Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

AMG 925

Catalog No: tcsc2486

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1401033-86-0

Formula:
$C_{26}H_{29}N_7O_2$

Pathway:
Cell Cycle/DNA Damage;Protein Tyrosine Kinase/RTK

Target:
CDK;FLT3

Purity / Grade:
>98%

Solubility:
DMSO :

Observed Molecular Weight:
471.55

Product Description

AMG 925 is a potent, selective, and orally available **FLT3**/**CDK4** dual inhibitor with **IC_{50}**s of 2±1 nM and 3±1 nM, respectively.

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IC50 & Target: IC50: 2±1 nM (FLT 3), 3±1 nM (CDK4), 8±2 nM (CDK6), 375±150 nM (CDK2), 1.90±0.51 μM(CDK1)[1]

In Vitro: AMG 925 also inhibits CDK6, CDK2, and CDK1 in kinase assays with IC_{50}s of 8±2 nM, 375±150 nM, 1.90±0.51 μM, respectively. A fair overall kinase selectivity of AMG 925 is as determined by KinomScan against a panel of 442 various kinases. Cellular selectivity (on-target vs. off-target activity) of AMG 925 is about 50-fold as evaluated by comparison of its growth-inhibiting activity in RB-positive (RB^+) and RB-negative (RB^-) non- acute myeloid leukemia (AML) cancer cell lines. AMG 925 potently inhibits growth of AML cell lines MOLM13 (FLT3-ITD; IC_{50}=19 μM) and Mv4-11 (FLT3-ITD; IC_{50}=18 μM)[1].

In Vivo: MOLM13 tumor-bearing mice are dosed twice daily by oral administration 6 hours apart with 12.5, 25, or 37.5 mg/kg AMG 925. Tumors are then harvested 3, 9, 12, and 24 hours after the first dose, and analyzed for levels of P-STAT5 and P-RB. Maximum inhibition of P-STAT5 and P-RB is achieved at 6 and 12 hours respectively at the 37.5 mg/kg dose of AMG 925. Interestingly, a rebound of P-STAT5 at 24 hours is observed, possibly as a result of compensational feedback. The pharmacodynamic responses of P-STAT5 and P-RB inhibition correlated with plasma concentrations of AMG 925. AMG 925 inhibits AML xenograft tumor growth by 96% to 99% without significant body weight loss. The antitumor activity of AMG 925 correlates with the inhibition of STAT5 and retinoblastoma protein (RB) phosphorylation, the pharmacodynamic markers for inhibition of FLT3 and CDK4, respectively. In addition, AMG 925 is also found to inhibit FLT3 mutants (e.g., D835Y) that are resistant to the current FLT3 inhibitors (e.g., AC220 and Sorafenib)[1].