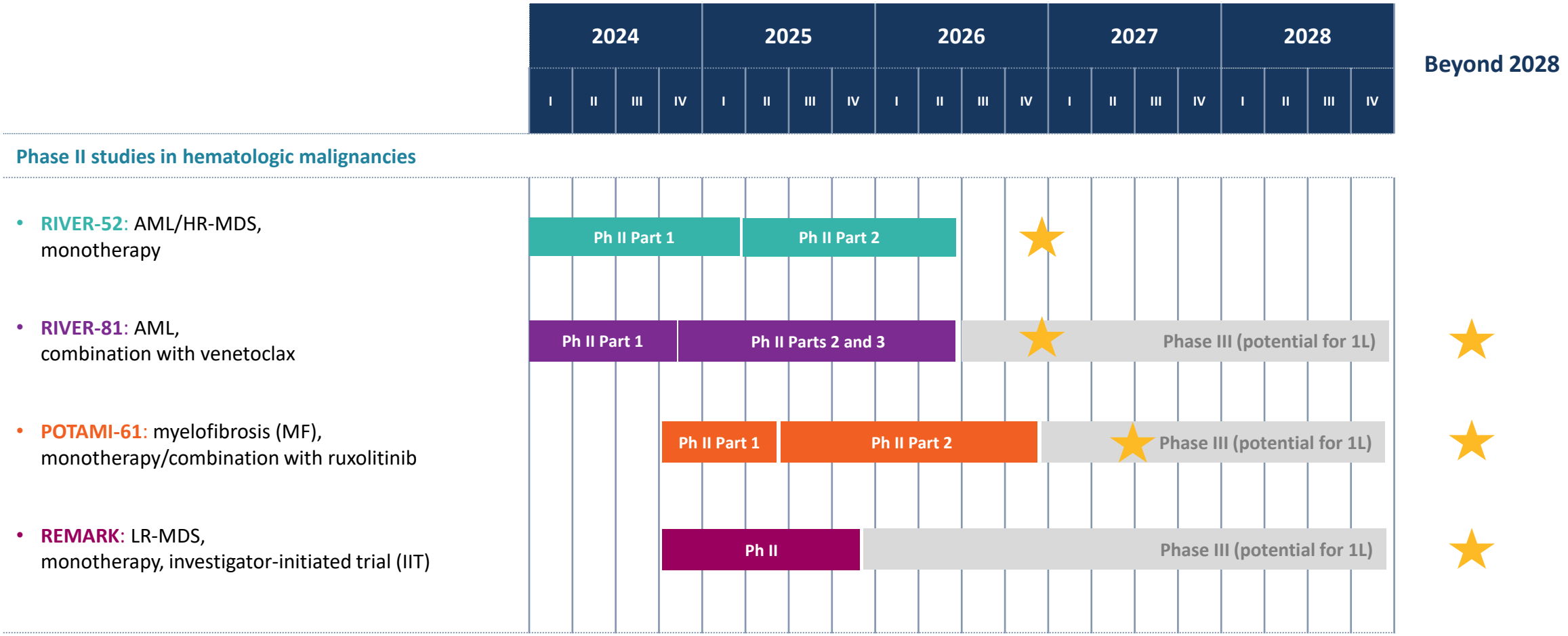


CR achieved end of C1 with persistent skin leukemia, resolved in C5

RBC-TI and Plt-TI on RVU120 treatment

Reduction of fibrosis grade and marrow CR

Current clinical development of RVU120 focuses on single agent trials in patients with AML, MDS, and MF and combinations in AML and MF



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

RVU120 monotherapy

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
- Estimated enrollment: **~40-140 patients**
- Up to **80 clinical sites** planned globally

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

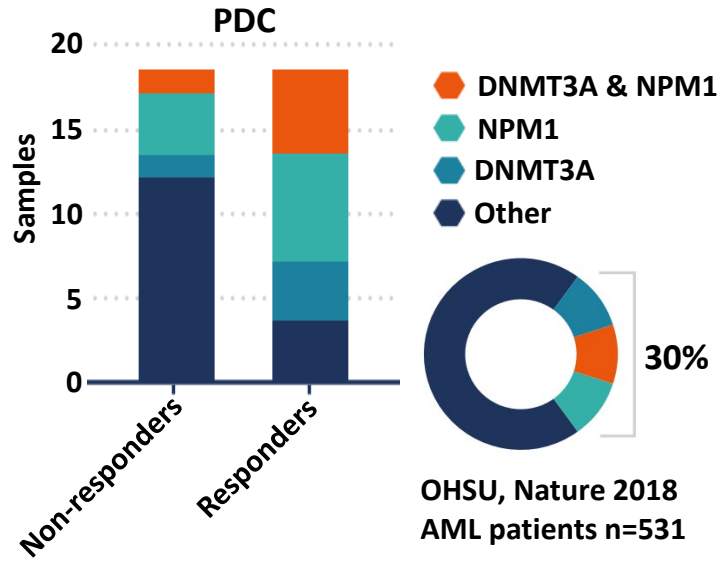
PART 2 (N = ~100 pts)

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

Results from the ongoing Part 1 will determine potential launch of Part 2

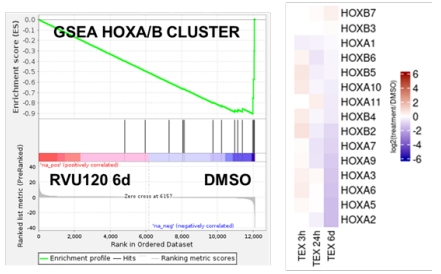
RIVER-52 Nonclinical Results and Signals of RVU120 Efficacy from Phase 1 (RIVER-51) Provide Rationale for Phase 2 study in NPM1 and DNMT3A Mutant Patients

- **Differential efficacy of RVU120 in AML models:**
  - In vitro screening of AML patient-derived cells revealed differential efficacy of RVU120 and other CDK8 inhibitors in NPM1 and/or DNMT3A mutants
  - RVU120 as monotherapy demonstrated high efficacy in NPM1 or DNMT3A-mutated patient-derived xenografts
- **Transcriptomic profiling provides mechanistic rationale:**
  Transcriptomic profiling indicated RVU120 represses MEIS1/HOXA/B gene expression programs, highly enriched in AML positive for NPM1 and DNMT3A mutations
- **Clinical Activity in Phase I:**
  One of two NPM1 mutant patients recruited in Phase I achieved complete remission (CR); transcriptomic profiling demonstrated repression of MEIS1/HOXA/B genes, consistent with nonclinical findings

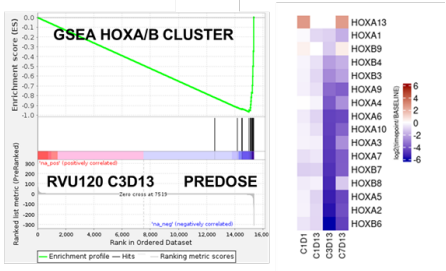


RVU120 downregulates homeobox cluster genes in TEX CD34+ leukemic cells and in AML patient 103-002 that achieved a complete remission

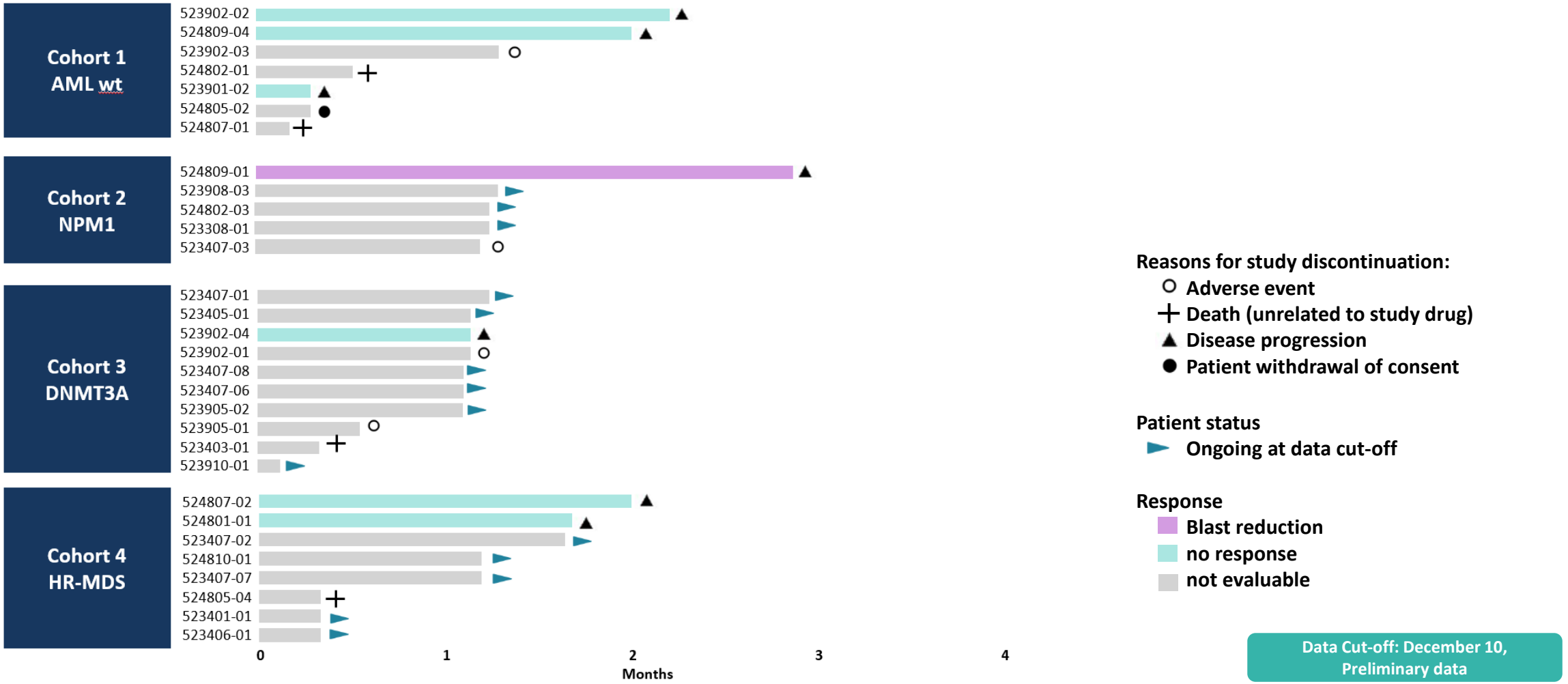
Preclinical data (TEX CD34+ cells)



