UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 30, 2024

MEI Pharma, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-41827**	**51-0407811**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

11455 El Camino Real, Suite 250 **San Diego, California** **(Address of Principal Executive Offices)**	**92130** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: 858 369-7100

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.00000002 par value	MEIP	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On July 22, 2024, MEI Pharma, Inc. (the "Company") announced that its Board of Directors had determined unanimously to begin an evaluation of the Company's strategic alternatives, including potential transactions as well as an orderly wind-down of the Company, if necessary, in order to maximize the value of its assets. The Company also announced that it intended to promptly discontinue the clinical development of voruciclib, while continuing to conduct certain non-clinical activities related to the Company's drug candidate assets.

The Company intends to utilize presentation materials (the "Corporate Presentation") in substantially the form attached to this Current Report on Form 8-K as Exhibit 99.1 in connection with the activities described above. These materials primarily describe the status of the Company's voruciclib program.

The information contained in the Corporate Presentation is summary information that should be considered in the context of the Company's filings with the Securities and Exchange Commission and other public announcements the Company may make by press release or otherwise from time to time. The Corporate Presentation speaks as of the date of this Current Report. While the Company may elect to update the Corporate Presentation in the future to reflect events and circumstances occurring or existing after the date of this Current Report, the Company specifically disclaims any obligation to do so.

By furnishing this Current Report on Form 8-K and furnishing the Corporate Presentation, the Company makes no admission as to the materiality of any information in this Current Report, including without limitation the Corporate Presentation. The Corporate Presentation contains forward-looking statements. See Page 2 of the Corporate Presentation for a discussion of certain forward-looking statements that are included therein and the risks and uncertainties related thereto.

The information set forth in this Item 7.01 of this Report, including without limitation the Corporate Presentation, is not deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as may be expressly set forth by specific reference in such a filing.

Item 9/01 Financial Statements and Exhibits

No.	**Description**
99.1	Corporate Presentation July 2024

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

MEI Pharma, Inc.

Date: July 30, 2024

By: Justin J. File

Justin J. File
Chief Financial Officer and Secretary

Voruciclib: An Oral CDK9 Inhibitor for AML and Other Malignancies

July 2024

Forward Looking Statements

Certain information contained in this communication that are not historical in nature are "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 including, without limitation, statements regarding: the potential, safety, efficacy, and regulatory and clinical progress of our product candidates, including the anticipated timing for initiation of clinical trials and release of clinical trial data and our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations. You should be aware that our actual results could differ materially from those contained in the forward-looking statements, which are based on management's current expectations and are subject to a number of risks and uncertainties, including, but not limited to, risk relating to our ability to successfully commercialize our product candidates; the availability or appropriateness of utilizing the FDA's accelerated approval pathway for our product candidates; final data from our pre-clinical studies and completed clinical trials potentially differing materially from reported interim data from ongoing studies and trials; costs and delays in the development and/ or FDA approval, or the failure to obtain such approval, of our product candidates; uncertainties or differences in interpretation in clinical trial results; uncertainty regarding the impact of rising inflation and the increase in interest rates as a result; potential economic downturn; activist investors; our inability to maintain or enter into, and the risks resulting from, our dependence upon collaboration or contractual arrangements necessary for the development, manufacture, commercialization, marketing, sales and distribution of any products; competitive factors; our inability to protect our patents or proprietary rights and obtain necessary rights to third party patents and intellectual property to operate our business; our inability to operate our business without infringing the patents and proprietary rights of others; general economic conditions; the failure of any products to gain market acceptance; our inability to obtain any additional required financing; technological changes; government regulation; changes in industry practice; and one-time events. We do not intend to update any of these factors or to publicly announce the results of any revisions to these forward-looking statements. Under U.S. law, a new drug cannot be marketed until it has been investigated in clinical studies and approved by the FDA as being safe and effective for the intended use.

Voruciclib Presents a Strong Value Proposition as the Only Oral CDK9 Inhibitor in Clinical Development in Combination with Venetoclax in AML

- Investment rationale
  - Opportunity to continue ongoing Phase 1 study (16-32 patients) to value inflection point by YE2024 and Phase 2 study (24 patients) in CY2025 for modest investment
- Initial focus on R/R AML
  - Significant medical need in large number of patients
    - Mutation agnostic therapy with potential to address >50% of AML patients
  - Clear and efficient path to marketing approval
- Voruciclib plus venetoclax
  - Durable responses observed in patients with R/R AML after venetoclax failure
  - On target effect observed on Mcl-1 and RNA Pol II
- Life cycle management
  - Market and scientific rationale to move to 1L AML
  - Utility where venetoclax is approved/used in other hematologic indications
  - Potential to address several solid tumors associated with MYC overexpression

Estimated R&D costs

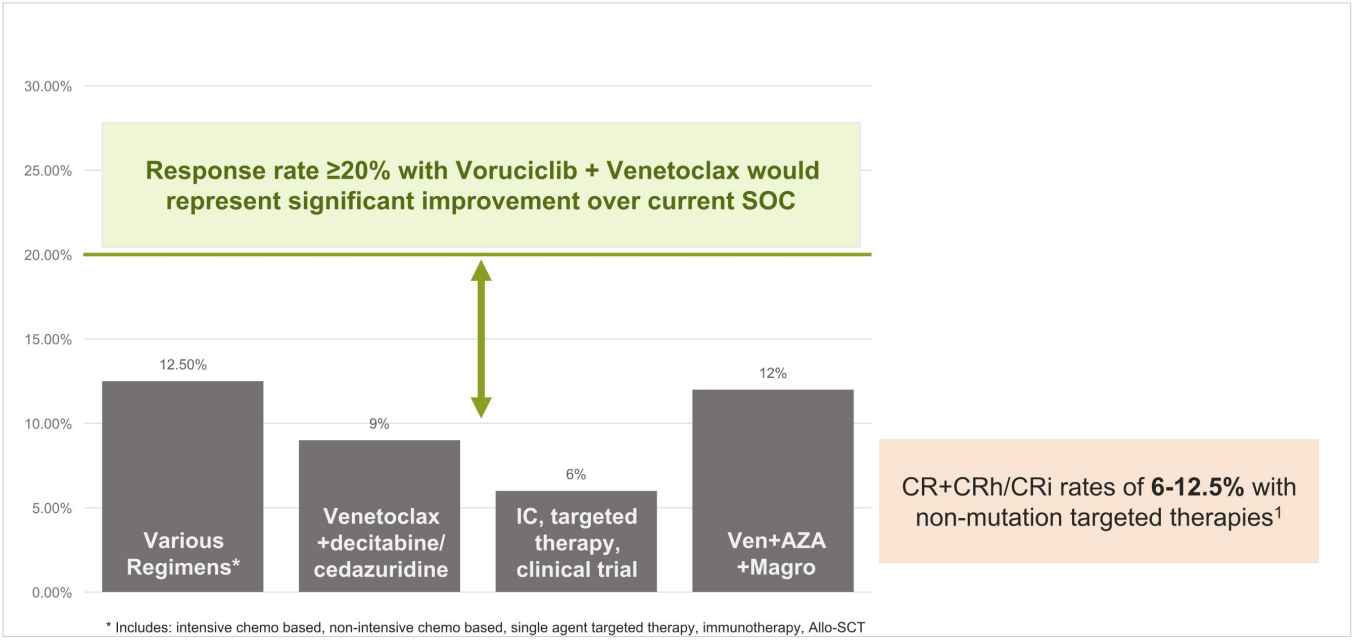
- Stage 1a: ~$1.2M
  - 16 patients
  - Evaluate 200 mg only
  - Readout December 2024
- Stage 1b: ~$1.1M
  - 16 patients
  - Evaluate 250 mg
  - Readout March 2025
- Stage 2: ~$2.4M
  - 24 patients
  - Dose 200 or 250 mg
  - Readout December 2025

TOTAL: ~ $4.7M to complete Phase 1 and Phase 2 studies with ~56 patients by YE2025

Program Overview: Voruciclib and Venetoclax Combination in R/R AML Patients

July 2024

Limited Treatment Options and Poor Outcomes for AML Patients Post Venetoclax Exposure



CR+CRh/CRi rates of **6-12.5%** with non-mutation targeted therapies[1]

1. Maiti, A., et. al., Haematologica 2021: 106(3. Maiti, A., et. al., *Blood* 2023: 142 (Supplement 1): 4289. Zainaldin, C., et. al., *Leuk Lymphoma* 2022: 63(13):3245-3248. Daver, N., *Blood* (2022) 140 (Supplement 1): 141–144:

Majority of R/R AML Patients Do Not Have Actionable Mutations and Need New Treatment Options

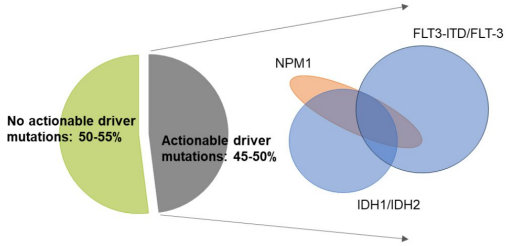
Despite the significant progress made against targetable mutations in AML…

50-55% of AML Patients Do Not Have Actionable Mutations[1,2]

In comparison, approximately 30%, 30% and 20% of AML patients have NPM1, FLT3 and IDH1/2 mutations, respectively[1].

Co-mutations in AML

Significant overlap across mutation sub-populations[1]



In one study, approximately 80% of patients with an NPM1 mutation had a co-mutation in either FLT3, IDH1/2 or both[2]

Diagram is for illustrative purposes.

