SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. General Information

Device Generic Name:	Injectable Dermal Filler
Device Trade Name:	SKINVIVE by JUVÉDERM®
Device Procode	LMH
Applicant's Name and Address:	Allergan Aesthetics, an AbbVie Company 2525 Dupont Drive Irvine, CA 92612
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P110033/S099
Date of FDA Notice of Approval:	June 11, 2026

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 midface in adults over the age of 21. SKINVIVE by JUVÉDERM® (P110033/S059) was approved on May 11, 2023 for intradermal injection to improve skin smoothness of the cheeks in adults over the age of 21. The SSED to support these indications is available on the CDRH website and is incorporated by reference herein. The current supplement was submitted to:

- Expand the indication for SKINVIVE by JUVÉDERM® for intradermal and/or subdermal injection to reduce neck lines for improvement of neck appearance in adults over the age of 21; and
- Add the use of TSK 25 G 1½″ STERiGLIDE™ cannula when used with needle for SKINVIVE by JUVÉDERM® neck treatment.

II. Indications for Use

SKINVIVE by JUVÉDERM® injectable gel is indicated for intradermal injection to improve skin smoothness of the cheeks in adults over the age of 21.

SKINVIVE by JUVÉDERM® injectable gel is indicated for intradermal and/or subdermal injection to reduce neck lines for improvement of neck appearance in adults over the age of 21.

III. Contraindications

- SKINVIVE by JUVÉDERM® is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- SKINVIVE by JUVÉDERM® contains trace amounts of gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- SKINVIVE by JUVÉDERM® 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 SKINVIVE by JUVÉDERM® labeling.

V. Device Description

SKINVIVE by JUVÉDERM® injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel implant. The gel consists of hyaluronic acid (HA) produced by *Streptococcus* species of bacteria at a concentration of 12 mg/mL, crosslinked with 1,4-Butanediol diglycidyl ether (BDDE), which contains 0.3% w/w lidocaine in a physiologic buffer. Each retail box of SKINVIVE by JUVÉDERM® contains 2 sterilized syringes prefilled with 1.0 ml of HA gel implant. Each syringe is sealed in a thermoformed tray with two 32 G ½″ needles. Syringes are fitted with a luer lock adaptor, a plunger rod, a rubber stopper tip cap, and a finger grip. Syringes are labeled with the name of the product, batch number, and expiration date.

VI. Alternative Practices and Procedures

There are several other alternatives for the correction of neck lines to improve neck appearance including other fillers, botulinum toxin, microfocused ultrasound, radiofrequency, resorbable suspension sutures, and laser treatments. 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

SKINVIVE by JUVÉDERM® received FDA approval on May 11, 2023 for intradermal injection to improve skin smoothness of the cheeks. SKINVIVE by JUVÉDERM® is marketed as JUVÉDERM® VOLITE™ in some countries outside of the United States. JUVÉDERM® VOLITE™ without lidocaine received CE Mark as JUVÉDERM®

VOLITE™ B in April 2015, and JUVÉDERM® VOLITE with lidocaine, also known as JUVÉDERM® VOLITE™ XC, received CE Mark as JUVÉDERM® VOLITE™ in April 2016. JUVÉDERM® VOLITE™ is available in the European Union for the treatment of superficial cutaneous depressions such as fine lines and for additional improvement of skin quality attributes such as hydration and elasticity.

SKINVIVE by JUVÉDERM® is marketed in countries in the following regions: North America, Latin America, South America, European Union and affiliated countries, Eastern Europe, Middle East, Africa, Asia-Pacific, and Australia/New Zealand.

SKINVIVE by JUVÉDERM® has not been withdrawn from any marketplace for any reason.

VIII. Potential Adverse Effects of the Device on Health

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

Common treatment site responses that can occur with the use of SKINVIVE by JUVÉDERM® and other soft tissue fillers include redness, bruising, tenderness to touch, lumps/bumps (mass), swelling, firmness (induration), pain after injection, discoloration, and itching.

Treatment-related adverse events (AEs) were reported in the US clinical study by the Treating Investigator at follow-up visits. Among the 148 participants treated with SKINVIVE by JUVÉDERM® (treatment and treated control group participants), 5 participants had 5 treatment-related AEs. These AEs were injection site papule (2.7%, 4/148) and injection site mass (0.7%, 1/148).

Postmarket Surveillance

SKINVIVE by JUVÉDERM® (also known as JUVÉDERM® VOLITE™ XC) has been marketed outside the US since 2016 and in the US since 2023.

The following AEs were received from postmarket surveillance for SKINVIVE by JUVÉDERM® with and without lidocaine with a frequency of 5 events or more in the neck area and were not observed in the clinical study (during the 6 months that participants 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: non-inflammatory nodule, use error, edema, erythema, vascular occlusion, inflammatory nodule, edema (injection site), unsatisfactory result, skin rash (dermatitis), induration, inflammation/irritation, dry skin, pruritus, anxiety (product/procedure), infection, allergic reaction/hypersensitivity, loss of correction, acne, inflammation (injection site irritation), abscess, varied injuries, blister, lack of correction, bleeding, device migration, neurological symptoms such as increase/decrease in sensation, urticaria, ischemia, vision abnormalities, necrosis, overcorrection, hematoma, flu-like symptoms, headache, herpes simplex, autoimmune/connective tissue disorders, incorrect injection placement, scar, cellulitis, cyst, drainage, dyspnea, and vasospasm. No vascular occlusion event was reported for neck treatment.

In many cases, AEs resolved without any treatment. Reported treatments for these events included (in alphabetical order): antibiotics, anticholinergics, anticoagulants, antihistamines, anti-inflammatories, antimetabolites, antivirals, arnica, blood thinners, hyaluronidase, hyperbaric oxygen treatment, ice, laser therapy, massage, radiofrequency therapy, steroids, ultrasound therapy, and warm compress.

Delayed-onset inflammation near the site of soft tissue filler injections is one of the known AEs associated with fillers. Cases of delayed-onset inflammation have been reported to occur at the soft tissue 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 AEs 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 intradermal and/or subdermal injection in the neck region using a needle or needle and cannula to improve neck appearance in adults over the age of 21. There was no change in the raw materials, manufacturing process, product specifications, or shelf life. Therefore, the nonclinical data previously presented in support of PMA P110033/S059 and subsequent supplements remain applicable and are incorporated herein by reference.

X. Summary of Primary Clinical Study

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of intradermal and/or subdermal injections in the neck using microdroplet,

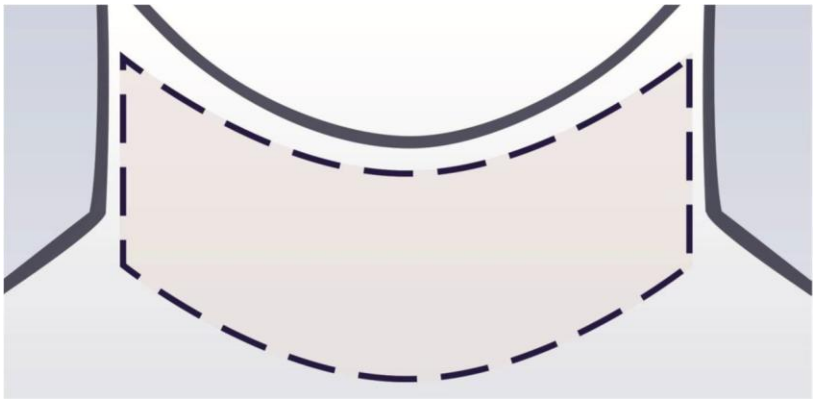
tunneling, or fanning techniques with a needle or a needle and cannula for improvement of neck appearance in the US under IDE G210148. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. STUDY DESIGN

Participants were treated between May 2, 2022 and February 27, 2024. The database for this PMA reflected data collected through December 4, 2024 and included 159 randomized participants. There were 13 investigational sites.

The study was a multicenter, evaluator-blind, randomized, no-treatment controlled pivotal study (2029-701-008) to evaluate the safety and effectiveness of SKINVIVE by JUVÉDERM® for the improvement of neck appearance. The neck treatment area was bounded superiorly by a horizontal line along the hyoid bone, inferiorly by the sternal notch and clavicles, and laterally by vertical lines dropped from each anterior tragus, as depicted in Figure 1.

Figure 1. Neck Treatment Area



Participants were randomized to treatment or no-treatment control in a 2:1 ratio. The 105 treatment group participants underwent treatment with SKINVIVE by JUVÉDERM® at the outset of the study followed by an optional touch-up treatment 30 days after initial treatment, if deemed necessary to achieve optimal improvement, and optional repeat treatment at Month 6.

The 54 no-treatment control participants attended follow-up visits through 6 months during the no-treatment control period. Thereafter, control participants were offered initial and touch-up treatments.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the 2029-701-008 study was limited to patients who met the following key inclusion criteria:

- Age 22 or over and in good general health
- Had *moderate* or *severe* transverse neck lines (Grade 2 or 3 on the Allergan Transverse Neck Lines Scale[1] [ATNLS]) as assessed live by the Evaluating Investigator

Patients were not permitted to enroll in the 2029-701-008 study if they met any of the following key exclusion criteria:

- Could not achieve at least a 1-grade improvement from the Evaluating Investigator's baseline score on the ATNLS given the allowed injection volume, in the opinion of the Treating Investigator
- Had atrophic skin in the neck area that might not be suitable for injection, in the opinion of the Treating Investigator
- Had neck deformity or significant skin laxity with severe redundant folds
- Had ever received permanent soft tissue fillers in the neck area or neck surgeries or procedures
- Had received semi-permanent soft tissue fillers in the neck area within 2 years before enrollment
- Had received HA fillers or autologous fat in the neck area within 12 months before enrollment
- Had received botulinum toxin in the neck area within 6 months before enrollment
- Had received deoxycholic acid injections or cryolipolysis in the submentum area within 6 months before enrollment
- Had a tendency to develop hypertrophic scarring

[1] Jones D, Carruthers A, Hardas B, Murphy DK, Sykes JM, Donofrio L, Carruthers J, Creutz L, Marx A, and Dill S. Development and validation of a photonumeric scale for evaluation of transverse neck lines. *Dermatol. Surg.* 2016; 42:S235-S242.

- Had history of anaphylaxis or allergy to lidocaine (or any amide-based anesthetics), HA products, or *Streptococcal* protein
- Had current cutaneous inflammatory or infectious processes (e.g., acne, herpes), abscess, an unhealed wound, or a cancerous or precancerous lesion on the neck
- Had active autoimmune disease
- Pregnant, nursing, or planning a pregnancy during the study

2. Follow-up Schedule

The follow-up schedule for the treatment group included safety visits at Day 3 (telephone call) and Day 14 after each treatment, and safety and effectiveness visits at Months 1, 2, 4, and 6 after the last treatment (initial or touch-up) and at Months 1, 2, and 4 after optional repeat treatment (**Table 1**).

Control participants attended follow-up visits at Months 1, 2, 4, and 6 during the no treatment- control period. If control participants opted to receive initial treatment and touch-up, their follow-up schedule included safety visits at Day 3 (telephone call) and Day 14 after each treatment, and safety and effectiveness visits at Months 1, 2, 4, and 6 after the last treatment (**Table 1**).

Table 1. Follow-up Visits

Follow-up Period	Treatment Group	Control Group
Control Period	Days 3 and 14 after each treatment, Months 1, 2, 4, 6	Months 1, 2, 4, 6
Optional Treatment Period	N/A	Days 3 and 14 after each treatment, Months 1, 2, 4, 6
Repeat Treatment Period	Days 3 and 14, Months 1, 2, 4	N/A

Adverse events and complications were recorded at all visits.

Pre- and post-procedure, the parameters measured during the study included Evaluating Investigators' assessment of the participants' overall horizontal neck lines severity and improvement in neck appearance using the validated 5-grade photonumeric ATNLS and the 5-point Global Aesthetic Improvement Scale (GAIS), respectively. In addition, participants performed self-assessments on the GAIS, validated FACE-Q *Appraisal of the Neck* questionnaire, and the satisfaction with neck (feel, appearance) and treatment on 4-point scales. Furthermore, the Treating Investigator evaluated treatment characteristics including injection ease and product moldability for initial, touch-up, and repeat treatments, and participants assessed their procedural pain.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

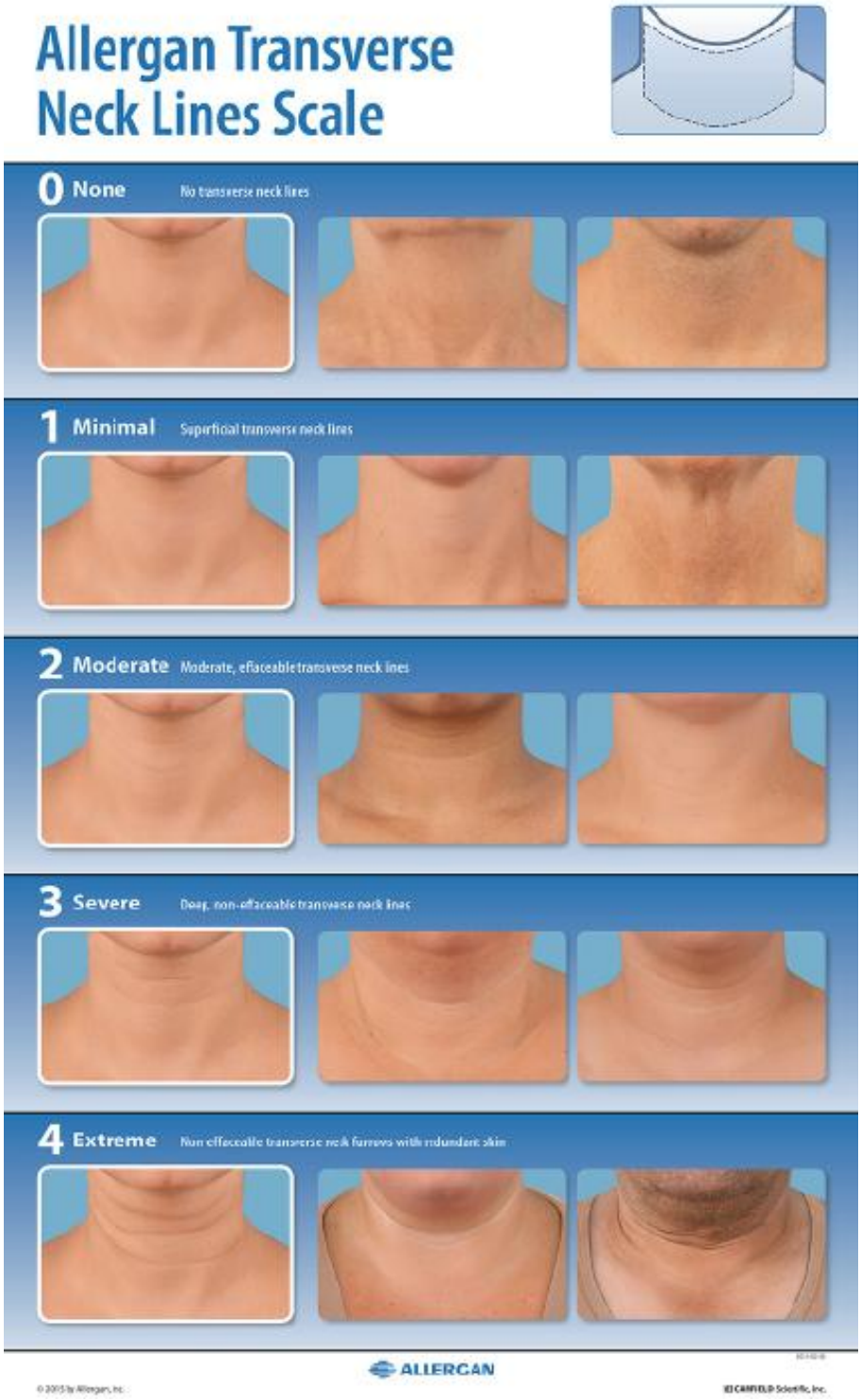
With regards to safety, participants used electronic diaries to record specific signs and symptoms of injection site responses (ISRs) experienced during the 30 days after the initial, touch-up, and repeat treatments. AEs were reported by the TI at follow-up visits.

With regards to effectiveness, the primary effectiveness measure for the study was the responder rate (≥ 1-grade improvement in ATNLS score from baseline) based on the blinded Evaluating Investigator's live assessment of horizontal neck lines using the validated 5-grade ATNLS at Month 1 after the last treatment (initial and touch-up) (**Table 2** and **Figure 2**).

Table 2. Allergan Transverse Neck Lines Scale

Score	Grade	Description
0	None	No transverse neck lines
1	Minimal	Superficial transverse neck lines
2	Moderate	Moderate, effaceable transverse neck lines
3	Severe	Deep, non-effaceable transverse neck lines
4	Extreme	Non-effaceable transverse neck furrows with redundant skin

Figure 2. Allergan Transverse Neck Lines Scale



Key secondary effectiveness measures included participant assessment using the validated *Appraisal of the Neck* module[2] of the FACE-Q™ questionnaire and independent, noncollaborative assessments by both the Evaluating Investigator and the participant of the improvement in the neck area using the 5-point Global Aesthetic Improvement Scale (GAIS).

A gatekeeping procedure was used for the primary endpoint and key secondary effectiveness endpoints following a predefined sequence to control the overall type I error rate at the 0.05 level. Both primary hypotheses had to have been rejected in order to test the secondary effectiveness endpoints in the sequential order specified below:

- Primary endpoint ATNLS responder status at Month 1 after last treatment
    - Between VOLITE and Control groups
    - Within VOLITE group against 50%
- GAIS responder status as assessed by the Evaluating Investigator at Month 1 after last treatment
- Change from baseline of Rasch-transformed score of participant responses to FACE-Q Appraisal of the Neck questionnaire at Month 1 after last treatment
    - Within VOLITE group
    - Between VOLITE and Control groups

Other effectiveness measures included participant assessments of the neck area using the Allergan Neck Satisfaction Scale (ANSS) and Allergan Neck Treatment Outcomes Scale (ANTOS) questionnaires, and MoistureMeterD® instrument measurements of changes in skin hydration in the treatment area.

With regard to success/failure criteria, a responder was defined as a participant with ≥ 1-grade improvement in ATNLS score from baseline. Effectiveness of SKINVIVE by JUVÉDERM® was demonstrated if the responder rate for the treatment group was statistically superior to that for the control group at 1 month and if the lower bound of the 95% CI was greater than 50%.

[2] Klassen AF, Cano SJ, Scott AM, Pusic AL. Measuring outcomes that matter to face-lift patients: development and validation of FACE-Q appearance appraisal scales and adverse effects checklist for the lower face and neck. Plast Reconstr Surg. 2014;133(1):21-30.

B. ACCOUNTABILITY OF PMA COHORT

At the time of database lock, data from all 159 randomized participants were available for analysis. Participant disposition is shown in **Table 3**.

Table 3. Participation Disposition

Disposition	Number of Participants		
	Treatment	Control	Total
Screened	**N/A**	**N/A**	**188**
Screen Failures	**N/A**	**N/A**	**29**
Randomized Participants	**105**	**54**	**159**
Completed Control Period Through 6 Months	**98**	**50**	**148**
Lost to Follow-up	6	3	9
Withdrawal by Participant	1	1	2
Completed Treated Period Through 6 Months (Including Treated Control Group)	**98**	**38**	**136**
Treatment and Control Group – Did Not Receive Optional Repeat Treatment (Completed Study)	**51**	**45**	**96**
Treatment Group – Received Optional Repeat Treatment (SRT Population)	**47[a]**	**N/A**	**47 [a]**
Withdrawal by Participant due to AE	2	N/A	2
Treatment Group – Completed Follow-up Period Through 6 Months After Repeat Treatment (Completed Study)	**45**	**N/A**	**45**

a. One participant was considered as continued into repeat treatment but did not actually receive repeat treatment and withdrew due to an AE.

Analysis Populations

The analysis populations were defined as shown in **Table 4** and summarized in **Table 5**.

Table 4. Analysis Populations Definitions

Population	Definition	Study Treatment Assignment
Intent-to-treat (ITT)	All randomized participants	As randomized
Observed Primary Endpoint	All ITT participants with baseline and Month 1 assessments on the ATNLS	As randomized
Safety	All randomized participants who have at least 1 study intervention (i.e., VOLITE XC or no-treatment)	As treated
SKINVIVE Treated (ST)	• All randomized participants who receive VOLITE XC treatment at the beginning of the control period • All randomized participants who receive optional VOLITE XC treatment after the control period	As treated
SKINVIVE Repeat Treatment (SRT)	Participants in the ST population who receive repeat treatment	As treated

Table 5. Summary of Analysis Populations

Population	Treatment	Control	Total
ITT	105	54	159
Observed Primary Endpoint	95	48	143
Safety	105	54	159
ST	105	43	148
SRT	46	N/A	46

C. STUDY POPULATION DEMOGRAPHICS AND BASELINE PARAMETERS

The demographics of the study population are typical for a pivotal study performed in the US. Participant demographics and pretreatment characteristics of the treatment and controls are presented in **Table 6**.

Table 6. Participant Demographics and Pretreatment Characteristics (ITT Population)

Demographic	Number of Participants		
	Treatment Group (VOLITE XC) N = 105 % (n/N)	Control Group N = 54 % (n/N)	Total N = 159 % (n/N)
Gender			
Female	96.2% (101/105)	98.1% (53/54)	96.9% (154/159)
Male	3.8% (4/105)	1.9% (1/54)	3.1% (5/159)
Age			
Median	52.0	48.0	51.0
Range	26 – 71	26 – 65	26 – 71
Race			
White	79.0% (83/105)	75.9% (41/54)	78.0% 124/159)
Black or African American	4.8% (5/105)	11.1% (6/54)	6.9% (11/159)
Asian	7.6% (8/105)	5.6% (3/54)	6.9% (11/159)
American Indian/Alaska Native	3.8% (4/105)	5.6% (3/54)	4.4% (7/159)
Native Hawaiian/Pacific Islander	1.9% (2/105)	0	1.3% (2/159)
Multiple	2.9% (3/105)	1.9% (1/54)	2.5% (4/159)
Ethnicity			
Hispanic or Latino	35.2% (37/105)	33.3% (18/54)	34.6% (55/159)
Not Hispanic or Latino	64.8% (68/105)	66.7% (36/54)	65.4% (104/159)
Fitzpatrick Skin Phototype*			
I	4.8% (5/105)	3.7% (2/54)	4.4% (7/159)
II	20.0% (21/105)	25.9% (14/54)	22.0% (35/159)
III	41.9% (44/105)	35.2% (19/54)	39.6% (63/159)
IV	21.9% (23/105)	24.1% (13/54)	22.6% (36/159)
V	8.6% (9/105)	5.6% (3/54)	7.5% (12/159)
VI	2.9% (3/105)	5.6% (3/54)	3.8% (6/159)
Baseline ATNLS Scale Score			
Moderate	33.3% (35/105)	40.7% (22/54)	35.8% (57/159)
Severe	66.7% (70/105)	59.3% (32/54)	64.2% (102/159)

*Fitzpatrick skin type classification based on Investigator live assessment of subjects; post-hoc photo assessments for treatment group: I 4.8% (5/105), II 20.0% (21/105), III 29.5% (31/105), IV 29.5 (31/105), V 2.9% (3/105) and VI 1.0% (1/105); for control group: I 3.7% (2/54), II 25.9% (14/54), III 35.2% (19/54), IV 27.8% (15/54), V 1.9% (1/54) and VI 5.6% (3/54); total treatment: I 4.4% (71/159), II 22.0% (35/159), III 39.6% (63/159), IV 28.9% (46/159), V 2.5% (4/159) and VI 2.5% (4/159)

Injections were administered using 32 G ½" needles with or without 25 G 1½" cannulas (48.6% of participants received cannula injections at initial or touch-up treatments). The most common injection technique was microdroplet, and the majority of participants received both subdermal injections and intradermal injections. In the treatment group, the median injection volume was 2.0 mL at initial treatment, 1.45 mL at touch-up treatment, and 1.6 mL at repeat treatment. The median injection volume administered for the treatment group for initial and touch-up treatments combined was 3 mL and ranged from 0.55 to 5 mL.

D. SAFETY AND EFFECTIVENESS RESULTS

1. Safety Results

The analysis of safety was based on the treated population (N = 148) at each follow-up timepoint (3 and 14 days and 1, 2, 4, and 6 months after initial/touch-up treatment; 3 and 14 days, and 1, 2, and 4 months after repeat treatment). The key safety outcomes for this study are presented below in **Table 7** and **Table 8**.

Adverse effects that occurred in the PMA clinical study:

Participants recorded specific signs and symptoms of ISRs in a 30-day electronic diary starting on the day of each initial, touch-up, and repeat treatment. ISRs are reactions associated with the injection procedure. Examples of ISRs are redness, bruising, tenderness to touch, lumps/bumps, swelling, firmness, pain after injection, discoloration, and itching.

Of the 148 participants who underwent treatment (from both the treatment and treated control groups), 147 participants completed the diaries, and of the 102 participants who received touch-up treatment, 100 completed the diaries. All 46 subjects who received repeat treatment also completed the diaries. Participants rated each ISR listed on the diary as *none* (no symptom or not applicable), *mild* (barely noticeable), *moderate* (uncomfortable), or *severe* (severely uncomfortable).

The severity and duration of all ISRs reported by > 5% of participants after initial treatment (from both the treatment and control groups) are summarized in **Table 7**. Most ISRs were mild severity, and their duration was short lasting (14 days or less). In general, ISRs were comparable across the initial, touch-up, and repeat treatments.

Table 7. Injection Site Responses by Severity and Duration After Initial Treatment Occurring in > 5% of Treated Participants (N=147)

ISR	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])	4-7 Days % (n/N[a])	8-14 Days % (n/N[a])	15-30 Days % (n/N[a])	> 30 Days % (n/N[a])
Any ISR	89.8% (132/147)	42.9% (63/147)	42.2% (62/147)	4.8% (7/147)	6.1% (9/147)	22.4% (33/147)	24.5% (36/147)	29.3% (43/147)	7.5% (11/147)
Redness	81.6% (120/147)	63.9% (94/147)	17.0% (25/147)	0.7% (1/147)	59.2% (87/147)	15.6% (23/147)	5.4% (8/147)	1.4% (2/147)	0%
Bruising	77.6% (114/147)	49.7% (73/147)	25.2% (37/147)	2.7% (4/147)	18.4% (27/147)	25.9% (38/147)	29.3% (43/147)	3.4% (5/147)	0.7% (1/147)
Tenderness to Touch	77.6% (114/147)	59.9% (88/147)	17.0% (25/147)	0.7% (1/147)	46.3% (68/147)	18.4% (27/147)	8.2% (12/147)	4.1% (6/147)	0.7% (1/147)
Lumps/Bumps	76.2% (112/147)	46.9% (69/147)	27.2% (40/147)	2.0% (3/147)	23.1% (34/147)	13.6% (20/147)	7.5% (11/147)	25.2% (37/147)	6.8% (10/147)
Swelling	70.7% (104/147)	56.5% (83/147)	13.6% (20/147)	0.7% (1/147)	40.1% (59/147)	18.4% (27/147)	8.8% (13/147)	2.7% (4/147)	0.7% (1/147)
Firmness	64.6% (95/147)	51.0% (75/147)	12.9% (19/147)	0.7% (1/147)	34.0% (50/147)	14.3% (21/147)	9.5% (14/147)	5.4% (8/147)	1.4% (2/147)
Pain After Injection	63.3% (93/147)	50.3% (74/147)	12.2% (18/147)	0.7% (1/147)	44.9% (66/147)	12.2% (18/147)	4.1% (6/147)	1.4% (2/147)	0.7% (1/147)
Discoloration	50.3% (74/147)	39.5% (58/147)	8.8% (13/147)	2.0% (3/147)	28.6% (42/147)	12.9% (19/147)	6.8% (10/147)	2.0% (3/147)	0%
Itching	34.7% (51/147)	29.9% (44/147)	3.4% (5/147)	1.4% (2/147)	21.8% (32/147)	8.2% (12/147)	4.1% (6/147)	0%	0.7% (1/147)

a. N denotes the number of participants 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

AEs were defined in accordance with ISO 14155 as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory finding) in study participants, users, or other persons, whether or not related to the investigational medical device. An AE was considered a treatment-emergent AE (TEAE) if the AE began or worsened (increased in severity or became serious) after first administration of SKINVIVE by JUVÉDERM® for the treatment group and after the date of randomization for the control group. A TEAE was considered a treatment-related TEAE if the event was deemed related to the procedure or the study device by the Treating Investigator.

Among the 148 participants treated with SKINVIVE by JUVÉDERM® (treatment and treated control group participants), 5 participants (3.4%) had 5 mild treatment-related TEAEs (**Table 8**). There were no treatment-related AEs after repeat treatment. All treatment-related TEAEs were at the injection site and resolved without sequelae.

