产品名称：**NVP-BSK805**
产品别名：**BSK805**

生物活性：					
Description	NVP-BSK805 is an ATP-competitive JAK2 inhibitor, with IC_{50}s of 0.48 nM, 31.63 nM, 18.68 nM, and 10.76 nM for JAK2 JH1 (JAK homology 1), JAK1 JH1, JAK3 JH1, and TYK2 JH1, respectively.				
IC_{50} & Target	JAK2 JH1	FL JAK2 V617F	FL JAK2 wt	TYK2 JH1	JAK3 JH1
	0.48 nM (IC_{50})	0.56 nM (IC_{50})	0.58 nM (IC_{50})	10.76 nM (IC_{50})	18.68 nM (IC_{50})
	JAK1 JH1				
	31.63 nM (IC_{50})				
In Vitro	NVP-BSK805 (BSK 805) is a JAK2 inhibitor, with IC50s of 0.48 nM, 31.63 nM, 18.68 nM, and 10.76 nM for JAK2 JH1 (JAK homology 1), JAK1 JH1, JAK3 JH1, and TYK2 JH1, respectively. NVP-BSK805 inhibits the full-length wild-type JAK2 (FL JAK2 wt) and FL JAK2 V617F activity, with IC50s of 0.58 ± 0.03 and 0.56 ± 0.04 nM. NVP-BSK805 is ATP-competitive, with aclculated Ki of 0.43 ± 0.02 nM. NVP-BSK805 suppresses the growth of JAK2V617F-bearing acute myeloid leukemia cell lines with GI50 of <100 nM. NVP-BSK805 blocks the STAT5 phosphorylation at ⩾100 nM concentrations, and shows a bias for JAK2 over JAK1 and JAK3 inhibition in the JAK2V617F-mutant cell lines[1]. NVP-BSK805 (5 μM) improves P-gp inhibitory activity. NVP-BSK805 increases sensitization of drug-resistant KBV20C cancer cells to VIC treatment at 10 μM, and such an effect is more effective than a 5 μM dose[2].				
In Vivo	NVP-BSK805 (BSK 805; 150 mg/kg, p.o.) blocks STAT5 phosphorylation, splenomegaly, and leukemic cell spreading in a Ba/F3 JAK2V617F cell-driven mouse model[1]. NVP-BSK805 (50, 75, and 100 mg/kg, p.o.) also suppresses rhEpo-mediated polycythemia and splenomegaly in BALB/c mice[1].				
References	[1]. Baffert F, et al. Potent and selective inhibition of polycythemia by the quinoxaline JAK2 inhibitor NVP-BSK805. Mol Cancer Ther. 2010 Jul;9(7):1945-55. [2]. Cheon JH, et al. The JAK2 inhibitors CEP-33779 and NVP-BSK805 have high P-gp inhibitory activity and sensitize drug-resistant cancer cells to vincristine. Biochem Biophys Res Commun. 2017 Sep 2;490(4):1176-1182.				

实验参考：	
Cell Assay	The antiproliferative activity of JAK2 inhibitors is determined by incubating cells for 72 hours (96 hours for MB-02 and MUTZ-8 cells) with an 8-point concentration range of NVP-BSK805 and cell proliferation relative to NVP-BSK805 is measured using the colorimetric WST-1 cell viability readout. Of each triplicate treatment, the mean is calculated and these data are plotted in XLfit 4 to determine the half-maximal growth inhibition (GI50) values[1].
Animal Administration	Mice[1] Concomitantly with NVP-BSK805 treatment, female BALB/c mice receive daily s.c. injections (in 100 μL saline buffer) of 10 units of rhEpo for 4 consecutive days. Controls are injected corresponding volumes of saline buffer. Mice are sacrificed 24 hours after the final dose and total blood, spleen, and bone marrow are taken for further analysis. Animals are 8 to 10 weeks of age at treatment start (20-25 g body weight) and are kept under optimal hygienic conditions with free access to food and water[1].
	[1]. Baffert F, et al. Potent and selective inhibition of polycythemia by the quinoxaline JAK2 inhibitor

References	NVP-BSK805. Mol Cancer Ther. 2010 Jul;9(7):1945-55. [2]. Cheon JH, et al. The JAK2 inhibitors CEP-33779 and NVP-BSK805 have high P-gp inhibitory activity and sensitize drug-resistant cancer cells to vincristine. Biochem Biophys Res Commun. 2017 Sep 2;490(4):1176-1182.