



Developing therapeutics  
at the forefront of oncology

# Corporate Presentation

May 2025



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

## Clinical and Preclinical Candidate Pipeline

### RVU120

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

### Dapolsertib (MEN1703, SEL24)

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

### RVU305

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

## Novel Multi-Target Discovery

### ONCO Prime Platform

- Multiple novel precision oncology targets, including synthetic lethality

### Novel ADC Payloads

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

### Immuno-oncology

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



## FULLY INTEGRATED RESEARCH & DEVELOPMENT ORGANIZATION

- **LISTING**: WSE:RVU; cash runway to H2 2026
- **TEAM**: ~200 employees, including ~100 scientists (with ~60 PhDs)
- **SITE**: Fully-owned, state-of-the-art 108,000 sq ft facility



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



**Pawel Przewięźlikowski, MSc, MBA**  
CEO and Founder



**Krzysztof Brzózka, PhD, MBA**  
CSO



**Hendrik Nogai, MD**  
CMO



**Kamil Sitarz, PhD, MBA**  
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**Vatnak Vat-Ho, MBA**  
CBO



**Justyna Żółtek, MSc**  
CPO



**Jakub Janowski, MSc**  
General Counsel



**Bartłomiej Konicki, MSc**  
Financial Director






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# Broad pipeline addressing emerging targets in oncology

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

# RVU120:

## First-in-Class CDK8/19 Inhibitor in Hematologic 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)



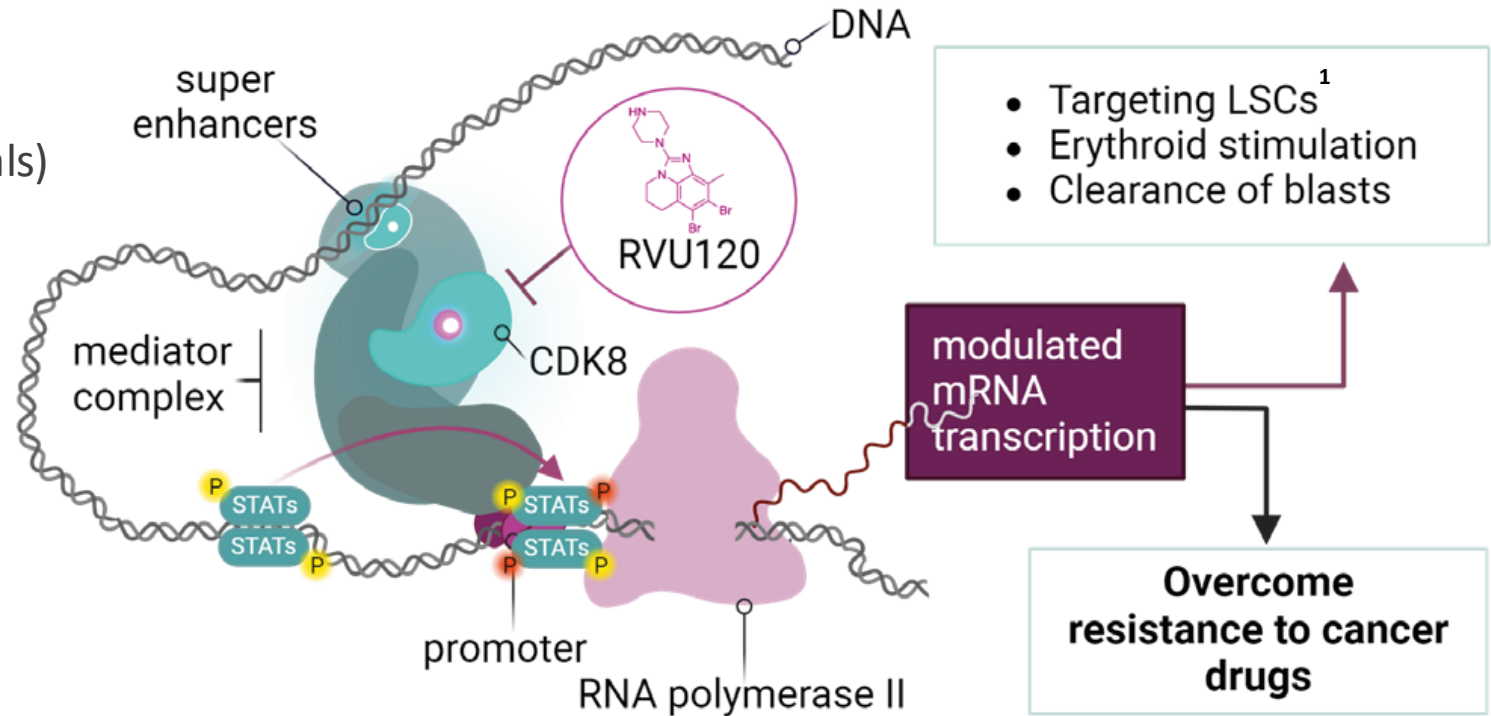
easy to formulate



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

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

## Solid Tumors

Medulloblastoma

ACC

Breast

Sarcoma

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

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

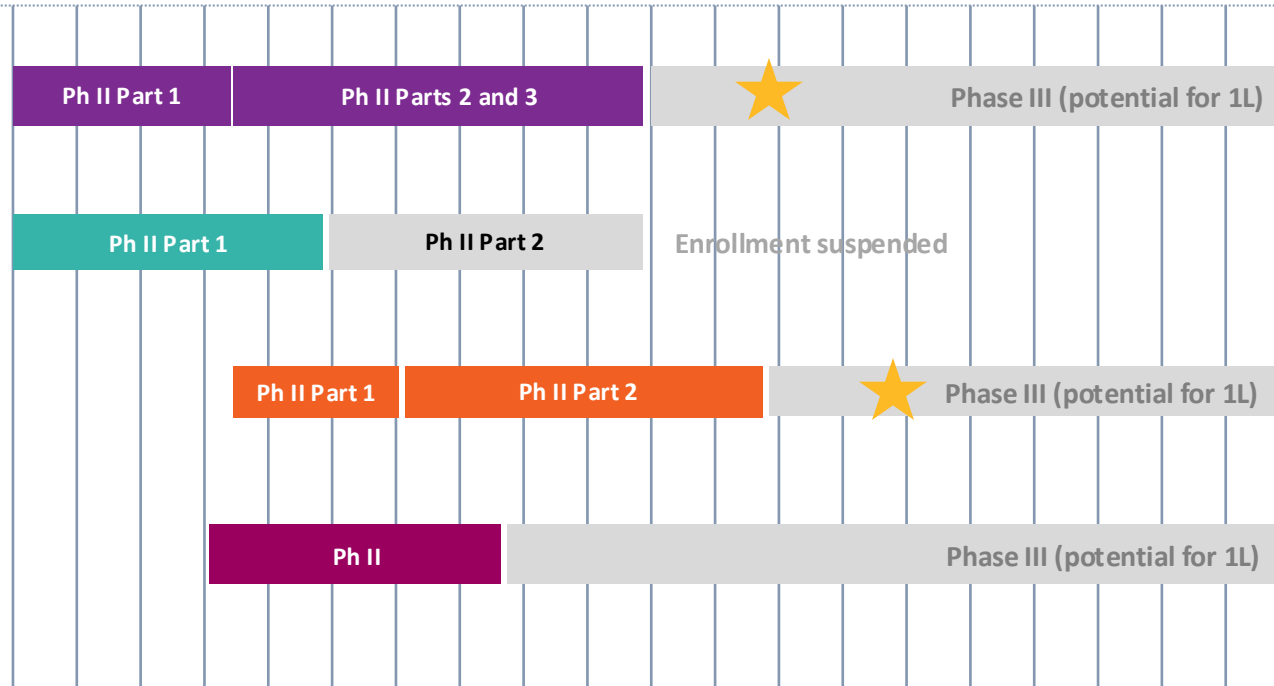


2024				2025				2026				2027				2028			
I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV

