Revumenib for Patients With Relapsed or Refractory *KMT2Ar* Acute Leukemia: Outcomes by Leukemia Type in the Phase 2 AUGMENT-101 Study

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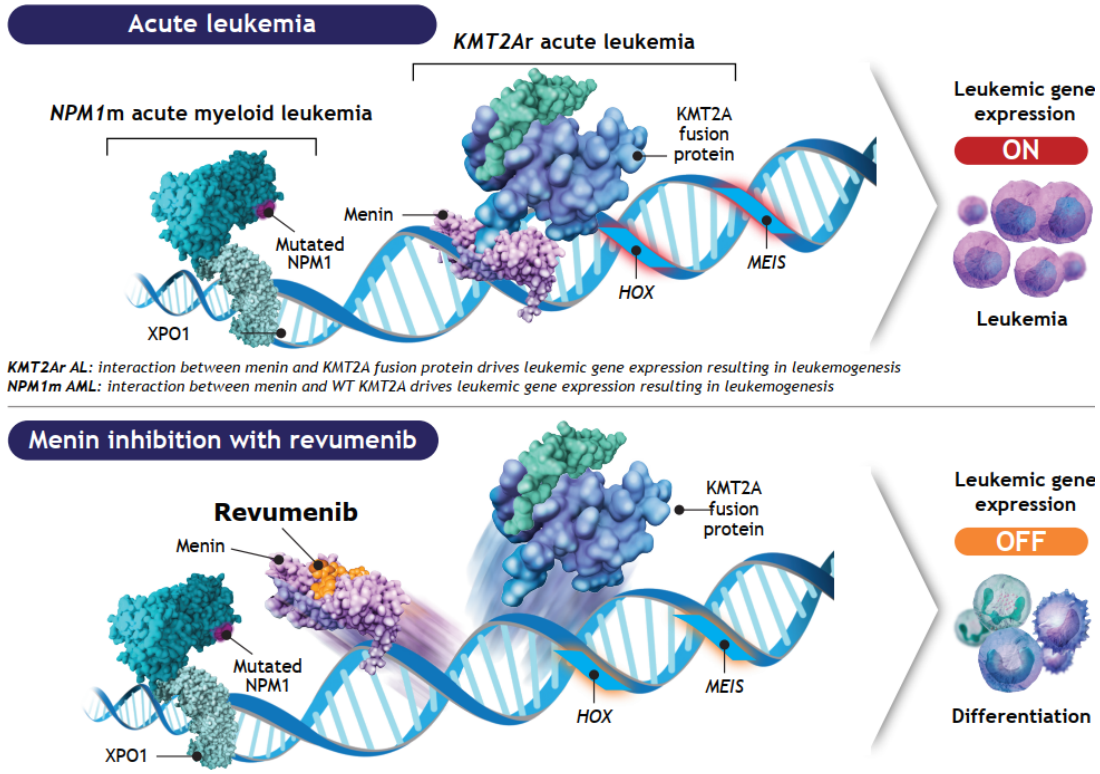
Revumenib: First-in-class menin inhibitor

- The menin-KMT2A protein interaction plays a critical role in leukemogenesis, and up to 10% of patients with AL have a *KMT2A* gene rearrangement (*KMT2A*r)[1,2]
- *KMT2A*r AML is aggressive, progresses rapidly, and has high rates of relapse[3]
- Revumenib is a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction that disrupts multiple drivers of leukemogenesis (*KMT2A*r and *NPM1*m)[4]
- Revumenib is the only menin inhibitor approved for R/R AL harboring a *KMT2A* translocation, and was recently approved for those with an *NPM1* mutation, in adult and pediatric patients (≥1 year) in the United States[5]



Objective: to further characterize the efficacy and safety of revumenib monotherapy in patients from AUGMENT-101 with R/R *KMT2A*r AL across AML, ALL, and MPAL subtypes

