

Product Data Sheet

Product Name: PD173074

Cat. No.: GC17943

Chemical Properties

Cas. No. 219580-11-7

Chemical Name 1-tert-butyl-3-[2-[4-(diethylamino)butylamino]-6-(3,5-dimethoxyphenyl)pyrido[2,3-d]pyrimidin-7-yl]urea

SMILES CCN(CC)CCCCNC1=NC2=NC(=C(C=C2C=N1)C3=CC(=CC(=C3)OC)OC)NC(=O)NC(C)(C)C

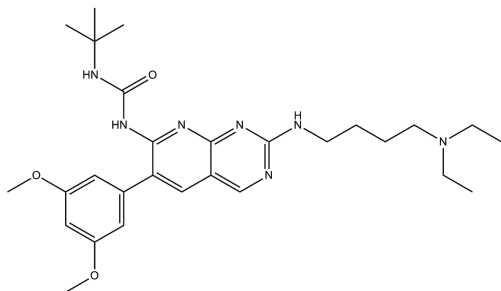
Formula $C_{28}H_{41}N_7O_3$ M.Wt 523.67

Solubility $\geq 26.1835\text{mg/mL}$ in DMSO, $\geq 108.4\text{ mg/mL}$ in EtOH with ultrasonic Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Kinase experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

The assay media for TK activity contained 25mM HEPES buffer (pH 7.4), 150mM NaCl, 10mM MnCl₂, 0.1mM sodium orthovanadate, 750µg/ml of random co-polymer of glutamic acid and tyrosine (4:1), various concentrations of Preparation Method inhibitor and 60–75ng of enzyme. The reaction (total volume, 100µL) was initiated by the addition of [γ -³²P]ATP (50µM ATP containing 0.4µCi [³²P]ATP per incubation. Samples were incubated for 10 minutes at 25°C and terminated by the addition of 30% trichloroacetic acid.

Reaction Conditions 10 minutes at 25°C

Applications PD173074 displayed selective inhibitory activity towards FGFR1TK at 26nM.

Cell experiment [2]:

Cell lines HepG2, Hep3B, human normal liver cell line HL7702

HepG2, Hep3B or HL7702 cells were seeded into 96-well plate at 5000cells/well. After adherence, the cells were treated with different concentrations of PD173074 (0.5, 1, 10, 20 and 50µM). 48h later, the cells were Preparation Method incubated with MTT solution (500µg/mL) for 4h at 37°C. The formazan was solubilized with DMSO and relative cell viability was measured at 490nm with a microplate reader. Growth inhibition in response to various concentrations of PD173074 was calculated using GraphPad Prism 7.0.

Reaction Conditions 0.5, 1, 10, 20 and 50µM; 48h

Applications PD173074 significantly arrested HepG2 and Hep3B cells in G1 phase and inhibited cell proliferation.

Animal experiment [3]:

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal models nude mice

H510 (1:1 cell suspension) or H69 cells were implanted into the flank of nude mice. When tumors became measurable, 50mg/kg PD173074/mice or equivalent volume of buffer alone were administered daily for 14 or 28d. In addition, mice received or did not receive two doses of 5mg/kg cisplatin. Tumor volume was monitored using a calliper. Animals were sacrificed when tumor burden reached 15mm in any dimension and survival recorded as a Kaplan-

Preparation Method Meier plot. Tissues were formalin fixed and paraffin embedded before staining as indicated in the figure legends. For the endomucin experiments, pictures were acquired using a $\times 10$ objective and analyzed using ImageJ. For activated Caspase 3 and cytokeratin 18 scoring, the number of positive cells in five high-power field views/tumor (five tumors per condition) was determined and results represented as bar graphs. The total number of nuclei per field was determined by manual counting using event flagging in Metamorph.

