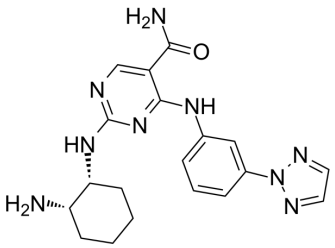
PRT062607

Cat. No.:	HY-15322
CAS No.:	1370261-96-3
Molecular Formula:	$C_{19}H_{23}N_9O$
Molecular Weight:	393.45
Target:	Syk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PRT062607(P505-15; PRT-2607; BIIB-057) is a highly specific and potent inhibitor of Syk with IC50 of 1-2 nM; >80-fold selective for Syk than Fgr, Lyn, FAK, Pyk2 and Zap70.IC50 value: 1-2 nM [1]Target:Syk kinase inhibitorin vitro: In human whole blood, P505-15 potently inhibited B cell antigen receptor-mediated B cell signaling and activation (IC50 0.27 and 0.28 μM, respectively) and Fcε receptor 1-mediated basophil degranulation (IC50 0.15 μM) [1]. P505-15 successfully inhibited SYK-mediated B-cell receptor signaling and decreased cell viability in NHL and CLL [2]. PRT318 and P505-15 effectively antagonize CLL cell survival after BCR triggering and in nurse-like cell-co-cultures. Moreover, they inhibit BCR-dependent secretion of the chemokines CCL3 and CCL4 by CLL cells, and leukemia cell migration toward the tissue homing chemokines CXCL12, CXCL13, and beneath stromal cells. PRT318 and P505-15 furthermore inhibit Syk and extracellular signal-regulated kinase phosphorylation after BCR triggering [3].in vivo: Similar levels of ex vivo inhibition were measured after dosing in mice (Syk signaling IC50 0.32 μM). Oral administration of P505-15 produced dose-dependent anti-inflammatory activity in two rodent models of rheumatoid arthritis [1]. Oral dosing in mice prevented BCR-mediated splenomegaly and significantly inhibited NHL tumor growth in a xenograft model. In addition, combination treatment of primary CLL cells with P505-15 plus fludarabine produced synergistic enhancement of activity at nanomolar concentrations [2].

CUSTOMER VALIDATION

- Int J Ophthalmol. 2022 Jul 18;15(7):1044-1052.
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REFERENCES

[1]. Coffey G, et al. Specific inhibition of spleen tyrosine kinase suppresses leukocyte immune function and inflammation in animal models of rheumatoid arthritis. J Pharmacol Exp Ther. 2012 Feb;340(2):350-9.

[2]. Spurgeon SE, et al. The selective SYK inhibitor P505-15 (PRT062607) inhibits B cell signaling and function in vitro and in vivo and augments the activity of fludarabine in chronic lymphocytic leukemia. J Pharmacol Exp Ther. 2013 Feb;344(2):378-87.

[3]. Hoellenriegel J, et al. Selective, novel spleen tyrosine kinase (Syk) inhibitors suppress chronic lymphocytic leukemia B-cell activation and migration. Leukemia. 2012 Jul;26(7):1576-83.

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