Table 8. Treatment-Related TEAEs by Severity and Outcome

TEAE	Participants % (n/N[a])	Severity			Outcome
		Mild % (n/N[a])	Moderate % (n/N[a])	Severe % (n/N[a])	
Initial/Touch-up Treatment					
Injection Site Papule	2.7% (4/148)	2.7% (4/148)	0%	0%	Resolved without sequelae
Injection Site Mass	0.7% (1/148)	0.7% (1/148)	0%	0%	Resolved without sequelae
Repeat Treatment					
None	N/A	N/A	N/A	N/A	N/A

There were 2 treatment-related TEAEs that began more than 30 days after initial/touch-up treatment: 1 mild injection site mass with onset 135 days after initial treatment that resolved in 8 days with massage, and 1 mild injection site papule with onset 178 days after initial treatment that resolved in 345 days without treatment. Neither of these were inflammatory reactions.

Safety Subgroup Analyses

Subgroup analyses for TEAEs were performed based on injection volumes and injections with and without cannula. As shown in **Table 9** and **Table 10** below, less than 7% of treated participants experienced a treatment-related TEAE in all subgroups, and there were none in the group receiving injections via cannula. Overall ISR rates were also similar for injections with and without cannula.

Table 9. Treatment-Related TEAEs by Median Volume Injected (3 mL) for Initial and Touch-Up Treatments Combined

TEAEs	≤ Median Volume Injected (N = 61)		> Median Volume Injected (N = 44)	
	Participants % (n)	Mild % (n)	Participants % (n)	Mild % (n)
Overall	6.6% (4)	6.6% (4)	2.3% (1)	2.3% (1)
Injection Site Papule	4.9% (3)	4.9% (3)	2.3% (1)	2.3% (1)
Injection Site Mass	1.6% (1)	1.6% (1)	0%	0%

Table 10. Treatment-Related TEAEs by Injection with and without Cannula for Initial and Touch-Up Treatments Combined

TEAEs	Needle Only (N = 78)		Needle + Cannula (N = 70)	
	Participants % (n)	Mild % (n)	Participants % (n)	Mild % (n)
Overall	6.4% (5)	6.4% (5)	0%	0%
Injection Site Papule	5.1% (4)	5.1% (4)	0%	0%
Injection Site Mass	1.3% (1)	1.3% (1)	0%	0%

Other Safety Assessments

Procedural Pain

Participants assessed procedural pain (pain during injection) immediately after completion of each treatment on an 11-point scale ranging from 0 (no pain) to 10 (worst pain imaginable). Pain was minimal, with mean treatment group scores of 1.9 for initial treatment, 2.3 for touch-up treatment, and 2.0 for repeat treatment. A total of 88.6% of participants received ice and/or topical anesthesia prior to initial treatment.

Vision Assessments

Snellen visual acuity showed that over 95% of participant eyes had the same or better visual acuity at all post-treatment assessments. No participant eyes showed a ≥ 3-line worsening in visual acuity related to treatment at any assessment, and none of the vision changes were related to intravascular injection.

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 effectiveness was based on the ITT population comprising 105 participants in the treatment group and 54 participants in the control group. The key effectiveness outcomes are presented in **Table 11** and **Table 12** below.

Primary Effectiveness Results

Success criteria for the primary endpoint were met. At 1 month after initial or optional touch-up treatment, the ATNLS responder rate for the treatment group based on a single blinded evaluator's live assessment (74.8%, 95% CI 66.20%-83.39%) was statistically superior ($p < 0.0001$) to that for the no-treatment control group (16.1%, 95% CI 5.70%-26.52%) in the ITT population , with the lower bound of the 95% CI exceeding 50% (**Table 11**).

Table 11. Primary Endpoint Results of ATNLS Responder Rates at Month 1 (ITT Population)

Analysis Population	Treatment Group Responder Rate % (n/N[a]) (95% CI)	Control Group Responder Rate % (n/N[a]) (95% CI)	Difference (Device-Control) % (95% CI)	p-value
ITT (with multiple imputation)[a]	74.8% (78.5/105) (66.20%, 83.39%)	16.1% (8.7/54) (5.70%, 26.52%)	58.7% (45.23%, 72.13%)	<.0001
Observed Primary Endpoint[b]	76.8% (73/95) (67.06%, 84.88%)	14.6% (7/48) (6.07%, 27.76%)	62.3% (46.23%, 74.21%)	N/A

[a] Missing primary endpoint data was imputed by treatment group using a multiple imputation model with age, sex, Fitzpatrick skin type, body mass index, site, and baseline ATNLS as covariates
[b] Number of participants with data at baseline and the specified timepoint

The blinded Evaluating Investigator ATNLS observed responder rates remained high at Month 1 (76.8%), Month 2 (78.0%), Month 4 (75.0%), and Month 6 (66.0%) after initial/touch-up treatment and remained above 88.1% after repeat treatment (**Table 12**).

Table 12. ATNLS Responder Rates Based on Observed Data (ITT and SRT Populations)

Timepoint After Initial/Touch-up Treatment	Treatment Group Responder Rate % (n/N[a])	Control Group Responder Rate % (n/N[a])
1 Month	76.8% (73/95)	14.6% (7/48)
2 Months	78.0% (78/100)	12.2% (5/41)
4 Months	75.0% (69/92)	9.5% (4/42)
6 Months	66.0% (64/97)	9.1% (4/44)
1 Month after Repeat Treatment	88.1% (37/42)	N/A
2 Months after Repeat Treatment	88.6% (39/44)	N/A
4 Months after Repeat Treatment	84.4% (38/45)	N/A

[a] Number of participants with data at baseline and the specified timepoint

3. Subgroup Analyses

The following baseline characteristics were evaluated for potential association with safety and effectiveness outcomes: sex, age, race, Fitzpatrick skin type, baseline ATNLS severity, injection volume, and injection with needle and needle and cannula.

The results of these analyses support the safety and effectiveness across these various subgroups. The study was not specifically powered for these subgroups.

Subgroup analyses of the observed Month 1 ATNLS responder rates appear to be similar between treatment groups across men and women of all races, Fitzpatrick skin types, and age groups studied, and for injections with needle and needle and cannula (**Table 13**).

Table 13. Subgroup Analyses of ATNLS Responder Rates Based on Observed Data at Month 1 (ITT Population)

Subgroup	Treatment Group % (n/N[a])	Control Group % (n/ N[a])
Baseline ATNLS Moderate	64.5% (20/31)	14.3% (3/21)
Baseline ATNLS Severe	82.8% (53/64)	14.8% (4/27)
Injection volume ≤ Median (3 mL)	85.2% (46/54)	N/A
Injection volume > Median (3 mL)	65.9% (27/41)	N/A
Injection with needle only	83.7% (41/49)	N/A
Injection with needle and cannula	69.6% (32/46)	N/A
Female	76.1% (70/92)	14.9% (7/47)
Male	100% (3/3)	0% (0/1)
White	75.0% (57/76)	16.7% (6/36)
Black or African American	100% (4/4)	0% (0/5)
Asian	71.4% (5/7)	0% (0/3)
American Indian or Alaska Native	100% (4/4)	33.3% (1/3)
Native Hawaiian or Pacific Islander	100% (2/2)	N/A
Multiple	50.0% (1/2)	0% (0/1)
Fitzpatrick I/II	76.0% (19/25)	28.6% (4/14)
Fitzpatrick III/IV	75.4% (46/61)	10.3% (3/29)
Fitzpatrick V/VI	88.9% (8/9)	0% (0/5)
≤ median age (51 years)	79.6% (43/54)	14.8% (4/27)
> median age (51 years)	73.2% (30/41)	14.3% (3/21)

a. Number of participants with data in specified subgroup

Secondary Effectiveness Results

The blinded EI GAIS responder rate (*improved* or *much improved*) at Month 1 was significantly better ($p < 0.0001$) for the treatment group 85.8% (90.1/105) than for the no-treatment control group 14.9% (8.1/54) based on multiple imputation for missing data in the ITT population. The participant GAIS responder rate was 89.4% (84/94) at Month 1 in the ITT population. The GAIS responder rates for the treatment group remained above 78% at all timepoints for both EI and participant assessments based on observed data (**Table 14**).

