RYVU THERAPEUTICS

Targeted therapeutics
at the forefront of oncology

CORPORATE PRESENTATION

September 2020

Note on the presentation and forward looking statements

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Ryvu at a glance

Developing small molecule therapies which address high value emerging targets and pathways in oncology

- Diverse pipeline with mechanisms of action spanning kinase inhibition, RNA transcription, synthetic lethality (SMARCA2, WRN, MTAPdel cancers) and immuno-oncology (A2A/A2B, STING, HPK1)
- Initial focus of pipeline on hematological malignancies, with near term expansion planned in solid tumors

Wholly owned, first-in-class, selective oral CDK8/19 inhibitor (SEL120) with therapeutic potential in multiple indications and clinical data in 2021 in Phase Ib study

- Applicable across indications: acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), hematological and solid tumors
- Trial in lead indication (AML/MDS) enrolling across 6 sites in USA with first data available in early 2021

First-in-class dual PIM/FLT3 kinase inhibitor (SEL24) for Acute Myeloid Leukemia (AML) in Phase II - partnered with Menarini

- Dual-targeting of PIM and FLT3 designed to facilitate broader activity and potentially more durable responses
- Single agent efficacy shown in relapsed/refractory AML patients with acceptable safety profile demonstrated in Phase I

Broad early-stage pipeline delivering potential near-term clinical candidates and robust internal drug discovery engine

- Significant pipeline momentum with 2 programs expected to enter the clinic in 2021 (A2A/A2B, STING) and 2 near-term preclinical or late discovery targets (HPK1, SMARCA2)
- Deep discovery capability and track-record in generating clinical candidates; validated by partnerships including Galapagos research collaboration

Listed on Warsaw Stock Exchange, market cap of $276m[1]

- One of the largest drug discovery companies in the region, headquartered in Kraków, Poland
- ~$44m cash position[2] and significant non-dilutive grant funding (>$26m secured till 2023)

1 28 September 2020. Exchange rate (NBP): 1 $ =3.74PLN
2 10 September 2020

Broad pipeline addressing emerging targets in oncology

CLINICAL PROJECTS

PROGRAM / TARGET NAME	INDICATION	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PARTNER	ANTICIPATED MILESTONES
SEL24/MEN1703 PIM/FLT3	AML					MENARINI	Phase I data EHA June 2020
SEL120 CDK8/19	AML/MDS					LEUKEMIA & LYMPHOMA SOCIETY	Phase I data H1 2021
	SOLID TUMORS						Intiation of Phase I 2021

DISCOVERY & PRECLINICAL PROJECTS

PROGRAM / TARGET NAME	INDICATION	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PARTNER	ANTICIPATED MILESTONES
IMMUNO-ONCOLOGY							
A2A/A2B	SOLID TUMORS						IND filing 2021
STING	SOLID TUMORS						IND filing 2021
HPK1	SOLID TUMORS						Pre-clinical candidate 2021
SYNTHETIC LETHALITY							
SMARCA2	SOLID TUMORS						
MTAP DELETIONS	SOLID TUMORS						
WRN	SOLID TUMORS						
DISCOVERY COLLABORATIONS						Galápagos MERCK	

Strong momentum from 2019 and 2020'YTD

SEPTEMBER	2019	First patient dosed with SEL120
OCTOBER		Corporate split between Ryvu Therapeutics and Selvita (CRO) completed, >$100M incremental value created for Ryvu shareholders
MARCH	2020	SEL24 – successfully completed Phase I in acute myeloid leukemia patients
MARCH		SEL120 – orphan drug designation in AML by FDA
MARCH		SEL24 – FDA approval for the initiation of Phase II
APRIL		Collaboration with Galapagos in inflammatory disorders announced
JUNE		Ryvu spin-out company NodThera raises $55 M Series B funding
JUNE		Clinical posters at EHA 2020 - SEL24 Phase I data, SEL120 trial in progress
JUNE		Data updates from SEL120 and multiple pre-clinical programs (STING, SMARCA, HPK1, A2A/A2B) presented at AACR Conference
JULY		Completed construction and move into a new fully-owned $20M research center in Krakow
JULY		PLN 143M ($39 M) raised in a follow-on public offering
AUGUST		Filed CTA for SEL120 Phase 1 study in Europe

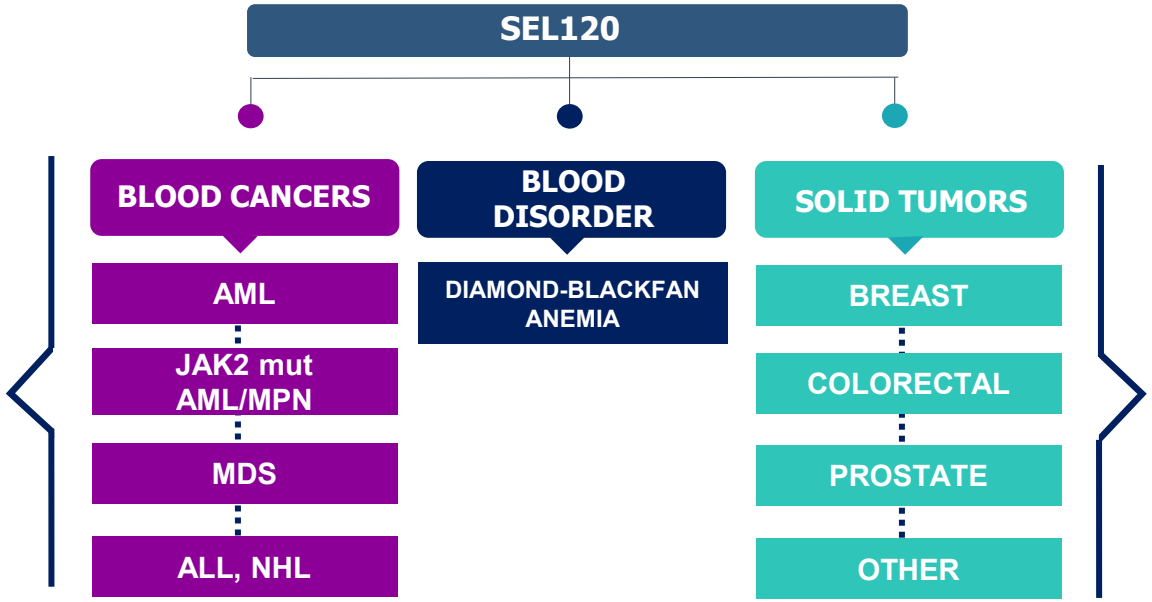
SEL120: Highly selective first-in-class CDK8/CDK19 inhibitor with broad potential in hematological malignancies and solid tumors

FDA | Orphan drug designation in AML in 2020

LEUKEMIA & LYMPHOMA SOCIETY | Therapy Acceleration Program (TAP) grant support
Total funding - $3.25 M

New treatment options in hematological disorders

- Direct cytotoxicity (induction of apoptosis)
- Eradication of Leukemic Stem Cells (LSC) known to be responsible for tumor relapse in AML
- Preclinical data indicate safe and synergistic combination with standard-of-care chemotherapy and approved targeted therapies
- Opportunity in another orphan indication (Diamond-Blackfan anemia)



Emerging therapeutic opportunities in solid cancers

- Precise, targeted mode of action by transcriptional regulation of cancer-dependent genes
- Preclinical data to support broad potential in multiple solid tumors with unmet medical needs
- Modulation of immune cell activity (NK cells) as additional component of anticancer activity

First therapeutic area of Ryvu focus: acute myeloid leukemia

Most common, highly aggressive type of acute leukemia in adults with poor outcomes in most patients[1]

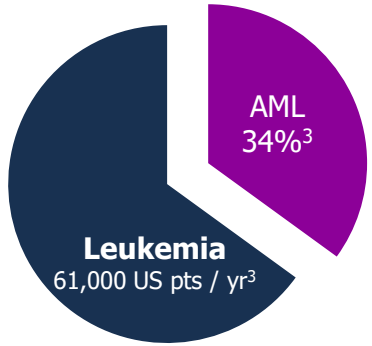
~20,000 new cases diagnosed
and >11,000 deaths in the US in 2018[2]

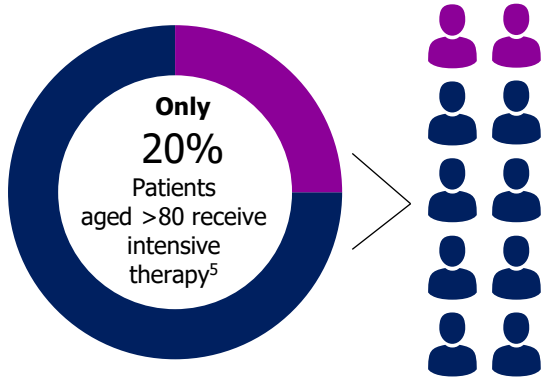
AML makes up 1% of all cancers
and 34% of all adult leukemia cases[2,3]

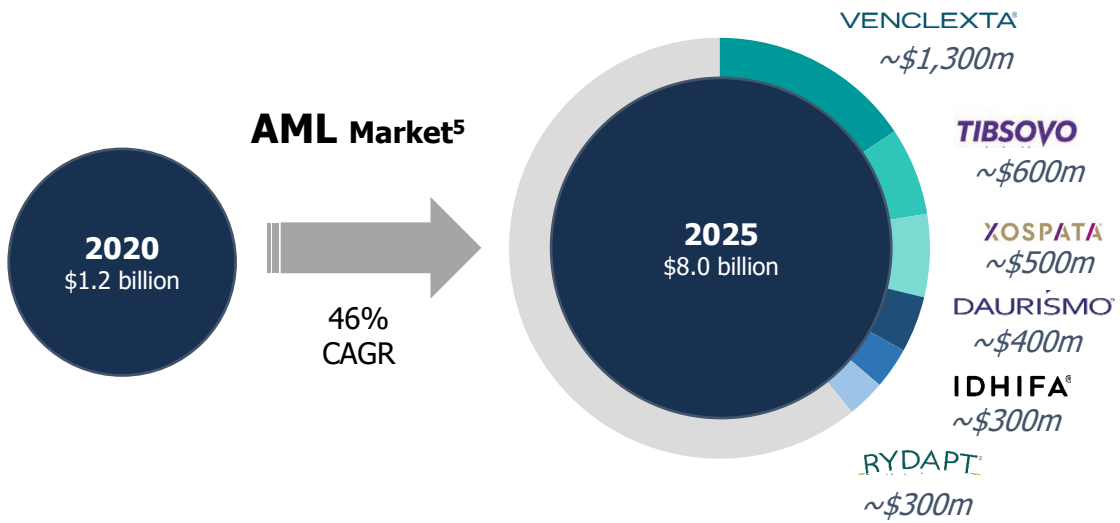
Occurs in a predominantly elderly, frail patient population;
75% of patients diagnosed with AML were aged >60 years[4]

