Safety and Efficacy of SLI-F06 in Wound Healing and Scar Appearance in Pre-Abdominoplasty Surgical Excisions and Post-Operative Scar Appearance in Subjects Undergoing Abdominoplasty

Phase I/IIa

Protocol: SLI-C40-001

Version: v.1.4

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Study Sponsor:
Scarless Laboratories Inc.
369 South Doheny Drive, Suite 1201
Beverly Hills, CA
USA 90211

Clinical Research Organization:
ethica CRO Inc.
8555 Transcanada Hwy, Suite 201
Montreal, Canada H4S 1Z6

PROTOCOL APPROVAL SIGNATURE PAGE

The following individuals approve this version of Protocol SLI-C40-001. All changes to this version of the protocol must have a prior written approval and require an amendment or administrative letter.

Accepted for the Sponsor – Scarless Laboratories Inc.

Printed Name	Title
Signature	Date

Accepted for the Clinical Research Organization - ethica CRO Inc.

Printed Name	Title
Signature	Date

INVESTIGATOR SIGNATURE PAGE

I agree to:

- Implement and conduct this study diligently and in strict compliance with the protocol, good clinical practices and all applicable laws and regulations.
- Maintain all information supplied by Scarless Laboratories Inc. in confidence and, when this information is submitted to an Institutional Review Board (IRB) or another group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Principal Investigator *(Printed Name)*	Signature	Date

SYNOPSIS

Protocol Version	Version 1.4 (13-Nov-2020)	**Investigational Product:**	SLI-F06
Study Number	SLI-C40-001		
Phase	Phase I - Safety/Proof of Concept (Part A) Phase IIa - Safety and Efficacy (Part B and Part B Extension)	**Control Treatment:**	Formulation Buffer (vehicle)
Indication	Intradermal injection for improvement of wound healing and post-operative scar appearance	**Study Sites:**	Approximately 3-4 sites
Title	Safety and Efficacy of SLI-F06 in Wound Healing and Scar Appearance in Pre-Abdominoplasty Surgical Excisions and Post-Operative Scar Appearance In Subjects Undergoing Abdominoplasty		
Sponsor	Scarless Laboratories Inc.		
Study Duration	Approximately 13.5 to 24 months per subject	**Number of Subjects**	Approximately 25 subjects
Treatment Groups	During Part A of the study, subjects will be randomized by side of the pannus (right or left) (see Section 6.2) for treatment with SLI-F06 or formulation buffer, wound tension (high or low), and by duration of follow-up post-excisions to 12 weeks (group 1) or 8 weeks (group 2) pre-abdominoplasty. Excision mapping and number of excisions will be determined by size of pannus as follows: • Small pannus: 25 cm length x 12 cm height mapping 6 small wounds (3 cm length x 1 cm width) and 6 large wounds (3 cm length x 2 cm width) will be generated per subject. 12 wounds per subject. • SLI-F06 at 6 excision sites (3 high tension, 3 low tension) • Formulation buffer at 6 excision sites (3 high tension, 3 low tension) • Medium pannus: 30 cm length x 14 cm height mapping 6 small wounds (3 cm length x 1 cm width) and 8 large wounds (3 cm length x 2 cm width) will be generated per subject. 14 wounds per subject. • SLI-F06 at 7 excision sites (4 high tension, 3 low tension) • Formulation buffer at 7 excision sites (4 high tension, 3 low tension) • Large pannus: 32 cm length x 18 cm height mapping 8 small wounds (3 cm length x 1 cm width) and 10 large wounds (3 cm length x 2 cm width) will be generated per subject. 18 wounds per subject. • SLI-F06 at 9 excision sites (5 high tension, 4 low tension) • Formulation buffer at 9 excision sites (5 high tension, 4 low tension) During Part B of the study, after undergoing abdominoplasty, subjects will be randomized by side of the incision (right or left), and will receive injections of SLI-F06 into one half of their abdominoplasty incision and injections of vehicle formulation buffer into the other half of their incision. During Part B Extension, no SLI-F06 or formulation buffer will be administered. It is an observational extension of the study.		
Study Design	This is a multicenter, double-blind study comparing the safety of SLI-F06 to control formulation buffer (vehicle), as well as comparing the improvement in scar appearance and wound strength. Each subject will serve as his or her own control. The study is divided into 2 parts where Part A is a Phase I safety/proof of concept study of small scars pre-abdominoplasty, and Part B is a Phase IIa study of post-abdominoplasty scars. In **Part A** of the study (i.e., Phase I safety/proof-of-concept), subjects desiring abdominoplasty and who consent to participate in the study will have their abdominoplasty site mapped to accommodate 12, 14 or 18 excisions depending on pannus size for standardized 3 cm length excisions (see Section 6.5). Subjects will be allocated to 2 groups with different durations of post-excision follow-up (i.e., 12 weeks or 8 weeks pre-abdominoplasty) according to when they were enrolled into the study. All participants will be enrolled in or transferred to the 12-week pre-abdominoplasty group (Group 1). However, if		

	consented participants, who are assigned to Group 2 (8-week pre-abdominoplasty), cannot transfer to Group 1, they will remain in Group 2. Each excision site will be treated post-operatively in precisely the same manner. Following completion of the follow-up period, the entire abdominoplasty site will be harvested and sent for analyses of histopathology and tensile strength. In **Part B** of the study (i.e., Phase IIa), **ALL** subjects who complete Part A will be randomly assigned to receive injections of SLI-F06 along one half (left or right) of the abdominoplasty incision and control injections along the other half. Injections will be on both sides of the incision. The subject will undergo routine wound care and will attend study follow-up visits following abdominoplasty at Day 8 and at Months 1, 2, 3, 6, 9, and 12. Participants will then be invited to participate in an observational extension of the study, Part B Extension. Numbering and timing of study visits will be extended from Visit 8b (M12) of Part B. The subject will attend study visits at Months 15, 18, 21 and 24 where they will undergo POSAS assessments (PI and Subject) and abdominal photography. No further treatments will be administered during this observational extension of the study.
Objectives	**Primary objectives:** • Part A: Assess the safety and tolerability of SLI-F06 in the treatment of planned surgical excisions. • Part B: Assess the safety and tolerability of SLI-F06 in the treatment of abdominoplasty incisions. • Part B Extension: Assess the efficacy of SLI-F06 treatment on the appearance of abdominoplasty incision scars. **Secondary objectives:** • Part A: – Assess the effect of SLI-F06 on scar appearance. – Assess the effect of SLI-F06 on wound strength. – Assess the effect of SLI-F06 on histological appearance of scars. – Assess immunogenicity effects of SLI-F06. • Part B: – Assess the effect of SLI-F06 on post-operative abdominoplasty scar appearance. – Assess immunogenicity effects of SLI-F06. • Part B Extension: – None
Inclusion Criteria (Parts A and B)	1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Visit 1a and 1b and practice a reliable method of contraception 2. Seeking or scheduled for standard elective abdominoplasty. 3. Willing to undergo directed excisions and follow-up prior to abdominoplasty and to undergo all follow-up visits after abdominoplasty. 4. Willing to undergo directed excisions under local anesthetic (i.e., does not require general anesthetic). 5. Be able to follow study instructions and likely to complete all required visits. 6. Sign the IRB-approved ICF (which includes the Photographic Release Form and HIPAA) prior to any study-related procedures being performed.
Inclusion Criteria (Part B Extension)	1. Current or previous participant in Part B of Study SLI-C40-001. 2. Sign the IRB-approved ICF (which includes the Photographic Release Form and HIPAA) prior to any study-related procedures being performed.
Exclusion Criteria (Parts A and B)	1. Female subjects that are pregnant, breast-feeding, or of childbearing potential and not practicing reliable birth control (as specified in Section 5.1). 2. Known hypersensitivity or previous allergic reaction to any constituent of the IP (i.e., SLI-F06). 3. History of diabetes mellitus or an HgB A1C greater than 5.7 percent. 4. Morbid obesity (i.e., BMI >40).

	5. History of prior abdominal surgery. 6. History of abdominal liposuction, cryolipolysis, focused ultrasound or other fat reduction procedures in or near the anterior abdomen within 12 months of Visit 2a. 7. History of poor or delayed wound healing such as a prior wound dehiscence, chronic wound or leg ulcer. 8. History of or evidence of a genetic collagen disorder such as Ehlers-Danlos syndrome. 9. Operating Physician unable to design an abdominoplasty incision area of at least 25 cm wide by 12 cm tall at the center of the fusiform. 10. The presence of any abnormality of the skin within the area of the proposed abdominoplasty that, in the opinion of the Principal Investigator (PI), could interfere with the excision process or grading of the resultant surgical scar. 11. Use of any concomitant medications/procedures or tobacco/inhaled nicotine products specified in Section 6.7.1 within a restricted time period. 12. Allergy to or intolerance of local anesthetics. 13. Medical or psychiatric conditions that may increase the risk associated with study participation or may interfere with interpretation of study results or compliance of the subject and, in the opinion of the PI, would make the subject inappropriate for study entry. 14. Any personal, familial, employment or financial situation that could impede the subject's ability to attend all study visits and successfully complete the entire clinical study. 15. Clinically significant alcohol or drug abuse, or history of poor cooperation or unreliability. 16. Exposure to any other investigational drug/device within 30 days prior to study entry.
Exclusion Criterion (Part B Extension)	1. None
Drug Administration	The solution of SLI-F06 or vehicle solution will be injected intradermally into **BOTH** edges of the surgical wound immediately prior to closure (Part A) and after closure (Part B). The concentration of SLI-F06 will be 25 mg/ml. In Part A, a total of 0.4 mL (10 mg) will be injected at each excision site. A total of 0.2 mL (5 mg) will be injected along **EACH SIDE** of the wound edge. As each wound edge is 3 cm in length, 0.05 mL will be injected per 0.75 cm of wound edge). The total exposure of SLI-F06 for subjects with small pannus will be approximately 60 mg (6 treated excisions), for subjects with a medium pannus will be approximately 70 mg (7 treated excisions), and for subjects with a large pannus will be approximately 90 mg (9 treated excisions). In Part B of the study, 0.05 mL will be injected per 0.75 cm of wound edge as above. A subject with an incision length of 25 cm (12.5 cm active treatment) would be exposed to 41.6 mg of SLI-F06, while subjects with an incision lengths of 30 cm (15 cm active treatment) or 32 cm (16 cm active treatment) would be exposed to 50 mg or 53.3 mg, respectively. In Part B Extension, there will be no exposure to SLI-F06 or vehicle solution.
Blinding	Subjects, PIs and study coordinators will be blinded to treatment assignments of vehicle versus active IP. Subjects may or may not be blinded to low or high wound tension; PIs will not be blinded to the degree of wound tension. A member of the site staff will be designated as the unblinded Independent Drug Reconstitutor (IDR). The IDR will consult a randomization schedule and prepare syringes of active product and vehicle (formulation buffer). Syringes will be labeled "left side" or "right side".
Procedures	*Refer to the Study Summary Table for a schedule of activities.*
Efficacy Evaluations	**Primary** • Patient and Observer Scar Assessment Scale (POSAS; PI Assessment) – Excisions and Abdominoplasty Incisions (Parts A, B, Part B Extension) **Secondary** • POSAS (Subject Assessment) – Abdominoplasty Incisions (Part B and Part B Extension)

	• POSAS (PI Assessment) – Abdominoplasty 5 cm Segments (Part B and Part B Extension) • POSAS (Subject Assessment) – Abdominoplasty 5 cm Segments (Part B and Part B Extension) • Independent Panel Review of scar photography using POSAS • Excision site histology • Tensile strength of scar **Exploratory** • POSAS (Subject Assessment) – Excisions (Part A)
Safety Evaluations	• Adverse Events (Part A and Part B) • Treatment Related Adverse Events (Part B Extension) • Clinical safety laboratory tests • Immunogenicity
Sample Size	Approximately 25 subjects will be enrolled. This is a Phase I safety/proof-of-concept + Phase IIa study and a formal sample size justification is not required. It is the opinion of the Sponsor that a total of 25 subjects will be sufficient to achieve the objectives of the study.
Statistical Methods	All statistical processing will be performed using SAS® version 9.4 or later unless otherwise stated. Statistical significance will be based on two-tailed tests of the null hypothesis resulting in p-values of 0.05 or less. For categorical parameters, the number and percentage of subjects or observations in each category will be presented. The denominator for percentage will be based on the number of subjects or observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n (number of subjects or observations), mean, standard deviation, median, and range. Comparisons between treatment groups will be performed using parametric or non-parametric testing, as appropriate. Statistical analyses will be conducted on an intent-to-treat (ITT) basis. An interim analysis will be conducted when all subjects have completed Study Part A.

