

# TEM1657 is a new small molecule for the topical and oral treatment of psoriasis



# temisis

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## Development of novel pharmaceutical APIs in dermatology

Temisis is a therapeutic company focusing on the development of small-molecule assets for the treatment of unmet needs in dermatology. Its main asset, TEM1657, shows similar efficacy as market reference corticosteroids to **remove psoriasis symptoms** at pre-clinical stage, but with **no observed side-effects**



# 1

## Rapid efficacy

Symptoms are significantly reduced after the first application of TEM1657 at 0.2%

# 2

## Complete remission of psoriasis symptoms

No erythema - Regulated desquamation - Normal skin thickness

# 3

## No side effect

No skin thinning (unlike corticosteroids), no observed side effect on animals in toxicity tests

## In vitro efficacy profile

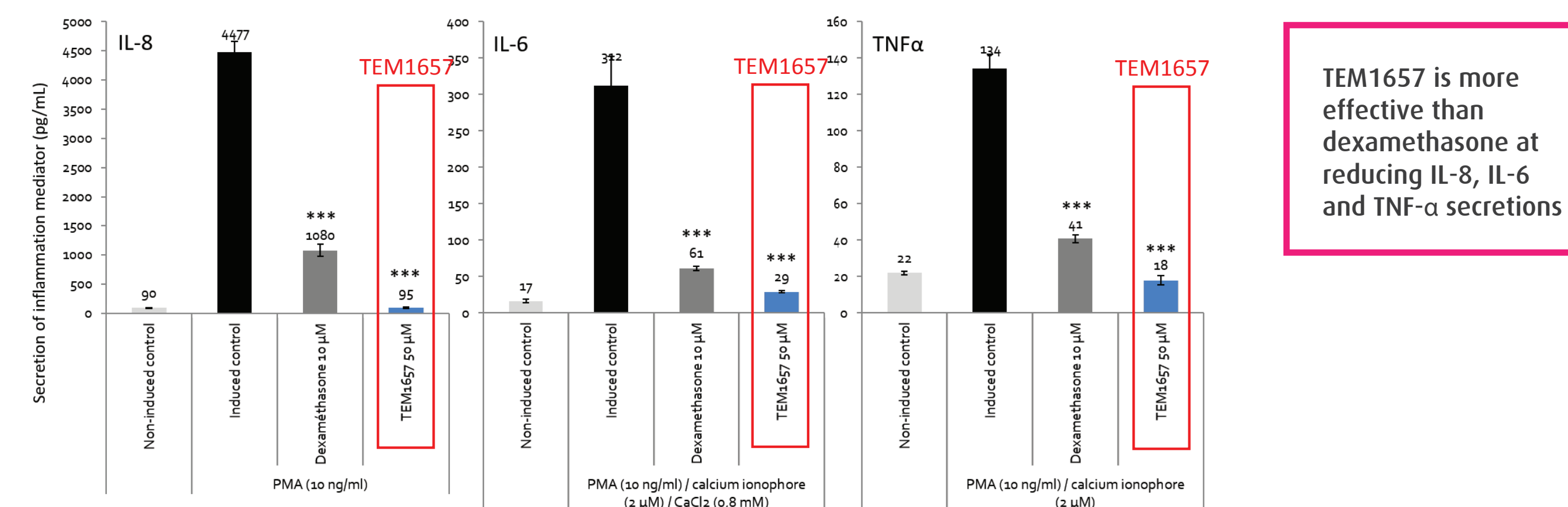
TEM1657 greatly reduces cytokines secretion in PMA-inflamed skin cells

### 1 Experimental design

Human keratinocytes (NHEK) were cultured, placed in contact with TEM1657, and 2h later, inflamed in different conditions (see table below) for the measurement of cytokines.

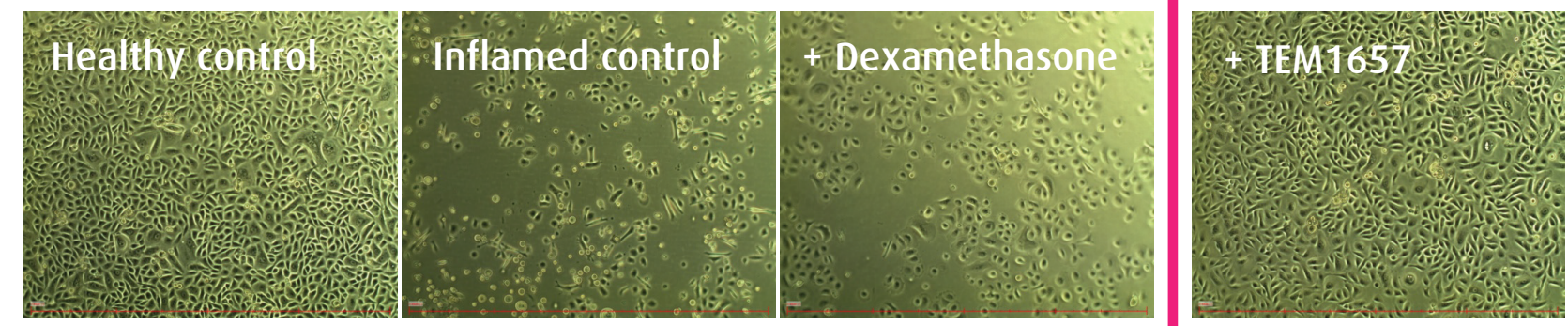
Cytokine quantified	Inflammation agent	Inflammation time
IL-8	PMA 10 ng / ml	24h
IL-6	PMA 10 ng / ml Calcium ionophore A23187 2 µM [Ca <sup>2+</sup> ] = 800 µM	24h
TNF-α	PMA 10 ng / ml calcium ionophore A23187 2 µM [Ca <sup>2+</sup> ] = 40 µM	24h

### 2 Cytokines secretion



TEM1657 is more effective than dexamethasone at reducing IL-8, IL-6 and TNF-α secretions

### 3 Microscopic view of the cells

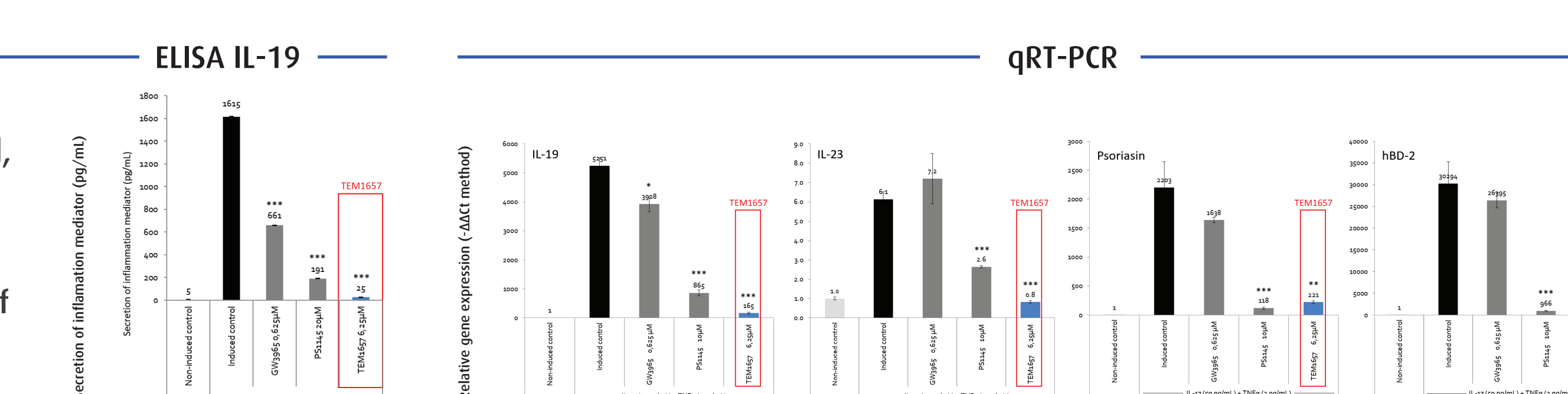


After 48h, not only did TEM1657 decrease the inflammation, but it also preserved cell integrity

