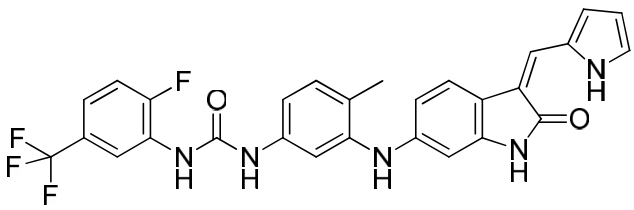
GNF-5837

SYN-1183



(Z)-1-(3-((3-((1H-pyrrol-2-yl)methylene)-2-oxoindolin-6-yl)amino)-4-methylphenyl)-3-(2-fluoro-5-(trifluoromethyl)phenyl)urea

CAS Registry No.: 1033769-28-6

Smiles String:
CC1=CC=C(NC(NC2=C(F)C=CC(C(F)(F)F)=C2)=O)C=C1NC3=CC(NC(/C4=C\C5=CC=CN5)=O)=C4C=C3

Molecular Weight: 535.49

Molecular Formula: C28H21F4N5O2

Lot Number: Refer to vial

1H-NMR: Available on request

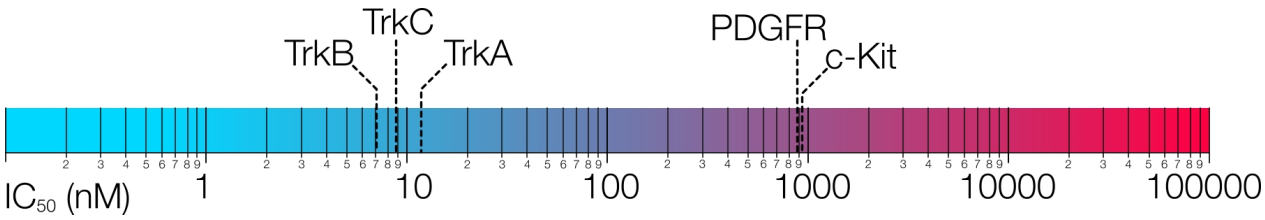
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

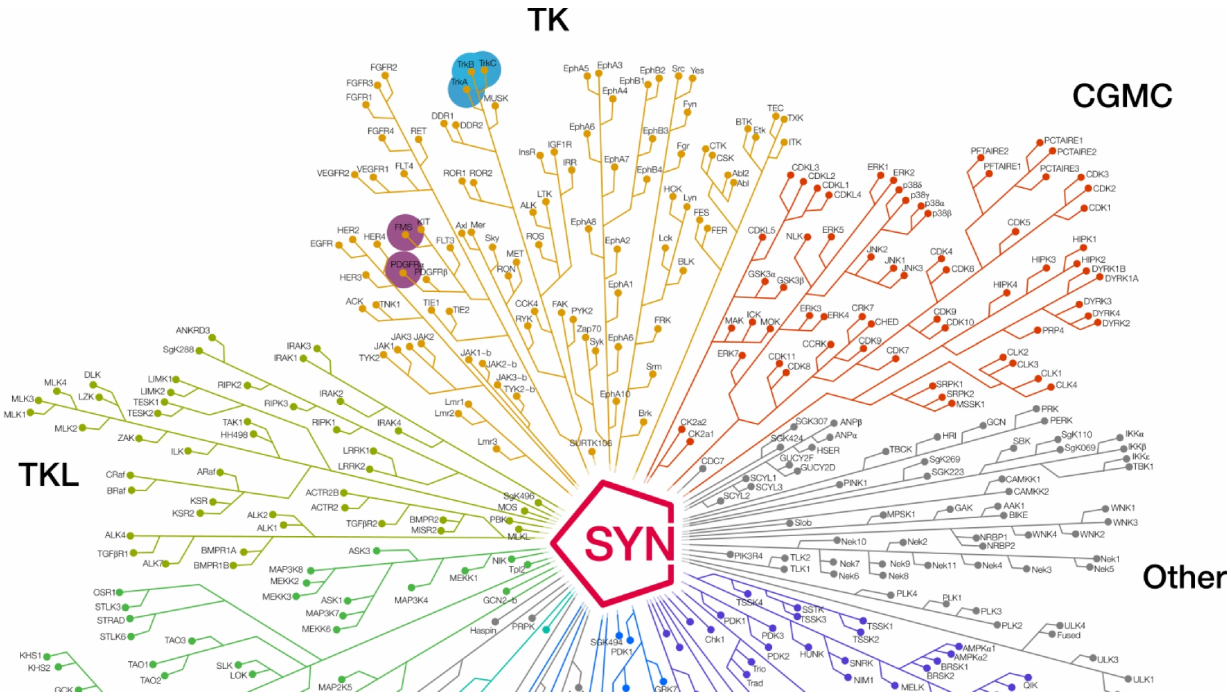
Description:

An orally bioavailable oxindole compound that and acts as a potent, reversible and type II DFG-out inhibitor of pan-Trk activity (IC50 = 8 and 12 nM for TrkA and TrkB). Shown to target Trk (tropomyosin receptor kinase) ATP binding cleft and an immediately adjacent hydrophobic pocket. Preferentially arrests the proliferation of Ba/F3 cells fused with Tel-TrkA, Tel-TrkB and Tel-TrkC (IC50 = 11, 9 and 7 nM, respectively) and in Ba/F3 and RIE cells expressing both TrkA and NGF (IC50 = 42 and 17 nM, respectively) over Mo7e-c-Kit and Rat-A10-PDGFR (IC50 = 1 and 0.5 μM) and Ba/F3-Tel-KDR and wt-Ba/F3 cells (IC50 = 3.0 and 5.6 μM). Displays ~100-fold greater selectivity among a panel of 59 closely related kinases and in 33 cellular kinase assays. Weakly active against relevant cytochrome P450 isozymes and hERG channel, and exhibit adequate microsomal stability, pharmacokinetic profile and efficacy in mice and rats. Suppresses tumor growth in a mouse RIE-TrkAmNGF xenograft model (50 mg/kg, p.o.).

Biological Activity



Kinome Mapping



Shipping and Storage Temperature

Shipping:
Ambient

Storage:
2 years -20C, Powder 1 month, -4C in DMSO, More than one month -80C in DMSO

Solubility

20 mM in DMSO

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.5355	5.3549	10.7098	26.7745

References

1. Albaugh P, Fan Y, Mi Y, Sun F, Adrian F, Li N, Jia Y, Sarkisova Y, Kreusch A, Hood T, Lu M, Liu G, Huang S, Liu Z, Loren J, Tuntland T, Karanewsky DS, Seidel HM, Molteni V. Discovery of GNF-5837, a Selective TRK Inhibitor with Efficacy in Rodent Cancer Tumor Models. ACS Med Chem Lett. 2012 Jan 1;3(2):140-5. doi: 10.1021/ml200261d. eCollection 2012.

Ordering Information

To order more of this or any other SYNkinase compound, go to synkinase.com, Call us Toll Free (US Only) at 1- 877-854-6273 or email orders@synkinase.com.