Clinical data (patient 103-002):



RIVER-52 Swimmer Plot : 14 ongoing patients out of 30 enrolled overall



Data Cut-off: December 10, Preliminary data

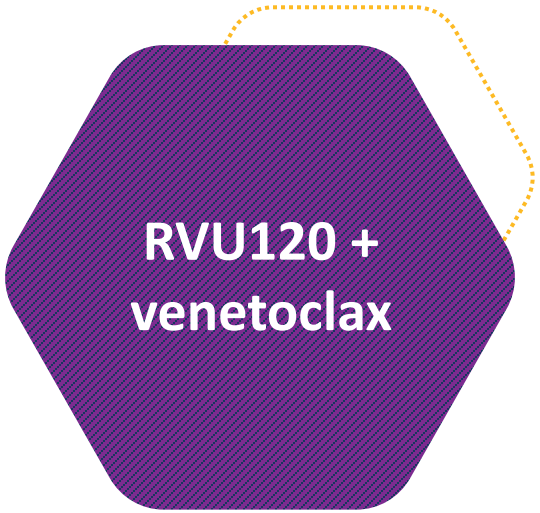
No new safety signal was identified
Systemic exposure of RVU120 following oral dosing of 250 mg QOD was confirmed to be consistent with previous studies
Data is immature for the interpretation of efficacy

RIVER-52 RVU120 appears to have a good safety profile, with the notable absence of QTc prolongation and differentiation syndrome

Agent (#pts)	Revumenib (N=94)	Ziftomenib (N=83)	RVU120 (N=20)
Trial	Phase 1/2 (AUGMENT-101)	Phase 1/1b (KOMET-001)	Phase 2 (RIVER-52)
Company	Syndax	Kura	Ryvu
DLT	Ph 1 QTc Pr	Gr 3 Pneumonia Gr 4/5 DS	No
DS (all)	**26 (28%)**	**12 (15%)**	**0 (0%)**
DS (≥ Gr3)	15 (16%)	10 (12%)	0 (0%)
Neutropenia (≥ Gr3)	27 (29%)	7 (8%)	2 (10%)
Febrile Neutropenia (≥ Gr3)	36 (38%)	18 (22%)	3 (15%)
Thrombocytopenia(≥ Gr3)	20 (21%)	5 (6%)	3 (15%)
Anemia	22 (21%)	20 (24%)	2 (10%)
QTc prolongation (any)	**24 (25%)**	**0 (0%)**	**1 (5%)**
QTc prolongation (≥ Gr3)	13 (14%)	0 (0%)	0 (0%)
Transaminitis	27 (29%)	16 (19%)	1 (5%)
Sepsis	11 (12%)	15 (18%)	1 (5%)

Data cut-off 01 Nov 2024

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 €13.3M 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

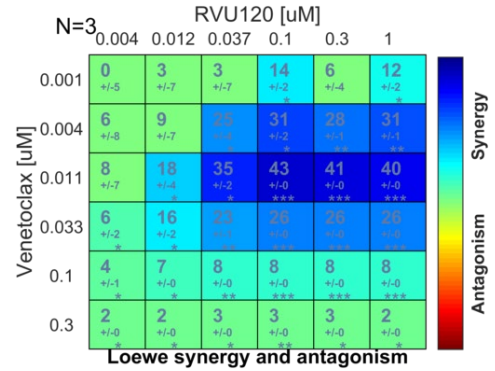
(1) 35 patients for: Part 1 (N=17 pts) and Stage 1 of Part 2 (N=18 pts); 97 patients for: complete planned enrollment into Parts 1, 2 and 3, including optional additional enrichment cohort.

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

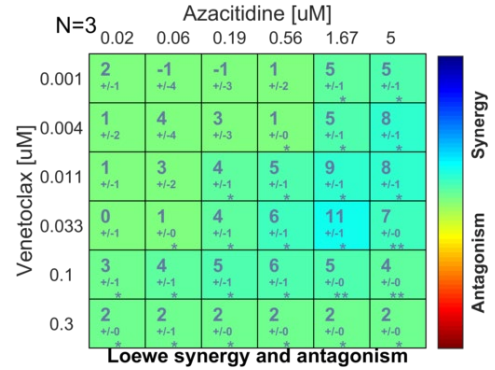
- **True Synergy and Superiority:**
  - RVU120 + ven demonstrates synergy across multiple AML cell lines and superiority over ven + aza
- **Remissions in Animal Studies:**
  - RVU120 + ven achieves remissions in animal models at doses that allow hematological recovery
- **Mechanism of Synergy:**
  - 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

