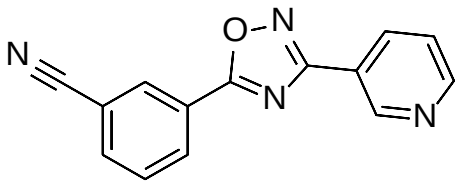
Product data sheet

MedKoo Cat#: 532373 Name: NS9283 CAS: 913830-15-6 Chemical Formula: $C_{14}H_8N_4O$ Exact Mass: 248.0698 Molecular Weight: 248.245	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
NS9283 is a positive allosteric modulator of α4β2 receptor. NS9283 increases the potency of Ach-evoked currents ~60 fold without effecting the maximum efficacy (HEK293-hα4β2 cells). It reduces the rate of recovery from desensitization and slows the rate of deactivation.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMF	10.0	40.28
DMF:PBS (pH 7.2) (1:1)	0.5	2.01
DMSO	7.71	31.04

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	4.03 mL	20.14 mL	40.28 mL
5 mM	0.81 mL	4.03 mL	8.06 mL
10 mM	0.40 mL	2.01 mL	4.03 mL
50 mM	0.08 mL	0.40 mL	0.81 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Olsen JA, Kastrup JS, Peters D, Gajhede M, Balle T, Ahring PK. Two distinct allosteric binding sites at α4β2 nicotinic acetylcholine receptors revealed by NS206 and NS9283 give unique insights to binding activity-associated linkage at Cys-loop receptors. J Biol Chem. 2013 Dec 13;288(50):35997-6006. doi: 10.1074/jbc.M113.498618. Epub 2013 Oct 29. PMID: 24169695; PMCID: PMC3861648.
2. Grupe M, Jensen AA, Ahring PK, Christensen JK, Grunnet M. Unravelling the mechanism of action of NS9283, a positive allosteric modulator of (α4)3(β2)2 nicotinic ACh receptors. Br J Pharmacol. 2013 Apr;168(8):2000-10. doi: 10.1111/bph.12095. PMID: 23278456; PMCID: PMC3623068.

In vivo study

1. Wang J, Blasio A, Chapman HL, Doebelin C, Liaw V, Kuryatov A, Giovanetti SM, Lindstrom J, Lin L, Cameron MD, Kamenecka TM, Pomrenze MB, Messing RO. Promoting activity of (α4)3(β2)2 nicotinic cholinergic receptors reduces ethanol consumption. Neuropsychopharmacology. 2020 Jan;45(2):301-308. doi: 10.1038/s41386-019-0475-8. Epub 2019 Aug 8. PMID: 31394567; PMCID: PMC6901472.

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2. Mohler EG, Franklin SR, Rueter LE. Discriminative-stimulus effects of NS9283, a nicotinic α4β2* positive allosteric modulator, in nicotine-discriminating rats. Psychopharmacology (Berl). 2014 Jan;231(1):67-74. doi: 10.1007/s00213-013-3207-5. Epub 2013 Aug 8. PMID: 23925734.

7. Bioactivity

Biological target:

NS9283 is a positive positive allosteric modulator of (α4)3(β2)2 nicotinic ACh receptors.

In vitro activity

NS9283 was demonstrated to increase the potency of ACh-evoked currents in HEK293-hα4β2 cells by left-shifting the concentration-response curve ~60-fold. Interestingly, this modulation did not significantly alter maximal efficacy levels of ACh. NS9283 strongly decreased the rate of deactivation kinetics and also modestly decreased the rate of activation. This resulted in a left-shift of the ACh window current of (α4)3(β2)2 nAChRs in the presence of NS9283.

Reference: Br J Pharmacol. 2013 Apr;168(8):2000-10. https://pubmed.ncbi.nlm.nih.gov/23278456/

In vivo activity

The present experiments tested the nicotine discriminative-stimulus effects of the α4β2* PAM NS9283 (A-969933) in the presence and absence of low-dose nicotine or nicotinic subtype-selective agonist. Rats were trained to discriminate 0.4 mg/kg nicotine from saline in a two-lever drug discrimination paradigm. In subsequent generalization tests, rats were administered nicotine, the α4β2*-preferring agonist ABT-594, and NS9283, alone or in two-drug combinations. Nicotine and ABT-594 showed dose-dependent nicotine generalization. NS9283 alone resulted in a non-significant increase in nicotine-appropriate lever selection. Combination of non-effective doses of nicotine or ABT-594 with escalating doses of NS9283 resulted in a complete conversion to 100 % nicotine-appropriate choice in the case of nicotine combination and incomplete, though significant, generalization for ABT-594.

Reference: Psychopharmacology (Berl). 2014 Jan;231(1):67-74. https://pubmed.ncbi.nlm.nih.gov/23925734/