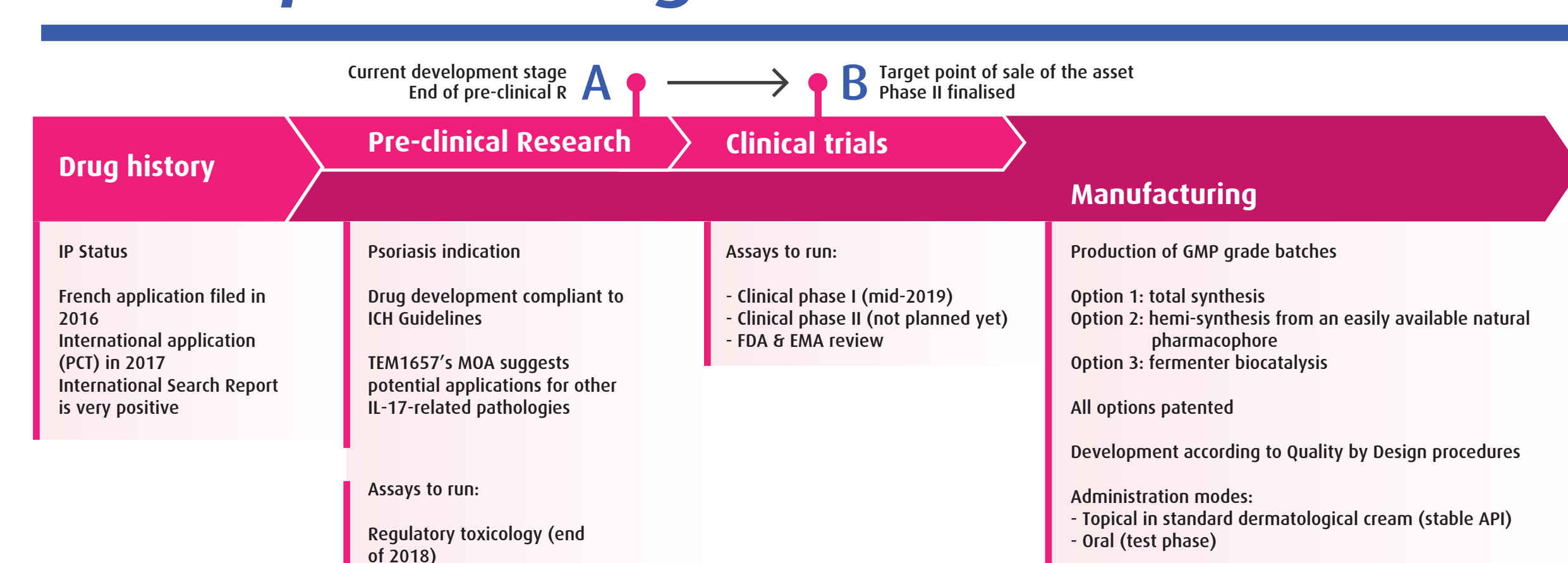
TEM1657 reduces inflammation in IL-17-induced keratinocytes

