SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Injectable Dermal Filler

Device Trade Name: JUVÉDERM® VOLUMA® XC

Device Procode: LMH

Applicant's Name and Address: Allergan Aesthetics, an AbbVie Company
2525 Dupont Drive
Irvine, CA 92612

Date of Panel Recommendation: June 10,2023

Premarket Approval Application (PMA) Number: P110033/S070

Date of FDA Notice of Approval: 10/06/2023

The original JUVÉDERM® VOLUMA® XC (PMA #P110033) was approved on October 22, 2013, and is indicated for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face in adults over the age of 21. JUVÉDERM® VOLUMA® XC was also approved on June 12, 2020, for an indication expansion for the deep (subcutaneous and/or supraperiosteal) injection for augmentation of the chin region to improve the chin profile in adults over the age of 21 (P110033/S047). The SSEDs to support the combined indication for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face and for augmentation of the chin region to improve the chin profile in adults are available on the CDRH website and are incorporated by reference here. The current supplement was submitted to expand the indication for JUVÉDERM® VOLUMA® XC for supraperiosteal injection to augment the temple region to improve moderate to severe temple hollowing in adults over the age of 21.

II. INDICATIONS FOR USE

JUVÉDERM® VOLUMA® XC is indicated for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face and for augmentation of the chin region to improve the chin profile, and for supraperiosteal injection to augment the temple region to improve moderate to severe temple hollowing in adults over the age of 21.

III. CONTRAINDICATIONS

- JUVÉDERM® VOLUMA® XC is contraindicated for patients with severe allergies

manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

- JUVÉDERM® VOLUMA® XC contains trace amounts of Gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- JUVÉDERM® VOLUMA® XC contains lidocaine and is contraindicated for patients with a history of allergies to such material.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the JUVÉDERM® VOLUMA® XC labeling.

V. DEVICE DESCRIPTION

JUVÉDERM® VOLUMA® XC is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel implant. The gel consists of hyaluronic acid (HA) produced by the *Streptococcus* species of bacteria, which is crosslinked with 1,4-butanediol diglycidyl ether (BDDE). It is formulated to a concentration of 20 mg/mL and 0.3% w/w lidocaine in a physiologic buffer. The HA gel is made primarily of crosslinked HA with some remaining lightly crosslinked and uncrosslinked HA. Each box of JUVÉDERM® VOLUMA® XC contains 2 prefilled disposable syringes each containing 1 mL of HA gel implant. Each syringe is fitted with a luer lock adaptor, a plunger rod, a rubber stopper tip cap, and a finger grip. Each syringe is labeled with the name of the product, batch number, and expiration date. JUVÉDERM® VOLUMA® XC is delivered by an injection into the temple region to improve moderate to severe temple hollowing.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative treatments to improve temple hollowing including: fat grafting, surgical implants, and soft tissue fillers such as HA, poly-L-lactic acid, and calcium hydroxylapatite. Each alternative has its own advantages and disadvantages. Patients should fully discuss these alternatives with their physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

JUVÉDERM® VOLUMA® XC received the CE Mark in December 2009 for restoration of facial volume and received FDA approval on October 22, 2013 for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face in adults over the age of 21. JUVÉDERM® VOLUMA® XC also received FDA approval on June 12, 2020 for an expansion of the indication for use to include augmentation of the chin region to improve the chin profile in adults over the age of 21. In addition to being marketed throughout EU and affiliated countries, JUVÉDERM® VOLUMA® XC is 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 under the tradename JUVÉDERM® VOLUMA® XC with Lidocaine.

JUVÉDERM® VOLUMA® XC 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.

Common treatment site responses that can occur with the use of JUVÉDERM® VOLUMA® XC, and other soft tissue fillers include tenderness, firmness (induration), swelling, pain, lumps/bumps (mass), bruising, redness, itching, and discoloration. Other adverse effects reported less frequently (in less than 1% of the study subjects) include injection site inflammation, injection site abscess, injection site cellulitis, gingival pain, and acne cyst.

Post-Market Surveillance

JUVÉDERM® VOLUMA® without lidocaine has been marketed outside the US since 2005, and JUVÉDERM® VOLUMA® XC (also known as JUVÉDERM® VOLUMA® with lidocaine) has been marketed outside the US since 2009 and in the US since 2013.

The following AEs were received from postmarket surveillance for JUVÉDERM® VOLUMA® with and without lidocaine with a frequency of 5 events or more and were not observed in the clinical study (during the 13 months that subjects were monitored in this study); this includes reports received globally from all sources including scientific journals and voluntary reports. All AEs obtained through postmarket surveillance are listed in order of number of reports received: edema, inflammatory reaction, non-inflammatory nodule, pain, loss/lack of correction, inflammatory nodule/granuloma, unsatisfactory result, hematoma, allergic reaction, bruising, infection, skin discoloration, device migration, neurological symptoms such as increase or decrease in sensation, vascular occlusion, abscess, anxiety, dermatitis, varied injuries, headache, vision abnormalities, drainage, flu-like symptoms, blister, overcorrection, scarring, necrosis, bleeding, malaise, cyst, dry skin, acne, dizziness, herpes, autoimmune disorder exacerbation, angioedema, lymphadenopathy, syncope, nausea, dyspnea, extrusion, telangiectasia, depression, vision loss, calcification, anaphylactic reaction, cardiac complications, biofilm, and deeper wrinkle.

Reported treatments include: antibiotics, steroids, antiseptic creams, hyaluronidase, anti-inflammatories, antihistamines, needle aspiration, eye drops, hyperbaric oxygen treatment, laser treatment, ice, massage, warm compress, analgesics, anti-virals, ultrasound therapy, excision, drainage, surgery, immunosuppressants, petroleum jelly, arnica, anticoagulants, anxiolytics, ACE inhibitors and vasodilators.

Vision abnormalities have been reported following injection of JUVÉDERM® VOLUMA®, with and without lidocaine, into the nose, glabella, periorbital area, cheek,

and/or temple, with a time to onset ranging from immediate to 1 week following injection. Reported treatments include anticoagulants, sympathomimetics, steroids, and surgery. Outcomes ranged from resolved to ongoing at the time of last contact. Events requiring medical intervention and events where resolution information is not available were reported after injection of JUVÉDERM® VOLUMA® with and without lidocaine in the highly vascularized areas of the glabella, nose, and periorbital area, which are outside the device indications for use (see Warnings section).

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.

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

IX. SUMMARY OF NONCLINICAL STUDIES

This supplement presented clinical data to support approval of a new indication for the supraperiosteal injection in the temple region to improve moderate to severe temple hollowing in adults over the age of 21. There was no change in product manufacturing or specifications or shelf-life (24 months). Therefore, the data previously presented in support of PMA P110033 are incorporated here by reference.

X. SUMMARY OF PRIMARY CLINICAL STUDY

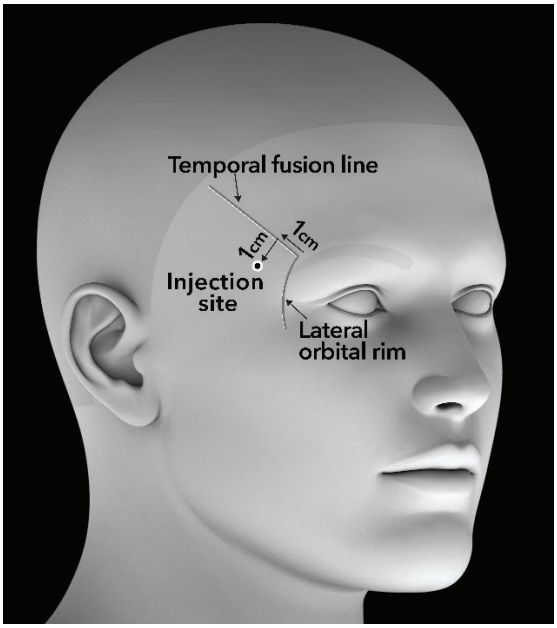
A. STUDY DESIGN

Subjects were treated between May 28, 2020 and October 17, 2022. The database for this PMA reflected data collected through November 16, 2022 and included 205 subjects. There were 15 investigational sites.

