产品名称：**RG2833**
产品别名：**RGFP109**

生物活性：

Description	RG2833 is a brain-penetrant **HDAC** inhibitor with **IC_{50}** of 60 nM and 50 nM for HDAC1 and HDAC3, respectively.	
IC_{50} & Target	HDAC3	HDAC1
	50 nM (IC_{50})	60 nM (IC_{50})
In Vitro	The Ki values of RG2833 for HDAC1 and HDAC3 are 32 nM and 5 nM, respectively. RG2833 is highly active in the whole tested concentration range from 1 to 10 μM. Continuous incubation with RG2833 slows the increase in frataxin protein, and when the compound is removed, frataxin protein levels rapidly increased in the cells from patient P13[1]. RG2833 produces significant increases in brain aconitase enzyme activity, together with reduction of neuronal pathology of the dorsal root ganglia (DRG)[2].	
In Vivo	RG2833 (150 mg/kg) is able to correct frataxin deficiency in the brain and heart of KIKI mice 24 hours after a single injection, but not when lower doses are used. When followed in time, the frataxin mRNA increase induced by RG2833 in the KIKI mouse can be first detected at 12 hours and reach a maximum at 24 hours in both brain and heart[1]. RG2833 (100 mg/kg, s.c.) is well tolerated in chronic dosing of mice without toxicity. RG2833 improves motor coordination of YG8R FRDA mice. RG2833 increases frataxin protein expression in the brain of YG8R FRDA mice[2]. RGFP109 (30 mg/kg, p.o. once daily for 6 days) has no acute effects on dyskinesia after single or 6 days once-daily treatment. One week following cessation of RGFP109, dyskinesia and duration of ON-time with disabling dyskinesia are reduced by 37% and 50%, respectively[3].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (147.31 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	2.9461 mL	14.7306 mL	29.4612 mL
	5 mM	0.5892 mL	2.9461 mL	5.8922 mL
	10 mM	0.2946 mL	1.4731 mL	2.9461 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 (7.37 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (7.37 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 (7.37 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.37 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 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 (7.37 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.37 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]. Rai M, et al. Two new pimelic diphenylamide HDAC inhibitors induce sustained frataxin upregulation in cells from Friedreich's ataxia patients and in a mouse model. PLoS One. 2010, 5(1), e8825. [2]. Sandi C, et al. Prolonged treatment with pimelic o-aminobenzamide HDAC inhibitors ameliorates the disease phenotype of a Friedreich ataxia mouse model. Neurobiol Dis. 2011, 42(3), 496-505. [3]. Johnston TH, et al. RGFP109, a histone deacetylase inhibitor attenuates L-DOPA-induced dyskinesia in the MPTP-lesioned marmoset: a proof-of-concept study. Parkinsonism Relat Disord. 2013, 19(2), 260-264.

实验参考：

Animal Administration	Mice are housed in conventional open cages with Litaspen Premium 8/20 bedding, paper wool nesting and standard fun tunnel environmental enrichment, with 13 h light, 11 h dark, 20-23°C and 45-60% humidity. The mice are given a diet of SDS RM3 Expanded food pellets and standard drinking water. Mice are given subcutaneous injections of 150 mg/kg RG2833 three times per week for 4.5 months, or 50 mg/kg 136 or 100 mg/kg RG2833 five times per week for 5 months, followed by culling for tissue collection 24 h after the final injection. [2]
Kinase Assay	Aconitase activities are determined by homogenization of mouse brain tissues on ice at 10% w/v in CellLytic MT Mammalian Tissue Lysis/Extraction buffer, followed by centrifugation at 800×g for 10 min at 4°C. Tissue lysates (50 μL) are then added to 200 μL of substrate mix (50 mM Tris/HCl pH 7.4, 0.4 mM NADP, 5 mM Na citrate, 0.6 mM $MgCl_2$, 0.1% (v/v) Triton X-100 and 1U isocitrate dehydrogenase) and the reactions are incubated at 37°C for 15 min, followed by spectrophotometric absorbance measurements every minute for 15 min at 340 nm 37°C to determine the reaction slope. Aconitase activities of mouse brain tissues are then normalized to citrate synthase activities, which are determined using a citrate synthase assay kit. [2]
References	[1]. Rai M, et al. Two new pimelic diphenylamide HDAC inhibitors induce sustained frataxin upregulation in cells from Friedreich's ataxia patients and in a mouse model. PLoS One. 2010, 5(1), e8825. [2]. Sandi C, et al. Prolonged treatment with pimelic o-aminobenzamide HDAC inhibitors ameliorates the disease phenotype of a Friedreich ataxia mouse model. Neurobiol Dis. 2011, 42(3),

	496-505. [3]. Johnston TH, et al. RGFP109, a histone deacetylase inhibitor attenuates L-DOPA-induced dyskinesia in the MPTP-lesioned marmoset: a proof-of-concept study. Parkinsonism Relat Disord. 2013, 19(2), 260-264.