SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Injectable Dermal Filler

Device Trade Name: *Sculptra*

Device Procode: LMH

Applicant's Name and Address: Q-Med AB, a Galderma affiliate
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SE-752 28 Uppsala, Sweden

Galderma Research & Development, LLC
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Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P030050/S039

Date of FDA Notice of Approval: April 18, 2023

The original PMA (P030050) was approved on August 3, 2004 and is indicated for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus under the product named *Sculptra*. The PMA supplement for *Sculptra Aesthetic* (P030050/S002) was approved on July 28, 2009 in immune-competent people as a single regimen for the correction of shallow to deep nasolabial fold (NLF) contour deficiencies and other facial wrinkles in which deep dermal grid pattern (cross-hatch) injection technique is appropriate.

Although *Sculptra* and *Sculptra Aesthetic* are identical in composition, both products were initially marketed under these two distinct trade names and utilized labeling specific to their respective indication. In PMA supplement P030050/S034, approved on November 23, 2021, *Sculptra* and *Sculptra Aesthetic* have been combined under the single product trade name (*Sculptra*) and labeling has been revised to include the combined information for both the approved lipoatrophy and aesthetic indications. P030050/S034 also included alternative reconstitution and injection procedures along with the addition of lidocaine to the product.

When the product name *Sculptra Aesthetic* is used, it is to align with the product name stated in the supportive documentation. The SSEDs to support the indications referred to above are available on the CDRH website and are incorporated by reference here.

The current supplement was submitted to expand the indication for *Sculptra* to include correction of fine lines and wrinkles in the cheek region for use in immune-competent subjects.

II. INDICATIONS FOR USE

Sculptra is indicated for correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles for use in immune-competent subjects.

Sculptra is indicated for correction of fine lines and wrinkles in the cheek region for use in immune-competent subjects.

Sculptra is intended for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

III. CONTRAINDICATIONS

Sculptra should not be used in any person who has hypersensitivity to any of the components of *Sculptra* (see DEVICE DESCRIPTION).

Sculptra should not be used in patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

Sculptra should not be used in patients with known history of or susceptibility to keloid formation or hypertrophic scarring.

Sculptra reconstituted with lidocaine hydrochloride (lidocaine) should not be used in patients with a history of allergies to lidocaine or other amide type local anesthetics.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the *Sculptra* Instructions for Use.

V. DEVICE DESCRIPTION

Sculptra is an injectable implant containing microparticles of poly-L-lactic acid (PLLA), sodium carboxymethylcellulose (USP), non-pyrogenic mannitol (USP) and sterile water for injection (SWFI) (USP). *Sculptra* is available in 367.5 mg dose vials and is to be

reconstituted prior to use by the addition of 5 mL or 8 mL SWFI (USP) to form a sterile, non-pyrogenic suspension.

Sculptra is produced by aseptic manufacturing and is supplied as a sterile dry powder in a clear glass vial sealed by a rubber bung covered by an aluminum ring and a plastic flip-off cap.

Sculptra is available in packages of two vials.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are other approved procedures in the United States for correction of NLF contour deficiencies, correction of fine lines and wrinkles in the cheek region and other facial wrinkles as well as for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

Alternative therapies for correction of NLF, lines and wrinkles in the cheek region and other facial wrinkles include bovine collagen dermal fillers, human collagen dermal fillers, hyaluronic acid-based dermal fillers and autologous fat transfer. Alternative therapies for treating lipoatrophy in people with human immunodeficiency virus include fillers, implants or surgery. Other methods for treatment of facial rhytids include injection of botulinum toxin, topical creams, chemical peels, laser skin resurfacing, dermabrasion, and surgical intervention. 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

Sculptra was initially developed by Biotech Industries S.A under the name *NEW-FILL*® and was approved for marketing and sale in the European Union in November 1999. The name *Sculptra* was added in January 2004.

Sculptra was approved by the FDA in August 2004 under P030050 for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus (HIV). The PMA supplement (P030050/S002) for *Sculptra Aesthetic* was approved on July 28, 2009 as a single regimen for the correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles in immunocompetent people where deep dermal grid pattern (cross-hatch) injection technique is appropriate. PMA supplement P030050/S034, approved on November 23, 2021 included alternative reconstitution and injection procedures along with the addition of lidocaine to the product and the combination of *Sculptra* and *Sculptra* Aesthetic under the single product trade name (*Sculptra*) with labeling that includes combined information for both the approved lipoatrophy and aesthetic indications.

On July 11, 2014 the Agency was informed that Q-Med AB located in Uppsala, Sweden acquired ownership and all rights of the product from Valeant Pharmaceuticals North America, LLC. The Agency was subsequently informed on July 22, 2014 that Galderma Laboratories, L.P. would be the US point of contact for Q-Med AB.

The product has since been approved in multiple countries globally: Argentina, Australia, Brazil, Canada, Chile, Colombia, EU/EFTA, Hong Kong, Israel, Lebanon, Malaysia, Mexico, New Zealand, Philippines, Puerto Rico, Russia, South Africa, Saudi Arabia, Singapore, South Korea, Taiwan, Turkey, UAE, UK and USA.

Sculptra has not been withdrawn from any marketplace for any reason.

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

Post-marketing surveillance

The adverse events received from post-marketing surveillance (voluntary reporting and published literature) for *Sculptra* in the US and other countries include:

- papules/nodules with or without inflammation or discoloration,
- lack of effect,
- swelling,
- mass formation/induration,
- pain/tenderness,
- granuloma (including ectropion)/foreign body reaction,
- visual disturbance including transient blurred vision, reduced visual acuity, increased lacrimation, eyelid ptosis, dry eye and blindness,
- bruising/hematoma,

- erythema,
- nerve injury including paresthesia, hypoesthesia and facial nerve paralysis,
- bacterial infections and abscess formation,
- inflammation,
- skin discoloration,
- injection site reactions including burning sensation, warmth and irritation,
- atrophy/scarring,
- pruritus,
- deformity/facial asymmetry,
- rash,
- hypersensitivity/allergic reaction and angioedema,
- dermatitis,
- bleeding,
- symptoms of reactivation of herpes infection,
- urticaria,
- vesicles/blisters/pustules,
- ischemia/necrosis,
- acne,
- device dislocation,
- telangiectasia,
- discharge,
- other dermatological events including alopecia, skin wrinkling, skin tightness, skin dryness, skin hypertrophy and photosensitive reaction,
- non-dermatological events including headache, pyrexia, malaise, arthralgia, anxiety, nausea, insomnia, dyspnea, fatigue, dizziness, muscular weakness or twitching, lymphadenopathy, and depression

When required, depending on event, treatments may include massage/manipulation, warm compress, nitroglycerine paste, corticosteroids, antibiotics, antihistamines, NSAIDs, aspiration/drainage of the product, saline injections and surgery. Events which did not resolve or where resolution information is not available at last contact were reported.

Scarring, mostly a non-serious event, was reported in association with skin discoloration, nodules, lumps, indurations, granulomas, hyperpigmentation, hypertrophic scars, and suspicion of keloid formation. Time to onset when specified ranged from within 1 week

to 24 months post-*Sculptra* injection and outcome ranged from 'recovered' to 'ongoing' at last contact.

Skin discoloration was reported as a non-serious event, typically reported in association with lumps and nodules. It has also been reported with blanching and telangiectasias. Time to onset when specified usually ranged from within 1 week to 12 months post-injection. Outcome ranged from 'recovered' to 'ongoing' at last contact.

Serious adverse events have rarely been reported. The most commonly reported serious adverse events for *Sculptra* with more than 5 reported events include papule/nodule, swelling/edema, pain, granuloma, symptoms of visual disturbance, infection/abscess, mass/induration, paresthesia and facial nerve paralysis, erythema, inflammation, bruising/hematoma, discoloration, deformity, scaring/atrophy, hypersensitivity, pruritus, rash, muscle disorders, ischemia/necrosis, urticaria and blisters.
Injection site nodules mostly occurred several months post-injection. Such nodules are occasionally associated with inflammation or discoloration, with time to onset ranging from 1-2 months to 14 months post-last injection. In some cases, the nodules were reported to resolve spontaneously or following treatment with, *e.g.* intralesional corticosteroids, others were described with a prolonged duration of up to 2 years. For those nodules that were larger in size, occurring in difficult anatomical regions (*e.g.* lower eyelid) or persisted after other treatments such as intralesional corticosteroids failed, surgical excision of the nodules was required.

Granulomas usually occur several months after injection; in few cases onset was more than 1-year post-injection. While events were reported as granuloma, only a few cases were confirmed by biopsy. Treatment ranged from subcision or intralesional corticosteroid with subsequent improvement, to surgical extraction. Of the few granuloma cases that required hospitalization, these were associated with infraorbital use or injection in the lip vermilion.

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. Visual disturbances including blindness have been reported following injection of *Sculptra* into the temple area, periorbital areas,

and/or cheek. Events requiring medical intervention, and events which did not resolve or where resolution information is not available were reported.

Serious edema was reported in association with erythema, pain, and heat sensation. The symptoms were mostly temporary, and with no significant impact on the quality of daily life reported. Treatment included corticosteroids, antihistamines and/or anti-inflammatories. Recovery occurred within 7-10 days without sequelae.