A multi-center, evaluator-blinded, randomized, parallel-group, controlled pivotal clinical study was conducted to evaluate the safety and effectiveness of JUVÉDERM® VOLUMA® XC injectable gel to improve temple hollowing. Subjects were randomized to treatment or no-treatment control in a 2:1 ratio. Treatment group subjects underwent treatment with JUVÉDERM® VOLUMA® XC at the outset of the study. The Treating Investigator (TI) determined the appropriate volume of JUVÉDERM® VOLUMA® XC to be injected in the temple area. To determine the injection site, the TI identified the point where the temporal fusion line meets the lateral orbital rim and moved superolaterally approximately 1 cm and then inferolaterally approximately 1 cm (**Figure 1**). The TI inspected and palpated the injection site to identify the location of any superficial vessels, including the superficial temporal artery. The precise injection site was to be slightly adjusted according to the subject's unique anatomy to lower the risk of injecting directly into vessels. The TI inserted the needle at the injection site at an 85- to 90-degree angle to the plane of the temple until it reached the periosteum. The TI injected a single bolus of

JUVÉDERM® VOLUMA® XC into the treatment area slowly using gentle, even pressure on the syringe. After injection, if more than one bolus was needed to achieve optimal results, the needle was repositioned in the injection area by slightly changing the injection angle or moving slightly from the initial injection point. No more than 3 different needle entry points were to be used for a single temple in a single treatment session. The no-treatment control subjects were offered optional treatment at 3 months.

Figure 1: Temple Area Treated



1. Clinical Inclusion and Exclusion Criteria

Enrollment in the 1878-702-008 study was limited to patients who met the following inclusion criteria:

- Age 22 or over and in good general health
- Seeking improvement of temple hollowing
- Had "Minimal", "Moderate," or "Severe" temple hollowing (Grade 2, 3, or 4 on the Allergan Temple Hollowing Scale[1] [ATHS]) for each temple as assessed by the Evaluating Investigator (EI) during live assessment (both temples must have qualified but did not need to have the same score).
- TI considered the subject's temple hollowing to be amenable to temporary improvement
- Ability to follow study instructions (including compliance with the safety e-diary) and likely to complete all required visits

[1] Carruthers J, Jones D, Hardas B, Murphy DK, Donofrio L, Sykes JM, Carruthers A, Creutz L, Marx A, and Dill S. Development and validation of a photonumeric scale for evaluation of volume deficit of the temple. *Dermatol. Surg.* 2016; 42(S1):S203-S210.

- Ability to complete effectiveness self-assessments without the use of glasses (contact lens use is acceptable if they will be used for all subject self-assessments)
- Written informed consent had been obtained

Patients were not permitted to enroll in the 1878-702-008 study if they met any of the following exclusion criteria:

- Could not achieve at least a 1-point improvement for each temple from the EI's baseline score on the ATHS given the allowed injection volume, in the opinion of the TI
- Had temple hollowing due to trauma, congenital malformations, or lipodystrophy, either congenital or acquired (including: congenital myotonic dystrophy, HIV-associated lipodystrophy, or acquired generalized lipodystrophy)
- Had experienced trauma to the temple area within 6 months before enrollment or had residual deficiencies, deformities, or scarring
- Had atrophic skin in the temple area that might not be suitable for injection, in the opinion of the TI
- Had temporal artery that ran across the area to be injected, obscuring the field
- Had temporal arteritis or history of temporal arteritis
- Had temporomandibular joint dysfunction or any other jaw issues
- Had recurrent temporal headaches such as temporal tendinitis migraine
- Had active or recurrent inflammation or infection in either eye
- Had tendency to develop hypertrophic scarring
- Had active autoimmune disease
- Had history of anaphylaxis or allergy to lidocaine (or any amide-based anesthetics), HA products, or Streptococcal protein
- Had current cutaneous or mucosal inflammatory or infectious processes (e.g., acne, herpes), abscess, an unhealed wound, or a cancerous or precancerous lesion, above the subnasale
- Had history of detached retina, retinal vascular occlusion (e.g., vein or arterial occlusion), narrow angle glaucoma, neovascular eye disease (e.g., diabetic retinopathy, age-related wet macular degeneration), or severely impaired/absent eye function in 1 or both eyes
- Had prior facial reconstructive surgeries, facelift, or browlift as well as surgeries on the temple area (e.g., biopsy)
- Had fat injection or permanent facial implants (e.g., polymethylmethacrylate, silicone, polytetrafluoroethylene) anywhere in the face
- Had semipermanent soft-tissue filler treatment (e.g., calcium hydroxyapatite, poly-L-lactic acid) in the temple or mid-face within 36 months before enrollment
- Had temporary dermal filler injections above the subnasale within 24 months before enrollment (Note: injections in the nasolabial fold were acceptable only if done at least 3 months prior to enrollment)
- Had botulinum toxin treatment above the subnasale within 6 months before enrollment

- Had mesotherapy or cosmetic facial procedures (such as face-lift, laser, photomodulation, intense pulsed light, radiofrequency, dermabrasion, moderate or greater depth chemical peel, or other ablative procedures) above the subnasale within 6 months before enrollment
- Had braces or other orthodontics or was planning such treatment during the study
- Had changes in use of over-the-counter or prescription oral or topical, anti-wrinkle products above the subnasale within 30 days before enrollment or planned changes during the study
- Was on a regimen of anti-coagulation therapy (e.g., warfarin, clopidogrel)
- Had received lasik surgery or other surgical intervention on the eye within 3 months prior to enrollment or was planning such a procedure
- Was enrolled in an investigational drug or device study or participation in such a study within 30 days of entry into this study
- Had tattoos, piercings, facial hair, or scars above and including the subnasale that would interfere with visual assessment of the temple
- Females who were pregnant, nursing, or planning a pregnancy
- Had a condition or was in a situation which in the TI's opinion may have put the subject at significant risk, may have confounded the study results, or may have interfered significantly with the subject's participation in the study
- Was an employee (or a relative of an employee) that was directly or indirectly involved in the conduct and administration of this study.
- Had plans for a significant weight change (more than 10% of body weight) during the study

2. Follow-up Schedule

Subjects in the treatment group were given initial study treatment and an optional touch-up treatment 1 month after initial treatment, if deemed necessary to achieve optimal improvement. After each treatment, subjects had safety follow-up visits at Day 3 (telephone call) and at Day 14 and safety and effectiveness follow-up visits at Months 1, 3, 6, 9 (safety telephone call), and 13 after the last treatment. At the Month 13 visit, subjects had the option of receiving repeat treatment, followed by Day 3 (telephone call) and Day 14 safety follow-ups, and visits at Months 1, 3, and 6. Alternatively, subjects exited the study after all Month 13 visit procedures were complete.

No treatment (control) group subjects participated in follow-up visits at 1 and 3 months during the "no treatment" control period. After the completion of the 3-month control period procedures, subjects were offered optional treatment and were followed for 6 months with the same assessments as the treatment group subjects, except that they did not receive treatment satisfaction questions. They also received safety telephone calls at Months 9 and 13.

Pre- and post-procedure, the objective parameters measured during the study included the Evaluating Investigators' (EIs') assessment of subjects' overall improvement of temple hollowing based on live assessment using the validated 5-point photonumeric ATHS. EIs also assessed subjects' improvement on the 5-point Global Aesthetic Improvement Scale (GAIS). In addition, subjects performed self-assessments on the GAIS, the validated FACE-Q *Satisfaction with Facial Appearance* questionnaire, the validated FACE-Q *Satisfaction with Temples* questionnaire, and the natural look and natural feel of the treatment on a 5-point scale. Furthermore, the TI evaluated treatment characteristics, including injection ease and product moldability for initial and touch-up treatments, and subjects assessed their procedural pain.

3. Clinical Endpoints

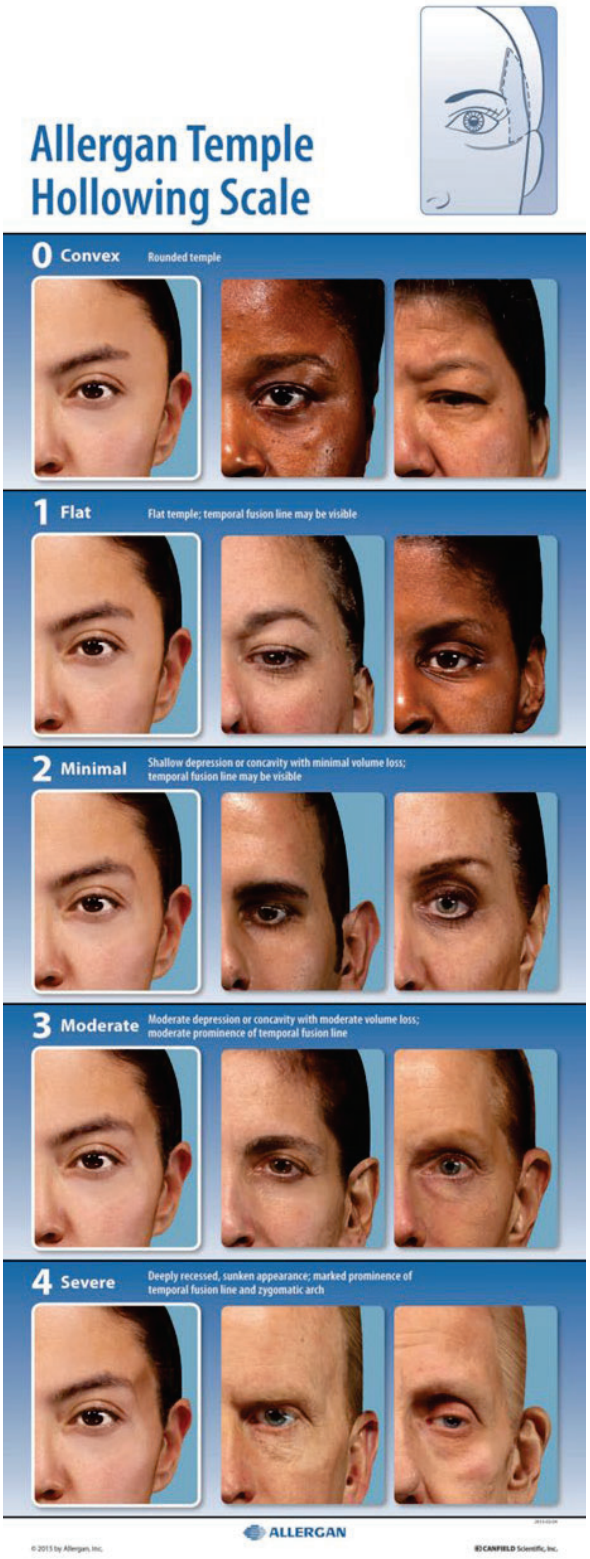
With regards to safety, study subjects used electronic diaries (e-diary) to record specific signs and symptoms of treatment site responses (TSRs) experienced during the first 14 days after the initial, touch-up, and repeat treatments. The initial e-diary was continued to be recorded on even-numbered days from Day 16 through Day 30. Subjects were instructed to rate each TSR listed on the e-diary as "Mild (barely noticeable)," "Moderate (uncomfortable)," "Severe (severe discomfort)," or "None." Adverse events (AEs) were reported by the TI at all follow-up visits where applicable.

With regards to effectiveness, the 3-month primary effectiveness measure was the blinded Evaluating Investigator's (EI) live assessment of temple hollowing using the validated 5-point photonumeric ATHS described in Table 1 and illustrated in **Figure 2**. The ATHS scale was previously validated in a live validation study of 298-subjects to assess the inter- and intra-rater reliability of the ATHS. Eight trained clinicians (raters) independently evaluated subjects in-person and assigned each subject an ATHS grade. Three weeks later, the same clinicians re-evaluated the same subjects (in-person) and assigned each subject an ATHS grade based on the live evaluation and without reliance on prior memory. The mean weighted kappa for the intra-rater agreement between the 2 validation sessions was 0.86. The mean weighted kappa for the inter-rater agreement during the second session was 0.81. Therefore, the results demonstrated that the ATHS is valid for its intended purpose.

Table 1: Allergan Temple Hollowing Scale

Score	Grade	Description
0	Convex	Rounded temple
1	Flat	Flat temple; temporal fusion line may be visible
2	Minimal	Shallow depression or concavity with minimal volume loss; temporal fusion line may be visible
3	Moderate	Moderate depression or concavity with moderate volume loss; moderate prominence of temporal fusion line
4	Severe	Deeply recessed, sunken appearance; marked prominence of temporal fusion line and zygomatic arch

Figure 2: Photonumeric Allergan Temple Hollowing Scale (ATHS)



Secondary effectiveness measures included statistical superiority at Month 3 compared to baseline of the mean overall score on the *Satisfaction with Facial Appearance* and *Satisfaction with Temple* modules of the validated FACE-Q questionnaire (0 to 100, where higher scores reflect a better outcome) as assessed by the subjects, and the level of improvement on the 5-point GAIS scale as assessed by the blinded EIs and the subjects.

Other effectiveness assessments included measurements of temple volume change from 3D images, subject self-perception of age, and subject assessments of satisfaction with the treatment result and natural look and feel, treatment meeting expectations, likelihood of continuing treatment, and assessment of willingness to recommend treatment.

With regards to success/failure criteria, a responder was defined as a subject with ≥ 1-point improvement in the ATHS score from baseline. Effectiveness of JUVÉDERM® VOLUMA® XC was demonstrated if at least 60% of subjects treated with JUVÉDERM® VOLUMA® XC were responders at Month 3, and if the responder rate for the treatment group was statistically superior to that of the no-treatment control group.

B. ACCOUNTABILITY OF PMA COHORT

At the time of database lock, data from all 205 enrolled subjects were available for analysis (Table 2). Of the 205 subjects, 34 were screen failures primarily due to ineligibility, and 171 were randomized per protocol, with 113 in the treatment group and 58 in the control group. Of the 171 randomized subjects, 162 (94.7%; 106 treatment, 56 control) completed the Month 3 primary endpoint visit, and 53 control group subjects (91.4%) opted to receive study treatment after the completion of the 3-month control period. A total of 137 subjects (80.1%; 91 treatment, 46 control) completed the study.

