CONTOUR Registry Study Protocol

Study No: ATX-101-15-40M

Study Title: CONTOUR: **Con**dition of Submental Fullness and **T**reatment **Ou**tcomes **R**egistry (A Registry of Submental Fullness, Treatment Options Administered, and Associated Outcomes)

Clinical Phase: 4

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PROTOCOL SYNOPSIS

Title	CONTOUR: **Con**dition of Submental Fullness and **T**reatment **Ou**tcomes **R**egistry (A Registry of Submental Fullness, Treatment Options Administered, and Associated Outcomes)
Protocol Number	ATX-101-15-40M
Phase	4
Objectives	The primary objective of this registry is to develop a comprehensive understanding of the condition of submental (SM) fullness due to submental fat (SMF), how it is treated in current clinical practice, and the risks and benefits associated with its treatment. This objective will be accomplished through the systematic collection of data on the following: • Practice patterns of physicians with patients who have SMF concerns • The population of patients who are eligible for SMF reduction treatment • Eligible patients who elect SMF reduction treatment • Treatment procedures • Treatment outcomes • Safety profile through adverse event reporting of the SMF reduction treatments administered
Study Design	This is a prospective, observational, multi-center registry. Patients enrolled in this study will provide information related to the condition and treatments of interest and will permit their physicians to provide any available data concerning their condition status and treatment, as indicated in the table of Data for Collection.
Treatment Procedures	The eligibility of patients for treatment, and the treatment administered, will be determined by the physician. Treatments will be administered by the physician or qualified designee (other care provider, such as nurse practitioner or physician assistant) according to their directions at each center.
Rationale	SM fullness associated with the accumulation of SMF can influence negative self-perception. While the SM region is visually important, at present, only surgical options (cosmetic surgery, liposuction) are available to reduce SMF. Currently available injectable products, ie, botulinum toxins and dermal fillers, are employed primarily in the aesthetic rejuvenation of the upper and mid-face and do not adequately address contouring the SM region. The use of energy based devices for lipolysis has been investigated as a less invasive approaches; but may still require accompanying surgery in more severely affected cases, and safety concerns remain. Recently, a pharmacologic treatment, deoxycholic acid injection (ATX-101) was approved by the FDA for improvement in the appearance of moderate to severe convexity or fullness associated with submental fat in adults. This registry will gather information on patterns of use and outcomes of treatments for SM fullness by reduction of SMF, beginning with currently used methods, and including newly approved products as they become adopted into the practice.
Duration of Registry	Data collection is anticipated to continue for approximately 15 months. The duration of individual patient participation will vary depending on the chosen treatment method and individual requirements.

Patient Population and Key Selection Criteria	• Adult male and female patients, aged 18 years and above, presenting with SM fullness due to the accumulation of unwanted SMF, and considered by their treating physician to be a candidate to receive treatment of SM fullness by reduction of SMF. If the patient decides to participate, then the following will be performed or assessed: • Signed informed consent and medical records release • No severe skin laxity, defined as superficial wrinkling, loose skin separated from deeper neck structures, and/or marked skin redundancy (draping and/or sagging), per the physician's judgment • No other cause of fullness in the SM region (eg, thyroid enlargement, cervical adenopathy) other than localized SMF • Not participating in an interventional clinical study, currently or within 30 days before enrollment • Did not previously participate in an interventional clinical study involving ATX-101
Number of Patients	Approximately 1000 patients will be recruited from approximately 100 sites in the US and Canada.
Study Procedures	Details of the physician's practice setting will be recorded once for each site; treatment logistics will be recorded at the first treatment session for each patient . Patients considering treatment for improvement of SM fullness due to SMF will be recruited. Eligible patients will be enrolled in the registry and data will be collected from patients who elect treatment until their SMF reduction treatment is completed or discontinued. Patients who do not initially elect treatment will be followed to determine whether or not they subsequently undergo treatment, and if not, until up to one year has elapsed since enrollment and no treatment has been elected. Physicians will treat and assess patients according to their discretion. At enrollment, data on previous relevant SMF and facial aesthetic treatment(s) will be collected from the patients, and as necessary, their medical records, along with baseline SMF assessments and information on treatment goals. Demography (birth date, sex, race, ethnic origin), Clinical Information (height, weight, lifestyle habits), and a brief medical history (including diabetes, cardiovascular disease) will be collected, Information including treatment received for SMF reduction, treatment procedures and outcomes, follow-up assessments of SMF, and adverse events (AEs) will be recorded at subsequent clinic visits or telephone contacts (Data for Collection). Patient medical history data will be updated, as appropriate, at the first treatment visit.
Data Collection Procedures	Electronic data capture (EDC) will be used for participating sites to record clinical data, data questionnaires and assessment data via electronic case report forms (eCRFs) accessed through a secure internet portal. Data entry screens will be designed to efficiently capture the desired data elements from patient medical records (Data for Collection).
Data Elements	**Physician Practice Profile** At each site, the physician will complete the Physician Practice Setting Questionnaire, including the following information: • Physician characteristics: - Clinical history / specialty, including board certification - Years of aesthetic practice - Percent of practice focused on facial aesthetics - Physician approach to discussing new treatment options - Number and roles of physicians and other healthcare providers (HCPs) in the

practice

- Aesthetic treatment options, including options for reducing SMF, offered by the clinic: types and relative frequencies
- Consent and intake details pertaining to aesthetics and chin and neck (cervicomental) region.
- Percent of patients presenting with SMF concerns and percent receiving SMF reduction treatment
- Referral of patients for SMF reduction treatment to or from other physicians

Patient Population (all patients)

Upon confirmation of eligibility and signed informed consent, the following information will be collected at the Enrollment visit for all patients:

- Informed consent / medical records release
- Demography & Clinical Information (birth date, sex, race, ethnic origin, height, weight, , lifestyle habits)
- Brief medical history (including diabetes, cardiovascular disease)
- Patient treatment history:
    - Previous facial aesthetic treatment(s) within past 24 months:
    - Treatment type (eg, toxins, fillers, devices, cosmetic surgery)
    - Location of treatment (eg. face, chin/neck)
- Patient Treatment Goals Questionnaire:
- History of SMF concern
- Patient's treatment goals in terms of aesthetic outcome
- Physician Treatment Goals Questionnaire
  - Physician's treatment goal in terms of aesthetic outcome
- Enrollment SMF assessments:
- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG) score
- Subject Self Rating Scale (SSRS) score
- Self-perception of age (SPA) scale score

Should a patient elect to receive treatment for SMF reduction, the site will also record:

- Treatment decision date(s)
- SMF reduction treatment type(s) selected

Treatment Logistics (treated patients)

At each site, for patients who elect treatment for SMF reduction (treated patients), the physician or designee will complete the following questionnaires and scales at the first treatment session(s) for each treatment selected (unless otherwise stated) for all treated patients:

- **Treatment Logistics Questionnaire**

Completed at the first treatment session for patients who elect treatment for SMF reduction (treated patients):

- Time spent by HCPs with patients, discussing treatment details and expectations
- HCP who prepared the treatment materials/equipment, HCP who prepared the patient for the procedure, and HCP who performed the procedure

- Other treatments (if any) combined in the same treatment session / area(s) and where these treatments were administered
- Clinic scheduling procedures for treatment session
- **Pain Numeric Rating Scale for Pain:**

At each treatment time point (Baseline, Follow-up, End-of-Treatment), all treated patients will be asked to provide a Pain Numeric Rating Scale score for the maximum pain experienced post-treatment by the patient.

