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
邮箱：shyysw@sina.com

产品名称：BMS-564929
产品别名：BMS-564929

生物活性：

Description	BMS-564929 is an androgen receptor (AR) agonist, binds to androgen receptor (AR) with a Ki of 2.11±0.16 nM.
IC_{50} & Target	Ki: 2.11±0.16 nM (Androgen receptor)[1]
In Vitro	BMS-564929 exhibits a potency (EC50, calculated as the concentration at which 50% of the maximum stimulatory effect of DHT is achieved) of 0.44±0.03 nM in the C2C12 myoblast cell line. In the PEC cell line, the EC50 for BMS-564929 is 8.66±0.22 nM. BMS-564929 is more than 1000-fold selective for AR vs. estrogen receptors (ER) α and β, glucocorticoid receptor (GR), and mineralocorticoid receptor (MR), and approximately 400-fold selective vs. progesterone receptor (PR). BMS-564929 shows no measurable activity in functional transactivation assays with ERα/β, GR, MR, or PR at concentrations up to 30 μM[1].
In Vivo	In sexually mature, castrated male rats, a well-characterized animal model, BMS-564929 (p.o.) shows substantially more potent activity in the levator ani, exhibiting an ED50 of 0.0009 mg/kg in the levator ani and an ED50 of 0.14 mg/kg in the prostate; a net 160-fold selectivity for muscle vs. prostate. Approximately 100% muscle stimulation is achieved at 0.1 mg/kg, reaching greater than 125% stimulation at 0.3 and 1 mg/kg. Compared with T propionate (TP) in the same model, BMS-564929 is more than 200 times more potent in stimulation of muscle and 80 times more selective for muscle vs. prostate[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**163.55 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2710 mL	16.3548 mL	32.7097 mL
	5 mM	0.6542 mL	3.2710 mL	6.5419 mL
	10 mM	0.3271 mL	1.6355 mL	3.2710 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 (8.18 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.18 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 (8.18 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.18 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]. Ostrowski J, et al. Pharmacological and x-ray structural characterization of a novel selective androgen receptor modulator: potent hyperanabolic stimulation of skeletal muscle with hypostimulation of prostate in rats. Endocrinology. 2007 Jan;148(1):4-12.

实验参考：

Animal Administration	Rats[1] Matched sets of castrated, sexually mature Harlan Sprague Dawley rats (42-56 d old, 200-250 g) are dosed once daily by oral gavage with BMS-564929 (0.00001-10 mg/kg) in solution/suspension of 80% PEG 400 and 20% Tween 20 for 14 d. Two control groups, one sham operated intact and one castrated, are dosed orally with the PEG/TW vehicle only, beginning on d 15 after surgery. Animals are dosed (vol/wt) at 1 mL/kg body weight. T propionate (TP) is dosed once daily sc in a 10% ethanol/90% peanut oil vehicle as a reference compound (0.03-10 mg/kg). After 14 d of treatment, the animals are killed by carbon dioxide asphyxiation, the levator ani and the ventral prostate are surgically removed and weighed, and serum is collected for LH measurements.
Kinase Assay	The human cancer epithelial breast cell lines MDA MB-453 and T47D, which endogenously express AR and progesterone receptor (PR), respectively, are used for radioligand competition binding assays. Binding assays are conducted by incubating BMS-564929 at various concentrations with either [^{3}H]DHT or [^{3}H]progesterone with the cells for 2 h at room temperature. For ERα and ERβ, fusion proteins expressed in *Escherichia coli*, consisting of maltose binding protein, a specific biotinylation sequence, an enterokinase cleavage site, and either the ERα or ERβ LBD is used. Binding reactions are conducted by incubating ERα and ERβ LBD with BMS-564929 and [^{3}H]E2 for 2 h at room temperature. Specific binding activity to the mineralocorticoid receptor (MR) by BMS-564929 is evaluated by competition binding assay using kidney cytosolic preparations and [^{3}H]aldosterone. The kidneys are obtained from adrenalectomized rats to remove the endogenous source of aldosterone and to increase the MR concentration in the cytosol of kidney cells. Binding reactions are incubated for 2 h on ice in the presence of excess mifepristone (RU486) to block nonspecific glucocorticoid receptor (GR) binding. A fluorescence polarization based assay is used for GR binding, as per manufacturer recommendations. Inhibitory constants (K_i, app) defining apparent binding affinity of test compounds to intracellular receptors are calculated from the observed inhibition of natural ligand binding at multiple concentrations of test compound. SHBG binding is performed using a standard charcoal assay. Reagents: 1 mg lyophilized SHGB powder (Tris), [^{3}H]DHT, 3% charcoal, and 0.4% Dextran in PBS; binding buffer: 50 mM Tris, pH 7.6, 100 mM NaCl, 1 mM EDTA, 1 mM DTT, and mock lysate (3.5 μg/100 μL buffer); stock solutions: stock SHBG protein: 1 mg/mL in water=20 μM; stock [^{3}H]DHT ligand: 9 μM; DHT: 10 mM in DMSO; BMS 564929:

	10 mM in DMSO. Compounds diluted in binding buffer are added to 40 nM [^{3}H]DHT and 20 nM SHBG protein in 200 µL volume and incubated for 1 h at room temperature. Total binding: 40 nM [^{3}H]DHT and 20 nM SHBG protein in 200 µL volume; nonspecific binding: 40 nM [^{3}H]DHT and 20 nM SHBG protein and 1 mM cold DHT in 200 µL volume. At the end of the incubation period, 200 µL of the charcoal solution (3% containing 0.04% dextran) is added to 200 µL of the reactions and shaken for 15 min before centrifugation. Supernatant (200 µL) is then transferred to the wells of a 24-well white Optiplate; 200 µL of scintillant are added with mixing. Radioactivity counts are read in Topcount[1].
References	[1]. Ostrowski J, et al. Pharmacological and x-ray structural characterization of a novel selective androgen receptor modulator: potent hyperanabolic stimulation of skeletal muscle with hypostimulation of prostate in rats. Endocrinology. 2007 Jan;148(1):4-12.