

A GENE-BASED AESTHETICS COMPANY

March 2022

JEUNE



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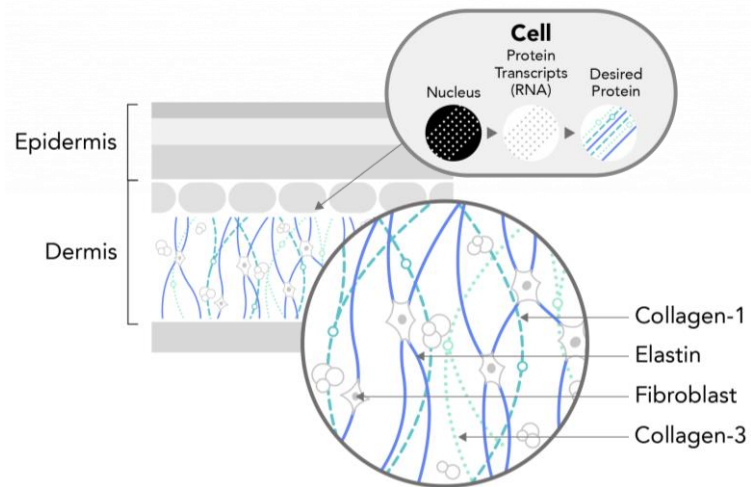


Introduction

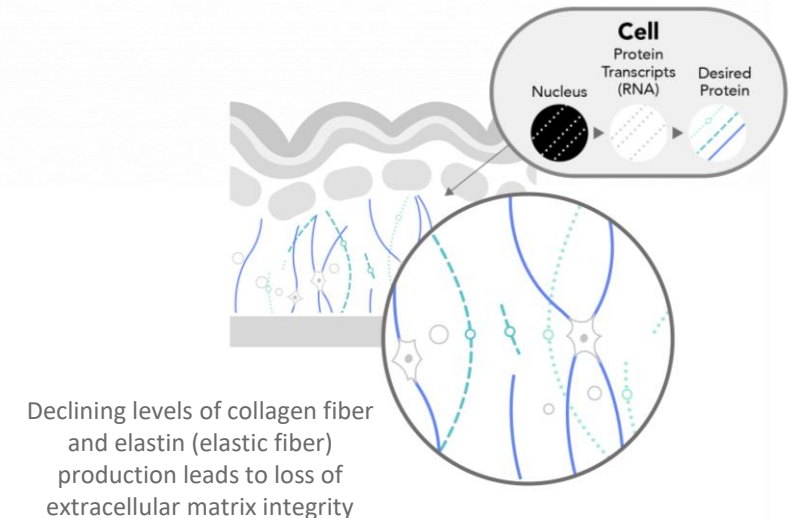
The Characteristic Look of Aging is Caused by Declining Levels of Key Proteins in the Skin's Extracellular Matrix

- Skin aging is a complex process that is caused by intrinsic factors (age) and extrinsic factors (e.g., sun, cigarette smoke, pollutants, diet etc.)
- These factors cause dermal matrix alterations, impaired collagen synthesis, and degradation of extracellular matrix which consequently affects overall quality and function of skin
- The primary function of the extracellular matrix is to give skin its mechanical and biochemical properties

YOUNGER / HEALTHY



AGED / PHOTODAMAGED



Jeune Aesthetics is Creating a New Category of Aesthetic Medicines Designed to Directly Address Underlying Biology



Damage

Using light and sound waves, **energy-based devices damage the skin** triggering a wound healing response



Fill

Whether bovine collagen, hyaluronic acid, or others, **fillers add artificial volume** to decrease the appearance of wrinkles



Paralyze

By inducing temporary denervation **toxins paralyze the underlying muscle** to prevent movement, thereby decreasing the appearance of wrinkles



Restore and Rebuild

Via targeted gene delivery directly to skin cells Jeune Aesthetics' gene-based treatments are designed to **restore protein production to rebuild** the underlying extracellular matrix structure, to improve skin quality and appearance

KB301 is designed to increase production of type III collagen

Presence of COL3 fibrils induces deposition of long-lasting COL1 fibrils

- COL3 appears early during collagen fibrillogenesis, and the subsequent replacement of this COL3 by COL1 is a critical step for collagen fibril maturation and extracellular matrix reorganization¹
- In addition, COL3 both regulates the dimensions of COL1 fibers² and enhances COL1 elasticity³
- As such, the appearance of early COL3 expression, and ensuing replacement with COL1, has been used as a marker of efficacy for injectable facial fillers in humans⁴
- COL3 provides tensile strength, and influences other functions such as cell adhesion, migration, proliferation, and differentiation through its interaction with integrins, which are cell surface receptors⁵

	Type I Collagen	Type III Collagen	Elastin
Percentage in the skin	70-80%	20-30%	2-3%
Aging alteration	Increases with growth, decreases with age	Abundant in baby skin, decreases with growth	Abundant in baby skin, peaks in mid-20s / early 30s and declines thereafter

1. Wang, P. et al., 2018. Wound healing. *Journal of the Chinese Medical Association*, 81(2), pp. 94-101.

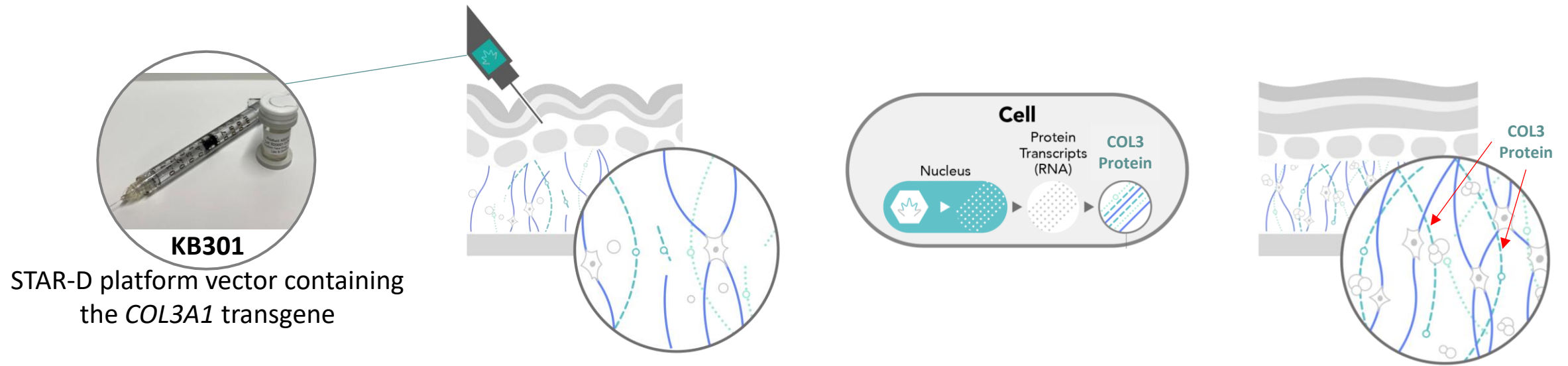
2. Liu, X. et al., 1997. Type III collagen is crucial for collagen I fibrillogenesis and for normal cardiovascular development.. *Proc Natl Acad Sci U S A*, 94(5), pp. 1853-6.

3. Asgari, M., Latifi, N., Heris, H.K. et al. In vitro fibrillogenesis of tropocollagen type III in collagen type I affects its relative fibrillar topology and mechanics. *Sci Rep* 7, 1392 (2017).

4. Yutskovskaya, Y., Kogan, E. & Leshunov, E., 2014. A randomized, split-face, histomorphologic study comparing a volumetric calcium hydroxylapatite and a hyaluronic acid-based dermal filler. *J Drugs Dermatol*, 13(9), pp. 1047-52.

5. Kim JK, Xu Y, Xu X, Keene DR, Gurusiddappa S, Liang X, Wary KK and Hook M, 2005. A novel binding site in collagen type III for integrins alpha1beta1 and alpha2beta1. *J Biol Chem* 280, 32512-20.

KB301 – Mode of Action



1 Ready to Use

- Shipped on dry ice and stored at below freezing at sites

2 Intradermal Injection

- Delivered via 33G needle
- Treatment area numbed with ice (no topical anesthesia required)

3 Protein Synthesis

- Once in the nucleus, STAR-D gene designed to allow normal cell machinery to make COL3 protein

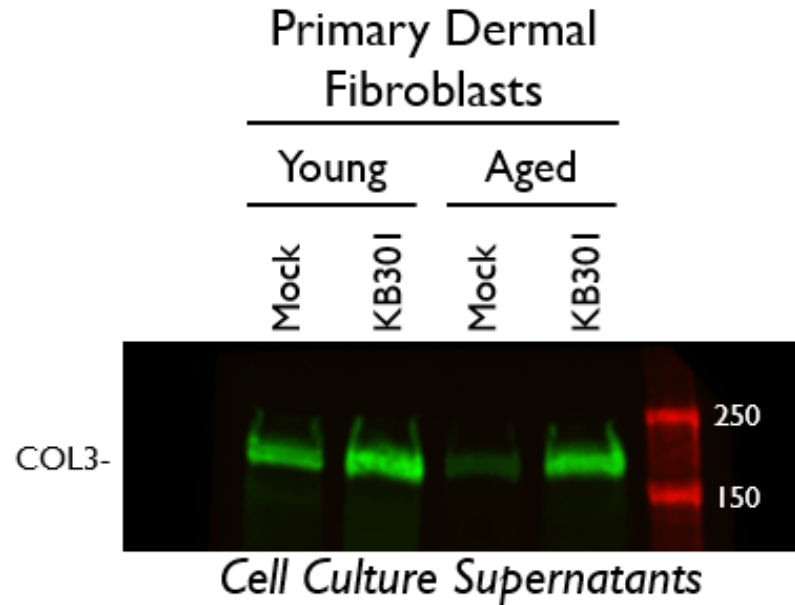
4 Protein Integration

- Newly made protein is secreted into the extracellular space where it rebuilds and restores the extracellular matrix



