# Product Data Sheet

Product Name: KPT-9274
Cat. No.: GC14615

## Chemical Properties

| | | | |
|---|---|---|---|
| Cas. No. | 1643913-93-2 | | |
| Chemical Name | (1Z,2E)-3-(6-aminopyridin-2-yl)-N-((5-(4-(4,4-difluoropiperidine-1-carbonyl)phenyl)-7-(4-fluorophenyl)benzofuran-2-yl)methyl)acrylimidic acid | | |
| SMILES | FC1=CC=C(C2=CC(C3=CC=C(C(N4CCC(F)(F)CC4)=O)C=C3)=CC5=C2OC(C/N=C(O)/C([H])=C([H])/C6=NC(N)=CC=C6)=C5)C=C1 | | |
| Formula | $C_{35}H_{29}F_3N_4O_3$ | M.Wt | 610.62 |
| Solubility | ≥ 22.45mg/mL in DMSO | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |
| Structure | KPT-9274 | | |

## Background

KPT-9274 is a selective and orally bioavailable allosteric inhibitor of PAK4 [1][2][3].

P21 protein (Cdc42/Rac)-activated kinase 4 (PAK4) is a serine/threonine-protein kinase and a member of the PAK family of proteins which are Rac1 and Cdc42 effectors. PAK4 is a mediator of filopodia formation and stabilizes β-catenin transcriptional activity, and is involved in disease progression for several solid tumors [1][2][3].

KPT-9274 is a selective and orally bioavailable PAK4 inhibitor. In MDA-MB-468 cells, KPT-9274 showed anti-tumor activity with IC50 value of 0.12 μM. KPT-9274 reduced PAK4 protein and the key downstream effectors of cell cycle (β-catenin, cyclin D1), cell migration (cofilin), autophagy (AMPK) and apoptosis (Caspase and PARP cleavage) [1]. In RCC cells, KPT-9274 dose-dependently inhibited cell viability [2]. In AML cell lines, KPT-9274 (1 nM-10 μM) inhibited cell proliferation in a dose-and time- dependent way and reduced protein and mRNA expression of PAK4 [3].

In mice inoculated with MDA-MB-231 or MDA-MB-468 cells, KPT-9274 were given orally once daily (5 or 7 days/week) without major toxicity. KPT-9274 induced a maximum TGI of ~55% and ~70% in MDA-MB-231 and MDA-MB-468 mice, respectively [1]. In subcutaneous xenograft mouse models, KPT-9274 inhibited RCC growth [2]. In human AML leukemia xenograft model, KPT-9274


***Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com***
***Address: 10292 Central Ave. #205, Montclair, CA, USA***

(150 mg/kg) significantly inhibited tumor growth, prevented invasion of MV4-11 cells, and improved overall survival [3].

References:

[1]. Senapedis W, George R, McCauley D, et al. Preclinical Evaluation of Novel PAK4 Allosteric Modulators Against Triple Negative Breast Cancer.

[2]. Aboud OA, Senapedis W, Landesman Y, et al. Inhibition of PAK4 attenuates renal cell carcinoma (RCC) growth.

[3]. Mitchell S, Orwick S, Cannon M, et al. In Vitro and In Vivo Anti-Leukemic Effects of KPT-9274, a Reported PAK4 Allosteric Modulator, in Acute Myeloid Leukemia: Promising Results Justifying Further Development in This Disease. 57th Annual Meeting & Exposition. Orlando, FL December 5-8, 2015.