



Developing therapeutics
at the forefront of oncology

Corporate Presentation

February 2025



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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 Przewiezlikowski, MSc, MBA
CEO and Founder



Krzysztof Brzozka, PhD, MBA
CSO



Hendrik Nogai, MD
CMO



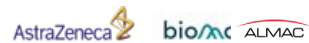
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NEUCA

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) (monotherapy)						Updated Ph II data in 2Q25
	R/R AML (RIVER-81) (combo with venetoclax)						Updated Ph II data in 2Q25
	LR-MDS (REMARK) (monotherapy)						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)						
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						
STING ADC	ONCOLOGY						

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



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)



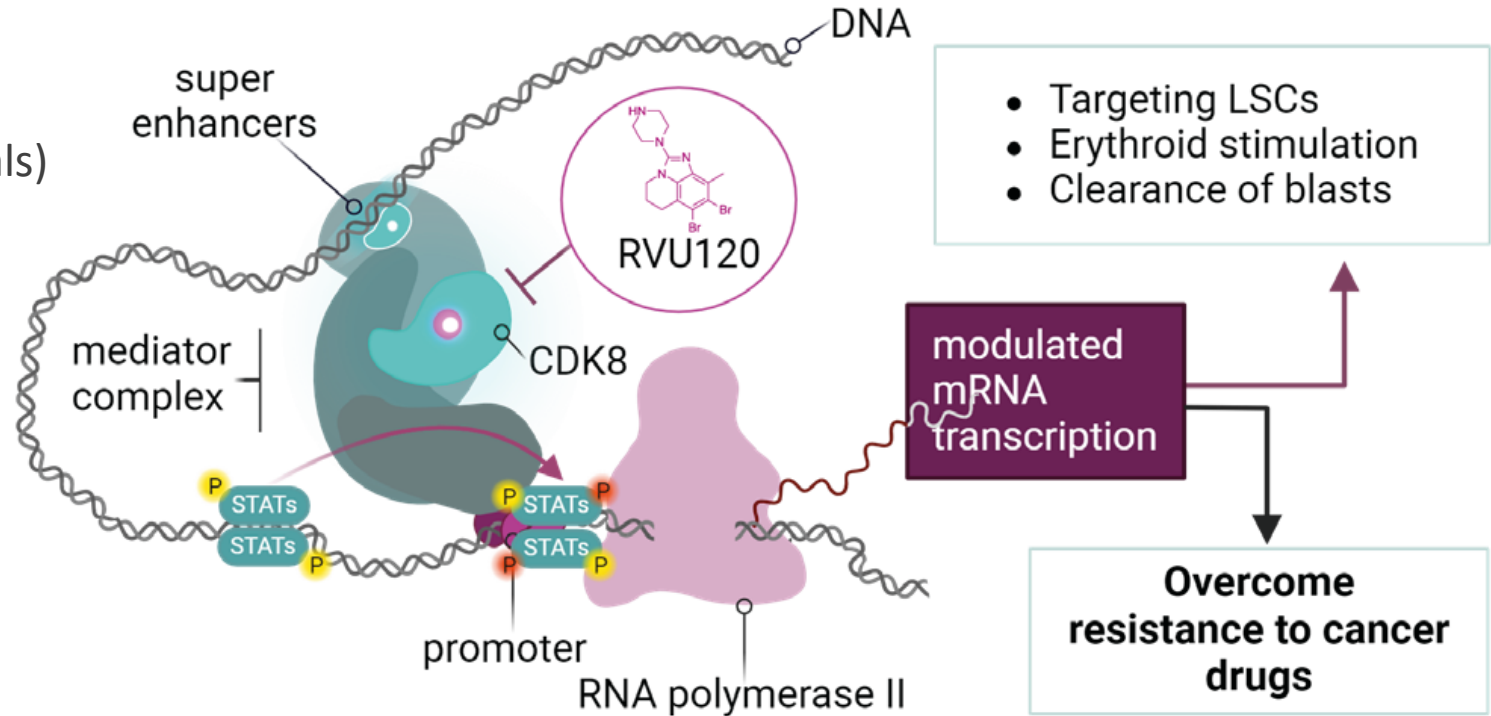
easy to formulate



orally bioavailable



favorable safety profile

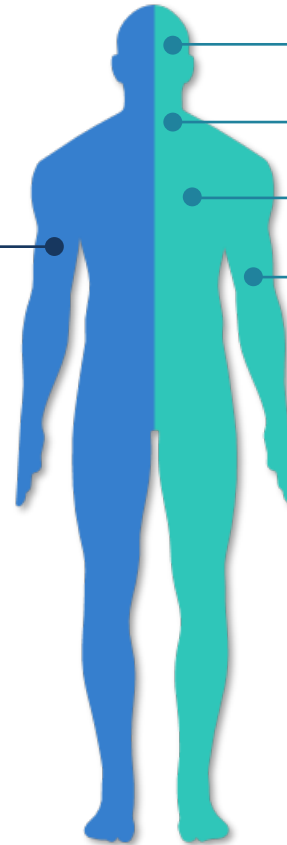


RVU120 is an innovative dual CDK8/19 inhibitor designed to target the expression of genes crucial for cancer cell survival and differentiation

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

Medulloblastoma

ACC

Breast

Sarcoma

- **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

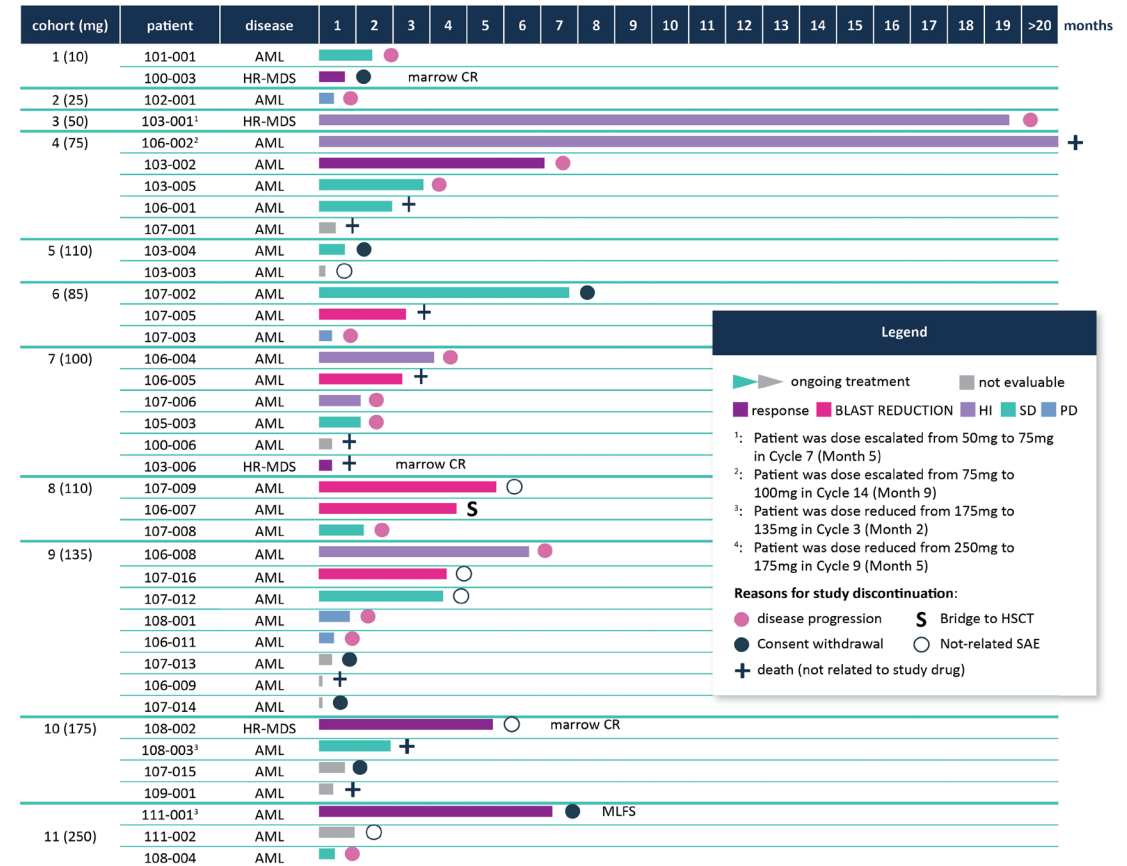
- 30 treated patients are evaluable for response (38 were treated in total)
- 9 patients achieved clinically significant BM blast reduction
 - (including 1 CR, 1 MLFS, 3 marrow CRs)
- 5 patients achieved erythroid hematological improvement (HI-E), 4 of those became transfusion-independent, of which 2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

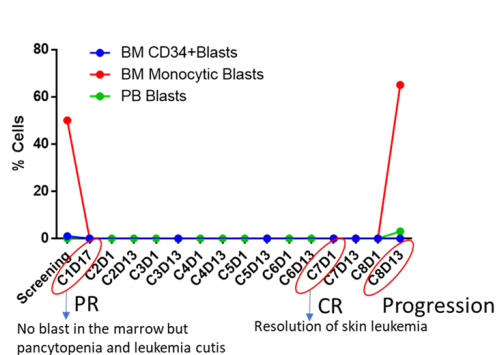
Data generated in RIVER-51 study support further development of RVU120 in AML, HR-MDS, LR-MDS and MF

