RYVU THERAPEUTICS

Targeted therapeutics
at the forefront of oncology

CORPORATE PRESENTATION

April 2020

Note on the presentation and forward looking statements

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Clinical stage company developing novel small molecule therapies addressing high value targets in oncology

ASSETS

- Fully-owned lead asset, first-in-class CDK8 inhibitor for blood cancers and solid tumors SEL120, first patient dosed in AML/MDS in September 2019.
- First-in-class dual PIM/FLT3 inhibitor SEL24/MEN1703 for blood cancers partnered globally with Menarini entered Phase 2 studies in March 2020
- All clinical trials of SEL24/MEN1703 and SEL120 are conducted in the U.S.

TWO PROJECTS IN CLINICAL TRIALS

STRATEGY

- Development of SEL120 in multiple hemato-oncology and solid tumor indications
- All Ryvu programs have been discovered internally - robust discovery engine addressing targeted cancer therapies and immunooncology
- Expected one new pre-clinical candidate per year for self development or partnering

HIGH VALUE UPSIDE

CORPORATE

- Listed on the Warsaw Stock Exchange (WSE:RVU)
- ~ $162M market capitalization
- ~ $20M* in cash and short-term investments
- > $25M** in grant funding secured until 2023
- >150 employees

MATURE CORPORATE GOVERNANCE

* October 2019, Q3 2019 report. Data for Q4 2019 will be released on April 9, 2020.
** Maximum non-dilutive research funding if all projects succeed according to the current research plans and grant contracts

Broad pipeline addressing emerging targets in oncology

CLINICAL PROJECTS

PROGRAM / TARGET NAME	INDICATION	DISCOVERY & PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER	ANTICIPATED MILESTONES
SEL24/MEN1703 PIM/FLT3	AML					MENARINI	Phase I completed, initiation of Phase II
SEL120/CDK8	AML/HR-MDS					LEUKEMIA & LYMPHOMA SOCIETY	Phase I data (2021)
	NEW INDICATIONS						

DISCOVERY & PRECLINICAL PROJECTS

IMMUNOONCOLOGY & IMMUNOMETABOLISM

PROGRAM / TARGET NAME	INDICATION	DISCOVERY & PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER	ANTICIPATED MILESTONES
A2A/B	SOLID TUMORS						
STING	SOLID TUMORS						
HPK1	SOLID TUMORS						
NOVEL TARGETS	SOLID TUMORS						

SYNTHETIC LETHALITY

SMARCA2	SOLID TUMORS						
NOVEL TARGETS	SOLID TUMORS						

COLLABORATIONS

CANCER METABOLISM	SOLID TUMORS					MERCK	

Differentiated internally discovered small-molecule drug candidates and new programs

TARGETED THERAPIES

SEL24/MEN1703
DUAL **PIM/FLT3**
INHIBITOR
CLINICAL

SEL120
SELECTIVE
CDK8 INHIBITOR
CLINICAL

SEL24
- Partnered globally with MENARINI group
- Dual targeting for broader efficacy and durable responses in AML
- Potential for patients who relapse or are unresponsive to FLT3-selective inhibitors

SEL120
- First-in-class unique mechanism: direct cytotoxicity and eradication of leukemic stem cells as a single-agent
- Administered independently of mutational status
- Safe and effective combo with SoC and recent emerging agents

IMMUNO-ONCOLOGY

DUAL ADENOSINE
A2A/A2B
ANTAGONIST
NON-GLP TOXICOLOGY

SMALL MOLECULE
SYSTEMIC
STING AGONIST
LATE LEAD OPTIMIZATION

SELECTIVE
HPK1 INHIBITOR
LEAD OPTIMIZATION

A2A/A2B
- The only dual A2A/A2B receptor antagonist known to efficiently overcome immunosuppression in the adenosine-rich tumor microenvironment
- Orders of magnitude more potent than known adenosine receptor antagonists in development, including AstraZeneca, Corvus

STING
- As efficacious in vivo in mice as the most potent disclosed STING agonists (GSK) while suitable for systemic as well as local delivery
- Induces long-term immunological memory
- Strong, direct binder to heterogenous STING alleles

HPK1
- Novel, emerging kinase target with unique dual potential in oncology: boosting immune response and making T cells more resistant to immunosuppressive tumor microenvironment
- First-in-class potential

SYNTHETIC LETHALITY

SMARCA4-SELECTIVE
SMARCA2
DEGRADER
HIT-TO-LEAD

SMARCA2
- Targets SWI/SNF chromatin remodeling complex implicated in multiple cancers, including NSCLC
- First-in-class potential
- Most selective disclosed SMARCA2 with confirmed synthetically lethal phenotype
- Unique allosteric ATPase inhibitors with PROTAC approach

OTHER S/L TARGETS
- MTAP, WRN and multiple other undisclosed targets
- Unmet indications in solid tumors

Corporate milestones 2019/2020

ACHIEVED IN 2019

- First patient dosed with SEL120 in first indications (AML and HR-MDS) – September 2019
- Completed the regulatory process of the split of Ryvu (oncology) and Selvita (drug discovery and development services) segments
- $10.5M non-dilutive grant funding received for discovery and Phase I development of a synthetic lethality program
- Two SEL120 posters at ASH:

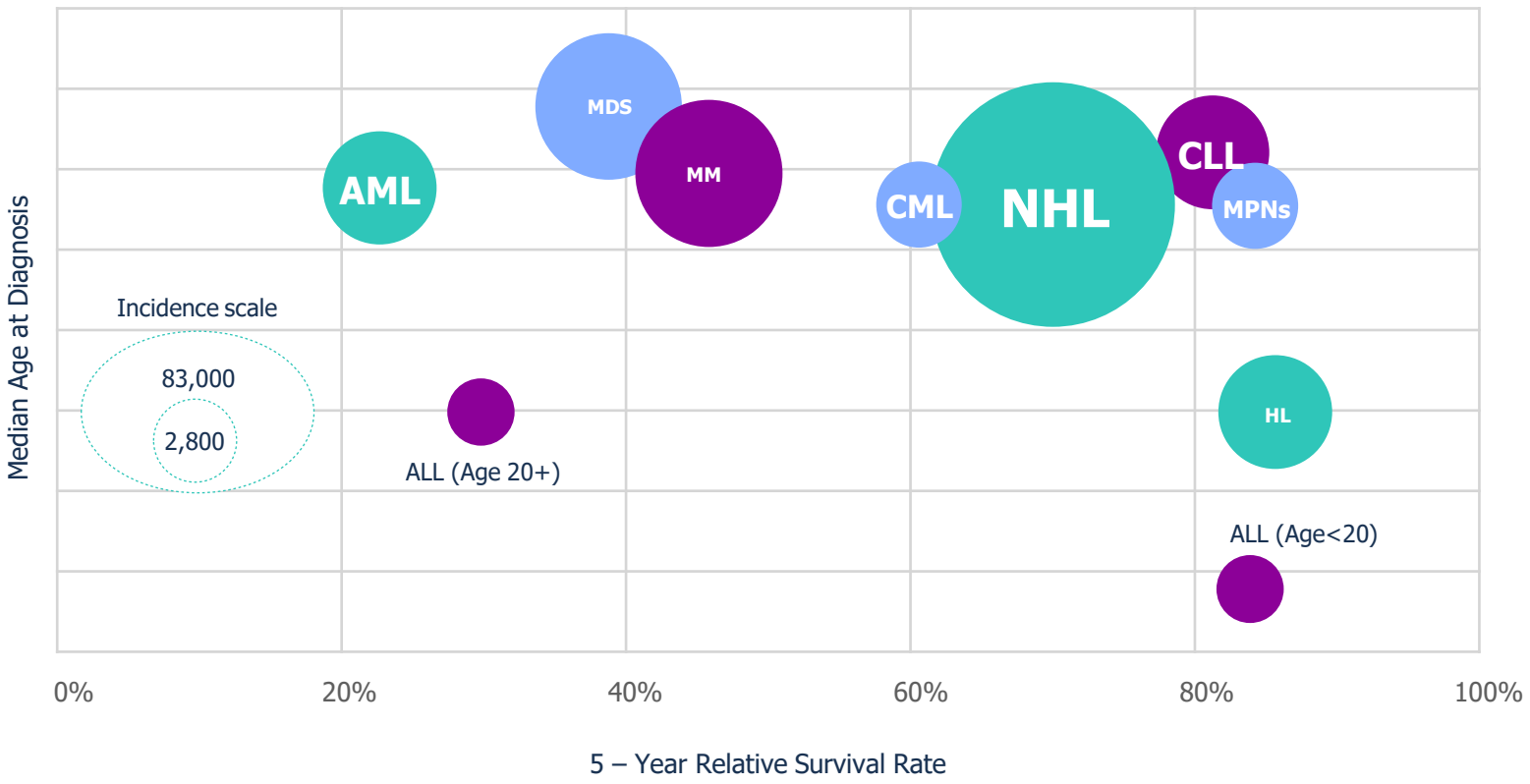
  Data from Preclinical Studies and Introduction to a Phase Ib Clinical Trial

  CDK8 Inhibitors Induce Transcriptional Reprogramming of AML Cells Associated with Differentiation
- SEL24 posters at ASCO, EHA and ASH

ACHIEVED/ANTICIPATED IN 2020

- SEL24
  - successful completion of Phase 1 Dose Escalation Study in AML announced on March 6, 2020
  - Phase 2 started
  - data from Phase 1 to be published by Menarini at an upcoming scientific conference
- SEL120
  - Orphan Drug Designation granted by the FDA on March 26, 2020
  - interim data from Phase 1b study by year-end
- Partnering deals in the pre-clinical pipeline
- One new pre-clinical candidate from internal discovery
- Differentiated data from pre-clinical programs in immunooncology, and synthetic lethality

First therapeutic area of focus: acute myeloid leukemia



AML: Lowest survival among all blood cancers

26% of patients surviving 5 years after the diagnosis

2nd Most common leukemia type in adults

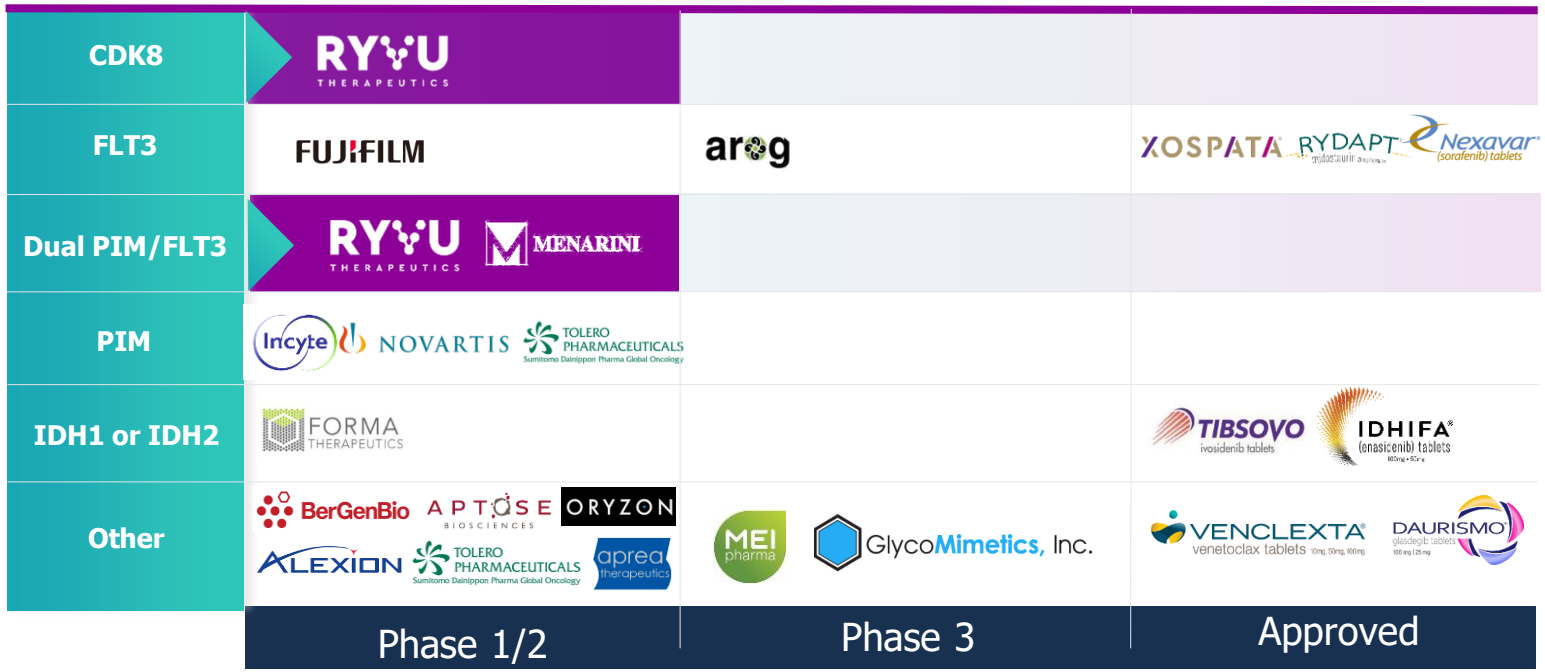
67 Median age at diagnosis (in years)
Highest incidence in the older adults
3-4 people/100 000 individuals

30% AML patients with a ITD mutation in the FMS-like tyrosine kinase 3 (FLT3) gene linked to a less favorable prognosis

