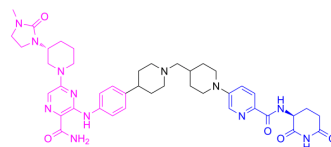


NX-5948

Cat. No.:	HY-153321		
CAS No.:	2649400-34-8		
Molecular Formula:	C ₄₂ H ₅₄ N ₁₂ O ₅		
Molecular Weight:	806.96		
Target:	Btk; PROTACs		
Pathway:	Protein Tyrosine Kinase/RTK; PROTAC		
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 : 50 mg/mL (61.96 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.2392 mL	6.1961 mL	12.3922 mL
	5 mM	0.2478 mL	1.2392 mL	2.4784 mL
	10 mM	0.1239 mL	0.6196 mL	1.2392 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 3.33 mg/mL (4.13 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 3.33 mg/mL (4.13 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 3.33 mg/mL (4.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NX-5948 (BTK-IN-24) is an orally active chimeric targeting molecule (CTM) that induces specific BTK protein degradation by the cereblon E3 ligase (CRBN) complex without degradation of other cereblon neo-substrates. NX-5948 mediates potent anti-inflammatory activity via BTK degradation with resultant inhibition of B cell activation. NX-5948 exhibits potent tumor growth inhibition in TMD8 xenograft models that contain either wild-type BTK or BTKi-resistant mutations. NX-5948 is efficacious in a mouse collagen-induced arthritis (CIA) model. NX-5948 can cross the blood brain barrier (BBB). NX-5948 is a PROTAC composed of the ligand for target protein, a linker, and a cereblon E3 ligase (CRBN) complex (Red: ligand for target protein; Blue: CRBN; Black: linker)^{[1][2][3]}.

IC₅₀ & Target	Cereblon								
In Vitro	<p>NX-5948 (BTK-IN-24; 0.0001-1000 nM; 4 h) is a potent degrader of BTK in primary human B cells (DC₅₀=0.34 nM) and inhibits BCR signaling^[1]. NX-5948 induces the degradation of BTK (DC₅₀< 1 nM) in lymphoma cell lines and PBMCs^[3]. NX-5948 (10 nM; 0.25, 0.5, 1, 2, 4, 6, 18, 24 h) catalyzes rapid BTK degradation within 1 hour and is complete within 2 hours in Ramos cells^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>								
In Vivo	<p>NX-5948 (BTK-IN-24; 10, 30 mg/kg; po; daily; Day 18 to 36) is efficacious and well-tolerated in a mouse collagen-induced arthritis (CIA) model and suppresses antibody titers and IL-6 cytokine levels^[1].</p> <p>NX-5948 (3, 10, 30 mg/kg; po) causes dose- and time-dependent reduction in BTK levels in circulating murine and non-human primate, cynomolgus monkey B cells^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Mouse collagen-induced arthritis (CIA) model^[1]</td> </tr> <tr> <td>Dosage:</td> <td>10, 30 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>PO; daily; Day 18 to 36</td> </tr> <tr> <td>Result:</td> <td>Showed efficacious and well-tolerated in a mouse CIA model.</td> </tr> </table>	Animal Model:	Mouse collagen-induced arthritis (CIA) model ^[1]	Dosage:	10, 30 mg/kg	Administration:	PO; daily; Day 18 to 36	Result:	Showed efficacious and well-tolerated in a mouse CIA model.
Animal Model:	Mouse collagen-induced arthritis (CIA) model ^[1]								
Dosage:	10, 30 mg/kg								
Administration:	PO; daily; Day 18 to 36								
Result:	Showed efficacious and well-tolerated in a mouse CIA model.								

REFERENCES

- [1]. Mark Noviski, et al. NX-5948, a Selective Degradator of BTK, Significantly Reduces Inflammation in a Model of Autoimmune Disease. 2021 Nurix Therapeutics, Inc.
- [2]. 4473 Initial Findings from a First-in-Human Phase 1a/b Trial of NX-5948, a Selective Bruton's Tyrosine Kinase (BTK) Degradator, in Patients with Relapsed/Refractory B Cell Malignancies. Annual Meeting & Exposition, Monday, December 11, 2023.
- [3]. Zi Liu, et al. An overview of PROTACs: a promising drug discovery paradigm. Mol Biomed. 2022 Dec 20;3(1):46.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA