# PRODUCT INFORMATION



C25-140

Item No. 39669

CAS Registry No.: 1358099-18-9

Formal Name: 3-[3,5-dimethyl-1-(3-methyl-1,2,4-

> triazolo[4,3-b]pyridazin-6-yl)-1Hpyrazol-4-yl]-1-[4-(phenylmethyl)-1-

piperidinyl]-1-propanone

MF:  $C_{26}H_{31}N_7O$ FW: 457.6 **Purity:** ≥98% Supplied as: A 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**

C25-140 is supplied as a solid. A stock solution may be made by dissolving the C25-140 in the solvent of choice, which should be purged with an inert gas. C25-140 is soluble in methanol and DMSO.

### Description

C25-140 is an inhibitor of the protein-protein interaction between the E3 ligase TNF receptor-associated factor 6 (TRAF6) and ubiquitin-conjugating enzyme E2 N (Ubc13;  $IC_{50}$  = 2.6  $\mu$ M).<sup>1</sup> It selectively inhibits the TRAF6-Ubc13 interaction over the interactions between Ubc13-OTUB1 and Ubc13-Uev1a. C25-140 (30 μM) also selectively inhibits TRAF6-dependent ubiquitination over a panel of various E3 ligase/E2 enzymes, but does inhibit cellular inhibitor of apoptosis 1 (cIAP1) and E1/E2 enzymes in cell-free assays. It reduces IL-1β-induced activation of NF-κB in mouse embryonic fibroblasts (MEFs) when used at a concentration of 50  $\mu$ M. Topical application of C25-140 (~1.5 mg/kg twice per day) reduces scaling and erythema in a mouse model of psoriasis induced by the TLR7 agonist imiquimod (Item No. 14956). It decreases disease severity in a mouse model of collagen-induced arthritis when administered at doses ranging from 6 to 14 mg/kg twice per day. C25-140 (5 mg/kg) also reduces alveolar septal thickening, pulmonary edema, and inflammatory cell infiltration in bronchoalveolar lavage fluid (BALF) in a mouse model of lung injury induced by mechanical ventilation with high tidal volumes.<sup>2</sup>

### References

- 1. Brenke, J.K., Popowicz, G.M., Schorpp, K., et al. Targeting TRAF6 E3 ligase activity with a small-molecule inhibitor combats autoimmunity. J. Biol. Chem. 293(34), 13191-13203 (2018).
- 2. Zeng, Q., Ye, L., Ling, M., et al. TLR4/TRAF6/NOX2 signaling pathway is involved in ventilation-induced lung injury via endoplasmic reticulum stress in murine model. Int. Immunopharmacol. 96:107774, (2021).

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

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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