Source: Leukemia & Lymphoma Society, 2018

Clinical landscape: small molecule targeted therapies for acute myeloid leukemia

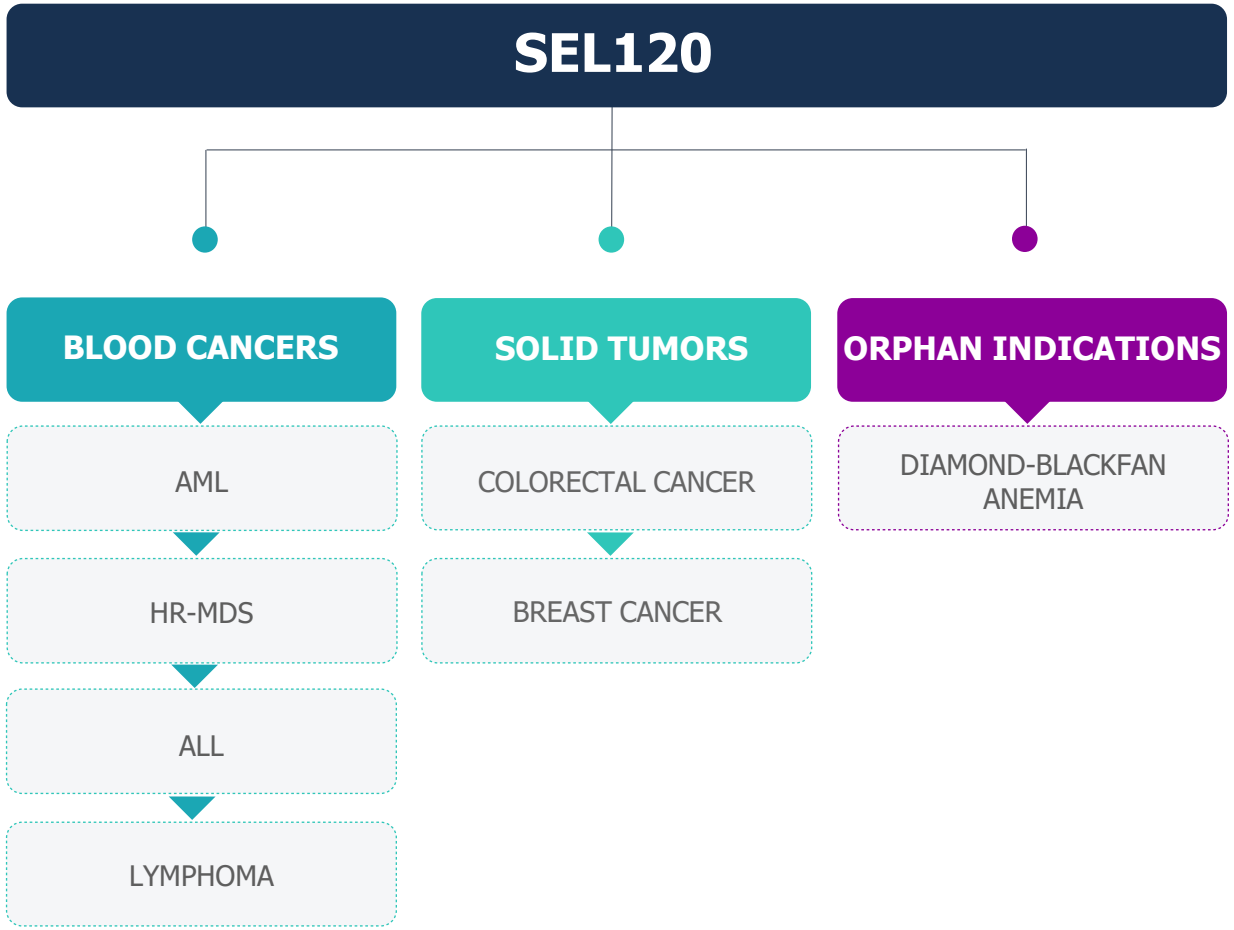
- SEL120 is the only CDK8 inhibitor actively developed in the clinic
- MEN1703/SEL24 is an unique, clinical dual PIM/FLT3 inhibitor



RYVU CLINICAL PROGRAMS FULLFIL UNMET NEEDS

- overcoming resistance to single-target mutation-specific inhibitors
- efficacy in broader patient populations
- reducing chemotherapy-based treatment regimens
- all oral regimen

SEL120: Highly selective first-in-class CDK8 inhibitor with broad potential in multiple indications



Biology of CDK8 different from other CDKs

- Different tumors responding to inhibitors
- Different toxicity profile
- Different stratification of responders and biomarkers of response

Therapeutic potential via two mechanisms of action

- Direct cytotoxicity (induction of apoptosis)
- Eradication of Leukemic Stem Cells (LSC) known to be responsible for tumor relapse in AML

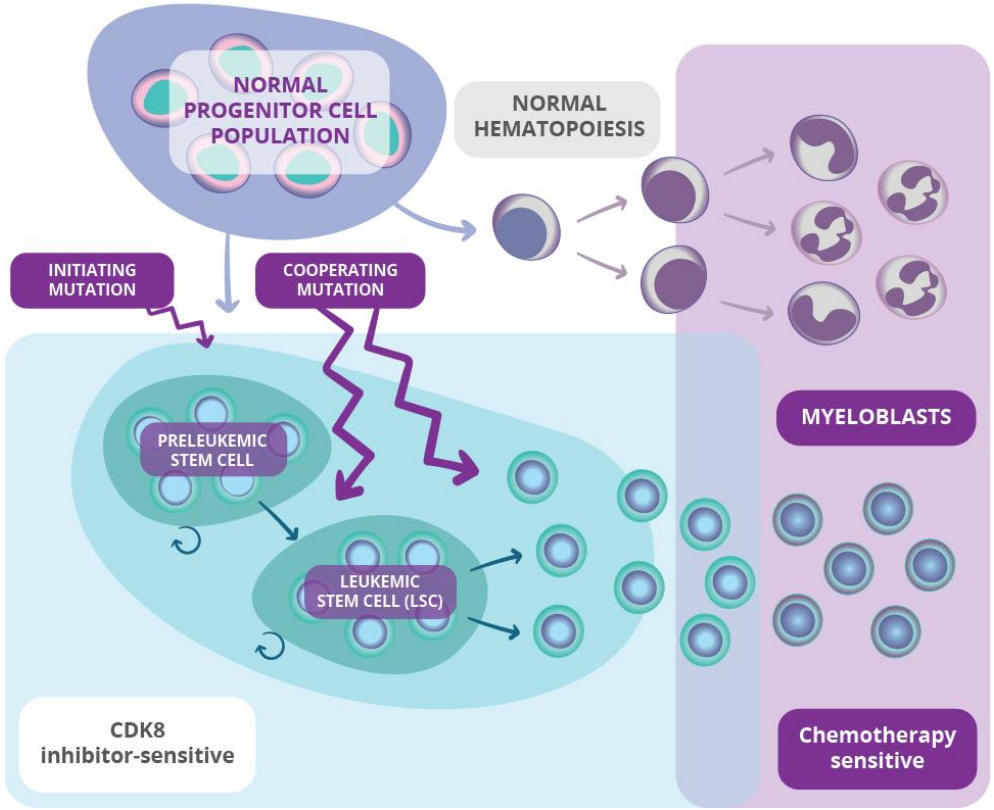
Different features compared to current treatments

- Can be given to patients independently of mutational status
- Can be safely and effectively combined with standard-of-care chemo (e.g. Ara-C), as well as with recent emerging compounds (e.g. venetoclax)

LEUKEMIA & LYMPHOMA SOCIETY

SEL120 has received $3.25 M from Leukemia & Lymphoma Society Therapy Acceleration Program (TAP)

SEL120: potential role of CDK8 in AML treatment



RATIONALE FOR CDK8 INHIBITORS IN AML

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

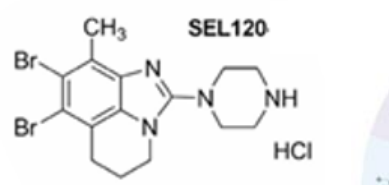
EFFICACY OF SEL120 - CDK8 INHIBITOR - IN AML

- 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

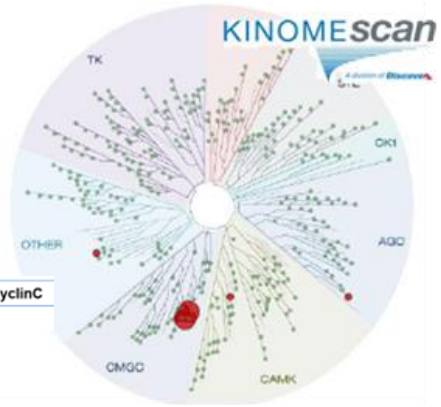
Excellent on-target activity of SEL120 in pSTAT positive AML cell models

SEL120 is a potent and selective CDK8 inhibitor

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



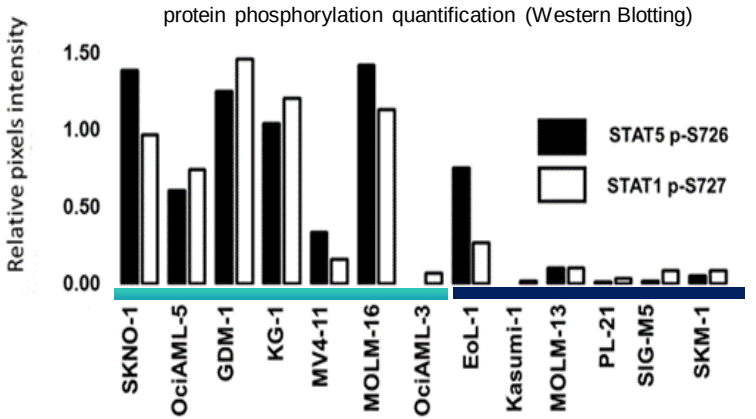
IC_{50} [nM]	CDK8/CyclinC	CDK19/CyclinC
SEL120	4.4	10.4

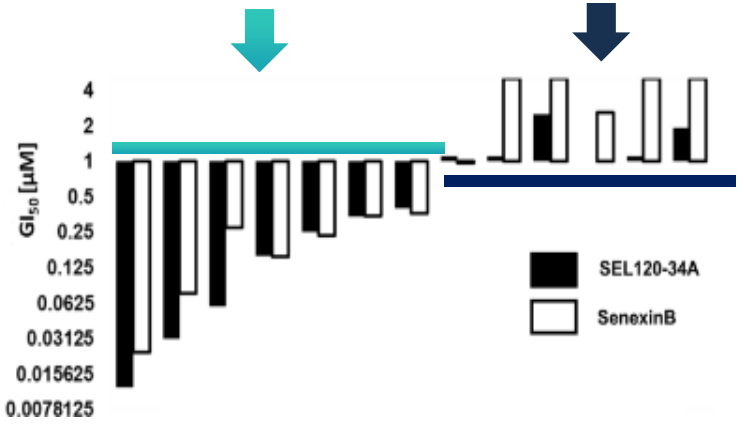


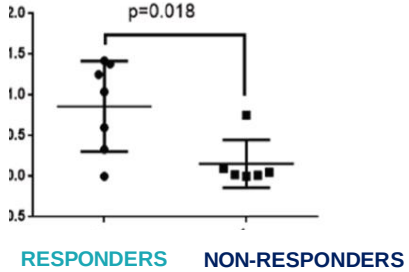
Spares CDK2, CDK4, CDK6, CDK7, CDK9, etc.

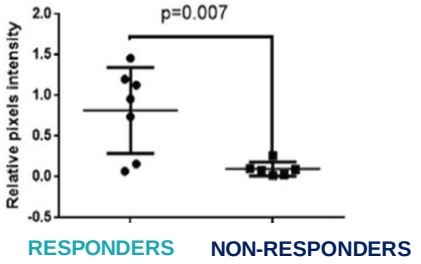
U.S. patent granted in 2017

pSTAT1/pSTAT5 levels discriminate responder/ non-responder

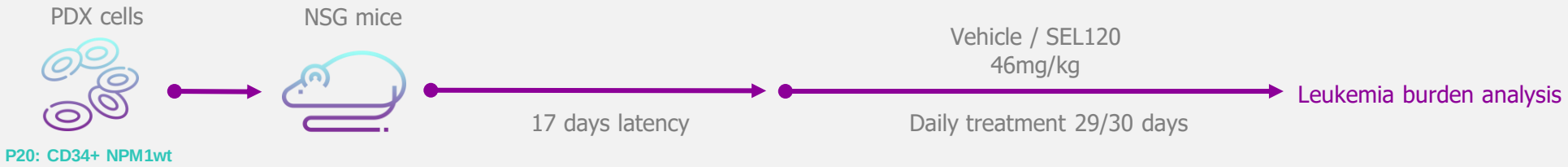




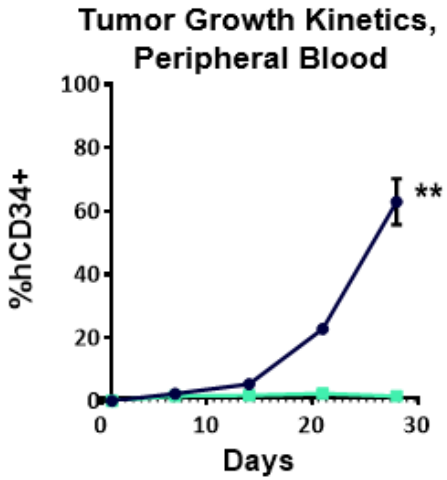


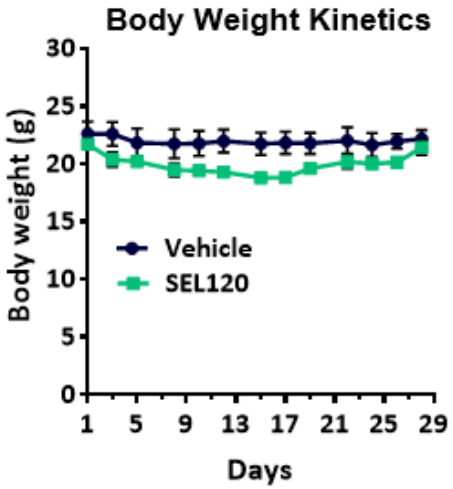


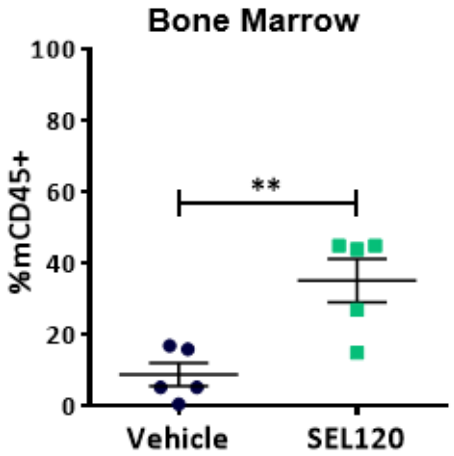
Complete regression with SEL120 in CD34+ AML patient-derived xenografts and bone marrow recovery