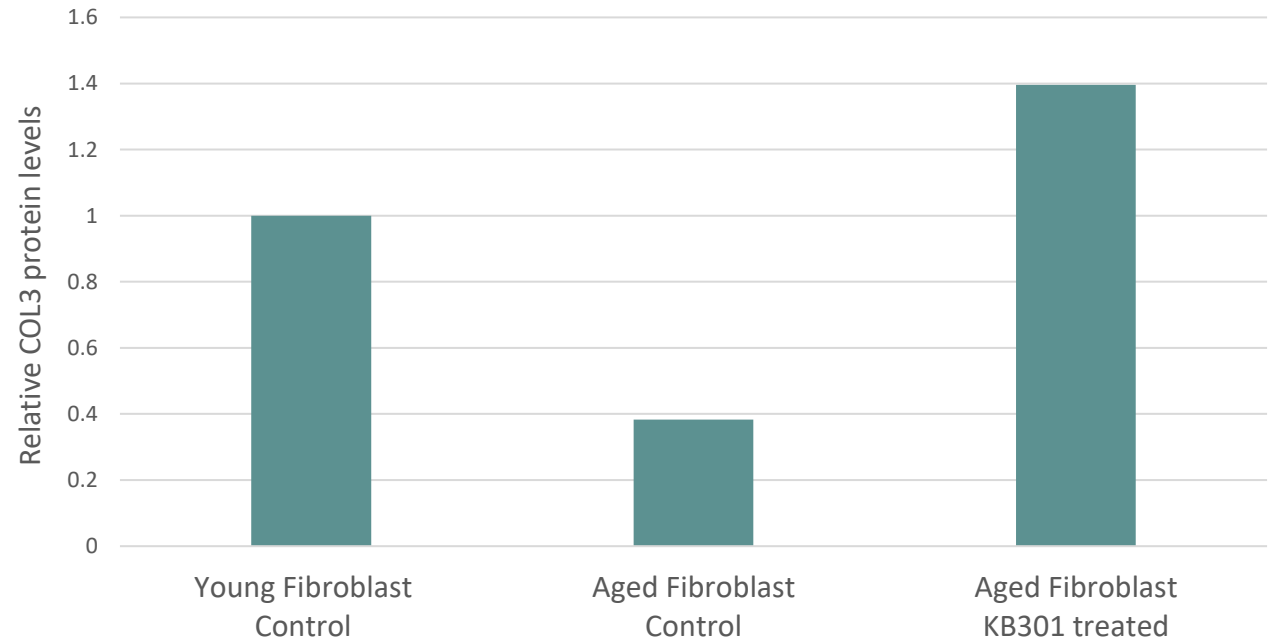
KB30 I

In Vitro Studies Show Aged-Human Fibroblasts can produce comparable amount of COL3 to young human Fibroblast after treating with KB301



Source: Data on File

Quantitative analysis of Western Blot data demonstrates treatment with KB301 restores levels of COL3 secretion to the younger phenotype



COL3 levels from Young Fibroblasts used as Reference Value = 1

PEARL-I Cohort I – Data Presented at SID 2021

Well tolerated with minimal adverse events

Design

- Open label, dose ranging study designed to evaluate safety and repeat dosing after intradermal injections in 7 subjects

Dosing

- Subjects received two (day 0 and day 30) intradermal bolus injections dosages (1e8, 2e8 and 4e8) in buttocks region
- Biopsy was taken on day 2 and day 32

Safety & Tolerability

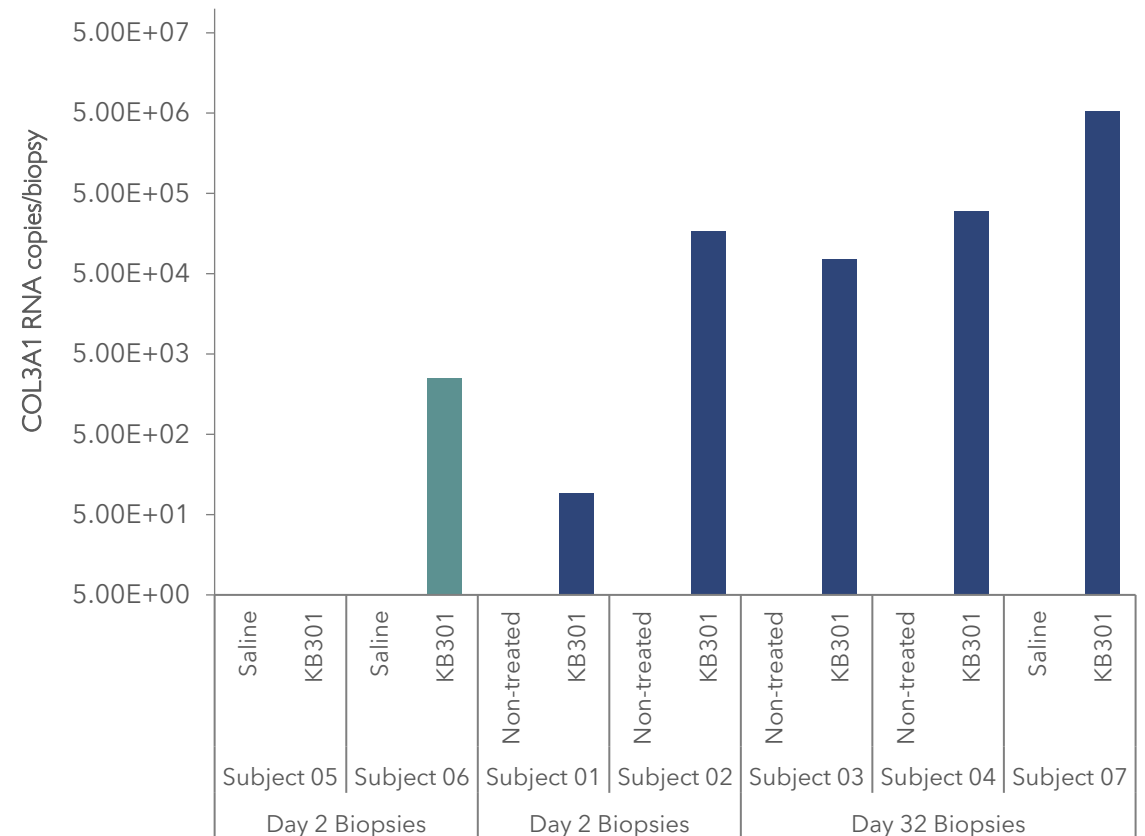
- Well tolerated with no systemic adverse events
- Injection site erythema and pain (grade 1 and 2) and adverse events related to punch biopsy were observed
- No vector shedding detected in blood, urine or skin swabs
- No meaningful change in lab results

Efficacy Measures

- COL3A1 transgene expression 2-days post-dose, as measured by qRT-PCR of skin biopsies
- Expression was observed with 2e8 and 4e8 dose as well as after second (30 days repeat) dosing

RNA copy levels were similar following first and second intradermal doses

KB301-Encoded COL3A1 Transcripts



PEARL-I Cohort 2 Safety & POC Efficacy Study Design



Hypothesis

KB301 will improve extracellular matrix of the aged/photo damaged skin thereby improving skin quality attributes such as fine lines, skin texture and thickness of the skin



Study Design

- Split face/knee design with treatment side randomized 2:1 for active arm
- Subjects administered KB301 high dose / low dose / placebo
- Intent to Treat = 27 subjects or 54 sites (36 active, 18 placebo) were recruited across 2 sites



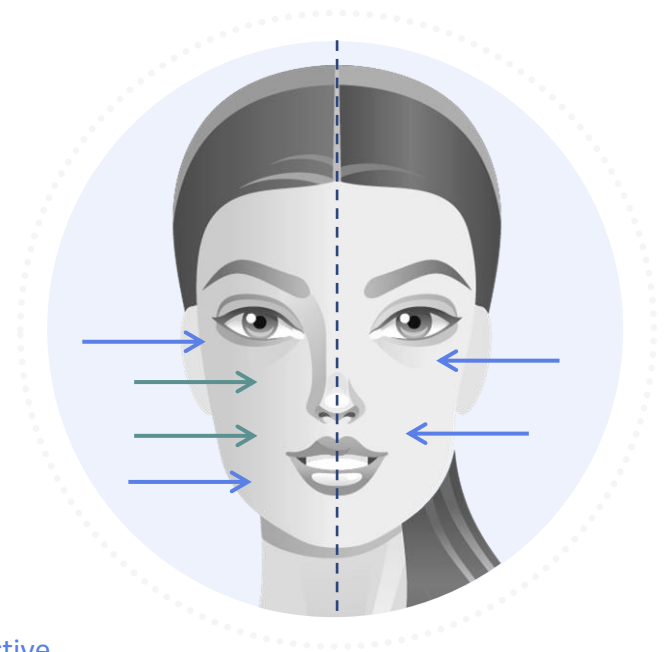
Safety and Tolerability

- Besides general physical examination, vector shedding in blood, urine or skin swabs and routine lab were performed to rule out any systemic side effects



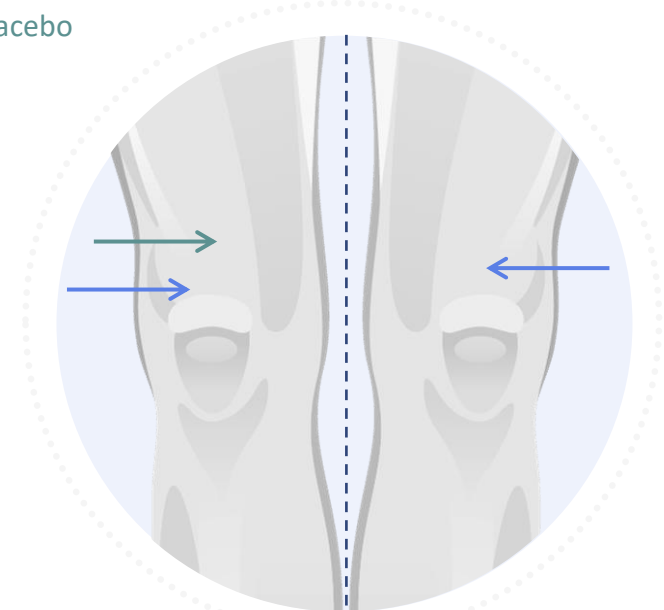
Efficacy Measures

- Jeune Aesthetics Skin Roughness Score (JASRS)¹
- Jeune Aesthetics Fine Lines Score (JAFLS)²
- Subject Satisfaction Score (SSS)
- Skin thickness over the knee