Lowest survival among all blood cancers;
only 26% patients surviving 5 years after diagnosis

30% AML patients with a ITD mutation in the FLT3 gene have a less favorable prognosis, 70% of patients refractory to current inhibitors targeting FLT3 mut

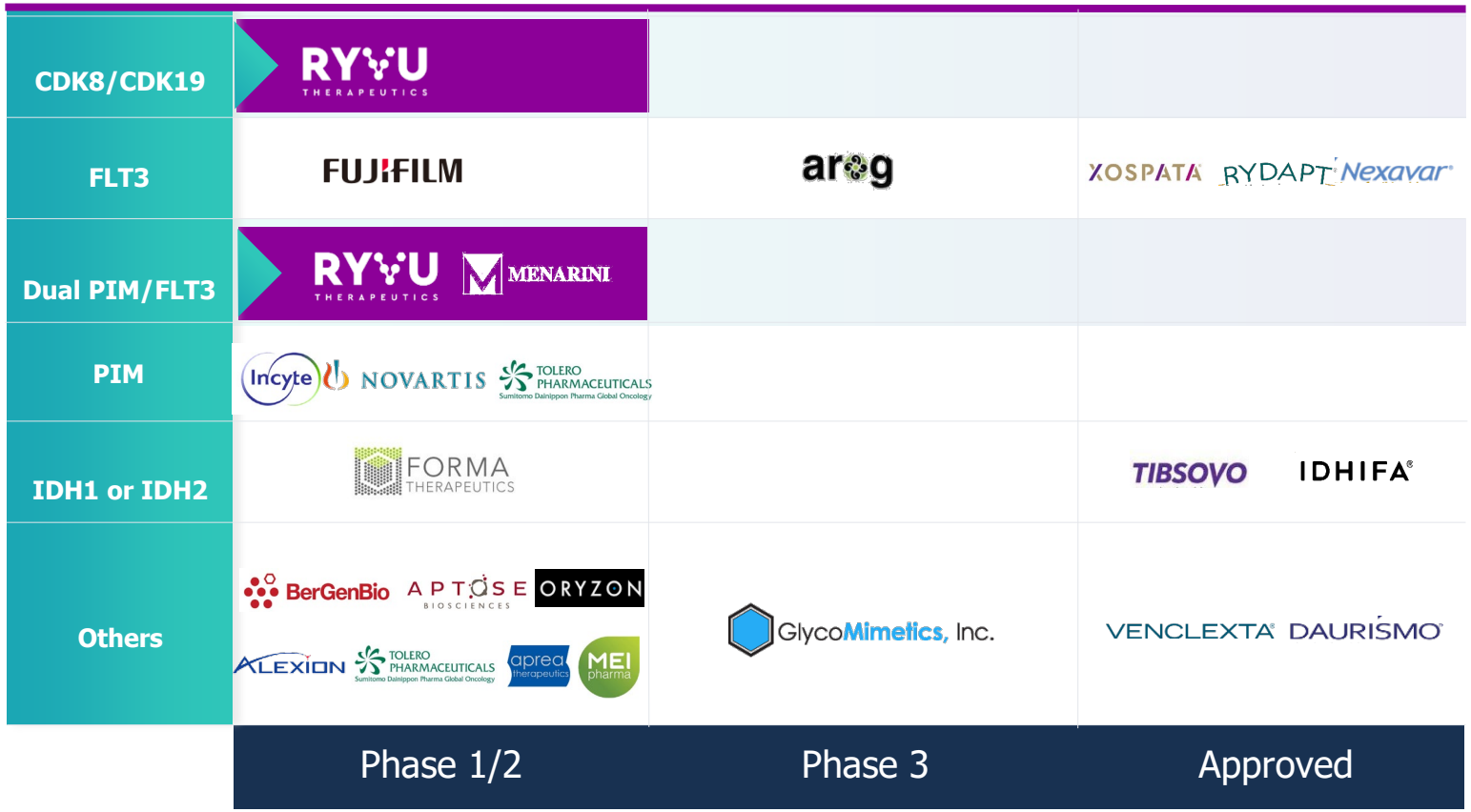






1 Mayo Clinic
2 Cancer.net
3 Leukemia & Lymphoma society
4 Walter, R; *Leukemia 2015*
5 Evaluate Pharma

Clinical landscape: targeted small molecule therapies for AML

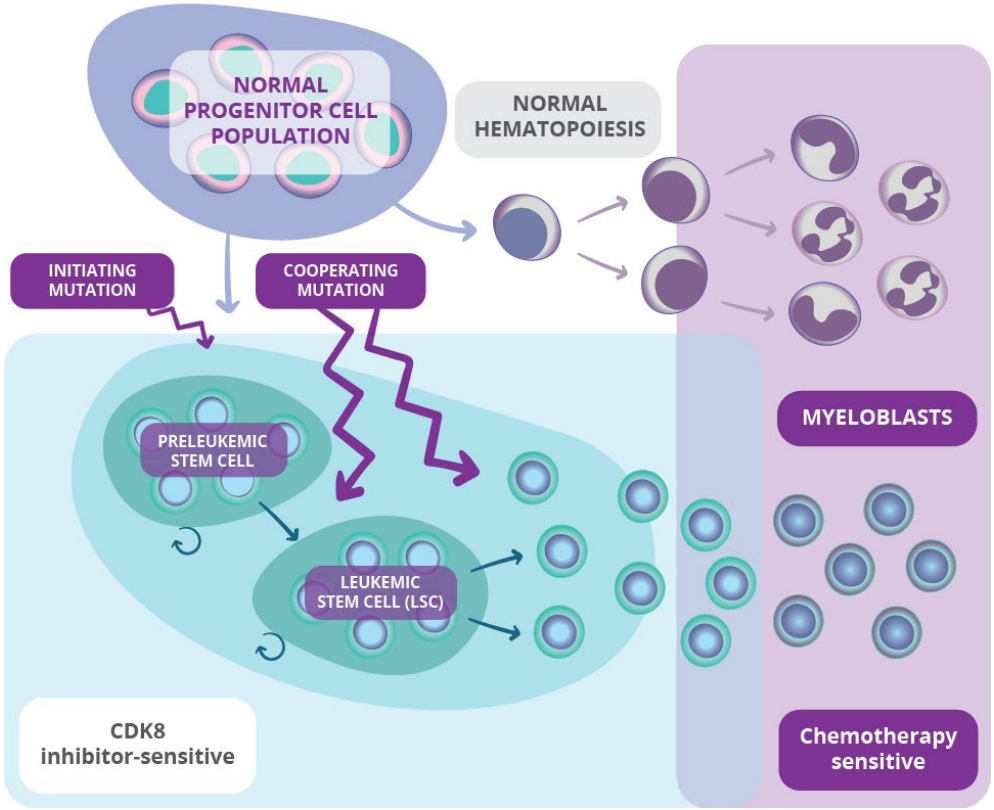


- SEL120 IS THE ONLY CDK8/CDK19 INHIBITOR IN CLINICAL DEVELOPMENT
- MEN1703/SEL24 IS AN UNIQUE, CLINICAL-STAGE DUAL PIM/FLT3 INHIBITOR

RYVU CLINICAL PROGRAMS DESIGNED TO FULFILL UNMET NEEDS IN AML

- OVERCOMING RESISTANCE TO SINGLE-TARGET MUTATION-SPECIFIC INHIBITORS
- EFFICACY IN BROADER PATIENT POPULATIONS
- REDUCING CHEMOTHERAPY-BASED TREATMENT REGIMENS
- FULLY ORAL REGIMEN

SEL120: potential role of CDK8/CDK19 in AML treatment



RATIONALE FOR CDK8/CDK19 INHIBITORS IN AML

- Transcriptional deregulation is a hallmark of AML
- CDK8 is a kinase subunit of the Mediator complex serving as a bridge between basal transcription and regulatory elements involved in:
  - Deregulation of super enhancers (SE)
  - Affected differentiation and pro/anti-apoptotic genes

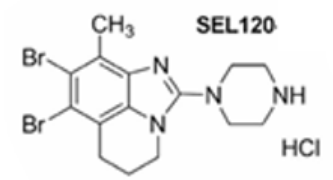
EFFICACY OF SEL120 - CDK8/CDK19 INHIBITOR - IN AML

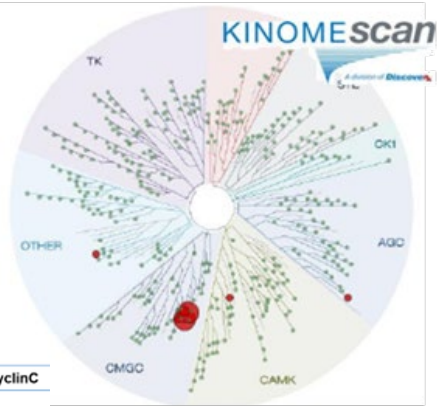
- Selectively targets leukemic cells, sparing normal blood cells (unaffected normal hematopoiesis)
- Promotes cell death (differential cytotoxicity on STAT5+ AML)
- Represses increased levels of anti-apoptotic proteins and induces lineage commitment genes in undifferentiated AML cells

Excellent on-target activity of SEL120 in pSTAT positive AML cell models

SEL120 is a potent and selective CDK8/CDK19 inhibitor

Low nM activity on CDK8/CDK19
and excellent kinase selectivity (broad kinome)



