



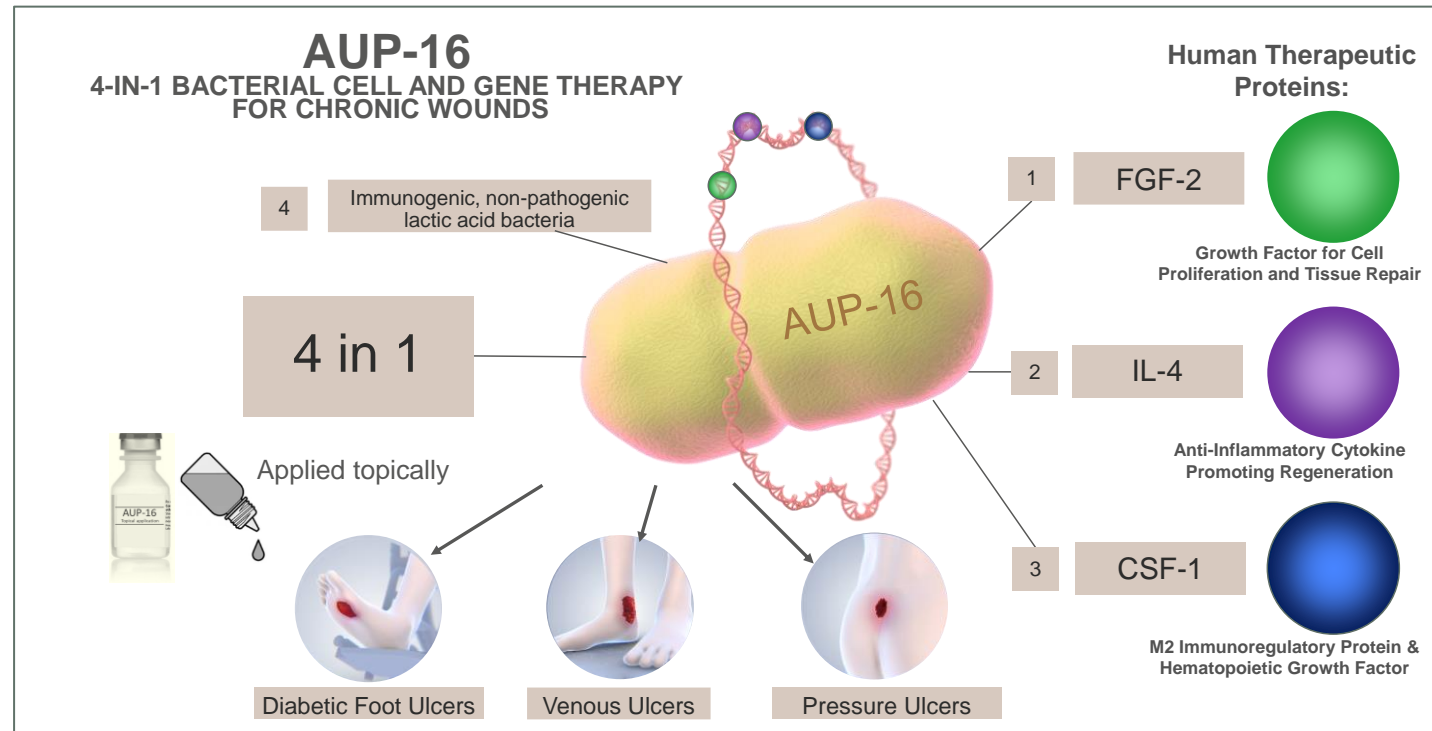
AUREALIS THERAPEUTICS

# AUP-16 MODE OF ACTION

MULTI-TARGET CELL & GENE THERAPIES FOR UNMET MEDICAL NEEDS

# INTRODUCTION

- Aurealis Therapeutics is a Swiss-Finnish clinical stage synthetic biology company developing bacteria-based cell & gene therapies for Chronic Wounds, Oncology and Inflammation
- Our lead clinical asset is AUP-16 (AUP1602-C), a topical four-in-one ATMP gene therapy for chronic wounds
- It consists of genetically engineered *Lactococcus lactis* producing and secreting human growth factors and cytokines in the wound tissue (Fibroblast growth factor 2, Interleukin 4, Colony stimulating factor 1)
- AUP-16 bacterium act as millions of nanoscale bioreactors in the wound, targeting all key components of wound healing: inflammation, proliferation, angiogenesis, and remodelling.