→ Active

→ Placebo



1. Adapted from Donofrio L, Carruthers A, Hardas B, et al. Development and validation of a photonumeric scale for evaluation of facial skin texture. *Dermatol Surg.* 2016;42(suppl 1):S219–S226.
2. Adapted from Carruthers J, Donofrio L, Hardas B et al. Development and validation of a photonumeric scale for evaluation of facial fine lines. *Dermatol Surg.* 2016;42:S227–S234. 101

Baseline Characteristics and Disposition

27 Subjects Enrolled in the Study; 23 fully completed

Criteria	Baseline in PEARL-I Study	Comments
Healthy Male and Female Subjects	Male: 1 Female: 26	
Between 30 and 70 years old at time of written consent	Average age: 65.1 years	Older age-range than us typical in aesthetic trials due to regulatory feedback
Subjects with Fitzpatrick skin type I through III	Type II: 93% subjects Type III: 7% subjects	The Fitzpatrick skin type describes a way to classify the skin, from I (most severe) through V by its reaction to exposure to sunlight.
Scored moderate, severe and extreme in fines line scale and moderate, severe and diffuse in skin texture scale	JAFLS ¹ : 23% Severe and 77% Extreme JASRS ² : 23% Severe and 77% Diffuse	Study enrolled mostly severe, extreme or diffuse Subjects based on regulatory feedback
Enrolled Subjects were first dosed behind the ear for safety prior to injections in the face and knee	27 Subjects were randomized to receive either KB301 or Placebo. 23 Subjects fully completed the Study	No AE related dropouts in the Study

1. Adapted from Carruthers J, Donofrio L, Haldas B et al. Development and validation of a photonumeric scale for evaluation of facial fine lines. *Dermatol Surg.* 2016;42:S227–S234. 101

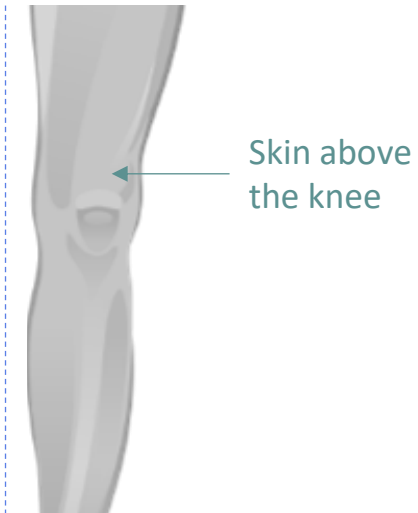
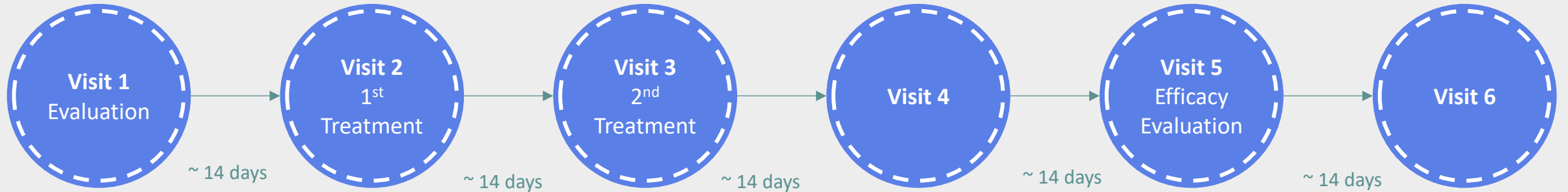
2. Adapted from Donofrio L, Carruthers A, Haldas B, et al. Development and validation of a photonumeric scale for evaluation of facial skin texture. *Dermatol Surg.* 2016;42(suppl 1):S219–S226.

A microscopic view of cells, likely chondrocytes, arranged in a grid-like pattern. The cells are dark, rounded, and have a central dark spot. A teal-colored rectangular overlay is positioned on the left side of the image, partially covering the cells. The word "Knee" is written in white text on the teal overlay.

Knee

Above the Knee: Treatment Schedule and Outcome Measurements

Treatment: 1ml of low dose of KB301 or placebo injected with 33G needle in area above knee



Outcome Measurements	Description	Comments
Safety	Safety and tolerability	Evaluated at all visits
	Injection site reactions (ISRs)	Evaluated after each injection
Efficacy	Subject Satisfaction Scores	Assessed by subjects on each side separately
	Skin fold assessment with calipers	Assessed at baseline and Visit 5
	Global assessment in Improvement	Assessed by blinded site investigator

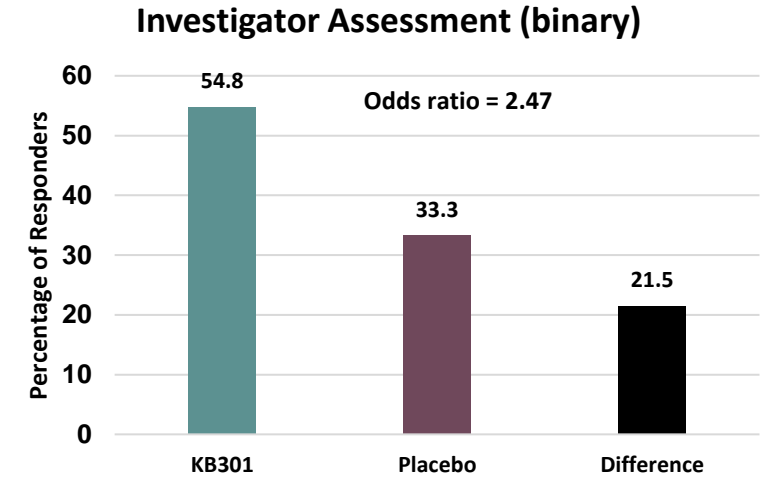
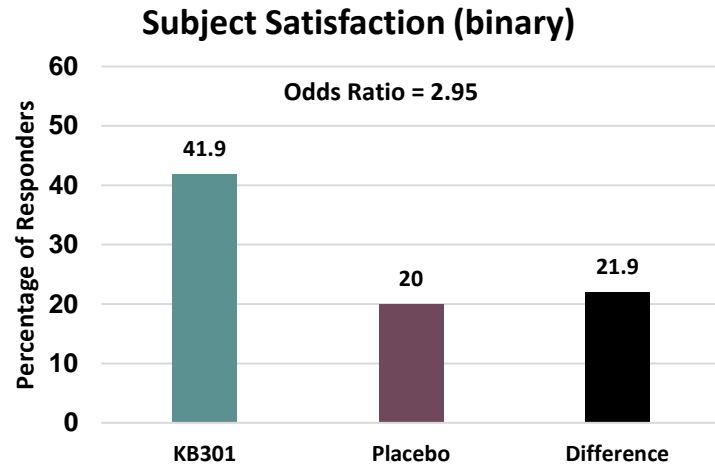
Above the Knee: Injection Site Reactions

Injection Site Reactions				
Above Knee AE Counts				
	KB301		PLACEBO	
	Visit 2	Visit 3	Visit 2	Visit 3
Blisters	1	0	0	0
Bruising	1	1	0	0
Bumps	1	0	0	0
Unspecified	1	0	1	0
Itching	3	0	0	0
Pain	2	1	0	0
Pruritus	2	1	0	0
Rash	2	0	0	0
Redness	8	0	0	0
Soreness	1	0	0	0
Swelling	15	6	1	0
Tenderness	5	1	0	0
Warmness	3	1	0	0
N	45	11	2	0

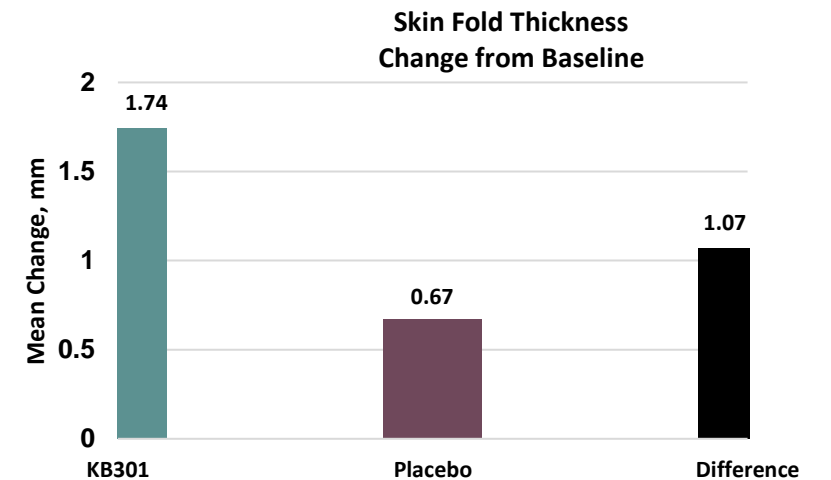
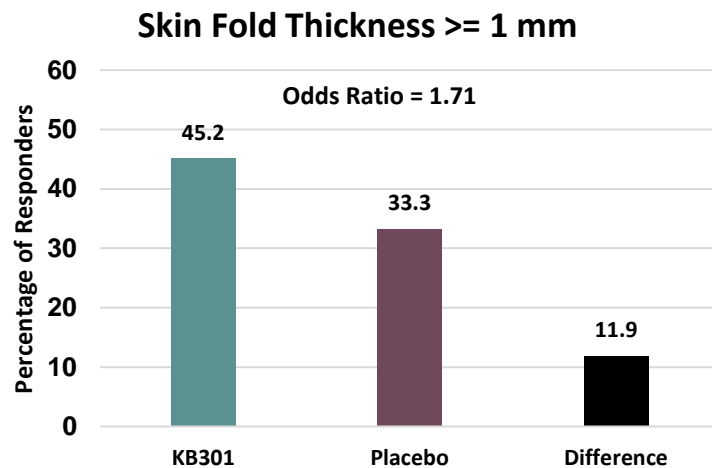
- 100% of the active adverse events were mild
- Injection site reactions minimized following the first injection