- For patients treated with ATX-101, patients will be asked to provide a Pain Numeric Rating Scale score for maximum pain experienced post-treatment by the patient at every treatment session.
- **Treatment Procedures Questionnaire**

At each treatment session (for patients treated with ATX-101 only), the site will complete the Treatment Procedures Questionnaire, including the following information:

- Comfort regimen used, type and effectiveness, pre- and post-treatment
- Protocol for post-treatment follow-up (eg, phone, visit) for each treatment session
- Total time spent by patients on treatment and post-treatment follow-up in office (including deviation from the scheduled time / other treatments given during the same appointment)
- Time interval between treatments
- Details of treatment method (treatment dependent)
- Patient Grid Questionnaire

Adverse Events

To be collected only for patients who elect treatment for SMF reduction. The following information will be recorded in the Electronic Data Capture (EDC) system:

- Frequency, severity, duration, medication or other treatment required, and outcome of adverse events (AEs) during and after each SMF reduction treatment session:
  - At each visit, patients will have treatment areas examined and be interviewed in an open-ended manner to solicit reports of AEs since the last visit.
  - Patient calls to clinic with post-treatment concerns or symptoms that meet the definition of AEs (eg, pain, swelling, bruising, numbness, induration) will be included in the AE record.

Treatment Outcomes and Follow-up

Following SMF reduction treatment initiation, patients and physicians will be asked to complete SMF assessments and scales at the **Follow-up** time point for each treatment**:**

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG) score
- Subject Self Rating Scale (SSRS) score
- Pain Numeric Rating Scale for Pain: maximum pain experienced post-treatment by the patient.

After each treatment completed, patients and physicians will be asked to complete the following SMF assessments, questionnaires, and scales for **End-of-Treatment** time point:

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score

	• Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score • Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score • Submental Skin Laxity Grade (SMSLG) score • Subject Self Rating Scale (SSRS) score • Patient Self-Perception of Age (SPA) scale score • Patient Global Questions • Patient End-of-Treatment Questionnaire, including the following information: - After treatment, would the patient undergo the treatment again? (eg, was the benefit greater than the risk) - After treatment, would the patient recommend this treatment to a friend? - Overall, is the patient aesthetically satisfied with the treatment outcome? - Did the patient's friends, spouse or co-workers notice a positive/negative aesthetic change? • Physician End-of-Treatment Questionnaire, including the following information: Physician's treatment goal in terms of aesthetic outcome: was the physician's treatment goal achieved? • Pain Numeric Rating Scale for Pain: maximum pain experienced post-treatment by the patient. • Clinical Information (height, weight) For patients that do not elect treatment for SMF reduction (untreated patients), patients will be asked to complete: • Patient End-of-Study Questionnaire to capture the patient reasons for not electing treatment(eg, benefits did not outweigh the risks for the treatment options, too expensive, etc.) • Clinical Information (height, weight)
Statistical Methods	A formal statistical analysis plan (SAP) that will provide details of all analyses and presentation of registry data will be approved prior to data analysis. Descriptive statistics will comprise the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum for continuous variables; and n and percent for categorical variables, with the number of patients who do not have missing values as the denominator. No imputation for missing data will be performed. Analyses will be conducted using observed cases.
Sample Size	Up to 1,000 patients are anticipated. The number and size of analysis groups will be determined by the treatments selected by the patients in this sample; therefore, group sizes may not be identical. In general, if the sample size in a treatment cohort is at least 250, this study is well-powered to observe an improvement of at least one grade in the CR-SMFRS (Section 8.1)
Analysis Populations	Analyses will be based upon all patients who were enrolled and have at least one post-baseline visit. Additional subgroups also may be examined, as deemed appropriate (eg, sex, initial assessment scores, prior treatments received).
Practice, Patient, and Treatment Data	Data will be summarized, by type of SMF reduction treatment, with descriptive statistics, and presented in listings.
Outcome Data	**SMF Assessments** Results for SMF assessments will be summarized with descriptive statistics at each time point. Changes from baseline will be summarized descriptively for each

	treatment cohort at each post-baseline assessment. Exploratory analysis of covariance (ANCOVA) methods will also be used to assess change from baseline at the end-of-treatment follow-up timepoint, where treatment type and baseline score will be included in the model. The ANCOVA results will be generated in SAS using PROC MIXED. Cochran-Mantel-Haenszel (CMH) tests for association, stratified by site, will be used to assess categorical responses. The qualification for a "responder" for each SMF assessment will be further defined in the SAP. For the CR-SMFRS and PR-SMFRS assessments, the number and percent of patients in each treatment cohort who have at least a 1-grade improvement will be presented, along with the corresponding 95% confidence interval (CI). Responses to the other SMF assessments will be summarized similarly. Questionnaire responses will be summarized using counts, percents, and 95% CIs for each treatment type.
Safety Data	AE and AE mitigation data will be summarized with descriptive statistics, by type of SMF reduction treatment, system organ class (SOC), and preferred term (PT), and presented in listings. The duration (days) and severity of pain, swelling, and bruising will be summarized by type of SMF reduction treatment, by treatment session, and overall. When a patient has an occurrence of a PT more than once, the patient's average duration for the PT will be computed for the overall summary. Pain scores from the Pain Numeric Rating Scale will be summarized with descriptive statistics by type of SMF reduction treatment and time point.

DATA FOR COLLECTION

	Site Screening	Enrollment (all patients)	Baseline (treated patients)	Follow-up (treated patients)	End-of-Study (untreated patients)	End-of-Treatment (treated patients)
Physician Practice Setting Questionnaire[a]	X					
Patient Population						
Informed consent / medical records release /brief medical history		X				
Demography & Clinical Information		X[f]			X[f]	X[f]
Patient Treatment History		X				
Patient Treatment Goals Questionnaire		X				
Physician Treatment Goals Questionnaire						
Treatment Logistics:						
Treatment Logistics Questionnaire			X[b]			
Pain Numeric Rating Scale			X[e]	X[e]		X[e]
Treatment Procedures Questionnaire			X[c]			
Adverse Events:						
Adverse Event Log			X[b]	X[b]		X[b]
Treatment Outcomes & Follow-up:						
SMF assessments:						
Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score		X		X[b]		X[b]
Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score		X		X[b]		X[b]
Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score		X		X[b]		X[b]
Submental Skin Laxity Grade (SMSLG)		X		X[b]		X[b]
Subject Self Rating Scale (SSRS)		X		X[b]		X[b]
Patient Self-Perception of Age (SPA) scale		X				X[b]
Patient Global Questions (PGQ)						X[b]
Patient End-of-Treatment Questionnaire						X[b]
Physician End-of-Treatment Questionnaire						X[b]
Patient End-of-Study Questionnaire					X[d]	

a: Physician Practice Setting Questionnaire is to be completed once for each site at the start of the study (following site initiation).