Table 14. GAIS Responder Rates Based on Observed Data (ITT and SRT Populations)

Timepoint After Treatment	Treatment Group (VOLITE XC) EI Responder Rate % (n/N[a])	Treatment Group (VOLITE XC) Participant Responder Rate % (n/N[a])	Control Group EI Responder Rate % (n/N[a])
1 Month	88.3% (83/94)	89.4% (84/94)	12.5% (6/48)
2 Months	89.0% (89/100)	85.9% (85/99)	9.8% (4/41)
4 Months	92.4% (85/92)	83.7% (77/92)	11.9% (5/42)
6 Months	80.4% (78/97)	78.4% (76/97)	9.1% (4/44)
1 Month after Repeat Treatment	95.2% (40/42)	92.9% (39/42)	N/A
2 Months after Repeat Treatment	97.7% (43/44)	81.8% (36/44)	N/A
4 Months after Repeat Treatment	95.6% (43/45)	86.7% (39/45)	N/A

a. Number of participants with data at the specified timepoint

The mean score on the *Appraisal of the Neck* module of the FACE-Q questionnaire for the treatment group improved from 45.2 at baseline by a mean of 25.7 to 70.2 at Month 1 (after initial treatment or optional touch-up) ($p < 0.0001$ based on multiple imputation for missing data in the ITT population) and 63.3 at Month 6 (based on observed data). These mean scores indicate that participants were less bothered by their neck after treatment with SKINVIVE by JUVÉDERM®. In the no-treatment control group, the mean score was 43.4 at baseline and was similar at Month 1 (mean of 42.9). The observed treatment group responder rate (participants who demonstrated improvement from baseline in overall score) for the treatment group remained above 78% at all timepoints (**Table 15**).

Table 15. FACE-Q Responder Rates Based on Observed Data (ST and SRT Populations)

Timepoint After Treatment	Treatment Group (VOLITE XC) Responder Rate % (n/N[a])
1 Month	89.2% (83/93)
2 Months	93.8% (91/97)
4 Months	84.8% (78/92)
6 Months	78.4% (76/97)
1 Month after Repeat Treatment	90.5% (38/42)
2 Months after Repeat Treatment	95.3% (41/43)
4 Months after Repeat Treatment	88.9% (40/45)

a. Number of participants with data at baseline and the specified timepoint

The treatment group satisfaction results from the individual questions of the FACE-Q *Appraisal of the Neck* questionnaire, which contribute to the overall score, ranged from 21% to 57.1% at baseline, from 71.0% to 87.1% at Month 1, and from 60.8% to 77.3% at Month 6 (**Table 16**).

Table 16. FACE-Q *Appraisal of the Neck* Questionnaire Questions (ST Population – Treatment Group)

Percentage of Participants who were *not at all* or *a little* bothered with:	% of Participant Responses at Baseline (N = 105) (n)	% of Participant Responses at Month 1 (N = 93) (n)	% of Participant Responses at Month 6 (N = 97) (n)
Having to cover up their neck with clothing	57.1% (60)	87.1% (81)	77.3% (75)
How their neck looks compared with other people their age	34.3% (36)	87.1% (81)	71.1% (69)
How deep the horizontal lines on their neck are	21.0% (22)	79.6% (74)	71.1% (69)
How their neck looks in collared shirts	43.8% (46)	84.9% (79)	75.3% (73)
Hanging skin on their neck	49.5% (52)	87.1% (81)	75.3% (73)
How their neck looks when they grimace	39.0% (41)	81.7% (76)	72.2% (70)
How their neck looks in profile	30.5% (32)	78.5% (73)	67.0% (65)
How wrinkled their neck skin looks	34.3% (36)	80.6% (75)	62.9% (61)
How old their neck makes them look	21.0% (22)	71.0% (66)	60.8% (59)
Sagging skin on their neck	42.9% (45)	83.9% (78)	73.2% (71)

Other Effectiveness Results

Other effectiveness assessments included skin hydration measurements from the MoistureMeter® D instrument, participant assessments of satisfaction with the treatment result and look and feel, and assessment of willingness to recommend treatment. As summarized in **Table 17**, the other effectiveness assessments showed observed satisfaction rates above 68.4% with neck skin smoothness (crepiness) post-treatment based on participant-reported improvements, and an observed objective mean increase from baseline of 4.6% in the percentage of water content in the skin at the 1-month primary timepoint based on the MoistureMeter® D measurements. Objective instrument observed measurements showed higher skin hydration scores compared to baseline at Month 2 (6.6%), Month 4 (3.6%), and Month 6 (1.4%) after initial/touch-up SKINVIVE by JUVÉDERM® treatment.

Table 17. Additional Treatment Group Effectiveness Results (ST Population)

Assessment	Month 1
MoistureMeter® D Instrument	
Percentage of Water Content (Mean Increase from Baseline)	4.6%
ANSS Questionnaire	
Participant Satisfaction with Natural Look (% *Satisfied* or *Very Satisfied*)	85.3%
Participant Satisfaction with Feel (% *Satisfied* or *Very Satisfied*)	83.2%
Participant Satisfaction with Smoothness (% *Satisfied* or *Very Satisfied*)	73.7%
Participant Happiness with Neck (% *Moderately* or *Very Happy*)	68.4%
ANTOS Questionnaire	
Participant Satisfaction with Treatment (% *Mostly Satisfied* or *Very Satisfied*)	71.6%
Participant Willingness to Recommend Treatment (% *Moderately*, *Quite a Bit*, or *Extremely* likely)	87.4%

Independent Photographic Assessment

An independent photographic assessment was conducted to evaluate the treatment of SKINVIVE by JUVÉDERM® in participants' necks. Three independent, blinded raters who did not participate in the pivotal study individually assessed evaluable pairs of baseline and Month 1 images displayed side by side from participants with the primary effectiveness measure, ATNLS, at both timepoints. For each randomized image pair, raters selected 1 of 3 options with regards to neck appearance: photo A looks clinically better, photo B looks clinically better, or no clinical difference, without knowing which image was post-treatment.

Photographs for 142 participants (94 in treatment group, 48 in control group) were assessed, and clinical improvement was achieved if at least 2 out of 3 blinded raters assessed the Month 1 image as clinically better than baseline. The Month 1 clinical improvement rate for the treatment group (68.1%, 64/94, 95% CI 57.67%-77.33%) was significantly better ($p < 0.0001$) than that for the no-treatment control group (14.6%, 7/48, 95% CI 6.07%-27.76%), with the point estimate greater than 50%. Thus, the independent photographic assessment provided support for the clinical improvement in neck appearance after SKINVIVE by JUVÉDERM® treatment that was observed in the pivotal study.

