CLINICAL INVESTIGATIONAL PLAN

PROTOCOL NUMBER: 43USSA2112

A prospective open-label study to evaluate safety and effectiveness of two different reconstitution volumes of poly-l-lactic acid (PLLA) for correction of wrinkles in the décolletage area

Clinical Trial Number (CTN): **43USSA2112**

Study Device: *Sculptra*

SPONSOR:

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The study should be conducted in compliance with the clinical trial agreement, the clinical investigational plan (CIP), good clinical practice (GCP), and applicable regional or national regulations. The international standard for clinical study of medical devices for human subjects, ISO14155:2020 should be followed. The International Conference on Harmonisation (ICH) guideline for GCP (E6 (R2)) should be followed as applicable for medical device. The study should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (1).

INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

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Further details on all participating Investigators and the complete administrative structure of the study are found in the study files. Note that administrative changes are to be documented in the study files without requiring a CIP amendment.

SYNOPSIS

Clinical Study Title:	A prospective open-label study to evaluate safety and effectiveness of two different reconstitution volumes of poly-l-lactic acid (PLLA) for correction of wrinkles in the décolletage area
Clinical Trial Number:	43USSA2112
Country Involved and Planned Number of Study Centers:	Country: USA No. of Study Centers: 2
Clinical Study Design:	This is a prospective open-label study to evaluate safety and effectiveness of two different reconstitution volumes of poly-l-lactic acid (PLLA) for correction of wrinkles in the décolletage area. Approximately 30 adult female subjects will be enrolled in the study and randomized 1:1 to receive either *Sculptra* reconstituted with 8 mL Sterile Water For Injection (SWFI) with the addition of 1 mL 2% lidocaine hydrochloride (HCl), or *Sculptra* reconstituted with 17 mL SWFI with the addition of 1 mL 2% lidocaine HCl. Subjects will be stratified by Galderma Décolletage Scale (GDS) severity score (moderate or severe) and by study center. Eligible subjects will be offered treatment with *Sculptra* in four sessions spaced one month (+2 weeks) apart. Safety and effectiveness data will be collected for up to 9 months following the initial treatment. The study visits are illustrated in the Clinical study flowchart. Assessments are outlined in the Schedule of Assessments and summarized in Sections 6 and 7. Effectiveness assessments include: • Photography • Grading of wrinkles in the décolletage area by the Treating Investigator using the GDS • Global aesthetic improvement by the Treating Investigator and Subject using Global Aesthetic Improvement Scale (GAIS). CCI [redacted] Safety assessments include: • An evaluation and an interview of the subjects at each visit to obtain information about any medical occurrence that meets the definition of an AE • Subject diary • Laboratory assessment CCI [redacted]
Indication:	Correction of moderate or severe wrinkles in the décolletage area.

Total Number of Subjects (Planned):	Approximately 30 adult female subjects will be enrolled.
Primary Effectiveness Objective and Endpoint:	**Objective** To evaluate the effectiveness of *Sculptra* for correction of wrinkles in the décolletage area. **Endpoint** Percentage of responders, defined by at least one grade improvement from baseline, on the Galderma Décolletage Scale (GDS), as assessed live by the Treating Investigator, at Month 9.
Secondary Effectiveness Objectives and Endpoints:	**Objective** To evaluate the effectiveness of *Sculptra* for correction of wrinkles in the décolletage area. **Endpoints** 1. Percentage of responders, defined by at least one grade improvement from baseline, on the Galderma Décolletage Scale (GDS), as assessed live by the Treating Investigator, at Month 6. 2. Percentage of responders, defined by having at least "Improved" (improved, much improved or very much improved) according to the Global Aesthetic Improvement Scale (GAIS), as assessed by the subject and the Treating Investigator separately, at Month 6 and 9. CCI [redacted]

CCI [redacted]

Safety Objective and Endpoints:	**Objective** To evaluate the safety of *Sculptra* for correction of wrinkles in the décolletage area. **Endpoints** 1. Incidence, intensity, time to onset and duration of Adverse Events (AEs) collected throughout the study period. 2. Incidence, intensity and number of days of pre-defined expected post-treatment events collected using subject diaries for 28 days from each treatment.
Subgroup Analyses:	AEs will be summarized by treatment group injection volume: 8 vs 17 mL.
Clinical Study Duration:	The planned clinical study duration (from First Subject First Visit to Last Subject Last visit) is approximately 13 months (including 3 months for enrollment). The planned duration of study participation for each enrolled subject is approximately 10 months. *One month is defined as four weeks in the study.*
Inclusion Criteria:	The subjects must meet the following criteria to be eligible for the study: 1. Subjects willing to comply with the requirements of the study and providing a signed written informed consent. 2. Non-pregnant, non-breastfeeding females, 22 years of age or older. 3. Subjects seeking treatment for wrinkles in the décolletage. 4. Subjects with grade 2 (moderate) or 3 (severe) on the Galderma Décolletage Scale (GDS). 5. Subjects willing to abstain from any other surgical or cosmetic procedures in the décolletage area for the duration of the study (e.g., mesotherapy or resurfacing procedure (laser, chemical peels or other ablative or non-ablative treatment)). CCI [redacted]

	CCI [redacted]
Exclusion Criteria:	The presence of any of the following exclusion criteria excludes a subject from enrollment in the study: 1. Known/previous allergy or hypersensitivity to any of the *Sculptra* constituents. CCI [redacted] 4. Previous tissue augmenting therapy, contouring or revitalization treatment in the décolletage, with any of the following prior to baseline visit: CCI [redacted] 8. Previous treatment/procedure in the treatment area in the previous 6 months that would interfere with the study injections and/or study assessments, e.g.: CCI [redacted]

GALDERMA EST. 1981	Title **43USSA2112 CIP Sculptra Decolletage**	Doc id **MA-50966**

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Investigational Product:	*Sculptra*, a sterile, freeze-dried, injectable PLLA available in 367.5 mg dose vials including 150 mg PLLA. Commercially available *Sculptra,* reconstituted in either 8 mL or 17 mL per vial using SWFI, with the addition of 1 mL 2% lidocaine HCl.
Comparator/Placebo Product:	Not applicable.
Treatment area: **Treatment regimen:** **Mode of administration:**	Each subject will be treated at baseline, and optionally at Month 1, Month 2 and Month 3, with a maximum of 2 vials of *Sculptra* per treatment session, i.e. a maximum of 8 vials in total per subject. Subjects are randomized to receive *Sculptra* reconstituted in 8 mL SWFI or 17 mL SWFI, with the addition of 1 mL 2% lidocaine HCl and the study product will be administered with a 25 Gauge (G) thin wall needle in an approximately 30-45 degree angle.

CCI [redacted]

Statistical Method:	Effectiveness assessments: Continuous endpoints will be summarized using descriptive statistics, e.g. mean, median, standard deviation (SD), minimum and maximum values. Categorical endpoints will be presented in frequency tables with number and percentage of observations for each level. Responder rate regarding GAIS and GDS will be presented together with a 95% confidence interval (based on the binomial distribution). Safety assessments: Safety assessments will be presented descriptively.
Sample Size:	The sample size of approximately 30 subjects is not based on a statistical calculation. The selected number of subjects is regarded as adequate for an initial evaluation of safety and effectiveness of *Sculptra* when injected in the décolletage area.
CCI [redacted]	[redacted]

GALDERMA EST. 1981	Title **43USSA2112 CIP Sculptra Decolletage**	Doc id **MA-50966**

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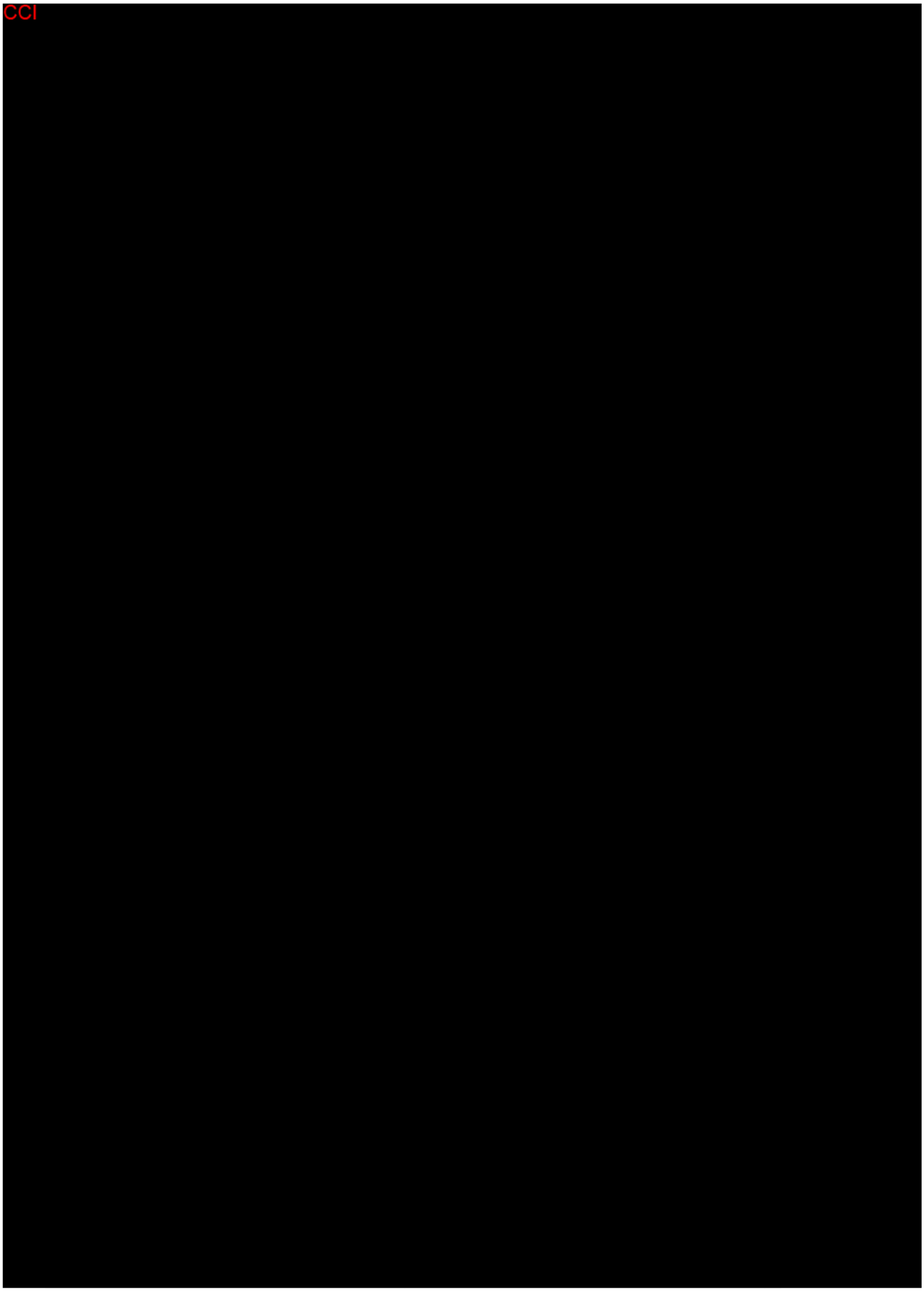

GALDERMA EST. 1981	Title **43USSA2112 CIP Sculptra Decolletage**	Doc id **MA-50966**

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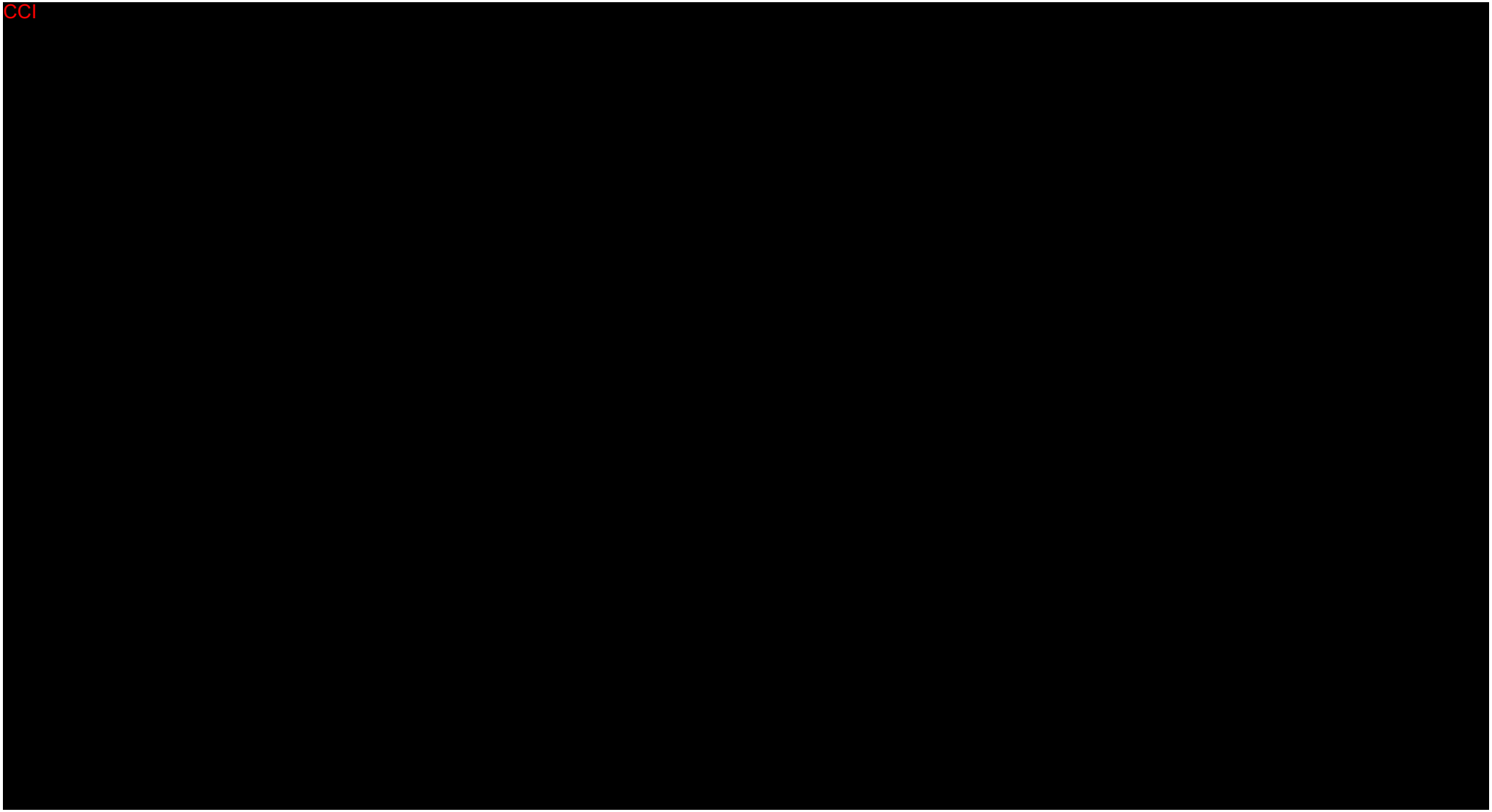

ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
AESI	Adverse Event of Special Interest
CFR	Code of Federal Regulations
CIP	Clinical Investigational Plan
CMC	Carboxymethylcellulose
CRO	Contract Research Organization
CTA	Clinical Trial Agreement
CTN	Clinical Trial Number
Device deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance (includes malfunctions, use errors, and inadequate labelling)
DBL	Database lock
DMP	Data management plan
eCRF	Electronic Case Report Form
FDA	Food and Drug Administration
FST	Fitzpatrick skin type
G	Gauge
GAIS	Global Aesthetic Improvement Scale
GCP	Good Clinical Practice
GDP	Good Documentation Practice
GDS	Galderma Décolletage Scale
HCl	Hydrochloride
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IDE	Investigational Device Exemption
IFU	Instructions For Use
Institution	Any public or private entity or agency or medical or dental facility where a clinical study is conducted.
Investigational product	Medical device being assessed for safety or performance in a study. “Investigational product” is the same as “study device”, “investigational device”, or” investigational medical device”.
Investigator	The Investigator or other qualified person, i.e. sub-Investigator, designated and supervised by the Investigator at a study site to perform critical study-related procedures or to make important study-related decisions as specified on the signature and delegation log
Investigator file	Essential documents relating to a clinical study as defined in applicable GCP guidance document and maintained by the Investigator.
IRB	Institutional Review Board

ISO	International Organization for Standardization
ITT	Intention-to-Treat
IUD	Intra uterine Device
MedDRA	Medical Dictionary for Regulatory Activities
NaCMC	Sodium carboxymethylcellulose
PI	Principal Investigator
PP	Per protocol
PLLA	Poly L- Lactic Acid
PT	Preferred Term
RA	Regulatory authority
ROPI	Report of Prior Investigations
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard deviation
SDV	Source Data Verification
SOC	System Organ Class
Sponsor file	Essential documents relating to a clinical study as defined in applicable GCP guidance document and maintained by the Sponsor.
Study files	The Investigator file and the Sponsor file
Study product	The investigational product
CCI	[redacted]
Study site	Institution or site where the study is carried out
SWFI	Sterile Water For Injection
USP	United States Pharmacopeia

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1. BACKGROUND INFORMATION

1.1 Medical background, indication and population description

The indication under investigation in this study is the correction of wrinkles in the décolletage area. Injectable fillers have been demonstrated to be safe and effective and provide volume restoration efficiently, without significant discomfort or downtime and have been used extensively for facial rejuvenation.(2, 3) CCI [redacted]

Sculptra is an injectable implant containing microparticles of poly-L-lactic acid (PLLA). *Sculptra* works as biostimulator that gradually builds collagen over time in the area injected, to help restore the skin's inner structure, and the appearance of fuller and more youthful looking skin.(5) *Sculptra* is marketed as *Sculptra* or *New-Fill* in different regions, but is hereinafter referred to as *Sculptra* in this document. *Sculptra* has previously been marked as *Sculptra Aesthetic* in the US. *Sculptra* is indicated for use in immune competent people as a single regimen for correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles. A description of the investigational device is provided in Section 5.1.

The benefits of treatment of wrinkles in the décolletage area with *Sculptra* have been reported in clinical studies and published literature.(6, 7) CCI [redacted]

In this study, the total volume of 18 mL, including 1 mL of 2% lidocaine, is being explored and compared with the results from the current labeled volume of 9 mL, including lidocaine, to assess if the larger volume is well-tolerated for treatment of wrinkles in the décolletage area.

The population in this study will comprise adult women, aged 22 years or older, with intent to undergo correction of wrinkles in the décolletage area. Subjects must have a Galderma Décolletage Scale (GDS) score of 2 (moderate) or 3 (severe) at enrollment and meet the eligibility criteria outlined in Section 4.2.1 and Section 4.2.2.

In this study each subject will be treated at baseline, and optionally at Month 1, Month 2 and Month 3, with a maximum of 2 vials of *Sculptra* per treatment session, i.e. a maximum of 8 vials in total per subject. Subjects will be randomized to receive *Sculptra* reconstituted in 8 mL Sterile Water For Injection (SWFI) or 17 mL SWFI, with the addition of 1 mL 2% lidocaine. Efficacy

assessments will include assessment of GDS, Global Aesthetic Improvement Scale (GAIS) and CCI at intervals of one month after each treatment and at Month 6 and Month 9 (see Sections 6 and 8). Also, CCI (see Sections 6 and 8). Safety assessments will include evaluation of Adverse Events (AE)s, in addition to evaluation of vision function assessment and pulmonary auscultation and percussion before and after treatment at each study visit (see Sections 7 and 8).

1.2 Study Device Profile

Sculptra is an injectable implant containing microparticles of PLLA, sodium carboxymethylcellulose (NaCMC) (USP), non-pyrogenic mannitol (USP) and SWFI (USP). *Sculptra* is available in 367.5 mg dose vials and is to be reconstituted prior to use to form a sterile, non-pyrogenic suspension. A detailed description of the investigational device is provided in Section 5.1.

In this study, *Sculptra* will be reconstituted in either 8 mL or 17 mL of SWFI, with the addition of 1 mL 2% lidocaine to form a sterile non-pyrogenic suspension. Data from this clinical study will be used to support a pivotal study, with proposed modifications to the current *Sculptra* label for the correction of wrinkles in the décolletage area.

A volume of 8 mL SWFI for reconstitution of *Sculptra* has already been investigated in an Investigational Device Exemption (IDE) study 43USSA1705 for the treatment of nasolabial folds and in study 43USSA1812 for the correction of cheek wrinkles. The positive risk/benefit profile from these studies contributed to the recent *Sculptra* label update with the use of larger volumes of SWFI for reconstitution.

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Furthermore, experienced physicians have recommended larger volume reconstitution procedures for *Sculptra* since the frequency of nodules and papules can be reduced with an increased reconstitution volume.(13, 14) Indeed an inverse relationship between the volume dilution of PLLA and the incidence of nodules has been reported (in facial and non-facial indications), with increasing volume dilution likely to decrease the likelihood of nodule formation. (8, 9)

The results from clinical investigations performed by the Sponsor are consistent with reports from published literature, where larger volumes for reconstitution (up to 18 mL)(11) have been used, and with best practice guidelines for the treatment of body skin laxity (i.e. non-facial areas) where a reconstitution volume of 16 mL PLLA for treatment of the décolletage area (i.e. 14 mL SWFI and 2 mL lidocaine 2%) has been recommended. (4) Reconstitution with 4 mL to 18 mL appears

to be safe and effective and addition of lidocaine to the product immediately prior to injection does not appear to impair safety.

1.2.1 Non-clinical documentation

The currently marketed *Sculptra* will be the product used in the clinical study. CCI [redacted]

CCI [redacted]

1.3 Risks and benefits

Anticipated benefits for subjects treated with Sculptra for the correction of wrinkles in the décolletage area include restoration of a more youthful appearance, with relatively long-lasting effects reducing the need for frequent touch-up procedures CCI [redacted] Overall, publications and clinical studies have demonstrated that treatment with Sculptra in the décolletage area was effective and well tolerated, and satisfactory aesthetic outcome results were obtained, with effects lasting for up to 2 years.(8, 9)

Since the initial approval of Sculptra in 1999 (EU) or 2004 (US), the amount of SWFI used to reconstitute Sculptra has gradually increased. Based on medical literature and physician experience, practitioners have reported improved clinical outcomes with increased reconstitution volumes that are up to two times higher than the volume recommended by the manufacturer and usually in combination with anesthetic solutions, like lidocaine 2%.(13) It has also been suggested, that a reduction in frequency of nodules/papules can be achieved with an increased reconstitution volume.(4, 8, 9). An increased reconstitution volume of 8 mL has been evaluated in study 43USSA1705 for the treatment of nasolabial folds and in study 43USSA1812 for the correction of cheek wrinkles, with both studies confirming that the alternative reconstitution volume did not

result in impaired safety or effectiveness.CCI [redacted]

Risks with Sculptra, as with any other injectable implant, include infections, perforation of blood vessels, trauma to nerves and lumps. The most common reported AEs after Sculptra treatments are formation of papules and nodules, swelling, mass/induration, of which most resolve with time.

Infection, and damage to body structures such as nerves or blood vessels at the injection site, have also been reported. Rare but serious AEs associated with the intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment, blindness, cerebral ischemia or cerebral hemorrhage, leading to stroke, skin necrosis, and damage to underlying facial structures.

Vascular occlusion resulting in ischemia/necrosis and visual disturbances including blindness have been reported following injection of any soft tissue filler in the face especially in the nose, glabella, periorbital areas, nasolabial folds and cheek, with a time to onset ranging from immediate to a few weeks following injection. For intravascular complications or embolic events, the treating physician should provide prompt medical attention and follow relevant clinical practice guidelines for handling these symptoms. (16) The treating physician should also review the Intravascular Treatment Protocol (17) provided separately as a supportive tool.

CCI [redacted]

CCI [redacted] Moreover, study Investigators will be carefully selected to assure proper device implantation and minimization of study risk and Investigators must meet the following criteria:

CCI [redacted]

Lidocaine can, in rare cases, elicit allergic reactions, and therefore subjects with a known allergy or hypersensitivity to local anesthetics should not be included in the study.

Additional information about reported AEs and anticipated risks are included in the study Instructions for use (IFU) (18) and the ROPI (15).

Stopping rules for the study are outlined in Section 7.11.

The potential risks related to treatment with Sculptra for correction of wrinkles in the décolletage area have been assessed and evaluated in accordance with requirements in the ISO 14971 standard and the Sponsor's established risk management procedures. CCI [redacted].

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESIS

2.1 Effectiveness objectives and endpoints

Primary Effectiveness objective:

To evaluate the effectiveness of *Sculptra* for correction of wrinkles in the décolletage area.

Secondary Effectiveness objectives:

To evaluate the effectiveness of *Sculptra* for correction of wrinkles in the décolletage area.

To compare the effectiveness of Sculptra for correction of wrinkles in the décolletage area between the two treatment groups.

2.1.1 Primary effectiveness endpoints

Percentage of responders, defined by at least one grade improvement from baseline, on the Galderma Décolletage Scale (GDS), as assessed live by the Treating Investigator, at Month 9

2.1.2 Secondary effectiveness endpoints

Objective

To evaluate the effectiveness of *Sculptra* for correction of wrinkles in the décolletage area.

Endpoints

1. Percentage of responders, defined by at least one grade improvement from baseline, on the Galderma Décolletage Scale (GDS), as assessed live by the Treating Investigator, at Month 6.
2. Percentage of responders, defined by having at least "Improved" (improved, much improved or very much improved) according to the Global Aesthetic Improvement Scale (GAIS), as assessed by the subject and the Treating Investigator separately, at Month 6 and 9.

CCI [redacted]

2.2 Safety objectives and endpoints

Safety objective:

To evaluate the safety of *Sculptra* for correction of wrinkles in the décolletage area.

Safety endpoints:

1. Incidence, intensity, time to onset and duration of Adverse Events (AE)s collected throughout the study period.
2. Incidence, intensity, time to onset and number of days of pre-defined expected post-treatment events collected using subject diaries for 28 days from each treatment.

3. STUDY DESIGN

3.1 Overall design

This is a prospective study to evaluate the safety and effectiveness of Sculptra for correction of wrinkles in the décolletage area.

Approximately 30 subjects will be enrolled in the study and randomized 1:1 to receive either Sculptra reconstituted with 8 mL SWFI with the addition of 1 mL 2% lidocaine hydrochloride (HCl) or Sculptra reconstituted with 17 mL SWFI with the addition of 1 mL 2% lidocaine HCl. Subjects will be stratified by GDS severity score (moderate or severe) and study center.

Eligible subjects will perform a screening visit and baseline visit; these visits may be combined, if appropriate. Eligible subjects will be offered treatment with Sculptra in four sessions spaced one month (+2 weeks) apart.

Subjects will be injected with Sculptra by the Treating Investigator at Baseline. Sufficient amount of product, as determined by the Treating Investigator, should be injected to achieve optimal correction, which is defined as at least a one grade improvement on the GDS and best correction that could be achieved as agreed upon by the Treating Investigator and the subject. Three additional treatment sessions may be performed if needed to achieve optimal correction, as determined by the Treating Investigator and subject. Treatment will stop when optimal correction has been achieved and subsequent visits will be follow-up visits.

CCI [redacted] Safety follow-up assessments will also be conducted one month after each treatment (Visits 3a, 4a, 5a and 6). Safety and effectiveness data will be collected for up to 9 months following the initial treatment.

CCI [redacted]

3.2 Study rationale and justification for design

The purpose of this study is to investigate the safety and effectiveness of *Sculptra* in two different reconstitution volumes for the correction of wrinkles in the décolletage area, with the objective of initiation of a pivotal study.

CCI [redacted]

Evaluations will be performed by the Treating Investigator and the Subject. The intention is to improve the aesthetic appearance compared to baseline. Evaluations will be performed using the validated GDS, validated CCI and the GAIS (for Investigators and subjects). CCI [redacted] GAIS improvement has been commonly accepted by the medical community in Europe and the United States as clinically meaningful indicator of global aesthetic improvement. CCI [redacted]

3.3 Number of subjects and investigational sites

Approximately 30 adult female subjects with intent to undergo correction of wrinkles in the décolletage area will be enrolled in the study. Subjects will be stratified by GDS severity score and study center.

3.4 Study duration

The planned clinical study duration (from First Subject First Visit to Last Subject Last visit) is approximately 13 months (including 3 months for enrollment). The planned duration of study participation for each enrolled subject is approximately 10 months.

One month is defined as four weeks in the study.

The End of Study is defined as the time point when the target number of subjects has been enrolled and all subjects have completed the last study visit.

3.5 Randomization

Before starting the study, a randomization list will be prepared under the supervision of a designated statistician from the Sponsor. Approximately 30 adult female subjects will be randomized 1:1 to receive either *Sculptra* reconstituted with 8 mL SWFI with the addition of 1 mL 2% lidocaine HCl or *Sculptra* reconstituted with 17 mL SWFI with the addition of 1 mL 2% lidocaine HCl. Subjects will be stratified by GDS severity score and study center. Randomization numbers will be allocated in ascending sequential order to each subject.

3.6 Blinding

Not applicable.

3.6.1 Emergency unblinding

Not applicable as the treating Investigator is not blinded to treatment.

3.7 Medical history

History of relevant surgical events, medical conditions and any prior dermatological procedures/ implants must be documented in the electronic case report forms (eCRF) using medical terminology prior to enrollment in the study.

3.8 Previous and concomitant therapies

3.8.1 Definition

Prior therapies are defined as therapies that have been used within 30 days of the screening visit or within the timelines specified in the Inclusion/Exclusion criteria and then stopped prior to the screening visit.