Serious erythema, serious pain, and serious pruritus reported with bruising and heat sensation, were reported within 24 hours post-injection. Treatment included corticosteroids, antihistamines and/or anti-inflammatories. Events resolved within 7-10 days post-injection without sequelae and with no significant impact on daily life.

Serious hypersensitivity reactions were reported mainly in association with facial swelling and Quincke's edema, with symptoms appearing from 1 day to 1-week post-injection. Patients recovered without sequelae after treatment with intravenous corticosteroids and antihistamines.

Serious infections such as subcutaneous abscesses, cellulitis, folliculitis, and methicillin-resistant *Staphylococcus aureus* at the injection site, were reported. Time to onset of event ranged from 1 day to 1 week. Of these cases a few required hospitalization with administration of intravenous antibiotics. All patients recovered or were recovering at the last contact.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory studies

Because no change in product manufacture or specification is proposed in this supplement, the biocompatibility studies previously presented in PMA P030050 and supplements support the labeling changes described herein.

B. Biocompatibility studies

The ISO 10993 biocompatibility program for *Sculptra* was re-evaluated in 2016 utilizing *Sculptra* batches produced under the current approved manufacturing conditions. Because no change in product manufacture or specification is proposed in this supplement, the biocompatibility studies previously presented in PMA P030050 and supplements support the labeling changes described herein.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for the use of *Sculptra* for the correction of fine lines and wrinkles in the cheek region. 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

Base study (0 to 12 months): Subjects were treated between 12 Nov 2019 and 13 Mar 2021 with subjects followed through Aug 12, 2021. Subjects may have participated in an Extension study for up to 24 months. In the Extension study, Control Subjects were treated and Base study Treatment subjects were followed with no further treatment. The database for this PMA supplement reflects data collected for both the Base and Extension studies through July 20, 2022 and included 149 subjects at 13 investigational sites in the US.

The study (43USSA1812) was a prospective, randomized, evaluator-blinded, no-treatment controlled multicenter study to assess the effectiveness and safety of treatment with *Sculptra* for correction of cheek wrinkles. One hundred forty-nine (149) subjects with intent to undergo correction of cheek wrinkles with a Galderma Cheek Wrinkles Scale (GCWS) At Rest score of 2 (moderate) or 3 (severe) on each side of the face were randomized (2:1) to either treatment with *Sculptra* (treatment group; 97 subjects) or no treatment (control group; 52 subjects). The treatment group received *Sculptra* reconstituted with 8 mL of SWFI with the addition of 1 mL 2% lidocaine. All subjects were offered to participate in an extension study in which treatment was administered to the control group at Month 12. No further treatment was administered to the treatment group in the extension. The extension study is complete. A total of 111 subjects (39 control group subjects, 72 treatment group subjects) entered the extension study.

Subjects were treated to optimal correction at four-week intervals (+5 weeks), with a maximum of four treatment sessions. Follow-up visits were conducted at Months 7, 9 and 12 after initial treatment.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the clinical study (43USSA1812) was limited to subjects who met the following key inclusion criteria:

   - Women or men over 21 years of age.
   - Intent to undergo correction of cheek wrinkles on both sides of the face and a Galderma Cheek Wrinkles Scale (GCWS) At Rest score of Moderate or

Severe on each side of the face, as assessed on Day 1 by the Blinded Evaluator and the Treating Investigator (agreement on score was not required and the GCWS At Rest score for each side of the face did not need to be equal; however, the difference between the two was limited to 1 grade).

Subjects were not permitted to be enrolled in the clinical study if they met any of the following key exclusion criteria:

- Known/previous allergy or hypersensitivity to any of the *Sculptra* constituents.
- History of allergy or hypersensitivity to lidocaine or other amide-type anesthetics, or topical anesthetics or nerve blocking agents.
- Previous use of any tissue augmenting therapy, contouring, or revitalization treatment in or near the area of treatment.
    - Calcium hydroxylapatite, Poly-L-Lactic acid, was prohibited.
    - Collagen or hyaluronic acid may not have been use within 12 months of enrollment.
- Previous treatment/procedure in the face in the previous 6 months that, in the Treating Investigator's opinion, would interfere with the study injections and/or study assessments or exposes the study subject to undue risk by study participation.

2. Follow-up Schedule

Base study (0 to 12 months): Qualified subjects were randomized to receive treatment with *Sculptra* reconstituted with 8 mL of SWFI (Treatment Group) or no treatment (Control Group). Subjects in the treatment group received treatment by the Treating Investigator at Day 1. The method of injection was at the discretion of the treating Investigator according to the study protocol. Subjects were treated to optimal correction, which was defined as at least a one-step improvement on the Galderma Cheek Wrinkles Scale (GCWS) At Rest and the best correction that can be achieved as agreed by Treating Investigator and subject.

After the first treatment, there was a 12-month follow-up period with 6 in-clinic visits after baseline/first treatment. Additional treatment was performed at one month (+5 weeks) after the last treatment in up to four sessions if deemed necessary to obtain optimal aesthetic result; this decision was agreed upon by the Treating Investigator and the subject. Follow-up visits without treatment were conducted at Months 7, 9 and 12.

The Treatment group (investigational product) received a maximum of 2 vials (9 mL total volume per vial with 1 mL added lidocaine solution included) of *Sculptra* per treatment session with a maximum of 9 mL per cheek. The Control group did not receive any treatment. Dose amount maximums were the same for all treatment sessions.

Subjects were contacted by telephone 72 hours after each treatment (i.e. initial, optional touch-up, as applicable) for safety follow-up.

Subjects evaluated injection site reactions in a 28-day diary, starting on the day of treatment and at each treatment time point.

Extension Study (12-24 months): During the extended follow-up period, control group subjects were offered *Sculptra* treatment (Designated as Group A), and treatment group subjects (Designated as Group B) returned for continued safety and effectiveness evaluations up to 24 months.

Group A subjects received the same safety assessments after treatment as in the Base study. Both Group A and B subjects had the same efficacy assessments as during the Base study.

3. Clinical Endpoints

Safety

The objective of the study was to evaluate the safety of *Sculptra* in the correction of cheek wrinkles.

Safety endpoints:

- Incidence, intensity, time to onset and duration of adverse events collected throughout the study period.
- Incidence, intensity and number of days of pre-defined expected post-treatment events collected using subject diaries for 28 days from each treatment.
- Safety assessment by a qualified staff member at all visits according to predefined methods at baseline and at all follow-up visits for the Treatment Group and the Control Group:
    - Cheek firmness, symmetry and function (smiling and chewing)
    - Device palpability (baseline assessment excluded)

- Mass formation
- Cheek sensation
- Visual Function Assessments

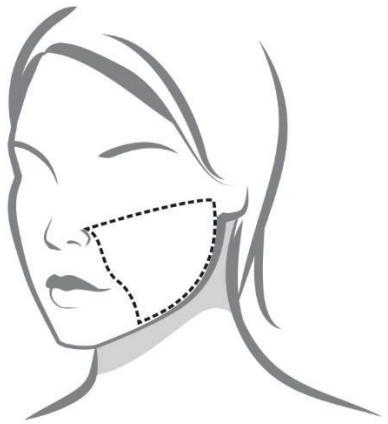
Effectiveness

The primary effectiveness endpoint was evaluated based on responder rates using the GCWS At Rest (Figure 1, Table 1), as assessed live by the Blinded Evaluator at Month 12. A responder was defined as a subject with at least a 1-grade improvement from baseline in both cheeks concurrently.

Table 1 Galderma Cheek Wrinkle Scale At Rest

None	No lines or wrinkles.
Mild	Only a few superficial lines
Moderate	Many superficial lines or a few shallow wrinkles
Severe	Many shallow wrinkles or a few moderate depth wrinkles.
Very severe	Many moderate wrinkles or at least one deep wrinkle with or without redundant folds.

Figure 1 Treatment Area Cheek region



Secondary effectiveness endpoints included responder rates over time up to Month 12 based on Blinded Evaluator assessment using GCWS At Rest and GCWS Dynamic, percentage of subjects having at least "Improved" on the Global Aesthetic Improvement Scale (GAIS) on both sides of the face combined as assessed live by the subject and the Treating Investigator separately, change from baseline in subject satisfaction using the Satisfaction with Cheeks FACE-Q questionnaire, subject

satisfaction scores using a 5-point subject satisfaction questionnaire and time in hours from treatment procedure until the earliest time the subject reported feeling comfortable returning to social engagement, based on subject diary reporting.

Extension study (12 to 24 months):
Effectiveness endpoints evaluated for the long- term extension included responder rate on both sides of the face as assessed by the Blinded Evaluator using GCWS At Rest and GCWS Dynamic at Months 19, 21, and 24 as well as Satisfaction with Cheeks FACE-Q™ questionnaire, subject satisfaction and GAIS at all visits, and time in hours from treatment procedure until the earliest time the subject reported feeling comfortable returning to social engagement based on subject diary reporting.

B. Accountability of PMA Cohort

Base study (0 to 12 months): A total of 149 subjects were enrolled and randomized. A total of 134 (89.9%) subjects completed the study (90.7% treatment group, 88.5% control group); the most common reason for study discontinuation was subjects being lost to follow-up (4 [4.1%] subjects in the treatment group, 2 [3.8%] subjects in the control group). One subject discontinued the study for medical reasons.

