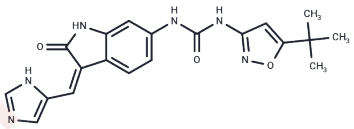
Data Sheet (Cat.No.T86102)

TargetMol

CSF1R-IN-22

Chemical Properties



CAS No. : 2760585-35-9

Formula: C20H20N6O3

Molecular Weight: 392.41

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	CSF1R-IN-22 (Compound C19), a potent orally administered CSF-1R selective inhibitor (IC50 <6 nM), significantly enhances CXCL9 secretion from M2 macrophages and promotes CD8+ T cell infiltration. Moreover, it amplifies the anti-tumor immune responses in conjunction with anti-PD-1 and triggers apoptosis in tumor cells. Additionally, CSF1R-IN-22 effectively reprograms M2-like TAMs (tumor-associated macrophages) to an M1 phenotype, modulates the tumor microenvironment (TME) by fostering the recruitment of CD8+ T cells, and diminishes the presence of immunosuppressive Tregs and MDSCs [1].
Targets(IC50)	Apoptosis,c-Fms
In vitro	CSF1R-IN-22 significantly inhibits the activation of the CSF-1R signaling pathway in BMDMs cells at concentrations of 0-2500 nM for 1 hour. At concentrations of 30-100 nM for 24 hours, CSF1R-IN-22 effectively reprograms M2 macrophages into M1 macrophages in both BMDMs and HMDMs cells. The supernatant from M2 macrophages treated with 10-100 nM of CSF1R-IN-22 for 20 hours significantly reduces the viability of MC-38 and CT-26 cells. A Western blot analysis using BMDMs cells at concentrations of 10, 30, and 100 nM for 1 hour showed a dose-dependent inhibition of the phosphorylation of CSF-1R and its downstream signaling proteins AKT and mTORC1. An apoptosis analysis with MC-38 and CT-26 cells at 10, 30, and 100 nM for 20 hours demonstrated that the processed M2 macrophage supernatant substantially increased the apoptosis rate, with an approximately 60% increase observed at the 100 nM concentration.
In vivo	CSF1R-IN-22 exhibited significant antitumor activity in C57BL/6 mice bearing MC-38 subcutaneous tumors at dosages of 5-20 mg/kg, orally once daily for 14 days. It enhanced the activity of cytotoxic T lymphocytes (CTLs), with high-dose groups outperforming PLX3397 [1]. When administered in combination with 100 μg/mouse PD-1 antibody, CSF1R-IN-22 (20 mg/kg; p.o.; once daily for 14 days) demonstrated enhanced antitumor effects. A positive correlation was observed between CXCL9 expression and survival rates [1]. Pharmacokinetic analysis in SD rats [1] showed that intravenous administration of 1 mg/kg resulted in an AUC 0-t of 9126.62 ng·h/mL, a half-life of 1.34 hours, a clearance rate of 0.10 L/h/kg, and a steady-state volume of distribution of 0.34 L/kg; oral administration of 10 mg/kg resulted in an AUC 0-t of 85939.36 ng·h/mL, a half-life of 2.41 hours, a clearance rate of 0.12 L/h/kg, and a maximum concentration of 10867.65 ng/mL, with a bioavailability of 94.2%. In the MC-38 tumor model in C57BL/6

In vivo	mice, CSF1R-IN-22 significantly inhibited tumor growth and induced apoptosis through oral administration of 5, 10, 20 mg/kg daily for 14 days, leading to significantly lower tumor mass compared to controls. The high-dose group showed a tumor growth inhibition (TGI) of 65% and a 30-day survival rate of 70%. An increase in M1 macrophage marker gene mRNA levels (Nos2, Tnf, Il6, Il1) and a decrease in M2 macrophage marker gene expression (Arg1, Chil3l, Rentla, Mrc1) were observed. Doses of 10 and 20 mg/kg significantly increased the proportion of CD3+CD8+ T cells, and reduced the proportion of immunosuppressive Treg cells and myeloid-derived suppressor cells (MDSCs) in tumor tissues. For mice treated with CSF1R-IN-22 (20 mg/kg) in combination with PD-1 in the MC-38 or MC-38-luc models, there was a significant reduction in tumor bioluminescence compared to the monotherapy groups. The combination therapy notably increased the proportion of CD3+CD8+ T cells and CTLs in tumor tissues, significantly decreasing the proportion of immunosuppressive Treg cells in the MC-38 tumor model. Enhanced infiltration of CD8+ T cells and CTLs was significantly associated with increased mRNA expression of Cxcl9. Mice treated with the combination therapy exhibited a survival rate of 100% at 70 days and 70% overcame tumor recurrence within 91 days after rechallenging MC-38 tumor cells. The use of a CXCL9 neutralizing antibody significantly reduced apoptosis and the proportion of CD3+CD8+ T cells.

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5484 mL	12.7418 mL	25.4836 mL
5 mM	0.5097 mL	2.5484 mL	5.0967 mL
10 mM	0.2548 mL	1.2742 mL	2.5484 mL
50 mM	0.051 mL	0.2548 mL	0.5097 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.