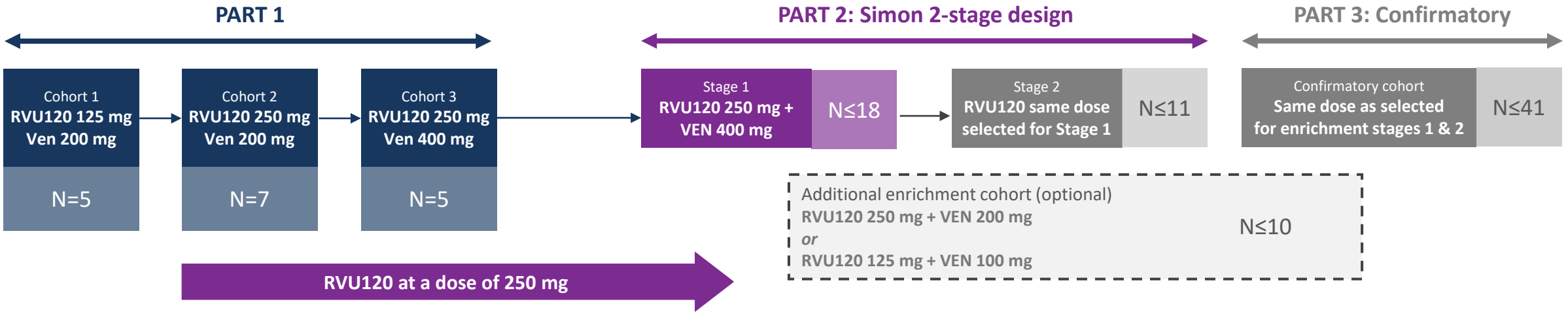


AZA + VEN



RIVER-81

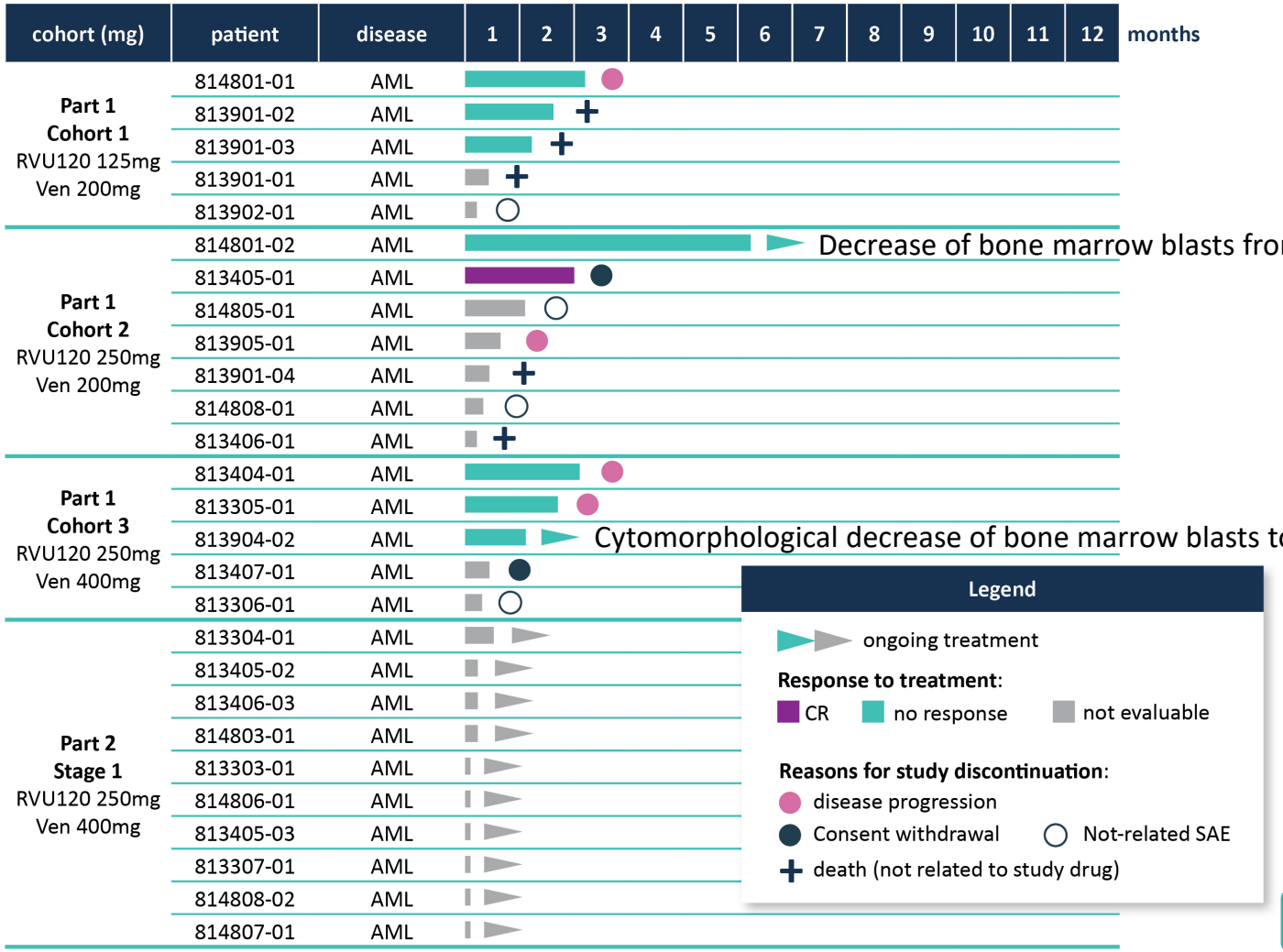
Part 1 (dose escalation) has been completed; currently enrolling into Part 2 at the highest dose from Part 1



- 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 initiated based on the observed safety and the early signs of efficacy of the combination
11 of 18 patients have already been treated in Stage 1 of Part 2

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



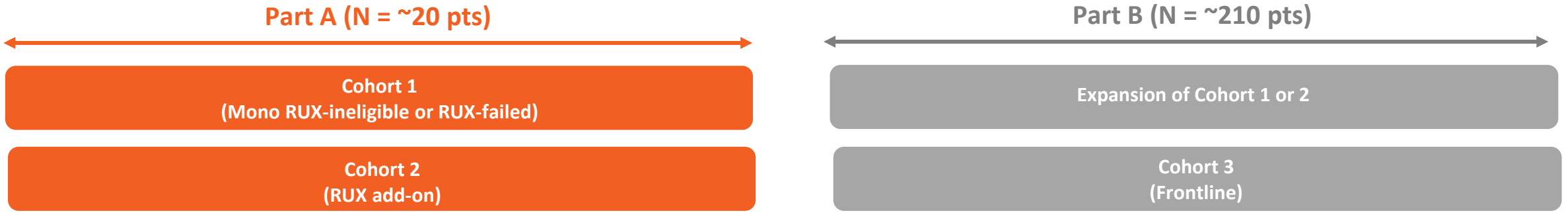
Data Cut-off: December 10, Preliminary data

Eight patients treated with RVU120 at a dose of 250 mg (RP2D) had at least one evaluable post-baseline assessment

POTAMI-61 Phase II study of RVU120 in myelofibrosis (MF) as mono and combo – first patient 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 December 11, 2024: **first patient dosed, 5 patients in screening, 12 sites activated** (17 sites planned by year-end)



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

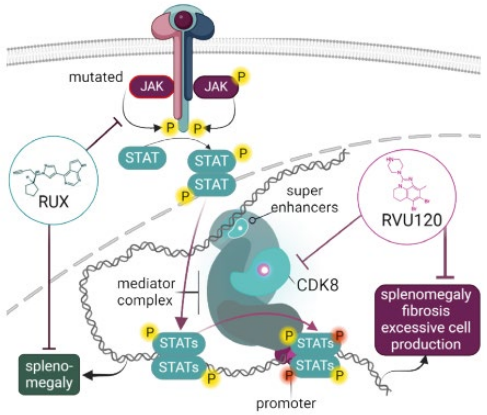
Opportunity in myelofibrosis

- 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

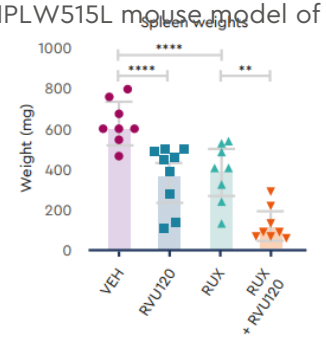
- CDK8 kinase is an important player in MPN pathogenesis, and RVU120 disrupts the downstream signaling events, mitigating MPN symptoms
- In preclinical studies, RVU120 effectively reduced splenomegaly, bone marrow fibrosis, and abnormal blood cell production. RVU120 has also demonstrated synergy in combination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



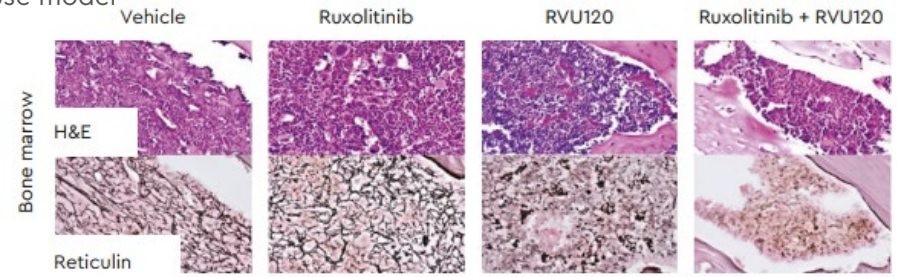
RVU120 reduces splenomegaly

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;**
  18 patients enrolled as of December 11, 2024
- 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

RYVU THERAPEUTICS

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

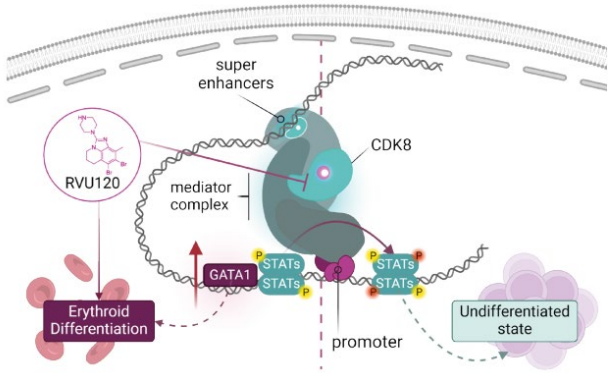
Opportunity in LR-MDS

- 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

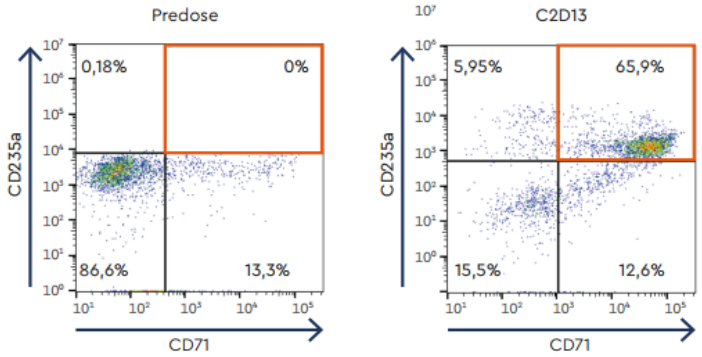
- MDS pathogenesis is influenced by gene expression alterations that hinder the maturation of hematopoietic cells.
- When aberrant stem cells from MDS patients are treated with RVU120, it triggers erythroid gene expression programs orchestrated by STAT5 and GATA1.
- Importantly, RVU120's activity does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



