SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Injectable Dermal Filler

Device Trade Name: *Restylane® Lyft with Lidocaine*

Device Procode: LMH

Applicant's Name and Address: Q-Med AB, a Galderma affiliate
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Uppsala, Sweden

Galderma Research and Development, LLC
Ross Avenue, Suite 1600
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P040024/S142

Date of FDA Notice of Approval: November 4, 2025

The original PMA P040024 was approved on March 25, 2005, and is indicated for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds (NLF). The PMA Supplements for *Perlane®* (PMA P040024/S006) and *Restylane® Lyft with Lidocaine* (P040024/S039) were approved on May 11, 2007 and January 29, 2010, respectively for implantation into the deep dermis to superficial subcutis for the correction of moderate to severe facial folds and wrinkles, such as nasolabial folds. The PMA Supplement for *Restylane® Lyft with Lidocaine* (P040024/S073) was approved on July 1, 2015, for subcutaneous to supraperiosteal implantation for cheek augmentation and correction of age-related midface contour deficiencies over the age of 21, and the PMA Supplement for *Restylane® Lyft with Lidocaine* (P040024/S099) for injection into the subcutaneous plane in the dorsal hand to correct volume deficit in patients over the age of 21 was approved on May 18. 2018. The SSEDs to support the indications are available on the CDRH website and are incorporated by reference here.

The current supplement was submitted to expand the indication for *Restylane® Lyft with Lidocaine*.

II. INDICATIONS FOR USE

Restylane® Lyft with Lidocaine is indicated for subcutaneous and/or supraperiosteal implantation for augmentation of the chin region to improve the chin profile in patients over the age of 21 with mild to moderate chin retrusion.

III. CONTRAINDICATIONS

- *Restylane® Lyft with Lidocaine* is contraindicated for use in patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- *Restylane® Lyft with Lidocaine* contains trace amounts of gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- *Restylane® Lyft with Lidocaine* is contraindicated for patients with bleeding disorders.
- *Restylane® Lyft with Lidocaine* should not be used in patients with previous hypersensitivity to local anesthetics of the amide type, such as lidocaine.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the *Restylane® Lyft with Lidocaine* labeling.

V. DEVICE DESCRIPTION

Restylane® Lyft with Lidocaine is a sterile gel of hyaluronic acid generated by Streptococcus species of bacteria, chemically cross-linked with 1.4-butanediol diglycidylether (BDDE), stabilized and suspended in phosphate buffered saline at pH=7 and concentration of 20 mg/mL with 0.3% lidocaine. *Restylane Lyft with Lidocaine* is supplied in a disposable glass syringe with a luer-lock fitting and is co-packed with two sterilized needles as indicated on the carton. The syringe and carton are labeled with the product name, lot number, and expiration date, with storage conditions on the product carton. *Restylane® Lyft with Lidocaine* is injected into the chin for augmentation of the chin region.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of chin retrusion. Other alternatives include fat grafting and implants. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Perlane® and *Restylane® Lyft with Lidocaine* received approval in the United States for the correction of moderate to severe facial folds and wrinkles in May 2007 and January 2010, respectively; the same device also received approval for age-related midface contour

deficiencies in July 2015 and for the correction of volume deficit in the dorsal hand in May 2018.

Restylane® Lyft with Lidocaine (also known previously as Perlane® Lidocaine outside of the US) has been commercially available in the European Union since 2009. The product is also currently marketed in countries in the following regions: North America, Latin America, South America, Eastern Europe, Middle East, Africa, Asia-Pacific, and Australia/New Zealand.

Restylane® Lyft with Lidocaine has not been removed from the marketplace for any reasons related to safety, effectiveness, patient or physician complaint, or dissatisfaction.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

The safety of *Restylane® Lyft with Lidocaine* for augmentation of the chin region to improve the chin profile was assessed in study 43USCH2208. Adverse Events (AEs) that occurred in ≥ 2.0% of subjects in the study, whether related or unrelated to the study product or procedure, (reported by Investigators from study visits), included COVID-19, sinusitis and implant site bruising. Treatment related adverse events included implant site bruising, nodule, exfoliation, hemorrhage, edema, papule and erythema. Pre-defined self-reported (subject diary data) expected post treatment events (i.e., pain, tenderness, redness, bruising, swelling, itching, or lumps/bumps) were also recorded.

For the specific adverse events that occurred in the clinical study, please see Section X below.

The adverse event reports received from post-marketing surveillance (from voluntary reporting and published literature) for the use of *Restylane® Lyft with Lidocaine* and *Perlane®* for all indications included reports of swelling/edema or inflammatory reactions immediate or delayed onset, up to several weeks after treatment.

The following events were also reported in decreasing order of frequency:

- mass formation including lumps or bumps/induration
- pain or tenderness
- short duration of effect
- erythema
- bruising/hematoma
- papules/nodules
- presumptive bacterial infections/abscess formation including purulent discharge, pustules and cellulitis
- inflammation
- injection site reactions including burning sensation, warmth and irritation

- neurological symptoms including hypoesthesia, paresthesia and facial nerve paralysis
- hypersensitivity/angioedema
- ischemia and necrosis including pallor, ulcer, livedo reticularis due to unintentional intravascular injection or embolization
- discoloration/hyperpigmentation
- asymmetry/deformity
- eye disorders including eye pain, eye swelling, eye irritation, increased lacrimation, eyelid ptosis and visual impairment such as blurred vision, reduced visual acuity and blindness
- pruritus
- skin atrophy/scarring
- granuloma/foreign body reaction
- device dislocation
- rash
- discharge/extravasation
- blisters/vesicles
- acne
- symptoms of reactivation of herpes infection
- urticaria
- capillary disorder such as telangiectasia
- dermatitis
- encapsulation
- muscle disorders such as muscle twitching, muscle tightness and muscle weakness
- other dermatological events including dry skin, skin tightness, skin wrinkling, skin exfoliation and localized alopecia
- non-dermatological events including headache, dizziness, sinusitis, dyspnea/respiratory disorder, influenza-like symptoms such as discomfort, fatigue/malaise and pyrexia, insomnia, nausea, anxiety/emotional disorder, dysphagia, lymphadenopathy and bone resorption.

When required, treatments for these events included ice, massage, warm compress, nitroglycerine paste, corticosteroids, antibiotics, anticoagulants, antihistamines, analgesics, antiviral agents, diuretic agents, aspiration/incision and drainage, surgery or enzymatic degradation (with hyaluronidase) of the product.

Adverse events received from post-marketing surveillance for *Restylane® Lyft with Lidocaine* and *Perlane®* used for cheek augmentation was in line with the reports listed above for all indications. In rare cases, a late onset (weeks to months) and recurrent inflammation was reported post injection. Concurrent localized events/symptoms were nodules or lumps, infection, and redness, swelling and pain. The treatments of these events included hyaluronidase, antibiotics, corticosteroids, analgesics, incision and drainage.

Reports of serious adverse events for *Restylane® Lyft with Lidocaine* and *Perlane®* are rare. The most commonly reported serious adverse events were infection/abscess,

ischemia/necrosis, visual impairment, hypersensitivity/allergic reactions, scarring, inflammation, and granuloma including cases of mass/induration. Concurrent serious events/symptoms included: swelling, pain/tenderness, erythema, neurological symptoms such as paresthesia and hypoesthesia, bruising, discoloration, papules/nodules, and overcorrection, and irregular skin.

Serious infections/abscesses were reported with a time to onset ranging from one day to two months following the injection. Most of the patients were recovered or recovering at the time of last contact. The treatments included antibiotics, analgesics, corticosteroids and hyaluronidase.

Serious hypersensitivity reactions were reported. Most cases had a time to onset ranging from immediately to few weeks post injection and were recovering or recovered at the time of last contact. The treatment included analgesics, antihistamine, antibiotics, and corticosteroids.

Serious granuloma/foreign body reaction including mass/induration, were reported with a time to onset ranging from one day to a year or longer. The outcomes were mostly recovered or recovering at the time of last contact. The treatment included analgesics, antihistamine, antibiotics, corticosteroids and excisions. Biopsies have been taken in some cases, but the majority of cases are non-biopsy confirmed.

Serious inflammation was reported with a time to onset from one to two weeks post injection. Most patients had recovered or were recovering at the time of last contact. Rare cases of inflammation with delayed onset up to several weeks or months post injection has been observed; particularly if the patient experienced local trauma, facial/dental infection, or local infection. The treatment included analgesics, antibiotics, and corticosteroids.

Vascular occlusion resulting in ischemia/necrosis and vision disturbances including blindness have been reported following injection of any soft tissue filler in the face especially in the nose, glabella, periorbital areas, nasolabial folds and cheek, with a time to onset ranging from immediate to a few weeks following injection. Vascular compromise may occur due to an inadvertent intravascular injection or as a result of vascular compression associated with implantation of any injectable product. This may manifest as blanching, discoloration, necrosis or ulceration at the implant site or in the area supplied by the blood vessels affected, or rarely as ischemic events in other organs due to embolization. Isolated rare cases of ischemic events affecting the eye leading to visual loss, and the brain resulting in cerebral infarction, following facial aesthetic treatments have been reported.

Reported treatments include anticoagulant, epinephrine, aspirin, hyaluronidase, corticosteroid treatment, analgesics, antibiotics, local wound care, drainage, hyperbaric oxygen and surgery. Outcome of the events ranged from resolved to ongoing at the time of last contact. In many of the events requiring medical intervention, the patient was injected into the highly vascularized areas of the glabella, nose, and periorbital area, which are outside the device indications for use.

Injection site bruising, swelling, erythema and pain mostly non-serious generally occurred within 1-2 days after treatment usually resolving within 1 to 4 weeks. Some occurrences have persisted for up to 6 months. Most instances of discoloration including hyperpigmentation, sometimes described as a blue or brown color, have occurred within the same day as treatment but have also occurred up to 6 months post treatment. These events typically resolve within a few days but with some infrequent instances lasting up to 18 months.

Rare instances of bone resorption following supraperiosteal injection of hyaluronic acid dermal filler into the face have been reported.

Delayed-onset inflammation near the site of dermal filler injections is one of the known adverse events associated with dermal fillers. Cases of delayed-onset inflammation have been reported to occur at the dermal filler treatment site following viral or bacterial illnesses or infections, vaccinations, or dental procedures. Typically, the reported inflammation was responsive to treatment or resolved on its own.

IX. SUMMARY OF NON-CLINICAL STUDIES

This supplement describes clinical data to support approval of a new indication for use. Because no change in product manufacture or specification was conducted, the nonclinical data previously presented in PMA P040024 and supplements support the new proposed indication for use.

A. Laboratory Studies

No additional studies were conducted due to this supplement.

B. Animal Studies

No additional studies were conducted due to this supplement.

C. Additional Studies

No additional studies were conducted due to this supplement.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of injection with *Restylane® Lyft with Lidocaine* for subcutaneous and/or supraperiosteal implantation for augmentation of the chin region in the US under IDE G230006. Data from this clinical study were the basis for the PMA approval decision.

A summary of the clinical study is presented below.

A. Study Design

Patients were treated between March 22, 2023 and July 31, 2023. The database for this Panel-Track Supplement reflected data collected through July 10, 2024 and included 175 patients. There were 12 investigational sites.

The study was a prospective, randomized, evaluator-blinded, parallel group, comparator-controlled, multicenter clinical study. The study was not designed to evaluate the safety of repeat use of the device.

Subjects were randomized 2:1 to treatment with either *Restylane® Lyft with Lidocaine* (115 subjects) or comparator control (60 subjects). Subjects received injections in the chin (sublabial crease, pogonion, and mentum) and surrounding areas (pre-jowl sulci) at baseline (initial treatment), with optional touch-up treatment 1 month (4 weeks) after initial treatment, if deemed necessary by Treating Investigator and subject to obtain optimal aesthetic improvement. *Restylane® Lyft with Lidocaine* was supplied in a sealed blister package containing a syringe with 1.0 mL sterile gel and two thin-wall 27-gauge × ½" needles for injection. Alternatively, commercially available thin-wall sterile needle (29-gauge × ½") and TSK Steriglide sterile blunt cannula (25- 27-gauge × 1½ or 2") that are approved for use in the US for midface correction could have been used in the study and were obtained by study centers.

Restylane® Lyft with Lidocaine was administered by supraperiosteal or subcutaneous injections with needle or cannula in the chin areas. Appropriate injection volume for the chin area was determined by the Treating Investigator but was not to exceed a maximum of 4.0 mL for initial and touch-up treatments combined.

The Treating Investigator was not blinded to study product. A Blinded Evaluator, to whom randomization and treatment were concealed, conducted the blinded assessments. As much as possible, the same Blinded Evaluator assessed a particular subject throughout the study; safety assessments were performed by non-blinded personnel.

The control device was an FDA approved hyaluronic acid filler which was a legally marketed alternative with similar indications for use.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the 43USCH2208 study was limited to patients who met the following inclusion criteria:

- Willing to comply with the requirements of the study, including being photographed, following post-treatment care instructions, completing the diary, attending all study visits, and providing a signed written ICF.
- Males or non-pregnant, non-breastfeeding females, 22 years of age or older.
- Mild or moderate (Grade 1 or 2, respectively) chin retrusion on the Galderma Chin Retrusion Scale (GCRS), at screening and baseline, as assessed by the

Blinded Evaluator as well as the Treating Investigator (agreement on grade was not required).
- Intent to receive treatment for augmentation and correction of retrusion in the chin region.
- Willing to abstain from any other facial and plastic surgical or cosmetic procedure(s) or implant for the duration of the study.
- If female of childbearing potential, agreed to use an acceptable form of effective birth control for the duration of the study and was willing to take a urine pregnancy test at the screening/enrollment visit and prior to treatment (negative test required).

Patients were <u>not</u> permitted to enroll in the 43USCH2208 study if they met any of the following exclusion criteria:

- History of allergy or hypersensitivity to injectable HA gel or to gram positive bacterial proteins.
- History of allergy or hypersensitivity to lidocaine or other amide type anesthetics.
- Previous facial surgery (including facial aesthetic surgery and liposuction) below the level of the horizontal line from the subnasale.
- Previous use of any permanent (non-biodegradable) or semi-permanent (e.g., calcium hydroxylapatite or poly-L-lactic acid) facial tissue augmentation therapy, lifting threads, permanent implants, autologous fat or HA filler or collagen filler below the level of the horizontal line from subnasale within 12 months.

2. <u>Follow-up Schedule</u>
   All patients were scheduled to return for follow-up examinations at 72 hours (telephone call), 14 days (visit), 1 month (visit – optional touch-up [72-hour telephone call post-touch-up]), 14 days post-touch-up (visit), 1-month post-touch-up (visit), and 3, 6, 9, and 12 months post-treatment.

   Pre-treatment, the following evaluations were conducted:
   - Palpability assessment
   - Sensory and functionality tests
   - GCRS assessed both by the Treating Investigator and the Blinded Evaluator
   - FACE-Q™ satisfaction with chin, assessed by subjects
   - FACE-Q™ satisfaction with outcome, assessed by subjects
   - FACE-Q™ satisfaction with lower face and jawline, assessed by subjects.

