

## IMS-P21 **Discovery of ASP5736, a Novel 5-HT<sub>5A</sub> Receptor Antagonist as an Antipsychotic Drug**

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The 5-HT<sub>5A</sub> receptor is a G-protein-coupled seven-transmembrane receptor and expresses predominantly in neural tissues such as hippocampus, thalamus, amygdala and cerebral cortex with little expression in peripheral tissues. 5-HT<sub>5A</sub> KO mice were reported to show increased exploratory activity in response to novel environments. These observations suggested that the 5-HT<sub>5A</sub> receptor is involved in regulation of mood, affective disorder, and cognitive function. Therefore, the 5-HT<sub>5A</sub> receptor is considered as a potential clinical target for the treatment of schizophrenia.

As part of our research program directed at the development of new 5-HT<sub>5A</sub> receptor antagonists, we have identified ASP5736 as a clinical candidate. ASP5736 is a potent and selective 5-HT<sub>5A</sub> receptor antagonist, and showed promising preclinical pharmacological profiles in several animal models of schizophrenia without specific toxicities such as sedation, catalepsy, or increase in plasma prolactin. In this presentation, we will show the synthesis, SAR of this novel series of 5-HT<sub>5A</sub> receptor antagonists, and pharmacological profiles of ASP5736.