Above the Knee: Efficacy Assessments

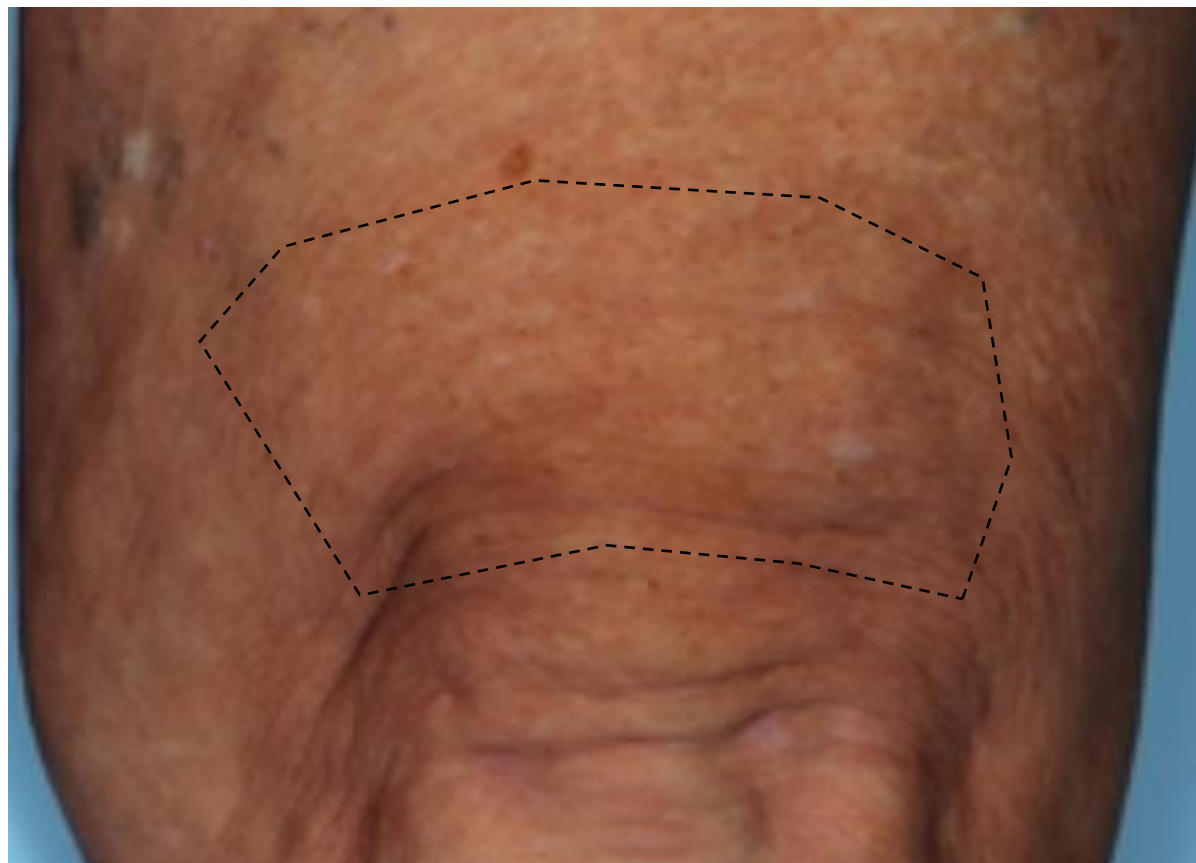
Meaningful Improvement in Subject Satisfaction, Investigator Assessment and Improvement in Thickness between Active and Placebo



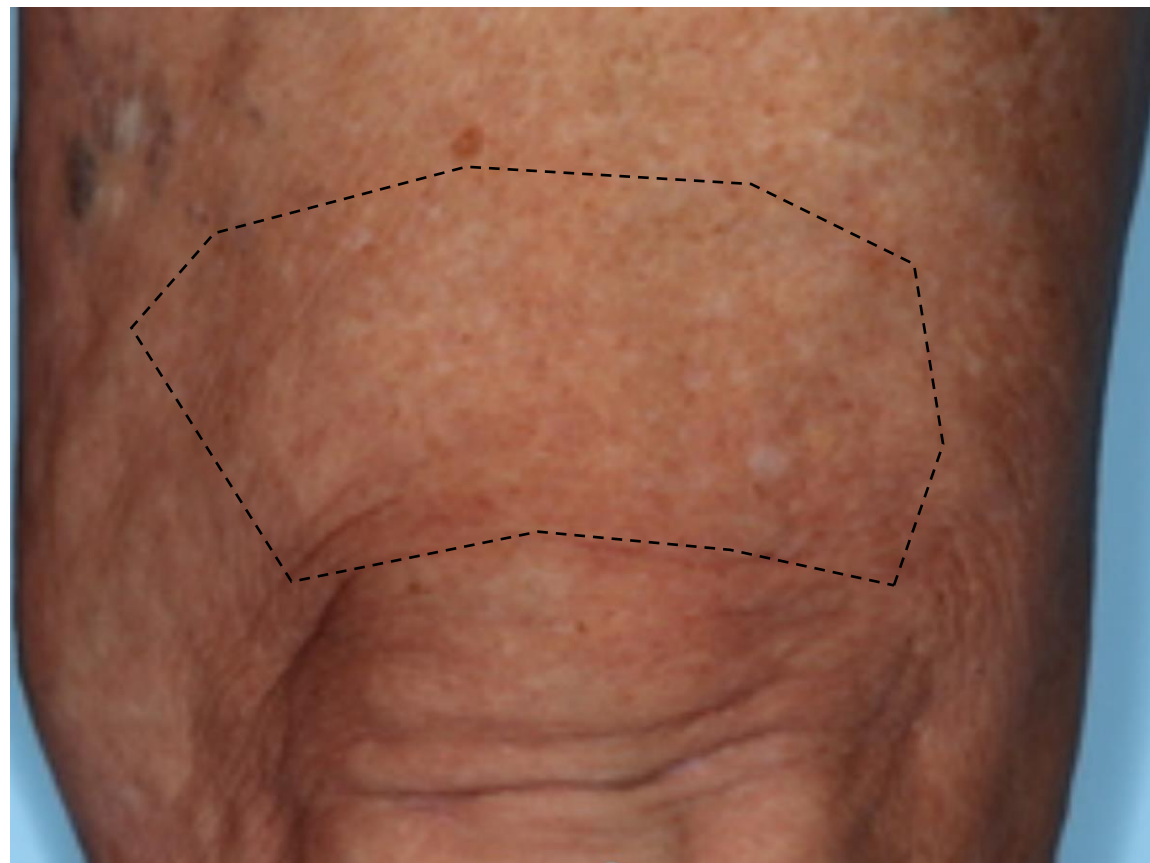
N for KB103 = 31 | N for Placebo = 15



Above the Knee: Before and After of Left Knee Treated with KB301 Low Dose



Baseline



Visit 5

Improvement in texture as well as fine lines and softening of the folds

Above the Knee: Before and After of Left knee treated with KB301 Low Dose



Baseline

Visit 5

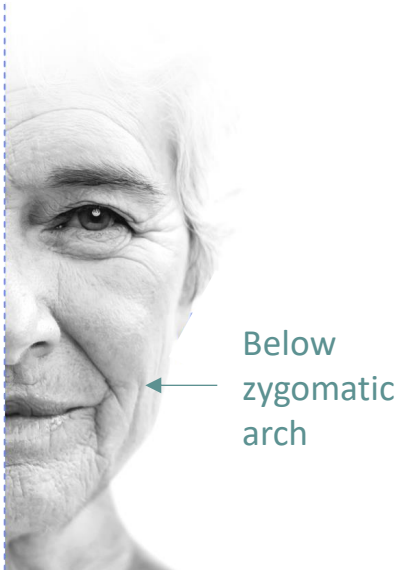
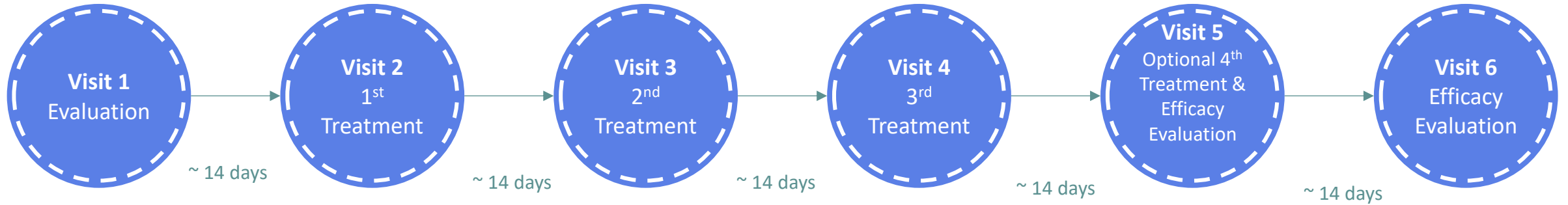
Improvement in texture as well as fine lines and softening of the folds



Lower Cheek

Lower Cheek: Treatment Schedule and Outcome Measurements

Treatment: 1ml of high or low dose of KB301, or placebo, injected with 33G needle in cheek areas below zygomatic arch (lower cheek)



Outcome Measurements	Description	Comments
Safety	Safety and tolerability	Evaluated at all visits
	Injection site reactions (ISRs)	Evaluated after each injection
Efficacy	Subject Satisfaction Scores	Assessed by subjects on each side separately
	Skin Texture Score and Fine Lines Score	Assessed by Blinded Independent Reviewer using photographs and evaluated based on scales that were developed <u>specific to this skin area but not specific to KB301</u>

Lower Cheek: Injection Site Reactions

Injection Site Reactions per Visit								
Below Zygomatic Arch AE Counts								
	KB301				PLACEBO			
	Visit 2	Visit 3	Visit 4	Visit 5	Visit 2	Visit 3	Visit 4	Visit 5
Blisters	1	0	0	0	0	0	0	0
Bruising ¹	1	1	0	0	1	0	0	0
Bumps	2	0	0	2	0	0	0	0
Erythema	2	0	0	0	0	0	0	0
Unspecified	1	0	0	0	1	0	0	0
Irritated	0	0	1	0	0	0	0	0
Itching	1	0	0	1	0	0	0	0
Redness	5	1	2	2	0	0	0	1
Soreness	0	0	1	0	0	0	0	0
Swelling ²	10	8	5	4	1	0	0	0
Tenderness	8	5	0	1	0	0	0	1
Warmness	1	2	0	0	0	0	0	0
N	32	17	9	10	3	0	0	2