Post-treatment, the objective parameters measured during the study included:

- Visual function assessments
- Palpability assessment
- Sensory and functionality tests
- Evaluation of changes in facial hair growth
- GAIS
- GCRS assessed both by the Treating Investigator and the Blinded Evaluator
- Investigator Satisfaction Questionnaire
- Subject Satisfaction Questionnaire
- FACE-Q™ satisfaction with chin, assessed by subjects
- FACE-Q™ satisfaction with outcome, assessed by subjects
- FACE-Q™ satisfaction with lower face and jawline, assessed by subjects.
- Subject pain assessment
- Returning to social engagement (subject assessment)

Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the Schedule of Events (**Table 1**) and tables summarizing safety and effectiveness.

Table 1. Schedule of Events

Procedure	Visit 1a Day -21 to 1 Screening	Visit 1b Day 1 BL/Tx	Visit 2 72 hrs after Tx (±24 hrs) TC	Visit 2a 14 days after Tx (+7 days) Follow-up	Visit 3 1 month[2,3] after initial treatment (+7 days) Follow-up/ Optional	Visit 3a[1] 72 hrs after Optional TU (±24 hrs) TC	Visit 3b[1] 14 days after Optional TU (+7 days) Follow-up	Visit 3c[1] 1 month[2] after Optional TU (+7 days) Follow-up	Visit 4 3 months[2] after last treatment (±14 days) Follow-up	Visit 5 6 months[2] after last treatment (±14 days) Follow-up	Visit 6 9 months[2] after last treatment (±14 days) Follow-up	Visit 7 12 months[2] after last treatment (+14 days) Follow-up/ EOS
Informed consent	X											
Medical history/prior therapies	X	X[4,5]										
Demographics	X											
Height/weight[6]		X[4]										X
Inclusion/exclusion criteria	X	X[4,5]			X[4,7]							
Urine pregnancy test[8]	X	X[4,5]			X[4,7]							
Randomization		X[4]										
Treatment with study product		X			X[7]							
Visual function assessments[9]	X	X[10]		X	X[10]		X	X	X	X	X	X
Evaluate device deficiencies		X			X[7]							
Dispense subject diary		X			X[7]							
Collect/review subject diary			X[11]	X[11]	X	X[11]	X[11]	X				
Photography		X[4]		X	X[4]		X	X	X	X	X	X
Palpability assessment	X[12]	X[4]		X	X[4]		X	X	X	X	X	X
Sensory and functionality tests	X[12]	X[4]		X	X[4]		X	X	X	X	X	X

Procedure	Visit 1a Day -21 to 1 Screening	Visit 1b Day 1 BL/Tx	Visit 2 72 hrs after Tx (±24 hrs) TC	Visit 2a 14 days after Tx (+7 days) Follow-up	Visit 3 1 month[2,3] after initial treatment (+7 days) Follow-up/ Optional	Visit 3a[1] 72 hrs after Optional TU (±24 hrs) TC	Visit 3b[1] 14 days after Optional TU (+7 days) Follow-up	Visit 3c[1] 1 month[2] after Optional TU (+7 days) Follow-up	Visit 4 3 months[2] after last treatment (±14 days) Follow-up	Visit 5 6 months[2] after last treatment (±14 days) Follow-up	Visit 6 9 months[2] after last treatment (±14 days) Follow-up	Visit 7 12 months[2] after last treatment (+14 days) Follow-up/ EOS
Evaluate changes in facial hair growth				X	X		X	X	X	X	X	X
Concomitant therapies	X	X[5]	X	X	X	X	X	X	X	X	X	X
Assessment of adverse events		X	X	X	X	X	X	X	X	X	X	X
Treating Investigator Assessments												
GAIS									X	X	X	X
GCRS	X	X[4,5]			X[4,7]							
Investigator Satisfaction Questionnaire									X			
Blinded Evaluator Assessment												
GCRS	X	X[4,5]							X	X	X	X
Subject Assessments												
GAIS									X	X	X	X
Subject Satisfaction Questionnaire									X	X	X	X
FACE-Q™ satisfaction with chin		X[4]							X	X	X	X
FACE-Q™ satisfaction with outcome									X	X	X	X
FACE-Q™ satisfaction with lower face and jawline		X[4]							X	X	X	X

Procedure	Visit 1a Day -21 to 1 Screening	Visit 1b Day 1 BL/Tx	Visit 2 72 hrs after Tx (±24 hrs) TC	Visit 2a 14 days after Tx (+7 days) Follow-up	Visit 3 1 month[2,3] after initial treatment (+7 days) Follow-up/ Optional	Visit 3a[1] 72 hrs after Optional TU (±24 hrs) TC	Visit 3b[1] 14 days after Optional TU (+7 days) Follow-up	Visit 3c[1] 1 month[2] after Optional TU (+7 days) Follow-up	Visit 4 3 months[2] after last treatment (±14 days) Follow-up	Visit 5 6 months[2] after last treatment (±14 days) Follow-up	Visit 6 9 months[2] after last treatment (±14 days) Follow-up	Visit 7 12 months[2] after last treatment (+14 days) Follow-up/ EOS
Subject pain assessment		X[13]			X[7,13]							
Returning to social engagement			X[14]		X[14]							

BL=baseline; EOS=End of Study; GAIS=Global Aesthetic Improvement Scale; GCRS=Galderma Chin Retrusion Scale; hrs=hours; TC=telephone call; TU=touch-up; Tx=treatment

1 Visit was scheduled only if optional touch-up had been performed.
2 One month was defined as 4 weeks.
3 If optional touch-up was not performed, this was a follow-up visit.
4 Prior to any planned treatment.
5 Omitted if the screening and baseline visits occurred on Day 1. Screening visit and baseline visit could have been combined if no drug washout was needed.
6 Subject self-reported. Height only needed to be collected at baseline.
7 Omitted if optional touch-up was not performed.
8 For females of childbearing potential.
9 Visual function assessments included Snellen visual acuity test, extraocular muscle function test, and confrontational visual field.
10 At the treatment visits, the visual function assessment tests were to be performed prior to and approximately 30 minutes post injection of the study product.
11 Review diary with subject over the phone or at follow-up visit.
12 As required at screening to confirm study eligibility. The safety assessments were to be done prior to treatment.
13 At the treatment visits, the subject pain assessment was performed prior to and after injection of the study product.
14 Time for returning to social engagements asked to the subject over the phone.

3. Clinical Endpoints

With regards to safety, endpoints included the incidence of all AEs, including safety assessments made by the Treating investigator at all visits and pre-identified injection related symptoms reported by subjects during the first 28 days after treatment as recorded in the subject diary. Subject pain was assessed before and immediately after treatment, using an 11-point Numeric Pain Scale (NPS).

Visual function assessments (i.e., Snellen visual acuity test, extraocular muscle function test, and confrontation visual field test) were performed at baseline and at all following physical visits. At treatment visits, the assessments were performed both prior to and post injection of the study product.

Presence of any unexpected lumpiness, mass, or non-uniform density by palpation of the chin were assessed at each physical follow-up visit after baseline/Day1 as well as any changes in hair growth (e.g., loss or growth) in the treated area at each physical follow up visit after baseline.

Additionally, presence of abnormal lower lip movement, function, and sensation (on 3 different locations), and presence of abnormal chin function and sensation (on 3 different locations), were assessed according to pre-defined methods, at baseline and at each physical follow-up visit.