STUDY SUMMARY

	Part A (Phase I Safety/Proof of Concept)						Part B (Phase IIa)									Part B Extension				
Visit Number	**1a**	**2a**	**3a**	**4a**	**5a**	**6a**	**1b**	**2b**	**SR**	**3b**	**4b**	**5b**	**6b**	**7b**	**8b**	**9b**	**10b**	**11b**	**12b**	**Optional Visit**
Assessment and Procedures	**Screening Period**	**Excisions**	**Suture Removal**				**Abdomin-oplasty**		**Suture Removal**											
	D -30 to 0	**D1**	**D8 ± 1d**	**D29 ± 2d**	**D57 ± 3d**	**D85 ± 3d**	**D0**	**D8 ± 1d**	**PI Discretion**	**M1 ± 3d**	**M2 ± 7d**	**M3 ± 14d**	**M6 ± 14d**	**M9 ± 14d**	**M12 ± 14d**	**M15 ± 14d**	**M18 ± 14d**	**M21 ± 14d**	**M24 ± 14d**	--
Informed Consent	X															X[5]	X[5]	X[5]		X[5]
Inc/Excl Criteria Parts A and B	X																			
Inc/Excl Criteria Part B Extension																X[6]	X[6]	X[6]		X[6]
Medical/Surgical History	X																			
Physical Exam	X																			
Urine Pregnancy Test [1]	X	X [1]					X					X	X	X	X					
Abdominoplasty Area Assessment & selection of Pannus Map size	X																			
Immunogenicity sampling	X		X	X	X	X		X		X	X	X	X	X	X					
Safety Laboratory Testing [2]	X [2]			X	Group 2	Group 1				X					X					
Photography [3]		X [3]	X [3]	X	X	X				X	X	X	X	X	X	X	X	X	X	X
Randomization		X					X													
Excisions		X																		
IP Injections		X					X													
Abdominoplasty/ Tissue Harvesting							X													
Suture removal			X						X											
POSAS grading (PI & Subject)			Post-removal of sutures	X	X	X				X	X	X	X	X	X	X	X	X	X	X
AE Assessment		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[7]	X[7]	X[7]	X[7]	X[7]
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Group 1; 12 week assessment																				
Exit from Part A / Start of Part B						**X**														
Group 2; 8 week assessment[4]																				
Exit from Part A / Start of Part B					**X**															

1 UPT if female of childbearing potential and if last UPT performed >7 days of V2a.

2 Safety laboratory results to be reviewed by the PI prior to excisions in order to confirm absence of any health condition(s) that would make the subject inappropriate for study entry.

3 Day 1 photography occurs prior to excisions and following closure of all excisions, and Day 8 photography occurs pre- and post-removal of sutures.

4 Only **currently enrolled** participants who cannot be moved from group 2 to group 1 will remain in group 2

5 First Part B extension visit can occur at any of these timepoints. Consent to be obtained during the first visit of Part B extension if not obtained at Visit 8b.

6 First Part B extension visit can occur at any of these timepoints. Inclusion/Exclusion criteria to be reviewed during the first visit of Part B extension.

7 Only Treatment Related AE (TRAE) will be assessed.

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CONTACT LIST

Medical Monitor
Stacy Smith, MD
2371 Lagoon View Drive
Cardiff By The Sea, CA 92007
Phone: 619.787.5723
Fax: 619.342.7428
ssmith@stacyrsmithmd.com

Sponsor Contact
Carol H Danielson, MS, DrPH
Scarless Laboratories, Inc.
369 South Doheny Dr.
Suite 1201
Beverly Hills, CA 90211
Phone: 520.907.5193
cdanielson@scarlessslabs.com

eCRO Clinical Project Manager
Sara Kasem
ethica CRO Inc.
8555 Transcanada Hwy, Suite 201
Montreal, Quebec, H4S 1Z6
Phone: 514.531.2315
Fax: 514.336.1142
skasem@ethicacro.com

eCRO Managing Director
Murray Jensen, MSc
ethica CRO Inc.
8555 Transcanada Hwy, Suite 201
Montreal, Quebec, H4S 1Z6
Phone: 514.262.9398
Fax: 514.336.1142
mjensen@ethicaCRO.com

24-Hour Emergency Phone Number
ethica CRO Inc.
514-262-9398

NOTE: Changes in the names, addresses or telephone numbers of these contacts will be considered administrative and will not require a protocol amendment before being implemented.

ABBREVIATIONS AND DEFINITIONS

Abdominoplasty excision area	The entire area of skin and subcutaneous tissue that is planned to be excised during the abdominoplasty procedure. The abdominoplasty excision area will contain 12-18 excision sites.
AE	Adverse Event
BL	Baseline
BMI	Body Mass Index
CFR	U. S. Code of Federal Regulations
CTR	Common Treatment Response
CRO	Clinical Research Organization
DHHS	Department of Health and Human Services
DP	Drug Product
Excision site	A mapped area designated for a single excision.
eCRF	electronic Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practices
HgB	Hemoglobin
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDR	Independent Drug Reconstitutor
IP	Investigational Product
IPR	Independent Panel Review
IRB	Institutional Review Board
ITT	Intent-to-Treat
LLT	Lowest Level Term
MedDRA	Medical Dictionary for Regulatory Activities
NSAID	Non-steroidal anti-inflammatory drug
OP	Operating Physician (typically also the PI)
PI	Principal Investigator (typically also the OP)
POC	Proof Of Concept
POSAS	Patient and Observer Scar Assessment Scale
PP	Per protocol
PT	Preferred Term
SAE	Serious Adverse Event
SAFT	Safety
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SDs	Source Documents
SOC	System Organ Class
TAN	Treatment Assignment Number
TRAE	Treatment Related Adverse Event
Tx	Treatment
UPT	Urine Pregnancy Test
USP	United States Pharmacopeia

1 INTRODUCTION

SLI-F06 is a synthetic 40-amino acid peptide that is being developed as a treatment to promote wound healing and improve scar appearance. The amino acid sequence of SLI-F06 is derived from an endogenous human protein that has been shown in animal models to promote accelerated wound healing, reduced scarring, and increased wound tensile strength. In these same animal models, the SLI-F06 has been demonstrated to retain similar pro-migration, pro-tensile strength, and anti-fibrotic properties as the endogenous protein.

SLI-F06 drug product (DP) is a sterile lyophilized powder consisting of SLI-F06 as the active ingredient and formulation buffer components. The DP will be reconstituted in clinic with USP Water for Injection and injected intradermally along both edges of a freshly made excision to achieve a primarily local effect.

The route of administration, dosage, dosage regimen and treatment period for the current study are based on large and small animal safety and efficacy studies. Pre-clinical toxicology testing of SLI-F06 includes a 5-day intravenous repeat dosing in rats, a 3-day subcutaneous repeat dosing in pigs, and a 3-day intradermal repeat dosing in a wounded pig model. The intended human drug exposure for the current study is far below the human equivalent dose that has demonstrated to be safe in animals. Please see the Investigator Brochure for a summary of all preclinical studies as well as a list of references.

The study population will consist of healthy patients planning to undergo elective abdominoplasty. During Part A of this study (i.e., Phase I Safety/Proof of Concept), each subject will receive 12, 14, or 18 small or large excisions at 8 weeks or 12 weeks pre-abdominoplasty. Wounds treated with SLI-F06 or vehicle will be followed until the time of abdominoplasty when the tissue is harvested. At the completion of study Part A, subjects will enter study Part B where they will undergo the abdominoplasty, have the abdominoplasty incision treated with SLI-F06, and be followed for an additional 12 months. At the completion of Part B, subjects will be invited to participate in the study Part B Extension where the abdominoplasty scar will be monitored for an additional 12 months.

This is a first-in-human study; there are currently no human experience or regulatory actions related to SLI-F06. The study will be conducted in compliance with the protocol, Good Clinical Practices, and all applicable regulatory requirements.

Please see the Investigator Brochure for additional information as well as a list of references.

2 STUDY OBJECTIVES

The primary objectives of this study are the following:

- Part A: Assess the safety and tolerability of SLI-F06 in the treatment of planned surgical excisions.
- Part B: Assess the safety and tolerability of SLI-F06 in the treatment of abdominoplasty incisions.
- Part B Extension: Assess the efficacy of SLI-F06 treatment on the appearance of abdominoplasty incision scars.

Secondary objectives include, but are not limited to, the following:

- Part A:
  - Assess the effect of SLI-F06 on scar appearance.
  - Assess the effect of SLI-F06 on wound strength.
  - Assess the effect of SLI-F06 on histological appearance of scars.
  - Assess immunogenicity effects of SLI-F06.
- Part B:
  - Assess the effect of SLI-F06 on post-operative abdominoplasty scar appearance.
  - Assess immunogenicity effects of SLI-F06.
- Part B Extension:
  - None

3 COMPLIANCE STATEMENT

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) and Good Clinical Practice (GCP), the Declaration of Helsinki, United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312).

The sites' Principal Investigator (PI) is responsible for ensuring the privacy, safety and welfare of the subjects during and after the study and must ensure that site personnel are appropriately trained. The PI must be familiar with the background and requirements of the study and with the properties of the IP as described in the Investigator Brochure. The PI at each site has the overall responsibility for the conduct and administration of the study at their site, and for contact with study site management, and local authorities.

3.1 Variations to the Protocol

No changes from the final approved (signed) protocol will be initiated without the prior approval by the IRB except 1) when necessary to eliminate immediate hazards to the subjects or when the change involves only logistics or administration, or 2) minor administrative or typographical corrections. The sites' PIs and the Sponsor must sign any protocol amendments.

3.2 Investigational Sites

Up to four (4) U.S. investigational sites will participate in this study. Each site must obtain written approval from a 21 CFR 56 compliant IRB prior to recruitment and enrollment of any subject into the study. Any changes to the study procedures must be made with the mutual agreement of the PI and the Sponsor, documented in an amendment to the protocol, and approved by the reviewing IRB.

3.3 Medical Monitor

A Medical Monitor will provide safety oversight for this clinical study. The Medical Monitor will review and evaluate SAEs upon receipt to ensure adherence to the FDA requirements for expedited reporting. Additionally, in consultation with the Sponsor's team, the Medical Monitor will review and evaluate all AEs approximately monthly, review safety reports, and will provide consultation and recommendations with regard to inclusion/exclusion criteria, concomitant medications/treatments, and subject discontinuations.

4 OVERVIEW OF STUDY DESIGN

4.1 Study Design

This is a multicenter, double-blind study comparing SLI-F06 to vehicle formulation buffer for the improvement in scar appearance and wound strength in routine surgical excisions, as well as post-operative abdominoplasty scar appearance. Each subject will serve as his or her own control.

Subjects desiring abdominoplasty and who consent to participate in the study will have their abdominoplasty site allocated and mapped into sections for standardized 3 cm length excisions (see Section 6.5). Number of excisions will be determined by pannus size (i.e., 12 excision sites for small pannus, 14 excision sites for medium pannus, 18 excision sites for large pannus).

All excisions to be treated with SLI-F06 will be on one side of the mapped area (i.e., left side or right side) and vehicle treated excisions will be on the other side of the mapped area. A randomization scheme will assign treatment for the left and right side of the pannus. Each excision site will be treated post-operatively in precisely the same manner.

Duration of follow-up will not be subject to randomization. Subjects will be allocated to 2 groups with different durations of post-excision follow-up (i.e., 12 weeks or 8 weeks pre-abdominoplasty) according to when they were enrolled into the study.

Following completion of the designated post-excision follow-up period, the entire abdominoplasty site will be harvested and sent for analyses of histopathology and tensile strength.

Subjects will then be randomly assigned to receive injections of SLI-F06 along one half (left or right) of the abdominoplasty incision and control injections along the other half. Injections will be on both sides of the incision. Subjects will undergo routine wound care and will attend study follow-up visits following abdominoplasty at Months 1, 2, 3, 6, 9, and 12. The entire incision will be treated post-operatively in precisely the same manner.

Subjects will then be invited to participate in an observational extension of the study, Part B Extension. Numbering and timing of study visits will be extended from Visit 8b (M12) of Part B. The subject will attend study visits at Months 15, 18, 21 and 24 where they will undergo POSAS assessments (PI and Subject) and abdominal photography. No further treatments will be administered during this observational extension of the study.

4.2 Study Design Rationale

4.2.1 Study Population

Up to 25 healthy adult subjects presenting for abdominoplasty surgery will be enrolled and randomized. This will include a subset of up to 6 subjects with a history of hypertrophic or keloidal scarring. The full description of the inclusion and exclusion criteria is found in Section 5.

4.2.2 Primary Effectiveness Outcome Measurements

The primary efficacy outcome parameter will be the difference in Patient and Observer Scar Assessment Scale (POSAS) scores, as assessed by the PI:

1) Between SLI-F06 treated excision sites and the vehicle treated excision sites at each timepoint during the Part A of the study;
2) Between the half of the abdominoplasty incision treated with SLI-F06 and the half of the incision treated with vehicle during Part B and Part B Extension of the study.

5 STUDY POPULATION

5.1 Inclusion Criteria

5.1.1 Part A and Part B

The inclusion criteria below are only applicable to Parts A and B. Refer to Section 5.1.2 for the Inclusion Criteria for Part B Extension.