Ninety-seven (97) subjects were treated with *Sculptra* reconstituted with 8 mL of SWFI with the addition of 1 mL 2% lidocaine and a reference group of fifty-two (52) subjects did not receive any treatment.

Table 2 Summary of Subject Disposition: All Subjects

Category	Control Group n (%)	Treatment Group n (%)	Total n (%)
Screened			183
Screening failures			34
Intent-to-treat population[a]	52	97	149
Safety population[b]	52 (100)	97 (100)	149 (100)
Per-protocol population[c]	45 (86.5)	86 (88.7)	131 (87.9)
Completed study, n (%)	46 (88.5)	88 (90.7)	134 (89.9)
Premature study discontinuation, n (%)	6 (11.5)	9 (9.3)	15 (10.1)
Primary reason for study discontinuation			
Medical reason	0	1 (1.0)	1 (0.7)
Withdrawal of informed consent (not due to coronavirus disease-19 concerns)	2 (3.8)	1 (1.0)	3 (2.0)
Withdrawal of informed consent (due to coronavirus disease-19 concerns)	1 (1.9)	3 (3.1)	4 (2.7)

Category	Control Group n (%)	Treatment Group n (%)	Total n (%)
Lost to follow-up	2 (3.8)	4 (4.1)	6 (4.0)
Other	1 (1.9)[d]	0	1 (0.7)

a All subjects who were randomized based on the as-randomized principle (i.e., according to the treatment they were randomized to).

b All subjects who were treated with *Sculptra* or randomized to no treatment control group. Subjects were analyzed based on the as-treated principle (i.e., according to the treatment they actually received).

c All intent-to-treat subjects who completed 12 months after the baseline visit without any deviations considered to have a substantial impact on the primary effectiveness outcome (this was determined by the Sponsor).

d One subject was a screen failure due to previous use of Radiesse; however, they were randomized erroneously but did not receive treatment.

Note: N = number of subjects; n = number of subjects in a specific category. Percentages calculated as 100 × (n/N) in the intent-to-treat population.

The safety population includes all subjects who were treated with *Sculptra* or randomized to the no treatment control group. Subjects were analyzed based on the as-treated principle (i.e., according to the treatment they actually received).

The Intent-to-treat (ITT) population includes all subjects who were randomized based on the as randomized principle (i.e., according to the treatment they were randomized to).

The per protocol (PP) population included all ITT subjects with a completed Month 12 after baseline assessment of the Blinded Evaluator GCWS At Rest and without any deviations considered to have a substantial impact on the primary effectiveness outcome.

Extension study (12 to 24 months):
Of the 134 subjects eligible for the extension study, 111 subjects enrolled in the extension study. The most common reason for subjects not participating in the extension study was the requirement for follow-up visits. A total of 104 (93.7%) subjects completed the extension study. The most common reason for study discontinuation was the subject being lost to follow-up (5 [4.5%] subjects).

C. Study Population Demographics and Baseline Parameters

Base study (0 to 12 months): The demographics of the study are typical for a pivotal study performed in the US for this indication. The demographics of the study population are presented in Table 3.

The majority of subjects were female (96.6%), White (90.6%), and not Hispanic or Latino (91.9%); the mean age was 60.7 years.

The most common Fitzpatrick Skin Type (FST) for all subjects was FST III (45.6%) and the least common was FST VI (3.4%). This study was designed to enroll an ethnically

diverse population by including at least fifteen subjects with FST IV and 14 subjects with FST V-VI. There was a total of 32 FST IV-VI subjects (21.5% of all subjects; 21.6% in treatment group and 21.2% in the control group). All subjects had a moderate or severe GCWS at rest score on both sides of the face.

Table 3 Subject demographics and baseline characteristics

	Control Group (N=52)	Treatment Group (N=97)	Total (N=149)
Age (years)			
n	52	97	149
Mean (SD)	60.4 (8.72)	60.9 (8.50)	60.7 (8.55)
Median	60.0	60.0	60.0
Min, Max	45, 88	41, 89	41, 89
Age Category, n (%)			
>=55 years	39 (75.0)	77 (79.4)	116 (77.9)
<55 years	13 (25.0)	20 (20.6)	33 (22.1)
Gender, n (%)			
Female	50 (96.2)	94 (96.9)	144 (96.6)
Male	2 (3.8)	3 (3.1)	5 (3.4)
Race, n (%)			
American Indian/Alaska Native	0	1 (1.0)	1 (0.7)
Asian	1 (1.9)	1 (1.0)	2 (1.3)
Black/African American	4 (7.7)	7 (7.2)	11 (7.4)
Native Hawaiian/Other Pacific Islander	0	0	0
White	47 (90.4)	88 (90.7)	135 (90.6)
Other	0	0	0
Multiple [1]	0	0	0
Ethnicity, n (%)			
Not Hispanic or Latino	47 (90.4)	90 (92.8)	137 (91.9)
Hispanic or Latino	5 (9.6)	7 (7.2)	12 (8.1)
Fitzpatrick Skin Type Score, n (%)			
I	2 (3.8)	4 (4.1)	6 (4.0)
II	18 (34.6)	25 (25.8)	43 (28.9)
III	21 (40.4)	47 (48.5)	68 (45.6)
IV	6 (11.5)	12 (12.4)	18 (12.1)
V	4 (7.7)	5 (5.2)	9 (6.0)
VI	1 (1.9)	4 (4.1)	5 (3.4)
Galderma Cheek Wrinkles Scale (GCWS) – At Rest, Blinded Evaluator, n (%)			
Left			
None	0	0	0

	Control Group (N=52)	Treatment Group (N=97)	Total (N=149)
Mild	0	0	0
Moderate	28 (53.8)	50 (51.5)	78 (52.3)
Severe	24 (46.2)	47 (48.5)	71 (47.7)
Very Severe	0	0	0
Galderma Cheek Wrinkles Scale (GCWS) – At Rest, Blinded Evaluator, n (%)			
Right			
None	0	0	0
Mild	0	0	0
Moderate	37 (71.2)	60 (61.9)	97 (65.1)
Severe	15 (28.8)	37 (38.1)	52 (34.9)
Very Severe	0	0	0

[1] 'Multiple' category includes subjects with more than one race selected on eCRF.

Note: N = Number of subjects, n = Number of subjects in specific category. Percentages calculated as 100 x (n/N). SD = Standard Deviation.

Extension Study (12 to 24 months): As subjects enrolled from the base study, the above demographics presented is representative of the study population.

Treatment regimen

Base study (0 to 12 months): The first treatment was administered at the baseline visit. Additional treatments were performed if deemed necessary to obtain optimal aesthetic result one month after the last treatment in up to four treatment sessions in total. Subjects were treated to optimal correction, which was defined as at least a 1 grade improvement on the GCWS At Rest and best correction that could have been achieved as agreed upon by the Treating Investigator and the subject.

Sculptra was injected using the following injection techniques; linear threading, bolus, fanning and cross-hatching technique, in the subdermal plane; subcutaneously or supraperiosteally. Subjects were given a maximum of two vials per session, with a maximum of one vial per side, (i.e. maximum 9 mL per side). Overall, a total mean injection volume of 54.11 mL was received per subject in the treatment group. The median injection volume (left + right sides) at each treatment session was 16.00 mL. The minimum volume injected was 7.5 mL in session 1, 8.0 mL in session 2, 3.0 mL in session 3, and 6.1 mL in session 4; the maximum volume injected at each treatment session was 18.0 mL. The mean number of treatments was 3.6 (range 1-4).

A summary of overall treatment administration characteristics for all treatment sessions is presented in Table 4. Subjects received a combination of injection techniques, at the discretion of the Treating Investigator using a 25 G needle. Linear retrograde (91.3%) and fanning (81.2%) were the most common injection techniques used. The majority of

subjects received one vial per session (96.8%). All subjects received injections in the subcutaneous region and 67% also received injections in the supraperiosteal plane.

61.2% of the subjects received anesthetics (local), even though lidocaine was added to the investigational product prior to injection. 83.8% of all subjects received injection concomitant procedures (i.e., massage, ice pack, or other) at the time of treatment.