b: To be completed only for patients who elect a SMF reduction treatment (treated patients). (Applicable time points: Baseline, Follow-up, End-of-Treatment).

c: To be completed only for patients treated with ATX-101. (Applicable data point(s): Treatment Procedures Questionnaire).

d: To be completed only for untreated patients. (Applicable data point: Patient End-of-Study Questionnaire)

e: To be completed only for patients who elect a SMF reduction treatment (treated patients) at the following applicable time points: Baseline, Follow-up, and End-of-Treatment. Patients treated with ATX-101 will be asked to provide pain scores at each ATX-101 treatment visit.

f: Demography (birth date, sex, race, ethnic origin) & Clinical Information (height, weight, lifestyle habits) to be collected at Enrollment; Clinical Information (height, weight) to be collected at End-of-Treatment / End-of-Study for all patients.

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ABBREVIATIONS AND ACRONYMS

AE	adverse event
ANCOVA	analysis of covariance
BMI	body mass index
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CR-SMFRS	Clinician-Reported Submental Fat Rating Scale
eCRF	electronic case report form
EDC	electronic data capture
GPP	Good Pharmacoepidemiology Practices
HCP	healthcare provider
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
MedDRA	Medical Dictionary for Regulatory Activities
PR-SMFIS	Patient-Reported Submental Fat Impact Scale
PR-SMFRS	Patient-Reported Submental Fat Rating Scale
PT	preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SM	Submental
SMF	submental fat
SMSLG	Submental Skin Laxity Grade
SOC	system organ class
SPA	Self-perception of Age
SSRS	Subject Self Rating Scale
SUSAR	suspected unexpected serious adverse reaction

1 INTRODUCTION

1.1 Background

Submental (SM) fullness associated with the accumulation of submental fat (SMF) can influence negative self-perception.[1,2] While the SM region is visually important, at present, only surgical options (cosmetic surgery, liposuction) are available for addressing SM fullness through SMF reduction, and not all patients are suitable candidates for, or willing to undergo, these invasive procedures and the potential complications.[3-8] Currently available injectable products, ie, botulinum toxins and dermal fillers, are primarily employed in the aesthetic rejuvenation of the upper and mid-face and do not adequately address contouring the SM region. The use of energy based devices for lipolysis has been investigated as a less invasive approach,[9] but may still require accompanying surgery in more severely affected cases,[10] and safety concerns remain.[11] Recently, a pharmacologic treatment, deoxycholic acid injection (ATX-101), was approved by the FDA for improvement in the appearance of moderate to severe convexity or fullness associated with submental fat in adults.[12]

1.2 Study Rationale

This registry will gather information on use patterns and outcomes of treatments for addressing SM fullness through SMF reduction, beginning with currently used methods, and including newly approved products as they become adopted into the practice.

2 OBJECTIVES

The primary objective of this registry is to develop a comprehensive understanding of the condition of SM fullness due to SMF, how it is treated in current clinical practice, and the risks and benefits associated with its treatment. This objective will be accomplished through the systematic collection of data on the following:

- Population of physicians with patients who have SMF concerns
- Population of patients who are eligible for SMF reduction treatment
- Eligible patients who elect SMF reduction treatment
- Treatment procedures
- Treatment outcomes
- Safety profile through adverse event reporting of the SMF reduction treatments administered

3 STUDY CONDUCT

3.1 Design of the Study

This is a prospective, non-interventional, longitudinal, multi-center registry to be conducted in patients with SM fullness due to SMF. Each participating physician will prescribe treatments based on his or her usual clinical practice, and no restriction on the use of commercially available treatments will be imposed. As this is a non-interventional study, the patient-physician relationship will not be affected, nor will there be any influence on the therapeutic management of the patient.

Study visits, procedures, and evaluations are summarized in Data for Collection and described in detail in Sections 5 and 6.

Patients considering treatment to reduce SMF will be recruited. Eligible patients will be enrolled in the registry, and patients who elect treatment will be followed until their SMF reduction treatment is completed or discontinued. Patients who do not initially elect treatment will be followed to determine whether or not they subsequently undergo treatmentuntil up to one year has elapsed since enrollment and no treatment has been elected. Reasons for treatment discontinuation, or for the decision to not receive treatment, will be recorded. Enrolled patients will be assessed regularly by their treating physician according to usual clinical practice. Data collection is anticipated to continue for approximately 15 months. The duration of individual patient participation will vary depending on the chosen treatment method and individual requirements.

At Enrollment, relevant data on previous SMF and facial aesthetic treatments will be collected from the patients, and as necessary, from their medical records. Additionally, baseline assessments of SMF will be performed. Details of the investigator's practice setting will be recorded after site initiation, and details of treatment logistics will be recorded at the first treatment session(s) (for each treatment selected) for patients who elect treatment for SMF reduction . Information, including treatment received for SMF reduction, treatment procedures and outcomes, follow-up assessments of SMF, and adverse events (AEs) will be recorded at subsequent clinic visits or telephone contacts. Patient medical history data will be updated, as appropriate, at the first treatment session (Baseline Treatment Visit).

3.2 Patient Discontinuation and Study Site or Study Termination

3.2.1 Withdrawal of Individual Patients Prior to Study Completion

A patient may be withdrawn from the registry prior to completion, or the decision to not receive treatment, for any of the following reasons:

- Withdrawal of patient consent

- Any other reason, including lack of willingness to complete assessment questionnaires, the patient's best medical interest, or decisions made by the investigator or the sponsor

If a patient withdraws or is withdrawn, the reason should be documented in the electronic case report form (eCRF).

3.2.2 Study or Study Site Termination

The Sponsor reserves the right, at any time, to discontinue enrollment of additional patients into the registry, at any site; or to discontinue the registry, for medical or administrative reasons.

4 STUDY POPULATION

4.1 Inclusion Criteria

A patient must meet all of the following criteria to be eligible for participation in the registry.

1. Adult male and female patients, aged 18 years and above, presenting with SM fullness due to the accumulation of unwanted SMF, and considered by their treating physician to be a candidate to receive treatment of SM fullness by reduction of SMF, if the patient decides
2. Signed informed consent by the patient, obtained before any study-related activities are undertaken
3. Willing to complete all patient assessment questionnaires
4. Signed release form by the patient, permitting abstraction of the patient's medical records at baseline and during participation in the registry

4.2 Exclusion Criteria

A patient who meets any of the following criteria is not eligible for participation in the registry.