AL, acute leukemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; *HOX*, homeobox; *KMT2A*, lysine methyltransferase 2A; *KMT2A*r, *KMT2A*-rearranged; *MEIS*, Meis homeobox; MPAL, mixed-phenotype acute leukemia; *NPM1*, nucleophosmin 1; *NPM1*m, *NPM1*-mutated; R/R, relapsed or refractory; XPO1, exportin-1. 1. Yokoyama A, et al. *Cell*. 2005;123(2):207-218. 2. Issa GC, et al. *Leukemia*. 2021;35(9):2482-2495. 3. Issa GC, et al. *Blood Cancer J*. 2021;11(9):162. 4. Issa GC, et al. *Nature*. 2023;615(7954):920-924. 5. REVUFORJ® (revumenib) tablets, for oral use [package insert]. Syndax Pharmaceuticals, Inc.; 2025.

AUGMENT-101 phase 2 study design (NCT04065399)

Phase 1: Dose escalation

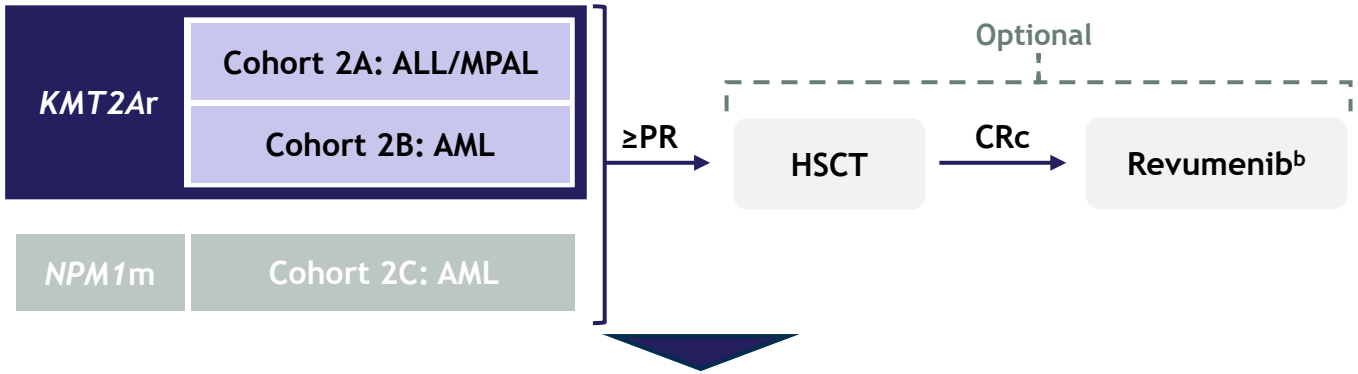
Revumenib RP2D

160 mg q12h orally (95 mg/m^2 if <40 kg) WITH strong CYP3A4i in 28-day cycles[a]

Patient population

Adult and pediatric patients with R/R AL with *KMT2A*r or *NPM1*m

Phase 2: Pivotal trial



FDA-approved dosage

160 mg q12h orally (95 mg/m^2 if <40 kg) WITH strong CYP3A4i in 28-day cycles[a]

or

270 mg q12h orally (160 mg/m^2 if <40 kg) WITHOUT strong CYP3A4i in 28-day cycles[a]

Phase 2 endpoints (DCO: Feb 29, 2024)

Primary

- CR + CRh rate
- Safety and tolerability

Key secondary

- CRc rate[c]
- ORR
- Duration of response
- Time to response
- OS

[a]Revumenib administered until unacceptable toxicity, end of Cycle 4 if no response, or PD without clinical benefit as defined by the investigator. [b]Maintenance therapy with revumenib after HSCT was allowed per protocol amendment for eligible patients, with maintenance treatment continued until disease progression or unacceptable toxicity. [c]CR + CRh + CRp + CRi. CR, complete remission; CRc, composite CR; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; HSCT, hematopoietic stem cell transplant; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial remission.

