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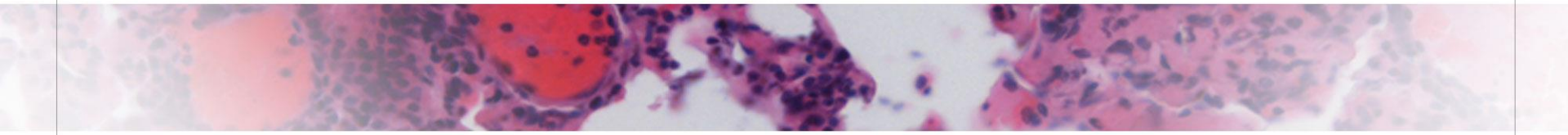

Preliminary Data Report on a Phase 1/2A First in Human Study of the Menin-KMT2A (MLL) inhibitor KO-539 in patients with relapsed or refractory acute myeloid leukemia

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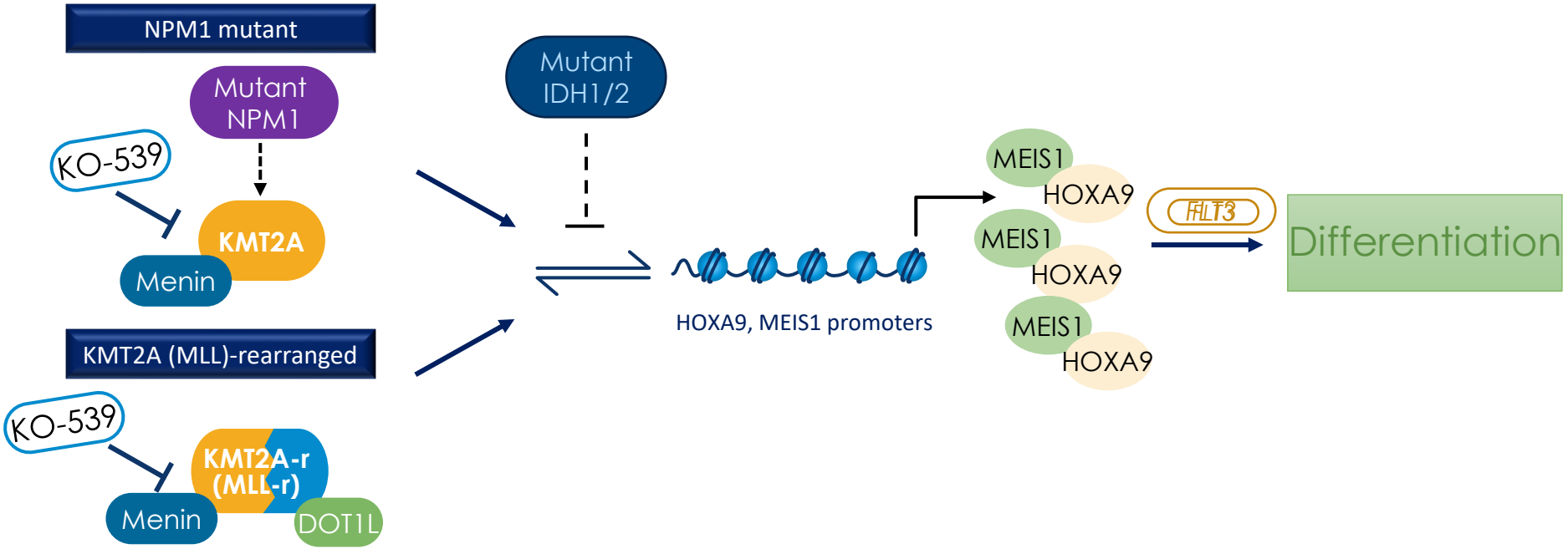
KO-539 is a Potent and Selective Oral Inhibitor of the Menin-KMT2A (MLL) Complex



