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Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family in GtoPdb v.2025.3

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Abstract

Type III RTKs include PDGFR, CSF-1R (Ems), Kit and FLT3, which function as homo- or heterodimers. Endogenous ligands of PDGF receptors are homo- or heterodimeric: PDGFA, PDGFB, VEGFE and PDGFD combine as homo- or heterodimers to activate homo- or heterodimeric PDGF receptors. SCF is a dimeric ligand for KIT. Ligands for CSF1R are either monomeric or dimeric glycoproteins, while the endogenous agonist for FLT3 is a homodimer.

Contents

This is a citation summary for Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family in the Guide to Pharmacology database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

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Database links

Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family
https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=322

Receptors

- PDGFRα(platelet derived growth factor receptor alpha)
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1803
- PDGFRβ(platelet derived growth factor receptor beta)
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1804
- Kit(KIT proto-oncogene, receptor tyrosine kinase)
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1805
- CSFR(colony stimulating factor 1 receptor)
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1806
- FLT3(fms related receptor tyrosine kinase 3)
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=1807

References

1. Adams JL, Smothers J, Srinivasan R and Hoos A. (2015) Big opportunities for small molecules in immuno-oncology. *Nat Rev Drug Discov* **14**: 603-22 [PMID:26228631]
2. Ahn Y, Vogeti L, Caldwell TM, Kaufman MD and Flynn DL. (2014) 2-aminopyrimidin-6-ones and analogs exhibiting anti-cancer and anti-proliferative activities Patent number: WO2014145025A2. Assignee: Deciphera Pharmaceuticals, Llc. Priority date: 15/03/2013.

Publication date: 18/09/2014.
3. Akeno-Stuart N, Croyle M, Knauf JA, Malaguarnera R, Vitagliano D, Santoro M, Stephan C, Grosios K, Wartmann M and Cozens R *et al.*. (2007) The RET kinase inhibitor NVP-AST487 blocks growth and calcitonin gene expression through distinct mechanisms in medullary thyroid cancer cells. *Cancer Res* **67**: 6956-64 [PMID:17638907]
4. Albert DH, Tapang P, Magoc TJ, Pease LJ, Reuter DR, Wei RQ, Li J, Guo J, Bousquet PF and Ghoreishi-Haack NS *et al.*. (2006) Preclinical activity of ABT-869, a multitargeted receptor tyrosine kinase inhibitor. *Mol Cancer Ther* **5**: 995-1006 [PMID:16648571]
5. Anastassiadis T, Deacon SW, Devarajan K, Ma H and Peterson JR. (2011) Comprehensive assay of kinase catalytic activity reveals features of kinase inhibitor selectivity. *Nat Biotechnol* **29**: 1039-45 [PMID:22037377]
6. Apsel B, Blair JA, Gonzalez B, Nazif TM, Feldman ME, Aizenstein B, Hoffman R, Williams RL, Shokat KM and Knight ZA. (2008) Targeted polypharmacology: discovery of dual inhibitors of tyrosine and phosphoinositide kinases. *Nat Chem Biol* **4**: 691-9 [PMID:18849971]
7. Břehová P, Řezníčková E, Škach K, Jorda R, Dejmek M, Vojáčková V, Šála M, Kovalová M, Dračínský M and Dolníková A *et al.*. (2023) Inhibition of FLT3-ITD Kinase in Acute Myeloid Leukemia by New Imidazo[1,2-*b*]pyridazine Derivatives Identified by Scaffold Hopping. *J Med Chem* **66**: 11133-11157 [PMID:37535845]
8. Bachelet I, Munitz A, Berent-Maoz B, Mankuta D and Levi-Schaffer F. (2008) Suppression of normal and malignant kit signaling by a bispecific antibody linking kit with CD300a. *J Immunol* **180**: 6064-9 [PMID:18424727]
9. Bae IH, Kim JS, Choi JY, Kang SJ, Ahn YG and Suh KH. (2020) Pyrimidine compounds and pharmaceutical compositions for preventing or treating cancers including the same Patent number: US10870639B2. Assignee: Hanmi Pharmaceutical Co Ltd. Priority date: 25/07/2018. Publication date: 22/12/2020.
10. Bendell J *et al.*. A Phase 1 Study of ARRY-382, an Oral Inhibitor of Colony-stimulating Factor-1 Receptor (CSF1R), in Patients with Advanced or Metastatic Cancers http://www.arraybiopharma.com/files/3014/4501/8593/382-101_AACR-NCI-EORTC_poster.pdf. Accessed on 14/04/2016.
11. Beria I, Bossi RT, Brasca MG, Caruso M, Ceccarelli W, Fachin G, Fasolini M, Forte B, Fiorentini F and Pesenti E *et al.*. (2011) NMS-P937, a 4,5-dihydro-1H-pyrazolo[4,3-h]quinazoline derivative as potent and selective Polo-like kinase 1 inhibitor. *Bioorg Med Chem Lett* **21**: 2969-74 [PMID:21470862]
12. Bibi S, Zhang Y, Hugonin C, Mangean MD, He L, Wedeh G, Launay JM, Van Rijn S, Würdinger T and Louache F *et al.*. (2016) A new humanized in vivo model of KIT D816V+ advanced systemic mastocytosis monitored using a secreted luciferase. *Oncotarget* **7**: 82985-83000 [PMID:27783996]
13. Blum A, Dorsch D, Linde N, Brandstetter S, Buchstaller HP, Busch M, Glaser N, Grädler U, Ruff A and Petersson C *et al.*. (2023) Identification of M4205−A Highly Selective Inhibitor of KIT Mutations for Treatment of Unresectable Metastatic or Recurrent Gastrointestinal Stromal Tumors. *J Med Chem* **66**: 2386-2395 [PMID:36728508]
14. Bold G, Altmann KH, Frei J, Lang M, Manley PW, Traxler P, Wietfeld B, Brüggen J, Buchdunger E and Cozens R *et al.*. (2000) New anilinophthalazines as potent and orally well absorbed inhibitors of the VEGF receptor tyrosine kinases useful as antagonists of tumor-driven angiogenesis. *J Med Chem* **43**: 2310-23 [PMID:10882357]
15. Brasel KA, Foster S, Cerretti DP, Sun J, Smothers JF and Mehlin C. (2009) Human c-fms antigen binding proteins Patent number: WO2009026303 A1. Assignee: Amgen Inc.. Priority date: 21/08/2007. Publication date: 26/02/2009.
16. Brewin J, Horne G and Chevassut T. (2013) Genomic landscapes and clonality of de novo AML. *N Engl J Med* **369**: 1472-3 [PMID:24106951]
17. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
18. Caldwell TM, Ahn YM, Bulfer SL, Leary CB, Hood MM, Lu WP, Vogeti L, Vogeti S, Kaufman MD and Wise SC *et al.*. (2022) Discovery of vimseltinib (DCC-3014), a highly selective CSF1R switch-control kinase inhibitor, in clinical development for the treatment of Tenosynovial Giant Cell Tumor (TGCT). *Bioorg Med Chem Lett* **74**: 128928 [PMID:35961460]
19. Cao ZX, Liu JJ, Zheng RL, Yang J, Zhong L, Xu Y, Wang LJ, Zhang CH, Wang BL and Ma S *et al.*. (2012) SKLB1028, a novel oral multikinase inhibitor of EGFR, FLT3 and Abl, displays exceptional activity in models of FLT3-driven AML and considerable potency in models of CML harboring Abl mutants. *Leukemia* **26**: 1892-5 [PMID:22402607]
20. Chan S, Zhang Y, Wang J, Yu Q, Peng X, Zou J, Zhou L, Tan L, Duan Y and Zhou Y *et al.*. (2022) Discovery of 3-Aminopyrazole Derivatives as New Potent and Orally Bioavailable AXL Inhibitors *Journal of Nedicinal Chemistry*
21. Chao Q, Sprankle KG, Grotzfeld RM, Lai AG, Carter TA, Velasco AM, Gunawardane RN, Cramer MD, Gardner MF and James J *et al.*. (2009) Identification of N-(5-tert-butyl-isoxazol-3-yl)-N'-{4-

