产品名称：**PIM447**
产品别名：**LGH447**

生物活性：		
Description	PIM447 (LGH447) is a potent, orally available, and selective pan-PIM kinase inhibitor, with Ki values of 6, 18, and 9 pM for PIM1, PIM2, and PIM3, respectively. PIM447 displays dual antimyeloma and bone-protective effects. PIM447 induces apoptosis[1][2].	
In Vitro	PIM447 (0.05-10 μM; 24-72 hours) shows antiproliferative effect on the multiple myeloma (MM) cells[2]. PIM447 (10 μM; 6-24 hours) induces apoptosis[2]. PIM447 (0.1-10 μM; 48 hours) increases the percentage of cells in the G0-G1 phase and decreases the proliferative phases (S and G2–M) of the cell cycle, in the two cell lines (MM1S and OPM-2 cells) at all doses[2].	
	Cell Viability Assay[2]	
	Cell Line:	MM1S, MM1R, RPMI-8226, MM144, U266, NCI-H929, OPM-2, RPMI-LR5, U266-Dox4, and U266-LR7 cells
	Concentration:	0.05, 0.1, 0.5, 1, 5, 10 μM
	Incubation Time:	24, 48, 72 hours
	Result:	Sensitive cell lines with IC_{50} values at 48 hours ranging from 0.2 to 3.3 μM (MM1S, MM1R, RPMI-8226, MM144, U266, and NCI-H929) and less sensitive cell lines with IC50 values at 48 hours >7 μmol/L (OPM-2, RPMI-LR5, U266-Dox4, and U266-LR7).
	Western Blot Analysis[2]	
	Cell Line:	MM1S cells
	Concentration:	10 μM
	Incubation Time:	6, 12, 24 hours
	Result:	Promoted the cleavage of initiator caspases, such as caspases 8 and 9, and also the cleavage of the effector caspases 3 and 7, together with PARP cleavage.
In Vivo	PIM447 (100 mg/kg; p.o.; 5 times for a week) reduces tumor burden[2].	
	Animal Model:	6-week-old female NOD-SCID-IL-2Rγ−/− (NSG) mice (bearing RPMI-8226-luc cells)[2]
	Dosage:	100 mg/kg
	Administration:	p.o.; 5 times for a week
	Result:	Clearly controlled tumor progression as measured by bioluminescence.
References	[1]. Burger MT, et al. Identification of N-(4-((1R,3S,5S)-3-Amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (PIM447), a Potent and Selective Proviral Insertion Site of Moloney Murine Leukemia (PIM) 1, 2, and 3 Kinase Inhibitor in Clinical Trials for Hematological Malignancies.J Med Chem. 2015 Nov 12;58(21):8373-86. [2]. Paíno T et al. The novel pan-PIM kinase inhibitor, PIM447, displays dual anti-myeloma and bone protective effects, and potently synergizes with current standards of care. Clin Cancer Res. 2016 Jul 20. [3]. Peters TL et al. Control of translational activation by PIM kinase in activated B-cell diffuse large B-cell lymphoma confers sensitivity to inhibition by PIM447. Oncotarget. 2016 Aug 20	