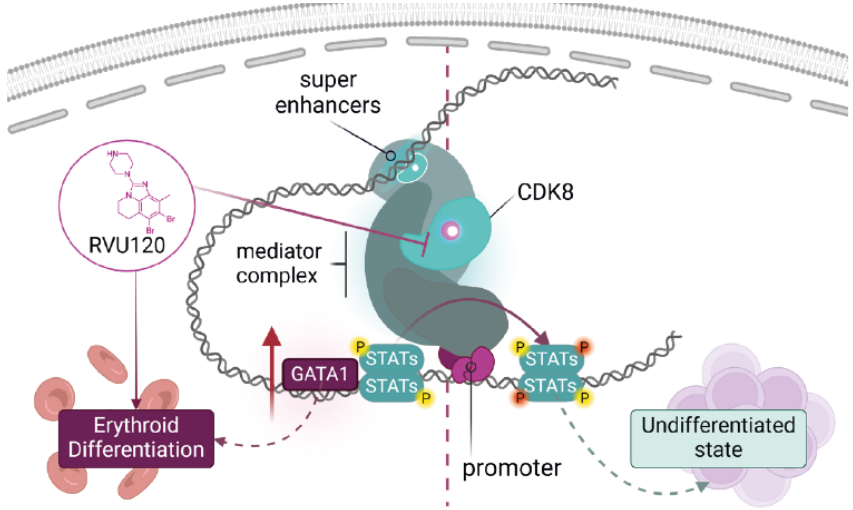
REMARK RVU120 has strong erythroid-stimulating activity in nonclinical anemia models and selected patients with AML/HR-MDS in Phase I (RIVER-51), providing the rationale for the Phase II clinical study in patients with LR-MDS

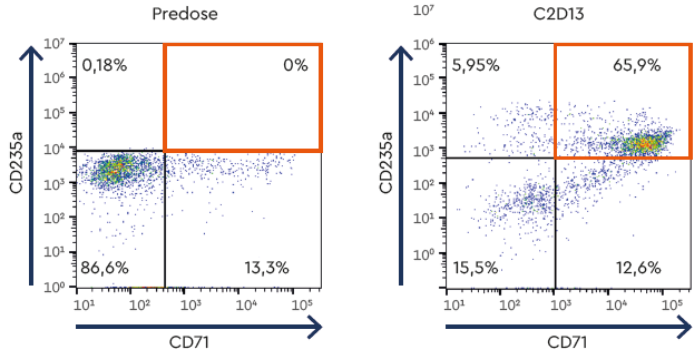
Nonclinical rationale

- 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

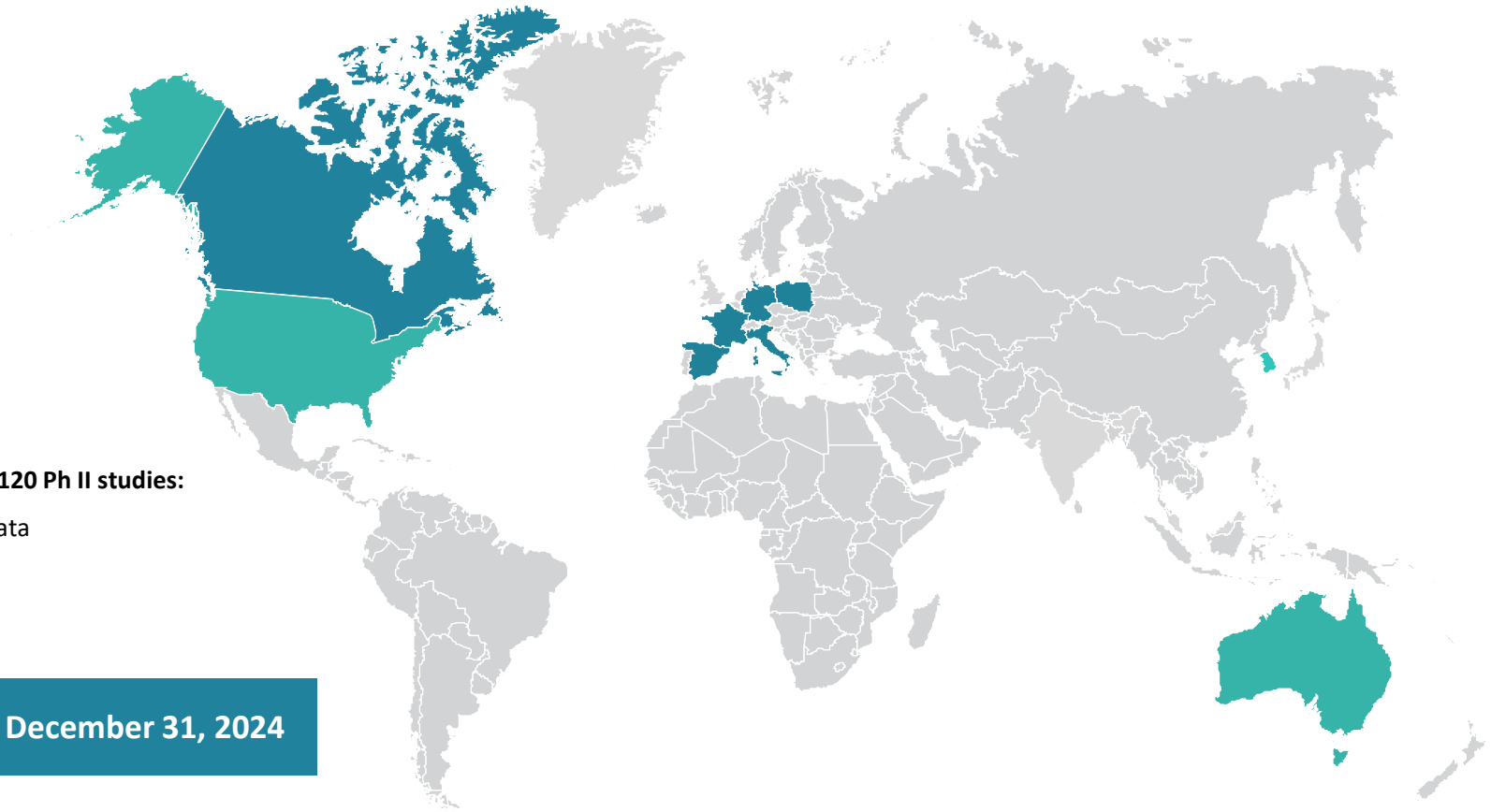
Related clinical observations

- 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





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

Expected status as of December 31, 2024

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+	~100	20+	80+

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

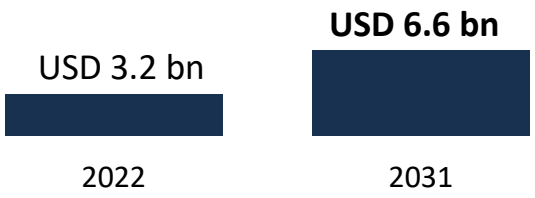
MDS (Myelodysplastic Syndrome)

- 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)

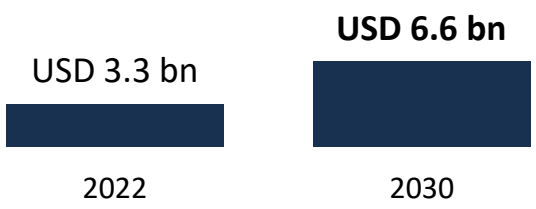
- MF is a bone marrow disease characterized by JAK mutations; often leads to severe anemia
- Chronic disease with long duration of therapy; US prevalence is est. to be ~13,000 patients[7]
- **Jakafi (ruxolitinib) sales in 2023 – USD 2.6 bn**
- **Morphosys acquired by Novartis for EUR 2.7 bn in Feb 2024**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

Global AML Market [4]



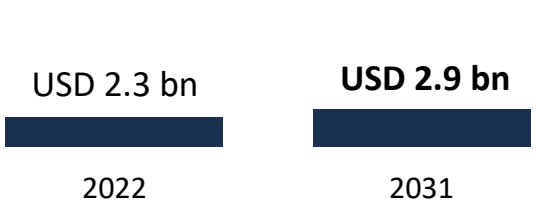
8.5% CAGR (2022-2031)

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 All studies on track for efficacy analysis in H1 2025

RVU120 program summary

RIVER-52 **Next data in Q2 2025**

- 1 of 2 evaluable NPM1+ pts with 50% blast reduction; 1 of 3 evaluable DNMT3A+ pts with disease stabilization
- Data from the first 10+ evaluable patients in Cohorts 2-4 expected in H1 2025

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

POTAMI-61 **Enrollment ongoing; initial data in Q2 2025**

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

REMARK **Enrollment ongoing; initial data in Q2 2025**

- First patient dosed in September 2024
- Initial efficacy data expected in Q2 2025

Accelerating enrollment across Phase II program

- Successful launch of all 4 Phase II studies: RIVER-52, RIVER-81, POTAMI-61, REMARK
- 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 still to Q1 2026

RYVU THERAPEUTICS

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

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

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

Novel Targeted Oncology Platform with Focus on Synthetic Lethality

RYVU THERAPEUTICS

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 Focus on selectivity, potency 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	File IND/CTA 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 high efficacy in large cell line panel
- **Favorable PK profile** demonstrated in PK studies in various species
- **Antitumor efficacy** achieved *in vivo* in responder CDX models