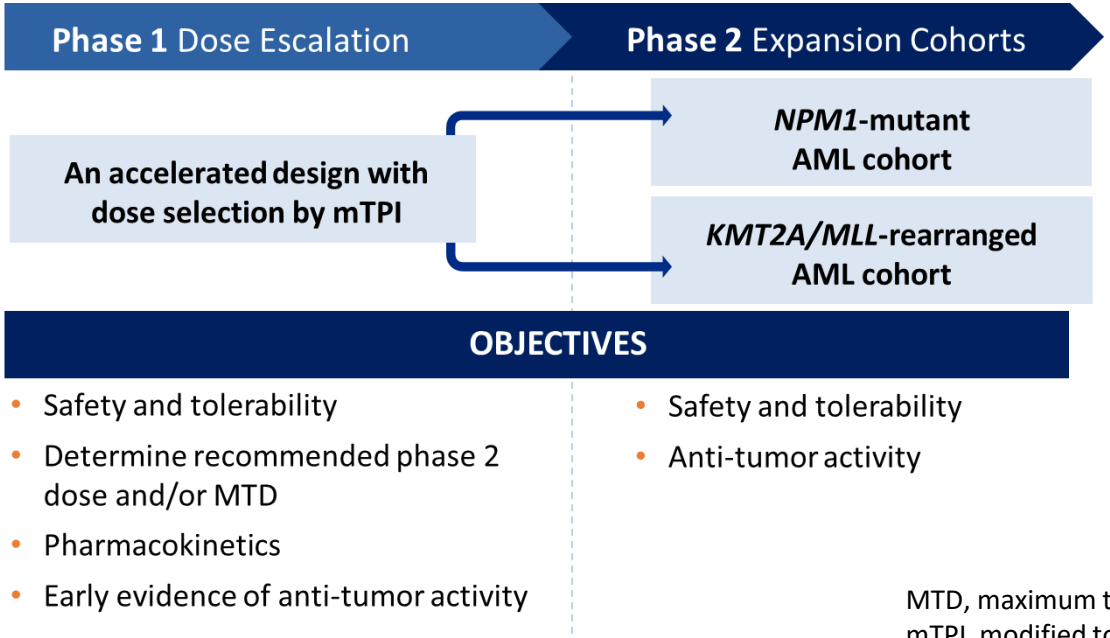
Key KO-539 Preclinical Toxicology and Pharmacokinetics Findings

- Toxicology/Safety Pharmacology
  - No evidence of QTc prolongation in dogs
  - Low torsadogenic risk based on key cardiac ion channels interactions

- Pharmacokinetics
  - Primarily metabolized by CYP3A4 generating biologically two active metabolites
  - KO-539 and metabolite(s) possess CYP3A4 inhibitory properties
  - High protein binding (>99%)

KOMET-001 is a Phase 1/2A First-in-Human Study of KO-539 in Patients with Relapsed/Refractory AML

komet Trial 001



NCT04067336

MTD, maximum tolerated dose
mTPI, modified toxicity probability interval

Patient Demographics and Baseline Characteristics

KOMET-001 Patients	N=12
Median Age, y (min, max)	67 (33, 80)
Gender, n (%)	
Male	8 (66.7%)
Female	4 (33.3%)
Race, n (%)	
White	8 (66.7%)
Number of prior lines of therapies, median (range)	3 (2-7)
Number of patients with prior transplant	1

Data as of 02 November 2020

Patient Status Summary

Disposition & Discontinuation

KOMET-001 Patients	N=12
Patients in Treatment	6
Patients in Follow-Up	1
Patients off Study	5

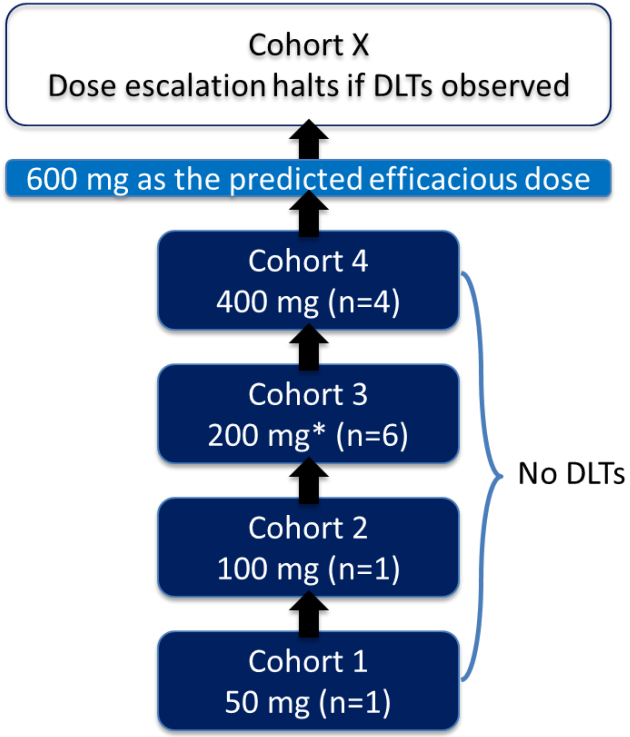
Reason for Study Treatment Discontinuation	N=6
Symptomatic Deterioration	1
Disease Progression as assessed by Investigator	4
Withdrawal of Consent	1

