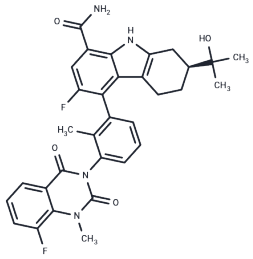
Data Sheet (Cat.No.T5138)

TargetMol

BMS-986142

Chemical Properties



CAS No. : 1643368-58-4

Formula: C32H30F2N4O4

Molecular Weight: 572.6

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	BMS-986142 is a potent and highly selective reversible BTK inhibitor (IC50: 0.5 nM).
Targets(IC50)	BTK
In vitro	Against a panel of 384 kinases, BMS-986142 is highly selective, with only five other kinases (Tec, ITK, BLK, Txk, BMX) inhibited with <100-fold selectivity for BTK. Four of these kinases are Tec family kinases, of which BTK is a member, and only Tec (IC50: 10 nM) is inhibited with 30-fold selectivity compared with BTK. BMS-986142 does not inhibit CD40L-induced expression of CD86 or CD69 on peripheral blood B cells (IC50>10,000 nM for both). When Ramos B cells are treated with anti-IgM to activate BCR, BMS-986142 inhibits BTK-dependent calcium flux (IC50: 9 nM) [2].
In vivo	BMS-986142 administration at doses of 4, 10, and 30 mg/kg produces dose-dependent decreases in clinically evident disease by 26%, 43%, and 79%, respectively. Notably, at a 4 mg/kg dose, BMS-986142, when used in conjunction with MTX, enhances clinical scores by achieving a 54% inhibition, compared to a 19% inhibition with MTX alone. Further, this co-administration at 4 mg/kg leads to a 53% reduction in inflammation and bone resorption, significantly more effective than the 24% and 10% reductions observed with each drug individually. Additionally, serum anti-collagen II IgG levels are notably reduced with 10 and 30 mg/kg doses of BMS-986142. The compound also demonstrates efficacy in delayed treatment protocols, showing dose-dependent improvements in clinical scores even when administration begins on day 21, with 2, 4, and 25 mg/kg doses resulting in clinical score reductions of 17%, 37%, and 67%, respectively, by study's end [2].
Animal Research	Male DBA/1 mice are injected subcutaneously at the base of the tail with bovine type II collagen (200 μg) admixed. The mice are boosted 21 days later in the same manner. For preventative administration, PO QD dosing is immediately started with BMS-986142 in EtOH: TPGS: PEG300 (5:5:90); for therapeutic administration, the start of dosing is delayed until the booster immunization on day 21. For BMS-986142 plus MTX preventative studies, mice receive vehicle; BMS-986142 at 4, 10, or 30 mg/kg; BMS-986142 at 4 mg/kg plus MTX 0.25 mg/kg; or MTX at 0.25 mg/kg daily. For BMS-986142 plus etanercept therapeutic studies, mice receive vehicle daily; BMS-986142 at 2, 4, or 25 mg/kg daily; BMS-986142 at 2 or 4 mg/kg daily plus etanercept at 15 mg/kg IP twice weekly (BIW); or etanercept at 15 mg/kg IP BIW. For BMS-986142 plus murine cytotoxic T

Animal Research	lymphocyte-associated protein 4 immunoglobulins (CTLA-4-Ig) preventative studies, mice receive vehicle daily; BMS-986142 at 10 or 30 mg/kg daily; murine CTLA-4-Ig at 0.05 or 0.2 mg/kg IP BIW; or BMS-986142 at 10 mg/kg daily plus murine CTLA-4-Ig at 0.05 or 0.2 mg/kg IP BIW. Dosing proceeds from day 0 through study completion (36 days).

Solubility Information

Solubility	DMSO: 45 mg/mL (78.59 mM),Sonication is recommended. H2O: Insoluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.49 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7464 mL	8.7321 mL	17.4642 mL
5 mM	0.3493 mL	1.7464 mL	3.4928 mL
10 mM	0.1746 mL	0.8732 mL	1.7464 mL
50 mM	0.0349 mL	0.1746 mL	0.3493 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Watterson SH, et al. Discovery of 6-Fluoro-5-(R)-(3-(S)-(8-fluoro-1-methyl-2,4-dioxo-1,2-dihydroquinazolin-3(4H)-yl)-2-methylphenyl)-2-(S)-(2-hydroxypropan-2-yl)-2,3,4,9-tetrahydro-1H-carbazole-8-carboxamide (BMS-1986142): A Reversible Inhibitor of Bruton's Tyrosine Kinase (BTK) Conformationally Constrained by Two Locked Atropisomers. J Med Chem. 2016 Oct 13;59(19):9173-9200.

Kathleen M. Gillooly, et al. Bruton'styrosine kinase inhibitor BMS-986142 in experimental models of rheumatoid arthritis enhances efficacy of agents representing clinical standard-of-care. PLoS One. 2017; 12(7): e0181782.