[7-(2-morpholin-4-yl-ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea dihydrochloride (AC220), a uniquely potent, selective, and efficacious FMS-like tyrosine kinase-3 (FLT3) inhibitor. *J Med Chem* **52**: 7808-16 [PMID:19754199]
22. Cho TP, Dong SY, Jun F, Hong FJ, Liang YJ, Lu X, Hua PJ, Li LY, Lei Z and Bing H *et al.*. (2010) Novel potent orally active multitargeted receptor tyrosine kinase inhibitors: synthesis, structure-activity relationships, and antitumor activities of 2-indolinone derivatives. *J Med Chem* **53**: 8140-9 [PMID:21028894]
23. Choi SJ, Moon MJ, Lee SD, Choi SU, Han SY and Kim YC. (2010) Indirubin derivatives as potent FLT3 inhibitors with anti-proliferative activity of acute myeloid leukemic cells. *Bioorg Med Chem Lett* **20**: 2033-7 [PMID:20153646]
24. Cirstea D, Hideshima T, Santo L, Eda H, Mishima Y, Nemani N, Hu Y, Mimura N, Cottini F and Gorgun G *et al.*. (2013) Small-molecule multi-targeted kinase inhibitor RGB-286638 triggers P53-dependent and -independent anti-multiple myeloma activity through inhibition of transcriptional CDKs. *Leukemia* **27**: 2366-75 [PMID:23807770]
25. Coffey G, Betz A, DeGuzman F, Pak Y, Inagaki M, Baker DC, Hollenbach SJ, Pandey A and Sinha U. (2014) The novel kinase inhibitor PRT062070 (Cerdulatinib) demonstrates efficacy in models of autoimmunity and B-cell cancer. *J Pharmacol Exp Ther* **351**: 538-48 [PMID:25253883]
26. Conway JG, McDonald B, Parham J, Keith B, Rusnak DW, Shaw E, Jansen M, Lin P, Payne A and Crosby RM *et al.*. (2005) Inhibition of colony-stimulating-factor-1 signaling in vivo with the orally bioavailable cFMS kinase inhibitor GW2580. *Proc Natl Acad Sci USA* **102**: 16078-83 [PMID:16249345]
27. Correia DV, d'Orey F, Cardoso BA, Lança T, Grosso AR, deBarros A, Martins LR, Barata JT and Silva-Santos B. (2009) Highly active microbial phosphoantigen induces rapid yet sustained MEK/Erk- and PI-3K/Akt-mediated signal transduction in anti-tumor human gammadelta T-cells. *PLoS ONE* **4**: e5657 [PMID:19479075]
28. Craggs G, Herve KJM and Marshall D. (2018) Antibodies Patent number: US9908939B2. Assignee: UCB Biopharma SRL. Priority date: 26/08/2014. Publication date: 06/03/2018.
29. Cruz-López O, Temps C, Longo B, Myers SH, Franco-Montalban F and Unciti-Broceta A. (2019) Synthesis and Characterization of a Click-Assembled 18-Atom Macrocycle That Displays Selective AXL Kinase Inhibitory Activity. *ACS Omega* **4**: 21620-21626 [PMID:31867559]
30. Cui JJ, Rogers EW, Ung J, Whitten J, Zhai D, Deng W, Zhang X, Huang Z, Liu J and Zhang H. (2019) Macrocyclic compounds and uses thereof Patent number: WO2019023417A1. Assignee: Tp Therapeutics, Inc.. Priority date: 28/07/2017. Publication date: 31/01/2019.
31. Czako B, Marszalek JR, Burke JP, Mandal P, Leonard PG, Cross JB, Mseeh F, Jiang Y, Chang EQ and Suzuki E *et al.*. (2020) Discovery of IACS-9439, a Potent, Exquisitely Selective, and Orally Bioavailable Inhibitor of CSF1R. *J Med Chem* **63**: 9888-9911 [PMID:32787110]
32. Davis MI, Hunt JP, Herrgard S, Ciceri P, Wodicka LM, Pallares G, Hocker M, Treiber DK and Zarrinkar PP. (2011) Comprehensive analysis of kinase inhibitor selectivity. *Nat Biotechnol* **29**: 1046-51 [PMID:22037378]
33. Dimoudis N, Fertig G, Fidler A, Pickl M, Ries C, Seeber S, Lanzendoerfer M and Krueger K.. (2011) Antibodies against human csf-1r and uses thereof. Patent number: US20110165156 A1. Assignee: Dimoudis N, Fertig G, Fidler A, Pickl M, Ries C, Seeber S, Lanzendoerfer M, Krueger K.. Priority date: 10/12/2009. Publication date: 07/07/2011.
34. Doody JF and Li Y. (2011) Antibodies against csf-1r. Patent number: WO2011123381 A1. Assignee: Imclone Llc. Priority date: 01/04/2010. Publication date: 06/10/2011.
35. Drexler HG. (1996) Expression of FLT3 receptor and response to FLT3 ligand by leukemic cells. *Leukemia* **10**: 588-99 [PMID:8618433]
36. Drygin D, Haddach M, Pierre F and Ryckman DM. (2012) Potential use of selective and nonselective Pim kinase inhibitors for cancer therapy. *J Med Chem* **55**: 8199-208 [PMID:22924342]
37. Dubreuil P, Letard S, Ciufolini M, Gros L, Humbert M, Castéran N, Borge L, Hajem B, Lermet A and Sippl W *et al.*. (2009) Masitinib (AB1010), a potent and selective tyrosine kinase inhibitor targeting KIT. *PLoS ONE* **4**: e7258 [PMID:19789626]
38. Eriksson A, Hermanson M, Wickström M, Lindhagen E, Ekholm C, Jenmalm Jensen A, Löthgren A, Lehmann F, Larsson R and Parrow V *et al.*. (2012) The novel tyrosine kinase inhibitor AKN-028 has significant antileukemic activity in cell lines and primary cultures of acute myeloid leukemia. *Blood Cancer J* **2**: e81 [PMID:22864397]
39. Evans EK, Gardino AK, Kim JL, Hodous BL, Shutes A, Davis A, Zhu XJ, Schmidt-Kittler O, Wilson D and Wilson K *et al.*. (2017) A precision therapy against cancers driven by *KIT/PDGFRA* mutations. *Sci Transl Med* **9** [PMID:29093181]
40. Fedorov O, Marsden B, Pogacic V, Rellos P, Müller S, Bullock AN, Schwaller J, Sundström M and Knapp S. (2007) A systematic interaction map of validated kinase inhibitors with Ser/Thr kinases. *Proc Natl Acad Sci USA* **104**: 20523-8 [PMID:18077363]
41. Flynn DL, Petillo PA and Kaufman MD. (2010) Cyclopropane amides and analogs exhibiting anti-cancer and anti-proliferative activities Patent number: WO2010051373. Assignee: Deciphera Pharmaceuticals, Llc. Priority date: 29/10/2008. Publication date: 06/05/2010.