1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Visit 1a (Study Part A) and 1b (Study Part B) and practice a reliable method of contraception throughout the study.

   A female is considered of childbearing potential unless she is:

   - *postmenopausal for at least 12 months prior to study treatment administration;*
   - *without a uterus and/or both ovaries; or*
   - *has been surgically sterile for at least 6 months prior to study treatment administration.*

   Reliable methods of contraception are:

   - *hormonal methods or intrauterine device in use ≥90 days prior to study treatment administration;*
   - *barrier methods plus spermicide in use at least 14 days prior to study treatment administration; or*
   - *vasectomized partner.*

   [Exception: Females of childbearing potential who are not sexually active are not required to practice contraception. These subjects may be enrolled at the site's PI's discretion if they are counseled to remain sexually inactive during the study or agree to use an approved method of contraception should they become sexually active and understand the possible risks in getting pregnant during the study.]

2. Seeking or scheduled for standard elective abdominoplasty.
3. Willing to undergo directed excisions and follow-up prior to abdominoplasty and to undergo all follow-up visits after abdominoplasty.
4. Willing to undergo directed excisions under local anesthetic (i.e., does not require general anesthetic).
5. Be able to follow study instructions and likely to complete all required visits.
6. Sign the IRB-approved ICF (which includes the Photographic Release Form and HIPAA) prior to any study-related procedures being performed.

5.1.2 Part B Extension:

The inclusion criteria below are only applicable to Part B Extension.

1. Current or previous participant in Part B of Study SLI-C40-001.
2. Sign the IRB-approved ICF (which includes the Photographic Release Form and HIPAA) prior to any study-related procedures being performed.

5.2 Exclusion Criteria

5.2.1 Parts A and B

The Exclusion Criteria below are only applicable to Parts A and B. Refer to Section 5.2.2 for the Exclusion Criteria for Part B Extension.

1. Female subjects that are pregnant, breast-feeding, or of childbearing potential and not practicing reliable birth control (as specified in Section 5.1).
2. Known hypersensitivity or previous allergic reaction to any constituent of the IP (i.e., SLI-F06).
3. History of diabetes mellitus or an HgB A1C greater than 5.7 percent.
4. Morbid obesity (i.e., BMI >40).
5. History of prior abdominal surgery. *[Note: laparoscopic surgery that did not result in open laparotomy or routine cesarean section surgery is acceptable provided the procedure occurred at least 3 years prior to Visit 1a]*
6. History of abdominal liposuction, cryolipolysis, focused ultrasound or other fat reduction procedures in or near the anterior abdomen within 12 months of Visit 2a.
7. History of poor or delayed wound healing such as a prior wound dehiscence, chronic wound or leg ulcer.
8. History of or evidence of a genetic collagen disorder such as Ehlers-Danlos syndrome.
9. Operating Physician unable to design an abdominoplasty incision area of at least 25 cm wide by 12 cm tall at the center of the fusiform.
10. The presence of any abnormality of the skin within the area of the proposed abdominoplasty that, **in the opinion of the PI**, could interfere with the excision process or grading of the resultant surgical scar (e.g., striae gravidarum, striae distensae, excessive nevi, numerous seborrheic keratoses, tattoos, etc.).
11. Use of any concomitant medications/procedures or tobacco/inhaled nicotine products specified in Section 6.7.1 within a restricted time period.
12. Allergy to or intolerance of local anesthetics.
13. Medical or psychiatric conditions that may increase the risk associated with study participation or may interfere with interpretation of study results or compliance of the subject and, **in the opinion of the PI**, would make the subject inappropriate for study entry.
14. Any personal, familial, employment or financial situation that could impede the subject's ability to attend all study visits and successfully complete the entire clinical study.
15. Clinically significant alcohol or drug abuse, or history of poor cooperation or unreliability.
16. Exposure to any other investigational drug/device within 30 days prior to study entry.

5.2.2 Part B Extension

The Exclusion Criteria below are only applicable to Parts B Extension.

1. None

5.3 Subject Withdrawal Criteria

Reasons for withdrawal may include, but are not limited to, the following:

- At the request of the PI or study Sponsor (e.g., for tolerability reasons, SAE, etc.).
- At the request of the subject.
- When the requirements of the protocol are not followed.

- When a concomitant therapy or interventional surgery required by the subject is likely to interfere with study results, (report all such information on the source documents and CRFs) and confer with the Sponsor if the subject should be withdrawn).
- When a subject is lost to follow-up. The PIs will try at least twice to reach the subject by telephone and document these attempts and then send a follow-up letter by certified mail before considering that the subject is lost to follow-up.

All premature discontinuations and their reasons must be carefully documented by the PI in the source documents, CRF, and (if applicable), on the AE form.

No subject who has received study injection(s) can be replaced if they discontinue prematurely for whatever reason. All data gathered on the subject prior to termination will be made available to the Sponsor.

Reasons for study completion/discontinuation as listed on the final report form are defined as follows:

- **Normal Study Completion** – Subject completes the study as planned in the protocol.
- **Adverse Event** – Complete AE form.
- **Death** – Complete SAE form.
- **Subject Request** – Consent withdrawal, subject moved, schedule conflicts.
- **Protocol Violation** – Contact the Sponsor or designee before making decision.
- **Lost to Follow-Up** – Document with 2 phone calls and a certified letter.
- **Pregnancy** – Subject will discontinue study drug immediately, but will be followed to term. Complete pregnancy form.
- **Study Terminated by Sponsor**
- **Other** – Specify in comments section of final CRF.

Subjects are free to withdraw from participating in this study at any time and for whatever reason, specified or unspecified, and without prejudice.

6 TREATMENT PLAN

6.1 Subject Numbering

Each screened subject will be assigned a unique 4-digit study subject number assigned by the investigational site, which will consist of a pre-assigned 1-digit investigational site number and a 3-digit chronological screening order number, starting with 001 (e.g., 1001, 1002). Subject Numbers will not be omitted or reused. Subjects withdrawn from the study will retain their Subject Number; new subjects will be allotted a new Subject Number.

6.2 Randomization

A hardcopy computer generated "Randomization Schedules" will link a bilateral (left, right) treatment assignment to each Subject Number (Section 6.1). Randomization to treatment assignment for Part A will be independent of Part B randomization. The Randomization Schedule will be maintained by the Independent Drug Reconstitutor (Section 6.3). During Part A, all excisions to be treated with SLI-F06 for a given subject will be on one side of the mapped area (i.e., left side or right side) and vehicle treated excisions will be on the other side of the mapped area. During Part B, one side of the abdominoplasty incision will be treated with SLI-F06 (i.e., left side or right side) and the other side of the incision will be treated with vehicle.

6.3 Blinding

To maintain study blind, the Independent Drug Reconstitutor (IDR) (i.e., pharmacist, study nurse or physician not responsible for subject follow-up) will have access to the Randomization Schedule, be aware of treatment assignment, and will prepare study medication. "Injectors", Investigators, and study coordinators responsible for subject assessment and follow-up, and study subjects will remain unaware of which study treatment was injected on either side of the pannus or abdominoplasty incision, but might not be blinded to the degree of wound tension.

The IDR will consult the Randomization Schedule, prepare syringes of SLI-F06 and vehicle, and label syringes accordingly with the designation of "left side" or "right side".

6.4 Unblinding

The treatment assignments for all enrolled subjects will be unblinded only after the conclusion of the study (or for interim analyses). Specifically, the blind will be broken only after all data are verified, entered into the database and validated, and the database is locked. If it is medically imperative to know what study treatment was injected on a particular side, the Investigator or authorized person will contact the IDR (or designee) to obtain the treatment assignment for that subject. Prior to unblinding, the investigator should attempt to contact the Medical Monitor and ethica CRO Inc. to discuss the rationale for unblinding. The rationale for breaking the code must be recorded in the subjects' medical record and eCRF.

6.5 Pannus Excision Sites - Study Part A

6.5.1 Excision Sites

Each excision site will be a 3 cm long fusiform excision. All excisions will be performed in an identical manner except for dimensions. Two types of fusiform excisions will be made (templates will be provided):

- **Low tension** wounds will have a 3 cm length with a maximum midpoint width of 1 cm;
- **High-tension** wounds will have a 3 cm length and a maximum midpoint width of 2 cm.

6.5.2 Pannus Map and Excision Template

The Investigator will assess the subject's abdomen (while supine) and will select the appropriate size of pannus map. If unable to select a suitable pannus map, the subject will be considered as a screen failure. The following sizes of pannus maps will be supplied to the site:

Small pannus map: For an abdominoplasty area of at least 25 cm length x 12 cm height. This map accommodates 6 small wounds (3 cm length x 1 cm width, green wounds) and 6 large wounds (3 cm length x 2 cm width, blue wounds) for a total of 12 wounds per subject. The excision sites will be numbered as shown in Figure 1 below:

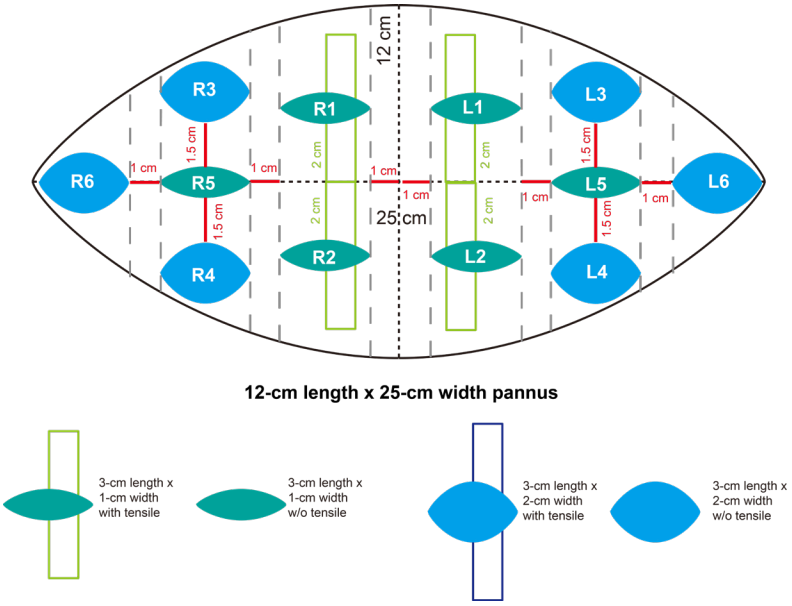


Figure 1. Small Pannus Map

Medium pannus map: For an abdominoplasty area of at least 30 cm length x 14 cm height. This map accommodates 6 small wounds (3 cm length x 1 cm width, green wounds) and 8 large wounds (3 cm length x 2 cm width, blue wounds) for a total of 14 wounds per subject. The excision sites will be numbered as shown in Figure 2 below:

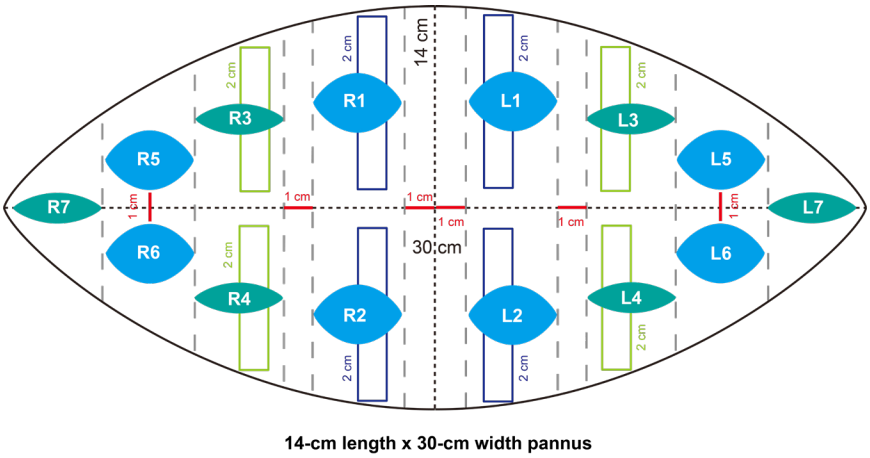


Figure 2. Medium Pannus Map

Large pannus map: For an abdominoplasty area of at least 32 cm length x 18 cm height. This map accommodates 8 small wounds (3 cm length x 1 cm width, green wounds) and 10 large wounds (3 cm length x 2 cm width, blue wounds) for a total of 18 wounds per subject. The excision sites will be numbered as shown in Figure 3 below:

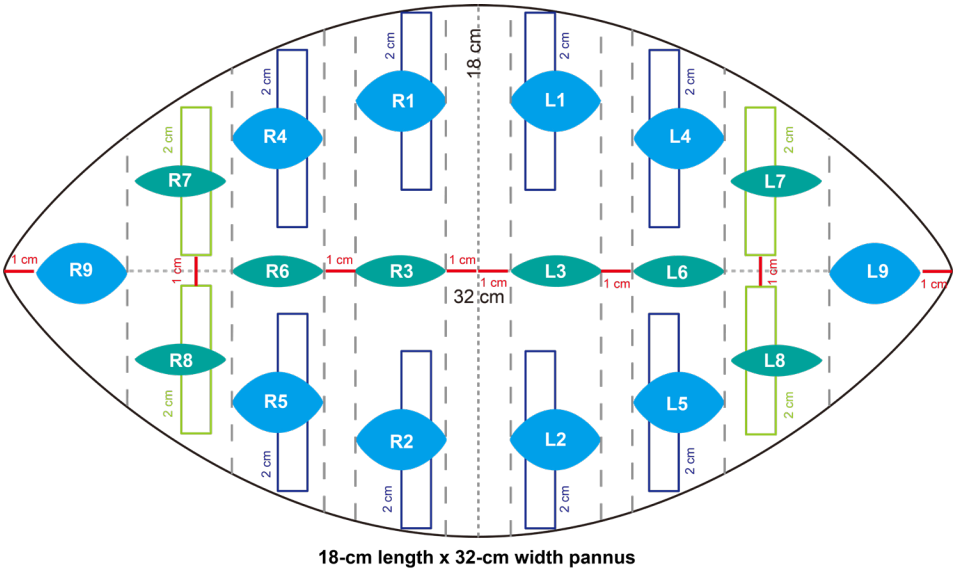


Figure 3. Large Pannus Map

6.5.3 Excision Site Mapping

The PI will designate the excision sites with the subject in the supine position and using the selected pannus map.