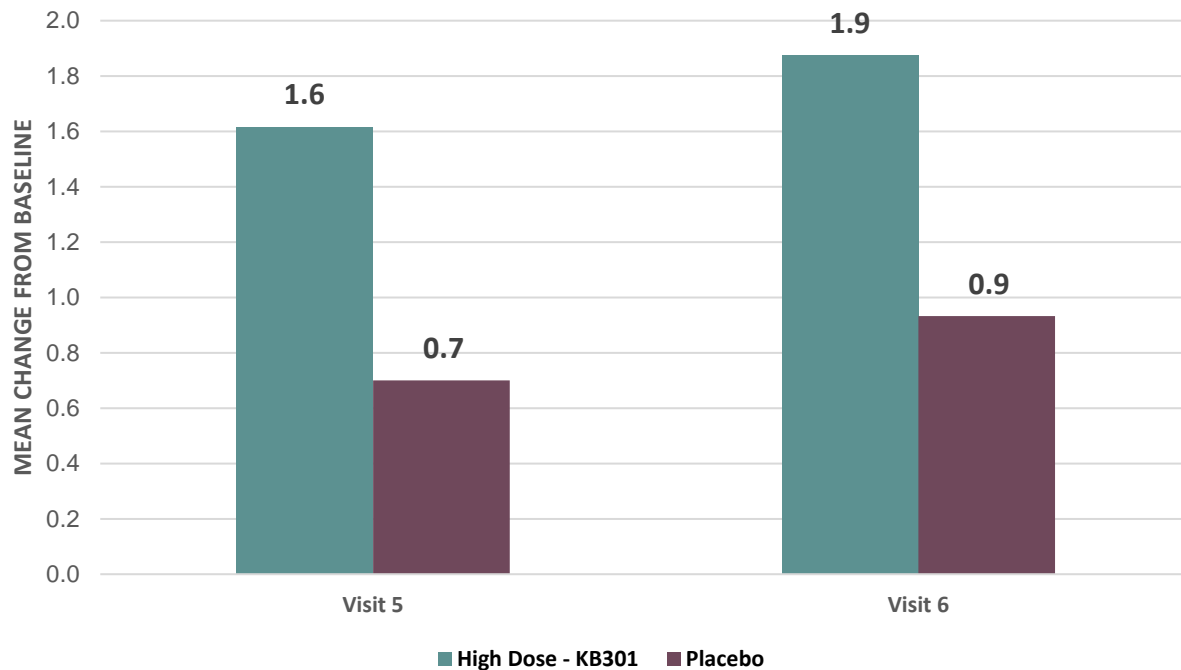
- 91% of the active adverse events (N = 68) were mild; 9% were moderate
- Injection site reactions minimized following the first injection

Lower Cheek: Efficacy Measures - Subject Satisfaction Efficacy Assessment

Difference in Mean Change from Baseline between High Dose KB301 and Placebo is Clinically Meaningful

High Dose

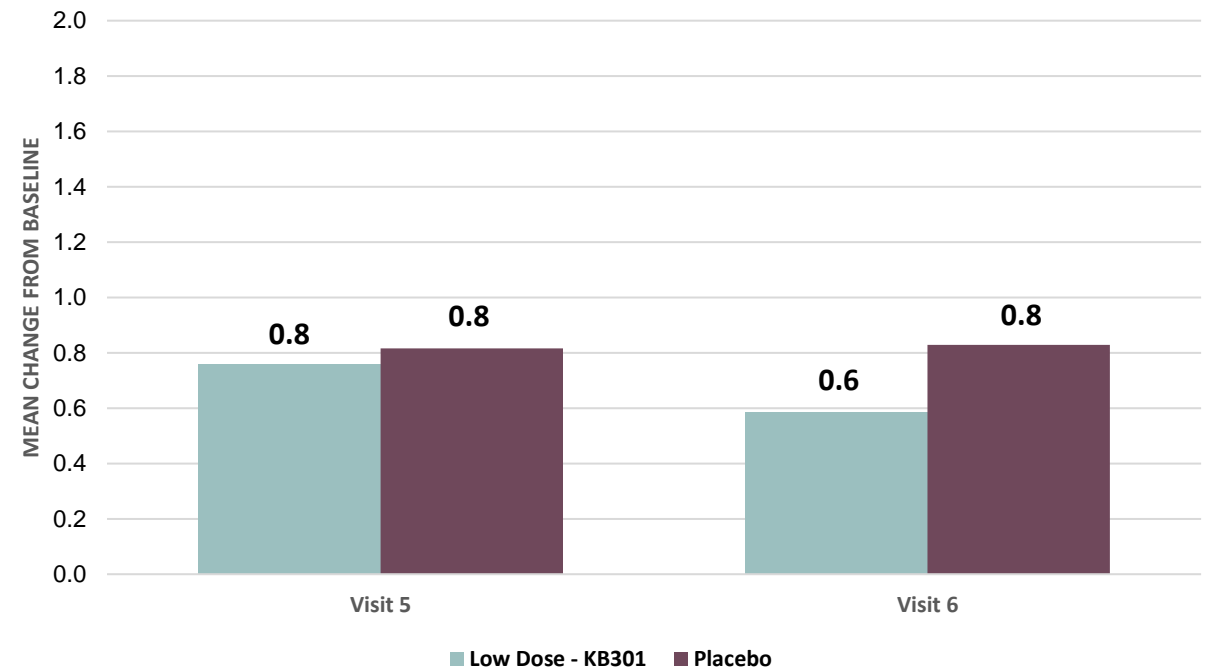
Subject Satisfaction Score - Below the Zygomatic Arch



N for High Dose = 19 for KB301 | N = 9 for Matching Placebo*

Low Dose

Subject Satisfaction Score - Below the Zygomatic Arch

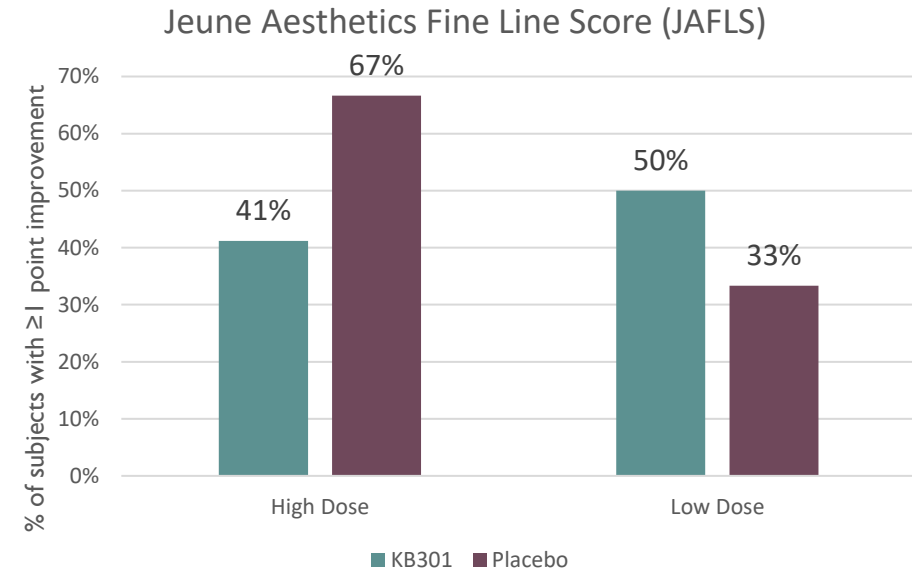
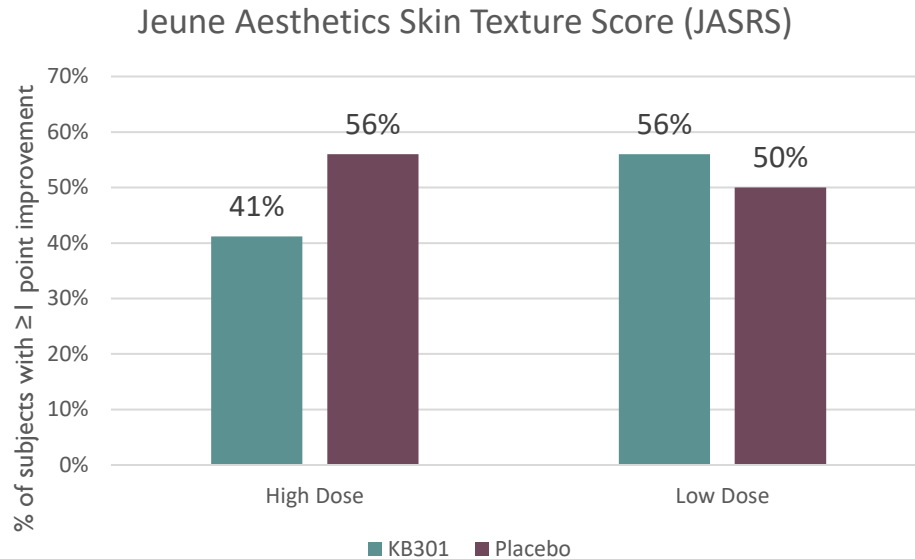


N for Low Dose = 12 for KB301 | N = 6 for Matching Placebo

*Assessment was done on 23 subjects.

