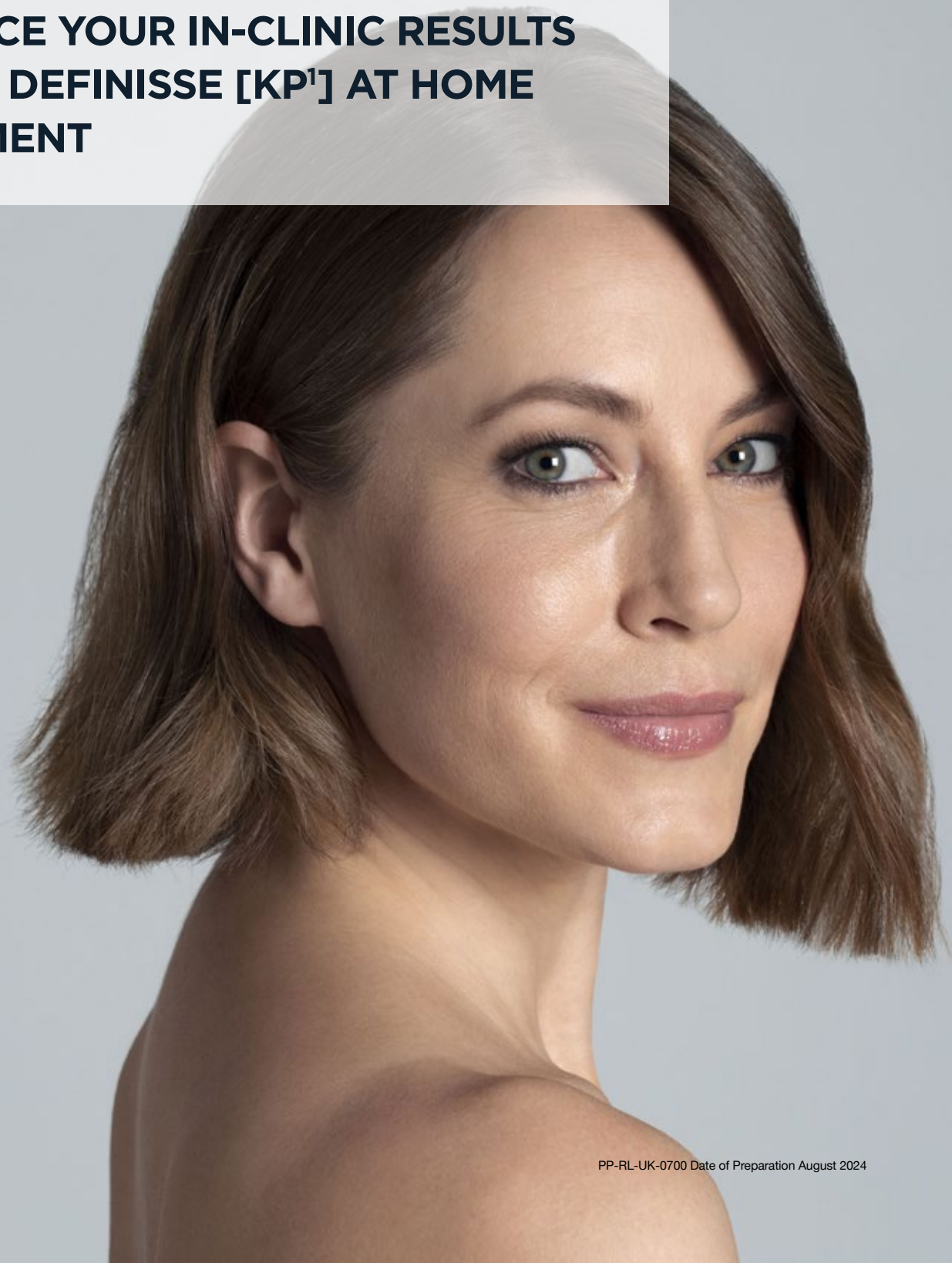
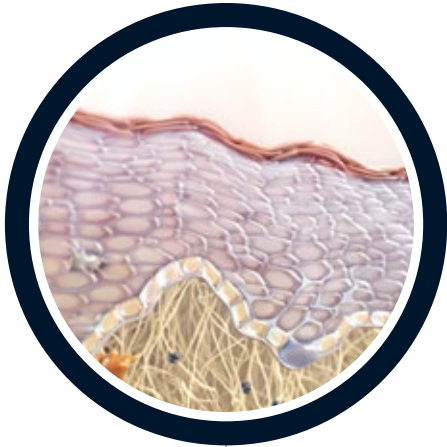


## Definisse [KP<sup>1</sup>]<sup>®</sup> Collagen Modulator

**ENHANCE YOUR IN-CLINIC RESULTS  
WITH A DEFINISSE [KP<sup>1</sup>] AT HOME  
TREATMENT**



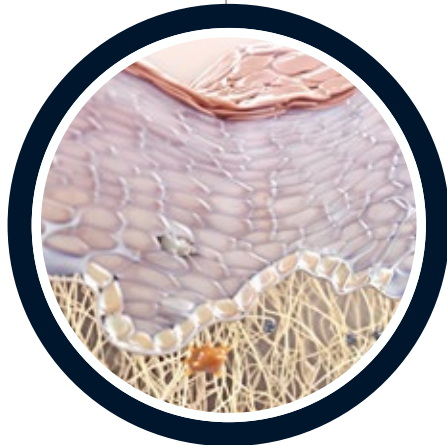
THE MAJOR MODIFICATIONS FOUND IN AGED SKIN ARE  
**QUANTITATIVE AND STRUCTURAL CHANGES  
IN COLLAGEN FIBERS<sup>1</sup>**



## YOUNG SKIN

abundant, tightly packed, and  
well-organized intact collagen fibrils<sup>1</sup>

VS.



