



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

产品名称: **AMG 487**  
产品别名: **AMG 487**

生物活性:

Description	AMG 487 is an orally active and selective antagonist of CXC chemokine receptor 3 (CXCR3) which inhibits the binding of CXCL10 and CXCL11 to CXCR3 with IC50s of 8.0 and 8.2 nM, respectively.				
IC50 & Target	125I-IP10-CXCR3	125I-ITAC-CXCR3			
	8 nM (IC50)	8.2 nM (IC50)			
In Vitro	AMG 487 inhibits CXCR3-mediated cell migration by the three CXCR3 chemokines (IP-10 IC50=8 nM, ITAC IC50=15 nM, and MIG IC50=36 nM). Furthermore, AMG 487 inhibits calcium mobilization in response to ITAC (IC50=5 nM)[1]. AMG487 (1 μM) develops into fewer lung metastases, and the lungs are significantly smaller than vehicle-treated lungs[2]. AMG487 abrogates proliferation/survival of C26 tumour cells[3].				
In Vivo	AMG 487 (0.03-10 mg/kg, s.c.) exhibits significant reduction in cellular infiltration into the lungs in a dose dependent manner[1]. AMG487 (5 mg/kg, s.c., twice daily) develops fewer metastases than that in vehicle-treated mice[2]. AMG487 (5 mg/kg, s.c.)-treated mice exhibits fewer pulmonary nodules than the control mice in both the models. AMG487 reduces the tumour volume[3].				
Solvent&Solubility	<b>In Vitro:</b>  DMSO : ≥ 41 mg/mL (67.93 mM)  H2O : < 0.1 mg/mL (insoluble)  * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	1.6568 mL	8.2838 mL	16.5675 mL
		5 mM	0.3314 mL	1.6568 mL	3.3135 mL
		10 mM	0.1657 mL	0.8284 mL	1.6568 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。				
	<b>In Vivo:</b>  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 (4.14 mM); Clear solution  此方案可获得 ≥ 2.5 mg/mL (4.14 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。				



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

	<p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: 2.5 mg/mL (4.14 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.5 mg/mL (4.14 mM)的均匀悬浊液, 悬浊液可用于口服和腹腔注射。</p> <p>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 20% 的 SBE-β-CD 生理盐水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.14 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。</p> <p>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。</p>
References	<p>[1]. Johnson M, et al. Discovery and optimization of a series of quinazolinone-derived antagonists of CXCR3. Bioorg Med Chem Lett. 2007 Jun 15;17(12):3339-43.</p> <p>[2]. Walser TC, et al. Antagonism of CXCR3 inhibits lung metastasis in a murine model of metastatic breast cancer. Cancer Res. 2006 Aug 1;66(15):7701-7.</p> <p>[3]. Cambien B, et al. Organ-specific inhibition of metastatic colon carcinoma by CXCR3 antagonism. Br J Cancer. 2009 Jun 2;100(11):1755-64.</p> <p>[4]. Henne KR, et al. Sequential metabolism of AMG 487, a novel CXCR3 antagonist, results in formation of quinone reactive metabolites that covalently modify CYP3A4 Cys239 and cause time-dependent inhibition of the enzyme. Drug Metab Dispos. 2012 Jul;40(7):142</p>
实验参考:	
Cell Assay	<p>Colon cancer cells are seeded at a density of 10<sup>4</sup> cells cm<sup>2</sup> and incubated either in serum-enriched medium or in base medium (containing 0.1% bovine serum albumin, BSA) supplemented or not with various concentrations of rCXCL9, rCXCL10 and rCXCL11 for the indicated periods of time before being either trypsin-detached, collected and enumerated or re-fed with fresh medium for 3 days, harvested and enumerated. The morphology of the CRC cells is observed through an inverted optical microscope at ×20 magnification, and photographs are taken at day 7. [3]</p>
Animal Administration	<p>Local tumor growth and spontaneous metastasis are evaluated by injecting 3×10<sup>5</sup> viable tumor cells s.c. proximal to the right abdominal mammary gland of syngeneic female mice. Tumor diameters are measured by caliper twice weekly, and mice are euthanized on an individual basis when the s.c. tumor measured 18 mm in diameter or earlier if the mouse seemed moribund. The lungs are removed and weighed, and surface tumor colonies are quantified in a blinded fashion under a dissecting microscope. Experimental metastasis is evaluated by injecting 9×10<sup>4</sup> viable tumor cells i.v. into the lateral tail vein of syngeneic female mice. All mice are euthanized on day 21 posttransplantation or earlier if the mice seemed moribund. The lungs are removed and weighed, and surface tumor colonies are quantified in a blinded fashion under a dissecting microscope. A 50% hydroxypropyl-β-cyclodextrin solution is prepared; at 20%, this solution serves as the vehicle. AMG487 is added to the 50% solution, and it is incubated in a sonicating water bath for 2 hours with occasional vortexing. Distilled water is added to give the appropriate final concentration of AMG487</p>



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

	in 20% of hydroxypropyl- $\beta$ -cyclodextrin. [2]
<b>Kinase Assay</b>	<p>Cells are then lysed and sonicated in 50 mM Hepes pH 7.5, 150 mM NaCl, 20 mM EDTA, 1 mM PMSF, 10 <math>\mu</math>g/mL leupeptin, 2 <math>\mu</math>g/mL aprotinin and 0.2% NP-40. Equal amount of lysates are mixed in substrate buffer (50 mM Hepes, 100 mM NaCl, 1 mM EDTA, 10% sucrose, 0.5% CHAPS, 5 mM dithiothreitol) with Ac-DEVD-AMC substrate and caspase-3/7 substrate in a microtiter plate.</p> <p>Production of fluorogenic substrate is measured continuously at 37°C in a spectrophotometer Ascent Fluoroskan and the caspase activity (expressed as U/mg of protein) is defined as the amount of enzyme cleaving 1 nmol of substrate/min. [3]</p>
<b>References</b>	<p>[1]. Johnson M, et al. Discovery and optimization of a series of quinazolinone-derived antagonists of CXCR3. Bioorg Med Chem Lett. 2007 Jun 15;17(12):3339-43.</p> <p>[2]. Walser TC, et al. Antagonism of CXCR3 inhibits lung metastasis in a murine model of metastatic breast cancer. Cancer Res. 2006 Aug 1;66(15):7701-7.</p> <p>[3]. Cambien B, et al. Organ-specific inhibition of metastatic colon carcinoma by CXCR3 antagonism. Br J Cancer. 2009 Jun 2;100(11):1755-64.</p> <p>[4]. Henne KR, et al. Sequential metabolism of AMG 487, a novel CXCR3 antagonist, results in formation of quinone reactive metabolites that covalently modify CYP3A4 Cys239 and cause time-dependent inhibition of the enzyme. Drug Metab Dispos. 2012 Jul;40(7):142</p>

源叶生物