Lower Cheek: Efficacy Measures – JASRS and JAFLS Scale Assessment

Evaluation by Blinded Independent Reviewer Showed No Separation between Active and Placebo Low or High Dose* with respect to exploratory JASRS and JAFLS measures



N for High Dose = 17 for KB301 | N = 9 for Matching Placebo**
N for Low Dose = 12 for KB301 | N = 6 for Matching Placebo

Observations by blinded evaluator: Moderate improvement in skin laxity; Improvement in solar dyschromia (redness); Improvement in telangiectasia (microvasculature)

*The Scales need further validation for KB301

**Assessment was done on 23 subjects

Lower Cheek: Before and After Right Side Treated with KB301 High Dose

Overall improvement in texture, fine lines and elasticity



Baseline



Visit 6

Lower Cheek: Before and After Same subject Observation on Week 6 KB301 vs. Placebo



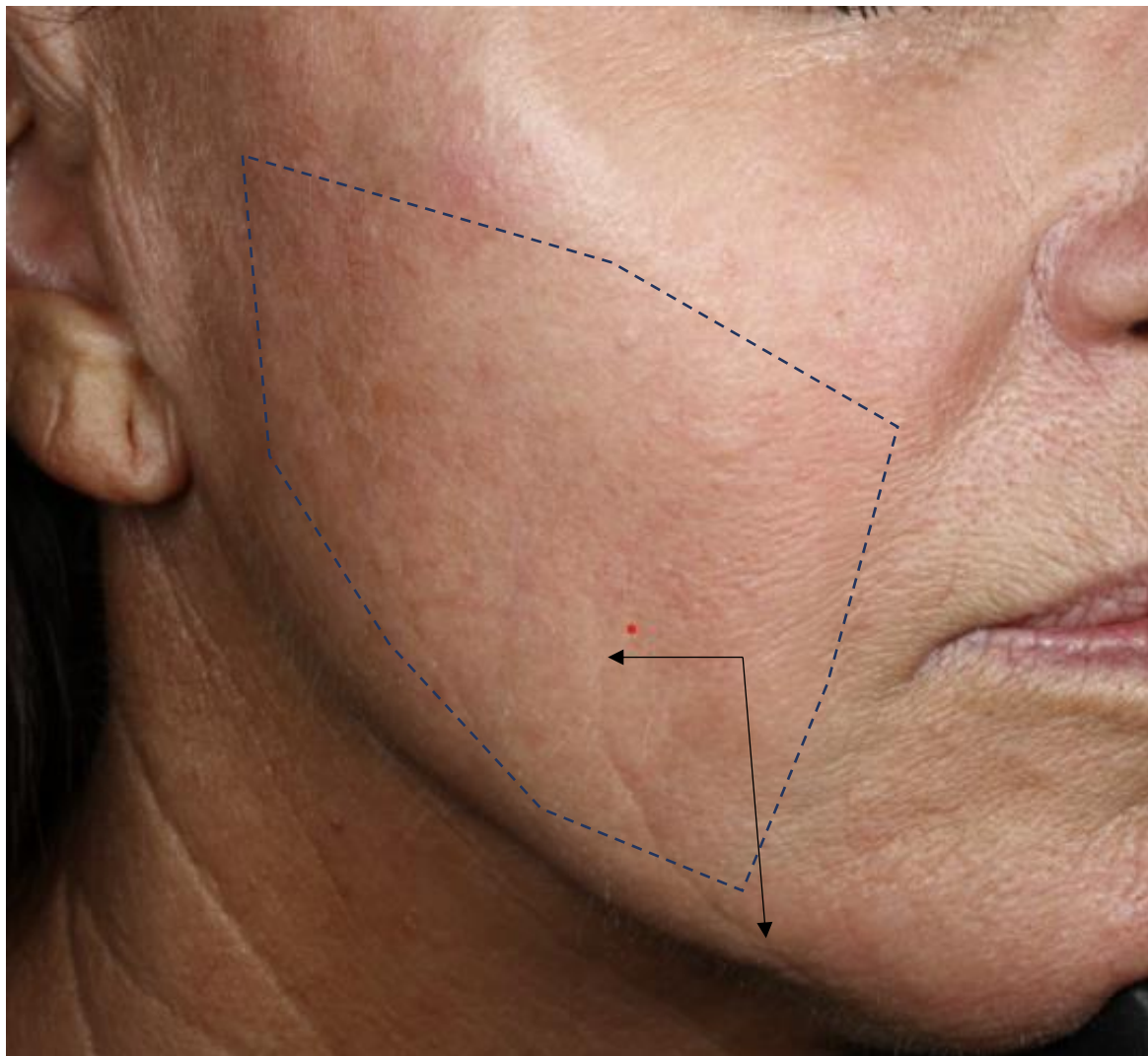
High Dose KB301 – Visit 6



Placebo – Visit 6

Lower Cheek: Before and After Right side treated with KB301 High Dose

Subject Reported: "Right Cheek Significantly improved from last visit. One wrinkle completely resolved"



Baseline



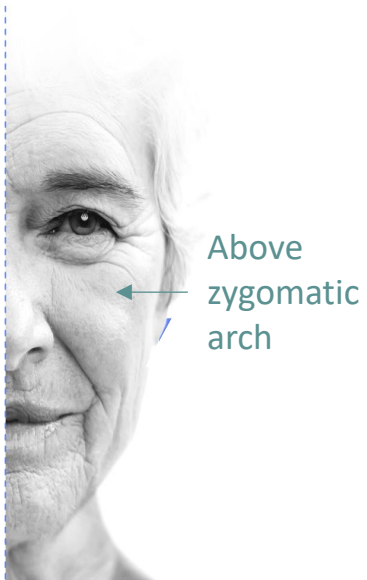
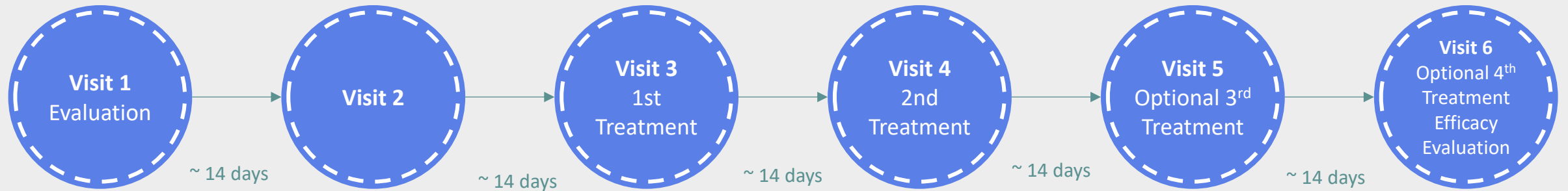
Visit 6



Upper Cheek

Upper Cheek: Treatment Schedule and Outcome Measurements

Treatment: 0.5 mL of low dose of KB301 or placebo injected with 33 G needle in cheeks above the zygomatic arch (upper cheek)



Outcome Measurements	Description	Comments
Safety	Safety and tolerability	Evaluated at all visits
	Injection site reactions (ISRs)	Evaluated after each injection
Efficacy	Subject Satisfaction Scores	Assessed by subjects on each side separately
	Blinded Independent Evaluator Assessment	No existing scale for this skin area. Clinically meaningful improvement assessed by blinded evaluator using Pictures

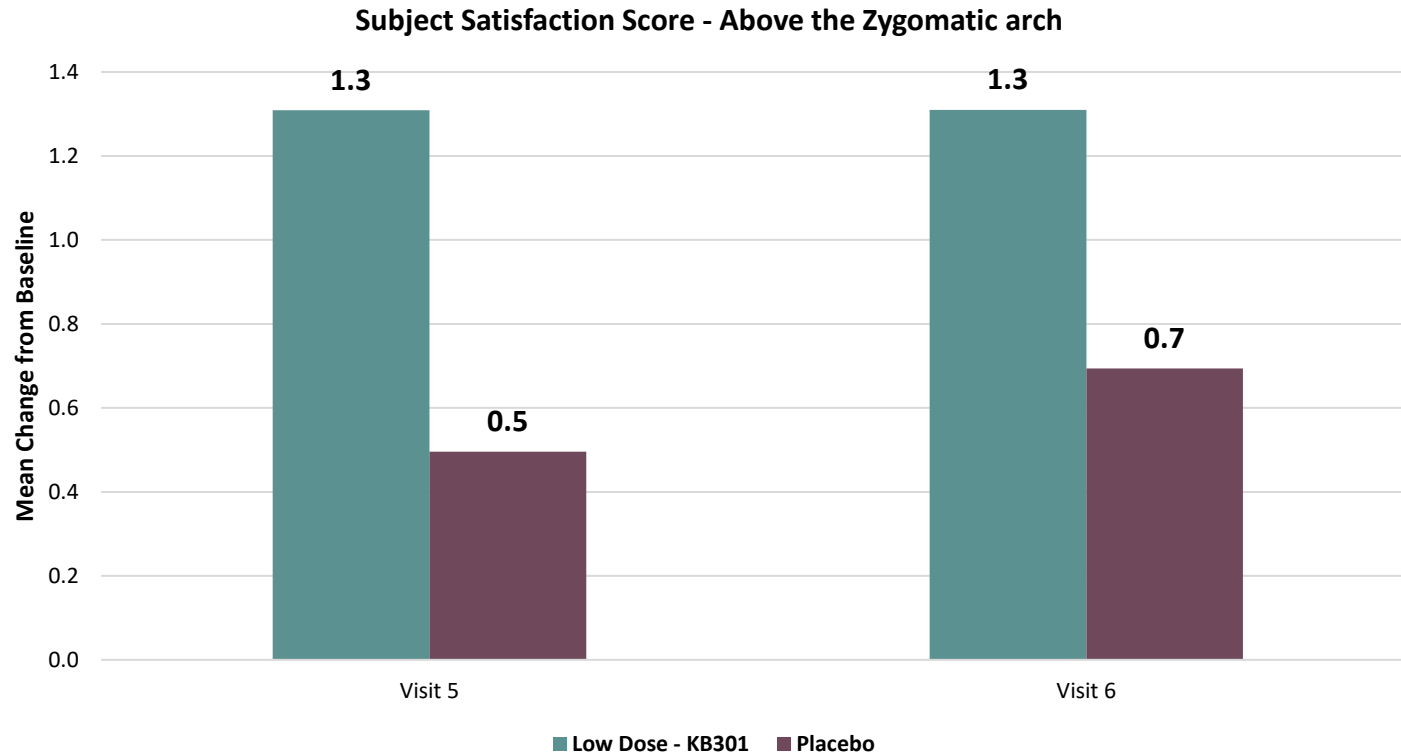
Upper Cheek: Injection Site Reactions

Injection Site Reactions per Visit								
Above Zygomatic Arch AE Counts								
	KB301				PLACEBO			
	Visit 3	Visit 4	Visit 5	Visit 6	Visit 3	Visit 4	Visit 5	Visit 6
Bruising	3	2	0	0	0	0	0	1
Bumps	0	0	2	0	0	0	0	0
Erythema	2	0	0	0	0	0	0	0
Irritated	0	1	1	0	0	0	0	0
Itching	0	0	1	0	0	0	0	0
Redness	3	2	1	0	0	0	0	0
Soreness	1	1	0	0	0	0	0	0
Swelling ¹	4	5	8	1	0	1	0	2
Tenderness	4	0	1	4	0	0	0	0
Warmness	2	0	0	0	0	0	0	0
N	19	11	14	5	0	1	0	3

