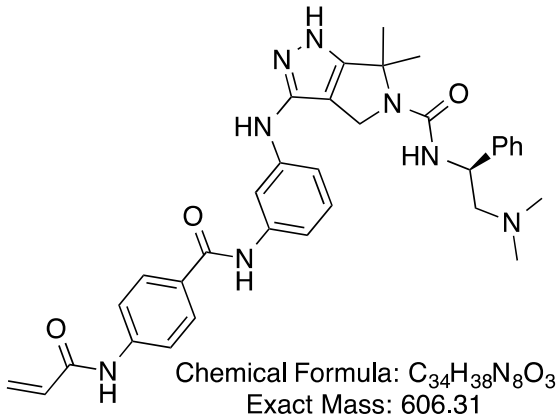
YKL-1-116



Chemical Formula: $C_{34}H_{38}N_8O_3$
Exact Mass: 606.31

Category	Parameter	Description
Compound	Name	YKL-1-116
	Citations	"Activation of the p53 Transcriptional Program Sensitizes Cancer Cells to Cdk7 Inhibitors" *Cell reports* 21.2 (2017): 467-481. "Targeting MYC dependency in ovarian cancer through inhibition of CDK7 and CDK12/13" *eLife* 2018 Nov 13; 7.
	Chemical descriptors	CC1(C)N(C(N[C@H](CN(C)C)C2=CC=CC=C2)=O)CC3=C1NN=C3NC4=CC(NC(C5=CC=C(NC(C=C)=O)C=C5)=O)=CC=C4
	Chemical name	(*S*)-3-((3-(4-acrylamidobenzamido)phenyl)amino)-*N*-(2-(dimethylamino)-1-phenylethyl)-6,6-dimethyl-4,6-dihydropyrrolo[3,4-*c*]pyrazole-5(1*H*)-carboxamide
	Entries in chemical databases	CID 121444083
	Availability	
In vitro profiling	Target (potency)	**CDK7**: IC_{50}= 7.6 nM (Invitrogen, biochemical assay)
	Target (potency)	**CDK9**: IC_{50} > 1 µM; **CDK2**: IC_{50} = 1.1 µM; **CHK2**: IC_{50} = 7.4 nM; **FGR**: IC_{50} = 5.1 nM; **HIP4K**: IC_{50} = 178 nM; **PRKCQ**: IC_{50} = 4.9 nM; **RET**: IC_{50} = 63.5 nM; **SRC**: IC_{50} = 3.9 nM (Invitrogen, biochemical assay)
	Selectivity	YKL-1-116 selectivity was assessed by KiNativ profiling in Jurkat cells @ 1 µM
	Potential reactivity	Cysteine reactive
	SAR	
	Mechanism of inhibition	Irreversible
	Structure of target-probe complex	N/A
	Additional comments	
Cellular profiling	Validation of cellular target	YKL-1-116 dose-dependently targets CDK7 in HCT116, Jurkat, Kuramochi, OVCAR8, and COV362 cancer cells as assessed by intracellular target engagement
	Validation of cellular specificity	OVCAR8 cells overexpressing a CDK7 mutant lacking the requisite cysteine (Cys312) is approximately 6-fold less sensitive to YKL-1-116 (Note: C312S mutant was overexpressed via viral transduction, leaving endogenous CDK7 unchanged); selectivity was also assessed by KiNativ profiling assay in Jurkat cells @ 1 µM
	Additional comments	
Pharmacodynamics	N/A	
Pharmacokinetics	N/A	

Synthetic scheme