BIIB091

Cat. No.: HY-139984

CAS No.: 2247614-80-6

Molecular Formula: $C_{28}H_{34}N_{10}O_2$

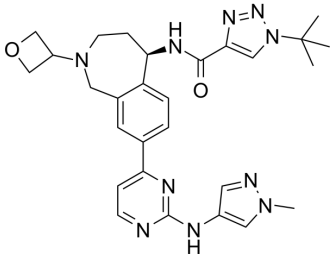
Molecular Weight: 542.64

Target: Btk

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 : 125 mg/mL (230.36 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8428 mL	9.2142 mL	18.4284 mL
	5 mM	0.3686 mL	1.8428 mL	3.6857 mL
	10 mM	0.1843 mL	0.9214 mL	1.8428 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: ≥ 2.08 mg/mL (3.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BIIB091 is a potent, selective, orally active and reversible BTK inhibitor, with an IC_{50} of <0.5 nM. BIIB091 binds the BTK protein to sequester TYR-551 into an inactive conformation with excellent affinity. BIIB091 can be used for the research of multiple sclerosis[1].

In Vitro

BIIB091 inhibits the phosphorylation of PLCγ2 in the Ramos human B-cell line, with an IC_{50} of 6.9 nM[1].
BIIB091 blocks anti-IgM-stimulated CD69 activation in PBMCs with an IC_{50} of 6.9 nM[1].
BIIB091 inhibits FcγR-induced ROS production in purified primary neutrophils, with an IC_{50} of 4.5 nM[1].
BIIB091 inhibits FcγRI and FcγRIII-mediated TNFα secretion upon simulation with FcγR agonists such as coated human IgG (all FcγR, IC_{50}=5.6 nM), anti-CD16 (FcγRIII, IC_{50}=8.0 nM), anti-CD64 (FcγRI IC_{50}=3.1 nM), and cross-linked anti-CD16 (FcγRIII IC_{50}=1.3 nM) in human monocytes[1].

BIIB091 inhibits the phosphorylation of BTK (IC_{50}=24 nM) and blocks both BCR mediated B cell and FcεR-induced basophil activation as measured by inhibition of CD69 and CD63 expression (IC_{50}=71 nM and IC_{50}=82 nM, respectively) in the whole blood assays[1].

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

In Vivo

BIIB091 (0.03-30 mg/kg; p.o. twice daily for 10 d) reduces the anti-NP IgM antibody titers (88%, 77%, 59%, 59%, 44%, 34%, and 22%) in the TI-2 immunization model[1].

Pharmacokinetics of BIIB091 in preclinical species[1]

species	IV (1 mg/kg)					PO (5 mg/kg) in HMPC/Tween			
	$T_{1/2}$ (h)	AUC_{inf} (h•ng/mL)	CL (mL/min/kg)	CL %Q_H	V_{dss} (L/kg)	T_{max} (h)	C_{max} (ng/mL)	AUC_{inf} (h•ng/mL)	%F
rat	2.1	748	10	22	0.4	0.9	693	1522	42
cyno	1.1	943	18	44	0.7	0.33	1104	1446	31
dog	6.0	1675	12	33	1.7	1.6	1440	6075	89

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

Animal Model:	C57BL/6 mice immunized with NP-Ficoll a thymus-independent type 2 (TI-2) antigen[1]
Dosage:	0.03, 0.1, 0.3, 1, 10, 30 mg/kg in a CMC/Tween suspension formulation
Administration:	P.o. twice daily for 10 days
Result:	Observed a significant reduction of the anti-NP IgM antibody titers (88%, 77%, 59%, 59%, 44%, 34%, and 22%).

REFERENCES

[1]. Hopkins BT, et al. Discovery and Preclinical Characterization of BIIB091, a Reversible, Selective BTK Inhibitor for the Treatment of Multiple Sclerosis. J Med Chem. 2021 Nov 4.

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