## AGED SKIN

collagen fibrils fragmented  
and coarsely distributed<sup>1</sup>

Increased collagen degradation and reduced collagen biosynthesis  
are both involved in a  
**ABERRANT COLLAGEN HOMEOSTASIS,**  
which results in a **NET COLLAGEN DEFICIENCY<sup>1,13</sup>**

# With age the skin's ability to replenish collagen naturally

**decreases** by about **1.0% - 1.5%** per year<sup>2</sup>

## THIS DECREASE IN COLLAGEN

is one of the characteristic hallmarks associated with the appearance of  
**FINE LINES AND DEEPER WRINKLES<sup>2</sup>**

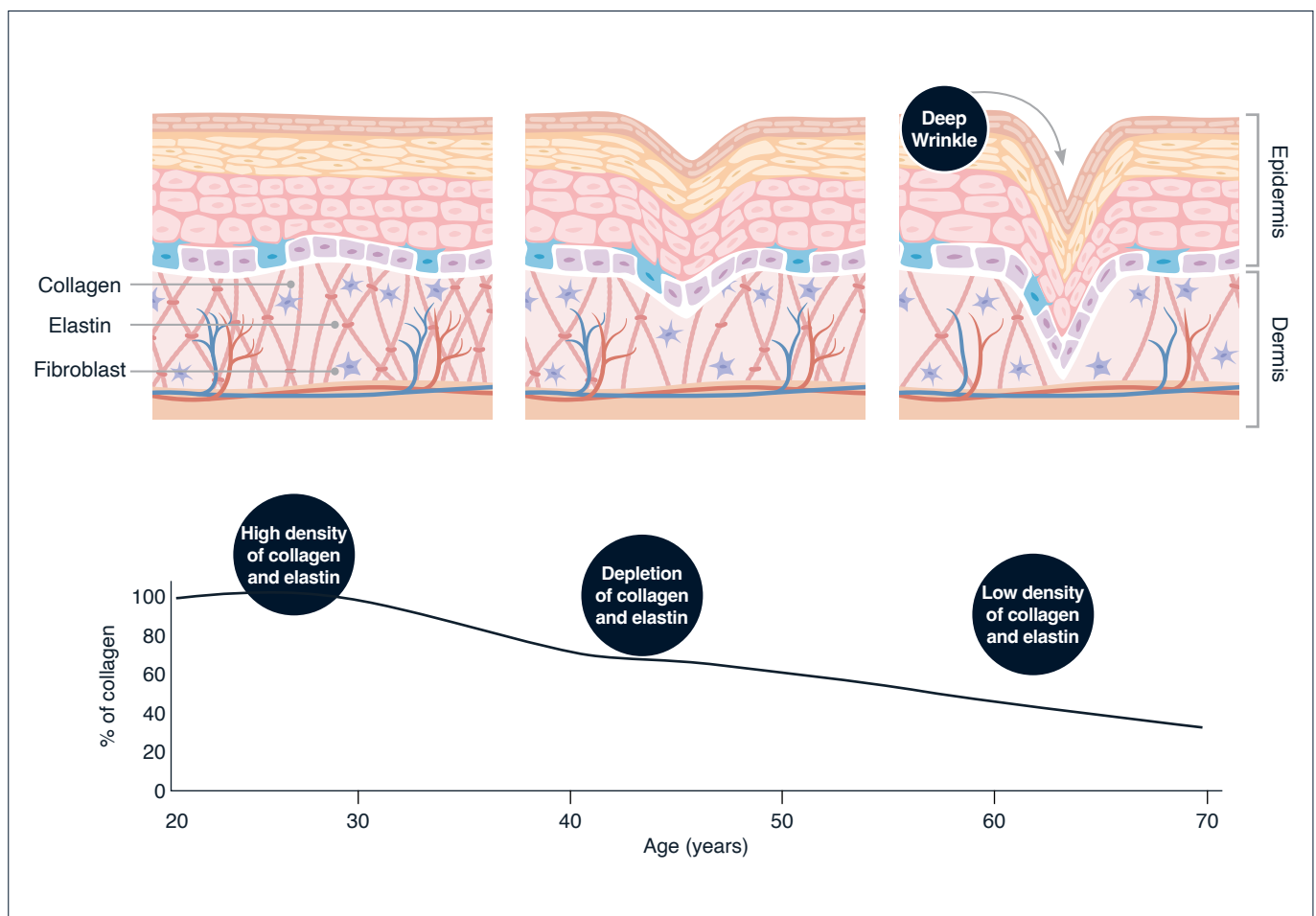


Figure 1. Modified from Figure 5, Reilly D. M. et al 2021<sup>2</sup>

# COLLAGEN DEGRADATION AND UNMET NEEDS



Collagen is responsible for the **stability** and **strength** of the body tissues<sup>3</sup>



**Type I collagen** is by far the most abundant protein in human skin, comprising greater than 90% of its dry weight. The unique physical properties of collagen fibers confer structural integrity to skin<sup>4</sup>



While many anti-ageing strategies focus on stimulating collagen production, **acting against collagen degradation** represents an innovative bio-inspired option **to slow down the ageing process**

## TWO FAMILIES OF ENZYMES ARE ABLE TO DEGRADE COLLAGEN:<sup>6</sup>

**Matrix Metallo  
Proteases (MMPs)**

**Serine  
Proteases**

Their activity is regulated by **endogenous modulators**:<sup>6,7</sup>

**TIMPs**

(Tissue Inhibitors of Metallo Proteinase)<sup>7</sup>

**Serpins**

(Serine Protease Inhibitors)<sup>6</sup>

# INTRODUCING THE REVOLUTIONARY [KP<sup>1</sup>]<sup>®</sup> BIO-INSPIRED RANGE

## DEFINISSE [KP<sup>1</sup>]<sup>®</sup> COLLAGEN MODULATOR

WITH THE EXCLUSIVE PEPTIDE [KP<sup>1</sup>], DERIVED FROM THE SERINE  
PROTEASE INHIBITOR SERPIN A1.<sup>8-10,13</sup>

Key Peptide One [KP<sup>1</sup>] showed a good collagen modulation, protecting collagen  
against degradation.<sup>6,11-13</sup>



USER BENEFITS: FIRMNESS, LESS WRINKLES, AND BRIGHTER SKIN



Each formulation combines [KP<sup>1</sup>] with high and low molecular  
weight Hyaluronic Acid (HA) and specific ingredients, for a  
radiant and younger-looking skin.

