产品名称：**BMS-754807**
产品别名：**BMS-754807**

生物活性：

Description	BMS-754807 is a potent and reversible inhibitor of IGF-1R/IR with IC_{50} of 1.8 and 1.7 nM, respectively and K_i of <2 nM for both, and also shows potent activities against Met, RON, TrkA, TrkB, AurA, and AurB with IC_{50} values of 6, 44, 7, 4, 9, and 25 nM, respectively.
IC_{50} & Target	IC50: 1.7 nM (IR), 1.8 nM (IGF-1R), 4 nM (TrkB), 6 nM (Met), 7 nM (TrkA), 9 nM (AurA), 25 nM (AurB), 44 nM (RON)
In Vitro	BMS-754807 effectively inhibits the growth of a broad range of human tumor cell lines with IC_{50} values of ranging from 5 to 365 nM. BMS-754807 also inhibits the proliferation of human rhabdomyosarcoma tumor cells Rh41 and human colon carcinoma Geo with IC_{50}s of 7 and 5 nM, respectively. BMS-754807 shows inhibitory activity in the proliferation of Rh41 cells with IC_{50} of 5 nM[1] BMS-754807 inhibits the phosphorylation of IGF-1R (IC_{50}=13 nM) and the downstream targets Akt (IC_{50}=22 nM) and MAPK (IC_{50}=13 nM) in the IGF-Sal cell line with IC_{50} consistent with the antiproliferative IC_{50} (7 nM) in this cell line[2]. BMS-754807 shows a median EC_{50} value of 0.62 μM against the PPTP cell lines. The median EC_{50} for the four Ewing sarcoma cell lines is less than that for the remaining PPTP cell lines (0.19 μM vs. 0.78 μM, P=0.0470) [3] BMS-754807 (0.25 and 0.5 μM) reduces the activated IGF-IR/IR (pIGF-IR/IR), causes a concurrent decrease in phosphorylated AKT in both lung cancer cell lines. BMS-754807 (0.5 μM) also reduces wound closure of lung cancer cells and reduces the ERK phosphorylation. BMS-754807 reduces cell viability in both A549 and NCI-H358 cells, with IC_{50} of 1.08 μM and 76 μM, respectively[4].
In Vivo	BMS-754807 (3.125 and 12.5 mg/kg, p.o.) inhibits tumor growth in IGF-1R-Sal tumor-bearing nude mice. BMS-754807 inhibits tumor growth in a selected group of epithelial (IGF-1R-Sal, GEO, and Colo205), hematopoietic (JJN3), and mesenchymal (RD1 and Rh41) xenograft tumor models with TGI ranging from 53% to 115%. BMS-754807 is effective at a dose level of 3.125 mg/kg twice daily and as low as 6.25 mg/kg once daily, in the highly sensitive Rh41 rhabdomyosarcoma. BMS-754807 (25 mg/kg) also shows synergy when combined with targeted agents in human tumor cell lines and human xenograft models[1]Furthmore, BMS-754807 is active at doses from 3 mg/kg upward in the IGF-Sal tumor model[2]. BMS-754807 (25 mg/kg, p.o.) induces significant differences in EFS distribution compared to controls in 18 of 32 evaluable solid tumor xenografts (56%) tested, but in none of the ALL xenografts studied[3]
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (216.69 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1669 mL	10.8345 mL	21.6689 mL
5 mM	0.4334 mL	2.1669 mL	4.3338 mL
10 mM	0.2167 mL	1.0834 mL	2.1669 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 (5.42 mM); Clear solution 方案可获得 ≥ 2.5 mg/mL (5.42 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% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.42 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.42 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂：10% DMSO → 90% corn oil Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.42 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]. Carboni JM, et al. BMS-754807, a small molecule inhibitor of insulin-like growth factor-1R/IR. Mol Cancer Ther, 2009, 8(12), 3341-3349. [2]. Franks SE, et al. BMS-754807 is cytotoxic to non-small cell lung cancer cells and enhances the effects of platinum chemotherapeutics in the human lung cancer cell line A549. BMC Res Notes. 2016 Mar 1;9:134. [3]. Wittman MD, et al. Discovery of a 2,4-disubstituted pyrrolo[1,2-f][1,2,4]triazine inhibitor (BMS-754807) of insulin-like growth factor receptor (IGF-1R) kinase in clinical development. J Med Chem, 2009, 52(23), 7360-7363. [4]. Kolb EA, et al. Initial testing (stage 1) of the IGF-1 receptor inhibitor BMS-754807 by the pediatric preclinical testing program. Pediatr Blood Cancer, 2011, 56(4), 595-603.

实验参考：

Cell Assay	Cells are grown at their optimal density in RPMI+GlutaMax. Cell proliferation is evaluated by incorporation of 3H-thymidine into DNA after exposure of cells to BMS-754807 for 72 h. Results are expressed as an IC_{50}, which is the drug concentration required to inhibit cell proliferation by 50% compared with untreated control cells. [1]
Animal Administration	The required numbers of animals needed to detect a meaningful response are pooled at the start of the experiment and each is given a subcutaneous implant of a tumor fragment (appr 20 mg) with a 13-gauge trocar. Tumors are allowed to grow to the predetermined size window (75-200 mg; tumors outside the range are excluded), and animals are evenly distributed to various treatment and control groups. There are typically eight mice per treatment and control groups, with the exception of experiments conducted in the Sal-IGF (same as IGF-1R-Sal) tumor model, in which there are

	typically five mice per treatment and control group. Treatment of each animal is based on individual body weight. Treated animals are checked daily for treatment-related toxicity/mortality. Each group of animals is weighed before the initiation of treatment (Wt1) and then again following the last treatment dose (Wt2). The difference in body weight (Wt2 − Wt1) provides a measure of treatment-related toxicity. [1]
References	[1]. Carboni JM, et al. BMS-754807, a small molecule inhibitor of insulin-like growth factor-1R/IR. Mol Cancer Ther, 2009, 8(12), 3341-3349. [2]. Franks SE, et al. BMS-754807 is cytotoxic to non-small cell lung cancer cells and enhances the effects of platinum chemotherapeutics in the human lung cancer cell line A549. BMC Res Notes. 2016 Mar 1;9:134. [3]. Wittman MD, et al. Discovery of a 2,4-disubstituted pyrrolo[1,2-f][1,2,4]triazine inhibitor (BMS-754807) of insulin-like growth factor receptor (IGF-1R) kinase in clinical development. J Med Chem, 2009, 52(23), 7360-7363. [4]. Kolb EA, et al. Initial testing (stage 1) of the IGF-1 receptor inhibitor BMS-754807 by the pediatric preclinical testing program. Pediatr Blood Cancer, 2011, 56(4), 595-603.