42. Foulks JM, Carpenter KJ, Luo B, Xu Y, Senina A, Nix R, Chan A, Clifford A, Wilkes M and Vollmer D *et al.*. (2014) A small-molecule inhibitor of PIM kinases as a potential treatment for urothelial carcinomas. *Neoplasia* **16**: 403-12 [PMID:24953177]
43. Fujisaki H, Kakuda H, Shimasaki N, Imai C, Ma J, Lockey T, Eldridge P, Leung WH and Campana D. (2009) Expansion of highly cytotoxic human natural killer cells for cancer cell therapy. *Cancer Res* **69**: 4010-7 [PMID:19383914]
44. Furet P, Bold G, Meyer T, Roesel J and Guagnano V. (2006) Aromatic interactions with phenylalanine 691 and cysteine 828: a concept for FMS-like tyrosine kinase-3 inhibition. Application to the discovery of a new class of potential antileukemia agents. *J Med Chem* **49**: 4451-4 [PMID:16854049]
45. Furuta T, Sakai T, Senga T, Osawa T, Kubo K, Shimizu T, Suzuki R, Yoshino T, Endo M and Miwa A. (2006) Identification of potent and selective inhibitors of PDGF receptor autophosphorylation. *J Med Chem* **49**: 2186-92 [PMID:16570914]
46. Gajiwala KS, Wu JC, Christensen J, Deshmukh GD, Diehl W, DiNitto JP, English JM, Greig MJ, He YA and Jacques SL *et al.*. (2009) KIT kinase mutants show unique mechanisms of drug resistance to imatinib and sunitinib in gastrointestinal stromal tumor patients. *Proc Natl Acad Sci USA* **106**: 1542-7 [PMID:19164557]
47. Gangwar RS, Landolina N, Arpinati L and Levi-Schaffer F. (2017) Mast cell and eosinophil surface receptors as targets for anti-allergic therapy. *Pharmacol Ther* **170**: 37-63 [PMID:27773785]
48. Gao M, Duan L, Luo J, Zhang L, Lu X, Zhang Y, Zhang Z, Tu Z, Xu Y and Ren X *et al.*. (2013) Discovery and optimization of 3-(2-(Pyrazolo[1,5-a]pyrimidin-6-yl)ethynyl)benzamides as novel selective and orally bioavailable discoidin domain receptor 1 (DDR1) inhibitors. *J Med Chem* **56**: 3281-95 [PMID:23521020]
49. Gao Y, Davies SP, Augustin M, Woodward A, Patel UA, Kovelman R and Harvey KJ. (2013) A broad activity screen in support of a chemogenomic map for kinase signalling research and drug discovery. *Biochem J* **451**: 313-28 [PMID:23398362]
50. Garton AJ, Crew AP, Franklin M, Cooke AR, Wynne GM, Castaldo L, Kahler J, Winski SL, Franks A and Brown EN *et al.*. (2006) OSI-930: a novel selective inhibitor of Kit and kinase insert domain receptor tyrosine kinases with antitumor activity in mouse xenograft models. *Cancer Res* **66**: 1015-24 [PMID:16424037]
51. Gazit A, Yee K, Uecker A, Böhmer FD, Sjöblom T, Ostman A, Waltenberger J, Golomb G, Banai S and Heinrich MC *et al.*. (2003) Tricyclic quinoxalines as potent kinase inhibitors of PDGFR kinase, Flt3 and Kit. *Bioorg Med Chem* **11**: 2007-18 [PMID:12670652]
52. Gebreyohannes YK, Burton EA, Wozniak A, Matusow B, Habets G, Wellens J, Cornillie J, Lin J, Nespi M and Wu G *et al.*. (2019) PLX9486 shows anti-tumor efficacy in patient-derived, tyrosine kinase inhibitor-resistant KIT-mutant xenograft models of gastrointestinal stromal tumors. *Clin Exp Med* **19**: 201-210 [PMID:30523507]
53. Genovese MC, Hsia E, Belkowski SM, Chien C, Masterson T, Thurmond RL, Manthey CL, Yan XD, Ge T and Franks C *et al.*. (2015) Results from a Phase IIA Parallel Group Study of JNJ-40346527, an Oral CSF-1R Inhibitor, in Patients with Active Rheumatoid Arthritis despite Disease-modifying Antirheumatic Drug Therapy. *J Rheumatol* **42**: 1752-60 [PMID:26233509]
54. Glaser KB, Li J, Marcotte PA, Magoc TJ, Guo J, Reuter DR, Tapang P, Wei RQ, Pease LJ and Bui MH *et al.*. (2012) Preclinical characterization of ABT-348, a kinase inhibitor targeting the aurora, vascular endothelial growth factor receptor/platelet-derived growth factor receptor, and Src kinase families. *J Pharmacol Exp Ther* **343**: 617-27 [PMID:22935731]
55. Goh KC, Novotny-Diermayr V, Hart S, Ong LC, Loh YK, Cheong A, Tan YC, Hu C, Jayaraman R and William AD *et al.*. (2012) TG02, a novel oral multi-kinase inhibitor of CDKs, JAK2 and FLT3 with potent anti-leukemic properties. *Leukemia* **26**: 236-43 [PMID:21860433]
56. Gomez-Nicola D and Perry VH.. (2014) Neurodegenerative diseases. *In Microglia in health and disease.* Edited by Tremblay M-È, Sierra A.: Springer: 437–53 [ISBN: 9781493914296]
57. Goodfellow VS, Loweth CJ, Ravula SB, Wiemann T, Nguyen T, Xu Y, Todd DE, Sheppard D, Pollack S and Polesskaya O *et al.*. (2013) Discovery, synthesis, and characterization of an orally bioavailable, brain penetrant inhibitor of mixed lineage kinase 3. *J Med Chem* **56**: 8032-48 [PMID:24044867]
58. Gou H, Zhou J, Ye Y, Hu X, Shang M, Zhang J, Zhao Z, Peng W, Zhou Y and Zhou Y *et al.*. (2016) The prevalence and clinical profiles of FLT3-ITD, FLT3-TKD, NPM1, C-KIT, DNMT3A, and CEBPA mutations in a cohort of patients with de novo acute myeloid leukemia from southwest China. *Tumour Biol* **37**: 7357-70 [PMID:26676635]
59. Gough KC, Maddison BC, Shikotra A, Moiseeva EP, Yang W, Jarvis S and Bradding P. (2015) Evidence for a novel Kit adhesion domain mediating human mast cell adhesion to structural airway cells. *Respir Res* **16**: 86 [PMID:26173671]
60. Greiner G, Gurbisz M, Ratzinger F, Witzeneder N, Simonitsch-Klupp I, Mitterbauer-Hohendanner G, Mayerhofer M, Müllauer L, Sperr WR and Valent P *et al.*. (2018) Digital PCR: A Sensitive and Precise Method for*KIT*D816V Quantification in Mastocytosis. *Clin Chem* **64**: 547-555 [PMID:29237714]