4. Pediatric Extrapolation

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

XI. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR §54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 31 investigators, of which none of the investigators were full-time or part-time employees of the sponsor, and 8 investigators had disclosable financial interests/arrangements as defined in 21 CFR §54.2(a), (b), (c), and (f) as described below.

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: no investigators
- Significant payment of other sorts: 8 investigators
- Proprietary interest in the product tested held by the investigator: no investigators
- Significant equity interest held by investigator in sponsor of covered study: no investigators

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.

XII. Summary of Supplemental Clinical Information

European Clinical Study (V12-001)

A prospective, single-arm study was conducted in France with injecting physicians from 6 countries to evaluate the safety and effectiveness of SKINVIVE by JUVÉDERM® without lidocaine for treatment of fine lines and improvement of skin quality. A total of 131 participants were treated with VOLITE without lidocaine on the face, and 96 were also treated on the neck. Touch-up treatment, if needed to correct asymmetry, occurred approximately 30 days after the initial treatment. Participants were followed for 9 months

after the last treatment. An optional repeat treatment was offered to participants at Month 9, with a follow-up visit 1 month after the repeat treatment.

1. Safety Results

ISRs after initial treatment in the neck were mostly mild severity and resolved within 1 week (**Table 18**). The incidence, severity, and duration of ISRs reported after repeat treatment were similar to or better than those reported after initial treatment.

Table 18. Injection Site Responses by Severity and Duration After Initial Treatment in the Neck with SKINVIVE by JUVÉDERM® without Lidocaine (Study V12-001)

ISR	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])	4-7 Days % (n/N[a])	8-14 Days % (n/N[a])	15-30 Days % (n/N[a])
Any ISR	91.7% (88/96)							
Redness	60.4% (58/96)	37.5% (36/96)	20.8% (20/96)	2.1% (2/96)	39.6% (38/96)	17.7% (17/96)	3.1% (3/96)	0%
Pain After Injection	20.8% (20/96)	16.7% (16/96)	4.2% (4/96)	0%	18.8% (18/96)	2.1% (2/96)	0%	0%
Tenderness to Touch	25.0% (24/96)	21.9% (21/96)	3.1% (3/96)	0%	13.5% (13/96)	11.5% (11/96)	0%	0%
Firmness	21.9% (21/96)	17.7% (17/96)	4.2% (4/96)	0%	17.7% (17/96)	4.2% (4/96)	17.7% (17/96)	17.7% (17/96)
Swelling	32.3% (31/96)	30.2% (29/96)	2.1% (2/96)	0%	26.0% (25/96)	4.2% (4/96)	0%	2.1% (2/96)
Lumps/ Bumps	45.8% (44/96)	31.3% (30/96)	12.5% (12/96)	2.1% (2/96)	17.7% (17/96)	12.5% (12/96)	8.3% (8/96)	7.3% (7/96)
Bruising	66.7% (64/96)	39.6% (38/96)	21.9% (21/96)	5.2% (5/96)	13.5% (13/96)	22.9% (22/96)	29.2% (28/96)	1.0% (1/96)
Itching	8.3% (8/96)	7.3% (7/96)	1.0% (1/96)	0%	6.3% (6/96)	1.0% (1/96)	1.0% (1/96)	0%
Discoloration	8.3% (8/96)	7.3% (7/96)	1.0% (1/96)	0%	6.3% (6/96)	1.0% (1/96)	1.0% (1/96)	0%

a. N denotes the number of participants who recorded responses in the diaries after initial treatment
b. Maximum severity reported in the diary
c. Maximum reported successive occurrence of an ISR

AEs were recorded when observed by the Investigator or reported by participants. After initial treatment (or touch-up treatment, if performed), treatment-related TEAEs were reported in 16.0% of participants (21/131) overall (including cheek, forehead, and neck injections). These TEAEs included injection site mass (9.2%, 12/131 participants), hemorrhage (3.1%, 4/131), bruising (1.5%, 2/131), hematoma (1.5%, 2/131), erythema (0.8%, 1/131), nodule (0.8%, 1/131), and oral herpes (0.8%, 1/131). All treatment-related TEAEs were mild to moderate in severity. Most treatment-related AEs required no action to be taken and resolved without sequelae. One participant experienced 2 events of moderate injection site nodule and erythema on the neck that began 122 days after treatment and received treatment with oral methylprednisolone. All treatment-related TEAEs resolved without sequelae. No treatment-related AEs were reported after repeat treatment.

2. Effectiveness Results

Significant improvement was shown in smoothness and fine lines on the cheeks based on validated photonumeric scales. Results presented herein focus on the validated FACE-Q *Satisfaction with Skin* questionnaire and treatment recommendation question, which were global assessments, as well as on skin hydration and other instrument measurements as these were performed on all treatment areas, including the neck.

Participants assessed satisfaction with their skin using the validated FACE-Q *Satisfaction with Skin* questionnaire. There was a statistically significant improvement ($p < 0.001$) from baseline in mean overall score at all timepoints through 9 months and 1 month after repeat treatment. The responder rate (participants who demonstrated improvement from baseline in overall score) stayed high from Month 1 (90.8%) to Month 6 (83.6%), Month 9 (75.8%), and Month 1 after repeat treatment (91.9%).

At Month 1, 87.0% of participants would recommend the treatment to a friend, and it stayed high to Month 6 (84.1%), Month 9 (86.7%), and Month 1 after repeat treatment (96.8%).

Skin hydration in the cheeks, forehead, and neck were measured using the MoistureMeter® D instrument (same tool used in the US pivotal neck study). The measurements showed an increase in all treatment areas through 9 months, which indicates improved skin hydration (**Table 19**).

Table 19. Study V12-001 MoistureMeterD® Skin Hydration Results

Treatment Area	Depth	Mean Change from Baseline in Total Dielectric Constant (unitless)				
		1 Month	4 Months	6 Months	9 Months	1 Month after Repeat Treatment
Cheek	0.5 mm	1.58	3.12	3.07	2.83	1.64
	1.5 mm	1.15	3.37	3.49	2.97	1.85
Forehead	0.5 mm	0.65	1.72	1.65	1.20	0.06
	1.5 mm	0.48	1.07	0.94	0.75	0.21
Neck	0.5 mm	0.94	1.92	1.87	1.49	1.68
	1.5 mm	1.01	1.61	1.81	1.03	0.57

Other instrument measures performed on the neck included the Fringe Project System for skin smoothness, Cutometer for elasticity, and the DermaScan C for skin thickness. Results from these instruments showed improvement in skin crepiness (skin smoothness, elasticity, and thickness) at 1 month after initial/touch-up treatment.

XIII. Panel Meeting Recommendation and FDA's Post-Panel Action

In accordance with the provisions of section 515(c)(3) of the act as amended by the safe medical devices act of 1990, this PMA was not referred to the general and plastic surgery devices advisory panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. Conclusions Drawn from the Clinical Study

E. EFFECTIVENESS CONCLUSIONS

The data submitted provide a reasonable assurance that the device is effective for improving neck appearance. The specific conclusions from the pivotal study are as follows:

- The primary endpoint was met that the Month 1 ATNLS responder rate for the treatment group (74.8%, 78.5/105) was clinically relevant and statistically superior

($p < 0.0001$) to that for the no-treatment control group (16.1%, 8.7/54), with the lower bound of the 95% CI for the treatment group exceeding 50%.

