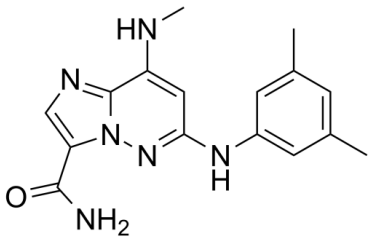
Data Sheet

Product Name:	TyK2-IN-2
Cat. No.:	CS-7482
CAS No.:	2098466-94-3
Molecular Formula:	$C_{16}H_{18}N_6O$
Molecular Weight:	310.35
Target:	JAK; Phosphodiesterase (PDE)
Pathway:	Epigenetics; JAK/STAT Signaling; Metabolic Enzyme/Protease; Stem Cell/Wnt
Solubility:	DMSO : ≥ 25 mg/mL (80.55 mM)



BIOLOGICAL ACTIVITY:

TyK2-IN-2 (Compoud 18) is a potent and selective **TYK2** inhibitor with **IC_{50}**s of 7 nM, 0.1 μM and 0.05 μM for **TYK2 JH2**, **IL-23** and **IFNα**, respectively. TyK2-IN-2 also inhibits **phosphodiesterase 4 (PDE4)** with an **IC_{50}** of 62 nM. TyK2-IN-2 can be used for the research of inflammatory and autoimmune diseases[1]. **In Vitro:** A co-crystal structure of TyK2-IN-2 (Compoud 18) bound to the TYK2 JH2 is solved. First, limited room between C8 and the hinge is seen, consistent with the loss in affinity seen with groups larger than methylamino at this position. There are also hydrogen bonds revealed between the NH of the C8 methylamine and from N1 of the IZP core to the 'hinge' (Val690). Additional hydrogen bonds are observed from the oxygen of the C3 amide to Lys642 and to the hinge carbonyl of Glu688 through a bridging water molecule. The pocket proximal to the C3 amide of the TYK2 JH2 domain contains a combination of residues which are largely unique relative to the kinome such as a small residue (Ala671) under the "gatekeeper" (Thr687) and the replacement of the highly kinase-conserved DFG motif by DPG which alters the positioning of the conserved catalytic Lys642 and Asp759. The ability of the C3 amide to fit and bind to this pocket is believed to be a key source of kinome selectivity for TyK2-IN-2 (Compoud 18)[1].

References:

[1]. Moslin R, et al. Identification of imidazo[1,2-b]pyridazine TYK2 pseudokinase ligands as potent and selective allosteric inhibitors of TYK2 signalling. Medchemcomm. 2016 Dec 15;8(4):700-712.

CAIndexNames:

Imidazo[1,2-b]pyridazine-3-carboxamide, 6-[(3,5-dimethylphenyl)amino]-8-(methylamino)-

SMILES:

CNC1=CC(NC2=CC(C)=CC(C)=C2)=NN3C1=NC=C3C(N)=O

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

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