1. Miyamoto, K., et. al., Int J Mol Sci. 2020;21(14):5114. 2. Malani, D., Cancer Discov. 2022;12(2):388-401

Large Addressable R/R AML Population for Mutation Agnostic Therapy

~7,500 Addressable Patient Population for Mutation Agnostic Therapy in Patients with R/R AML

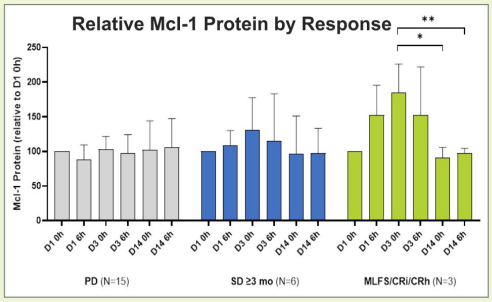
Sources: Clarivate November 2023

Voruciclib: An Oral CDK9 Inhibitor with Clinical Activity in R/R AML and On-Target Biologic Effect

- 161 patients enrolled to date in 4 Phase 1 studies
  - 65 pts with AML: 21 single agent and 44 in combination with venetoclax (VORU+VEN)
  - 19 pts with B-cell malignancies
  - 77 pts with solid tumors
- Current focus on R/R AML, with substantial clinical, PK and PD datasets
  - CRi/MLFS observed in patients with disease progression after venetoclax
  - Target dose of 150-250 mg/day for phase 2 based on clinical responses and PK/PD data
  - Decrease in Mcl-1 and RNA Poll II^{Ser2} phosphorylation observed in patient samples
- Potential completion of VORU+VEN dose/schedule optimization using 21 days/cycle in H2-2024
- Ready for phase 2 stage in H1-2025

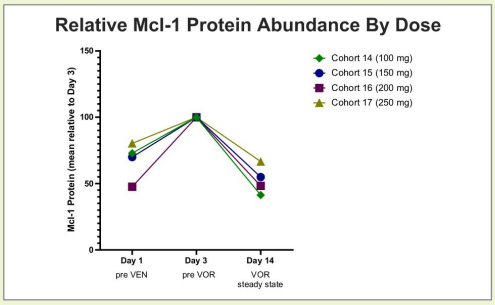
Decrease in Mcl-1 Protein with VORU+VEN Demonstrates On-Target Biological Activity

Greater Decrease in Mcl-1 in Responders[1]



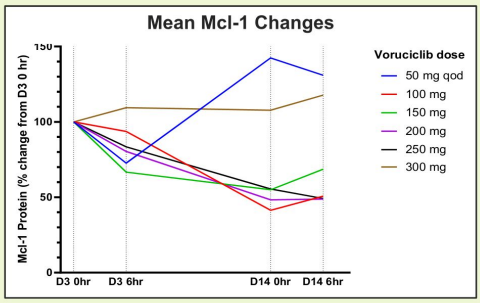
*p ≤ 0.05; **p ≤ 0.01

Mcl-1 Increases After Venetoclax then Decreases with Voruciclib[1]



Mcl-1 increases after venetoclax dosing (D1 0h – D3 0h) and decreases after 1st voruciclib dosing (D3 6h), continuing after 12 daily doses (D14 0h)

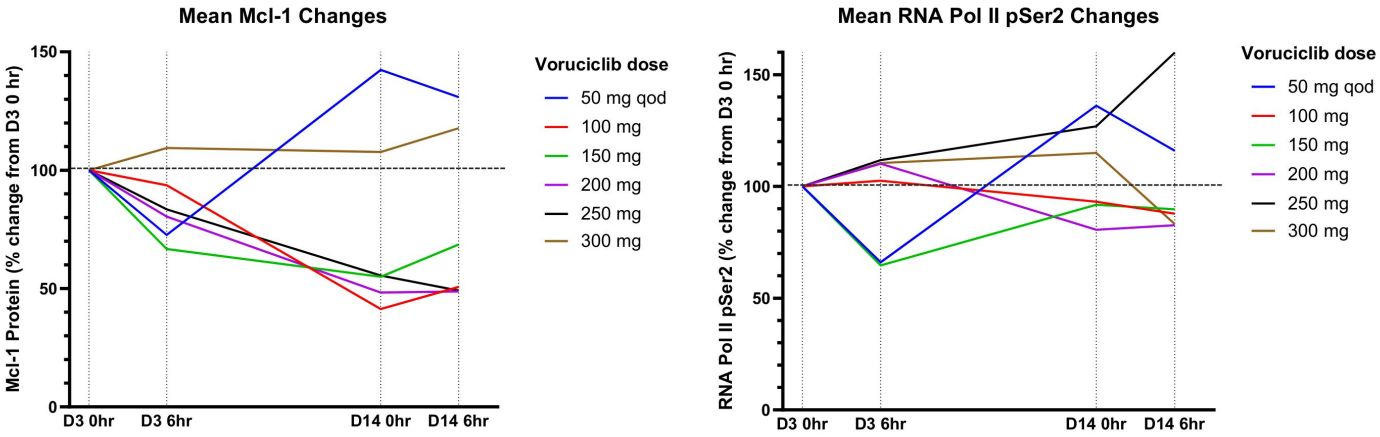
Consistent Decreases in Mcl-1 Across Dose Levels



1. Mcl-1 protein expressed as mean fluorescence normalized to D1 0h or D3 0h

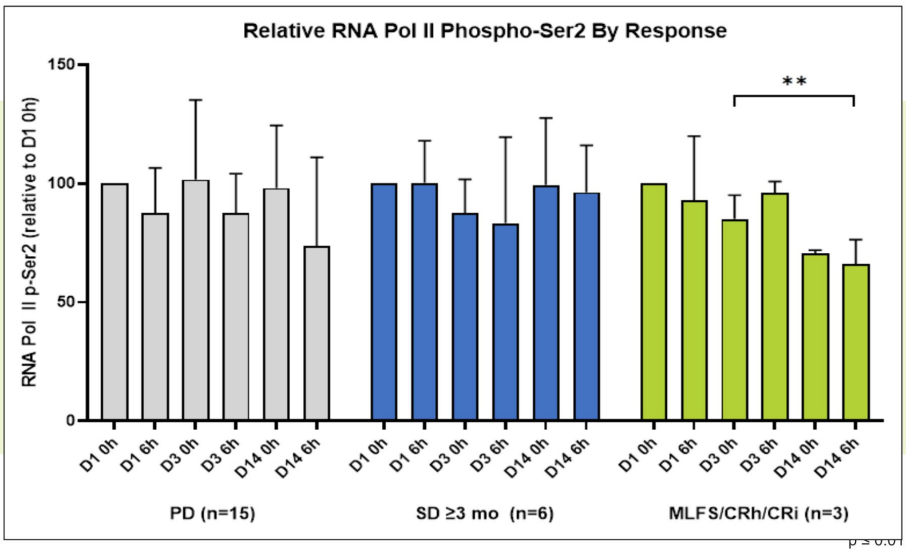
On-Target Decreases in Mcl-1 and Phosphorylation of RNA Pol II^{Ser2} Across Doses

- Mcl-1 protein expression and phosphorylation of RNA Pol II^{Ser2} values decreased from before first voruciclib dose to day 14 at the end of voruciclib dosing



Patients with Clinical Responses Have Strongest Decreases in RNA Pol II^{Ser2} Phosphorylation Following VORU+VEN at 100-300 mg

- Clinical responders (MLFS/CRh/Cri) showed significant decreases in RNA Pol II phospho-Ser2 on Day 14 compared to pre VORU dosing on Day 3
- Data normalized to each patient's C1D1 pre dose

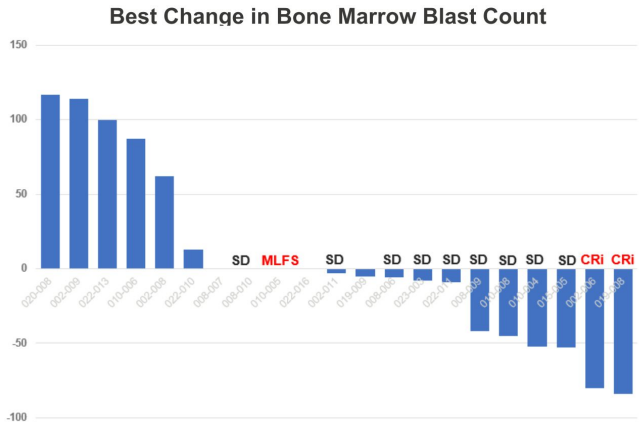


Anti-Leukemic Activity Observed After Venetoclax Failure

31% (10/32) of Patients Administered VORU at 100-300 mg for 14 days/cycle + VEN had Disease Control

- 3 patients achieved a response
  - 2 had a CRi
    - 1 underwent HSCT transplant
    - 1 had a CRi for 6 months then progressed
  - 1 had a MLFS, ongoing at 9+ months
- 7 patients had stable disease ≥3 months
  - 13 patients had stable disease <3 months

~50% of Patients with Pre/Post Bone Marrow Biopsy Had a Decrease in Blast Counts

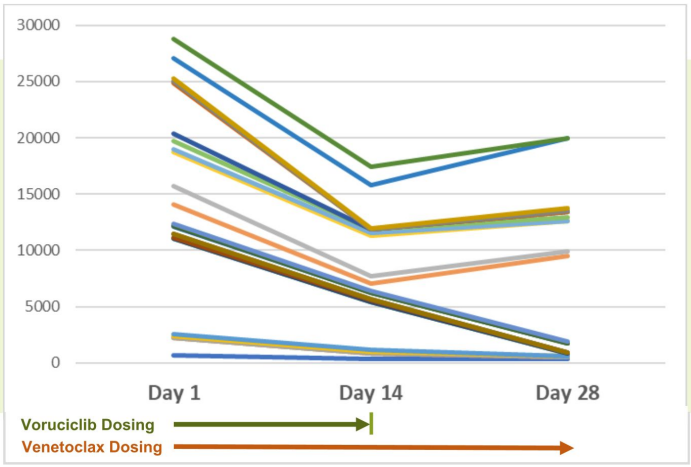


Importance of Evaluating Voruciclib on Days 1 to 21 of 28-Day Cycle in Combination with Venetoclax to Extend Voruciclib Exposure and Prevent Blast Rebound on Venetoclax Alone

Increasing duration of VORU exposure may prevent blast rebound and enhance efficacy

- 18/24 pts (75%) had decreased peripheral blasts on Day 14 of Cycle 1, at the end of voruciclib and venetoclax combination dosing
- 8/18 pts (44%) had peripheral blasts rebound between Day 14 and 28, when voruciclib was stopped and patient received venetoclax alone

Peripheral Blast Counts Decrease on VORU+VEN & Rebound on VEN Alone in Days 15-28