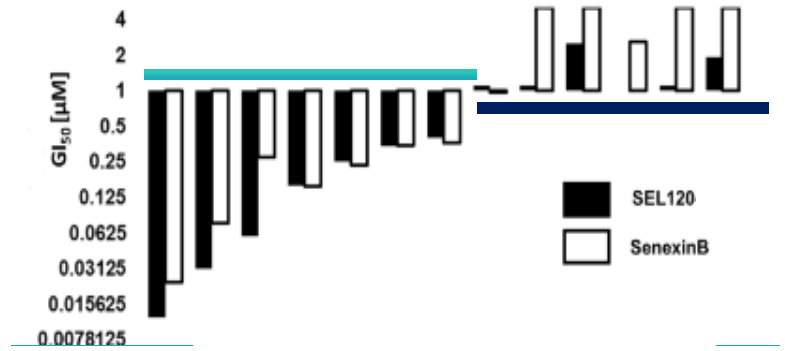


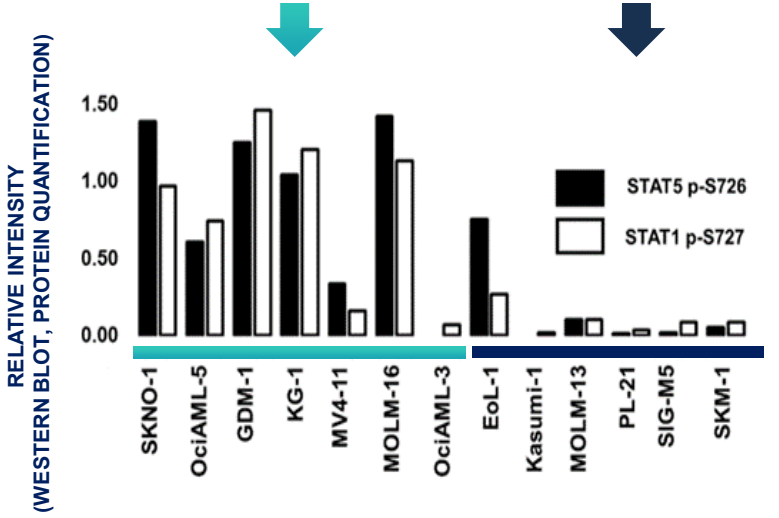
IC_{50} [nM]	CDK8/CyclinC	CDK19/CyclinC
SEL120	4.4	10.4

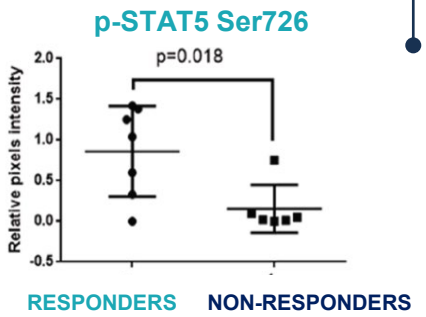
- Spares CDK2, CDK4, CDK6, CDK7, CDK9, etc.
- Type I, ATP-competitive mechanism of binding and inhibition of CDK8/19 activity
- Lack of binding to off-targets potentially associated with toxicity of pre-clinical EMD Serono CDK8/19 inhibitors (such as JNK1 or GSK3b)[1]
- Higher selectivity based on comparison of gene expression effects[2]
- Composition of matter patents granted in 2017

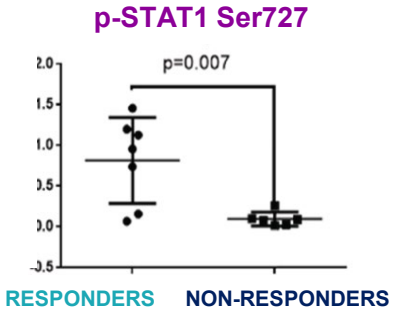
[1]*Chen et al. 2019*
[2]*Rzymski et al. 2017*

pSTAT1/pSTAT5 levels discriminate responder/ non-responder



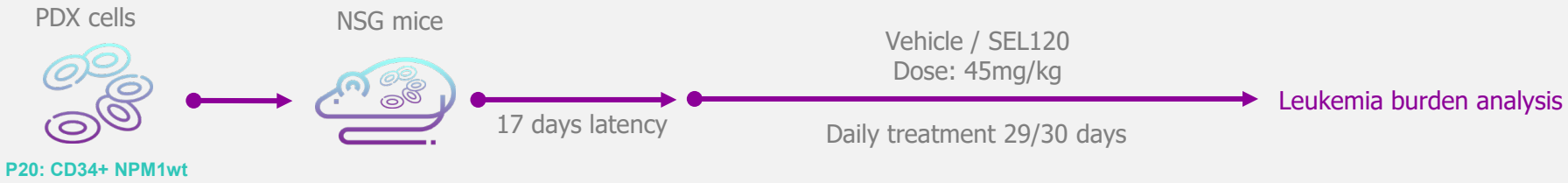




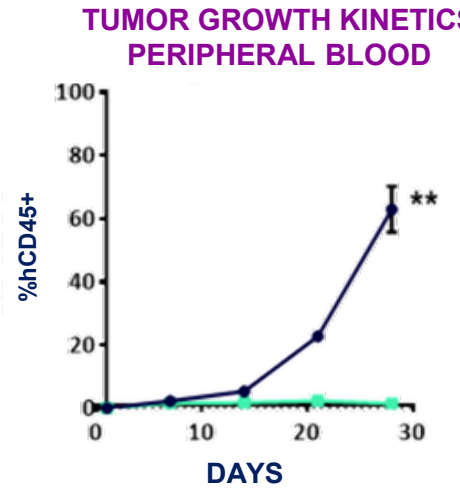


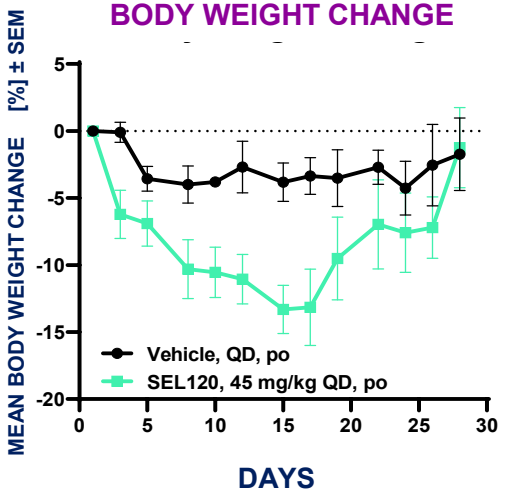
SEL120 induces complete regression and bone marrow recovery in AML

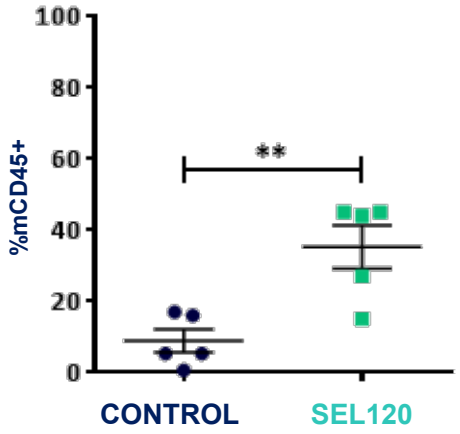
In CD34+ AML patient-derived xenografts

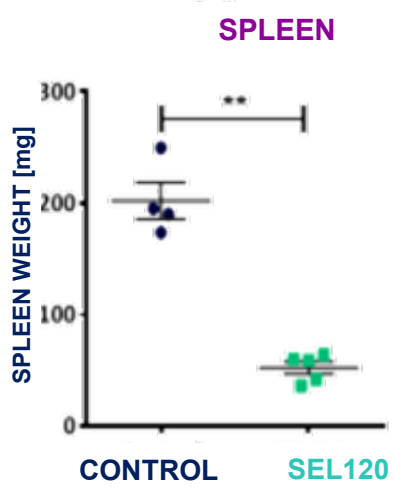


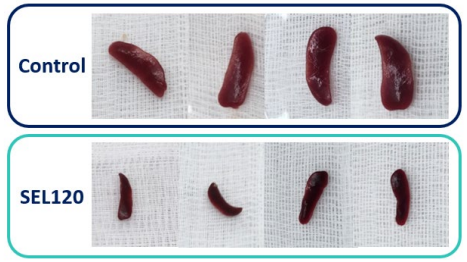
COMPLETE REGRESSION (PERIPHERAL BLOOD)	HEMATOLOGIC RECOVERY (BONE MARROW)	REDUCED SPLENOMEGALY









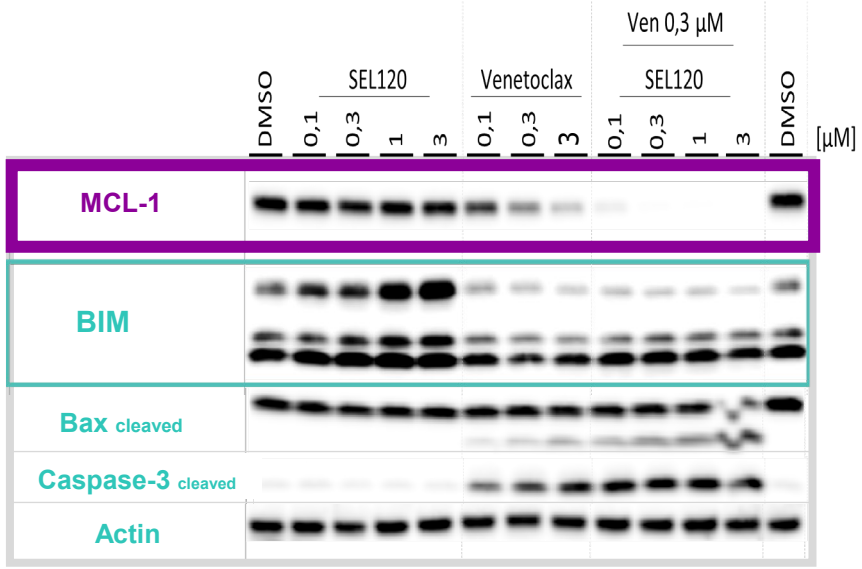


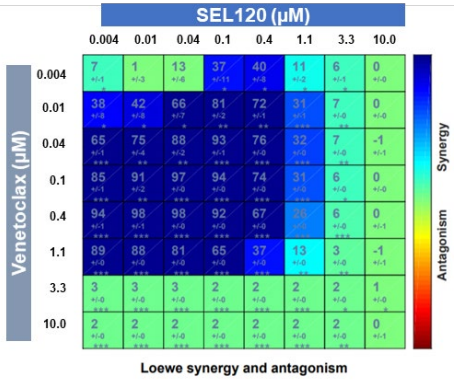
Research performed at: CENTRUM ONKOLOGII – INSTYTUT IM. MARII SKŁODOWSKIEJ-CURIE ODDZIAŁ W GLIWICACH

RYVU THERAPEUTICS

SEL120 strongly synergizes with Venetoclax

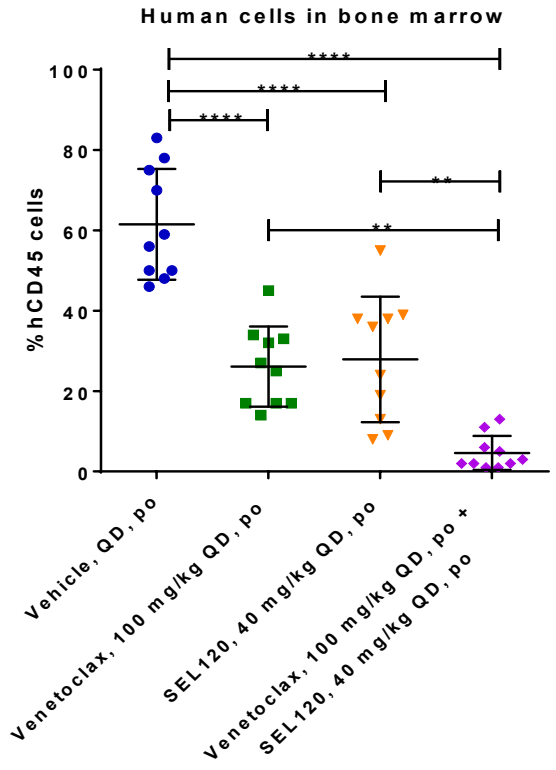
SEL120 potentially addresses treatment resistant disease through safe, indirect MCL-1 downregulation in cancer cells