- 98% of the active adverse events (N = 49) were mild; 2% were moderate
- Injection site reactions minimized following the first injection

Upper Cheek: Efficacy Measures

Difference in Mean Change from Baseline between Low Dose KB301 and Placebo is Clinically Meaningful

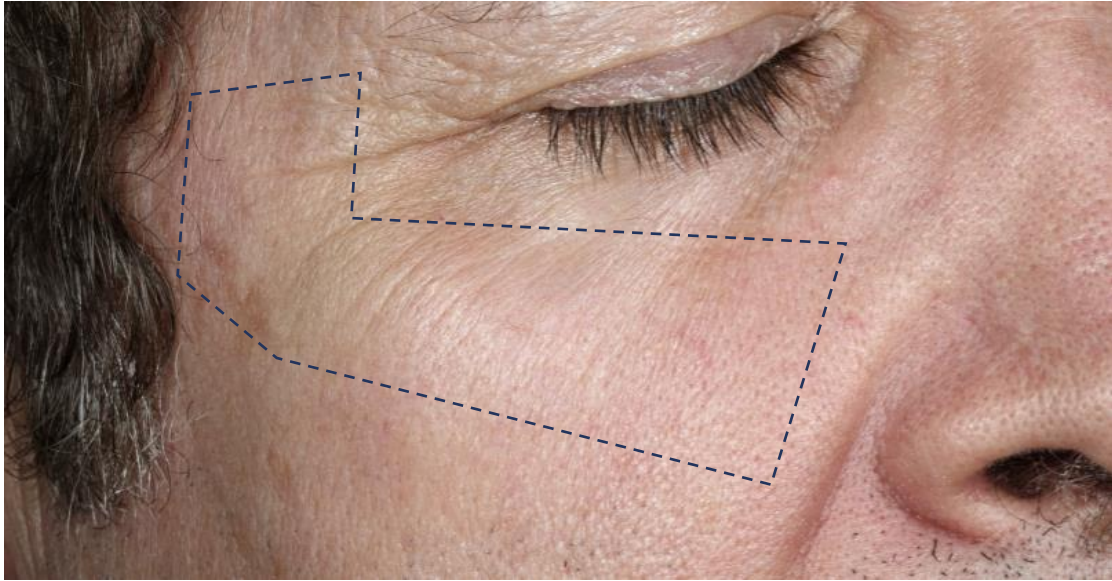


N for KB301= 31 for KB301 | N = 15 for Placebo

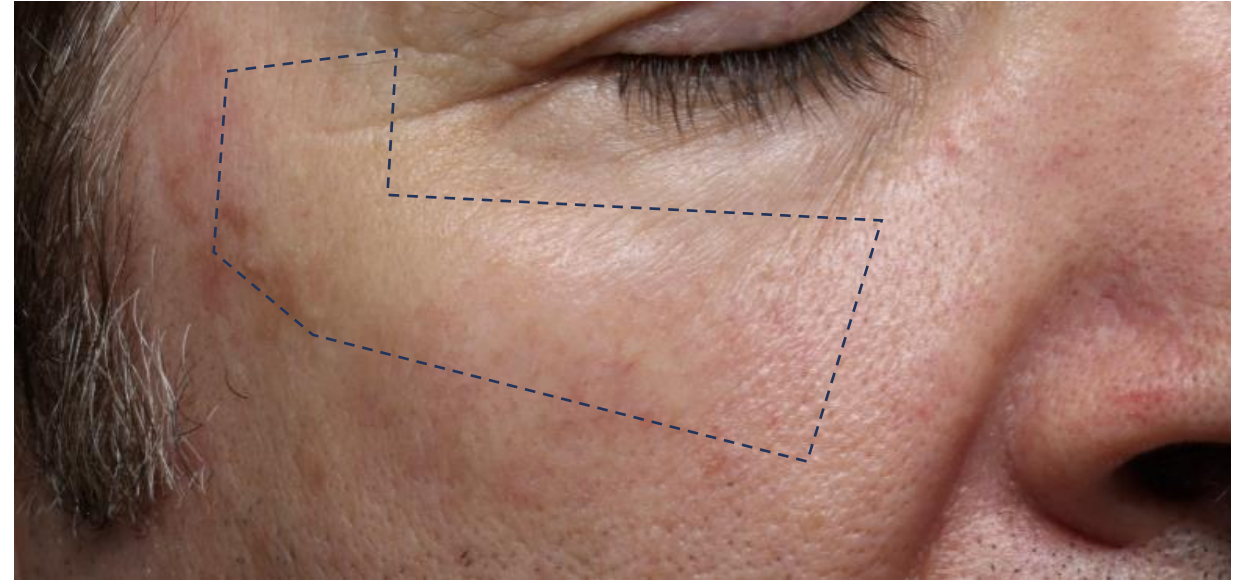
Grading	Description	Comments
Clinical Improvement	Performed by Blinded Independent Reviewer using pictures due to lack of scale for skin area	No meaningful difference between active and placebo

Upper Cheek: Before and After with low dose of KB301

Improvement in fine lines as well as reduction on lateral canthal line because of increased elasticity of the skin



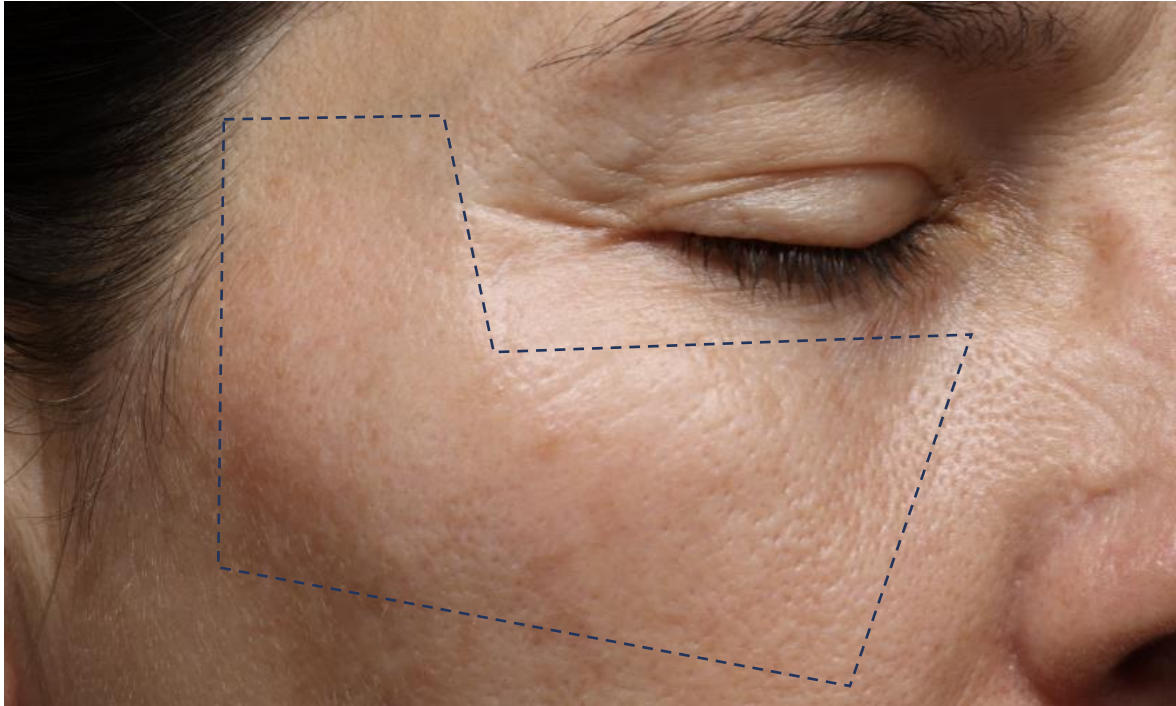
Baseline



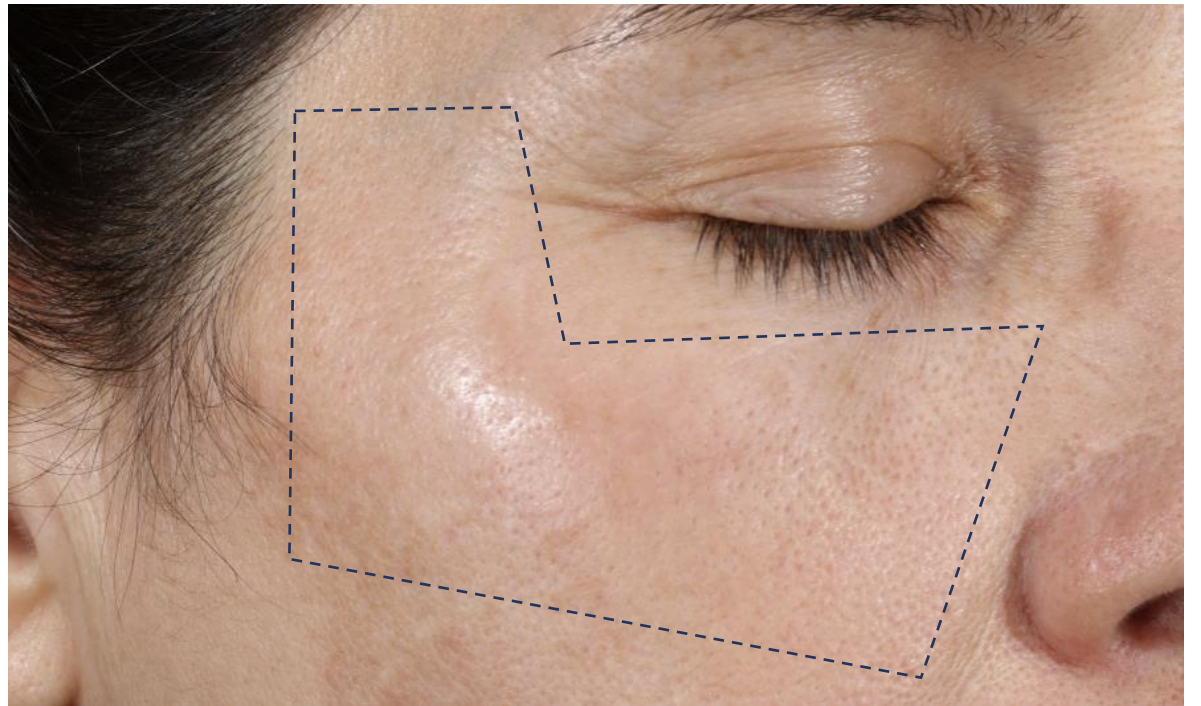
Visit 6

Upper Cheek: Before and After Pictures with low dose of KB301

Improvement in fine lines as well as reduction on lateral canthal line because of increased elasticity of the skin



