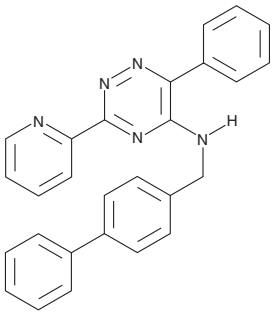
PRODUCT INFORMATION

ML-228

Item No. 14568

CAS Registry No.:	1357171-62-0
Formal Name:	N-([1,1'-biphenyl]-4-ylmethyl)-6-phenyl-3-(2-pyridinyl)-1,2,4-triazin-5-amine
Synonym:	CID-46742353
MF:	$C_{27}H_{21}N_5$
FW:	415.5
Purity:	≥95%
UV/Vis.:	λ_{max}: 268, 328 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ML-228 is supplied as a crystalline solid. A stock solution may be made by dissolving the ML-228 in the solvent of choice. ML-228 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of ML-228 in ethanol and DMF is approximately 30 mg/ml and approximately 25 mg/ml in DMSO.

ML-228 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ML-228 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. ML-228 has a solubility of approximately 0.25 mg/ml in a 1:2 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The hypoxia-inducible factor (HIF) transcription factors are members of the basic-helix-loop-helix (bHLH) family of transcription factors and play important roles in maintaining cellular oxygen homeostasis.[1,2] HIF-1α has emerged as an important drug target in breast and prostate cancer, cardiovascular disease, and ischemia.[3,4] ML-228 is an activator of the HIF signaling pathway, as demonstrated by HIF response element (HRE) reporter assay (EC_{50} = 1.2 µM), HIF-1α nuclear translocation assay (EC_{50} = 1.3 µM), and increased VEGF expression (EC_{50} = 1.6 µM).[5] Its activity in the HRE assay is blocked by excess iron, suggesting that ML-228 can chelate iron.[5] Molecular modeling indicates that ML-228 does not modulate HIF signaling by binding to prolyl hydroxyases.[5] ML-228 also significantly inhibits ligand binding to several channels, receptors, and transporters, including ERG potassium channel, 5-HT_{2B} and A_3 adenosine receptors, and dopamine transporter.[5]

Reference

1. Wang, G.L., Jiang, B.H., Rue, E.A., *et al. Proc. Natl. Acad. Sci. U. S. A.* **92(12)**, 5510-5514 (1995).
2. Safran, M. and Kaelin, W.G., Jr. *J. Clin. Invest.* **111(6)**, 779-783 (2003).
3. William, C., Masson, N., Tian, Y.M., *et al. Proc. Natl. Acad. Sci. U. S. A.* **99(16)**, 10423-10428 (2002).
4. Welsh, S., Williams, R., Kirkpatrick, L., *et al. Mol. Cancer Ther.* **3(3)**, 233-244 (2004).
5. Theriault, J.R., Felts, A.S., Bates, B.S., *et al. Bioorg. Med. Chem. Lett.* **22(1)**, 76-81 (2012).

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