Beyond 2028

## Phase II studies in hematologic malignancies

- **RIVER-81:** AML, combination with venetoclax



★ Approval process  
in selected regions

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

## 15 of 30 evaluable patients showed clinical benefit across dose levels

### Clinical benefits

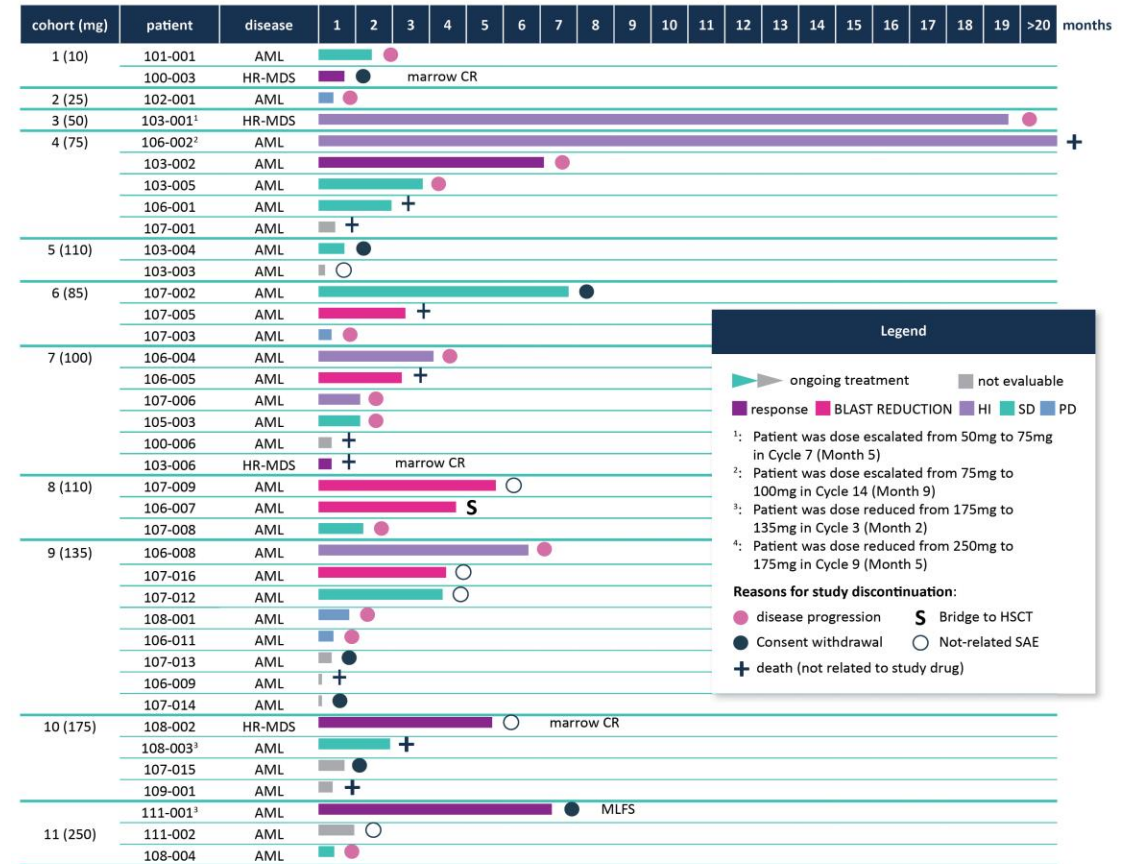
- 30 treated patients are evaluable for response (38 were treated in total)
- 9 patients achieved clinically significant BM blast reduction
  - (including 1 CR, 1 MLFS, 3 marrow CRs)
- 5 patients achieved erythroid hematological improvement (HI-E), 4 of those became transfusion-independent, of which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

### NPM1 and DNMT3A mutations

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

### HR-MDS

- 4 pts with HR-MDS treated were failing 1-5 prior lines of treatment
- 3 of these pts had >10 % blasts at baseline, all of them met the Cheson criterion of marrow CR during treatment with RVU120



### Favorable safety profile

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

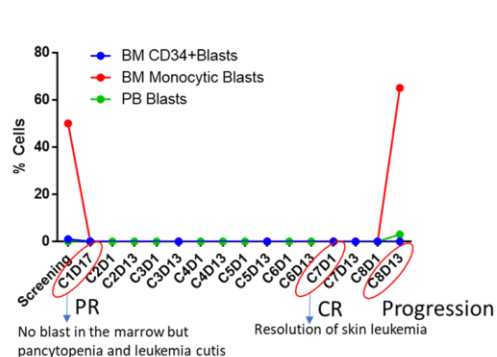
# Data generated in RIVER-51 study support further development of RVU120 in AML, LR-MDS and MF

## Significant blast reductions

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

### P103-002 AML

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



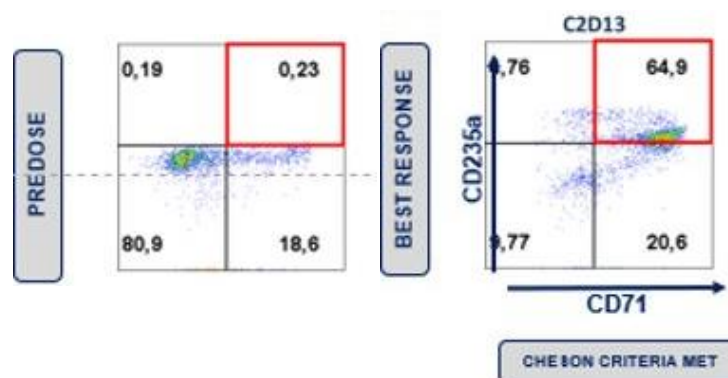
CR achieved end of C1 with persistent skin leukemia, resolved in C5

## 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



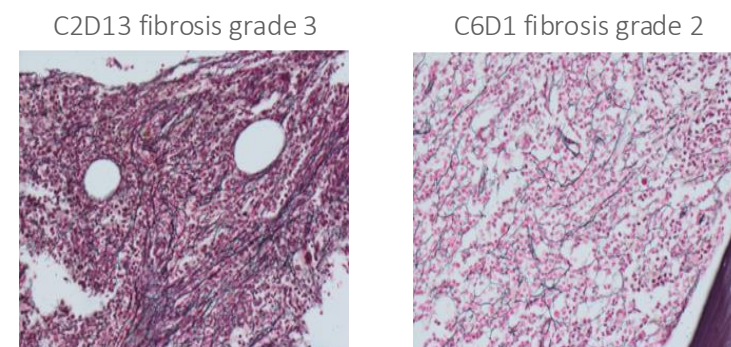
RBC-TI and Plt-TI on RVU120 treatment

## 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



Reduction of fibrosis grade and marrow CR

# RIVER-81

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

RVU120 +  
venetoclax

### STUDY DESIGN

- Primary endpoints:
  - Rate of CR, CRh, CRi, with and without MRD, and DoR
- Secondary endpoints: Transfusion independence, PFS, RFS, OS
- For Part 2: including PRO and HRQoL change from baseline
- Population: r/r ven-failed AML, no alternative treatments
- Estimated enrollment: **~35-97 patients<sup>(1)</sup>**
- Up to **50 clinical sites** planned globally



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

PART 1 (N = 17 pts)

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

PART 2 (N = ~39 pts)

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

PART 3 (N = ~41 pts)

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

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

## 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

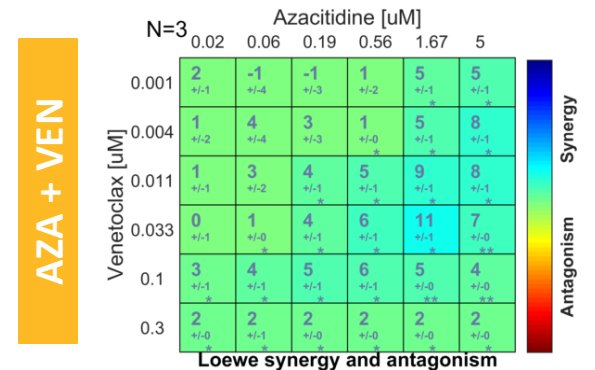
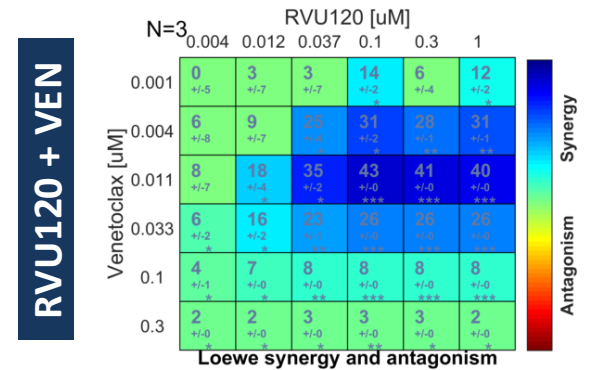
### • Remissions in Animal Studies:

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

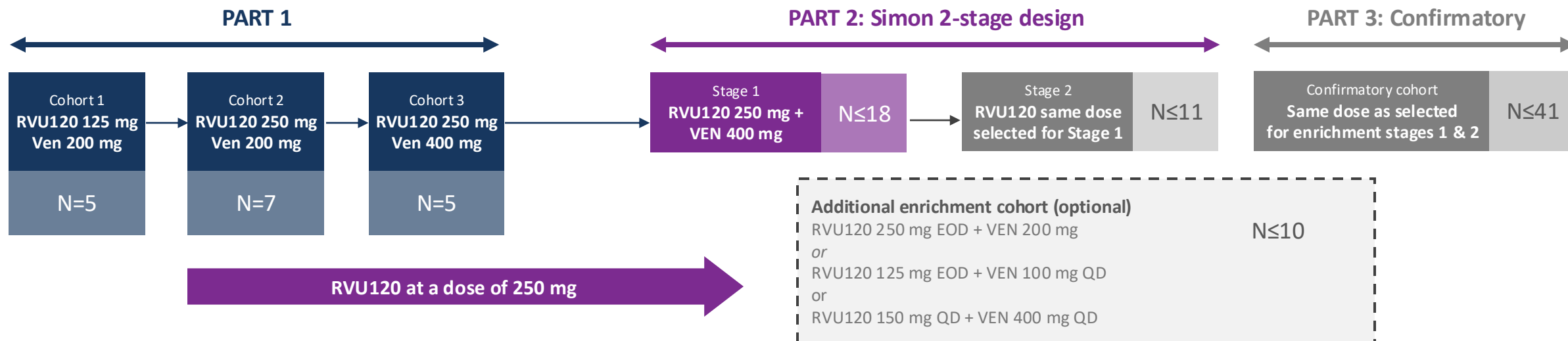
### • Mechanism of Synergy:

- 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



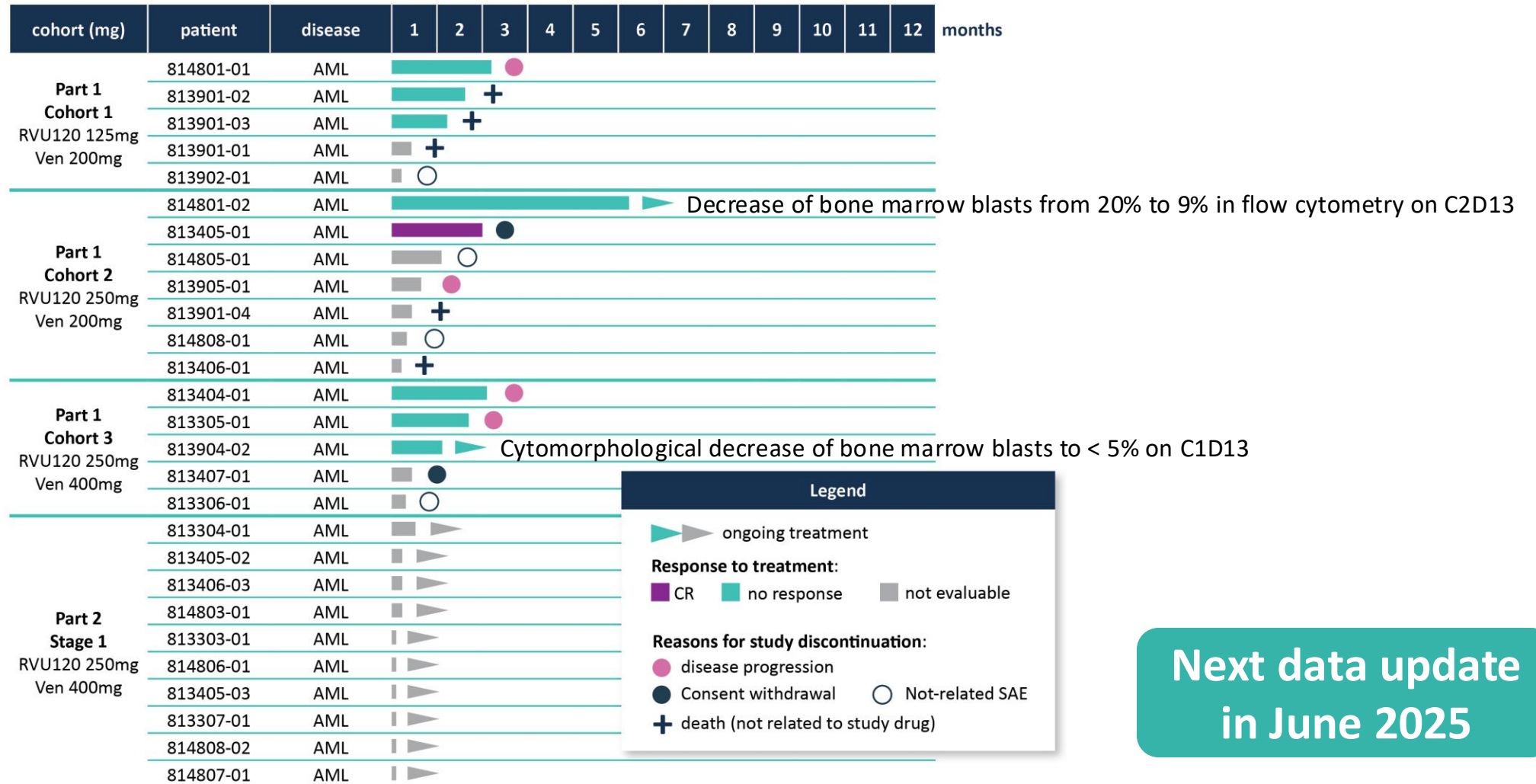
### STUDY PLAN



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

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

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



Next data update  
in June 2025

Data Cut-off: December 10, 2024  
Preliminary data



# POTAMI-61

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

### STUDY DESIGN

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

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

#### Part A (N = ~20 pts)

**Cohort 1**  
(Mono RUX-ineligible or RUX-failed)

**Cohort 2**  
(RUX add-on)

#### Part B (N = ~210 pts)

Expansion of Cohort 1 or 2

**Cohort 3**  
(Frontline)

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

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

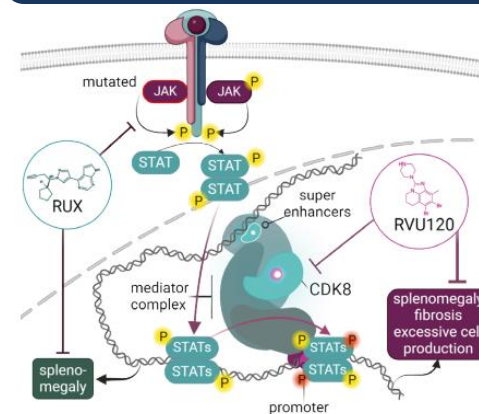
## Opportunity in myelofibrosis

- 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

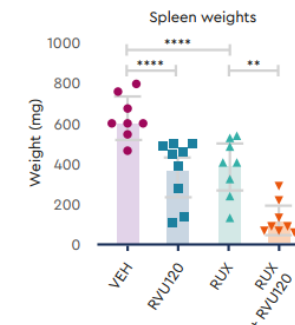
- CDK8 kinase is an important player in MPN pathogenesis, and RVU120 disrupts the downstream signaling events, mitigating MPN symptoms
- In preclinical studies, RVU120 effectively reduced splenomegaly, bone marrow fibrosis, and abnormal blood cell production. RVU120 has also demonstrated synergy in combination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



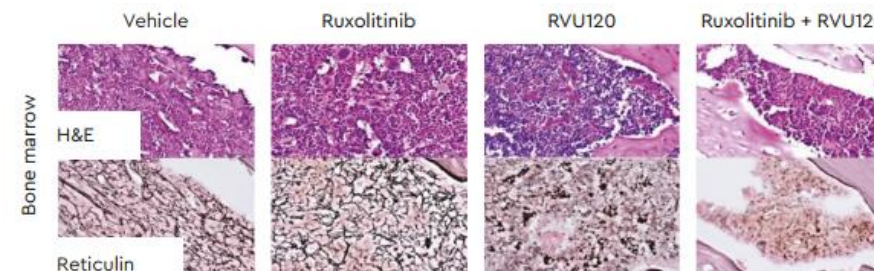
## RVU120 reduces splenomegaly

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

## PHASE II

### 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

### EXPLORATORY RVU120 AS A SINGLE AGENT

Patients failing available options

Enrollment of ~40 patients planned  
Ongoing assessment of Phase II data  
will drive further development

**First data update  
in December 2025**

### IIT

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

EMSCO  
MYELODYSPLASTIC  
SYNDROMES



#### Prof. Uwe Platzbecker

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

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

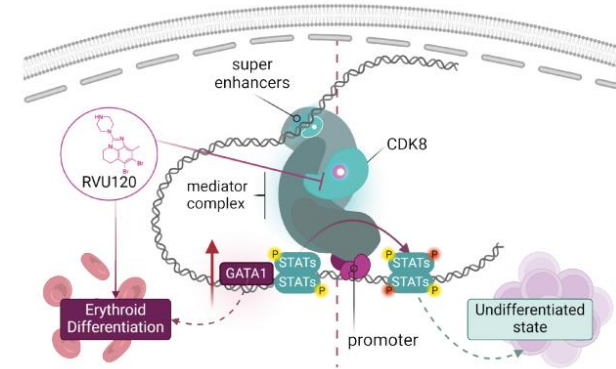
## Opportunity in LR-MDS

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

## RVU120 in LR-MDS

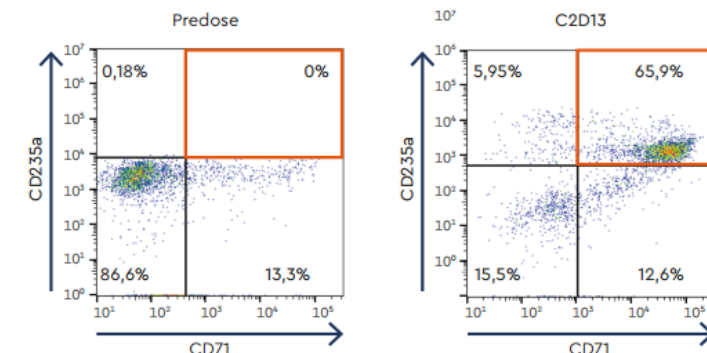
- MDS pathogenesis is influenced by gene expression alterations that hinder the maturation of hematopoietic cells.
- When aberrant stem cells from MDS patients are treated with RVU120, it triggers erythroid gene expression programs orchestrated by STAT5 and GATA1.
- Importantly, RVU120's activity does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