# SEVERE, NON-HEALING DIABETIC WOUNDS HEAL WITH AUP-16 TARGETING FOUR KEY WOUND HEALING MECHANISMS

## AUREALIS 4-IN-1 PRODUCT AUP-16

**TARGET 1**  
INFLAMMATION



**TARGET 2**  
PROLIFERATION



**TARGET 3**  
ANGIOGENESIS



**TARGET 4**  
EPITHELIALIZATION



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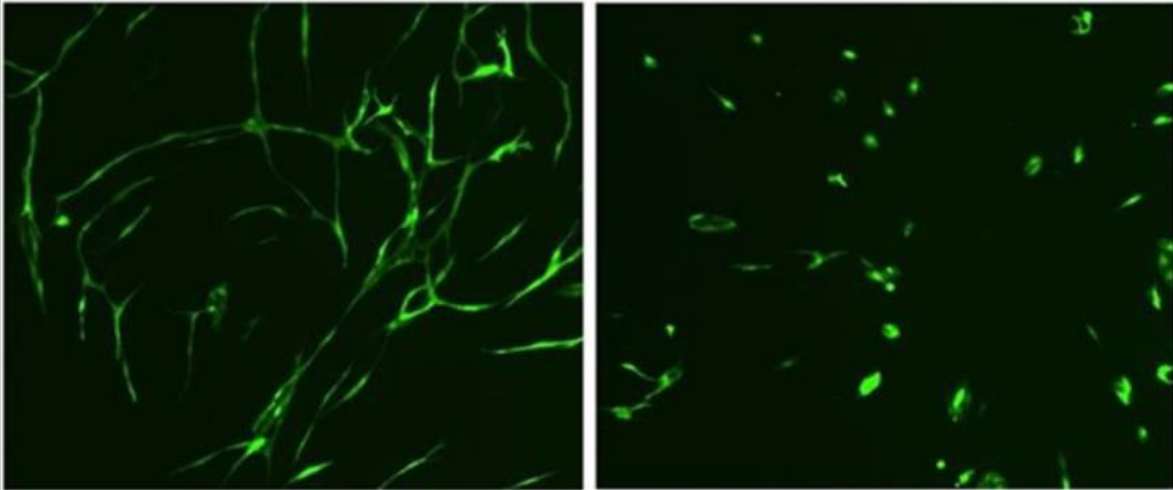
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# AUP-16 PRE-CLINICAL EFFICACY DATA - HUMAN CELL CULTURES

## AUP-16 INDUCES GROWTH OF NEW BLOOD VESSELS (ANGIOGENESIS)

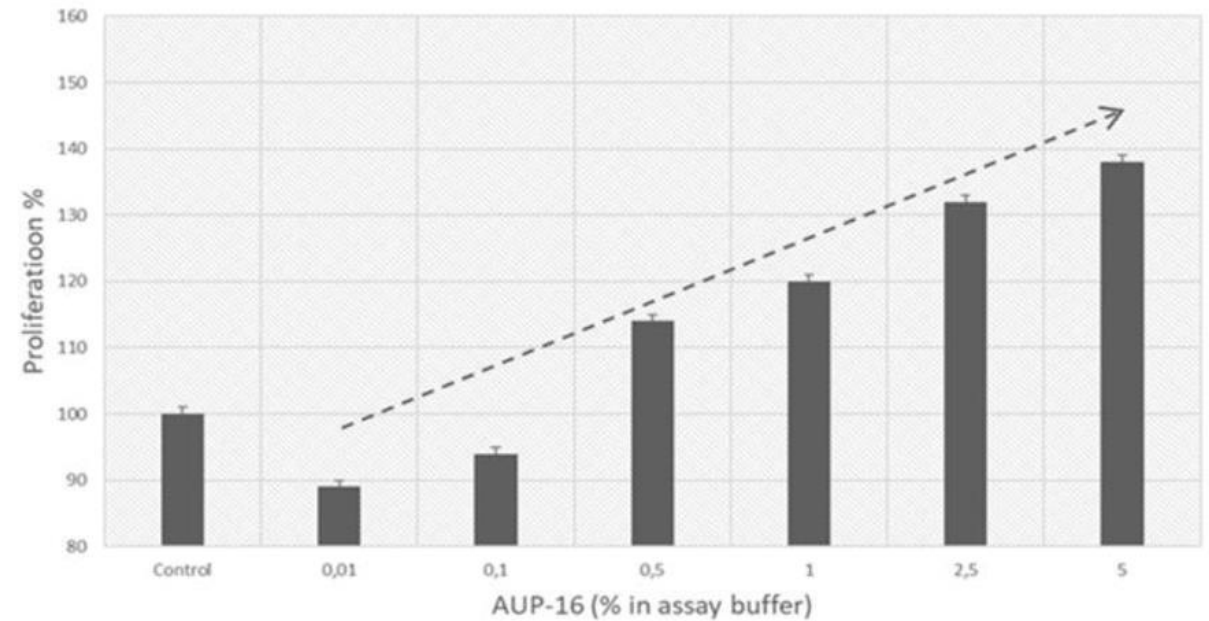
AUP-16

Placebo



Human endothelial cell sprouting assay

## AUP-16 INDUCES DOSE DEPENDENT HUMAN DERMAL FIBROBLAST PROLIFERATION

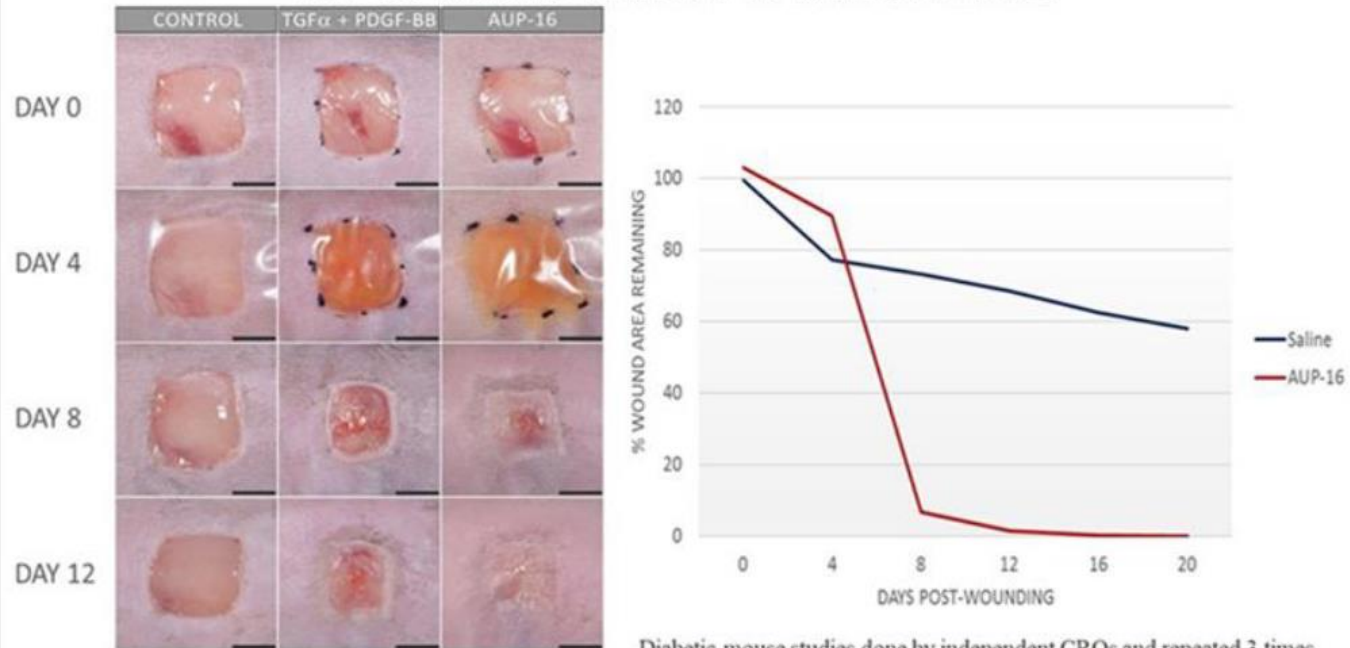


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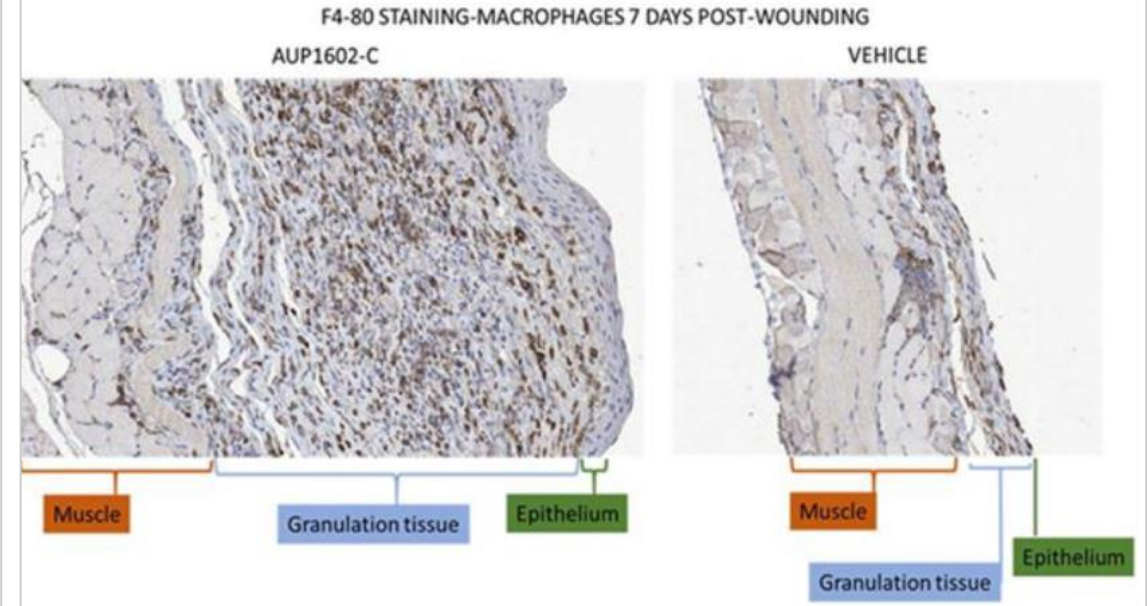
# AUP-16 PRE-CLINICAL EFFICACY DATA – ANIMAL STUDIES

**AUP-16 WOUND HEALING IN DIABETIC MICE**



Diabetic mouse studies done by independent CROs and repeated 3 times with similar results. Dose, frequency and different formulation also done.

**AUP-16 ACTIVATES MACROPHAGES IN DIABETIC MICE WOUNDS**



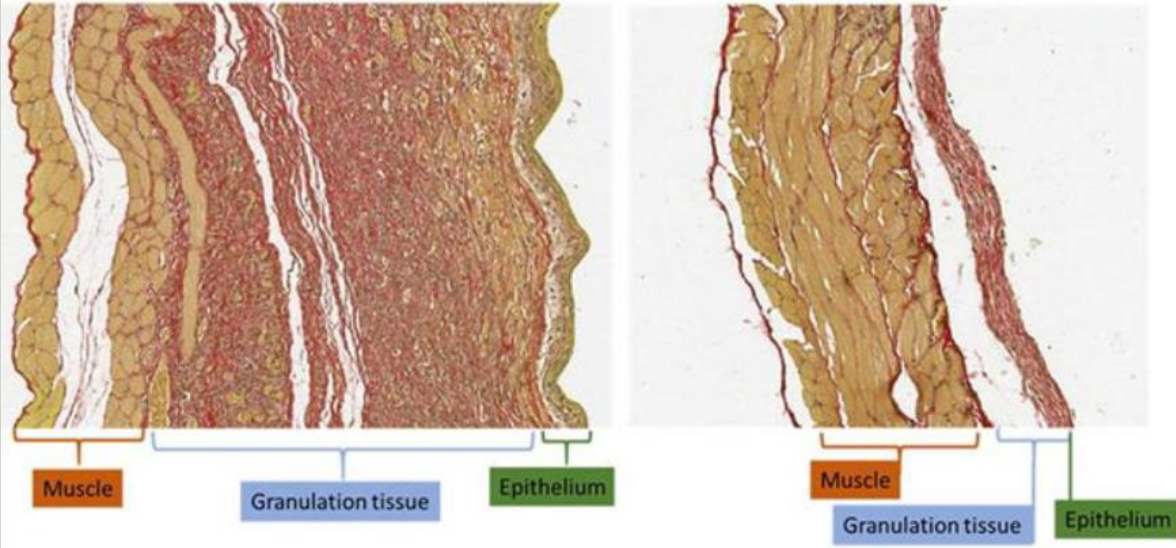
# AUP-16 PRE-CLINICAL EFFICACY DATA – ANIMAL STUDIES (CTD.)

## AUP-16 PROMOTES GRANULATION TISSUE AND COLLAGEN FORMATION IN DIABETIC MICE WOUNDS

PSR STAINING-COLLAGEN (Red) 7 DAYS POST-WOUNDING

AUP16

VEHICLE

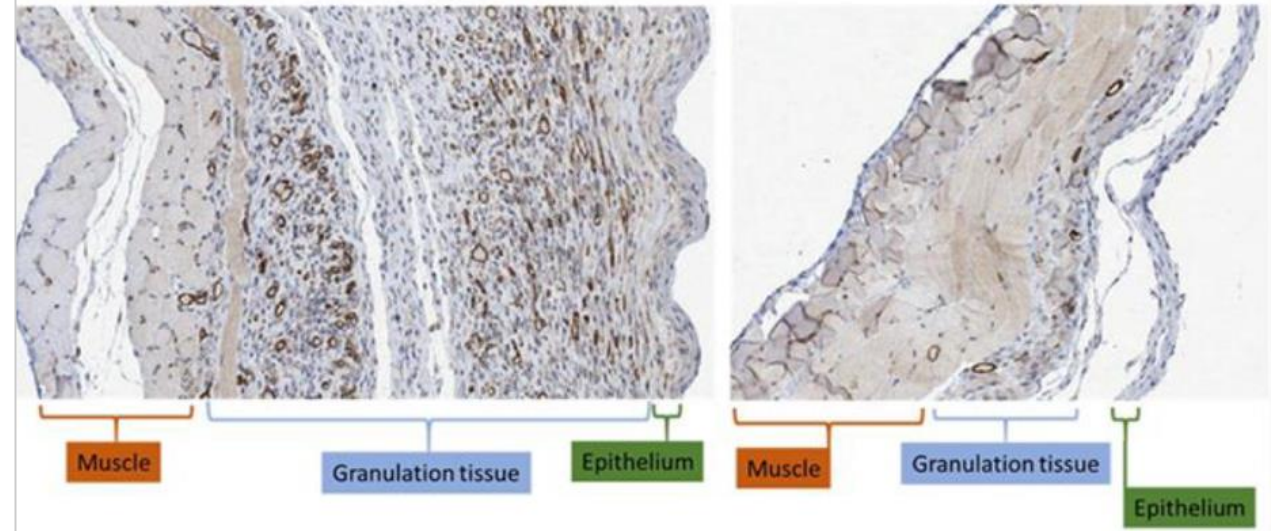


## AUP-16 PROMOTES ANGIOGENESIS IN DIABETIC MICE WOUNDS

CD31 STAINING-ANGIOGENESIS 7 DAYS POST-WOUNDING

AUP1602-C

VEHICLE



STEP 1

Conversion of chronic inflammation to acute inflammation

Upon application, the lactic acid bacteria trigger an immune response, activating resident macrophages and recruiting more immune cells to the wound site. This wake-up step re-boots the chronic inflammatory wound to an acute inflammatory wound.



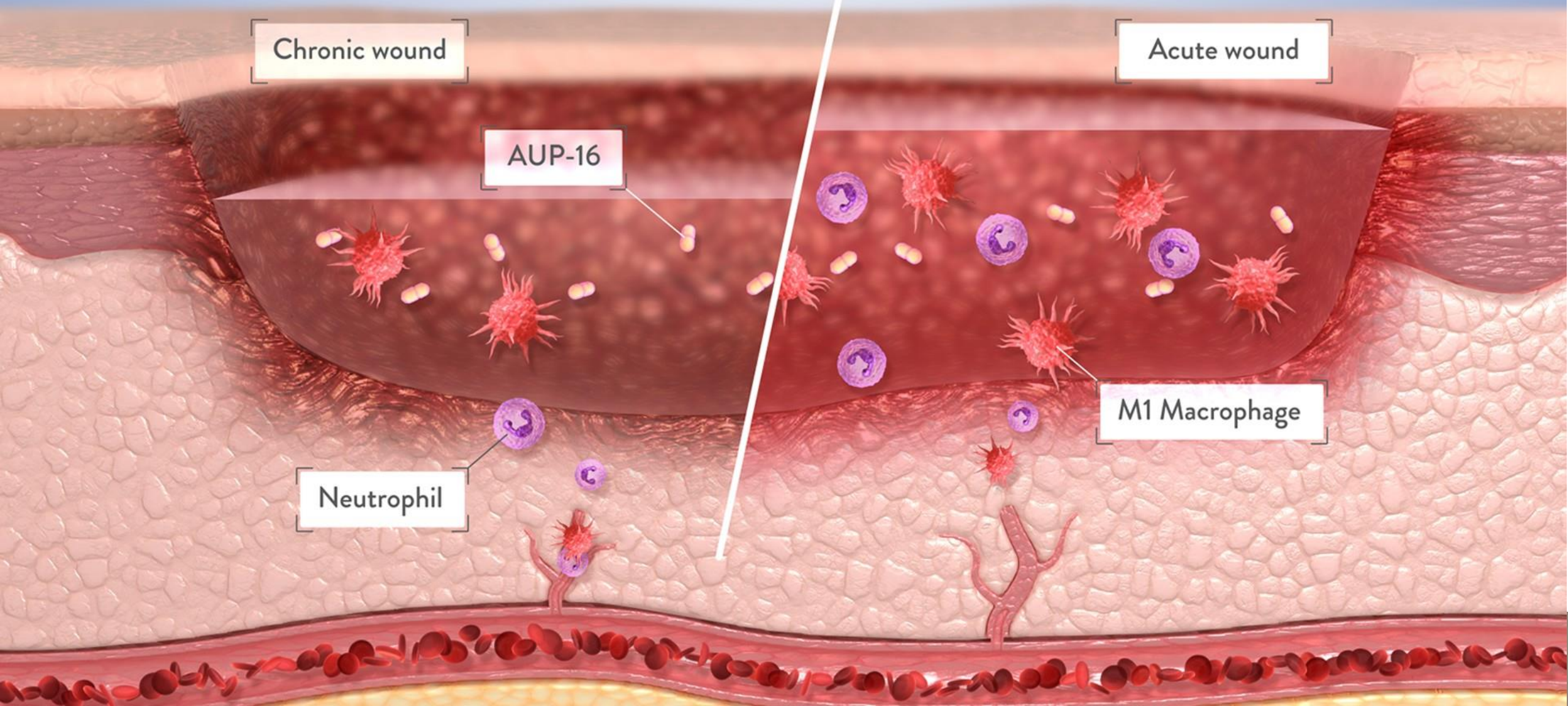
Chronic wound

Acute wound

AUP-16

Neutrophil

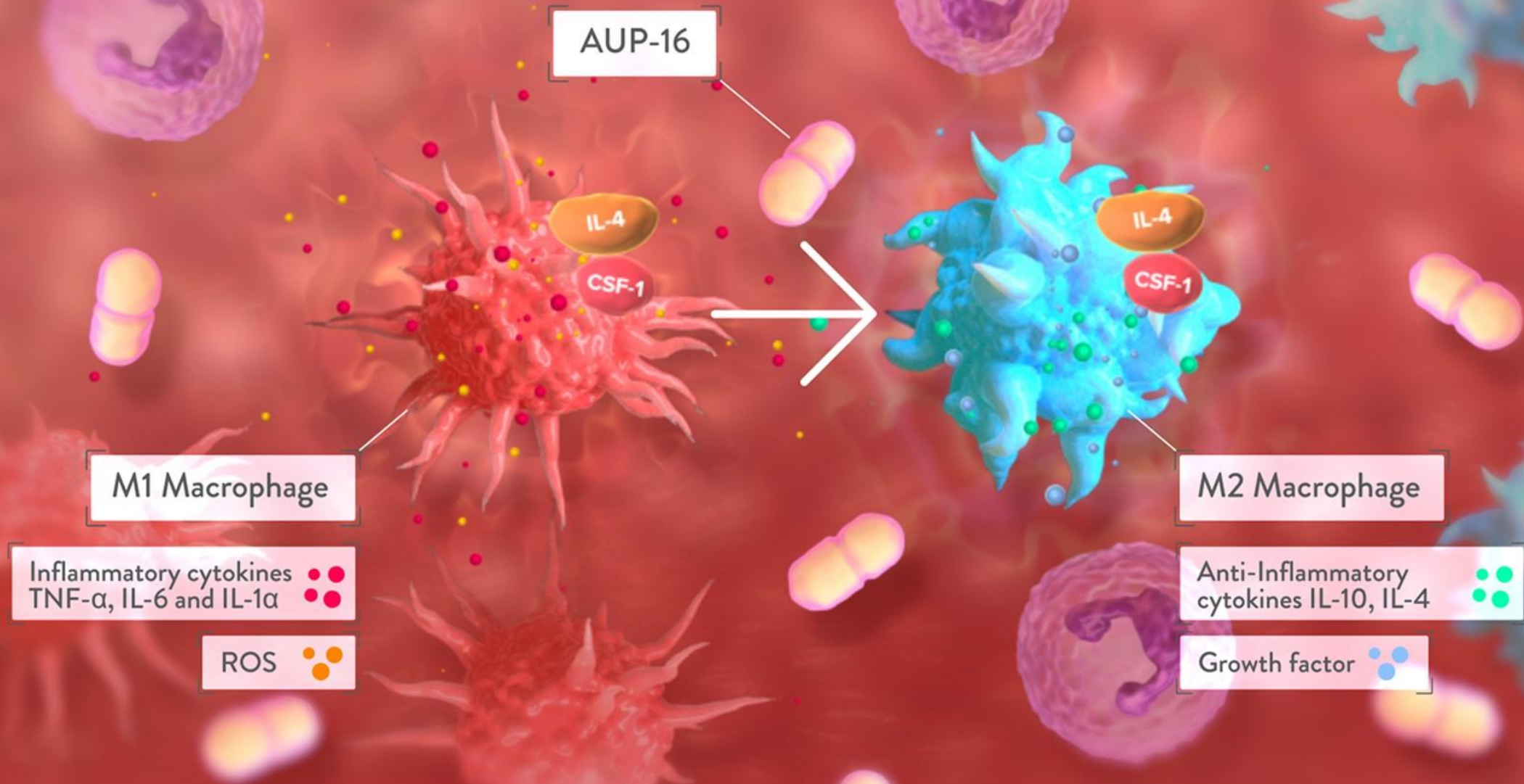
M1 Macrophage



## STEP 2

Converting the hostile inflammatory environment to wound healing inflammatory environment

The proteins produced by AUP-16, in particular IL4 and CSF1, change the setup of the immune cells, cytokines, and growth factors, and convert the wound from a hostile M1 pro-inflammatory state to M2 anti-inflammatory