Product Datasheet

RGB-286638 free base (orb1223052)

Catalog Number	orb1223052
Category	Small Molecules
Description	RGB-286638 free base is a novel CDK inhibitor with IC50s of 1 nM/2 nM/3 nM/4 nM/5 nM for cyclin T1-CDK9/cyclin B1-CDK1/cyclin E-CDK2/cyclin D1-CDK4/cyclin E-CDK3/p35-CDK5 respectively; less potent against cyclin H-CDK7 and cyclin D3-CDK6.(In Vitro):RGB-286638 is an indenopyrazole-derived CDK inhibitor (CDKI) with Ki-nanomolar activity against transcriptional CDKs. RGB-286638 inhibits several tyrosine and serine/threonine non-CDK enzymes, i.e. GSK-3β, TAK1, AMPK, Jak2, MEK1. The dose- and time-dependent effect of treatment with RGB-286638 (12.5-100nM) is investigated on the growth of human p53-wt (MM.1S, MM.1R, and H929) and p53-mutant (U266, OPM1, and RPMI) MM cells by MTT assay, assessing viability at 24 and 48 hours. The half-maximally effective concentrations (EC50) range between 20 and 70 nM at 48 hours. Dose-dependent differences in growth among p53-wt and -mutant cells are observed after 50nM treatment, with p53-wt MM.1S, MM.1R and H929 being slightly more sensitive to RGB-286638 treatment at 48h.(In Vivo):Dose-finding studies with RGB-286638 identify 40 mg/kg/day IV treatment as the maximum tolerated dose in SCID mice. Five days IV treatment with RGB-286638 significantly suppresses MM tumor growth, with maximum TGI (%) noted at day 14 following end of treatment at 85.06% and 86.34% in the 30 mg/kg and 40 mg/kg treated cohorts respectively. The log10 cell kill (LCK Td: 4.5 days) is 1.6 for both treated groups. RGB-286638 treatment is also associated with improved survival, evidenced by first death at day 24 in controls versus day 43 in both treated groups. No toxic deaths occurred during this study: maximum percentage of body weight (BW) loss is observed on day 5 (8.4%) at 30 mg/kg dosage schedule, and on day 15 (9.9%) after 40 mg/kg dosing, with weight recovery in the following two weeks.
Target	c-Kit
Purity	>98% (HPLC)
MW	545.63

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Target Areas	CDK1/cyclinB1| CDK2/cyclinE| CDK3/cyclinE| CDK4/cyclinD1| CDK9/cyclinT1| p35-CDK5
Solubility (25°C)	DMSO : ≥ 36 mg/mL. 65.98 mM
CAS Number	784210-88-4
Formula	$C_{29}H_{35}N_7O_4$
SMILES	COCCN1CCN(CC1)Cc1ccc(cc1)c1n[nH]c2c1C(=O)c1c2cccc1NC(=O)NN1CCOCC1
Storage	Storage temperature: -20°C. Stability: ≥ 2 years
Note	For research use only
Expiration Date	12 months from date of receipt.

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