Table 2: Participation Disposition

Disposition	Number of Subjects		
	Treatment	Control	Total
Enrolled	**N/A**	**N/A**	**205**
Screen Failures	**N/A**	**N/A**	**34**
Randomized Subjects	**113**	**58**	**171**
Completed Control Period (Month 3 Primary Endpoint)	**106**	**56**	**162**
Continued After Control Period	**106**	**53**	**159**
Lost to Follow-up	9	4	13
Withdrawal by Subject	6	3	9
Completed Follow-up Period Through 13 Months After Treatment	**91**	**46**	**137**
Treatment Group – Did Not Receive Optional Repeat Treatment (Completed Study)	**51**	**N/A**	**51**
Treatment Group – Received Optional Repeat Treatment (VMT Population)	**40**	**N/A**	**40**
Lost to Follow-up	3	N/A	3
Withdrawal by Subject	2	N/A	2
Treatment Group – Completed Follow-up Period Through 6 Months After Repeat Treatment (Completed Study)	**35**	**N/A**	**35**

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a study performed in the US. Subject demographics and pre-treatment characteristics are presented in Table 3. At baseline, 26 subjects (15.2%, 19 treatment, 7 control) had minimal, 87 subjects (50.9%, 54 treatment, 33 control) had moderate, and 58 subjects (33.9%, 40 treatment, 18 control) had severe temple hollowing based on EI assessments on the ATHS.

Table 3: Demographics and Pretreatment Characteristics (N = 171)

	JUVÉDERM® VOLUMA® XC	
Female	85.0% (96/113)	81.0% (47/58)
Male	15.0% (17/113)	19.0% (11/58)
Age		
Median	54.0	55.5
Range	32-82	25-75
White	83.2% (94/113)	82.8% (48/58)
Black or African American	10.6% (12/113)	10.3% (6/58)
Asian	1.8% (2/113)	1.7% (1/58)
American Indian / Alaska Native	0.9% (1/113)	0% (0/58)
Multiple	3.5% (4/113)	5.2% (3/58)
Ethnicity		
Hispanic or Latino	23.9% (27/113)	24.1% (14/58)
Not Hispanic or Latino	76.1% (86/113)	75.9% (44/58)
Fitzpatrick Skin Type		
I/II	34.5% (39/113)	34.5% (20/58)
III/IV	53.1% (60/113)	58.6% (34/58)
V/VI	12.4% (14/113)	6.9% (4/58)
Baseline ATHS Score		
Minimal	16.8% (19/113)	12.1% (7/58)
Moderate	47.8% (54/113)	56.9% (33/58)
Severe	35.4% (40/113)	31.0% (18/58)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the cohort of subjects available at each follow-up timepoint (1, 3, 6, 9, and 13 months after initial/touch-up treatment and 1, 3 and 6 months after repeat treatment). The key safety outcomes for this study are presented below.

Subjects recorded specific signs and symptoms of TSRs in a 30-day e-diary after initial treatment (daily for the first 14 days and every other day for the final 16 days) and in a 14-day daily diary after touch-up and repeat treatments. Of the 165 subjects who underwent treatment (from both the treatment and control groups), 161 subjects completed the diaries, and of the 111 subjects who received touch-up treatment, 108 completed the diaries. All 40 subjects who received repeat treatment also completed the diaries. Subjects rated each TSR listed on the diary as "Mild (barely noticeable)," "Moderate (uncomfortable)," "Severe (severe discomfort)," or "None."

After initial treatment with JUVÉDERM® VOLUMA® XC, 59.0% of the subjects (95 of 161) with diary entries reported experiencing at least 1 TSR. Subjects rated TSRs as predominantly mild (70.5% , 67 of 95 reported TSRs) or moderate (26.3% , 25 of 95 reported TSRs) in severity, with a majority of TSRs resolving within 3 days (60.0%, 57

of 95 reported TSRs). The incidence of TSRs for the touch-up and maintenance treatments was lower than that for initial treatment.

TSRs reported by > 5% of subjects after initial treatment are summarized by severity and duration in Table 4.

Table 4: Treatment Site Responses (TSR) by Maximum Severity Occurring in > 5% of Subjects After Initial Treatment to Improve Temple Hollowing (N=161)

TSR	Incidence % (n/N[a])	Severity[b]			Duration[c]			
		Mild % (n/N[a])	Moderate % (n/N[a])	Severe %(n/N[a])	≤ 3 Days % (n/N[a])	7 Days % (n/N[a])	8-14 Days % (n/N[a])	15-30 Days % (n/N[a])
Any TSR	59.0% (95/161)	41.6% (67/161)	15.5% (25/161)	1.9% (3/161)	35.4% (57/161)	12.4% (20/161)	7.5% (12/161)	3.7% (6/161)
Pain After Injection	50.9% (82/161)	37.9% (61/161)	11.2% (18/161)	1.9% (3/161)	37.9% (61/161)	8.7% (14/161)	3.7% (6/161)	0.6% (1/161)
Tenderness to Touch	49.7% (80/161)	42.9% (69/161)	5.6% (9/161)	1.2% (2/161)	34.2% (55/161)	9.9% (16/161)	4.3% (7/161)	1.2% (2/161)
Redness	41.0% (66/161)	34.2% (55/161)	5.6% (9/161)	1.2% (2/161)	34.2% (55/161)	4.3% (7/161)	1.9% (3/161)	0.6% (1/161)
Firmness	37.9% (61/161)	33.5% (54/161)	3.7% (6/161)	0.6% (1/161)	29.2% (47/161)	4.3% (7/161)	2.5% (4/161)	1.9% (3/161)
Swelling	30.4% (49/161)	26.1% (42/161)	4.3% (7/161)	0%	21.1% (34/161)	5.0% (8/161)	3.7% (6/161)	0.6% (1/161)
Lumps/Bumps	26.1% (42/161)	23.0% (37/161)	3.1% (5/161)	0%	20.5% (33/161)	3.7% (6/161)	1.2% (2/161)	0.6% (1/161)
Bruising	16.1% (26/161)	14.9% (24/161)	1.2% (2/161)	0%	11.2% (18/161)	3.1% (5/161)	1.9% (3/161)	0%
Headache	9.3% (15/161)	6.8% (11/161)	1.9% (3/161)	0.6% (1/161)	9.3% (15/161)	0%	0%	0%
Discoloration	6.8% (11/161)	5.6% (9/161)	1.2% (2/161)	0%	6.2% (10/161)	0.6% (1/161)	0%	0%

a N denotes the number of subjects who recorded responses in the diaries after initial treatment
b Maximum severity reported in the diary
c Duration is calculated as total days from first to last date of occurrence

TSRs reported by ≤ 5% of subjects included difficulty chewing, difficulty opening mouth, eye twitching, increased sensation, jaw stiffness, jaw tightness, poor cosmetic result, vasodilation, and wrinkles.

Among the 165 subjects treated with JUVÉDERM® VOLUMA® XC, 17.6% (29 subjects) experienced 51 treatment-related TEAEs following initial and touch-up treatment. All of the treatment-related TEAEs after initial/touch-up treatment were either mild (96.1%, 49 of 51 treatment-related TEAEs) or moderate (3.9%, 2 of 51 treatment-related TEAEs) in severity.

