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产品名称：N-(6-Amino-2-pyridinyl)-4'-cyano-[1,1'-biphenyl]-4-sulfonamide
产品别名：PF-915275

生物活性：

Description	PF-915275 is a potent, selective and orally active human 11β-hydroxysteroid dehydrogenase type 1 (11βHSD1) inhibitor with a Ki of 2.3 nM and an EC50 of 15 nM (in HEK293 cells). The dose-dependent effect of PF-915275 on conversion of cortisone to cortisol in primary human and monkey hepatocytes, with an EC50 of 20 and 100 nM, respectively[1][2][3].
IC_{50} & Target	Ki: 2.3 nM (11βHSD1); EC50: 15 nM (11βHSD1)[1]
In Vitro	PF-915275 is a potent inhibitor of 11βHSD1 (in vitro HEK293, EC50 of 15 nM) in this human 11βHSD1 overexpressed cell line when coincubated in the presence of 300 nM enzyme substrate. Consistent with the species differences between human and rodent observed in biochemical assays, PF-915275 is a poor inhibitor of 11βHSD1 in rat FAO hepatoma cells, with an EC50 of 14,500 nM. PF-915275 demonstrates species-dependent potency for inhibiting cellular conversion of cortisone to cortisol in dog, monkey, and human in primary hepatocytes, with activity in human hepatocytes/monkey hepatocytes/dog hepatocytes. PF-915275 does not significantly inhibit 11βHSD2 (only 1.5% inhibition when tested at 10 μM). The dose-dependent effect of PF-915275 on conversion of cortisone to cortisol in primary human and monkey hepatocytes, with an EC50 of 20 and 100 nM, respectively[1].
In Vivo	The inhibition of either cortisone or prednisone turnover with PF-915275 yields similar EC50 values to that in human hepatocytes (EC50 by PF-915275 is 18 and 13 nM using cortisone and prednisone substrates, respectively) in vivo 11βHSD1 activity[1]. PF-915275 dose-dependently inhibits 11βHSD1-mediated conversion of prednisone to prednisolone. A maximum of 87% inhibition is observed, with the highest tested dose of 3 mg/kg[1]. The half-life of PF-915275 is 22 hours in monkey[1]. PF-915275 (0.1-3 mg/kg; oral administration; for 8 hours; male cynomolgus monkeys) treatment shows a trend in dose-dependent lowering of fed plasma insulin after 8 h of dosing in these monkeys. Plasma insulin levels are significantly lowered (by 54 and 60%, respectively) at 1 and 3 mg/kg PF-915275 treatment. Plasma glucose or lipid levels are not altered with treatment[1].
Animal Model:	Adult male cynomolgus monkeys (2-5 kg)[1]
Dosage:	0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg
Administration:	Oral administration; for 8 hours
Result:	There was a trend in dose-dependent lowering of fed plasma insulin after 8 h of dosing in these monkeys. Plasma insulin levels were significantly lowered (by 54 and 60%,

In Vitro:

DMSO : ≥ 31 mg/mL (88.47 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing	1 mM	2.8540 mL	14.2698 mL	28.5396 mL

<table>
<tr><td rowspan="3">Solvent&Solubility</td><td rowspan="2">Stock Solutions</td><td>5 mM</td><td>0.5708 mL</td><td>2.8540 mL</td><td>5.7079 mL</td></tr>
<tr><td>10 mM</td><td>0.2854 mL</td><td>1.4270 mL</td><td>2.8540 mL</td></tr>
<tr><td colspan="5">*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: ≥ 0.83 mg/mL (2.37 mM); Clear solution
此方案可获得 ≥ 0.83 mg/mL (2.37 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 8.3 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: ≥ 0.83 mg/mL (2.37 mM); Clear solution
此方案可获得 ≥ 0.83 mg/mL (2.37 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 8.3 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: ≥ 0.83 mg/mL (2.37 mM); Clear solution
此方案可获得 ≥ 0.83 mg/mL (2.37 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 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</td></tr>
<tr><td>References</td><td colspan="5">[1]. Bhat BG, et al. Demonstration of proof of mechanism and pharmacokinetics and pharmacodynamic relationship with 4'-cyano-biphenyl-4-sulfonic acid (6-amino-pyridin-2-yl)-amide (PF-915275), an inhibitor of 11 -hydroxysteroid dehydrogenase type 1, in cynomolgus monkeys. J Pharmacol Exp Ther. 2008 Jan;324(1):299-305.
[2]. Siu M, et al. N-(Pyridin-2-yl) arylsulfonamide inhibitors of 11beta-hydroxysteroid dehydrogenase type 1: Discovery of PF-915275. Bioorg Med Chem Lett. 2009 Jul 1;19(13):3493-7.
[3]. Courtney R, et al. Modulation of 11beta-hydroxysteroid dehydrogenase (11betaHSD) activity biomarkers and pharmacokinetics of PF-00915275, a selective 11betaHSD1 inhibitor. J Clin Endocrinol Metab. 2008 Feb;93(2):550-6.</td></tr>
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