- The secondary endpoints were met:
    - At Month 1 the overall mean score on the FACE-Q *Appraisal of the Neck* questionnaire was 70.2 for the treatment group, improved by a mean of 25.7 from baseline, which was significantly better ($p < 0.0001$) than that for the no-treatment control group.
    - At Month 1 the Evaluating Investigator GAIS responder rate for the treatment group (85.8%, 90.1/105) was significantly better ($p < 0.0001$) than that for the no-treatment control group (14.9%, 8.1/54).
    - At Month 1 the participant GAIS responder rate for the treatment group was high (89.4%, 84/94).
- Two-thirds of treatment group participants 66.0% (64/97) showed continued improvement in neck lines (≥1-grade ATNLS improvement based on blinded Evaluating Investigator's assessment) at 6 months after initial/touch-up treatment.
- Participants were significantly less bothered with their overall neck appearance compared to baseline ($p < 0.0001$) at 1 month after SKINVIVE by JUVÉDERM® neck treatment based on the FACE-Q *Appraisal of the Neck* questionnaire and the FACE-Q Appraisal of the Neck responder rate at 6 months was 78.4% (76/97) for the treatment group.
- Over 85% of participants had overall aesthetic improvement at 1 month after SKINVIVE by JUVÉDERM® treatment, and the improvement lasted through 6 months (EI GAIS: 80.4% (78/97) and Participant GAIS: 78.4% (76/97) at 6 months after initial/touch-up treatment) based on Evaluating Investigator and participant GAIS assessment of the neck.
- Over 80% of participants were not at all or a little bothered by having to cover up their neck with clothing, how their neck looks compared with other people their age, or how wrinkled their neck skin looks at 1 month after SKINVIVE by JUVÉDERM® neck treatment based on the FACE-Q *Appraisal of the Neck* questionnaire.
- Over 80% of participants were satisfied with how their neck felt to the touch, how natural their neck appeared, and would recommend SKINVIVE by JUVÉDERM® neck treatment.

- Objective instrument observed measurements showed higher skin hydration scores compared to baseline at Month 1 (4.6%) and Month 6 (1.4%) after initial/touch-up SKINVIVE by JUVÉDERM® treatment.
- Participant responses to patient-reported outcome questionnaires showed observed satisfaction rates above 68.4% with neck skin smoothness (crepiness).
- At Month 6, repeat treatment required approximately half the initial/touch-up injection volume (1.6 mL versus 3.0 mL), and it resulted in an ATNLS responder rate of 88.1% at Month 1
- At Month 6, repeat treatment required approximately half the initial/touch-up injection volume (1.6 mL versus 3.0 mL), and it resulted in an ATNLS responder rate of 88.1% at Month 1
- Subgroup analyses of the observed Month 1 ATNLS responder rates appear to be similar between treatment groups across men and women of all races, Fitzpatrick skin types, and age groups studied, and for injections with needle and cannula

F. SAFETY CONCLUSIONS

The risks of the device are based on data collected in the clinical study conducted to support the indication expansion, as well as evaluation of device use in the postmarket setting. The data submitted provide a reasonable assurance that the device is safe for intradermal or subdermal injection with a needle or needle and cannula in the neck to improve neck appearance in adults over the age of 21. The specific conclusions from the pivotal study are as follows:

- For initial, touch-up, and repeat treatments, most ISRs were mild in severity and resolved within 2 weeks.
- The most common ISRs were redness, bruising, tenderness to touch, and lumps/bumps.
- Participants assessed procedural pain during injection as minimal.
- The most common treatment-related TEAE after initial/touch-up treatment was injection site papule, with all others occurring in less than 1% of participants.
- All treatment-related TEAEs were mild in severity and resolved without sequelae.
- No treatment-related TEAEs occurred after repeat treatment.

- There were no deaths, unanticipated adverse device effects, or treatment-related serious AEs.
- SKINVIVE by JUVÉDERM® neck treatment did not compromise vision.
- Subgroup analyses of ISRs and treatment-related TEAEs demonstrated that SKINVIVE by JUVÉDERM® treatment for neck lines is safe with both needle and needle and cannula.

G. BENEFIT-RISK CONCLUSIONS

The probable benefits of the device are based on the data collected in the pivotal clinical study conducted to support PMA approval of the neck indication as described above. The results of the 2029-701-008 study demonstrated the effectiveness of SKINVIVE by JUVÉDERM® for improvement of neck appearance. The predefined primary endpoint was met in that the treatment group ATNLS responder rate at 1 month was statistically superior ($p < 0.0001$) to that for the no-treatment control group, and the lower bound of the 95% CI exceeded 50%.

The key secondary effectiveness endpoints further demonstrated that SKINVIVE BY JUVÉDERM® is effective for improvement of neck appearance based on patient-reported outcome measures and other subjective and objective measures. The treatment versus no-treatment control difference in overall scores on the FACE-Q *Appraisal of the Neck* questionnaire was significantly greater ($p < 0.0001$) at 1 month after initial or optional touch-up treatment, and FACE-Q Appraisal of the Neck responder rate at 6 months was 78.4% (76/97) for the treatment group. Based on Evaluating Investigator and participant GAIS assessments, over 85% of treatment group participants had overall aesthetic improvement of their neck at Month 1, and improvement was observed through 6 months (EI GAIS: 80.4% (78/97) and participant GAIS: 78.4% (76/97) at 6 months after initial/touch-up treatment).

The probable risks of the device are based on the data collected in the pivotal clinical study conducted to support PMA approval of the neck indication as described above. The clinical study results demonstrated that the safety profile of SKINVIVE by JUVÉDERM® injection for improvement of neck appearance is acceptable and consistent with other approved JUVÉDERM® products. Most participants in the clinical study experienced common ISRs, such as redness, bruising, tenderness to touch, and lumps/bumps after treatment. All TEAEs were mild in nature and resolved without sequelae. There were 2 treatment-related TEAEs that began more than 30 days after treatment (mild injection site mass and papule) that resolved without sequelae, neither of which were inflammatory reactions. Furthermore, there were no treatment-related serious AEs and no unanticipated AEs.

1. Patient Perspective

Patient perspectives considered during the review included:

- The mean change from baseline at Month 1 in the FACE-Q *Appraisal of the Neck* score was 25.7 for the treatment group compared to -0.7 for the no-treatment control group.
- The participant GAIS responder rate at Month 1 for the treatment group was 89.4%.

The data support a favorable benefit-risk profile of SKINVIVE by JUVÉDERM® for intradermal and/or subdermal injection with a needle or a needle and cannula in the neck to improve neck appearance in adults over the age of 21.

H. 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. The data demonstrate the benefits of SKINVIVE by JUVÉDERM® to reduce neck lines for improvement of neck appearance outweigh the risks, and the intended patient populations will achieve clinically significant results. The benefits and risks of soft tissue fillers are sufficiently well understood for patients to make informed decisions about their use.

XV. CDRH Decision

CDRH issued an approval order on June 11, 2026. The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality Management System (QMSR) regulation (21 CFR 820).

XVI. Approval Specifications

Directions for Use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.