**Definisse [KP<sup>1</sup>]<sup>®</sup>**  
redensifying cream

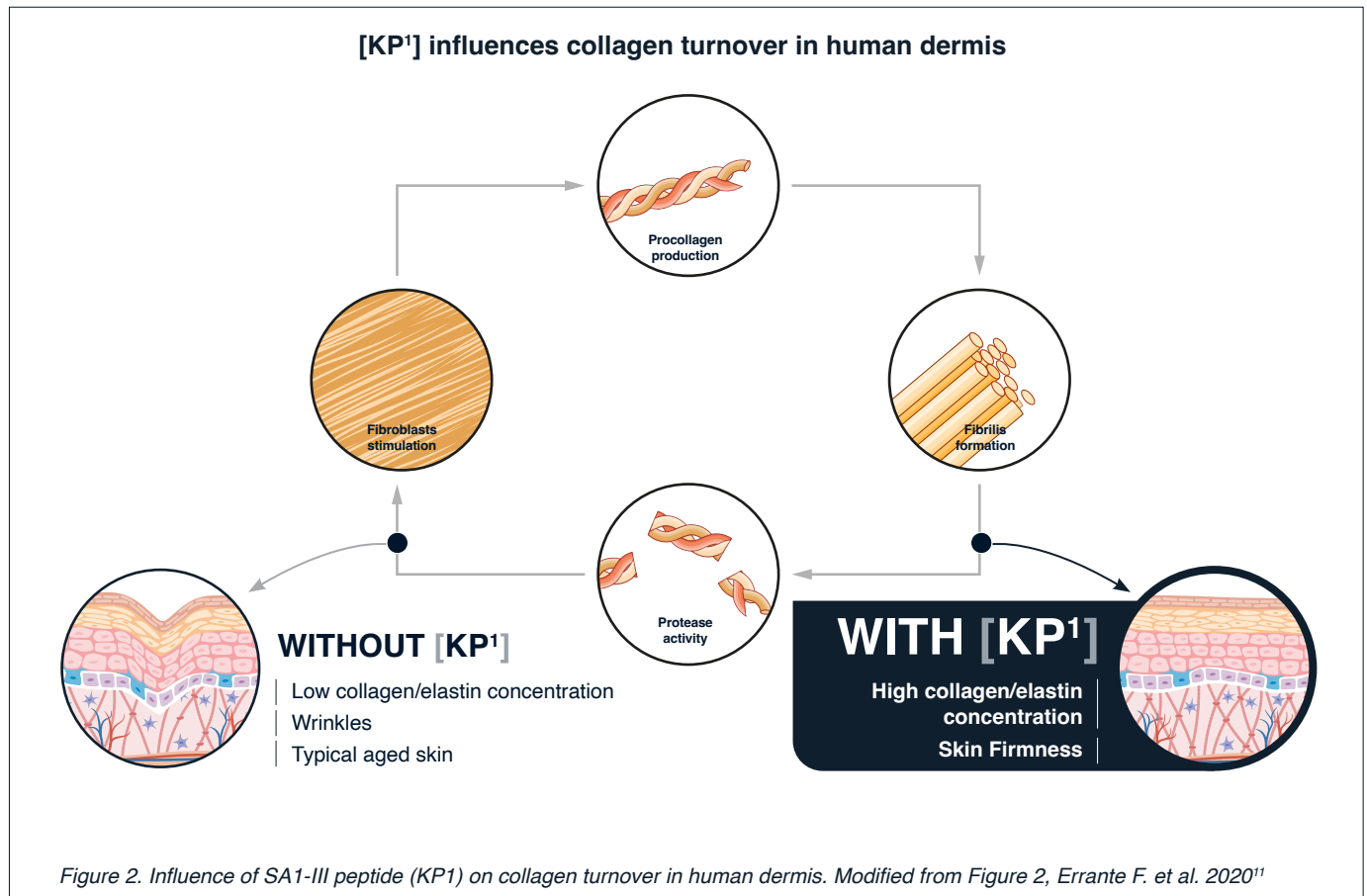
**Definisse [KP<sup>1</sup>]<sup>®</sup>**  
regenerating serum

