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#### ACCEPTED MANUSCRIPT

# In vivo and in vitro ADMET profiling and in vivo pharmacodynamic investigations of a selective $\alpha 7$ nicotinic acetylcholine receptor agonist with a spirocyclic $\Delta^2$ -isoxazoline molecular skeleton

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#### **Abstract**

( $\pm$ )-3-Methoxy-1-oxa-2,7-diaza-7,10-ethanospiro[4.5]dec-2-ene sesquifumarate ( $\pm$ )-1 was previously characterized as the most selective agonist at  $\alpha$ 7 neuronal nicotinic acetylcholine receptors in a series of spirocyclic quinuclidinyl- $\Delta^2$ -isoxazoline derivatives. In this study, we performed different in vitro biological assays aimed at characterizing the ADMET properties of ( $\pm$ )-

1. Then, we tested the compound in vivo in behavioral studies including classical novel object recognition and inhibitory avoidance tests in the rat, and a spatial memory assay in zebrafish involving a rapid T-maze task. The results indicated an overall favorable profile for  $(\pm)$ -1 in view of potential therapeutic applications targeting the central nervous system.

*Keywords:* α7 Nicotinic acetylcholine receptors - Agonist - eADMET - Novel object recognition test - Episodic memory passive avoidance test - Learning/memory in zebrafish

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