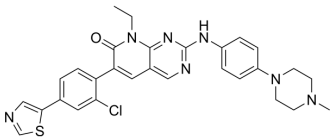
FRAX597

Cat. No.:	HY-15542A
CAS No.:	1286739-19-2
Molecular Formula:	$C_{29}H_{28}ClN_7OS$
Molecular Weight:	558.1
Target:	PAK
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 14.29 mg/mL (25.60 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7918 mL	8.9590 mL	17.9179 mL
	5 mM	0.3584 mL	1.7918 mL	3.5836 mL
	10 mM	0.1792 mL	0.8959 mL	1.7918 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 1.43 mg/mL (2.56 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.43 mg/mL (2.56 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.43 mg/mL (2.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

FRAX597 is a potent group I p21-activated Kinases (PAKs) inhibitor with IC_{50} of 8, 13 and 19 nM for PAK1, 2 and 3.

IC_{50} & Target

PAK1	PAK2	PAK3
8 nM (IC_{50})	13 nM (IC_{50})	19 nM (IC_{50})

In Vitro

FRAX597 is determined to be a potent, ATP-competitive inhibitor of group I PAKs (PAK 1-3), with biochemical IC_{50} values as follows: PAK1 IC_{50}=8 nM, PAK2 IC_{50}=13 nM, PAK3 IC_{50}=19 nM. The IC_{50} toward PAK4, a member of group II PAKs is >10 μM. At

	a concentration of 100 nM FRAX597 displays a significant (>80% inhibition) inhibitory capacity toward YES1 (87%), RET (82%), CSF1R (91%), TEK (87%), PAK1 (82%), and PAK2 (93%). When measured using the Kinase Glo Assay in the presence of 20 nM protein and 1 μM ATP, FRAX597 displayed an IC_{50} value of 48 nM against wild type PAK1, while IC_{50} values against the V342F and V342Y PAK1 mutants are higher than 3 μM and 2 μM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Analysis of the flux reading for the animals in the two cohorts demonstrates a significantly slower tumor growth rate in FRAX597-treated mice compared with control mice. After 14 days of treatment the animals are sacrificed and the tumors excised and weighed. FRAX597-treated cohort shows significantly lower average tumor weight compared with the control cohort [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	30,000 SC4 cells/well are plated in 12-well dishes in triplicate. Cell growth media with or without FRAX597 (1 μM) is replaced daily. At indicated time points, cells from individual wells are trypsinized and counted using a Coulter counter. Statistical analysis is performed using a Student's t test. For cell cycle analysis, cells are harvested, washed once with PBS and fixed in cold 70% ethanol. Fixed cells are resuspended in propidium iodide (PI) buffer (50 μg/mL PI, 250 mg/mL RNase A in PBS) and incubated overnight at 4°C in the dark. Cell cycle distribution is evaluated using Coulter Epics XL flow cytometer. Data are analyzed using WinMDI software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] $Nf2^{-/-}$ SC4 Schwann cells are transduced by lentiviruses carrying pLuc-mCherry and sorted by FACS. 5×10^4 cells are transplanted into the sciatic nerve sheath of NOD/SCID mice (8 weeks of age) by intraneural injection. Tumor progression is monitored weekly by bioluminescence imaging (BLI) on an IVIS-200 system. The representative images from bioluminescence imaging (BLI) of mice carrying orthotopic tumors treated with FRAX597 (100 mg/kg) or vehicle control at day 14 of treatment. NOD/SCID mice are injected intraneurally with 5×10^4 SC4/pLuc-mCherry cells and are enrolled into treatment after 10 days. Mice are treated daily for 14 days and imaged every 3 days to follow tumor development. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharm Sin B. 2020 Apr;10(4):603-614.
- Br J Cancer. 2022 Nov 1.
- Antioxid Redox Signal. 2020 Aug 7.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Licciulli S, et al. FRAX597, a small molecule inhibitor of the p21-activated kinases, inhibits tumorigenesis of neurofibromatosis type 2 (NF2)-associated Schwannomas. J Biol Chem. 2013 Oct 4;288(40):29105-14.

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

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