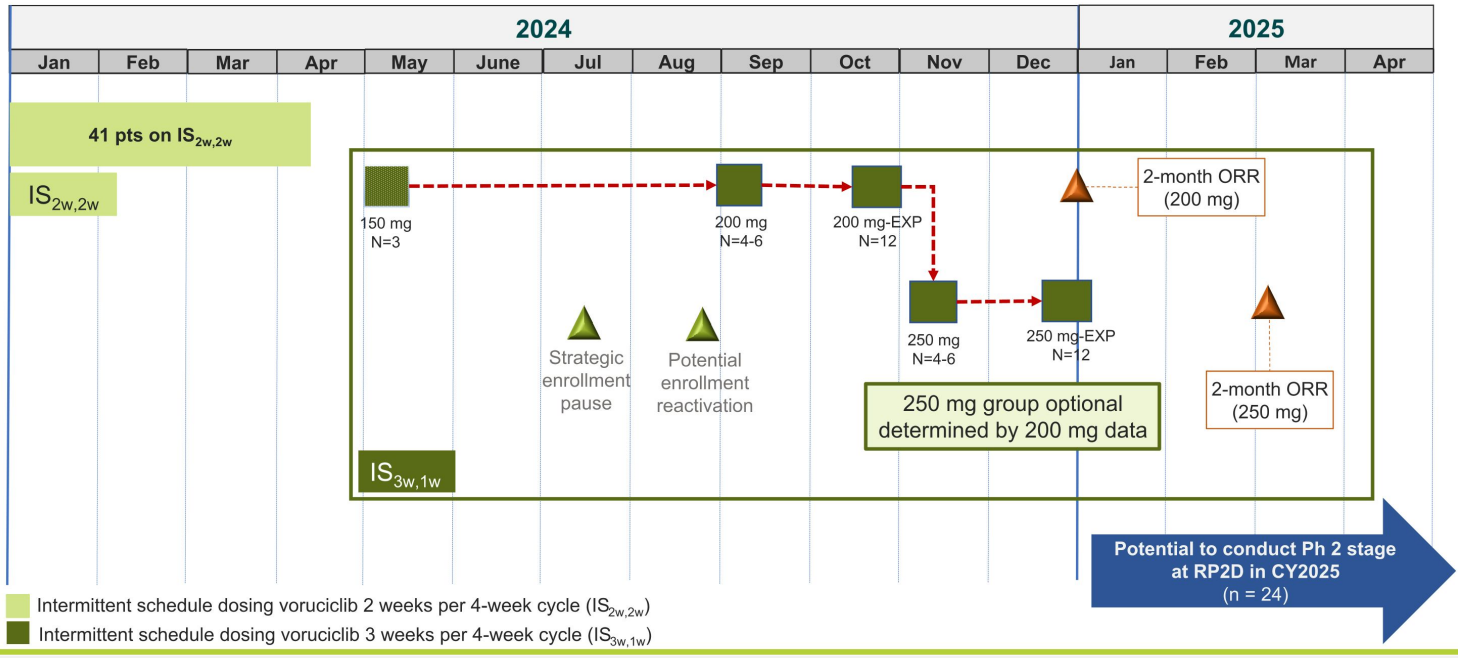


Voruciclib Plus Venetoclax is Well-Tolerated in Heavily Pre-Treated Patients with R/R AML

- MTD not reached on 14 days/cycle schedule evaluated to date
- Dose escalation stopped at 300 mg because plasma concentrations achieved exceed concentrations shown to be effective in nonclinical models
  - Target dose for PD effect projected to be 150-250 mg
- No DLTs observed at doses evaluated
- No discontinuations due to drug-related toxicities

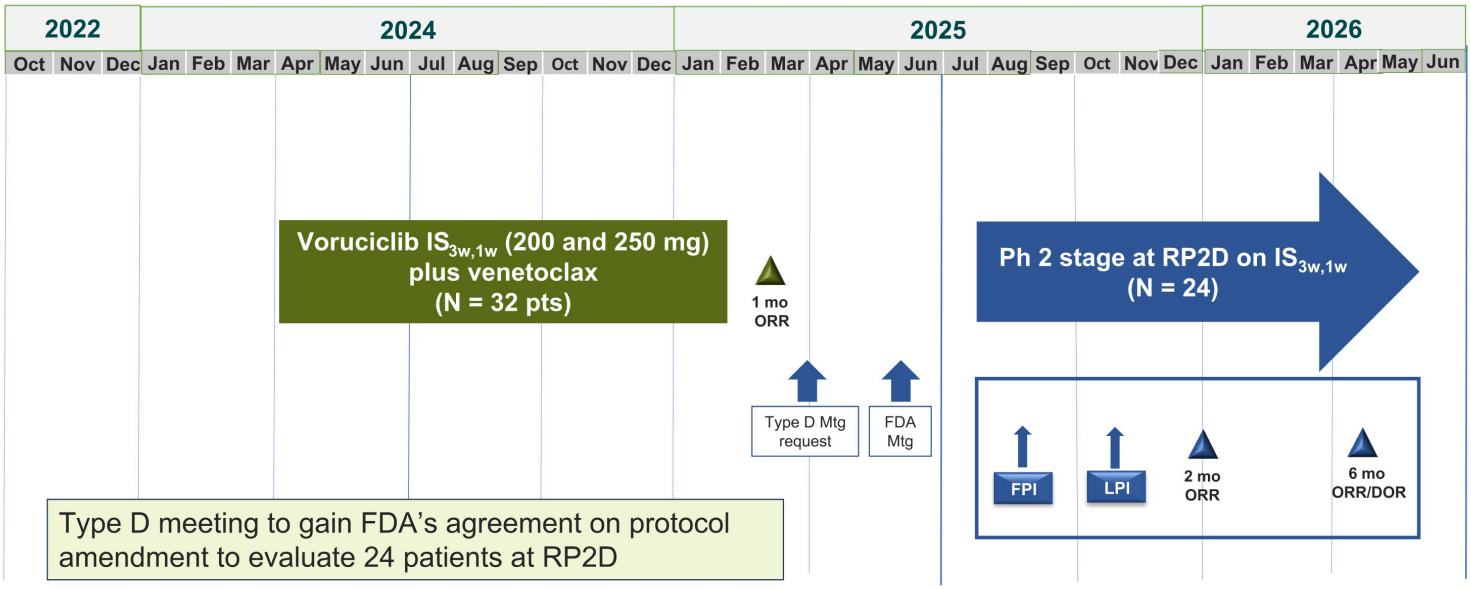
Remaining Cohorts (16-32 Patients) to Be Evaluated in the Dose Optimization Stage in H2-2024

Assumes Reactivation of Enrollment in September 2024



Timeline for Stage 2 at RP2D with 24 Patients Enrolled

Topline Results in Q4-2025



Phase 3 Ready Package for Voruciclib + Venetoclax in R/R AML in 2026

- Phase 1/2 study enrolling up to 120 patients with R/R AML
  - 100 patients in combination with venetoclax, with ~40 patients at RP2D
- Extensive PK data on > 150 patients
- Pharmacodynamics data for Mcl-1 and RNA Pol
- Pharmacology studies
  - Food effect study
  - Nonclinical pharmacology studies
    - In vitro CYP and transporters
    - Protein binding in human liver microsomes
- 3-month toxicology studies in dogs and rats
- Ph 3 ready API/drug product, including process development, DOE, & analytical method development

Registration Strategy in R/R AML

- Phase 3 study design
  - Randomized placebo-controlled vs SOC (HMA, LDAC, Venetoclax alone
  - R/R AML, not to exceed 3 prior lines of therapy, exclude TP53 mutations
  - Overall survival as primary endpoint for full approval
  - Possible accelerated approval based on CR+CRh rate
  - Sample size = 300 pts for survival HR ~0.6 (8.3 months vs 5 months)
  - Enrollment ~24 months
- Other studies for NDA package
  - TQT study
  - ADME study
  - DDI study
  - Food effect study (if change in commercial formulation)
  - Hepatic impairment study (TBD)

Intellectual Property & Market Exclusivity

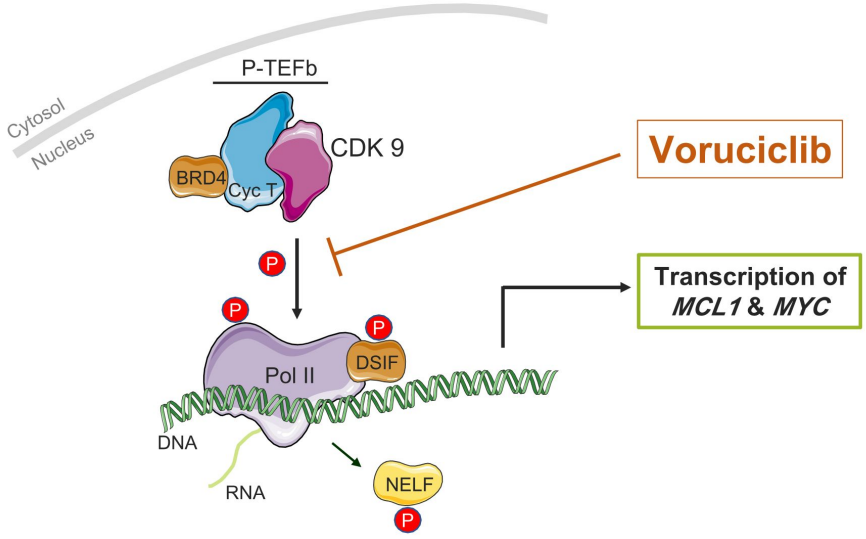
- MEI Pharma has acquired exclusive worldwide rights to develop, manufacture and commercialize voruciclib from Presage Biosciences, Inc.
- 14 issued patents, 2 allowed and 7 pending U.S. non-provisional patent applications with the USPTO covering the composition of matter, pharmaceutical compositions, and methods of use to treat cancer for voruciclib
- Pending U.S. patent application covering composition of matter for voruciclib polymorph has a projected expiration date in 2040, if issued, which may be potentially extended by about one year of patent term adjustment (PTA) to **2041** due to patent office prosecution delays, and up to five years of patent term extension (PTE) to **2046** due to regulatory delays
- Allowance of patent application in Japan covering composition of matter for voruciclib polymorph is expected upon minor formalities being addressed.
- There are over 90 allowed or issued foreign patents, 3 pending U.S. provisional patent applications, and approximately 60 pending foreign patent applications for voruciclib, related compounds, and related methods of use
- Acute Myeloid Leukemia is also an orphan designation with the FDA, which qualifies for a potential seven years of market exclusivity upon regulatory approval in the U.S