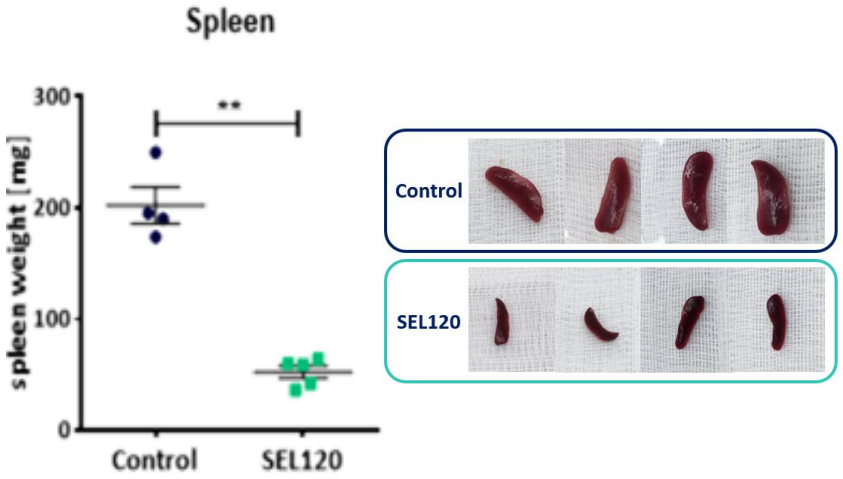


COMPLETE REGRESSION (PERIPHERAL BLOOD)	HEMATOLOGIC RECOVERY (BONE MARROW)	REDUCED SPLENOMEGALY









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

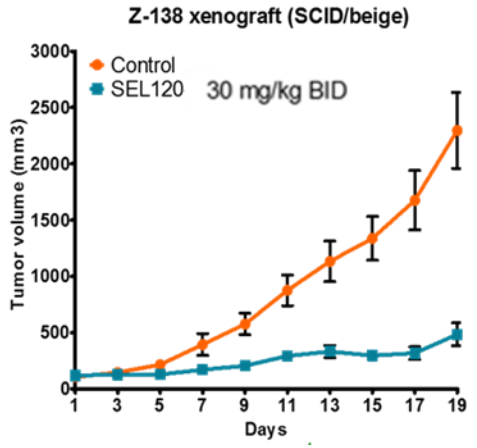
RYVU THERAPEUTICS

SEL120: Broad potential in oncology beyond AML and orphan blood disease

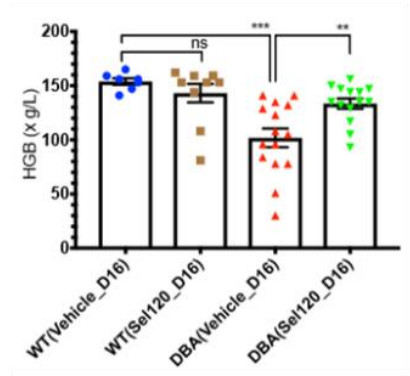
QUICK FACTS

- SEL120 treatment results in on-target efficacy in preclinical models of AML and solid tumors
- Emerging therapeutic opportunities in solid cancers (breast and prostate cancer) and orphan hematological disorders

MANTLE CELL LYMPHOMA

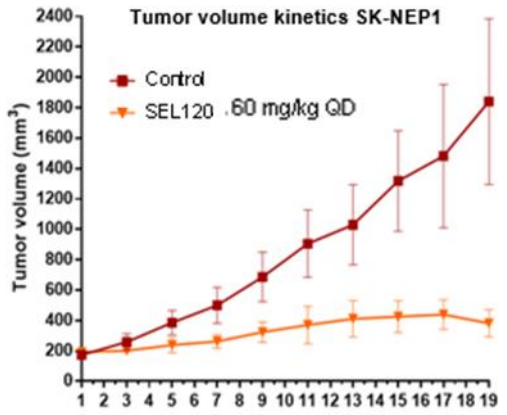


DIAMOND BLACKFAN ANEMIA*

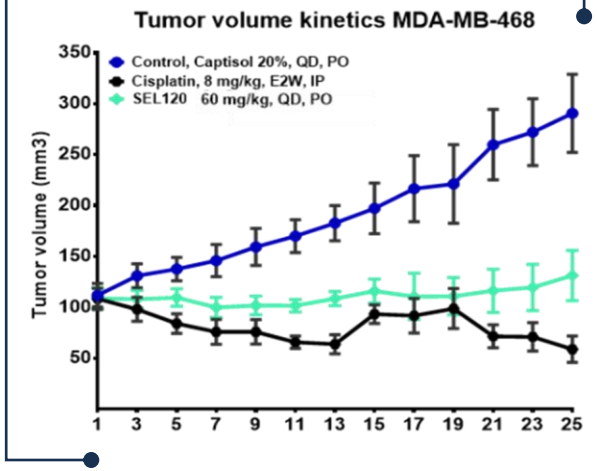


SciLifeLab CBCS CHEMICAL BIOLOGY CONSORTIUM SWEDEN

WILMS' TUMOR

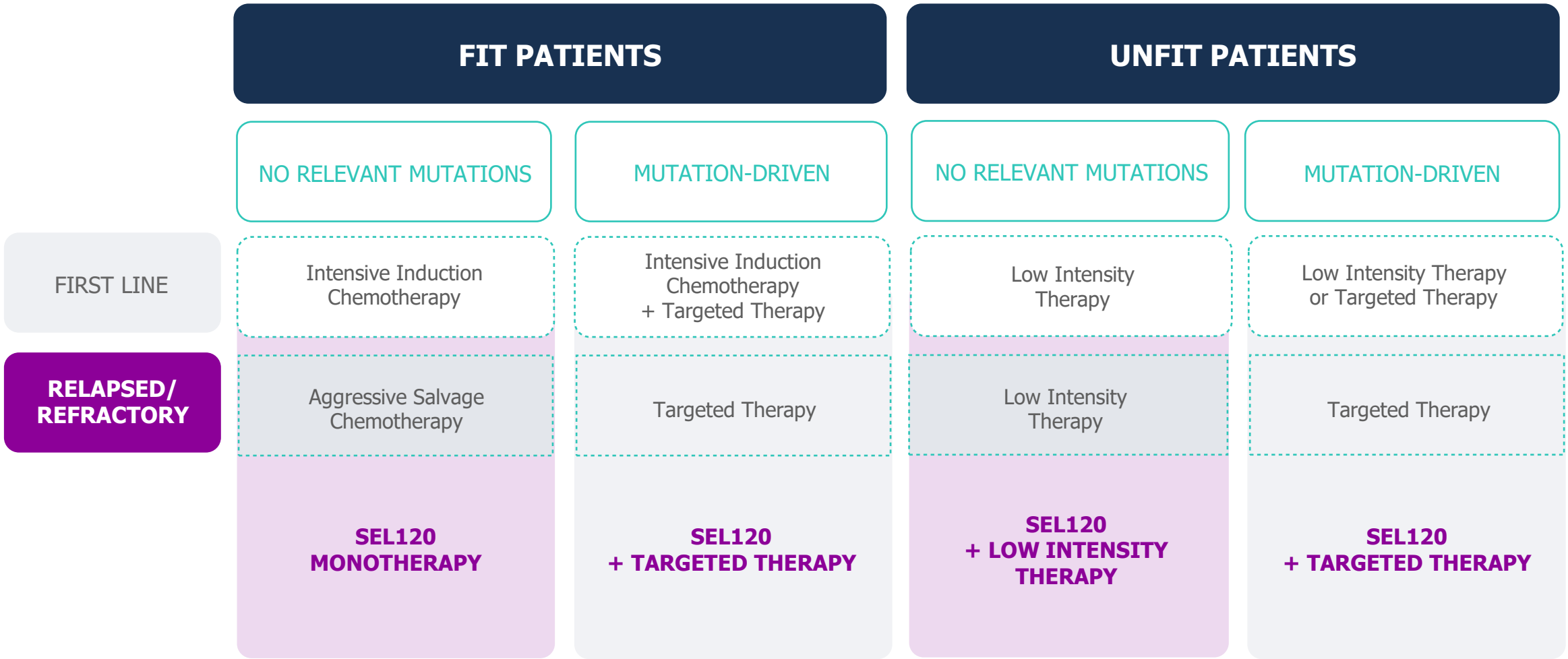


BREAST CANCER



* Small Molecule Screens Identify CDK8-Inhibitors as Candidate Diamond-Blackfan Anemia Drugs – Lund University, Jun Chen, MD, PhD – Presentation at ASH 2018

Potential medical need for SEL120 in AML patients



SEL120: Phase 1b study – first patient dosed in September 2019

Study title: A Phase 1b Study of SEL120 in Patients with Acute Myeloid Leukemia or High-Risk Myelodysplastic Syndrome

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

PRIMARY OBJECTIVES:
- To assess safety and tolerability of SEL120 in patients with relapsed/refractory AML or HR-MDS
- To determine the recommended dose of SEL120 in patients with AML or HR-MDS

SECONDARY OBJECTIVES:
- To evaluate the pharmacokinetics of SEL120 in patients with AML or HR-MDS
- To evaluate the preliminary anti-leukemic activity of SEL120 in patients with AML or HR-MDS

EXPLORATORY OBJECTIVE:
- To evaluate the pharmacodynamics of SEL120 in patients with AML or HR-MDS

Cleveland Clinic
Northside Hospital
Washington University in St. Louis School of Medicine
The University of Texas MD Anderson Cancer Center
SCRI
Tennessee Oncology

Orphan Drug Designation received from the FDA on March 27, 2020
Interim data from Phase 1b study in 2020. Final data in 2021

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

CLINICAL RATIONALE

- PIM and FLT3 are oncogenes involved in AML
- Dual targeting creates potential for broader activity, more durable responses than selective FLT3 inhibitors such as gilteritinib
- Potential for treating patients that have relapsed on selective FLT3 inhibitors - PIM kinases are largely responsible for the development of resistance to FLT3 inhibitors
- On 5th of March 2020 Menarini informed Ryvu of the successful completion of Phase 1 dose escalation study for SEL24/MEN1703 and establishing of the recommended dose for Phase 2 studies of the drug, triggering a milestone payment for Ryvu
- Phase 2 dose expansion started in USA and planned in Europe

VALUE THROUGH GLOBAL DEAL WITH MENARINI group

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

- Partnered globally with Menarini (37th largest pharma company in the world, based in Italy) in 2017
- 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

SEL24: Phase 1/2 study of SEL24/MEN1703

Study title: A Phase 1/2 Study of SEL24 in Patients With Acute Myeloid Leukemia

- Study was initiated as the first clinical trial testing a dual PIM/FLT3 inhibitor in patients with AML regardless of the FLT3 status and potentially overcome resistance to FLT3 inhibitor treatment

RECENT CONFERENCE UPDATES

55th ASCO Annual Meeting 2019
"CLI24-001: First-in-human study of SEL24/MEN1703, an oral dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia" (abstract #256995)

24th EHA Meeting 2019
"CLI24-001: First-in-human study of SEL24/MEN1703, an oral dual PIM/FLT3 kinase inhibitor, in patients with acute myeloid leukemia" (abstract #PF281)

61ST ASH Congress 2019
"CLI24-001 (DIAMOND-01): First in Human Study of SEL24/MEN1703, First in Class, Orally Available Dual PIM/FLT3 Kinase Inhibitor, in Patients with Acute Myeloid Leukemia (Poster III #3920)

AIM OF THE STUDY: determine the recommended Phase 2 dose (RP2D), the PK profile and the single agent activity in R/R or newly diagnosed AML patients

PLANS:

- Menarini will publish study results at an upcoming scientific conference
- Cohort expansion at the recommended Phase 2 dose (RP2D) to confirm the safety profile and assess drug efficacy starting at multiple clinical sites in the U.S. in Q2
- Expansion in Europe in 2020

the MENARINI group

Study locations

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

NORTHSIDE HOSPITAL

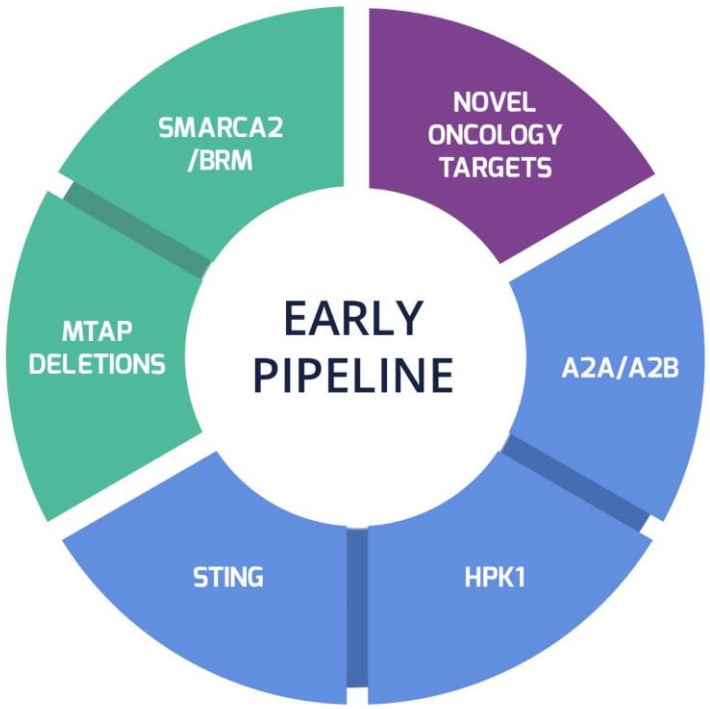
FRED HUTCH CURES START HERE®

Cleveland Clinic

VANDERBILT-INGRAM CANCER CENTER

Broad early discovery pipeline addressing major cancer-related molecular pathways