Table 4 Overall treatment administration characteristics (Treatment group) (Safety population)

Characteristic	Treatment 1 (N=97) n (%)	Treatment 2 (N=95) n (%)	Treatment 3 (N=86) n (%)	Treatment 4 (N=67) n (%)	Total (N=345) n (%)
Number of vials used					
One	92 (94.8)	91 (95.8)	86 (100)	65 (97.0)	334 (96.8)
Two	5 (5.2)	4 (4.2)	0	2 (3.0)	11 (3.2)
Was 25-gauge needle used for injection					
Yes	97 (100)	95 (100)	86 (100)	67 (100)	345 (100)
Injection method[a]					
Linear antegrade	38 (39.2)	39 (41.1)	36 (41.9)	25 (37.3)	138 (40.0)
Linear retrograde	87 (89.7)	85 (89.5)	79 (91.9)	64 (95.5)	315 (91.3)
Bolus	20 (20.6)	22 (23.2)	18 (20.9)	14 (20.9)	74 (21.4)
Fanning	78 (80.4)	77 (81.1)	73 (84.9)	52 (77.6)	280 (81.2)
Cross hatching	33 (34.0)	34 (35.8)	38 (44.2)	26 (38.8)	131 (38.0)
Depth of injection, left side					
Subcutaneous	97 (100)	95 (100)	86 (100)	67 (100)	345 (100)
Supraperiosteal	67 (69.1)	63 (66.3)	56 (65.1)	45 (67.2)	231 (67.0)
Depth of injection, right side					
Subcutaneous	97 (100)	95 (100)	86 (100)	67 (100)	345 (100)
Supraperiosteal	67 (69.1)	63 (66.3)	56 (65.1)	45 (67.2)	231 (67.0)
Any anesthetics used before injection	62 (63.9)	61 (64.2)	53 (61.6)	35 (52.2)	211 (61.2)
Topical	56 (57.7)	55 (57.9)	49 (57.0)	31 (46.3)	191 (55.4)
Local injection	6 (6.2)	6 (6.3)	4 (4.7)	4 (6.0)	20 (5.8)
None	35 (36.1)	34 (35.8)	33 (38.4)	32 (47.8)	134 (38.8)
Any injection concomitant procedures	79 (81.4)	81 (85.3)	74 (86.0)	55 (82.1)	289 (83.8)
Massage	60 (61.9)	64 (67.4)	60 (69.8)	42 (62.7)	226 (65.5)
Ice pack	61 (62.9)	59 (62.1)	51 (59.3)	37 (55.2)	208 (60.3)
Other	6 (6.2)	6 (6.3)	6 (7.0)	5 (7.5)	23 (6.7)
None	18 (18.6)	14 (14.7)	12 (14.0)	12 (17.9)	56 (16.2)
Any technical problems	0	1 (1.1)	1 (1.2)	0	2 (0.6)

a Injector was to check all that applied.

Note: N = number of treatments given to subjects in safety population, n = number of treatments given for specific category. Percentages calculated as 100 × (n/N).

Extension study (12 to 24 months):

Only Group A subjects received treatment with *Sculptra* in the Extension study and followed the same treatment schedule as the Base study. Overall, similar injection volumes were seen in the Extension study.

Overall, a total mean injection volume of 62.84 mL was received per subject in Group A. The median injection volume (left + right sides) at each treatment ranged from 16.50 to 16.80 mL. The minimum volume injected was 8.5 mL at treatment 4 and 9.0 mL at treatments 1, 2, and 3; the maximum volume injected at each treatment was 18.0 mL.

D. Safety and Effectiveness Results

1. Safety Results

Base study (0 to 12 months)**:** The analysis of safety was based on all 149 subjects included in the study. The key safety outcomes for this study are presented below in Tables 5 – 9. Subject reported injection related events are presented in Table 5 and Table 6. Adverse events (AEs) are presented in Table 7, Table 8 and Table 9.

Pre-defined Injection Related Events:

Base study (0 to 12 months): Pre-printed diary forms were used by subjects to record the presence of pre-defined expected post-treatment events in the treated area, i.e. bruising, redness, swelling, pain, tenderness, itching, lumps/bumps, and "other" for 28 days following each treatment. Subjects rated each treatment site response as "None", "Mild", "Moderate" or "Severe".

Overall, for either side of the face, 92 (98.9%) subjects in the treatment group reported symptoms. The most common symptoms overall were tenderness (93.5%), bruising (93.5%), swelling (87.1%), and pain (including burning) (83.9%). Overall, almost all symptoms were mild or moderate in intensity (97.8%) and the majority resolved within 14 days (76.1%).

Device and Injection Related Events:

Adverse events (AEs) were evaluated by Investigators throughout entirety of the study. In addition, Vision function assessments: Snellen Visual Acuity Test, Extraocular Muscle Function Test and Confrontation Visual Field Test, was performed both prior to and post injection of the study product at baseline, before and after treatments, and all physical scheduled follow-up visits. At all physical visits, a study staff member who was qualified by training and experience to perform safety assessments assessed each subject's cheek sensation; firmness and symmetry; and mass formation. After treatment with the study product, product palpability was performed at each physical visit.

No clinically meaningful changes from baseline in visual function assessments or functionality, sensation, cheek firmness and symmetry, mass formation, or abnormal device palpability were observed.

One subject experienced a unilateral 1-line change in the Snellen Visual Acuity test from Baseline at Month 1 post injection (0+, -1), but reported no ocular symptoms or vision loss.

All other eye and safety assessments were normal throughout the completion of the Month 1 visit for the subject. Subject did not return for additional assessments.

Three subjects in the control group experienced a change in Snellen Visual Acuity test from baseline to a post-baseline visit. These occurrences are due to the subjects not wearing their corrective lenses for the post-baseline assessments.

An overview of adverse events is presented below in Table 7. An overall summary of AEs following treatment is presented in Tables 8 and 9. Out of the 97 subjects randomized to treatment, a total of 20 subjects (20.6%) experienced an AE considered related to study treatment. The most common (>1.0% of subjects in the treatment group) related AEs were injection site bruising (11 [11.3%] subjects), dizziness (2 [2.1%] subjects), and headache (2 [2.1%]) subjects.

All AEs related to study product or injection procedure reported in the treatment group were mild or moderate in intensity. Three (3.1%) subjects experienced related AEs of moderate intensity (one experienced 2 events of moderate injection site pain, one subject experienced moderate dizziness, and one subject experienced moderate injection site bruising) and all events resolved by the end of the study.

One (1.0%) subject in the treatment group experienced an adverse event of special interest (AESI), an AE of hypermetropia with late onset (>21 days after the most recent treatment) related to study product or injection procedure, mild in intensity. The duration of the event was 37 days and was resolved without action taken.

One subject experienced multiple small, palpable skin nodules in the treatment area on both her left and right cheeks (PT: injection site nodule) on Day 332, 180 days after her most recent injection The AEs (for both the left and right cheeks) were considered mild in intensity and were ongoing at study completion. No action was taken with regard to the AEs.

One subject experienced a 5-6 mm small, oblong lump that was palpable on her lower left cheek, near the corner of their mouth (PT: skin mass [small lump]) on Day 49, 9 days after her most recent injection. The AE was considered mild in intensity, related to study

product and injection procedure, and resolved on Day 327 (was considered chronic and/or stable). No action was taken with regard to the AE.

A summary of the duration (days) of AEs related to study product or injection procedure is provided in Table 9.

Three subjects in the treatment group experienced serious adverse event (SAE)s. None of these were considered related to study product or injection procedure.

One subject had an AE leading to study discontinuation (which was also considered an SAE unrelated to treatment (adenocarcinoma)). No subject died during the study.

21.3% (20/94) of females experienced a related adverse event, while no male subjects (0/5) had a related adverse event. Due to the small number of male subjects, conclusions cannot be drawn.

Device Deficiencies

A total of 2 product complaints in a total of 650 vials were reported during the study from 2 sites. One complaint was in regard to a chipped vial being noticed during reconstitution (which was placed in quarantine) and the other complaint stated that there was more foam and less opacity to the study product when compared to the visual 48-hour reconstitution. There were no AEs reported due to these deficiencies.

Table 5 Frequency and intensity of pre-defined events reported in the daily diary

	Treatment Group (N=97)			
Symptom	Any n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Number of Subjects with Diaries at Visit: 93				
Overall Any Symptom	92 (98.9)	61 (66.3)	29 (31.5)	2 (2.2)
Pain (including burning)	78 (83.9)	70 (89.7)	8 (10.3)	0
Tenderness	87 (93.5)	78 (89.7)	9 (10.3)	0
Redness	59 (63.4)	53 (89.8)	5 (8.5)	1 (1.7)
Bruising	87 (93.5)	64 (73.6)	21 (24.1)	2 (2.3)
Swelling	81 (87.1)	64 (79.0)	16 (19.8)	1 (1.2)
Itching	25 (26.9)	24 (96.0)	1 (4.0)	0
Lumps/Bumps	48 (51.6)	44 (91.7)	4 (8.3)	0

Note: N = Number of subjects in Safety Population, n = Number of subjects in specific category. For 'Any' column, percentages calculated as 100 x (n/number of subjects with response indicating symptom or none at applicable treatment session). For intensity columns, percentages calculated as 100 x (n/number of subjects at treatment session with that symptom). Subjects reporting multiple events of the same symptom are counted once for that event within the most severe category.

Table 6 Frequency and duration of pre-defined events reported in the daily diary

Symptom	Treatment Group (N=97) 1 Day n (%)	2-7 Days n (%)	8-14 Days n (%)	15-28 Days n (%)
Number of Subjects with Diaries at Visit: 93				
Overall Any Symptom	3 (3.3)	23 (25.0)	44 (47.8)	22 (23.9)
Pain (including burning)	19 (24.4)	54 (69.2)	4 (5.1)	1 (1.3)
Tenderness	7 (8.0)	64 (73.6)	14 (16.1)	2 (2.3)
Redness	15 (25.4)	39 (66.1)	4 (6.8)	1 (1.7)
Bruising	6 (6.9)	21 (24.1)	41 (47.1)	19 (21.8)
Swelling	7 (8.6)	62 (76.5)	11 (13.6)	1 (1.2)
Itching	12 (48.0)	12 (48.0)	1 (4.0)	0
Lumps/Bumps	8 (16.7)	30 (62.5)	7 (14.6)	3 (6.3)

Note: N = Number of subjects in Safety Population, n = Number of subjects in specific category. Percentages calculated as 100 x (n/number of subjects who reported 'Mild' or higher for the respective symptom in their subject diary).

