

# Soluble Adenylyl Cyclase (sAC) Inhibitors for the Treatment of Psoriasis

<b>Therapeutic Area</b>	Dermatology	<b>Indications</b>	Psoriasis
<b>Modality</b>	Small Molecule	<b>Development Stage</b>	Pre-clinical

## Overview

### Background

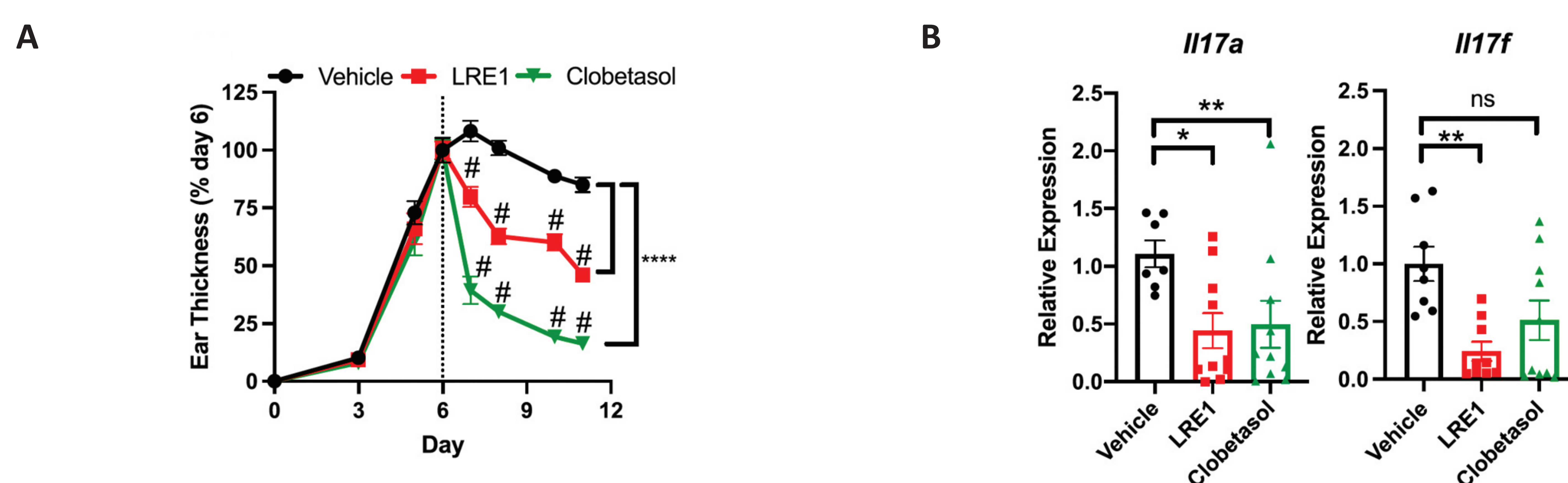
- Inflammatory diseases of the skin, including psoriasis and atopic dermatitis, affect millions of people every year
- Whereas biologics and other systemic therapies are effective for patients with severe disease, those with mild to moderate disease are limited to topical anti-inflammatories
- However, corticosteroids, the most effective topicals, have significant skin and systemic side effects
- Soluble adenylyl cyclase (sAC) is an important source of the second messenger cAMP, which is critical for the activation of T cells during the inflammatory response
- Unmet Need: Broadly effective non-steroidal anti-inflammatory for topical treatment of psoriasis

### Technology Advantages

- No overt toxicity was noted in in vivo studies, despite high dosages
- Demonstrated efficacy via topical administration
- Comparable efficacy to topical steroids but with superior safety profile
- Could be used as combination therapy with topical steroids or systemic biologics

