# A GENE-BASED AESTHETICS COMPANY

March 2022

JEUNE

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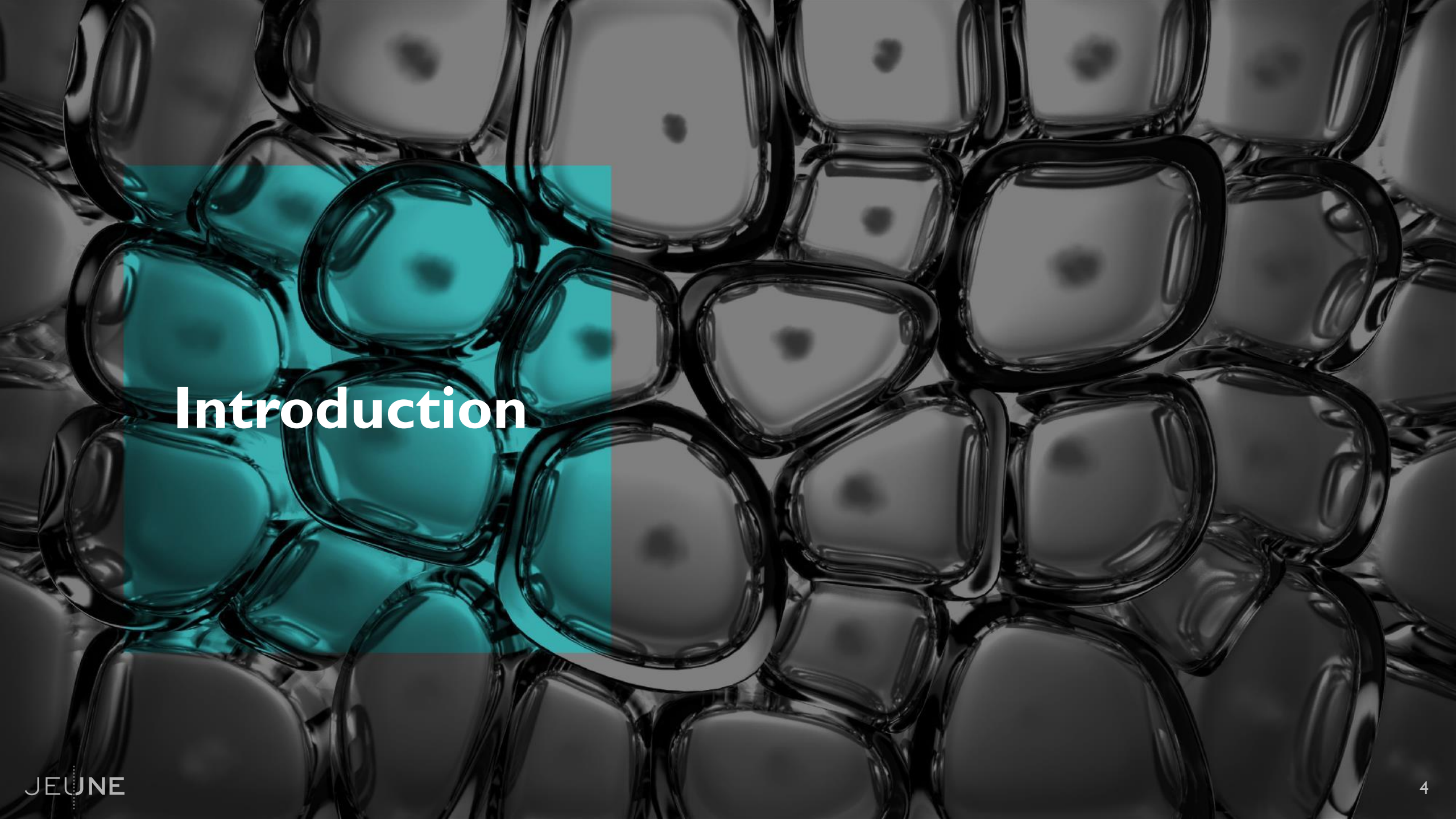
# Agenda

1 **Introduction**
- Krish Krishnan, Chairman, Jeune Aesthetics

2 **PEARL - 1 Clinical Study and Next Steps**
- Dr. Bhushan Hardas, President, Jeune Aesthetics, Inc.

3 **KOL Perspective**
- Dr. Steve Yoelin, Study Investigator

4 **Q&A**

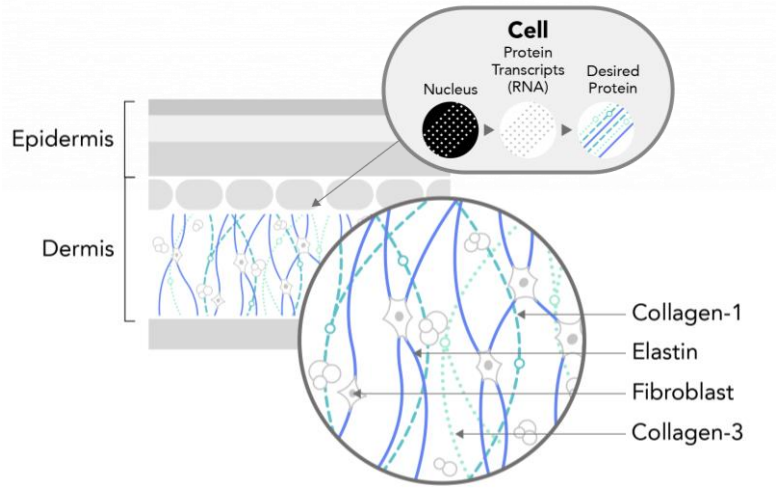


# Introduction

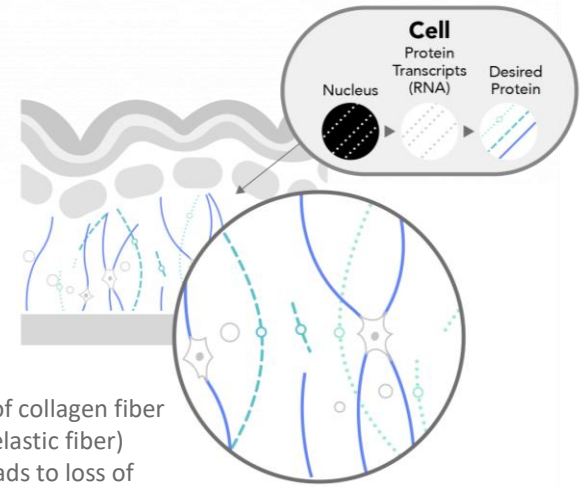
# The Characteristic Look of Aging is Caused by Declining Levels of Key Proteins in the Skin's Extracellular Matrix

- 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




Declining levels of collagen fiber and elastin (elastic fiber) production leads to loss of extracellular matrix integrity

# 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

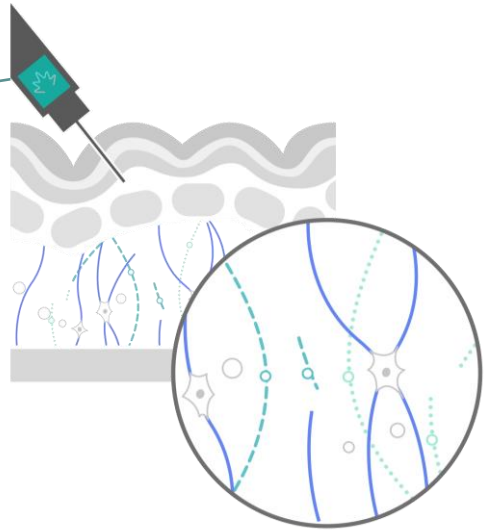
- COL3 appears early during collagen fibrillogenesis, and the subsequent replacement of this COL3 by COL1 is a critical step for collagen fibril maturation and extracellular matrix reorganization[1]
- In addition, COL3 both regulates the dimensions of COL1 fibers[2] and enhances COL1 elasticity[3]
- 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 humans[4]
- 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 receptors[5]

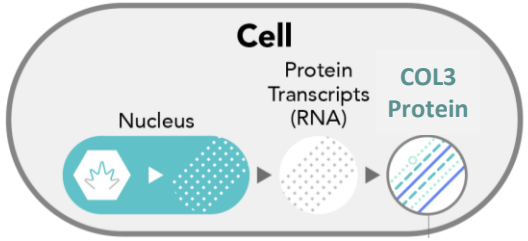
| | Type I Collagen | Type III Collagen | Elastin |
|---|---|---|---|
| Percentage in the skin | 70-80% | 20-30% | 2-3% |
| Aging alteration | Increases with growth, decreases with age | Abundant in baby skin, decreases with growth | Abundant in baby skin, peaks in mid-20s / early 30s and declines thereafter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

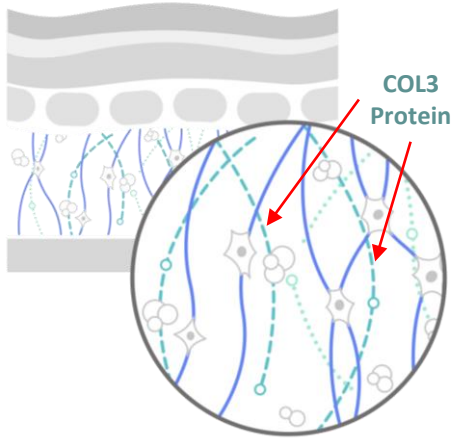

1. *Wang, P. et al., 2018. Wound healing. Journal of the Chinese Medical Association, 81(2), pp. 94-101.*
2. *Liu, X. et al., 1997. Type III collagen is crucial for collagen I fibrillogenesis and for normal cardiovascular development.. Proc Natl Acad Sci U S A, 94(5), pp. 1853-6.*
3. *Asgari, M., Latifi, 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


STAR-D platform vector containing the *COL3A1* transgene





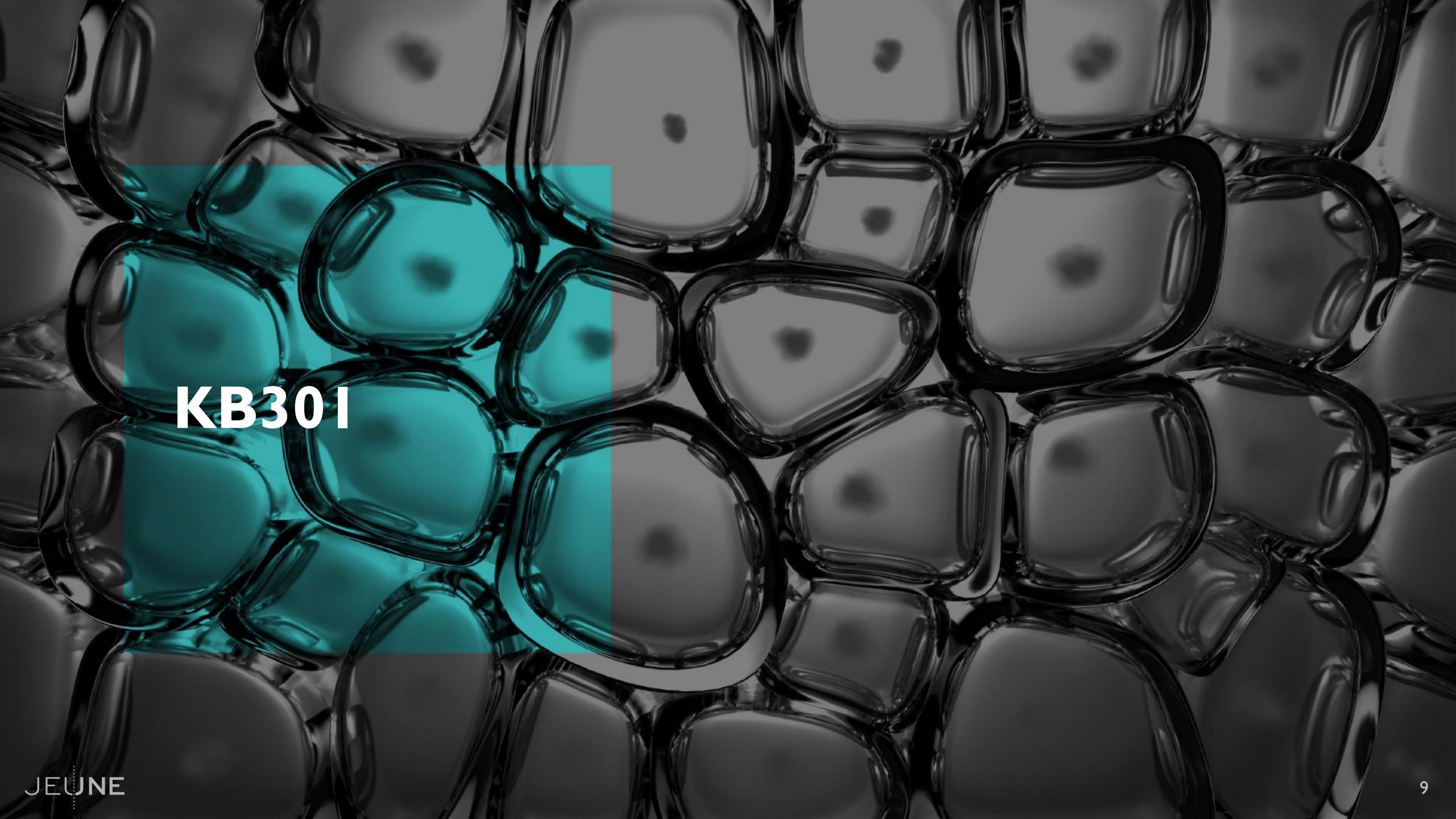




**1 Ready to Use**
- Shipped on dry ice and stored at below freezing at sites

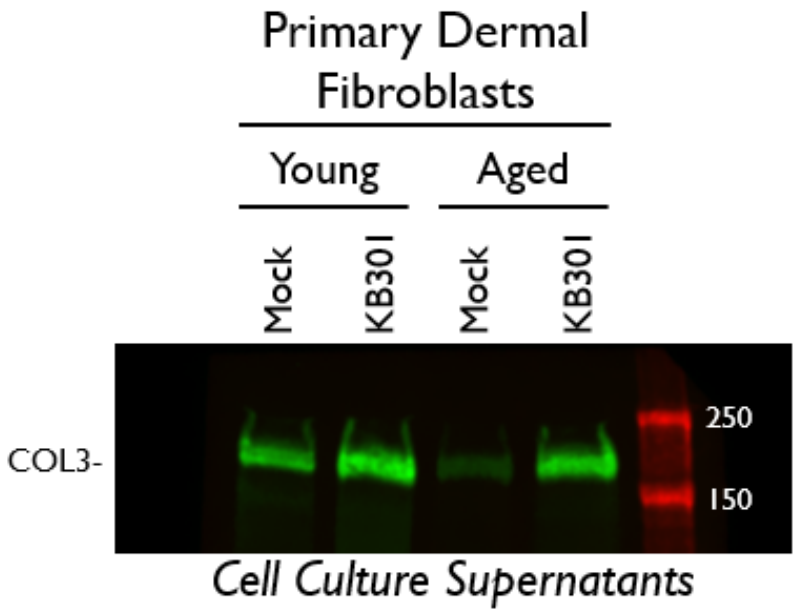
**2 Intradermal Injection**
- Delivered via 33G needle
- Treatment area numbed with ice (no topical anesthesia required)

