



JEUNE

A Gene-Based Aesthetics  
Company

KB303, AN INNOVATIVE AND  
MINIMALLY INVASIVE HSV-I-  
BASED THERAPY TO IMPROVE  
SKIN ELASTICITY

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# Aging skin is characterized by declining protein levels and dermal matrix alteration

- The primary function of the extracellular matrix (ECM) is to give skin its mechanical and biochemical properties
- Skin aging is a complex process that is caused by intrinsic (age) and extrinsic (eg, UV exposure, cigarette smoke, pollutants, diet, etc.) factors
- These factors cause dermal alterations, impaired collagen synthesis, and degradation of the extracellular matrix which consequently affects overall quality and function of the skin
- Due to their low turnover rate, elastin (ELN) fibers are particularly prone to the accumulation of damage, resulting in a loss of skin resilience and elasticity with age



# KB303 is designed to enable local elastin replacement

## Vector Platform Highlights

### Clinically validated platform

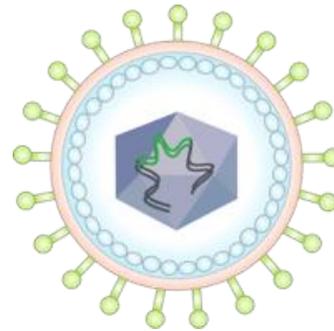
- Jeune product candidates based on Krystal's clinically validated Skin TARgeted Delivery (STAR-D) platform
  - The STAR-D platform is an engineered, replication incompetent HSV-1, which has a natural affinity for skin cells
- Safety, efficacy, and redosability have been validated in rare disease settings with hundreds of doses of STAR-D-based products administered in the clinic to date

### Positioned to fundamentally address – and reverse – the biologic changes associated with age and damage

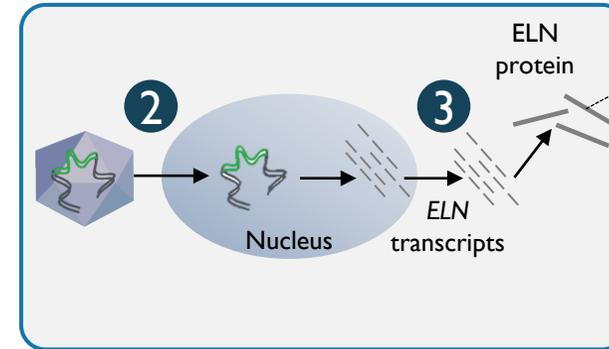
- KB303 enables a patient's cells to produce new elastic fibers to supplement or replace the damaged or absent fibers present in aged or photodamaged skin, enabling directed biorejuvenation

## KB303 Mechanism of Action

### KB303: An Engineered HSV-1 Vector Encoding Human ELN



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Fibroblasts & Keratinocytes

1 Our skin-targeted vector, built on our STAR-D platform, is injected into the dermis where it finds and transduces epithelial cells

2 Once in the nucleus of transduced cells, the vector genome is deposited episomally (does not disrupt the host cell genome)

3 Subsequently, the cell uses the *ELN* gene template to make copies, or transcripts, which are then translated into functional protein