Leading to a differentiated clinical strategy

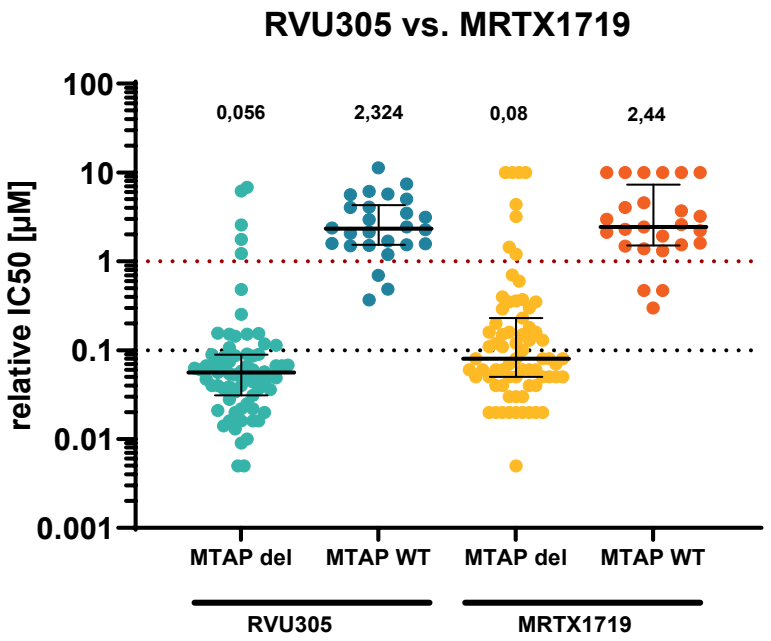
Ongoing translational work will support the selection of

- 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

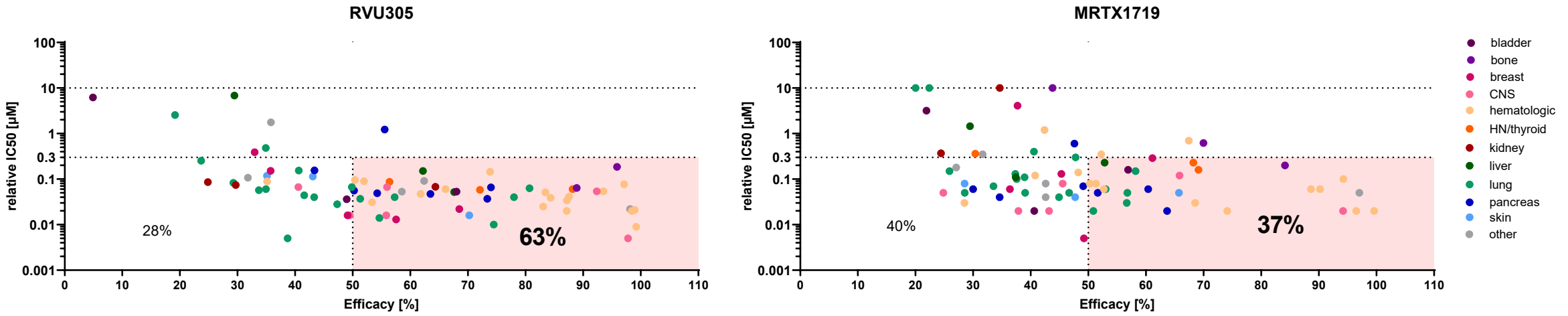
- Panel of MTAP-deleted and MTAP-wt cells was profiled with RVU305 in a 5-day CellTiter-Glo assay
- A differential response to Ryvu PRMT5 MTA-cooperative inhibitor is seen between cells with different MTAP status
- RVU305 shows higher potency than MRTX1719 (comparing to results published by Engstrom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



RVU305 shows strong antiproliferative activity in cell lines

RVU305 shows superior potency and efficacy in cell line panel vs. MRTX1719

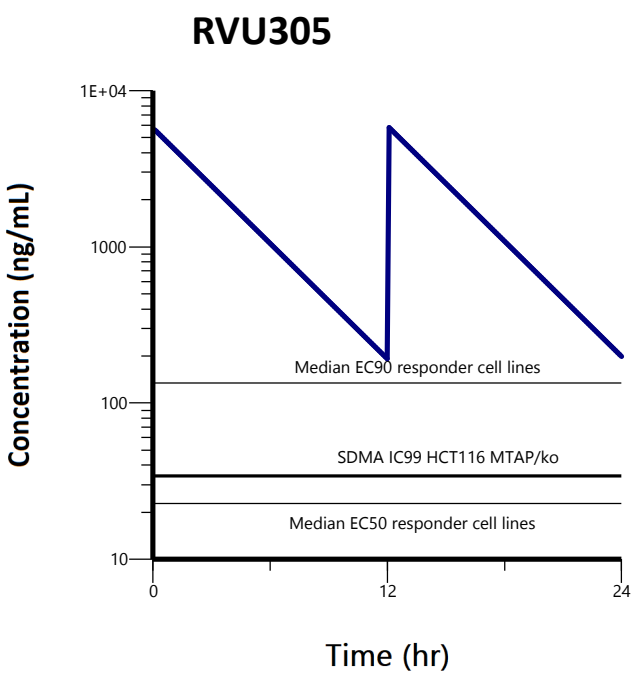
RVU305 shows a better profile of potency and efficacy in the cell line panel with 63% of the cell lines below a threshold of 300nM IC50 (at which most sensitive MTAP WT cell line responded) and efficacy above 50% comparing to 37% for MRTX1719

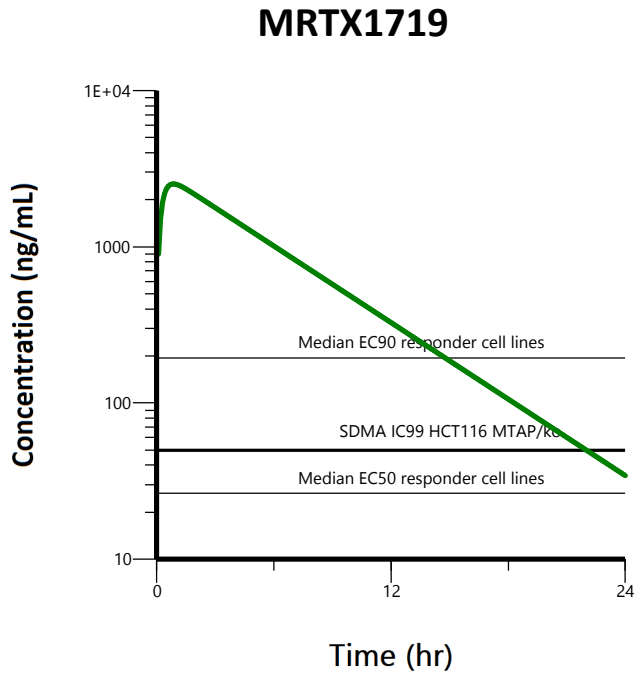


Favorable PK profile for RVU305 is promising for clinical development

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



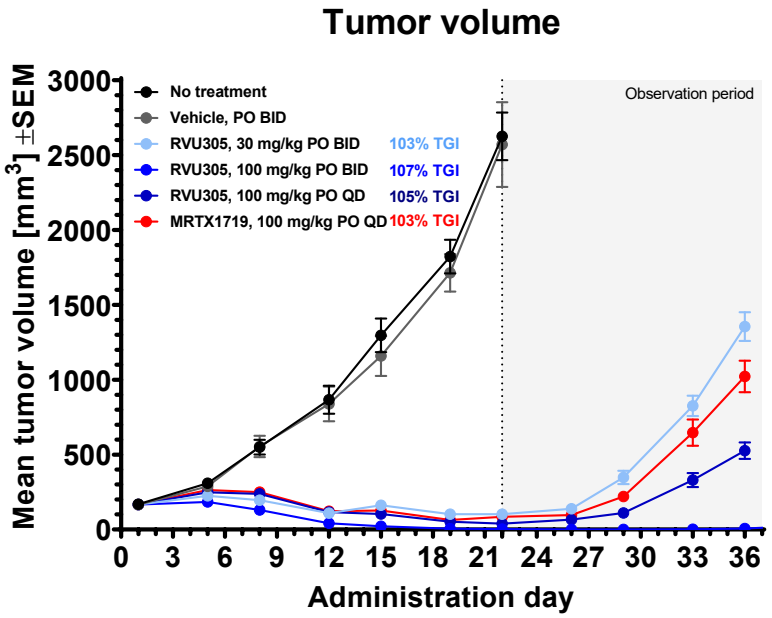


SDMA EC99 (measured via ELISA assay in HCT116 MTAP knockout cells) was used as a target engagement marker. The 2D viability assay median EC50/90 values were derived from panel of multiple MTAP/del cell lines (BXPC3, Lu99, HUPT4, MiaPaca2, A549, DoHH2, HCT116-MTAP-DEL).