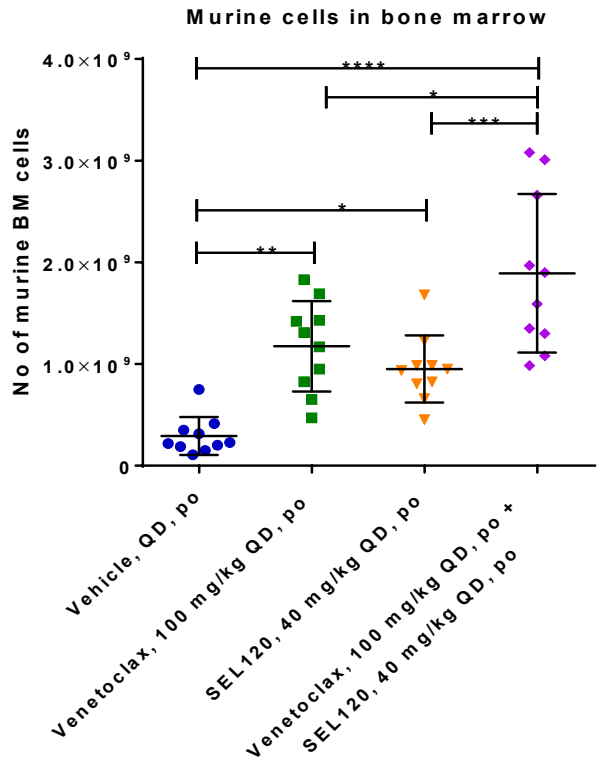




Compelling potential for SEL120 in combination with Venetoclax

COMPLETE REGRESSION | **HEMATOLOGIC RECOVERY (BONE MARROW)**





SEL120: Phase Ib study – first patient dosed in September 2019

Phase 1b Study of SEL120 in Patients with Acute Myeloid Leukemia or Myelodysplastic Syndrome

1 STUDY POPULATION:
- Patients with relapsed /refractory AML or high risk MDS
- No upfront patient stratification

2 PRIMARY OBJECTIVE:
- To assess safety and tolerability
- To determine the recommended dose

3 SECONDARY OBJECTIVE:
- To evaluate pharmacokinetics
- To evaluate the preliminary anti-leukemic activity

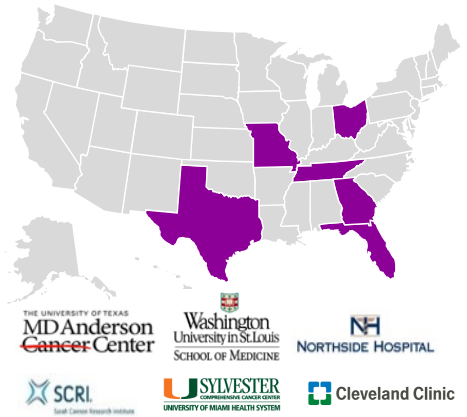
4 EXPLORATORY OBJECTIVE:
- To evaluate pharmacodynamics

PROJECT MILESTONES

- **H1 2021** – INITIAL RESULTS FROM PHASE Ib
- **H2 2021** – FINAL RESULTS FROM PHASE Ib
- **H1 2022** – PHASE II IN AML/MDS
- **2022+** – INTERIM RESULTS FROM PHASE II

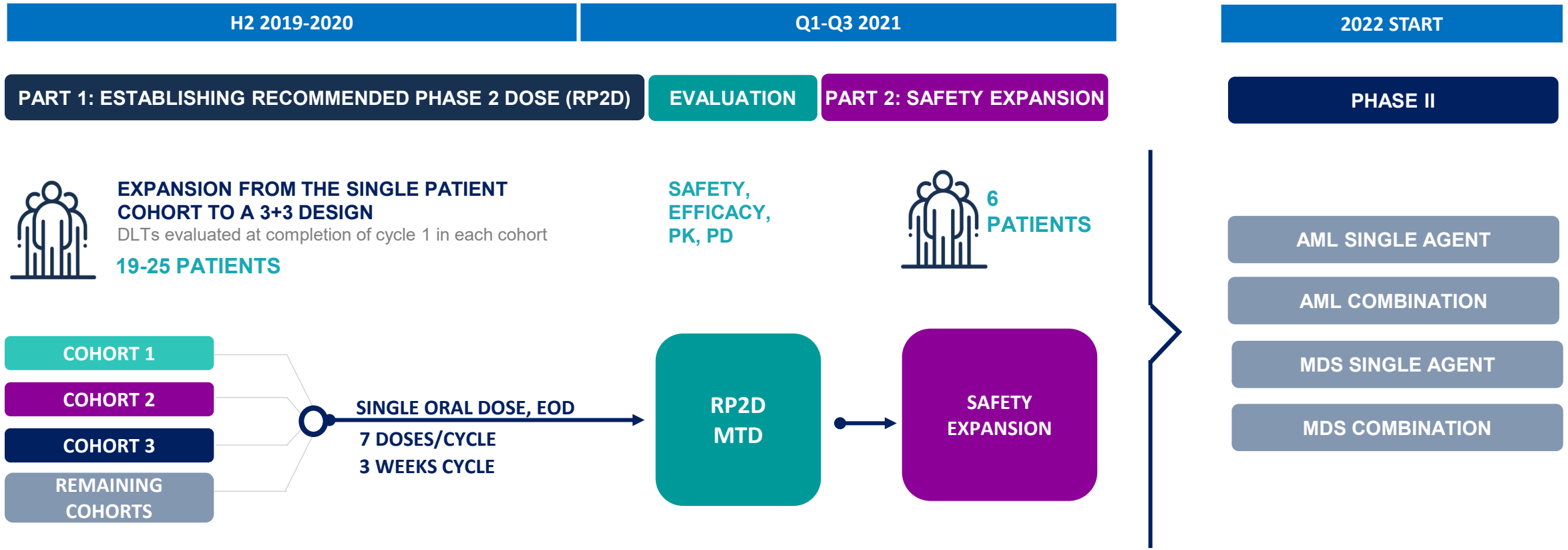
STATUS AND PLANS

6 ACTIVE SITES IN USA IN 2020



3 SITES EXPANSION IN EUROPE IN 2020/2021
- **2 SITES IN POLAND – CTA APPLICATION FILED IN AUGUST 2020**
- 1 SITE IN ANOTHER EU COUNTRY - planned

SEL120 study design in AML/MDS and further plans



Positioning of SEL120 in AML treatment regimen and strategic expansion

AML TREATMENT PROTOCOL UNFIT PATIENTS

	NO RELEVANT MUTATIONS	MUTATION - DRIVEN
FIRST LINE	LOW INTENSITY CHEMOTHERAPY	LOW INTENSITY CHEMOTHERAPY OR TARGETED THERAPY
RELAPSED/REFRACTORY	LOW INTENSITY CHEMOTHERAPY	TARGETED THERAPY
SEL120	SEL120 + LOW INTENSITY CHEMOTHERAPY (e.g. Azacitidine)	SEL120 + TARGETED THERAPY (e.g. Venetoclax)

RYVU STRATEGY FOR DEVELOPMENT OF SEL120 IN AML/MDS

STAGE 1 — POSITIONING IN THIRD+ LINE TREATMENT

- Monotherapy
- Patients unfit for intensive chemotherapy
- Relapsed/refractory AML, high risk MDS

STAGE 2 — POSITIONING IN SECOND/THIRD LINE

- Monotherapy and combination with SoC
- Combo with Venetoclax or chemotherapies
- Patients unfit for intensive chemotherapy
- Relapsed/refractory to frontline or follow up treatment AML, high risk MDS

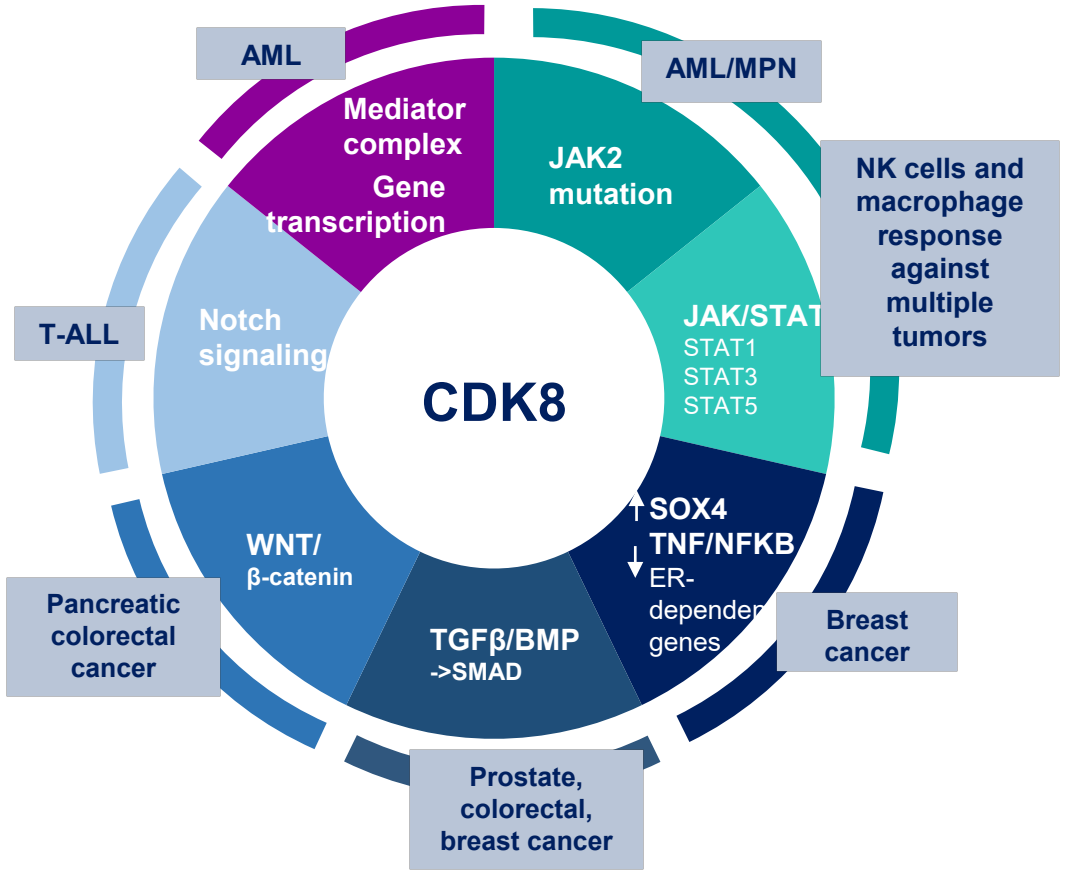
STAGE 3 — POSITIONING IN FIRST LINE TREATMENT

