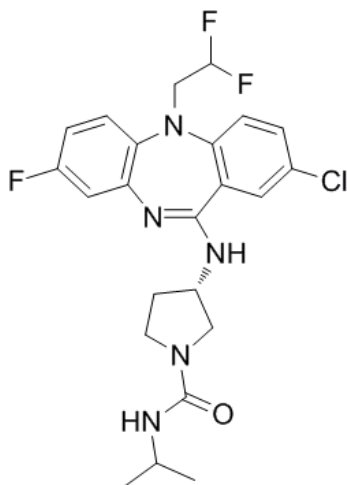


Cat. No.: GC32830



Product Data Sheet

**Kinase
experiment:**

Inhibition of PAK1 kinase activity is measured using the Caliper assay. The assay is performed using 384-well microtiter plates. Compounds (NVS-PAK1-1) are tested as 8-point dose responses. The assays are prepared by addition of 50 nL of compound solution in 90% DMSO directly into the empty plate. Subsequently, 4.5 μ L of the enzyme solution is added to each well and the resulting solution is pre-incubated at 30°C for 60 min, followed by addition of 4.5 μ L of the peptide/ATP-solution. After 60 min incubation at 30°C, reactions are terminated by addition of 16 μ L per well of the stop solution. Plates with terminated kinase reactions are transferred to the Caliper LC3000 workstations for reading. Product formation is measured in a microfluidic mobility shift assay. IC50 values are derived from percent inhibition values at different compound concentrations by non-linear regression analysis[1].

References:

[1]. Karpov AS, et al. Optimization of a Dibenzo-diazepine Hit to a Potent and Selective Allosteric PAK1 Inhibitor. ACS Med Chem Lett. 2015 May 22;6(7):776-81.

Background

NVS-PAK1-1 is a potent and selective allosteric PAK1 inhibitor with an IC50 of 5 nM.

NVS-PAK1-1 demonstrates high selectivity for inhibition of PAK1 over other PAK isoforms and the kinome in general. NVS-PAK1-1 has a biochemical PAK1 Kd of 7 nM and a PAK2 Kd of 400 nM. NVS-PAK1-1 shows excellent activity in biochemical assays and an exceptional selectivity profile against other known kinases. NVS-PAK1-1 at 6-20 μ M inhibits the phosphorylation of the downstream substrate MEK1 Ser289. Consistent with the observation, NVS-PAK1-1 inhibits proliferation of Su86.86 cell line only above a concentration of 2 μ M. In contrast, by applying a mixture of NVS-PAK1-1 and PAK2 shRNA, inhibition of downstream signaling and cell proliferation at a significantly lower 0.21 μ M concentration are achieved[1].

NVS-PAK1-1 shows a relatively poor stability in rat liver microsomes (RLM) and this would limit its application for in vivo studies ($t_{1/2}$ in RLM 3.5 min)[1].

Caution: Product has not been fully validated for medical applications. For research use only.

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[1]. Karpov AS, et al. Optimization of a Dibenzodiazepine Hit to a Potent and Selective Allosteric PAK1 Inhibitor. ACS Med Chem Lett. 2015 May 22;6(7):776-81.

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