Pannus maps will have pre-punched holes at the center of each fusiform. With the subject in a supine position, the PI will place the map over the pannus and, using permanent ink, will place a "dot" on the skin through each hole, thus indicating the center of each planned excision.

Two sterilizable ink stamps will be provided to each investigative site. One stamp will trace the fusiform for high-tension excision sites, and the other stamp will trace the fusiform for low-tension excision sites. Referring to the pannus map, the OP will select the appropriate "excision stamp" (i.e., high vs. low tension as per R1, L1, R2, etc.), place the stamp over the previously marked dot, and apply a tracing outlining the fusiform to be excised. Each tracing will be orientated horizontally, as per the pannus map.

6.5.4 Sequence of Excisions

Bilateral matched excisions (e.g., R1/L1, R2/L2, etc.) are to be performed in sequence. Each individual excision should be injected and then closed prior to performing the next excision (i.e., do not perform all of the excisions, followed by all of the closures). Injection of study drug is to be performed before closure (i.e., excise skin, undermine if needed, hemostasis, inject study drug, then skin closure).

It is acknowledged that during the excision process, the topography of the pannus will change and the final placement, orientation, and number of excisions may not match pre-defined pannus mapping. In such cases, the abdominoplasty map should be updated and annotated accordingly in order to match the final placement, orientation, and number of excisions.

6.5.5 Pre-operative Preparation and Patient Monitoring

Prophylactic antibiotics are allowed on a case-by-case basis, at the discretion of the Investigator. Use of sedative/pain medication (e.g., 10mg diazepam, hydrocodone with acetaminophen, etc.) or nitrous oxide is allowed on a case-by-case basis to relieve anesthetic injection pain and anxiety, at the discretion of the Investigator. Routine patient monitoring (e.g., BP, HR, oxygen saturation, etc.) is to be conducted at the discretion of the Investigator.

6.5.6 Anesthetic Preparation and Administration

At each excision site, local injections of dilute anesthetic solution with epinephrine should be used as per the site's standard practice (e.g., 0.05-0.1% lidocaine with ~1:1,000,000 epinephrine) with or without sodium bicarbonate. Use of dilute anesthetic solutions containing epinephrine is suggested in order to optimize hemostasis. Total lidocaine dosage should not exceed established lidocaine guidelines of 7 mg/kg with respect to mg lidocaine per kg patient weight. Use of 1% rather than 2% is suggested to minimize over-dosing errors.

6.5.7 Excision Procedures

A #15 scalpel will be used to excise the skin up to the subcutaneous fat (minimize fat removal).

As the intent of this study is to test scar formation in wounds closed under tension, undermining of wound edges should be avoided if possible. If undermining is required, the surgeon will use only the minimal amount needed to close the wound and will undermine at the level of the subcutaneous fat about 1 cm deep to the dermis (avoid undermining more than 1 cm horizontally from the cut wound edge if possible). The use of undermining will be recorded in the CRF.

Hemostasis should be achieved by light pressure, topical epinephrine (1:100,000 dilution on Telfa strips), or additional injection of the dilute anesthetic solution only. Electrocautery will be avoided if possible. At this point, study treatment will be injected (i.e., after excision, potential undermining, and hemostasis, but before wound closure). See Section 6.5.8 below.

As per Figure 4 below, the deep dermal and subcutaneous layers will be closed using 2 equally spaced #4-0 poliglycaprone 25 (e.g., Monocryl) simple, buried, deep dermal interrupted sutures (the knot should be closer to the subcutaneous fat, deep to the deep dermis). The 3 cm wound will be divided into thirds (i.e., each third will be 1 cm). Sutures will be placed at the 1 cm and 2 cm locations in the wound while avoiding any sutures in the middle cm of the 3 cm long wound).

The skin edge will be closed with 4 equally (approximate) spaced #5-0 polypropylene (e.g., Prolene) simple interrupted sutures that are approximately 4 mm from the skin edge and effectively evert the skin edge. Ensure that a 0.6 cm suture-free area remains at the midpoint of the wound

and note gap size in mm in the center of the wound after all sutures are placed (i.e., “0 mm” indicates no gap).

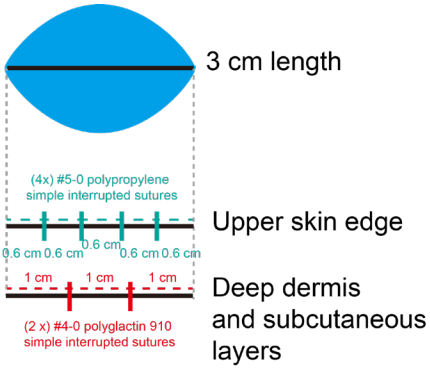


Figure 4. Suture Placement for Excision Closure

- Avoid placing suture material in the middle of the wound.
- Divide the deep dermal layer into thirds and place 2 absorbable (e.g., Vicryl) sutures.
- Divide the outer skin layer into fifths and place 4 non-absorbable sutures.

6.5.8 Administration of Investigational Product (Excisions)

Excisions are to be injected on each edge of the wound, immediately prior to closure, using a 29G needle. The solution of SLI-F06 or vehicle solution will be injected intradermally into **BOTH** edges of the surgical wound immediately prior to closure. The concentration of SLI-F06 will be 25 mg/ml.

The needle should be inserted into the dermis, and while keeping parallel to both the dermis and the wound edge, the needle will be advanced 0.75 cm.

A total of 0.4 mL (10 mg) will be injected at each excision site. A total of 0.2 mL (5 mg) will be injected along **EACH SIDE** of the wound edge. As each wound edge is 3 cm in length, 0.05 mL will be injected per 0.75 cm of wound edge).

Investigational Product will be injected into the dermis while the needle is withdrawn (avoiding injection into the subcutaneous fat). Care should be taken to avoid ‘bare areas” along the wound edge where no study treatment is injected (i.e., the needle should always slightly advance into the area of the previous needle insertion).

6.5.9 Wound Care (Excisions)

A sterile dressing of non-stick gauze (i.e., Telfa or similar) and paper surgical tape will be applied along with ~1 gram of petrolatum ointment. Wounds may be individually dressed, or all dressed together (Investigator preference).

Extreme care will be taken to ensure the uniform application of post-operative care to each excision site. Subjects will be instructed to apply new bandages once per day after bathing/showering. Each excision site will have sutures removed at the next clinic visit (nominally in 8 days).

Upon suture removal, use of adhesive strips is prohibited. The CRF will capture any use of adhesive strips and any such use will be treated as a protocol violation.

6.6 Abdominoplasty Incision – Study Part B

6.6.1 Surgical Preparation and Patient Monitoring

Surgical preparation and patient monitoring during surgery will be performed according to the surgeons' standard practice and best medical judgment on a per-patient basis.

6.6.2 Surgical Anesthesia

Surgical anesthesia will be administered according to the surgeons' standard practice and best medical judgment on a per-patient basis.

6.6.3 Abdominoplasty Surgery

Prior to handing off the pannus specimen, the orientation of the pannus will be confirmed by placing a simple, non-absorbable suture in the top midline (leaving a short tail of ~1 cm) and a simple non-absorbable suture on the patient's left corner of the pannus (leaving a long tail ~5-10 cm).

Abdominoplasty will be performed according to the surgeons' standard practice and best medical judgment on a per-patient basis.

Closure of the abdominoplasty incision will be performed according to the surgeons' standard practice and best medical judgment on a per-patient basis.

Study treatment will be injected immediately after incision closure.

6.6.4 Administration of Investigational Product (Abdominoplasty)

On the upper and lower wound edges and using a surgical marker, a line will be drawn at the exact center of the abdominoplasty incision, separating the left from the right side. The randomization code will dictate which study treatment will be injected into the left and right sides of the incision.

Using a 29G needle, each edge of the incision wound is to be injected immediately after closure. The needle should be inserted into the dermis. Injections should run parallel and 1 mm from the incisional line. Injections will start 1 cm from the mid-point on each side of both wound edges and will proceed laterally. While keeping parallel to both the dermis and the wound edge, the needle will be advanced 0.75 cm and a total volume of 0.05 ml of study treatment for each 0.75 cm of wound edge will be injected into the dermis while the needle is withdrawn back to the injection point (avoiding injection into the subcutaneous fat). Injections will be repeated in the same manner until the entire length of the wound edge (i.e., left or right side, as per the randomization schedule) has been injected. Care should be taken to avoid 'bare areas" (except for the 2 cm area at the mid-point) along the incision line where no study treatment is injected (i.e., the needle should always advance slightly into the area of the previous needle insertion) (see Fig. 5).

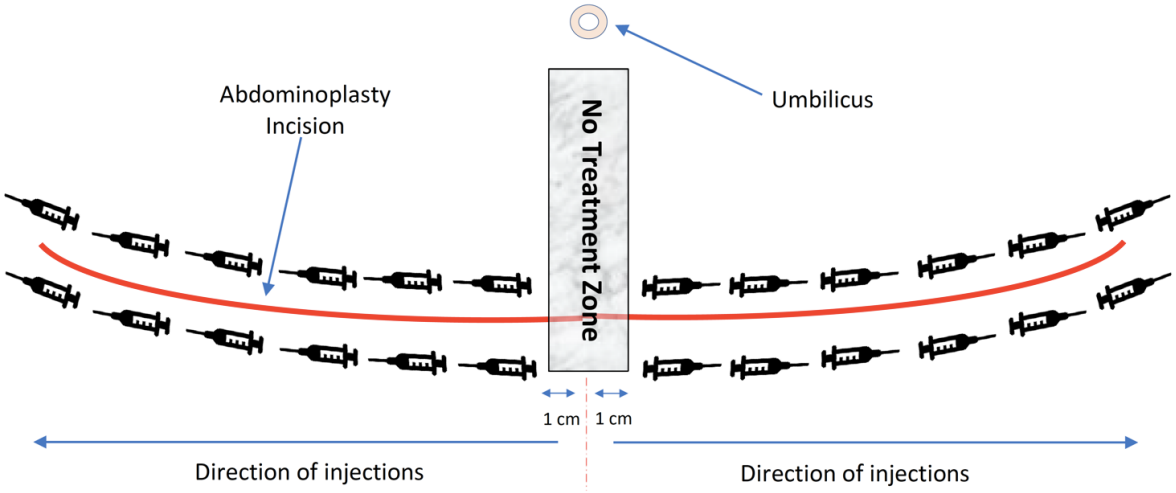


Figure 5. Injection of the abdominoplasty incision

6.6.5 Wound Care (Abdominoplasty)

Post-surgical wound care will be administered according to the surgeons' standard practice and best medical judgment on a per-patient basis. Care must be taken to ensure the uniform application of post-operative care to the entire incision area.

The timing of suture removal, if applicable, is at the discretion of the Investigator as per the Investigator's standard of care. Sutures will be removed as per the Investigator's standard of care, and with appropriate consideration for the suturing method employed (e.g., subcuticular, absorbable vs. non-absorbable sutures, use of DERMABOND, etc.).

Upon suture removal, if applicable, the use of adhesive strips will be recorded in the CRF. If adhesive strips are used, all efforts should be made to ensure identical use of strips on the left and right side of the incision. The use of adhesive strips will be recorded in the CRF.

6.7 Observational Extension - Part B Extension

6.7.1 Participant Recruitment

Ongoing subjects and subjects who exited Part B of the study will be asked to join the Part B extension. A new informed consent form will be signed.