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- [redacted]
- [redacted]
- [redacted]

3.8.2 Categories

The following three categories are to be considered for prior and concomitant therapies:

- Drugs/therapies CCI [redacted]
- Medical and surgical procedures CCI [redacted]
- Aesthetic procedure CCI [redacted]

CCI [redacted]

3.8.3 Authorized concomitant therapies

Unless listed in prohibited concomitant therapies (Section 3.8.4), all therapies are authorized.

3.8.4 Prohibited concomitant therapies

The following therapies are prohibited during the study because they may interfere with the effectiveness and/or safety assessment of the study product(s) and/or injection procedure:

CCI [redacted]

- Planned aesthetic surgery in the décolletage area or of the breasts.
- Tissue augmenting therapy, contouring or revitalization treatment with fillers, fat-injections, collagen, Calcium Hydroxyapatite (CaHa), PLLA or lifting threads, tissue grafting, tissue augmentation with permanent implants, silicone or fat in the décolletage area.
- Needling, mesotherapy, lipolytic injection, intense pulsed light (IPL), radiofrequency, ultrasound, cryotherapy, laser or light treatment, photo modulation, chemical peeling, dermabrasion or other ablative/non-ablative procedures are prohibited in the décolletage area.
- Neurotoxin injections in or near the décolletage area or lower platysma bands.
- Tattoo or piercing in the décolletage.
- Participation in any interventional clinical study.

If a prohibited therapy becomes a necessary treatment for the safety or best interest of the subject, the Sponsor should be notified, time permitting, to discuss possible alternatives prior to administration of a prohibited therapy.

If a subject receives prohibited therapy during the clinical study, the Sponsor should be notified to discuss the pertinence and the modalities for the subject to continue in the clinical study.

3.8.5 Documentation and recording instructions

Prior and concomitant therapies are to be recorded in source documents and on the appropriate form in the eCRF. Concomitant therapies are to be recorded, reviewed, and updated at each visit. Any new concomitant therapy or modification of an existing therapy may be linked to an AE. A corresponding AE form must be completed to account for the change in therapy, except in some cases such as therapy used for prophylaxis, or dose modification for a chronic condition.

4. STUDY POPULATION

The study population will comprise adult women, aged 22 years or older, with intent to undergo correction of décolletage wrinkles. Subjects must have a GDS score of 2 (moderate) or 3 (severe) at enrollment. Study Inclusion criteria are presented in Section 4.2.1. Study Exclusion criteria are presented in Section 4.2.2.

4.1 Subject information and informed consent

The Sponsor will provide an approved sample subject information and informed consent form (ICF) to each site. Prior to performing any study procedure, the subject must be informed (in non-technical terms) by the Investigator (or designee) orally, and in writing, about the nature, importance, intended purpose, possible benefits, possible risks of the current trial and the opinion of the Institutional Review Board (IRB). Furthermore, they will be informed about randomized allocation to treatment groups, and alternative treatments available. The subjects will be informed that the participation in the trial is entirely voluntary and that they might withdraw from the study at any time without stating any reason and without prejudicing future medical treatment.

Subjects must also be informed that clinical records relevant to the study may be disclosed to the Sponsor, the monitor, a quality assurance auditor and to authorities responsible, in order to verify adherence to applicable laws and GCP. Data will be collected, recorded, processed, and may be transferred to other countries. The data will not contain any information that can be used to identify any subject. The subject must be assured that all personal data will be treated with the utmost confidentiality.

The information shall be provided in a language clearly and fully understandable to the subject. Subjects must be allowed sufficient time to make a decision and consent freely to participate in the study. Subjects will be required to read, sign, date the ICF, summarizing the discussion prior to screening/ before any study-related activities are performed. Subjects will sign and date one copy of the ICF, the Investigator/designee providing the information and obtaining the consent will also sign. The copy will be retained by the subject and the original will be retained on file by the Investigator. By signing the ICF, subjects agree that they will complete all evaluations required by the study, unless they withdraw voluntarily, or are terminated from the study, for any reason.

Photographs collected during the study will be analyzed and stored in a database by the Sponsor and its representatives in order to evaluate the effect of the treatment in the study. The subjects will be recognizable on the photographs, but their names will not be disclosed.

If information concerning the device and/or the trial that may be relevant to the subject becomes available during the study, the Sponsor will provide this to the Investigator (in written form) and

the subject must be informed accordingly. If new significant information becomes available, or there are changes to study procedures that may affect the subject's willingness to participate in the study, the ICF must be revised. The subjects must re-consent to the most current ICF version.

The ICFs and any subject information materials will be submitted for approval by the IRB and RA (as applicable). Any changes to the subject information leaflet and ICF also require approval by the IRB and RA.

4.2 Clinical study population characteristics

4.2.1 Inclusion criteria

The subjects must meet the following criteria to be eligible for the study:

1. Subjects willing to comply with the requirements of the study and providing a signed written informed consent.
2. Non-pregnant, non-breastfeeding females, over the age of 22.
3. Subjects seeking treatment for the décolletage.
4. Subjects with grade 2 (moderate) or 3 (severe) on the Galderma Décolletage Scale (GDS).
5. Subjects willing to abstain from any other surgical or cosmetic procedures in the décolletage area for the duration of the study CCI

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4.2.2 Exclusion criteria

The presence of any of the following exclusion criteria excludes a subject from enrollment in the study:

1. Known/previous allergy or hypersensitivity to any of the *Sculptra* constituents.

CCI [redacted]

4. Previous tissue augmenting therapy, contouring or revitalization treatment in the décolletage, with any of the following prior to baseline visit:

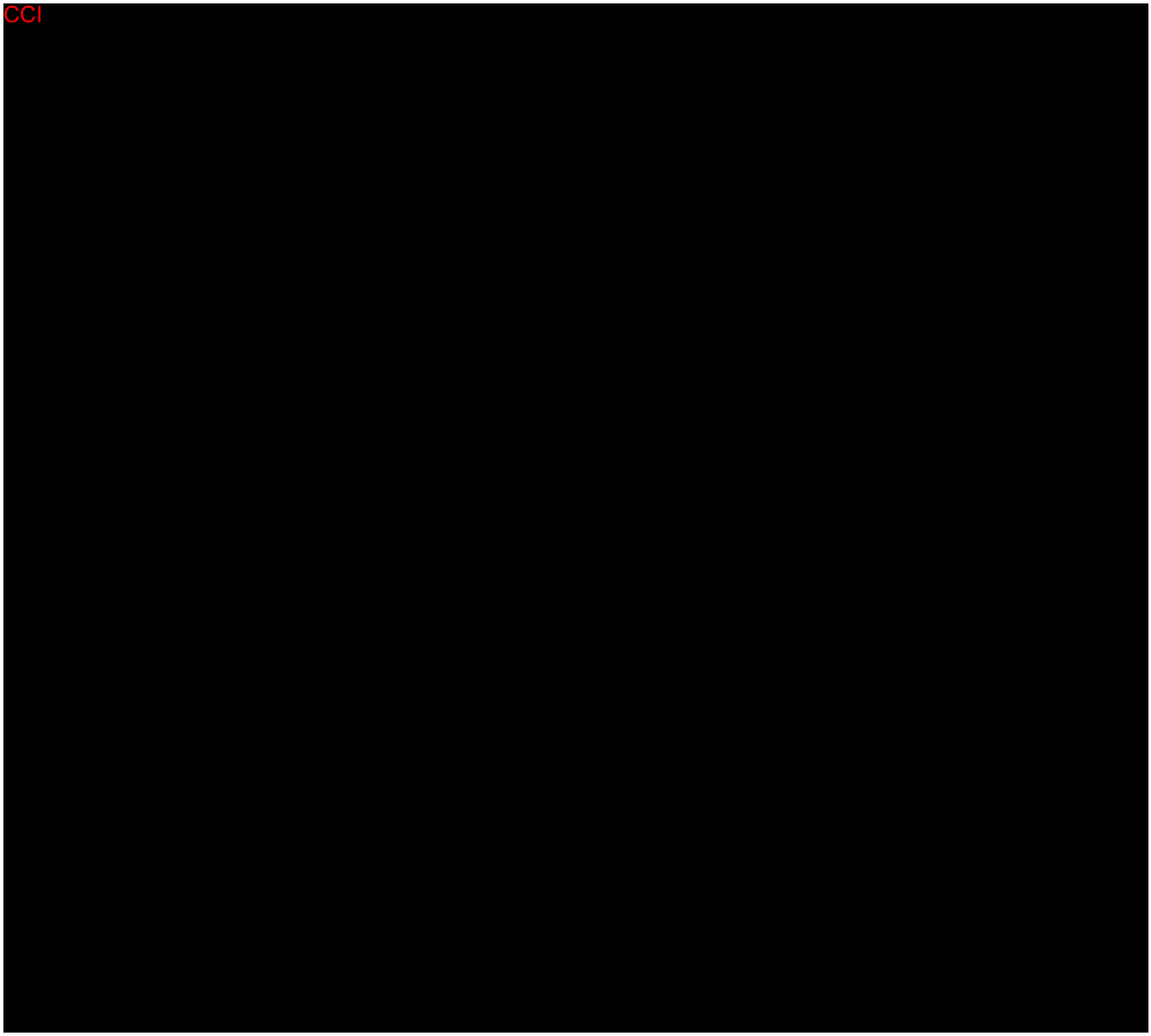
CCI [redacted]

5. Any plastic surgery or permanent surgical implant in the treatment area.

CCI [redacted]

8. Previous treatment/procedure in the treatment area in the previous 6 months that would interfere with the study injections and/or study assessments, e.g.:

CCI [redacted]



4.3 Subject identification number

Prior to any study procedures being conducted, the subject must sign the ICF. Each subject who has signed the ICF will be assigned a screening number. Upon randomization, each subject will be assigned a subject identification number that will be allocated in ascending order within each center. A screen failure is a subject who signed the informed consent, but was never enrolled (i.e. was randomized and/or received treatment) in the study. For screen failures, the subject source documents should indicate which assessments have been made and the reason why the subject was determined to be a screen failure. A screen failure should not be re-entered in the study.

For the duration of the clinical study, each subject will be identified using the subject number for all documentation and discussion.

4.4 Procedures/Reasons for subject discontinuation/withdrawal

Each subject must be advised in the ICF that the subject has the right to withdraw from the study at any time, for any reason, without prejudice. Subjects may also be discontinued from this study if the Investigator determines that it is in the subject's best interest to do so and may be withdrawn at the Investigator's discretion at any time.

The withdrawal criteria are:

- **Medical Reasons:** If the subject suffers from a medical condition and/or AEs that, in the judgment of the Investigator makes it medically necessary to withdraw the subject. The specific rationale for Investigator-initiated withdrawal of a subject for medical reasons should document the specific condition for withdrawing the subject.

- **Withdrawal by Subject:** Includes consent withdrawal, subject relocation, schedule conflicts. A subject can withdraw their consent to participate in the study at their own request or be withdrawn from participation in the study at the request of their legally authorized representative, at any time for any reason.

- **Lost to follow-up:** If a subject does not return for a scheduled visit, reasonable efforts shall be made to contact the subject. The subject should only be declared lost to follow-up after confirmation that no responses/answers were obtained from three documented phone calls and a certified letter (receipt of delivery requested).

- **Other:** This category is to be used for a subject who discontinues due to a reason other than those specified in the pre-defined categories above. The reason for discontinuation should be explained.

The reason and date for withdrawal should be documented in the subject's source documents and eCRFs. When possible, an explanatory comment should be added to further explain the reason for the withdrawal. If withdrawal of a subject occurs during a regular study visit, the eCRF for that specific visit shall be completed as far as possible.

If withdrawal of a subject occurs between regular study visits, the subject should, when possible, (irrespective of the reason for withdrawal) be scheduled for a termination visit to document the outcome of the secondary endpoints for the subject.

If a subject is withdrawn from the study, all data collected until the time of withdrawal will be used in the analyses. Subjects who receive the investigational device and are withdrawn or discontinued will not be replaced. For AEs still ongoing at the time of withdrawal, see Section 7.8.6.

4.5 Suspension or premature termination

Enrollment and injections at an investigational site will be temporarily halted if a Serious Adverse Event (SAE) occurs for a vascular embolic event that leads to skin necrosis, vision loss, or stroke and is determined by the Investigator to be directly, or possibly, related to the investigational device or injection procedure. The SAE will be investigated by the Sponsor.

CCI [redacted]

[redacted]

CCI [redacted]

5. STUDY INTERVENTION

5.1 Description of the investigational device

Sculptra is a PLLA injectable implant in the form of a sterile non-pyrogenic suspension, which is reconstituted from a sterile dry powder by the addition of SWFI. The suspension contains microparticles of PLLA. PLLA is a biocompatible, biodegradable, synthetic polymer from the alpha-hydroxy-acid family.

Each vial of *Sculptra* contains:

- Poly-L-lactic acid (PLLA)150 mg
- Sodium carboxymethylcellulose (NaCMC) 90 mg
- Non-pyrogenic mannitol 127.5 mg

PLLA is the main active ingredient from which the device has achieved its intended purpose. NaCMC acts as a suspending agent for maintaining an even distribution of PLLA particles following reconstitution. Mannitol enhances the lyophilization process and provides the suspension with a consistency that is suitable for injection.

Table 1 Description of the Investigational Study Device

Investigational Study Device	
Trade Name or Equivalent	*Sculptra*
Treatment Substance	Poly-L-lactic acid (PLLA)
Concentration	367.5 mg dose vials including 150 mg PLLA. To be reconstituted with either 8 mL SWFI or 17 mL SWFI.
Packaging	Single use vial
Storage Conditions	Store at room temperature, up to 30°C (86°F). DO NOT FREEZE. Refrigeration is not required.
Additional Anesthetic	1 mL of Lidocaine HCl 2% will be added to the vial immediately prior to injection. Topical or local injection anesthetics may be used at the discretion of the Treating Investigator.
Recommended Maximum Volume per treatment session	• Maximum of 17 mL of *Sculptra* (+1 mL 2% lidocaine HCl) per vial, maximum of 2 vials administered per treatment session **OR** • Maximum of 8 mL of *Sculptra* (+1 mL 2% lidocaine HCl) per

	vial, maximum of 2 vials administered per treatment session.
Frequency intervals	Four (4) injection sessions with 1-month (+2 weeks) intervals.
Injection needle size	25 Gauge (G) thin wall needle
Mixing Instructions	*Sculptra* will be reconstituted in 8 mL SWFI or 17 mL SWFI and used directly after mixing. 1 mL 2% lidocaine HCl will be added directly prior to injection. [redacted] CCI [redacted]
CCI [redacted]	
Injection Depth	Subdermal regions
CCI [redacted]	

5.2 Description of the reference product

Not applicable.

5.3 Additional products and materials

The following will be supplied by the study sites:

- Antiseptic (such as alcohol)
- Topical or local anesthesia.

