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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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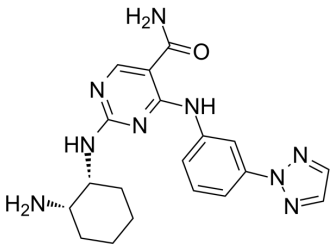
PRT062607

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:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (254.16 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5416 mL	12.7081 mL	25.4162 mL
	5 mM	0.5083 mL	2.5416 mL	5.0832 mL
	10 mM	0.2542 mL	1.2708 mL	2.5416 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.35 mM); Clear solution

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

- Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2207280119.
- Int J Ophthalmol. 2022 Jul 18;15(7):1044-1052.
- Harvard Medical School LINCS LIBRARY

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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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