产品名称：Poziotinib (HM781-36B)
产品别名：NOV120101

生物活性：

Description	Poziotinib (HM781-36B) is an orally active, irreversible pan-HER inhibitor, which effectively inhibits $EGFR^{wt}$, HER-2 and HER-4 with IC_{50}s of 3.2, 5.3 and 23.5 nM, respectively. Poziotinib (HM781-36B) also shows excellent inhibitory activities against mutated EGFRs, including $EGFR^{T790M}$ and $EGFR^{L858R/T790M}$, with IC_{50}s of 4.2 and 2.2 nM, respectively. Excellent antitumor activity[1][2]
IC_{50} & Target	IC50: 3.2 nM ($EGFR^{wt}$), 5.3 nM (HER-2), 23.5 nM (HER-4) 4.2 nM ($EGFR^{T790M}$), 2.2 nM ($EGFR^{L858R/T790M}$)[2]
In Vitro	The IC50 levels of Poziotinib (HM781-36B) for N87 and SNU216 were 0.001 and 0.004 μM, respectively, which was 10-1000 fold lower than the IC50 levels of other HER family TKIs. HM781-36B more potently inhibited the phosphorylation of HER family and downstream proteins, and induced apoptosis and G1 arrest compared to gefitinib or lapatinib[1]. Poziotinib (HM781-36B) also shows excellent selectivity with other kinases with greater than 100- to 1,000-fold IC50 values compared with EGFR family members. Poziotinib (HM781-36B) possesses a functional α, β - unsaturated carbonyl group as Michael acceptor moiety at the C6 position that allows covalent modifications of the EGFR kinase domain active site[2]. The addition of HM781-36B induced potent growth inhibition in both DiFi cells with EGFR overexpression and SNU-175 cells (IC50=0.003 and 0.005 μM, respectively). Furthermore, HM781-36B induced G1 arrest of the cell cycle and apoptosis, and reduced the levels of HER family and downstream signaling molecules, pERK and pAKT, as well as nonreceptor/cytoplasmic tyrosine kinase, BMX[3].
In Vivo	The growth of tumors in mice treated with HM781-36B alone or in combination with 5-FU was significantly inhibited compared with control mice, and tumor volume in mice receiving coadministraion of HM781-36B and 5-FU was smaller than tumor volume in mice receiving HM781-36B only[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 135 mg/mL** (**274.76 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0353 mL	10.1763 mL	20.3525 mL
	5 mM	0.4071 mL	2.0353 mL	4.0705 mL
	10 mM	0.2035 mL	1.0176 mL	2.0353 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.25 mg/mL (4.58 mM); Clear solution

	此方案可获得 ≥ 2.25 mg/mL (4.58 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.25 mg/mL (4.58 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (4.58 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
References	[1]. Nam HJ, et al. Antitumor activity of HM781-36B, an irreversible Pan-HER inhibitor, alone or in combination with cytotoxic chemotherapeutic agents in gastric cancer. Cancer Lett. 2011 Mar 28;302(2):155-65. [2]. Cha MY, et al. Antitumor activity of HM781-36B, a highly effective pan-HER inhibitor in erlotinib-resistant NSCLC and other EGFR-dependent cancer models. Int J Cancer. 2012 May 15;130(10):2445-54. [3]. Kang MH, et al. Antitumor Activity of HM781-36B, alone or in Combination with Chemotherapeutic Agents, in Colorectal Cancer Cells. Cancer Res Treat. 2015 Mar 5.