6.8 Concomitant Medications and Procedures

For Study Parts A and B, any medication or procedure, including over-the-counter preparations, that the subject takes during the study protocol period is considered concomitant medication and will be captured on the Concomitant Medications page of the eCRF.

Every attempt should be made to keep concomitant therapy dosing constant during the study. Any change to concomitant therapy should be noted in source documents and the eCRF.

For Study Part B Extension, no concomitant medication will be recorded in the eCRF or source documents unless it is needed to treat a Treatment Related AE.

6.8.1 Prohibited Treatment and Procedures

Necessary therapies that will not interfere with the response to treatment or interpretation of results

may be provided to the subject at the discretion of the PI.

As per Table 1 below, the following medications are prohibited during the course of the study and appropriate washout periods noted below (calculated from Visit 2a) must be respected:

Table 1. Prohibited medications and procedures

Description	Washout Period
• Systemic corticosteroids (e.g., prednisone, triamcinolone, etc.) *[NOTE: inhaled and insufflated corticosteroids of stable dosing are acceptable]*	4 weeks
• Topical corticosteroids in or around the treatment areas *[NOTE: low/medium potency corticosteroids may be used in areas removed from the treatment area with caution to ensure no contamination of the treatment area]*	4 weeks
• Antimetabolite medications (e.g., methotrexate, azathioprine, 6-mercaptopurine, etc.)	8 weeks
• Antineoplastic agents	4 weeks
• Chronic NSAID use (i.e., use for more than 7 days out of the prior 14 days) *[NOTE: short courses of NSAIDS are allowable to manage acute pain/inflammation syndromes but should be limited to 7 days or less]*	4 weeks
• Oral hypoglycemic agents or any form of insulin	2 years
• Agents that prolong bleeding times (i.e., coumarin, heparin, clopidogrel, Factor Xa inhibitors, vitamin E supplementation ≥30,000 IU per day, etc.)	4 weeks
• Investigational drug or device	30 days
• Tobacco/inhaled nicotine products (cigarettes, pipe, snuff, cigars, vaporizers)	6 months
• Incisional surgery of any kind from the level of the umbilicus to the knees	12 months
• Any cosmetic surgery (e.g., facelift, breast enhancement, etc.).	Prohibited during study Parts A and B (Not applicable to Part B Extension)

All treatment/procedures received by the subject within 30 days prior to Visit 1a and throughout the treatment period, including the name of the treatment/procedure, must be recorded in the eCRF with end dates, if applicable. Use of prohibited treatment/procedures must be recorded in the eCRF up to the extent of the prohibited time period indicated above.

In the event such prohibited therapies are administered during the study period, the Medical Monitor will be contacted to discuss the details of the event. Subject participation will not automatically be discontinued. At a minimum, the event will be documented by the site staff as a protocol deviation, as instructed by the Medical Monitor. Depending upon the nature of the prohibited therapy and the timing relative to the determination of the primary endpoint, the Medical Monitor may make a decision to discontinue the subject.

The decision to administer a prohibited medication/treatment is done with the safety of the study participant as the primary consideration. If the permissibility of a specific medication/treatment is in question, the Medical Monitor should be contacted before the prohibited medication/treatment is administered.

7 STUDY DRUG MATERIALS AND MANAGEMENT

7.1 SLI-F06 (Investigational Product)

SLI-F06 drug product will be provided by the Sponsor as a lyophilized powder. It consists of SLI-F06 and the formulation buffer components in a lyophilized cake. It will be reconstituted with USP Water for Injection just prior to use.

7.2 Formulation Buffer

Formulation buffer will be provided as a lyophilized powder consisting of L-histidine, disodium phosphate, D-mannitol, and deionized water. Adjusted to pH 6.5 with NaOH or HCl as required. It will be reconstituted with USP Water for Injection just prior to use.

7.3 Packaging and Labeling

Product supplies will be packaged in glass vials with labeling for storage conditions.

7.4 Storage, Handling, and Disposal of Investigational Product

Upon receipt of the study drug, the PI is responsible for ensuring that the designated staff member will conduct a complete inventory of study materials and assumes responsibility for their storage, dispensing and disposal. In accordance with federal regulations, the PIs must keep all study materials in a secure location with restricted access. The PI will keep a record of the inventory and dispensing of all study drugs. All supplies sent to the PIs will be accounted for and, in no case, used in any unauthorized situation.

Lyophilized SLI-F06 and lyophilized formulation buffer will be stored at -20ºC (-25°C to -15°C). Lyophilized formulation buffer will be brought to room temperature (20°C to 25°C) and reconstituted with USP Water for Injection. Reconstitute each vial with 1mL USP Water for Injection to create a 25mg/mL solution and, then store on ice or keep in the refrigerator at 4°C (refrigerated reconstituted product or product on ice must be used within 8 hours). Note that one vial will be sufficient to load 2 syringes or treat 2 wounds (Part A). For the abdominoplasty (Part B, one vial will be sufficient to treat approximately 15 cm of a single wound edge.

All used and unused supplies will be returned to Sponsor/designee for destruction at the conclusion of the study.

7.5 Dosing and Administration

SLI-F06 will be supplied as a lyophilized powder (25 mg/vial) and will be diluted with 1 ml USP Water for Injection to make a 25 mg/ml solution. Formulation buffer (25 mg of lyophilized powder per vial) will be diluted with 1 ml USP Water for Injection to make a 25 mg/ml solution.

Immediately prior to closure, excisions will be injected along BOTH wound edges at 0.05 mL per 0.75 cm of single wound edge. The total dose of SLI-F06 for each subject is based on the number of excisions and abdominoplasty incision length. Total dose exposure follows:

Part A:
- 90 mg of SLI-F06 (9 treated excisions) for subjects with large pannus
- 70 mg of SLI-F06 (7 treated excisions) for subjects with smaller pannus
- 60 mg of SLI-F06 (6 treated excisions) for subjects with smaller pannus

Part B:
- 41.7 mg of SLI-F06 for subjects with a 25 cm wound (12.5 cm active treatment)
- 50.0 mg of SLI-F06 for subjects with a 30 cm wound (15 cm active treatment)
- 53.3 mg of SLI-F06 for subjects with a 32 cm wound (16 cm active treatment)

Part B Extension:
- There will be no exposure to SLI-F06 or vehicle solution.

8 DATA COLLECTION

8.1 Electronic Case Report Form

Treatment and follow-up of subjects will be recorded in a 21 CFR part 11 compliant eCRF. Data will be first recorded into the medical record and study specific source document worksheets prior to entry into the eCRF.

8.2 Laboratory Data

Laboratories utilized in this study (clinical safety, immunogenicity, tensile strength, and histology) will provide electronic data transfers that will be maintained separate from the eCRF.

8.3 Photography

Photographs of treatment areas will be taken according to a standardized protocol incorporating appropriate quality control processes. A reshoot may be requested if quality standards are not met.

9 STUDY EVALUATIONS

9.1 Informed Consent

The PI (or designate) will explain the benefits and risks of participation in the study to each subject and will obtain written informed consent. Written informed consent must be obtained prior to the subject entering the study (before initiation of any study related procedure).

9.2 Study Part A

9.2.1 Visit 1a (Screening Period; Day -30 to 0)

- Written informed consent
- Inclusion / exclusion criteria for Part A and Part B
- Medical history and demographics
- Physical exam
- UPT (if female subject of childbearing potential)
- Concomitant medications/treatments
- Abdominoplasty area assessment and selection of pannus map size
- Immunogenicity sampling
- Safety laboratory sampling
- Concomitant medications/treatments

9.2.2 Visit 2a (Abdominal Excisions; Day 1)

- UPT (if female of childbearing potential and if last UPT was >7 days before V2a)
- Randomization
- Excisions
- IP Injection
- Abdominal area photography (pre- and post-excisions)
- Adverse events assessment
- Concomitant medications/treatments

9.2.3 Visit 3a (Suture Removal; Day 8; ±1 day)

- Immunogenicity sampling
- Abdominal area photography
- Suture removal
- POSAS grading (post-suture removal)
- Adverse events assessment
- Concomitant medications/treatments

9.2.4 Visit 4a (Day 29; ±2 days)

- Immunogenicity sampling
- Safety laboratory sampling
- Abdominal area photography
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment

9.2.5 Visit 5a (Day 57; ±3 days)

- Immunogenicity sampling
- Safety laboratory sampling (Group 2 only)
- Abdominal area photography
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment
- ***Group 2 subjects enter Study Part B***

9.2.6 Visit 6a (Day 85; ±3 days)

- Immunogenicity sampling
- Safety laboratory sampling (Group 1 only)
- Abdominal area photography
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment
- ***Group 1 subjects enter Study Part B***

9.3 Study Part B

9.3.1 Visit 1b (Day 0; Abdominoplasty)

- UPT (prior to abdominoplasty, if female subject of childbearing potential)
- Abdominoplasty/tissue harvesting*
- Randomization
- IP injections
- Concomitant medications/treatments
- Adverse events assessment

** the abdominoplasty will be performed according to the surgeons' standard practice and best medical judgment on a per-patient basis*

9.3.2 Visit 2b (Day 8; ±1 day)

- Immunogenicity sampling
- Concomitant medications/treatments
- Adverse events assessment

9.3.3 Suture Removal Visit (Timing of visit at the discretion of the Investigator)

- Suture Removal
- Concomitant medications/treatments
- Adverse events assessment

9.3.4 Visit 3b (Month 1 ± 3d)

- Immunogenicity sampling
- Safety Laboratory Testing
- Abdominal area photography
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment

9.3.5 Visit 4b, 5b, 6b, and 7b (Month 2 ± 7d, Months 3, 6, and 9 ± 14d)

- UPT (if female subject of childbearing potential; except for V4b)
- Immunogenicity sampling
- Abdominal area photography*
  * If photographs do not meet the Sponsor and/or Photography vendor quality standards, participants will be asked to return to the study site for a reshoot (except for V4b).
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment

9.3.6 Visit 8b (Months 12 ± 14d)

- UPT (if female subject of childbearing potential)
- Immunogenicity sampling
- Safety Laboratory Testing
- Abdominal area photography*
  * If photographs do not meet the Sponsor and/or Photography vendor quality standards, participants will be asked to return to the study site for a reshoot (except for V4b).
- POSAS grading
- Concomitant medications/treatments
- Adverse events assessment
- Study Exit

  Subject does not consent to Part B extension
  - If a photography reshoot IS NOT required, Study Exit date will be the date the V8b photography report is received.
  - If one or more photography reshoots ARE required, Study Exit date will be the date on which the last reshoot photography report is received or the date the participant decline additional photography session.

  Subject consent to Part B extension
  - Participant will be exited from Part B.
  - Subject will enter Part B Extension.

9.4 Study Part B Extension

A subject first visit in Part B extension may be conducted at an alternative timepoint than Visit 9b and a scheduled visit may be cancelled as per the directive of the Sponsor.

9.4.1 Visit 9b, 10b, and 11b (Months 15, 18, 21 ± 14d)

- Written Informed Consent*
- Inclusion/ exclusion criteria Part B extension**
- Abdominal area photography
  - If photographs do not meet the Sponsor and/or Photography vendor quality standards, subjects will be asked to return to the study site for a reshoot.
- POSAS grading
- Treatment Related Adverse Events assessment

- **To be performed during first visit of Part B Extension if consent not obtained at Visit 8b.*

- *** To be performed during first visit of Part B Extension.*

9.4.2 Visit 12b (Month 24 ± 14d)

- Abdominal area photography
  - If photographs do not meet the Sponsor and/or Photography vendor quality standards, subjects will be asked to return to the study site for a reshoot.
- POSAS grading
- Treatment Related Adverse Events assessment

9.4.3 Study Exit

The Final visit may be conducted at any timepoint (Month 15, 18, 21 or 24)

- If a photography reshoot IS NOT required, Study Exit date will be the date the photography report is received for the last visit.
- If one or more photography reshoots ARE required, Study Exit date will be the date on which the last reshoot photography report from the last visit is received or the date the participant decline additional photography session.

9.4.4 Optional Visit

The Sponsor may request that an Optional Visit(s) be conducted at an alternative timepoint.

- Written Informed Consent*
- Inclusion/ exclusion criteria Part B extension**
- Abdominal area photography
  - If photographs do not meet the Sponsor and/or Photography vendor quality standards, participants will be asked to return to the study site for a reshoot.
- POSAS grading
- Treatment Related Adverse Events assessment

**To be performed if first visit of Part B Extension and consent not obtained at Visit 8b.*
*** To be performed if first visit of Part B Extension Visit.*

9.5 Efficacy

9.5.1 Primary Efficacy Variable

9.5.1.1 POSAS (PI Assessment) – Excisions/Abdominoplasty Incisions (Parts A, B, and B Extension)

The Patient and Observer Scar Assessment Scale (POSAS; Appendix B) will be used to assess the various parameters of each excision site and the abdominoplasty incision. At each observation time point, the **PI** will grade each scar using the "Observer Scale" of the POSAS. The PI assessment will be conducted after the subject POSAS assessment so as not to influence the subject's grading.