With regards to effectiveness, the following clinical endpoints were assessed:

The primary endpoint was the change from baseline in the Blinded Evaluators' live assessment using the Galderma Chin Retrusion Scale (GCRS; **Table 2**, **Figure 1**) at 3 months after the last treatment. The effectiveness analyses were based on the intention-to-treat (ITT) population, defined as all randomized subjects. Responders were defined as having at least 1 point improvement from baseline (as assessed by the blinded evaluator) at 3 months after the last treatment.

Table 2. Galderma Chin Retrusion Scale (GCRS)

Score	Grade	Description
0	No Retrusion	The most anterior portion of the chin is at or near a vertical line drawn from the vermillion border of the lower lip
1	Mild Retrusion	The most anterior portion of the chin is clearly recessed, but less than midway, between vertical lines drawn from the vermillion border of the lower lip and the oral commissure.
2	Moderate Retrusion	The most anterior portion of the chin is recessed approximately midway between vertical lines drawn from the vermillion border of the lower lip and the oral commissure.
3	Severe Retrusion	The most anterior portion of the chin is clearly posterior to the midway point between vertical lines drawn from the vermillion border of the lower lip and the oral commissure.

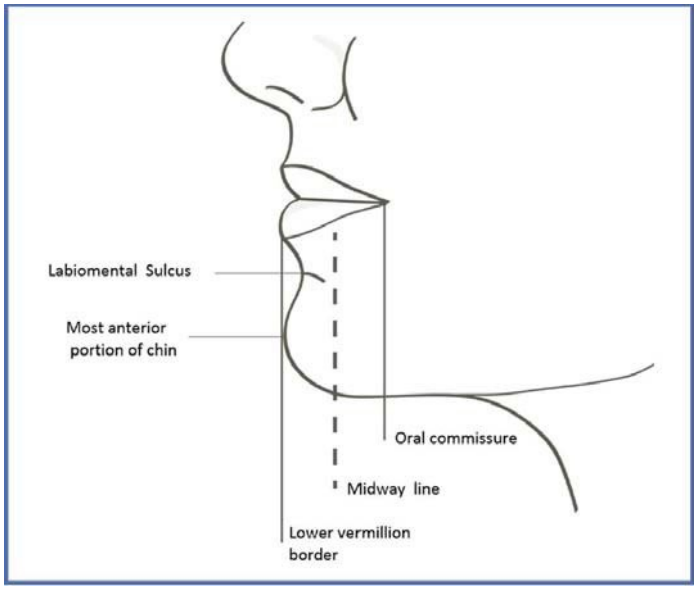

Figure 1. Lines used in the GCRS Descriptors

The secondary effectiveness endpoints included response rates based on the Blinded Evaluators' live assessment using the GCRS (a responder was defined as a subject with at least 1 grade improvement from baseline); the aesthetic improvement as assessed by subjects and the Treating investigator separately using Global Aesthetic Improvement Scale (GAIS), at 3, 6, 9, and 12 months after the last treatment, change from baseline in FACE-Q™ Satisfaction with Chin, FACE-Q™ Satisfaction with outcome, and validated FACE-Q™ Lower Face and Jawline Rasch-transformed total scores as well as proportions of subjects in each response category for each individual question. Additional secondary endpoints included proportion of Treating Investigators and Subjects, respectively, in each response category for every question in the Investigator Satisfaction Questionnaire (ISQ) at 3 months and Subject Satisfaction Questionnaire (SSQ) at 3, 6, 9, and 12 months after the last treatment,

time in hours until the subject feels comfortable returning to social engagement after treatment, based on a follow-up question via telephone at 72 hours after treatment, and improvement rate based on the Independent Photographic Review (IPR) assessment using random pairings of baseline and post-baseline photographs from physical visits at 3 and 12 months after the last treatment (an improved subject was defined as a subject for whom 2 of the 3 IPRs correctly identified the post-treatment image in the pair).

The exploratory endpoint for the study was change from baseline in topography of the chin region by 3-dimensional (3D) imaging at 3 and 12 months after the last treatment, assessed only for selected sites and a limited number of subjects.

With regard to success/failure criteria, the primary objective of the study was to demonstrate non-inferiority of Restylane Lyft to comparator control for augmentation of the chin region to improve the chin profile by comparing change from baseline in the Blinded Evaluators' live assessment of the Galderma Chin Retrusion Scale (GCRS) at 3 months after the last treatment with a pre-specified non-inferiority margin of 0.5.

Individual patient success was defined as at least one step improvement on the GCRS.

B. Accountability of PMA Cohort

At the time of database lock, of 175 patients enrolled in the PMA study, 92% (161) patients are available for analysis at the completion of the study, the 12 months post-operative visit.

A total of 186 subjects were screened and 175 subjects (115 *Restylane® Lyft with Lidocaine*, 60 comparator control) were randomized (ITT population). Randomization was stratified by FST (I-III, IV or V-VI). Subjects in the FST I-III stratum were further stratified by study center; subjects in the FST IV or FST V-VI strata were not further stratified by study center due to the smaller sample size in these groups.

Of the 174 subjects who were treated (115 *Restylane® Lyft with Lidocaine*, 59 comparator control; Safety population), 161 (92.0%) subjects completed the study (93.9% *Restylane® Lyft with Lidocaine*, 88.3% comparator control). There were 7 (6.1%) *Restylane® Lyft with Lidocaine* subjects and 7 (11.7%) comparator subjects who did not complete the study, with the most common reason being lost to follow-up (3 [42.9%] *Restylane® Lyft with Lidocaine* subjects, 5 [71.4%] comparator control subjects); only a single subject discontinued due to an AE.

In the overall ITT population, 168 subjects (111 *Restylane® Lyft with Lidocaine* [96.5%], 57 comparator control [95.0]) comprised the per protocol population (PP), defined as completing the primary endpoint assessment at 3 months after baseline or last treatment without any deviations considered to have substantial impact on the primary effectiveness.

A summary of subject accountability is provided in **Table 3** and a presentation of the set of patients which are included in which analysis cohort is provided in **Table 4**.

Table 3. Summary of Subject Disposition

Category	*Restylane® Lyft with Lidocaine* n (%)	Comparator Control n (%)	Total n (%)
Screened			186
Screening failures[1]			11 (5.9)
Randomized[1]	115 (61.8)	60 (32.3)	175 (94.1)
Treated[2]	115 (100)	59 (98.3)	174 (99.4)
Completed Study[2]	108 (93.9)	53 (88.3)	161 (92.0)
Did Not Complete Study[2]	7 (6.1)	7 (11.7)	14 (8.0)
Reason did not complete study[3]			
Withdrew consent	3 (42.9)	1 (14.3)	4 (28.6)
Lost to follow-up	3 (42.9)	5 (71.4)	8 (57.1)
Adverse event	1 (14.3)	0	1 (7.1)
Other	0	1 (14.3)	1 (7.1)

1 Denominator for percentages was the number of screened subjects.
2 Denominator for percentages was the number of subjects per treatment in the Intention-to-Treat Population (all subjects who were randomized).
3 Denominator for percentages was the number of subjects per treatment who did not complete the study.

Table 4. Analysis Populations

Category	Restylane Lyft with Lidocaine	Comparator Control	Overall
Intention-to-treat population, N[1]	115	60	175
Per-protocol population, n (%)[2]	111 (96.5)	57 (95.0)	168 (96.0)
Safety population[3]	115	59	174

1 All subjects who were randomized.
2 All subjects in the intention-to-treat population who completed the primary endpoint assessment at 3 months after baseline or last treatment without any deviations considered to have substantial impact on the primary effectiveness. Denominator for percentages was the number of subjects per treatment in the intention-to-treat population.
3 All subjects who were treated with *Restylane Lyft with Lidocaine* or comparator control.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a clinical study performed in the US among patients intending to undergo aesthetic procedures.

The majority of subjects were white (72.6% - 127/175), predominantly female (89.1% - 156/175), and mostly non-Hispanic or Latino (69.1% - 121/175), with a mean age of 45.3 years. Subject demographics and Baseline characteristics for the ITT population are presented in **Table 5**.

Table 5. Summary of Subject Demographics (Intent To Treat Population)

Parameter	*Restylane® Lyft with Lidocaine* (N=115)	Comparator Control (N=60)	Overall (N=175)
Age at baseline (years)			
Mean (standard deviation)	44.4 (12.14)	47.0 (12.97)	45.3 (12.46)
Median	44.0	46.5	44.0
Minimum, maximum	23, 74	22, 77	22, 77
Age category at baseline			
≤ITT population median age (44 years)	63 (54.8)	25 (41.7)	88 (50.3)
>ITT population median age (44 years)	52 (45.2)	35 (58.3)	87 (49.7)
Sex at birth, n (%)			
Female	104 (90.4)	52 (86.7)	156 (89.1)
Male	11 (9.6)	8 (13.3)	19 (10.9)
Gender identity, n (%)			
Female	105 (91.3)	52 (86.7)	157 (89.7)
Male	10 (8.7)	8 (13.3)	18 (10.3)
Race, n (%)			
White	82 (71.3)	45 (75.0)	127 (72.6)
Black/African American	28 (24.3)	14 (23.3)	42 (24.0)
Asian	9 (7.8)	5 (8.3)	14 (8.0)
Chinese	3 (2.6)	1 (1.7)	4 (2.3)
Filipino	2 (1.7)	2 (3.3)	4 (2.3)
Japanese	2 (1.7)	1 (1.7)	3 (1.7)
Vietnamese	2 (1.7)	1 (1.7)	3 (1.7)
Other	2 (1.7)	1 (1.7)	3 (1.7)
Ethnicity, n (%)			
Hispanic or Latino	37 (32.2)	17 (28.3)	54 (30.9)
Not Hispanic or Latino	78 (67.8)	43 (71.7)	121 (69.1)
Fitzpatrick Skin Types (cohort at randomization), n (%)			
I-III	61 (53.0)	33 (55.0)	94 (53.7)
IV	28 (24.3)	14 (23.3)	42 (24.0)
V-VI	26 (22.6)	13 (21.7)	39 (22.3)
Baseline body mass index (kg/m^2)			
Mean (standard deviation)	26.171 (5.3488)	26.480 (5.6313)	26.277 (5.4331)
Median	25.030	26.000	25.190
Minimum, maximum	17.17, 45.60	16.80, 41.60	16.80, 45.60
Baseline Galderma Chin Retrusion Scale (Blinded Evaluator), n (%)			
1 (Mild retrusion)	52 (45.2)	27 (45.0)	79 (45.1)
2 (Moderate retrusion)	63 (54.8)	33 (55.0)	96 (54.9)
Baseline Galderma Chin Retrusion Scale (Treating Investigator), n (%)			
1 (Mild retrusion)	57 (49.6)	28 (46.7)	85 (48.6)
2 (Moderate retrusion)	58 (50.4)	32 (53.3)	90 (51.4)

The mean total volume of *Restylane® Lyft with Lidocaine* injection into the chin for the Initial Treatment and touch-up combined was 3.39 mL (range 1.00 to 4.00). Subcutaneous and supraperiosteal depth of injection was used in the majority of treatments.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the Safety cohort of 174 patients/procedures, etc. available for the 12-month evaluation. The key safety outcomes for this study are presented below and in Tables **6** to **8**. Adverse effects are reported in **Table 6**.

Adverse effects that occurred in the PMA clinical study:

A total of 28 (24.3%) *Restylane® Lyft with Lidocaine* subjects and 17 (28.8%) comparator control subjects experienced at least one AE during the study. Adverse events that occurred in >2.0% of the study population consisted of COVID-19 (5/115 [4.3%] *Restylane® Lyft with Lidocaine* subjects and 2/59 [3.4%] comparator control subjects), sinusitis (4/115 [3.5%] *Restylane® Lyft with Lidocaine* subjects and no comparator control subjects), and implant site bruising (3/115 [2.6%] *Restylane® Lyft with Lidocaine* subjects and no comparator control subjects). The majority of subjects who experienced unrelated AEs had events that were at most mild or moderate in intensity; 2/115 (1.7%) *Restylane® Lyft with Lidocaine* subjects experienced severe events. Two (1.7%) *Restylane® Lyft with Lidocaine* subjects experienced Serious Adverse Events (SAEs) that were considered unrelated to study product or injection procedure. One (0.9%) *Restylane® Lyft with Lidocaine* subject and none of the comparator control subjects experienced an AE leading to study discontinuation.

Eight (7.0%) *Restylane® Lyft with Lidocaine* subjects and 3 (5.1%) comparator control subjects experienced an AE that were considered related to study product or injection procedure. The most common AE related to study product or injection procedure was implant site bruising (3/115 [2.6%] *Restylane® Lyft with Lidocaine* subjects and no comparator control subjects). All AEs considered related to study product or injection procedure were mild in intensity. No subject died, and no subject experienced a treatment related SAE during the study. No subject in either group experienced an Adverse Event of Special Interest (AESI), defined as visual disturbances or abnormal findings in functionality tests, stroke or skin necrosis.

A complete summary of Investigator reported treatment related adverse events by preferred term (PT) is provided in **Table 6**. All AEs related to study product or injection procedure reported in the *Restylane® Lyft with Lidocaine* and comparator control groups were mild in intensity.

The minimum mean duration for any related AE was 1.0 day (implant site edema) and the maximum mean duration was 192.5 days (implant site nodule) in the *Restylane® Lyft with Lidocaine* group. The minimum mean duration was 15.0 days (implant site exfoliation), and the maximum mean duration was 145.0 days (implant site nodule) in the comparator control group.

The mean time to onset of related AEs varied, ranging from 0 days (implant site hemorrhage, implant site edema, injection site papule) to 8.0 days (implant site exfoliation) in the *Restylane® Lyft with Lidocaine* group and from 1.0 day (implant site exfoliation, implant site erythema) to 4.0 days (implant site nodule) in the comparator control group. There were no late-onset AEs.

Table 6. Treatment-Related Adverse Events by Preferred Term (Safety Population)

Preferred Term	*Restylane® Lyft with Lidocaine* (N=115) n (%)	Comparator Control (N=59) n (%)
Subjects with at least 1 treatment-related adverse event	8 (7.0)	3 (5.1)
Implant site bruising	3 (2.6)	0
Implant site nodule	2 (1.7)	1 (1.7)
Implant site exfoliation	1 (0.9)	1 (1.7)
Implant site hemorrhage	1 (0.9)	0
Implant site edema	1 (0.9)	0
Injection site papule	1 (0.9)	0
Implant site erythema	0	1 (1.7)

Note: Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 25.1. Subjects were counted once for each preferred term. Treatment-related adverse events have a relationship of reasonable possibility to investigational treatment or injection procedure, as identified by the investigator.

Three *Restylane® Lyft with Lidocaine* subjects experienced a device deficiency during the study: luer lock disengaged from the syringe leading to leakage of product; needle disengaged from the luer lock; leakage and loose connection. There were no AEs reported due to these deficiencies.

No clinically meaningful changes from baseline in visual function assessments or functionality, sensation, palpability, and hair growth were observed in either treatment group.