MEI Pharma

Voruciclib Mechanism of Action and Nonclinical Studies

Voruciclib Modulates 2 Important CDK9 Interactions for MCL1 and MYC

- Transcription of short-lived mRNAs by RNA polymerase II is regulated by promoter proximal pausing
- CDK9 activates RNA polymerase II, which is important for the transcription of MCL1 and MYC that support proliferation and survival of malignant cells
- Voruciclib inhibits CDK9-mediated RNA Pol II phosphorylation, blocking gene transcription elongation and mRNA maturation leading to decreased Mcl-1 and Myc proteins

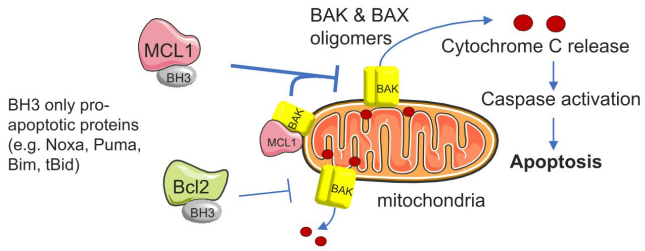


P-TEFb regulation of promoter proximal pausing and transcription of short-lived mRNA

Dey, et al. Sci Reports (2017) 7(1):8007. Li, et al. Transcription (2018) 9(2):88. Luedtke, et al. Signal Transduct Ther (2020) 5(1):17. Dollinger, et al. J Mol Biol (2021) 433(14):1666897. Wiley, et al. Cancer Research (2021) 81(13 supp):1962

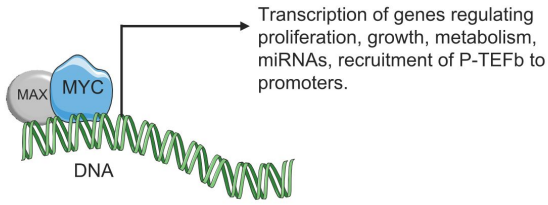
MCL1 and MYC Proteins are Important for Cell Proliferation and Survival

MCL1 is an anti-apoptotic BCL2 family member



- Prevents cell death and contributes to cancer cell survival
- MCL1 amplification or increased expression in AML, MM, HCC, prostate, and SCLC.

MYC is an oncogenic transcription factor



- Contributes to cancer cell survival
- MYC amplification or increased expression in 70% of cancers

CDK 9 regulates expression of MCL1 and MYC genes

Dey, et al. Sci Reports (2017) 7(1):8007. Li, et al. Transcription (2018) 9(2):88. Luedtke, et al. Signal Transduct Ther (2020) 5(1):17. Dollinger, et al. J Mol Biol (2021) 433(14):1666897. Wiley, et al. Cancer Research (2021) 81(13 supp):1962. Huska, et al, Methods in Mol Biol (2019).

High Mcl-1 Levels Associated With Poor Prognosis and Resistance to Venetoclax in AML

- High levels of Mcl-1 found consistently high in nearly all bone marrow samples in newly diagnosed and relapsed AML[1]
- High level of Mcl-1 associated with poor outcome in AML[2]
  - Provide survival advantage and sustained growth of the disease
  - Lead to chemotherapy resistance
- Mcl-1 protein has a short half-life (~0.5 hr) which makes it dependent on continuous gene transcription
- Mcl-1 upregulation is an established venetoclax resistance mechanism[3]
  - Venetoclax inhibits BCL2 but can lead to stabilization of Mcl-1

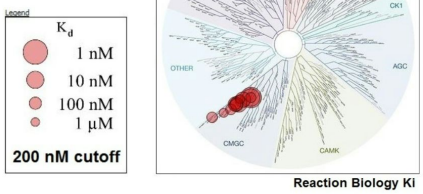
1. Glaser et al, Gene Dev 2012;26(2):120-125
2. Li et al, Onco Target Ther 2019;12:3295-3304
3. Carter et al, Haematologica 2022;107(1):58-76.

Voruciclib Is a Selective and Potent Oral CDK9 Inhibitor

- **Orally administered**
  - Patient convenience
  - Half-life of 26-32 hours allows once a day dosing
- **Potent**
  - Biochemical IC_{50} 0.63 nM
  - IC_{50} from 0.2 to 1.7 µM in various cell lines
- **Preferential distribution to tissues *vs* plasma**
  - >10-fold higher tissue accumulation
- **Selective**
  - Higher specificity and longer residence time on CDK9
  - Greater selectivity against CDKs *vs* other kinases

CDK / Cyclin	Ki (nM)	Residence Time
CDK9 / T2	0.63	105
CDK9 / T1	1.68	151
CDK6 / D1	2.92	3.5
CDK4 / D1	3.96	4.8
CDK1 / A2	9.10	55
CDK2 / A2	55.1	19

Selectivity to CDK9 *vs* other kinases

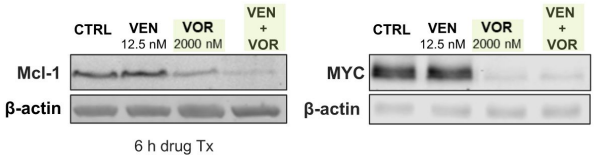


Reaction Biology Ki

Dey, et al. Sci Reports (2017) 7(1):8007. Luedtke, et al. Signal Transduct Ther (2020) 5(1):17. Wiley, et al. Cancer Research (2021) 81(13 supp):1962

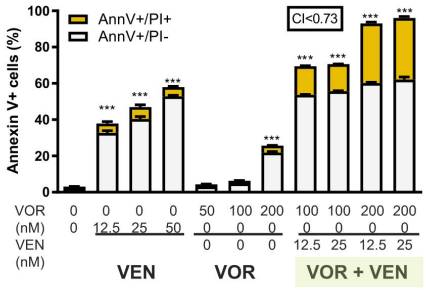
Preclinical Studies Demonstrate Voruciclib Suppresses Mcl-1 and Synergizes with Venetoclax in AML Murine Xenograft Model

Suppresses Mcl-1 and MYC Protein Levels

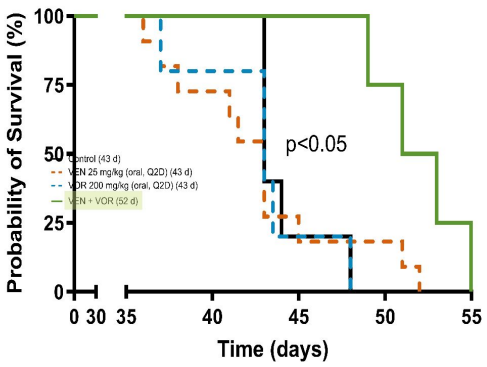


6 h drug Tx

Increases Apoptosis



Extends Survival in MV4-11 Tumor



Luedtke, et al. Signal Transduct Ther (2020)

Voruciclib Results in R/R AML

Completed Single-Agent Dose Escalation/Expansion in R/R AML & B-cell Malignancies (N = 40)

Treatment Well Tolerated with Evidence of Anti-Leukemic Activity

Voruciclib up to 200 mg for days 1-14 in a 28-day Cycle Demonstrated Anti-Leukemic Activity . . .

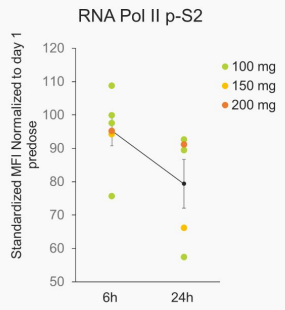
21 patients with heavily pretreated AML (median = 3 prior lines)

- 1 MLFS (81 yo, 4 prior lines, adverse mutations & cytogenetics)
- 5 of 10 patients at 200 mg had stable disease
- 2 patients had differentiation syndrome demonstrative of biological activity

. . . and Was Well-tolerated

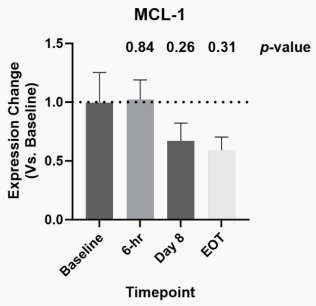
- No dose-limiting toxicity on $IS_{2w,2w}$ dosing
- MTD not reached
- Dose escalation stopped at 200 mg to focus on venetoclax combination
- No drug-related neutropenia
- No Grade 3+ drug related toxicity
- No discontinuation due to drug related toxicity

On-Target Biologic Activity With Effect on Key Biomarkers



AML

Decreased RNA Pol II phosphorylation



CLL

Reduced Mcl-1 mRNA

Davids et al, Blood (2023) 142 (Supplement 1): 4286

Completed Dose Escalation/Expansion of Voruciclib 2 Weeks/Cycle ($IS_{2w,2w}$) Plus Venetoclax in R/R AML Showed Evidence of Clinical Activity With a Well Tolerated Regimen

- Dosing schedule
  - Voruciclib days 1-14 (day 3-14 in cycle 1)
  - Venetoclax 200 mg on days 1-21 and 400 mg on days 22-28
- 41 patients enrolled
  - 29 in dose escalation cohorts at 50-300 mg
  - 12 in expansion cohort at 300 mg
- Clinical activity
  - 2 CRh and 1 MLFS
  - Improved blast counts
- Well tolerated
  - No DLTs observed
  - MTD not reached
  - No discontinuation due to drug-related adverse events
- PK does not show drug-drug interaction
- Decreases in Mcl-1 protein expression and phosphorylation of RNA Pol II^{ser2}

Baseline Characteristics in Dose Escalation/Expansion Cohorts (N = 41)

Patients Heavily Pretreated With High Rate of Adverse Cytogenetic and Molecular Features

- **Median age 67 years (range 34-89)**
- **18 patients (44%) had ≥3 prior lines of therapy**
- **39 (95%) previously treated with venetoclax**
- **27 (66%) had Adverse 2017 ELN Risk Category**