FOCUS ON NOVEL TARGETS THAT LEVERAGE IN-HOUSE EXPERTISE

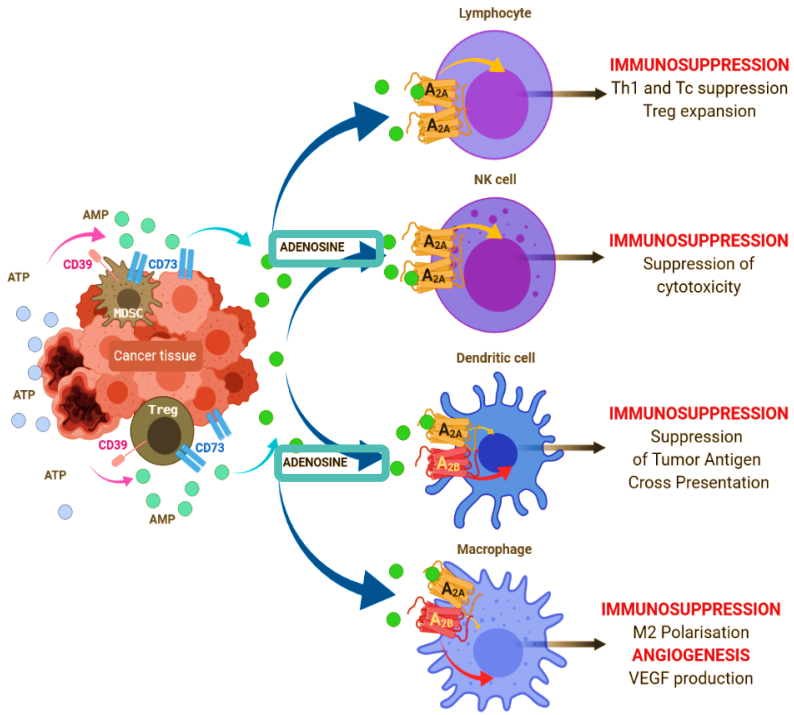


- Synthetic lethality: potential pre-clinical candidates in 2021
- Immunoncology & immunometabolism: two potential initiation of IND-enabling studies in 2020
- Novel targets

- Novel targets and attractive fast follower programs
- Deep expertise focused on novel immunokinases, helicases, ATPases
- Challenging scaffold proteins
- Excellent know how from hit ID to clinical candidate
- Strong medicinal chemistry division
- Discovery engine to generate one new clinical candidate per year

Ryvu develops dual A2A/A2B adenosine receptor antagonists

Dual targeting of A_{2A}/A_{2B} should result in enhanced immunostimulatory responses



Adenosine is a potent and widespread immunosuppressive factor in TME that hampers the antitumor activity of all types of immune cells.

STATUS	**PRECLINICAL DEVELOPMENT (non-GLP Tox studies)**
RYVU STARTEGY	Best-in-class dual antagonist of two adenosine receptors (A2A/B) capable to restore adenosine suppressed function at high adenosine concentrations
SYNERGISTIC POTENTIAL	Synergistic potential in combination with immunotherapies (anti-PD1/PDL1, CAR-T), targeted therapies and chemotherapy
UPCOMING VALUE INFLECTION POINTS	**Current stage: non-GLP Tox studies** **IND-enabling studies in 2020**

RYVU APPROACH PROVIDES STRONG PRECLINICAL COMPETITIVE ADVANTAGE

	DUAL A2A/A2B ANTAGONIST	HIGH ADENOSINE CONCENTRATION: 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	✗	✗	✗	✗	✗

Ryvu has small molecule, direct, systemic STING agonists with confirmed antitumor efficacy in a mouse model

KEY SUCCESS FACTORS COMPETITIVE EDGE

- **Small molecule, direct STING agonists with multiple routes of administration (intravenous, subcutanous, intratumoral)**
- Antitumor efficacy after systemic administration comparable to the best clinical small molecule agonist (GSK) and outperforming the intratumoral agents (Aduro)
- Standalone agonists or antibody-drug conjugates (ADC)
- Wide range of patients may benefit: active in multiple STING haplotypes

VALUE INFLECTION POINTS MILESTONES

- **Preclinical candidate nomination for IND-enabling studies: 2020**
- Clinical development: 2021

1. **Ryvu has unique, direct small-molecule STING agonists, with a chemotype distinct from any other known agonists** with secured intellectual property

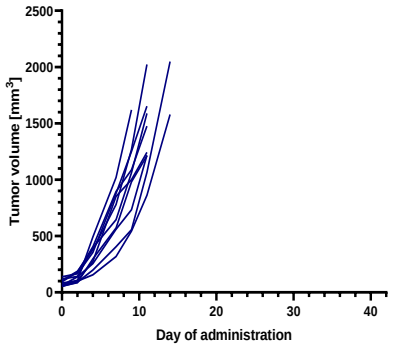
3. ▪ Iimmunostimulatory activity on antigen presenting cells) in nanomolar concentration range
   ▪ *In vitro* and *in vivo* reactivation of immunosuppressive macrophages

4. ▪ Stable remissions and immunological memory in a CT26 mouse colorectal carcinoma model

Ryvu STING agonists lead to elimination of established tumors after systemic administration on par with the most potent disclosed STING agonist (GSK)

Ryvu STING agonist leads to dose-dependent tumor regression and complete remissions (CRs) in CT26 mouse model after intravenous administration on par with reference STING agonist diABZI (GSK) currently in Phase 1 clinical trials

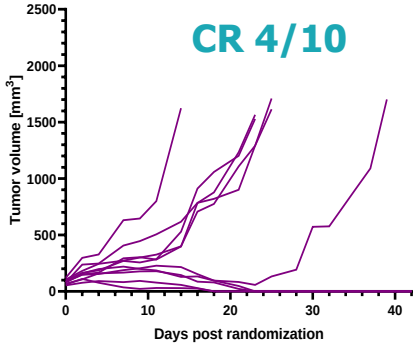
CONTROL GROUP



REFERENCE GSK diABZI

1.5 mg/kg, E3Dx3, IV

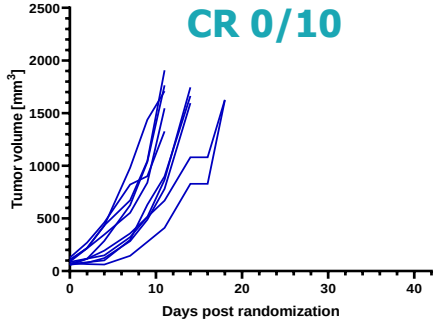
CR 4/10



RYVU STING AGONIST, INTRAVENOUS ADMINISTRATION

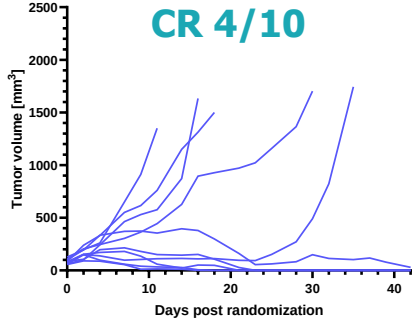
1 mg/kg, E3Dx3, IV

CR 0/10



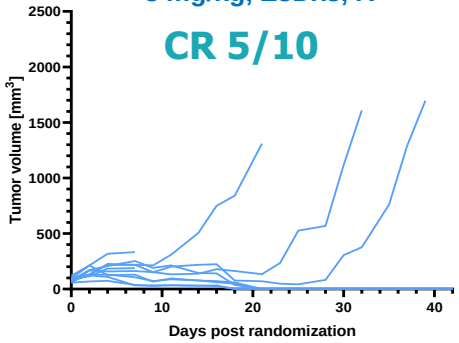
2 mg/kg, E3Dx3, IV

CR 4/10



3 mg/kg, E3Dx3, IV

CR 5/10



Ryvu develops selective SMARCA2 inhibitors and degraders targeting SMARCA4 loss of function tumors based on synthetic lethality mechanism

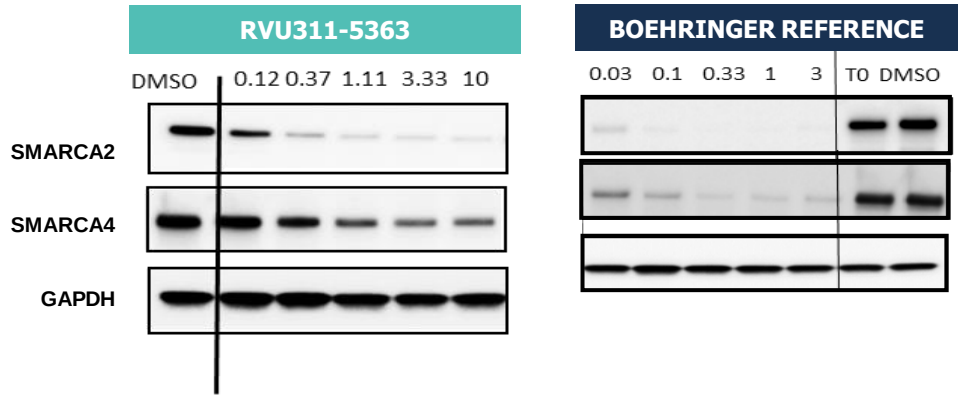
RYVU APPROACH

STATUS	**HIT TO LEAD STAGE**
RYVU STRATEGY SUCCESS FACTORS	Unique mechanism of action: Allosteric small molecule inhibitors of SMARCA2 ATPase activity with PROTACs probe based on proprietary Ryvu series
WELL DEFINED PATIENTS POPULATION	▪ 5-10% NSCLC with inactivating (LOF) and truncating mutations SMARCA4 (BRG1) ▪ Other SMARCA4 mut cancers (GI, Skin, Cervical, Bladder, Colorectal)
COMPETITIVE ADVANTAGE	First-in-class potential The only disclosed, most selective SMARCA2 over SMARCA4 ATPase PROTAC inhibitors known with confirmed synthetic lethal phenotype *in vitro*, competitors series based on bromodomain ligands
UPCOMING VALUE INFLECTION POINT	Optimized lead with *in vivo* PoC in relevant mouse models carrying mutation in SMARCA4: 2020

RYVU SMARCA2 PROTACs SELECTIVELY DEGRADE SMARCA2

SMARCA2/SMARCA4 selectivity is critical for a therapeutic window

			RVU311-5363	REFERENCE
PHYS-CHEM	MW/ clogP/ PSA		<1400/5.1/292	<1000/3.7/209
BINDING TO SMARCA2 (RECOMBINANT PROTEIN)	MST	- DNA Kd [µM]	**0.7**	**no binding (BRD domain)**
DEGRADATION	Remaining SMARCA2 after 24h		**10%**	**2%**
	Remaining SMARCA4 after 24h		**46%**	**9%**



Covid-19 impact on Ryvu Therapeutics

Clinical trials:

- Industry risk: Clinical trials in locations impacted by Covid-19 such as the US may be impacted 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 will mainly dependent on site decisions
- **As of March 30, 2020 five SEL120 sites confirmed continued patient enrollment, one site suspended enrollment**

Laboratory operations:

- Ryvu introduced the first risk Covid-19 management steps already in February and reduced laboratory operations to critical experiments from March 30
- Most non-lab associates work from home
- Planned full restart of laboratory activities on April 12 depending on the situation in Krakow/Poland
- Thanks to the early government intervention (March 12) Poland is so far one of the countries least impacted by Covid-19 in Europe (as of March 30 <300 cases and <10 deaths per day, 16% average daily case dynamic between March 24 and March 31, trending lower)
- Outsourcing – limited capacity at some European CROs. Key providers less impacted. Risk-management with Asian CROs.

Other industry specific risks

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

Currency risk

- $ (US. dollar) has gained 8% vs PLN (Polish zloty) since January 1, 2020

Ryvu investment highlights and near term milestones

- Developing **novel small molecule therapies** that address **emerging targets in oncology**
- Targeting **kinases, synthetic lethality, immune response and immuno-metabolism** pathways
- Validation from strategic **collaborations**
- **Partnership options** for early stage candidates
- **Limited cash burn** thanks to non-dilutive grants and cost-efficient discovery platform, significant resources located in Poland
- **Potential milestone payments** and royalties from partnered programs
- Steady **generation of differentiated candidates**

Contact data

Pawel Przewiezlikowski
Chief Executive Officer
pawel.przewiezlikowski@ryvu.com

Ryvu Therapeutics S.A.
www.ryvu.com
ryvu@ryvu.com

Appendix

Management team with strong clinical and shareholder value creation track record

PAWEL PRZEWIEZLIKOWSKI, MSc, MBA

CEO and Founder

SETAREH SHAMSILI M.D., Ph.D.

CMO

KRZYSZTOF BRZOZKA Ph.D., MBA

CSO

PETER LITTLEWOOD Ph.D.

Director of DMPK

LUIGI STASI Ph.D.

Director of Chemistry

MONIKA DOBRZANSKA Ph.D.

