

## PF-543 (Sphingosine kinase I inhibitor)

Catalog number: B-0026

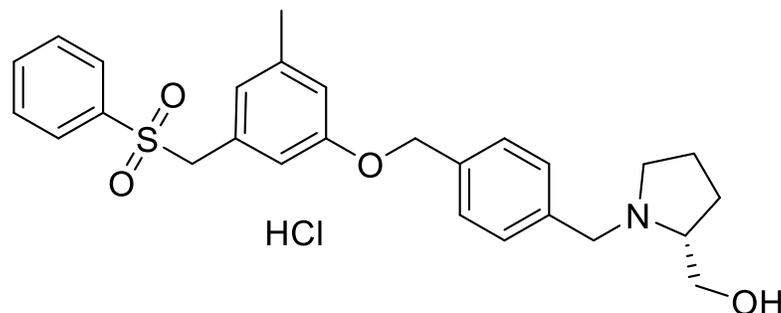
Molecular Formula:  $C_{27}H_{32}ClNO_4S$

MW: 502.07

CAS: 1415562-82-1 (free base)

Solubility: water (20 mg/mL), DMSO

Storage and Handling:  $-20^{\circ}C$  or below



**Background:** PF-543 is a potent inhibitor of sphingosine kinase 1 (SK1;  $IC_{50}$  = 2–3.6 nM) that less effectively inhibits SK2 ( $IC_{50}$  = 356 nM).<sup>1</sup> It does not significantly block the activity of other protein and lipid kinases, or bind sphingosine-1-phosphate receptors, when tested at a concentration of 10  $\mu$ M.<sup>1</sup> PF-543 prevents the phosphorylation of sphingosine in cancer cells and in whole blood ( $EC_{50}$  = 8.4 and 27 nM, respectively).<sup>1</sup> Through its effects on SK1, PF-543 prevents sickling, hemolysis, and inflammation in sickling cell disease transgenic mice.<sup>2</sup> Unlike inhibitors that are selective for SK2, PF-543 does not impair DNA synthesis in human pulmonary arterial smooth muscle cells.<sup>3</sup>

**References:** 1) M. E. Schnute, M. D. McReynolds, T. Kasten, *et al.* "Modulation of cellular S1P levels with a novel, potent and specific inhibitor of sphingosine kinase-1" *Biochemistry Journal* 2012, 444, 79–88. 2) Y. Zhang, V. Berka, A. Song, *et al.* Elevated sphingosine-1-phosphate promotes sickling and sickle cell disease progression. *J. Clin. Invest.* 2014, 124, 2750–2761. 3) H. S. Byun, S. Pyne, N. Macritchie, *et al.* Novel sphingosine-containing analogues selectively inhibit sphingosine kinase (SK) isozymes, induce SK1 proteasomal degradation and reduce DNA synthesis in human pulmonary arterial smooth muscle cells. *Med. Chem. Comm.* 2013, 4, 1–15.

**Hazardous Properties and Cautions:** The toxicological and pharmacological properties of this compound are not fully known. For further information see the MSDS on request. This product is manufactured and shipped only in small quantities, intended for research and development in a laboratory utilizing prudent procedures for handling chemicals of unknown toxicity, under the supervision of persons technically qualified to evaluate potential risks and authorized to enforce appropriate health and safety measures. As with all research chemicals, precautions should be taken to avoid unnecessary exposures or risks.

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