(Note: Topical or local anesthesia may be used at the discretion of the Treating Investigator before the treatment. The type of anesthesia, administration route, product name, and quantity used must be recorded in the eCRF.)

25 G sterile needles to be used for treatment is provided by the Sponsor.

The following supplies are for reconstitution of *Sculptra* and for the addition of lidocaine and are to be provided by the end-user:

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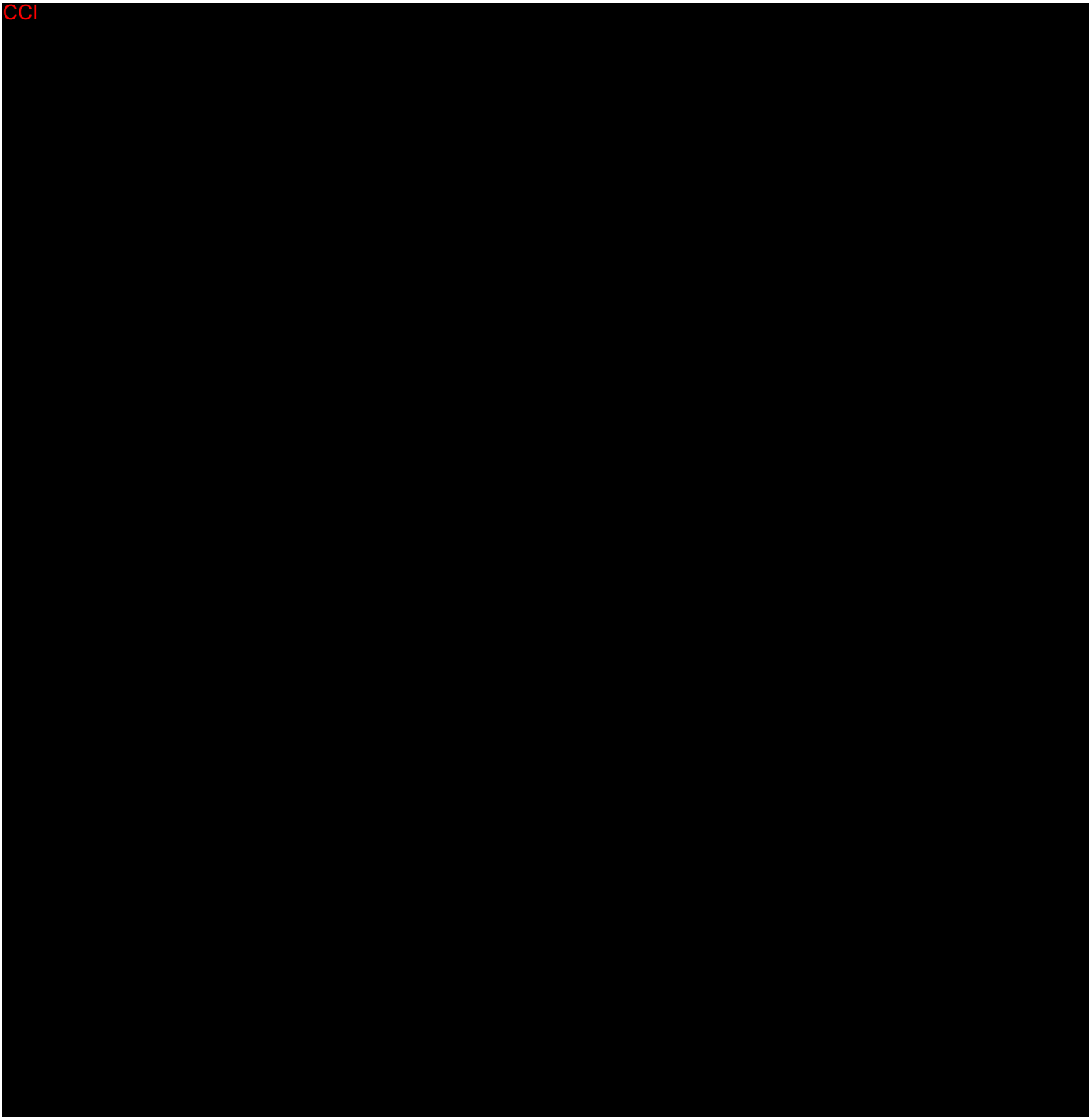

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Version: 2.0

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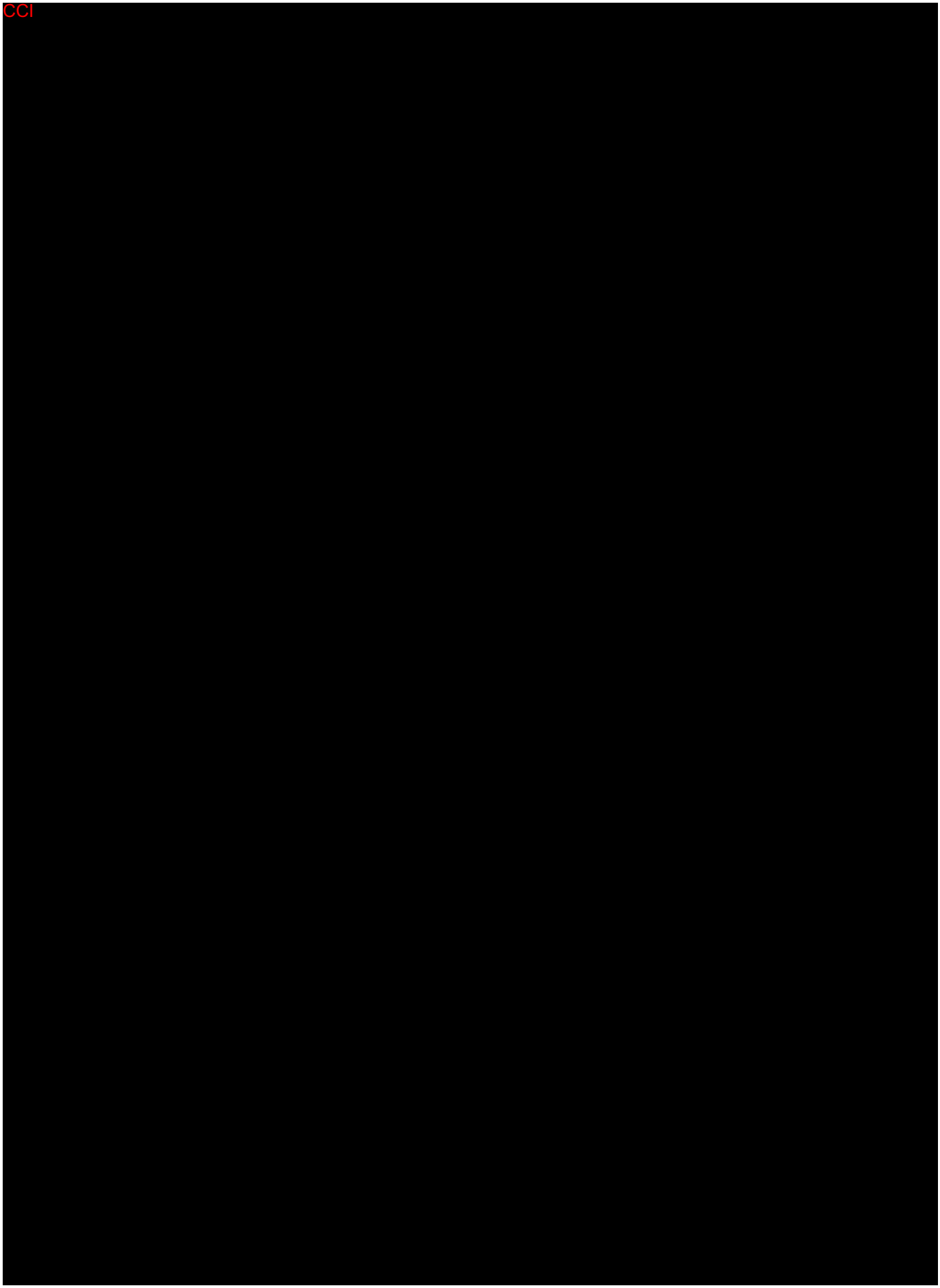

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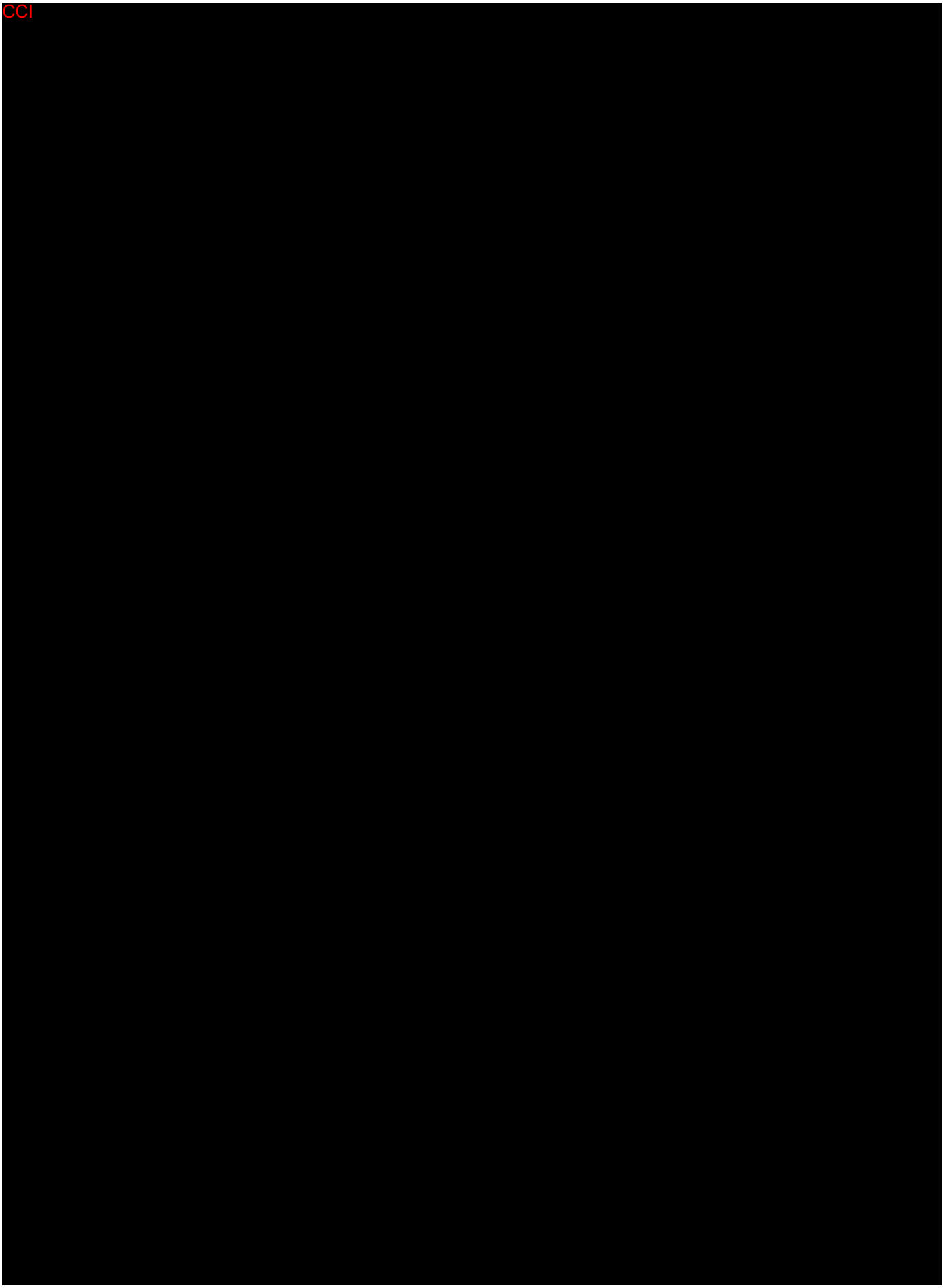

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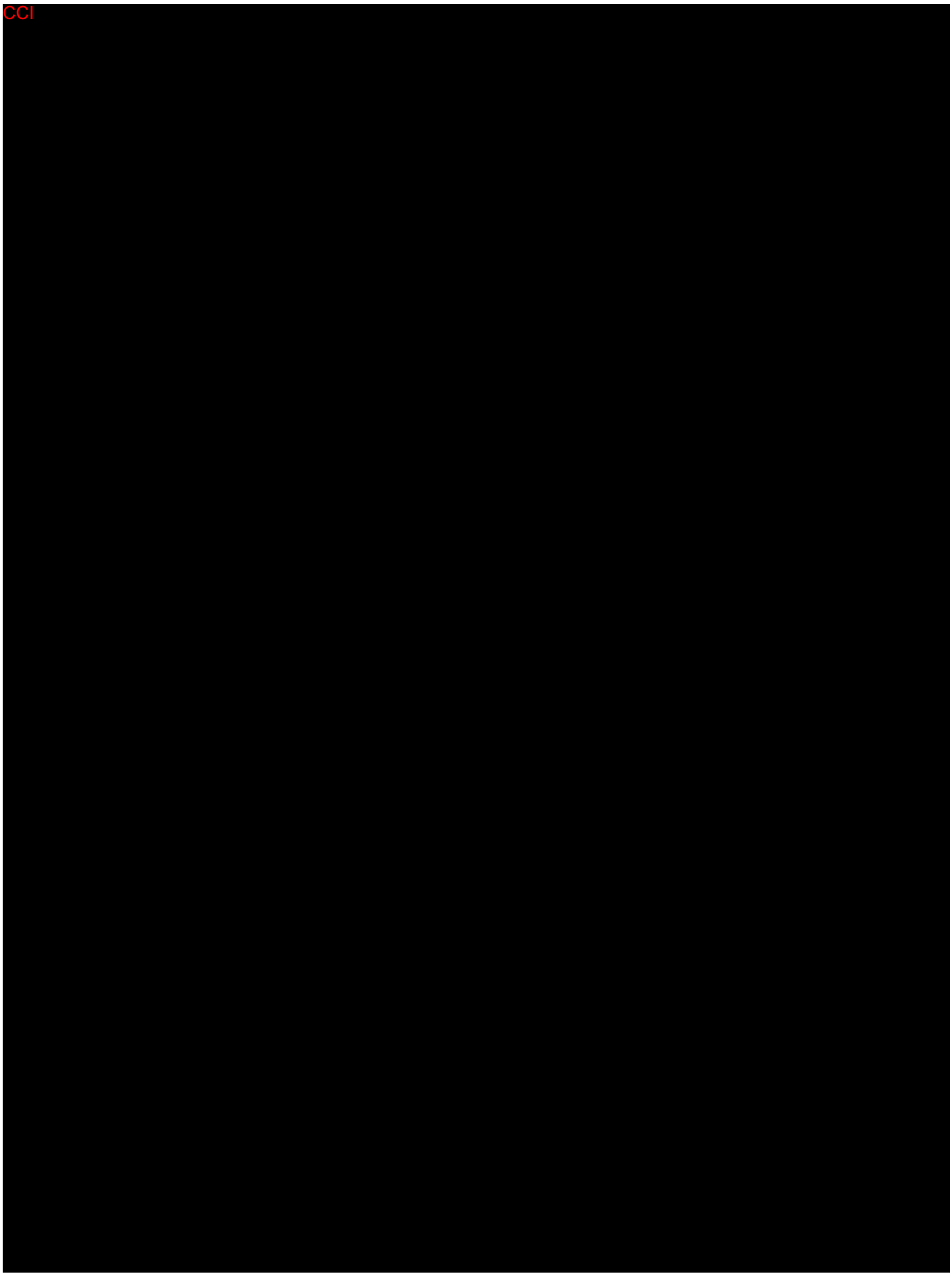

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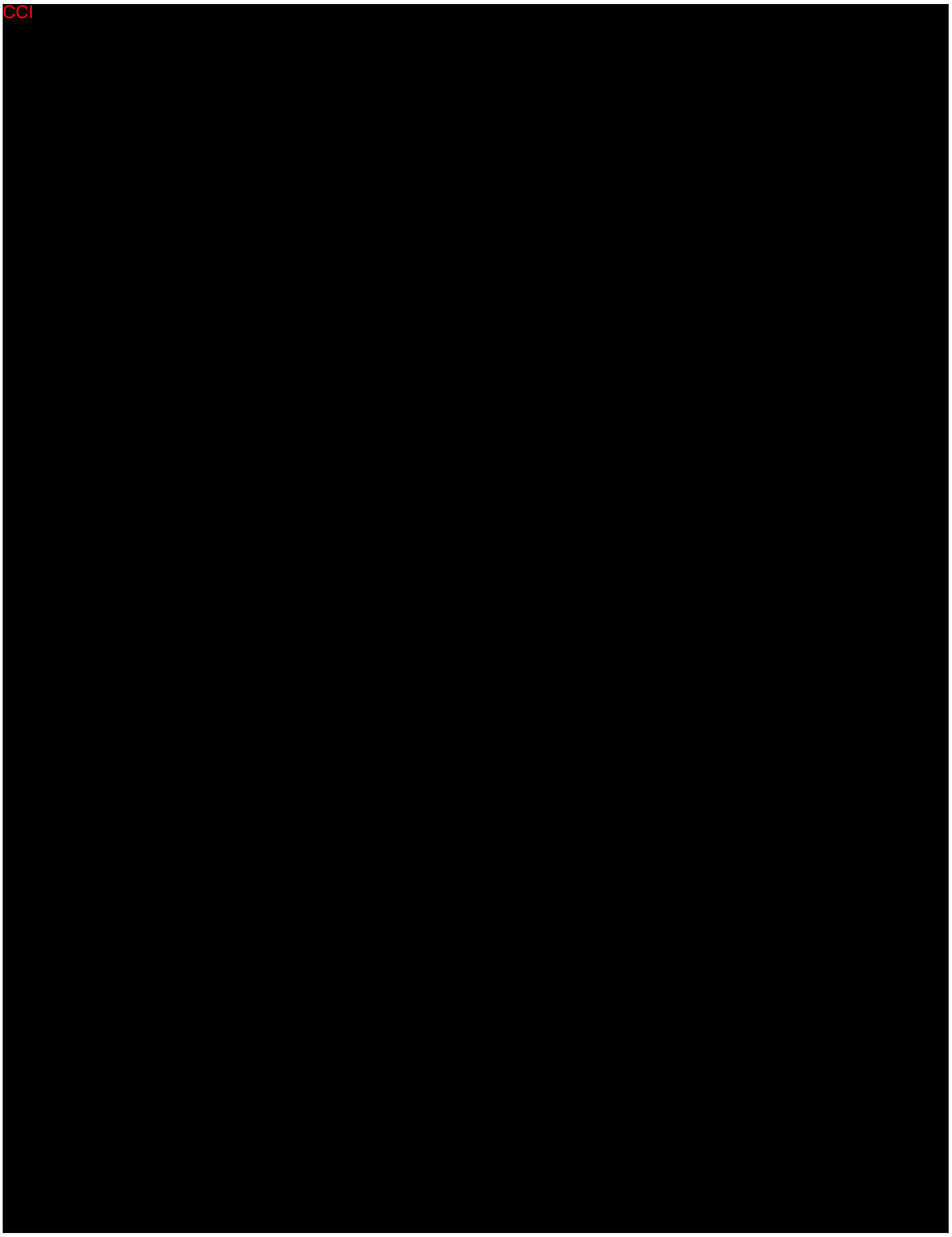

5.6.4 Treatment regimen (dose and interval)

Eligible subjects will be randomized to receive *Sculptra*, reconstituted to either 8 mL or 17 mL per vial using SWFI, with the addition of 1 mL 2% lidocaine HCl (immediately prior to injection). Subjects will receive a single regimen of *Sculptra*, which consists of up to 4 injection sessions with 1-month (+2 weeks) intervals. A maximum of 2 vials of *Sculptra* are permitted per treatment session. CCI [redacted]

CCI [redacted]

5.6.5 Post-treatment care

The injected sites should be gently massaged by the treating Investigator to distribute the product evenly. Topical cooling may be applied to reduce initial swelling and bruising. CCI [redacted]

5.6.6 Post-trial provisions

In time, the implant will be degraded in the body and additional treatments will be necessary to maintain the aesthetic result. No additional treatment will be provided beyond what is described as part of the study protocol. Subjects who seek continued treatment should discuss available treatment options with their health care provider after study completion and exit from the study.

5.6.7 Treatment compliance

The treatment will be administered by the Treating Investigator at the investigational site and will be recorded in the eCRF.

6. EFFECTIVENESS ASSESSMENTS

The methods for collecting effectiveness data are described in this section. To minimize inter-observer variability, every effort should be made to ensure that the same person who made the initial baseline assessments completes all corresponding follow-up evaluations.

The methods for collecting effectiveness data are:

- Photography
- Grading of wrinkles in the décolletage area by the Treating Investigator using the GDS.
- Global aesthetic improvement by the Treating Investigator and Subject using GAIS.

CCI [redacted]

6.1 Photography

Photographs shall be taken at the time points indicated in the Schedule of Assessments. Photographs should be captured prior to the first injection of the study device and before each additional treatment. CCI [redacted]

6.2 Galderma Décolletage Scale (GDS)

CCI [redacted]

GALDERMA EST. 1981	Title **43USSA2112 CIP Sculptra Decolletage**	Doc id **MA-50966**

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[redacted]

6.3 Global Aesthetic Improvement Scale (GAIS)

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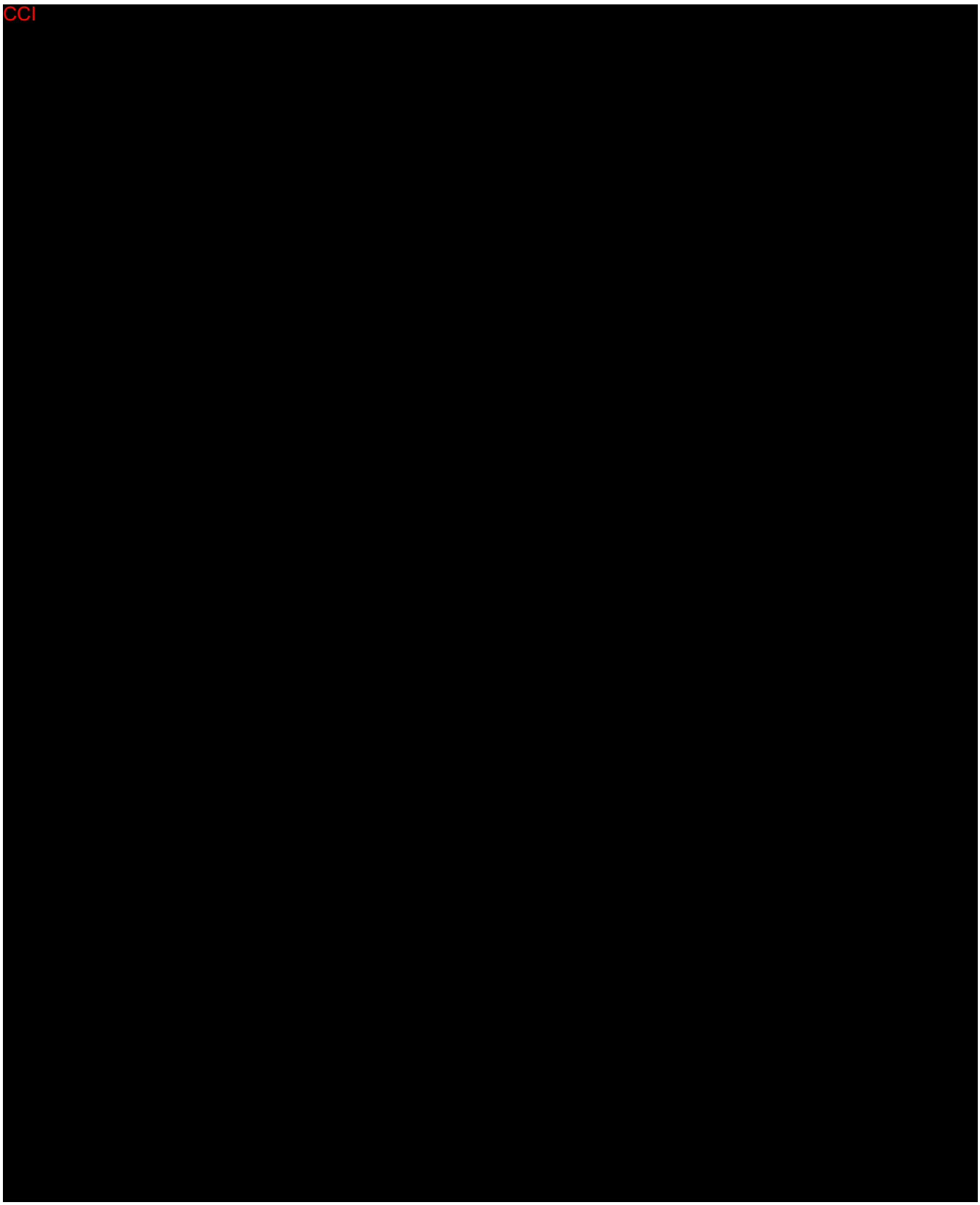

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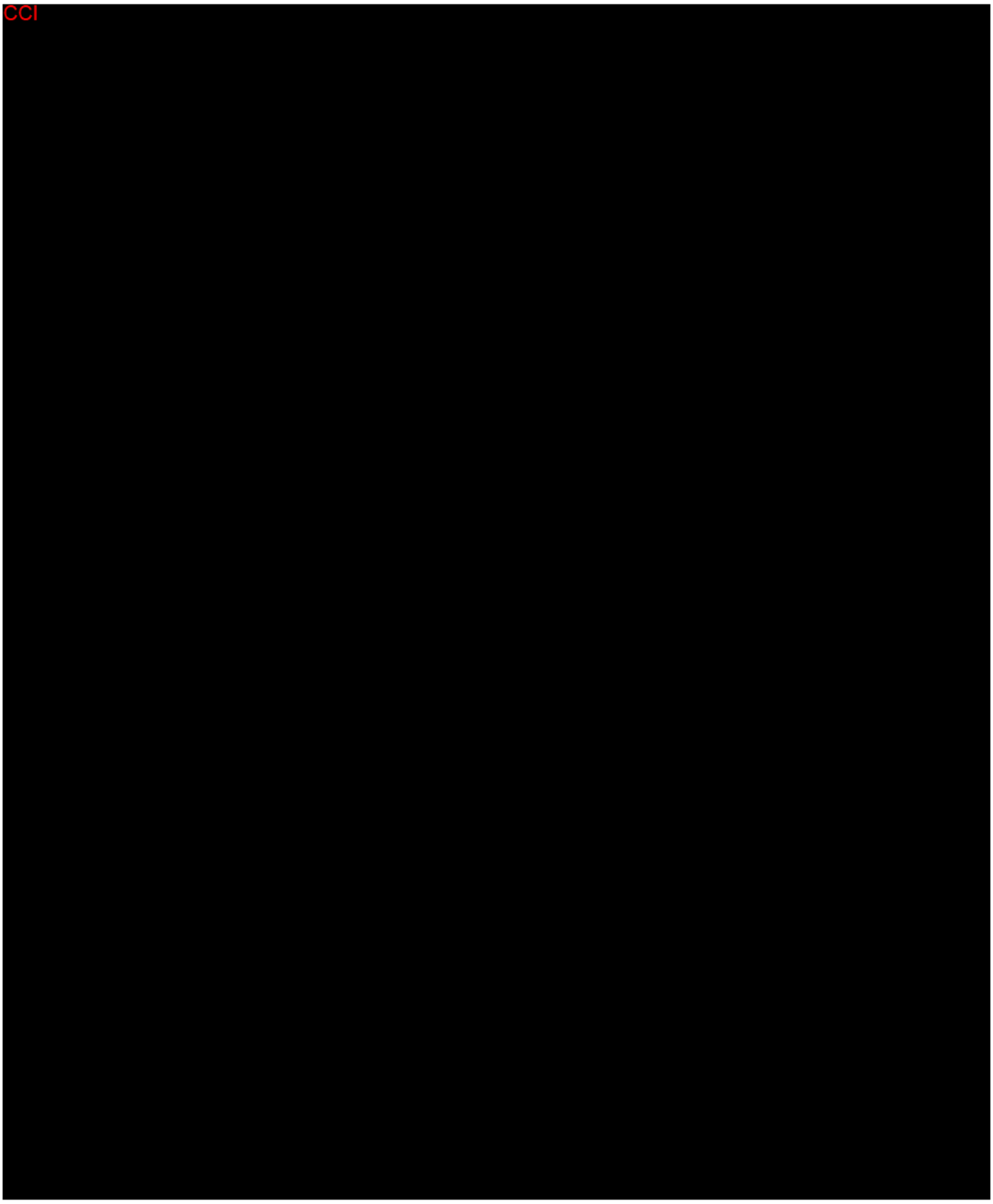

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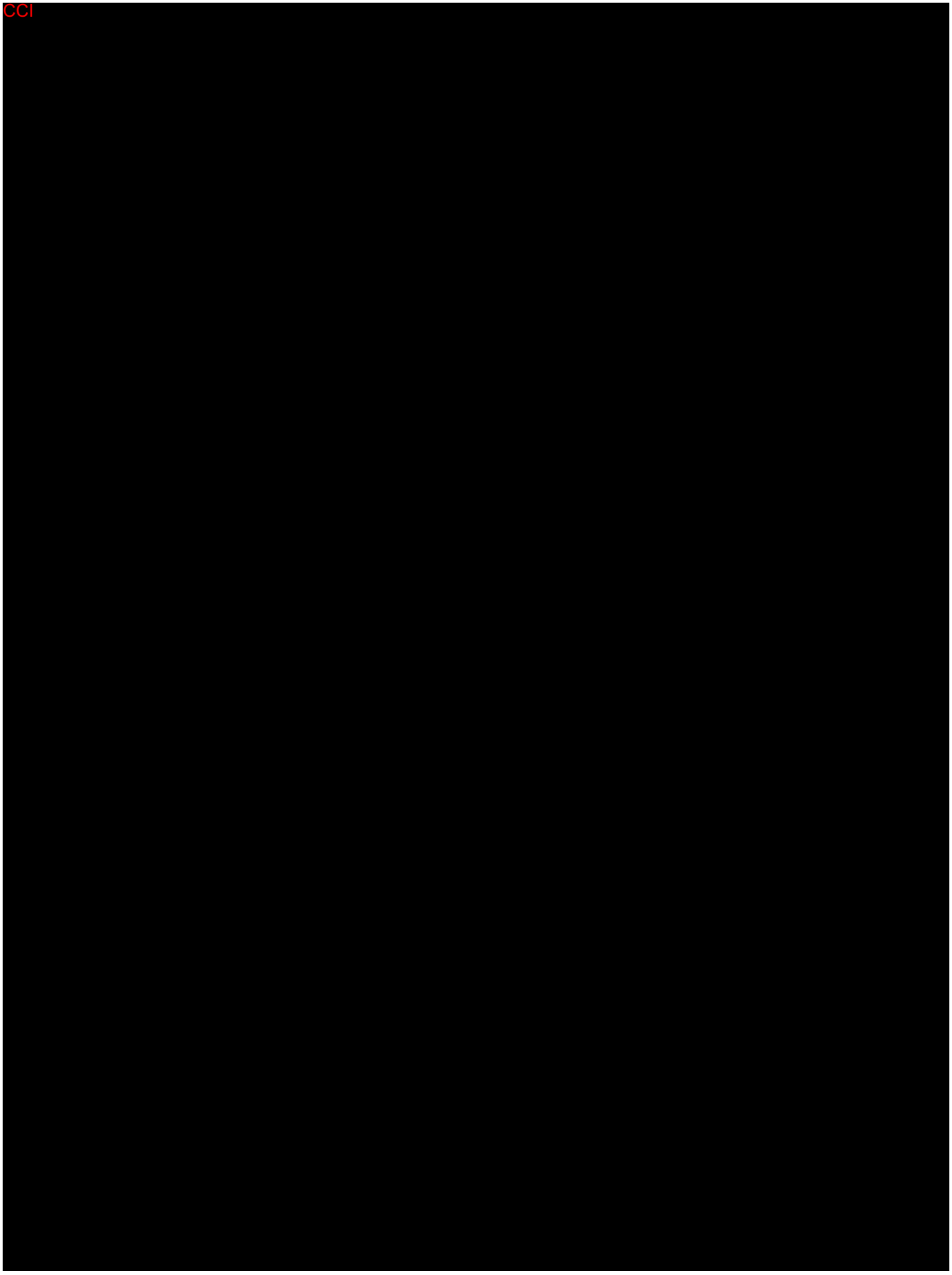

CCI [redacted]

7. SAFETY ASSESSMENTS

Safety assessments for this study include:

- An evaluation and an interview of the subjects at each visit to obtain information about any medical occurrence that meets the definition of an AE
- Subject diary
- Laboratory assessment
- CCI [redacted]

Information on AEs can also be obtained from signs and symptoms detected during each examination by the Investigator or designee, which should include visual inspection of the treatment area.

AEs must be documented in the source document and eCRF without regard for cause or relation to the investigational device. Events that occur after Screening, but prior to randomization, should be recorded in the subject's medical history.

It is the responsibility of the Treating Investigator to determine the severity of the AE and relatedness of the event to the study device and/or injection procedures. AEs must be reported as outlined in Section 7.8.

CCI [redacted]

7.2 Subject diary data

A subject diary will be dispensed to all subjects for daily completion for 28 days beginning on the injection day for each treatment with direct questioning for injection site responses: pain, tenderness, redness, bruising, swelling, itching and other. The presence and maximum intensity (grading for subject diary in Table 3) shall be assessed for the treated area.

Injection site responses that have not been pre-defined in the diary may also be recorded in the diary under "other".

Diary data will be counted and displayed separately from other AE data.

Table 3 **Grading for subject diary data**

Category	Description
None	Symptom did not occur in treated area being evaluated
Mild	Tolerable
Moderate	Affects Daily Activities
Severe	Disabling

7.3 Laboratory assessment/Pregnancy testing

For all women of childbearing potential, including those currently using contraception, a urine pregnancy test will be performed at screening and all injection visits (prior to treatment). The test result must be negative for the subject to receive any treatment with the study device. The test result will be documented in source data and the eCRF.

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[redacted]

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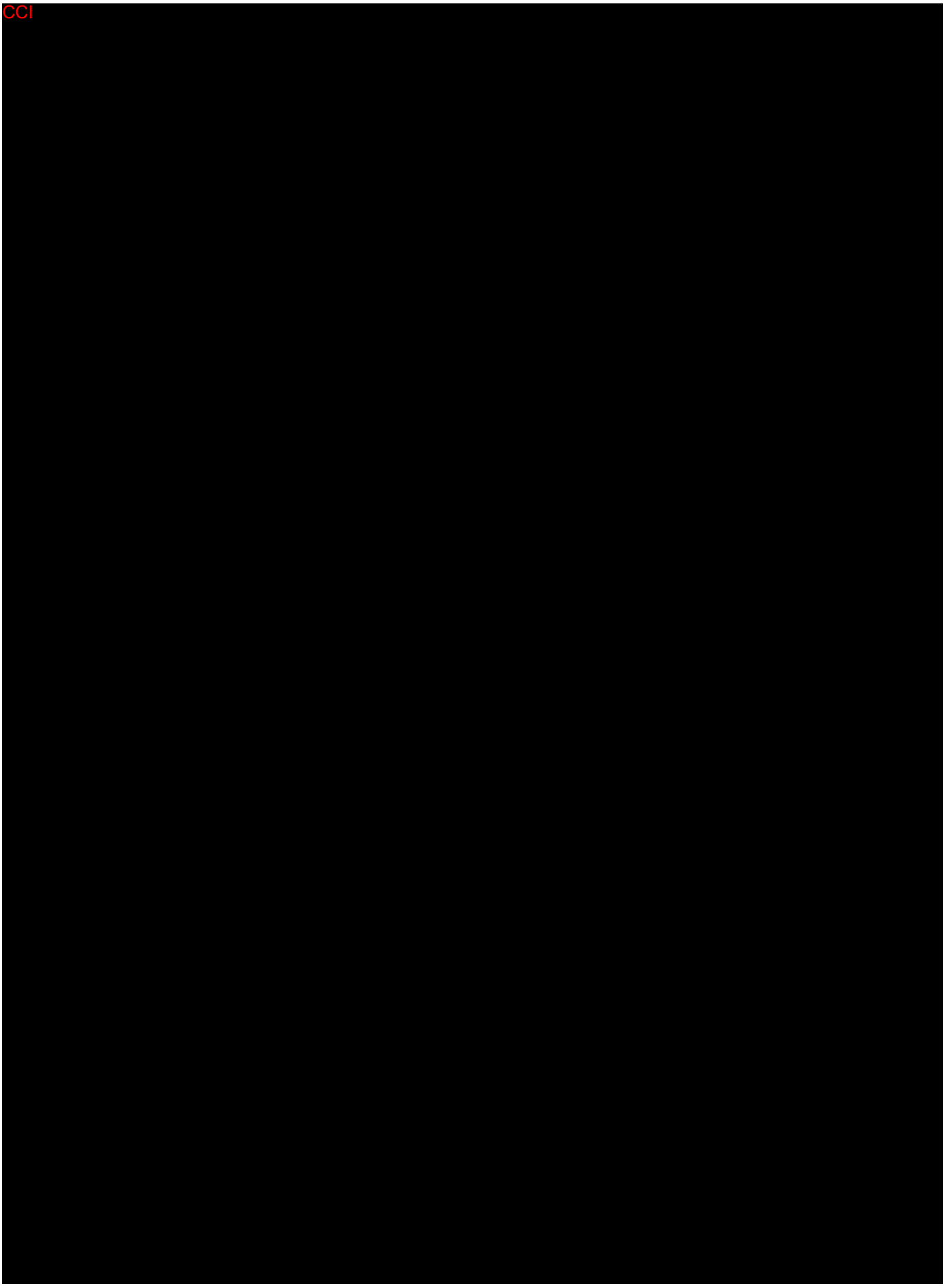

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[redacted]

7.6 Adverse events

7.6.1 Definition of an Adverse Event (AE)

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons[a], whether or not related to the study product.

This definition includes:

a) events related to the investigational product or the reference product

b) events related to the procedures involved

7.6.2 Definition of a Serious Adverse Event (SAE)

An SAE is an AE that:

a) led to death,

b) led to serious deterioration in the health of the subject, that either resulted in

1. a life-threatening[b] illness or injury, or
2. a permanent impairment of a body structure or body function, or
3. in-patient or prolonged hospitalization[c], or
4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

c) led to fetal distress, fetal death, or a congenital abnormality or birth defect

In cases of doubt, whether an AE fulfils a serious criterion or not, there should be a predisposition to report as a SAE rather than not report as such (see Section 7.8.3).

7.6.3 Definition of Unanticipated Adverse Effect

An anticipated AE for *Sculptra* is any AE included in the study specific IFU. An unanticipated adverse device effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the investigational device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence, or any other unanticipated serious problem associated with a device that relates to the right, safety or welfare of the subject (see US requirement CFR 812.3 (s)).

---

[a] For users or other persons, this definition is restricted to events related to the investigational device.

[b] The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event, which hypothetically might have caused death if it were more severe. (Source: ICH-E2A clinical safety data management: definitions and standards for expedited reporting).

[c] Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a SAE. (Source: ISO14155:2011).

CCI

[redacted]

7.6.5 Pregnancy

Pregnancy itself is not regarded as an AE.

If there is a pregnancy during the study period, the subject must be withdrawn from any subsequent study treatment but should continue to be followed within the study and the outcome of pregnancy must be reported even if the delivery occurs after study completion. Details of pregnancy reporting are outlined in Section 7.8.5.

7.7 Safety recording instructions

Each subject with an AE occurring after enrollment through study exit should be fully recorded in the source document(s) for further transcription into the eCRF. Each subject should be questioned about AEs at each study visit following randomization and treatment. The question asked should be: ”Since your last clinical visit; have you had any health problems?” Information on AEs can also be obtained from signs and symptoms detected during each examination, or from a laboratory test, observations made by the study site personnel, subject diaries, or spontaneous reports from the subjects or their relatives.

When an AE is related to a device deficiency (refer to Section 7.9), including technical device malfunction, the AE shall be recorded on the AE form/module in the eCRF and the technical complaint shall be reported separately on the clinical study complaint form, provided separately in the Investigator file, and the eCRF.

Investigators, or other study site personnel, shall record all AEs in the eCRF, including:

a) Event term (recorded in standard medical terminology and avoiding abbreviations)
b) Affected area
c) Start date (first day with symptoms)
d) Stop date (last day with symptoms)
e) Intensity (mild, moderate, or severe according to definition in Section 7.7.1)
f) Seriousness (serious or not serious, according to definition in Section 7.6.2)
g) Causal relationship to study product or study product injection procedure (yes or no, see Section 7.7.2)
h) Action taken (none, medication treatment, non-pharmacological treatment, or other procedures/tests, subject withdrawn)
i) Outcome of the AE (ongoing, recovered, recovered with sequelae, death, chronic/ stable, not recovered at the end of the study)

The AE form/module in the eCRF must be signed and dated by the Investigator.
The pre-defined, expected post-treatment events shall be assessed separately. These events shall be collected daily by subjects in a diary for up to 28 days after each treatment.

7.7.1 Assessment of Intensity

Intensity will be recorded for each reported AE. The following definitions of intensity must be used:

Mild: Awareness of symptoms or signs, but easily tolerated (acceptable)
Moderate: Enough discomfort to interfere with usual activity (disturbing)
Severe: Incapacity to work or to do usual activity (unacceptable)

If the intensity changes within one day, the maximum intensity of the AE during that day must be recorded.

7.7.2 Assessment of Causal relationship and Seriousness

Each AE, serious as well as non-serious, shall be assessed by the Investigator for causal relationship with the study device and its use (the injection procedure) and for seriousness (Yes or No) of the event.
A two-point scale ("Yes" or "No" response) shall be used for the causality assessments. The Investigators shall be asked to indicate a response to each of the following questions in the eCRF:

- "Do you consider that there is a reasonable possibility that the event may have been caused by the study device?", and
- "Do you consider that there is a reasonable possibility that the event may have been caused by the study device injection procedure?"

If any of these questions is answered with "Yes", the AE is considered related.
Each AE will also be assessed for causal relationship and seriousness by the Sponsor, in order to fulfil regulatory requirements.

7.8 Safety reporting procedures and timelines

7.8.1 Reporting of Adverse Events (AE)s

AE reporting on each subject shall start upon randomization. The reporting shall continue during each follow-up visit (including telephone contacts and extra visits between planned visits) until the last scheduled visit in the study. All AEs, non-serious as well as serious, must be reported as an AE in the eCRF.

Any events that occur after the subject signs the ICF, but before randomization, will be recorded in the subject's medical history.

7.8.2 Reporting of Adverse Events of Special Interest (AESIs)

CCI [redacted]

CCI [redacted]

Appropriate follow-up should be conducted in order to determine the cause, severity, seriousness, outcome, and relationship to the study device or procedures. In case of difficulty obtaining all the required information within 24 hours, an initial report can be submitted, with follow-up information provided within 24 hours of awareness of the new information.

The following information should be provided when reporting an AESI:

- Study Number CTN 43USSA2112
- Subject identification (age, subject number and initials)
- Date and time when the AE occurred
- Adverse event description
- Medical history related to the event
- Treatment specification
- Seriousness of the event
- Relatedness to study device or procedure
- Event outcome (with resolution date and time, if applicable)
- Prior exposure to similar device
- Investigations performed as a result of the AE
- Interventions for treatment of the AE
- Name and signature of Investigator

If the Investigator assesses an AESI to be serious, an SAE report should be submitted as specified in Section 7.8.3.

Upon receipt of the AESI report, the Medical Monitor and Sponsor will review the information provided, assess the event, and report as applicable to RA and IRB.

CCI

CCI [redacted]

The SAE form must be signed and dated by the Investigator. If the initial 24-hour SAE report does not contain full information, or if it is made without using the SAE form, the fully completed and signed SAE form shall be e-mailed to the CRO. A copy of the fully completed SAE form shall be kept at the site.