61. Griffith J, Black J, Faerman C, Swenson L, Wynn M, Lu F, Lippke J and Saxena K. (2004) The structural basis for autoinhibition of FLT3 by the juxtamembrane domain. *Mol Cell* **13**: 169-78 [PMID:14759363]
62. Gucký T, Řezníčková E, Radošová Muchová T, Jorda R, Klejová Z, Malínková V, Berka K, Bazgier V, Ajani H and Lepšík M *et al.*. (2018) Discovery of N^2-(4-Amino-cyclohexyl)-9-cyclopentyl- N^6-(4-morpholin-4-ylmethyl-phenyl)- 9H-purine-2,6-diamine as a Potent FLT3 Kinase Inhibitor for Acute Myeloid Leukemia with FLT3 Mutations. *J Med Chem* **61**: 3855-3869 [PMID:29672049]
63. Gómez-Nicola D, Fransen NL, Suzzi S and Perry VH. (2013) Regulation of microglial proliferation during chronic neurodegeneration. *J Neurosci* **33**: 2481-93 [PMID:23392676]
64. Hadari Y, Mandel-Bausch EM Carr FJ, Jones TD and Perry LCA. (2020) Anti-kit antibodies and uses thereof Patent number: US10781267B2. Assignee: Celldex Therapeutics Inc. Priority date: 25/07/2012. Publication date: 22/09/2020.
65. Harris PA, Boloor A, Cheung M, Kumar R, Crosby RM, Davis-Ward RG, Epperly AH, Hinkle KW, Hunter 3rd RN and Johnson JH *et al.*. (2008) Discovery of 5-[[4-[(2,3-dimethyl-2H-indazol-6-yl)methylamino]-2-pyrimidinyl]amino]-2-methyl-benzenesulfonamide (Pazopanib), a novel and potent vascular endothelial growth factor receptor inhibitor. *J Med Chem* **51**: 4632-40 [PMID:18620382]
66. Heinrich MC, Griffith D, McKinley A, Patterson J, Presnell A, Ramachandran A and Debiec-Rychter M. (2012) Crenolanib inhibits the drug-resistant PDGFRA D842V mutation associated with imatinib-resistant gastrointestinal stromal tumors. *Clin Cancer Res* **18**: 4375-84 [PMID:22745105]
67. Hilberg F, Roth GJ, Krssak M, Kautschitsch S, Sommergruber W, Tontsch-Grunt U, Garin-Chesa P, Bader G, Zoephel A and Quant J *et al.*. (2008) BIBF 1120: triple angiokinase inhibitor with sustained receptor blockade and good antitumor efficacy. *Cancer Res* **68**: 4774-82 [PMID:18559524]
68. Ho CY, Ludovici DW, Maharoof US, Mei J, Sechler JL, Tuman RW, Strobel ED, Andraka L, Yen HK and Leo G *et al.*. (2005) (6,7-Dimethoxy-2,4-dihydroindeno[1,2-c]pyrazol-3-yl)phenylamines: platelet-derived growth factor receptor tyrosine kinase inhibitors with broad antiproliferative activity against tumor cells. *J Med Chem* **48**: 8163-73 [PMID:16366598]
69. Huang Z, Li H, Zhang Q, Lu F, Hong M, Zhang Z, Guo X, Zhu Y, Li S and Liu H. (2017) Discovery of Indolinone-Based Multikinase Inhibitors as Potential Therapeutics for Idiopathic Pulmonary Fibrosis. *ACS Med Chem Lett* **8**: 1142-1147 [PMID:29152045]
70. Jarusiewicz JA, Jeon JY, Connelly MC, Chen Y, Yang L, Baker SD and Guy RK. (2017) Discovery of a Diaminopyrimidine FLT3 Inhibitor Active against Acute Myeloid Leukemia. *ACS Omega* **2**: 1985-2009 [PMID:28580438]
71. Jensen BM, Metcalfe DD and Gilfillan AM. (2007) Targeting kit activation: a potential therapeutic approach in the treatment of allergic inflammation. *Inflamm Allergy Drug Targets* **6**: 57-62 [PMID:17352689]
72. Johnson CN, Berdini V, Beke L, Bonnet P, Brehmer D, Coyle JE, Day PJ, Frederickson M, Freyne EJ and Gilissen RA *et al.*. (2014) Fragment-based discovery of type I inhibitors of maternal embryonic leucine zipper kinase. *ACS Med Chem Lett* **6**: 25-30 [PMID:25589925]
73. Kammasud N, Boonyarat C, Sanphanya K, Utsintong M, Tsunoda S, Sakurai H, Saiki I, André I, Grierson DS and Vajragupta O. (2009) 5-Substituted pyrido[2,3-d]pyrimidine, an inhibitor against three receptor tyrosine kinases. *Bioorg Med Chem Lett* **19**: 745-50 [PMID:19110422]
74. Kane JL Jr, Matthews G, Metz M, Kothe M, Liu J and Scholte A. (2015) Tropomyosin-related kinase (Trk) inhibitors Patent number: US9174986B2. Assignee: Genzyme Corp.. Priority date: 10/12/2013. Publication date: 03/11/2015.
75. Kelly LM, Yu JC, Boulton CL, Apatira M, Li J, Sullivan CM, Williams I, Amaral SM, Curley DP and Duclos N *et al.*. (2002) CT53518, a novel selective FLT3 antagonist for the treatment of acute myelogenous leukemia (AML). *Cancer Cell* **1**: 421-32 [PMID:12124172]
76. Khanwelkar RR, Chen GS, Wang HC, Yu CW, Huang CH, Lee O, Chen CH, Hwang CS, Ko CH and Chou NT *et al.*. (2010) Synthesis and structure-activity relationship of 6-arylureido-3-pyrrol-2-ylmethylideneindolin-2-one derivatives as potent receptor tyrosine kinase inhibitors. *Bioorg Med Chem* **18**: 4674-86 [PMID:20570526]
77. Kim JL, Dineen TA and Guzi T. (2020) Pyrrolotriazine derivatives for treating kit- and pdgfra-mediated diseases Patent number: WO2020210293A1. Assignee: Blueprint Medicines Corporation. Priority date: 08/04/2020. Publication date: 15/10/2020.
78. Kim MH, Tsuhako AL, Co EW, Aftab DT, Bentzien F, Chen J, Cheng W, Engst S, Goon L and Klein RR *et al.*. (2012) The design, synthesis, and biological evaluation of potent receptor tyrosine kinase inhibitors. *Bioorg Med Chem Lett* **22**: 4979-85 [PMID:22765894]
79. Kitagawa D, Yokota K, Gouda M, Narumi Y, Ohmoto H, Nishiwaki E, Akita K and Kirii Y. (2013) Activity-based kinase profiling of approved tyrosine kinase inhibitors. *Genes Cells* **18**: 110-22 [PMID:23279183]
80. Kiyoi H, Naoe T, Nakano Y, Yokota S, Minami S, Miyawaki S, Asou N, Kuriyama K, Jinnai I and Shimazaki C *et al.*. (1999) Prognostic implication of FLT3 and N-RAS gene mutations in acute

myeloid leukemia. *Blood* **93**: 3074-80 [PMID:10216104]
81. Kong D, Tian Q, Chen Z, Zheng H, Stashko MA, Yan D, Earp HS, Frye SV, DeRyckere D and Kireev D *et al.*. (2024) Discovery of Novel Macrocyclic MERTK/AXL Dual Inhibitors. *J Med Chem* **67**: 5866-5882 [PMID:38556760]
82. Kristensen T, Vestergaard H, Bindslev-Jensen C, Mortz CG, Kjaer HF, Ollert M, Møller MB, Broesby-Olsen S and Mastocytosis Centre Odense University Hospital (MastOUH). (2017) Prospective evaluation of the diagnostic value of sensitive KIT D816V mutation analysis of blood in adults with suspected systemic mastocytosis. *Allergy* **72**: 1737-1743 [PMID:28432683]
83. Lam B, Arikawa Y, Cramlett J, Dong Q, de Jong R, Feher V, Grimshaw CE, Farrell PJ, Hoffman ID and Jennings A *et al.*. (2016) Discovery of TAK-659 an orally available investigational inhibitor of Spleen Tyrosine Kinase (SYK). *Bioorg Med Chem Lett* **26**: 5947-5950 [PMID:27839918]
84. Lee HK, Kim HW, Lee IY, Lee J, Lee J, Jung DS, Lee SY, Park SH, Hwang H and Choi JS *et al.*. (2014) G-749, a novel FLT3 kinase inhibitor, can overcome drug resistance for the treatment of acute myeloid leukemia. *Blood* **123**: 2209-19 [PMID:24532805]
85. Lee KH, Yen WC, Lin WH, Wang PC, Lai YL, Su YC, Chang CY, Wu CS, Huang YC and Yang CM *et al.*. (2021) Discovery of BPR1R024, an Orally Active and Selective CSF1R Inhibitor that Exhibits Antitumor and Immunomodulatory Activity in a Murine Colon Tumor Model. *J Med Chem* **64**: 14477-14497 [PMID:34606263]
86. Lee LY, Hernandez D, Rajkhowa T, Smith SC, Raman JR, Nguyen B, Small D and Levis M. (2017) Preclinical studies of gilteritinib, a next-generation FLT3 inhibitor. *Blood* **129**: 257-260 [PMID:27908881]
87. Lefranc J, Schulze VK, Hillig RC, Briem H, Prinz F, Mengel A, Heinrich T, Balint J, Rengachari S and Irlbacher H *et al.*. (2020) Discovery of BAY-985, a Highly Selective TBK1/IKKε Inhibitor. *J Med Chem* **63**: 601-612 [PMID:31859507]
88. Lewis RT, Bode CM, Choquette DM, Potashman M, Romero K, Stellwagen JC, Teffera Y, Moore E, Whittington DA and Chen H *et al.*. (2012) The discovery and optimization of a novel class of potent, selective, and orally bioavailable anaplastic lymphoma kinase (ALK) inhibitors with potential utility for the treatment of cancer. *J Med Chem* **55**: 6523-40 [PMID:22734674]
89. Li B, Wang A, Liu J, Qi Z, Liu X, Yu K, Wu H, Chen C, Hu C and Wang W *et al.*. (2016) Discovery of N-((1-(4-(3-(3-((6,7-Dimethoxyquinolin-3-yl)oxy)phenyl)ureido)-2-(trifluoromethyl)phenyl)piperidin-4-yl)methyl)propionamide (CHMFL-KIT-8140) as a Highly Potent Type II Inhibitor Capable of Inhibiting the T670I "Gatekeeper" Mutant of cKIT Kinase. *J Med Chem* **59**: 8456-72 [PMID:27545040]
90. Liao AT, Chien MB, Shenoy N, Mendel DB, McMahon G, Cherrington JM and London CA. (2002) Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors. *Blood* **100**: 585-93 [PMID:12091352]
91. Lin H, Lee E, Hestir K, Leo C, Huang M, Bosch E, Halenbeck R, Wu G, Zhou A and Behrens D *et al.*. (2008) Discovery of a cytokine and its receptor by functional screening of the extracellular proteome. *Science* **320**: 807-11 [PMID:18467591]
92. Liu B, Kang N, Yang F, Zhang W, Yan X, Wang H, Bai S, Cheng CC, Xu J and Hu W *et al.*. (2025) Discovery of FLT3-ITD Inhibitor Clifutinib: A Novel Biphenylacetylene Urea Derivative in Clinical Trials for the Treatment of Relapsed/Refractory FLT3-ITD^{+} Acute Myeloid Leukemia. *J Med Chem* **68**: 7955-7972 [PMID:40213868]
93. Liu F, Li S, Chen P, Gu Y, Wang S, Wang L, Chen C, Wang R and Yuan Y. (2023) Salvianolic acid B inhibits hepatic stellate cell activation and liver fibrosis by targeting PDGFRβ. *Int Immunopharmacol* **122**: 110550 [PMID:37451016]
94. Liu G, Campbell BT, Holladay MW, Ford Pulido JM, Hua H, Gitnick D, Gardner MF, James J, Breider MA and Brigham D *et al.*. (2012) Discovery of AC710, a Globally Selective Inhibitor of Platelet-Derived Growth Factor Receptor-Family Kinases. *ACS Med Chem Lett* **3**: 997-1002 [PMID:24900421]
95. Liu W, Bai Y, Zhou L, Jin J, Zhang M, Wang Y, Lin R, Huang W, Ren X and Ma N *et al.*. (2024) Discovery of LWY713 as a potent and selective FLT3 PROTAC degrader with in vivo activity against acute myeloid leukemia. *Eur J Med Chem* **264**: 115974 [PMID:38007910]
96. Loizos N and Huber J. (2012) Antibodies against PDGFRa Patent number: US8128929. Assignee: Imclone Llc. Priority date: 17/06/2006. Publication date: 06/04/2012.
97. Luo H, Quan H, Xie C, Xu Y, Fu L and Lou L. (2010) HH-GV-678, a novel selective inhibitor of Bcr-Abl, outperforms imatinib and effectively overrides imatinib resistance. *Leukemia* **24**: 1807-9 [PMID:20703259]
98. Ma H, Nguyen B, Li L, Greenblatt S, Williams A, Zhao M, Levis M, Rudek M, Duffield A and Small D. (2014) TTT-3002 is a novel FLT3 tyrosine kinase inhibitor with activity against FLT3-associated leukemias in vitro and in vivo. *Blood* **123**: 1525-34 [PMID:24408321]
99. Machrouhi F, Ouhamou N, Laderoute K, Calaoagan J, Bukhtiyarova M, Ehrlich PJ and Klon AE. (2010) The rational design of a novel potent analogue of the 5'-AMP-activated protein kinase inhibitor compound C with improved selectivity and cellular activity. *Bioorg Med Chem Lett* **20**: 6394-9 [PMID:20932747]