- Combination (dublet or triplet) with SoC
- Regimen e.g. with Venetoclax+Azacitidine
- Patients unfit for intensive chemotherapy
- First line, treatment naïve, AML/MDS

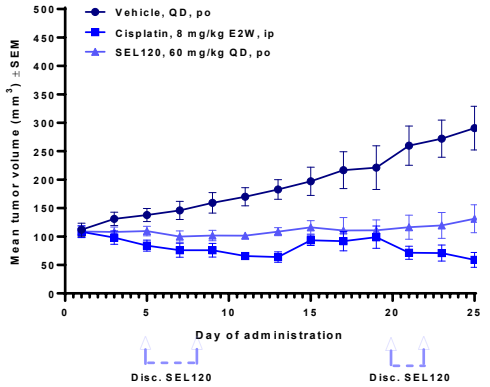
SEL120 beyond blood cancers: potential role of CDK8/CDK19 in solid tumors

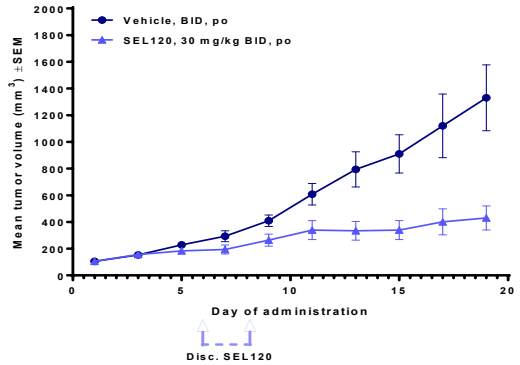
SEL120: expansion plan in multiple solid tumors and other heme malignancies

Phase I start: 2021, preliminary results: 2022



TNBC BREAST AND COLORECTAL CANCER MODELS





CDK8/CDK19 inhibitors have potential in multiple solid tumors

- Ryvu confirmed in vitro or in vivo potential in breast, colorectal and prostate cancer

Unique MoA differentiates CDK8/CDK19 from other CDK family members

- Do not interfere with cell cycle progression (like CDK1, CDK2, CDK4/6)
- Unique across family mediator of transcriptional reprogramming (induction of silent genes, not physiological transcription) preventing metastasis and drug-resistance
- Different stratification of responders and biomarkers of response
- First generation of CDK8/19 inhibitors unsuccessful due to toxic off-target effects and suboptimal PK/PD profile

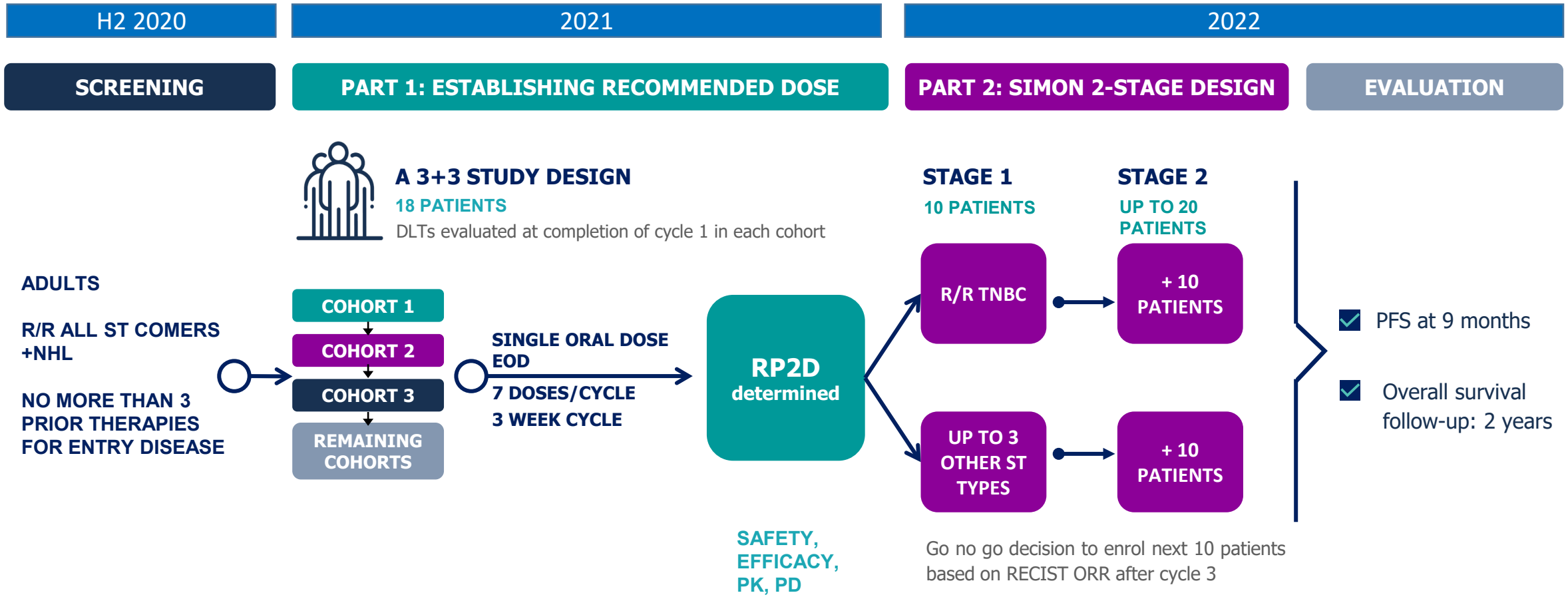
CDK8/19 inhibitors designed to provide targeted and safer treatment options

- Selective targeting cancer cells while sparing healthy ones
- (e.g. CDK4/6, CDK9 affect both normal and cancer cells – possible cytopenias, no bone marrow recovery)
- Selective regulation of transcription in a cancer gene specific context
- (e.g. CDK7/9 involved in general transcriptional programs of normal genes)

Chart inspired by Pharmaceuticals 2019, 12,92 + Ryvu data

SEL120: expansion plan in multiple solid tumors and other heme malignancies – preliminary plan

Phase I start: 2021, preliminary results: 2022



SEL24/MEN1703 is a differentiated, first-in-class PIM/FLT3 dual kinase inhibitor

1. PIM and FLT3 are oncogenes involved in AML
2. Dual targeting creates potential for broader activity, more durable responses than selective FLT3 inhibitors such as gilteritinib
3. Potential for treating patients that have relapsed on selective FLT3 inhibitors - PIM kinases are largely responsible for the development of resistance to FLT3 inhibitors

VALUE THROUGH GLOBAL DEAL WITH the MENARINI group

DEVELOPED BY RYVU UP TO INITIATION OF CLINICAL STUDIES AND OUT-LICENSING

- Partnered globally with Menarini in 2017
  TOP 40 global pharma company, based in Italy
- Menarini is fully responsible for clinical development and funds translational research at Ryvu

$5.6M	UPFRONT PAYMENT
$104M	TOTAL POTENTIAL VALUE OF MILESTONES & REFUND OF R&D COSTS
xx%	UP TO DOUBLE-DIGIT ROYALTIES FOR RYVU FROM MENARINI

ONGOING CLINICAL TRIALS

Study title: A Phase I/II Study of SEL24 in Patients With Acute Myeloid Leukemia

SITES

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

NORTHSIDE HOSPITAL

FRED HUTCH CURES START HERE®

Cleveland Clinic

VANDERBILT-INGRAM CANCER CENTER

INITIAL RESULTS OF THE PHASE I STUDY:

- determined the recommended Phase II dose (RP2D), the PK profile and the single agent activity in R/R or newly diagnosed AML patients
- Study results published at EHA 2020 conference
- Ryvu has received 1.9 M milestone payment for successful completion of Phase I studies

PROJECT PROGRESS:

- Cohort expansion at the recommended Phase II dose (RP2D) to confirm the safety profile and assess drug efficacy starting at multiple clinical sites in the U.S. and Europe started
- First Phase II patients in US (July 2020) and Europe (September 2020)

Initial Phase I data for SEL24/MEN1703 demonstrates compelling single agent efficacy

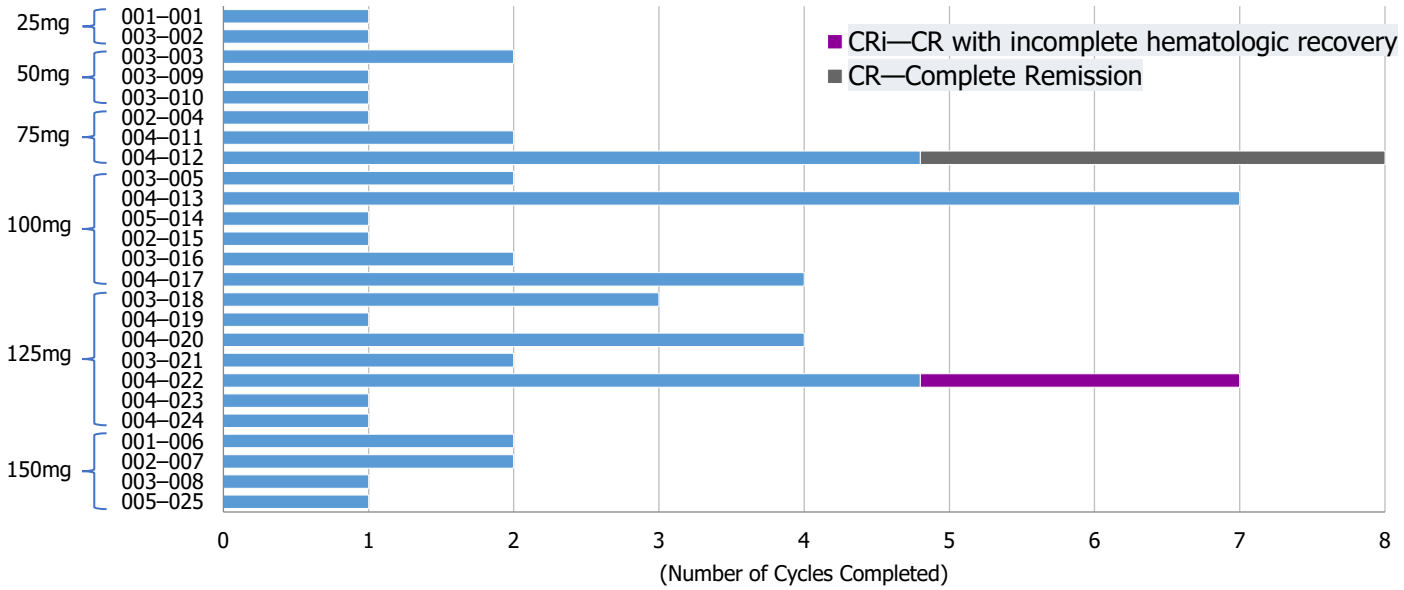
Acceptable safety data with complete responses observed