## Mechanism of RVU120 in LR-MDS



## Clinical evidence of erythropoiesis demonstrated with RVU120

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



## REMARK

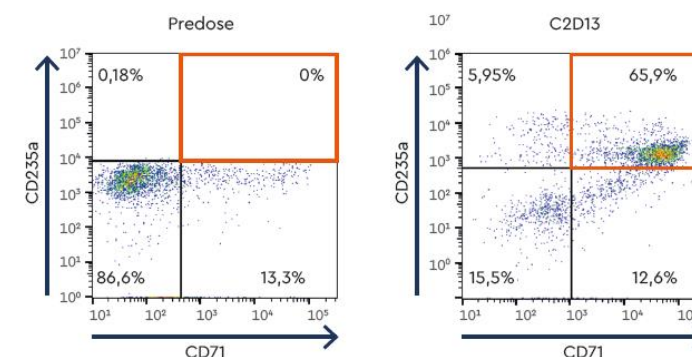
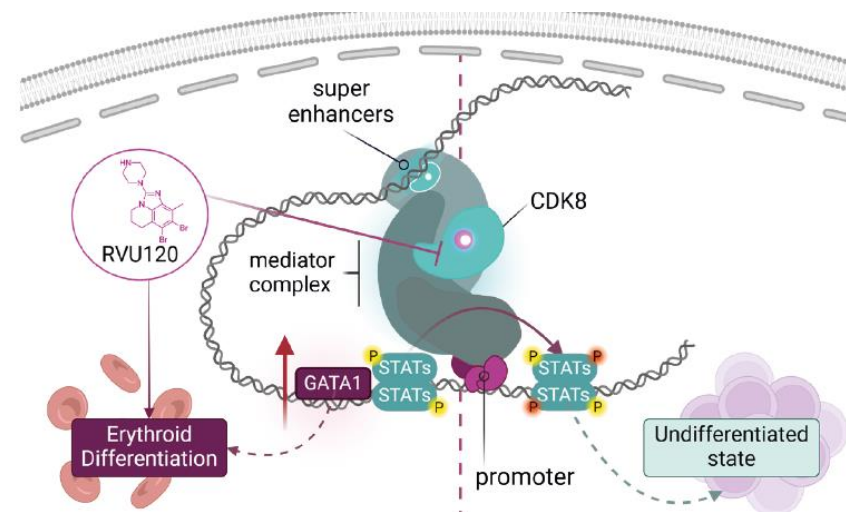
RVU120 has strong erythroid-stimulating activity in nonclinical anemia models and selected patients with AML/HR-MDS in Phase I (RIVER-51), providing the rationale for the Phase II clinical study in patients with LR-MDS

### Nonclinical rationale

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

### Related clinical observations

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



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

## 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

### PART 1 (N = ~40 pts)

#### Genetically defined and disease specific cohorts:

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

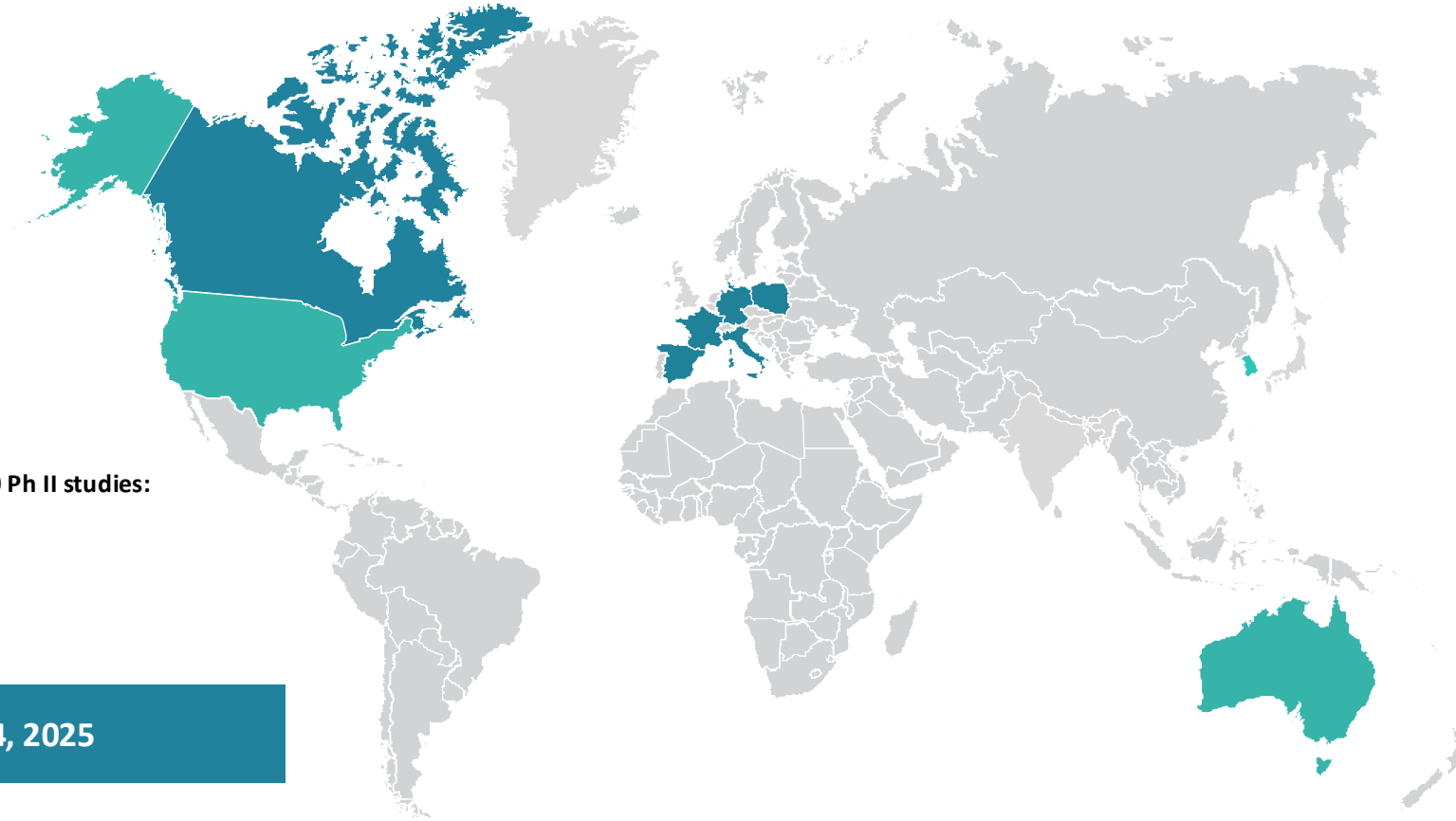
#### Clinical Benefit (CR/CRh/CRi/Hi) in any of the cohorts



### Part 2: Enrollment Suspended

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





Global site locations  
and patient population

Global CROs  
and clinical vendors

Regulatory authorities  
worldwide

Status as of February 24, 2025

Number of Ph II clinical  
trials initiated  
in 2024

4

Number of countries  
across studies

5

Number of activated  
clinical sites globally

110+

Number of patients  
enrolled

~120

Number of clinical vendors  
managed

20+

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

70+



**AML** (Acute Myeloid Leukemia)

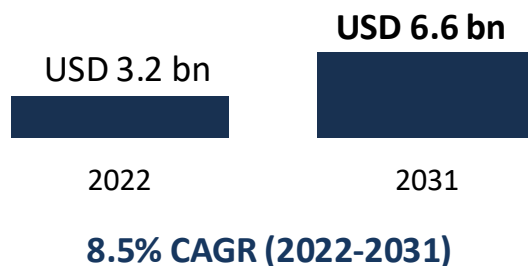
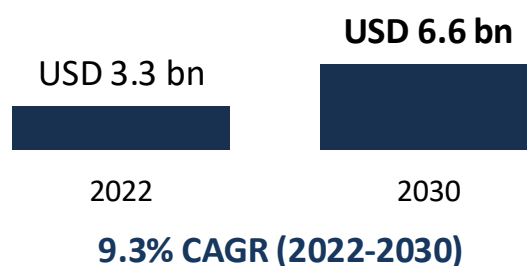
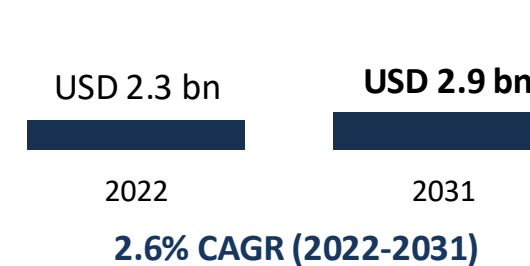
- The most common, highly aggressive type of acute leukemia occurring in adults; unfavorable outcomes for most patients<sup>(1)</sup>
- Annual incidence in the US at ~20,800 with an est. 11,220 deaths in the US in 2024<sup>(2)</sup>
- **Venclexta (venetoclax) sales estimated to exceed USD 3.5 bn in 2025<sup>(3)</sup>**
- **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<sup>(4)</sup>
- **Reblozyl (luspatercept) projected peak sales of USD 3.2 bn by 2029<sup>(5)</sup>**
- **Rytelo (imetelstat) projected peak sales of USD 1.2 bn<sup>(6)</sup>**

**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<sup>(7)</sup>
- **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<sup>(4)</sup>****Global MDS Market<sup>(4)</sup>****Global MF Market<sup>(7)</sup>**

