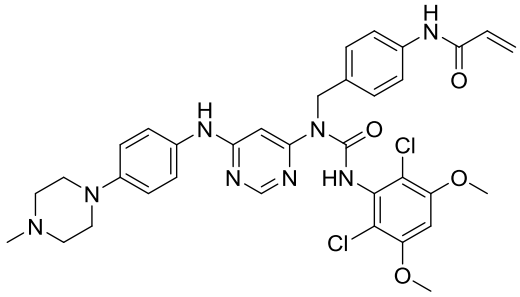
FGFR/EGFR dual inhibitor (FIIN-3)



Chemical Formula: $C_{34}H_{36}Cl_2N_8O_4$
Molecular Weight: 691.61

Category	Parameter	Description
Compound	Name	FGFR/EGFR dual inhibitor (FIIN-3)
	Citation	*Proc Natl Acad Sci U S A*. 2014 Nov 11;111(45):E4869-77
	Chemical descriptors	COC1=CC(OC)=C(Cl)C(NC(N(CC2=CC=C(C=C2)NC(C=C)=O)C3=CC(NC4=CC=C(C=C4)N5CCN(CC5)C)=NC=N3)=O)=C1Cl
	Chemical name	*N*-(4-((3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-methylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)ureido)methyl)phenyl)acrylamide
	Availability	
In vitro profiling	Target (potency)	**FGFR1/2/3/4** (13, 21, 31 and 35 nM IC50s in Z'-Lyte assay) **EGFR** (43 nM IC50 in Z'-Lyte assay)
	Additional Target (potency)	
	Selectivity	S(1) = 0.04, S(10) = 0.08 (DiscoverX KinomeScan)
	Potential reactivity	None to our knowledge
	SAR	
	Mechanism of inhibition	ATP-competitive
	Structure of target-probe complex	
Cellular profiling	Validation of cellular target	FIIN-3 dose-dependently inhibited proliferation of FGFR1/2/3/4 dependent Ba/F3 cells with EC50s between 1~93 nM, EGFR VIII dependent Ba/F3 cells with EC50 of 135 nM. FIIN-3 also effectively inhibited FGFR1 and FGFR2 gatekeeper or other mutants in cells which were resistant to many current FGFR inhibitors. The potency against FGFR dependent cancer cell lines were correlated. FIIN-3 at 1.0 μM effectively inhibited stimulated proliferation of SKOV-3 cells with EGF Compound phenotypes were compared to literature. The cellular effects were correlated with *in vitro* biochemical activities.
	Validation of cellular specificity	FIIN-2 inhibited RET dependent Ba/F3 cells proliferation with EC50 of 211 nM.
Pharmacodynamics		

Pharmacokinetics

Synthetic scheme