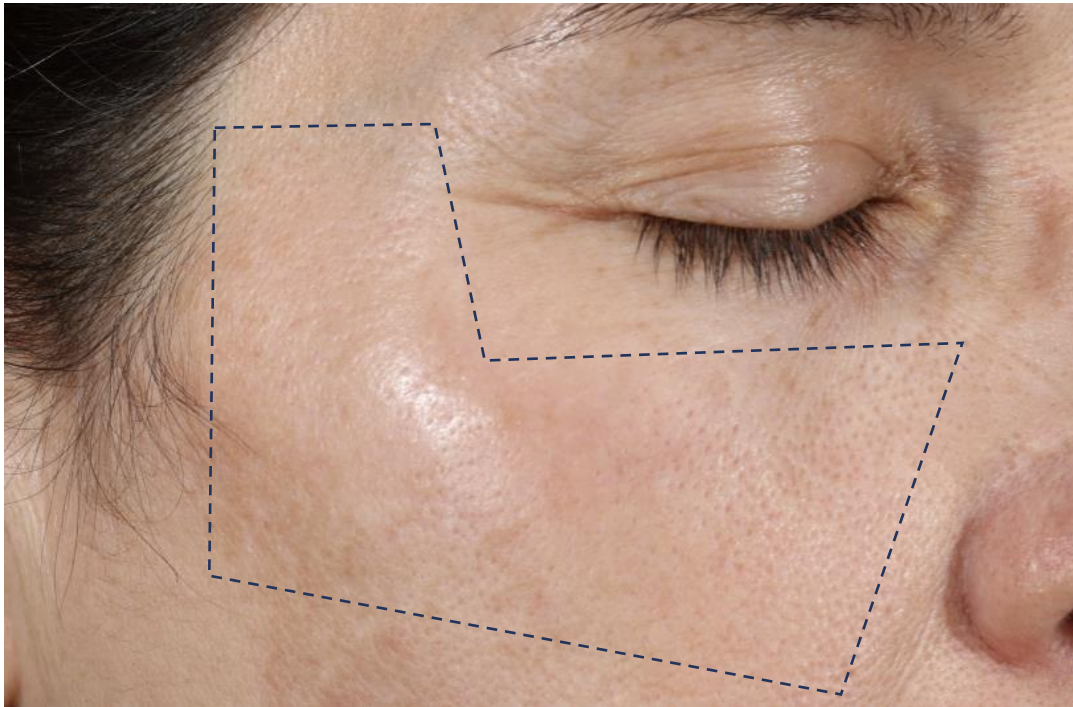
Baseline



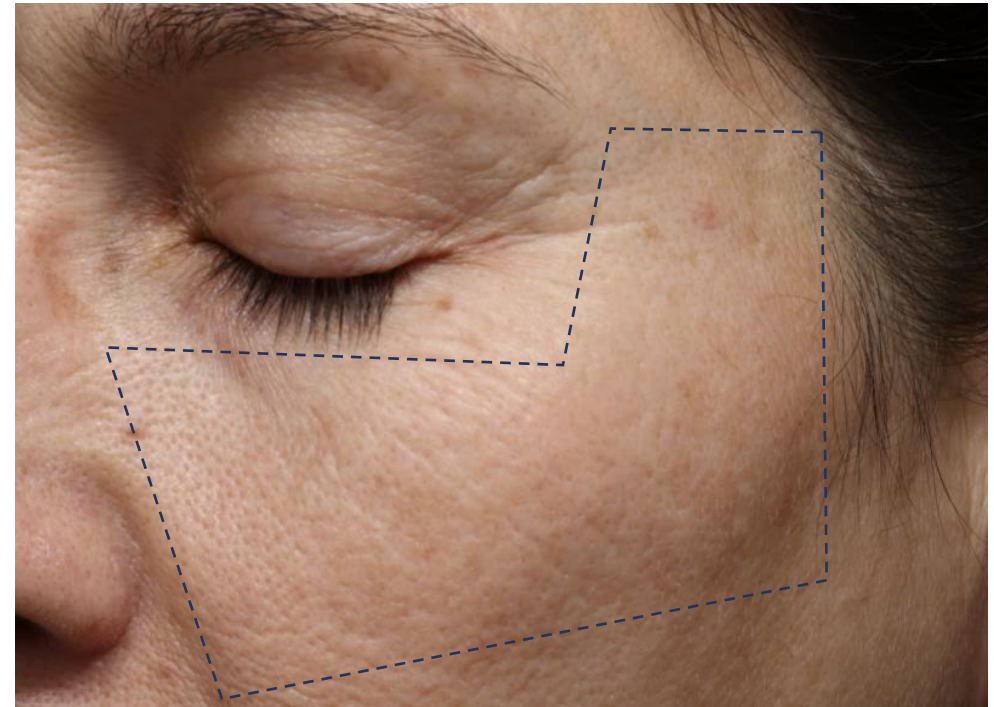
Visit 6

Upper Cheek: Same Subject KB301 vs Placebo on Visit 6

Improvement in fine lines as well as reduction on lateral canthal line because of increased elasticity of the skin



KB301 low dose – Visit 6



Placebo - Visit 6

Phase I Cohort 2 Summary

1

Repeat administration of KB301 was well tolerated across subjects with minimal injection site reactions; all injection site reactions resolved within 3-5 days post injection

- Systemic Adverse Events (drug or placebo related) included: mild body ache (n=4), mild fatigue (n=4), mild headache (n=2), mild chills (n=2); moderate muscle pain on one side of the body (placebo side, n=1)

2

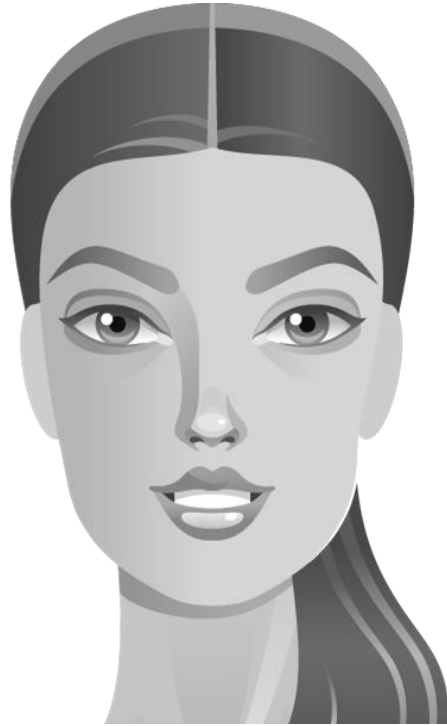
Treatment of KB301 has demonstrated clinical benefit vs placebo, including improved Subject Satisfaction Scores across three areas compared with placebo

- **Above the Knee:** KB301 injection in the area above the knee was associated with improved thickness as well as improved Subject Satisfaction and Investigator Assessment compared with placebo, indicating potential opportunity beyond face (e.g., back of the hand)
- **Lower cheek:** while exploratory Skin Texture Scale and Fine Line Scale did not demonstrate separation of treated vs placebo, KB301 treatment resulted in improved skin laxity, solar dyschromia and telangiectasia as well as improved Subject Satisfaction Scores in the high dose cohort
- **Upper cheek:** KB301 treatment was associated with improved elasticity, reduced fine lines as well as improved Subject Satisfaction Scores in the high dose cohort



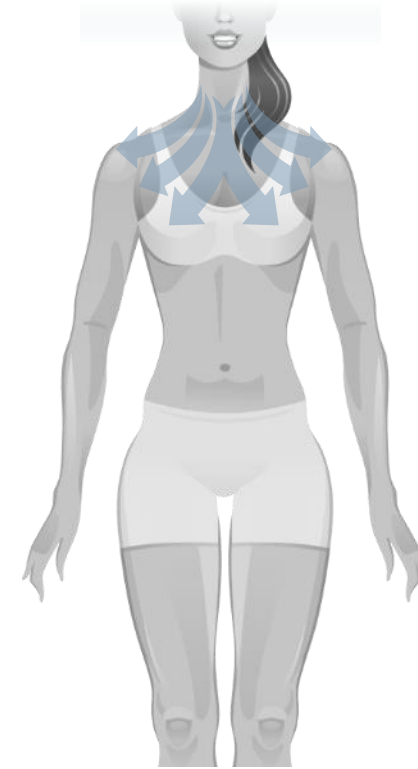
Market Opportunity

KB301 Has Potential to Provide Differentiated Benefit in Large and Growing Markets



Global Facial Injectables Market¹

\$13B → \$26B
2020 by 2026



Global Skincare Devices Market²

\$18B → \$50B
2018 by 2028

Source: ISAPS International Survey on Aesthetic / Cosmetic Procedures
Note: Not all products or indications approved in the US.

1. August 2021 – Grand View Research - Facial Injectable Market Size & Share Report, 2021-2028.
2. November 2020 – Research and Markets - Global Skincare Devices Market (2020 to 2030) - by Product, Distribution Channel, Application and End-user.



Closing and Q&A

A GENE-BASED AESTHETICS COMPANY

March 2022

JEUNE