Portfolio Management Director

MATEUSZ NOWAK Ph.D., MBA

Director of Early
Discovery & Innovation

TOMASZ RZYMSKI Ph.D., MBA

Director of Biology

KAMIL SITARZ Ph.D.

Director of R&D Operations

TOMASZ NOCUN, MSc, MBA

Director of Research Financing

Supervisory Board assembling industry veterans and financing experts

RAFAL CHWAST
MSc

Board Member and CFO at the New Style group.

Past: VP and CFO at Comarch, responsible for financial supervision of group's subsidiaries, raising capital through the stock exchange. CEO of the Association of Stock Exchange Issuers, and member of the Capital Market Council.

AXEL GLASMACHER
M.D.

Independent consultant.
Past: Senior VP and Head of the Clinical R&D Hematology Oncology at Celgene. Worked on: Revlimid®, Idhifa® and Vidaza®.

Research and teaching at University Hospital in Bonn.

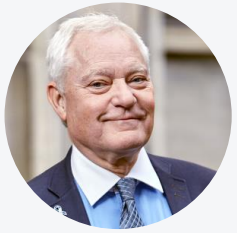
BOD: 4D Pharma. Medical advisory: Oncopeptides.

COLIN GODDARD
Ph.D.

Chairman and CEO of BlinkBio.
Past: CEO of OSI Pharmaceuticals for 12 years: Tarceva ® development & launch, through to $4 billion acquisition by Astellas.

BOD: Mission Therapeutics and Endocyte.

PhD in cancer chemotherapy and post-doc at the NCI, Bethesda, MD.



JARL ULF JUNGNELIUS
M.D.

CMO at NOXXON Pharma.
Past: VP of Clinical Research and Development, Solid Tumors at Celgene. Contributed to Abraxane®, Alimta®, Gemzar® and Revlimid®.

BOD: Isofol Medical, Biovica, Oncopeptides, Monocl.
M.D. from Karolinska Institutet.

PIOTR ROMANOWSKI
M.D. Ph.D., CHAIRMAN

Partner at PwC

Past; Partner at McKinsey & Company and Board Member in the banking sector

MD, PhD (cancer genetics) from Medical Academy of Gdansk, Poland; PhD (cell cycle regulation) from University of Cambridge, UK.

THOMAS TURALSKI

Portfolio Manager leading investment team at Revidea Ventures.

Past: 11yrs at Perceptive Advisors responsible e.g. for investment in Myogen, Morphosys and Pharmacyclics and Acerta Pharma, where he was a member of the founding team as well as BOD.

Graduate of Columbia University.

TADEUSZ WESOLOWSKI
Ph.D.

Highly experienced investor and manager.

Past: Founder and CEO of PROSPER, for more than 17 years one of the leading pharmaceutical distributors in Poland.

BOD: Neuca, wholesale distributor of pharmaceuticals.

Nowy Styl Group
COMARCH
Celgene
oncopeptides
(osi) pharmaceuticals
BlinkBio
Celgene
Takeda
Pfizer
Lilly
pwc
McKinsey & Company
revidea ventures
PERCEPTIVE ADVISORS
AcertaPharma
NEUCA

Scientific advisory board assembles expertise across hematology, oncology and precision medicine

GREG NOWAKOWSKI M.D.

Mayo Clinic

HEINZ-JOSEF LENZ M.D.

University of Southern California

RALF-DIETER HOFHEINZ M.D.

Mannheim University Hospital

MICHAEL SAVONA M.D.

Vanderbilt University

CEZARY SZCZYLIK M.D., Ph.D.

ECZ Otwock, Poland

ALWIN KRAEMER M.D.

University of Heidelberg

PRZEMYSLAW JUSZCZYNSKI M.D., Ph.D.

Warsaw Institute of Hematology & Transfusion

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Roche

morphosys

CLINICAL COLLABORATIONS OR ASSOCIATIONS

EMD SERONO

Genentech

Bristol-Myers Squibb

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Roche

AMGEN

MERCK

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Incyte

Baxalta

GILEAD

Celgene

CLINICAL COLLABORATIONS OR ASSOCIATIONS

gsk

Pfizer

NOVARTIS

astellas

CLINICAL COLLABORATIONS OR ASSOCIATIONS

Roche

Danish Cancer Society

CLINICAL COLLABORATIONS OR ASSOCIATIONS

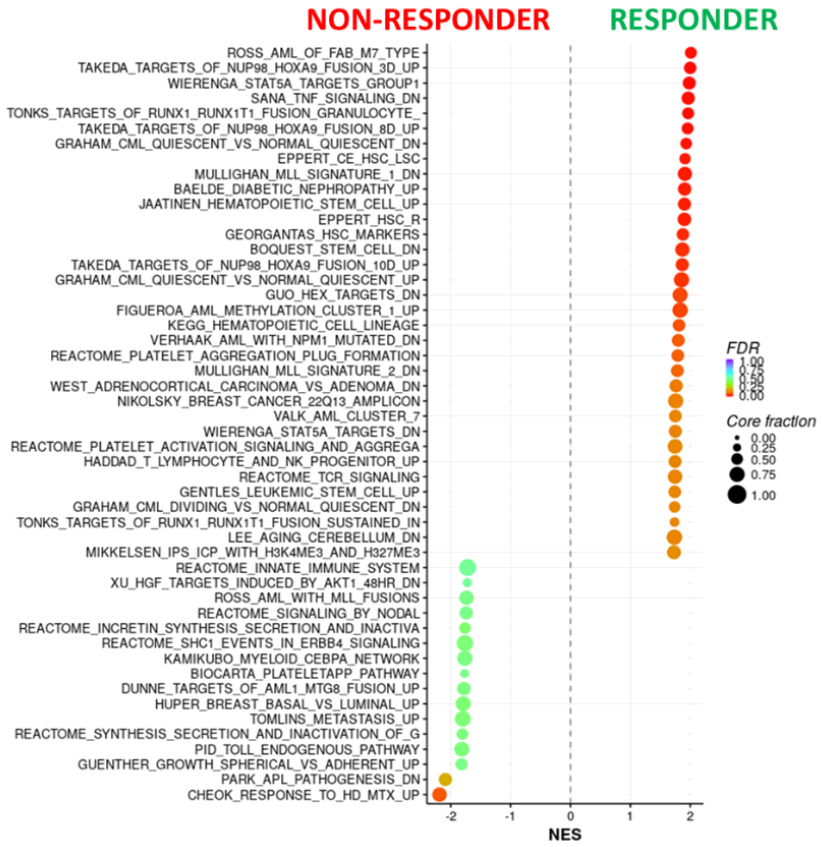
DANA-FARBER CANCER INSTITUTE

AMERICAN SOCIETY OF HEMATOLOGY

AACR

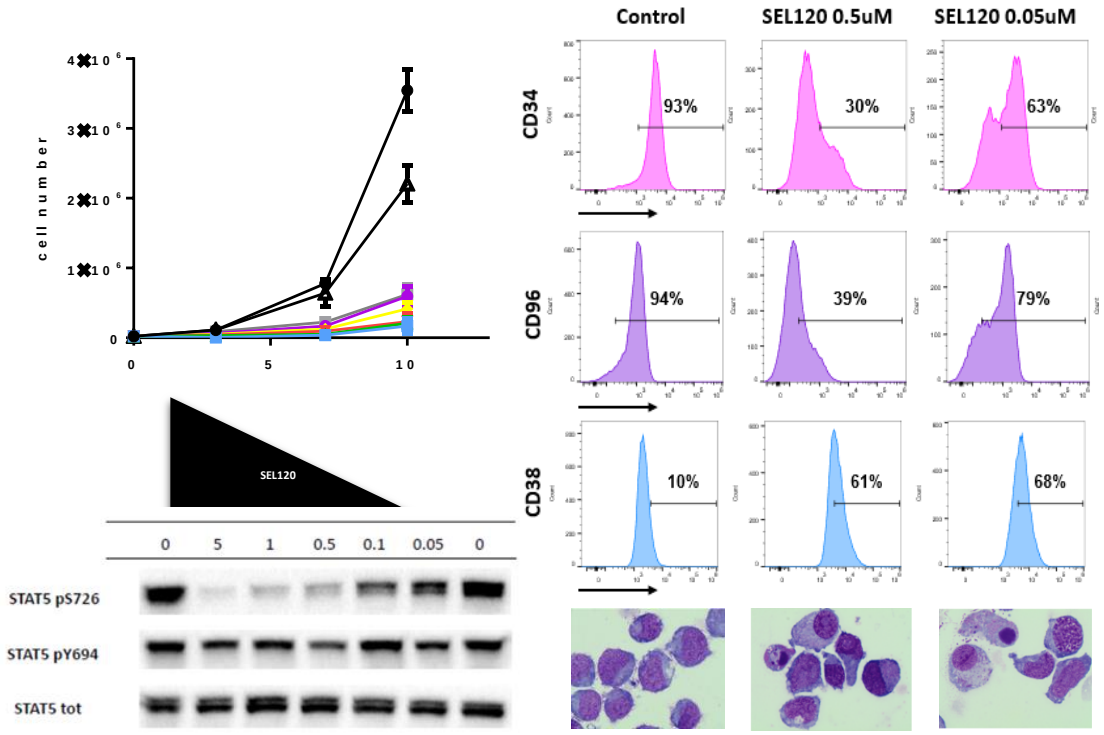
SEL120 specifically targets STAT5+/CD34+ AML cells and induces differentiation in leukemic stem cells

STAT5 AND LSC GENE SIGNATURES DISCRIMINATE RESPONDER/NON-RESPONDERS



EFFICACY AND LINEAGE COMMITMENT IN CD34+ AML LSC

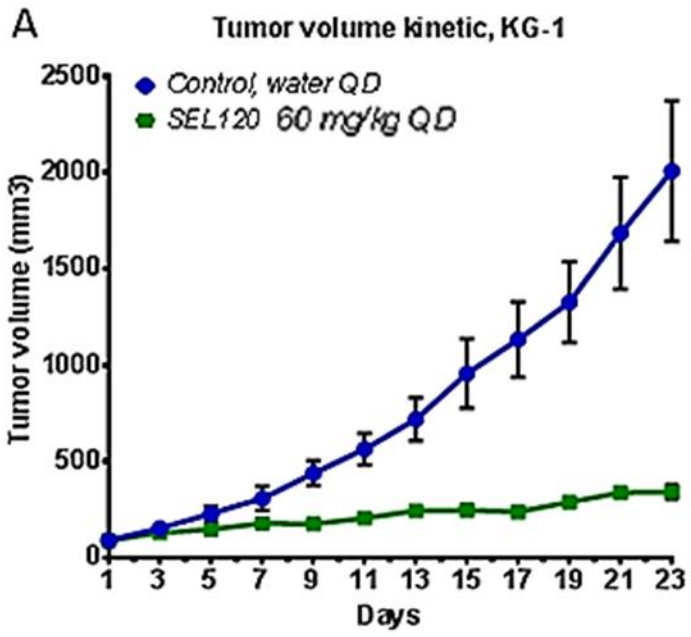
AML LSC model (CD34+, CD96+, CD123+, CD38-)



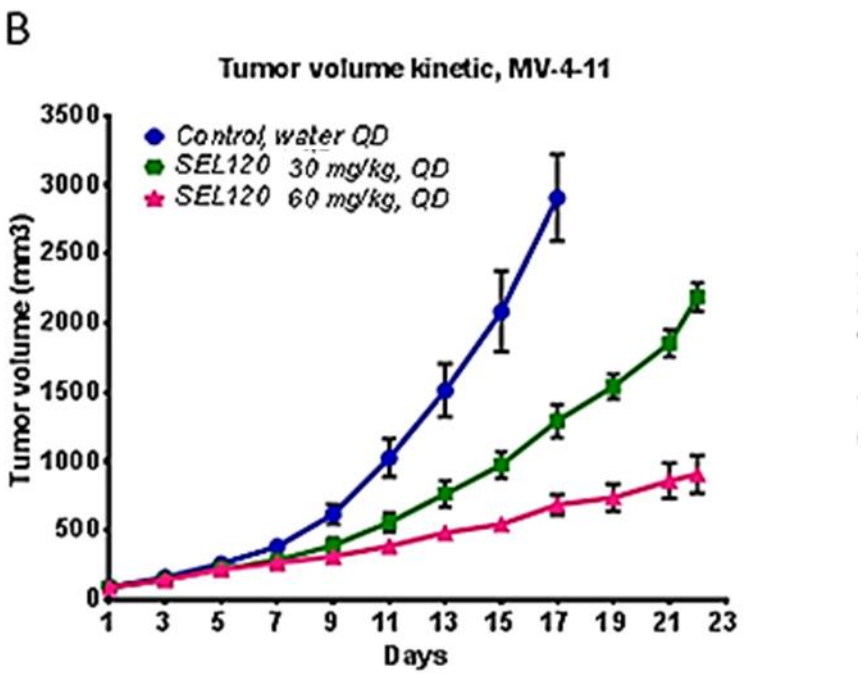
Single agent efficacy of SEL120 *in vivo*

- Favorable PK enables once daily oral administration or less frequently
- Efficacy *in vivo* correlates with inhibition of specific CDK8 biomarkers pSTAT1/STAT5

SINGLE AGENT EFFICACY IN CD34+ AND $_{p}$STAT5+ AML MODELS *IN VIVO*



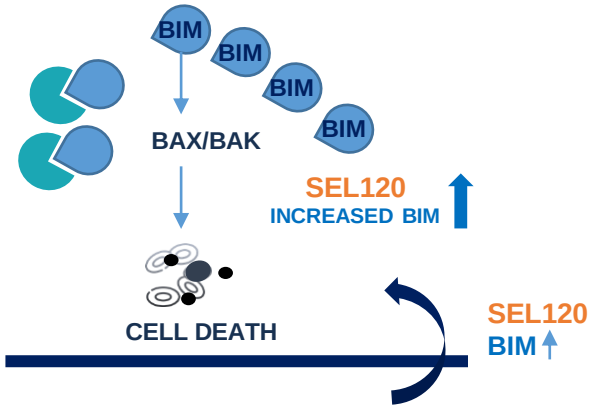
SINGLE AGENT EFFICACY IN CD34- AND $_{p}$STAT5+ AML MODELS *IN VIVO*