**Definisse [KP<sup>1</sup>]<sup>®</sup>**  
revitalising eye contour

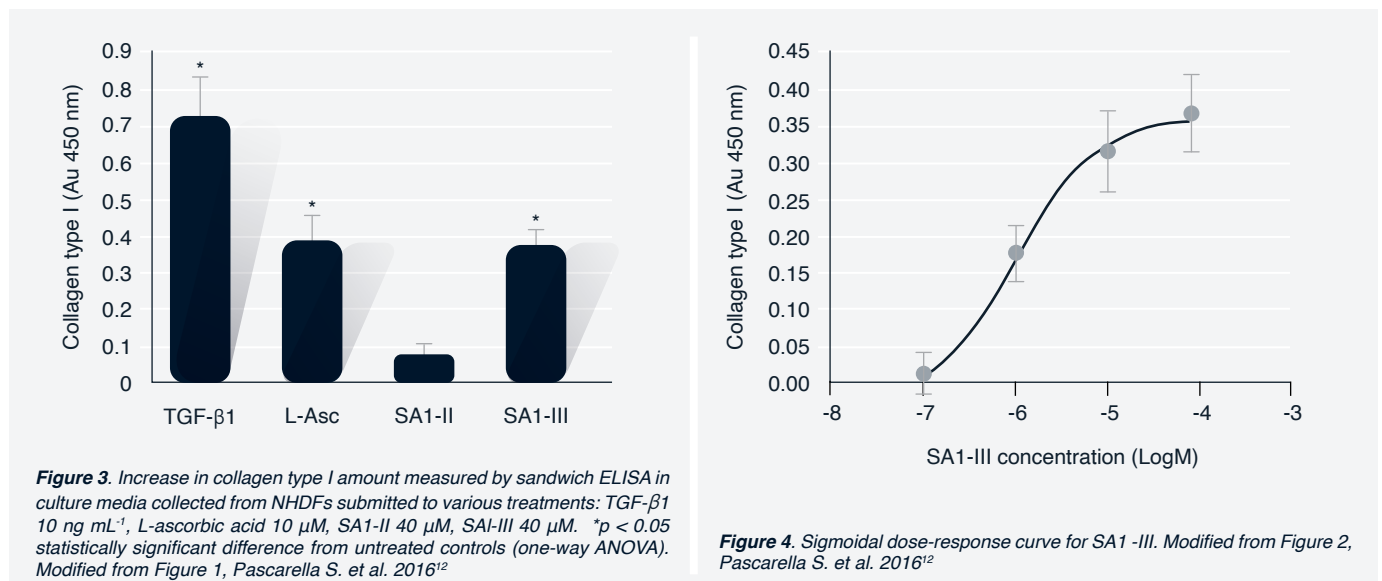


## [KP<sup>1</sup>] COLLAGEN MODULATOR

KEY PEPTIDE ONE - FIRST IN CLASS BIO-ACTIVE PEPTIDE



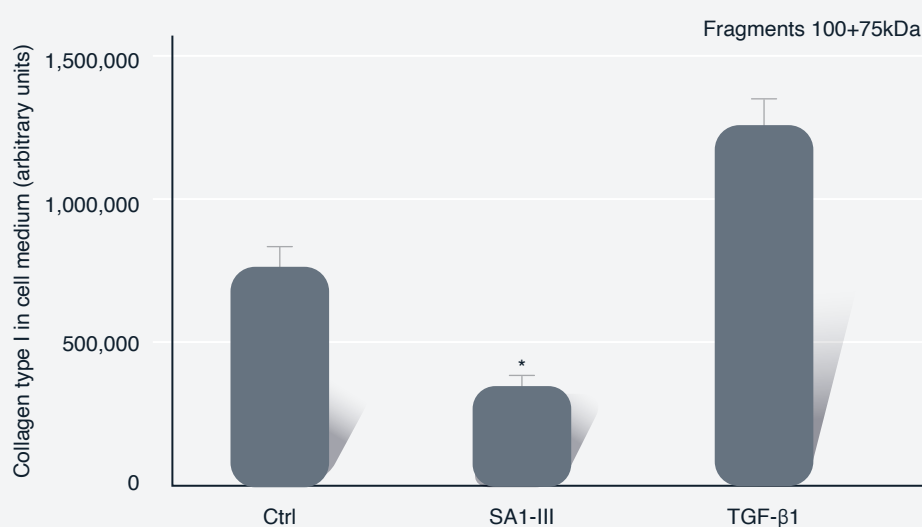
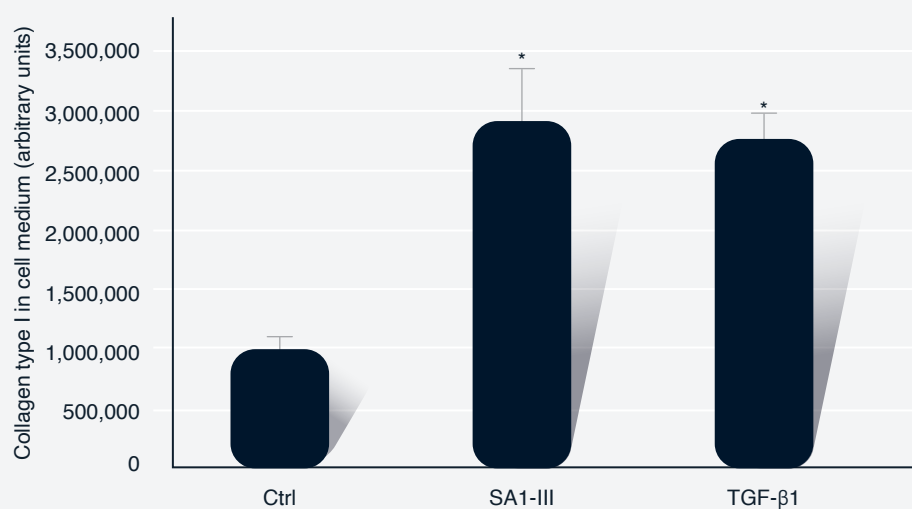
Peptide [KP<sup>1</sup>] (termed SA1-III\* in the scientific literature) **is able to increase collagen type I concentration** in cultured normal human dermal fibroblasts (NHDFs).<sup>12</sup>



\*SA1-III: Scientific name Serpin A1-III



Further *in vitro* studies demonstrate that peptide [KP<sup>1</sup>] (termed SA1-III\*) increases collagen type I concentration in cultured human dermal fibroblasts **through reduction of collagen degradation**.<sup>13</sup>



**Figure 5.** Effect of SA1-III (20  $\mu$ M) peptide and TGF- $\beta$  (10 ng/mL) on soluble collagen levels in cell-conditioned medium (72 h treatment). The results are shown for NHDFs for collagen type I (upper level) and for the collagen fragments (lower panel). There is a strong decrease in all fragment forms upon SA1-III treatment. Modified from Figure 3, Cipriani C. et al. 2018<sup>6</sup>

\*SA1-III: Scientific name Serpin A1-III

\* $P < 0.05$  statistically significant difference from the corresponding control(Ctrl).



# Definisse [KP<sup>1</sup>]<sup>®</sup> regenerating serum

## Collagen Modulator Bio-peptide



Clinically proven effective in addressing dullness and reducing fine lines and wrinkles.<sup>8</sup>



### USER BENEFITS

The concentrated, fast-absorbing formula provides immediate and long-lasting hydration, promoting a luminous, nourished, and velvety-smooth skin.<sup>8</sup>



### [KP<sup>1</sup>] Collagen Modulator Bio-peptide

RELIFE's exclusive, first-in-class, bio-active peptide.<sup>8</sup>

With<sup>8</sup>

- **White Truffle Extract** fragrance-less, that increases skin elasticity and performs a filler effect
- **2 next-generation HAs**, that increase hydration and promote new collagen substrate production
  - **High molecular weight HA** sits on the surface of the skin to prevent dehydration
  - **Very low molecular weight HA** can penetrate deeper into the skin significantly improving hydration
- **Vitamin B5**, stimulates the physiological skin regeneration.