Significant blast reductions

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

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

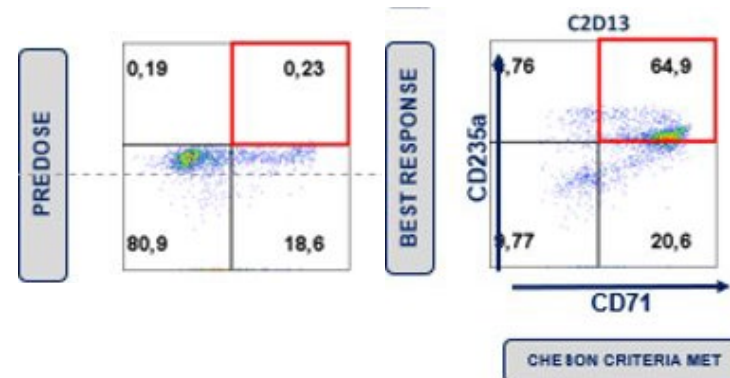


Transfusion independence

- >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

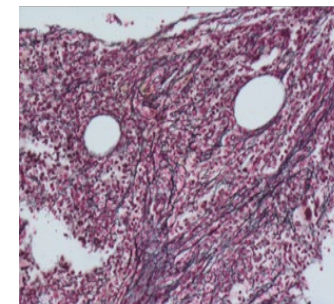
Improvement of BM architecture

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

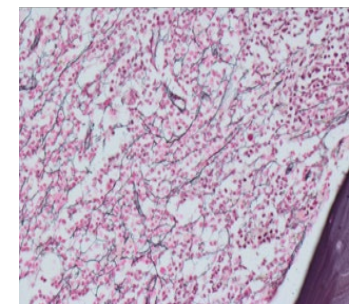
P108-002 HR-MDS

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

C2D13 fibrosis grade 3



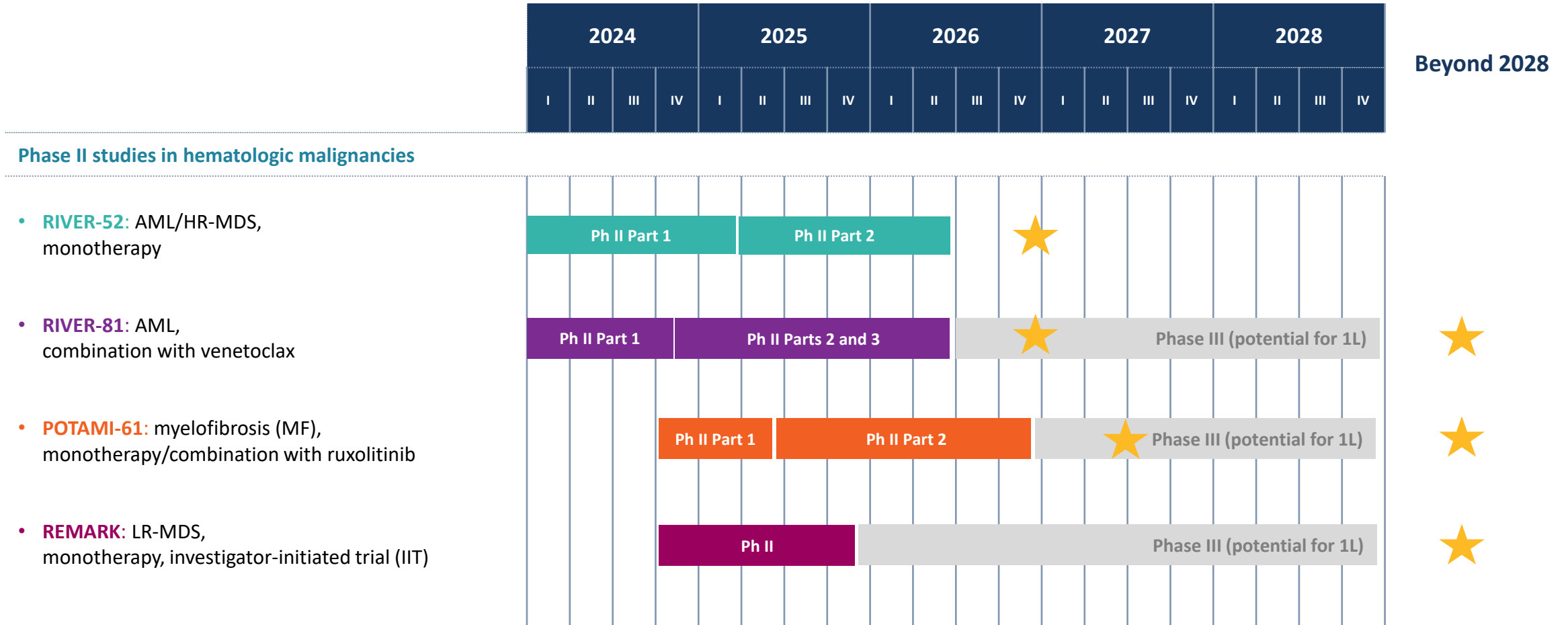
C6D1 fibrosis grade 2



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

Reduction of fibrosis grade and marrow CR

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



★ Approval process in selected regions

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

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:**

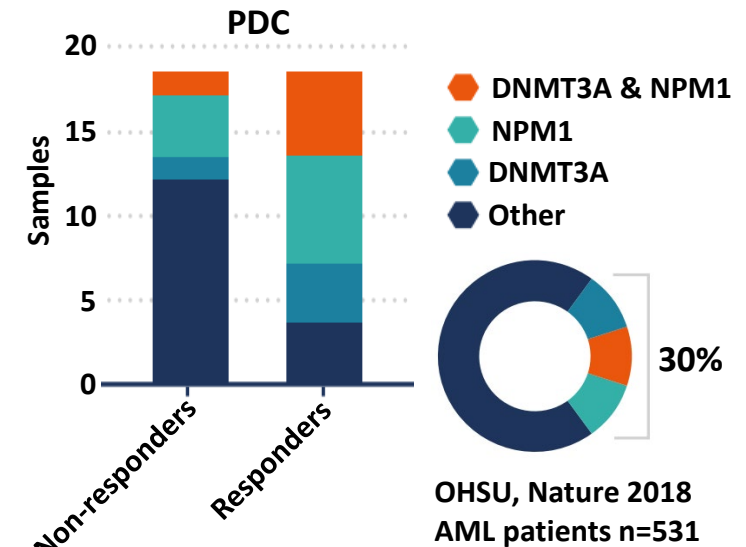
- In vitro screening of AML patient-derived cells revealed differential efficacy of RVU120 and other CDK8 inhibitors in NPM1 and/or DNMT3A mutants
- RVU120 as monotherapy demonstrated high efficacy in NPM1 or DNMT3A-mutated patient-derived xenografts

- 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

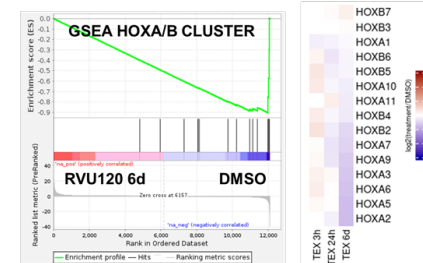
- Clinical Activity in Phase I:**

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

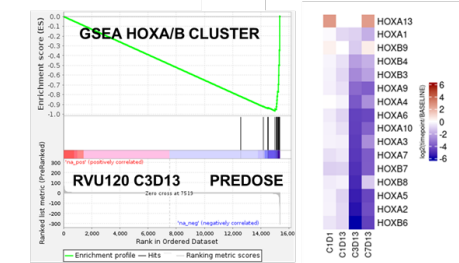


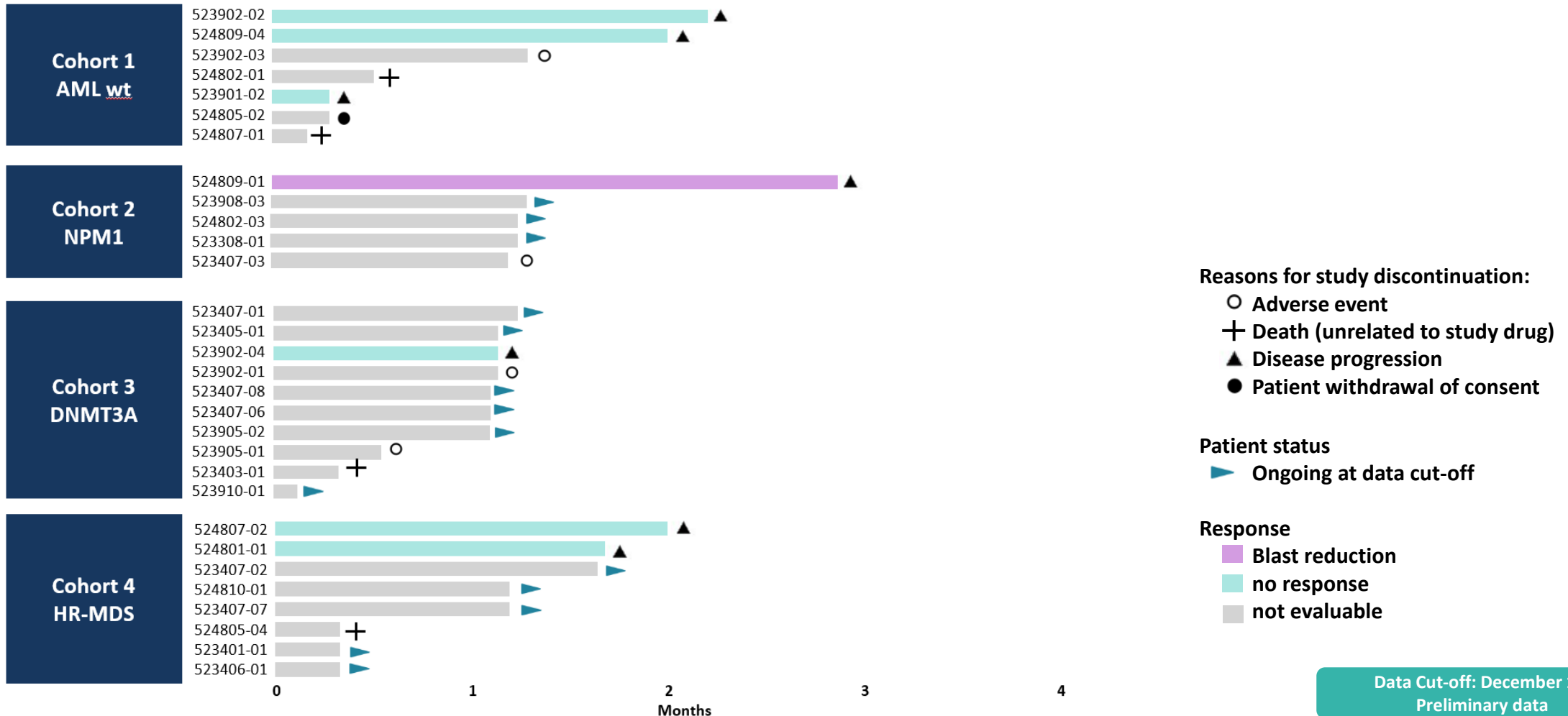
RVU120 downregulates homeobox cluster genes in TEX CD34+ leukemic cells and in AML patient 103-002 that achieved a complete remission