Dosage form 50mg/kg; up to 28 days; goral gavage

Applications In the H-510 xenograft, tumor growth was impaired similar to that seen with single-agent cisplatin administration, increasing median survival compared with control sham-treated animals. Crucially, the effect of cisplatin was significantly potentiated by coadministration of PD173074. In H-69 xenografts, PD173074 induced complete responses lasting >6 months in 50% of mice.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

- [1] Dimitroff, C J et al. "Anti-angiogenic activity of selected receptor tyrosine kinase inhibitors, PD166285 and PD173074: implications for combination treatment with photodynamic therapy." *Investigational new drugs* vol. 17,2 (1999): 121-35. doi:10.1023/a:1006367032156
- [2] Qiao, Chuchu et al. "PD173074 significantly HepG2 and Hep3B inhibited cell proliferation." *PloS one* vol. 15,6 e0234708. 18 Jun. 2020, doi:10.1371/journal.pone.0234708
- [3] Pardo, Olivier E et al. "The fibroblast growth factor receptor inhibitor PD173074 blocks small cell lung cancer growth in vitro and in vivo." *Cancer research* vol. 69,22 (2009): 8645-51. doi:10.1158/0008-5472.CAN-09-1576

Background

PD173074 is an ATP-competitive FGFR1 and VEGFR2 inhibitor with an IC₅₀ value of 26nM and 100-200nM, respectively, showing higher selectivity for FGFR1 over PDGFR and c-Src^[1]. PD173074 weakly inhibits the activities of Src, InsR, EGFR, PDGFR, MEK, and PKC^[2].

in vitro, PD173074 (0.5, 1, 10, 20 and 50μM; 48h) blocks G1/S transition via CUL3-mediated ubiquitin protease in HepG2 and Hep3B cells^[3]. PD173074 (0.25 or 1μmol/L, 20μL/well; 4h) reverses MRP7 (ABCC10)-mediated multidrug resistance^[4]. PD173074 (0-100μM; 30min) binds to the C-terminus of oncofetal architectural chromatin factor high-mobility group AT-hook 2 (HMGA2) and modulates its DNA-binding and transcriptional activation functions^[5].

in vivo, PD173074 (50mg/kg; up to 28 days; goral gavage) blocks small cell lung cancer growth in a nude mice model^[6]. PD173074 (20 mg/kg; 3 days; i.p) block FGFR-dependent urothelial carcinoma growth in a Balb/c mice model^[7]. PD173074 (20mg/kg; once per day; 10 days; i.p) improves antitumor immunity and impairs breast cancer metastasis in a Balb/c mice model^[8].

References:

- [1] Dimitroff, C J et al. "Anti-angiogenic activity of selected receptor tyrosine kinase inhibitors, PD166285 and PD173074: implications for combination treatment with photodynamic therapy." *Investigational new drugs* vol. 17,2 (1999): 121-35. doi:10.1023/a:1006367032156
- [2] Tan, Li et al. "Development of covalent inhibitors that can overcome resistance to first-generation

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

FGFR kinase inhibitors.” *Proceedings of the National Academy of Sciences of the United States of America* vol. 111,45 (2014): E4869-77. doi:10.1073/pnas.1403438111

[3] Qiao, Chuchu et al. “PD173074 blocks G1/S transition via CUL3-mediated ubiquitin protease in HepG2 and Hep3B cells.” *PloS one* vol. 15,6 e0234708. 18 Jun. 2020, doi:10.1371/journal.pone.0234708

[4] Anreddy, Nagaraju et al. “PD173074, a selective FGFR inhibitor, reverses MRP7 (ABCC10)-mediated MDR.” *Acta pharmaceutica Sinica. B* vol. 4,3 (2014): 202-7. doi:10.1016/j.apsb.2014.02.003

[5] Ahmed, Syed Moiz et al. “The FGFR inhibitor PD173074 binds to the C-terminus of oncofetal HMGA2 and modulates its DNA-binding and transcriptional activation functions.” *FEBS letters* vol. 597,15 (2023): 1977-1988. doi:10.1002/1873-3468.14675

[6] Pardo, Olivier E et al. “The fibroblast growth factor receptor inhibitor PD173074 blocks small cell lung cancer growth in vitro and in vivo.” *Cancer research* vol. 69,22 (2009): 8645-51. doi:10.1158/0008-5472.CAN-09-1576

[7] Lamont, F R et al. “Small molecule FGF receptor inhibitors block FGFR-dependent urothelial carcinoma growth in vitro and in vivo.” *British journal of cancer* vol. 104,1 (2011): 75-82. doi:10.1038/sj.bjc.6606016

[8] Ye, Tinghong et al. “Inhibition of FGFR signaling by PD173074 improves antitumor immunity and impairs breast cancer metastasis.” *Breast cancer research and treatment* vol. 143,3 (2014): 435-46. doi:10.1007/s10549-013-2829-y

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA