产品名称：2-[(2-氯-4-氟苯基)甲基]-3-(4-氟苯基)-7-(三氟甲基)-2H-吲唑；WAY 252623

产品别名：LXR-623

生物活性：

Description	LXR-623 is a brain-penetrant partial LXRα and full LXRβ agonist, with IC_{50}s of 24 nM and 179 nM, respectively.
IC_{50} & Target	IC50: 24 nM (LXR-α), 179 nM (LXR-β)[2][3]
In Vitro	LXR-623 potently kills U87EGFRvIII and GBM39 cells in vitro while completely sparing NHAs. LXR-623 also increases ABCA1 protein and decreases LDLR protein levels in all three cell lines. LXR-623 suppresses LDLR expression, increases expression of the ABCA1 efflux transporter, and induces substantial cell death in all of the GBM samples tested. LXR-623 (5 μM) also induces GBM cell death through activation of LXRβ[1]. LXR-623 treatment of human PBMC in vitro significantly increases transcription of ABCA1 and ABCG1[4].
In Vivo	LXR-623 (400 mg/kg, p.o.) crosses the blood-brain barrier, induces target gene expression, and achieves therapeutic levels in GBM cells in the brain with minimal activity in the periphery. LXR-623 inhibits tumor growth, promotes tumor cell death, and prolongs the survival of mice bearing intracranial patient-derived GBMs[1]. LXR-623 (1.5, 5 mg/kg/day) significantly reduces progression of atherosclerosis in animals compared with the placebo group[2]. WAY-252623 (15 and 50 mg/kg) results in a significant reduction of atherosclerosis in a dose-dependent manner. WAY-252623 (20, 60, and 120 mg/kg/day, p.o.) displays neutral lipid effects in this CETP-expressing Syrian hamster[3]. Moreover, LXR-623 (50 mg/kg) induces gene expression in rodent peripheral blood cells in rat. LXR-623 (0, 15 and 50 mg/kg) dose-dependently upregulates transcription of ABCA1 and ABCG1 in monkey whole blood cells proportional to dose[4].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 47 mg/mL (111.17 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3653 mL	11.8265 mL	23.6530 mL
	5 mM	0.4731 mL	2.3653 mL	4.7306 mL
	10 mM	0.2365 mL	1.1826 mL	2.3653 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 (5.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.91 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 (5.91 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.91 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]. Villa GR, et al. An LXR-Cholesterol Axis Creates a Metabolic Co-Dependency for Brain Cancers. Cancer Cell. 2016 Nov 14;30(5):683-693. [2]. Giannarelli C, et al. Synergistic effect of liver X receptor activation and simvastatin on plaque regression and stabilization: an magnetic resonance imaging study in a model of advanced atherosclerosis. Eur Heart J. 2012 Jan;33(2):264-73. [3]. Quinet EM, et al. LXR ligand lowers LDL cholesterol in primates, is lipid neutral in hamster, and reduces atherosclerosis in mouse. J Lipid Res. 2009 Dec;50(12):2358-70. [4]. DiBlasio-Smith EA, et al. Discovery and implementation of transcriptional biomarkers of synthetic LXR agonists in peripheral blood cells. J Transl Med. 2008 Oct 16;6:59.

实验参考：

Animal Administration	Five-week-old female athymic nu/nu mice are used in the experiment. A total of 1×10^5 U87EGFRvIII IRFP720 or GBM39 IRFP720 cells in 5 μL of PBS is intracranially injected into the mouse brain. Tumors are allowed to establish over the course of 7-10 days and engraftment of tumors is quantitatively confirmed via FMT signal intensity. Tumor growth is monitored using an FMT 2500 fluorescence tomography system. For drug treatment studies, vehicle (0.5% methylcellulose, 2% Tween 80 in water) or LXR-623 (400 mg/kg) resuspended in vehicle are administered to mice via oral gavage daily starting at day 7 postinjection. [1]
References	[1]. Villa GR, et al. An LXR-Cholesterol Axis Creates a Metabolic Co-Dependency for Brain Cancers. Cancer Cell. 2016 Nov 14;30(5):683-693. [2]. Giannarelli C, et al. Synergistic effect of liver X receptor activation and simvastatin on plaque regression and stabilization: an magnetic resonance imaging study in a model of advanced atherosclerosis. Eur Heart J. 2012 Jan;33(2):264-73. [3]. Quinet EM, et al. LXR ligand lowers LDL cholesterol in primates, is lipid neutral in hamster, and reduces atherosclerosis in mouse. J Lipid Res. 2009 Dec;50(12):2358-70. [4]. DiBlasio-Smith EA, et al. Discovery and implementation of transcriptional biomarkers of synthetic LXR agonists in peripheral blood cells. J Transl Med. 2008 Oct 16;6:59.