**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

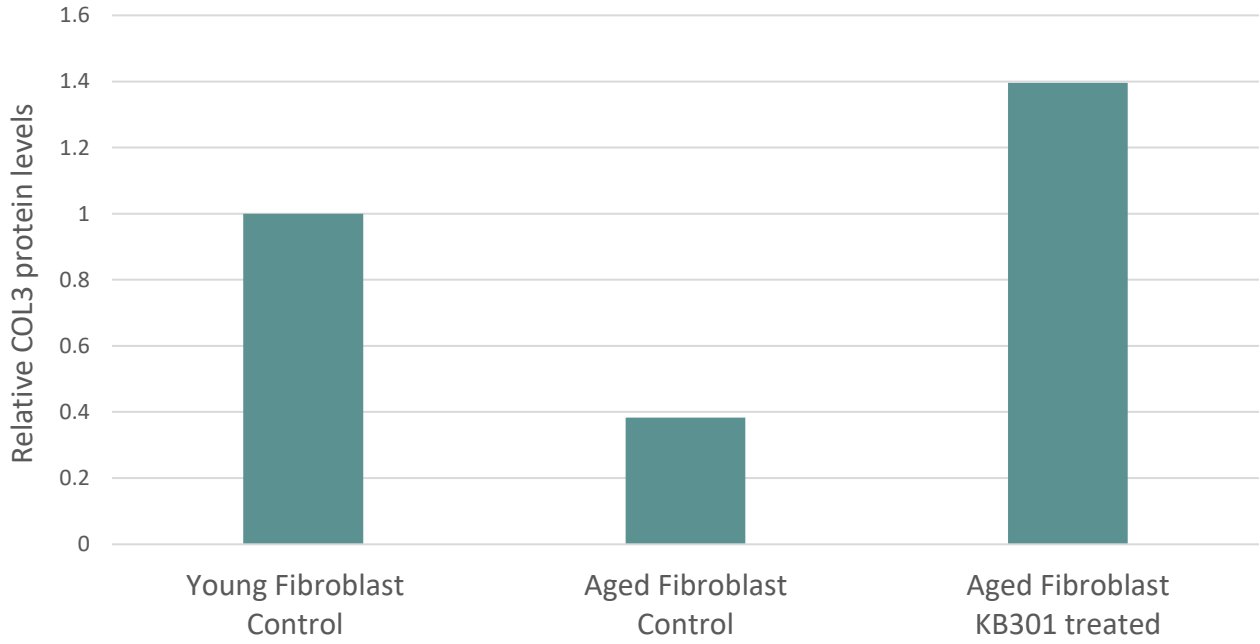

KB301

# 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*

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# PEARL-1 Cohort 1 – 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

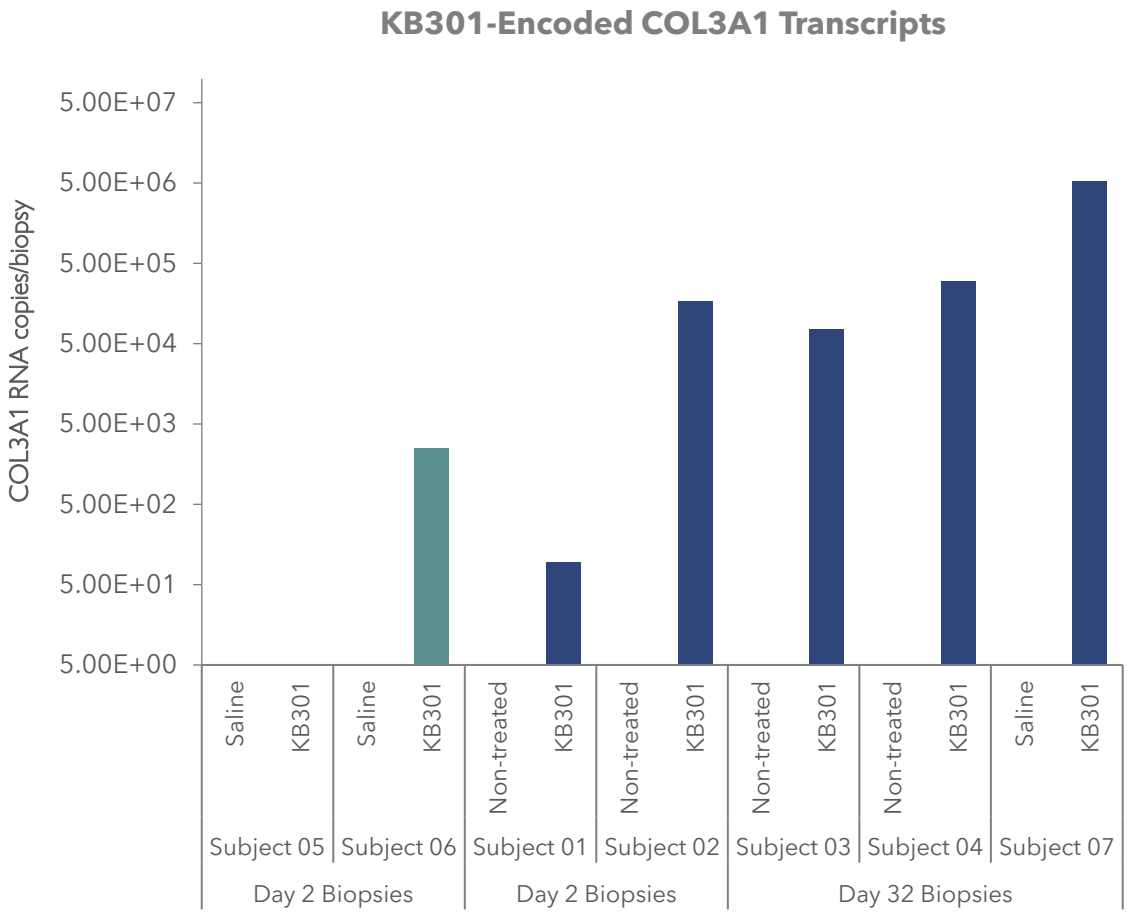
## Safety & Tolerability

- 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



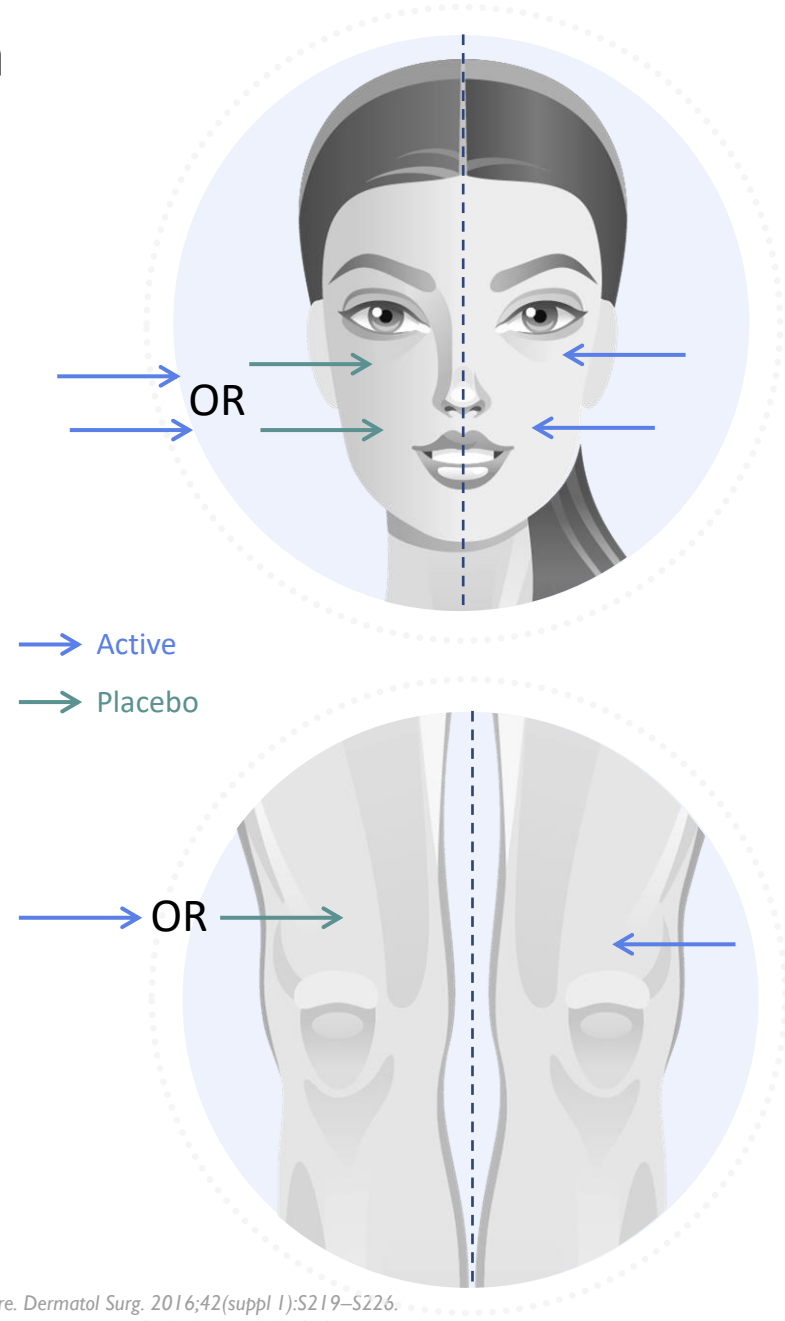
# PEARL-1 Cohort 2 Safety & POC Efficacy Study Design

## 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

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*

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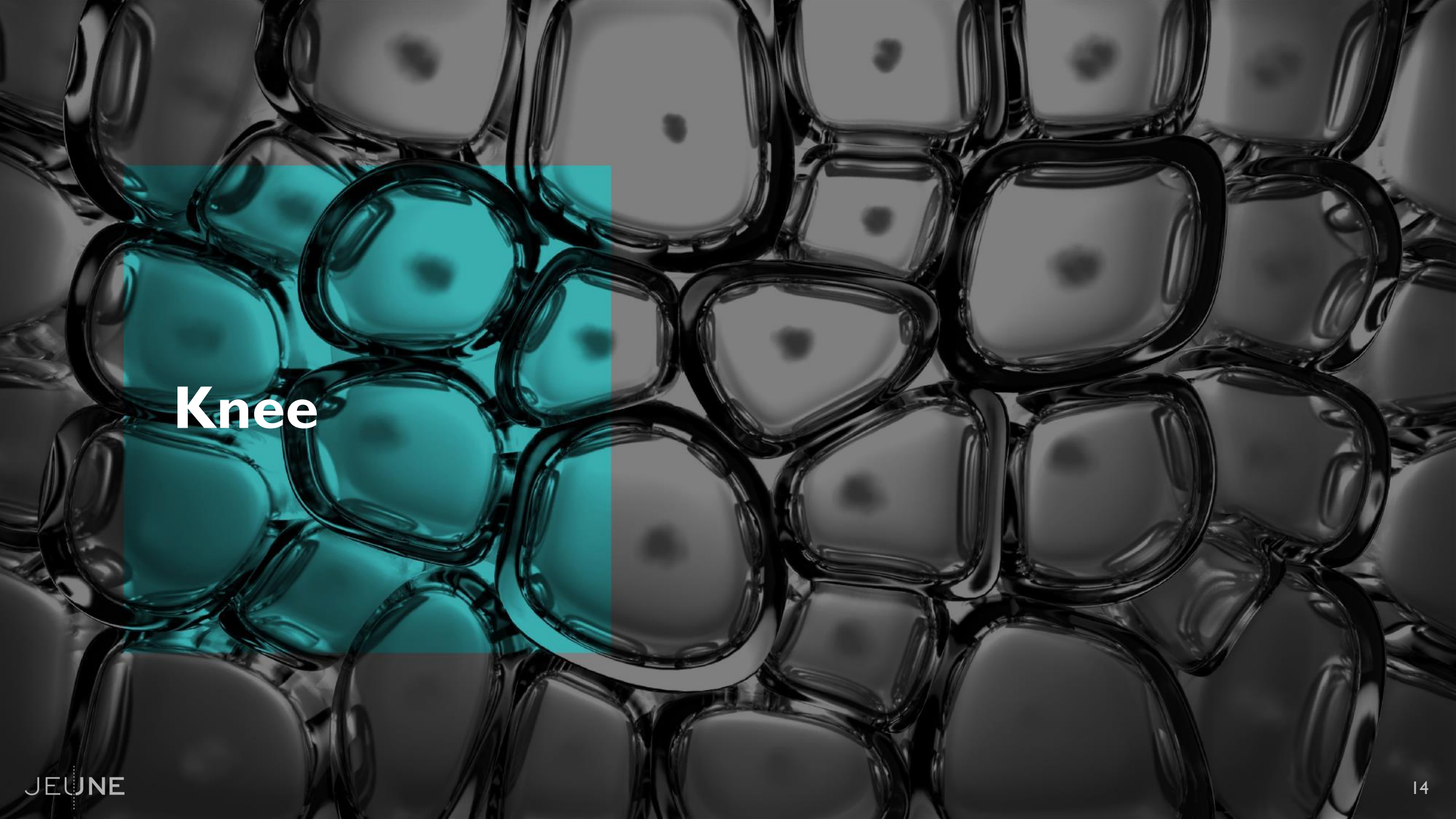
# Baseline Characteristics and Disposition

27 Subjects Enrolled in the Study; 23 fully completed

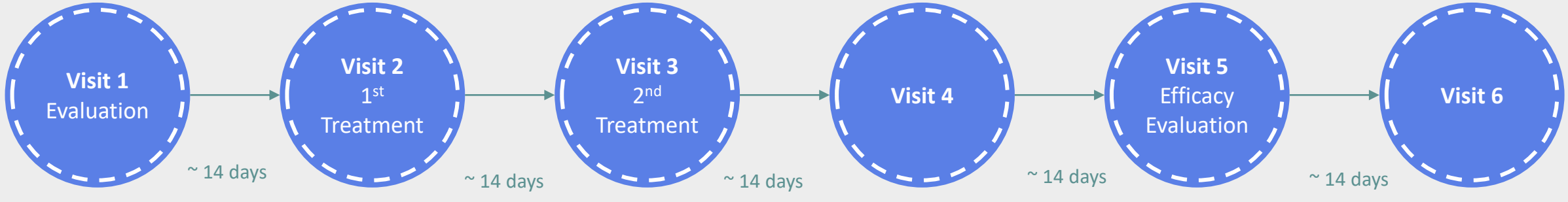
| Criteria | Baseline in PEARL-1 Study | Comments |
|---|---|---|
| Healthy Male and Female Subjects | Male: 1<br>Female: 26 | |
| Between 30 and 70 years old at time of written consent | Average age: 65.1 years | Older age-range than us typical in aesthetic trials due to regulatory feedback |
| Subjects with Fitzpatrick skin type I through III | Type II: 93% subjects<br>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<br>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 |