## RVU120 program summary

### RIVER-81

#### Next data in June 2025

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

### POTAMI-61

#### Enrollment ongoing; initial data in June 2025

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

### REMARK

#### Enrollment ongoing; initial data in December 2025

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



### Accelerating enrollment across Phase II program

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



### Safety and efficacy as expected early in Phase II

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



### On track in 2025 for key data

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

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



## PARTNERSHIP AGREEMENT WITH MENARINI GROUP (2017)

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

## PROVEN SAFETY AND CLINICAL ACTIVITY

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

## DLBCL

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

## Future Opportunities

- Ongoing translational work supports potential development in other hematologic indications

## Partnership

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

**First patient in DLBCL dosed on March 26, 2025**

# Phase II in DLBCL



## DAPOLSERTIB PROFILE

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



## CLINICAL STUDIES TO DATE

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



## PHASE II in DLBCL

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

# RVU305: MTA-cooperative PRMT5 inhibitor

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



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

## RVU305/PRMT5i

### KEY RATIONALE and MOA

PRMT5 MTA-cooperative inhibitors exert synthetic lethal phenotype in MTAP deleted cells

### NOVELTY

Best-in-class potential: selectivity, potency, brain penetration and safety

### TOP TUMOR INDICATIONS

MTAP deletions, up to 15% of all cancers, one of the largest genetically-defined population: GBM, lung, pancreatic, DLBCL, bladder, esophageal

### STATUS

Complete IND-enabling studies in H2 2025

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

RVU305 demonstrates superior preclinical properties vs. competitors

Leading to a differentiated clinical strategy

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

Ongoing translational work will support the selection of

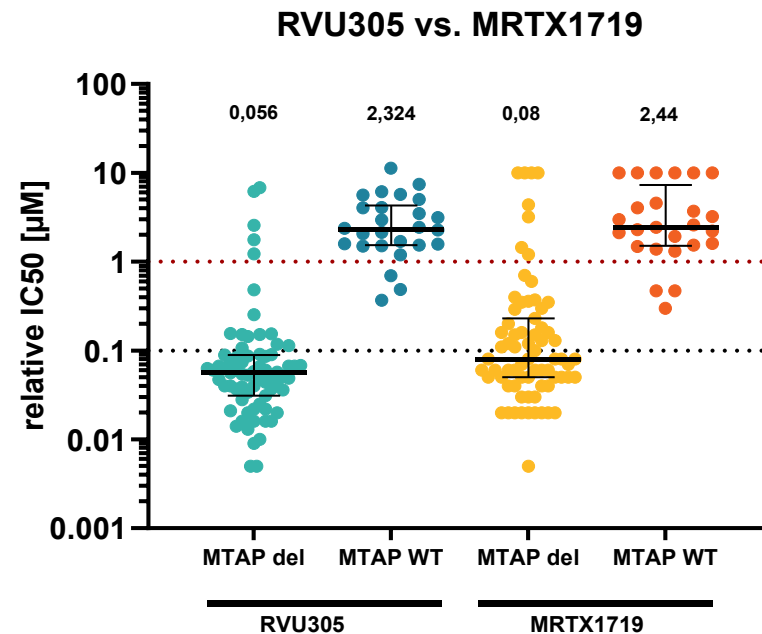
- Indications/tumors
- Drug combination partners
- Patient sub-populations



# RVU305 shows superiority in multiple cell lines

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

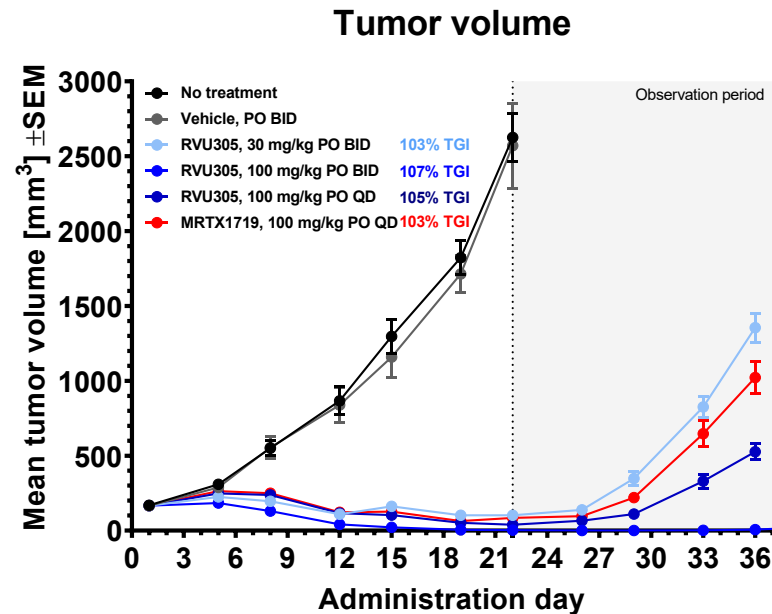
- Panel of MTAP-deleted and MTAP-wt cells was profiled with RVU305 in a 5-day CellTiter-Glo assay
- A differential response to Ryvu PRMT5 MTA-cooperative inhibitor is seen between cells with different MTAP status
- RVU305 shows higher potency than MRTX1719 (comparing to results published by Engstrom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



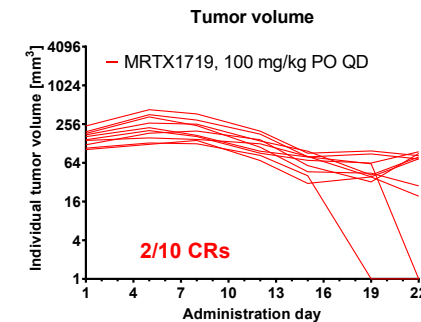
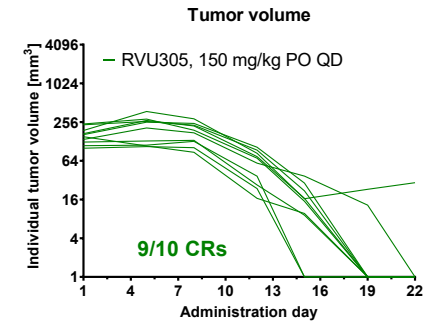
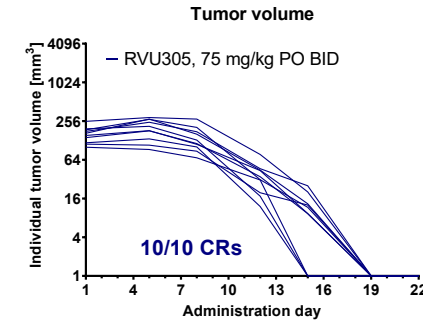
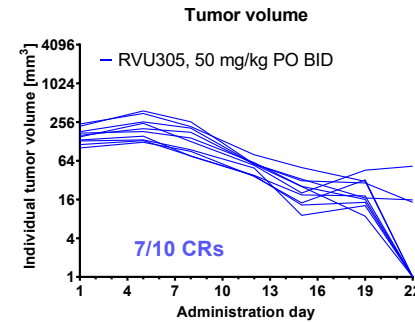
# RVU305 shows significant antitumor efficacy *in vivo*

## Strong antitumor efficacy

DoHH2 MTAP-deleted model (DLBCL)



## Complete responses demonstrated in vivo: favorable vs. MRTX1719

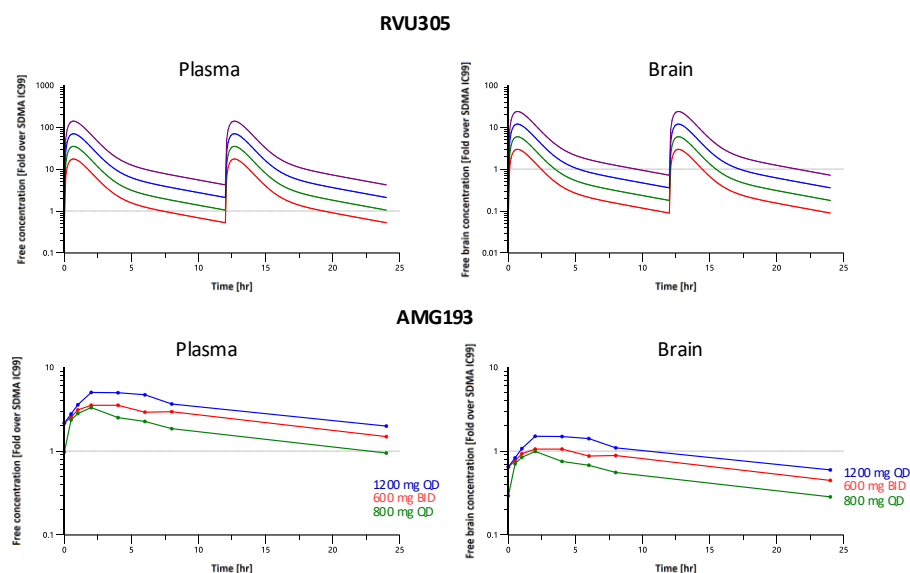


DoHH2 MTAP-deleted model. Individual tumor volumes in a log<sub>2</sub> scale from efficacy study in which RVU305 was administered orally (PO) once (QD) or twice (BID) daily, and MRTX1719 was administered PO QD to SCID mice bearing DoHH2 (DLBCL carcinoma) tumors (n=10 animals/group). Either no tumor growth (10 mg/kg BID) or tumor volume regression (other BID dose levels and QD administration) were present after RVU305 treatment.

