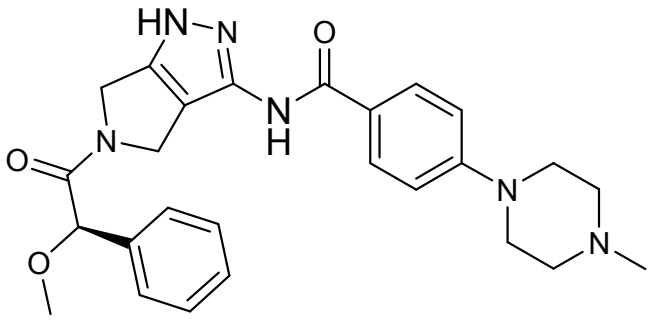
Danusertib

SYN-1095



(R)-N-(5-(2-methoxy-2-phenylacetyl)-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-3-yl)-4-(4-methylpiperazin-1-yl)benzamide

CAS Registry No.: 827318-97-8

Smiles String:
CN1CCN(CC1)c2ccc(cc2)C(=O)Nc3c4c([nH]n3)CN(C4)C(=O)[C@@H](c5ccccc5)OC

Molecular Weight: 474.55

Molecular Formula: C26H30N6O3

Lot Number: Refer to vial

1H-NMR: Available on request

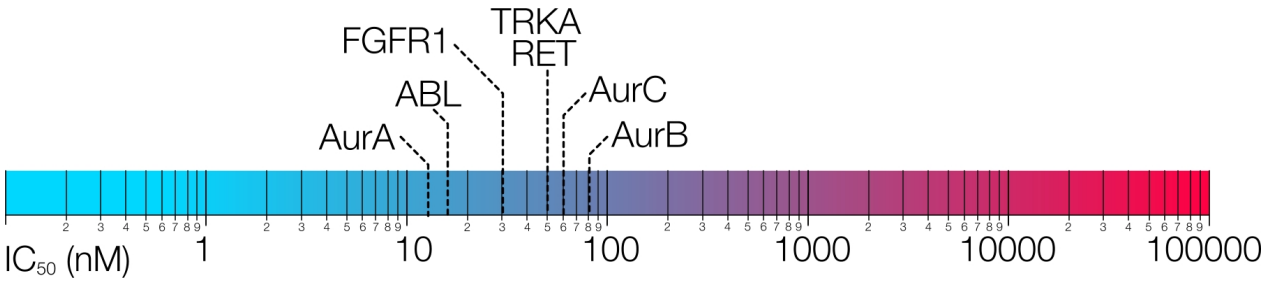
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