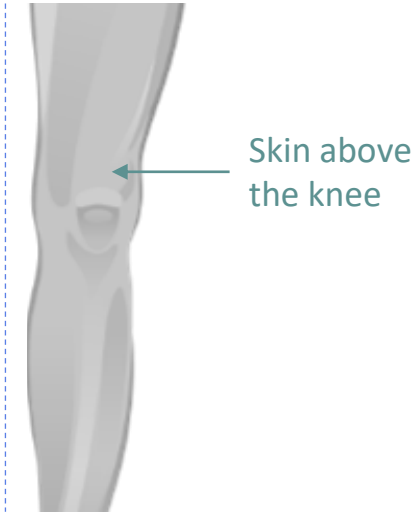
1. *Adapted from Carruthers J, Donofrio L, Hardas B et al. Development and validation of a photonumeric scale for evaluation of facial fine lines. Dermatol Surg. 2016;42:S227–S234. 101*
2. *Adapted from Donofrio L, Carruthers A, Hardas B, et al. Development and validation of a photonumeric scale for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


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 |

# Adverse Events

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)

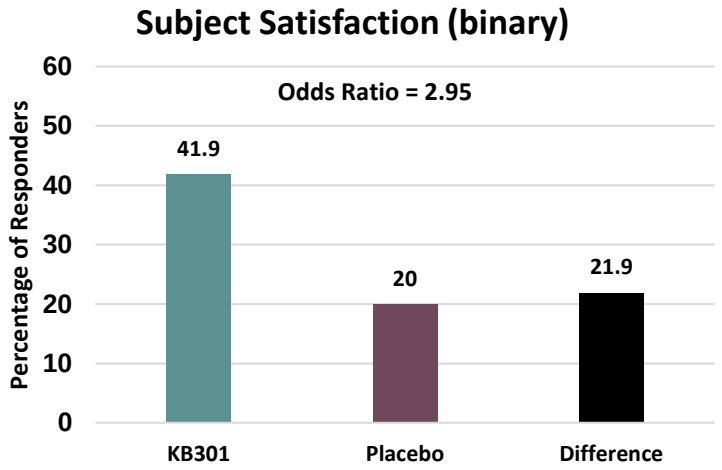
Local adverse Event **: Above the knee** (Injection site reactions)

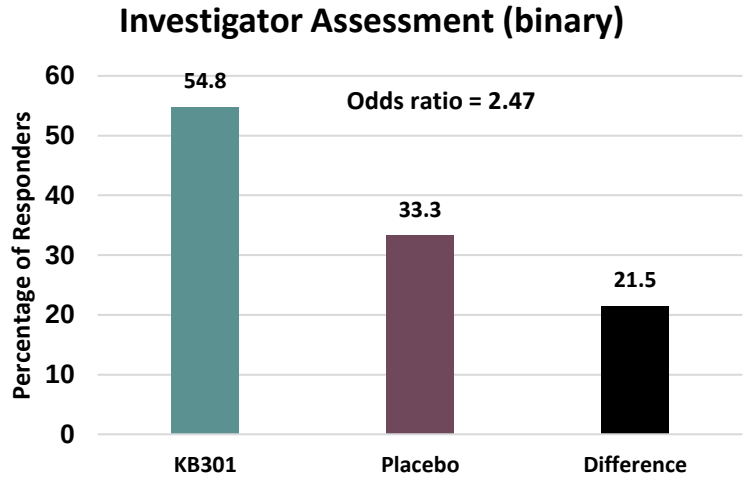
| Injection Site Reactions | | | | |
|---|---|---|---|---|
| | Above Knee AE Counts | | | |
| | KB301 | | PLACEBO | |
| | Visit 2 | Visit 3 | Visit 2 | Visit 3 |
| Blisters | 1 | 0 | 0 | 0 |
| Bruising | 1 | 1 | 0 | 0 |
| Bumps | 1 | 0 | 0 | 0 |
| Unspecified | 1 | 0 | 1 | 0 |
| Itching | 3 | 0 | 0 | 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

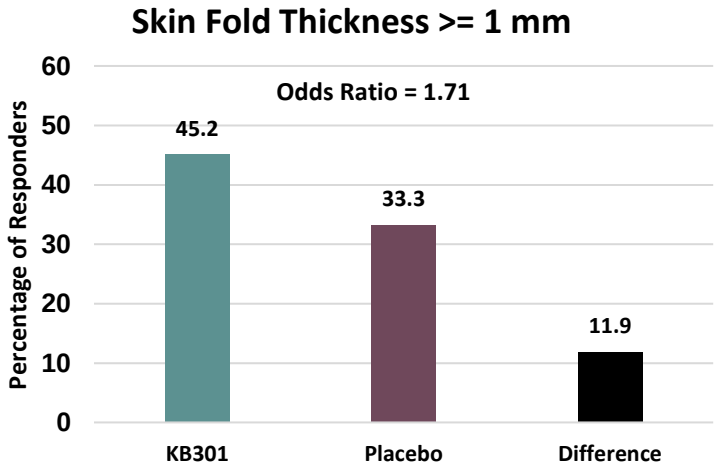
# Above the Knee: Efficacy Assessments

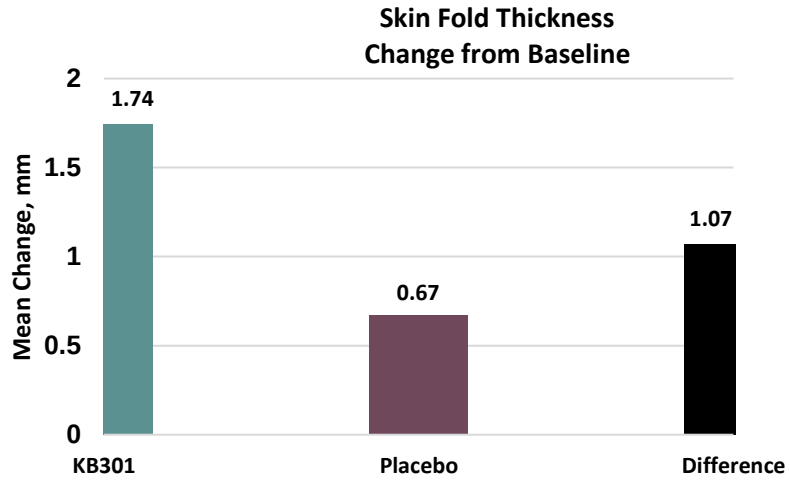
## Meaningful Improvement in Subject Satisfaction, Investigator Assessment and Improvement in Thickness between Active and Placebo



