IMS-P24 **Identification of 5-HT6 Antagonists without a Basic Amine Moiety**

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Antagonism of the 5-HT6 receptor is a promising mechanism for improving cognitive function and has also been shown to affect food intake and body weight regulation in rodent models of obesity. Rational design utilizing 5-HT6 ligand-receptor pharmacaphore models led to the discovery of a novel class of benzofuro[3,2-c]pyridine derivatives as potent 5-HT6 receptor antagonists. An overview of the SAR of the series will be provided. Typically the 5-HT6 pharmacophore has been associated with a basic amine. Surprisingly several analogues replacing the basic amine with an acetamide or an alcohol moiety retained low nM potency and exquisite selectivity against other off-targets, challenging the requirement of the basic amine for potent binding at the 5-HT6 receptor.