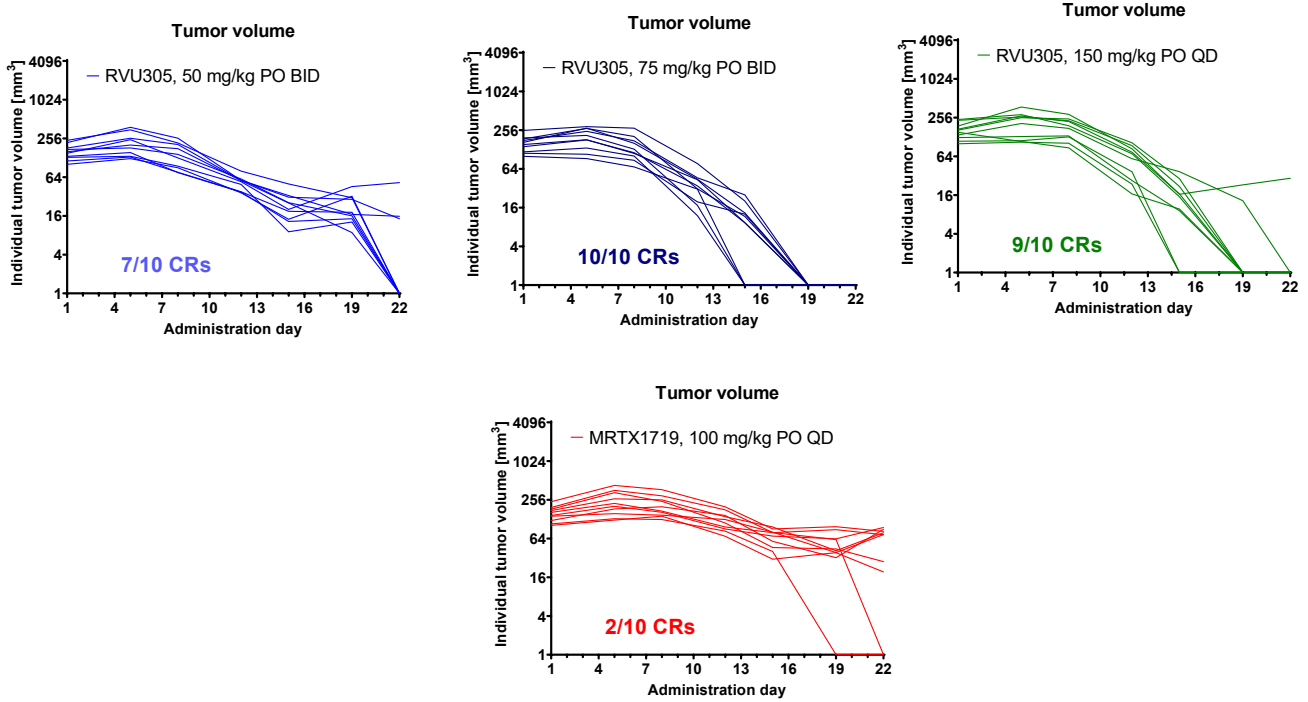
RVU305 shows significant antitumor efficacy *in vivo*

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 best-in-class potential vs. clinical competitors

	MRTX1719	TNG908	TNG462	AMG193	RVU305
Potency [1]	+++	+	+++	++	+++
Viability fold shift MTAP KO/MTAP WT	+++	+	++	++	++++
Residence time	+++	+	ND	ND	+++
% of highly sensitive MTAP deleted cell lines in Omniscreen[2]	36%	ND	ND	ND	**63%**
Brain penetrance	-	+++	-	-	-
In vivo PK[3]	+	+	++	+++	+++
Potential for drug-drug interactions	+++	+	++	+++	+++
Expected target coverage at clinical dose and schedule[4]	++	+	+++	++	++++
Clinical safety	+++	ND	ND	+++	ND

1) Viability *in vitro* in MTAP del cell line model
2) Based on published data on MRTX1719 compared with Ryvu Omniscreen panel on RVU305
3) Overall murine PK profile including clearance
4) Based on the overall preclinical profile and simulations

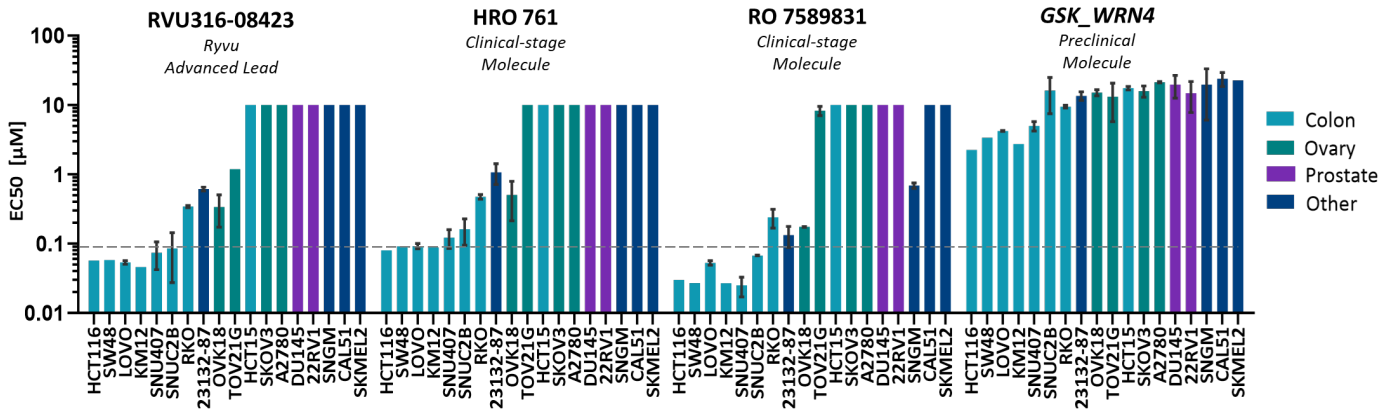
37

Werner Syndrome Helicase (WRN) inhibitors at Ryvu

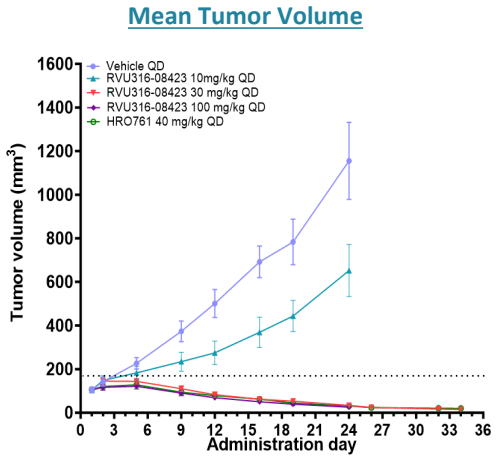
WRN Inhibitor Program at Ryvu

KEY RATIONALE and MOA	Synthetic lethality of WRN with microsatellite instability (MSI-high)
NOVELTY	Best-in-class potential Focus on selectivity, potency and safety
TOP TUMOR INDICATIONS	Tumor agnostic with MSI-high vulnerability (~10-30% of colorectal, endometrial, gastric, ovarian cancers)
STATUS	Lead Optimization

01 **Third generation of Ryvu WRN inhibitors shows strong in vitro potency in MSI-H cell lines, comparing favorably to competitor benchmarks**



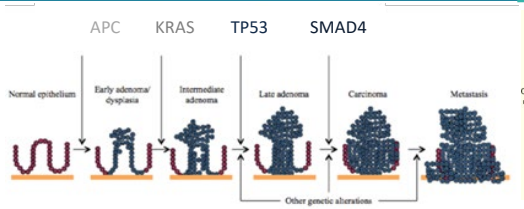
02 **Potent and dose-dependent inhibition of tumor growth in SW48 CDX CRC model compares favorably to competitor benchmark**



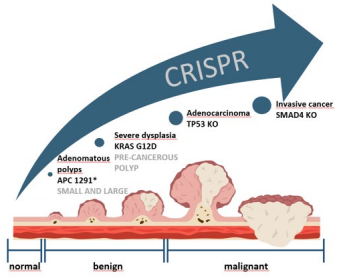
Driving novel synthetic lethal target discovery with Ryvu's ONCO Prime platform