In vitro synergy of SEL120 in combination with Venetoclax (ABT-199)

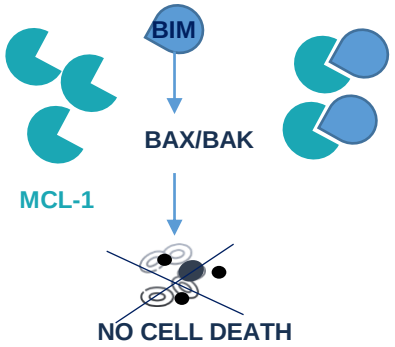
VENETOCLAX SENSITIVE

MCL-1 ↓ **NOT ENOUGH MCL-1** TO SEQUESTER ALL THE RELEASED BIM

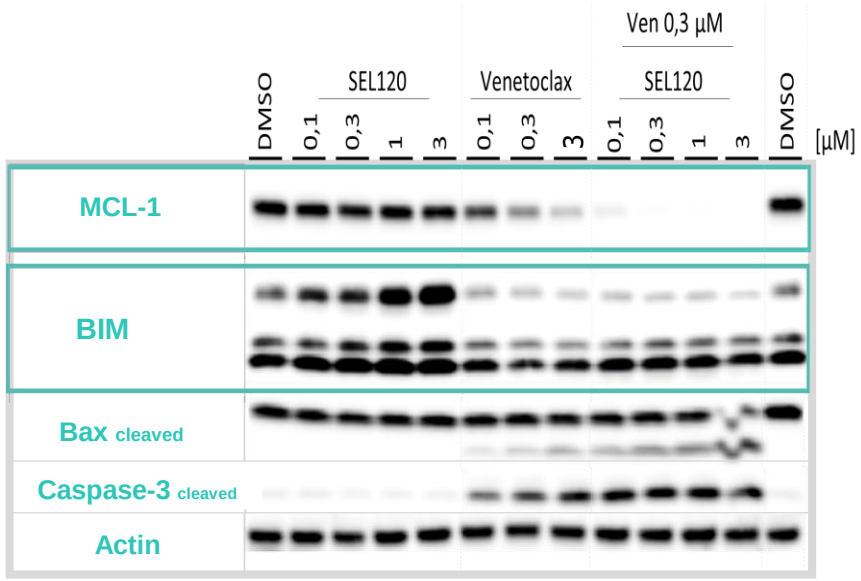


VENETOCLAX RESISTANT

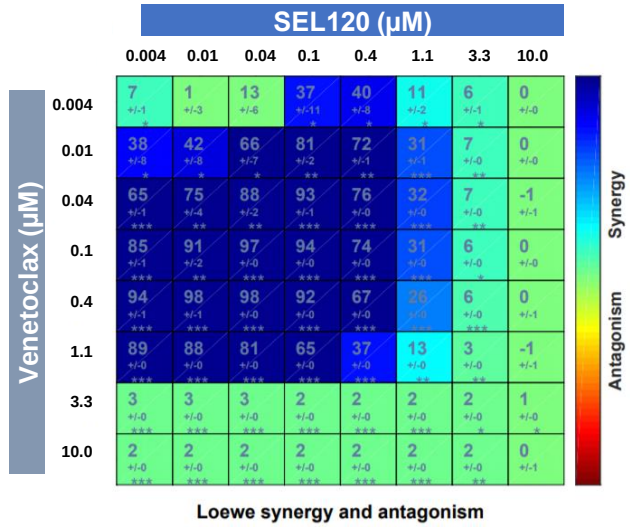
MCL-1 ↑ MCL-1 SEQUESTERS ALL THE RELEASED BIM



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

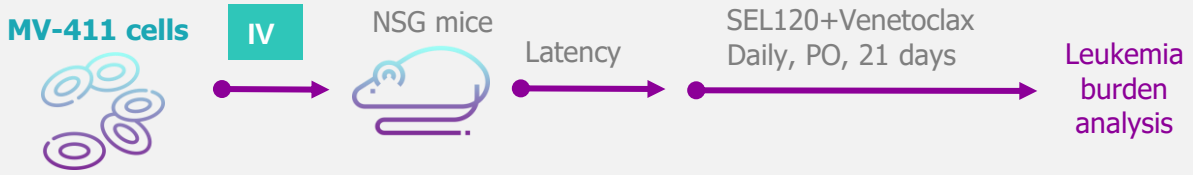


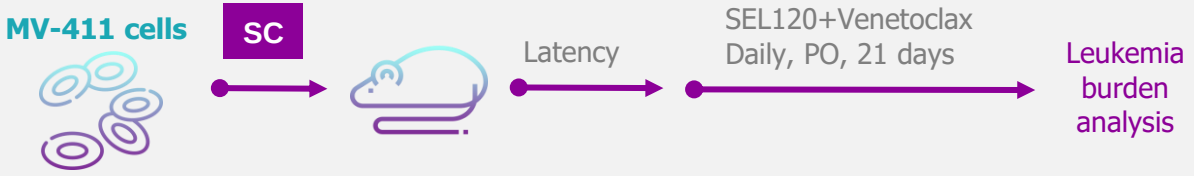
Compelling potential for SEL120 in combination with Venetoclax at low concentrations



In vivo synergy of SEL120 in combination with Venetoclax (ABT-199)

AML regression and bone marrow recovery *in vivo*

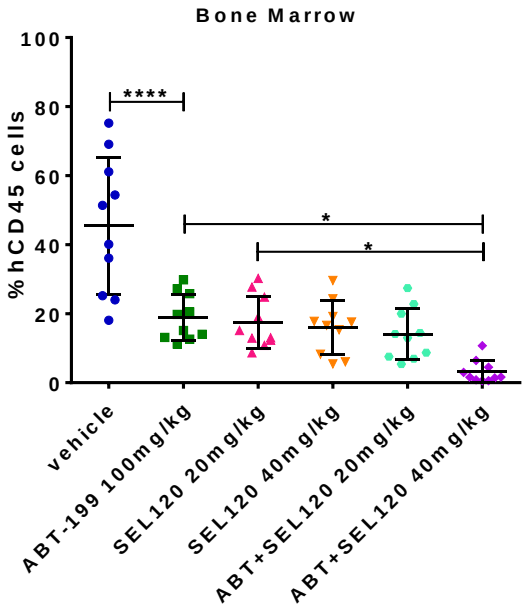


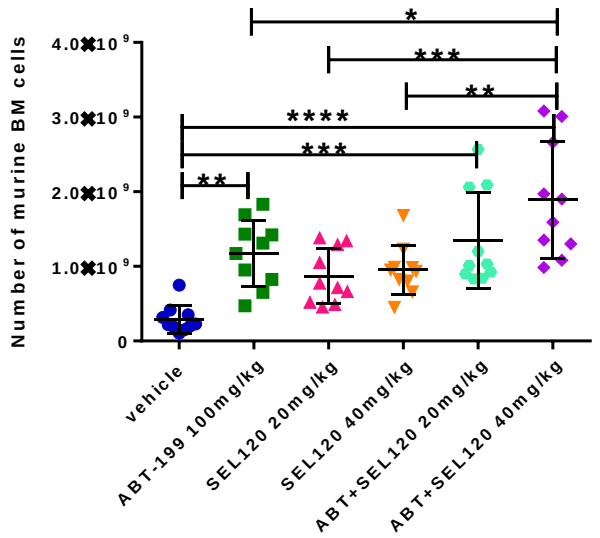


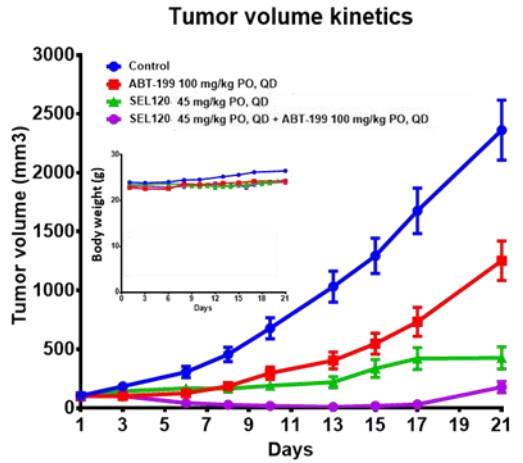
COMPLETE REGRESSION

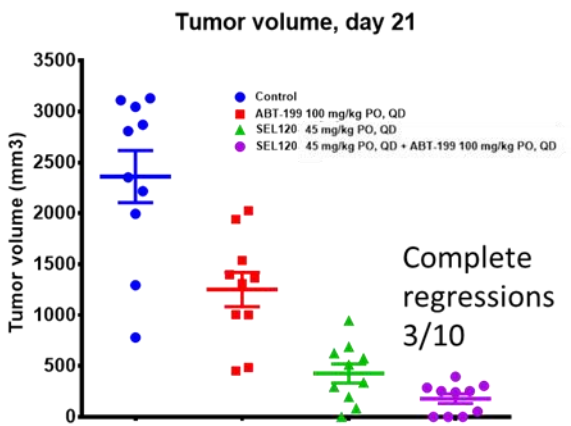
HEMATOLOGIC RECOVERY (BONE MARROW)

TUMOR GROWTH INHIBITION AND COMPLETE REGRESSIONS









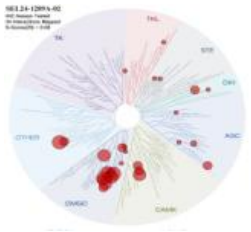
Simultaneously targeting FLT3 and PIM may provide improved efficacy and durability over narrowly targeted agents

SEL24/MEN1703 VS PIM INHIBITOR AZD1208 AND FLT3 INHIBITOR QUIZARTINIB IN AML CELL LINES

SEL24/MEN1703

Dual PIM/FLT3 inhibitor

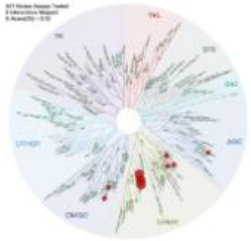
RYVU THERAPEUTICS MENARINI



AZD1208(*)