100. Mackarehtschian K, Hardin JD, Moore KA, Boast S, Goff SP and Lemischka IR. (1995) Targeted disruption of the flk2/flt3 gene leads to deficiencies in primitive hematopoietic progenitors. *Immunity* **3**: 147-61 [PMID:7621074]
101. Mahboobi S, Teller S, Pongratz H, Hufsky H, Sellmer A, Botzki A, Uecker A, Beckers T, Baasner S and Schächtele C *et al.*. (2002) Bis(1H-2-indolyl)methanones as a novel class of inhibitors of the platelet-derived growth factor receptor kinase. *J Med Chem* **45**: 1002-18 [PMID:11855980]
102. Mahboobi S, Uecker A, Sellmer A, Cénac C, Höcher H, Pongratz H, Eichhorn E, Hufsky H, Trümpler A and Sicker M *et al.*. (2006) Novel bis(1H-indol-2-yl)methanones as potent inhibitors of FLT3 and platelet-derived growth factor receptor tyrosine kinase. *J Med Chem* **49**: 3101-15 [PMID:16722630]
103. Manthey CL, Johnson DL, Illig CR, Tuman RW, Zhou Z, Baker JF, Chaikin MA, Donatelli RR, Franks CF and Zeng L *et al.*. (2009) JNJ-28312141, a novel orally active colony-stimulating factor-1 receptor/FMS-related receptor tyrosine kinase-3 receptor tyrosine kinase inhibitor with potential utility in solid tumors, bone metastases, and acute myeloid leukemia. *Mol Cancer Ther* **8**: 3151-61 [PMID:19887542]
104. Marathe P, Tang Y, Sleczka B, Rodrigues D, Gavai A, Wong T, Christopher L and Zhang H. (2010) Preclinical pharmacokinetics and in vitro metabolism of BMS-690514, a potent inhibitor of EGFR and VEGFR2. *J Pharm Sci* **99**: 3579-93 [PMID:20166197]
105. Marsilje TH, Pei W, Chen B, Lu W, Uno T, Jin Y, Jiang T, Kim S, Li N and Warmuth M *et al.*. (2013) Synthesis, structure-activity relationships, and in vivo efficacy of the novel potent and selective anaplastic lymphoma kinase (ALK) inhibitor 5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)phenyl)-N4-(2-(isopropylsulfonyl)phenyl)pyrimidine-2,4-diamine (LDK378) currently in phase 1 and phase 2 clinical trials. *J Med Chem* **56**: 5675-90 [PMID:23742252]
106. Matsuno K, Ushiki J, Seishi T, Ichimura M, Giese NA, Yu JC, Takahashi S, Oda S and Nomoto Y. (2003) Potent and selective inhibitors of platelet-derived growth factor receptor phosphorylation. 3. Replacement of quinazoline moiety and improvement of metabolic polymorphism of 4-[4-(N-substituted (thio)carbamoyl)-1-piperazinyl]-6,7-dimethoxyquinazoline derivatives. *J Med Chem* **46**: 4910-25 [PMID:14584942]
107. Mead AJ, Linch DC, Hills RK, Wheatley K, Burnett AK and Gale RE. (2007) FLT3 tyrosine kinase domain mutations are biologically distinct from and have a significantly more favorable prognosis than FLT3 internal tandem duplications in patients with acute myeloid leukemia. *Blood* **110**: 1262-70 [PMID:17456725]
108. Mendel DB, Laird AD, Xin X, Louie SG, Christensen JG, Li G, Schreck RE, Abrams TJ, Ngai TJ and Lee LB *et al.*. (2003) In vivo antitumor activity of SU11248, a novel tyrosine kinase inhibitor targeting vascular endothelial growth factor and platelet-derived growth factor receptors: determination of a pharmacokinetic/pharmacodynamic relationship. *Clin Cancer Res* **9**: 327-37 [PMID:12538485]
109. Miller CA, Wilson RK and Ley TJ. (2013) Genomic landscapes and clonality of de novo AML. *N Engl J Med* **369**: 1473 [PMID:24106950]
110. Mortensen DS, Perrin-Ninkovic SM, Shevlin G, Zhao J, Packard G, Bahmanyar S, Correa M, Elsner J, Harris R and Lee BG *et al.*. (2015) Discovery of mammalian target of rapamycin (mTOR) kinase inhibitor CC-223. *J Med Chem* **58**: 5323-33 [PMID:26083478]
111. Murata K, Kumagai H, Kawashima T, Tamitsu K, Irie M, Nakajima H, Suzu S, Shibuya M, Kamihira S and Nosaka T *et al.*. (2003) Selective cytotoxic mechanism of GTP-14564, a novel tyrosine kinase inhibitor in leukemia cells expressing a constitutively active Fms-like tyrosine kinase 3 (FLT3). *J Biol Chem* **278**: 32892-8 [PMID:12815052]
112. Nakanishi Y, Akiyama N, Tsukaguchi T, Fujii T, Sakata K, Sase H, Isobe T, Morikami K, Shindoh H and Mio T *et al.*. (2014) The fibroblast growth factor receptor genetic status as a potential predictor of the sensitivity to CH5183284/Debio 1347, a novel selective FGFR inhibitor. *Mol Cancer Ther* **13**: 2547-58 [PMID:25169980]
113. Nam K, Kim J, Park D, Jeon Y, Yang YI and Kang HK. (2021) Quinoline derivatives as inhibitors of axl/mer rtk and csf1r Patent number: US20210163448A1. Assignee: QURIENT CO Ltd. Priority date: 31/05/2019. Publication date: 03/06/2021.
114. Nicolas G, Pottier C, Charbonnier C, Guyant-Maréchal L, Le Ber I, Pariente J, Labauge P, Ayrignac X, Defebvre L and Maltête D *et al.*. (2013) Phenotypic spectrum of probable and genetically-confirmed idiopathic basal ganglia calcification. *Brain* **136**: 3395-407 [PMID:24065723]
115. Ohno H, Kubo K, Murooka H, Kobayashi Y, Nishitoba T, Shibuya M, Yoneda T and Isoe T. (2006) A c-fms tyrosine kinase inhibitor, Ki20227, suppresses osteoclast differentiation and osteolytic bone destruction in a bone metastasis model. *Mol Cancer Ther* **5**: 2634-43 [PMID:17121910]
116. Okaniwa M, Hirose M, Arita T, Yabuki M, Nakamura A, Takagi T, Kawamoto T, Uchiyama N, Sumita A and Tsutsumi S *et al.*. (2013) Discovery of a selective kinase inhibitor (TAK-632) targeting pan-RAF inhibition: design, synthesis, and biological evaluation of C-7-substituted 1,3-benzothiazole derivatives. *J Med Chem* **56**: 6478-94 [PMID:23906342]
117. Olmos-Alonso A, Schetters ST, Sri S, Askew K, Mancuso R, Vargas-Caballero M, Holscher C, Perry VH and Gomez-Nicola D. (2016) Pharmacological targeting of CSF1R inhibits microglial