## Key Data

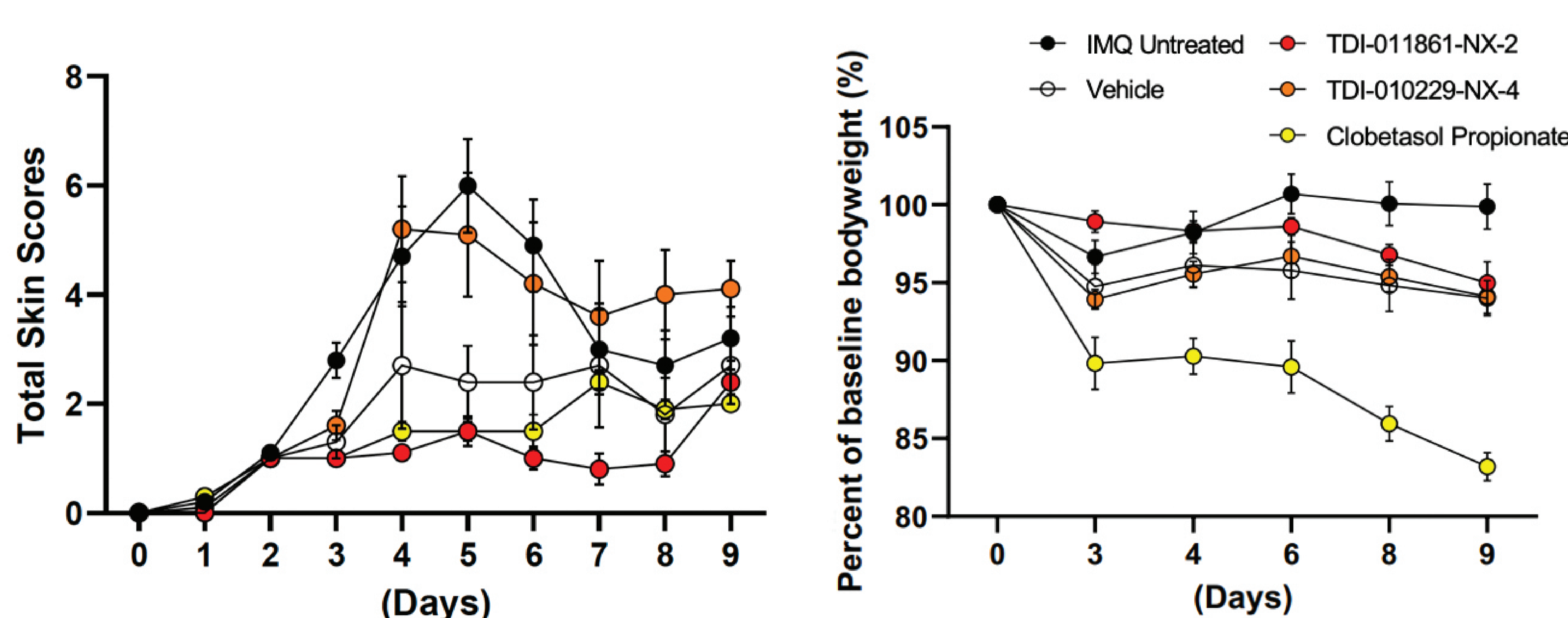
### sAC inhibitors reduce imiquimod-induced immune response in mice



Imiquimod-induced inflammatory response, measured by ear thickness, in mice treated with imiquimod for 6 days followed by continued imiquimod treatment and either vehicle (DMSO), sAC inhibitor (LRE1), or clobetasol for 5 days. (B) Quantitative RT-PCR analysis of IL17a and IL17f expression in skin from the experiment described in (A)

\*LRE1 is a research tool compound and was the starting point for development of lead compound TDI-11861

### Effects of topical treatment with TDI-11861 on skin score and baseline body weight *in vivo*



Topical treatment with TDI-11861 significantly ameliorates total skin scores similarly to the group treated with the positive control clobetasol propionate, but without a substantial change in baseline body weight

## IP Status & Publication(s)

### Intellectual Property

**Patent Number**  
PCT application filed

**Patent Family**  
PCT

### Publication(s)

- You, J. et al. (2023). Soluble adenylyl cyclase contributes to imiquimod-mediated inflammation and is a potential therapeutic target in psoriasis. *Experimental Dermatology*.
- Fushimi, M. et al. (2021). Discovery of TDI-10229: a potent and orally bioavailable inhibitor of soluble adenylyl cyclase (SAC, ADCY10). *ACS Medicinal Chemistry Letters*, 12(8), 1283–1287.