Ryvu's CRISPR-based target Discovery Platform

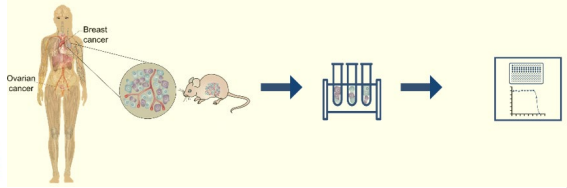
Engineered Model



Isogenic Primary Cells Recreating the stages of tumor development



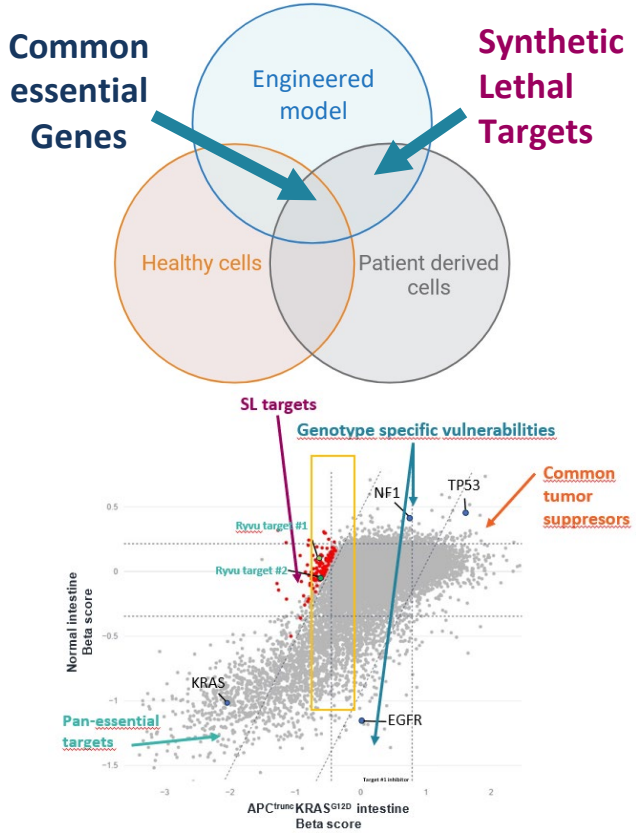
Patient-Derived Cells (PDCs)



Tumor heterogeneity & relevant transcriptomic profile

Awarded USD 6.6M grant
Polish Agency for Enterprise Development[1]

Discovering Novel Synthetic Lethal Targets



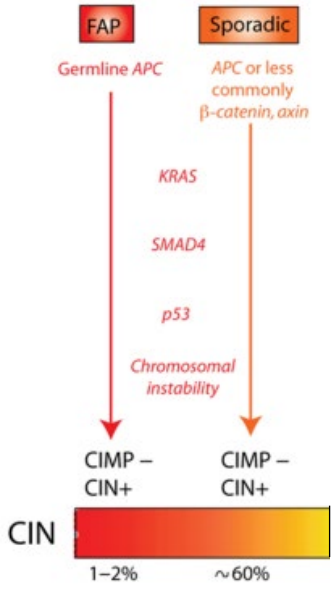
1) ONCO Prime is co-financed by the European Union under the Operational Programme European Funds for Modern Economy 2021-2027. Project title: "ONCO Prime: new possibilities for personalised anti-cancer therapy based on patient-derived primary cell cultures, omics characterisation, and functional assays".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

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

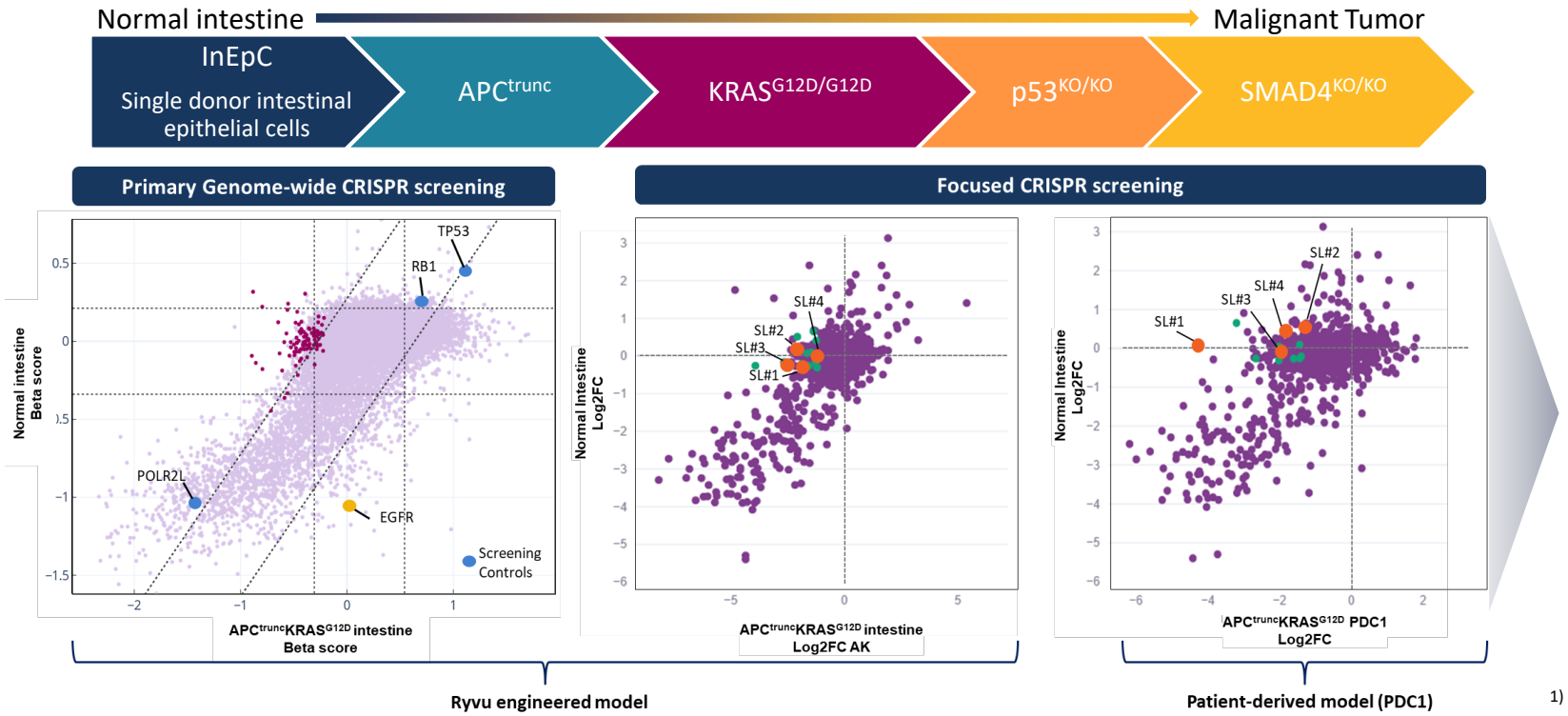
CRC

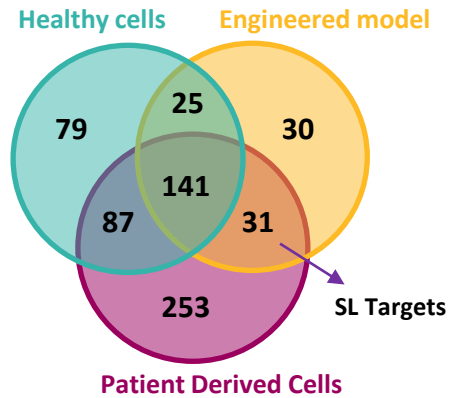
- **The third most prevalent cancer worldwide**
- Estimated number of colorectal cancers in the US for 2024 are 153,000 new cases[1]
- Diagnosed usually at an advanced stage. Mortality still remains high.
  Five-year survival shown by SEER database is **around 65%**, the survival drops to **13%** at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

