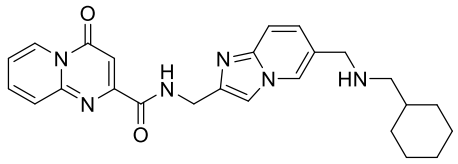
Product data sheet

MedKoo Cat#: 408159 Name: STM2457 CAS#: 2499663-01-1 Chemical Formula: $C_{25}H_{28}N_6O_2$ Exact Mass: 444.2274 Molecular Weight: 444.539	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

STM2457 is a highly potent and selective first-in-class catalytic inhibitor of METTL3. Treatment of tumours with STM2457 leads to reduced AML growth and an increase in differentiation and apoptosis. These cellular effects are accompanied by selective reduction of m6A levels on known leukaemogenic mRNAs and a decrease in their expression consistent with a translational defect. Pharmacological inhibition of METTL3 in vivo leads to impaired engraftment and prolonged survival in various mouse models of AML, specifically targeting key stem cell subpopulations of AML.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	89	200.21
Ethanol	89	200.21

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.25 mL	11.25 mL	22.50 mL
5 mM	0.45 mL	2.25 mL	4.50 mL
10 mM	0.22 mL	1.12 mL	2.25 mL
50 mM	0.04 mL	0.22 mL	0.45 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

TBD

In vivo study

Yankova E, Blackaby W, Albertella M, Rak J, De Braekeleer E, Tsagkogeorga G, Pilka ES, Aspris D, Leggate D, Hendrick AG, Webster NA, Andrews B, Fosbeary R, Guest P, Irigoyen N, Eleftheriou M, Gozdecka M, Dias JML, Bannister AJ, Vick B, Jeremias I, Vassiliou GS, Rausch O, Tzelepis K, Kouzarides T. Small-molecule inhibition of METTL3 as a strategy against myeloid leukaemia. Nature. 2021 May;593(7860):597-601. doi: 10.1038/s41586-021-03536-w. Epub 2021 Apr 26. PMID: 33902106.

7. Bioactivity

Biological target:

STM2457 is a highly potent and selective first-in-class catalytic inhibitor of RNA Methyltransferase METTL3 with an IC50 of 16.9 nM. STM2457 is highly specific for METTL3 and showed no inhibition of other RNA methyltransferases.

Product data sheet

In vitro activity

TBD

In vivo activity

Treatment of tumours with STM2457 leads to reduced AML growth and an increase in differentiation and apoptosis. These cellular effects are accompanied by selective reduction of m6A levels on known leukaemogenic mRNAs and a decrease in their expression consistent with a translational defect. We demonstrate that pharmacological inhibition of METTL3 in vivo leads to impaired engraftment and prolonged survival in various mouse models of AML, specifically targeting key stem cell subpopulations of AML. Collectively, these results reveal the inhibition of METTL3 as a potential therapeutic strategy against AML, and provide proof of concept that the targeting of RNA-modifying enzymes represents a promising avenue for anticancer therapy.

Reference: Yankova E, Blackaby W, Albertella M, Rak J, De Braekeleer E, Tsagkogeorga G, Pilka ES, Aspris D, Leggate D, Hendrick AG, Webster NA, Andrews B, Fosbeary R, Guest P, Irigoyen N, Eleftheriou M, Gozdecka M, Dias JML, Bannister AJ, Vick B, Jeremias I, Vassiliou GS, Rausch O, Tzelepis K, Kouzarides T. Small-molecule inhibition of METTL3 as a strategy against myeloid leukaemia. Nature. 2021 May;593(7860):597-601. doi: 10.1038/s41586-021-03536-w. Epub 2021 Apr 26. PMID: 33902106.