1. Severe skin laxity, defined as superficial wrinkling, loose skin separated from deeper neck structures, and/or marked skin redundancy (draping and/or sagging), per the physician's judgment
2. Any other cause of fullness in the SM area (eg, thyroid enlargement, cervical adenopathy) other than localized SMF
3. Participating in an interventional clinical study, currently or within 30 days before enrollment
4. Participated previously in an interventional clinical study involving ATX-101

5 STUDY PROCEDURES

5.1 Site Enrollment, Training, and Questionnaires

The Sponsor or designee will invite qualified investigators to participate in the registry study. Investigators will be required to obtain approval from the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC), and will be responsible for maintaining all related documents, before enrollment of any patient into the registry.

Designated study personnel will participate in a training program that will encourage consistency of process and procedures at the investigative sites and ensure collection of high-quality data for this registry. All sites will be trained on the protocol, registry logistics, and the electronic data capture (EDC) system. Retraining will be conducted as needed. Investigators will be reminded of the processes and importance of reporting AEs, SAEs, and other information.

The investigator or designee at each initiated site will complete the following questionnaires regarding practices at that site:

- Physician Practice Setting Questionnaire (Section 5.2.1; to be completed once for each site at the beginning of study participation)
- Treatment Logistics Questionnaire (Section 5.3.2; to be completed at the first treatment session(s) (for each treatment selected) for patients who elect treatment for SMF reduction for all treatments)
- Treatment Procedures Questionnaire (Section 5.3.2; to be completed at every treatment session only for patients treated with ATX-101)

Patients considering treatment of SM fullness by reduction of SMF will be recruited. After written informed consent is obtained (Section 9.1), each screened patient will be assigned a unique study identification number. Eligibility will be determined by review of the inclusion/exclusion criteria.

5.1.1 Enrollment Visit

Patients who are enrolled in the registry will have information abstracted from their medical records and undergo the baseline assessments (Section 5.3.1).

5.1.2 Baseline Treatment Visit

Information about the patient's treatment procedures, any AEs, and treatment outcomes will be recorded at the first treatment session(s) for each treatment selected for all patients who elect treatment for SMF reduction (treated patients) (Section 5.3.2). The number of and time between treatment visits will vary with the treatment type and specific needs of the patient.

5.1.3 Follow-up Visit

The follow-up visit will take place after the patient's first treatment session or Baseline Treatment Visit (for each treatment selected) at the treatment mid-point. Depending on the number of treatment sessions (dependent on treatment type), the timing of the follow-up visit may vary at the mid-point of their treatment (Section 5.3.4). Information on AE/SAEs and treatment outcomes will be recorded.

5.1.4 Final Visit

The patient's Final Visit will take place either at the last scheduled follow-up visit after completion of all SMF reduction treatment(s), within 3 months of the last treatment session (for each treatment selected), when a patient elects to discontinue treatment, or prior to study closure (treated patients). Information on AE/SAEs, treatment outcomes, and End-of Study assessments will be recorded (section 5.3.4). For patients who do not elect treatment for SMF reduction (untreated patients), the reason for not selecting treatment will be captured at this time point.

STUDY ASSESSMENTS

5.2 Site Characteristics

5.2.1 Physician Practice Profile

At each site, the investigator or designee will provide information about the practice setting, including the following:

Physician Practice Setting Questionnaire:

- Characteristics of physicians:
  - Clinical practice history and specialty, including board certification
  - Years of aesthetic practice
  - Percent of practice focused on aesthetics versus medical or reconstructive
  - Physician approach to discussing new treatment options
  - Number and roles of physicians and other healthcare providers (HCPs) in the practice
- Aesthetic treatment options, including options for treating SM fullness through SMF reduction, offered by the clinic: types and relative frequencies
- Consent and intake details pertaining to aesthetics and chin and neck (cervicomental) region.
- Percent of patients in the practice who present with SMF concerns, and percent of these patients who elected to receive treatment of SM fullness through SMF reduction
- Referral of patients for SMF reduction treatment to and from other physicians

5.3 Patient and Treatment Characteristics

5.3.1 Demographic and Baseline Assessments

The following information will be collected at the Enrollment time point

Demography:

- Birth date
- Sex
- Race
- Ethnic origin

Clinical Information:

- Height
- Weight
- Lifestyle habits (eg, smoking)

Brief medical history (including diabetes, cardiovascular disease)

Patient Treatment History:

- Previous facial aesthetic treatment(s) within past 24 months:
  - Treatment type (eg, toxins, fillers, devices, cosmetic surgery)
  - Location of treatment (eg. face, chin/neck)

Patient Treatment Goals Questionnaire, including the following information:

- History of SMF concern
- Patient's treatment goal in terms of aesthetic outcome

Physician Treatment Goals Questionnaire, including the following information:

- Physician's treatment goal in terms of aesthetic outcome

Baseline SMF assessments:

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG) score
- Subject Self Rating Scale (SSRS) score
- Self-perception of age (SPA) scale score

5.3.2 Baseline Treatment Assessments

At the Baseline time point, the investigator or designee will provide information about treatment logistics within the practice, and patients will be asked to provide post-treatment data, including the following information:

Treatment Logistics Questionnaire:

Completed by the physician or designee at the first treatment session(s) for each treatment selected for all patients who elect treatment for SMF reduction (for all treatments):

- Patient preparation for the procedure / specific instructions
- HCP who prepared the treatment materials/equipment, HCP who prepared the patient for the procedure, and HCP who performed the procedure
- Time spent with patients, by both the physician and qualified designee, discussing treatment details and expectations
- Total time spent by patients on treatment and post-treatment follow-up in office (including deviation from the scheduled time / other treatments given during the same appointment)
- SMF reduction treatment selected and treatment schedule
- Other treatments (if any) combined in the same treatment session / area(s) where these treatments were administered
- Clinic scheduling procedures for treatment sessions

Pain Numeric Rating Scale for Pain:

At each treatment time point (Baseline, Follow-up, End-of-Treatment), all treated patients will be asked to provide a Pain Numeric Rating Scale score for the maximum pain experienced post-treatment by the patient.

- For patients treated with ATX-101, patients will be asked to provide a Pain Numeric Rating Scale score for maximum pain experienced post-treatment by the patient at every treatment session.

Treatment Procedures Questionnaire:

Completed by the physician or designee at every treatment session only for patients treated with ATX-101.

- Other treatments (if any) combined in the same treatment session / area(s) where these treatments were administered
- Time spent with patients, by both the physician and qualified designee, discussing treatment details and expectations
- Total time spent by patients on treatment and post-treatment follow-up in office (including deviation from the scheduled time / other treatments given during the same appointment)
- Details of treatment method (treatment dependent)

- Mitigation procedures administered before and after treatment
- Time interval between successive treatments
- Patient Grid Questionnaire (only if grid was used)

Adverse Events:

- Frequency, severity, duration, medication or other treatment required, and outcome of AEs during and after each SMF reduction treatment session
  - At the Baseline visit, patients will have treatment areas examined and be interviewed in an open-ended manner to solicit reports of AEs since the last visit.
  - Patient calls to clinic with post-treatment concerns /symptoms that meet the definition of AEs (eg, pain, swelling, bruising, numbness) will be included in the AE record.