Table 7 Adverse Event Overview

Subjects with at least 1:	**Control Group (N=52) n (%)**	**Treatment Group (N=97) n (%)**
Adverse event	3 (5.8)	43 (44.3)
Serious adverse event	0	3 (3.1)
Adverse event leading to study discontinuation	0	1 (1.0)
Adverse event related to study product or injection procedure	0	20 (20.6)
Adverse event unrelated to study product or injection procedure	3 (5.8)	30 (30.9)
Serious adverse event unrelated to study product or injection procedure	0	3 (3.1)
Adverse event of special interest	0	1 (1.0)
Adverse event with late onset (>21 days after most recent treatment) related to study product or injection procedure	0	1 (1.0)
No adverse event	49 (94.2)	54 (55.7)

Note: N = number of subjects, n = number of subjects in specific category. Percentages calculated as 100 × (n/N). Subjects reporting more than 1 event in a category were counted only once in that category (n); multiple events in a similar category were instead counted for each occurrence.

Table 8 Related Adverse Events by preferred term (Safety population)

Preferred Term	Treatment Group (N=97) n (%)
Subjects with at least 1 related adverse event	20 (20.6)
Injection site bruising	11 (11.3)
Dizziness	2 (2.1)
Headache	2 (2.1)
Abnormal sensation in eye	1 (1.0)
Injection site erythema	1 (1.0)
Injection site irritation	1 (1.0)
Injection site nodule	1 (1.0)
Injection site pain	1 (1.0)
Injection site discolouration	1 (1.0)
Injection site swelling	1 (1.0)
Skin mass (small lump)[a]	1 (1.0)

a One subject experienced 2 events of skin mass on Day 49, 9 days after the most recent injection; reported terms were small lump on lower left cheek, near corner of mouth and small lump below left corner of mouth. The AE was considered mild in intensity, related to study product and injection procedure. These were considered chronic and stable (not resolved) at the end of study participation but did resolve without medical intervention after the subject exited the study per report from the Investigator.

Note: N = number of subjects in safety population, n = number of subjects in specific category. Percentages calculated as 100 × (n/N). Subjects reporting more than 1 event in a category were counted only once in that category (n). Events were coded by Medical Dictionary for Regulatory Activities version 23.1.

Table 9 Related Adverse Events by Duration

System Organ Class Preferred Term	Treatment Group (N=97)
Abnormal sensation in eye	1
Mean (SD)	3.0 (-)
Median	3.0
Min, Max	3, 3
Injection site bruising	11
Mean (SD)	11.4 (5.77)
Median	9.0
Min, Max	6, 22
Injection site discolouration	1
Mean (SD)	4.0 (-)
Median	4.0
Min, Max	4, 4
Injection site erythema	1
Mean (SD)	13.0 (-)

System Organ Class Preferred Term	Treatment Group (N=97)
Median	13.0
Min, Max	13, 13
Injection site irritation	1
Median	3.0
Min, Max	3, 3
Injection site nodule	1
Mean (SD)	1.0 (-)
Min, Max	1, 1
Injection site pain	1
Mean (SD)	1.0 (-)
Median	1.0
Injection site swelling	1
Mean (SD)	11.0 (-)
Median	11.0
Min, Max	11, 11
Dizziness	2
Mean (SD)	1.0 (0.00)
Median	1.0
Min, Max	1, 1
Mean (SD)	1.0 (0.00)
Median	1.0
Min, Max	1, 1
Skin mass	1
Median	279.0
Min, Max	279, 279

Events are coded by MedDRA version 23.1.
Note: For 3 related events (2 subjects) ongoing at end of study, stop date is censored at the later of last vi sit date or end of study date. Duration is derived as: stop date minus start date + 1.
Subjects reporting more than one event in a category are counted only once in that category at longest dur ation.

Extension study (12-24 months)

During the extension study, a total of 9 (23.1%) subjects in Group A experienced an AE considered related to study product or injection procedure. No subject in Group A experienced an AE with late onset (>21 days after the most recent treatment), an AESI, or an AE leading to study discontinuation.

During the extension study, no new related AEs were reported in Group B. One subject (1.4%) experienced an AE with late onset (>21 days after the most recent treatment)

related to study product or injection procedure in the base study was which ongoing when enrolled in the extension study. The subject withdrew prior to the AE resolving. No subject in Group B experienced an AESI or an AE leading to study discontinuation.

No subjects in the extension study experienced an SAE considered related to study product or procedure.

A summary of related AEs is presented in Table 10.

TABLE 10 RELATED ADVERSE EVENTS BY PREFERRED TERM (EXTENSION POPULATION)

Preferred Term	Group A (N=39) n (%)	Group B (N=72) n (%)
Subjects with at least 1 related adverse event	9 (23.1)	1 (1.4)
Injection site bruising	5 (12.8)	0
Injection site pain	2 (5.1)	0
Injection site pruritus	1 (2.6)	0
Injection site swelling	1 (2.6)	0
Injection site nodule	0	1 (1.4)
Sinusitis	1 (2.6)	0

Source: CSR, Table 14.3.2.1

Note: N = number of subjects in extension population, n = number of subjects in specific category. Percentages calculated as 100 × (n/N). Subjects reporting more than 1 event in a category were counted only once in that category (n). Events were coded by Medical Dictionary for Regulatory Activities version 23.1. Group A subjects were untreated in the Base study but received *Sculptra Aesthetic* in the Extension study; Group B subjects received *Sculptra Aesthetic* in the Base study but were untreated in this extension study.

Subject diaries captured self-assessed, pre-defined, expected, post-treatment symptoms. The most common symptoms for Group A were tenderness, swelling, bruising, pain (including burning), and redness. Almost all symptoms were mild or moderate in intensity (94.9%).

TABLE 11
SUMMARY OF SUBJECT DIARY SYMPTOMS, OVERALL (GROUP A)
(EXTENSION POPULATION)

Characteristic	Group A (N=39) n (%)
Number of subjects with diaries at visit	
Overall, Any Symptom	39 (100)
Pain (including burning)	32 (82.1)
Tenderness	37 (94.9)
Redness	32 (82.1)
Bruising	36 (92.3)
Swelling	37 (94.9)
Itching	15 (38.5)
Lumps/bumps	26 (66.7)

Source: CSR,Table 14.3.8.1
Note: N = number of subjects in extension population; n = number of subjects in specific category. Percentages calculated as 100 × (n/number of subjects with response indicating symptom or none at applicable treatment session). Subjects reporting multiple events of the same symptom were counted only once for that event within the most severe category. Group A subjects were untreated in the Base study but received *Sculptra Aesthetic* in the Extension study.

Snellen visual acuity assessment had no subjects in Group A with a change from any treatment visit pre-injection to any treatment visit (post-injection). Only 1 subject (2.6%) in Group A had a visual acuity line change at any follow-up visit. The one subject had ≥2 visual acuity line change at Month 13 (pre-injection), but was normal at the post-injection visit at Month 13 and throughout the rest of the study.

2. Effectiveness Results

Base study (0 to 48 weeks): The analysis of effectiveness was based on the ITT population of 149 subjects with data available up to the Month 12 evaluation. Three (2.0%) subjects (2 [2.1%] subjects in the treatment group and 1 [1.9%] subject in the control group) experienced protocol deviations that resulted in their exclusion from the PP population. Both subjects in the treatment group experienced an out-of-window visit and the 1 subject in the control group received a prohibited medication or procedure. The primary effectiveness endpoint was the responder rate based on the GCWS At Rest, as assessed live by the Blinded Evaluator, at Month 12. A responder was defined as a subject with at least a 1-grade improvement from baseline in both cheeks concurrently. As shown in Table 12, there was a statistically significantly higher responder rate based on the GCWS At Rest (Blinded Evaluator) at Month 12 for the treatment group compared

with the control group (70.7% versus 25.9%, respectively; p<.0001). Similar results were observed for the PP population using observed cases analysis.

Table 12 Responder Rate Based on the GCWS At Rest (Blinded Evaluator) at Month 12 (Multiple Imputation Analysis - Intent to Treat Population)

Statistic	Control Group	Treatment Group
Observed cases responder rate, n/N (%)[a]	12/46 (26.1)	63/88 (71.6)
Estimated responder rate[b]	25.9	70.7
95% confidence interval[c]	13.4, 38.3	61.1, 80.4
P-value[d]		
Mean[e]		<.0001
Maximum[e]		<.0001
Difference 95% confidence interval[c,f]		29.4, 60.3

GCWS = Galderma Cheek Wrinkles Scale

a Defined as at least a 1-grade improvement from baseline on both sides of the face concurrently.

b Estimated with 10 imputation datasets and full conditionals, which included the assigned treatment, side of face, and all GCWS up to Month 12 (inclusive).

c Confidence interval calculated using multiple imputation methods.

d Two-sided p-value as calculated via Fisher's exact test.

e Across 10 imputation data sets.

f Difference confidence interval calculated using normal approximation.

Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit. Ten datasets were multiply imputed; only subjects with a baseline score were included. One subject (control group) who did not have a baseline value was excluded from analysis. Fourteen subjects (5 control group, 9 treatment group) had Month 12 scores imputed.

Primary Endpoint: The primary effectiveness endpoint was the responder rate based on the GCWS At Rest, as assessed live by the Blinded Evaluator, at Month 12. A responder was defined as a subject with at least a 1-grade improvement from baseline in both cheeks concurrently. As shown in Table 12, there was a statistically significantly higher responder rate based on the GCWS At Rest (Blinded Evaluator) at Month 12 for the treatment group compared with the control group (70.7% versus 25.9%, respectively; p<.0001). Similar results were observed for the PP population using observed cases analysis.

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Females reported a responder rate of 72.9% (62/85) compared to males that reported 33.3% (1/3). Due to the small number of male subjects, conclusions cannot be drawn.

Secondary Effectiveness Analyses

The following secondary endpoints were evaluated to assess secondary effectiveness.

Blinded Evaluator Responder Rate, Over Time

Responder rates, defined as a subject with at least a 1-grade improvement from baseline in both cheeks concurrently, over time based on Blinded Evaluator assessment, displayed in Table 13, demonstrate there was a statistically significantly higher responder rate for the treatment group compared with the control group based on the GCWS At Rest (Blinded Evaluator) also at Months 7 (66.2% versus 38.6%, respectively; p = 0.0043) and 9 (70.6% versus 31.1%, respectively; p<.0001).

Table 13 Responder Rate based on GCWS At Rest (Blinded Evaluator) by visit (Observed cases analysis - ITT population)

Statistic	Control Group	Treatment Group
Month 7 responder rate, n/N (%)[a]	17/44 (38.6)	51/77 (66.2)
95% confidence interval[b]	24.4, 54.5	54.6, 76.6
P-value[c]		0.0043
Difference 95% confidence interval[d]		9.7, 45.4
Month 9 responder rate, n/N (%)[a]	14/45 (31.1)	60/85 (70.6)
95% confidence interval[b]	18.2, 46.6	59.7, 80.0
P-value[c]		<.0001
Difference 95% confidence interval[d]		22.8, 56.1
Month 12 responder rate, n/N (%)[a]	12/46 (26.1)	63/88 (71.6)
95% confidence interval[b]	14.3, 41.1	61.0, 80.7
P-value[c]		<.0001
Difference 95% confidence interval[d]		29.7, 61.3

GCWS = Galderma Cheek Wrinkles Scale

a Defined as at least a 1-grade improvement from baseline on both sides of the face concurrently.

b Confidence interval calculated using Clopper-Pearson method (based on binomial distribution).

c Two-sided p-value as calculated via Fisher's exact test.

d Difference confidence interval calculated using normal approximation.

Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit.

GCWS Dynamic. As displayed in Table 14, there was a statistically significantly higher responder rate for the treatment group compared with the control group based on the GCWS Dynamic (Blinded Evaluator) at Months 7 (67.5% versus 27.3%, respectively; p<.0001), 9 (64.7% versus 22.2%, respectively; p<.0001), and 12 (70.5% versus 28.3%, respectively; p<.0001).

Table 14 Responder Rate based on the GCWS Dynamic (Blinded Evaluator) by visit (Observed cases analysis - ITT population)

Statistic	Control Group	Treatment Group
Month 7 responder rate, n/N (%)[a]	12/44 (27.3)	52/77 (67.5)
95% confidence interval[b]	15.0, 42.8	55.9, 77.8
P-value[c]		<.0001
Difference 95% confidence interval[d]		23.5, 57.1
Month 9 responder rate, n/N (%)[a]	10/45 (22.2)	55/85 (64.7)
95% confidence interval[b]	11.2, 37.1	53.6, 74.8
P-value[c]		<.0001
Difference 95% confidence interval[d]		26.6, 58.3
Month 12 responder rate, n/N (%)[a]	13/46 (28.3)	62/88 (70.5)
95% confidence interval[b]	16.0, 43.5	59.8, 79.7
P-value[c]		<.0001
Difference 95% confidence interval[d]		26.1, 58.3

a Defined as at least a 1-grade improvement from baseline on both sides of the face concurrently.
b Confidence interval calculated using Clopper-Pearson method (based on binomial distribution).
c Two-sided p-value as calculated via Fisher's exact test.
d Difference confidence interval calculated using normal approximation.
Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit.

Independent Photographic Review

Improvement rate based on the Independent Photographic Reviewer's (IPR) assessment using random pairings of 2D-photographs from baseline and Month 12 were conducted at study completion. An improved subject was defined as a subject for whom the IPR correctly identified the Month 12 photograph in the pair of pre- and post-treatment photographs at rest[1]. The responder rate was 37% in the treatment group and 16% in the no treatment group. The IPR responder rates are expected to be lower due to the challenges and limitations of evaluating changes in wrinkle severity on 2D-photography.

Subject and Treating Investigator Global Aesthetic Improvement Scale (GAIS)

As shown in Table 15, the percentage of responders (as assessed by the GAIS - Treating Investigator) ranged from 68.1% to 96.3% across Month 1 through Month 12 for the treatment group and from 4.3% to 6.8% across Month 7 through Month 12 for the control group. Excluding Month 1, CIs were >80% for the treatment group from Month 2 through Month 12.

[1] Note: The definition of responder for the control group was changed to match the same definition for the treatment group.

Table 15 GAIS Improvement Rates by Treating Investigator by visit (ITT population)

Time Point	Control Group	Treatment Group
Month 1 responder: any improvement, n/N (%)[a]		64/94 (68.1)
95% confidence interval[b]		57.7, 77.3
Month 2 responder: any improvement, n/N (%)[a]		78/87 (89.7)
95% confidence interval[b]		81.3, 95.2
Month 3 responder: any improvement, n/N (%)[a]		78/81 (96.3)
95% confidence interval[b]		89.6, 99.2
Month 7 responder: any improvement, n/N (%)[a]	3/44 (6.8)	74/77 (96.1)
95% confidence interval[b]	1.4, 18.7	89.0, 99.2
Month 9 responder: any improvement, n/N (%)[a]	2/45 (4.4)	79/85 (92.9)
95% confidence interval[b]	0.5, 15.2	85.3, 97.4
Month 12 responder: any improvement, n/N (%)[a]	2/46 (4.3)	83/88 (94.3)
95% confidence interval[b]	0.5, 14.8	87.2, 98.1

a A responder was defined as a subject that had "very much improved", "much improved", or "improved" on both sides of the face.

b Confidence interval calculated using Clopper-Pearson method (based on binomial distribution). Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit. Global Aesthetic Improvement Scale was first assessed in the control group at Month 7.

Aesthetic improvement compared to baseline, as evaluated by subject assessment (GAIS), is also summarized in Table 16. The percentage of responders ranged from 57.4% to 93.5% across Month 1 through Month 12 for the treatment group and from 6.5% to 7.0% across Month 7 to Month 12 for the control group. Excluding Months 1 and 2, CIs were >80% for the treatment group from Month 3 through Month 12.

Table 16 GAIS Improvement Rates by Subject by visit (ITT population)

Time Point	Control Group	Treatment Group
Month 1 responder: any improvement, n/N (%)[a]		54/94 (57.4)
95% confidence interval[b]		46.8, 67.6
Month 2 responder: any improvement, n/N (%)[a]		69/87 (79.3)
95% confidence interval[b]		69.3, 87.3
Month 3 responder: any improvement, n/N (%)[a]		72/81 (88.9)
95% confidence interval[b]		80.0, 94.8
Month 7 responder: any improvement, n/N (%)[a]	3/43 (7.0)	72/77 (93.5)
95% confidence interval[b]	1.5, 19.1	85.5, 97.9
Month 9 responder: any improvement, n/N (%)[a]	3/44 (6.8)	76/85 (89.4)
95% confidence interval[b]	1.4, 18.7	80.9, 95.0
Month 12 responder: any improvement, n/N (%)[a]	3/46 (6.5)	81/88 (92.0)
95% confidence interval[b]	1.4, 17.9	84.3, 96.7

a A responder was defined as a subject that had "very much improved", "much improved", or "improved" on both sides of the face.

b Confidence interval calculated using Clopper-Pearson method (based on binomial distribution). Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit. Global Aesthetic Improvement Scale was first assessed in the control group at Month 7.

FACE-Q™

The FACE-Q™ scores were used to assess treatment outcome from the subject's perspective. FACE-Q change from baseline scores indicate subjects were more satisfied with the appearance of their cheeks following treatment. A summary of the change from baseline in Satisfaction with Cheeks FACE Q™ Questionnaire Rasch-transformed scores over time is presented in Table 17. The mean score at baseline (prior to treatment) was 35.2 and 33.9 for the treatment and control groups, respectively. Based on the Rasch transformed scores, subjects were more satisfied with how their cheeks looked following treatment at all post-baseline visits from Month 1 through Month 12 (mean increase from baseline range: 21.3 to 40.0), whereas subjects in the control group were not more satisfied with how their cheeks looked at all post-baseline visits from Month 7 through Month 12 (mean decrease from baseline range: -3.6 to -4.1).