In addition, the Investigator shall report SAEs to the responsible IRB without undue delay. The Investigator is responsible for checking what reporting procedures are applicable for his/her IRB regarding SAEs and final report of the outcome of the study and to comply with such reporting procedures during the study period.

CCI [redacted]

The Sponsor is responsible for reporting to the RA, if applicable and according to national regulations.

7.8.4 Reporting of unanticipated adverse device effects

The Investigator shall submit to the Sponsor and to the reviewing IRB, a report of any unanticipated adverse device effect occurring during the study as soon as possible, but no later than 10 working days after the Investigator first learns of the effect (see US requirement 21 CFR 812:150 (a.)).

7.8.5 Pregnancy Reporting

A pregnancy confirmed during the study period must be reported by the Investigator on a pregnancy report form immediately upon knowledge of the pregnancy and the form must be submitted to the CRO according to contact details specified in Section 7.8.2. The report can be prospective or retrospective. Follow-up shall be conducted to obtain outcome information on all prospective reports.

Cases that led to fetal distress, fetal death or a congenital abnormality or birth defect, are to be regarded as SAEs and shall be reported on the exposure *in utero* report form to the Sponsor immediately but no later than 24 hours after the Investigator's awareness. These events shall be handled as SAEs during data processing. Other complications during the pregnancy that are related

to the pregnant woman which fulfil any serious criteria, such as pre-eclampsia requiring hospitalization, shall be reported and handled as SAEs. Elective abortions without complications shall not be reported as AEs.

7.8.6 Follow-up of unresolved events ongoing at termination of the study

All serious as well as non-serious AEs with a causal relationship to the study device or treatment procedure and ongoing at study end, shall be followed up after the subject's participation in the study is over. Such events shall be followed-up after the last study visit until resolved, assessed as chronic or stable, or the subject is lost to follow-up. Follow-up information shall be reported on the AE follow-up form.

7.8.7 Reporting and follow-up of events occurring after subject termination of the study

All AEs with a causal relationship to the study device or treatment procedure that the Investigator becomes aware of, serious as well as non-serious, with onset after the study termination (subject's last study visit) shall be reported to the Sponsor. The report should as a minimum include the information described in Section 7.7. The report can be sent via e-mail according to contact details specified in Section 7.8.2. The events shall thereafter be followed-up until resolved, considered chronic or stable, or the subject is lost to follow-up.

7.9 Device deficiencies

7.9.1 Definition of a device deficiency

A device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety[d], or performance.
Note: Device deficiencies include malfunctions, use errors, and inadequate labelling.

7.9.2 Recording instructions

When a device deficiency is discovered, Part A of the clinical study complaint form must be completed by the Investigator and the source data recorded in the eCRF. The type of complaint must be described and injury to the subject or user, or unintended exposure to study device, must be reported as applicable. If an injury has occurred, an AE or an SAE form must be completed as applicable (refer to Section 7.8). If no SAE was experienced as a result of the device deficiency, the Investigator must assess whether or not the device deficiency could have led to an SAE if:

- Suitable action had not been taken,
- Intervention had not been made or,
- Circumstances had been less fortunate

In Part B of the clinical study complaint form, the Sponsor will make the same assessment.

7.9.3 Reporting of device deficiencies

The Investigator must send the completed clinical study complaint form to the CRO.
A device deficiency that led to a SAE and any device deficiency that could have led to a SAE must be reported to the CRO within 24 hours after the Investigator's awareness (for contact information, see Section 7.8.2). If the form is completed within the eCRF system, refer to the eCRF completion guidelines.

[d] Inadequacy of device safety refers to properties of the device which could have or have led to an AE.

If the Investigator or the Sponsor assesses that the device deficiency could have led to a SAE, the Sponsor is responsible for reporting the device deficiency to RA and the Investigator is responsible for reporting it to the IRB.
The deficient study device shall be retained by the study site until the Sponsor has confirmed whether the device shall be returned to the Sponsor for further evaluation, or if it can be destroyed at the study site.

7.10 Independent data monitoring committee

Not applicable to this study.

7.11 Study Stopping rules

CCI [redacted]

8. DESCRIPTION OF STUDY VISITS

A description of the study visits is provided in the CCI [redacted]

A written signed informed consent (including Health Insurance Portability and Accountability Act of 1996 (HIPAA)) must be obtained prior to performing any study-related evaluations and/or procedures. The subject must be provided with a fully completed dated and signed copy.

8.1 Visit 1 - Screening (Day -30 to Day 1) – all subjects

The following activities and screening assessments will be performed within 30 days prior to baseline.
Note: The screening visit and baseline visit (Day 1) may be performed on the same day.

- Obtain Informed Consent prior to conducting any study specific procedure.
- Assess eligibility: Review inclusion/exclusion criteria.
- Perform Urine Pregnancy test for all females of childbearing potential. Test result must be negative for the subject to be eligible for the study.
- Obtain demographic and baseline data: date of birth, height, weight, cup size, ethnicity, race and Fitzpatrick Skin Type (FST).

- FST is a skin classification system that categorizes different skin colors, and their reactions to ultraviolet (UV) light.(21) For determination of the FST, see Table 4.
- Height and cup-size may be self-reported, weight must be measured at the clinic.

- Record the subject's medical history (including any prior dermatological procedures or breast procedures (e.g. augmentation, implants, breast reduction surgery)).
- Record the subject's prior and concomitant therapies.
- CCI [redacted]
- GDS assessment – Treating Investigator.
- Schedule the baseline treatment visit (Day 1) if performed on a different day than screening.

CCI [redacted]

8.2 Visit 2a, Baseline and First Treatment (Day 1) - all subjects

The screening visit and baseline visit (Day 1) may be performed on the same day. *If the screening visit and baseline visit are performed on the same day assessments will not be duplicated.*

Assessments prior to treatment:

- Re-confirm eligibility criteria
- Obtain weight measured at clinic.
- Review for changes in concomitant therapies.
- Perform Urine Pregnancy test for all females of childbearing potential (prior to treatment). Test result must be negative for the subject to be eligible for treatment.
- Record the subject's medical history
- Randomize the subject.

- Obtain Photography
- CCI
- [redacted]
- GDS assessment – Treating Investigator
- CCI

Once the subject is deemed eligible for treatment by the Treating Investigator, the following procedures should be completed:

- *Sculptra* administration
- Evaluate the subject for post-treatment AEs – Treating Investigator.
- CCI
- [redacted]
- Evaluate for device deficiencies.
- Dispense diary and instruct subject on daily diary completion. Remind subject to bring the diary to the next on-site visit.
- CCI

CCI [redacted]

CCI [redacted]

8.2 Visit 3a, Treatment 2/Follow-up (1 month [+ 2 weeks] after Treatment 1) – all subjects

Assessments prior to treatment:

- Re-confirm eligibility criteria.
- Review for changes in concomitant therapies.
- Perform Urine Pregnancy test for all females of childbearing potential (prior to treatment, if applicable). Test result must be negative for the subject to be eligible for treatment.
- Obtain Photography.
- CCI [redacted]
- [redacted]
- AE assessment.
- Collect subject diary from treatment 1.
- GAIS assessment – Treating Investigator and Subject.
- GDS assessment – Treating Investigator.
- CCI [redacted]
- Schedule the next on-site visit (1 month [+ 2 weeks] after Treatment 2).

Treatment and assessments post-treatment, for subjects who receive a second treatment:

- Sculptra administration (optional).
- Evaluate the subject for post-treatment AEs – Treating Investigator.
- CCI [redacted]
- [redacted]
- Evaluate for device deficiencies.
- Dispense diary and instruct subject on daily diary completion. Remind subject to bring the diary to the next on-site visit. (If applicable, if a second treatment is administered.)

CCI [redacted]

CCI [redacted]

8.5 Visit 4a, Treatment 3/Follow-up (1 month [+ 2 weeks] after Treatment 2) – all subjects

Assessments prior to treatment:

- Re-confirm eligibility criteria.
- Review for changes in concomitant therapies.
- Perform Urine Pregnancy test for all females of childbearing potential (prior to treatment, if applicable). Test result must be negative for the subject to be eligible for treatment.
- Obtain Photography.
- CCI [redacted]
- AE assessment.
- Collect subject diary from treatment 2 (if applicable, if a second treatment was administered).
- GAIS assessment – Treating Investigator and Subject.
- GDS assessment – Treating Investigator.
- CCI [redacted]
- Schedule the next on-site visit (1 month [+ 2 weeks] after Treatment 3).

Treatment and assessments post-treatment, for subjects who receive a third treatment:

- Sculptra administration (optional).
- Evaluate the subject for post-treatment AEs – Treating Investigator.
- CCI [redacted]
- Evaluate for device deficiencies.
- Dispense diary and instruct subject on daily diary completion. Remind subject to bring the diary to the next on-site visit. (If applicable, if a third treatment is administered.)

CCI [redacted]

- CCI [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

8.8 Visit 5a, Treatment 4/Follow-up (1 month [+ 2 weeks] after Treatment 3) – all subjects

Assessments prior to treatment:

- Re-confirm eligibility criteria.
- Review for changes in concomitant therapies.
- Perform Urine Pregnancy test for all females of childbearing potential (prior to treatment, if applicable). Test result must be negative for the subject to be eligible for treatment.
- Obtain Photography.
- CCI [redacted]

[redacted]

- AE assessment.
- Collect subject diary from treatment 3 (if applicable, if a third treatment was administered).
- GAIS assessment – Treating Investigator and Subject.
- GDS assessment – Treating Investigator.

CCI [redacted]

- Schedule the next on-site visit at Month 6 (+2 weeks) after Baseline.

Treatment and assessments post-treatment, for subjects who receive a fourth treatment:

- Sculptra administration.
- Evaluate the subject for post-treatment AEs – Treating Investigator.
- CCI [redacted]

[redacted]

- Evaluate for device deficiencies.
- Dispense diary and instruct subject on daily diary completion. Remind subject to bring the diary to the next on-site visit. (If applicable, if a fourth treatment is administered.)

CCI [redacted]

8.11 Visit 6, Safety follow-up (1 month [+ 2 weeks] after Treatment 4) – for subjects that received treatment at Visit 5a.

- Review for changes in concomitant therapies.
- AE assessment.
- CCI [redacted]
- Collect and review subject diary.

8.12 Visit 7, Follow-up (month 6 [+ 2weeks] after baseline) - all subjects

- Obtain weight measured at clinic.
- Review the subject's concomitant therapies.
- Obtain Photographs.
- Assess for AEs- Treating Investigator
- CCI [redacted]

- CCI [redacted]
- GAIS assessment – Treating Investigator and Subject.
- GDS assessment – Treating Investigator.
- CCI [redacted]

8.13 Visit 8/Final visit/Early termination, (month 9 [±2 weeks] after baseline) - all subjects

- Obtain weight measured at clinic.
- Review the subject's concomitant therapies.
- Obtain Photographs.
- Assess for AEs- Treating Investigator
- CCI [redacted]
- GAIS assessment – Treating Investigator and Subject.
- GDS assessment – Treating Investigator.
- CCI [redacted]

8.14 Unscheduled Visits

- Unscheduled visits can be performed if necessary (for example in case of an AE requiring specific treatment).
- Unscheduled visits related to the study should be documented and all AEs must be captured.

9. STATISTICAL DESIGN AND ANALYSIS

9.1 General

A comprehensive Statistical Analysis Plan (SAP) with a detailed description of all statistical analyses will be developed.

All study data will be listed in subject data listings.

All statistical analyses, including summary tables and data listings, will be performed using SAS. Confidence intervals will be two-sided and constructed at a confidence level of 95%.

All endpoints will be summarized descriptively. Continuous endpoints will be summarized using mean, median, standard deviation (SD), minimum and maximum values, for the observed value as well as the change from baseline. Categorical endpoints will be presented in frequency tables with number and percentage of observations for each level.

9.2 Analysis populations

The following populations will be defined:

- Safety — Includes all subjects who were treated with *Sculptra*. Subjects are analyzed based on the as treated principle (i.e. according to the treatment actually received).
- Intention-to-treat (ITT) — Includes all subjects who were randomized based on the as randomized principle (i.e. according to the treatment they were randomized to).
- Per protocol (PP) — Includes all subjects in the ITT who complete the visit 9 months after baseline without any deviations considered to have substantial impact on the primary effectiveness outcome.

The ITT is the primary population for all effectiveness analyses. The primary effectiveness analysis will be repeated using the PP analysis set if there is at least a 10% difference in the number of subjects between the PP and ITT sets. Safety analysis is performed based on the safety population set. The disposition of subjects will be presented in tables and/or figures as appropriate.

9.3 Demographics, baseline assessments, and subject characteristics

Demographic endpoints, baseline assessments, and subject characteristics will be presented by treatment group, based on the ITT analysis set using descriptive statistics, as appropriate.

9.4 Effectiveness analysis

Continuous endpoints will be summarized using descriptive statistics, e.g. mean, median, SD, minimum and maximum values. Categorical endpoints will be presented in frequency tables with number and percentage of observations for each level.

Responder rate regarding GAIS and GDS will be presented together with a 95% confidence interval (based on the binomial distribution). The difference in responder rate regarding GAIS and GDS will be calculated between the two groups presented together with a 95% confidence interval.

No adjustment to the level of significance will be performed; p-values obtained for any endpoint other than the primary will only be provided for ease of interpretation of the results.

9.5 Safety analysis

The number and percentage of subjects reporting each pre-defined, expected, post-treatment symptom, as collected in the 28-day diary, will be presented in total and by maximum intensity. Number of days with the event will be presented by treatment group and category: 1, 2-7, 8-14, and 15-28 days.

All AEs will be coded according to medical dictionary for regulatory activities (MedDRA) and summarized by system organ class (SOC), preferred term (PT) and treatment.

AEs related to the study device or injection procedure and unrelated AEs will be presented by maximum intensity, SOC and PT. For related AEs, the number of days to onset and the duration of the event will be summarized by SOC and PT using mean, SD, min, max and median. Action taken for related AEs will also be summarized by SOC and PT. Serious AEs will be listed. To evaluate consistency of AEs across different subgroups, AEs will also be summarized by treatment group injection volume: 8 vs 17 mL.

In addition, a summary of all AEs will be provided, which will include (but is not limited to):

- number of subjects with at least one AE and number of events (in total as well as SAEs)
- number of subjects with at least one related AE and number of events (in total as well as SAEs)
- number of subjects with at least one un-related AE and number of events (in total as well as SAEs)
- number of subjects who did not have an AE

9.6 Handling of missing data

The number of missing values will be summarized and reported as appropriate. For the ITT analysis of the Treating Investigator GDS Responder rate at Month 9 after baseline (primary endpoint), missing values will be assumed to be missing due to lack of effect. Therefore, the primary method of imputation will use the baseline observation carried forward (BOCF) method. Impact of missing data on the primary endpoint will be evaluated by performing sensitivity analysis based on the observed cases, as well as worst-case and best-case imputation in the ITT set.
All other effectiveness endpoints will be evaluated based on the observed cases in ITT.
Descriptive statistics of all safety data will be performed on observed cases in the Safety population

CCI [redacted]

9.8 Independent data monitoring committee

Not applicable to this study.