	N = 41
Number of prior therapies	
Median (range)	2 (1-6)
≥3 prior	18 (44%)
Prior allogeneic stem cell transplant	8 (20%)
Prior venetoclax	39 (95%)
1st line	25 (64%)
≥2nd line	14 (26%)
Prior HMAs	39 (95%)
Prior anthracyclines	21 (51%)

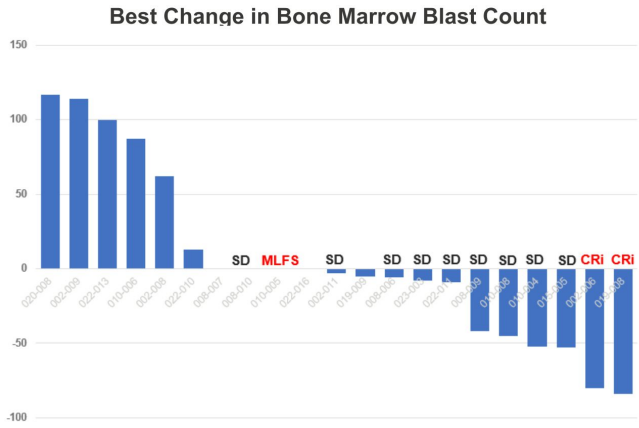
	Total (N=41)
2017 ELN Risk Category	
Favorable	4 (10%)
Intermediate	7 (17%)
Adverse	30 (73%)
Poor Cytogenetics (n = 40)	
Patients with adverse cytogenetics	20 (50%)
Adverse Molecular Mutations (n = 36)	
TP53	10 (28%)
ASLX1	14 (39%)
RUNX1	8 (22%)
GATA2	4 (11%)
Baseline Bone Marrow Blast	
Median (range)	33% (2-77%)

Anti-Leukemic Activity Observed After Venetoclax Failure

31% (10/32) of Patients Administered VORU at 100-300 mg for 14 days/cycle + VEN had Disease Control

- 3 patients achieved a response
  - 2 had a CRi
    - 1 underwent HSCT transplant
    - 1 had a CRi for 6 months then progressed
  - 1 had a MLFS, ongoing at 9+ months
- 7 patients had stable disease ≥3 months
  - 13 patients had stable disease <3 months

~50% of Patients with Pre/Post Bone Marrow Biopsy Had a Decrease in Blast Counts



Covariate Analyses From All Cohorts on $IS_{2W,2W}$ (41 Patients)

AML Type

- Poor risk AML had low disease control rate (<40%) *vs* favorable risk AML with higher disease control rate (≥50%)

	AML Type	No. Pts (N=41)	CRi/MLFS	SD ≥3 mo	"Good Outcome" CRi/MLFS/SD	"Poor Outcome" PD + SD <3 mo
Poor Risk	AML with MDS related changes	18	1	6	7 (39%)	11 (61%)
	AML with RUNX-1	5	0	1	1 (20%)	4 (80%)
	Pure erythroid leukemia	2	0	0	0	2 (100%)
	AML without maturation	1	0	0	0	1 (100%)
Favorable Risk	AMML	7	1	3	4 (57%)	3 (43%)
	AML with maturation	3	1	1	2 (67%)	1 (33%)
	NPM-1 mutation	2	0	1	1 (50%)	1 (50%)

Covariate Analyses From All Cohorts on $IS_{2W,2W}$ (41 Patients)

ELN 2017 Risk Group

- Patients with Adverse risk had low disease control rate (≤10%) *vs* patients with Intermediate/Favorable risk who had higher disease control rate (≥50%)

ELN 2017 Risk Group	No. Pts (N=41)	CR/MLFS	SD ≥3 mo	"Good Outcome" CRi/MLFS/SD	"Poor Outcome" PD + SD <3 mo
Adverse	30	1	2	3 (10%)	27 (90%)
Intermediate	7	1	5	6 (86%)	1 (14%)
Favorable	4	1	1	2 (50%)	2 (50%)

Covariate Analyses From All Cohorts on $IS_{2W,2W}$ (41 Patients)

Molecular Mutations

- Patients with adverse risk mutations (RUNX1, TP53, SRSF2) had low disease control rate, particularly for TP53
- Patients with ASXL1, considered poor risk in general but reported by Sellas to be associated with better outcome when treated with GFH009, led to 2 CRi with VORU+VEN

Molecular Mutation	No. Pts (N=36)	CR/MLFS	SD ≥3 mo	"Good Outcome" CRi/MLFS/SD	"Poor Outcome" PD + SD <3 mo
TP53	10	0	0	0	10 (100%)
RUNX-1	8	1	0	1 (12.5%)	7 (87.5%)
SRSF2	6	0	2	2 (33%)	4 (67%)
ASXL1	14	2	4	6 (43%)	8 (57%)

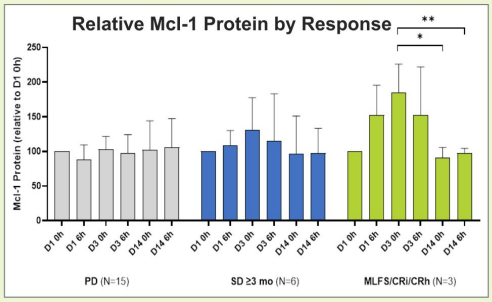
Voruciclib Dosed up to 300 mg for 14 Days per Cycle Was Generally Well-Tolerated with No Apparent Dose Response to Adverse Events Reported

Treatment Emergent Adverse Events in ≥10% of Patients

	(50 mg QOD) (N=6)	(50 mg QD) (N=3)	(100 mg QD) (N=4)	(150 mg QD) (N=4)	(200 mg QD) (N=4)	(250 mg QD) (N=4)	(300 mg QD) (N=4)	Total (N=29)
Nausea	0	0	2 (50.0)	3 (75.0)	2 (50.0)	1 (25.0)	2 (50.0)	10 (34.5)
Platelet Count Decreased	0	1 (33.3)	1 (25.0)	3 (75.0)	1 (25.0)	1 (25.0)	1 (25.0)	8 (27.6)
Febrile Neutropenia	0	1 (33.3)	2 (50.0)	2 (50.0)	0	1 (25.0)	1 (25.0)	7 (24.1)
Anaemia	0	0	2 (50.0)	2 (50.0)	0	1 (25.0)	1 (25.0)	6 (20.7)
Hypokalaemia	0	0	2 (50.0)	1 (25.0)	2 (50.0)	1 (25.0)	0	6 (20.7)
Cough	2 (33.3)	0	1 (25.0)	1 (25.0)	1 (25.0)	0	0	5 (17.2)
Diarrhoea	1 (16.7)	0	1 (25.0)	1 (25.0)	1 (25.0)	1 (25.0)	0	5 (17.2)
Dyspnoea	2 (33.3)	0	1 (25.0)	1 (25.0)	0	1 (25.0)	0	5 (17.2)
Fatigue	0	0	0	3 (75.0)	1 (25.0)	0	1 (25.0)	5 (17.2)
Stomatitis	2 (33.3)	0	1 (25.0)	1 (25.0)	0	0	0	4 (13.8)
Vomiting	0	0	1 (25.0)	0	0	2 (50.0)	1 (25.0)	4 (13.8)
Anxiety	1 (16.7)	0	2 (50.0)	0	0	0	0	3 (10.3)
Corona Virus Infection	1 (16.7)	0	0	1 (25.0)	1 (25.0)	0	0	3 (10.3)
Hypotension	1 (16.7)	0	1 (25.0)	1 (25.0)	0	0	0	3 (10.3)

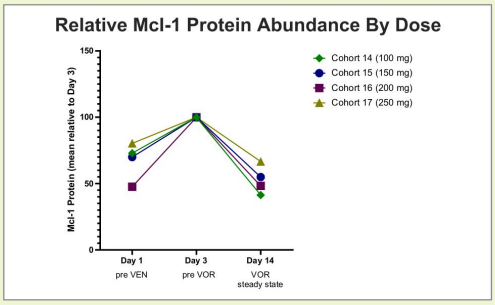
Decrease in Mcl-1 Protein with VORU+VEN Demonstrates On-Target Biological Activity

Greater Decrease in Mcl-1 in Responders[1]



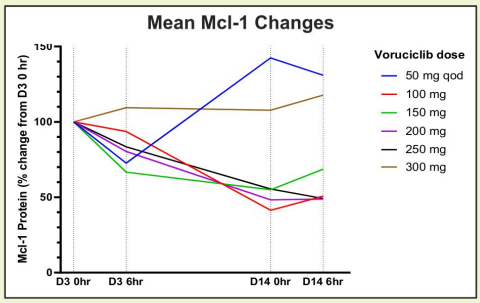
*p ≤ 0.05; **p ≤ 0.01

Mcl-1 Increases After Venetoclax then Decreases with Voruciclib[1]



Mcl-1 increases after venetoclax dosing (D1 0h – D3 0h) and decreases after 1st voruciclib dosing (D3 6h), continuing after 12 daily doses (D14 0h)

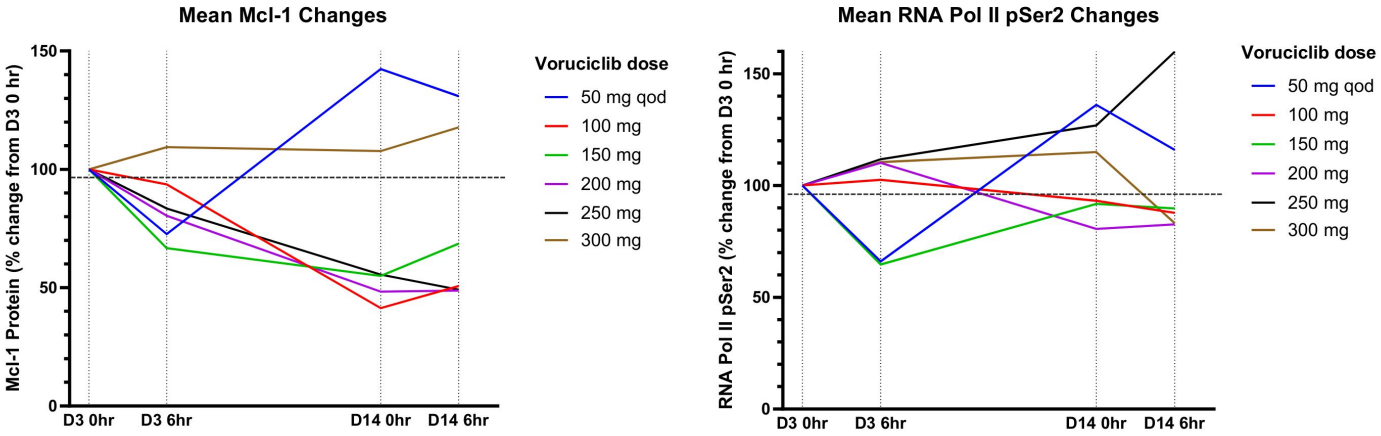
Consistent Decreases in Mcl-1 Across Dose Levels