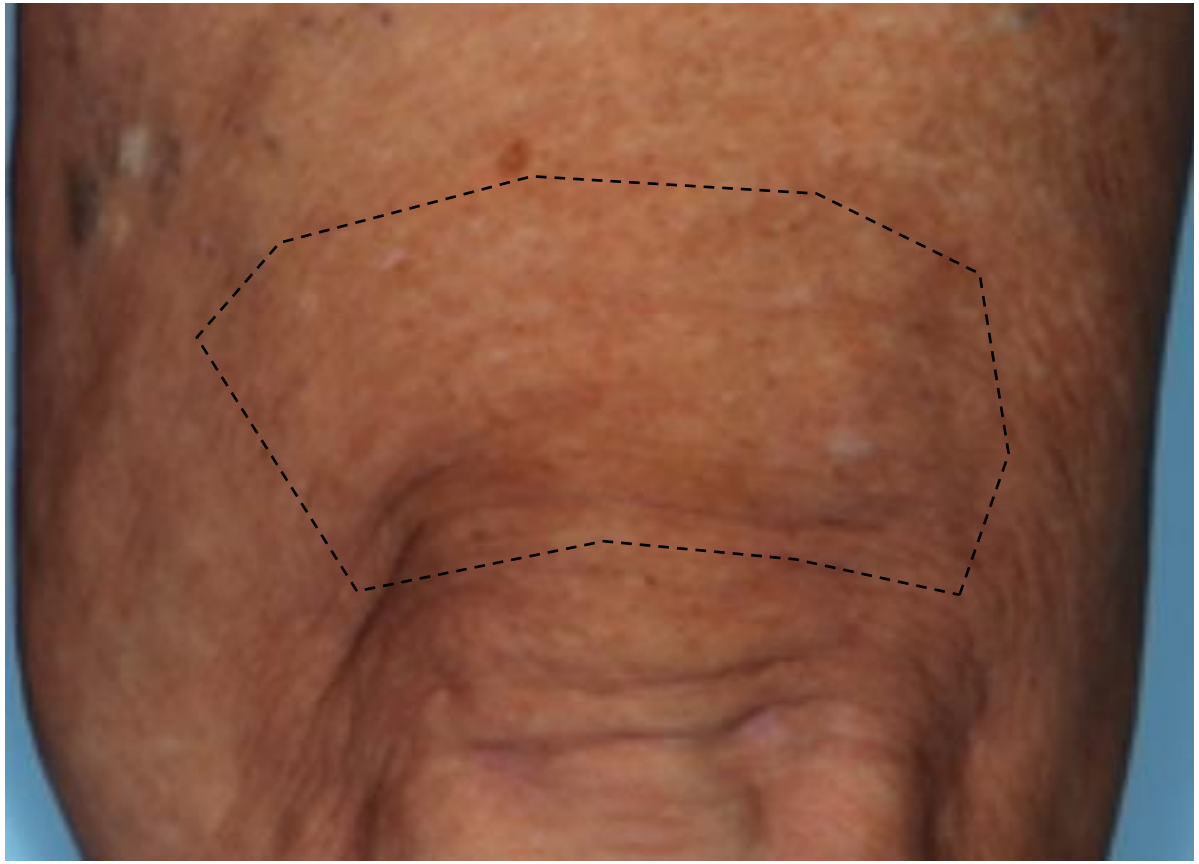




N for KB103 = 31 | N for Placebo = 15

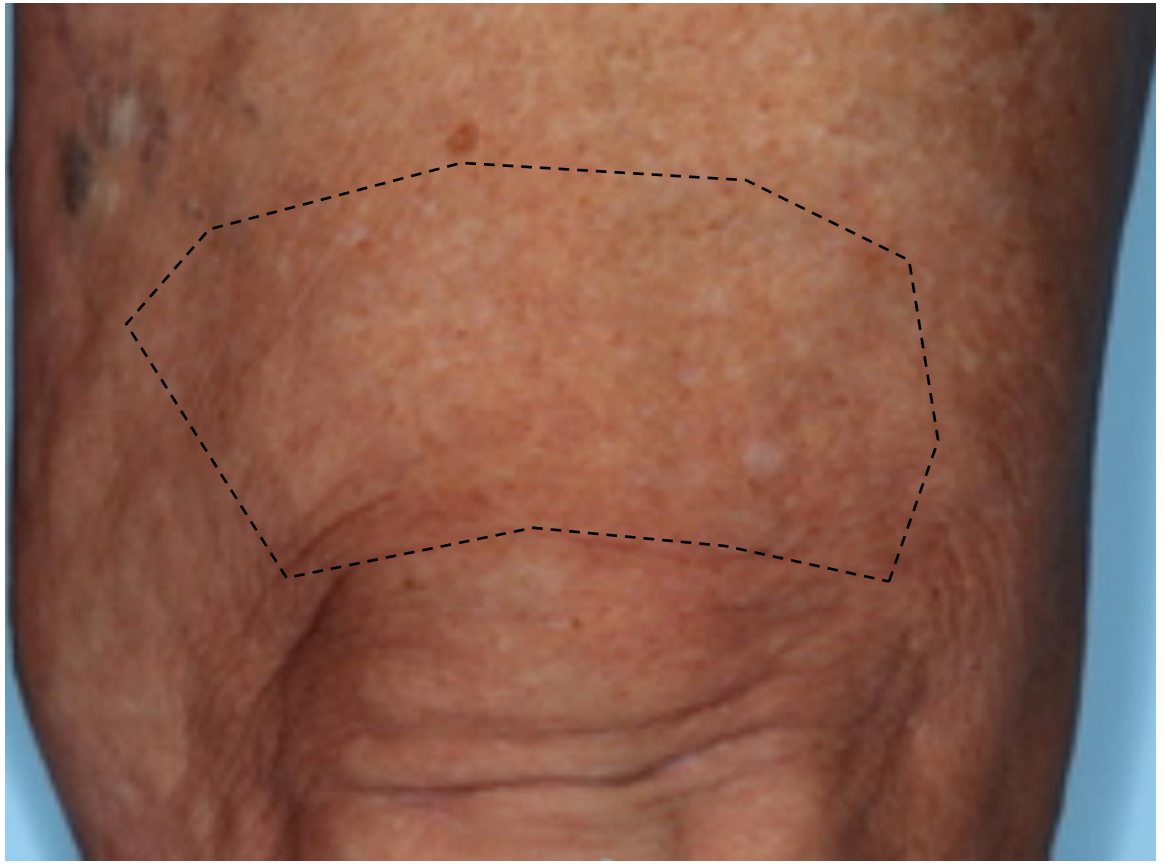


# Above the Knee: Before and After of Left Knee Treated with KB301 Low Dose



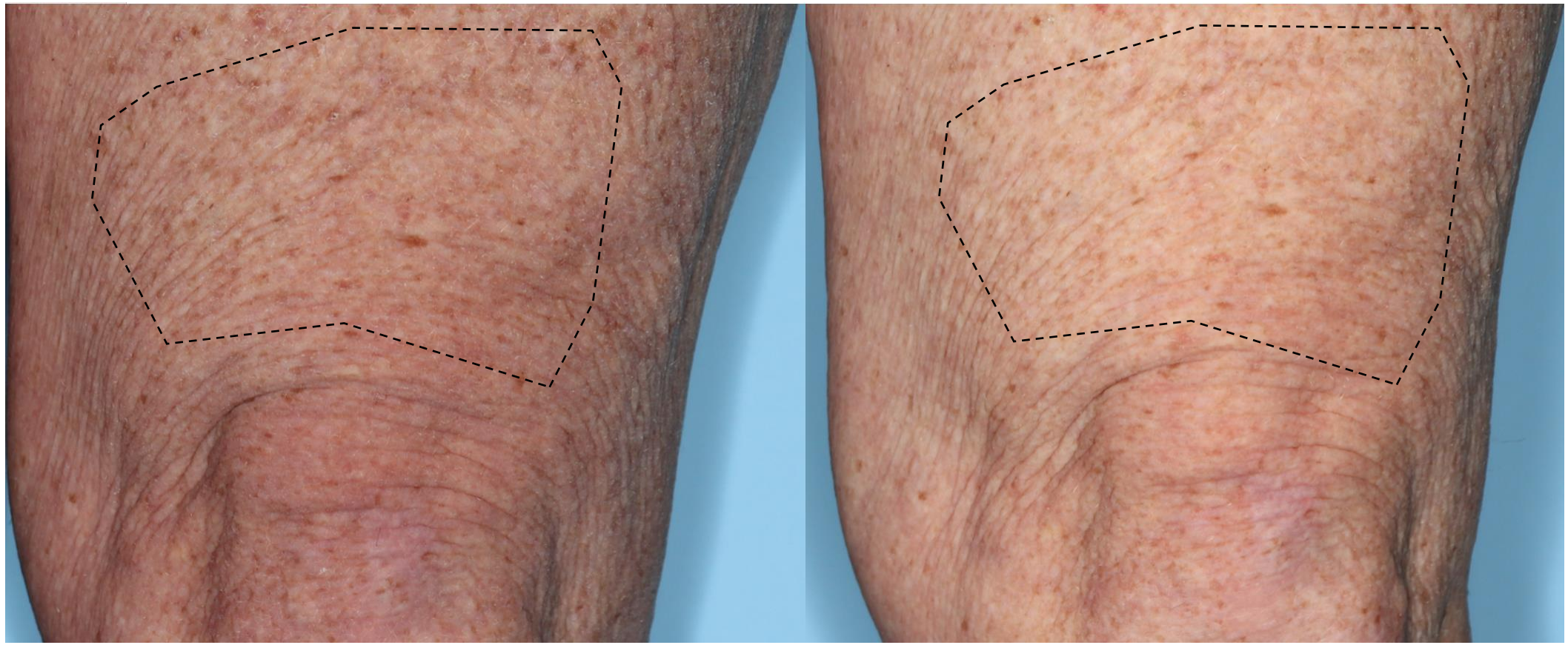
Baseline



Visit 5

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

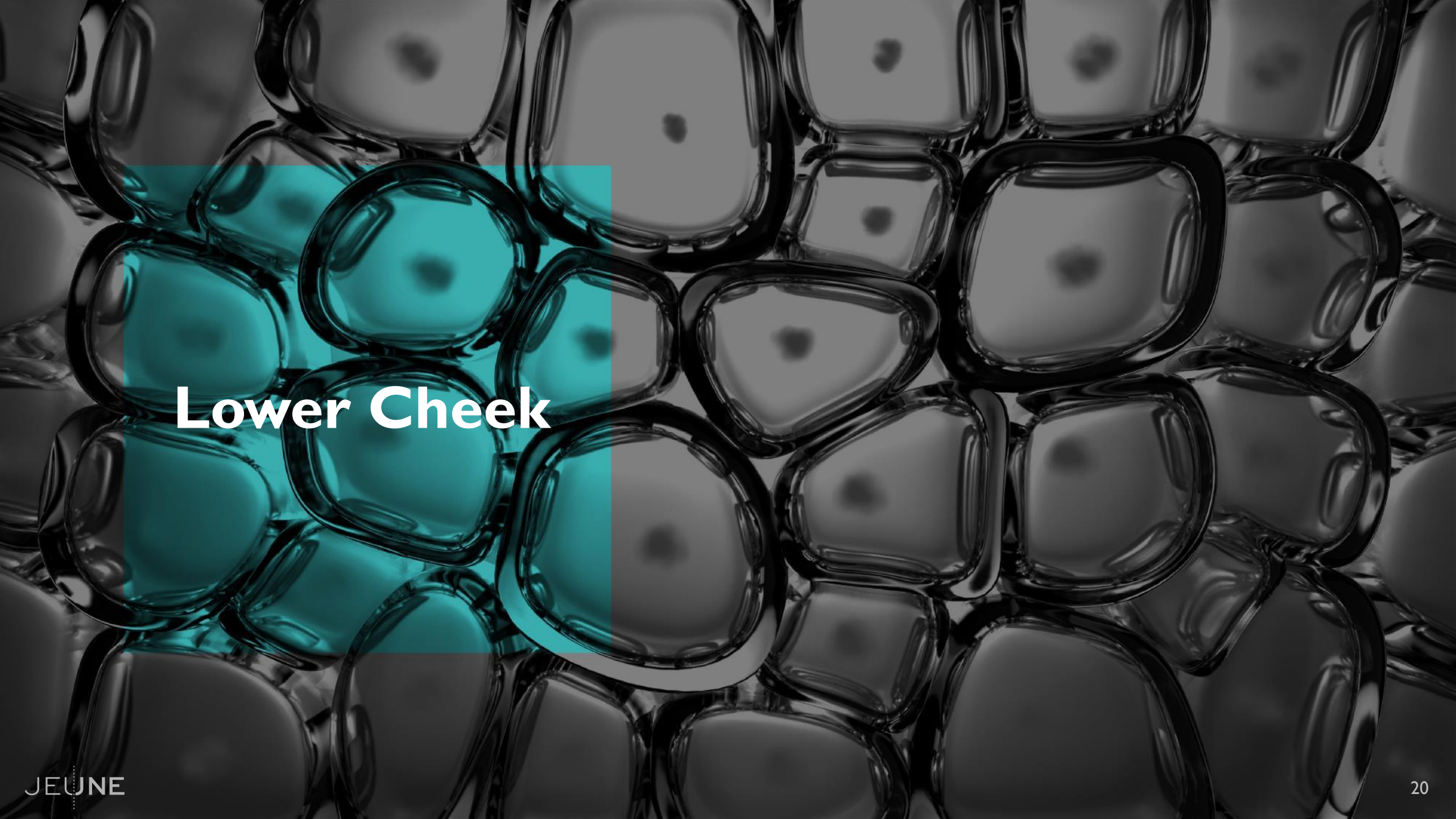
# Above the Knee: Before and After of Left knee treated with KB301 Low Dose



Baseline

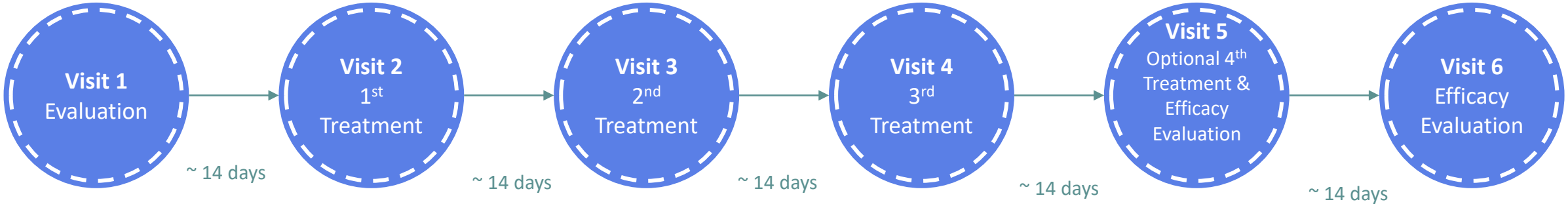
Visit 5

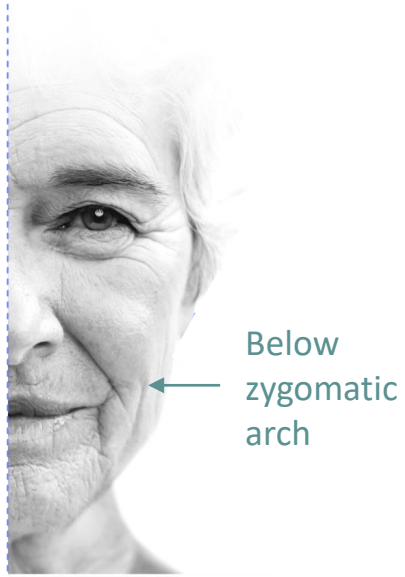
Improvement in texture as well as fine lines and softening of the folds


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 specific to this skin area but not specific to KB301 |

# Local adverse Event : Below zygomatic arch (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 |

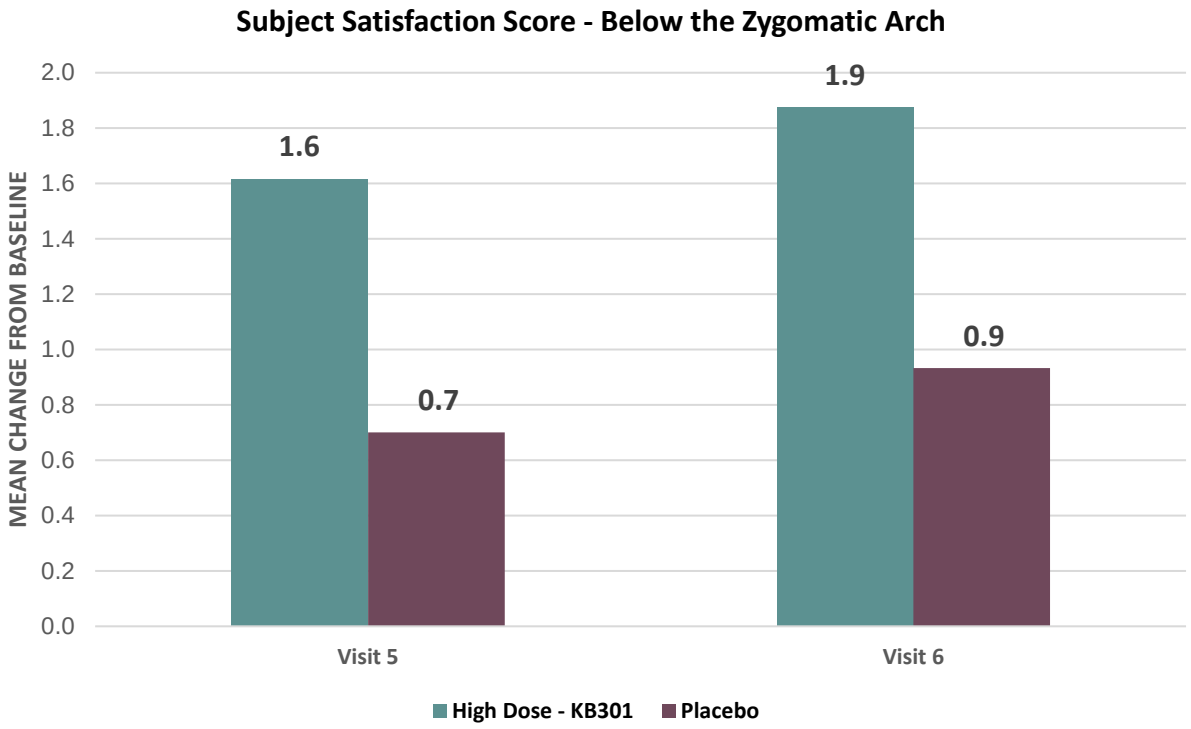
- 91% of the active adverse events (N = 68) were mild; 9% were moderate
- Injection site reactions minimized following the first injection

1. *All were mild except 1 were moderate*
2. *All were mild except 3 were moderate*
3. *All were mild except 2 were moderate*

# Lower Cheek: Efficacy Measures - Subject Satisfaction Efficacy Assessment

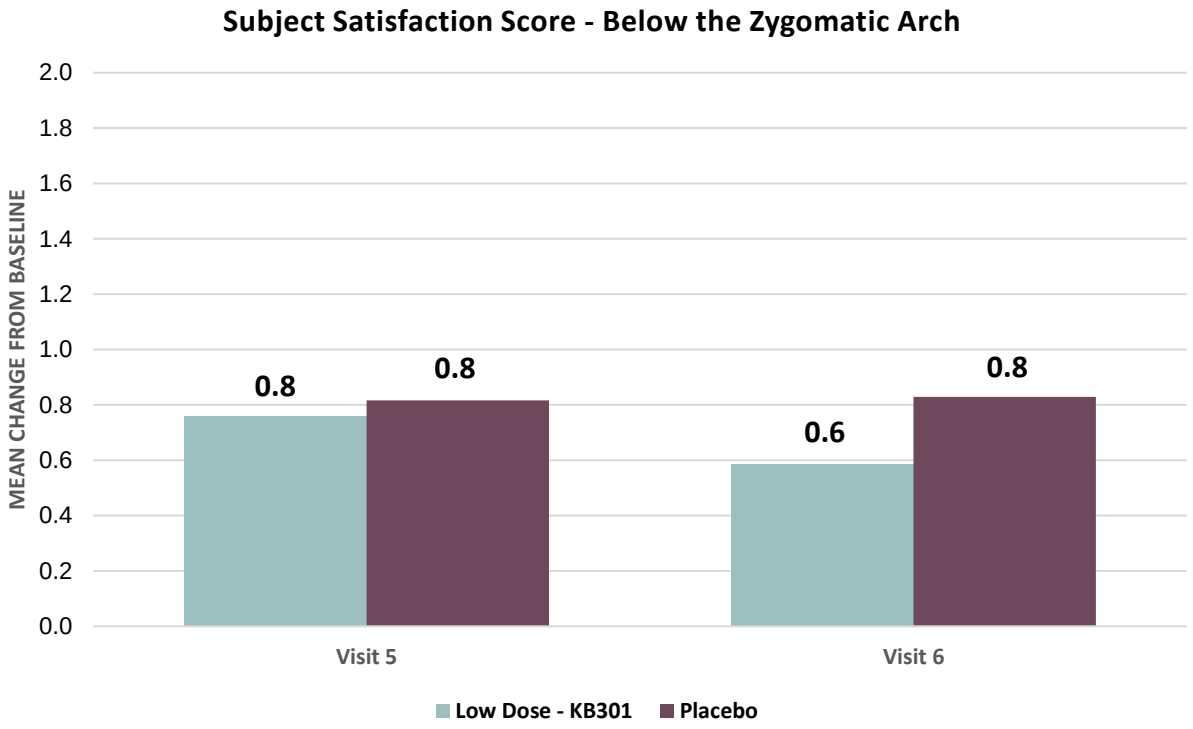
## Difference in Mean Change from Baseline between High Dose KB301 and Placebo is Clinically Meaningful

### High Dose




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

### Low Dose

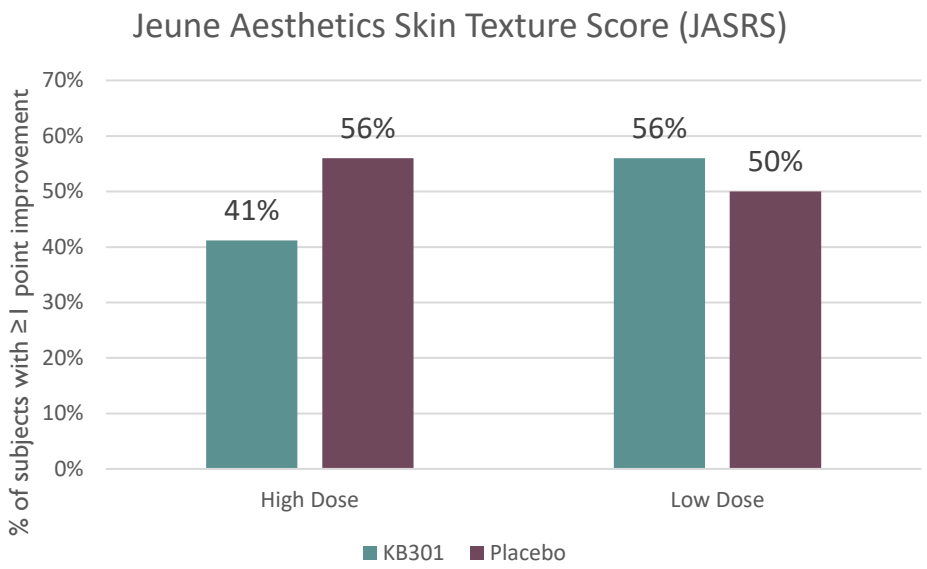


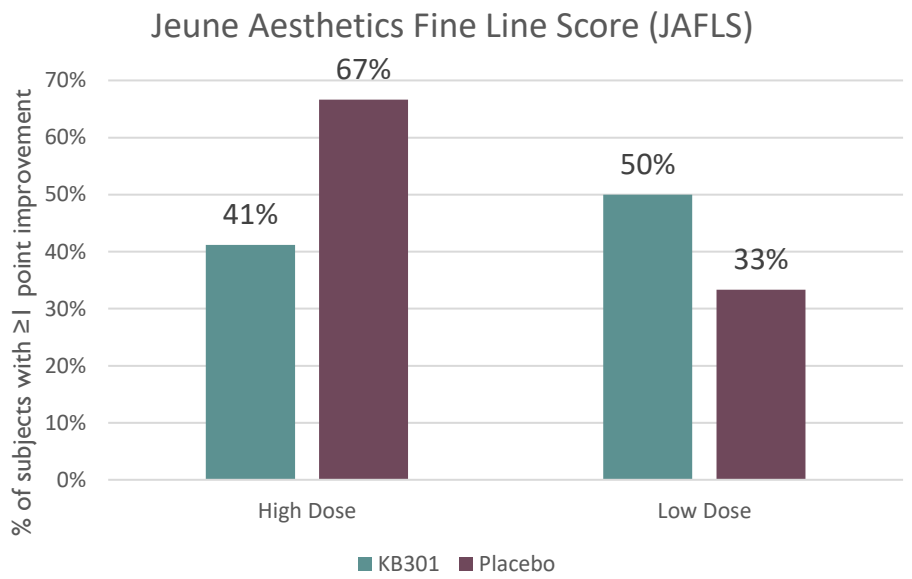

N for Low Dose = 12 for KB301| N = 6 for Matching Placebo

*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

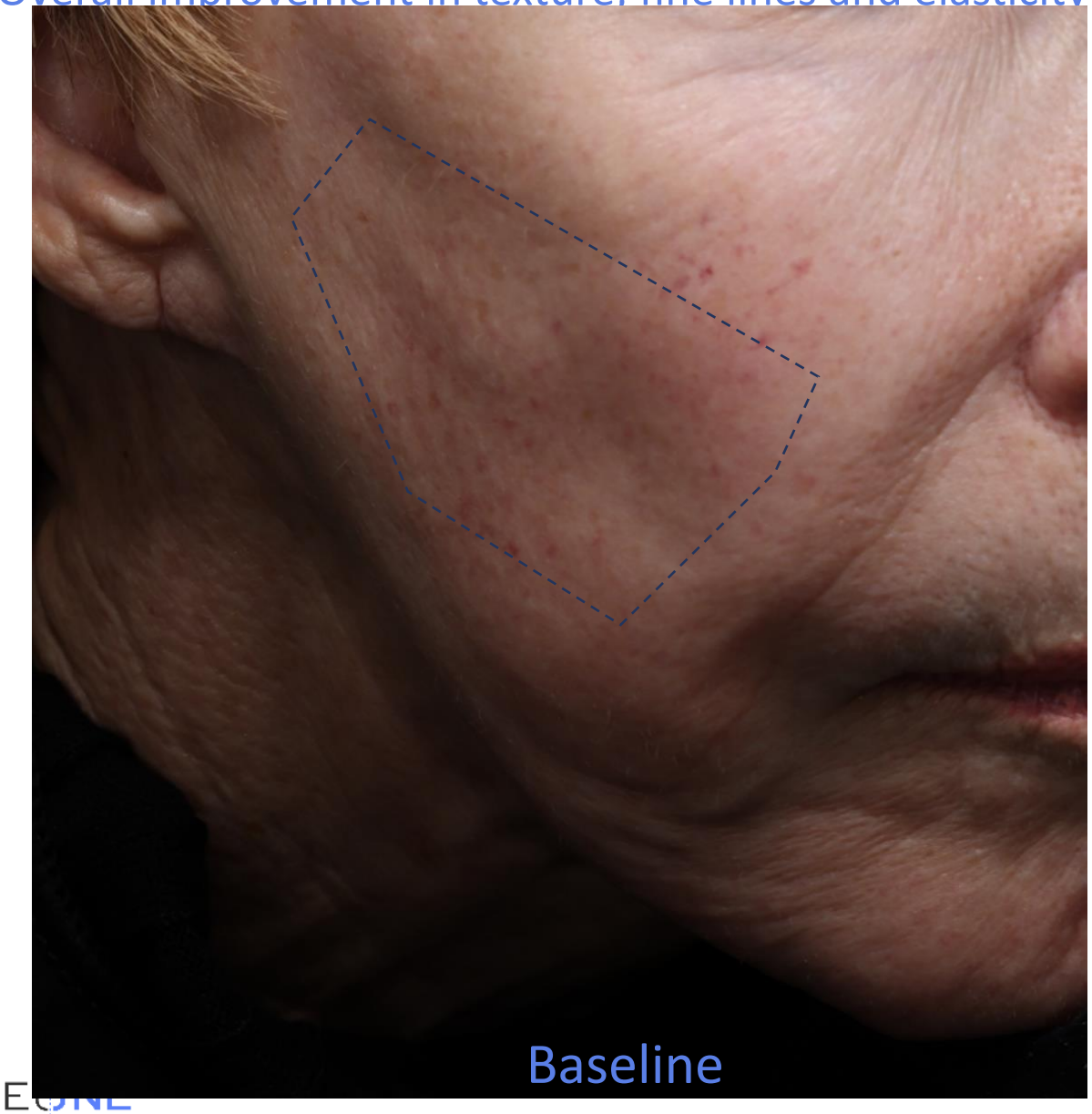
**Observations by blinded evaluator:** Moderate improvement in skin laxity; Improvement in solar dyschromia (redness); Improvement in telangiectasia (microvasculature)

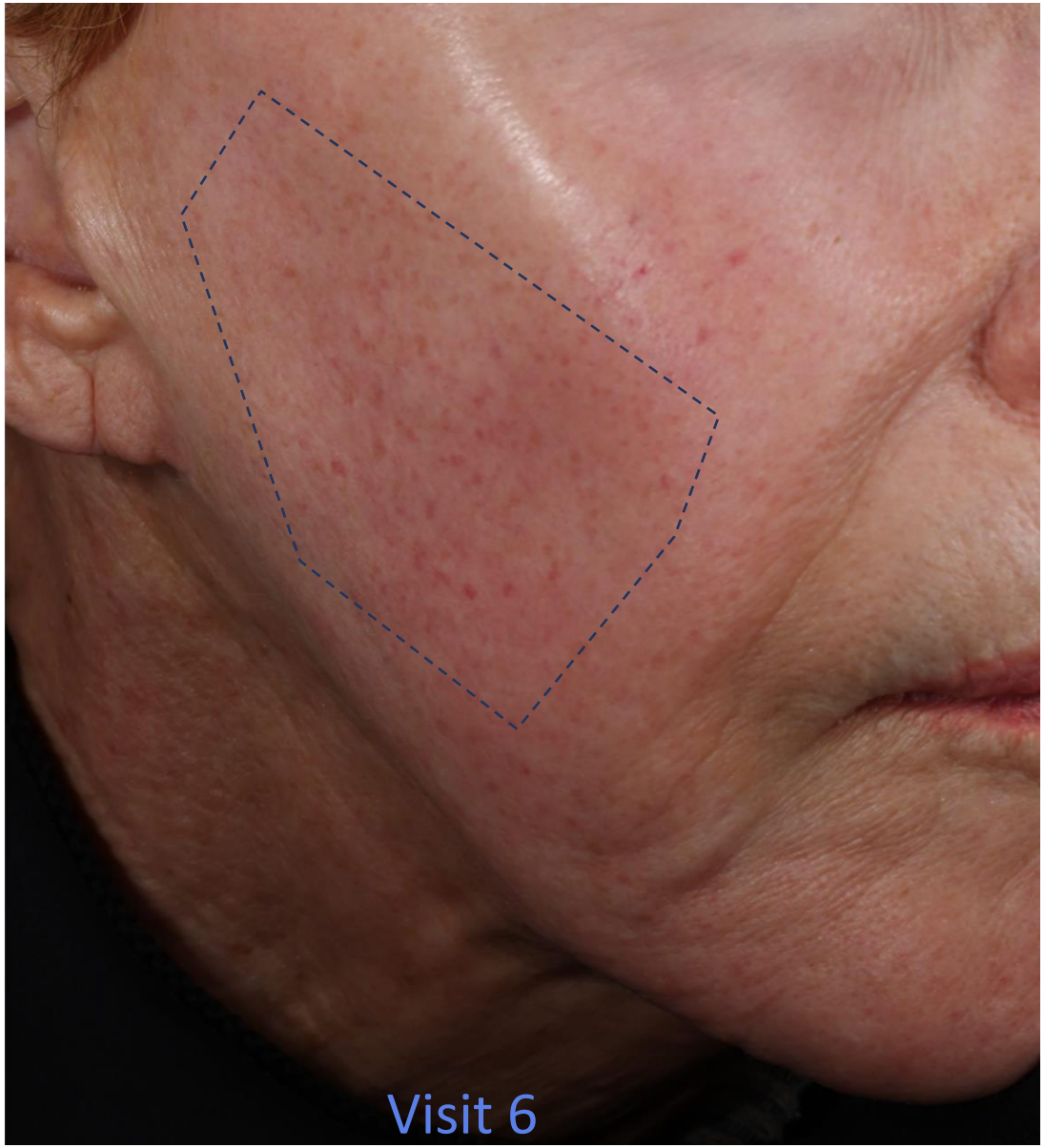
**The Scales need further validation for KB301*
***Assessment was done on 23 subjects*

JEUNE

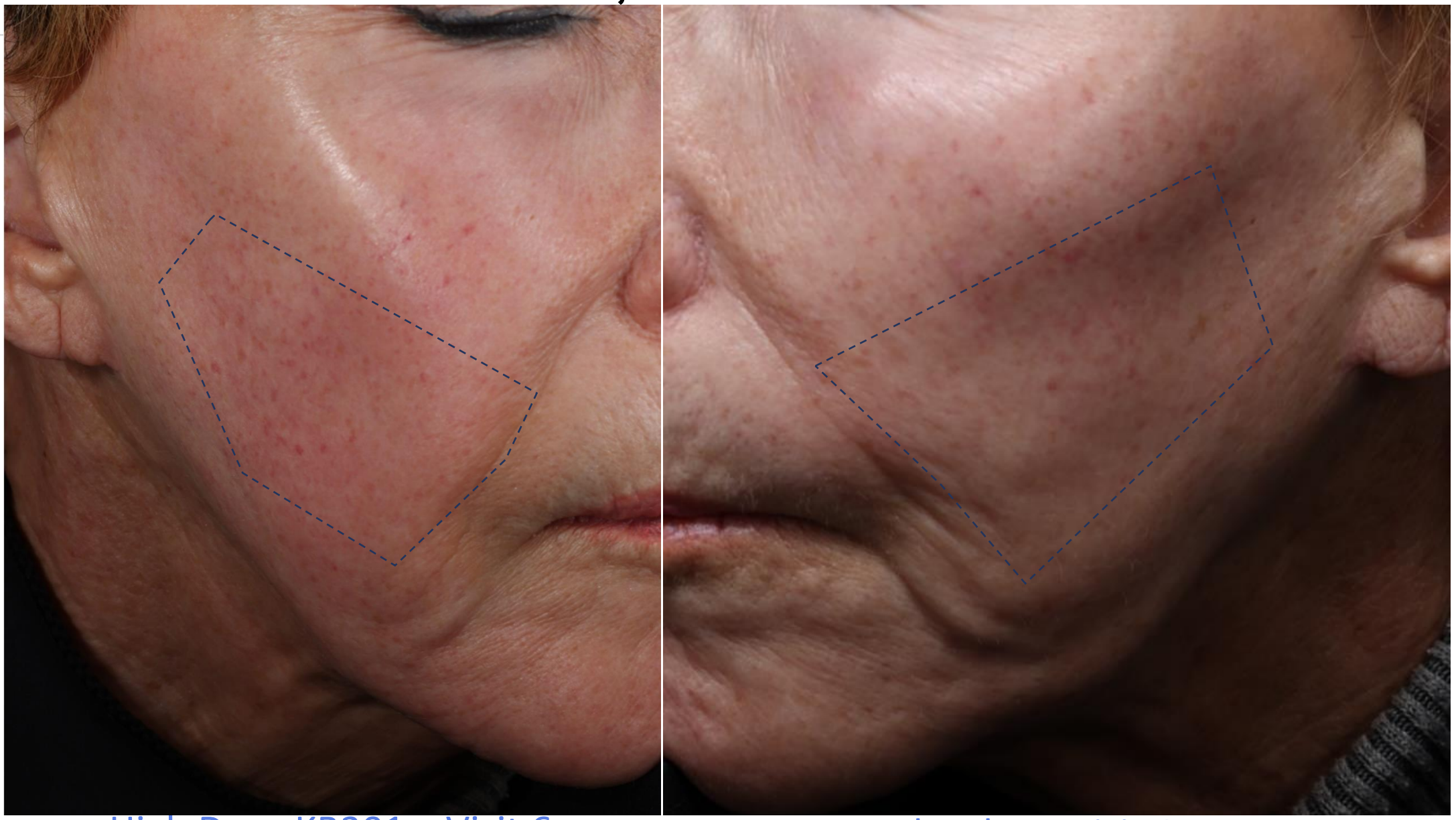
# Lower Cheek: Before and After Right Side Treated with KB301 High Dose

