

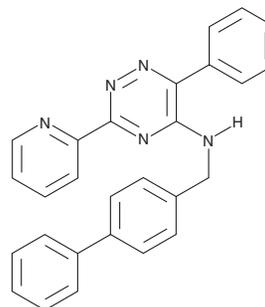
# PRODUCT INFORMATION



## 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<sub>27</sub>H<sub>21</sub>N<sub>5</sub>  
**FW:** 415.5  
**Purity:** ≥95%  
**UV/Vis.:** λ<sub>max</sub>: 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.<sup>1,2</sup> HIF-1 $\alpha$  has emerged as an important drug target in breast and prostate cancer, cardiovascular disease, and ischemia.<sup>3,4</sup> ML-228 is an activator of the HIF signaling pathway, as demonstrated by HIF response element (HRE) reporter assay (EC<sub>50</sub> = 1.2  $\mu$ M), HIF-1 $\alpha$  nuclear translocation assay (EC<sub>50</sub> = 1.3  $\mu$ M), and increased VEGF expression (EC<sub>50</sub> = 1.6  $\mu$ M).<sup>5</sup> Its activity in the HRE assay is blocked by excess iron, suggesting that ML-228 can chelate iron.<sup>5</sup> Molecular modeling indicates that ML-228 does not modulate HIF signaling by binding to prolyl hydroxylases.<sup>5</sup> ML-228 also significantly inhibits ligand binding to several channels, receptors, and transporters, including ERG potassium channel, 5-HT<sub>2B</sub> and A<sub>3</sub> adenosine receptors, and dopamine transporter.<sup>5</sup>

### 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).

#### WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

#### SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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