DISCOVERY OF A RENAL OUTER MEDULLARY POTASSIUM (ROMK) CHANNEL INHIBITOR CLINICAL CANDIDATE FOR THE TREATMENT OF HEART FAILURE.

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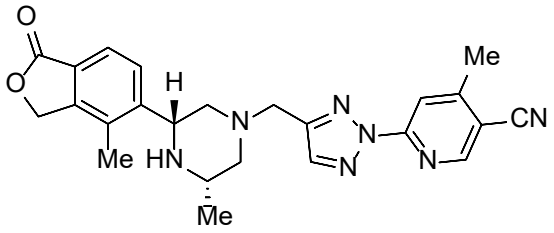
The renal outer medullary potassium (ROMK) channel plays a critical role in renal sodium and potassium hemostasis. Inhibition of the ROMK channel could provide a novel diuretic mechanism for patients with heart failure that are not well controlled on current diuretic therapy. A series of small molecule piperazine based ROMK inhibitors was designed with excellent potency, selectivity, and ADME properties. This work culminated in the discovery of BMS-986308, which demonstrated excellent in vivo efficacy and was advanced into the clinic.



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