### 1 Experimental design

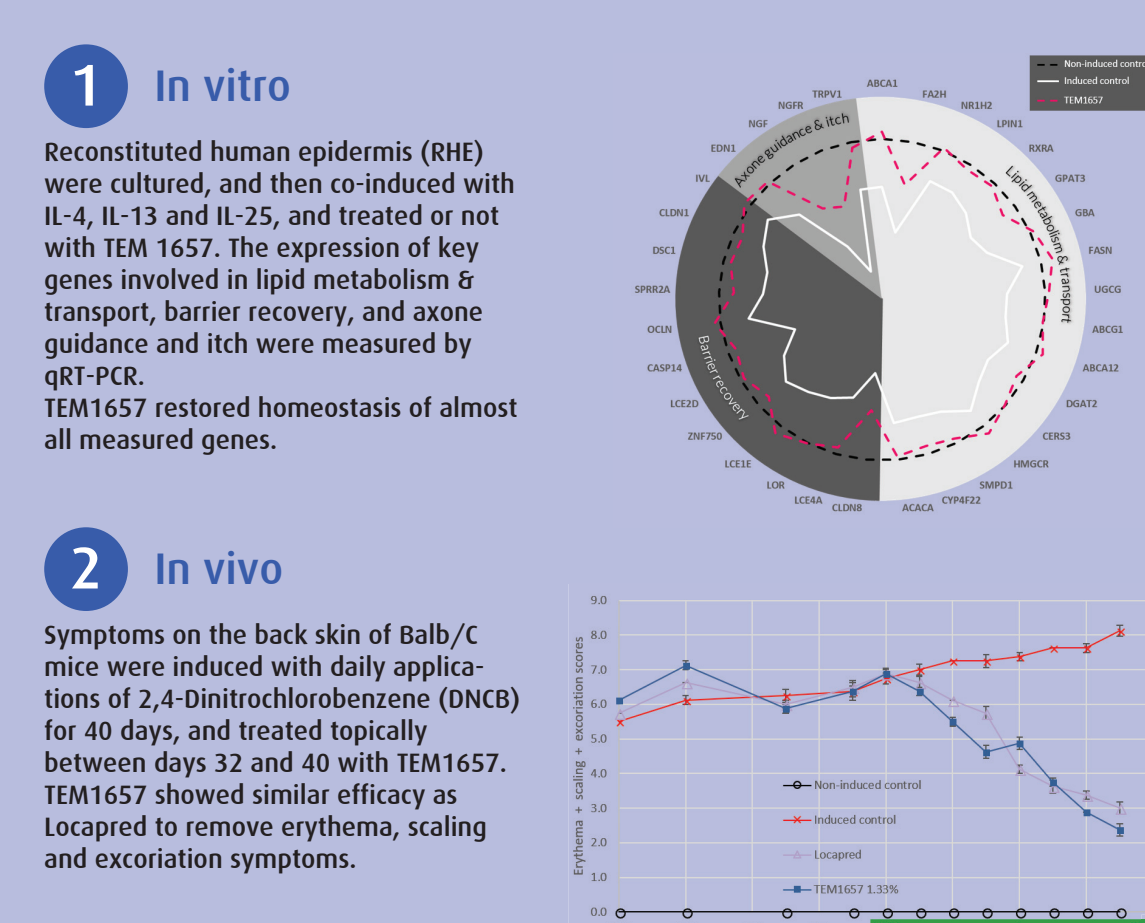
Human keratinocytes (NHEK) were cultured, and then co-induced with IL-17 and TNFα, and treated or not with TEM1657. Psoriasis associated markers were measured: secretion of IL-19 (ELISA), and expression of inducible genes encoding IL-19, IL-23, psoriasis, and hBD-2 (qRT-PCR).