### How to use:

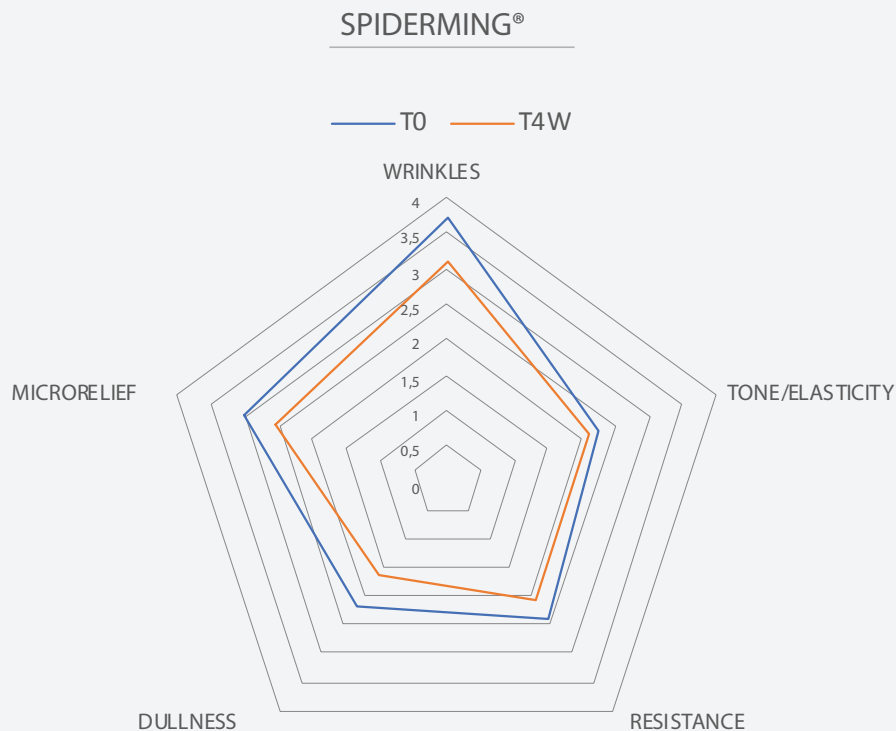
Apply a few drops to clean skin in the morning and evening by massaging until completely absorbed. Can be used in combination with aesthetic medicine treatments to improve results.<sup>8</sup>

30 ml

Dermatologically tested<sup>8</sup>



After 4 weeks of treatment, the skin appeared overall “younger”



After 4 weeks of application the treatment induced significant improvements in the following parameters:.\*<sup>14</sup>

- Significant variation of “**Crow’s Feet**” profilometry was found after 4 weeks (T4W)\*:<sup>13</sup>  
-17.1% in the average roughness in  $\mu\text{m}$  of the analysed profile (Ra parameter)
- +32.0%<sup>†</sup> in the **skin hydration** values
- +3.3%<sup>§</sup> in the **skin deep hydration** values
- Statistically significant improvement<sup>†</sup> in the **skin elasticity** values:  
-28.4% in the skin extensibility value (R0 parameter)  
+8.7% in the gross elasticity value (R2 parameter)
- Statistically significant improvement<sup>§</sup> in the **skin roughness** values:  
-13.4% in the average roughness value (Sa parameter)  
-14.3% in the average maximum roughness value (Sz parameter)
- + 2.67%<sup>†</sup> in the **skin echogenicity density** values (R2 parameter)

\*Clinical instrumental test on 20 female subjects 37-60 years old who applied Definisse [KP<sup>1</sup>]<sup>®</sup> regenerating serum twice a day for 4 weeks<sup>14</sup>

<sup>†</sup>Statistically significant ( $p < 0.0001$ )

<sup>§</sup>Statistically significant ( $p < 0.001$ )

# Definisse [KP<sup>1</sup>]<sup>®</sup> redensifying cream

## Collagen Modulator Bio-peptide



Clinically proven effective in achieving significant improvement on five anti-ageing parameters after only 4 weeks of use: hydration, elasticity, density, roughness, and brightness.<sup>9</sup>



### USER BENEFITS

The lightweight, easy-to-absorb formula provides immediate and long-lasting hydration, leaving the skin nourished, firm, and velvety smooth.<sup>9</sup>