Demographic and baseline disease characteristics

Characteristic	Efficacy population[a] (N = 97)			Safety population[b] (N = 116)		
	AML (n = 78)	ALL (n = 13)	MPAL (n = 6)	AML (n = 95)	ALL (n = 15)	MPAL (n = 6)
Age, median (range), y	37.5 (1.3–75.0)	37.0 (0.6–73.0)	16.0 (1.0–53.0)	37.0 (1.3–75.0)	31.0 (0.6–73.0)	16.0 (1.0–53.0)
Age group, n (%)						
<18 y	14 (17.9)	3 (23.1)	3 (50.0)	20 (21.1)	5 (33.3)	3 (50.0)
18 to <65 y	55 (70.5)	7 (53.8)	3 (50.0)	64 (67.4)	7 (46.7)	3 (50.0)
≥65 y	9 (11.5)	3 (23.1)	0	11 (11.6)	3 (20.0)	0
Female, n (%)	45 (57.7)	8 (61.5)	2 (33.3)	56 (58.9)	9 (60.0)	2 (33.3)
Race, n (%)						
White	56 (71.8)	9 (69.2)	4 (66.7)	66 (69.5)	10 (66.7)	4 (66.7)
Non-White	12 (15.4)	2 (15.4)	0	12 (12.6)	2 (13.3)	0
Other[c]	10 (12.8)	2 (15.4)	2 (33.3)	17 (17.9)	3 (20.0)	2 (33.3)
Prior lines of therapy, median (range)	2 (1–11)	3 (1–8)	2 (1–4)	2 (1–11)	3 (1–8)	2 (1–4)
≥3, n (%)	30 (38.5)	9 (69.2)	2 (33.3)	38 (40.0)	11 (73.3)	2 (33.3)
≥4, n (%)	15 (19.2)	5 (38.5)	2 (33.3)	19 (20.0)	6 (40.0)	2 (33.3)
Prior therapy, n (%)						
Venetoclax	57 (73.1)	3 (23.1)	2 (33.3)	67 (70.5)	4 (26.7)	2 (33.3)
HSCT	39 (50.0)	4 (30.8)	3 (50.0)	52 (54.7)	4 (26.7)	3 (50.0)

- Median (range) duration of follow-up[d] was 5.9 (0.3–25.7) months for AML, 3.9 (0.3–22.3) for ALL, and 5.4 (0.9–7.4) for MPAL

Data cutoff: February 29, 2024. [a]Efficacy population: patients with centrally confirmed *KMT2Ar* AL who had ≥5% baseline bone marrow blasts within 28 days prior to start of study treatment. [b]Safety population: all enrolled patients who received ≥1 dose of revumenib during the study. [c]Includes "other," "multiple," and "unknown." [d]In the safety population.

Efficacy: Response

Parameter	Efficacy population (N = 97)		
	AML (n = 78)	ALL (n = 13)	MPAL (n = 6)
ORR,[a] n (%)	52 (66.7)	6 (46.2)	4 (66.7)
95% CI[b]	55.1–76.9	19.2–74.9	22.3–95.7
Best overall response, n (%)			
CR	11 (14.1)	3 (23.1)	1 (16.7)
CRh	7 (9.0)	0	0
CRp	15 (19.2)	1 (7.7)	1 (16.7)
CRi	1 (1.3)	0	1 (16.7)
MLFS	18 (23.1)	1 (7.7)	1 (16.7)
PR	0	1 (7.7)	0
PD	6 (7.7)	1 (7.7)	0
No response	15 (19.2)	6 (46.2)	0
Other[c]	5 (6.4)	0	2 (33.3)
Patients remaining on study, n (%)	24 (30.8)	1 (7.7)	2 (33.3)

- 21 patients proceeded to HSCT while in remission, including 19 with AML and 2 with MPAL
  - As of data cutoff, 9/19 (47.4%) patients with AML who underwent HSCT resumed revumenib treatment after HSCT
- Median (range) duration of treatment[d]
  - AML: 2.6 (0.1–14.9) months
  - ALL: 2.0 (0.2–4.9) months
  - MPAL: 1.7 (0.7–3.9) months

Data cutoff: February 29, 2024. [a]CRc + MLFS + PR. [b]Exact 95% CIs of response rate are 2-sided and calculated using the Clopper-Pearson method. [c]Includes those with unknown or missing status. [d]In the safety population. CI, confidence interval; MLFS, morphologic leukemia-free state.