Selective PIM inhibitor

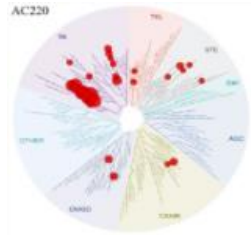
AstraZeneca

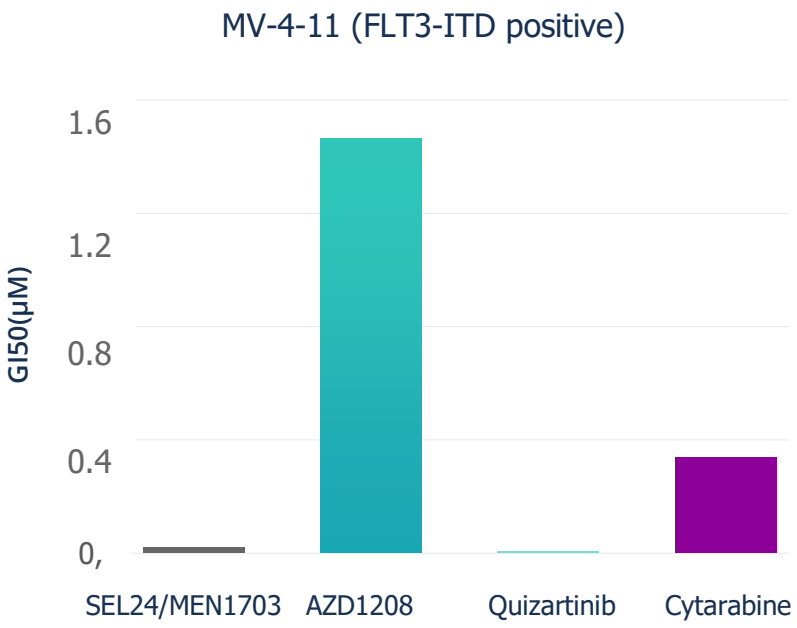


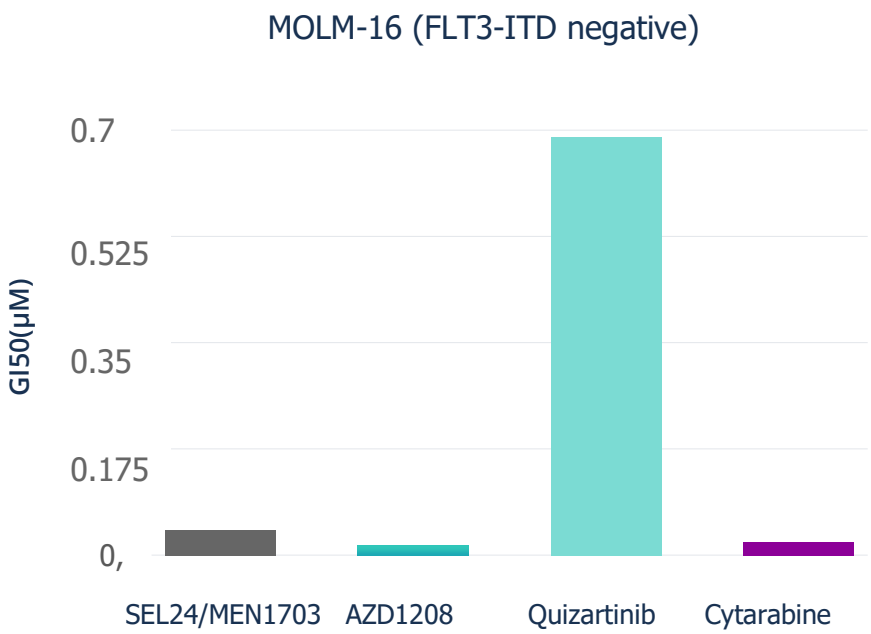
Quizartinib

Selective FLT3 inhibitor

Daiichi-Sankyo



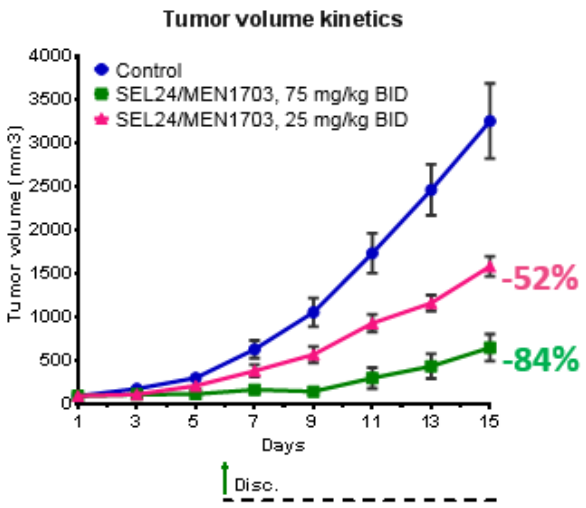




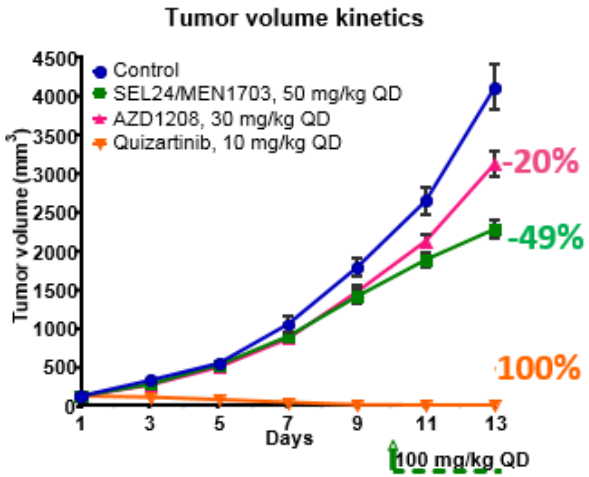
Potent efficacy of oral SEL24/MEN1703 in models of multiple AML subtypes

FLT3-ITD POSITIVE

MV-4-11

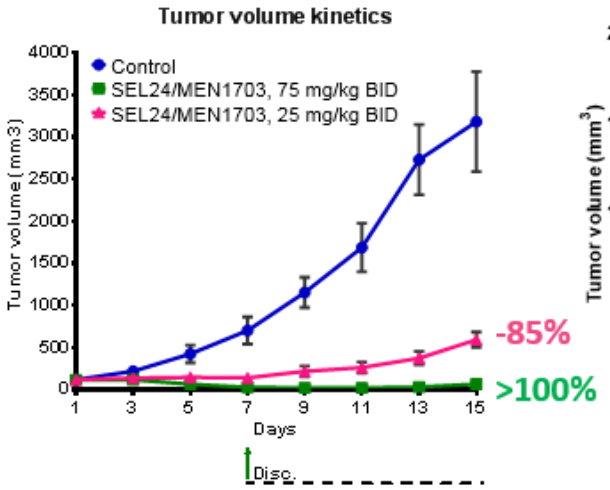


MOLM-13

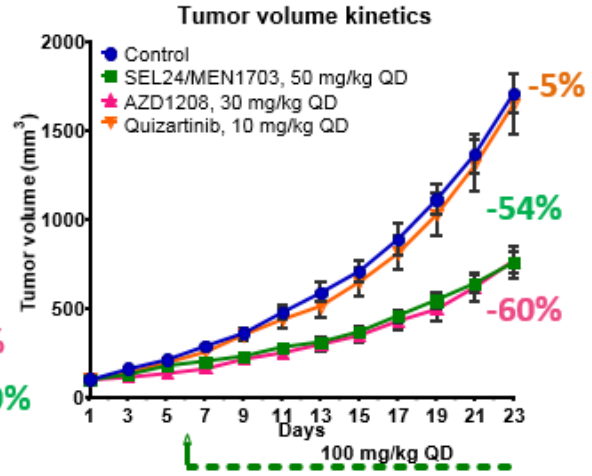


FLT3-ITD NEGATIVE

MOLM-16



KG-1



BID – twice a day, QD –once a day

RVU330 - best-in-class dual A2A/A2B antagonist

KEY SUCCESS FACTORS COMPETITIVE ADVANTAGE

- Best-in-class potential
  The only dual A2A/A2B antagonist efficient in high adenosine tumor environment
- Dual mode of action manifesting in activity in all immune cell types, unlike competitors compounds, providing potentially more pronounced anti-tumor effect
- May be efficacious in patients in which „1st wave" A2A (repositioned PD drugs) do not work

PLANNED INFLECTION POINTS AND MILESTONES

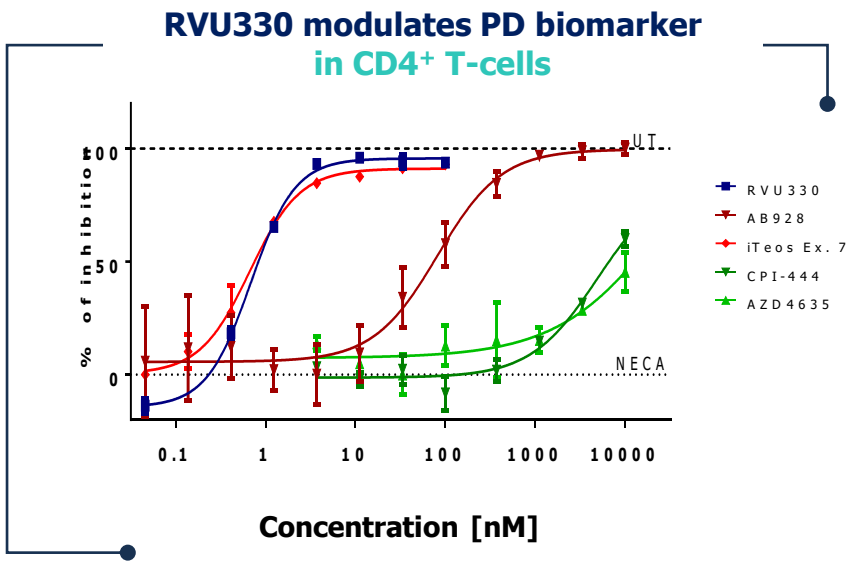
- **Nomination of preclinical candidate and initiation of IND enabling studies: H1 2020**
- **Initiation of phase I clinical trials: 2021**

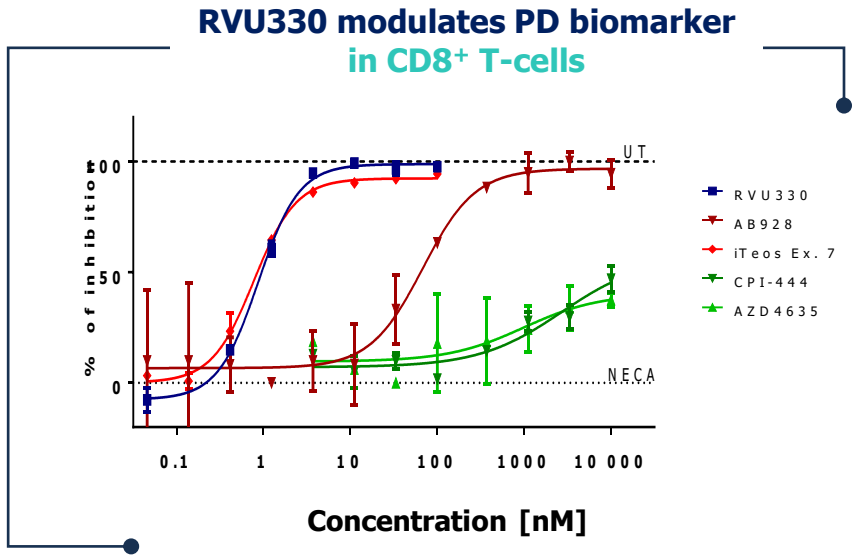
1 **Ryvu developed most potent, known A2A/A2B antagonist** with nanomolar activity *in vitro* in functional immune assays outperforming competitors

2 **Confirmed immunostimulatory mode of action**

- Induction of antitumor cytokine production by T cells and dendritic cells – stimulation of both innate and adaptive immunity
- Macrophages repolarization
- NK cells mobilization
- **Exceptionally potent, superior to clinical competitors, blockade of CREB** phosphorylation in human whole blood assay – clinical biomarker used by most of competitors (Arcus, Corvus)

RVU330 efficiently modulates pCREB (main PD clinical biomarker used by competitors) in *in vitro* human whole blood assay



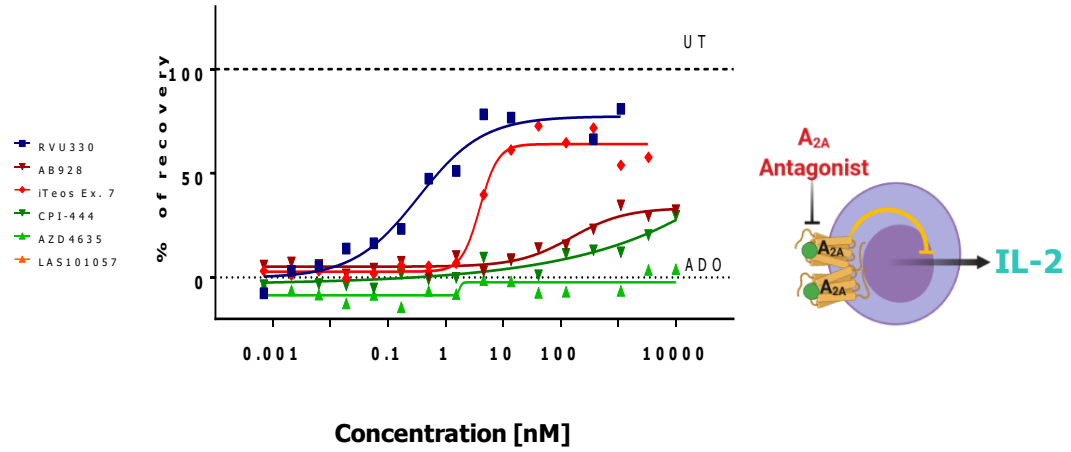


	AZD4635	CPI-444	AB928	Example 7	RVU330
pCREB WBA CD4+ T cells EC_{50} [nM]	1186 ±860	7798 ± 1734	182 ± 140	1.1 ± 0.6	1.6 ± 0.9
pCREB WBA CD8+ T cells EC_{50} [nM]	> 10 000	> 10 000	83.7 ± 0.1	2.4 ± 2.3	2.2 ± 1.4

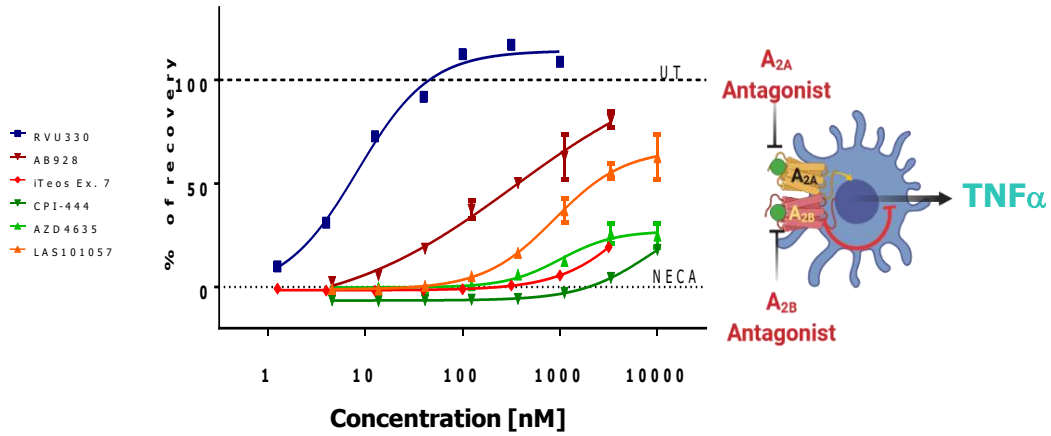
37

RVU330 A2A/B antagonists outperform competitors in *in vitro* activation of immune cells at high adenosine concentrations

RVU330 restores functional activity CD4⁺ T cells that is suppressed by high adenosine concentration (IL-2 production)



RVU330 reactivates dendritic cells (moDC) suppressed by high adenosine concentration (TNFα production)

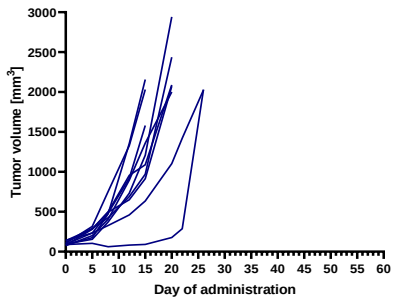


AstraZeneca CORVUS PHARMACEUTICALS ARCUS BIOSCIENCES iTeos Therapeutics RYVU

	AZD4635	CPI-444	AB928	Example 7	RVU330
TNFa moDCS - EC_{50} [nM]	>10 000	>10 000	699 ± 144	> 3 000	13 ± 5
IL-2 $CD4^+$ CELLS - EC_{50} [nM]	>10 000	>10 000	203 ± 97	4 ± 0.1	0.4 ± 0.2