ESTABLISHED RECOMMENDED PHASE II DOSE

EXPANSION FROM THE SINGLE PATIENT COHORT TO A 3+3 DESIGN

DLTs evaluated at completion of cycle 1 in each cohort

INDIVIDUAL TREATMENT DURATION



N=25 patients treated
22 patients evaluable
(cut-off date 11-Feb-20)

68 years median age
(range 25-84)

PATIENTS
- **2** newly diagnosed
- **11** primary refractory AML
- **12** relapsed AML

FREQUENT MUTATIONS
- **5 (20%)** FLT3/ITD.
- 4 (16%) DNMT3A
- 4 (16%) IDH1
- 2 (8%) IDH2
- 2 (8) NMP1

RESULTS

- **Establishment of recommended dose and evaluation of safety profile**
  - SEL24 has acceptable safety profile up to 125mg
  - RD defined at 125mg
  - Treatment-Emergent Adverse Events – mostly hematologic or infectious. Transient peak in transaminases was detected by C1 D14 in almost all cohorts (Grade ≤2 and reversible in the 7 days OFF treatment period up to the RP2D)
- **Objective response / single agent efficacy in FLT3 wild-type patients**
  - Complete remission at 75mg in a 81 y.o. patient, with DNMT3A/IDH2 mutant AML progressed on enasidenib
  - Complete response with incomplete hematological recovery at 125mg in a 75 y.o. patient with ASXL1/EZH2 mutant AML relapsed after chemotherapy and decitabine

Differentiated internally discovered small-molecule drug candidates and new programs

BEST IN CLASS

A2A/A2B ANTAGONIST

Current challenges
- × Based on internal data generated at Ryvu the disclosed competitors' antagonists are unable to overcome immunosuppression at high adenosine concentrations (typical to TME)
- × Selective A2A antagonists do not affect antigen presenting cells to prime immune system

Differentiation
- ○ Dual A2A/A2B antagonists acting on multiple subtypes of immune cells offering more pronounced anti-tumor response
- ○ *In vitro* efficacy in immune cells superior to known A2A/B antagonists

Competitive agents
AstraZeneca, CORVUS PHARMACEUTICALS, Genentech / ARCUS BIOSCIENCES, MERCK / iTeos Therapeutics

Next milestone
- ○ Initiate IND enabling studies (2020)
- ○ File IND (2021)

STING

Current challenges
- × First generation intratumoral STING agonists provided limited signs of clinical efficacy
- × Limited possibilities to reach multiple metastasis with IT agonists
- × Refractory STING alleles to first generation STING agonists do not cover whole patient population

Differentiation
- ○ Direct, small molecule STING agonists
- ○ Active in multiple human STING haplotypes
- ○ Anti-tumor efficacy after systemic administration in preclinical mouse models on par or superior to competitors

Competitive agents
NOVARTIS / ADURO BIOTECH, gsk, MERCK, spring bank pharmaceuticals

Next milestone
- ○ Initiate IND enabling studies (2020)
- ○ File IND (2021)

FIRST IN CLASS

HPK1

Novel Biology Insights
- ○ Unique dual potential to modulate both innate and adaptive anti-cancer immunity
- ○ Synergistic enhancement of T and DC cells function simultaneously making T cells resistant to immunosuppression

Cancer Targets
- ○ Hematopoietic progenitor kinase 1 (HPK1, MAP4K1)
- ○ Important in regulation of the signalling cascade triggered by TCR activation in lymphocytes T
- ○ Potentially multiple tumor types

Competitive agents
NIMBUS THERAPEUTICS, Takeda / ARIAD, Genentech, Incyte, BAYER, Treadwell Therapeutics

Next milestone
- ○ Non-GLP toxicology (H1 2021)

SMARCA2

Novel Biology Insights
- ○ Targets SWI/SNF chromatin remodelling complex
- ○ Implicated in multiple cancers, including NSCLC

Cancer Targets
- ○ Solid tumors with SMARCA4 loss of function mutations

Competitive agents
NOVARTIS, AURIGENE, Epizyme, Boehringer Ingelheim, ARVINAS, KYMERA

Next milestone
- ○ Lead selection (2021)

OTHER S-L TARGETS

Novel Biology Insights
- ○ Synthetic lethality arises when simultaneous mutations of gene pairs lead to cell death, whilst individual mutations does not cause a lethal effects

Cancer Targets
- ○ MTAP deletion cancers
- ○ WRN helicase in MSI high and other tumors
- ○ Multiple other undisclosed targets

Competitive agents
agios, IDEAYA BIOSCIENCES, Epizyme, NIMBUS THERAPEUTICS

Next milestone
- ○ Lead selection (>2021)

Ryvu develops dual A2A/A2B adenosine receptor antagonists

STATUS	**IN 2019 RVU330 WAS SELECTED AS A PRECLINICAL CANDIDATE** **NON-GLP TOX STUDIES ARE ONGOING**
KEY DIIFERENTIATION COMPETITIVE ADVANTAGE	**Strong potential of best-in-class drug:** The only disclosed dual A2A / A2B antagonist exhibiting immunostimulatory activity in vitro at high concentrations of adenosine

MILESTONES FOR RVU330

Q3 2020	COMPLETION OF NON-GLP TOX STUDIES
2H 2020	INITIATION OF IND ENABLING STUDIES
2020	PRELIMINARY TRANSLATIONAL STUDIES ALLOWING TO IDENTIFY PATIENTS WITH POTENTIAL BEST TREATMENT BENEFITS
2H 2021	IND FILING
2022+	PHASE I CLINICAL TRIALS

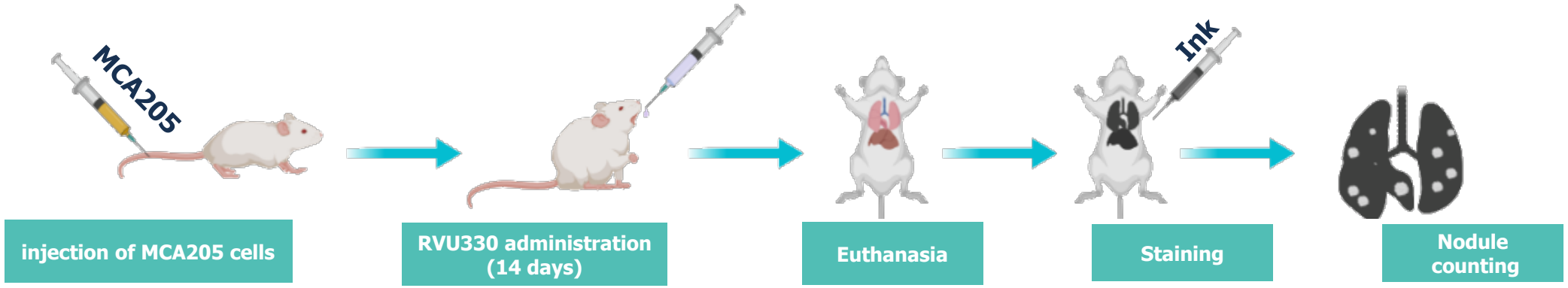
RYVU APPROACH OF TARGETING BOTH A2A AND A2B RECEPTORS PROVIDES STRONG PRECLINICAL COMPETITIVE ADVANTAGE

HIGH ADENOSINE CONCENTRATION

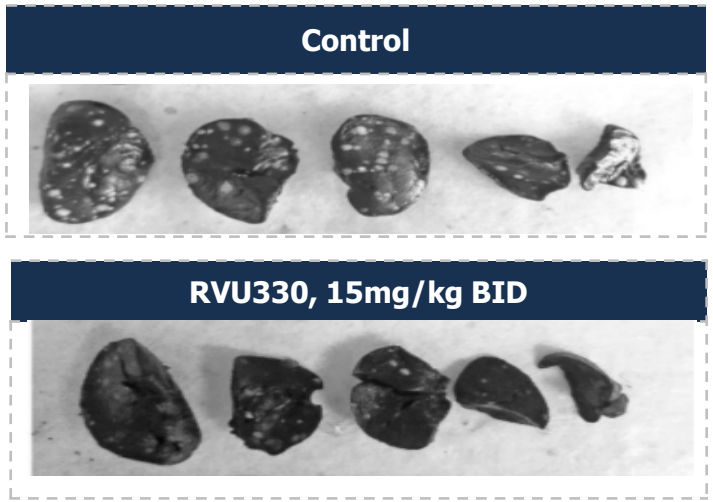
	DUAL A2A/A2B ANTAGONIST	ACTIVE IN HIGH ADENOSINE CONCENTRATION	ACTIVATION OF T CELLS	ACTIVATION OF DENDRITIC CELLS	pCREB BIOMARKER INHIBITION HUMAN WHOLE BLOOD
RYVU	✓	✓	✓	✓	✓
ARCUS BIOSCIENCES	✓	✗	✓	✓	✓
iTeos Therapeutics	✗	✓	✓	✗	✓
CORVUS PHARMACEUTICALS	✗	✗	✗	✗	✗
AstraZeneca	✗	✗	✗	✗	✗
NOVARTIS	✗	✗	✗	✗	✗

	AZD4635 Astra Zeneca	CPI-444 Corvus	AB928 Arcus	Example 7 iTeos	RVU330 Ryvu
TNFa moDCS - EC_{50} [nM]	>10 000	>10 000	699 ± 144	> 3 000	13.4 ± 5.1
IL-2 $CD4^+$ CELLS - EC_{50} [nM]	>10 000	>10 000	203 ± 97	4 ± 0.1	0.4 ± 0.2