Efficacy: Response

Parameter	Efficacy population (N = 97)		
	AML (n = 78)	ALL (n = 13)	MPAL (n = 6)
CR + CRh rate, n (%)	18 (23.1)	3 (23.1)	1 (16.7)
95% CI[a]	14.3–34.0	5.0–53.8	0.4–64.1
Duration of response,[b] mo Median (95% CI)	7.7 (3.4–NR)	NR (0.9–NR)	1.8 (NE–NE)
Time to response,[b] mo Median (range)	2.0 (0.9–4.6)	1.9 (0.9–2.8)	3.2 (3.2–3.2)
CRc rate,[c] n (%)	34 (43.6)	4 (30.8)	3 (50.0)
95% CI[a]	32.4–55.3	9.1–61.4	11.8–88.2
MRD-negative status,[d,e] n/N (%)			
CR + CRh	9/14 (64.3)	1/3 (33.3)	1/1 (100)
CRc	18/30 (60.0)	1/4 (25.0)	2/2 (100)

- CR + CRh was achievable and similar across AL subtypes
- MRD negativity, as assessed by investigators, was achievable regardless of AL subtype

Data cutoff: February 29, 2024. [a]Exact 95% CIs of response rate are 2-sided and calculated using the Clopper-Pearson method. [b]Kaplan-Meier method used and 2-sided 95% CI calculated based on the Greenwood method. [c]CR + CRh + CRp + CRi. [d]MRD status percentage based on number of responders with MRD status available. [e]MRD assessment conducted locally by flow cytometry. MRD, measurable residual disease; NE, not estimable; NR, not reached.

Safety: Treatment-emergent AEs

Event in ≥25% of safety population, n (%)	Safety population (N = 116)					
	AML (n = 95)		ALL (n = 15)		MPAL (n = 6)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE[a]	95 (100)	88 (92.6)	15 (100)	12 (80.0)	6 (100)	6 (100)
Hematologic AEs						
Febrile neutropenia	36 (37.9)	35 (36.8)	6 (40.0)	6 (40.0)	4 (66.7)	4 (66.7)
Anemia	27 (28.4)	19 (20.0)	2 (13.3)	2 (13.3)	2 (33.3)	2 (33.3)
Non-hematologic AEs						
Nausea	45 (47.4)	4 (4.2)	6 (40.0)	2 (13.3)	1 (16.7)	0
Vomiting	33 (34.7)	3 (3.2)	7 (46.7)	1 (6.7)	0	0
QTcF prolongation	30 (31.6)	15 (15.8)	3 (20.0)	0	1 (16.7)	0
Diarrhea	29 (30.5)	1 (1.1)	6 (40.0)	2 (13.3)	0	0
Differentiation syndrome	27 (28.4)	14 (14.7)	2 (13.3)	2 (13.3)	2 (33.3)	1 (16.7)
Epistaxis	25 (26.3)	3 (3.2)	4 (26.7)	0	1 (16.7)	0

- Revumenib was well tolerated and no new safety signals were identified across AL subtypes

Data cutoff: February 29, 2024. [a]AEs that started on or after first administration of study drug and within 30 days of last dose. For patients who resumed study drug post HSCT, only AEs from the period prior to HSCT are included.
AE, adverse event; QTcF, Fridericia's corrected QT interval.

Safety: Treatment-related AEs

Event in ≥15% of safety population, n (%)	Safety population (N = 116)					
	AML (n = 95)		ALL (n = 15)		MPAL (n = 6)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any revumenib-related AE[a]	83 (87.4)	55 (57.9)	8 (53.3)	4 (26.7)	5 (83.3)	4 (66.7)
Hematologic AEs						
Anemia[b]	16 (16.8)	13 (13.7)	1 (6.7)	1 (6.7)	2 (33.3)	2 (33.3)
Febrile neutropenia[b]	14 (14.7)	14 (14.7)	2 (13.3)	2 (13.3)	2 (33.3)	2 (33.3)
Non-hematologic AEs						
Nausea[b]	29 (30.5)	2 (2.1)	3 (20.0)[c]	2 (13.3)	0	0
QTcF prolongation[b]	28 (29.5)	15 (15.8)	3 (20.0)	0	1 (16.7)	0
Differentiation syndrome	27 (28.4)	14 (14.7)	2 (13.3)	2 (13.3)	2 (33.3)	1 (16.7)[d]
Vomiting[b]	20 (21.1)	1 (1.1)	5 (33.3)[c]	1 (6.7)	0	0