Table 5 summarizes treatment-related AEs that occurred with a frequency of > 1%. Treatment-related TEAEs occurring in ≤ 1% of subjects included implant site pain, injection site edema, injection site joint discomfort, injection site joint movement impairment, injection site paresthesia, mastication disorder and vasodilation, all occurring in 0.6% (1/165) of subjects.

Table 5: Treatment-Related Adverse Events Occurring in > 1% of Treated Subjects for Improvement of Temple Hollowing (N = 165)

Adverse Event	Treated Subjects % (n/N)
Pain in Jaw	6.1% (10/165)
Headache	4.8% (8/165)
Injection Site Pain	1.8% (3/165)
Injection Site Discomfort	1.2% (2/165)
Injection Site Mass	1.2% (2/165)
Temporomandibular Joint Syndrome	1.2% (2/165)
Trismus	1.2% (2/165)

The treatment-related TEAEs occurred within 1 week after treatment for 16.4% (27/165) of subjects and resolved without sequalae within 1 week for 15.2% (25/165) of subjects. There were 7 treatment-related TEAEs that began 1 week after treatment affecting 3.0% (5 of 165) of the subjects, which were injection site mass, pain in jaw, headache, and mastication disorder. There were no treatment-related TEAEs that began more than 30 days after treatment.

For initial/touch-up treatment, 4 subjects (2.4%, 4/165) had 6 treatment-related TEAEs that lasted longer than 30 days, including mild trismus that lasted 42 days, mild injection site mass in the left temple that lasted 56 days, mild injection site pain in both temples that lasted 32 days, and mild injection site mass in both temples that lasted 66 days. All the treatment-related TEAEs lasting longer than 30 days resolved without intervention. There were no treatment-related SAEs observed in the study.

Fewer treatment-related TEAEs occurred after maintenance treatment than after initial/touch-up treatment (Table 6). Among the 40 subjects who received maintenance treatment, 12.5% (5/40) experienced treatment-related TEAEs. All TEAEs after maintenance treatment were mild or moderate in severity, did not require any intervention and most resolved within 30 days without sequelae. There were no serious TEAEs after maintenance treatment.

Table 6: Summary of treatment-emergent Adverse Events (TEAEs) for Maintenance Treatment (Safety Population)

	After Maintenance Treatment		After Initial Treatment	
	Subjects (N=40) n (%)	Events	Subjects (N=40) n (%)	Events
All TEAEs	13 (32.5)	18	14 (35.0)	26
Treatment-related TEAEs	5 (12.5)	7	6 (15.0)	11
At Injection Site	1 (2.5)	2	1 (2.5)	1
Not at Injection Site	4 (10.0)	5	6 (15.0)	10
All SAEs	4 (10.0)	4	1 (2.5)	2
Treatment-related SAEs	0 (0)	0	0 (0)	0
Discontinued due to TEAE	0 (0)	0	0 (0)	0
Deaths	0 (0)	0	0 (0)	0
COVID-19 infection TEAEs	3 (7.5)	3	2 (5.0)	2

Procedural Pain

Subjects assessed procedural pain (pain during injection) immediately after completion of initial, touch-up, and maintenance treatments on an 11-point scale ranging from 0 (no pain) to 10 (worst pain imaginable). Pain was minimal, with mean scores in the treatment group of 1.3 (ranging from 0 to 7) for initial treatment, 1.0 (ranging from 0 to 7) for touch-up treatment, and 1.8 (ranging from 0 to 10) for maintenance treatment.

Facial Function Assessments

Subject assessments on the Jaw Functional Limitation Scale in the JUVÉDERM® VOLUMA® XC Treated (VT) population showed a median score of zero (no limitation) at baseline and a change from baseline of zero at all postbaseline timepoints in overall score and scores for the 3 subscales of mastication, mobility, and verbal and nonverbal communication, indicating that treatment did not affect jaw function for the subjects.

Vision Assessments

Subjects were assessed on visual acuity and functionality after the completion of initial, touch-up, and maintenance treatments. Snellen visual acuity showed that 11 of 156 (7.1%) subjects had worsening of their visual acuity while 10 of 156 (6.4%) subjects showed improvement of their visual acuity at Month 1 post initial/touch-up treatments. At Month 1 post maintenance treatment, 5 of 36 (13.9%subjects had improvement of their visual acuity and none of the subjects had worsening in visual acuity. The visual acuity remained the same for all other subjects post initial/touch-up and maintenance treatments. The TI confirmed that the change in Snellen scores was not clinically significant for any subject eyes that worsened. No eyes showed a ≥ 3-line worsening in visual acuity at any assessment.

Confrontational visual fields and ocular motility assessments showed that 100% of eyes were full to confrontation and had full duction and version at all timepoints.

2. Effectiveness Results

The analysis of primary effectiveness was based on the 113 treatment group and 58 control group evaluable subjects at the 3-month timepoint. Key effectiveness outcomes are presented below.

Primary effectiveness results:

JUVÉDERM® VOLUMA® XC provided a clinically and statistically significant improvement of moderate to severe temple hollowing compared to the no-treatment control group. The primary effectiveness endpoint was met in that greater than 60% of subjects in the treatment group were responders (80.4% improved by ≥ 1-point compared with their pre-treatment assessment), and the responder rate for the treatment group was significantly greater ($p < 0.0001$) than the responder rate for the control group (a difference of 66.9%) at Month 3 (Table 7). JUVÉDERM® VOLUMA® XC was found to be effective in all Fitzpatrick skin phototypes, for males and females, and across the studied age range. The median total volume used to achieve optimal improvement in the treatment group was 3.65 mL (range, 0.4-8.0 mL) for both temples, with median of 2.0 mL for initial treatment and 1.5 mL for touch-up treatment. Injection volumes were similar for both left and right temples.

Table 7: Effectiveness Summary Responder Rate at 3 Months Based on Evaluating Investigators' Live Assessments of Subjects

	Responder Rate at Month 3	p-value
Treatment Group	80.4% (90.8/113)	N/A
Control Group	13.5% (7.8/58)	
Difference in Responder Rates (Treatment rate - Control rate)	66.9%	< 0.0001

JUVÉDERM® VOLUMA® XC provided improvement in moderate to severe temple hollowing that lasted for more than 1 year. The ATHS responder rate for the treatment group was 81.7% (85/104) at the 1-month follow up visit and 73.3% (66/90) at the 13-month follow up visit.

Secondary effectiveness results:

The blinded EI and subject GAIS responder rates at Month 3 were 83.8% (88/113) and 92.9% (92/99) respectively, for the treatment group. The EI and subject GAIS responder rate was 10.7% (6/56) and 2.0% (1/51) respectively, for the untreated control group. The EI and subject GAIS responder rates remained high for the treatment group from Month 1 (86.5% and 91.4%, respectively) through Month 13 (72.2% and 78.9%, respectively).

Subject satisfaction with facial appearance, as measured by the FACE-Q *Satisfaction with Facial Appearance* demonstrated significant improvements after treatment with overall mean score of 41.5 at baseline improving to a mean score of 66.3 at Month 3 ($p <$

0.0001). In the no-treatment control group, the mean score was 39.6 at baseline and decreased to a mean score of 32.7 at Month 3. Improvements were seen from baseline to Month 3 in treatment group responses of *somewhat* or *very satisfied* in the individual FACE-Q *Satisfaction with Facial Appearance* questions:

- How symmetric their face looks: 54.0% of subjects were *somewhat* or *very satisfied* at baseline, which improved to 89.0% at Month 3
- How balanced their face looks: 49.6% improved to 88.0%
- How well-proportioned their face looks: 54.0% improved to 87.0%
- How their face looks at the end of the day: 33.6% improved to 72.0%
- How fresh their face looks: 23.0% improved to 68.0%
- How rested their face looks: 25.0% improved to 72.7%
- How their face looks in profile (side view): 31.3% improved to 71.7%
- How their face looks in photos: 31.3% improved to 74.7%
- How their face looks when they first wake up: 29.5% improved to 67.7%
- How their face looks under bright lights: 23.2% improved to 64.6%

At Month 13, the majority of treatment group subjects were still *somewhat* or *very satisfied* on each of the above questions.