9.5.2 Secondary Efficacy Variables

9.5.2.1 POSAS (Subject Assessment) – Abdominoplasty Incisions (Parts B and B Extension)

At each observation time point, the **subject** will be directed to grade the left and right side of the incision scar separately using the "Patient Scale" criteria of the POSAS. Then, each side of the abdominoplasty incision (left and right) will be divided into 5cm sections starting from the midpoint moving outwards to the end of the incision. The subject will use the "Patient Scale" criteria of the POSAS to assess the middle 3cm section within each 5cm section of the incision

line. Sections that are less than 5cm (as well as their paired contralateral section) will not be assessed (Refer to Figure 6). After the subject has completed his/her grading, the PI will grade the incisional scar using the "Observer Scale" of the POSAS.

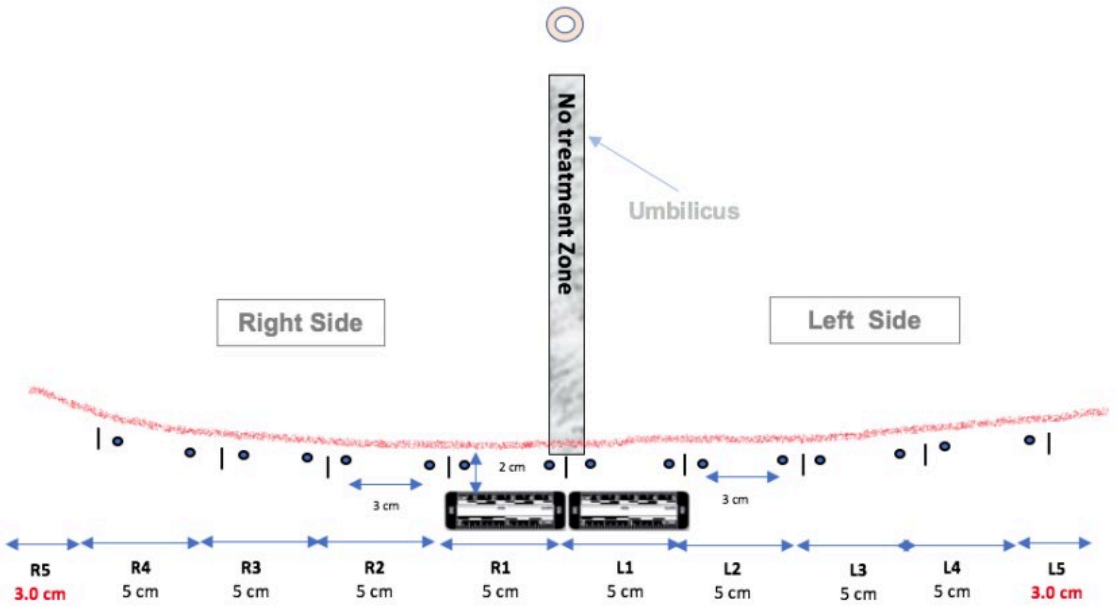


Figure 6. 5cm sections of Abdominoplasty Incision

9.5.2.2 POSAS (PI assessment) – Abdominoplasty 5 cm sections (Parts B and B Extension)

Using a standard clear plastic 15 cm ruler and surgical marker, each side of the abdominoplasty incision (left and right) will be divided into 5cm sections starting from the midpoint moving outwards to the end of the incision. Markings will be placed 2 cm below the scar incision in order to not obstruct the scar. The PI will use the POSAS to assess the middle 3cm section within each 5cm section of the incision line. Sections that are less than 5cm (as well as their paired contralateral section) will not be assessed (Refer to Figure 6).

Photography will be taken of each individual section including those that are less than 5 cm (as well as their contralateral section) in order to obtain photographs of the scar terminus. A 5cm adhesive ruler will be adhered at least 2 cm underneath each 5 cm section in order to confirm accuracy of the 5cm markings. Pre- identified labels (i.e., L1, L2, L3, etc.) will be adhered directly above each section.

9.5.2.3 Independent Panel Review - Photography

At each observation time point, close-up photographs of each excision will be taken. Upon study completion, a panel of raters will review the photographs in a blinded fashion. Assessors will grade scars using the "Observer Scale" of the POSAS (pliability and vascularity will not be assessed).

9.5.2.4 Histology

Study Part A only. Histologic appearance of excision sites will be assessed and compared. Logistics and assay specifics will be provided in a separate manual.

9.5.2.5 Tensile Strength

Study Part A only. *Ex vivo* tensile strength of excision sites will be assessed and compared. Logistics and assay specifics will be provided in a separate manual.

9.5.3 Exploratory Efficacy Variables

9.5.3.1 POSAS (Subject Assessment) – Excisions (Part A)

At each observation time point during study Part A, the **subject** will be directed to grade each excision scar separately using the "Patient Scale" criteria of the POSAS. After the subject has completed his/her grading, the PI will grade each excision scar using the "Observer Scale" of the POSAS.

9.6 Safety

9.6.1 Clinical Safety Laboratory Tests

Standard clinical laboratory analyses (CBC/Diff, chemistry) will be conducted on blood samples collected at Screening V1a, V4a (Day 29), V5a (Day 57 - Group 2 only), V6a (Day 85 - Group 1 only), V3b (M1) and at study exit.

Clinically significant results, in the opinion of the PI, should be reported as AEs. If an AE requires laboratory testing, the results of the test must be obtained by the investigative site and filed in the subject's documentation.

9.6.2 Immunogenicity Testing

During Study Part A, immunogenicity analyses will be conducted on blood samples collected from subjects at Screening V1a, V3a (Day 8), V4a (Day 29), V5a (Day 57) and V6a (Day 85 - Group 1 only). During Study Part B, immunogenicity analyses will be conducted at V2b (Day 8), V3b (M1), V4b (M2), V5b (M3), V6b (M6), V7b (M9), and V8b (12M).

Logistics and assay specifics will be provided in a separate manual.

9.6.3 Adverse Events

During Parts A and B, all observed or volunteered AEs regardless of treatment group or suspected causal relationship to the study treatment will be recorded in the eCRF. Subjects will be questioned for the occurrence of any new or worsening signs or symptoms at each visit.

During Part B Extension, all Treatment-Related AEs (TRAEs) will be recorded in the eCRF. Subjects will be questioned for the occurrence of any new or worsening signs or symptoms at each visit.

9.6.3.1 Definition of Adverse Event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a medicinal product and which does not necessarily have a causal relationship with the study drug. AEs include any unfavorable and unintended illness, sign, symptom, clinically significant laboratory test abnormality, or disease temporally associated with the use of a medicinal product that has appeared or worsened during the course of the clinical trial, regardless of causal relationship to the study drug(s) under study. AEs include any illness, sign, symptom, or out-of-range and clinically significant laboratory finding that has appeared or worsened during the course of the clinical trial, regardless of causal relationship to the study. Typical signs and symptoms of minor excisional surgery are NOT to be considered adverse events UNLESS:

- They persist longer than expected by the investigator
- They are more severe than expected by the investigator

Findings that should be considered typical of minor excisional surgery include:

- Pain
- Pruritus
- Erythema
- Bruising
- Tenderness
- Crusting/ Scabbing
- Any other finding that the investigator would expect to observe in routine, uncomplicated minor excisional surgery

The collection of non-serious AEs and serious adverse events (SAEs) will begin following the subject's exposure to SLI-F06.

9.6.3.2 Documenting Adverse Experiences

During Parts A and B, the PI is responsible to document all AEs that occur during the study. AEs should be documented as a single medical diagnosis. When this is not possible, AEs should be documented in terms of signs/symptoms observed by the PI or reported by the subject at each study visit. Each AE that appears to be independent of any prior event will be reported separately.

All AEs occurring after the subject first exposure to SLI-F06 through the last study visit must be reported, regardless of AE causality. All AEs, whether in response to a query, observed by the study site personnel, or reported spontaneously by the subject, will be recorded. Any clinically significant AEs deemed related to treatment reported or observed at the final study/treatment visit will be followed until stabilization or resolution (or up to 30 days after final study visit).

At each visit during the study, the subject will be assessed for the occurrence of new and ongoing AEs. The following data will be collected on all AEs and recorded on the appropriate CRF:

- Event name (diagnosis preferred, if unknown, record the signs/symptoms)
- Onset date and end date
- Maximum intensity (severity)
- Seriousness
- Action taken regarding study drug
- Corrective treatment, if given
- Outcome
- PI’s assessment of causality

Vital sign abnormalities are to be recorded as AEs only if they are clinically significant (for example: are symptomatic, requiring corrective treatment, leading to discontinuation or fulfilling a seriousness criterion).

For findings considered typical of minor excisional surgery that persist or become more severe than expected, the investigator should determine:

- The start date – when the finding exceeds what may be typically seen with minor excisional surgery.
- Maximum intensity (severity) – using the definitions for adverse event severity found in section 9.6.3.4, the investigator should assign a severity to the adverse event. For events that change in severity, the maximum severity attained should be recorded.

- The end date – the investigator should record the date that the finding returns to a typical severity or duration, NOT necessarily when the finding is fully recovered. For example, a subject who notes pain well above what would be expected for three days after the procedure but has very minor pain thereafter for six additional days should have an adverse event of pain lasting three days, not pain lasting nine days.

During Part B Extension, the PI is responsible to document all TRAEs that occur during the study. TRAEs should be documented as a single medical diagnosis. When this is not possible, TRAEs should be documented in terms of signs/symptoms observed by the PI or reported by the subject at each study visit. Each TRAE that appears to be independent of any prior event will be reported separately.

9.6.3.3 Serious Adverse Events

All AEs will be assessed as either serious or non-serious. An SAE is defined as any untoward medical occurrence that at any dose:

- Results in death
- Is immediately life threatening, (the term "life threatening" in the definition of "serious" refers to an event in which the subject is 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)
- Requires in patient hospitalization or prolongation of existing hospitalization (hospitalization for elective surgery for a baseline condition is not considered an AE)
- Results in persistent or significant disability/incapacity (permanent or substantial disruption of a person's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect
- Is a medically important event that may not be immediately life threatening or result in death or hospitalization but may jeopardize the subject and may require medical or surgical intervention to prevent one of the above listed outcomes. Examples of such events include, but are not limited to, allergic bronchospasm requiring intensive treatment in an emergency room or at home; blood dyscrasias or convulsions that do not result in inpatient hospitalization.

Note: A spontaneous abortion will be considered an SAE, and must be reported per Reporting of SAEs under Section 9.5.3.6.

9.6.3.4 Assessment of Severity

The severity assigned to an AE should be determined by the maximum severity of the AE. The categories described below should be used to estimate the severity of AEs:

- **Mild:** Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required
- **Moderate:** Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required
- **Severe:** Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization or prolongation of current hospitalization possible; may be incapacitating or life threatening

9.6.3.5 Assessment of Causality

The PI should assess the relationship of the AE to the study drug as either "Related" or "Not Related". The following should be taken into account when assessing AE causality:

- **Related:** There is at least a reasonable possibility that the AE/SAE is related to the study drug. Reasonable possibility means that there is evidence to suggest a causal relationship between the drug and the AE.
- **Not Related:** There is little or no reasonable possibility that the AE/SAE is related to the study drug. This assessment implies that the AE/SAE has little or no temporal relationship to the study drug and/or a more likely or certain alternative etiology exists.

9.6.3.6 Reporting of Serious Adverse Events

Adverse events classified as "serious" require expeditious handling and reporting to Sponsor or designee within 24 hours of investigational center notification to comply with regulatory requirements.

All SAEs, whether related or unrelated to study drug, must be immediately reported to the ethica CRO within 24 hours of the PI's awareness of the event. All SAEs must be reported via confirmed facsimile or email transmission and must be submitted on a written SAE report form signed by the PI within 24 hours of the PI's awareness of the event. **Please refer to the SLI-C40-001 Safety and Medical Monitoring Plan for the listing of appropriate contacts.**

PIs should not wait to receive additional information to fully document the event before notifying ethica CRO of an SAE. If only limited information is initially available, follow-up reports are required. Additional relevant information such as hospital records and autopsy reports should be provided to the Sponsor as soon as they are available. Should the PI become aware of an SAE (regardless of its relationship to IP) that occurs within 30 days after stopping the study drug, the SAE must be reported in accordance with procedures specified in this protocol.

All deaths of subjects, regardless of cause, and which are known to the PI will be reported on the appropriate CRF for up to 30 days after the administration of study drug, regardless of the PI's opinion regarding drug relationship. Documentation of the subject's cause of death and a copy of the autopsy/hospital report will also be provided. The Medical Monitor must be notified within 24 hours of knowledge of the event by telephone (and/or fax/email) of all subject deaths. Written follow-up must be received by ethica CRO within five (5) calendar days of initial notification.