proliferation and prevents the progression of Alzheimer's-like pathology. *Brain* **139**: 891-907 [PMID:26747862]
118. Onnes MC, Tanno LK and Elberink JN. (2016) Mast Cell Clonal Disorders: Classification, Diagnosis and Management. *Curr Treat Options Allergy* **3**: 453-464 [PMID:27942432]
119. Pan BS, Chan GK, Chenard M, Chi A, Davis LJ, Deshmukh SV, Gibbs JB, Gil S, Hang G and Hatch H *et al*.. (2010) MK-2461, a novel multitargeted kinase inhibitor, preferentially inhibits the activated c-Met receptor. *Cancer Res* **70**: 1524-33 [PMID:20145145]
120. Panek RL, Lu GH, Klutchko SR, Batley BL, Dahring TK, Hamby JM, Hallak H, Doherty AM and Keiser JA. (1997) In vitro pharmacological characterization of PD 166285, a new nanomolar potent and broadly active protein tyrosine kinase inhibitor. *J Pharmacol Exp Ther* **283**: 1433-44 [PMID:9400019]
121. Pardanani A. (2019) Systemic mastocytosis in adults: 2019 update on diagnosis, risk stratification and management. *Am J Hematol* **94**: 363-377 [PMID:30536695]
122. Patch RJ, Baumann CA, Liu J, Gibbs AC, Ott H, Lattanze J and Player MR. (2006) Identification of 2-acylaminothiophene-3-carboxamides as potent inhibitors of FLT3. *Bioorg Med Chem Lett* **16**: 3282-6 [PMID:16580199]
123. Patil NK, Bohannon JK, Luan L, Guo Y, Fensterheim B, Hernandez A, Wang J and Sherwood ER. (2017) Flt3 Ligand Treatment Attenuates T Cell Dysfunction and Improves Survival in a Murine Model of Burn Wound Sepsis. *Shock* **47**: 40-51 [PMID:27454384]
124. Patwardhan PP, Ivy KS, Musi E, de Stanchina E and Schwartz GK. (2016) Significant blockade of multiple receptor tyrosine kinases by MGCD516 (Sitravatinib), a novel small molecule inhibitor, shows potent anti-tumor activity in preclinical models of sarcoma. *Oncotarget* **7**: 4093-109 [PMID:26675259]
125. Patyna S, Laird AD, Mendel DB, O'farrell AM, Liang C, Guan H, Vojkovsky T, Vasile S, Wang X and Chen J *et al*.. (2006) SU14813: a novel multiple receptor tyrosine kinase inhibitor with potent antiangiogenic and antitumor activity. *Mol Cancer Ther* **5**: 1774-82 [PMID:16891463]
126. Pearson MA and Fabbro D. (2004) Targeting protein kinases in cancer therapy: a success? *Expert Rev Anticancer Ther* **4**: 1113-24 [PMID:15606337]
127. Peng SZ, Liao CB, Chen HK, Ho CH, Huang HJ and Chiou SY. (2018) Quinoxaline compounds as type iii receptor tyrosine kinase inhibitors Patent number: WO2018071348A1. Assignee: Development Center For Biotechnology, Dcb-Usa Llc. Priority date: 09/10/2017. Publication date: 19/04/2018.
128. Peng X, Hou P, Chen Y, Dai Y, Ji Y, Shen Y, Su Y, Liu B, Wang Y and Sun D *et al*.. (2019) Preclinical evaluation of 3D185, a novel potent inhibitor of FGFR1/2/3 and CSF-1R, in FGFR-dependent and macrophage-dominant cancer models. *J Exp Clin Cancer Res* **38**: 372 [PMID:31438996]
129. Pierre F, Stefan E, Nédellec AS, Chevrel MC, Regan CF, Siddiqui-Jain A, Macalino D, Streiner N, Drygin D and Haddach M *et al*.. (2011) 7-(4H-1,2,4-Triazol-3-yl)benzo[c][2,6]naphthyridines: a novel class of Pim kinase inhibitors with potent cell antiproliferative activity. *Bioorg Med Chem Lett* **21**: 6687-92 [PMID:21982499]
130. Pollard JR and Mortimore M. (2009) Discovery and development of aurora kinase inhibitors as anticancer agents. *J Med Chem* **52**: 2629-51 [PMID:19320489]
131. Qi B, Yang Y, Gong G, He H, Yue X, Xu X, Hu Y, Li J, Chen T and Wan X *et al*.. (2019) Discovery of N^1-(4-((7-(3-(4-ethylpiperazin-1-yl)propoxy)-6-methoxyquinolin-4-yl)oxy)-3,5-difluorophenyl)-N^3-(2-(2,6-difluorophenyl)-4-oxothiazolidin-3-yl)urea as a multi-tyrosine kinase inhibitor for drug-sensitive and drug-resistant cancers treatment. *Eur J Med Chem* **163**: 10-27 [PMID:30503936]
132. Ramurthy S, Taft BR, Aversa RJ, Barsanti PA, Burger MT, Lou Y, Nishiguchi GA, Rico A, Setti L and Smith A *et al*.. (2020) Design and Discovery of *N*-(3-(2-(2-Hydroxyethoxy)-6-morpholinopyridin-4-yl)-4-methylphenyl)-2-(trifluoromethyl)isonicotinamide, a Selective, Efficacious, and Well-Tolerated RAF Inhibitor Targeting RAS Mutant Cancers: The Path to the Clinic. *J Med Chem* **63**: 2013-2027 [PMID:31059256]
133. Renhowe PA, Pecchi S, Shafer CM, Machajewski TD, Jazan EM, Taylor C, Antonios-McCrea W, McBride CM, Frazier K and Wiesmann M *et al*.. (2009) Design, structure-activity relationships and in vivo characterization of 4-amino-3-benzimidazol-2-ylhydroquinolin-2-ones: a novel class of receptor tyrosine kinase inhibitors. *J Med Chem* **52**: 278-92 [PMID:19113866]
134. Roberts WG, Ung E, Whalen P, Cooper B, Hulford C, Autry C, Richter D, Emerson E, Lin J and Kath J *et al*.. (2008) Antitumor activity and pharmacology of a selective focal adhesion kinase inhibitor, PF-562,271. *Cancer Res* **68**: 1935-44 [PMID:18339875]
135. Roberts WG, Whalen PM, Soderstrom E, Moraski G, Lyssikatos JP, Wang HF, Cooper B, Baker DA, Savage D and Dalvie D *et al*.. (2005) Antiangiogenic and antitumor activity of a selective PDGFR tyrosine kinase inhibitor, CP-673,451. *Cancer Res* **65**: 957-66 [PMID:15705896]
136. Rosnet O, Bühring HJ, Marchetto S, Rappold I, Lavagna C, Sainty D, Arnoulet C, Chabannon C, Kanz L and Hannum C *et al*.. (1996) Human FLT3/FLK2 receptor tyrosine kinase is expressed at the surface of normal and malignant hematopoietic cells. *Leukemia* **10**: 238-48 [PMID:8637232]
137. Russi AE, Walker-Caulfield ME, Ebel ME and Brown MA. (2015) Cutting edge: c-Kit signaling