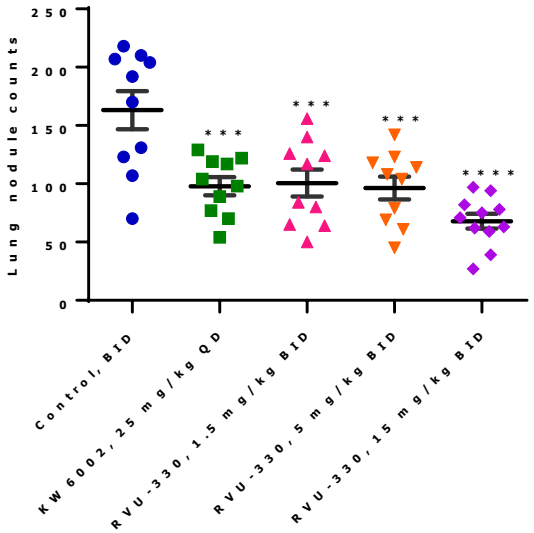
RVU330 IS EFFICACIOUS AS MONOTHERAPHY IN MCA205 SYNGENEIC MODEL



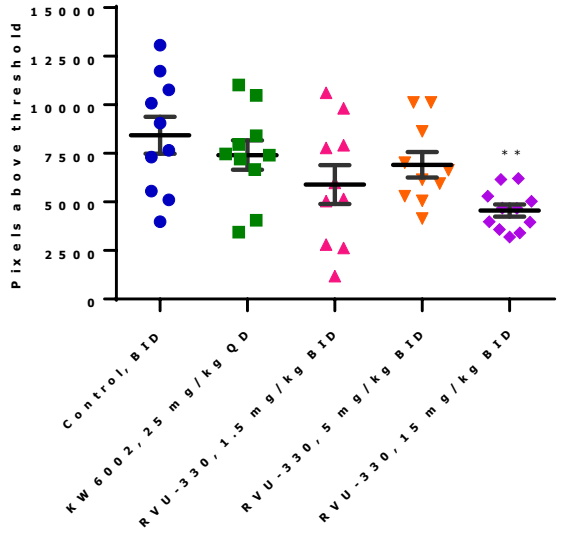
LUNG LOBES AFTER STAINING WITH VISIBLE WHITE MCA205 NODULES



NODULE COUNTS IN LUNGS



TOTAL AREA OF NODULES IMAGE ANALYSIS



Small molecule, direct, systemic STING agonists with strong anti-tumor efficacy

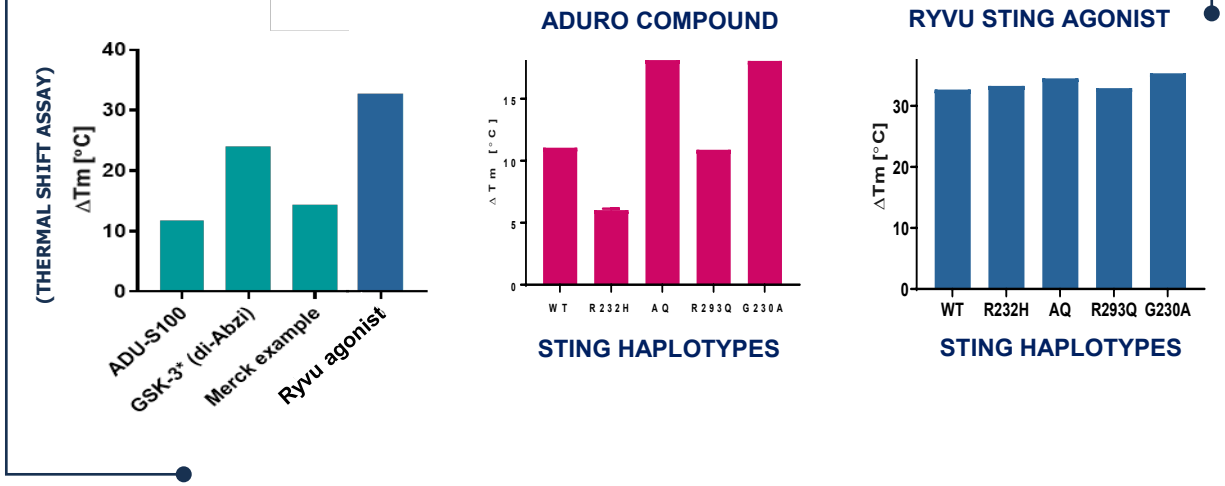
STATUS	**STAGE: SELECTION OF PRELINICAL CANDIDATE** STRONG ANTITUMOR EFFICACY AFTER SYSTEMIC ADMINISTRATION **OPTIMIZATION AND PROFILING OF COMPOUNDS - POTENTIAL CANDIDATES FOR IND STUDIES**
KEY DIFFERENTIATION COMPETITIVE ADVANTAGE	**Small molecule, direct STING agonists with systemic route of administration and activity on all STING haplotypes (broad patient population may benefit);** Potential for antibody drug conjugation (ADC)

MILESTONES FOR STING AGONISTS

Q1-Q3 2020	PROFILING AND ASSESSMENT OF THE POTENTIAL FOR BEST COMPOUNDS – DRUG CANDIDATES
2020	PRELIMINARY TRANSLATIONAL STUDIES ALLOWING TO IDENTIFY PATIENTS WITH POTENTIAL BEST TREATMENT BENEFITS
1H 2021	INITIATION OF IND STUDIES
2H 2021	IND FILING
2022+	PHASE 1 CLINICAL TRIALS

STRONG COMPETITIVE ADVANTAGE

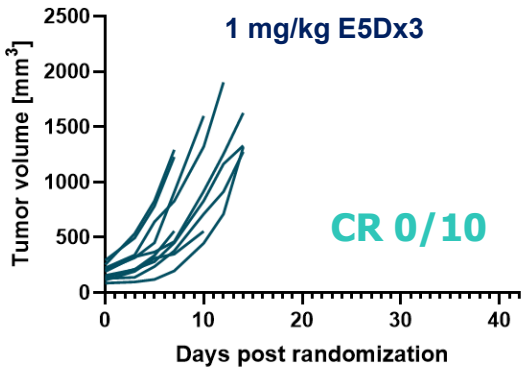
A broad patient population carrying multiple STING haplotypes may benefit

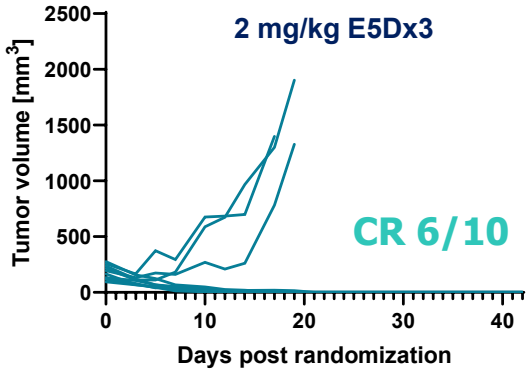


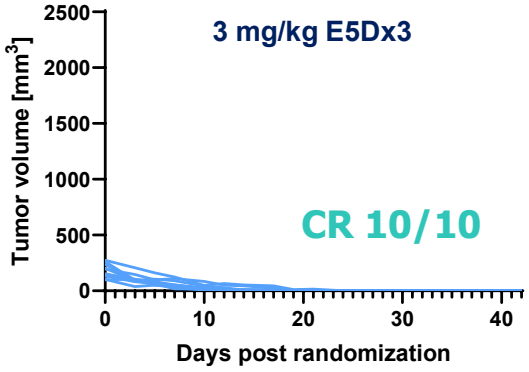
RVU312-4787 CLEARS TUMORS IN EMT6 MOUSE TUMOR MODEL

EMT6 MOUSE BREAST CANCER MODEL – INTRAVENOUS ADMINISTRATION

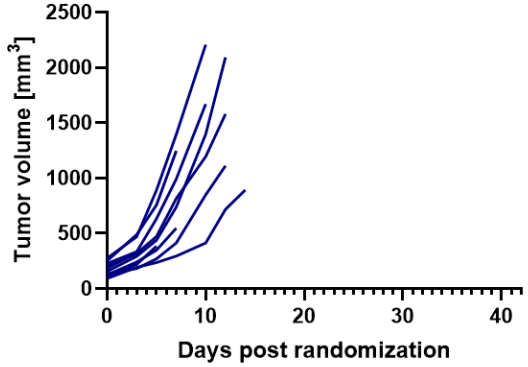
RVU-24024



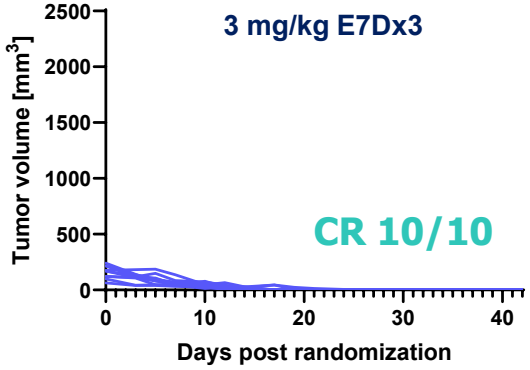




CONTROL GROUP



RVU-24024



	Complete remissions	Mice alive
EMT6 CONTROL	-	0/10
EMT6 3 mg/kg E5D	10/10	10/10
EMT6 2 mg/kg E5D	6/10	6/10
EMT6 1 mg/kg E5D	0/10	0/10
EMT6 3 mg/kg E7D	10/10	10/10

Ryvu has selective, potent HPK1 inhibitors with anti-tumor efficacy in mice

RYVU APPROACH

STATUS	**LEAD OPTIMIZATION**
APPROACH	▪ Small molecule, selective, orally bioavailable inhibitors of HPK1 kinase activity
CURRENT DIFFERENTIAL FACTORS	▪ High selectivity against kinases from TCR pathway ▪ Immunostimulatory activity in immunosuppresed, resistant hPBMC and T cells across species

MILESTONES FOR HPK1 INHIBITOR

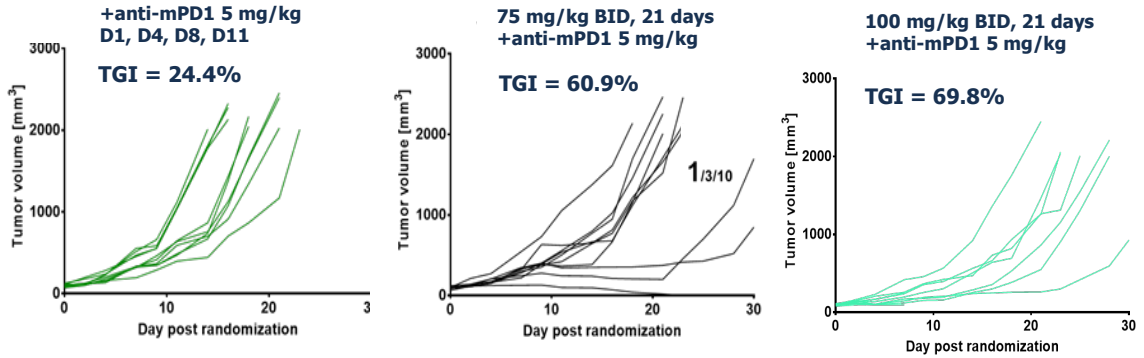
2H 2020-2021	LEAD OPTIMIZATION
2021-2022	PRECLINICAL DEVELOPMENT
2022	INITIATION OF IND-ENABLING STUDIES
2022+	IND FILING