The PI should take all appropriate measures to ensure the safety of the subjects, notably he/she should follow a subject with an SAE until the event has resolved or the condition has stabilized. This may imply that follow-up will continue after the subject has left the study, and that additional investigations may be requested by the Sponsor. When an SAE persists at the end of the study, the PI will conduct follow-up contacts with the subject until the PI/Sponsor agree the event is satisfactorily resolved and/or stabilized. If at any time after 30 days after administration of study drug, the PI becomes aware of an SAE which he/she feels is related to study drug or procedure, this must also be reported immediately (within 24 hours of knowledge of occurrence) by telephone and confirmed facsimile transmission/email to ethica CRO.

9.6.3.7 Expedited Serious Adverse Event Reports

Expedited SAE reports are those that are both unexpected based on the reference document (Investigator Brochure) and are related (i.e., the relationship cannot be ruled out) to the study drug.

These expedited reports are subject to reporting timelines of 7 and/or 15 calendar days to the regulatory reporting agency(ies). The Sponsor will notify regulatory authorities of these SAEs and all participating investigational centers in writing for submission by the PI to the IRB.

Upon receiving such notices, the PI must review and retain the notice with the Investigator Brochure and immediately submit a copy of this information to the responsible IRB according to local regulations. The PI and IRB will determine if the informed consent requires revision. The PI should also comply with the IRB procedures for reporting any other safety information.

9.6.3.8 Pregnancy

During Parts A and B, all female subjects of childbearing potential must use an effective method of birth control (as defined in Section 5.1) during the course of the study, in a manner such that risk of contraceptive failure is minimized. Abstinence is allowed as a birth control method.

Before enrolling a female subject of childbearing potential in this clinical trial, the PI must review the following information about study participation:

- Informed consent requirements
- Contraceptives in current use

Following review of this information and appropriate subject counseling, the PI or designee (obtaining the consent) and the subject must sign the informed consent before study enrolment.

During the study, all female subjects of childbearing potential should be instructed to contact the PI immediately if they suspect they might be pregnant (e.g., missed or late menstrual period).

If a subject or PI suspects that the subject may be pregnant prior to study enrolment, the study drug must be withheld until the results of laboratory pregnancy testing are available. If pregnancy is confirmed, the subject must not receive study drug and must not be enrolled in the study.

If pregnancy is suspected while the subject is receiving study treatment, the study drug must immediately be withheld until the result of pregnancy testing is known. If pregnancy is confirmed, the study drug will be permanently discontinued, and the subject will be followed until the pregnancy comes to term.

For Part B-Extension, all female subjects of childbearing potential are not required to use a birth control method as pregnancy will not impact their study participation. However, if they suspect they might be pregnant (e.g., missed or late menstrual period), they should be instructed to contact the PI immediately.

All confirmed pregnancies must be reported via confirmed facsimile or email transmission and must be submitted on an Unanticipated Problem Reporting form within 24 hours of the PI's awareness of the pregnancy. Any pregnancy complications that meet the criteria of a SAE (e.g., a spontaneous abortion, stillbirth, congenital anomaly, etc.) are considered SAEs. The SAE form must be submitted of PI awareness using the same reporting as procedure for an SAE under Section 9.6.3.6.

10 STATISTICS

All statistical processing will be performed using SAS® version 9.4 or later. Statistical significance will be based on two-tailed tests of the null hypothesis resulting in p-values of 0.05 or less. A statistical analysis plan (SAP), describing all statistical analyses will be provided as a separate document. The SAP will be finalized prior to unblinding of the study treatments.

10.1 Sample Size Determination

Approximately 25 subjects will be enrolled. This is a POC study and a formal sample size justification is not required for this study. It is the opinion of the Sponsor that a total of 25 subjects will be sufficient to achieve the objectives of the study.

10.2 Assessments of Efficacy

Efficacy analyses will be conducted on an intent-to-treat (ITT) basis (see Section 10.4).

For categorical parameters, the number and percentage of subjects/observations in each category will be presented. The denominator will be based on the number of subjects/observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n (number of subjects or observations), mean, standard deviation, median, and range.

Comparisons between treatment groups will be performed using parametric or non-parametric testing, as appropriate.

10.3 Assessment of Safety

For Parts A and B, safety analysis will be conducted on the Safety Population (SAFT), by tabulations of AEs, safety laboratory parameters and immunogenicity outcomes.

Subjects will be followed for AEs (local and systemic) throughout the study. Events specific to treatment sites will be recorded by excision site (Study Part A) and per side (Study Part B) to allow comparison of study treatments.

For Part B Extension, Safety analysis will be conducted on the ITT population. Subjects will be followed for Treatment-Related AEs (local and systemic) throughout the study.

10.3.1 Adverse Events

All AEs occurring during the study will be recorded and classified on the basis of MedDRA terminology. Descriptions of AEs will include the date of onset, the date the AE ended, the severity of the AE, the relationship to study medication, the action taken regarding study medication usage, the action taken to treat the AE, and the outcome. All reported treatment-emergent AEs (TEAEs) will be summarized by the number of Subjects reporting AEs, system organ class, severity, seriousness, and relationship to study medication. TEAEs are those AEs with an onset on or after the date of initial IP exposure.

AEs will be summarized by treatment group and severity, and by treatment group and relationship to IP. Each subject will be counted only once within a system organ class or a preferred term by using the AEs with the greatest relationship within each category.

All information pertaining to AEs noted during the study will be listed by subject, detailing verbatim given by the PI, preferred term, system organ class, start date, stop date, severity, actions taken, and drug relatedness.

10.3.2 Safety Laboratory Tests

Determination of clinical significance for all out-of-range laboratory values will be made by each PI, and Adverse Event reports will be generated as necessary.

10.3.3 Immunogenicity

Changes from baseline in immunogenicity outcomes will be summarized with descriptive statistics and text, as appropriate.

10.3.4 Concomitant Medications

All previous therapies and concomitant medications will be classified based on terminology from the WHO Drug Dictionary. Previous therapies and concomitant medications data will be presented in data listings.

No concomitant medication will be recorded in the eCRF for Part B Extension.

10.4 Analysis Populations

10.4.1 Primary Population for Efficacy Analysis

The ITT population will be the primary population for efficacy and safety analyses and will consist of all randomized subjects who received at least one injection of IP and provided at least one post-baseline evaluation, and will be analyzed in the treatment group they were allocated.

A per-protocol (PP) population will neither be identified nor analyzed.

10.4.2 Populations for Safety Analysis

The SAFT population will be used for safety analysis and will consist of all randomized subjects who received one injection of IP, and will be analyzed as per the treatment actually received.

10.4.3 Sub-Populations

A subset of subjects with a history of keloidal scarring will be analyzed for efficacy and safety in a separate report. Comparisons between this subject population and the general population will not be made.

10.5 Subject Disposition

A tabulation of subject disposition will be provided which will include the numbers of subjects who enter, complete, and discontinue the study. The reasons for discontinuation will be included.

10.6 Protocol Deviations and Violations

All protocol deviations and violations will be reported to the Sponsor and recorded throughout the study. A tabulation of protocol deviations will be included in the final study report.

10.7 Multicenter Issues

The study will be conducted at multiple investigational centers in the United States with the intention of pooling the results for analysis.

10.8 Missing Efficacy Data Imputations

Data will be analyzed as observed; no imputations will be made for missing data.

10.9 Statistical Hypothesis Testing and Control of Multiplicity

Not Applicable.

10.10 Compliance

No compliance analyses are planned.

10.11 Interim Analyses

An interim analysis will be performed utilizing data from study Part A.

11 QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Study Monitoring

An initiation visit will be conducted with the PI/OP, IDR and study coordinator(s) by Sponsor and/or its designee. During this meeting, an extensive review and discussion of the protocol, all study procedures, source documents, and eCRFs will be conducted. Evaluation scales will be reviewed extensively.

The study monitors/clinical research associates will be trained prior to study initiation. Following this training, an overview of the study disease and study material background will be understood. Specific monitoring guidelines and procedures to be followed during monitoring visits will also be utilized. For Parts A and B, all data will be approximately 100% source document verified by the site monitors. All subject source records must be made available to the monitors.

For Part B Extension, sites will be monitored remotely. On-site monitoring will not be conducted.

The conduct of the study will be closely monitored by the Sponsor (or designate) following GCP guidelines. The reports of these verifications will also be archived with the study report. In addition, inspections or on-site audits may be carried out by local and/or federal authorities. The PIs will allow the Sponsor's representatives and any regulatory agency to examine all study records, corresponding subject medical records, clinical dispensing records and storage area, and any other documents considered source documentation. The PIs agree to assist the representative, if required.

11.2 Audits and Inspections

The study will be conducted under the Sponsorship of the Sponsor in conformation with all appropriate local and federal regulations, as well as ICH guidelines. Interim and end-of-study audits of raw data, study files, and final report may be conducted by the Sponsor’s Quality Assurance Department or designee.

The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems to ensure that studies are conducted and data are generated, documented, and reported in compliance with the protocol, GCP, and applicable regulatory requirements. In addition, the Sponsor will be responsible for securing agreement from all involved parties to ensure direct access to all study related investigational centers, source data/documents, CRFs, and reports for the purpose of monitoring and auditing by the Sponsor, and inspection by regulatory authorities.

11.3 Protocol Deviations

The PIs must read the protocol thoroughly and must follow the instructions exactly.

A deviation from the protocol is an unintended and/or unanticipated departure from the procedures and/or processes approved by the Sponsor and the IRB and agreed to by the PI. Deviations usually have an impact on individual patients or a small group of patients and do not involve inclusion/exclusion or primary endpoint criteria.

A protocol violation occurs when there is non-adherence to the protocol that results in a significant, additional risk to the patient, when the patient or PI has failed to adhere to significant protocol requirements (inclusion/exclusion criteria) and the patient was enrolled without prior Sponsor approval, or when there is non-adherence to FDA regulations and/or ICH GCP guideline.

The issue of noncompliance may be either on the part of the subject, the PI, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the site to use continuous vigilance to identify and promptly report deviations to ethica CRO Inc.

All protocol deviations and violations must be addressed in study subject source documents. A completed copy of the ethica CRO Inc. Protocol Deviation Form must be maintained in the regulatory file, as well as in the subject's source document. Protocol deviations must be sent to the IRB per its guidelines.

The protocol must be rigorously adhered to; however, exceptions will be made in emergency situations when the protection, safety, and well-being of the subject requires immediate intervention based on the judgment of the PI.

12 ETHICS AND ADMINISTRATIVE ISSUES

12.1 Ethical Conduct of the Study

This study will be conducted in accordance with the ethical principles originating from the Declaration of Helsinki, ICH guidelines, GCP, and in compliance with local regulatory requirements. The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of GCP.

12.2 Ethics Review

This protocol, proposed informed consent form and other information to subjects, and all appropriate amendments will be reviewed and approved by an Institutional Review Board (IRB). A signed and dated notification of the IRB approval will be provided to the Sponsor and PI prior to study initiation. The name and occupation of the chairman and members of the IRB will be supplied to the Sponsor to the extent allowable by the IRB. The PI will provide required progress reports and report all SAEs to the IRB as required by the IRB.

12.3 Written Informed Consent

This study will be conducted in compliance with 21 CFR Part 50 for informed consent.

Written informed consent will be obtained from each subject before any procedures or assessments are done and after the aims, methods, anticipated benefits, potential hazards, compensation and/or honoraria, and insurance arrangements are in force. It will also be explained to the subject that they are free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment.

The site will keep the original consent forms and copies will be given to the subjects.

12.4 Subject Data Protections

Subject data will be protected by ensuring that no captured data contain subject names, addresses, telephone numbers, email addresses, or other personally identifying information. It is acknowledged that subject initials, demographics (including birthdates), medical histories, and prior concomitant medication uses, along with the name and address of the enrolling PI may allow for personal identification of study participants. Other than where necessary to meet regulatory requirements, all data collected in this study will be presented in tabulated (i.e., aggregate) form and listings containing information that could be used to identify an individual subject will not be included in any public disclosures of the study data or the study results.

12.5 Data Monitoring Committee

Not applicable.

12.6 Financial Disclosure

Financial disclosures will be obtained from Investigators and Co-Investigators to document any potential conflicts of interest.

12.7 Investigator Obligation

The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of Good Clinical Practice (GCP).

12.8 Changes to the Protocol

The PIs must read the protocol thoroughly and must follow the instructions exactly. Whenever

possible, any planned deviations should be agreed to by prior discussion between the Sponsor and the PI, with appropriate documentation of Sponsor approval prior to effecting the changes agreed upon. Any amendment to the protocol containing major modifications (particularly if it may involve an increased risk to the subjects) will be approved by the IRB before it may be implemented. No change in the conduct of the study can be instituted without written approval from the Sponsor.

12.9 Confidentiality Regarding Study Subjects

All the data furnished to the PI and his/her staff and all data obtained through this protocol will be regarded as confidential and proprietary in nature and will not be disclosed to any third party, except for the FDA or other regulatory body, without written consent from the Sponsor.