differentially regulates type 2 innate lymphoid cell accumulation and susceptibility to central nervous system demyelination in male and female SJL mice. *J Immunol* **194**: 5609-13 [PMID:25972476]
138. Schubert C, Schalk-Hihi C, Struble GT, Ma HC, Petrounia IP, Brandt B, Deckman IC, Patch RJ, Player MR and Spurlino JC *et al.*. (2007) Crystal structure of the tyrosine kinase domain of colony-stimulating factor-1 receptor (cFMS) in complex with two inhibitors. *J Biol Chem* **282**: 4094-101 [PMID:17132624]
139. Scott DA, Bell KJ, Campbell CT, Cook DJ, Dakin LA, Del Valle DJ, Drew L, Gero TW, Hattersley MM and Omer CA *et al.*. (2009) 3-amido-4-anilinoquinolines as CSF-1R kinase inhibitors 2: Optimization of the PK profile. *Bioorg Med Chem Lett* **19**: 701-5 [PMID:19114305]
140. Shim AH, Liu H, Focia PJ, Chen X, Lin PC and He X. (2010) Structures of a platelet-derived growth factor/propeptide complex and a platelet-derived growth factor/receptor complex. *Proc Natl Acad Sci USA* **107**: 11307-12 [PMID:20534510]
141. Shiotsu Y, Kiyoi H, Ishikawa Y, Tanizaki R, Shimizu M, Umehara H, Ishii K, Mori Y, Ozeki K and Minami Y *et al.*. (2009) KW-2449, a novel multikinase inhibitor, suppresses the growth of leukemia cells with FLT3 mutations or T315I-mutated BCR/ABL translocation. *Blood* **114**: 1607-17 [PMID:19541823]
142. Strachan DC, Ruffell B, Oei Y, Bissell MJ, Coussens LM, Pryer N and Daniel D. (2013) CSF1R inhibition delays cervical and mammary tumor growth in murine models by attenuating the turnover of tumor-associated macrophages and enhancing infiltration by CD8(+) T cells. *Oncoimmunology* **2**: e26968 [PMID:24498562]
143. Sun L, Liang C, Shirazian S, Zhou Y, Miller T, Cui J, Fukuda JY, Chu JY, Nematalla A and Wang X *et al.*. (2003) Discovery of 5-[5-fluoro-2-oxo-1,2- dihydroindol-(3Z)-ylidenemethyl]-2,4- dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide, a novel tyrosine kinase inhibitor targeting vascular endothelial and platelet-derived growth factor receptor tyrosine kinase. *J Med Chem* **46**: 1116-9 [PMID:12646019]
144. Sun L, Tran N, Liang C, Tang F, Rice A, Schreck R, Waltz K, Shawver LK, McMahon G and Tang C. (1999) Design, synthesis, and evaluations of substituted 3-[(3- or 4-carboxyethylpyrrol-2-yl)methylidenyl]indolin-2-ones as inhibitors of VEGF, FGF, and PDGF receptor tyrosine kinases. *J Med Chem* **42**: 5120-30 [PMID:10602697]
145. Tap WD, Wainberg ZA, Anthony SP, Ibrahim PN, Zhang C, Healey JH, Chmielowski B, Staddon AP, Cohn AL and Shapiro GI *et al.*. (2015) Structure-Guided Blockade of CSF1R Kinase in Tenosynovial Giant-Cell Tumor. *N Engl J Med* **373**: 428-37 [PMID:26222558]
146. Taylor ML, Sehgal D, Raffeld M, Obiakor H, Akin C, Mage RG and Metcalfe DD. (2004) Demonstration that mast cells, T cells, and B cells bearing the activating kit mutation D816V occur in clusters within the marrow of patients with mastocytosis. *J Mol Diagn* **6**: 335-42 [PMID:15507672]
147. Thomas M, Huang WS, Wen D, Zhu X, Wang Y, Metcalf CA, Liu S, Chen I, Romero J and Zou D *et al.*. (2011) Discovery of 5-(arenethynyl) hetero-monocyclic derivatives as potent inhibitors of BCR-ABL including the T315I gatekeeper mutant. *Bioorg Med Chem Lett* **21**: 3743-8 [PMID:21561767]
148. Tian S, Quan H, Xie C, Guo H, Lü F, Xu Y, Li J and Lou L. (2011) YN968D1 is a novel and selective inhibitor of vascular endothelial growth factor receptor-2 tyrosine kinase with potent activity in vitro and in vivo. *Cancer Sci* **102**: 1374-80 [PMID:21443688]
149. Tovar C, Higgins B, Deo D, Kolinsky K, Liu JJ, Heimbrook DC and Vassilev LT. (2010) Small-molecule inducer of cancer cell polyploidy promotes apoptosis or senescence: Implications for therapy. *Cell Cycle* **9**: 3364-75 [PMID:20814247]
150. Trudel S, Li ZH, Wei E, Wiesmann M, Chang H, Chen C, Reece D, Heise C and Stewart AK. (2005) CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma. *Blood* **105**: 2941-8 [PMID:15598814]
151. Turner AM, Bennett LG, Lin NL, Wypych J, Bartley TD, Hunt RW, Atkins HL, Langley KE, Parker V and Martin F *et al.*. (1995) Identification and characterization of a soluble c-kit receptor produced by human hematopoietic cell lines. *Blood* **85**: 2052-8 [PMID:7536489]
152. Verstraete K, Vandriessche G, Januar M, Elegheert J, Shkumatov AV, Desfosses A, Van Craenenbroeck K, Svergun DI, Gutsche I and Vergauwen B *et al.*. (2011) Structural insights into the extracellular assembly of the hematopoietic Flt3 signaling complex. *Blood* **118**: 60-8 [PMID:21389326]
153. Wang D, Tang F, Wang S, Jiang Z and Zhang L. (2012) Preclinical anti-angiogenesis and anti-tumor activity of SIM010603, an oral, multi-targets receptor tyrosine kinases inhibitor. *Cancer Chemother Pharmacol* **69**: 173-83 [PMID:21638122]
154. Wang T, Lamb ML, Block MH, Davies AM, Han Y, Hoffmann E, Ioannidis S, Josey JA, Liu ZY and Lyne PD *et al.*. (2012) Discovery of Disubstituted Imidazo[4,5-b]pyridines and Purines as Potent TrkA Inhibitors. *ACS Med Chem Lett* **3**: 705-9 [PMID:24900538]
155. Wedge SR, Kendrew J, Hennequin LF, Valentine PJ, Barry ST, Brave SR, Smith NR, James NH, Dukes M and Curwen JO *et al.*. (2005) AZD2171: a highly potent, orally bioavailable, vascular endothelial growth factor receptor-2 tyrosine kinase inhibitor for the treatment of cancer.