1. Mcl-1 protein expressed as mean fluorescence normalized to D1 0h or D3 0h

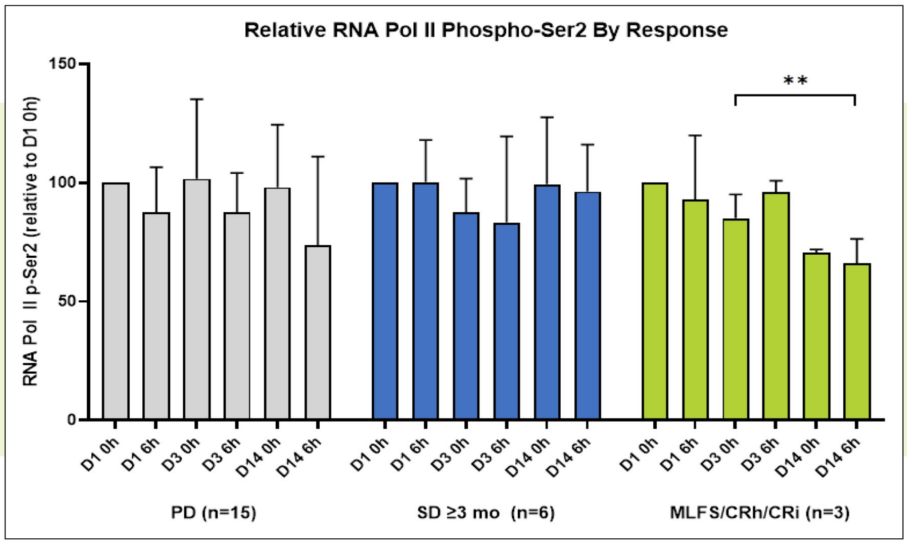
On-Target Decrease in Mcl-1 and RNA Pol II^{Ser2} Phosphorylation

- Mcl-1 and phosphorylation of RNA Pol II^{Ser2} mean values decreased from before first voruciclib dose to day 14 on the last day of voruciclib dosing
- Change not as evident at 300 mg (compensatory pathways?) and 50 mg (dose too low)



Patients with Clinical Responses Have Strongest Decreases in RNA Pol II^{Ser2} Phosphorylation Following VORU+VEN at 100-300 mg

- Clinical responders (MLFS/CRh/Cri) showed significant decreases in RNA Pol II phospho-Ser2 on Day 14 compared to pre VORU dosing on Day 3
- Data normalized to each patient's C1D1 pre dose



**p ≤ 0.01

Assessment of Voruciclib PD Responses by Raw Values

- Flow cytometry analysis of PBMC samples
- Changes in fluorescence signal for individual subjects analyzed for acute response (6 hr post-dose on day 3 or day 14 vs pre-dose on same day) or steady state response (day 14 pre-dose compared to day 3 pre-dose)
- Response defined as ≥20% decrease from baseline values

% of Patients with Mcl-1 and p-Ser2 RNA Pol II Responses

	100-250 mg Acute or Steady State	50-300 mg Acute or Steady State
Mcl-1	71.4%	53.6%
p-Ser2 RNA Pol II	35.7%	39.2%

Assessment of Voruciclib PD Responses by Raw Values

			Target Dose Range			
PD Assessment	**Cohort 12 (50 mg QOD)**	**Cohort 14 (100 mg)**	**Cohort 15 (150 mg)**	**Cohort 16 (200 mg)**	**Cohort 17 (250 mg)**	**Cohort 18 + EXP1 (300 mg)**
PD day 3 and/or day 14, N	3	4	3	4	3	11
Pts with Mcl-1 decrease (≥ 20%) post VOR (acute or steady state) % (N)	66.7% (2)	75% (3)	66.7% (2)	50% (2)	100% (3)	27.3% (3)
Pts with pSer2-RNA Pol II decrease (≥ 20%) post VOR (acute or steady state) % (N)	66.7% (2)	50% (2)	66.7% (2)	25% (1)	0% (0)	36% (4)
PD steady state day 14, N	1	3	2	1	2	11
Pts with Mcl-1 decrease (≥ 20%) VOR steady state (day 14 pre-dose compared to day 3 pre-dose) % (N)	100% (1)	100% (3)	50% (1)	100% (1)	100% (2)	9% (1)
Pts with pSer2-RNA Pol II decrease (≥ 20%) VOR steady state (day14 pre-dose compared to day 3 pre-dose) % (N)	0% (0)	33% (1)	0% (0)	100% (1)	0% (0)	9% (1)

Voruciclib PK Analysis 50-300 mg

Mean (%CV) single dose and multiple dose voruciclib C_{max} and AUC_{24}

	Cohort 12	Cohort 13	Cohort 14	Cohort 15	Cohort 16	Cohort 17	Cohort 18 + EXP1
Voruciclib dose Venetoclax dose	50 mg QOD 200 mg QD	50 mg QD 200 mg QD	100 mg QD 200 mg QD	150 mg QD 200 mg QD	200 mg QD 200 mg QD	250 mg QD 200 mg QD	300 mg QD 200 mg QD
C1D3 (single dose) voruciclib PK parameters							
n	5	2 [A]	3	2 [A]	2 [A]	1 [A]	4
C_{max}, ng/mL	95.1 (22%)	54.5, 40.9	258 (105%)	242, 267	425, 198	1040	662 (64%)
AUC_{24}, ng×h/mL	1301 (16%) [B]	n.c.	2507 (65%)	3590, 4454	4015, 2814	15443	9250 (49%)
C1D13/14 (multiple dose) voruciclib PK parameters							
n	4	2 [A]	4	3	2 [A]	4	13
C_{max}, ng/mL	200 (22%)	245, 124	313 (65%)	468 (29%)	378, 318	1240 (41%)	1267 (37%)
AUC_{24}, ng×h/mL	2488 (29%) [C]	4666, 2036	5767 (69%)	8323 (34%)	8283, 4587	19024 (33%)	21526 (38%)

Note: Multiple dose PK was assessed on C1D13 in Cohort 12 and C1D14 in Cohorts 13 to 18
n.c.: not calculated (insufficient data or PK samples not collected)
[A] Individual values are shown for n<3; [B] n=4; [C] n=3

- Voruciclib multiple dose exposures on C1D14 was generally proportional to the dose in the range 50 mg to 300 mg.
- Voruciclib PK profiles are consistent with historical single agent data; it is inferred that venetoclax does not affect voruciclib PK

Venetoclax PK at 50-250 mg

Mean (%CV) multiple dose venetoclax C_{max} and AUC_{24} values

	Cohort 12	Cohort 13	Cohort 14	Cohort 15	Cohort 16	Cohort 17	Cohort 18 + EXP1	Historical Venetoclax Data (Study M12-175)	
Venetoclax dose Voruciclib dose	200 mg QD 50 mg QOD	200 mg QD 50 mg QD	200 mg QD 100 mg QD	200 mg QD 150 mg QD	200 mg QD 200 mg QD	200 mg QD 250 mg QD	200 mg QD 300 mg QD	CLL/SLL 200 mg QD	NHL 200 mg QD
C1D13/14 (multiple dose) venetoclax PK parameters									
n	3	3	4	3	3	4	14	7	3
C_{max}, µg/mL	1.77 (36%)	1.49 (72%)	1.40 (127%)	0.95 (59%)	1.2 (13%)	1.27 (22%)	0.96 (62%)	1.44 (39%)	1.11 (27%)
AUC_{24}, µg×h/mL	17.04, 22.98 [A]	38.89, 7.54 [A]	21.8 (135%)	10.6 (39%)	14.9 (28%)	15.3 (30%)	12.26 (61%) [B]	24.28 (44%)	16.26 (28%)

Note: Multiple dose PK was assessed on C1D13 in Cohort 12 and C1D14 in Cohorts 13 to 18

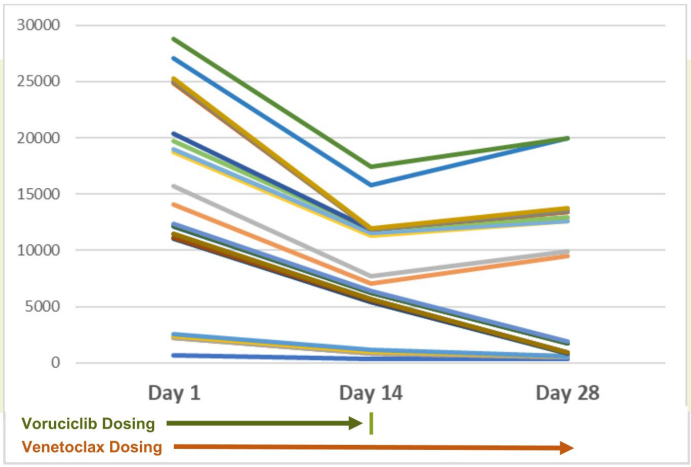
[A] Individual values are shown for n<3; [B] n=13

- Voruciclib once daily administration did not have an effect on venetoclax pharmacokinetics.