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

RVU305 shows optimal systemic target coverage and excellent brain penetration

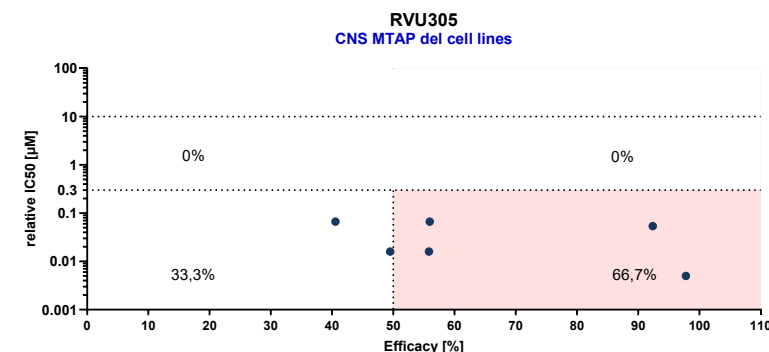
Predicted free RVU305 exposure in projected human escalation phases



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

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

RVU305 exhibits high potency and efficacy against CNS cell lines



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

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

# RVU305 has a potentially best-in-class profile



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

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

\* Viability in vitro in MTAP-del cell line model

^ Based on head-to-head comparison in cynomolgus brain PK experiment and simulations

# Based on Mirati data and Omniscreen panel, where 0.3uM (the level of response WT cells) was used as a cutoff for sensitivity

## Early pipeline

# Dual-pronged strategy with potential to generate multiple oncology medicines

## Novel precision oncology drug discovery platform

ONCO Prime

ADCs

## Next-generation novel ADC payloads

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



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

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



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

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



Leveraging Ryvu's internal competencies  
and ADC collaboration with Exelixis

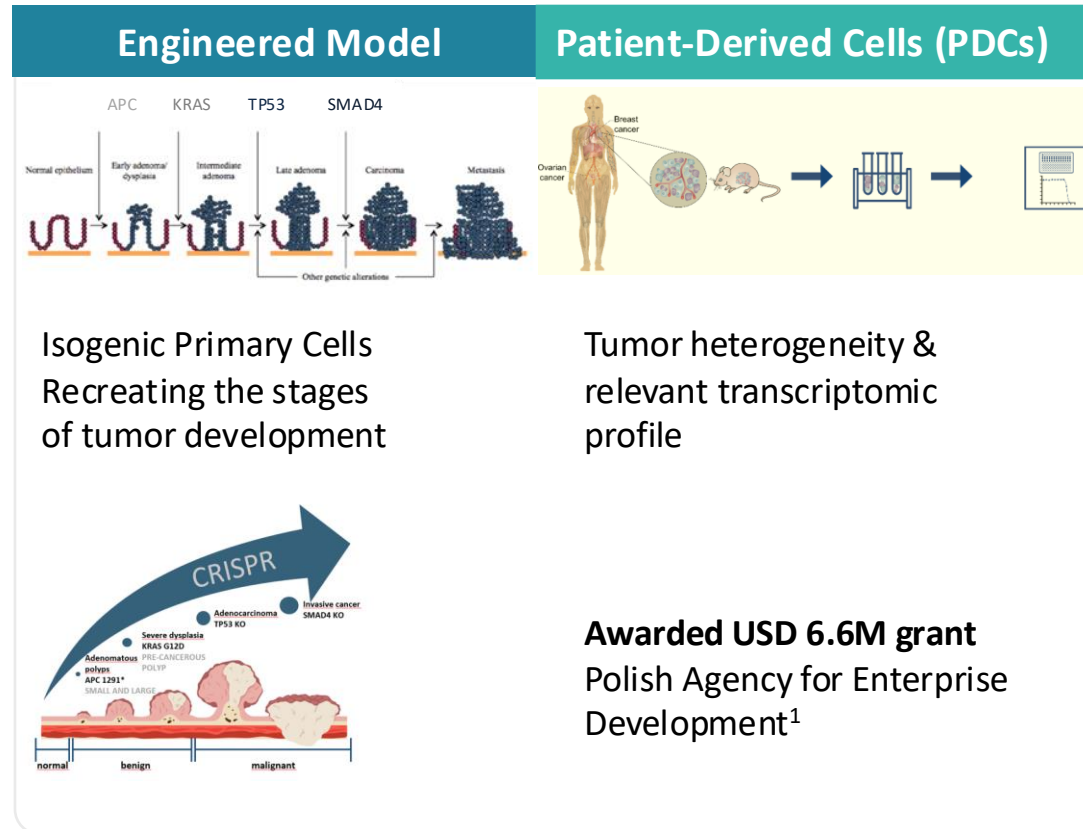
# ONCO Prime: Novel Precision Oncology

Multi-asset platform generating  
first-in-class therapeutics

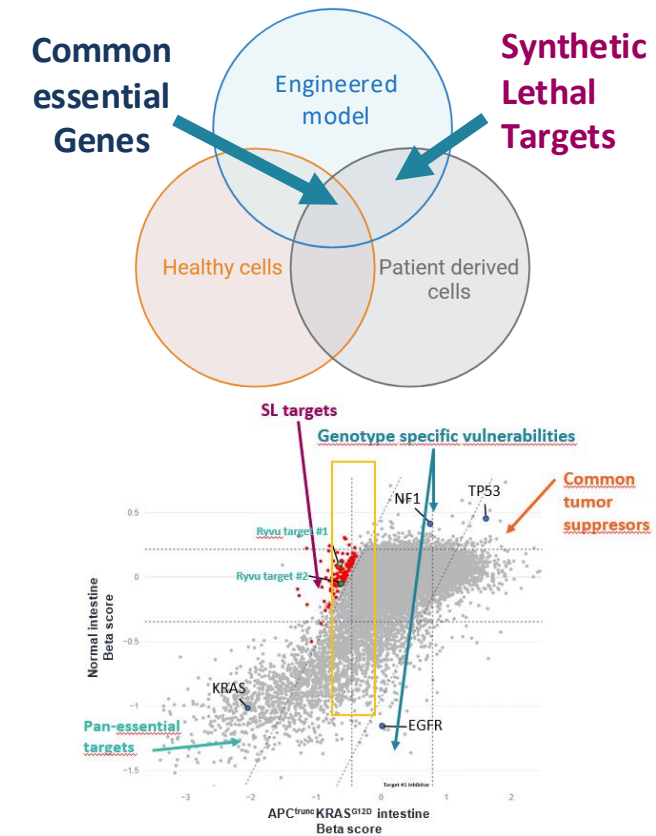


# Driving novel precision oncology drug discovery with Ryvu's ONCO Prime platform

## Ryvu's CRISPR-based target Discovery Platform



## Discovering Novel Precision Oncology Targets, including Synthetic Lethal Targets



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



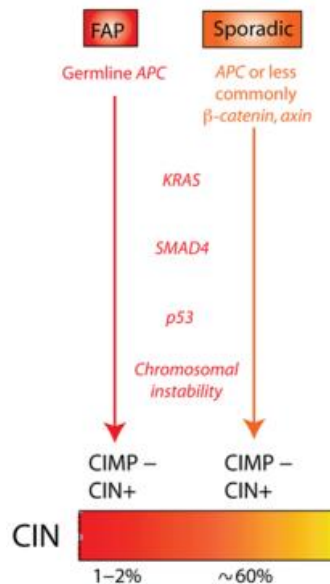
# Initial ONCO Prime data presented in CRC; broad applicability across oncology



