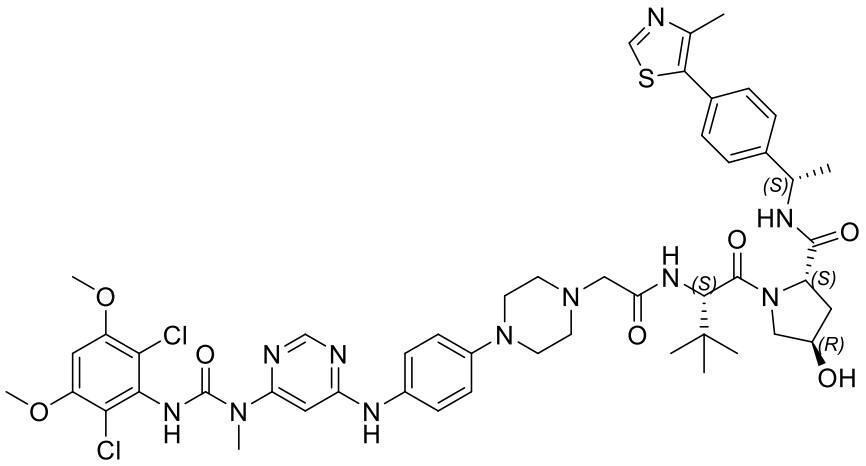
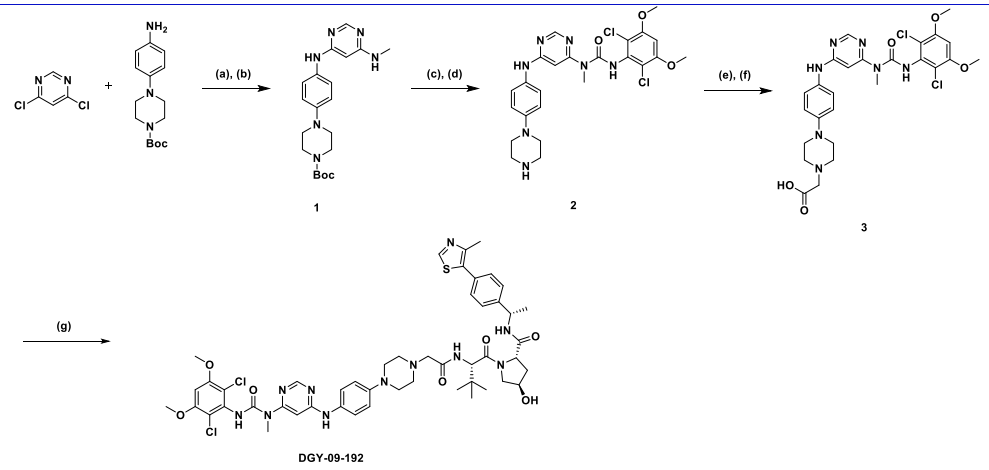
DGY-09-192



Chemical Formula: $C_{49}H_{59}Cl_2N_{11}O_7S$
Molecular Weight: 1017.04

Category	Parameter	Description
Compound	Name	DGY-09-192
	Citation	*Angew. Chem. Int. Ed. 2021, 60, 15905-15911.*
	Chemical descriptors	COC1=CC(OC)=C(Cl)C(NC(=O)N(C)C2=CC(NC3=CC=C(C=C3)N3CCN(CC(=O)N[C@H](C(=O)N4C[C@H](O)C[C@H]4C(=O)N[C@@H](C)C4=CC=C(C=C4)C4=C(C)N=CS4)C(C)(C)C)CC3)=NC=N2)=C1Cl
	Chemical name	(2S,4R)-1-((S)-2-(2-(4-(4-((6-(3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-methylureido)pyrimidin-4-yl)amino)phenyl)piperazin-1-yl)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-((S)-1-(4-(4-methylthiazol-5-yl)phenyl)ethyl)pyrrolidine-2-carboxamide
	Entries in chemical databases	**CID** 44607530
	Availability	N/A
In vitro profiling	Target (potency)	FGFR2 (IC50 = 34 nM Invitrogen assay)
	Target (potency)	FGFR1 (IC50 = 23.8 nM Invitrogen assay)
	Selectivity	
	Potential reactivity	
	SAR	
	Mechanism of inhibition	degradation
	Structure of target-probe complex	N/A
Cellular profiling	Validation of cellular target	FGFR2 (DC50 = 70 nM in KATO III cells), FGFR1 (DC50 = 4.35 nM in CCLP1 cells), FGFR2-PHGDH fusion (degradation at 50 nM)
	Validation of cellular specificity	The degrader compound also results in PDE6D degradation at 100 nM in KATO III cells
Pharmacodynamics		DGY-09-192 inhibited ERK, FRS2 and AKT phosphorylation and slow down tumor growth in xenograft model of FGFR2-PHGDH fusion

Pharmacokinetics	IP administration: T1/2 = 4.25 h, CL = 6.84 ml/min/Kg
Synthetic scheme	

(a) DIEA, IPA, rt. (b) CH_3NH_2, THF, DIEA, *n*-BuOH, 120 ºC (c) aniline, triphosgene, THF, DIEA, ice bath to rt, then **1**, DIEA, PhMe, 80 ºC (d) TFA, DCM (e) K_2CO_3, DMF, t-butyl bromoacetate, rt. (f) TFA, DCM (g) VHL ligand, DIEA, HATU, DMF, rt.