Reason for Study Discontinuation	N=5
Death	2
Physician Decision	2*
Other	1

Data as of 02 November 2020

*both patients expired soon after physician decision to discontinue study participation

KO-539 Demonstrates Encouraging Early Clinical Activity



Clinical activities observed in 6 patients (efficacy evaluable = 8)				
Dose	Mutational Profile	CYP3A4 inhibitor	# of prior regimens	Clinical Activity
400 mg	RUNX1, SRSF2, ASXL1, TET2, STAG2, BCOR, PTPN11	Yes	3	Decreased peripheral blasts
200 mg	U2AF1, TET2, p53, DNMT3A, PTPN11	No	4	Stable disease
	NPM1, FLT3-ITD, TET2, CUX1	Yes	4	Morphological leukemia-free state
	NPM1, DNMT3A, KMT2D	Yes	7	CR, MRD-
100 mg	SETD2, RUNX1	Yes	2	CR, MRD+
50 mg	KMT2A-r	Yes	2	Decreasing hydrea requirement

*Expanded to characterize PK

Data as of 02 November 2020

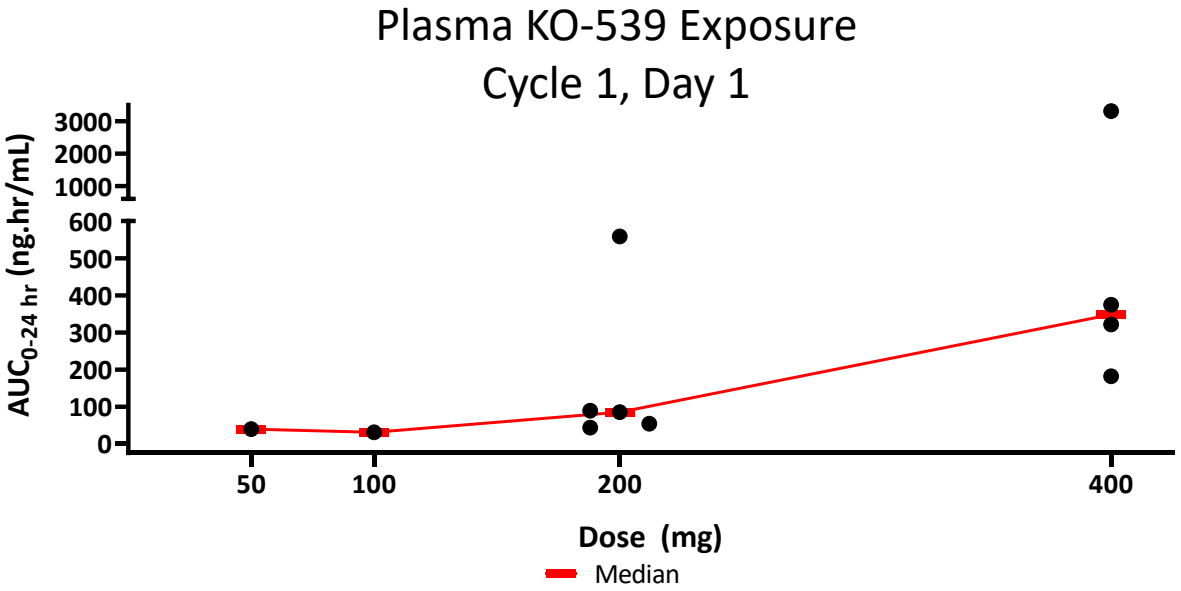
Continuous Daily Dosing of KO-539 Has Been Well-Tolerated with a Manageable Safety Profile