Preclinical data (TEX CD34+ cells)



Clinical data (patient 103-002):





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

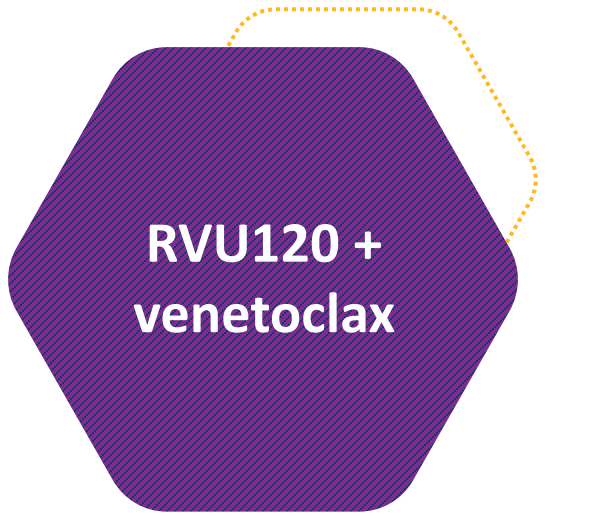
RVU120 appears to have a good safety profile, with the notable absence of QTc prolongation and differentiation syndrome

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



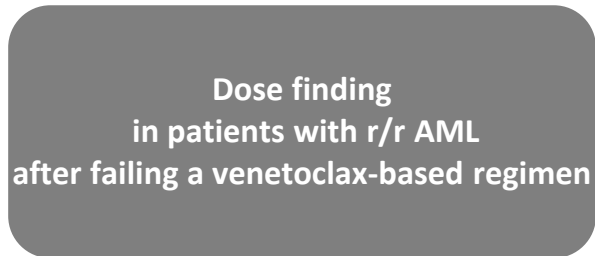
STUDY DESIGN

- 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

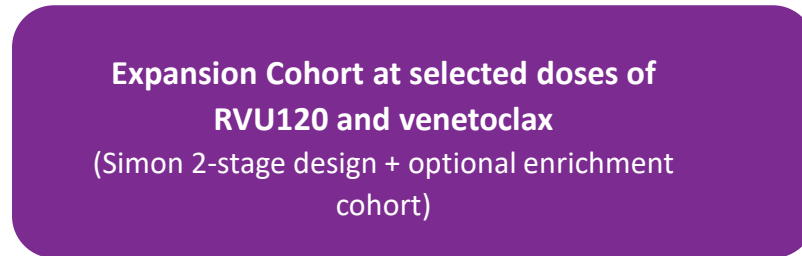


RIVER-81 is supported in part by a €13.3M grant from the Polish Medical Research Agency (ABM)

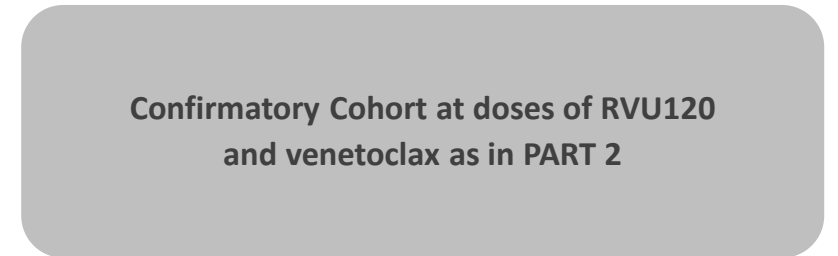
PART 1 (N = 17 pts)



PART 2 (N = ~39 pts)



PART 3 (N = ~41 pts)



(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

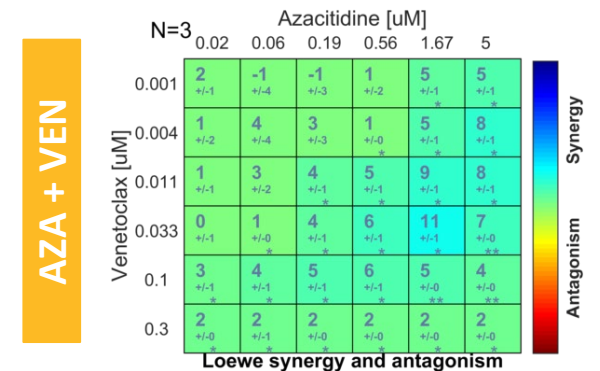
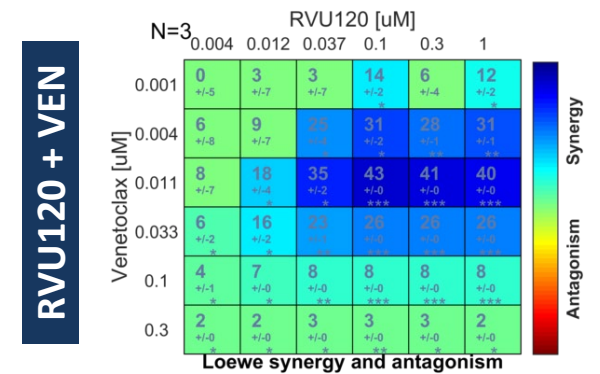
- **Remissions in Animal Studies:**

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

- **Mechanism of Synergy:**

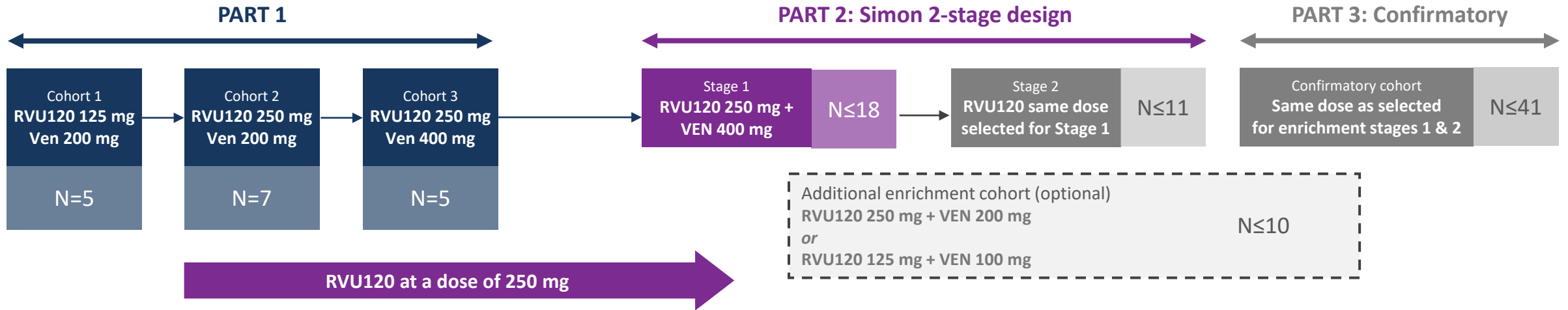
- MCL-1 is a known mediator of ven resistance. RVU120 induces caspase-dependent degradation of MCL-1
- MCL-1 inhibitors were tested in this setting, but prohibitive cardiotoxicity prevented further development
- The safety profile of RVU120 allows exploration of this concept
- Effectiveness on Leukemic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

