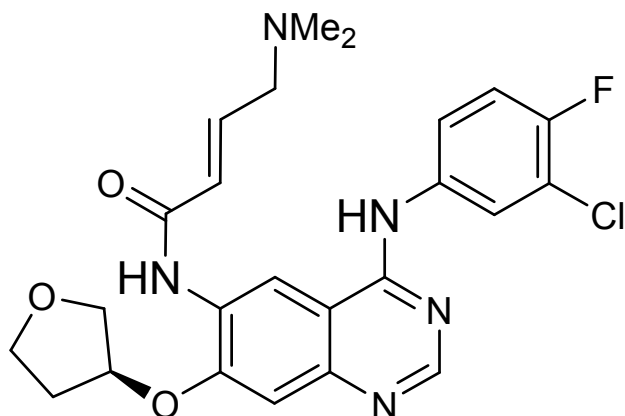


Afatinib

SYN-1100

(S,E)-N-(4-(3-chloro-4-fluorophenylamino)-7-(tetrahydrofuran-3-yloxy)quinazolin-6-yl)-4-(dimethylamino)but-2-enamide

CAS Registry No.: 439081-18-2

Smiles String:

CN(C)C/C=C/C(=O)Nc1cc2c(cc1O[C@H]3CCOC3)ncnc2Nc4ccc(c(c4)Cl)F

Molecular Weight: 485.94

Molecular Formula: C₂₄H₂₅ClFN₅O₃

Lot Number: Refer to vial

¹H-NMR: Available on request

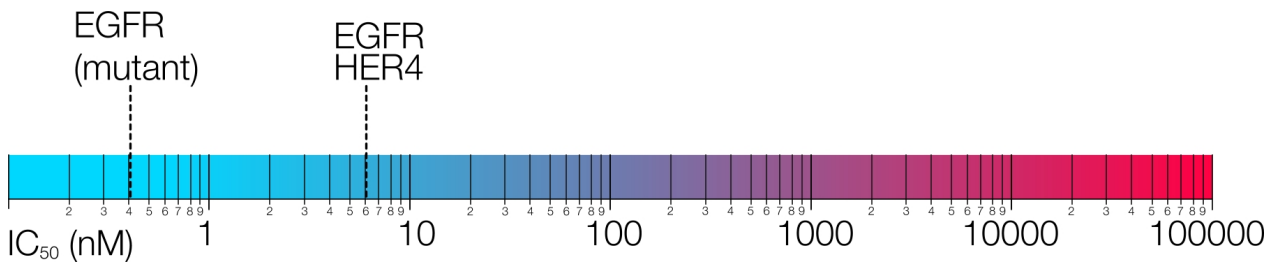
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

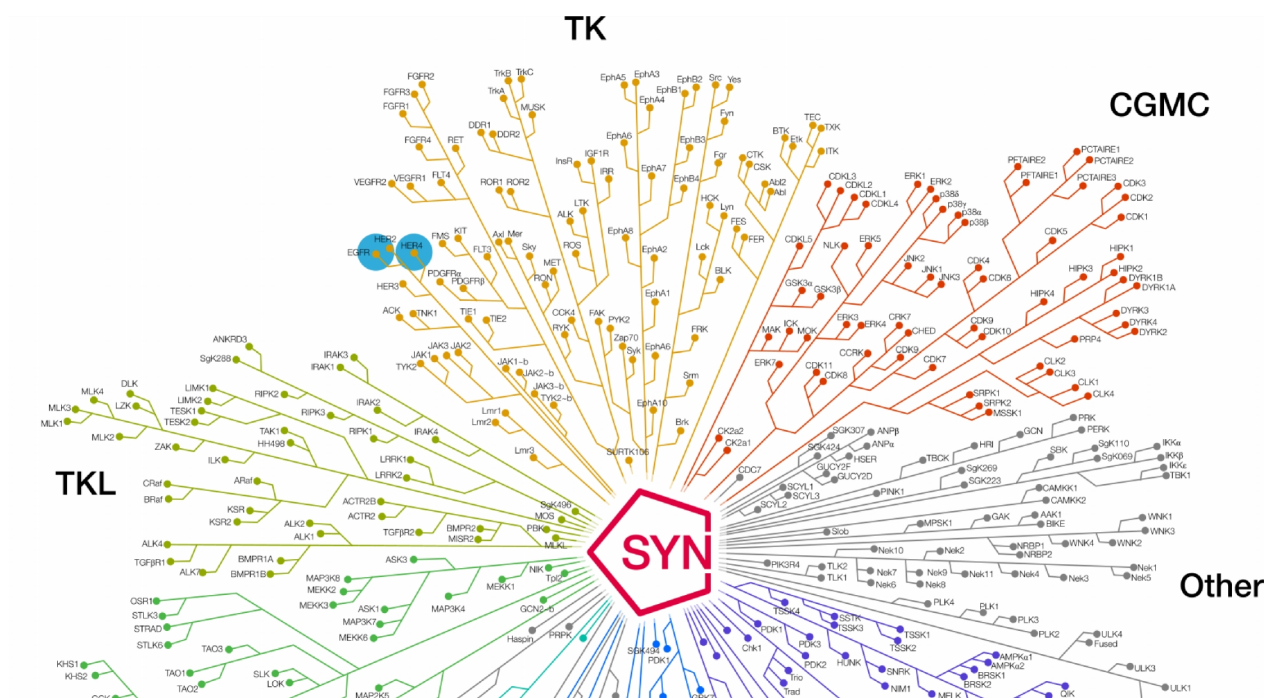
Description:

Afatinib is an irreversible kinase inhibitor and binds to the kinase domains of EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4) to inhibit tyrosine kinase autophosphorylation. This results in a downregulation of ErbB signaling and subsequent inhibition of proliferation of cell lines expressing wild-type EGFR, selected EGFR exon 19 deletion mutations, or exon 21 L858R mutations. It also inhibited in vitro proliferation of cell lines overexpressing HER2. Overall, tumor growth was inhibited by Afatinib very effectively with low nanomolar IC₅₀ values ranging from approximately 6nM to below 500 nM.

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

DMSO 97 mg/mL, Ethanol 15 mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.4860	4.8600	9.7200	24.3000

References

1. Barf T, Kaptein A. Irreversible protein kinase inhibitors: balancing the benefits and risks. *J Med Chem.* 2012 Jul 26;55(14):6243-62. doi: 10.1021/jm3003203. Epub 2012 Jun 8.
2. Ward RA, Anderton MJ, Ashton S, Bethel PA, Box M, Butterworth S, Colclough N, Chorley CG, Chuaqui C, Cross DA, Dakin LA, Debreczeni JÉ, Eberlein C, Finlay MR, Hill GB, Grist M, Klinowska TC, Lane C, Martin S, Orme JP, Smith P, Wang F, Waring MJ. Structure- and reactivity-based development of covalent inhibitors of the activating and gatekeeper mutant forms of the epidermal growth factor receptor (EGFR). *J Med Chem.* 2013 Sep 12;56(17):7025-48. doi: 10.1021/jm400822z. Epub 2013 Aug 30.
3. Stevens KL, Alligood KJ, Alberti JG, Caferro TR, Chamberlain SD, Dickerson SH, Dickson HD, Emerson HK, Griffin RJ, Hubbard RD, Keith BR, Mullin RJ, Petrov KG, Gerding RM, Reno MJ, Rheault TR, Rusnak DW, Sammond DM, Smith SC, Uehling DE, Waterson AG, Wood ER. Synthesis and stereochemical effects of pyrrolidinyl-acetylenic thieno[3,2-d]pyrimidines as EGFR and ErbB-2 inhibitors. *Bioorg Med Chem Lett.* 2009 Jan 1;19(1):21-6. doi: 10.1016/j.bmcl.2008.11.023. Epub 2008 Nov 13.

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.

Product Datasheet (Rev. 1.1)