

# PF-04447943

Catalog No: tcsc0942



## Available Sizes

**Size:** 5mg

**Size:** 10mg

**Size:** 25mg

**Size:** 50mg



## Specifications

**CAS No:**

1082744-20-4

**Formula:**

$C_{20}H_{25}N_7O_2$

**Pathway:**

Metabolic Enzyme/Protease

**Target:**

Phosphodiesterase (PDE)

**Purity / Grade:**

>98%

**Solubility:**

DMSO :  $\geq$  54.6 mg/mL (138.07 mM)

**Observed Molecular Weight:**

395.46

## Product Description

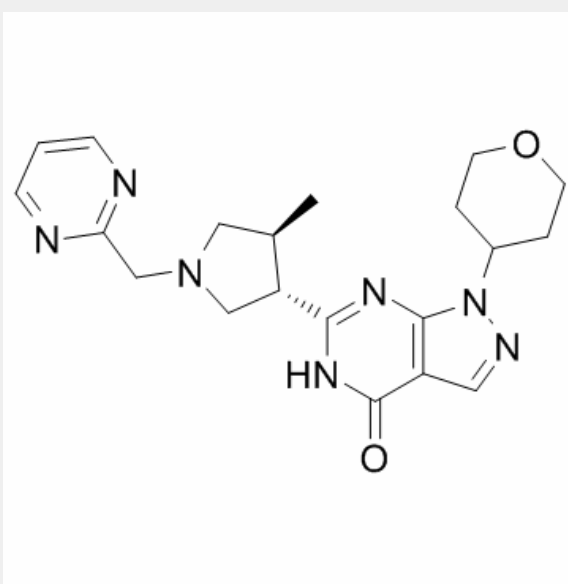
PF-04447943 is a potent inhibitor of human recombinant **PDE9A** ( $IC_{50}$ =12 nM) with >78-fold selectivity, respectively, over other

PDE family members (**IC<sub>50</sub>**>1000 nM).

IC50 & Target: IC50: 12 nM (PDE9A)<sup>[1]</sup>

**In Vitro:** Using recombinant human, rhesus, and rat PDE9A2 in a cell free assay PF-04447943 is shown to have a  $K_i$  of  $2.8 \pm 0.26$ ,  $4.5 \pm 0.13$ , and  $18.1 \pm 1.9$  nM (n=4, 11 and 9 respectively). PF-04447943 is found to be highly selective over other PDE enzymes (PDE1,  $K_i = 8600 \pm 2121$  nM, n = 5; PDE2A3,  $K_i > 99,000$  nM; PDE3A,  $K_i > 50,000$  nM; PDE4A,  $K_i > 29,000$  nM; PDE5A,  $K_i = 14,980 \pm 5025$  nM, n=5; PDE6C,  $K_i = 5324 \pm 2612$  nM, n=4; PDE7A2,  $K_i > 75,000$  nM; PDE8A,  $K_i > 50,000$  nM; PDE10,  $K_i > 51,250 \pm 20,056$  nM, n=4; PDE11,  $K_i > 80,000$  nM) and no other significant activity at ~60 other receptors/enzymes. In HEK whole cells expressing rhesus PDE9A2, PF-04447943 inhibits ANP (0.3  $\mu$ M) stimulated cGMP with an  $IC_{50}$  of  $375 \pm 36.9$  nM (n=16)<sup>[2]</sup>.

**In Vivo:** Based on i.v. and p.o. dosing, pharmacokinetic studies with PF-04447943 in the rat indicates a  $T_{max}$  of 0.3 h,  $T_{1/2}$  of 4.9 h, Cl of 21.7 mL/min/kg and an oral bioavailability of 47%. Thirty minutes following oral administration in rats (1-30 mg/kg), PF-04447943 concentrations dose-dependently increase in blood, brain and cerebrospinal fluid (CSF). The brain:plasma exposure ratios 30 min after dosing range from 0.13 at the 1 mg/kg dose to 0.33 at the 30 mg/kg dose. CSF levels are approximately 50% of brain levels. In mice, PF-04447943 (3, 10, 30 mg/kg p.o.) dose-dependently increases plasma and brain concentrations of PF-04447943 while the brain to plasma ratio ranged from 0.26 to 0.7 although this is not entirely dose dependent. CSF cGMP levels increase in a dose-dependent manner from a basal level of 3 pmol/mL to 13.3 pmol/mL (3.5-fold) at the 30 mg/kg dose. CSF cGMP levels also increase in a dose-dependent manner from a basal level of 3 pmol/mL in vehicle treated animals to 13.3 pmol/mL (3.5-fold) at the 30 mg/kg dose. CSF cGMP levels are elevated at all doses tested with a maximal effect of 3.5 fold increase above controls at 30 mg/kg<sup>[2]</sup>.



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!