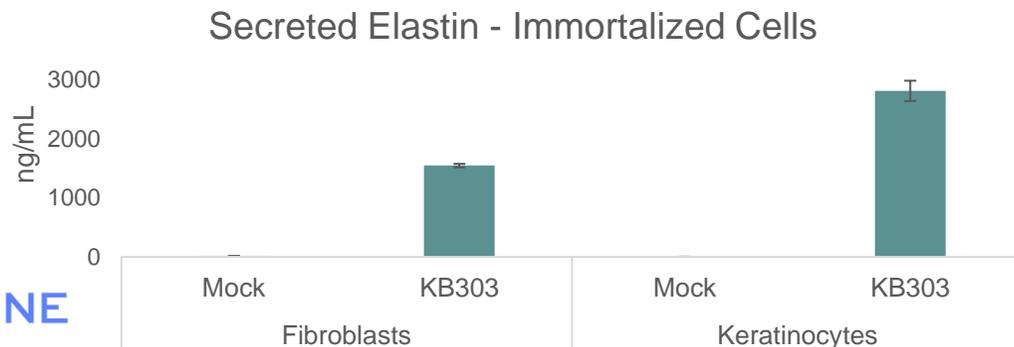
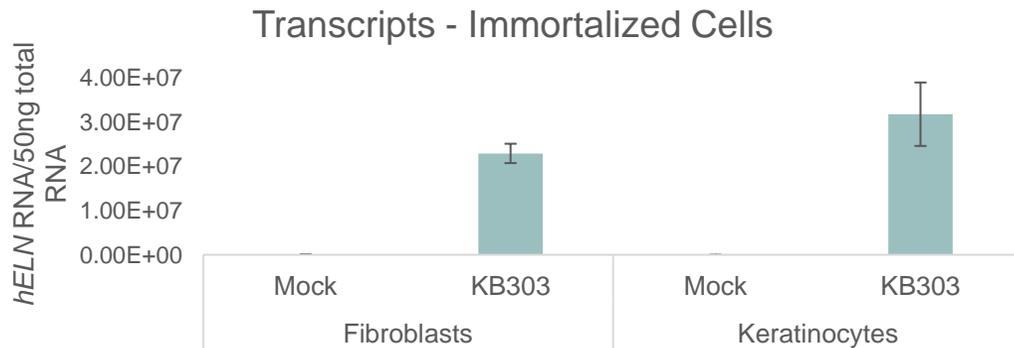
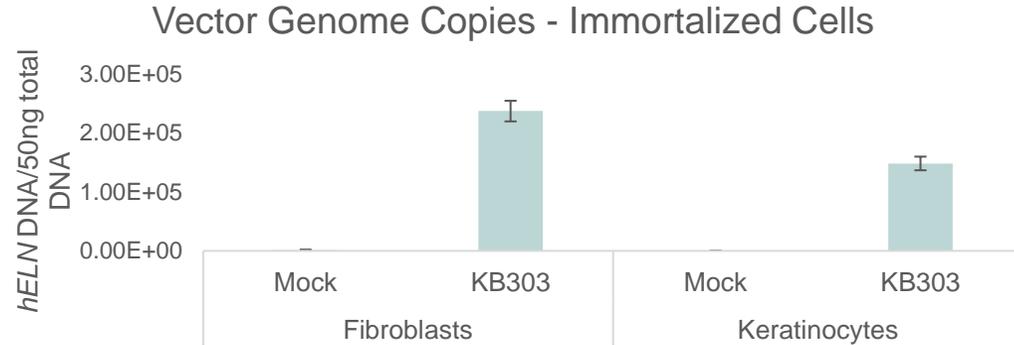
4 The new ELN protein is then secreted into the extracellular space where it forms functional elastic fibers

A black and white profile photograph of a woman with voluminous, curly hair. The image is partially obscured by a dark purple rectangular overlay on the left side, which contains white text. The woman's face is in profile, looking towards the left of the frame. Her hair is thick and curly, framing her face. The lighting is soft, highlighting the texture of her skin and hair.

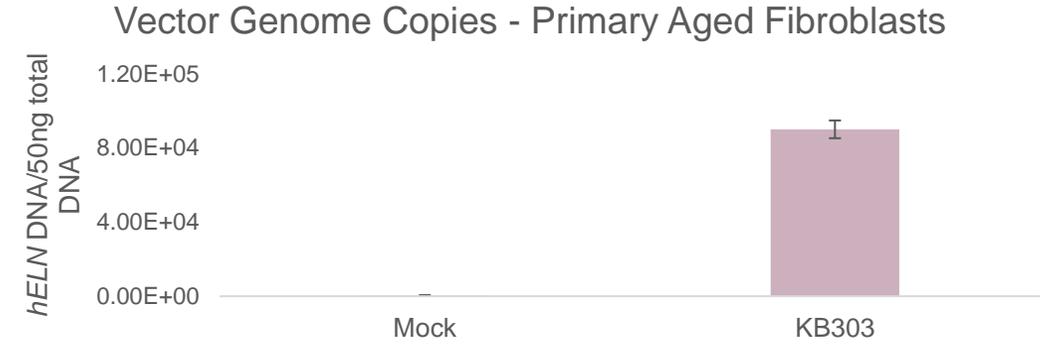
In vitro assessments of  
KB303 in clinically relevant  
human skin cells