The percentage of subjects self-reporting (subject diary data) pre-defined, expected post-treatment events (i.e., pain, tenderness, redness, bruising, swelling, itching, or lumps/bumps) was similar between the *Restylane® Lyft with Lidocaine* and

comparator control groups at the initial treatment (97.3% and 100%, respectively) and touch-up treatment (88.9% to 90.9%, respectively). Pre-defined, expected post treatment events are summarized in **Table 7**.

Over time, the percentage of subjects with each pre-defined diary symptom was similar between the *Restylane® Lyft with Lidocaine* and comparator control groups for the initial treatment and touch-up treatment (**Table 8**). All symptoms were resolved by day 28.

Table 7. Summary of Subject Diary Symptoms by Injection Timepoint and Maximum Intensity (Safety Population)

Characteristic	*Restylane® Lyft with Lidocaine*				Comparator Control			
	Tolerable n (%)	Affects Daily Activities n (%)	Disabling n (%)	Total n (%)	Tolerable n (%)	Affects Daily Activities n (%)	Disabling n (%)	Total n (%)
Initial Treatment (N=111 for *Restylane® Lyft with Lidocaine* and N=59 for Comparator Control)								
Pain (including burning)	77 (85.6)	12 (13.3)	1 (1.1)	90 (81.1)	43 (84.3)	8 (15.7)	0	51 (86.4)
Tenderness	92 (89.3)	10 (9.7)	1 (1.0)	103(92.8)	46 (83.6)	9 (16.4)	0	55 (93.2)
Redness	55 (98.2)	1 (1.8)	0	56 (50.5)	34 (94.4)	2 (5.6)	0	36 (61.0)
Bruising	58 (86.6)	9 (13.4)	0	67 (60.4)	30 (85.7)	5 (14.3)	0	35 (59.3)
Swelling	79 (90.8)	7 (8.0)	1 (1.1)	87 (78.4)	45 (90.0)	5 (10.0)	0	50 (84.7)
Itching	33 (91.7)	2 (5.6)	1 (2.8)	36 (32.4)	22 (95.7)	1 (4.3)	0	23 (39.0)
Lumps/bumps	66 (88.0)	8 (10.7)	1 (1.3)	75 (67.6)	46 (97.9)	1 (2.1)	0	47 (79.7)
Total	81 (75.0)	26 (24.1)	1 (0.9)	108(97.3)	47 (79.7)	12 (20.3)	0	59 (100)
Touch-up Treatment (N=99 for *Restylane® Lyft with Lidocaine* and N=44 for Comparator Control)								
Pain (including burning)	57 (93.4)	4 (6.6)	0	61 (61.6)	26 (86.7)	4 (13.3)	0	30 (68.2)
Tenderness	72 (93.5)	5 (6.5)	0	77 (77.8)	30 (88.2)	3 (8.8)	1 (2.9)	34 (77.3)
Redness	39 (92.9)	3 (7.1)	0	42 (42.4)	25 (100)	0	0	25 (56.8)
Bruising	39 (90.7)	4 (9.3)	0	43 (43.4)	17 (94.4)	1 (5.6)	0	18 (40.9)
Swelling	63 (96.9)	2 (3.1)	0	65 (65.7)	26 (89.7)	3 (10.3)	0	29 (65.9)
Itching	21 (95.5)	1 (4.5)	0	22 (22.2)	9 (90.0)	1 (10.0)	0	10 (22.7)
Lumps/bumps	53 (100)	0	0	53 (53.5)	28 (96.6)	0	1 (3.4)	29 (65.9)
Total	80 (90.9)	8 (9.1)	0	88 (88.9)	34 (85.0)	5 (12.5)	1 (2.5)	40 (90.9)

N=number of subjects who completed at least 1 diary entry and were injected.

Note: Percentages for symptom intensity columns were based on the total number of subjects who reported 'Tolerable' or higher for a respective symptom in their subject diary. The total column percentages were based on the number of subjects who completed at least 1 diary entry and were injected.

Table 8. Pre-Defined, Expected, Post-Treatment Symptoms by Injection Timepoint and Duration (Safety Population)

	Restylane® Lyft with Lidocaine					**Comparator Control**				
Injection timepoint/ Symptom	**1-3 Days**	**4-7 Days**	**8-13 Days**	**14-28 Days**	**> 28 Days**	**1-3 Days**	**4-7 Days**	**8-13 Days**	**14-28 Days**	**> 28 Days**
Initial Treatment (N=111 for *Restylane® Lyft with Lidocaine* and N=59 for Comparator Control)										
Pain	60 (66.7)	22 (24.4)	7 (7.8)	1 (1.1)	0	35 (68.6)	12 (23.5)	4 (7.8)	0	0
Tenderness	36 (35.0)	43 (41.7)	15 (14.6)	9 (8.7)	0	20 (36.4)	20 (36.4)	12 (21.8)	3 (5.5)	0
Redness	43 (76.8)	10 (17.9)	3 (5.4)	0	0	21 (58.3)	11 (30.6)	3 (8.3)	1 (2.8)	0
Bruising	16 (23.9)	31 (46.3)	17 (25.4)	3 (4.5)	0	7 (20.0)	19 (54.3)	8 (22.9)	1 (2.9)	0
Swelling	47 (54.0)	32 (36.8)	6 (6.9)	2 (2.3)	0	26 (52.0)	14 (28.0)	8 (16.0)	2 (4.0)	0
Itching	27 (75.0)	6 (16.7)	1 (2.8)	2 (5.6)	0	11 (47.8)	7 (30.4)	2 (8.7)	3 (13.0)	0
Lumps/Bumps	22 (29.3)	26 (34.7)	11 (14.7)	16 (21.3)	0	16 (34.0)	12 (25.5)	8 (17.0)	11 (23.4)	0
Total	20 (18.5)	37 (34.3)	27 (25.0)	24 (22.2)	0	10 (16.9)	18 (30.5)	17 (28.8)	14 (23.7)	0
Touch-up Treatment (N=111 for *Restylane® Lyft with Lidocaine* and N=59 for Comparator Control)										
Pain	40 (65.6)	16 (26.2)	5 (8.2)	0	0	22 (73.3)	8 (26.7)	0	0	0
Tenderness	35 (45.5)	29 (37.7)	9 (11.7)	4 (5.2)	0	18 (52.9)	12 (35.3)	4 (11.8)	0	0
Redness	32 (76.2)	5 (11.9)	3 (7.1)	2 (4.8)	0	21 (84.0)	3 (12.0)	0	1 (4.0)	0
Bruising	17 (39.5)	14 (32.6)	12 (27.9)	0	0	9 (50.0)	4 (22.2)	3 (16.7)	2 (11.1)	0
Swelling	35 (53.8)	20 (30.8)	9 (13.8)	1 (1.5)	0	15 (51.7)	12 (41.4)	1 (3.4)	1 (3.4)	0
Itching	12 (54.5)	7 (31.8)	2 (9.1)	1 (4.5)	0	7 (70.0)	2 (20.0)	1 (10.0)	0	0
Lumps/Bumps	22 (41.5)	10 (18.9)	9 (17.0)	12 (22.6)	0	12 (41.4)	8 (27.6)	4 (13.8)	5 (17.2)	0
Total	33 (37.5)	22 (25.0)	16 (18.2)	17 (19.3)	0	13 (32.5)	14 (35.0)	5 (12.5)	8 (20.0)	0

N = Number of subjects who completed at least one diary entry and were injected at a given timepoint for a given treatment group.
Note 1: Percentages are based on the total number of subjects who reported 'Tolerable' or higher for a respective symptom in their subject diary.
Note 2: The duration is defined as the sum of days when a sign/symptom was scored 'Tolerable' or higher.

