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INU-101

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## Abstract

11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1) is a cortisol regenerating enzyme that amplifies tissue glucocorticoid levels, especially in the liver and adipose tissue. Knockout mice or a selective inhibitor of 11 $\beta$ -HSD1 improves metabolic syndrome parameters in preclinical models and human clinical trials. Here, we evaluated the therapeutic potential of INU-101, a potent and selective oral inhibitor of 11 $\beta$ -HSD1. The in vitro activity of 11 $\beta$ -HSD1 was measured using the homogeneous time-resolved fluorescence (HTRF) assay. Differentiated adipocytes were used to evaluate the cellular 11 $\beta$ -HSD1 activity. To determine the inhibitory effects on 11 $\beta$ -HSD1 in tissues, we performed ex vivo studies using liver and adipose tissue isolated from C57BL/6J mice and Cynomolgus monkeys. KKAY mice, *ob/ob*

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