12.10 Information to Study Personnel

The PI, with the assistance of ethica CRO Inc., is responsible for ensuring that all study personnel are qualified for their designated roles and for providing information about the study to all staff members involved in the study or in any element of subject management, both before starting the practical performance of the study and during the course of the study (e.g., when new staff become involved).

The ethica CRO Inc. site monitor is responsible for initiating the site, for ensuring site compliance with the protocol and for closing out the site at the end of the study. Additional information available during the study should be given as agreed upon, either by the PI or the site monitor, and always when new staff members become involved in the study.

12.11 Reporting and Publication of Results

Scarless Laboratories Inc., as the Sponsor, has a proprietary interest in this study. Authorship and manuscript composition will reflect joint cooperation among multiple PIs and sites and Scarless Laboratories Inc. personnel. Authorship will be established prior to the writing of the manuscript. As this study involves multiple sites, no individual publications will be allowed prior to completion of the final report of the multicenter study except as agreed with Scarless Laboratories Inc.

All information, including but not limited to information regarding the IP or the Sponsor's operations supplied by the Sponsor to the PI and not previously published, along with any data generated as a result of this study are considered confidential and remain the sole property of the Sponsor. The PI agrees to maintain this information in confidence and will use the information only to perform the study.

The Sponsor or its designate is responsible for preparing a clinical study report.

The Sponsor or its designate is responsible for publicly registering this study on http://www.clinicaltrials.gov prior to initiating enrolment.

12.12 Financing and Insurance

A separate financial agreement (Clinical Study Agreement) will be made between the Sponsor and the PI at each site.

The study is covered under a Scarless Laboratories Inc. liability insurance policy. The certificate of insurance will be provided upon request.

13 DATA HANDLING AND RECORD KEEPING

13.1 Case Report Form

In this study the case report form will be an eCRF. The study coordinator must complete the eCRF for each subject within a timely manner of the visit occurring.

The site monitor, Clinical Project Manager (CPM), or Clinical Data Manager (CDM) will review the completed eCRF for accuracy, completeness and consistency with source documentation (i.e., medical records, source document worksheets, etc.). The site monitor or CDM will submit requests for correction/clarification of data (e.g., queries) to the study coordinator when inconsistencies are identified during monitoring and source data verification or during the edit check process.

All corrections and alterations of eCRF data must be made by the study coordinator in a timely manner and according to the instructions provided. Completed eCRFs for each visit (i.e., those reviewed by ethica CRO Inc. and with no remaining queries) should then be reviewed and electronically signed by the PI.

A full audit trail detailing corrections and alterations made to the eCRF will be maintained.

Upon study completion, an electronic copy of the eCRF for each subject will be provided to the site.

13.2 Inspection of Records

PIs must maintain detailed records on all study subjects who are enrolled in the study or undergo screening. Data will be recorded in the subject's source documents and in applicable study logs provided by the Sponsor. Source documents include subject medical records, hospital charts, clinic charts, PI subject study files, as well as the results of diagnostic tests (e.g., laboratory tests). All required data should be recorded in the study documentation completely for prompt data review. Upon study completion or at any other time specified by the Sponsor or designee, the appropriate study documents must be submitted.

The PI must keep accurate separate records (source documentation) of all subject visits, being sure to include all pertinent study related information. At a minimum, this includes the following information:

- A statement indicating that the subject has been enrolled in the study and the subject number.
- Date that informed consent was obtained.
- Evidence that the subject meets study eligibility requirements (e.g., medical history, screening evaluations).
- Dates of all study related visits and results of any evaluations/procedures performed, including who performed each assessment at each visit.
- Use of any concurrent medications during the study.
- Documentation of study drug accountability.
- Any and all side effects and AEs must be thoroughly documented to conclusion of Part B.
- Treatment related AEs must be thoroughly documented to conclusion of Part B Extension.
- Results of any diagnostic tests conducted during the study.
- The date the subject exited the study and a statement indicating that the subject completed the study or was discontinued early, including the reason for discontinuation.

Notes describing telephone conversations and all electronic mail with the subject or the Sponsor (Sponsor's designee) concerning the study must be recorded or kept on file. All source documents must be made available to the Sponsor and the Sponsor's designated monitor upon request.

13.3 Archiving of Study Documentation

Essential documents are any records that demonstrate the compliance of the subject, PIs, Sponsor, and site monitor with the study protocol, with standards of GCP, and with all applicable regulatory requirements. Essential documents (including but not limited to study-related correspondence (including emails), subject records, subject privacy documentation, records of the distribution and use of the IP, and copies of eCRFs should be retained and available for audit by the Sponsor's auditor and regulatory authorities until at least 2 years after the latest among the following scenarios: completion or termination of the study, the last approval of a marketing application, no pending or contemplated marketing applications, or formal discontinuation of clinical development of the IP. These documents should be retained for a longer period, however, if mandated by the applicable regulatory requirements, by conditions imposed by the IRB, or by an agreement with the Sponsor. It is the responsibility of the Sponsor to inform the PI when these documents no longer need to be retained.

The Sponsor must be notified in writing if the PI chooses to store the records at a different physical address than the site address or if the PI wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably qualified, responsible person.

14 APPENDICES

Appendix A: Protocol Version History

Appendix B: Patient and Observer Scar Assessment Scale (POSAS)

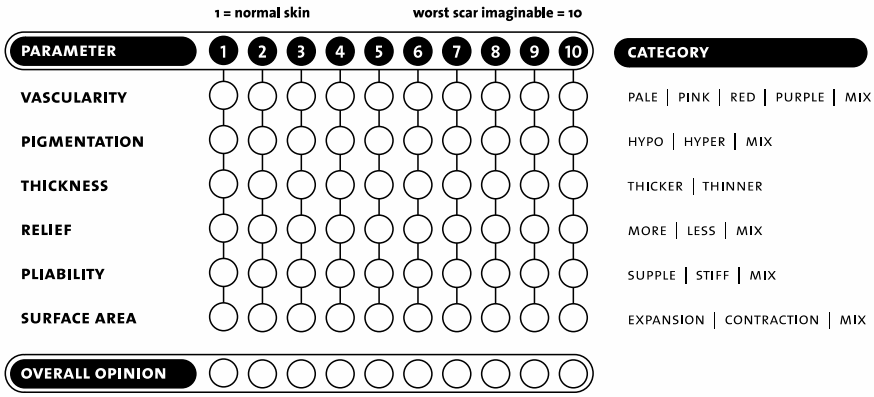
APPENDIX A: PROTOCOL VERSION HISTORY

Version and Date	Description
Version 1.0, 07-May-2018	*Initial protocol*
Version 1.1, 26-Jun-2018	*Clarifications provided to Section 6.5.3.*
Version 1.2, 31-Oct-2018	*1) Some text was modified/added to increase clarity and comprehension.* *2) Pannus maps were revised to permit additional space between excision sites as well as precision regarding skin strips to be used to test tensile strength. Overall, subjects will be exposed to slightly fewer excisions during Part A of the study. Text has been appropriately modified throughout the protocol to accommodate the new mapping.* *3) The study treatment will now be injected immediately prior to closing wounds, as opposed to injections immediately after closure.* *4) Protocol sections have been added to define Pre-operative Preparation and Patient Monitoring, Anesthetic Preparation and Administration, Excision Procedures, Administration of Investigational Product, and Wound Care.* *5) These amendments do not increase risk for study participants.*
Version 1.3, 15-Jan-2019	*1) The Pre-Screening Visit (day -45 to -15) and Screening (day -15 to 0) were combined into a single visit (i.e., Screening Period; day-30 to 0).* *2) Precision was made to confirm that safety laboratory results obtained during the Screening Period will be reviewed by the PI to confirm absence of any health condition(s) that would make the subject inappropriate for study entry.* *3) If the UPT conducted during the Screening Period was performed >7 days of V2a, it will now be repeated prior to performing excisions.* *4) The timing for the removal of sutures post-abdominoplasty is now at the discretion of the Investigator (i.e., standard of care), rather than mandatorily occurring at 2b (day 8 post-abdominoplasty).* *5) To accommodate Investigators removing abdominoplasty sutures as per standard of care, a Suture Removal Visit added has been added to Part B of the study (timing to be at the discretion of the PI).* *6) Immunogenicity testing for ADAs at Visits 4b, 5b, 7b and 8b will now be conducted without consideration of previous test results (i.e., rather than subjects negative for ADAs at a preceding visit not be re-tested).* *7) Photography will now be conducted at Visit 2A (pre- and post-excision).* *8) The POSAS will now also be conducted at Visit 3a (post-suture removal).* *9) Text describing administration of IP for excisions (Section 6.5.8) has been edited to be concise and more precise.* *10) Text describing administration of IP for abdominoplasty (Section 6.6.4) has been edited to be concise and more precise.* *11) Excision site mapping has been simplified with the use of paper pannus maps and sterilizable ink stamps.* *12) The maximal exposure to lidocaine while conducting excisions has been now defined as 7mg/kg.* *13) Incisional surgery of any kind from the level of the umbilicus to the knees has been added to the list of prohibited procedures (Section*

	6.7.1). *14) The shelf-life of refrigerated reconstituted Investigational Product has been increased to 6 hours, up from 4 hours.* *15) Precision was made to confirm that randomization to treatment assignment for Part B will be independent of the randomization to treatment assignment for Part A (Section 6.2).* *16) The Subject assessment of POSAS will now be a secondary endpoint (abdominoplasty incisions/Part B) and an exploratory endpoint (excisions/Part A), rather than a primary endpoint (Section 9.4.2.1).*
Version 1.4, 13-Nov-2020	*1) Clarification that typical signs and symptoms after a minor excisional surgery are not to be considered adverse events unless meeting certain criteria (Sections 9.6.3.1 and 9.6.3.2).* *2) All current participants, whereas possible, will be moved to Group 1; 12-week follow-up after excisions. All future participants will be enrolled in Group 1; 12-week follow-up after excision. (Section 4.1)* *3) Group 3; 4-week follow-up after excision was removed (Section 4.1)* *4) For part B, the IP will now be administered immediately after wound closure (not before wound closure as previously described). Injections will start 1 cm from the mid-point on each side of both wound edges and will proceed laterally (Sections 6.6.3 and 6.6.4).* *5) Addition of a 2 cm area at the midpoint of the incision that will have no IP administered (Sections 6.6.3 and 6.6.4).* *6) Addition of a secondary efficacy assessment. Each side of the abdominoplasty incision will be divided into 5cm sections starting from the midpoint and moving outwards to the end of the incision. The Participant will use the "Patient Scale" criteria of the POSAS and the PI will use the "Observer Scale" criteria of the POSAS to assess the middle 3cm section within each of the 5cm section (Sections 9.5.2.1 and 9.5.2.2)* *7) The shelf-life of refrigerated reconstituted Investigational Product has been increased to 8 hours, up from 6 hours.* *8) Some text was modified/added to increase clarity and comprehension in Sections 9.6.1 and 9.6.2* *9) If photographs don't meet the Sponsor and/or Photography Vendor quality standards, participants will be asked to return to the study site for a reshoot for V5b, V6b, V7b, and V8b (Sections 9.3.5 and 9.3.6).* *10) If participant does not consent to study Part B extension, the participant study exit date is the date the last V8b photography report is received or the date the participant declines additional reshoot photography sessions (Section 9.3.6.)* *11) Protocol sections and wording have been updated to incorporate details about addition of Part B extension. Protocol has been extended for an additional 12 months to assess the efficacy of SLI-F06 treatment on abdominoplasty incision scar appearance over a longer period of time* *12) Addition of wording on how participants will be recruited and consented for the Part B extension (Section 4.1)* *13) These amendments do not increase risk for study participants.*

APPENDIX B: PATIENT AND OBSERVER SCAR ASSESSMENT SCALE

POSAS Observer Scale



Explanation

The observer scale of the POSAS consists of six items (vascularity, pigmentation, thickness, relief, pliability and surface area).
All items are scored on a scale ranging from 1 ('like normal skin') to 10 ('worst scar imaginable').
The sum of the six items results in a total score of the POSAS observer scale. Categories boxes are added for each item. Furthermore, an overall opinion is scored on a scale ranging from 1 to 10.
All parameters should preferably be compared to normal skin on a comparable anatomic location.

Explanatory notes on the items:

- **VASCULARITY** Presence of vessels in scar tissue assessed by the amount of redness, tested by the amount of blood return after blanching with a piece of Plexiglas
- **PIGMENTATION** Brownish coloration of the scar by pigment (melanin); apply Plexiglas to the skin with moderate pressure to eliminate the effect of vascularity
- **THICKNESS** Average distance between the subcutical-dermal border and the epidermal surface of the scar
- **RELIEF** The extent to which surface irregularities are present (preferably compared with adjacent normal skin)
- **PLIABILITY** Suppleness of the scar tested by wrinkling the scar between the thumb and index finger
- **SURFACE AREA** Surface area of the scar in relation to the original wound area

POSAS Patient Scale