5.3.3 Treatment Outcomes and Follow-up:

The following information will be collected at the Follow-up time point, which should occur after the first treatment session for each treatment selected (Baseline Treatment Visit) at the treatment mid-point. Depending on the number of treatment sessions (dependent on treatment type), the timing of the Follow-up time point may vary.

For patients who elect treatment for SMF reduction (treated patients), the following information will be captured at the Follow-up time point (Follow-up):

Pain Numeric Rating Scale for Pain:

At each treatment time point (Baseline, Follow-up, End-of-Treatment), all treated patients will be asked to provide a Pain Numeric Rating Scale score for the maximum pain experienced post-treatment by the patient.

- For patients treated with ATX-101, patients will be asked to provide a Pain Numeric Rating Scale score for maximum pain experienced post-treatment by the patient at every treatment session.

Adverse Events:

- Frequency, severity, duration, medication or other treatment required, and outcome of AEs during and after each SMF reduction treatment session
  - At the Follow-up visit, patients will have treatment areas examined and be interviewed in an open-ended manner to solicit reports of AEs since the last visit.
  - Patient calls to clinic with post-treatment concerns /symptoms that meet the definition of AEs (eg, pain, swelling, bruising, numbness) will be included in the AE record.

Follow-up SMF assessments:

The following SMF assessments will be performed at the Follow-up visit (Follow-up) for each SMF treatment selected:

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG) score
- Subject Self Rating Scale (SSRS) score

These assessments were developed by Kythera for use in premarketing trials. The SMFIS and SSRS have been used in multiple Phase 3 trials and have produced aligned results with respect to satisfaction with the SMF reduction treatment and positive impacts on visual and emotional aspects of treatment.

5.3.4 End-of-Study Assessments

The following information will be collected at the Final Visit(s), which should occur within 3 months after the last treatment session(s) for treated patients, at the discontinuation visit, or prior to study closure (for untreated patients) in order to capture patient and physician feedback regarding treatment decisions.

For patients who elect treatment for SMF reduction (treated patients), the following information will be captured at the Final Visit (End-of-Treatment):

Clinical Information:

- Height
- Weight

Adverse Events:

- Frequency, severity, duration, medication or other treatment required, and outcome of AEs during and after each SMF reduction treatment session
  - At the end-of-treatment visit, patients will have treatment areas examined and be interviewed in an open-ended manner to solicit reports of AEs since the last visit.
  - Patient calls to clinic with post-treatment concerns /symptoms that meet the definition of AEs (eg, pain, swelling, bruising, numbness) will be included in the AE record.

Pain Numeric Rating Scale for Pain:

- At each treatment time point (Baseline, Follow-up, End-of-Treatment), all treated patients will be asked to provide a Pain Numeric Rating Scale score for the maximum pain experienced post-treatment by the patient.
  - For patients treated with ATX-101, patients will be asked to provide a Pain Numeric Rating Scale score for maximum pain experienced post-treatment by the patient at every treatment session.

End-of-Treatment SMF assessments:

The following SMF assessments will be performed at the Final Visit (End-of-Treatment) for each SMF treatment selected:

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG) score
- Subject Self Rating Scale (SSRS) score
- Self-Perception of Age (SPA) score
- Patient Global Questions (PGQ)

Physician End-of-Treatment Questionnaire:

Completed by the physician or designee at the End-of-Treatment visit, for patients who elect treatment for SMF reduction (treated patients):

- Physician's treatment goal in terms of aesthetic outcome: was the physician's treatment goal achieved?
- Treatment Adverse Events:
  - Does the physician feel that any training received for the treatment procedure accurately informed them of the adverse effects their patients experienced during and following treatment?
  - What could have been done better?

Patient End-of-Treatment Questionnaire:

Completed by the patient at the End-of-Treatment visit for patients who elect treatment for SMF reduction (treated patients):

- After treatment, would the patient undergo the treatment again? (eg, was the benefit greater than the risk)
- After treatment, would the patient recommend treatment to a friend?
- Treatment Adverse Events:
  - Does the patient feel their physician accurately prepared them for the adverse effects that occurred during and following treatment?
  - What could have been done better?
- Overall, is the patient aesthetically satisfied with the treatment outcome?
- Did the patient's friends, spouse/significant other or co-workers notice a positive/negative aesthetic change?

For patients that do not elect treatment for SMF reduction (untreated patients), the following feedback will be requested from the patient at study discontinuation/ prior to study closure:

Clinical Information:

- Height
- Weight

Patient End-of-Study Questionnaire:

- Patient reason for not electing treatment (eg. benefits did not outweigh the risks for the treatment options, too expensive, etc.)

6 ADVERSE EVENT DEFINITIONS AND REPORTING

6.1 Definitions

6.2 Adverse Event

An adverse event (AE) is any undesirable medical occurrence or worsening of an existing condition that occurs after SMF reduction treatment, irrespective of whether the event is considered treatment related. Abnormal laboratory values should not be reported as AEs; however, any clinical consequences of an abnormality must be reported as such. Safety reporting of non-serious (AEs) and /or serious adverse events (SAEs) will only be done for patients who elect treatment for SMF reduction.

6.2.1 Serious Adverse Event

A serious AE (SAE) is defined as an event that may constitute a significant medical hazard or side effect, regardless of the investigator or sponsor's opinion about its relationship to SMF reduction treatment. Serious events include, but may not be limited to, any event that:

- Is fatal
- Is life-threatening (places the patient at immediate risk of death while the event is occurring)
- Requires inpatient hospitalization or prolongs hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is a significant medical hazard

Significant untoward medical events that may not be life-threatening or result in death or hospitalization, or events that require intervention to prevent one of the outcomes listed above or that may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition, may be considered serious. Allergan considers all cancer adverse events as serious. In addition, Allergan considers any abortion (spontaneous or nonspontaneous) as a serious adverse event.

Elective hospitalizations for conditions that existed before SMF reduction treatment are not to be considered SAEs.

6.3 Reporting Procedures for All Adverse Events

All AEs observed by the investigator or reported by the patient will be recorded on the appropriate CRF, irrespective of relationship to SMF reduction treatment. Medically significant AEs will be followed until resolved or considered stable. For each event, the investigator will record a description, dates of onset and resolution, severity, and relationship to SMF reduction treatment. The investigator may be required to provide follow-up information.

Any AE that results in withdrawal from the study must be reported to Allergan after the decision to withdraw is made.

Any death occurring during the study must be reported to Allergan within 24 hours of discovery of the event. This includes any death that occurs within 30 days after the patient's final visit, irrespective of when the final visit occurs.