# KB303 transduces human fibroblasts and keratinocytes, inducing ELN secretion

## KB303 capably transduces keratinocytes and fibroblasts



## KB303 transduction led to secretion of elastin protein in primary aged (75yo) human dermal fibroblasts

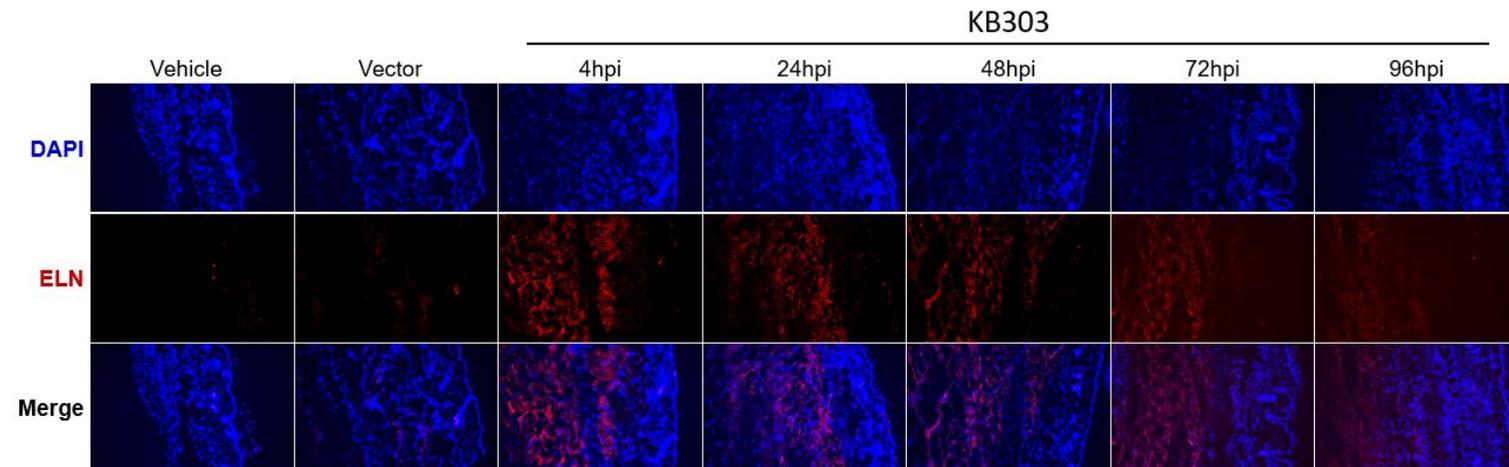
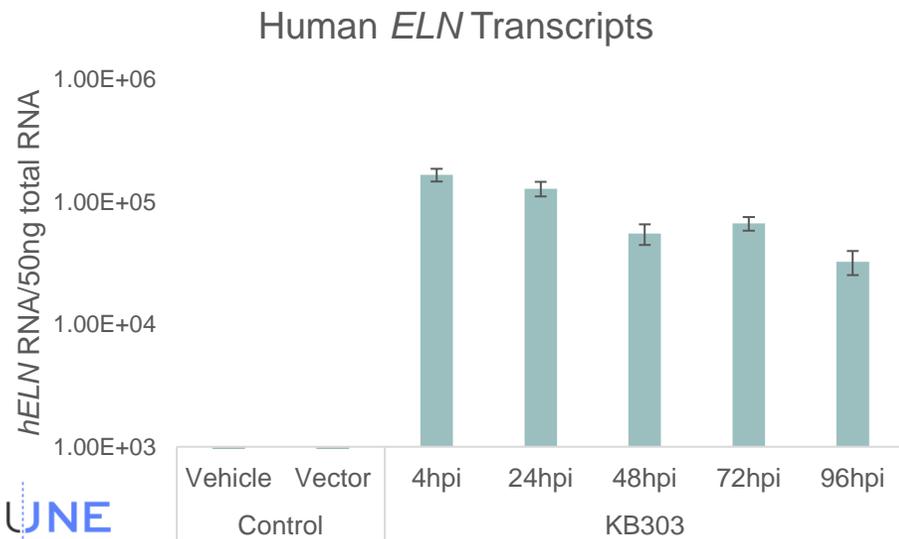
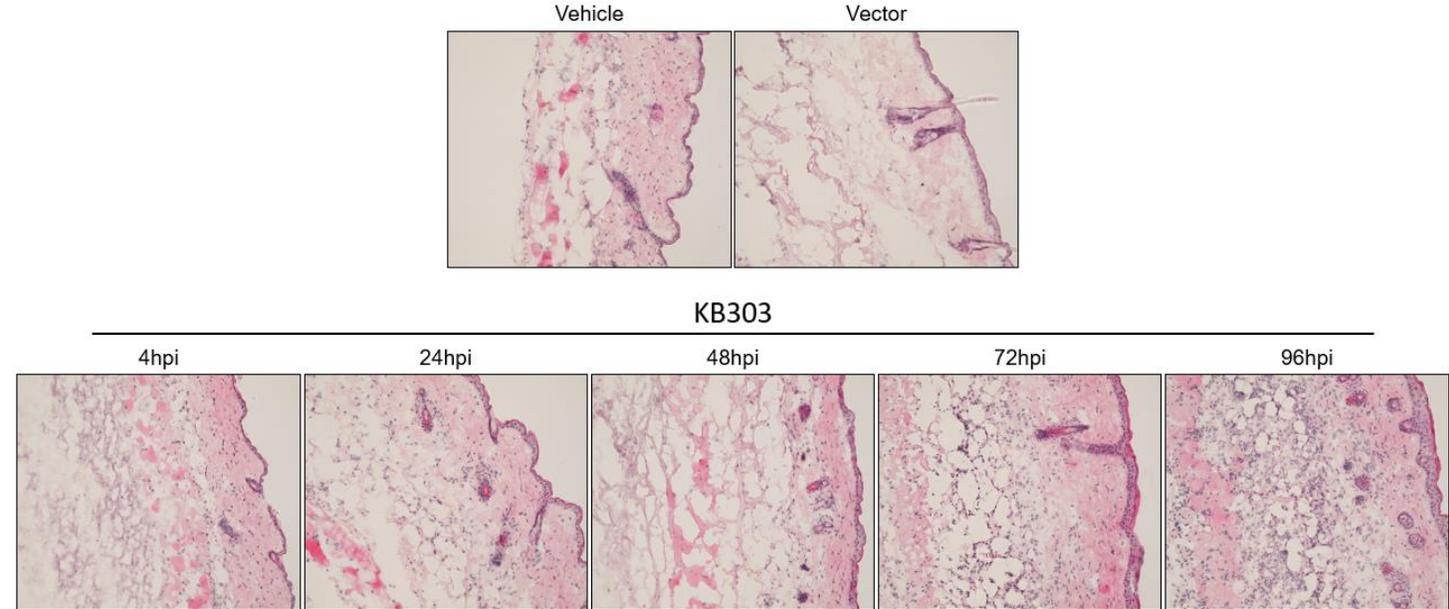
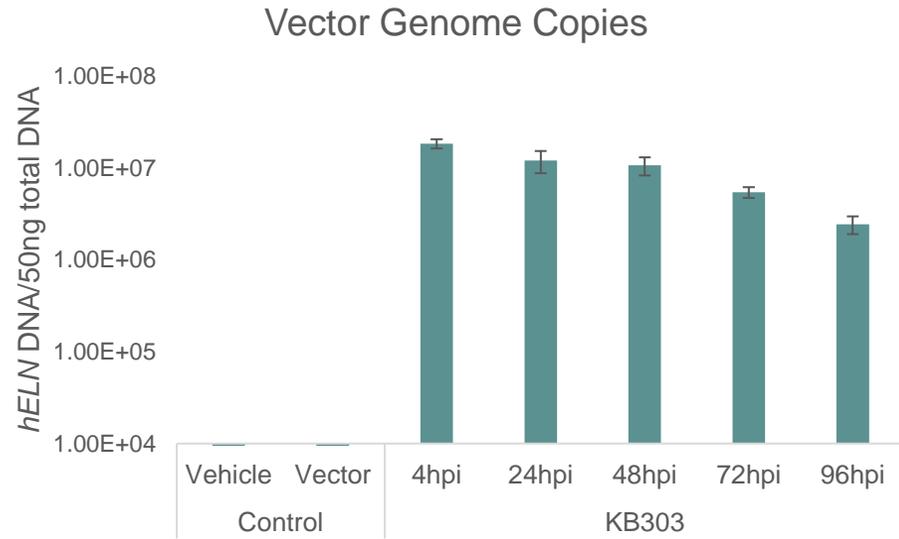