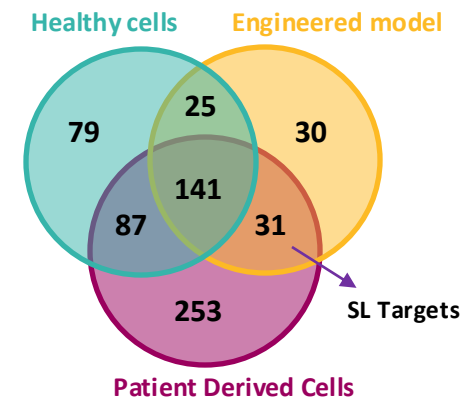
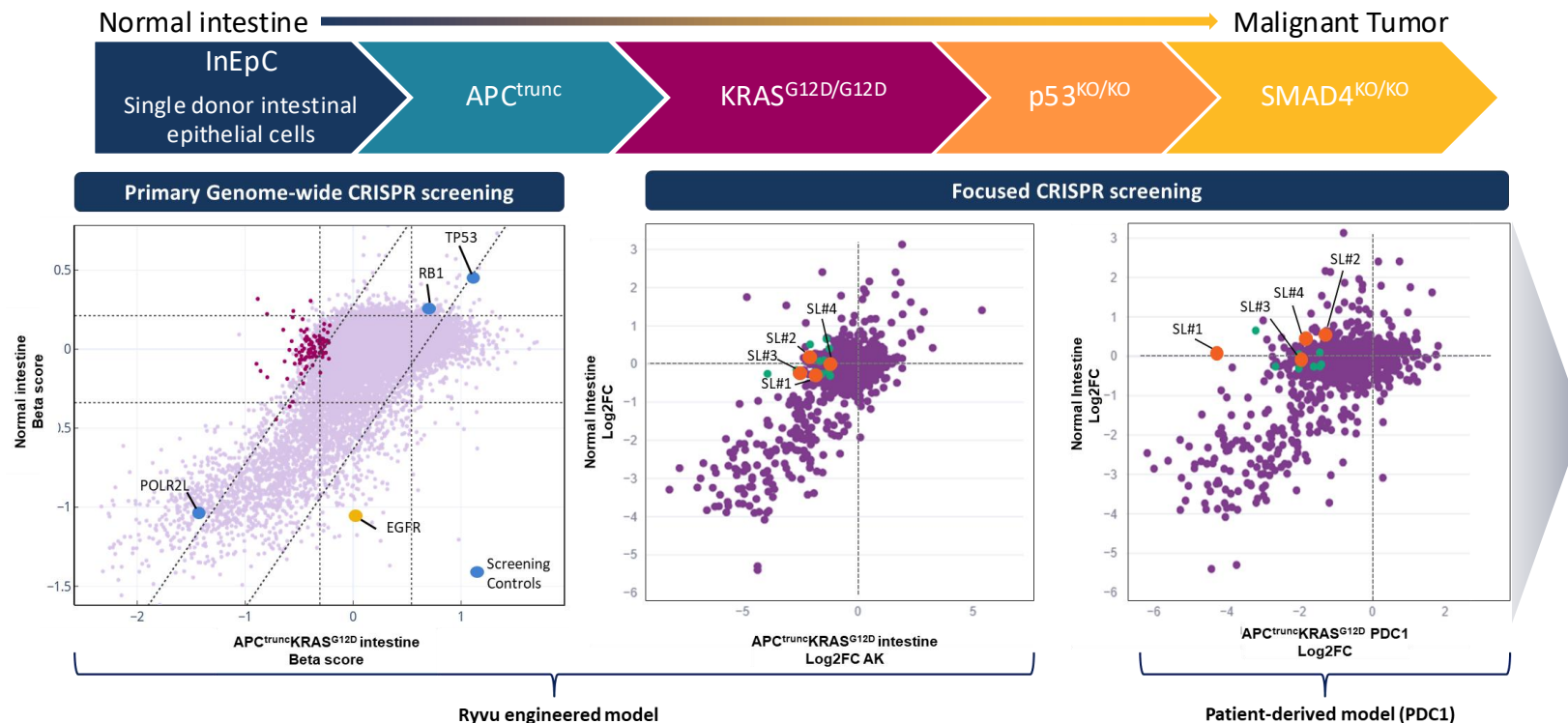
## CRC

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

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



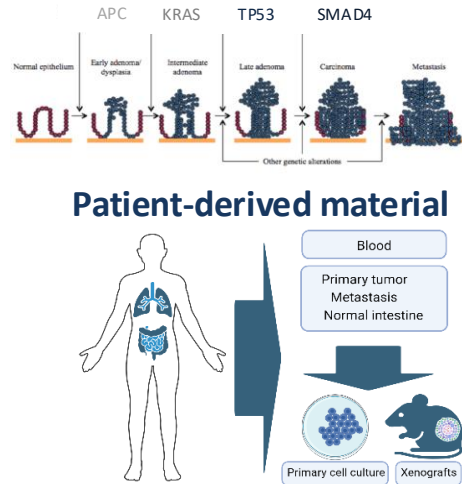
Based on East et al. 2017



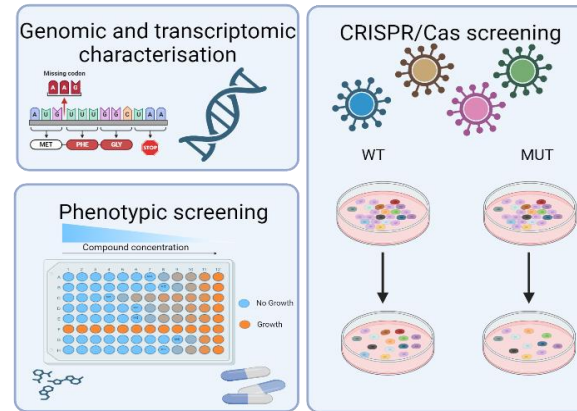
1) American Cancer Society

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

## Modeling cancer progression



## High Throughput Screenings



## Novel Targets & Treatments



Ryvu's OncoPrime platform has **broad potential to discover novel precision oncology targets, including synthetic lethal targets** across a variety of tumor types – initial case study data presented in colorectal cancer



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



Our approach allows exploring novel treatment strategies via phenotypic screening

