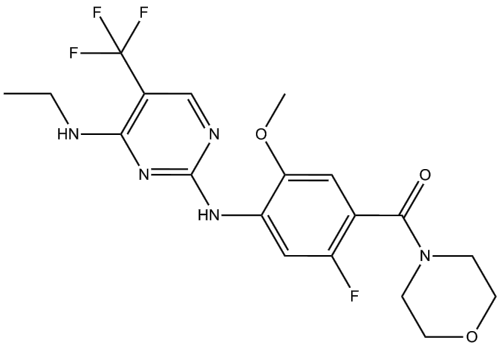
Product Data Sheet

Product Name: GNE-7915
Cat. No.: GC12121

Chemical Properties

Cas. No.	1351761-44-8		
Chemical Name	(4-((4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-yl)amino)-2-fluoro-5-methoxyphenyl)(morpholino)methanone		
SMILES	CCNC1=C(C(F)(F)F)C=NC(NC2=CC(F)=C(C(N3CCOCC3)=O)C=C2OC)=N1		
Formula	$C_{19}H_{21}F_4N_5O_3$	M.Wt	443.4
Solubility	≥ 22.15mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Background

GNE-7915 is a highly potent, selective, and brain-penetrable leucine-rich repeat kinase2 (LRRK2) inhibitor, with Ki and IC50 of 1 nM and 9 nM, respectively.
GEN-7915 is extensive inhibitor across 187 screened kinases, except TTK kinase. In an extended profile across 392 kinases, GNE-7915 only bound to 10 enzymes to a significant extent (>50% probe displaced at 100 nM). GNE-7915 and its progenitors are the first selective LRRK2 inhibitors to penetrating the brain barrier. [1]
GEN-7915 has been shown to induce dephosphorylation of LRRK2 in the brain of transgenic mice.

Caution: Product has not been fully validated for medical applications. For research use only.
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GNE-7915 is not reported to cause cellular or genetic toxicity, and has progressed into preclinical studies in cynomolgus monkeys [3]. The use of in silico modelling, extensive in vitro assays and resource-efficient in vivo techniques to produce GNE-7915, reflects a trend towards the concerted optimisation of potency, selectivity and pharmacokinetic properties in early-stage drug development [1]. GNE-7915 can inhibit TNFαand CXCL10 at higher concentrations (≥ 3 μM) in both WT and LRRK2 KO experiments [2].

References:

1.Kavanagh ME, Doddareddy MR, Kassiou M. The development of CNS-active LRRK2 inhibitors using property-directed optimisation. Bioorg Med Chem Lett. 2013 Jul 1;23(13):3690-6. doi: 10.1016/j.bmcl.2013.04.086. Epub 2013 May 9.

2.Luerman GC, Nguyen C, Samaroo H et al. Phosphoproteomic evaluation of pharmacological inhibition of leucine-rich repeat kinase 2 reveals significant off-target effects of LRRK-2-IN-1. J Neurochem. 2014 Feb;128(4):561-76. doi: 10.1111/jnc.12483. Epub 2013 Nov 11.

3.Estrada AA, Liu X, Baker-Glenn C et al. Discovery of highly potent, selective, and brain-penetrable leucine-rich repeat kinase 2 (LRRK2) small molecule inhibitors. J Med Chem. 2012 Nov 26;55(22):9416-33. doi: 10.1021/jm301020q. Epub 2012 Oct 15.

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