## Development stage



TEM1657 is also efficacious on atopic dermatitis

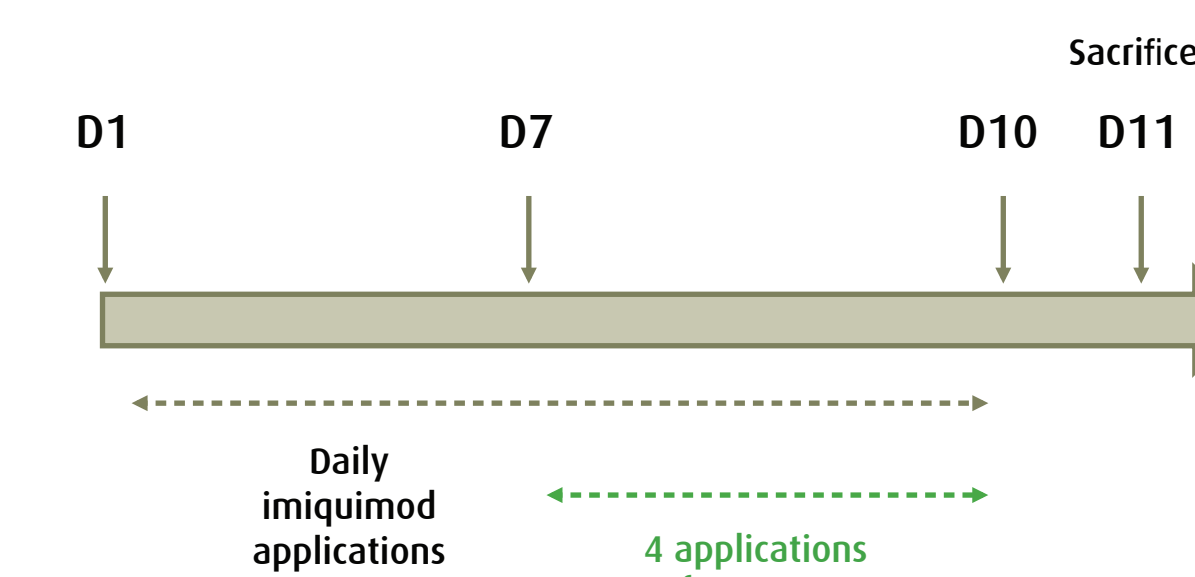


## In vivo efficacy profile

Topical applications of TEM1657 cure psoriasis in Balb/c mice

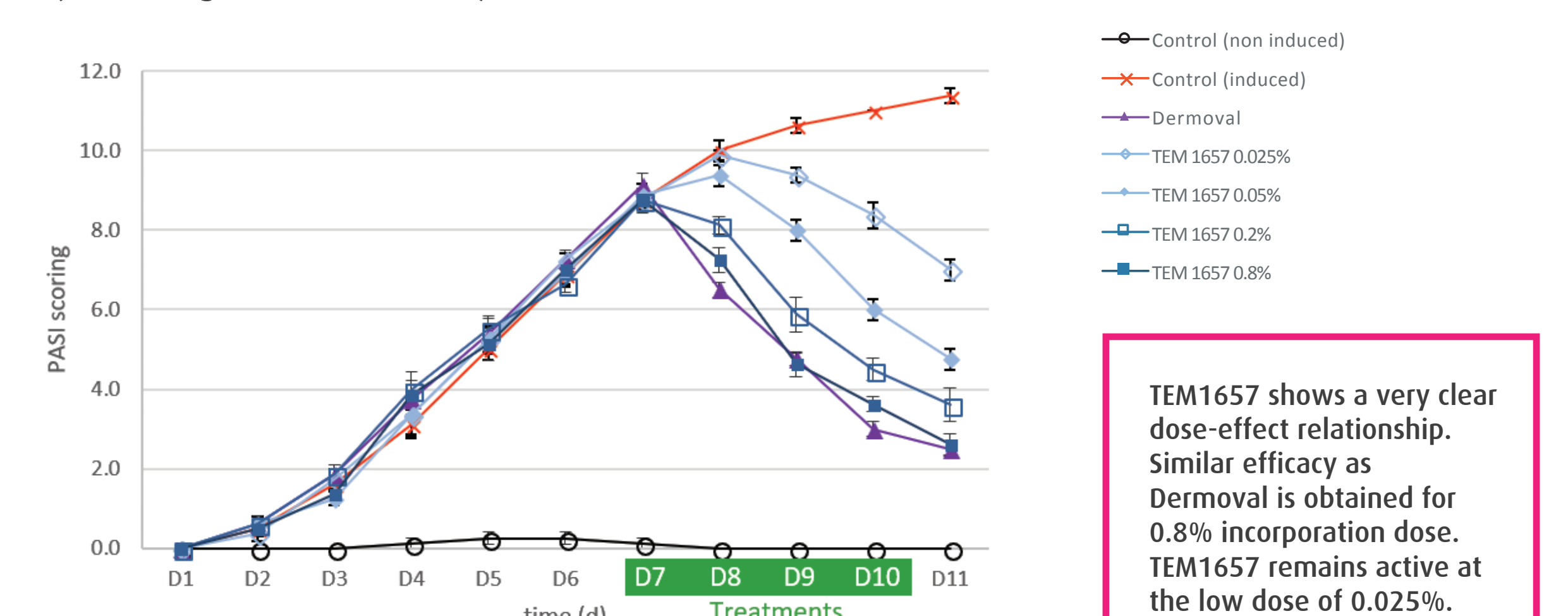
### 1 Experimental design

Psoriasis symptoms were induced on the back skin of Balb/c mice in imiquimod model. TEM1657 was topically applied on days 7 to 10 (see experimental planning below).



