产品名称：AD80
产品别名：AD80

生物活性：

Description	AD80, a multikinase inhibitor, inhibits RET, RAF,SRCand S6K, with greatly reduced mTOR activity.		
IC_{50} & Target	RAF	RET	SRC
In Vitro	AD80 is a polypharmacological agent with an optimal balance of activity against Ret, Raf, Src, Tor and S6K that show high efficacy with very low toxicity. AD80 and AD81 inhibits RET, RAF, SRC and S6K, with greatly reduced mTOR activity relative to AD57 and AD58.AD80 is optimal for Ras–Erk pathway inhibition. AD80 inhibits proliferation of MZ-CRC-1 and TT thyroid cancer cells in culture, probably through the induction of apoptosis. Immunoblot analysis demonstrates potent downregulation of phosphorylated Ret and several downstream biomarkers within these cells[1]. AD80 coordinately inhibits S6K1 together with the TAM family tyrosine kinase AXL.AD80 avoides S6K1 phosphorylation and mTOR co-association, resulting in durable suppression of S6K1-induced signaling and protein synthesis[2].		
In Vivo	Oral administration of either AD80 or AD81 results in a notable 70-90% of animals developing to adulthood in *Drosophila ptc>dRet^{MEN2B}*model, a considerable improvement over the efficacy observed with AD57. AD80 also promotes enhanced tumour growth inhibition and reduces body-weight modulation relative to vandetanib in a mouse xenograft model[1]. AD80 rescues 50% of mice transplanted with PTEN-deficient leukemia cells[2].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 150 mg/mL (316.84 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1122 mL	10.5612 mL	21.1224 mL
	5 mM	0.4224 mL	2.1122 mL	4.2245 mL
	10 mM	0.2112 mL	1.0561 mL	2.1122 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。

References

[1]. Dar AC, et al. Chemical genetic discovery of targets and anti-targets for cancer polypharmacology.Nature. 2012 Jun 6;486(7401):80-4.

[2]. Liu H, et al. Pharmacologic Targeting of S6K1 in PTEN-Deficient Neoplasia.Cell Rep. 2017 Feb 28;18(9):2088-2095.

实验参考：

Cell Assay	MZ-CRC-1 (MEN2B) and TT (MEN2A) cells are treated with AD80 (0.2 nM to 20 μM) for 7 days and cell viability is quantitated by MTT assay[1].
Animal Administration	Mice: Mice showing established growing tumors are separated into vehicle or drug treatment groups. A similar range of tumor sizes is selected for each experiment (vehicle vs AD57; vehicle vs AD80 vs Vandetanib). Vehicle, AD57 (20 mg/kg), AD80 (30 mg/kg), or Vandetanib (50mg/kg) are

	administered by oral gavage (PO; per os or by mouth) once daily, five times a week. Tumor and body weight measurements are performed 3 times a week[2].
References	[1]. Dar AC, et al. Chemical genetic discovery of targets and anti-targets for cancer polypharmacology.Nature. 2012 Jun 6;486(7401):80-4. [2]. Liu H, et al. Pharmacologic Targeting of S6K1 in PTEN-Deficient Neoplasia.Cell Rep. 2017 Feb 28;18(9):2088-2095.