MV4-11



RIVER-81

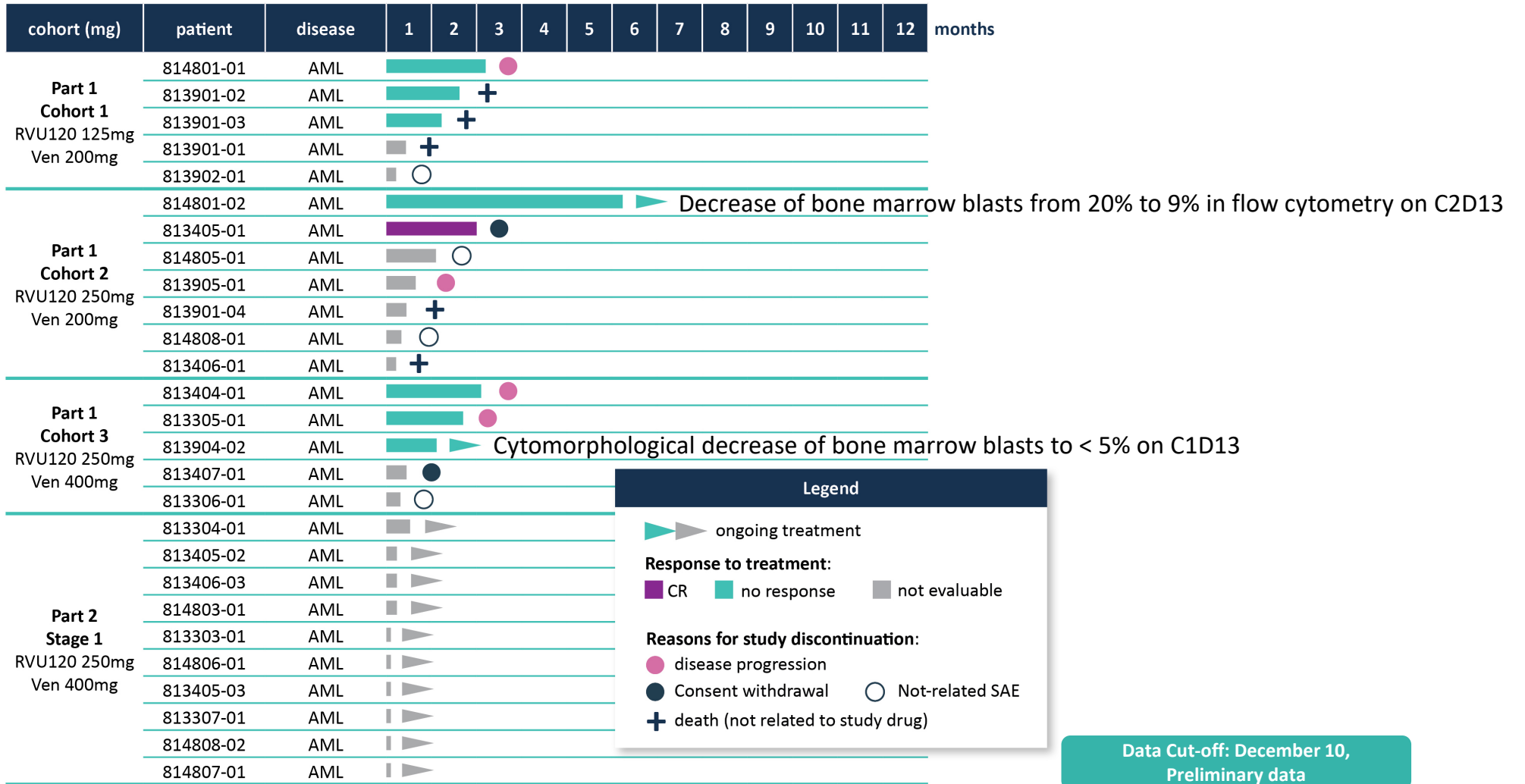
Part 1 (dose escalation) has been completed;
currently enrolling into Part 2 at the highest dose from Part 1



- 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 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

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



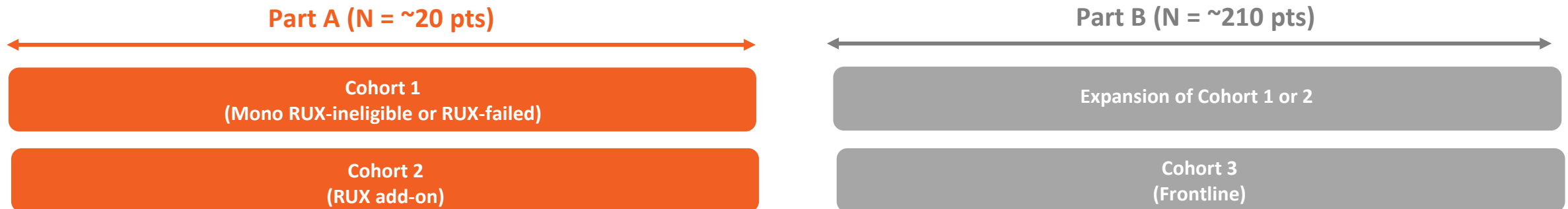
Eight patients treated with RVU120 at a dose of 250 mg (RP2D) had at least one evaluable post-baseline assessment

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

Confidential

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

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

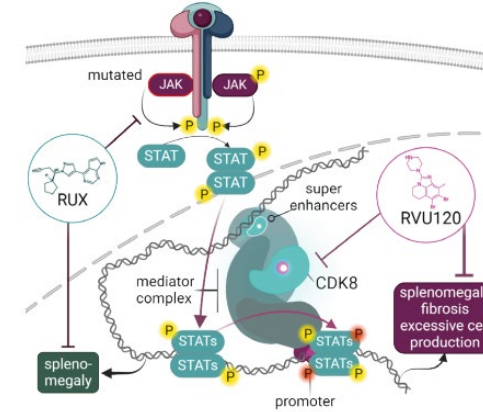
Opportunity in myelofibrosis

- 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

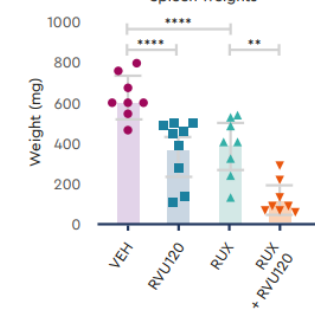
- CDK8 kinase is an important player in MPN pathogenesis, and RVU120 disrupts the downstream signaling events, mitigating MPN symptoms
- In preclinical studies, RVU120 effectively reduced splenomegaly, bone marrow fibrosis, and abnormal blood cell production. RVU120 has also demonstrated synergy in combination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



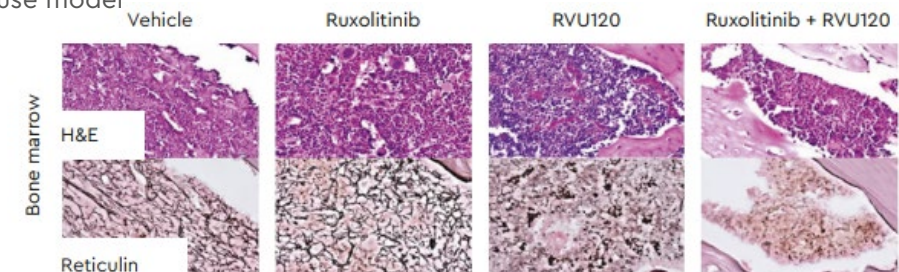
RVU120 reduces splenomegaly

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)



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

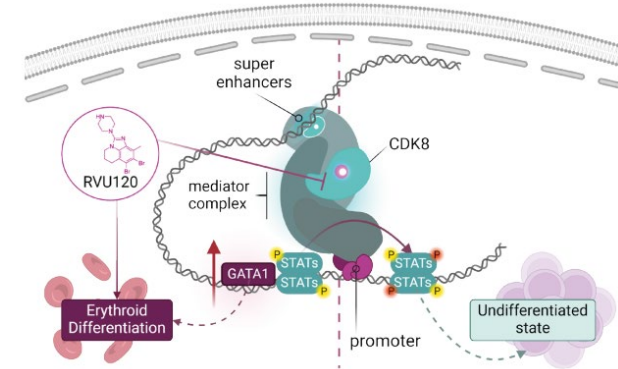
Opportunity in LR-MDS

- 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

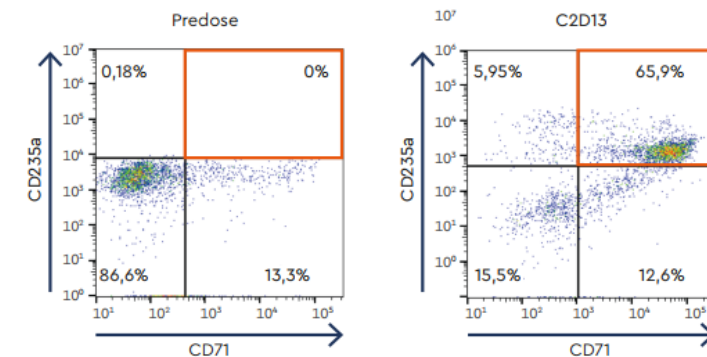
- MDS pathogenesis is influenced by gene expression alterations that hinder the maturation of hematopoietic cells.
- When aberrant stem cells from MDS patients are treated with RVU120, it triggers erythroid gene expression programs orchestrated by STAT5 and GATA1.
- Importantly, RVU120's activity does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

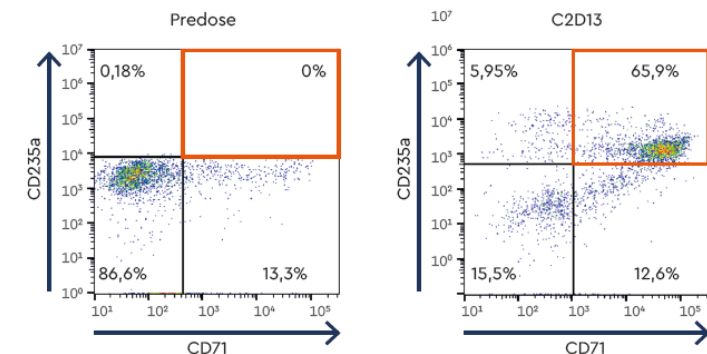
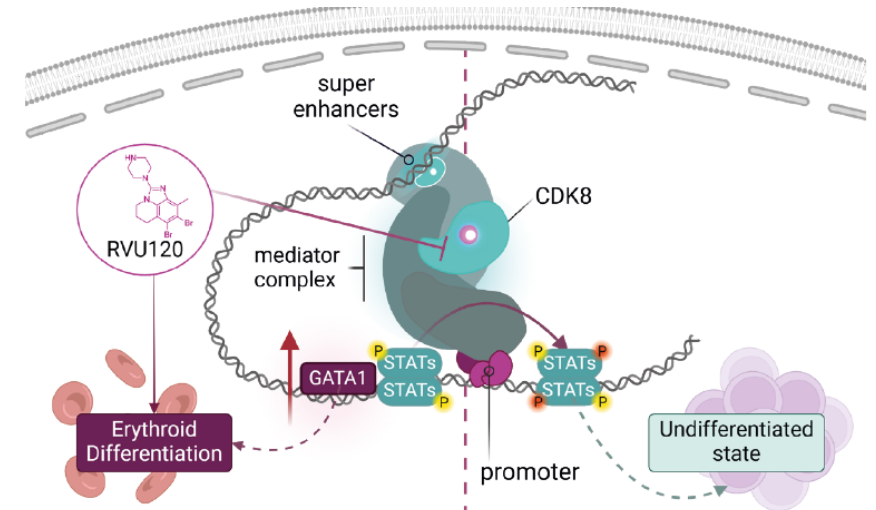
RVU120 has strong erythroid-stimulating activity in nonclinical anemia models and selected patients with AML/HR-MDS in Phase I (RIVER-51), providing the rationale for the Phase II clinical study in patients with LR-MDS