Now Evaluating Voruciclib on Days 1 to 21 of 28-Day Cycle in Combination with Venetoclax to Extend Voruciclib Exposure and Prevent Blast Rebound

- 18/24 pts (75%) had decreased blasts on Day 14, at the end of voruciclib and venetoclax combination dosing
- 8/18 pts (44%) had blasts rebound between Day 14 and 28, when voruciclib was stopped while continuing venetoclax
- Increasing duration of voruciclib exposure may prevent blast rebound and enhance efficacy

Peripheral Blast Counts Decrease on Voruciclib + Venetoclax and Rebound on Venetoclax Alone in Days 15-28



Patient Enrollment in VORU $IS_{3w,1w}$ + Venetoclax Cohorts Paused for Strategic Reasons After Completing Enrollment at 150 mg Dose

- 3 patients enrolled in VORU+VEN group at 150 mg on $IS_{3w,1w}$
  - No DLTs
  - 1 patient had a 49% reduction in bone marrow blasts
- Enrollment halted for strategic reasons despite investigator support for evaluation of 3-week schedule
- Enrollment of dose escalation and expansion cohorts on 3-week schedule can be completed by year-end 2024 if enrollment is reactivated in early September
  - Significant gain in efficiency and lower cost if current protocol is reactivated with the same sites and CRO
- Estimated R&D cost to complete dose optimization on $IS_{3w,1w}$

Patients Enrolled	Investigators/CRO	Consultants	Total
16 (at 200 mg)	$852,200	$386,000	$1,238,200
16 (at 250 mg)	$852,200	$177,000	$1,034,200
32 (at 200 mg and 250 mg)	$1,709,400	$563,000	$2,272,400

Estimated R&D Cost to Evaluate 200 mg Only

	Activity	Unit cost	No. Units	Total cost
Clinical study	Investigator cost	$ 30,000	16	$ 480,000
	CRO	$ 30,000	6	$ 180,000
	PK assays + analysis	$ 3,000	16	$ 48,000
	Correlative studies	$ 3,000	16	$ 48,000
	Drug supply	$ 700	16	$ 11,200
	TOTAL			**$ 767,200**
IND maintenance FDA/sites	IB/DSUR preparation (Sept 2024)	$ 40,000	1	$ 40,000
	IRB approvals	$ 5,000	9	$ 45,000
	TOTAL			**$ 85,000**
Consultants/R&D only	Medical monitor ($400 x 60h/m)	$ 24,000	6	$ 144,000
	Clin Ops ($250 x 80h/m)	$ 20,000	6	$ 120,000
	Drug supply/clin ops ($200 x50h/m)	$ 10,000	6	$ 60,000
	Biometrics (statistician, programmer)	$ 8,000	4	$ 32,000
	Reg Aff and Reg Ops	$ 5,000	6	$ 30,000
	TOTAL			**$ 386,000**
Study total				**$ 1,238,200**

Estimated R&D Cost to Evaluate 200 mg and 250 mg

	Activity	Unit cost	No. Units	Total cost
Clinical study	Investigator cost	$ 30,000	32	$ 960,000
	CRO	$ 50,000	9	$ 450,000
	PK assays + analysis	$ 3,000	32	$ 96,000
	Correlative studies	$ 3,000	32	$ 96,000
	Drug supply	$ 700	32	$ 22,400
	TOTAL			**$ 1,624,400**
IND maintenance FDA/sites	IB/DSUR preparation (Sept 2024)	$ 40,000	1	$ 40,000
	IRB approvals	$ 5,000	9	$ 45,000
	TOTAL			**$ 85,000**
Consultants	Medical monitor ($400 x 60h/m)	$ 24,000	9	$ 216,000
	Clin Ops ($250 x 80h/m)	$ 20,000	9	$ 180,000
	Drug supply/clin ops ($200 x50h/m)	$ 10,000	9	$ 90,000
	Biometrics	$ 8,000	4	$ 32,000
	Reg Aff and Reg Ops	$ 5,000	9	$ 45,000
	TOTAL			**$ 563,000**
Study total				**$ 2,272,400**

Estimated R&D Cost to Evaluate 24 Patients at RP2D in Phase 2

	Activity	Unit cost	No. Units	Total cost
Clinical study	Investigator cost	$ 30,000	24	$ 720,000
	Amendment approval at sites	$ 3,000	9	$ 27,000
	CRO	$ 50,000	12	$ 600,000
	PK assays + analysis	$ 3,000	24	$ 72,000
	Drug supply	$ 700	24	$ 16,800
	Biometrics consultants	$ 8,000	6	$ 48,000
	TOTAL			**$ 1,483,800**
IND maintenance FDA/sites	IB/DSUR preparation (Sept 2025)	$ 40,000	1	$ 40,000
	IRB approvals	$ 5,000	9	$ 45,000
	TOTAL			**$ 85,000**
Consultants/R&D only	Medical monitor ($500 x 60h/m)	$ 30,000	12	$ 360,000
	Clin Ops ($250 x 80h/m)	$ 25,000	12	$ 300,000
	Drug supply/clin ops ($200 x50h/m)	$ 10,000	12	$ 120,000
	Reg Aff and Reg Ops	$ 5,000	12	$ 60,000
	TOTAL			**$ 840,000**
Study total				**$ 2,408,800**

Voruciclib is the Only Oral CDK9 Inhibitor in Clinical Development in Combination with Venetoclax in AML

Drug	Company	Target(s)	CDK9 IC_{50} (nM)	ROA	Indications (ongoing studies)	Stage
Voruciclib	MEI Pharma	CDK 9	0.63	oral	**AML (+venetoclax)**	Ph 1
Fadraciclib	Cyclacel Pharma	CDK 2, 9	26.2	oral	**AML (single agent)**, MDS, T and B-cell lymphoma, biliary tract, endometrial, ovarian, breast, HCC, CRC	Ph 1/2
BTX-A51	Edgewood Oncology	CDK 7,9 CK1-alpha	4	oral	**AML (+azacytidine)**, MDS, advanced solid tumors, breast	Ph 1
SLS-009	Sellas	CDK 9	0.9	IV	**AML (+venetoclax/+azacytidine)**, PTCL, DLBCL, CLL, lymphoma	Ph 1
KB-0742	Kronos Bio	CDK 9	6	oral	NHL, DLBCL, refractory solid tumors	Ph 2
PRT-2527	Prelude Therapeutics	CDK 9	0.98	IV	NHL, TCL, advanced solid tumors (completed)	Ph 1
Enitociclib	Vincerx Pharma	CDK 9	3-16	IV	MYC-driven advanced cancers: DLBCL, PTCL & solid tumors	Ph1

Scientific Rationale for Voruciclib Development in B-cell Malignancies & Solid Tumors

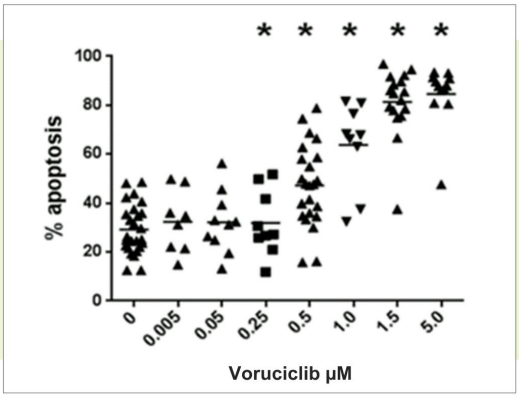
Life Cycle Opportunities for Voruciclib

- Lymphoid malignancies with MCL1 amplification or increased expression
  - PTCL
  - CLL in combination with venetoclax
  - MCL
  - DLBCL
  - Multiple myeloma
- Solid tumors with MCL1 amplification or increased expression
  - Prostate cancer
  - Small cell lung cancer (SCLC)
  - Hepatocellular carcinoma (HCC)

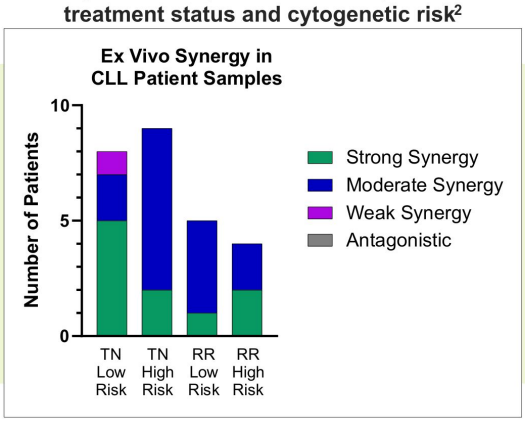
- Cancers with MYC amplification or increased expression (e.g., TNBC, SLCL, HCC, ovarian cancer)
  - PDX tumor models ongoing
- Cancers with KRAS mutations (NSCLC, CRC)
  - Synergy with KRAS G12C inhibitors observed in cell lines

Voruciclib Shows Single Agent Efficacy and Synergizes with Venetoclax in CLL Cells

Voruciclib induces apoptosis in CLL cells[1]



Voruciclib + Venetoclax shows synergy in all CLL patient samples tested: independent of treatment status and cytogenetic risk[2]



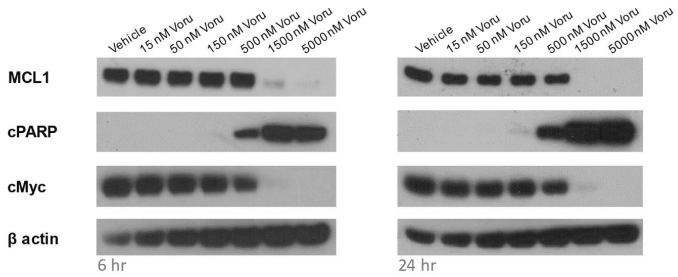
- TN: treatment naïve. RR: Relapsed / refractory
- Low risk=IGHV mutated plus low risk FISH . High risk=IGHV unmutated and/or high-risk FISH(11q-or 17p-)
- CLL cells assayed with human stromal cells.
- Synergy based on Combination Index values: Strong synergy (0-0.3), Moderate synergy (0.31-0.7), Weak synergy (0.71-1.0), Antagonsitic (>1.0)

[1]Danilov et al, ASH 2016. [2]Lesnick et al. J Clin Oncol. 2020;38(15_suppl):e20009

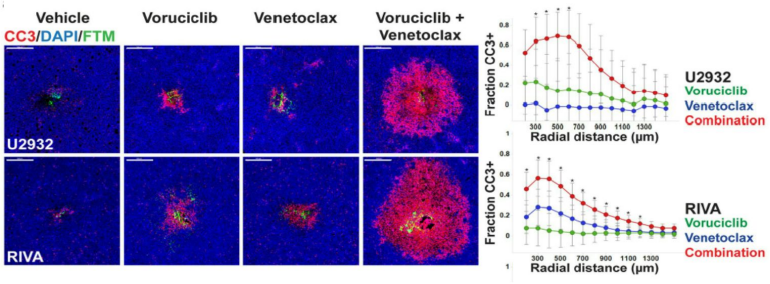
Voruciclib Synergizes with Venetoclax in DLBCL Nonclinical Models