Overall improvement in texture, fine lines and elasticity



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

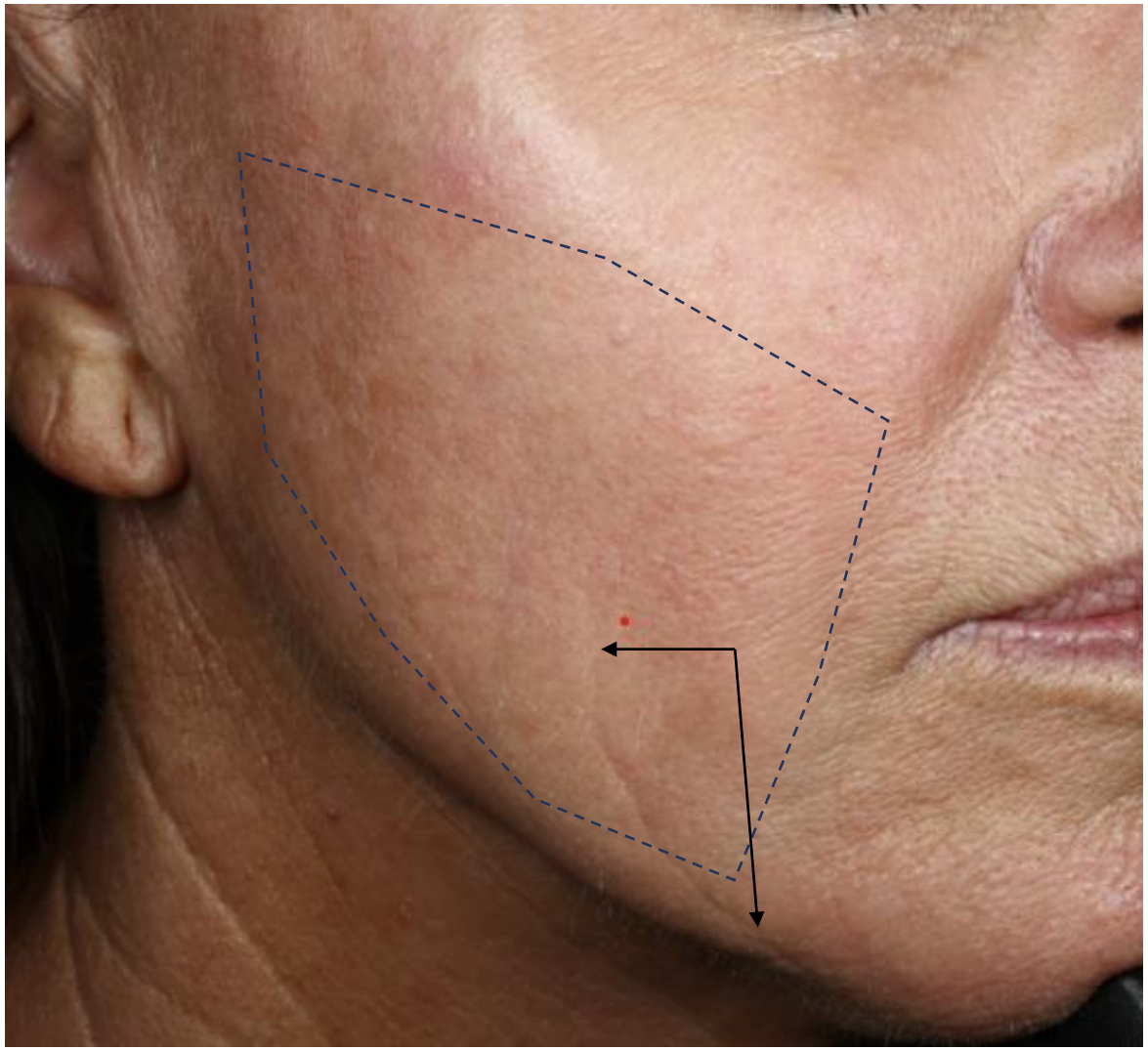


High Dose KB301 – Visit 6

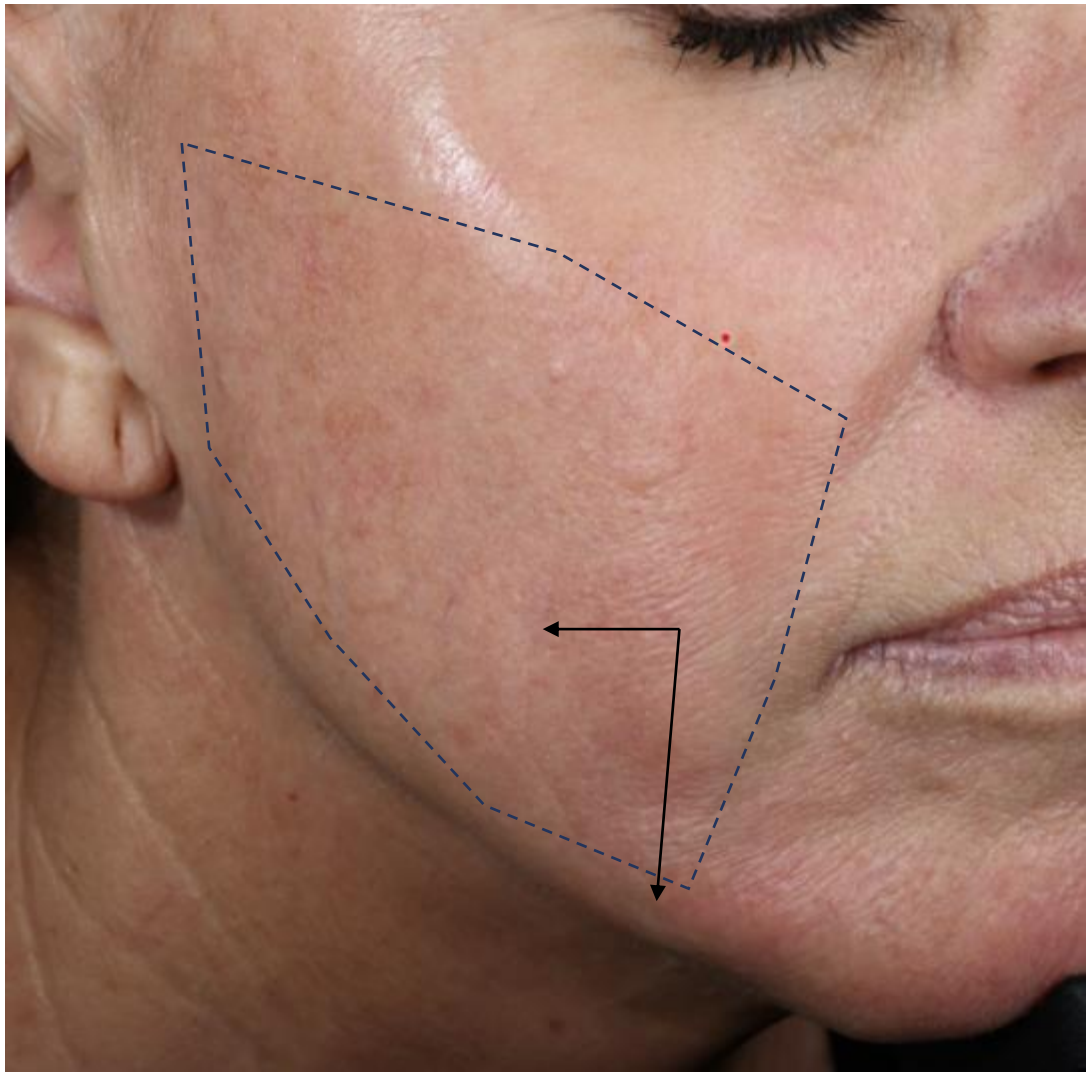
Placebo – Visit 6

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

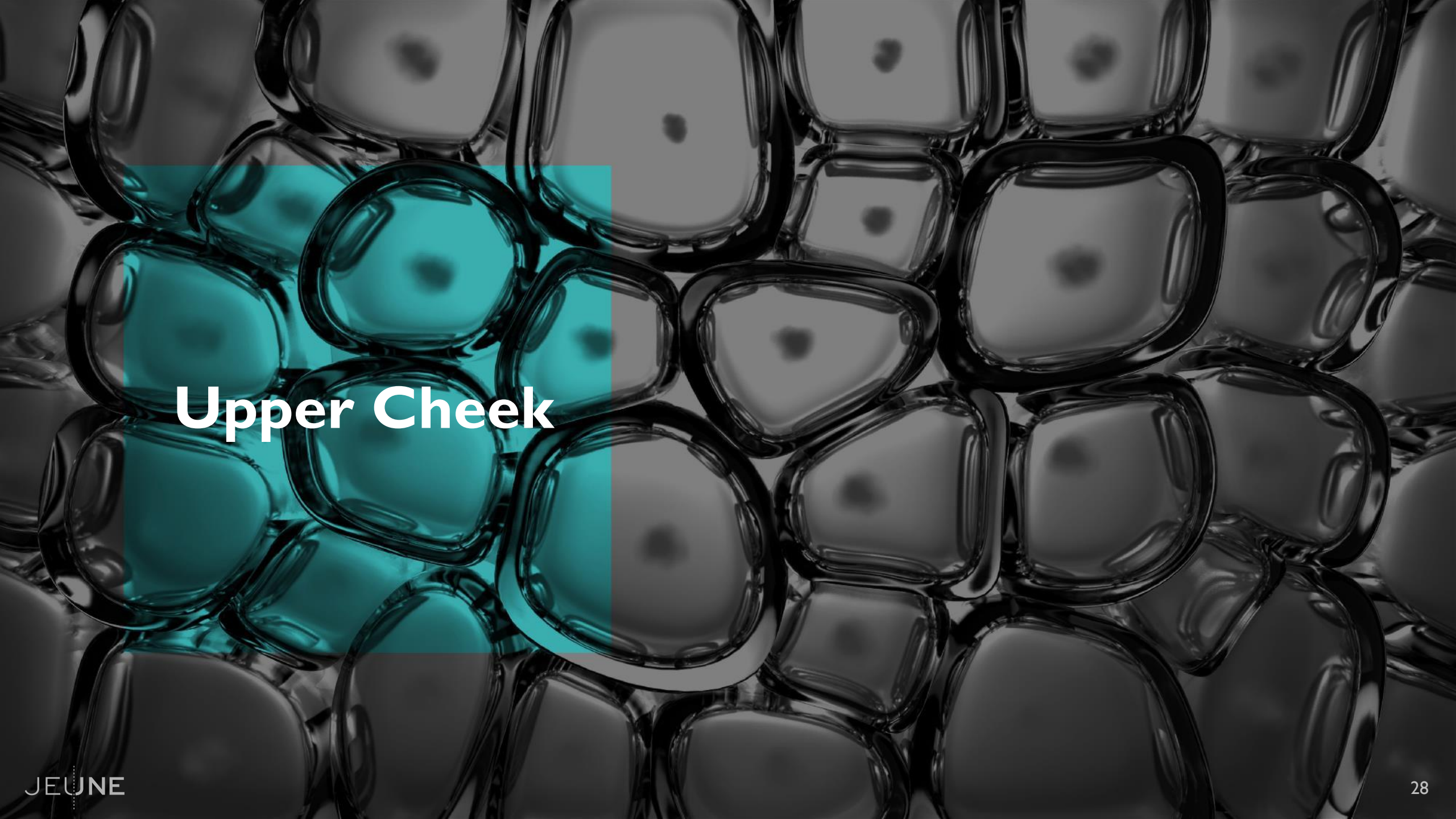
*Subject Reported: "Right Cheek Significantly improved from last visit. One wrinkle completely resolved"*



Baseline



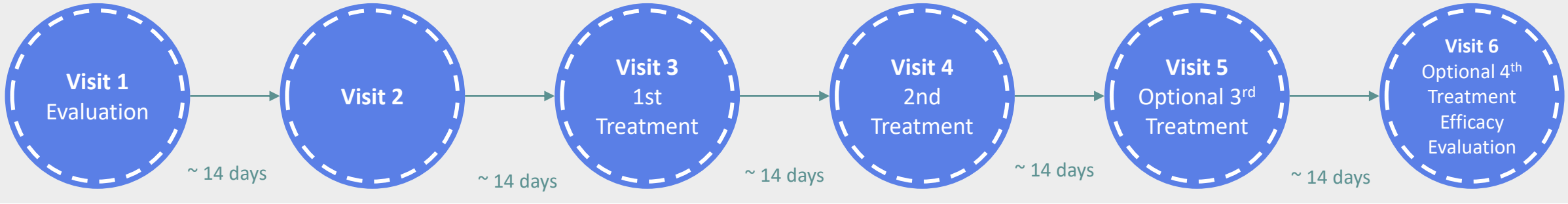
Visit 6

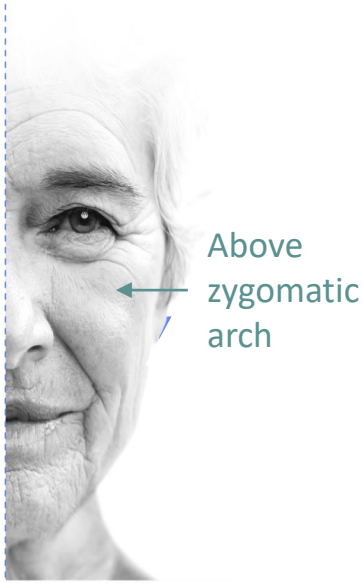


# Upper Cheek

# 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 |

# Local adverse Event : Above zygomatic arch (Injection site reactions)

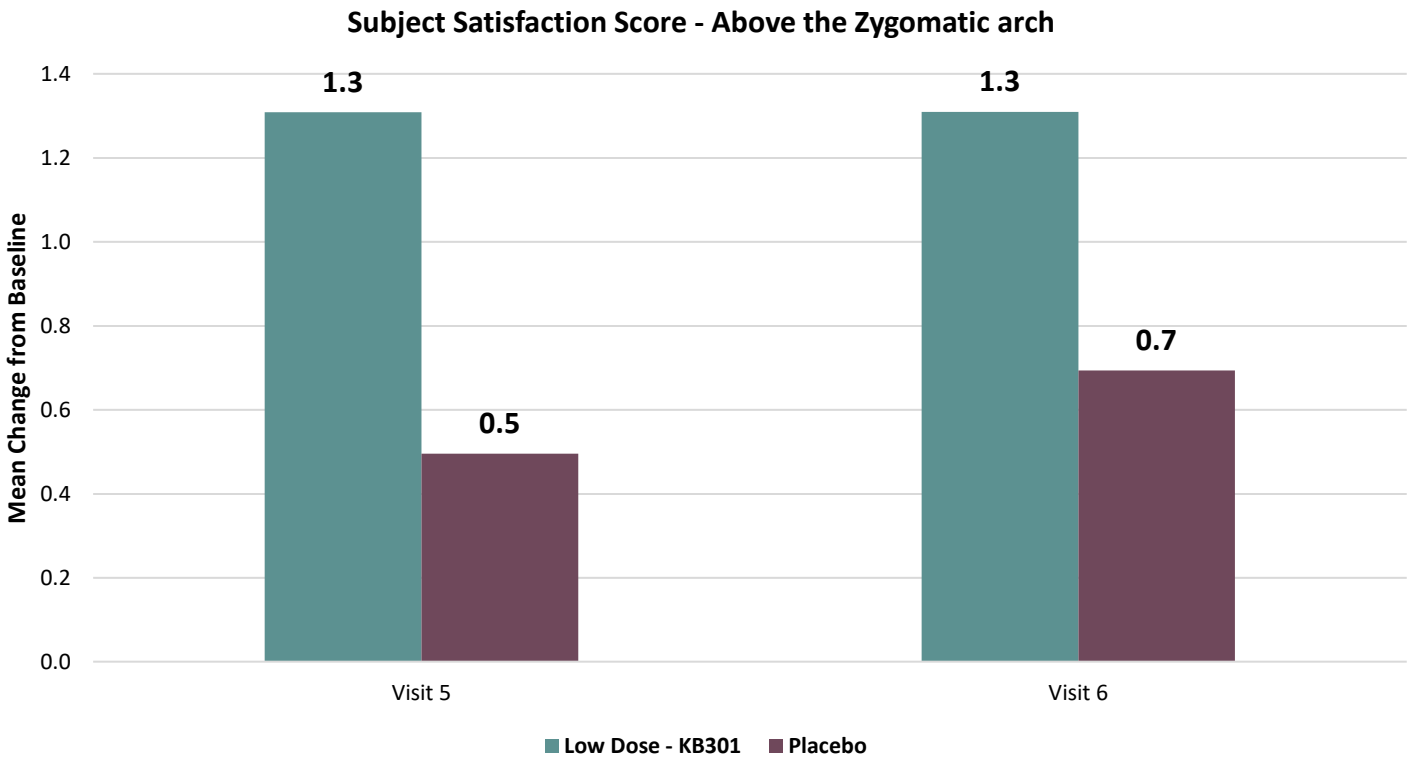
| Injection Site Reactions per Visit | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Above Zygomatic Arch AE Counts | | | | | | | | |
| | KB301 | | | | PLACEBO | | | |
| | Visit 3 | Visit 4 | Visit 5 | Visit 6 | Visit 3 | Visit 4 | Visit 5 | Visit 6 |
| Bruising | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 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