Pregnancy If a female patient becomes pregnant during the study, the investigator will notify Allergan immediately after the pregnancy is confirmed. Pregnancies are reportable to Allergan in the same timeframe as SAEs:

- Upon learning of a pregnancy occurring in a patient, notify Allergan within 24 hours
- Follow pregnancy until the outcome is known and once this known you must report the outcome to Allegan
- Use the Relevant Allergan Pregnancy Reporting Form
- Pre-Pregnancy and Post-Pregnancy information should be collected, as relevant
- Also complete a SAE Form if outcome results in a serious criteria

6.3.1 Assessment of Severity

Severity of AEs will be determined using the following scale:

- Mild: the patient is aware of a sign or symptom but it is easily tolerated
- Moderate: discomfort or interference with usual activity
- Severe: incapacitating with inability to engage in usual activity

6.3.2 Assessment of Relationship to Treatment

The investigator will determine the relationship of each AE to SMF reduction treatment using the question: "Is there a reasonable possibility that the event may have been caused by treatment or the treatment procedure?

Answer 'yes' or 'no' for each AE."

The guideline below should be used to consider relatedness:

No = there is not a reasonable possibility that the event may have been caused by treatment. The AE:

- May be judged to be due to extraneous causes such as disease or environment or toxic factors
- May be judged to be due to the patient's clinical state or other therapy being administered
- Is not biologically plausible
- Does not reappear or worsen when treatment is re-administered
- Does not follow a temporal sequence from administration of treatment

Yes = there is a reasonable possibility that the event may have been caused by treatment. The AE:

- Follows a temporal sequence from administration of treatment
- Is a known response to the treatment based on clinical or nonclinical data
- Could not be explained by the known characteristics of the patient's clinical state, environmental or toxic factors, or other therapy administered
- Disappears or decreases upon cessation or reduction of treatment
- Reappears or worsens when treatment is re-administered

6.4 Reporting Procedures for Serious Adverse Events

All SAEs must be reported to Allergan as soon as possible but no later than 24 hours of awareness on the day of discovery or notification of the event and according to IEC/IRB requirements and the institution at which the study is conducted, if applicable. SAE information and any follow-up information will be recorded on a SAE Form and transmitted to Allergan using the contact information provided by Allergan. Allergan or its designee will be responsible for reporting any SAEs and suspected unexpected serious adverse reactions (SUSARs) in accordance with all applicable laws and regulations.

Upon awareness of an SAE complete the SAE form and submit to Allergan immediately but no later than 24 hours of awareness by fax or email to: Fax:+1-714-796-9504 (Back-Up Fax No.: +1-714-246-5295) E-mail: IR-Clinical-SAE@allergan.com

Allergan may issue queries for follow-up information until resolution or stabilization of the event following conclusion of the CONTOUR study. In the event that SAEs are identified following the conclusion of the CONTOUR study (not previously reported to Allergan), the Investigator may report the SAE if there is reason to believe the event may be related to SMF treatment.

7 DATA MANAGEMENT

All data collected in the context of this registry study will be stored and evaluated in accordance with regulatory requirements and applicable guidance for electronic records.

7.1 Medical Record Abstraction

Electronic case report forms (eCRFs) will be used. Data will be extracted from the patient's medical record and entered into the EDC system as summarized in Data for Collection. Patients will be identified by use of the ID number assigned to them when they enroll in the registry.

Before the first patient's medical record is abstracted, the Sponsor and/or designee will meet with the investigator and the study center's personnel to train them on recording the data on the eCRFs using the EDC system.

7.2 Electronic Case Report Forms and Data Capture System

Only authorized personnel will have access to the EDC system. Data will be entered into eCRFs in accordance with instructions from the Sponsor and/or designee. Each investigator is responsible for ensuring that accurate data are entered into the EDC system in a timely manner.

Online logic checks will be built into the system, so that missing or illogical data are not submitted. In the event that inconsistent data persist, queries may be issued electronically to the study center and answered electronically by that study center's personnel. The identifying information (assigned user name, date, and time) for both the originator of the query and the originator of the data change (if applicable), as well as the investigator's approval of all changes performed on the data, will be collected.

The investigator will be responsible for reviewing eCRFs, resolving data queries generated by the Sponsor and/or designee via the system, providing missing or corrected data, approving all changes performed on the patient data, and endorsing these data within the EDC system. This approval method will include applying an electronic signature, a uniquely assigned user name, and a password that together will represent a traditional handwritten signature.

8 STATISTICAL METHODS

A formal statistical analysis plan (SAP) that will provide details of all analyses and presentation of registry data will be approved prior to database lock and data analysis.

Descriptive statistics will comprise the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum for continuous variables; and n and percent for categorical variables, with the number of patients who do not have missing values as the denominator.

For this registry, no imputation for missing data will be performed. Analyses will be conducted using observed cases.

8.1 Sample Size

Up to 1000 patients are anticipated. No pre-specified statistical hypotheses will be tested, therefore no formal power calculations were performed. Instead, the precision of 95% confidence intervals around key response variables was estimated. Note that the number and size of analysis groups will be determined by the treatments selected by the patients in this sample; therefore, group sizes may not be identical.

Table 1 below provides 2-sided 95% confidence interval (CI) around an expected response rate of 67.5% for CR-SMFRS score in patients treated with ATX-101 during Phase 3 clinical trials, where response was defined as an improvement of at least one grade.

Table 1 Precision and 95% Confidence Intervals for Various Sample Sizes, Based on an Expected Patient Response Rate of 67.5%

Sample size (N)	95% CI		
250	61.7, 73.3	500	63.4, 71.6
750	64.1, 70.9		

Table 2 below provides the 2-sided 95% CI around expected levels of patient satisfaction rates.[13]

Table 2 Precision and 95% Confidence Intervals for Various Combinations of Sample Size and Patient Satisfaction Rates

	Probable Rates of Patient-reported Satisfaction		
	80%	85%	90%
Sample Size (N)	95% CI	95% CI	95% CI
250	75.0, 85.0	80.6, 89.4	86.3, 93.7
500	76.5, 83.5	81.9, 88.1	87.4, 92.6
750	77.1, 82.9	82.4, 87.6	87.9, 92.1

8.2 Study Populations and Analyses

8.2.1 Study Populations

Efficacy and safety analyses will be based upon all enrolled patients who had at least one post-baseline visit, whether or not they elected to received treatment. Additional groups also may be examined, as deemed appropriate, and will be defined in the SAP (eg, sex, initial assessment scores, prior treatments received).

8.2.2 Analyses

Data will be summarized, by type of SMF reduction treatment, with descriptive statistics, and presented in listings. No formal statistical hypotheses are established for this protocol, but exploratory analyses involving inferential tests will be performed as described below.

Demographic and baseline characteristics will be summarized. Post-baseline values and change from baseline in selected outcome variables will be summarized, by type of SMF reduction treatment, with descriptive statistics, and, where appropriate, graphical presentations, and presented in listings.