2. Effectiveness Results

The analysis of effectiveness was based on the 175 evaluable patients at the 3-month time point. Key effectiveness outcomes are presented below.

Primary Effectiveness Results

The primary objective of the study was met. The mean change from baseline in GCRS score for the *Restylane® Lyft with Lidocaine* treatment group was -0.94. For the control group, the mean change from baseline in GCRS score was -1.02. The confidence interval for the difference in Blinded Evaluator GCRS assessment at Month 3 for both the ITT and PP analysis populations was entirely below 0.5. Thus, non-inferiority of *Restylane® Lyft with Lidocaine* to comparator control was demonstrated.

Results from the observed cases analysis were consistent with the primary ITT analysis.

Secondary Effectiveness Results

For the *Restylane® Lyft with Lidocaine* group, the responder rate, based on the Blinded Evaluator GCRS, was 83.6% at Month 3, 75.5% at Month 6, 69.1% at Month 9, and 69.7% at Month 12.

Table 9. Effectiveness Results Through Month 12: Responder Rates Based on the Galderma Chin Retrusion Scale as assessed by the Blinded Evaluator (ITT Population)

Time point after last treatment	*Restylane® Lyft with Lidocaine*, % (n/N)
Month 3	83.6 (92/110)
Month 6	75.5 (83/110)
Month 9	69.1 (76/110)
Month 12	69.7 (76/109)

In the *Restylane® Lyft with Lidocaine* group, the responder rate (responder defined as a subject for whom at least 2 of the 3 IPRs correctly identified the post-treatment image in the pair at a given post-baseline visit) was 87.7% at Month 3 and 88.5% at Month 12.

In *Restylane® Lyft with Lidocaine* subjects, GAIS responder rates (as assessed by the Treating Investigator) ranged from 99.1% at Month 3 to 95.4% at Month 12.

In *Restylane® Lyft with Lidocaine* subjects, GAIS responder rates (as assessed by the subject) ranged from 94.5% at Month 3 to 89.0% at Month 12.

Subjects treated with *Restylane® Lyft with Lidocaine* would recommend the treatment to a friend (94.5% at Month 3 and 93.6% at Month 12).

The percentage of subjects who would choose to receive treatment again with *Restylane® Lyft with Lidocaine* was 91.8% at Month 3 and 92.7% at Month 12, while almost all subjects treated with *Restylane® Lyft with Lidocaine* were satisfied with how quickly they could go back to social engagements after treatment at Month 3 (96.4%).

Based on the FACE-Q™ Satisfaction with Chin Questionnaire Rasch-transformed total scores, subjects were satisfied with how their chin looked following treatment with *Restylane® Lyft with Lidocaine* at all post baseline visits from Month 3 through Month 12 (mean increase from baseline was: 47.7 at Month 3 and 44.0 at Month 12).

Based on the FACE-Q™ Satisfaction with Lower Face and Jawline Questionnaire Rasch transformed total scores, subjects were satisfied with their lower face and jawline at all post-baseline visits from Month 3 through Month 12 when treated with *Restylane® Lyft with Lidocaine* (mean increase from baseline was: 46.3 at Month 3 and 44.0 at Month 12).

In terms of treatment outcome satisfaction, based on the FACE-Q™ Satisfaction with Outcome Questionnaire Rasch transformed total scores, subjects treated with *Restylane® Lyft with Lidocaine* were satisfied with their treatment outcome at the majority of visits from Month 3 through Month 12 for the group (mean:75.7 at Month 3 and 72.1 at Month12).

Based on the ISQ at Month 3, all Treating Investigators responded as “agree” or “strongly agree” that, for subjects treated with *Restylane® Lyft with Lidocaine*, the treatment results were natural looking (100%) and almost all Treating Investigators responded that they were satisfied with how the product enabled them to structure and sculpt the chin (99.1%).

In subjects treated with *Restylane® Lyft with Lidocaine*, the median time to feeling comfortable returning to social engagement was 6.7 hours after initial treatment and 2.0 hours after touch-up treatment.

Other Effectiveness Results

At Month 3 and Month 12, the mean change from baseline for positive volume change, total volume change, and pogonion projection was confirmed based on 3D imaging.

3. Subgroup Analyses

The following baseline characteristics were evaluated for potential association with safety and effectiveness outcomes: study site, race, ethnicity, sex at birth, age category (above or below median age), FST (I-III versus IV-VI), injection volume (above or below median volume), and injection tool (needle/needle and cannula).

Consistency of the primary effectiveness analysis results across all subgroups was found and no clinically meaningful differences were observed for AE incidence across the subgroups.

The study was not specifically powered for study site, race, ethnicity, sex at birth, age, FST, injection volume, or injection tool subgroups.

4. Pediatric Extrapolation
In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 12 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Not applicable.

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary effectiveness endpoint of study 43USCH2208 was the change from baseline in the Blinded Evaluators' live assessment using the GCRS at 3 months after the last

treatment; Results were similar in the ITT and PP populations, where non-inferiority of *Restylane® Lyft with Lidocaine* to comparator control was established.

Additionally, no clinically meaningful differences in the change from baseline to Month 3 in the Blinded Evaluator GCRS were observed between the *Restylane® Lyft with Lidocaine* and comparator control groups when summarized by study site, race, ethnicity, sex at birth, age category, FST, injection volume, or injection tool.

The secondary effectiveness endpoints evaluated the responder rate based on the Blinded Evaluators' live assessment of the GCRS at Months 3, 6, 9, and 12 (a responder was defined as a subject with at least 1-grade improvement from baseline on the GCRS); the responder rate based on the IPR assessment using random pairings of baseline and post-baseline photographs at Months 3 and 12 (an improved subject was defined as a subject for whom 2 of the 3 IPRs correctly identified the post treatment image in the pair); the percentage of responders, defined by having at least "improved" (improved, much improved or very much improved) on the GAIS as assessed by the subject and Treating Investigator separately, at Months 3, 6, 9, and 12; proportion of subjects in each response category for every question in the SSQ at 3, 6, 9, and 12 months after the last treatment; FACE-Q™ Satisfaction with Outcome Rasch-transformed total score, and change from baseline in FACE-Q™ Satisfaction with Chin and FACE-Q™ Satisfaction with Lower Face and Jawline Rasch-transformed total scores, as well as proportion of subjects in each response category for each of the individual questions for the FACE-Q™ Satisfaction with Chin and Satisfaction with Outcome questionnaires at Months 3, 6, 9, and 12; proportion of Treating Investigators in each response category for every question in the ISQ at 3 months after the last treatment; and the time in hours until the subject felt comfortable returning to social engagement after treatment, based on follow-up question at 72 hours after treatment.

Results for secondary effectiveness endpoints indicated *Restylane® Lyft with Lidocaine* was effective for subcutaneous and/or supraperiosteal implantation for augmentation of the chin region to improve the chin profile in patients over the age of 21 with mild to moderate chin retrusion. Based on questionnaire response data, Treating Investigators and subjects were satisfied with both treatment and outcome.

Additionally, the vast majority of subjects in the *Restylane® Lyft with Lidocaine* and comparator control groups would recommend the treatment to a friend (94.5% at Month 3 and 93.6% at Month 12 compared to 94.5% at Month 3 and 90.7% at Month 12, respectively), and would choose to receive the treatment again.

B. Safety Conclusions

The risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above.

The safety endpoints included the incidence, intensity, time to onset, and duration of AEs collected throughout the study and the incidence, intensity, and number of days of

pre-defined, expected, post treatment events collected using subject diaries for 28 days following each treatment.