- No dose discontinuations due to treatment-related AEs
- No evidence of QT prolongation or other clinically significant ECG changes

Treatment-related AEs (N=12)	Grade ≥ 3 (all)	Grade 1,2 (≥ 10%)
Pancreatitis	1 (8.3%)	0%
Lipase increased	1 (8.3%)	0%
Neutrophil count decreased	1 (8.3%)	0%
Tumor lysis syndrome	1 (8.3%)	0%
Deep vein thrombosis	1 (8.3%)	0%
Nausea	0%	3 (25%)
Rash	0%	2 (16.7%)
Diarrhea	0%	2 (16.7%)

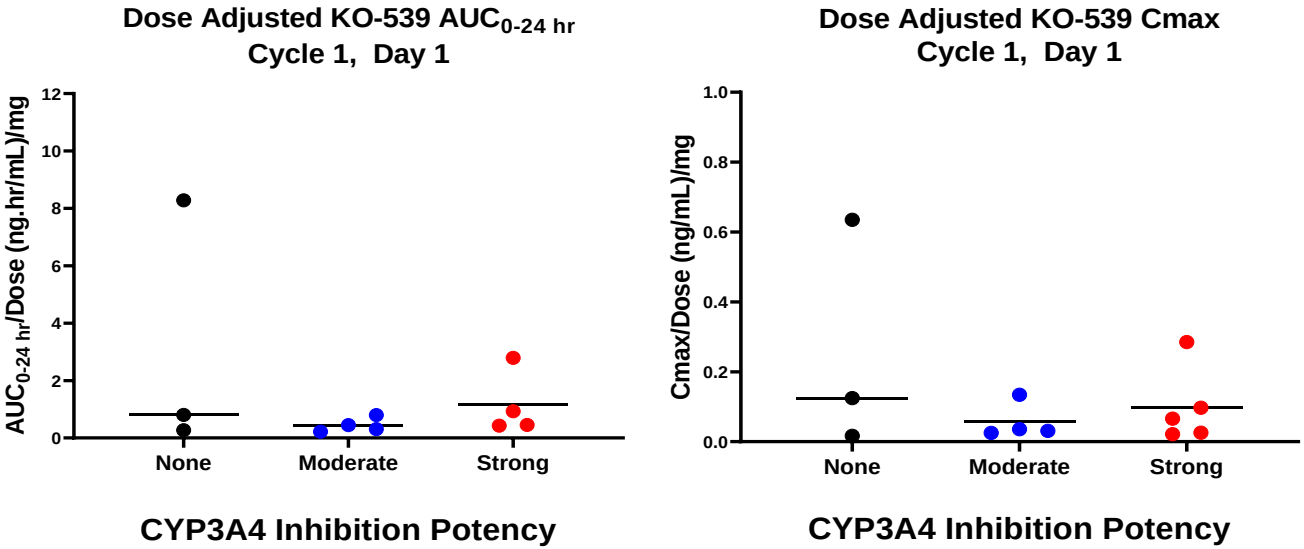
Data as of 02 November 2020

Dose-related Increase in Exposure and Wide Inter-Patient Variability in Patients



n=11; exposure (i.e., $AUC_{0\text{-}24\ hr}$) not evaluable in one patient

KO-539 Pharmacokinetics in Patients Do Not Appear to be Affected by Co-administration of an CYP3A4 Inhibitor



Line represents median value

($AUC_{0\text{-}24\ hour}$: n=11; not evaluable in one patient; Cmax: n=12)

Moderate CYP3A4 inhibitor: Fluconazole, Isavuconazole
Strong CYP3A4 inhibitor: Itraconazole, Posaconazole, Voriconazole, Ketoconazole

Conclusions

- KO-539 is a potent and selective inhibitor of the Menin-KMT2A (MLL) complex
- KO-539 demonstrates early encouraging clinical activity in different genomic subgroups
- KO-539 has been well tolerated and with a manageable safety profile to date
- Plasma KO-539 exposure increases with dose
- KO-539 pharmacokinetics and clinical activity do not appear to be affected by co-administration of an CYP3A4 inhibitor
- KOMET-001 is continuing to enroll patients for phase 1 dose escalation, with plans to expand to phase 2 once recommended phase 2 dose is determined

Acknowledgements

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