### [KP<sup>1</sup>] Collagen Modulator Bio-peptide

RELIFE's exclusive, first-in-class, bio-active peptide.<sup>9</sup>

With<sup>9</sup>

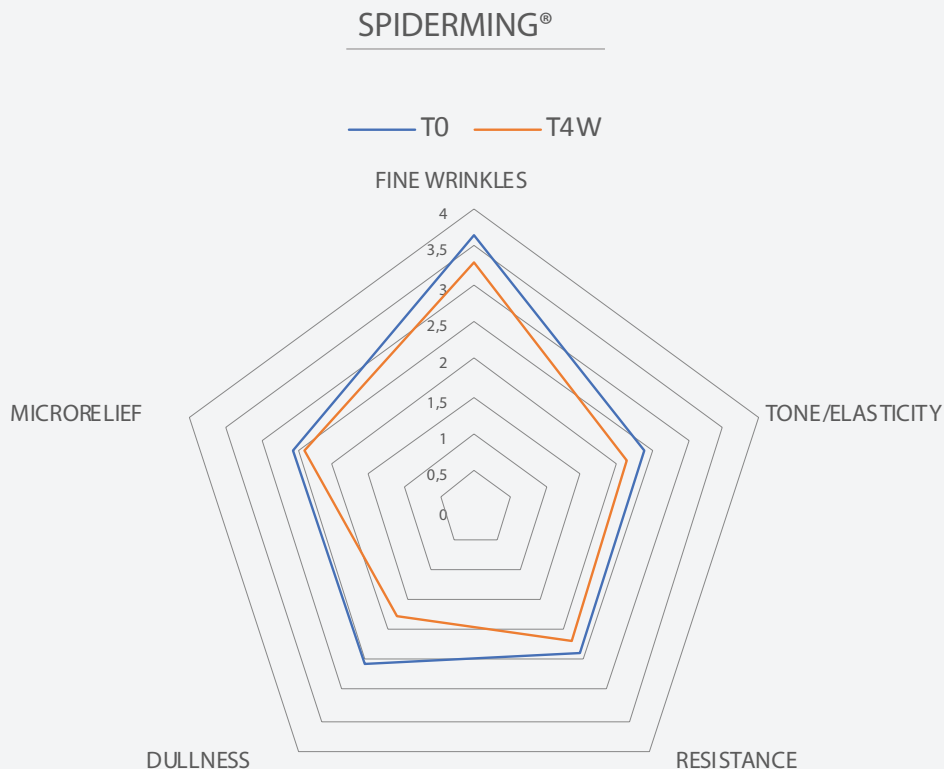
- **Phytosphingosine**, that helps to maintain the skin barrier function
- **Creatine for cosmetic use**, that increases cellular energy
- **2 next-generation HAs**, that increase hydration and promote new collagen substrate production
  - **High molecular weight HA** sits on the surface of the skin to prevent dehydration
  - **Very low molecular weight HA** can penetrate deeper into the skin significantly improving hydration
- **Vitamin B5**, stimulates the physiological skin regeneration
- **Vitamin E**, with antioxidant properties
- **Avocado oil**, that nourishes the skin
- **Lactil<sup>®</sup>**, that is a blend of humectants in aqueous solution acting as a substitute of the "Natural Moisturizing Factor" (NMF) of human skin

### How to use:

Apply to clean skin in the morning and evening by massaging until completely absorbed.  
Can be used in combination with aesthetic medicine treatments to improve results<sup>9</sup>

50 ml  
Dermatologically tested<sup>9</sup>

After 4 weeks of treatment, the skin appeared overall “younger”



After 4 weeks of application the treatment induced significant improvements in the following parameters:<sup>\*15</sup>

- Significant variation of “**Crow’s Feet**” profilometry was found after 4 weeks (T4W)<sup>\*:13</sup>  
-10.4% in the average roughness in  $\mu\text{m}$  of the analysed profile (Ra parameter)
- Statistically significant improvement<sup>†</sup> in the **skin elasticity** values:  
-14.3% in the skin extensibility value (R0 parameter)  
+5.8% in the gross elasticity value (R2 parameter)
- Statistically significant improvement in the **skin roughness** values:  
-13%\*\* in the average roughness value (Sa parameter)  
-10.1%<sup>§</sup> in the average maximum roughness value (Sz parameter)
- + 2.23%<sup>§</sup> in the **skin echogenicity density** values (R2 parameter)
- +43.1%<sup>†</sup> in the in the mean basal values of **skin hydration** values

<sup>\*</sup>Clinical instrumental test on 20 female subjects 40-65 years old who applied Definisse [KP<sup>1</sup>]<sup>®</sup> regenerating serum twice a day for 4 weeks<sup>15</sup>

<sup>†</sup>Statistically significant ( $p < 0.0001$ )

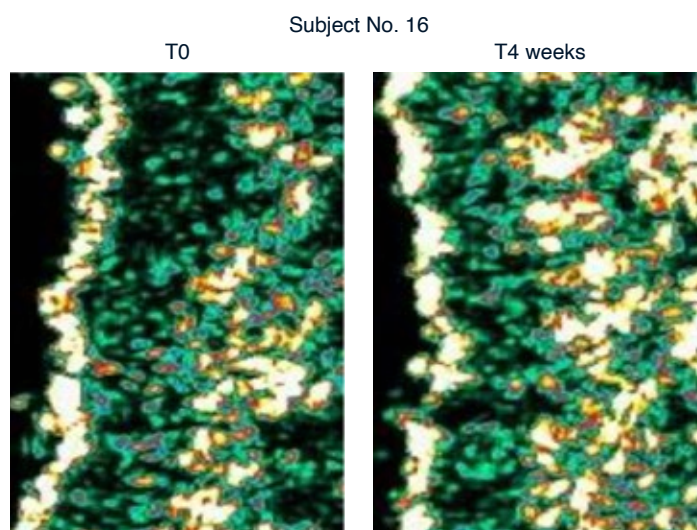
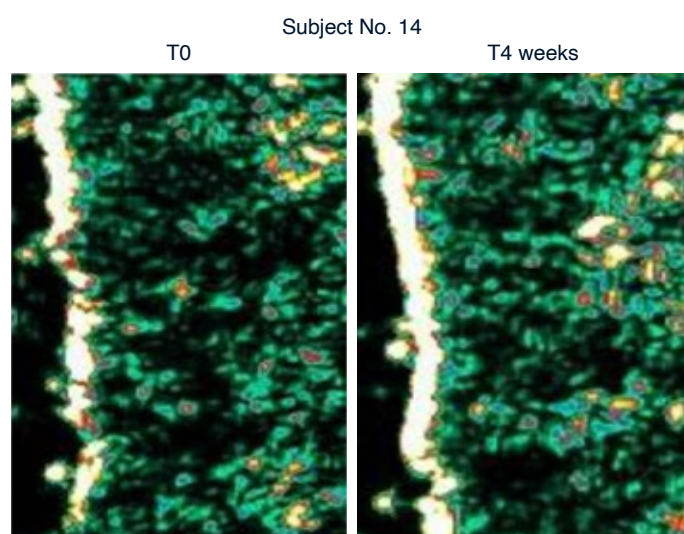
<sup>§</sup>Statistically significant ( $p < 0.001$ )

<sup>\*\*</sup>Statistically significant ( $p < 0.01$ )

# AFTER 4 WEEKS

**INCREASE OF THE SKIN DENSITY VALUES  
RELATED TO INCREASE OR A REORGANISATION  
OF THE DERMAL STRUCTURES: COLLAGEN  
FIBERS, CELLS AND EXTRACELLULAR MATRIX.<sup>16</sup>**

Increase of the echogenic structures (white colour).