### 2 PASI scoring

Efficacy of TEM1657 at different incorporation doses was compared to Dermoval cream (containing 0.05% Clobetasol).



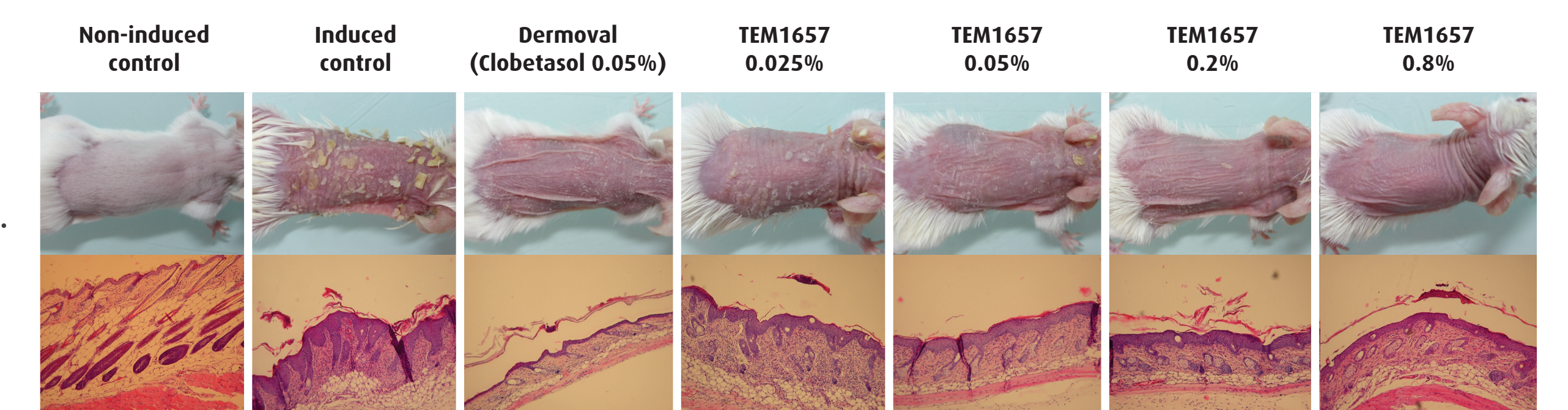
TEM1657 shows a very clear dose-effect relationship. Similar efficacy as Dermoval is obtained for 0.8% incorporation dose. TEM1657 remains active at the low dose of 0.025%.

### 3 Skin shape & histology

TEM1657 restores skin shape in a dose-dependent manner.