KB303 in vivo  
pharmacokinetics &  
pharmacodynamics

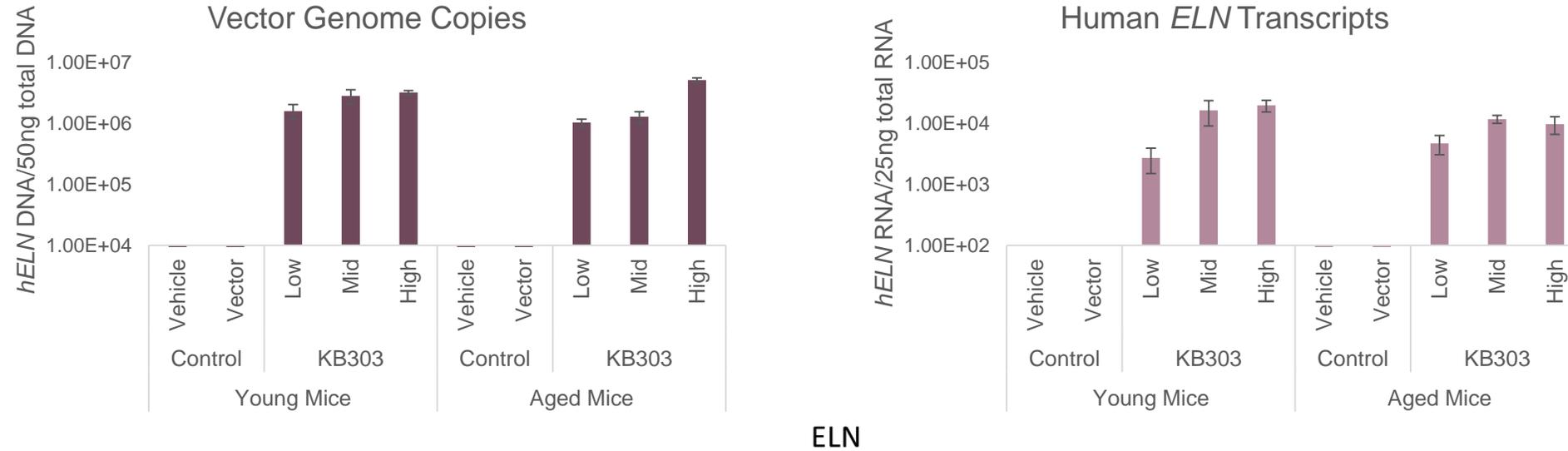
# KB303 produced ELN as early as four hours post intradermal injection in mice

Human ELN protein deposition observed in dermal tissue without apparent toxicity in young animals



# In vivo dose-ranging analysis of KB303 in young and aged mice

A dose-dependent increase in *ELN* expression observed in young and aged mice

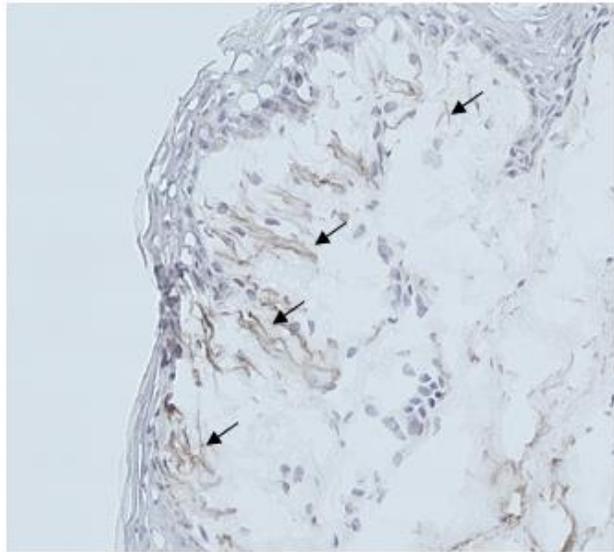


Human ELN immunohistochemistry (IHC)