1. *All were mile except one was moderate.*

# Upper Cheek: Efficacy Measures

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

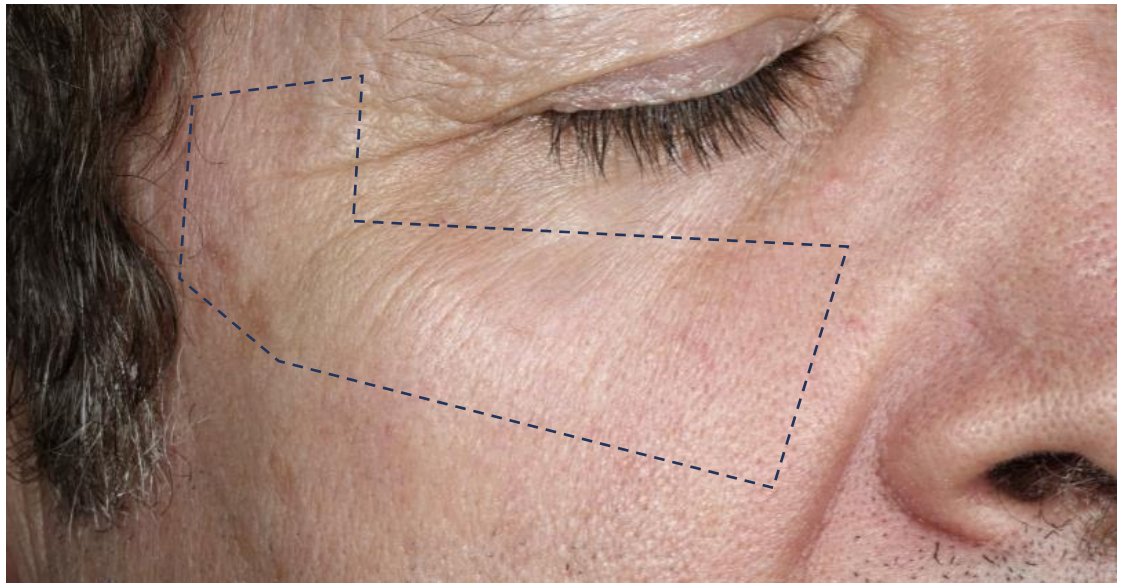



| Grading | Description | Comments |
|---|---|---|
| Clinical Improvement | Performed by Blinded Independent Reviewer using pictures due to lack of scale for skin area | No meaningful difference between active and placebo |

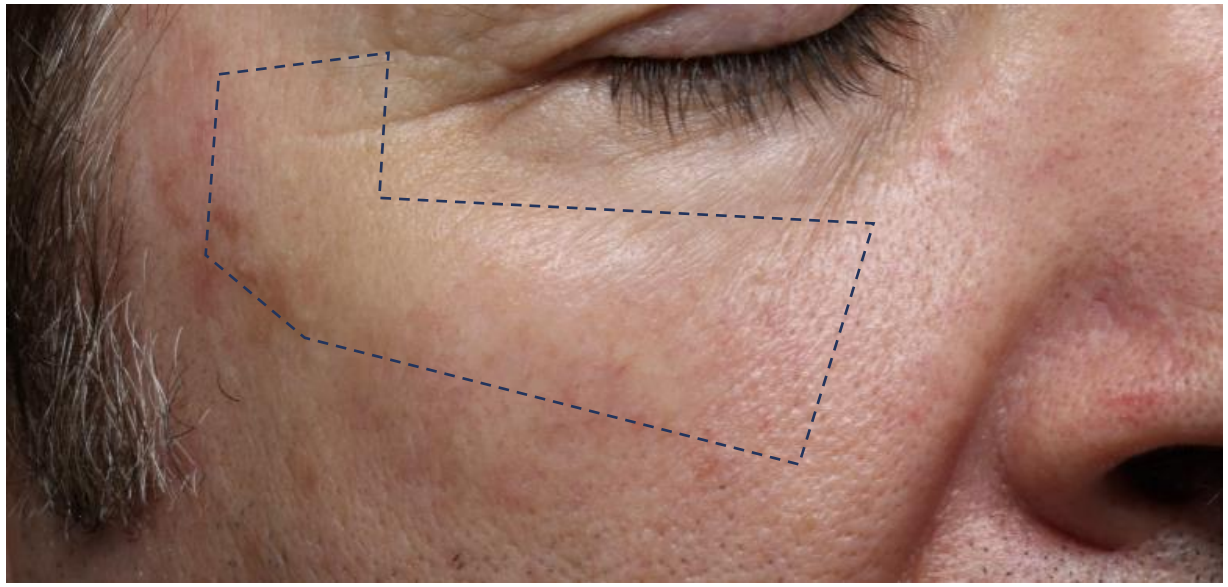
N for KB301= 31 for KB301 | N = 15 for Placebo