Subject satisfaction with temples as measured by the FACE-Q *Satisfaction with Temples* questionnaire also demonstrated significant improvements after treatment, with overall mean score of 34.5 at baseline and 77.4 at Month 3 ($p < 0.0001$). In the untreated control group, the mean score was 30.9 at baseline and decreased to a mean of 26.5 at Month 3. Improvements were seen from baseline to Month 3 in treatment group responses of *somewhat* or *very satisfied* in the individual FACE-Q *Satisfaction with Temples* questions shown below;

- How their temples look compared with other people their age: 33.9% of subjects were *somewhat* or *very satisfied* at baseline, which improved to 86.7% at Month 3
- How well their temples fit in with the rest of their face (balanced): 28.6% improved to 85.7%
- How well the shape of their temples compliments the shape of their face: 23.2% improved to 84.7%
- How their temples look in photos: 33.0% improved to 89.9%
- How their temples look under a bright light: 24.1% improved to 86.9%
- The age their temples make them look: 17.9% improved to 84.7%
- How their temples look when they turn their face slightly to the side: 21.4% improved to 89.9%
- How their temples look from the side (profile view): 29.2% improved to 88.9%
- The shape of their temples: 22.1% improved to 87.0%
- How their temples look in a mirror (straight on): 23.0% improved to 89.0%
- How full their temples look: 17.7% improved to 86.0%
- How youthful their temples make them look: 13.4% improved to 83.7%

At Month 13, the majority of treatment group subjects were still *somewhat* or *very satisfied* on each of the above questions.

Other effectiveness results:

Other effectiveness assessments included measurements of temple volume change from 3D images, subject self-perception of age, and subject assessments of satisfaction with the treatment result, natural look and feel, treatment meeting expectations, likelihood of continuing treatment, and assessment of willingness to recommend treatment. These effectiveness assessments showed high levels of satisfaction based on subject-reported improvements, and objective measurements showed an increase in volume compared to baseline (Table 8). Improvement continued through 13 months.

Table 8: Additional Treatment Group Effectiveness Results (UVÉDERM® VOLUMA® XC Treated VT Population)

Assessment	3 Months	Conclusion
Temple Volume Change (Mean Change per Temple)	1.0 cc	The measurement showed an increase after treatment
Subject Self-Perception of Age (Mean Years Younger Than Baseline)	5 years	Subjects reported looking younger after treatment
Subject Satisfaction with Treatment (% *Satisfied* or *Definitely Satisfied*)	91.0%	Subjects reported satisfaction with treatment
Subject Satisfaction with Natural Look (% *Satisfied* or *Definitely Satisfied*)	89.0%	Subjects reported satisfaction with natural look after treatment
Subject Satisfaction with Natural Feel (% *Satisfied* or *Definitely Satisfied*)	91.0%	Subjects reported satisfaction with natural feel after treatment
Subject Assessment of Treatment Meeting Expectations (% responding yes)	87.0%	Subjects reported treatment met expectations
Subject Likelihood of Continuing Treatment (% responding yes)	93.0%	Subjects reported likely to continue treatment
Subject Willingness to Recommend Treatment (% responding yes)	98.0%	Subjects reported willingness to recommend treatment

Follow-up After Maintenance Treatment

Maintenance treatment with JUVÉDERM® VOLUMA® XC was administered to 40 subjects. The effectiveness profile after maintenance treatment was similar to that after initial treatment. The ATHS responder rate after maintenance treatment was 82.9% (29/35) at 1 month, 73.5% (25/34) at 3 months, and 71.4% (25/35) at 6 months.

3. Subgroup Analysis

The baseline ATHS severity subgroup was evaluated for potential association with outcomes and the effectiveness data is presented in Table 9. Additionally, analyses of the primary effectiveness variables (ATHS responder rate at Month 3) were performed for the subgroups of injection volume, Fitzpatrick skin, phototypes, sex, and age. JUVÉDERM® VOLUMA® XC was found to be effective in all subgroups except the

baseline ATHS minimal subgroup (Table 10). Baseline ATHS severity subgroup analysis for safety is presented in Table 11.

Table 9: Effectiveness Results by Baseline ATHS Subgroups

Assessment	Group	Baseline ATHS Subgroup		
		Minimal	Moderate	Severe
ATHS Responder Rate, n/N (%)	**Voluma XC**	9/17 (52.9%)	43/51 (84.3%)	34/37 (91.9%)
	Control	1/6 (16.7%)	3/32 (9.4%)	3/18 (16.7%)
Investigator GAIS Responder Rate, n/N (%)	**Voluma XC**	12/17 (70.6%)	45/51 (88.2%)	31/37 (83.8%)
	Control	2/6 (33.3%)	2/32 (6.3%)	2/18 (11.1%)
Subject GAIS Responder Rate, n/N (%)	**Voluma XC**	15/16 (93.8%)	44/48 (91.7%)	33/35 (94.3%)
	Control	0/4 (0.0%)	0/30 (0.0%)	1/17 (5.9%)
FACE-Q Satisfaction with Facial Appearance Mean Change from Baseline, mean (n)	**Voluma XC**	26.4 (17)	21.5 (48)	26.7 (35)
	Control	-7.5 (4)	-7.2 (30)	-5.2 (17)
FACE-Q Satisfaction with Temple Mean Change from Baseline, mean (n)	**Voluma XC**	42.9 (17)	40.9 (48)	45.0 (35)
	Control	-4.0 (4)	-5.1 (30)	-2.6 (17)

Table 10: Subgroup Analyses of ATHS Responder Rates at Month 3 Initial Treatment Population in Control Period

Subgroups	Control (N=58) % (n/N)	Voluma XC Treatment (N=113) % (n/N)
Injection volume < Median	N/A	78.4% (40/51)
Injection volume ≥ Median	N/A	85.2% (46/54)
Fitzpatrick I/II	5.0% (1/20)	81.6% (31/38)
Fitzpatrick III/IV	9.4% (3/32)	81.1% (43/53)
Fitzpatrick V/VI	75.0% (3/4)	85.7% (12/14)
Female	13.0% (6/46)	84.1% (74/88)
Male	10.0% (1/10)	70.6% (12/17)
Age < Median (55 years)	14.3% (3/21)	76.9% (40/52)
Age ≥ Median 55 years	11.4% (4/35)	86.8% (46/53)