9.9 Withdrawals and deviations

All withdrawn subjects will be listed individually, including at least subject number, date and reason for withdrawal, and last visit performed.

Subjects with CIP deviations will be listed individually, including subject number and observed deviation. Depending on the seriousness of the deviation, the subject may be excluded from the PP population, which shall be documented prior to database lock (DBL).

Deviations from the statistical plan will be documented in the Clinical Study Report (CSR). If the statistical plan needs to be changed before DBL, but after the finalization of the SAP, the SAP will be amended.

9.10 Sample size

CCI [redacted]

10. DATA HANDLING AND MANAGEMENT

For ethical compliance and application to IRB and/or RA, please see Sections 11.1 and 11.2, respectively.

10.1 Protection of Personal Data

All processing of personal data must be carried out in accordance with national legislation concerning the protection of personal data. The Institution and the Investigator are responsible for complying with all requirements pursuant to national legislation in which the Institution and the Investigator are located. The Sponsor will ensure that all requirements for data processing are fulfilled.

The Investigator understands that clinical studies conducted under an IDE are exempt from the study subject identifier confidentiality provisions of the HIPAA, and the study subject should be made aware of this exception in the informed consent. The Institution and Investigator are jointly responsible for providing sufficient information to all subjects to enable them to give their informed consent not only to the participation in the investigation, but also to the processing of Personal Data. Such information includes information regarding the purposes of the processing, the length of time during which Personal Data will be stored, the right of access to stored Personal Data and the right to correction or purging of incorrect or obsolete Personal Data. A subject may also withdraw his or her consent at any time.

A subject who withdraws his or her consent to the processing of Personal Data must be considered to have withdrawn from the investigation, but the data collected until the consent was withdrawn may be used in the statistical analyses.

Authorized representatives from the Sponsor or a RA may visit the investigational site to perform audits/inspections, including source data verification (SDV), i.e., comparing data in the subjects' medical records and the eCRF. Data and information will be handled with strict confidentiality.

The study shall include collection and processing of personal data as specified in the Regulation (EU) 2016/679 (General Data Protection Regulation, GDPR) on the protection of individuals with regard to the processing of personal data. For the purposes of the study, the Sponsor will be considered the data controller, and the Institution and Investigator will both be considered data processors.

10.2 Personnel training

The study monitor will ensure that the Investigator and study site personnel understand all requirements of the protocol, and their regulatory responsibilities as an Investigator. Training will be provided at the Investigator's meeting and may also be provided at the study site, and/or by instruction manuals. In addition, the study monitor will be available for consultation with the Investigator and will serve as the liaison between the study site and the Sponsor.

Study sites must adhere to good documentation practice (GDP) for all maintained records and for any applicable changes to these records. GDP principles must be adhered to, and all records must be attributable, legible, contemporaneous, original, accurate, complete, chronological, consistent and permanent. All relevant study site personnel must undergo training in the key elements of GDP at the site initiation visit (SIV), and training must be documented for each person.

10.3 Data management and documentation

Data management based on GCP refers to the activities defined to achieve safe routines to enter clinical data information into a database, efficiently and to avoid errors. The data management routine includes procedures for database set-up and management, data entry and verification, data validation, and documentation of the performed activities including information of discrepancies in the process. The data management process will be described in detail in the data management plan (DMP).

The database, the data entry screens and program will be designed in accordance with the CIP and the eCRF template. Data validation will be performed by computerized logical checks and manual review. Drugs and events will be coded in accordance with World Health Organization (WHO) Drug and MedDRA dictionaries as specified in the DMP. Safety data (SAE and if applicable AESI) in the clinical database will be reconciled against the data in the safety database.

When all efforts have been made to ensure that the data recorded in the eCRFs and entered in the database is as correct and complete as possible, the clinical database will be locked. Study data will be transferred to SAS datasets, which thereafter will be write-protected. Statistical analyses will be generated in SAS using data from the locked datasets.

10.3.1 Data entry and collection

An electronic data capture application, compliant with regulatory requirements for software validation US FDA 21CFR11 will be used to collect, modify, maintain, archive, retrieve, and transmit study data. An eCRF is required and shall be completed electronically for each screened subject (screening visit) and enrolled subjects (subsequent visits).

The eCRF includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Study data shall be entered directly from the source documents, which are to be defined at each site before inclusion of the first subject.

Authorized study site personnel designated by the Investigator shall complete data collection. Appropriate training and security measures shall be completed with all authorized investigation site personnel prior to the study being initiated and any data being entered into the system for any subject.

The study data is the sole property of the Sponsor and shall not be made available in any form to third parties without written permission from the Sponsor, except for authorized representatives of appropriate RA. At the end of the study, electronic data are retained by the Sponsor and a copy (provided by the vendor) is retained at the study site as part of the Investigator file. Any delegation of collection of data shall be specified and recorded.

All data shall be entered in English. The eCRFs should always reflect the latest observations on the subjects participating in the study. Therefore, the eCRFs shall be completed as soon as possible during, or after, the subject's visit. The subject's identity must always remain confidential, i.e. the name and address of the subjects must not be registered in the eCRFs or in the database. The Investigator must verify that all data entries in the eCRFs are accurate and correct. If some assessments are not done, or if certain information is not available, not applicable or unknown, the Investigator shall indicate this in the eCRF. The Investigator shall electronically sign off the study data. By signing, the Investigator takes responsibility for the accuracy, completeness, and legibility of the data reported to the Sponsor in the eCRF.

The monitor shall review the eCRFs and evaluate them for completeness and consistency. Each eCRF shall be compared with the respective source documents to ensure that there are no discrepancies between critical data. All entries, corrections, and alterations shall be made by the Investigator or his/her authorized designee. The monitor cannot enter data in the eCRFs. Once study data have been submitted to the central server via the eCRF, corrections to the data fields will be audit trailed, meaning that the reason for change, the name of the person who made the change, together with time and date will be logged. Roles and rights of the site personnel responsible for entering study data into the eCRF shall be determined in advance. If discrepant data is detected during review of the data, either by the Sponsor or by its representatives, the responsible data manager or monitor shall raise a query in the electronic data capture application. The query shall state the question or data to be changed and shall be resolved in the system by the Investigator or his/her authorized designee. The appropriate study site personnel shall answer the queries in the eCRF within a reasonable timeframe. Answered queries will be audit trailed by the electronic data capture application, meaning that the name of study site personnel, time, and date are logged. Answered queries will then be closed by the appropriate study personnel (i.e. data manager, site monitor, etc.).

eCRF records will be automatically appended with the identification of the creator, by means of their unique UserID. Specified records shall be electronically signed by the Investigator to document his/her review of the data and acknowledgement that the data are accurate. This will be facilitated by means of the Investigator's unique UserID and password; date and time stamps will be added automatically at the time of electronic signature. If an entry in an eCRF requires change, the correction shall be made in accordance with the relevant software procedures.

All changes will be fully recorded in a protected audit trail and a reason for the change shall be stated. Once all data have been entered, verified, and validated, the database will be locked.

10.3.2 Source documentation

Source documents are all documents used by the Investigator or hospital, that relate to the subject's medical history, that verifies the existence of the subject, the inclusion and exclusion criteria, and all records covering the subject's participation in the study. They include laboratory notes, memoranda, material dispensing records, subject files, etc.

The Investigator is responsible for maintaining source documents. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry and should be explained, if necessary. Source documents shall be made available for inspection by the monitor at each monitoring visit. The Investigator must submit a completed eCRF for each subject for whom signed informed consent has been collected.

All supportive documentation submitted with the eCRF, such as laboratory or hospital records, shall be clearly identified with the CTN and subject number. Any personal information, including name, shall be removed or rendered illegible, to preserve individual confidentiality.

10.3.3 Archiving / record keeping

The Investigator/Institution shall permit study-related monitoring, audits, IRB review, and RA inspections and shall provide direct access to the source data/medical record including the identity of all participating subjects (sufficient information to link records, i.e. eCRF, medical records, original signed ICFs and detailed records of study product accountability). The records shall be retained by the Investigator as required by local legislation and international guidelines. Any transfer of responsibility for storage of the records shall be documented and the Sponsor must be informed in writing.

The Sponsor shall verify that each subject has consented in writing to direct access to the original medical record/source data (by the use of written subject information and signed informed consent). The data recorded in the eCRFs will be checked for consistency with the source documents/medical record by the monitor during monitoring (SDV). In order to be able to perform SDV, information about each subject's participation in the study must be detailed in the medical record or other relevant source.

All records pertaining to the conduct of the study, including signed eCRFs, ICFs, study product accountability records, source documents, and other study documentation must be retained for as long as is specified in the CTA after study completion, or longer if required by national legislation. The Sponsor will inform the site(s) as to when these documents no longer need to be retained. Measures shall be taken to prevent accidental or premature destruction of these documents (e.g. protection against damage and unauthorized access, preferably by storage in a fireproof cabinet).

After study completion and DBL, a security sealed CD with electronic study data shall be provided by the eCRF vendor for archiving.

It is the Investigator's responsibility to inform the Sponsor in writing if the Investigator file is moved or if the responsibility for the documents is transferred elsewhere.

10.4 Quality control / quality assurance

10.4.1 Quality Control

On-site monitoring of the study will be arranged by the Sponsor according to GCP guidelines to verify that the rights and well-being of the subjects are protected, the reported data are accurate, complete, verifiable from source documents, and that the conduct of the study complies with the approved CIP, subsequent amendment(s), GCP and the applicable regulatory requirements.

Any CIP deviation shall be documented appropriately, verified, discussed, and collected by the monitor and appropriate actions will be taken. The Investigator is responsible for promptly reporting any deviations from the CIP that affects the rights, safety or well-being of the subject or the scientific integrity of the study, including those that occur under emergency circumstances, to the Sponsor as well as the IRB if required by national regulations. Deviations will be reviewed to determine the need to amend the CIP or to terminate the study.

10.4.2 Quality Assurance

The study site may be subject to quality assurance audit by the Sponsor as well as inspection by appropriate RA. It is important that the Investigator and other relevant study site personnel are available during the monitoring visits, possible audits, and inspections, and that sufficient time is devoted to the monitoring process.

Each participating member of the study site team shall provide a curriculum vitae (CV) or equivalent that demonstrates their qualifications to conduct the study. It is the responsibility of the Investigator to ensure that all personnel involved in the study are fully informed of all relevant aspects of the study, including detailed knowledge of and training in all procedures to be followed. All Investigators and other responsible persons shall be listed together with their function in the study on the signature and delegation log.

10.4.3 Changes to the Clinical Investigation Plan

The Investigator and other site personnel involved in the study must not implement any changes to the CIP without agreement with the Sponsor and prior review and documented approval from the IRB and RA, if applicable, except where necessary to eliminate an immediate hazard to the subjects. All changes to the final CIP, or any other information given to the subject, must be documented in a dated and version-controlled written protocol amendment. However, administrative changes may be documented in the Sponsor file without requiring a protocol amendment. The Sponsor will assess if the changes require prior FDA approval and inform the Investigator when such approval has been received.

11. ETHICAL CONSIDERATIONS

11.1 Statement of ethical compliance

The study shall be conducted in compliance with the CTA, the clinical investigational plan (CIP), GCP, and applicable regional or national regulations. The study shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (1964, and its amendments in force at the initiation of the study) insofar as such revisions are consistent with US treaty obligations and in accordance with US law.(1)

The study shall follow the international standard for clinical study of medical devices for human subjects, International Organization for Standardization (ISO) 14155:2020 as applicable for US regulations and the International Conference on Harmonisation (ICH) guideline for GCP (E6) as applicable for medical devices.

11.2 Application to institutional review board (IRB) and regulatory authorities (RA)

It is the responsibility of the Principal Investigator (PI) to obtain approval of the CIP/CIP amendment(s) from the IRB. The study must not begin until the required favorable opinion

from the IRB has been obtained. The Investigator must file all correspondence with the IRB in the Investigator file and copies of IRB approvals must be forwarded to the Sponsor. Any additional requirements imposed by the IRB or regulatory authorities (RA) must be followed.

The study requires application for approval from the US Food and Drug Administration (FDA). The study must not be started until the Sponsor has received written approval, or until the statutory waiting period from the appropriate authority has elapsed. The Sponsor will provide the Investigator with a copy of the relevant document.

The collection, access to, processing, and transfer of protected health information, or sensitive personal data, must be carried out in accordance with applicable rules and regulations.

12. FINANCING, INDEMNIFICATION AND INSURANCE

The CTA outlines the compensation and payment terms of the study. The CTA must be signed before the first subject is screened in the study. If there are differences between the CTA and the CIP regarding certain rights and obligations, the CTA is the prevailing document. Q-Med AB's obligations in this clinical study are covered by Galderma's global general liability program. An insurance certificate will be provided upon request. The Institution/Investigator is obligated to maintain insurance coverage for their obligations in the clinical study in accordance with the CTA.

13. PUBLICATION POLICY

The Investigator's, Institution's, and Q-Med AB's obligations regarding intellectual property rights, confidentiality, and publications are described in detail in the CTA.

The aim is to submit the results of this study for publication in the public database ClinicalTrials.gov and to submit to a medical journal for a first joint publication of the results. All authors listed on the publication of results of this multicenter study must have made a substantial, direct, intellectual contribution to the work. Authorship will be based on (1) substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and (2) drafting the work, or revising it critically, for important intellectual content; and (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved[e]. Conditions 1, 2, 3, and 4 must all be met for designation as an author. Those who do not meet all four criteria will be acknowledged. Among the authors that fulfil the above-mentioned criteria, one author will be appointed by Q-Med AB to take primary responsibility for the overall work as primary author.

[e] Defining the role of authors and contributors, compiled by the International Committee of Medical Journal Editors (ICMJE) (http://www.icmje.org).

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15. APPENDICES

APPENDIX 1 INVESTIGATOR SIGNATURE PAGE

Signed agreement of the Clinical Investigation Plan (CIP)

Clinical Trial Number (CTN):	43USSA2112
Title of the CIP:	A prospective open-label study to evaluate safety and effectiveness of two different reconstitution volumes of poly-l-lactic acid (PLLA) for correction of wrinkles in the décolletage area

I, the undersigned, have read and understand the CIP specified above, and agree on the contents. The CIP, the clinical trial agreement (CTA) and the additional information given in the study specific instructions for use (IFU) and the report of prior investigations (ROPI) will serve as a basis for co-operation in this study.

Principal Investigator

Printed name	Signature	Date

Study site

GALDERMA EST. 1981	Title **43USSA2112 CIP Sculptra Decolletage**	Doc id **MA-50966**

SIGNATURES PAGE

Date	Signed by
PPD	
Justification	Approved by Technical Expert

PPD	
Justification	Approved by Owner

PPD	
Justification	Compiled by

PPD	
Justification	Approved by