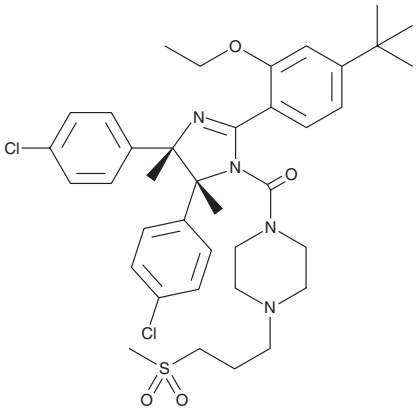
PRODUCT INFORMATION

RG-7112

Item No. 25673



CAS Registry No.:	939981-39-2
Formal Name:	[(4S,5R)-4,5-*bis*(4-chlorophenyl)-2-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydro-4,5-dimethyl-1H-imidazol-1-yl][4-[3-(methylsulfonyl) propyl]-1-piperazinyl]-methanone
Synonym:	RO5045337
MF:	$C_{38}H_{48}Cl_2N_4O_4S$
FW:	727.8
Purity:	≥98%
UV/Vis.:	λ_{max}: 214, 251 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

RG-7112 is supplied as a crystalline solid. A stock solution may be made by dissolving the RG-7112 in the solvent of choice. RG-7112 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of RG-7112 in these solvents is approximately 20, 12.5, and 25 mg/ml, respectively.

Description

RG-7112 is an inhibitor of mouse double-minute 2 protein (MDM2; IC_{50} = 0.018 µM), an E3 ubiquitin ligase that ubiquitinates the tumor suppressor p53 and also acts as a negative regulator of p53 transcriptional activity.[1] RG-7112 binds to the p53 binding pocket of MDM2. It increases the levels of p53 and its transcriptional targets in SJSA-1 osteosarcoma cells.[1,2] It inhibits proliferation in cancer cell lines expressing wild-type p53 (IC_{50}s = 0.18-2.2 µM) and cell lines expressing mutant p53 (IC_{50}s = 5.7-20.3 µM). RG-7112 also prevents and reduces tumor growth in an SJSA-1 mouse xenograft model when administered at doses of 50 and 100 mg/kg per day, respectively.[2] However, it inhibits thrombopoiesis *in vivo*, decreasing platelet counts in rats when administered at doses of 50 and 100 mg/kg and in cynomolgus monkeys at doses of 10 and 20 mg/kg.[3]

References

1. Vu, B., Wovkulich, P., Pizzolato, G., *et al.* Discovery of RG7112: A small-molecule MDM2 inhibitor in clinical development. *ACS Med. Chem. Lett.* **4(5)**, 466-469 (2013).
2. Tovar, C., Graves, B., Packman, K., *et al.* MDM2 small-molecule antagonist RG7112 activates p53 signaling and regresses human tumors in preclinical cancer models. *Cancer Res.* **73(8)**, 2587-2597 (2013).
3. Iancu-Rubin, C., Mosoyan, G., Glenn, K., *et al.* Activation of p53 by the MDM2 inhibitor RG7112 impairs thrombopoiesis. *Exp. Hematol.* **42(2)**, 137-145 (2014).

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