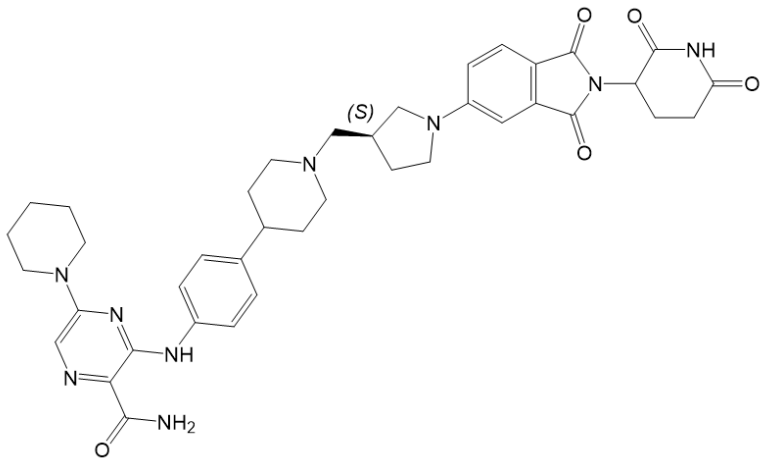
Name: NX-2127 Cat#: EX-A7600

Chemical Structure of NX-2127:



Chemical Name	2-Pyrazinecarboxamide, 3-[[4-[1-[[(3S)-1-[2-(2,6-dioxo-3-piperidinyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl]-3-pyrrolidinyl]methyl]-4-piperidinyl]phenyl]amino]-5-(1-piperidinyl)-

Molecular Weight	719.83	Storage	3 years -20°C powder 6 months -80°C in solvent Away from light
Formula	C39H45N9O5		
CAS No.	2416131-46-7	Synonyms	NX 2127; NX2127

Solubility (25°C) *	In vitro	DMSO	Soluble
		Ethanol	N/A
		Water	N/A
	In vivo （should be freshly prepared each time）		

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Selleck tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.

Preparing Stock Solutions:

Mass / Volume / Concentration	1 mg	5 mg	10 mg
1 mM	1.3892 mL	6.9461 mL	13.8922 mL
5 mM	0. 2778 mL	1.3892 mL	2.7784 mL
10 mM	0. 1389 mL	0. 6946 mL	1.3892 mL

*The above data is based on the product molecular weight 719.83.

Biological Activities:

Description	NX-2127 is an orally and potent BTK inhibitor, inducing degradation of the mutated BTK^{C481S} in cells. NX-2127 inhibits proliferation of BTK^{C481S} mutant TMD8 cells. NX-2127 catalyzes the degradation of Ikaros (IKZF1) and Aiolos (IKZF3) with of 25 nM and 54 nM, respectively. NX-2127 stimulates T cell activation and increasesIL-2 production in primary human T Cells[1][2].
In Vitro	NX-2127 inhibits proliferation of BTK-C481S mutant TMD8 cells with an EC50 value <30 nM[1]. NX-2127 increases IL-2 production in primary human T Cells[1].
In Vivo	NX-2127 (1 mg/kg; po; once daily for 14 days) demonstrates potent degradation of BTK in cynomolgus monkeys in vivo[1]. NX-2127 (po) leads to dose-proportional exposure in plasma and BTK degradation to <10% of baseline levels in circulating and splenic B cells[1]. NX-2127 results in superior tumor growth inhibition (TGI) in both WT TMD8 and C481S mutant xenograft models in mouse[1].

References	[1]. Robbins D W, et al. Nx-2127, a degrader of BTK and IMiD neosubstrates, for the treatment of B-cell malignancies. Blood, 2020, 136: 34. [2]. Mato A, et al. A first-in-human phase 1 trial of NX-2127, a first-in-class oral BTK degrader with IMiD-like activity, in patients with relapsed and refractory B-cell malignancies. 2022.