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

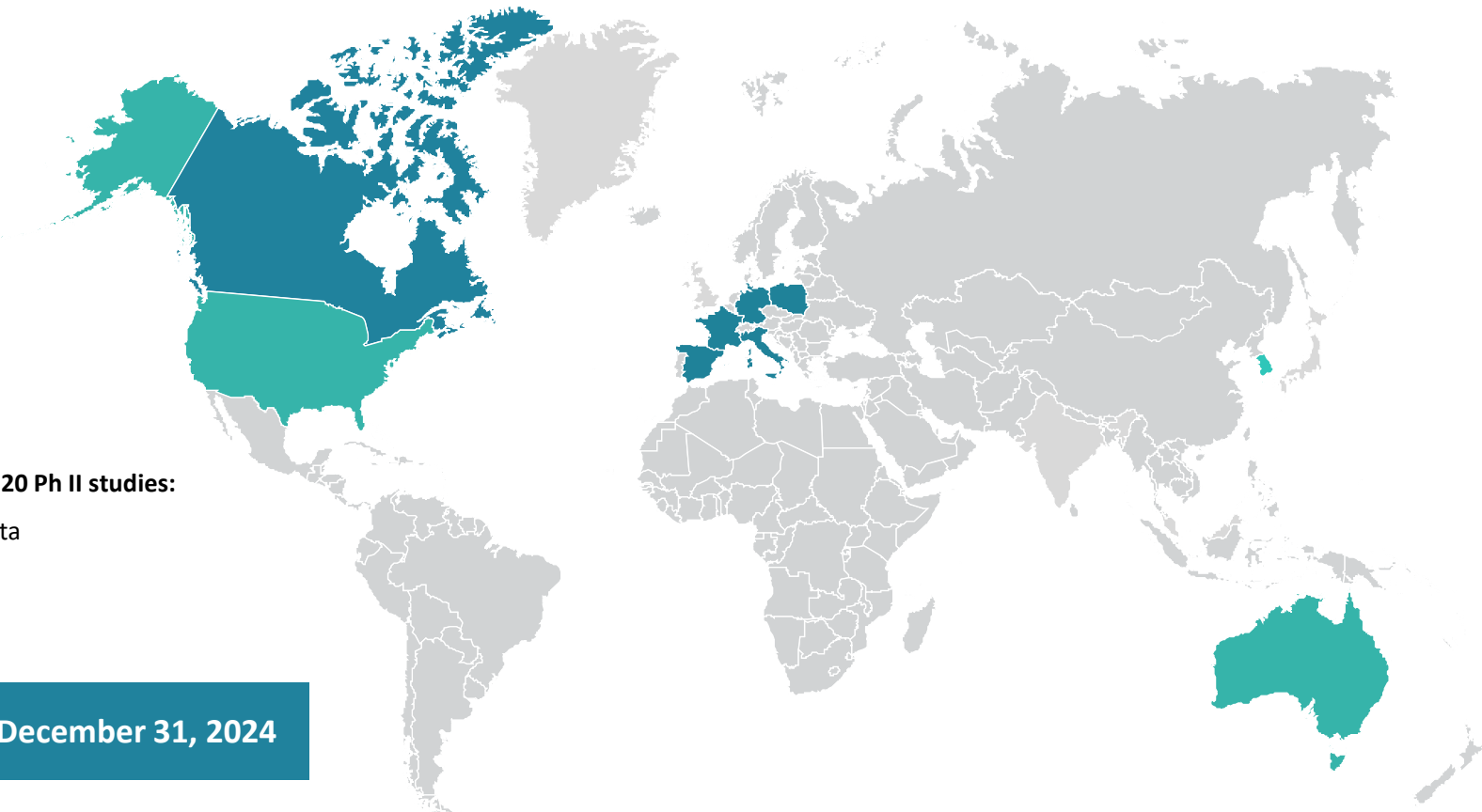
Related clinical observations

- 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



RVU120

Phase II clinical development with a global footprint



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

4

Number of countries across studies

6

Number of activated clinical sites globally

110+

Number of patients enrolled

~100

Number of clinical vendors managed

20+

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

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

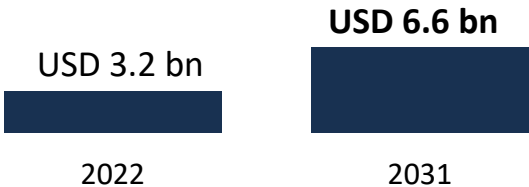
MDS (Myelodysplastic Syndrome)

- 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)

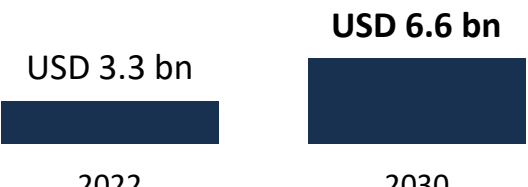
- MF is a bone marrow disease characterized by JAK mutations; often leads to severe anemia
- Chronic disease with long duration of therapy; US prevalence is est. to be ~13,000 patients⁽⁷⁾
- **Jakafi (ruxolitinib) sales in 2023 – USD 2.6 bn**
- **Morphosys acquired by Novartis for EUR 2.7 bn in Feb 2024**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

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

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



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
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 demonstrates superior preclinical properties vs. competitors

Leading to a differentiated clinical strategy

- **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

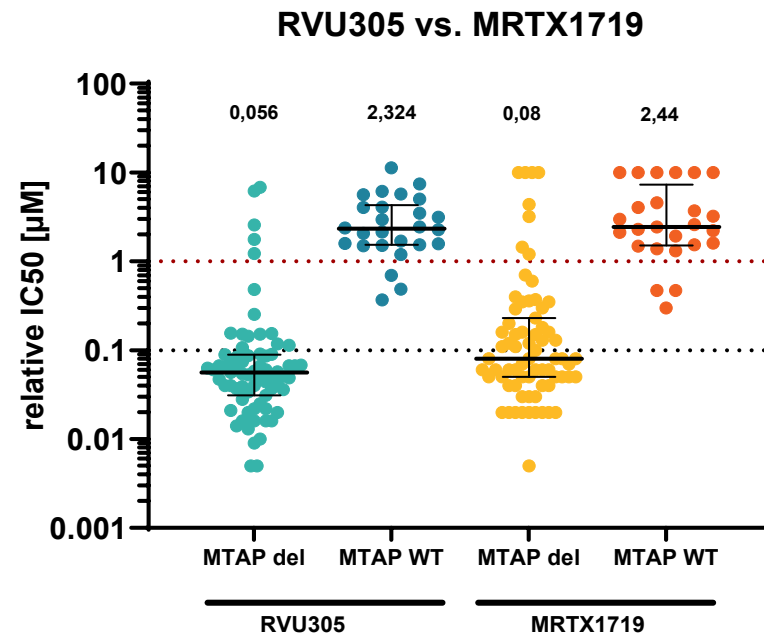
Ongoing translational work will support the selection of

- 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

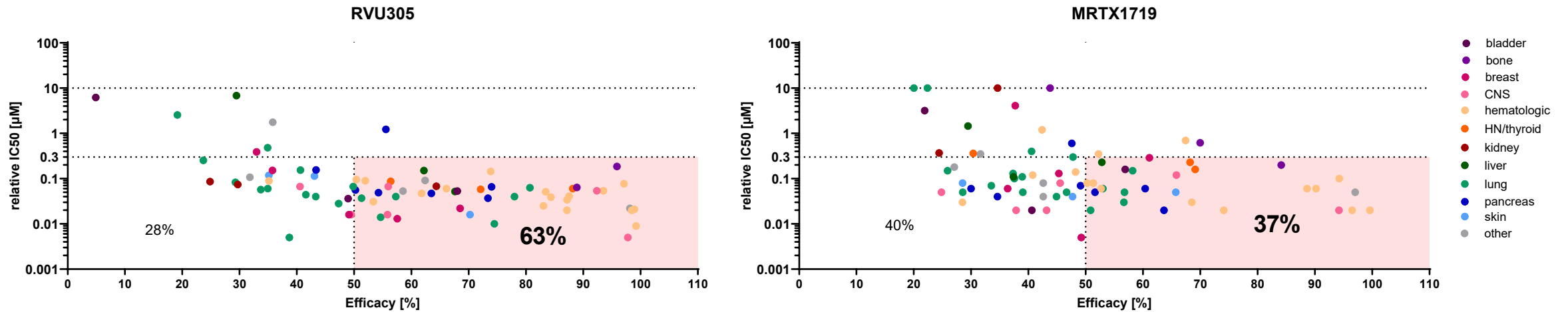
- Panel of MTAP-deleted and MTAP-wt cells was profiled with RVU305 in a 5-day CellTiter-Glo assay
- A differential response to Ryvu PRMT5 MTA-cooperative inhibitor is seen between cells with different MTAP status
- RVU305 shows higher potency than MRTX1719 (comparing to results published by Engstrom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



RVU305 shows strong antiproliferative activity in cell lines

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

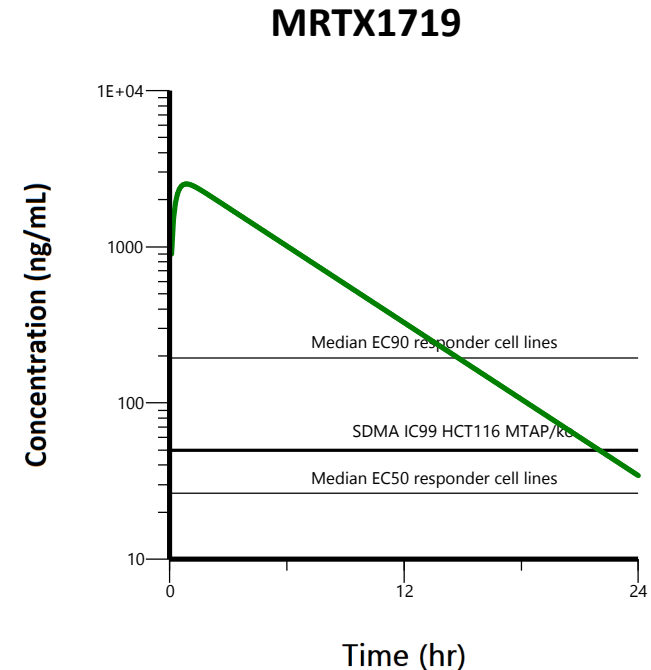
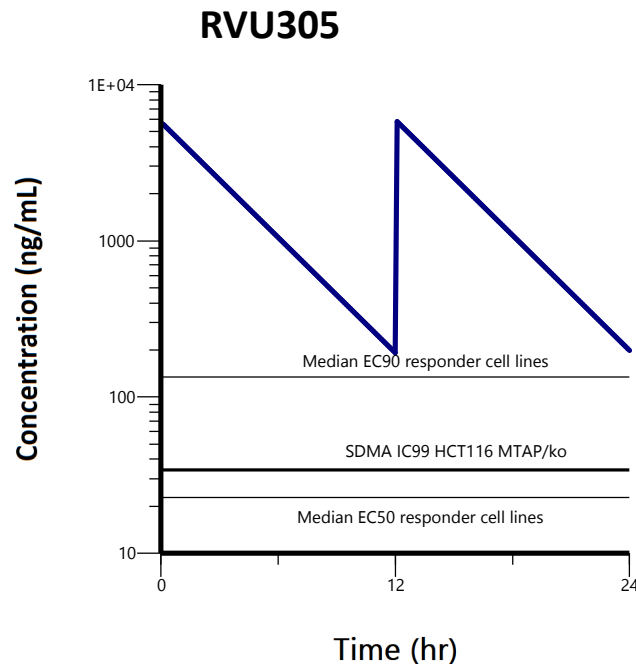
RVU305 shows a better profile of potency and efficacy in the cell line panel with 63% of the cell lines below a threshold of 300nM IC50 (at which most sensitive MTAP WT cell line responded) and efficacy above 50% comparing to 37% for MRTX1719



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

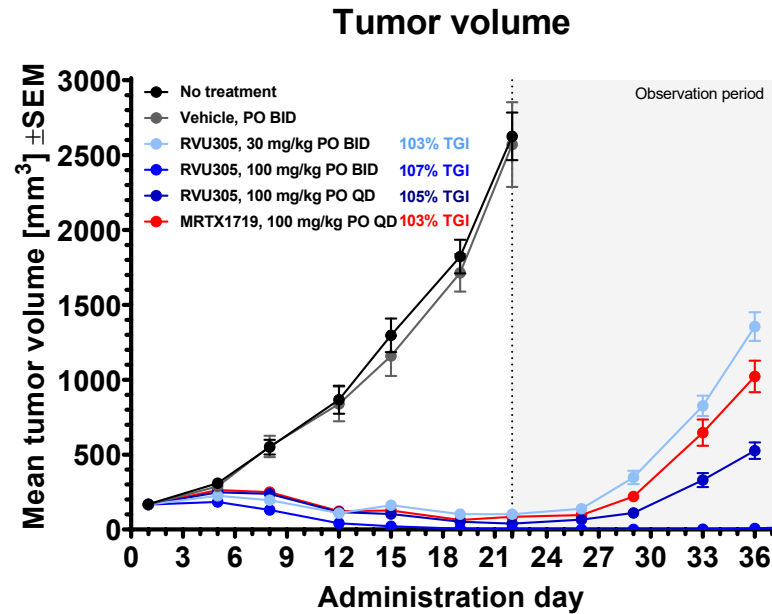


SDMA EC99 (measured via ELISA assay in HCT116 MTAP knockout cells) was used as a target engagement marker. The 2D viability assay median EC50/90 values were derived from panel of multiple MTAP/del cell lines (BXPC3, Lu99, HUPT4, MiaPaca2, A549, DoHH2, HCT116-MTAP-DEL).

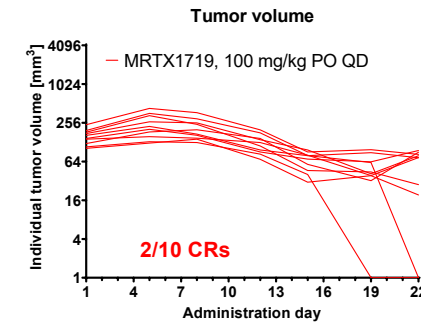
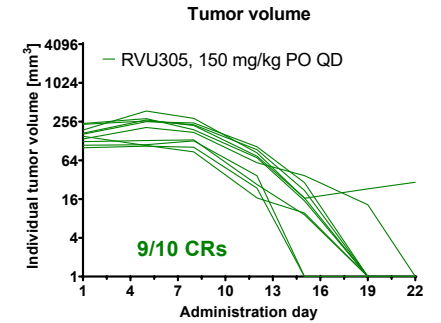
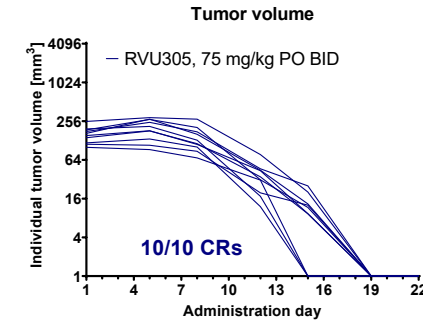
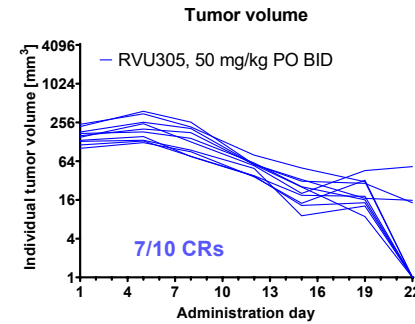
RVU305 shows significant antitumor efficacy *in vivo*

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

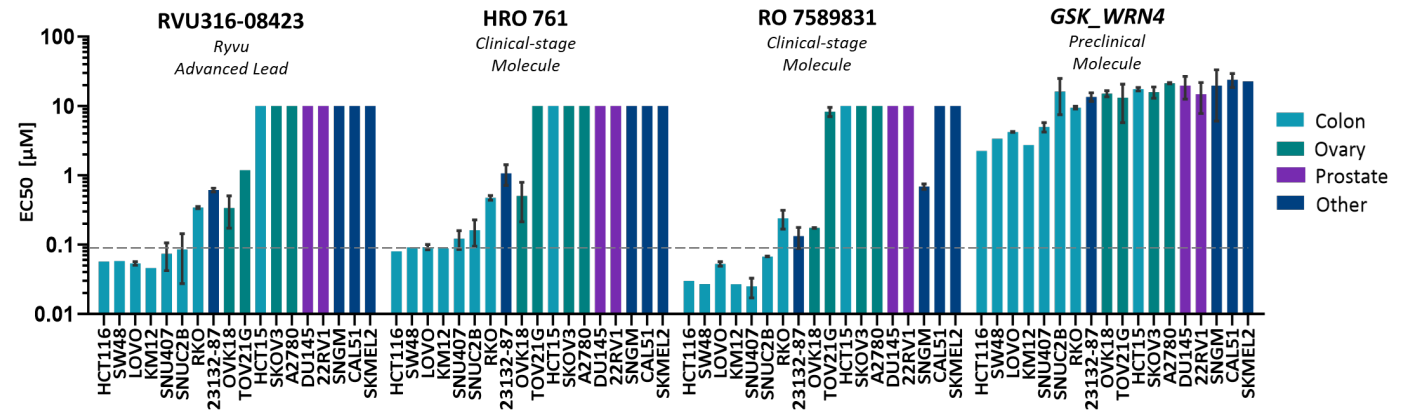
4) Based on the overall preclinical profile and simulations