- DS and QTcF prolongation events were manageable per protocol guidance, without any patients receiving DS prophylaxis
  - Majority of DS and QTcF prolongation events occurred during the first cycle, with a median (range) duration of 12 (3–31) and 1 (1-8) days, respectively
- Low rate of treatment discontinuation due to TRAEs (n = 6; 5.2%)
  - No patients discontinued revumenib due to cytopenias, DS, or QTcF prolongation

Data cutoff: February 29, 2024. [a]Relatedness judged by the investigator as possibly related, probably related, or definitely related to study drug. [b]None were grade 4 or 5. [c]One event led to treatment discontinuation. [d]Grade 4 event.
DS, differentiation syndrome; TRAE, treatment-related AE.

Conclusions

- Revumenib monotherapy provides **clinically meaningful** responses in patients with R/R *KMT2Ar* AL **regardless of leukemia type**
  - MRD negativity was achievable in patients achieving CR + CRh across AL subtypes
  - Durable responses were seen in patients who achieved CR + CRh across AL subtypes
- The well-characterized safety profile of revumenib is consistent with prior reports and is similar across AL subtypes
  - Differentiation syndrome was manageable, without any patients having received prophylaxis
  - No patients discontinued treatment due to cytopenias, differentiation syndrome, or QTcF prolongation

These findings continue to support revumenib as an effective treatment option for patients with *KMT2Ar* AL, demonstrating its potential to improve outcomes across multiple leukemia types in this difficult-to-treat population

Two phase 3, randomized, double-blind trials in newly diagnosed AML
(open to enrollment)

REVEAL-ND NPM1
Revumenib + IC in newly diagnosed *NPM1*m AML

Patient population (N ≈ 468)
- Age ≥12 years and ≥40 kg
- Newly diagnosed, untreated AML
- *NPM1*m AML (locally determined, centrally confirmed)

Randomize 1:1

Induction (1-2 cycles)	Consolidation (1-3 cycles)
Revumenib + IC	Revumenib + cytarabine
Placebo + IC	Placebo + cytarabine

(Double-blind treatment)

HSCT (optional)
Patients may undergo HSCT after initial induction chemo or after consolidation

Monotherapy continuation
- Revumenib
- Placebo

Treatment for up to 2 years (from Cycle 1, Day 1)

Survival follow-up

Primary endpoints
- EFS
- MRD-CR

Secondary endpoints
- OS
- CR
- ORR
- DoCR
- DoCRc
- DoR
- QoL

EVOLVE-2
Revumenib + venetoclax + azacitidine in newly diagnosed *NPM1*m or *KMT2A*r AML ineligible for IC

Patient population (N ≈ 448)
- Age ≥75 years or age 18-74 years with comorbidities
- Newly diagnosed *NPM1*m or *KMT2A*r AML
- Ineligible for IC

Randomize 1:1
- Revumenib + venetoclax + azacitidine

(Double-blind treatment)
- Placebo + venetoclax + azacitidine

Dual primary endpoints
- OS
- CR

REVEAL-ND NPM1

EVOLVE-2

REVEAL-ND NPM1: NCT07211958; EVOLVE-2: NCT06652438.
DoCR, duration of CR; DoCRc, duration of composite CR; DoR, duration of response; EFS, event-free survival; IC, intensive chemotherapy; MRD-CR, MRD-negative CR; ND, newly diagnosed.

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Additional revumenib clinical data presented at ASH 2025

Revumenib in R/R AML with *NPM1*m

Poster 3418

Revumenib + intensive chemotherapy in ND AML

Poster 3425

Real-world treatment patterns of ND AML with *NPM1*m

Poster 3385

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