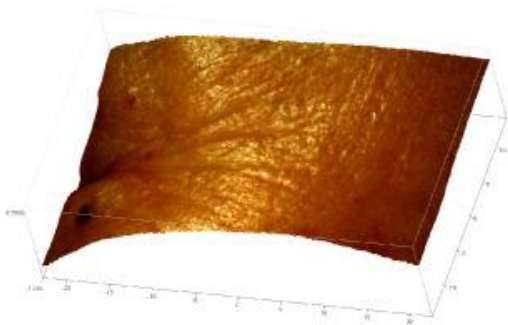
Some examples of digital images of skin echogenicity/density obtained by  
Ultrasound Scanner Dermascan C® Ver. 3 (Cortex Technology).

## **AFTER 4 WEEKS**

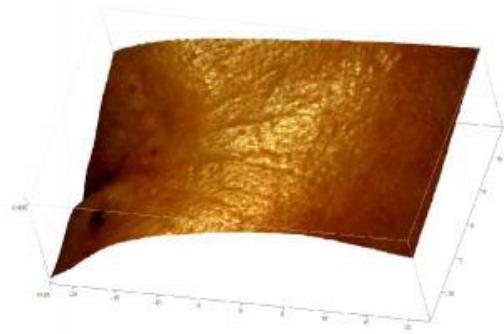
**SIGNIFICANT IMPROVEMENT OF THE SKIN  
ROUGHNESS AFTER ONLY 4 WEEKS OF USE.<sup>16</sup>**

Subject No. 8

T0

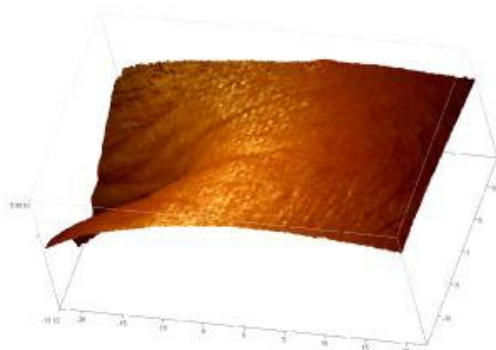


T4 weeks

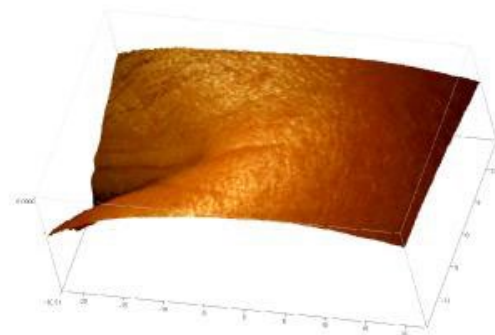


Subject No. 13

T0



T4 weeks



Some examples of 3D digital images obtained by Primos Pico Optical 3D Skin Measuring Device<sup>16</sup>

# Definisse [KP<sup>1</sup>]<sup>®</sup> revitalising eye contour

## Collagen Modulator Bio-peptide



A complete cosmetic treatment for the eye area that reduces wrinkles, dark circles, and under-eye puffiness due to an effective combination of 3 peptides and 3 latest-generation hyaluronic acids.<sup>10</sup>



### USER BENEFITS

Lightweight and easy-to-absorb formula that provides immediate and long-lasting hydration for fresh looking skin around the eyes.<sup>10</sup>



### [KP<sup>1</sup>] Collagen Modulator Bio-peptide

RELIFE's exclusive, first-in-class, bio-active peptide.<sup>10</sup>

With<sup>10</sup>

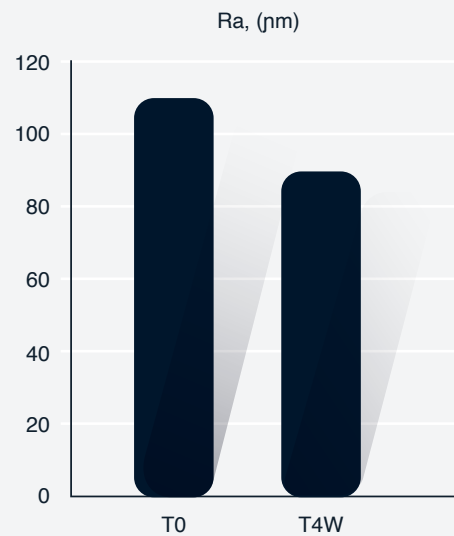
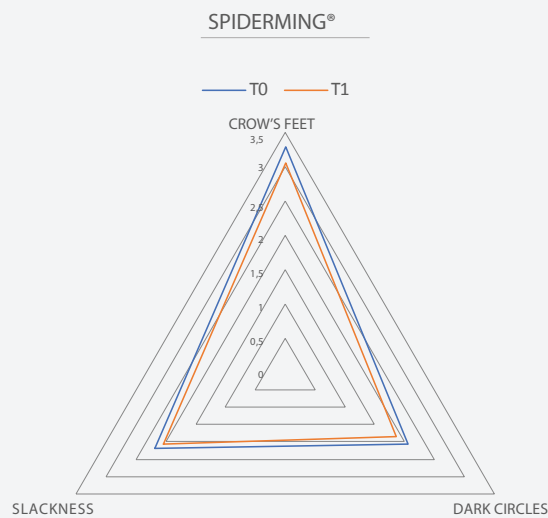
- **Argireline<sup>®</sup>**, a synthetic peptide, that helps inhibit the repetitive contraction of facial expression muscles, thereby reducing hyperkinetic facial lines
- **Acetil-tetrapeptide-5** proven effectiveness in reducing dark circles and under-eye puffiness
- **3 different types of HA** promote new collagen substrate production:
  - **High molecular weight HA** sits on the surface of the skin to prevent dehydration
  - **Very low molecular weight HA** can penetrate deeper into the skin significantly improving hydration
  - **Cross-linked HA**, has a significantly higher ability to hydrate the skin than other HAs, and double the ability to reduce wrinkles and wrinkle depth
- **Vitamin B5**, stimulates the physiological skin regeneration
- **Vitamin E**, with antioxidant properties
- **Avocado oil**, that nourishes the skin