- Voruciclib induces dose-dependent reduction in MYC and MCL1 proteins in DLBCL cell lines
- Voruciclib synergizes with venetoclax to induce caspase cleavage after CIVO intra-tumoral injections
- Voruciclib and venetoclax synergize to reduce tumor growth in DLBCL mouse xenograft models

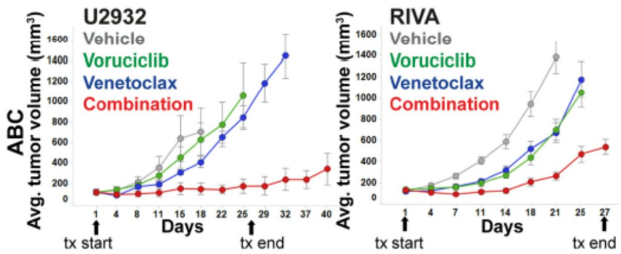
VOR reduces MCL1 & MYC in DLBCL cell lines



Synergy increases apoptosis in tumors



Synergy inhibits tumor growth



Dey, et al. Scientific Reports, 2017
Dey et al. Blood, 2016. ASH conference poster #4167. Presage Biosciences (Data on file)

Single-Agent Phase 1 Studies in Solid Tumors Demonstrated Reduction in MYC and was Generally Well-tolerated at Expected Therapeutic Doses

2 weeks on, 1 week off schedule (N = 29 pts)

- 75 to 850 mg
- MTD = 600 mg
- 41% disease control rate

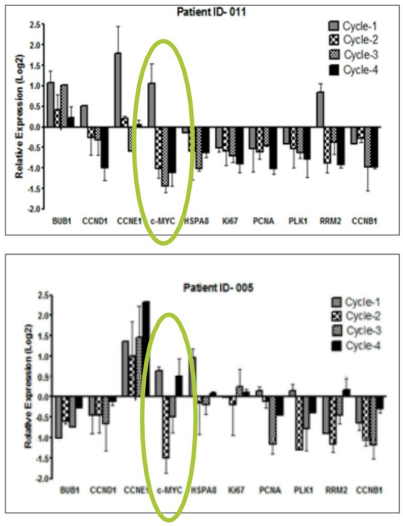
Daily continuously schedule (N = 39 pts)

- 75 to 500 mg
- MTD = 350 mg
- 31% disease control rate

Safety data

- No evidence of myelosuppression
- Most common AEs involved GI tract

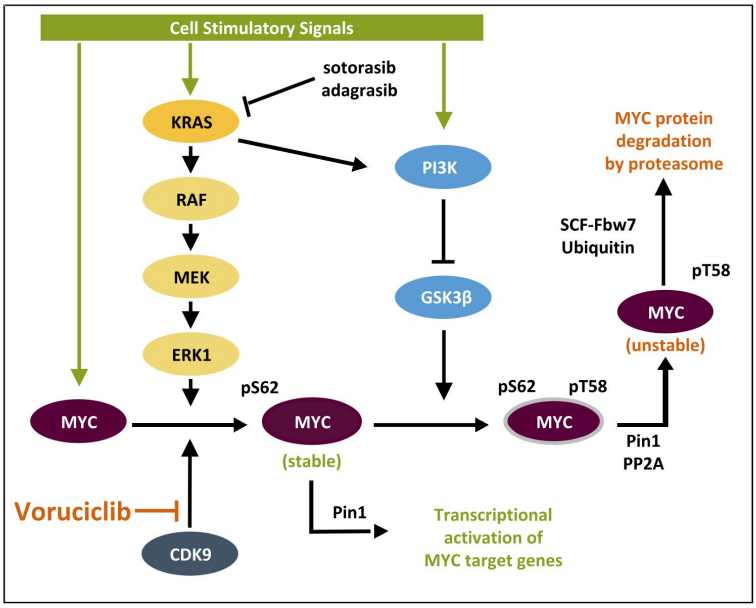
- 10 gene biomarkers evaluated in blood in daily dosing study
- c-MYC expression decreased in ~60% patients tested (n=25)



Gupta et al, ASCO 2012; Hao et al, ASCO 2012; MEI Data on file

CDK9 can influence MYC protein stability in KRAS mutant cancer cells

- Mutations in *KRAS* at G12, G13, and Q61 are oncogenic drivers in many cancers, including lung, colorectal, pancreatic, bone marrow, and endometrial carcinomas.
- *KRAS* mutations are frequently accompanied by stabilization of the MYC oncoprotein through increased *MYC* transcription and decreased protein degradation.
- MYC protein stability is mediated by phosphorylation of MYC on Ser 62 by ERK and CDK9 kinases.



Wiley, SE. et al. AACR, 2021.

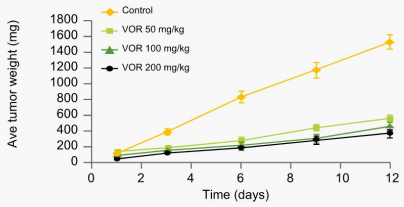
Voruciclib Inhibits *KRAS* Mutant Cell Lines *In Vitro* and *In Vivo* in Xenograft Mice

VOR inhibited proliferation of KRAS mutant cell lines from multiple indications

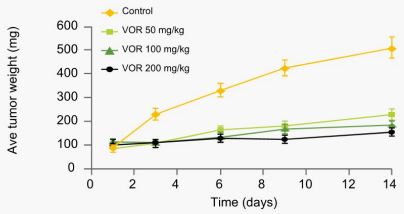
- CRC
- Esophageal
- Multiple Myeloma
- NSCLC
- Ovarian
- PDAC

VOR inhibited proliferation of cell lines with various KRAS mutations

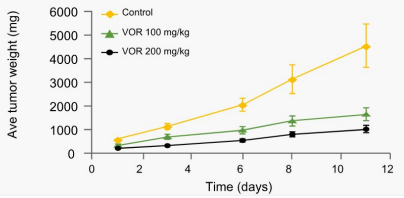
- G12C, G12D, G12A, G12V
- G13C, G13D
- Q61H



HCT-116
(CRC, KRAS G13D)



SW-480
(CRC, KRAS G12V)

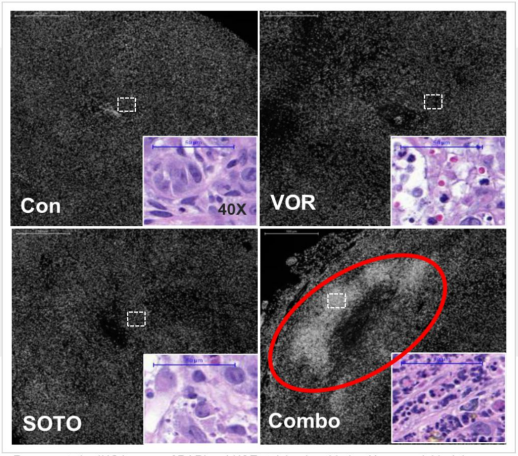


H460
(NSCLC, KRAS Q61H)

Wiley, SE. et al. AACR, 2021 & unpublished.

Synergy of CDK9 Inhibition with Direct KRAS Inhibitors

Voruciclib Synergizes with Sotorasib in an *In Vivo* MIA Paca-2 Tumor Model



Representative IHC images of DAPI and H&E staining in a Murine Xenograph Model

Cell death around each microinjection site measured by nuclear condensation and fragmentation

Voruciclib Synergizes With *Kras* G12c Inhibitors *In Vitro*

Cell Line	*KRAS* mut	Sensitivity to G12C Inhibitors	Synergy Scores: Voruciclib + Sotorasib	Synergy Scores: Voruciclib + Adagrasib
NCI-H23	G12C	High		
HCC1171	G12C	High		
MIA Paca-2	G12C	High		
SW837	G12C	Moderate - High		
NCI-H2030	G12C	High		
Calu-1	G12C	Moderate - High		
HCC-44	G12C	Moderate - High		
NCI-H1373	G12C	Moderate - High		
NCI-H358	G12C	High		
NCI-H1792	G12C	Moderate - High		
KYSE-410	G12C	Low - High		
Panc 04.03	G12D	Low		
Gp2D	G12D	Low		
LS-513	G12D	Low - Moderate		
AsPC-1	G12D	Low		
HPAF-II	G12D	Low		
TOV-21G	G13C	Low		

Low Moderate High

Non-small cell lung cancer cell lines
Pancreatic adenocarcinoma cell lines
Colorectal cancer cell lines
Esophageal cancer cell line
Ovarian cell line

Wiley, SE. et al. AACR, 2021.

Voruciclib Presents a Strong Value Proposition as the Only Oral CDK9 Inhibitor in Clinical Development in Combination with Venetoclax in AML

- Investment rationale
  - Opportunity to continue ongoing Phase 1 study (16-32 patients) to value inflection point by YE2024 and Phase 2 study (24 patients) in CY2025 for modest investment
- Initial focus on R/R AML
  - Significant medical need in large number of patients
    - Mutation agnostic therapy with potential to address >50% of AML patients
  - Clear and efficient path to marketing approval
- Voruciclib plus venetoclax
  - Durable responses observed in patients with R/R AML after venetoclax failure
  - On target effect observed on Mcl-1 and RNA Pol II
- Life cycle management
  - Market and scientific rationale to move to 1L AML
  - Utility where venetoclax is approved/used in other hematologic indications
  - Potential to address several solid tumors associated with MYC overexpression

Estimated R&D costs

- Stage 1a: ~$1.2M
  - 16 patients
  - Evaluate 200 mg only
  - Readout December 2024
- Stage 1b: ~$1.1M
  - 16 patients
  - Evaluate 250 mg
  - Readout March 2025
- Stage 2: ~$2.4M
  - 24 patients
  - Dose 200 or 250 mg
  - Readout December 2025

TOTAL: ~ $4.7M to complete Phase 1 and Phase 2 studies with ~56 patients by YE2025

Voruciclib: An Oral CDK9 Inhibitor for AML and Other Malignancies

July 2024