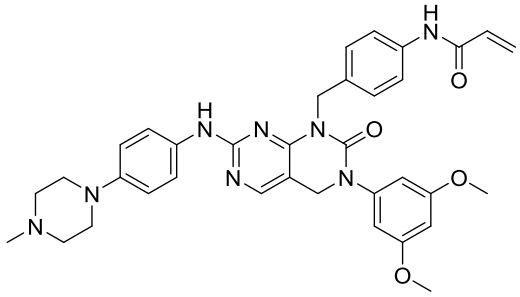
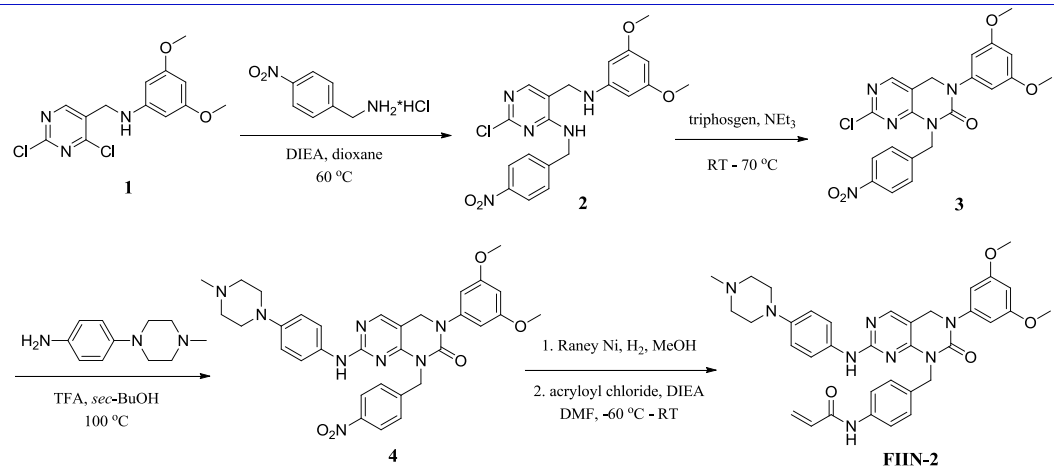
pan-FGFR inhibitor (FIIN-2)



Chemical Formula: $C_{35}H_{38}N_8O_4$
Molecular Weight: 634.74

Category	Parameter	Description
Compound	Name	pan-FGFR inhibitor (FIIN-2)
	Citation	*Proc Natl Acad Sci U S A*. 2014 Nov 11;111(45):E4869-77
	Chemical descriptors	COC1=CC(OC)=CC(N2CC3=CN=C(NC4=CC=C(N5CCN(C)CC5)C=C4)N=C3N(C2=O)CC6=CC=C(NC(C=C)=O)C=C6)=C1
	Chemical name	*N*-(4-((3-(3,5-dimethoxyphenyl)-7-((4-(4-methylpiperazin-1-yl)phenyl)amino)-2-oxo-3,4-dihydropyrimido[4,5-d]pyrimidin-1(2*H*)-yl)methyl)phenyl)acrylamide
	Availability	
In vitro profiling	Target (potency)	**FGFR1/2/3/4** (3.1, 4.3, 27 and 45 nM IC50s in Z'-Lyte assay)
	Additional Target (potency)	**EGFR** (204 nM IC50 in Z'-Lyte assay)
	Selectivity	S(1) = 0.03, S(10) = 0.06 (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-2 dose-dependently inhibited FGFR1/2/3/4 dependent Ba/F3 cells proliferation with EC50s between 1~93 nM. FIIN-2 also effective 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. 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 196 nM, slightly inhibited EGFR dependent Ba/F3 cells proliferation with EC50 around 500 nM,
Pharmacodynamics		
Pharmacokinetics		

Synthetic scheme



1 **2** **3** **4** **FIIN-2**