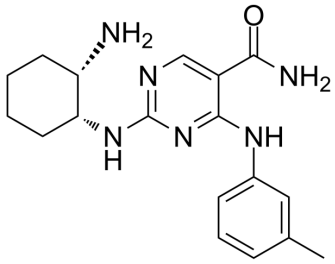
PRT-060318

Cat. No.:	HY-12974
CAS No.:	1194961-19-7
Molecular Formula:	$C_{18}H_{24}N_6O$
Molecular Weight:	340.42
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

H_2O : 5.6 mg/mL (16.45 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9375 mL	14.6877 mL	29.3755 mL
5 mM	0.5875 mL	2.9375 mL	5.8751 mL
10 mM	0.2938 mL	1.4688 mL	2.9375 mL

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

BIOLOGICAL ACTIVITY

Description

PRT-060318 (PRT318) is a novel selective inhibitor of the tyrosine kinase Syk with an IC_{50} of 4 nM.

IC_{50} & Target

IC50: 4 nM (Syk)[1]

In Vitro

PRT318 is a potent inhibitor of purified Syk kinase with an IC_{50} of 4 nM. Syk kinase is inhibited by 92%, whereas all other kinases retains more than 70% at a concentration of 50 nM of PRT318[1]. PRT318 and P505-15 effectively antagonize CLL cell survival after B-cell receptor (BCR) triggering and in nurse-like cell-co-cultures. 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 inhibit Syk and extracellular signal-regulated kinase phosphorylation after BCR triggering[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

PRT318 completely inhibits HIT immune complex-induced aggregation of both human and transgenic HIT mouse platelets. Pretreatment of mice with PRT318 markedly reduces HIT IC-induced thrombosis in the lungs. The Thrombosis Score is significantly lower for PRT318-treated mice compared with control[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	PRT318 is dissolved in DMSO. Cells are incubated for 14 days in 24-well plates. CLL cells are cultured under standardized conditions on NLC or in suspension, in the presence or absence of PRT318 and P505-15. At 24, 48, 72 h, CLL cells are collected and assayed for cell viability[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Heparin-induced thrombocytopenia (HIT) model mice are treated with KKO (20 mg/kg body weight, intraperitoneally) on day 0. The mice are divided into sex- and weight-matched experimental and control groups. On days 1 to 7, experimental mice (n=6) receives PRT318 (30 mg/kg body weight) orally via gavage twice a day, whereas control mice (n=6) receives vehicle only (sterile water). Both groups receives heparin (1600 U/kg body weight, subcutaneously) once daily. Mice are anesthetized by isoflurane inhalation for injections and blood collections[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- bioRxiv. 2019 Jan.

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REFERENCES

[1]. Reilly MP, et al. PRT-060318, a novel Syk inhibitor, prevents heparin-induced thrombocytopenia and thrombosis in a transgenic mouse model. Blood. 2011 Feb 17;117(7):2241-6.

[2]. 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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