Cancer Res **65**: 4389-400 [PMID:15899831]
156. Wedi B. (2023) Inhibition of KIT for chronic urticaria: a status update on drugs in early clinical development. *Expert Opin Investig Drugs* **32**: 1043-1054 [PMID:37897679]
157. Weisberg E, Boulton C, Kelly LM, Manley P, Fabbro D, Meyer T, Gilliland DG and Griffin JD. (2002) Inhibition of mutant FLT3 receptors in leukemia cells by the small molecule tyrosine kinase inhibitor PKC412. *Cancer Cell* **1**: 433-43 [PMID:12124173]
158. Weisberg E, Roesel J, Bold G, Furet P, Jiang J, Cools J, Wright RD, Nelson E, Barrett R and Ray A *et al.*. (2008) Antileukemic effects of the novel, mutant FLT3 inhibitor NVP-AST487: effects on PKC412-sensitive and -resistant FLT3-expressing cells. *Blood* **112**: 5161-70 [PMID:18820131]
159. Werner MH and Kelly TA. (2020) Compositions and methods for inhibiting kinases Patent number: US20200046699A1. Assignee: Inhibikase Therapeutics Inc. Priority date: 25/10/2017. Publication date: 13/02/2020.
160. Wilhelm SM, Carter C, Tang L, Wilkie D, McNabola A, Rong H, Chen C, Zhang X, Vincent P and McHugh M *et al.*. (2004) BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis. *Cancer Res* **64**: 7099-109 [PMID:15466206]
161. William AD, Lee AC, Blanchard S, Poulsen A, Teo EL, Nagaraj H, Tan E, Chen D, Williams M and Sun ET *et al.*. (2011) Discovery of the macrocycle 11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)]heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decaene (SB1518), a potent Janus kinase 2/fms-like tyrosine kinase-3 (JAK2/FLT3) inhibitor for the treatment of myelofibrosis and lymphoma. *J Med Chem* **54**: 4638-58 [PMID:21604762]
162. William AD, Lee AC, Goh KC, Blanchard S, Poulsen A, Teo EL, Nagaraj H, Lee CP, Wang H and Williams M *et al.*. (2012) Discovery of kinase spectrum selective macrocycle (16E)-14-methyl-20-oxa-5,7,14,26-tetraazatetracyclo[19.3.1.1(2,6).1(8,12)]heptacosa-1(25),2(26),3,5,8(27),9,11,16,21,23-decaene (SB1317/TG02), a potent inhibitor of cyclin dependent kinases (CDKs), Janus kinase 2 (JAK2), and fms-like tyrosine kinase-3 (FLT3) for the treatment of cancer. *J Med Chem* **55**: 169-96 [PMID:22148278]
163. Wodicka LM, Ciceri P, Davis MI, Hunt JP, Floyd M, Salerno S, Hua XH, Ford JM, Armstrong RC and Zarrinkar PP *et al.*. (2010) Activation state-dependent binding of small molecule kinase inhibitors: structural insights from biochemistry. *Chem Biol* **17**: 1241-9 [PMID:21095574]
164. Wong J and Vasquez M. (2011) Antibodies That Bind CSF1R Patent number: US20110274683 A1. Assignee: Five Prime Therapeutics, Inc.. Priority date: 04/05/2010. Publication date: 10/11/2011.
165. Wood FL, Shepherd S, Hayes A, Liu M, Grira K, Mok Y, Atrash B, Faisal A, Bavetsias V and Linardopoulos S *et al.*. (2019) Metabolism of the dual FLT-3/Aurora kinase inhibitor CCT241736 in preclinical and human in vitro models: Implication for the choice of toxicology species. *Eur J Pharm Sci* **139**: 104899 [PMID:30953752]
166. Wu Y, Wang B, Wang J, Qi S, Zou F, Qi Z, Liu F, Liu Q, Chen C and Hu C *et al.*. (2019) Discovery of 2-(4-Chloro-3-(trifluoromethyl)phenyl)-*N*-(4-((6,7-dimethoxyquinolin-4-yl)oxy)phenyl)acetamide (CHMFL-KIT-64) as a Novel Orally Available Potent Inhibitor against Broad-Spectrum Mutants of c-KIT Kinase for Gastrointestinal Stromal Tumors. *J Med Chem* **62**: 6083-6101 [PMID:31250638]
167. Xie Z, Wu B, Liu Y, Ren W, Tong L, Xiang C, Wei A, Gao Y, Zeng L and Xie H *et al.*. (2020) Novel Class of Colony-Stimulating Factor 1 Receptor Kinase Inhibitors Based on an *o*-Aminopyridyl Alkynyl Scaffold as Potential Treatment for Inflammatory Disorders. *J Med Chem* **63**: 1397-1414 [PMID:31934767]
168. Xu Z, Zhang N, Wang T, Sun Q and Wang Y. (2017) Fused pyrimidine compound, and intermediate, preparation method, composition and application of Patent number: CN106366093A. Assignee: Guangzhou Re Pharmaceutical Technology Co Ltd. Priority date: 21/07/2016. Publication date: 01/02/2017.
169. Yan SB, Peek VL, Ajamie R, Buchanan SG, Graff JR, Heidler SA, Hui YH, Huss KL, Konicek BW and Manro JR *et al.*. (2013) LY2801653 is an orally bioavailable multi-kinase inhibitor with potent activity against MET, MST1R, and other oncoproteins, and displays anti-tumor activities in mouse xenograft models. *Invest New Drugs* **31**: 833-44 [PMID:23275061]
170. Yang T, Hu M, Chen Y, Xiang M, Tang M, Qi W, Shi M, He J, Yuan X and Zhang C *et al.*. (2020) *N*-(Pyrimidin-2-yl)-1,2,3,4-tetrahydroisoquinolin-6-amine Derivatives as Selective Janus Kinase 2 Inhibitors for the Treatment of Myeloproliferative Neoplasms. *J Med Chem* **63**: 14921-14936 [PMID:33256400]
171. Yang T, Hu M, Qi W, Yang Z, Tang M, He J, Chen Y, Bai P, Yuan X and Zhang C *et al.*. (2019) Discovery of Potent and Orally Effective Dual Janus Kinase 2/FLT3 Inhibitors for the Treatment of Acute Myelogenous Leukemia and Myeloproliferative Neoplasms. *J Med Chem* **62**: 10305-10320 [PMID:31670517]
172. Yeh V, Li X, Liu X, Loren J, Molteni V, Nabakka J, Nguyen B, Michael H and Petrassi J. (2013) COMPOUNDS AND COMPOSITIONS AS c-KIT KINASE INHIBITORS Patent number: WO2013033070A1. Assignee: Irm Llc. Priority date: 28/08/2012. Publication date: 07/03/2013.
173. Yen SC, Chen LC, Huang HL, Ngo ST, Wu YW, Lin TE, Sung TY, Lien ST, Tseng HJ and Pan SL

et al.. (2021) Investigation of Selected Flavonoid Derivatives as Potent FLT3 Inhibitors for the Potential Treatment of Acute Myeloid Leukemia. *J Nat Prod* **84**: 1-10 [PMID:33393294]
174. Yoshida A, Ookura M, Zokumasu K and Ueda T. (2014) Gö6976, a FLT3 kinase inhibitor, exerts potent cytotoxic activity against acute leukemia via inhibition of survivin and MCL-1. *Biochem Pharmacol* **90**: 16-24 [PMID:24735609]
175. You WK, Sennino B, Williamson CW, Falcón B, Hashizume H, Yao LC, Aftab DT and McDonald DM. (2011) VEGF and c-Met blockade amplify angiogenesis inhibition in pancreatic islet cancer. *Cancer Res* **71**: 4758-68 [PMID:21613405]
176. Yuzawa S, Opatowsky Y, Zhang Z, Mandiyan V, Lax I and Schlessinger J. (2007) Structural basis for activation of the receptor tyrosine kinase KIT by stem cell factor. *Cell* **130**: 323-34 [PMID:17662946]
177. Zarrinkar PP, Gunawardane RN, Cramer MD, Gardner MF, Brigham D, Belli B, Karaman MW, Pratz KW, Pallares G and Chao Q *et al*.. (2009) AC220 is a uniquely potent and selective inhibitor of FLT3 for the treatment of acute myeloid leukemia (AML). *Blood* **114**: 2984-92 [PMID:19654408]
178. Zhang J, Ibrahim PN, Bremer R, Spevak W and Cho H. (2015) Compounds and methods for kinase modulation, and indications therefor Patent number: US9096593B2. Assignee: Plexxikon Inc. Priority date: 20/09/2013. Publication date: 08/04/2015.
179. Zhao B, Zhang M, Yu H, Yang S, Chen Z and Xu Y. (2019) N-(azaaryl)cyclolactam-1-carboxamide derivative, preparation method therefor, and use thereof Patent number: WO2018214867A9. Assignee: Shanghai Hoyu Biomedical Technology Co., Ltd.. Priority date: 22/05/2018. Publication date: 03/10/2019.
180. Zhao C, Zhang Y, Zhang J, Li S, Liu M, Geng Y, Liu F, Chai Q, Meng H and Li M *et al*.. (2023) Discovery of Novel Fedratinib-Based HDAC/JAK/BRD4 Triple Inhibitors with Remarkable Antitumor Activity against Triple Negative Breast Cancer. *J Med Chem* **66**: 14150-14174 [PMID:37796543]
181. Zhao J, Zhang D, Zhang W, Stashko MA, DeRyckere D, Vasileiadi E, Parker RE, Hunter D, Liu Q and Zhang Y *et al*.. (2018) Highly Selective MERTK Inhibitors Achieved by a Single Methyl Group. *J Med Chem* **61**: 10242-10254 [PMID:30347155]
182. Zhou Y, Chen Y, Tong L, Xie H, Wen W, Zhang J, Xi Y, Shen Y, Geng M and Wang Y *et al*.. (2012) AL3810, a multi-tyrosine kinase inhibitor, exhibits potent anti-angiogenic and anti-tumour activity via targeting VEGFR, FGFR and PDGFR. *J Cell Mol Med* **16**: 2321-30 [PMID:22304225]
183. Zhou Y, Shan S, Li ZB, Xin LJ, Pan DS, Yang QJ, Liu YP, Yue XP, Liu XR and Gao JZ *et al*.. (2017) CS2164, a novel multi-target inhibitor against tumor angiogenesis, mitosis and chronic inflammation with anti-tumor potency. *Cancer Sci* **108**: 469-477 [PMID:28004478]
184. Zisman LS. (2014) Non-selective kinase inhibitors Patent number: WO2014110200A1. Assignee: Zisman LS. Priority date: 10/01/2013. Publication date: 17/07/2014.