Table 17 Satisfaction with cheeks FACE-Q™ questionnaire: Rasch-transformed scores in subject satisfaction over time (ITT Population)

		Control Group (N=52)		Treatment Group (N=97)	
Visit	Statistic	Score	Change from Baseline	Score	Change from Baseline
Baseline	n	50		97	
	Mean (standard deviation)	33.9 (13.62)	--	35.2 (19.16)	--
	Median	35.0	--	35.0	--
	Minimum, maximum	0, 63	--	0, 100	--
Month 1	n			94	94
	Mean (standard deviation)	--	--	56.3 (23.73)	21.3 (24.25)
	Median	--	--	63.0	20.0
	Minimum, maximum	--	--	0, 100	-35, 80
	95% confidence interval	--	--	--	16.4, 26.3
Month 2	n			87	87
	Mean (standard deviation)	--	--	65.9 (25.50)	31.6 (28.45)
	Median	--	--	63.0	35.0
	Minimum, maximum	--	--	0, 100	-44, 87
	95% confidence interval	--	--	--	25.6, 37.7
Month 3	n			81	81
	Mean (standard deviation)	--	--	73.3 (22.41)	38.6 (26.51)
	Median	--	--	77.0	45.0
	Minimum, maximum	--	--	13, 100	-78, 78
	95% confidence interval	--	--	--	32.8, 44.5
Month 7	n	43	42	77	77
	Mean (standard deviation)	30.6 (20.17)	-4.1 (20.34)	74.0 (23.03)	38.6 (26.30)
	Median	35.0	-2.0	70.0	38.0
	Minimum, maximum	0, 63	-40, 50	0, 100	-40, 87
	95% confidence interval	--	-10.5, 2.2	--	32.7, 44.6
Month 9	n	45	44	85	85
	Mean (standard deviation)	30.2 (19.10)	-3.6 (21.36)	73.4 (23.48)	37.9 (26.63)
	Median	35.0	0.0	77.0	38.0
	Minimum, maximum	0, 63	-40, 40	0, 100	-28, 87
	95% confidence interval	--	-10.1, 2.9	--	32.2, 43.6
Month 12	n	46	45	88	88
	Mean (standard deviation)	30.6 (20.64)	-3.6 (21.76)	75.6 (24.36)	40.0 (29.07)
	Median	35.0	-5.0	77.0	46.0
	Minimum, maximum	0, 91	-40, 47	0, 100	-44, 87
	95% confidence interval	--	-10.1, 3.0	--	33.8, 46.1

Note: N = number of subjects; n = number of subjects in specific category. Confidence interval calculated via t-distribution.

Subject Satisfaction Questionnaire

A summary of subject satisfaction questionnaire results over time is provided below.

Across Month 7 to Month 12, the percentages of subjects in the treatment group who responded with "very good" or "excellent" for the following questions were as follows:

- Made them look younger (48.1% to 52.9%)
- Made them feel better about themselves (49.4% to 54.1%)
- Improved their self-confidence (46.6% to 50.6%)
- Improved overall satisfaction with their appearance (46.6% to 55.3%)
- Made them look/feel more confident in their life (45.5% to 50.6%)
- Made them look the way they felt (44.3% to 50.6%)
- Improved their skin firmness (52.3% to 60.0%)
- Improved their skin radiance (51.1% to 57.6%)
- Improved their skin sagging (40.9% to 49.4%)
- Made their skin look more refreshed (50.0% to 57.6%)

Across Month 7 to Month 12, the majority of subjects in the treatment group responded as "agree" or "strongly agree" that:

- The treatment results were natural looking (85.9% to 93.5%)
- The subtle treatment results over time were worth it (80.0% to 81.8%)

Across Month 7 to Month 12, the majority of subjects in the treatment group would recommend the treatment to a friend (range: 88.6% to 89.6%).

Across Month 7 to Month 12, the majority of subjects in the treatment group would choose to receive the treatment again (range: 84.4% to 89.4%).

Time to Return to Social Engagement

Based on subject diaries, the median time to feeling comfortable returning to social engagement across the 4 treatment sessions ranged from 3.9 hours (treatment 1) to 7.1 hours (treatment 4). Overall, across all treatment sessions, 90% of subjects felt comfortable returning to social engagement by 7.1 hours post-treatment. The remaining 10% did not complete the return to social engagement assessment. There were no subjects with missing or incomplete data from the subject diary that reported related adverse events associated with social circumstances or social avoidant behavior.

3. Subgroup Analyses

The primary effectiveness analysis was repeated in subgroups defined by age group (<55 years, ≥55 years) and FST group (I-III, IV-VI). The responder rate was higher for subjects <55 years of age 88.9%) compared with subjects ≥55 years of age (67.1%) in the treatment group; however, the responder rate was higher in the treatment group compared with the control group for both younger (<55 years of age) and older (≥55 years of age) subjects. The responder rate was higher for subjects with FST IV-VI (87.5%) compared with subjects with FST I-III (68.1%) in the treatment group; however, the responder rate was higher in the treatment group compared with the control group for both subjects with FST I-III and subjects with FST IV-VI. Regardless of age group or FST group, the responder rate was higher in the treatment group versus the control group for all subgroups.

Extension study (12 to 24 months):
GCWS data showed that the effects of Sculptra treatments were maintained through 24 months as displayed in Table 18 below.

TABLE 18
RESPONDER RATE BASED ON THE GCWS AT REST (BLINDED EVALUATOR) BY VISIT (OBSERVED CASES ANALYSIS - EXTENSION POPULATION)

Statistic	Group B
Month 19 responder rate, n/N (%)[1]	56/66 (84.8)
95% confidence interval[2]	73.9, 92.5
Month 21 responder rate, n/N (%)[1]	50/65 (76.9)
95% confidence interval[2]	64.8, 86.5
Month 24 responder rate, n/N (%)[1]	50/65 (76.9)
95% confidence interval[2]	64.8, 86.5

Source: CSR, Table 14.2.1.1
GCWS = Galderma Cheek Wrinkles Scale
1 Defined as at least a 1-grade improvement from pre-treatment on both sides of the face concurrently.
2 Confidence interval calculated using Clopper-Pearson method (based on binomial distribution).
Note: N = Number of subjects, n = Number of subjects in specific category. Percentages calculated as 100 x (n/N) out of the number of subjects at each visit. Group B subjects received *Sculptra Aesthetic* in Study 43USSA1812 but were untreated in this extension study.

The percentage of responders (as assessed by the GAIS - Treating Investigator), ranged from 93.8% to 97.0% across Month 19 (first assessment time point) through Month 24 for Group B, with CIs >80% for Group B from Month 19 through Month 24. The percentage

of responders (as assessed by the GAIS – subject assessment), ranged from 86.2% to 93.8% across Month 19 through Month 24 for Group B, with CIs >80% for Group B at Month 21. In general, subjects remained satisfied with the treatment throughout this extension study. The treated control subjects reported similar improvements in GAIS. The results are displayed in Table 19.

TABLE 19
GLOBAL AESTHETIC IMPROVEMENT SCALE IMPROVEMENT RATES BY TREATING INVESTIGATOR AND BY SUBJECT BY VISIT (EXTENSION POPULATION)

	By treating investigator	By subject
Time Point	**Group B**	**Group B**
Month 19 responder: any improvement, n/N (%)[1]	64/66 (97.0)	58/67 (86.6)
95% confidence interval[2]	89.5, 99.6	76.0, 93.7
Month 21 responder: any improvement, n/N (%)[1]	63/65 (96.9)	61/65 (93.8)
95% confidence interval[2]	89.3, 99.6	85.0, 98.3
Month 24 responder: any improvement, n/N (%)[1]	61/65 (93.8)	56/65 (86.2)
95% confidence interval[2]	85.0, 98.3	75.3, 93.5

Source: CSR; Table 14.2.4.1, Table 14.2.4.2

1. A responder was defined as a subject that had "very much improved," "much improved," or "improved" on both sides of the face.
2. Confidence interval calculated using Clopper-Pearson method (based on binomial distribution).

Note: N = number of subjects; n = number of subjects in specific category. Percentages calculated as 100 × (n/N) out of the number of subjects at each visit. Global Aesthetic Improvement Scale was first assessed in Group B at Month 19. Group A subjects were untreated in Study 43USSA1812 but received *Sculptra Aesthetic* in this extension study; Group B subjects received *Sculptra Aesthetic* in Study 43USSA1812 but were untreated in this extension study.

4. Pediatric Extrapolation

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

D. 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.

Clinical study 43USSA1812 included thirteen investigators; with two having disclosable financial interests/arrangements and one blinded evaluator as defined in section 54.2(f) as described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: [0 investigators]

- Significant payment of other sorts: [3 investigators]
- Proprietary interest in the product tested held by the investigator: [0 investigators]
- Significant equity interest held by investigator in sponsor of covered study: [0 investigators]

Therefore, approximately 77% of sites (10 out of 13) did not report financial interests. Of the investigator sites that disclosed financial interests, they did not enroll the majority of subjects (34/149). Enrollment for each of the study sites ranged from 4-13%, therefore no study site had a majority of the subject population which minimizes the potential effect that a single site could have on the study results. To further mitigate any potential bias, the primary effectiveness endpoint was measured by a blinded independent evaluator in which treatment of the subject was concealed.

