

# IMS-P10 **Design, Synthesis and Structure–Activity Relationships of 5-alkylaminoquinolines: Potent, Orally Active Corticotropin-Releasing Factor-1 Receptor Antagonists**

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Corticotropin-releasing factor (CRF) is a 41-amino acid peptide that acts as the prime regulator of the hypothalamic-pituitary-adrenal (HPA) axis. CRF is a major modulator of the body's overall response to stressors and there is evidence supporting the hypothesis that over production of CRF may underlie the pathology of stress-related disorders, such as depression and anxiety. CRF<sub>1</sub> receptor is the most abundant subtype found in the pituitary and is involved in the regulation of adrenocorticotrophic hormone (ACTH), a key mediator of the body's response to stress. Therefore a CRF<sub>1</sub> receptor antagonist is hypothesized to be a valuable target for the treatment of stress-related disorders.

To date, several CRF<sub>1</sub> receptor antagonists have been reported and prototypical antagonists have common structural features. Here we report the generation of 5-alkylaminoquinolines as novel CRF<sub>1</sub> receptor antagonists that have distinctive structural features compared to the currently known antagonists.