

Certificate of Analysis

www.tocris.com

Product Name: PF 06463922

Catalog No.: 5640

Batch No.: 1

CAS Number: 1454846-35-5

IUPAC Name: (10*R*)-7-Amino-12-fluoro-10,15,16,17-tetrahydro-2,10,16-trimethyl-15-oxo-2*H*-4,8-methenopyrazolo[4,3-*h*][2,5,11]benzoxadiazacyclotetradecine-3-carbonitrile

1. PHYSICAL AND CHEMICAL PROPERTIES

Batch Molecular Formula: C₂₁H₁₉FN₆O₂·³/₄H₂O

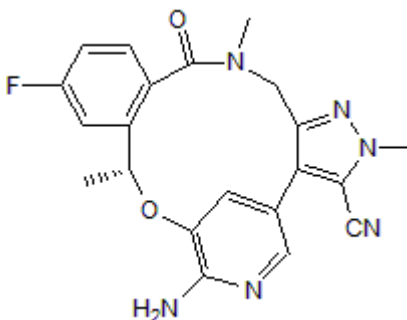
Batch Molecular Weight: 419.92

Physical Appearance: White solid

Solubility: DMSO to 100 mM
ethanol to 100 mM

Storage: Store at -20°C

Batch Molecular Structure:



2. ANALYTICAL DATA

HPLC: Shows 99.4% purity

¹H NMR: Consistent with structure

Mass Spectrum: Consistent with structure

Optical Rotation: [α]_D = -108.6 (Concentration = 0.58, Solvent = Methanol)

Microanalysis:

	Carbon	Hydrogen	Nitrogen
Theoretical	60.07	4.92	20.01
Found	60.36	4.89	19.68

Caution - Not Fully Tested • Research Use Only • Not For Human or Veterinary Use

Product Information

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Description:

High affinity and selective ALK and ROS1 inhibitor (K_i values are <0.02, <0.07 and 0.7 nM for ROS1, wild-type ALK and ALK-L1196M, respectively). Exhibits >100-fold selectivity for ROS1 over a panel of 204 other kinases. Inhibits proliferation of BaF3 cells containing crizotinib-resistant ROS1 mutation in vitro. Inhibits tumor growth in relevant mouse models. Orally available and brain penetrant.

Physical and Chemical Properties:

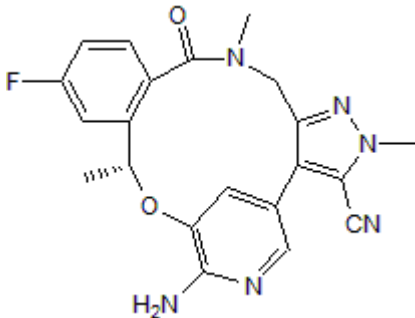
Batch Molecular Formula: $C_{21}H_{19}FN_6O_2 \cdot \frac{3}{4}H_2O$

Batch Molecular Weight: 419.92

Physical Appearance: White solid

Minimum Purity: >98%

Batch Molecular Structure:



Storage: Store at -20°C

Solubility & Usage Info:

DMSO to 100 mM

ethanol to 100 mM

Stability and Solubility Advice:

Some solutions can be difficult to obtain and can be encouraged by rapid stirring, sonication or gentle warming (in a 45-60°C water bath).

Information concerning product stability, particularly in solution, has rarely been reported and in most cases we can only offer a general guide. Our standard recommendations are:

SOLIDS: Provided storage is as stated on the product label and the vial is kept tightly sealed, the product can be stored for up to 6 months from date of receipt.

SOLUTIONS: We recommend that stock solutions, once prepared, are stored aliquoted in tightly sealed vials at -20°C or below and used within 1 month. Wherever possible solutions should be made up and used on the same day.

Licensing Information:

Sold for research purposes under agreement from Pfizer Inc.

References:

Zou *et al* (2015) PF-06463922 is a potent and selective next-generation ROS1/ALK inhibitor capable of blocking crizotinib-resistant ROS1 mutations. *Proc.Natl.Acad.Sci.U.S.A.* **112** 3493. PMID: 25733882.

Johnson *et al* (2014) Discovery of (10*R*)-7-amino-12-fluoro-2,10,16-trimethyl-15-oxo-10,15,16,17-tetrahydro-2*H*-8,4-(metheno)pyrazolo[4,3-*h*][2,5,11]-benzoxadiazacyclotetradecine-3-carbonitrile (PF-06463922), a macrocyclic inhibitor of anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 (ROS1) with preclinical brain exposure and broad-spectrum potency against ALK-resistant mutations. *J.Med.Chem.* **57** 4720. PMID: 24819116.

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