Werner Syndrome Helicase (WRN) inhibitors at Ryvu

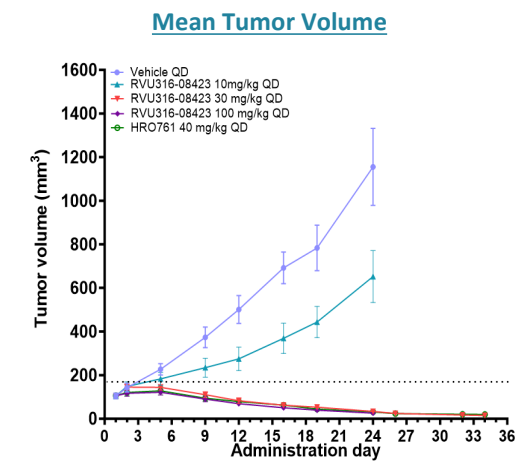
WRN Inhibitor Program at Ryvu

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

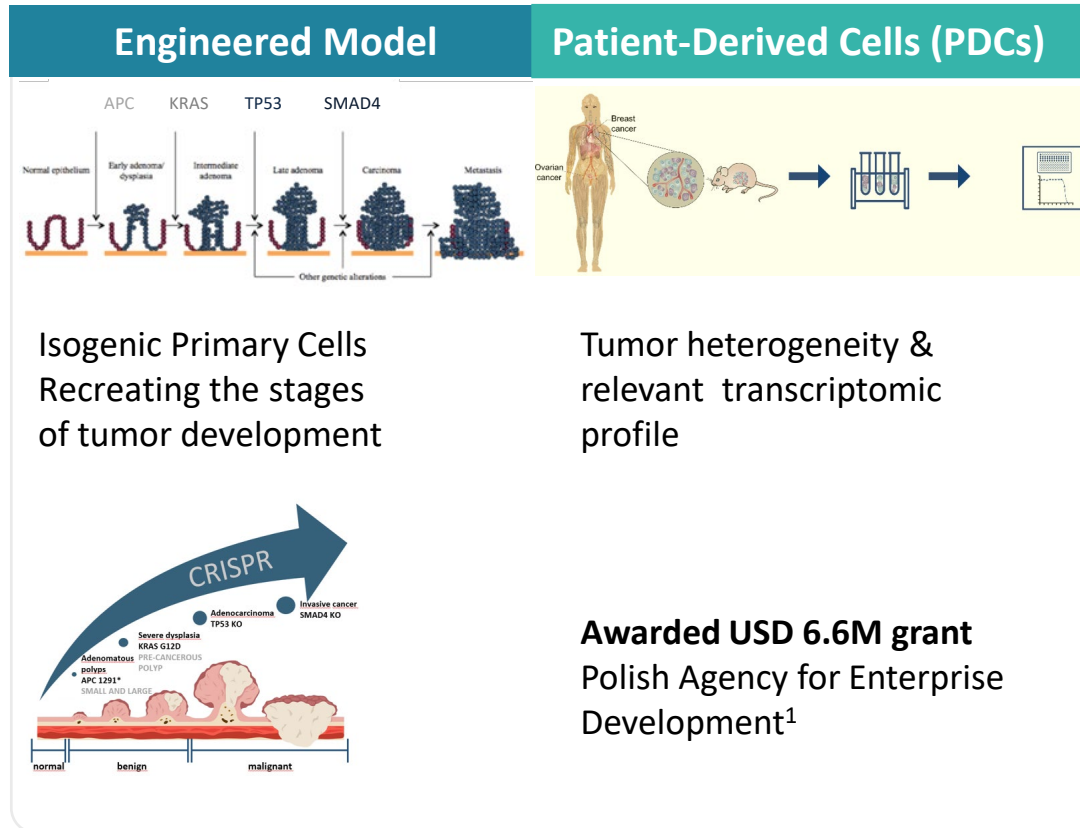


02 Potent and dose-dependent inhibition of tumor growth in SW48 CDX CRC model compares favorably to competitor benchmark

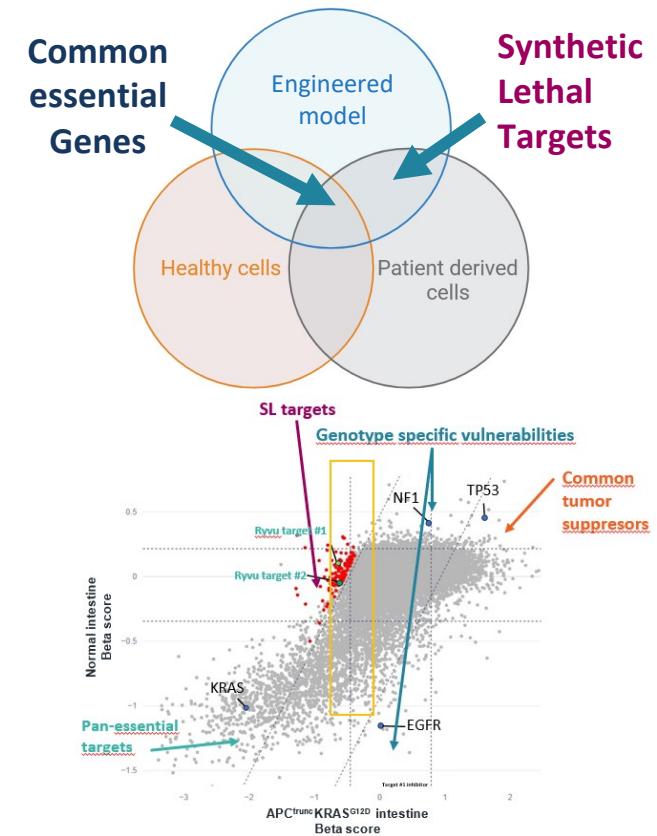


Driving novel synthetic lethal target discovery with Ryvu's ONCO Prime platform

Ryvu's CRISPR-based target Discovery Platform



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

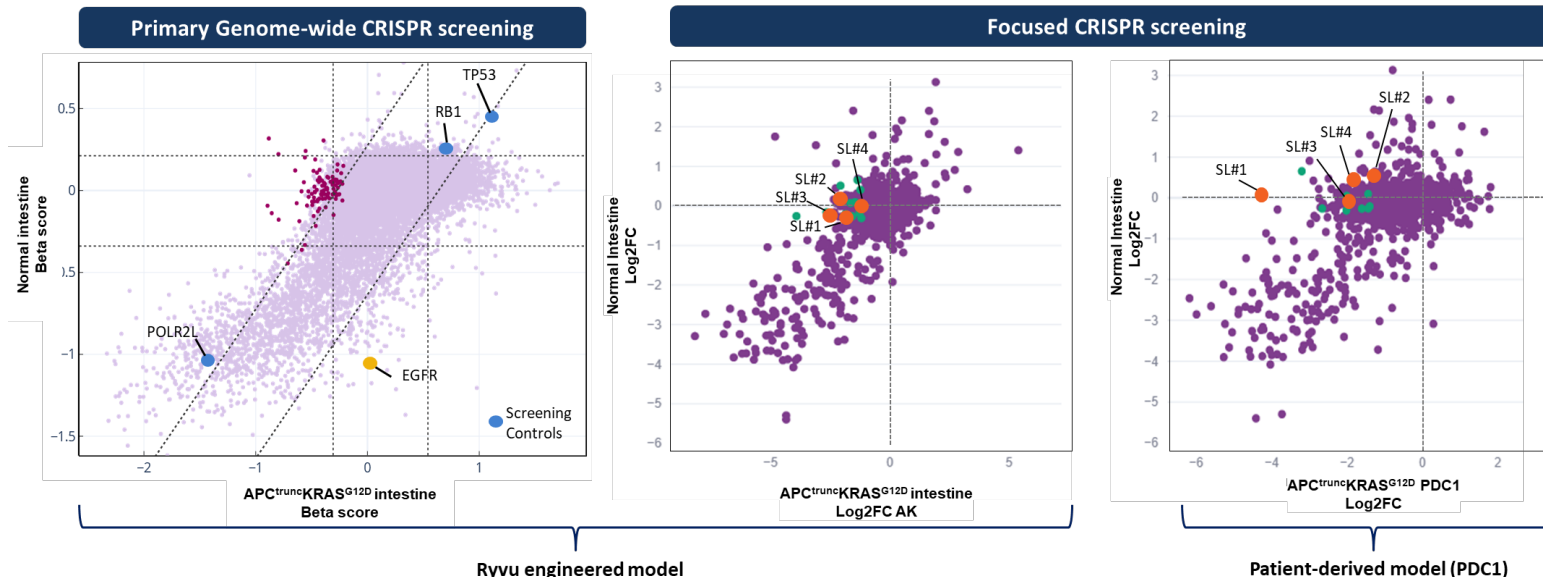
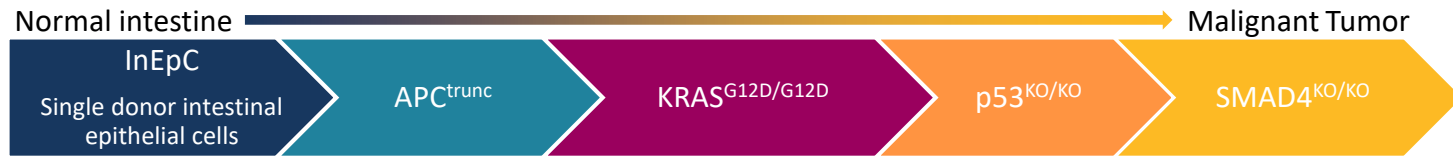


- The third most prevalent cancer worldwide
- Estimated number of colorectal cancers in the US for 2024 are 153,000 new cases¹
- Diagnosed usually at an advanced stage. Mortality still remains high. Five-year survival shown by SEER database is **around 65%**, the survival drops to **13%** at stage 4.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

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

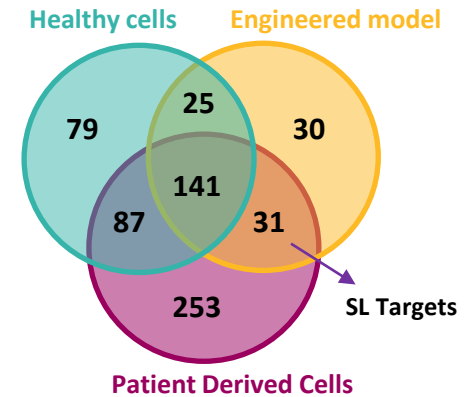


Based on East et al. 2017



Ryvu engineered model

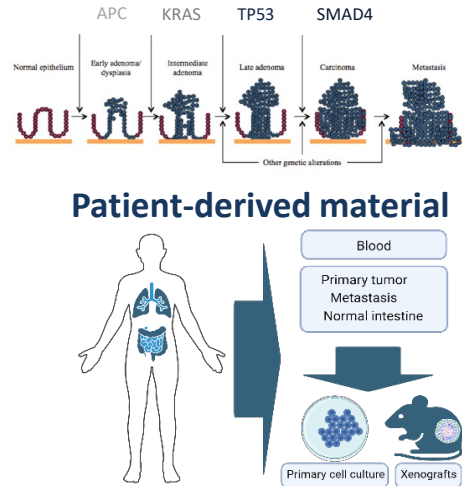
Patient-derived model (PDC1)