8.2.2.1 Main Efficacy Endpoint: Submental Fat (SMF) Assessments

The following SMF assessments (Appendix 11) are planned at each visit:

- Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) score
- Patient-Reported Submental Fat Rating Scale (PR-SMFRS) score
- Patient-Reported Submental Fat Impact Scale (PR-SMFIS) score
- Submental Skin Laxity Grade (SMSLG)
- Subject Self Rating Scale (SSRS)
- Patient Self-Perception of Age (SPA) scale
- Patient Global Questions

Overall and individual component summaries for each scale, where applicable, will be provided using descriptive statistics at each timepoint. Changes from baseline will be summarized descriptively for each treatment cohort at each post-baseline assessment. Exploratory analysis of covariance (ANCOVA) methods will also be used to assess change from baseline at the end-of-treatment follow-up timepoint, where treatment type and baseline score will be included in the model. The ANCOVA results will be generated in SAS using PROC MIXED. Cochran-Mantel-Haenszel (CMH) tests for association, stratified by site, will be used to assess the responses.

For CR-SMFRS and PR-SMFRS assessments, the number and percent of patients in each treatment cohort who are responders, ie, have at least a 1-grade improvement, will be presented, along with the corresponding 95% CI. Responses to the other SMF assessments will be summarized similarly.

For the SSRS, a subject is defined as a responder for the assessment if the response was positive relative to the score's neutral response option (ie, "slightly satisfied," "somewhat satisfied," or "extremely satisfied" where neutral is "neither satisfied nor dissatisfied").

An SMSLG responder at an assessment time is defined as a subject who stayed the same SMSLG score or had improvement in SMSLG score relative to baseline. This scale is different from the others in that "no change" is counted as a responder. The reason for this distinction is

that the intent is not to investigate whether ATX-101 reduces/improves skin laxity, but rather to investigate whether ATX-101 is associated with an undesirable increase in skin laxity. Accordingly, the categories are, effectively, skin laxity either "did not increase" or "did increase."

8.2.2.2 Other Efficacy Endpoints: Physician and Patient Questionnaires

The categorical responses observed for the physician and patient questionnaires will be summarized using counts, percents, and 95% CIs for each treatment type.

8.2.2.3 Safety Analysis

AEs will be coded using MedDRA Version 18.0 or later. AE and AE mitigation data will be summarized with descriptive statistics, by type of SMF reduction treatment, system organ class (SOC), and preferred term (PT), and presented in listings. The duration (days) and severity of pain, swelling, and bruising will be summarized by type of SMF reduction treatment, by treatment session, and overall. When a patient has an occurrence of a PT more than once, the patient's average duration for the PT will be computed for the overall summary. Pain scores from the Pain Numeric Rating Scale will be summarized with descriptive statistics by type of SMF reduction treatment and time point.

9 ETHICAL AND ADMINISTRATIVE ISSUES

9.1 Informed Consent

Before any protocol-specified procedures are carried out, the investigator or designee will explain details of the protocol and procedures to patients. Patients will be informed that they are free to withdraw from the registry at any time.

Each patient must sign an informed consent form (ICF), approved by the IRB/IEC, indicating their consent to participate. ICFs will conform to the requirements of the International Society for Pharmacoepidemiology (ISPE) code of Good Pharmacoepidemiology Practices (GPP). The original signed ICFs must remain in the patient's file in the clinic. Each patient will receive a copy of the signed ICF.

Each patient enrolled in the registry also must sign a medical records release form permitting abstraction of medical data for entry in the registry EDC system. Individual patient data included in the registry database will be treated in compliance with all applicable laws and regulations regarding privacy protection.

9.2 Institutional Review Board / Independent Ethics Committee Approval

The protocol and the ICF must be reviewed and approved by the site's IRB/IEC before the registry is initiated. The investigator is then responsible for informing the IRB/IEC of the completion of the registry and should provide any required status and/or safety report(s).

9.3 Adherence to the Protocol

The registry must be conducted as described in the approved protocol, except for an emergency situation in which proper care for the safety of the patient requires intervention. Any significant deviation from the protocol must be reported immediately to the Sponsor and IRB/IEC.

9.4 Protocol Amendment

Any amendment to the protocol will be created by the Sponsor or designee, and subsequently submitted by the site to the IRB/IEC and appropriate regulatory authority for approval. If the protocol amendment substantially alters the registry design or increases the potential risk or discomfort to the patients, updated written consent for continued participation in the registry must be obtained.

9.5 Monitoring of the Study

The Sponsor and its representatives will monitor the registry at the site according to the Monitoring Plan. At the monitoring visits, the progress of the registry and any procedural or data issues will be discussed with the investigator and/or designee. Patient source documents should be available for review; the investigator will permit the Sponsor, representatives of the Sponsor, the IRB/IEC, or regulatory authorities to inspect facilities and original records relevant to this registry.

9.6 Retention of Patient Records

When the registry is completed, the investigator must retain the essential documents for as long as needed to comply with regulatory guidelines and Sponsor requirements. The investigator will notify the Sponsor prior to moving or destroying any of the registry documents.

9.7 Confidentiality and Publication

The information in this and related documents from the Sponsor includes trade secrets and commercial information that are confidential and may not be disclosed, unless such disclosure is required by federal or other laws or regulations. In any event, persons to whom the information is disclosed must be informed that the information is confidential and may not be further disclosed by them.

Individual patient medical information obtained as a result of this registry is considered confidential, and disclosure to third parties, other than those noted below, is prohibited. Such medical information may be given to the patient's personal physician or to other appropriate medical personnel responsible for the patient's welfare.

Data generated as a result of this registry are to be available for inspection on request of the Sponsor's representative, the IRB/IEC, or local regulatory agency.

None of the parties involved in the management/conduct/analysis of this registry may publish any study-related data without the written permission of the Sponsor.

9.8 Bias and Limitations of the Study

9.8.1 Selection Bias

Sites will be selected from practices that see a large number of aesthetic patients with a variety of issues, including SMF. Physicians will attempt to consecutively enroll all patients who consent and meet the selection criteria, regardless of demography, health status, or other considerations.

9.8.2 Confounding Bias

An objective of this study is to better understand characteristics of practices, providers, and patients that influence the selection and outcomes of aesthetic treatments. The intent is to collect sufficient data to evaluate these predictors and adjust for them, as applicable, in the analyses. The collection of retrospective and baseline information will permit outcomes to be compared in light of differences prior to treatment selection.

9.8.3 Effect Modification

Characteristics such as obesity, age, skin laxity, etc. will be associated not only with treatment routing (selection bias) but also with outcomes. Again, this information will be used as appropriate in evaluating outcome data.

9.8.4 Patients Lost to Follow-Up

Some proportion of patients may discontinue the study. Investigators will be encouraged to share the patient’s data with him/her, in an effort to encourage the patient to remain involved in the study. Patients who do not choose a treatment for reduction of their SMF, or who withdraw treatment, will be asked to complete final visit assessments and record the reason in the Patient End-of-treatment Questionnaire. Steps may be taken to evaluate the presence of, and ameliorate, potential bias associated with differential attrition. Details will be provided in the Statistical Analysis Plan.

9.9 Registry Reports

Study results may be summarized periodically for presentation at professional conferences and sessions (Section 9.7).

