IMS-P19 **Discovery of a Novel and Potent Dual Orexin 1/Orexin 2 Receptor Antagonist, E2006, for the Treatment of Sleep Disorders**

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The orexin receptors, two distinct G-protein coupled receptors (OX1R, OX2R) widely expressed in the brain, play a central role in the regulation of sleep and wakefulness. OX1R and OX2R exert their functions through the binding of endogenous neuropeptides orexin-A (33 amino acid residues) and orexin-B (28 amino acid residues). Due to the therapeutic potential of modulating these receptors, it has been an active research area for the treatment of disorders associated with sleep-awake state control. Actually, several orexin receptor antagonists have advanced to clinical trials for the treatment of insomnia. Our investigational drug, E2006, is a novel and potent orexin receptor dual antagonist which has demonstrated preliminary efficacy and good tolerability in a Phase 1 clinical trial with insomnia subjects. E2006 has subsequently advanced to the Phase 2 clinical trial stage. In this presentation, we will describe the discovery of E2006 in which drug design, synthesis and structure-activity relationship will be highlighted.