### How to use:

Apply to clean skin in the morning and evening by massaging until completely absorbed.  
Can be used in combination with aesthetic medicine treatments to improve results<sup>10</sup>

15 ml  
Dermatologically tested<sup>10</sup>

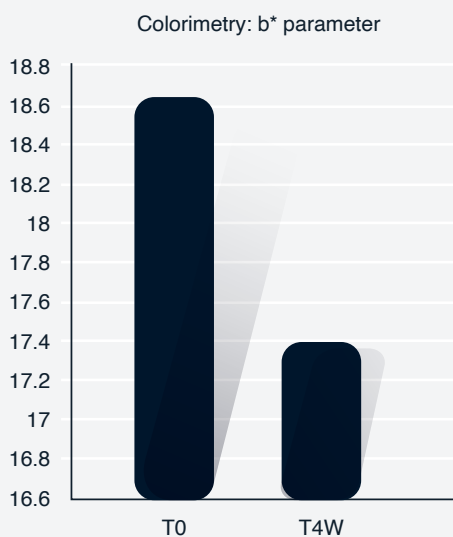
After 4 weeks of treatment, the skin appeared overall “younger”



Significant variation of “*Crow’s Feet*” profilometry was found after 4 weeks (T4W)\*:<sup>17</sup>

**-19.2%** for Ra parameter  
average roughness in  $\mu\text{m}$  of the analysed profile  
**statistically significant** ( $p < 0.05$ )

## Skin pigmentation



The **reduction of b\* parameter**  
(bluish/brown pigmentation)  
was significant ( $p < 0.05$ )  
and also **clinically evident**.<sup>17</sup>

\*Clinical instrumental test on 20 female subjects 37-65 years old who applied Definisse [KP1]<sup>®</sup> regenerating serum twice a day for 4 weeks<sup>17</sup>



YOU CAN'T STOP TIME BUT  
YOU CAN MAKE IT BEAUTIFUL

BEAUTIFY TIME

WITH

Definisse [KP<sup>1</sup>]<sup>®</sup>

Collagen Modulator Bio-peptide



*Enhance your in-clinic results  
with a breakthrough at home treatment*

## References

1. Shin J. W. et al. 2019. Molecular mechanisms of dermal aging and anti-ageing approaches. Int. J. Mol. Sci. 20:2126.
2. Reilly D. M. et al. 2021. Skin collagen through the lifestages: importance for skin health and beauty. Plast. Aesthet. Res. 8:2.
3. Avila Rodríguez M. I. et al. 2018. Collagen: a review on its sources and potential cosmetic applications. J. Cosmet. Dermatol. 17(1):20-26.
4. Fisher G. J. et al. 2008. Looking older: fibroblast collapse and therapeutic implications. Arch. Dermatol. 144(5): 666-672.
5. Mohiuddin A. K. 2019. Skin aging & modern age anti-ageing strategies. Int. J. Clin. Dermatol. Res. 7(4):209-240.
6. Cipriani C. et al. 2018. Serpin A1 and the modulation of type I collagen turnover: Effect of the C-terminal peptide 409-418 (SA1-III) in human dermal fibroblasts. Cell. Biol. Int. 9999:1-9.
7. Murphy G. 2011. Tissue inhibitors of metalloproteinases. Genom. Biol. 12:233.
8. Definisse [KP<sup>1</sup>]<sup>®</sup> regenerating serum leaflet
9. Definisse [KP<sup>1</sup>]<sup>®</sup> redensifying cream leaflet
10. Definisse [KP<sup>1</sup>]<sup>®</sup> revitalising eye contour leaflet
11. Errante F. et al. 2020. Cosmeceutical pseptides in the framework of sustainable wellness economy. Front. Chem. 8: 572923.
12. Pascarella S. et al. 2016. Serpin A1 C-terminal peptides as collagen turnover modulators. Chem Med Chem. 11:1850-1855.
13. Rovero P. et al. 2022. The clinical evidence-based paradigm of topical anti-ageing skincare formulations enriched with bio-active peptide SA1-III (KP1) as collagen modulator: from bench to bedside. Clin. Cosmet. Investig. Dermatol. 15:2693-2703.
14. Derming S.r.l. Anti-age efficacy and tolerance evaluation of a face serum. Test code: E0121 (report); 2021.
15. Derming S.r.l. Anti-age efficacy and tolerance evaluation of a face cream. Test code E0221 (report); 2021
16. Definisse [KP<sup>1</sup>]<sup>®</sup> Regenerating Serum. 2022. Instrumental and Subjective Evaluation of the Anti-age Efficacy of a Cosmetic Product. Institute of Skin and Product Evaluation (ISPE s.r.l.). Milan.
17. Derming S.r.l. Clinical study for the tolerability and anti-age efficacy of an eye-contour treatment. test code: E0321 (report); 2021.



A. MENARINI FARMACEUTICA INTERNAZIONALE SRL  
Menarini House, Mercury Park, Wycombe Lane,  
Wooburn Green, Buckinghamshire, HP10 0HH

Incorporated in Italy with Limited Liability

Branch registered in England  
No: BR016024

Tel: 01628 856400  
For general enquiries contact: info@relifecompany.co.uk

### Adverse events should be reported.

Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or App Store. Adverse events should also be reported to A. Menarini Farmaceutica Internazionale SRL.  
Phone no. 0800 0851497 or email: [medinformation@relifecompany.co.uk](mailto:medinformation@relifecompany.co.uk)