# KB303 induces elastic fiber formation and deposition in the ECM of treated skin

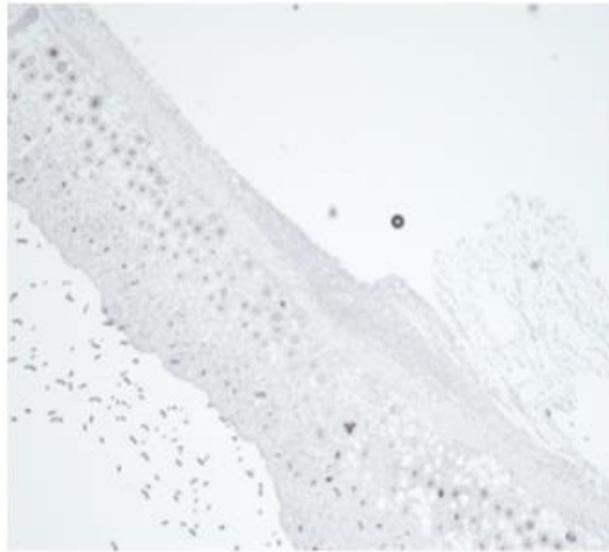
## Mouse skin

Normal Human skin



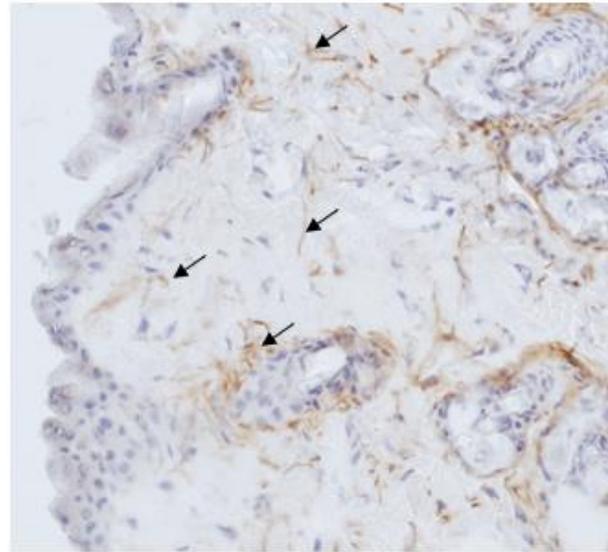
Human ELN IHC

Vector Control



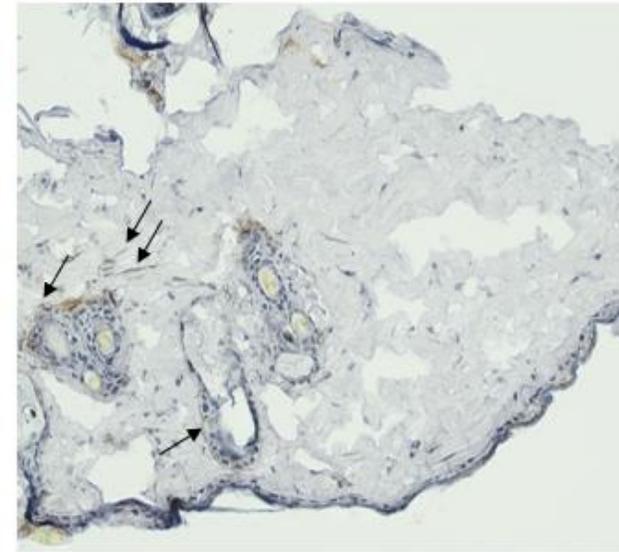
Human ELN IHC

KB303



Human ELN IHC

KB303



Human ELN IHC/VVG

*Arrows denote human elastic fibers*

# Breaking new ground in aesthetic medicine

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## KB303 data summary

- In vitro
  - KB303 readily transduced clinically relevant skin cells, inducing full-length ELN expression and subsequent protein secretion into the extracellular space
- In vivo
  - Successful vector transduction and ELN expression was observed in a dose-dependent manner at both the transcript and protein levels in young and aged immunocompetent mice
  - Immunofluorescence / immunohistochemistry data revealed that the exogenously expressed human protein localized to the mouse dermis, signifying proper delivery to the targeted skin layer
  - Histologic evaluation of skin tissue sections indicated no obvious signs of vector-induced toxicity
  - IHC/Verhoeff-Van Gieson (VVG) staining confirmed proper elastic fiber formation and deposition

Results from these in vitro and in vivo proof-of-concept studies and safety assessments support the future clinical investigation of KB303 for the treatment of age- or environment-related loss in cutaneous elasticity

A clinical trial investigating treatment with KB301 to address the loss of type 3 collagen is ongoing



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