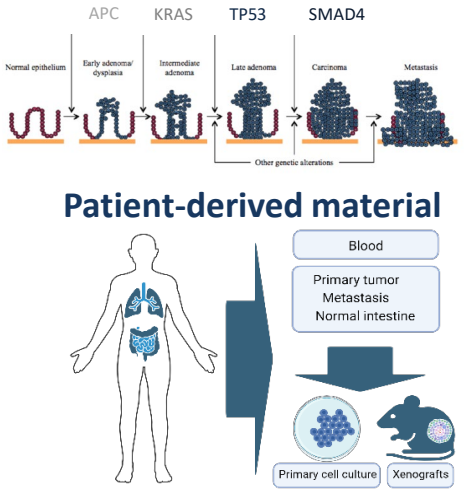




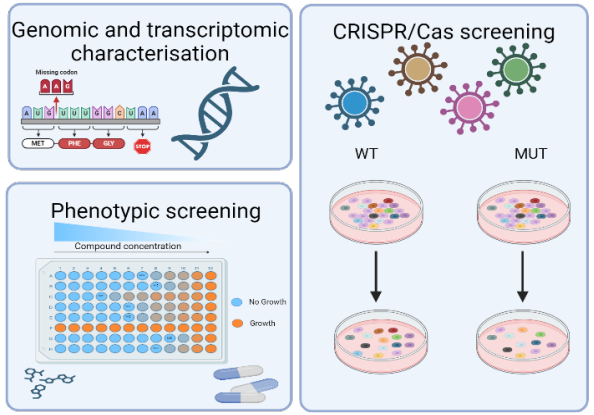
1) American Cancer Society

ONCO Prime is accelerating the development of novel synthetic lethal targets

Modeling cancer progression



High Throughput Screenings

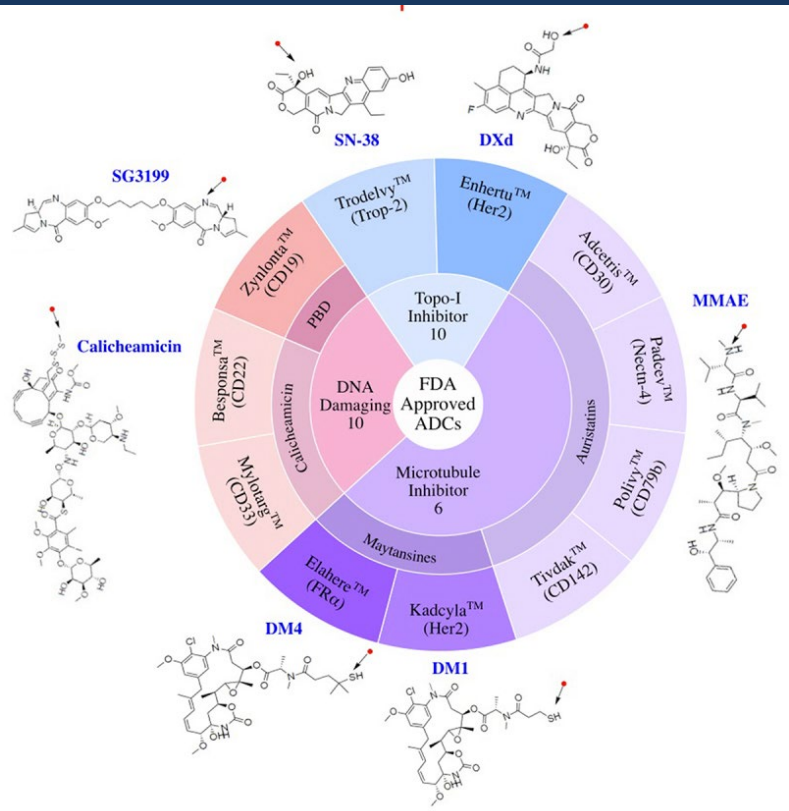


Novel Targets & Treatments

- Ryvu's OncoPrime platform has **broad potential to discover novel 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

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

Approved ADCs use three main types of payloads

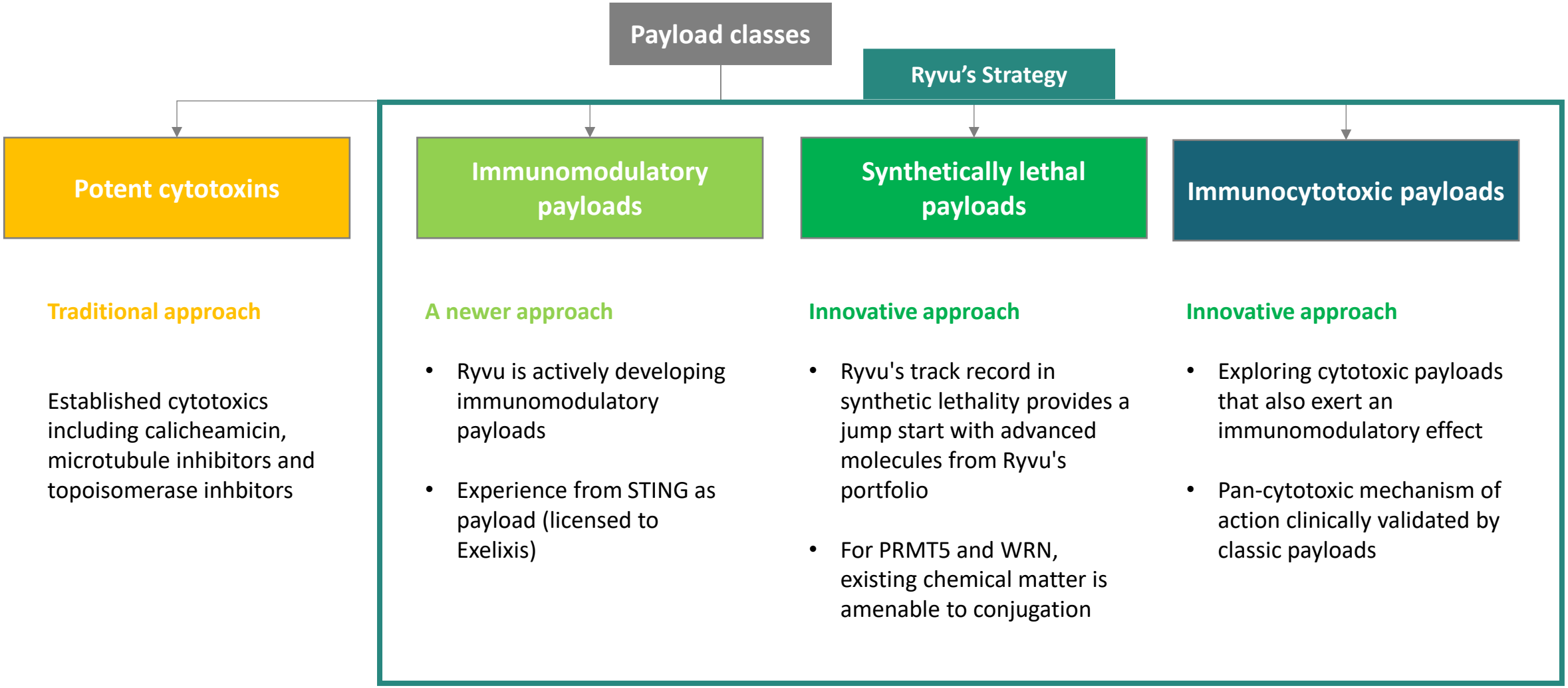


Maecker et al., MAbs, 2023.

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’s ADC payload strategy is focused on novel and potent mechanisms



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 (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, 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

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	Good	Good	Good	dsRNA and INF response ↑, immunopeptidome ↑	Good	Good
Target 2	Several clin. cand. grade	Good	Medium	Good	Micronuclei mediated INF response ↑, ICD	Poor **	Poor **
Target 3	Several clin. cand. grade	Good	Medium	ND	↓ pSTAT3, INF response ↑, DC maturation, ICD	Poor	Good
Target 4	One clin. cand. grade	Poor	Poor	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

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Corporate Progress

Financial Results: Q3 2024

$ million	2023*	Q3 YTD 2023*	Q3 YTD 2024*
Revenues	**16.3**	**11.9**	**18.6**
Partnering	*11.2*	*8.4*	*13.2*
Grants	*4.9*	*3.3*	*5.3*
Total Costs**	**37.6**	**27.4**	**38.2**
Clinical Pipeline	*13.0*	*6.4*	*17.4*
Early Pipeline	*15.8*	*13.9*	*14.2*
G&A	*8.8*	*7.1*	*6.6*
EBIT**	**-21.3**	**-15.5**	**-19.6**
EBITDA**	**-18.7**	**-13.6**	**-17.6**
Net Results***	**-20.0**	**-13.5**	**-18.5**

Partnering revenues in Q3 YTD 2024:
Exelixis ($1.2 million), BioNTech ($7.8 million recognized)

Cash position November 4, 2024

$58.1M

Ryvu Employees

>300

Employees with PhD

~100

* Recalculated from PLN using 4.1823 PLN/USD, 4.2337 PLN/USD and 3.9600 PLN/USD – for 2023, Q3 YTD 2023 and Q3 YTD 2024, respectively

** Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of $2.0m, $1.7m and $0.7m in 2023, Q3 YTD 2023 and Q3 YTD 2024 respectively) and valuation of NodThera (+$0.9m (increase of costs) in 2023, +$0.2m in Q3 YTD 2023, and +0,2m in Q3 YTD 2024, respectively)

*** Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of $2.0m, $1.7m and $0.7m, in 2023, Q3 YTD 2023 and Q3 YTD 2024 respectively)

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

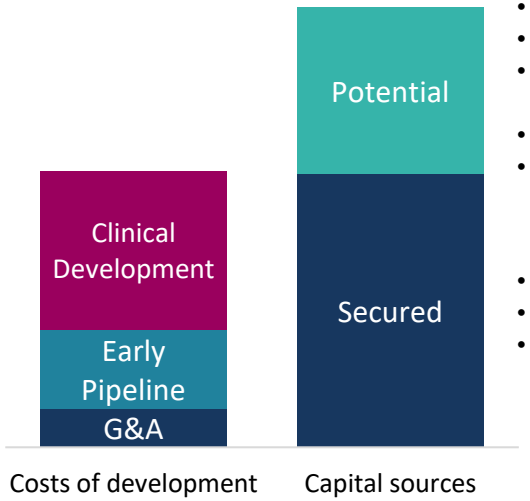
2025 KEY GOALS AND FINANCING

PIPELINE

- **RVU120 broad development (including potential fast-to-market strategy in AML/HR-MDS)**
- SEL24 (MEN1703) to enroll 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

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 **Corporate Split: Selvita and Ryvu**	Nov 2014 Oct 2019
Ticker: WSE	RVU
52-Week Range[1]	PLN 35.15 – 61.00
Average Daily Volume (YTD) [1]	9,848
Market cap[1]	PLN 900 M (USD 220M)
Shares outstanding	23.1 M
Cash[2]	USD 58.1M

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

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 03 January 2025 2. As of 04 November 2024 3. From stooq.pl as of 12 December 2024.

Thank you

CONTACT DATA:

Ryvu Therapeutics S.A.

www.ryvu.com

ryvu@ryvu.com

ir@ryvu.com