产品名称：Varlitinib
产品别名：ARRY-334543; ASLAN001

生物活性：

Description	Varlitinib (ARRY-334543; ASLAN001) is a potent, reversible, small molecule pan-EGFR inhibitor with IC_{50}s of 7, 2, 4 nM for HER1, HER2 and HER4, respectively.		
IC_{50} & Target	HER1	HER2	HER4
	7 nM (IC_{50})	2 nM (IC_{50})	4 nM (IC_{50})
In Vitro	In cell-based assays using tumor cells that over-express EGFR (A431) or ErbB-2 (BT474), Varlitinib (ARRY-334543) potently inhibits substrate phosphorylation. Varlitinib is shown to be highly selective for EGFR/ErbB-2, and does not show any significant activity when screened against a panel of 104 kinases[2].		
In Vivo	Varlitinib treatment potently inhibits tumor growth with complete tumor regression observed at dosing of 100 mg/kg twice a day. After five days of Varlitinib treatment, phosphorylation of HER1-3, RAS/RAF/MEK/MAPK, p70S6K, S6 ribosomal, 4EBP1, Cdk-2, Cdc-2 and retinoblastoma are strongly inhibited. Varlitinib treatment results in a significant reduction in survivin and a concomittant increase in Caspase 3 cleavage products[1]. In murine xenograft models, Varlitinib (ARRY-334543) demonstrates significant dose-related (25, 50, 100 mg/kg) tumor growth inhibition in A431-derived tumors when administered orally, twice a day, for 21 days[2].		

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (107.08 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1416 mL	10.7080 mL	21.4160 mL
	5 mM	0.4283 mL	2.1416 mL	4.2832 mL
	10 mM	0.2142 mL	1.0708 mL	2.1416 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: ≥ 2.5 mg/mL (5.35 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.35 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 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% corn oil

Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.35 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Hsieh C, et al. Varlitinib to demonstrate anti-tumour efficacy in patient-derived hepatocellular carcinoma xenograft models. Journal of Clinical Oncology 34, no. 15_suppl [2]. Miknis G, et al. ARRY-334543, A potent, orally active small molecule inhibitor of EGFR and ErbB-2.Proc Amer Assoc Cancer Res, Volume 46, 2005

实验参考：

Animal Administration	Mice: The effects of Varlitinib is tested in patient-derived HCC xenograft in SCID mice (HCC29-0909A) with co-expression of HER1, HER2 and HER3 recepors. Mice are treated with Varlitinib when the tumors reach the size of approximately 100-150 mm^3. Tumor size measurements are performed twice a week and tumor volumes are calculated[1].
References	[1]. Hsieh C, et al. Varlitinib to demonstrate anti-tumour efficacy in patient-derived hepatocellular carcinoma xenograft models. Journal of Clinical Oncology 34, no. 15_suppl [2]. Miknis G, et al. ARRY-334543, A potent, orally active small molecule inhibitor of EGFR and ErbB-2.Proc Amer Assoc Cancer Res, Volume 46, 2005