Erythema, induration and desquamation are removed.

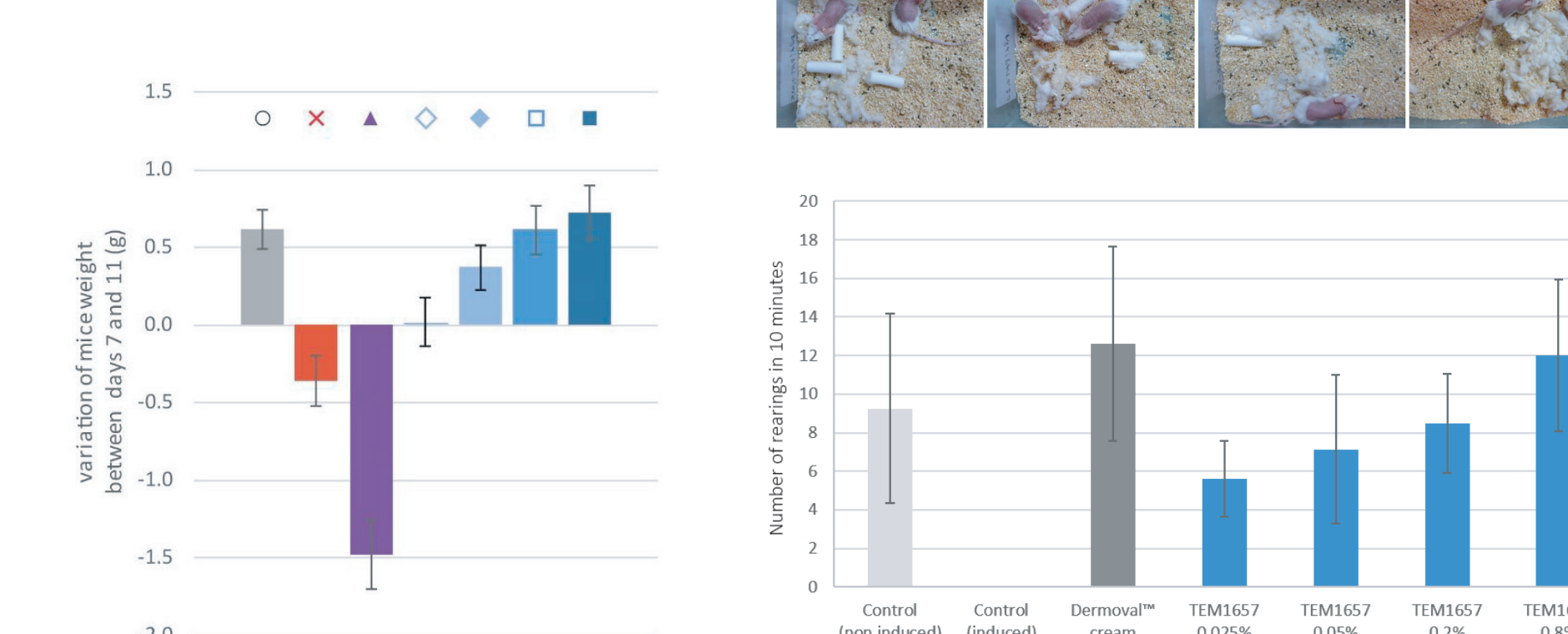
Acanthosis is reduced, and the number of immune cells in the dermis is decreased. Contrarily to Dermoval, no skin atrophy is observed.



### 4 Mice well-being

Body weight variation during treatments.

TEM1657 restores mice well-being and appetite (dose-dependent tendency).



TEM1657 restores natural mice behavior to chew on friable objects (dose dependent tendency).

TEM1657 also restores natural mice exploratory behavior (dose dependent tendency).

### 5 Spleen weight and immunity

Contrarily to Dermoval, TEM1657 does not induce splenotrophy, but rather restores normal spleen size, dose dependently.