# 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



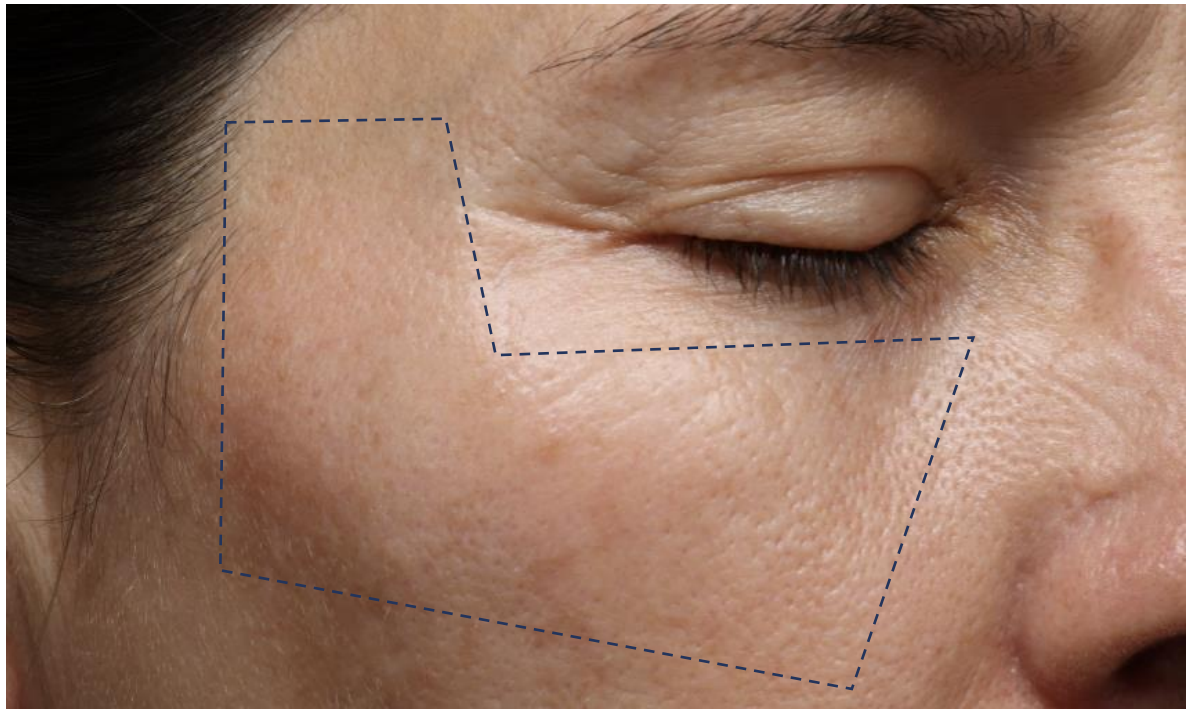
Baseline



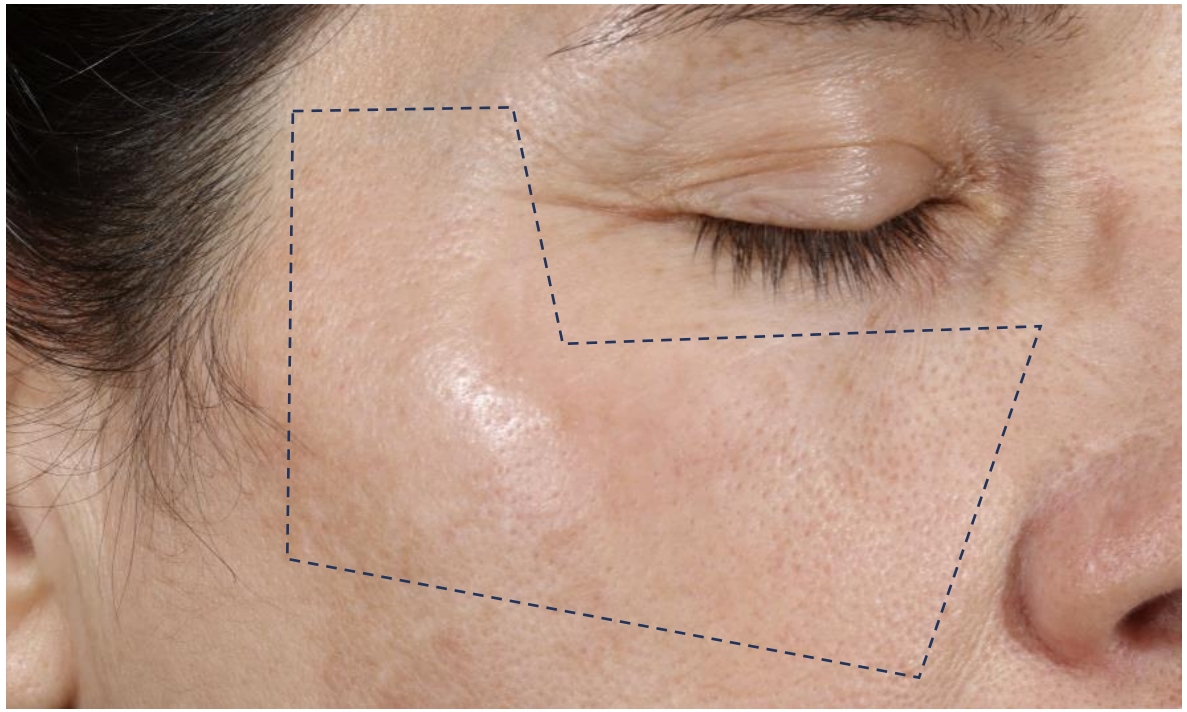
Visit 6

# 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



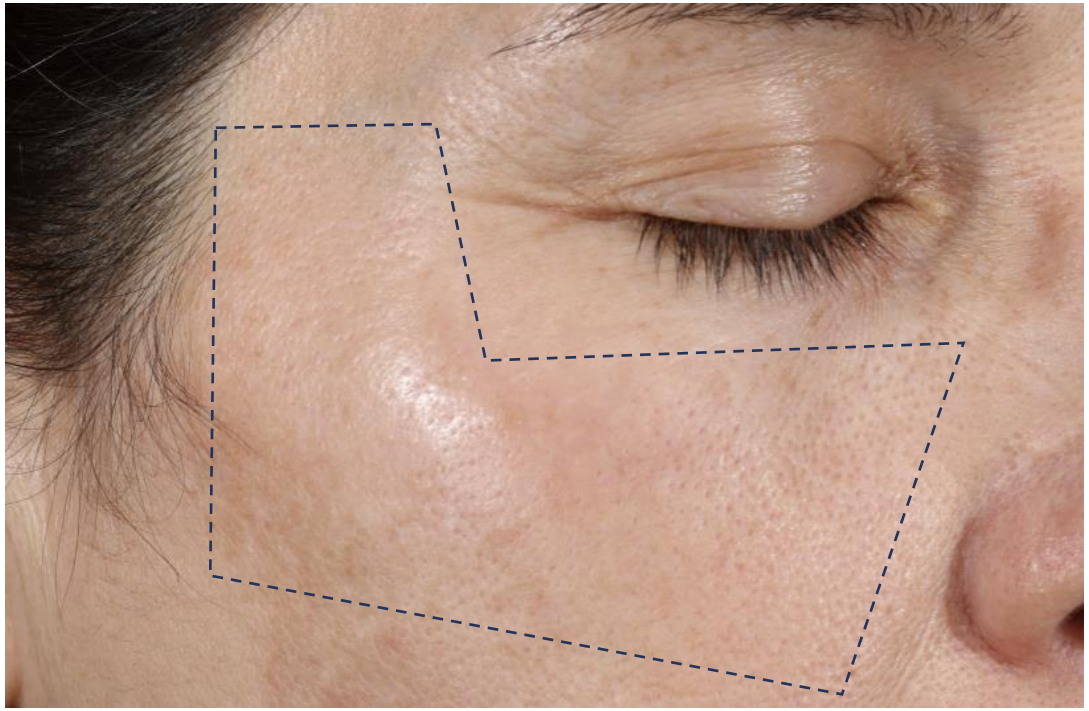
Baseline



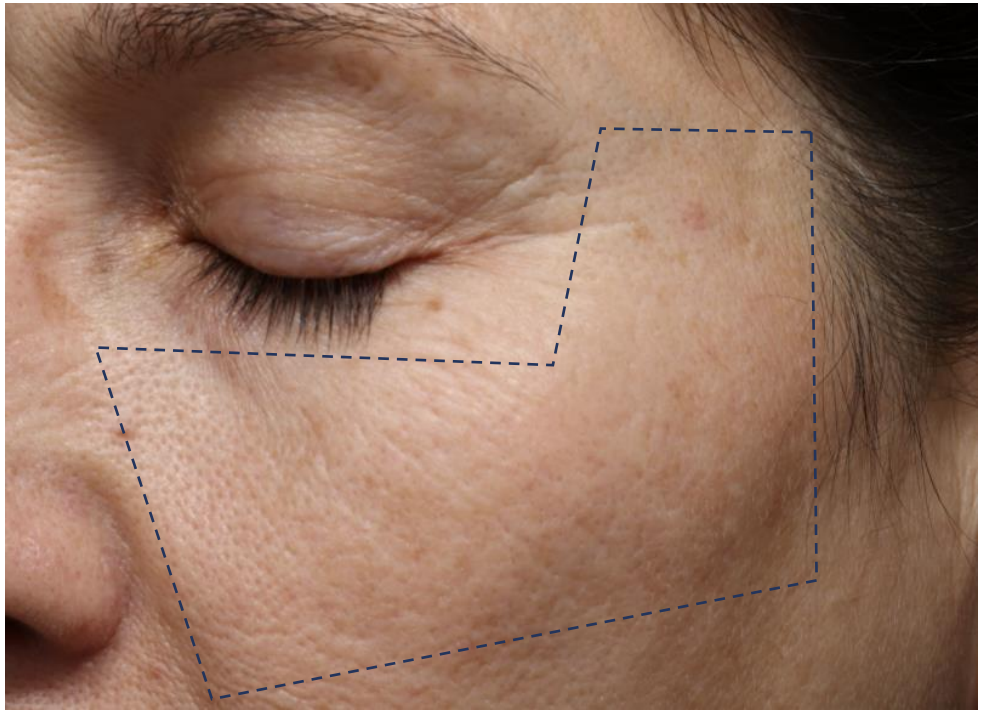
Visit 6

# 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 1 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)

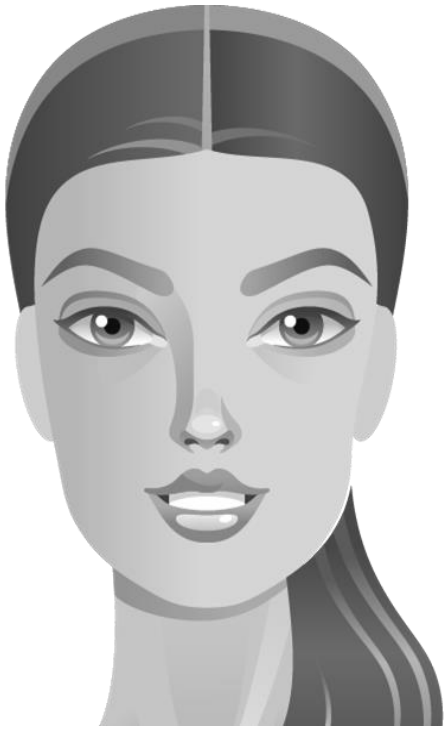
2

## 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

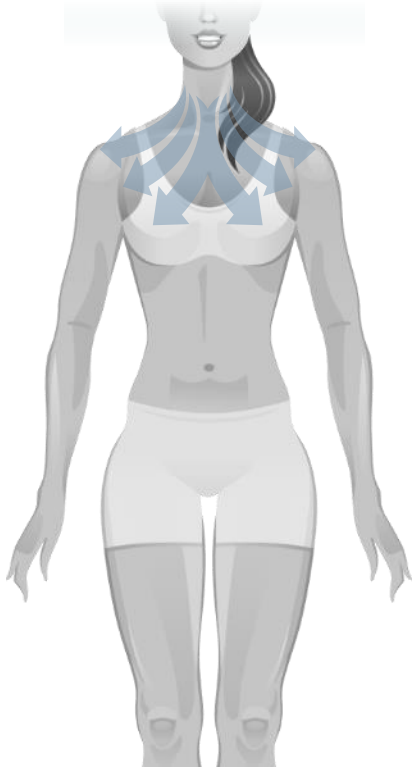
# KB301 Has Potential to Provide Differentiated Benefit in Large and Growing Markets



## Global Facial Injectables Market[1]

$13B → $26B

2020 by 2026



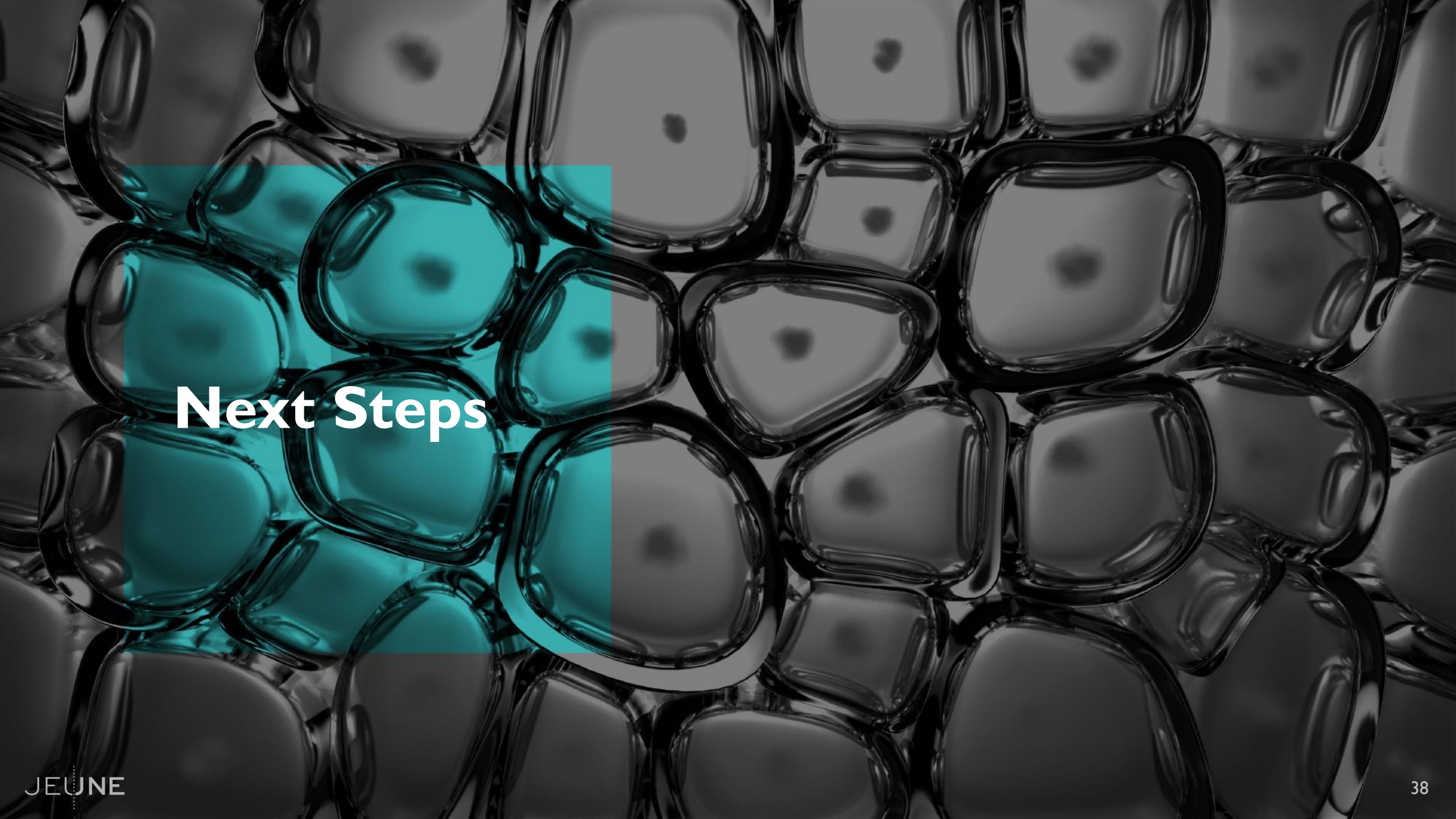
## Global Skincare Devices Market[2]

$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.



# Next Steps

# Next Steps: Cohort 2 Durability Trial Protocol Summary

## Lower and Upper Cheek Only

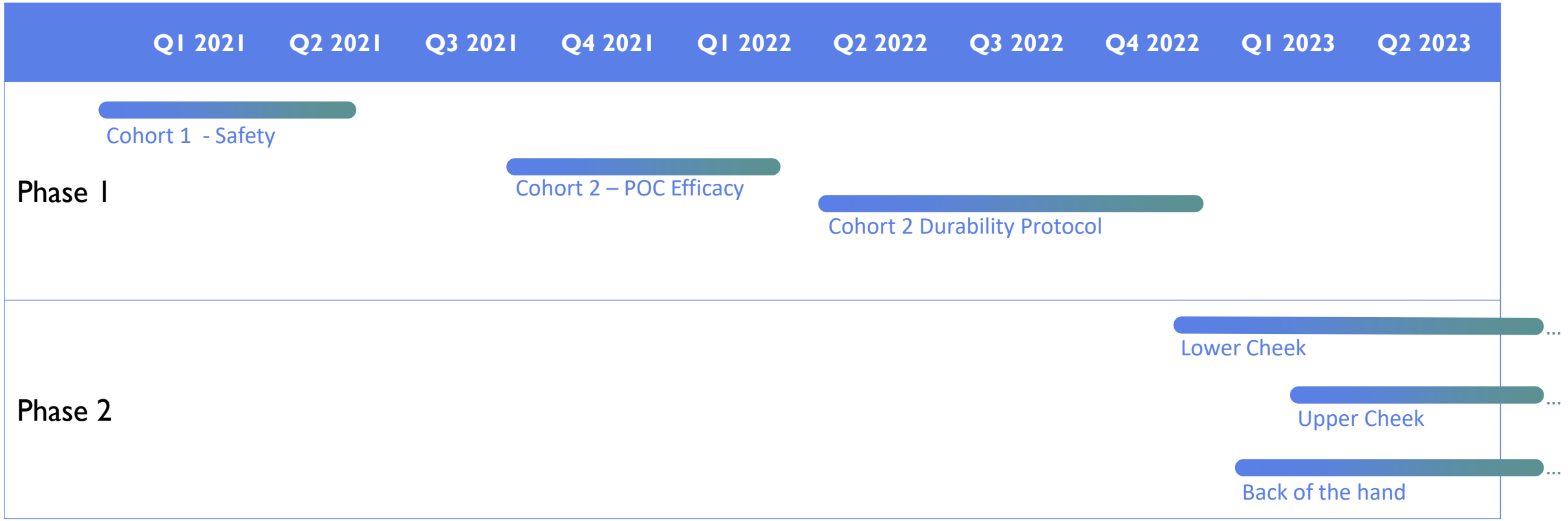
### Design

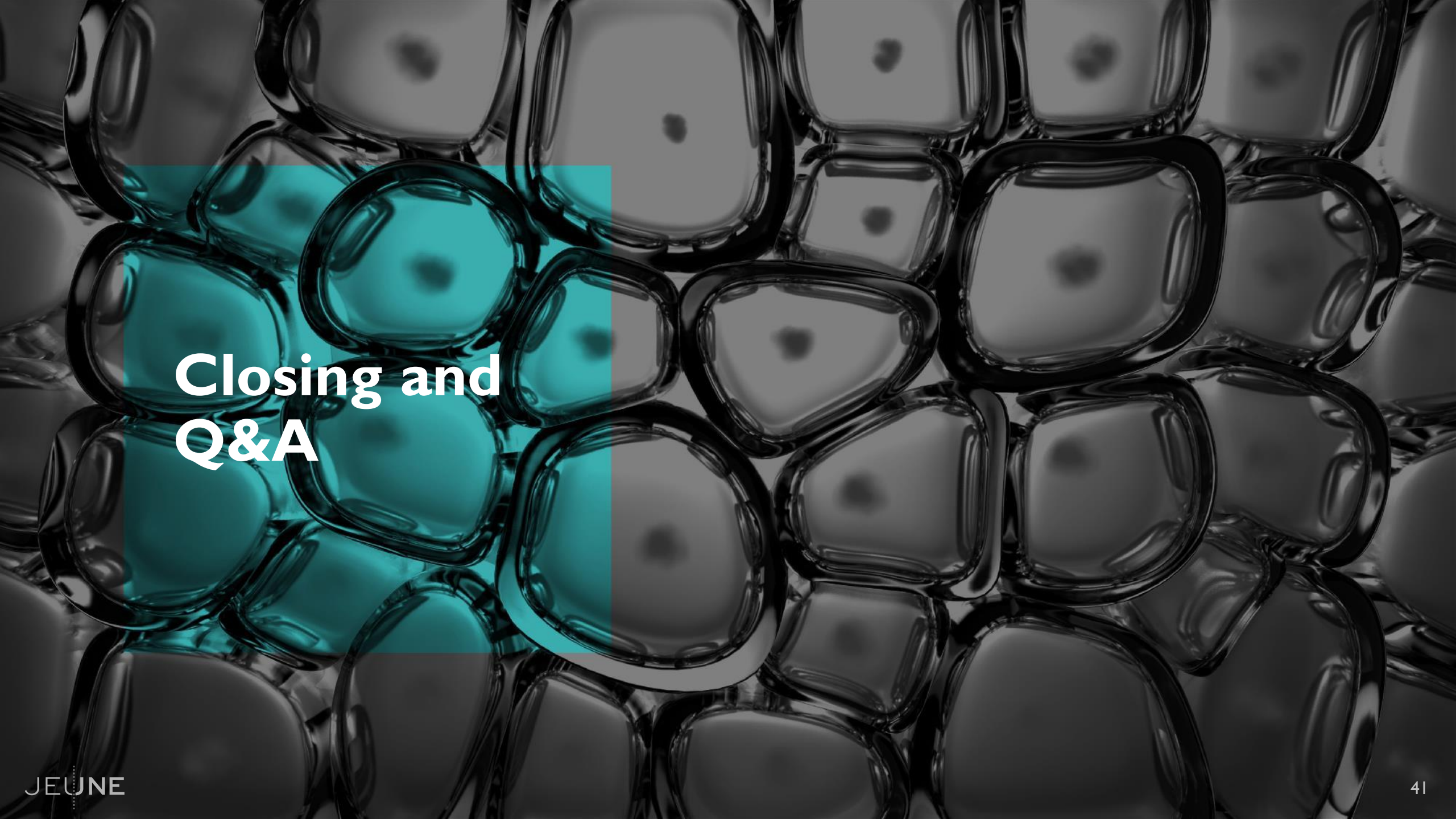
- Cohort 2 subjects will be enrolled at 2 sites
- Open label study where subjects that received placebo injection will now receive KB301 on that specific site
- Lower Cheek sites will receive KB301 high dose while Upper Cheek sites will receive KB301 low dose
- 6 total visits
- Could be extended depending upon outcome

### Endpoints

- Safety and tolerability of KB301
- Jeune Aesthetics Skin Roughness Score (JASRS)
- Jeune Aesthetics Fine Lines Score (JAFLS)
- Subject Satisfaction Score (SSS)
- Evaluation of on-going durability on sites that received KB301 in prior study

# Next Steps: KB301 Clinical Development Plan





# Closing and Q&A

# A GENE-BASED AESTHETICS COMPANY

March 2022

JEUNE