Table 11: Safety Results by Baseline ATHS Subgroups

Assessment	Baseline ATHS Subgroup		
	Minimal	Moderate	Severe
Any Treatment-related TEAEs, n/N (%)	5/24 (20.8%)	16/84 (19.0%)	8/57 (14.0%)
Injection Site Discomfort	0/24 (0.0%)	2/84 (2.4%)	0/57 (0.0%)
Injection Site Pain	1/24 (4.2%)	1/84 (1.2%)	1/57 (1.8%)
Injection Site Joint Movement Impairment	0/24 (0.0%)	1/84 (1.2%)	0/57 (0.0%)
Injection Site Mass	0/24 (0.0%)	1/84 (1.2%)	1/57 (1.8%)
Injection Site Paraesthesia	0/24 (0.0%)	1/84 (1.2%)	0/57 (0.0%)
Implant Site Pain	0/24 (0.0%)	0/84 (0.0%)	1/57 (1.8%)
Injection Site Joint Discomfort	0/24 (0.0%)	0/84 (0.0%)	1/57 (1.8%)
Injection Site Oedema	0/24 (0.0%)	0/84 (0.0%)	1/57 (1.8%)
Pain in Jaw	4/24 (16.7%)	4/84 (4.8%)	2/57 (3.5%)
Temporomandibular Joint Syndrome	0/24 (0.0%)	2/84 (2.4%)	0/57 (0.0%)
Trismus	0/24 (0.0%)	2/84 (2.4%)	0/57 (0.0%)
Mastication Disorder	0/24 (0.0%)	1/84 (1.2%)	0/57 (0.0%)
Headache	0/24 (0.0%)	4/84 (4.8%)	4/57 (7.0%)
Vasodilatation	0/24 (0.0%)	0/84 (0.0%)	1/57 (1.8%)
Any Serious Adverse Events (SAE), n/N (%)	0/24 (0.0%)	4/84 (4.8%)	3/57 (5.3%)
Any Treatment Site Responses (TSRs) after Initial Treatment, n/N (%)	19/24 (79.2%)	42/80 (52.5%)	34/57 (59.6%)

Prespecified safety analyses, including the TSRs (Table 12) and Treatment-related AEs (Table 13) in subgroups of baseline ATHS moderate to severe severity, injection volume, Fitzpatrick skin type, and investigational site demonstrated that JUVÉDERM® VOLUMA® XC is safe in these specified subgroups. Additionally, JUVÉDERM® VOLUMA® XC was evaluated for safety and effectiveness across the subject age subgroups (Table 14, Table 15 and Table 16). Although the responder rate for the 30-39 age group is lower than the rest of the populations, it is difficult to draw any conclusions due to the relatively small sample size in that subgroup.

Table 12. Subgroup Analyses of Subjects with Treatment Site Responses (TSR) after Initial Treatment (Voluma XC Treated Population)

Subgroup	Any TSR % of Subjects	Pain After Injection % of Subjects	Tenderness to Touch % of Subjects	Redness % of Subjects	Firmness % of Subjects	Swelling % of Subjects	Lumps /Bumps % of Subjects	Bruising % of Subjects	Discoloration % of Subjects	Itching % of Subjects
Injection volume < median (n=54)	57.4%	51.9%	44.4%	44.4%	38.9%	25.9%	16.7%	16.7%	9.3%	5.6%
Injection volume ≥ median (n=55)	54.5%	47.3%	49.1%	36.4%	32.7%	29.1%	27.3%	10.9%	0%	1.8%
Fitzpatrick I/II (n=56)	50.0%	42.9%	44.6%	33.9%	33.9%	33.9%	28.6%	16.1%	7.1%	3.6%
Fitzpatrick III/IV (n=89)	65.2%	58.4%	55.1%	46.1%	41.6%	29.2%	24.7%	15.7%	7.9%	3.4%
Fitzpatrick V/VI (n=16)	56.3%	37.5%	37.5%	37.5%	31.3%	25.0%	25.0%	18.8%	0%	6.3%
Female (n=136)	61.8%	53.7%	51.5%	43.4%	41.2%	31.6%	27.9%	18.4%	7.4%	4.4%
Male (n=25)	44.0%	36.0%	40.0%	28.0%	20.0%	24.0%	16.0%	4.0%	4.0%	0%
Age < median (n=73)	61.6%	54.8%	52.1%	39.7%	39.7%	28.8%	27.4%	12.3%	4.1%	4.1%
Age ≥ median (n=88)	56.8%	47.7%	47.7%	42.0%	36.4%	31.8%	25.0%	19.3%	9.1%	3.4%

Table 13. Subgroup Analyses of Subjects with Treatment-Related AEs in the Treatment Period (Voluma XC Treated Population)

Subgroup	Any TRAE % of Subjects	Injection Site Discomfort	Injection Site Pain	Injection Site Joint Movement Impairment	Injection Site Mass	Injection Site Paraesthesia	Implant Site Pain	Injection Site Joint Discomfort	Injection Site Oedema	Pain in Jaw	Temporoman-dibular Joint Syndrome	Trismus	Mastication Disorder	Headache	Vasodilatation
Injection volume < median (n=54 subjects)	14.0%	1.2%	1.2%	1.2%	1.2%	1.2%	0.0%	0.0%	0.0%	2.3%	2.3%	2.3%	0.0%	2.3%	0.0%
Injection volume ≥ median (n=55 subjects)	21.5%	1.3%	2.5%	0.0%	1.3%	0.0%	1.3%	1.3%	1.3%	10.1%	0.0%	0.0%	1.3%	7.6%	1.3%
Fitzpatrick I/II (n=56 subjects)	16.1%	1.8%	1.8%	0.0%	1.8%	1.8%	1.8%	1.8%	1.8%	7.1%	0.0%	0.0%	0.0%	5.4%	1.8%
Fitzpatrick III/IV (n=89 subjects)	22.0%	1.1%	2.2%	1.1%	1.1%	0.0%	0.0%	0.0%	0.0%	6.6%	2.2%	2.2%	1.1%	5.5%	0.0%
Fitzpatrick V/VI (n=16 subjects)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Female (n=136 subjects)	19.4%	1.4%	1.4%	0.7%	1.4%	0.7%	0.7%	0.7%	0.7%	7.2%	0.7%	1.4%	0.7%	5.8%	0.7%
Male (n=25 subjects)	7.7%	0.0%	3.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.8%	0.0%	0.0%	0.0%	0.0%
Age < median (n=73 subjects)	17.6%	2.7%	1.4%	1.4%	0.0%	0.0%	0.0%	0.0%	0.0%	8.1%	1.4%	1.4%	0.0%	2.7%	0.0%
Age ≥ median (n=88 subjects)	17.6%	0.0%	2.2%	0.0%	2.2%	1.1%	1.1%	1.1%	1.1%	4.4%	1.1%	1.1%	1.1%	6.6%	1.1%

Table 14. Effectiveness Analysis at Month 3 by Subject Age Subgroups (Initial Treatment Population in Control Period)

Effectiveness Measures	Group	Subject Age Subgroups (mITT Population) % of Subjects					
		30 – 39 years	40 – 49 years	50 – 59 years	60 – 69 years	70 – 79 years	≥ 80 years
ATHS Responder Rate, % (n/N)	Voluma XC	50.0% (4/8)	81.0% (17/21)	85.4% (35/41)	88.5% (23/26)	75.0% (6/8)	100.0% (1/1)
	Control	0.0% (0/4)	30.0% (3/10)	3.8% (1/26)	15.4% (2/13)	33.3% (1/3)	NA
Investigator GAIS Responder Rate, % (n/N)	Voluma XC	75.0% (6/8)	90.5% (19/21)	78.0% (32/41)	84.6% (22/26)	100.0% (8/8)	100.0% (1/1)
	Control	25.0% (1/4)	30.0% (3/10)	3.8% (1/26)	7.7% (1/13)	0.0% (0/3)	NA
Subject GAIS Responder Rate, % (n/N)	Voluma XC	100.0% (8/8)	95.2% (20/21)	90.0% (36/40)	91.7% (22/24)	100.0% (5/5)	100.0% (1/1)
	Control	0.0% (0/4)	10.0% (1/10)	0.0% (0/22)	0.0% (0/12)	0.0% (0/3)	NA
FACE-Q Satisfaction with Facial Appearance Mean Change from Baseline, mean (n)	Voluma XC	16.5 (8)	16.2 (21)	29.7 (41)	26.3 (24)	8.0 (5)	56.0 (1)
	Control	-17.3 (4)	-5.8 (10)	-6.4 (22)	-3.8 (12)	-7.3 (3)	NA
FACE-Q Satisfaction with Temple Mean Change from Baseline, mean (n)	Voluma XC	31.0 (8)	38.0 (21)	47.9 (41)	41.9 (24)	40.2 (5)	51.0 (1)
	Control	-11.5 (4)	-8.4 (10)	-1.9 (22)	0.9 (12)	-17.3 (3)	NA