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data

DI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

***Sculptra* Post-Marketing Safety Data**

There has been no significant change in AE and SAE reporting frequencies for spontaneously reported adverse events. As such, the safety profile of the product and benefit/risk ratio is judged to remain unchanged.

DII. 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 Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

DIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Assessment of product effectiveness is based on the results of Pivotal Study NCT 04124692 submitted to PMA P030050 and presented in the *Sculptra* Instructions for Use. Conclusions drawn from clinical study 43USSA1812 and the extension provide a

reasonable assurance that the device is effective when used for the correction of lines and wrinkles in the cheek region in subjects over the age of 21.

Conclusions from the Base study (0 to 12 months) and Extension Study (12 to 24 months) are:

- *Sculptra*, reconstituted in 8 mL SWFI + 1 mL of lidocaine HCl, was effective in the correction of cheek wrinkles, based on assessment of aesthetic improvement and satisfaction by subjects and Investigators.

- *Sculptra*, reconstituted with 8 mL SWFI + 1 mL lidocaine HCl, demonstrated a statistically significantly higher responder rate based on the GCWS At Rest (Blinded Evaluator) at Month 12 compared with the control group (70.7% versus 25.9%, respectively; p<.0001).

- A statistically significantly higher responder rate for the treatment group compared with the control group based on the GCWS At Rest (Blinded Evaluator) was observed at Months 7 (66.2% versus 38.6%, respectively; p = 0.0043) and 9 (70.6% versus 31.1%, respectively; p<.0001).

- Response rates based on the GCWS At Rest (Blinded Evaluator) for Extension study Group B subjects were 84.8% at Month 19, 76.9% at Month 21, and 76.9% at Month 24 demonstrating effectiveness up to Month 24.

- A statistically significantly higher responder rate for the treatment group compared with the control group based on the GCWS Dynamic (Blinded Evaluator) was observed at Months 7 (67.5% versus 27.3%, respectively; p<.0001), 9 (64.7% versus 22.2%, respectively; p<.0001), and 12 (70.5% versus 28.3%, respectively; p<.0001).

- The Month 12 improvement rates based on independent photographic review for the left and right cheeks were 53.6% (45/84 subjects; 95% CI: 42.4, 64.5) and 57.1% (48/84 subjects; 95% CI: 45.9, 67.9), respectively, for the treatment group and 29.5% (13/44 subjects; 95% CI: 16.8, 45.2) and 34.1% (15/44 subjects; 95% CI: 20.5, 49.9) for the control group.

- The percentage of responders (as assessed by the GAIS - Treating Investigator) ranged from 68.1% to 96.3% across Month 1 through Month 12 for the treatment group and from 4.3% to 6.8% across Month 7 through Month 12 for the control group. Excluding Month 1, CIs were >80% for the treatment group from Month 2 through Month 12.

- The percentage of responders (as assessed by the GAIS - Treating Investigator) ranged from 93.8% to 97.0% across Month 19 (first assessment time point) through

Month 24 for Group B, with CIs >80% for Extension study Group B from Month 19 through Month 24.

- The percentage of responders (as assessed by the GAIS – subject assessment) ranged from 57.4% to 93.5% across Month 1 through Month 12 for the treatment group and from 6.5% to 7.0% across Month 7 to Month 12 for the control group. Excluding Months 1 and 2, CIs were >80% for the treatment group from Month 3 through Month 12.

- The percentage of responders (as assessed by the GAIS – subject assessment) ranged from 86.2% to 93.8% across Month 19 through Month 24 for Extension study Group B, with CIs >80% for Group B at Month 21.

- Across Month 7 to Month 12, subject satisfaction questionnaire results showed that the majority of subjects in the treatment group would choose to receive the treatment again (range: 84.4% to 89.4%).

- Based on the Satisfaction with Cheeks FACE Q™ Questionnaire Rasch-transformed scores, subjects were more satisfied with how their cheeks looked following treatment at all post-baseline visits from Month 1 through Month 12 (mean increase from baseline range: 21.3 to 40.0), whereas subjects in the control group were not more satisfied with how their cheeks looked at all post-baseline visits from Month 7 through Month 12 (mean decrease from baseline range: -3.6 to -4.1).

- Based on subject diaries, the median time to feeling comfortable returning to social engagement across the 4 treatment sessions ranged from 3.9 hours (treatment 1) to 7.1 hours (treatment 4).

B. Safety Conclusions

Assessment of product safety is based on the results of the Pivotal Study NCT04124692 submitted to PMA P030050 and supplements as presented in the *Sculptra* Instructions for Use. The safety of using *Sculptra* for correction of fine lines and wrinkles in the cheek region has been evaluated in clinical studies 43USSA1812 and the extension.

Conclusions from the Base study (0 to 12 months) are:

- *Sculptra*, reconstituted with 8 mL SWFI + 1 mL lidocaine HCl, was generally safe and well tolerated.
- A total of 43 (44.3%) subjects in the treatment group and 3 (5.8%) subjects in the control group experienced at least 1 AE during the study. The only AE

experienced by >5.0% of subjects in the treatment group was injection site bruising (11.3%).

- Twenty (20.6%) subjects in the treatment group experienced an AE considered related to study product or injection procedure. The most common (>1.0% of subjects) related AEs were injection site bruising (11 [11.3%] subjects), dizziness (2 [2.1%] subjects), and headache (2 [2.1%]) subjects.
- All AEs related to study product or injection procedure were mild or moderate in intensity. Three (3.1%) subjects experienced related AEs of moderate intensity (1 subject experienced 2 events of moderate injection site pain, 1 subject experienced moderate dizziness, and 1 subject experienced moderate injection site bruising); all events resolved by the end of the study.
- One subject experienced 2 treatment-emergent AEs of injection site nodule (1 on the left cheek and 1 on the right cheek) and 1 subject experienced a treatment-emergent AE of skin mass (small lump on lower left cheek, near corner of mouth). Each event was considered mild in intensity, related to study product and/or injection procedure, and no action was required.
- Three (3.1%) subjects in the treatment group experienced treatment-emergent SAEs (1 subject experienced osteoarthritis, 1 subject experienced back pain, and 1 subject experienced obstruction gastric and small intestine adenocarcinoma [this event also led to premature study discontinuation]); all SAEs were considered unrelated to study product or injection procedure. No subject died during the study.

Conclusions from the Extension Study (12 to 24 months) are:

Sculptra, reconstituted with 8 mL SWFI + 1 mL lidocaine HCl, was generally safe and well tolerated up through 24 months.

- A total of 9 (23.1%) subjects in Group A experienced an AE considered related to study product or injection procedure. No subject in Group A experienced an AE with late onset (>21 days after the most recent treatment), an AESI, or an AE leading to study discontinuation.
- A total of 15 (20.8%) subjects in Group B experienced at least 1 AE. One subject (1.4%) experienced an AE with late onset (>21 days after the most recent treatment) related to study product or injection procedure in the Base study and was ongoing when enrolled in the extension study. The subject withdrew prior to the AE resolving.
- No subject in Group B experienced an AESI or an AE leading to study discontinuation.
- No subjects in the extension study experienced an SAE considered related to study product or procedure.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the clinical studies conducted to support PMA approval as described above. The primary potential benefit of the device is a perceived improvement in the visual appearance of fine lines and wrinkles in the cheek region, as assessed by the blinded Evaluator using GCWS At Rest and Dynamic, improved global aesthetic appearance according to investigator and subject GAIS assessments, and subject satisfaction with treatment per the FACE-Q questionnaire and subject satisfaction questionnaire.

The probable risks of the device are also based on data collected in the clinical studies conducted to support PMA approval as described above. The risks associated with correction of fine lines and wrinkles in the cheek region using *Sculptra* primarily include injection site reactions (e.g., pain, tenderness, redness, bruising, swelling, itching, lumps/bumps). Most of the pre-defined, expected post-treatment events were tolerable in severity, and resolved within 14 days.

1. Patient Perspective
   Patient perspectives considered during the review included:
   - At 12 months, 92.0% (81/88) of the treatment group subjects reported improvement in the overall aesthetic appearance of the fine lines and cheek wrinkles on the GAIS. Most treatment group subjects continued to report improvement on the GAIS at 24 months (86.2% (56/65)).
   - Based on the Satisfaction with Cheeks module of the FACE-Q ™ Questionnaire Rasch-transformed scores, subjects were more satisfied with how their cheeks looked following treatment at all post-baseline visits from Month 1 through Month 24 (mean increase from baseline range: 21.3 to 40.0)
   - Subjects reported the median time to feeling comfortable returning to social engagement across the 4 treatment sessions as 3.9 hours (Treatment 1) to 7.1 hours (Treatment 4).

In conclusion, given the available information above, the data support that for correction of fine lines and wrinkles in the cheek region 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.

DIV. CDRH DECISION

CDRH issued an approval order on April 18, 2023.

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

DV. 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.