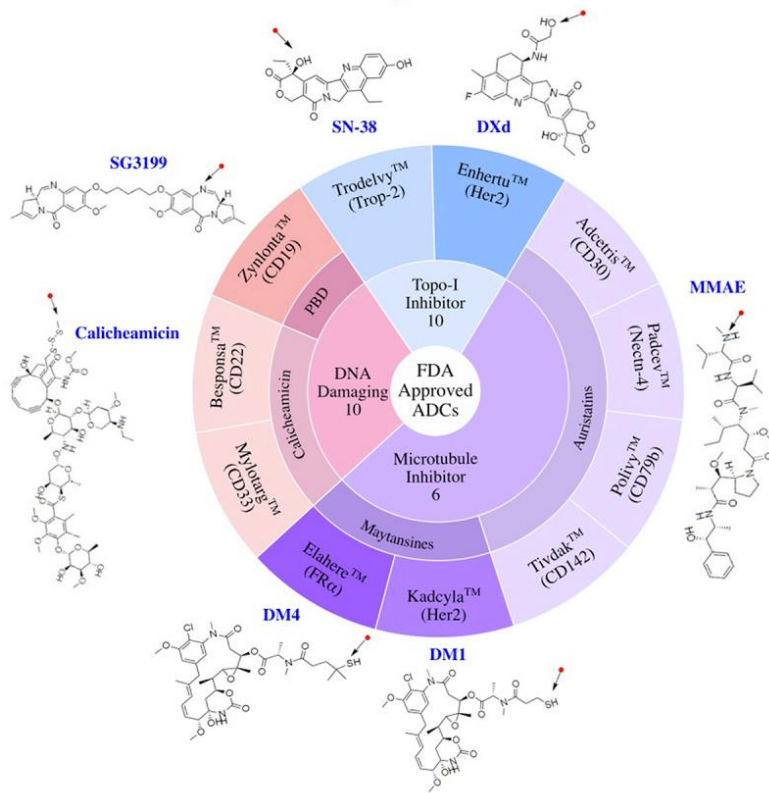
# ADCs with Novel Payloads

Generating multiple first-in-class therapeutics



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

## Approved ADCs use three main types of payloads

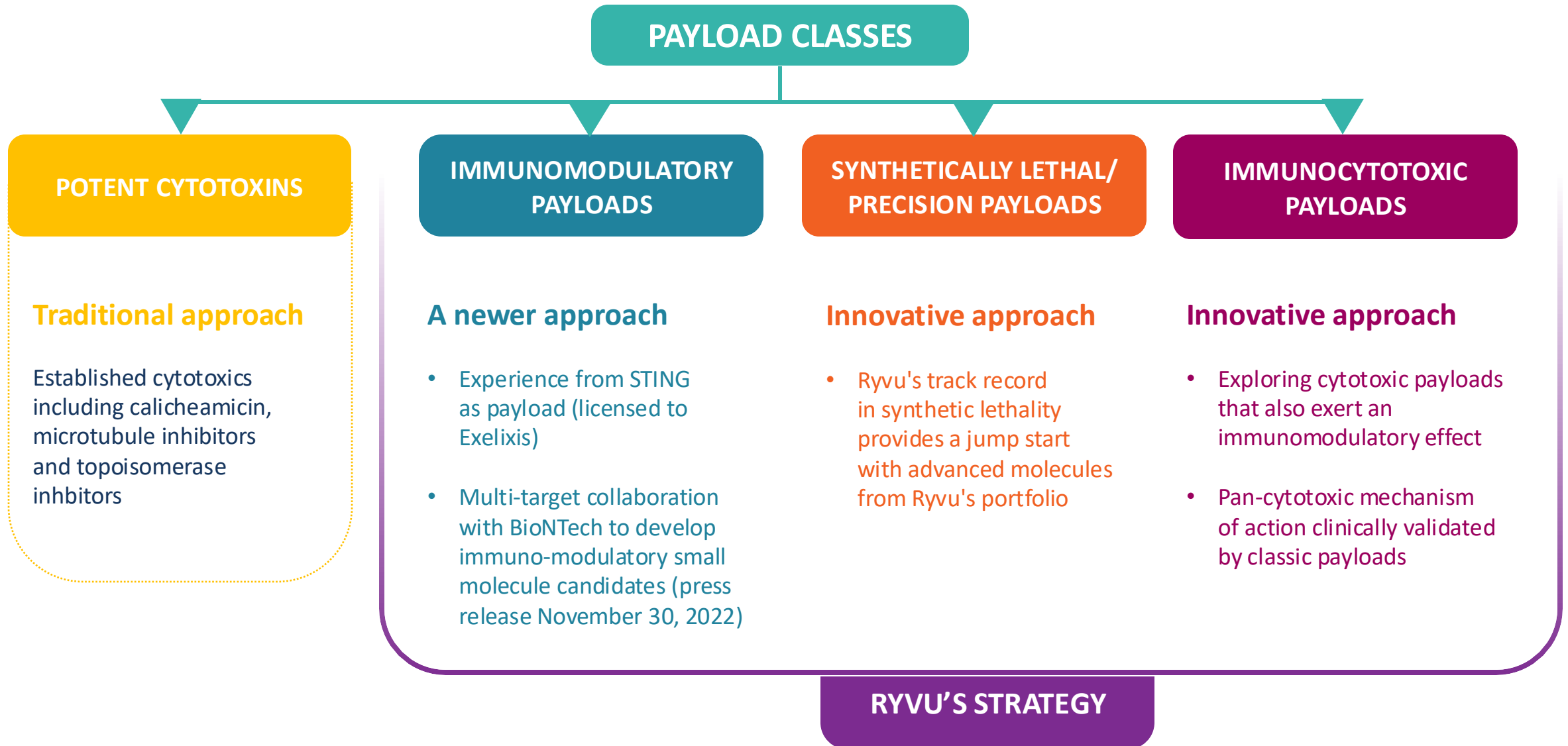


Maecker et al., MAbs, 2023.

## Novel payloads have the potential to improve on...

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

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



# 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



Common essentials  
Immunomodulating and pan-cytotoxic

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

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



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



## Partnership

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



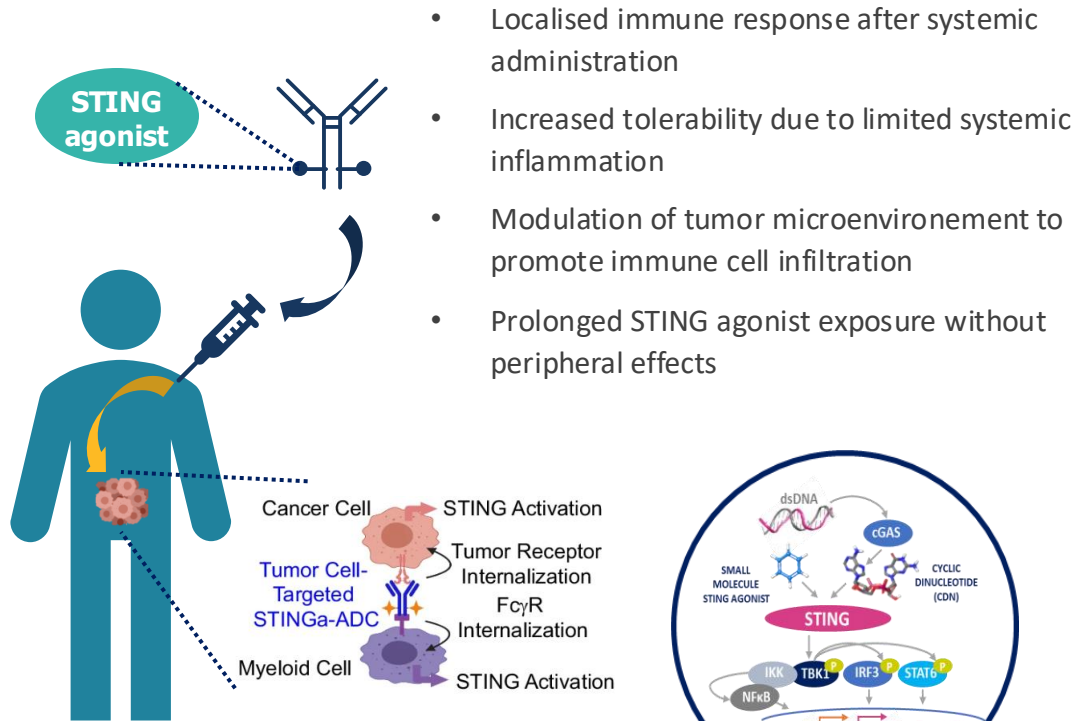
## Key Financial Terms

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



# STING activating Antibody-Drug Conjugates

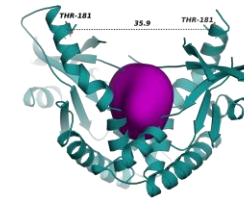
## STING activating Antibody-Drug Conjugates



**RYU**  
THERAPEUTICS

**EXELIXIS**<sup>®</sup>

- Proprietary STING agonist chemotype
- Small-molecule, non-CDN structures
- ADC-amenable
- Robust STING-specific activity in vitro and in vivo
- ADC development expertise
- Antibodies against cancer-relevant antigens
- Linker and conjugation technology



Antibody-  
drug  
conjugate



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

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

Largest-ever Ryvu deal: November 2022

BIONTECH

RYVU  
THERAPEUTICS



## Partnership



## Key Financial Terms

- Multi-target research collaboration: Ryvu is conducting discovery and research activities to develop multiple small molecule programs targeting immune modulation in cancer and potentially other disease areas based on targets selected by BioNTech; BioNTech will hold exclusive worldwide development and commercialization rights.
- Partnership revised in Q1 2025 to focus on earlier-stage projects
- Ryvu received €40 million from BioNTech, comprised of €20 million in upfront cash and a €20 million equity investment
- All R&D funded by BioNTech
- Ryvu is eligible for R&D and commercial milestones, and low single-digit royalties on product sales

# Corporate Progress



# Financial Results: Q1 YTD 2025

€ million	2024*	Q1 YTD 2024*	Q1 YTD 2025*
<b>Revenues</b>	<b>23.7</b>	<b>5.9</b>	<b>5.0</b>
<i>Partnering</i>	<i>18.1</i>	<i>5.0</i>	<i>4.0</i>
<i>Grants</i>	<i>5.6</i>	<i>0.9</i>	<i>1.0</i>
<b>Total Costs**</b>	<b>51.0</b>	<b>10.8</b>	<b>11.4</b>
<i>Clinical Pipeline</i>	<i>25.7</i>	<i>4.0</i>	<i>5.9</i>
<i>Early Pipeline</i>	<i>16.6</i>	<i>4.7</i>	<i>3.8</i>
<i>G&amp;A</i>	<i>8.7</i>	<i>2.1</i>	<i>1.7</i>
<b>EBIT**</b>	<b>-27.4</b>	<b>-4.9</b>	<b>-6.4</b>
<b>EBITDA**</b>	<b>-24.9</b>	<b>-4.3</b>	<b>-5.8</b>
<b>Net Results***</b>	<b>-24.9</b>	<b>-4.2</b>	<b>-5.8</b>

Partnering revenues in Q1 2025:  
BioNTech (€2.7M)

Cash position as of May 19, 2025

**€37.6M (PLN 161.1M)**

In addition, the company has secured approximately €19.8M (PLN 84.8M) in non-dilutive grant funding.

Ryvü  
Employees

~200

Employees  
with PhD

~60

\* Recalculated from PLN using 4.3042 PLN/EUR, 4.3211 PLN/EUR and 4.1848 PLN/EUR – for 2024, Q1 YTD 2024 and Q1 YTD 2025, respectively

\*\* Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of €1.0m, €0.3m and €0.2m in 2024, Q1 YTD 2024 and Q1 YTD 2025 respectively) and valuation of NodThera (+€0.0m (increase of costs), +€0.0m (increase of costs) and +€2.4 (increase of costs) in 2024, Q1 YTD 2024 and Q1 YTD 2025 respectively)

\*\*\* Excluding the impact of the non-dilutive, cash-neutral Employee Incentive Scheme (of €1.0m, €0.3m and €0.2m, in 2024, Q1 YTD 2024 and Q1 YTD 2025 respectively)

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

## 2025 / KEY GOALS AND FINANCING

### PIPELINE

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

### BUSINESS

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

## RVU120 PROGRESS SUMMARY

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

## 2025 / KEY ANTICIPATED EVENTS

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

## STRONG CASH POSITION WITH MULTIPLE POTENTIAL INFLOWS

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

# Ryvu equity summary

<b>IPO on WSE</b>	Nov 2014
<b>Corporate Split: Selvita and Ryvu</b>	Oct 2019
<b>Ticker: WSE</b>	RVU
<b>52-Week Range<sup>1</sup></b>	PLN 17.62 – 55.80
<b>Average Daily Volume<sup>1</sup></b>	115,212
<b>Market cap<sup>1</sup></b>	PLN 753M (EUR 177M)
<b>Shares outstanding</b>	23.1 M
<b>Cash<sup>2</sup></b>	EUR 37.6M

## Analyst Coverage



Vladimira  
Urbankova



Beata Szparaga-  
Waśniewska



Krzysztof  
Radojewski



Katarzyna  
Kosiorek



Łukasz  
Kosiarski



Tomasz  
Krukowski

## Top Holders<sup>3</sup>

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

1. As of 22 May, 2025   2. As of 19 May 2025   3. From stooq.pl as of May 6, 2025.

# Thank you

**CONTACT DATA:**

**Ryvu Therapeutics S.A.**

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