Table 15. Treatment Site Responses after Initial Treatment by Subject Age Subgroups (Voluma XC Treated Population)

Age Subgroups	Any TSR % of Subjects	Pain After Injection % of Subjects	Tenderness to Touch % of Subjects	Redness % of Subjects	Firmness % of Subjects	Swelling % of Subjects	Lumps /Bumps % of Subjects	Bruising % of Subjects	Discoloration % of Subjects	Itching % of Subjects
Total (n=161)	59.0%	50.9%	49.7%	41.0%	37.9%	30.4%	26.1%	16.1%	6.8%	3.7%
30 – 39 years (n=11)	81.8%	63.6%	72.7%	45.5%	45.5%	18.2%	18.2%	9.1%	0.0%	0.0%
40 – 49 years (n=30)	56.7%	53.3%	50.0%	26.7%	43.3%	36.7%	33.3%	16.7%	3.3%	3.3%
50 – 59 years (n=69)	58.0%	53.6%	49.3%	47.8%	31.9%	27.5%	27.5%	17.4%	10.1%	5.8%
60 – 69 years (n=40)	62.5%	50.0%	50.0%	42.5%	42.5%	40.0%	25.0%	20.0%	7.5%	2.5%
70 – 79 years (n=10)	30.0%	10.0%	20.0%	20.0%	30.0%	10.0%	0.0%	0.0%	0.0%	0.0%
≥ 80 years (n=1)	100.0%	100.0%	100.0%	100.0%	100.0%	0.0%	100.0%	0.0%	0.0%	0.0%

Table 16. Treatment-Related AEs after Initial/Touch-up Treatment by Subject Age Subgroups (Voluma XC Treated Population)

Age Subgroups	Any Treatment-Related AE %	Injection Site Discomfort	Injection Site Pain	Injection Site Joint Movement Impairment	Injection Site Mass	Injection Site Paraesthesia	Implant Site Pain	Injection Site Joint Discomfort	Injection Site Oedema	Pain in Jaw	Temporomandibular Joint Syndrome	Trismus	Mastication Disorder	Headache	Vasodilatation
30 – 39 years (n=12)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
40 – 49 years (n=30)	13.3%	3.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	0.0%	0.0%	0.0%	3.3%	0.0%
50 – 59 years (n=71)	25.4%	1.4%	4.2%	1.4%	2.8%	1.4%	0.0%	0.0%	0.0%	7.0%	1.4%	1.4%	1.4%	0.0%	0.0%
60 – 69 years (n=40)	17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	2.5%	2.5%	2.5%	5.0%	2.5%	2.5%	0.0%	5.0%	2.5%
70 – 79 years (n=11)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
≥ 80 years (n=1)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

4. Pediatric Extrapolation

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

E. 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 1878-702-008 study included 32 Treating and Evaluating Investigators in total. 21 of the 32 investigators have, by way of a signed Financial Disclosure/Certification Form, verified that they have no applicable financial arrangement with AbbVie defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

Eleven (11) of the 32 investigators have financial arrangements with AbbVie to be disclosed under 21 CFR 54.2 (b), not affecting the outcome of the 1878-702-008 clinical study. The nature of these disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) is described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: 11
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

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.

XI. 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.

XII. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

A. EFFECTIVENESS CONCLUSIONS

JUVÉDERM® VOLUMA® XC met the prespecified primary endpoint, and the secondary endpoints support product effectiveness. The balance of the data indicate that JUVÉDERM® VOLUMA® XC is effective for supraperiosteal injection to augment the temple region to improve moderate to severe temple hollowing in adults over the age of 21.

B. SAFETY CONCLUSIONS

The potential risks and adverse effects of the device are based on data collected in the clinical study conducted to support the indication expansion as described above as well as evaluation of device use in the postmarket setting. The data submitted provide a reasonable assurance that the device is safe for supraperiosteal injection in the temple region to improve moderate to severe temple hollowing in adults over the age of 21. The specific conclusions are:

- For initial, touch-up, and maintenance treatments, most TSRs were mild to moderate in severity and resolved within 14 days.
- The most common TSRs were pain at injection site, tenderness to touch, and redness.
- Subjects assessed procedural pain during injection as minimal.
- The most common treatment-related AEs after initial/touch-up treatment were jaw pain and headache, with all others occurring in less than 2% of subjects.
- Most treatment-related AEs began within 1 week of treatment, were mild in severity, and resolved within 1 week.
- There were no deaths, unanticipated adverse device effects, or treatment-related serious AEs.

C. BENEFIT-RISK CONCLUSIONS

The probable benefits of the device are based on the results of the 1878-702-008 study, which demonstrated the effectiveness of the product for improving moderate to severe temple hollowing. The predefined primary endpoint was met in that at least 60% of the treatment group subjects were responders, defined as those who had at least a 1-point improvement on the ATHS in both temples, and the responder rate was statistically higher for the treatment group compared to the control group ($p < 0.0001$).

Patient Perspective

The secondary and other effectiveness endpoints further demonstrated that JUVÉDERM® VOLUMA® XC is effective to improve moderate to severe temple hollowing based on subjective and objective measures. The FACE-Q Satisfaction with Facial Appearance and Satisfaction with Temples questionnaires overall mean scores for the treatment group improved significantly at Month 3 ($p < 0.0001$). Based on EI and subject GAIS assessments, over 80% of treatment group subjects had overall aesthetic improvement of their temples at Month 3. These effectiveness results were corroborated by objective calculations from 3D imaging that demonstrated increase in temple volume through 13 months.

The clinical study results demonstrated that the safety profile of JUVÉDERM® VOLUMA® XC injection for moderate to severe temple hollowing is acceptable and consistent with the clinical study data on JUVÉDERM® VOLUMA® XC for cheek augmentation (VOLUMA-002 study) and chin augmentation (VOLUMA-006 study). There were no unanticipated AEs, with most subjects in all 3 studies experiencing

common TSRs, such as pain after injection, tenderness to touch, and redness after treatment, the majority of which were mild in severity and resolved within 1 week of onset. AEs were generally mild in nature for temple hollowing treatment, and the majority resolved within 1 week in all 3 studies. Furthermore, the temple hollowing study reported no treatment-related SAEs.

Based on clinical study data, the probable benefits of JUVÉDERM® VOLUMA® XC in improving moderate to severe temple hollowing outweigh the probable risks, as determined by the short-term adverse outcomes seen after treatment balanced against the improvement seen on the ATHS, GAIS, and subject satisfaction.

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.

XIII. CDRH DECISION

CDRH issued an approval order on 10/06/2023.

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

XIV. 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.