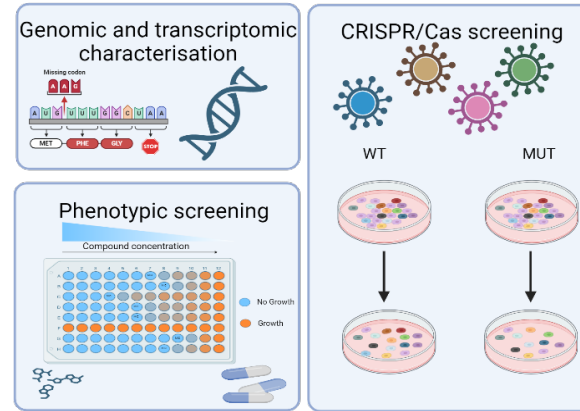
1) American Cancer Society

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



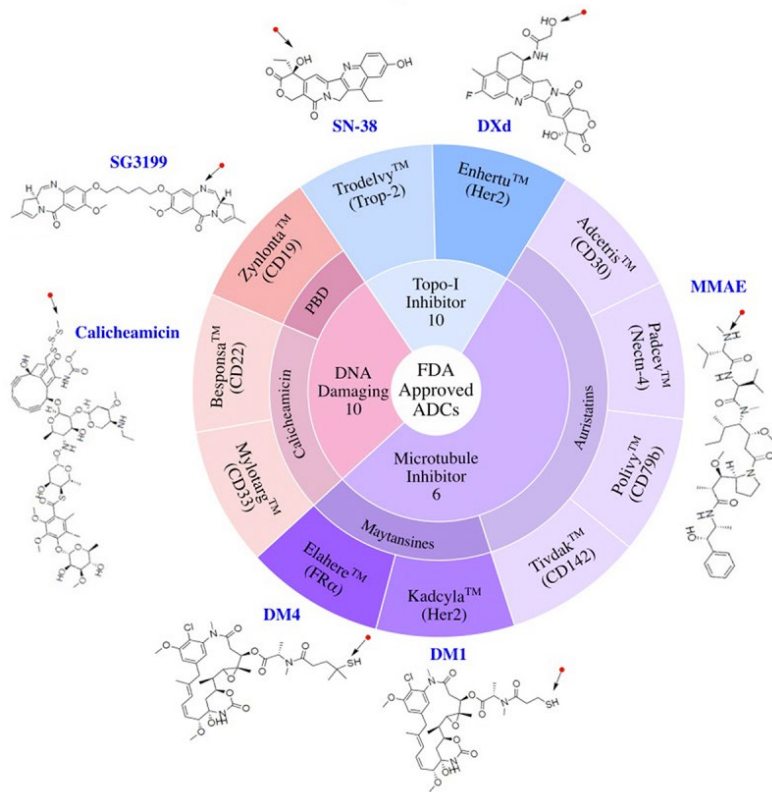
Ryvu Target Discovery platform has identified **several novel targets** for **KRAS-driven tumors**



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

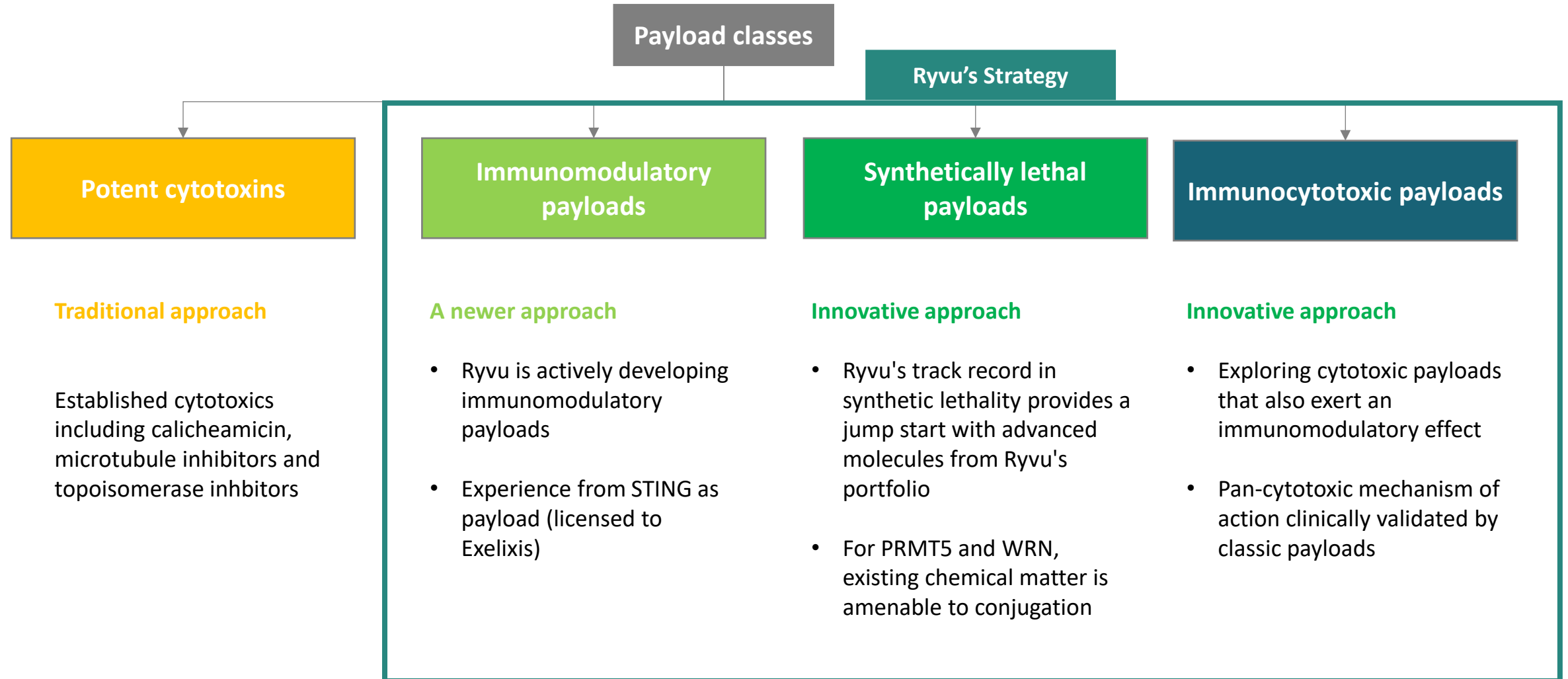


Maecker et al., MAbs, 2023.

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



Key Financial Terms

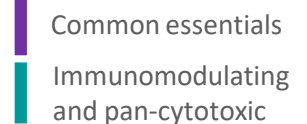
- Exclusive license agreement to combine Ryvu's small molecule STING agonists and STING biology know-how with Exelixis' antibody engineering, antibody-drug conjugate (ADC) technologies and drug development expertise
- Ryvu retains global rights for the development and commercialization of standalone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

- \$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	●	●	●	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

Corporate Progress



Financial Results: Q3 2024

\$ million	2023*	Q3 YTD 2023*	Q3 YTD 2024*
Revenues	16.3	11.9	18.6
<i>Partnering</i>	11.2	8.4	13.2
<i>Grants</i>	4.9	3.3	5.3
Total Costs**	37.6	27.4	38.2
<i>Clinical Pipeline</i>	13.0	6.4	17.4
<i>Early Pipeline</i>	15.8	13.9	14.2
<i>G&A</i>	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

Cash position
November 4, 2024

\$58.1M

Ryvu
Employees

>300

Employees
with PhD

~100

Partnering revenues in Q3 YTD 2024:

Exelixis (\$1.2 million), BioNTech (\$7.8 million recognized)

* 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

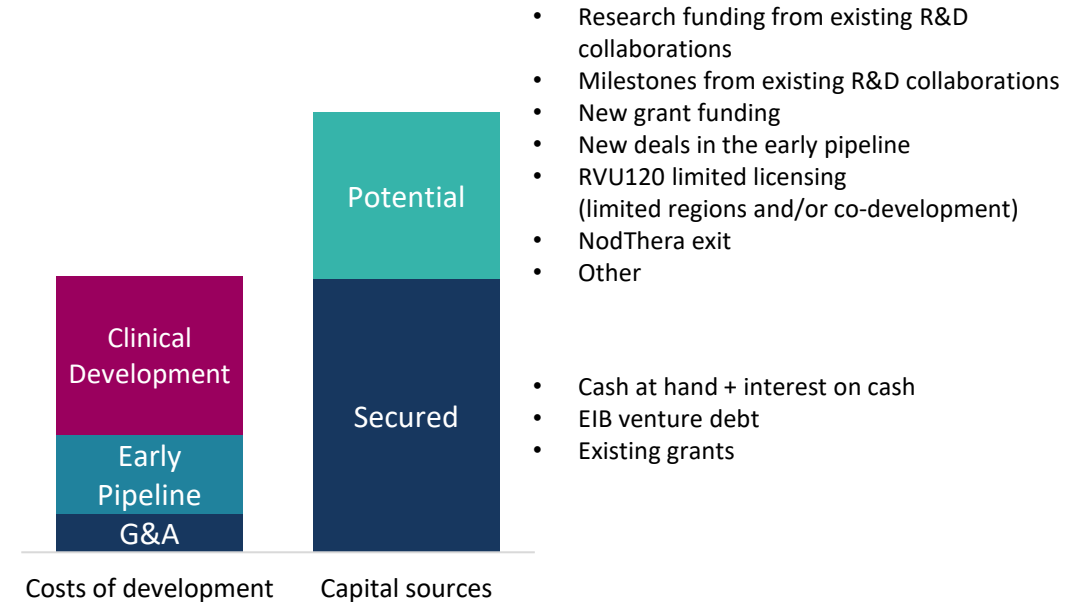
2025 KEY GOALS AND FINANCING

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**



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 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



Vladimira
Urbankova



Beata Szparaga-
Waśniewska



Krzysztof
Radojewski



Katarzyna
Kosiorek



Łukasz
Kosiarski



Bank Pekao
Biuro Maklerskie

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

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