Restylane® Lyft with Lidocaine was generally safe and well tolerated and had a similar safety profile as comparator control. As reported in the subject diaries, the percentage of subjects experiencing pre-defined, expected post treatment events (i.e., pain, tenderness, redness, bruising, swelling, itching, or lumps/bumps) was similar between the *Restylane® Lyft with Lidocaine* and comparator control groups at the initial treatment (97.3% and 100%, respectively) and touch-up treatment (88.9% to 90.9%, respectively). The majority of reported symptoms were tolerable in the *Restylane® Lyft with Lidocaine* and comparator control groups (range: 85.6% to 100% and 83.6% to 100%, respectively).

Eight (7.0%) *Restylane® Lyft with Lidocaine* subjects and 3 (5.1%) comparator control subjects experienced an AE considered related to study product or injection procedure. All AEs considered related to study product or injection procedure were mild in intensity. The most common AE related to study product or injection procedure was implant site bruising (3/115 [2.6%] *Restylane® Lyft with Lidocaine* subjects and no comparator control subjects). No subject experienced a severe AE related to study product or injection procedure, and no subject experienced an AESI. The maximum mean duration was 192.5 days in the *Restylane® Lyft with Lidocaine* group and 145 days in the comparator control group, both events comprised implant site nodule. There were no late-onset events.

No subject died or experienced a treatment related SAE during the study. Two (1.7%) *Restylane® Lyft with Lidocaine* subjects and no comparator control subjects experienced an SAE considered unrelated to study product or injection procedure. One (0.9%) *Restylane® Lyft with Lidocaine* subject experienced an AE leading to premature study discontinuation that was also an SAE and considered unrelated to study product or injection procedure. Three *Restylane® Lyft with Lidocaine* device deficiencies were reported during the study. There were no AEs reported due to these deficiencies.

The mean NPS post injection was similar in the *Restylane® Lyft with Lidocaine* and comparator control groups at Month 1. No clinically meaningful changes from baseline in visual function assessments or functionality, sensation, palpability, and hair growth were observed.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

A complete summary of effectiveness is provided in Section A and demonstrates *Restylane® Lyft with Lidocaine* was efficacious in the improvement of chin profile, with non-inferiority to comparator control based on the change from baseline on the Blinded Evaluators' live assessment of the chin at Month 3 using the GCRS. Treatment

with *Restylane® Lyft with Lidocaine* also resulted in Investigator and Subject satisfaction and global aesthetic improvement similar to that of comparator control through Month 12.

Additionally, there was no evidence for or against a specific subgroup of patients demonstrating a substantial difference in the response to *Restylane® Lyft with Lidocaine* treatment and comparator control groups when summarized by study site, race, ethnicity, sex at birth, age category, FST, injection volume, or injection tool.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

A thorough safety assessment was conducted in this study providing a robust safety dataset as further evidence of a positive benefit/risk assessment of treatment with *Restylane® Lyft with Lidocaine*. The majority of related AEs were anticipated from previous exposure to *Restylane® Lyft with Lidocaine* for other indications. No pre-specified subgroup was determined to be a vulnerable population based on AE assessments. No clinically meaningful changes from baseline in visual function assessments or functionality, sensation, palpability, and hair growth were observed.

Restylane® Lyft with Lidocaine, like that of comparator control, was generally safe and well tolerated for chin region augmentation through Month 12.

Additional factors to be considered in determining probable risks and benefits for Restylane® *Lyft with Lidocaine* included: A majority (97.3%, 108/111) of the subjects experienced common treatment site responses which included tenderness, pain, swelling, lumps/bumps, bruising, redness, and itching. The majority of reported symptoms were tolerable (range: 85.6% to 100%), and the majority of subjects with pre-defined diary symptoms had resolution of their symptoms within the first 7 days of treatment. The most common AE related to study product or injection procedure was implant site bruising (3 [2.6%]. All AEs considered related to study product or injection procedure were mild in intensity. The minimum mean duration for any related AE was 1.0 day (implant site oedema) and the maximum mean duration was 192.5 days (implant site nodule). Summary of safety conclusions is provided above.

In the subgroup analyses, the percentages of subjects who experienced an AE related to study product or injection procedure were similar among:

- Males (9.1%) and Females (6.7%)
- Median age category (44 years): ≤ median age (7.9%) and > median age (5.8%)
- White subjects (5.3%), Black subjects (9.1%), and subjects of other races (11.8%)
- Ethnic groups Latino (8.1%) and not Hispanic or Latino (6.4%)
- Fitzpatrick skin type: FST I-III (6.6%) and FST IV-VI (7.4%)

The probable benefits outweigh the probable risks, as determined by the short-term adverse outcomes seen after injection. The risks of short-term adverse outcomes seen after injection are sufficiently well understood for patients to make informed decisions about the device.

1. Patient Perspective

   Patient perspectives considered during the review included:

- Subjects were asked to complete the SSQ at Baseline, 3, 6, 9 and 12 months after last treatment. The SSQ contained 6 items on overall satisfaction with the aesthetic outcome, 14 items on overall satisfaction with the treatment, 2 items regarding if the subject would recommend the treatment and do the treatment again, and at Month 3 only, 1 item on satisfaction regarding the return to social engagement. SSQ data across Month 3 to Month 12 the majority of subjects showed that they were happy with the treatment and aesthetic outcome, and greater subject satisfaction with *Restylane® Lyft with Lidocaine* compared with comparator control was noted at the majority of visits through Month 12. Additionally, most subjects would recommend the treatment to a friend and would undergo repeat treatment in the future.
- A follow-up telephone call was scheduled for 72 hours after each treatment, where the treated subject was to be asked when (in hours after treatment) s/he felt comfortable returning to social engagement, such as returning to the office or other public workplace, having dinner in a public restaurant, attending a social event/gathering such as a dinner party, etc.
- Subjects completed adapted versions of the FACE-Q™ Satisfaction with outcome, Satisfaction with chin, and Satisfaction with lower face and jawline questionnaires at Baseline, 3, 6, 9 and 12 months after last treatment. Based on the FACE-Q™ Satisfaction with Chin Questionnaire Rasch-transformed total scores, subjects were satisfied with how their chin looked, with their lower face and jawline, and with their treatment outcome following treatment at all post-baseline visits from Month 3 through Month 12 for both the *Restylane® Lyft with Lidocaine* group and the comparator control group. At the majority of visits, the mean FACE-Q™ Satisfaction with Chin Questionnaire Rasch-transformed total score was higher for *Restylane® Lyft with Lidocaine* compared with comparator control.
- Subjects who received treatment assessed their pain in the chin at each treatment visit, before and immediately following injection, rating their pain using an 11-point NPS where 0 is no pain and 10 is the worst pain imaginable. In both the *Restylane® Lyft with Lidocaine* group and the comparator control groups, the mean post-injection NPS score was at the lower end of the scale (under 2).
- Subject self-reported safety endpoints, including the incidence, intensity, and number of days of pre-defined, expected, post-treatment events collected using subject diaries for 28 days following each treatment were collected. the

percentage of subjects experiencing pre-defined, expected post-treatment events was similar between the *Restylane Lyft with Lidocaine* and comparator control groups at both the initial treatment and touch-up treatments.

In conclusion, given the available information above, the data support that for subcutaneous and/or supraperiosteal implantation for augmentation of the chin region to improve the chin profile in patients over the age of 21 with mild to moderate chin retrusion, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XV. CDRH DECISION

CDRH issued an approval order on November 4, 2025.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES

Not applicable.