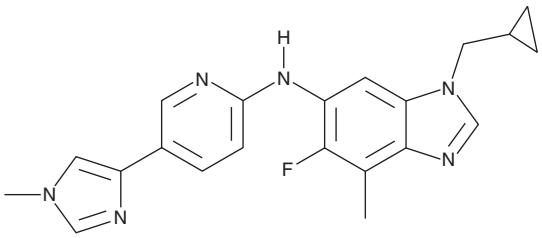
PRODUCT INFORMATION

ONO-8590580

Item No. 35297

CAS Registry No.:	1802661-73-9
Formal Name:	1-(cyclopropylmethyl)-5-fluoro-4-methyl-N-[5-(1-methyl-1H-imidazol-4-yl)-2-pyridinyl]-1H-benzimidazol-6-amine
MF:	$C_{21}H_{21}FN_6$
FW:	376.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 266, 290, 320 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ONO-8590580 is supplied as a crystalline solid. A stock solution may be made by dissolving the ONO-8590580 in the solvent of choice, which should be purged with an inert gas. ONO-8590580 is soluble in DMSO.

Description

ONO-8590580 is a negative allosteric modulator of α_5 subunit-containing $GABA_A$ receptors that binds at the benzodiazepine binding site.[1] It binds to α_1, α_2, α_3, and α_5 subunit-containing $GABA_A$ receptors (K_is = 140, 32, 24, and 7.9 nM, respectively). It is selective for inhibiting GABA-induced currents in HEK293 cells expressing human recombinant $\alpha_5\beta_3\gamma_2$ subunits (EC_{50} = 1.1 nM) over those expressing human recombinant $\alpha_1\beta_3\gamma_2$, $\alpha_2\beta_3\gamma_2$, or $\alpha_3\beta_3\gamma_2$ subunits for which it has little to no activity. ONO-8590580 (300 nM) enhances long-term potentiation in rat hippocampal brain slices. It decreases MK-801-induced memory deficits in the rat passive avoidance test when administered at doses ranging from 3 to 20 mg/kg. ONO-8590580 (20 mg/kg, p.o.) decreases MK-801- and scopolamine-induced increases in the latency to complete, and the number of errors made in, the eight-arm radial maze test in rats. It does not induce anxiety-like or proconvulsant behavior in rats in the elevated zero maze or pentylenetetrazole-induced seizure test when administered at a dose of 20 mg/kg.

Reference

1. Kawaharada, S., Nakanishi, M., Nakanishi, N., *et al*. ONO-8590580, a novel $GABA_A$ α_5 negative allosteric modulator enhances long-term potentiation and improves cognitive deficits in preclinical models. *J. Pharmacol. Exp. Ther.* **366(1)**, 58-65 (2018).

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