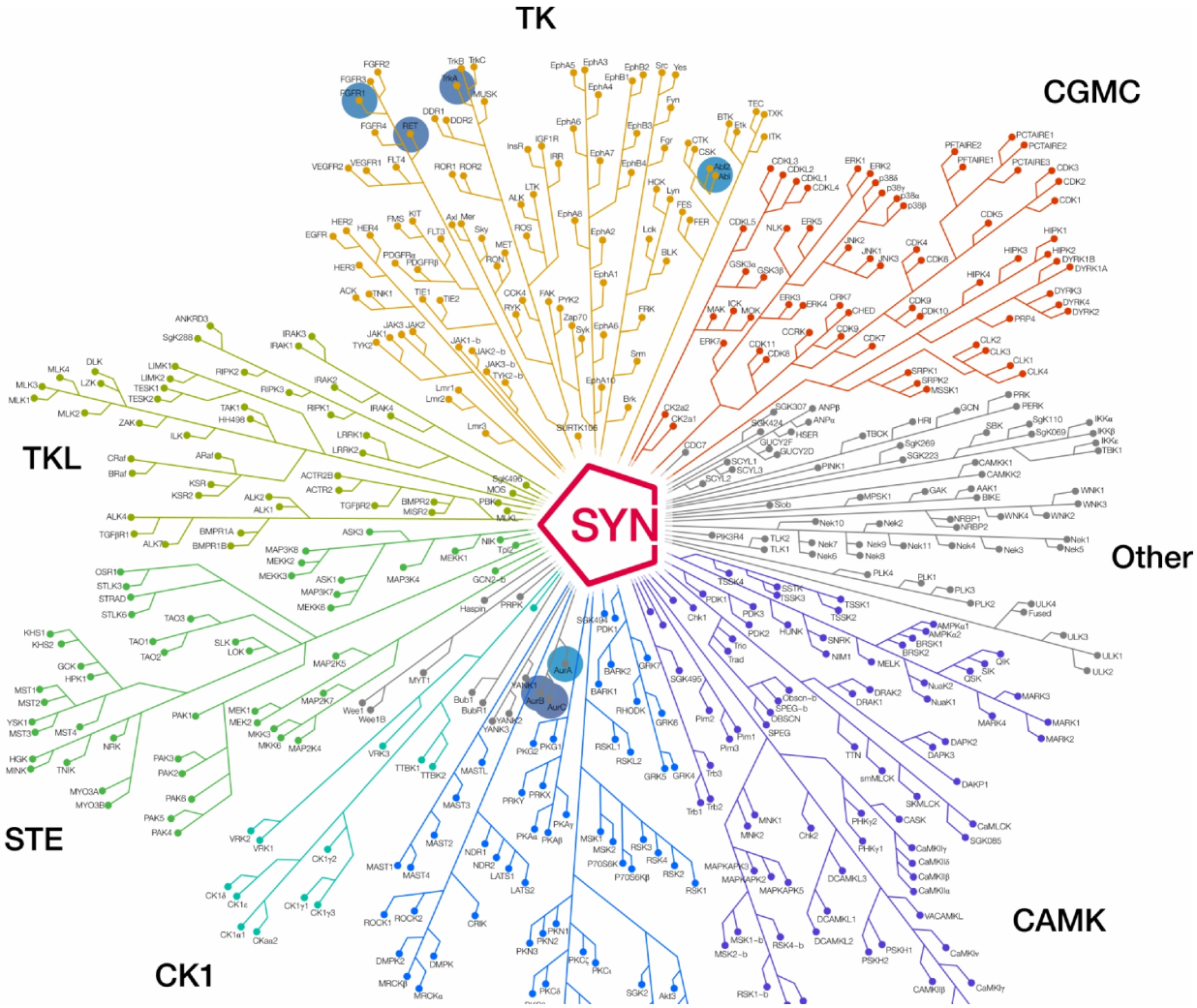
Description:

Aurora kinases are key regulators of protein phosphorylation during mitosis, and these serine/threonine kinases interact with other cellular proteins to help control chromosome assembly and segregation during mitosis. Aurora kinases are often highly expressed in malignancies and solid tumors. Danusertib (PHA-739358) is a small molecule pan-Aurora kinase inhibitor that also has activity against other cancer-relevant kinases such as Bcr-Abl tyrosine kinase. Other off target effects of Danusertib include inhibition of receptor tyrosine kinases such as FGFR-1, and TrkA. Danusertib demonstrates nanomolar IC50 values for the Aurora kinases all under 100 nM and it also demonstrates potent anti-proliferation effects in cell proliferation assays with IC50 values ranging from 20 nM for A2780 cells to <200 nM.

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 95 mg/mL, Ethanol 34mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.4746	4.7460	9.4920	23.7300

References

1. Fraedrich K, Schrader J, Ittrich H, Keller G, Gontarewicz A, Matzat V, Kromminga A, Pace A, Moll J, Bläker M, Lohse AW, Hörsch D, Brümmendorf TH, Benten D. Targeting aurora kinases with danusertib (PHA-739358) inhibits growth of liver metastases from gastroenteropancreatic neuroendocrine tumors in an orthotopic xenograft model. Clin Cancer Res. 2012 Sep 1;18(17):4621-32. doi: 10.1158/1078-0432.CCR-11-2968. Epub 2012 Jul 2.

2. Fancelli D, Moll J, Varasi M, Bravo R, Artico R, Berta D, Bindi S, Cameron A, Candiani I, Cappella P, Carpinelli P, Croci W, Forte B, Giorgini ML, Klapwijk J, Marsiglio A, Pesenti E, Rocchetti M, Roletto F, Severino D, Soncini C, Storici P, Tonani R, Zugnoni P, Vianello P.,4,5,6-tetrahydropyrrolo[3,4-c]pyrazoles: identification of a potent Aurora kinase inhibitor with a favorable antitumor kinase inhibition profile. J Med Chem. 2006 Nov 30;49(24):7247-51.

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.