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11 APPENDIXES: RATING INSTRUMENTS

11.1 Submental Skin Laxity Grade (SMSLG)

Grade	Laxity Description
1 **None**	• No or minimal superficial wrinkling • Skin well apposed to deeper neck structures • No skin redundancy - No skin draping (vertical folds) - No skin sagging (horizontal folds)
2 **Mild**	• Mild superficial wrinkling • Skin well apposed to deeper neck structures • Minimal skin redundancy - Slight skin draping (vertical folds) - Slight skin sagging (horizontal folds)
3 **Moderate**	• May have mild to moderate superficial wrinkling • Skin has mild to moderate separation from deeper neck structures • Moderate skin redundancy - Moderate skin draping (vertical folds) - Moderate skin sagging (horizontal folds)
4 **Severe**	• Mild to marked superficial wrinkling • Loose skin separated from deeper neck structures • Marked skin redundancy - Marked skin draping (vertical folds) - Marked skin sagging (horizontal folds)

Assessment Procedures

The SMSLG is an integration of three features: skin wrinkling, adherence to underlying neck structures (bone and muscle) and redundancy (horizontal and vertical folds). Each grade (none, mild, moderate and severe) defines the maximal allowed limit for skin wrinkling, adherence to underlying structures and redundancy.

SMSLG is based on assessor's clinical evaluation of the subject, including palpation of the chin and neck area; anterior, oblique, and profile views of the chin and neck; as well as observation of pronation, supination, and lateral movement of the head. The score is determined using the definitions in the rating scale and representative photographs associated with each score. The final determination of the score will be made while the subject's head is in the Frankfort plane posture. The score will be recorded as a whole number.

11.2 Clinician-Reported Submental Fat Rating Scale (CR-SMFRS)

Score	SMF Description
0	Absent Submental Convexity: No localized submental fat evident
1	Mild Submental Convexity: Minimal, localized submental fat
2	Moderate Submental Convexity: Prominent, localized submental fat
3	Severe Submental Convexity: Marked, localized submental fat
4	Extreme Submental Convexity

SMF score based on investigator's clinical evaluation of the subject, including palpation of the chin and neck area; anterior, oblique, and profile views of the chin and neck; as well as observation of pronation, supination, and lateral movement of the head. The score is determined using the definitions in the rating scale and representative photographs associated with each score. The final determination of the score will be made while the subject's head is in the Frankfort plane posture as described in the CR-SMFRS. The score will be recorded as a whole number. At screening and baseline, the score is determined in conjunction with protocol entry criteria (eg, absence of loose skin, diffuse submental fat, and prominent platysmal bands at rest that interfere with evaluation of localized fat).

11.3 Patient-Reported Submental Rating Scale (PR-SMFRS)

The subject will be instructed to position his or her head in a manner similar to that described for CR-SMFRS assessment and asked to respond to the question below.

PR-SMFRS

Please look in the mirror at **the area under your chin** to help you answer the following question:

How much fat do you have under your chin right now? Mark ☒ in one box below	
☐	No chin fat at all
☐	A slight amount of chin fat
☐	A moderate amount of chin fat
☐	A large amount of chin fat
☐	A very large amount of chin fat

11.4 Patient-Reported Submental Fat Impact Scale (PR-SMFIS)

PR-SMFIS

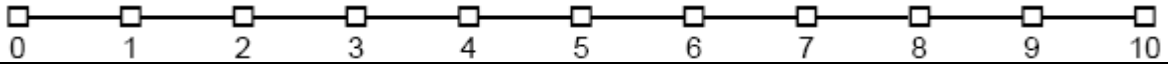
Please look in the mirror at **the area under your chin** to help you answer the following questions:

1.

How happy are you with the appearance of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not happy at all — Extremely happy

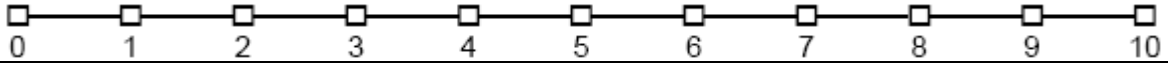


2.

How bothered are you by the appearance of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not bothered at all — Extremely bothered

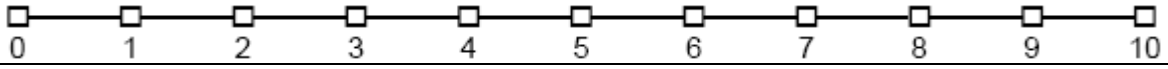


3.

How self-conscious are you about the appearance of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not self-conscious at all — Extremely self-conscious



4.

How embarrassed are you about the appearance of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not embarrassed at all — Extremely embarrassed

0 1 2 3 4 5 6 7 8 9 10

5.

How much older do you look because of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not older at all — Extremely older

0 1 2 3 4 5 6 7 8 9 10

6.

How overweight do you look because of your chin fat?

Mark▪☒ in one box below and do not mark between the boxes

Not overweight at all — Extremely overweight

0 1 2 3 4 5 6 7 8 9 10

11.5 Subject Self Rating Scale (SSRS)

The subject will be asked to respond to the question below. No photographs or reference to previous ratings or evaluations will be used.

Baseline: Considering your appearance in association with your face and chin, how satisfied do you feel with your appearance at the present time?

0 - Extremely dissatisfied

1 - Dissatisfied

2 - Slightly dissatisfied

3 - Neither satisfied nor dissatisfied

4 - Slightly satisfied

5 - Satisfied

6 - Extremely satisfied

Postbaseline: Considering your appearance in association with your face and chin, how satisfied do you feel with your appearance at the present time whether or not in your judgment it is due entirely to treatment?

0 - Extremely dissatisfied

1 - Dissatisfied

2 - Slightly dissatisfied

3 - Neither satisfied nor dissatisfied

4 - Slightly satisfied

5 - Satisfied

6 - Extremely satisfied

11.6 Patient Global Questions

1.

Since the start of this study, how would you rate the fat under your chin right now? Mark▪☒ in one box below	
☐	A great deal worse
☐	Moderately worse
☐	A little worse
☐	About the same
☐	A little better
☐	Moderately better
☐	A great deal better

2.

Since the start of this study, how would you rate the definition between your chin and neck right now? Mark▪☒ in one box below	
☐	A great deal worse
☐	Moderately worse
☐	A little worse
☐	About the same
☐	A little better
☐	Moderately better
☐	A great deal better

3.

How satisfied are you with the treatment you received in this study? Mark▪☒ in one box below	
☐	Extremely dissatisfied
☐	Moderately dissatisfied
☐	A little dissatisfied
☐	Neither dissatisfied or satisfied
☐	A little satisfied
☐	Moderately satisfied
☐	Extremely satisfied

11.7 Self-perception of Age

Please indicate how old you think you appear, compared to your actual age. If you do not look your age, please indicate how many years, younger or older, you appear.

☐ I appear _____ years younger than my actual age.

☐ I appear my actual age.

☐ I appear _____ years older than my actual age.

11.8 Pain Numeric Rating Scale

Pain Numeric Rating Scale

On a scale of 0 to 10, with 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your worst pain level associated with treatment for submental fullness reduction?

0	1	2	3	4	5	6	7	8	9	10
No Pain										**Worst Pain Imaginable**