RYVU SMALL MOLECULE HPK1 INHIBITORS SHOW EFFICACY IN MOUSE SYNGENEIC MODEL COMPARABLE TO CLINICAL REFERENCE COMPOUND

		RVU-918	RVU-293	UHN	TAKEDA/ ARIAD	GENENTECH	INCYTE	BAYER
hHPK1	IC50 [nM]	1.0	1.4	2.7	0.55	4.5	33	2.9
	Ki [nM]	0.1	0.3	0.7	0.1	1.6	20.7	0.4

EFFICACY IN CT26 (MOUSE MODEL OF COLON CANCER)

COMBINATION WITH ANTI-mPD-1



*currently Treadwell Therapeutics, in phase I clinical trials

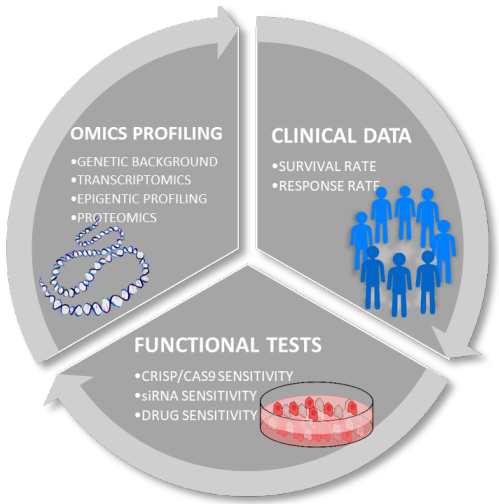
Ryvu established proprietary SYNTHETIC LETHALITY PLATFORM

Ryvu has a powerful engine to identify and validate novel synthetic lethal targets in oncology

1 FIND CONTEX-SPECIFIC NOVEL DRUG TARGETS

DATA MINING
FILTERING AND INTEGRATION

OMICS DATA FOR CELLS AND PATIENTS
HIGH CONTENT GENE INTERROGATION



2 IDENTIFY NOVEL SYNTHETIC LETHAL TARGETS

NETWORK ANALYSIS
CANCER DEPENDENCY MAP

CORRELATION STUDIES USING
RYVU PROPRIETARY BIOINFORMATIC TOOL: MULTIDEP AND SURV-LRT

3 NEW SYNTHETIC LETHAL TARGETS IDENFIED

EXPERIMENTAL VALIDATION
DRUG SCREENING

ISOGENIC PAIRS
CELL LINES/PDC PANEL

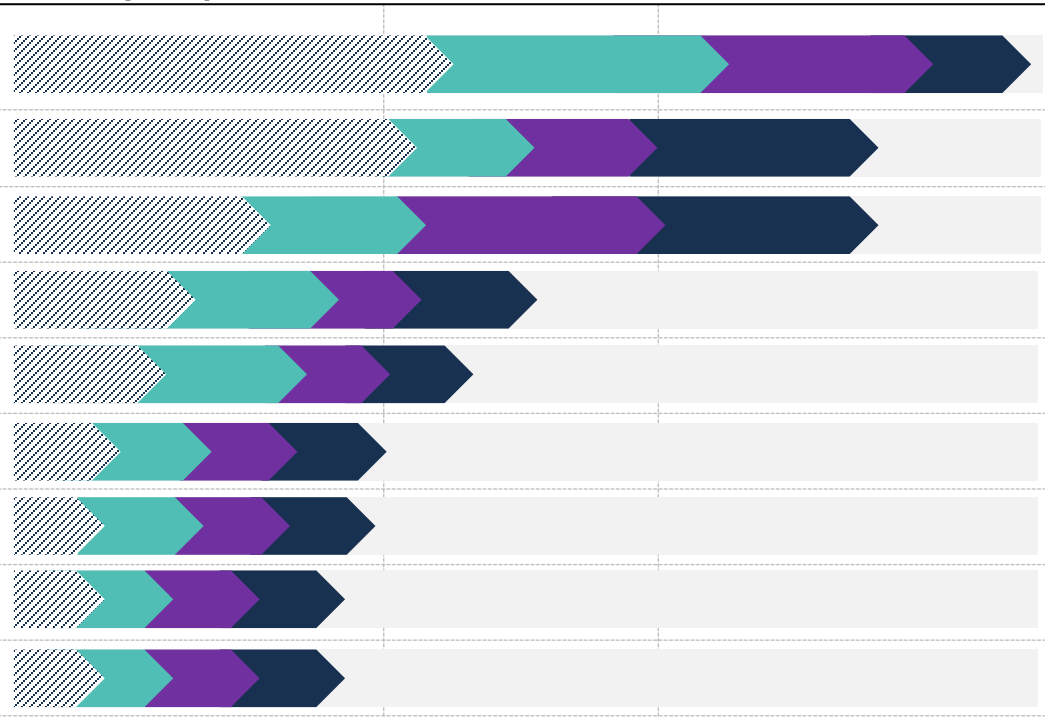
SYNTHETIC LETHAL TARGETS – DISCOVERY STAGE

- ✓ **SMARCA2 INHIBITORS: HIT-TO-LEAD**
- ✓ **WRN INHIBITORS: HIT ID**
- ✓ **TARGETING MTAP DELETED CANCERS: HIT ID**

- First in class WRN inhibitors selectively targeting tumors with microsatellite instabililty (MSI)
- 10-30% of colorectal, endometrial, gastric and ovarian tumors with microsatellite instability

Broad pipeline addressing emerging targets in oncology

Ryvu drives value creation from its multiple data readouts



Program/ target name	Indication	Partners / Collaborators	Anticipated Milestones 2020	2021	2022+
SEL24 / MEN1703 PIM / FLT3	AML		✓ Ph. I data ✓ Ph. II initiation	• Ph. II interim data	• Ph. II complete
SEL120 CDK8	AML / MDS	LEUKEMIA & LYMPHOMA SOCIETY®	• Ph. I dose escalation	• Initial Ph. Ib data • Final Ph. Ib data	• Ph. II initiation • Interim data
	Solid tumors		• Ph. I preparations	• Ph. I top line results	• Ph. II initiation • Interim data
A2A/A2B	Solid tumors		• IND enabling studies	• IND filing	• Ph. I dose escalation
STING	Solid tumors		• IND enabling studies	• IND filing	• Ph. I dose escalation
HPK1	Solid tumors		• Lead optimization	• Non-GLP tox	• IND enabling studies
SMARCA2	Solid tumors		• *In vivo* PoC	• Lead optimization	• IND enabling studies
WRN	Solid tumors		• Hit ID	• Hit-to-lead	• Lead optimization • IND
MTAP	Solid tumors		• Hit ID	• Hit-to-lead	• Lead optimization • IND

2020	2021	2022+
2 Clinical stage assets	**3-4** Clinical stage assets	**4+** Clinical stage assets
1 Human PoC	**2** Human PoCs	**3+** Human PoCs
5+ Early pipeline programs	**7+** Early pipeline programs	**10+** Early pipeline programs

Ryvu R&D Center for Innovative Drugs

Move completed in July 2020

2017	August 2018	April 2020	June 2020	July 2020
Preparations for the investment; obtaining a grant from the Ministry of Development	**Initiation of construction works**	**Completion of major construction works**	**Obtained occupation permits, first laboratories launched**	**All labs and offices fully operational**

Usable area of the Center	**> 86,000 sq. ft**	Investment budget	**> $20M**
# workplaces	**~300 associates**	Value of the grant from the Polish Ministry of Development	**~$9M**

- Investment initiated in 2017 – before the corporate split from Selvita CRO
- Provides Ryvu with adequate and consolidated research infrastructure
- Has enabled the spin-out of Selvita (CRO) and value creation of >$100M for Ryvu shareholders
- Ryvu has secured funds for investment from joint pre-split cash balance

* Exchange rate used – average NBP for 2019 – 1 USD = 3.8395 PLN

Covid-19 impact on Ryvu Therapeutics

Clinical trials:

- Industry risk: Clinical trials in locations impacted by Covid-19 such as the US has been by Covid-19 pandemic in multiple ways (slow or suspended enrollment, difficulties in patient monitoring, delayed DRCs, etc.)
- Clinical studies provide patients suffering from life threatening disorders such as AML and hrMDS with potential new therapeutic options – risk/benefit management policies are mainly dependent on individual site decisions
- Expected negative impact on enrollment – data availability in H1 2021 vs. Q4 2020 originally planned

Research operations:

- Thanks to the early government intervention Poland has been so far one of the countries least impacted by Covid-19 in Europe. (as of Sept. 28 total of 88,636 cases and 2,447 deaths for 38 million people). Lockdowns were transient and limited in scope.
- Second Covid-19 wave started in Poland in August with up to ~2,000 daily cases in September
- Ryvu introduced the first risk Covid-19 management steps already in February and reduced laboratory operations to critical experiments from for two weeks in March
- Full restart of laboratory activities in April with appropriate additional risk management procedures. Since then Ryvu labs have been operating at ~90% capacity, now using extra space in the new research center to maximize social distancing.
- Outsourcing – limited capacity at some CROs. Key providers less impacted. Risk-management with Asia and European Asian CROs.
- More difficult and slower access to some research materials.

Other industry specific risks

- Slowed-down business development (pharma demand)
- Market volatility and more difficult access to capital

Ryvu investment highlights and near term milestones

- Developing small molecule therapies which **address high value emerging targets and pathways in oncology**
- Diverse pipeline targeting **kinases, synthetic lethality and immuno-oncology**
- First-in-class selective **CDK8 inhibitor (SEL120)** with **potential across multiple indications**
- Validation from strategic **collaborations** including **partnership with Menarini on SEL24/MEN1703**
- Extensive early stage pipeline **delivering near term clinical candidates**
- Robust internal drug discovery engine and **partnership options** early stage candidates
- **Limited cash burn** thanks to non-dilutive grants and cost-efficient discovery platform, significant resources located in Poland

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