and regenerative state. In addition, the lactic acid bacteria itself has anti-inflammatory properties.

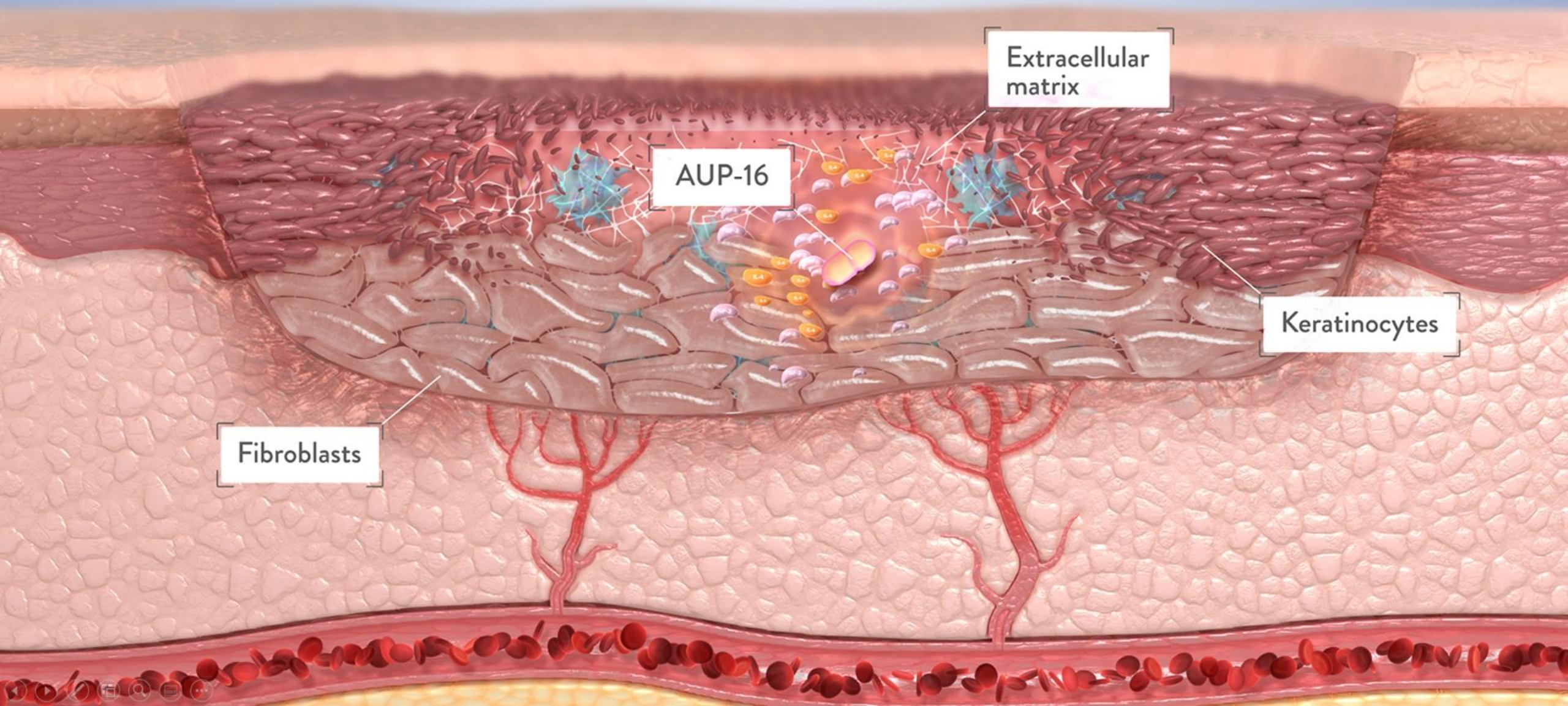




STEP 3

Proliferation

IL4 and FGF2 induce granulation tissue formation i.e. proliferation of fibroblasts, production of extracellular matrix, growth of new blood vessels, and initiate growth of skin epithelium. IL4 and CSF1 maintain the M2 regenerative state for the time needed to complete the wound healing.