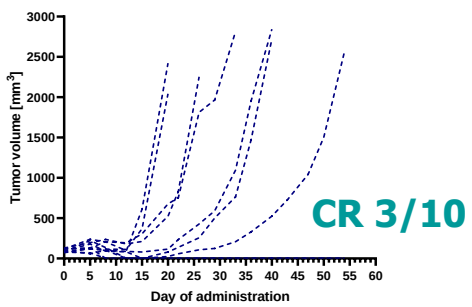
Ryvu STING agonist outperforms antitumor efficacy of Aduro agonist and provides immunological memory in mouse CT26 colorectal carcinoma model

CONTROL GROUP



REFRENCE ADURO ADU-S100

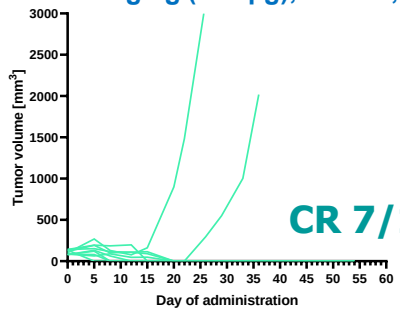
5 mg/kg (100 µg), EODx3, IT



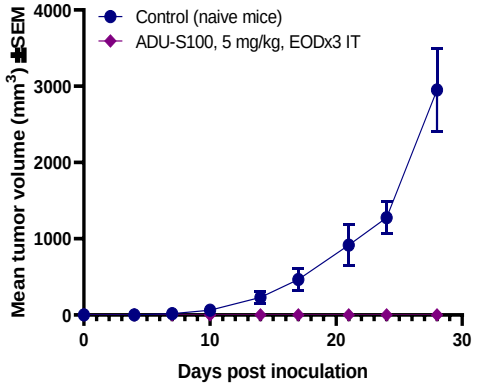
CR 3/10

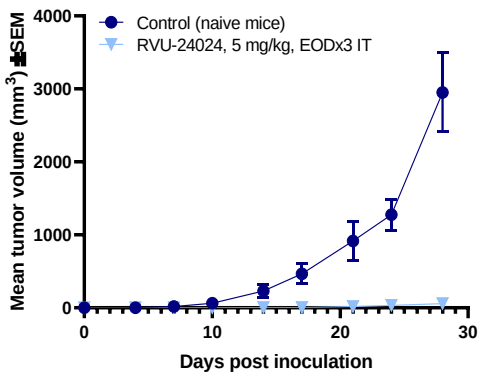
RYVU STING AGONIST

5 mg/kg (100 µg), EODx3, IT



CR 7/10





1. Subcutaneous inoculation with CT26 mouse colorectal carcinoma cells
2. **INTRATUMORAL ADMINISTRATION OF STING AGONIST**
3. **MICE WITH TUMOR REGRESSION**
4. RE-CHALLENGE Subcutaneous inoculation with CT26 mouse colorectal carcinoma cells
5. **LONG-TERM IMMUNOLOGICAL MEMORY** No tumor growth

Ryvu is developing next-generation direct STING agonists for immunotherapy of resistant tumors

STING agonists mobilize immune system sensitizing resistant tumors to therapy

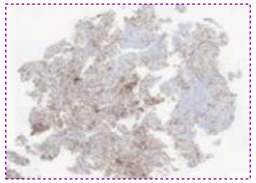
COLD, RESISTANT TUMORS

AIM: ACTIVATION OF IMMUNE RESPONSE

STING AGONISTS

HOT, INFLAMED TUMORS

AIM: OVERCOME IMMUNOSUPPRESSION



STING agonists are immune boosters inducing long-term immunological memory

STING agonists stimulate immune system facilitating tumor neoantigen presentation by dendritic cells, activation of CD8+ T cells and release of proinflammatory cytokines

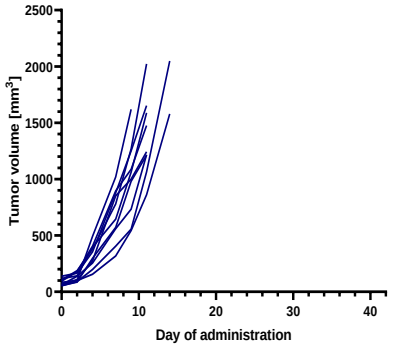
RYVU STRATEGY

STATUS	**LEAD TO CANDIDATE STAGE**
RYVU STRATEGY	Best-in-class small molecule direct, systemic STING agonists active across STING haplotypes
SYNERGISTIC POTENTIAL	Malignant tumors resistant to checkpoint inhibitor monotherapy; Synergistic potential in combination with immunotherapy (anti-PD1/PDL1, CTLA4), chemotherapy and radiotherapy

Ryvu STING agonists lead to elimination of established tumors after systemic administration

Ryvu STING agonist leads to dose-dependent tumor regression anc complete remissions (CRs) in CT26 mouse model after intravenous administration on par with the most potent disclosed reference STING agonist (GSK) currently in Phase 1 clinical trials

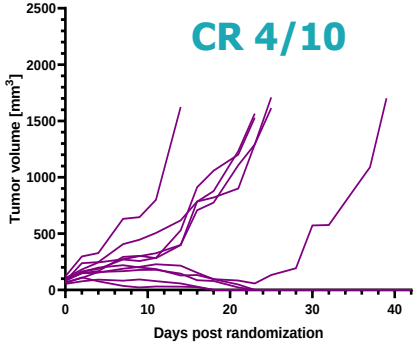
CONTROL GROUP



REFERENCE GSK diABZI

1.5 mg/kg, E3Dx3, IV

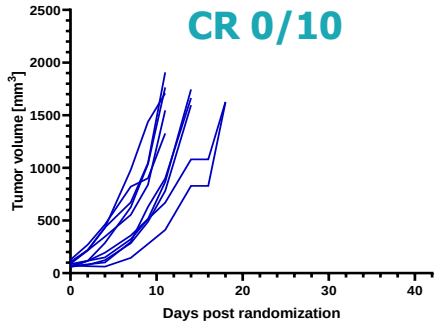
CR 4/10



RYVU STING AGONIST, INTRAVENOUS ADMINISTRATION

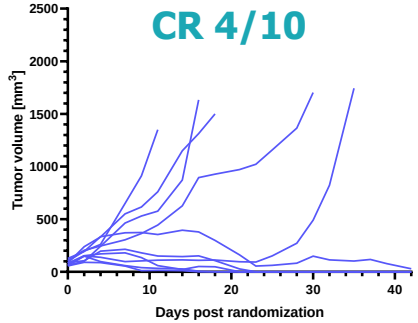
1 mg/kg, E3Dx3, IV

CR 0/10



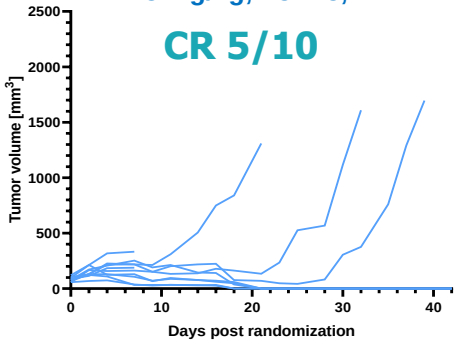
2 mg/kg, E3Dx3, IV

CR 4/10



3 mg/kg, E3Dx3, IV

CR 5/10



Ryvu is developing SMARCA2 inhibitors with first-in-class potential

TOP SUCCESS FACTORS, COMPETITIVE ADVANTAGE

- First in class potential:
  Most selective SMARCA2 over SMARCA4 inhibitors known with confirmed synthetic lethal phenotype *in vitro*
- Unique mechanism of action:
  Allosteric small molecule inhibitors of SMARCA2 ATPase activity
  Selective PROTACs based on proprietary Ryvu series
- Well defined patient population

UPCOMING VALUE INFLECTION POINTS

- ***In vivo* PoC in relevant mouse models carring mutation in SMARCA4: 2020**

1. Ryvu has the only disclosed program of small molecule allosteric inhibitors of ATPase activity and PROTAC series selectively degradating SMARCA2 showing synthetic lethal phenotype *in vitro*; competitor series based on bromodomain ligands
2. Strong responder hypothesis – validated panel of cancer cell lines carrying SMARCA4 LOF mutations;
   - clearly defined patient population
3. ▪ Confirmed targeted cell death in SMARCA4 mutated cancer cell lines (synthetic lethal phenotype) and strong differentiation factors from known competitors
4. ▪ Powerful Synthetic Lethality Platform consisting of unique bioinformatic tools and cellular models allowing identyfication and validation of novel synthetic lethal targets in oncology

Successful Ryvu spin-out company, NodThera

Discovery and development of next generation NLRP3 inflammasome inhibitors

nodthera

~8.6%
OWNED BY RYVU

NodThera investors

SOFINNOVA PARTNERS

5AM VENTURES

EPIDAREX CAPITAL

F-PRIME CAPITAL PARTNERS

PIONEERING DEVELOPMENT IN THE FIELD OF INFLAMMASOME/NLRP3 BIOLOGY

First Ryvu deal in the immunology area

NodThera Ltd. was launched in 2016 by Epidarex Capital, based on research conducted at Ryvu since 2012

Focused on the treatment of diseases driven by chronic inflammation

Productive medicinal chemistry platform

Addressing inflammation and fibrosis that drive NASH

In June 2018 NodThera announced closing of $40M Series A

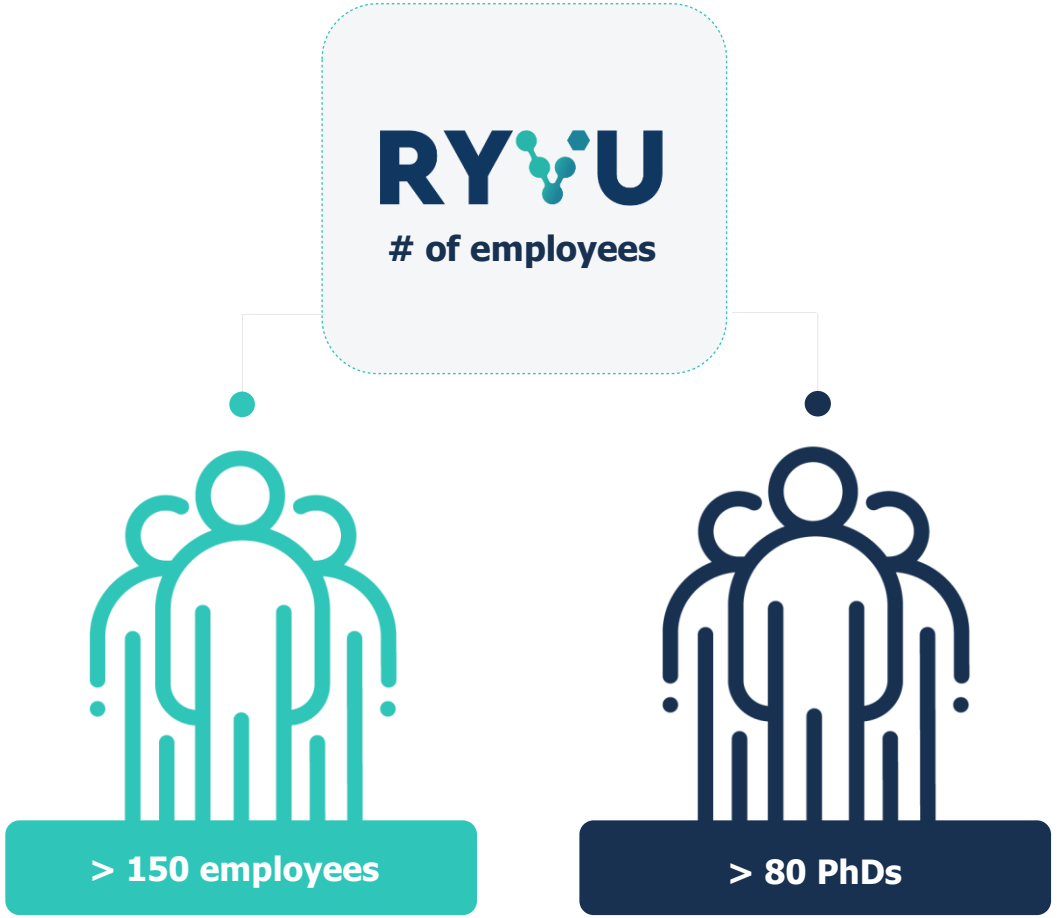
The financing was co-led by Sofinnova and 5AM Ventures, with further participation from Epidarex Capital and F-Prime Capital Partners

In October 2019 Series A was extended by $11M

Financial results – Ryvu (Selvita Oncology segment, exc. NodThera) 2018 and Q1-3 2019

$ million	2018	Q1-3 2019
Revenues	9.7	6.7
Partnering	*2.6*	*0.9*
Grants	*7.1*	*5.8*
Costs	16.6	15.7
EBIT	-6.9	-9.0
EBITDA (without impact of MSSF 16)	-5.8	-7.8
CAPEX	-4.3	-6.0

Cash position October 2019: **> $20M**



What sets Ryvu apart

BROAD, DIVERSIFIED PIPELINE IN SMALL MOLECULE ONCOLOGY

- Mix of wholly-owned and partnered programs
- Potential first-in-class, clinical stage candidates
- Diverse kinase, synthetic lethality, immuno-oncology and immunometabolism programs
- Strong early data relative to competitors

HIGH THROUGHPUT DISCOVERY ENGINE

- 80 Ph.D.- level scientists
- History of identifying molecules with differentiated properties
- Plan to generate one new clinical candidate per year
- Platforms, by design, address key challenges of current treatments
- Focus on internal development and partnering

SCIENTIFIC AND ORGANIZATIONAL EXPERTISE

- Driven by breakthrough science
- Global partnerships with Menarini and Merck KGaA
- Research validated by Leukemia & Lymphoma Society
- Efficient R&D organization
- Secured non-dilutive financing with follow-on opportunities