Product Name	:	GMB-475
Synonyms	:	——
Cat No.	:	M22049
CAS Number	:	
Molecular Formula	:	C43H4F3NOS
Formula Weight	:	861.93
Chemical Name	:	——
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 proteinGMB-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.
Pathway	:	Angiogenesis
Target	:	Bcr-Abl
Receptor	:	Bcr-Abl1
Solubility	:	DMSO:95 mg/mL(110.22 mM;Need ultrasonic)
SMILES	:	CC1=C(SC=N1)C1=CC=C(CNC(=O)C2CC(O)CN2C(=O)C(NC(=O)COCCOC2=CC=C(C=C2)C2=CC(NC3=CC=C(OC(F)(F)F)C=C3)=NC=N2)C(C)(C)C)C=C1
Storage	:	(-20℃)
Stability	:	≥ 2 years
Reference	:	

1.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.