Rosacea is a chronic inflammatory skin disorder characterized by itching, redness, and impaired skin barrier function. It has been reported that mast cell activation plays a crucial role in its pathogenesis. This study investigates the therapeutic potential of GE1111, a novel MRGPRX2 antagonist, in rosacea in vitro and in vivo models.

In the in vitro model, LL-37, a potent MRGPRX2 agonist, was used to stimulate LAD-2 mast cells, HaCaT keratinocytes, and RAW 264.7 macrophages. The effects on tight junction protein claudin 1, inflammatory cytokines, and macrophage phagocytosis were evaluated using immunohistochemistry, western blotting, RT-qPCR, and fluorescence imaging techniques. A mouse model of rosacea induced by LL-37 was employed to assess the therapeutic effects of GE1111 in vivo. GE1111 treatment reduced mast cell degranulation associated with rosacea. It also decreased immune cell infiltration and MCP-1 levels, indicating reduced skin inflammation. GE1111 preserved the expression of the tight junction protein Involucrin and reduced the inflammatory mediator peroxisome proliferator-activated receptor, which was evaluated by immunohistochemical analysis. Gene and protein expression analysis supported these findings, showing suppression of inflammatory cytokines and MRGPRX2 signaling pathways in rosacea skin lesions.

In conclusion, GE1111 showed promising therapeutic potential in both in vitro and in vivo studies, suggesting its efficacy in targeting MRGPRX2-mediated interactions between mast cells, keratinocytes, and macrophages in rosacea.