



ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

## NON-CLINICAL AND HUMAN PHARMACOLOGY OF THE POTENT AND SELECTIVE TOPICAL RAR $\gamma$ AGONIST TRIFAROTENE

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Introduction: Retinoids have a dominant role in topical acne therapy and to date, only RAR $\beta$  and RAR $\gamma$  dual agonists have reached the market.

Objectives: to confirm the hypothesis that developing RAR $\gamma$  -selective agonists could yield a new generation of topical acne treatments that would increase safety margins while maintaining the robust efficacy of previous drugs.

Materials and Methods: Structural knowledge derived from the X-Ray structure of known RAR $\gamma$ -selective molecule. Design, synthesis and in vitro evaluation of a novel triaryl series of RAR $\gamma$  agonists were performed including structure activity and property relationship.

Results: Results revealed an unique and isotype specific pocket in the RAR $\gamma$  ligand binding domain thus enabling the optimization of a novel triaryl series of RAR $\gamma$  selective agonist for topical administration.

Conclusions: Structural information led to the discovery of Trifarotene, a new RAR $\gamma$  -selective agonist as a potential new generation of topical acne treatments.

