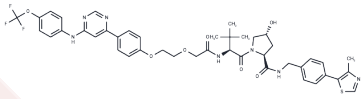
Data Sheet (Cat.No.T8488)

TargetMol

GMB-475

Chemical Properties



CAS No. :	2490599-18-1
Formula:	C43H46F3N7O7S
Molecular Weight:	861.93
Storage:	Store at low temperature,Keep away from direct sunlight Powder: -20°C for 3 years | In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.

Biological Description

Description	GMB-475 is a BCR-ABL1 tyrosine kinase degrader based on PROTAC, overcoming BCR-ABL1-dependent drug resistance. GMB-475 targets BCR-ABL1 protein and recruits the E3 ligase Von Hippel Lindau (VHL).resulting in ubiquitination and subsequent degradation of the oncogenic fusion protein
Targets(IC50)	Apoptosis,Bcr-Abl,STAT,E3 Ligase Ligand-Linker Conjugates,JAK,PROTACs
In vitro	GMB-475 inhibited the proliferation of certain clinically relevant BCR-ABL1 kinase domain point mutants and further sensitized Ba/F3 BCR-ABL1 cells to inhibition by imatinib, while demonstrating no toxicity toward Ba/F3 parental cells.?Reverse phase protein array analysis suggested additional differences in levels of phosphorylated SHP2, GAB2, and SHC associated with BCR-ABL1 degradation.?Importantly, GMB-475 reduced viability and increased apoptosis in primary CML CD34+ cells, with no effect on healthy CD34+ cells at identical concentrations.?GMB-475 degraded BCR-ABL1 and reduced cell viability in primary CML stem cells.?Together, these findings suggest that combined BCR-ABL1 kinase inhibition and protein degradation may represent a strategy to address BCR-ABL1-dependent drug resistance, and warrant further investigation into the eradication of persistent leukemic stem cells, which rely on neither the presence nor the activity of the BCR-ABL1 protein for survival.

Solubility Information

Solubility	DMSO: 245 mg/mL (284.25 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (5.8 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.1602 mL	5.8009 mL	11.6019 mL
5 mM	0.232 mL	1.1602 mL	2.3204 mL
10 mM	0.116 mL	0.5801 mL	1.1602 mL
50 mM	0.0232 mL	0.116 mL	0.232 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Burslem GM, et al. Targeting BCR-ABL1 in Chronic Myeloid Leukemia by PROTAC-mediated Targeted Protein Degradation. Cancer Res. 2019 Jul 16. pii: canres.1236.2019.