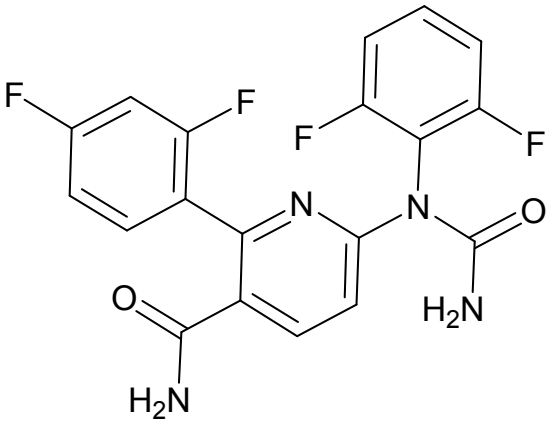
VX-702

SYN-1093



1-(5-carbamoyl-6-(2,4-difluorophenyl)pyridin-2-yl)-1-(2,6-difluorophenyl)urea

CAS Registry No.: 745833-23-2

Smiles String:
c1cc(c(c(c1)F)N(c2ccc(c(n2)c3ccc(cc3F)F)C(=O)N)C(=O)N)F

Molecular Weight: 404.32

Molecular Formula: C19H12F4N4O2

Lot Number: Refer to vial

1H-NMR: Available on request

HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

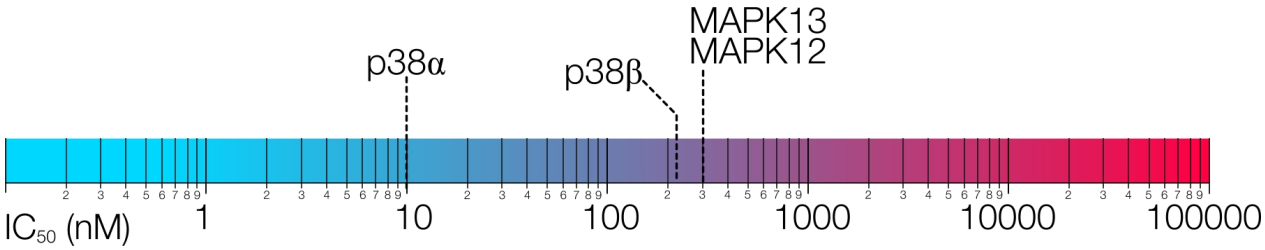
Description:

The kinases called p38 MAP kinases (MAPKs) are intracellular, soluble serine-threonine kinases which belong to a large family of proteins that include the extracellular regulated kinases (ERKs) and c-Jun N-terminal kinases (JNKs). So far four p38 isoforms have been identified, namely p38 α , p38 β , p38 γ and p38 δ , a.k.a., p38- α (MAPK14), - β (MAPK11), - γ (MAPK12 / ERK6), and - δ (MAPK13 / SAPK4). The ubiquitously expressed s p38 α has been the most extensively studied and is believed to be the most physiologically relevant in the regulation of the inflammatory response. The role of the three other isoforms is not currently well understood, however their primary sites of expression are known. Similar to p38 α , p38 β is also ubiquitously expressed, while p38 γ is expressed predominately in skeletal muscle and p38 δ is expressed primarily in the lung, kidney, testis, small intestine and pancreas. The small molecule inhibitor VX-702 is a potent p38 kinase family inhibitor that has been studied for its effects on inflammation and the inflammatory response. VX-702 dose-dependently inhibited the production of

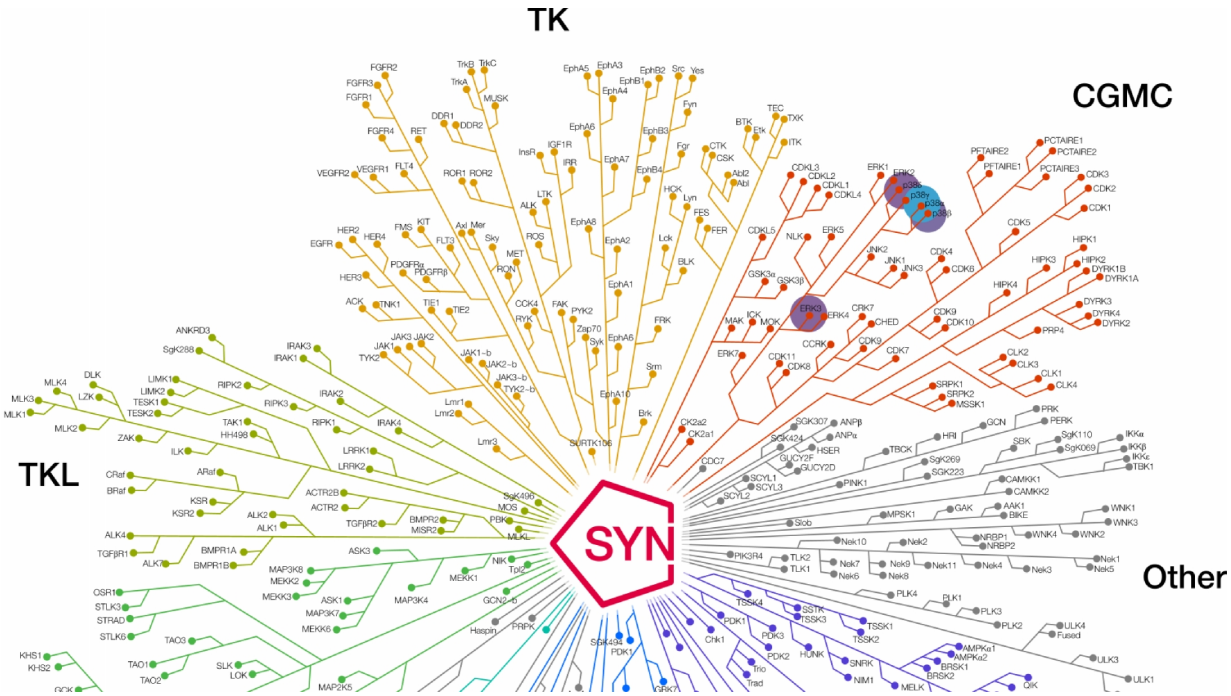
IL-6, IL-1 β and TNF α (IC50 = 59, 122 and 99 ng/ml, respectively) [PMID: 17117592], and in anti-platelet aggregation assays, pre-incubation of platelets with VX-702 (1 µM) completely or partially inhibited platelet agonist induced p38 activation (IC50 = 4 to 20 nM). More recently VX-702 has been studied as a potential treatment for rheumatoid arthritis (RA). VX-702 appears to be most effective against MAPK14, followed by MAPK11 and the remaining members of the family, however exact in vitro IC50 values have not been published. However a large amount of data is available for in vitro

growth inhibition assays where VX-702 exhibits potent activity, having low IC50 values beginning at ~16 nM and ending at < 400 μM for the numerous cell lines tested [CHEMBL1090090].

Biological Activity



Kinome Mapping



Shipping and Storage Temperature

Shipping:
Ambient

Storage:
2 years -20C, Powder 1 month, -4C in DMSO, More than one month -80C in DMSO

Solubility

DMSO 81mg/mL, Ethanol 1mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.4043	4.0432	8.0864	20.2160

References

1. Kuliopulos A, Mohanlal R, Covic L. Effect of selective inhibition of the p38 MAP kinase pathway on platelet aggregation. Thromb Haemost. 2004 Dec;92(6):1387-93.

Ordering Information

To order more of this or any other SYNkinase compound, go to synkinase.com, Call us Toll Free (US Only) at 1- 877-854-6273 or email orders@synkinase.com.