Extracellular matrix

AUP-16

Keratinocytes

Fibroblasts

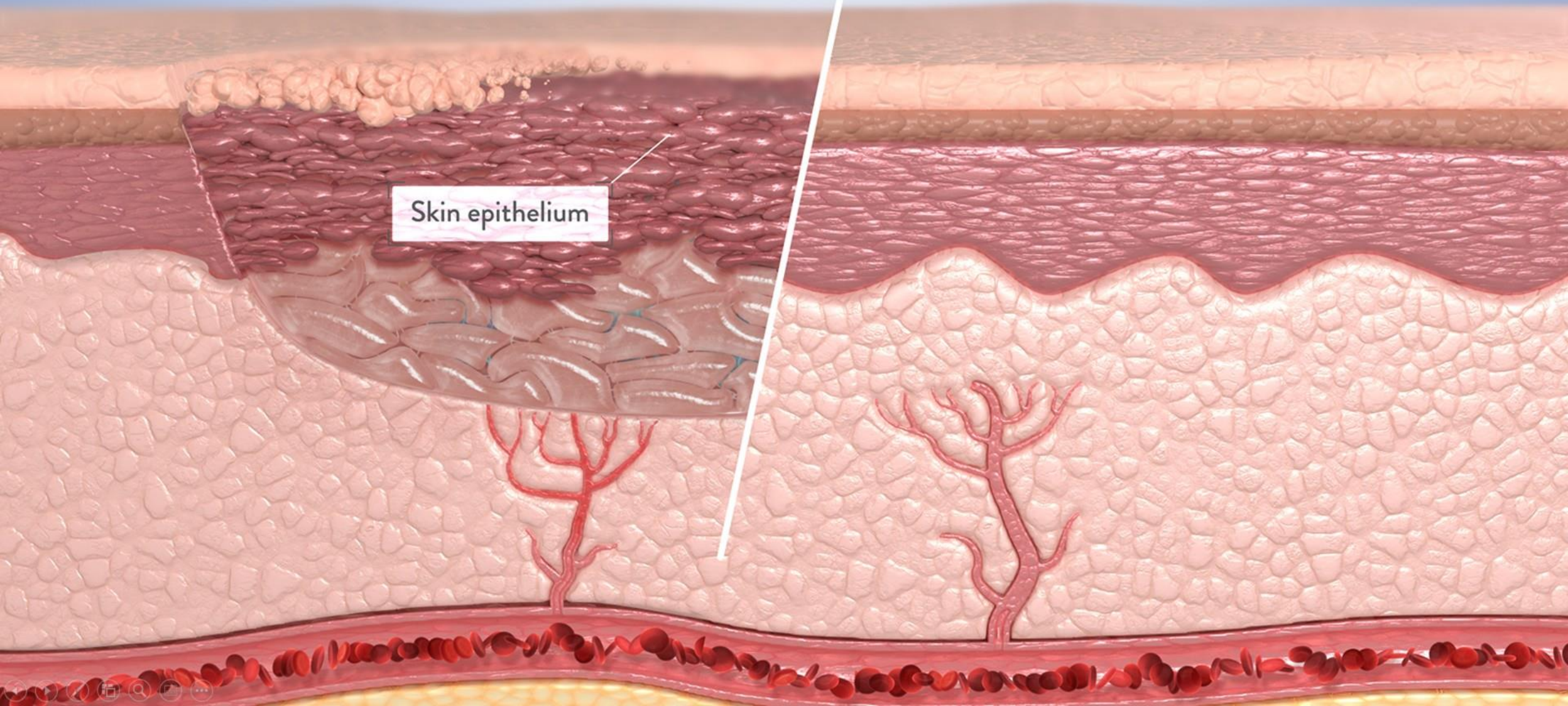
STEP 4

Remodelling

Finally, the skin epithelium regrows to close the wound and the skin layers are reinforced to form intact, durable skin. FGF2 accelerates re-epithelization, keratinocyte proliferation and epithelial to mesenchymal transition, and has anti-scarring effect.



Skin epithelium





# CONTACT:

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