A PROSPECTIVE, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL OF DAXIBOTULINUMTOXINA FOR INJECTION FOR THE MANAGEMENT OF PLANTAR FASCIITIS

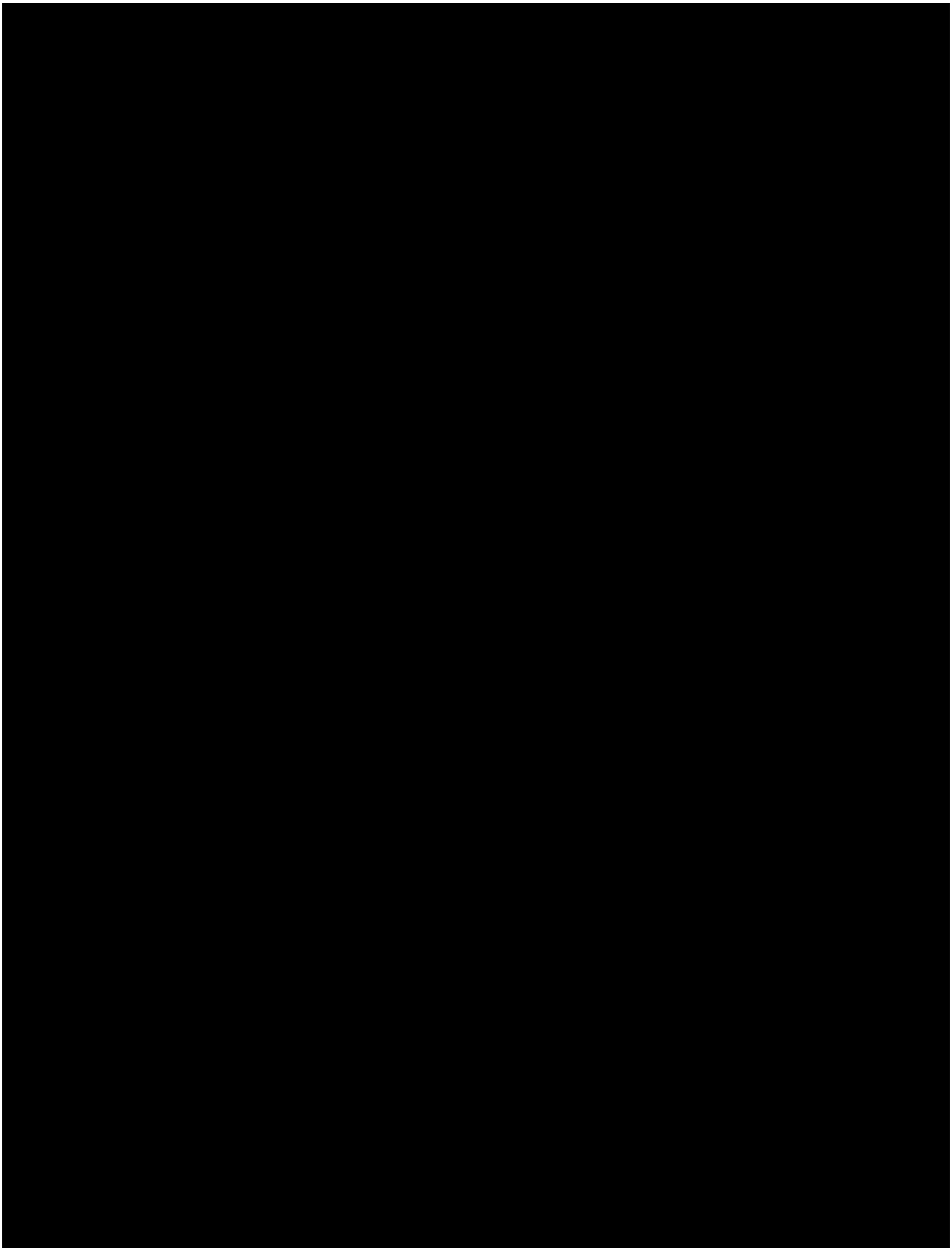
Protocol Number: 1720201

National Clinical Trial (NCT) Identified Number: NCT03137407

Sponsor: Revance Therapeutics, Inc.

Version Number: 4.0

14 Dec 2017



INVESTIGATOR'S AGREEMENT

I have carefully read the protocol entitled: "*A Prospective, Randomized, Double-Blinded, Placebo-Controlled Trial of DaxibotulinumtoxinA for Injection for the Management of Plantar Fasciitis*" and,

I will provide copies of the protocol, any subsequent protocol amendments and access to all information provided by the Sponsor to the trial personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the investigational drug and the trial protocol.

I agree to conduct this clinical trial according to the attached protocol, in compliance with all applicable laws and regulations, and in accordance with the ethical principles stipulated in the Declaration of Helsinki.

_____	_____
Investigator Signature	**Date**
_____	
Printed Name	
_____	
Institution Name	
_____	
Address	
_____	_____
City, State, Postal Code, Country	**Phone Number**

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Council for Harmonisation Good Clinical Practice (ICH GCP) and applicable United States (US) Code of Federal Regulations (CFR) Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the Investigational New Drug (IND) sponsor, funding agency and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

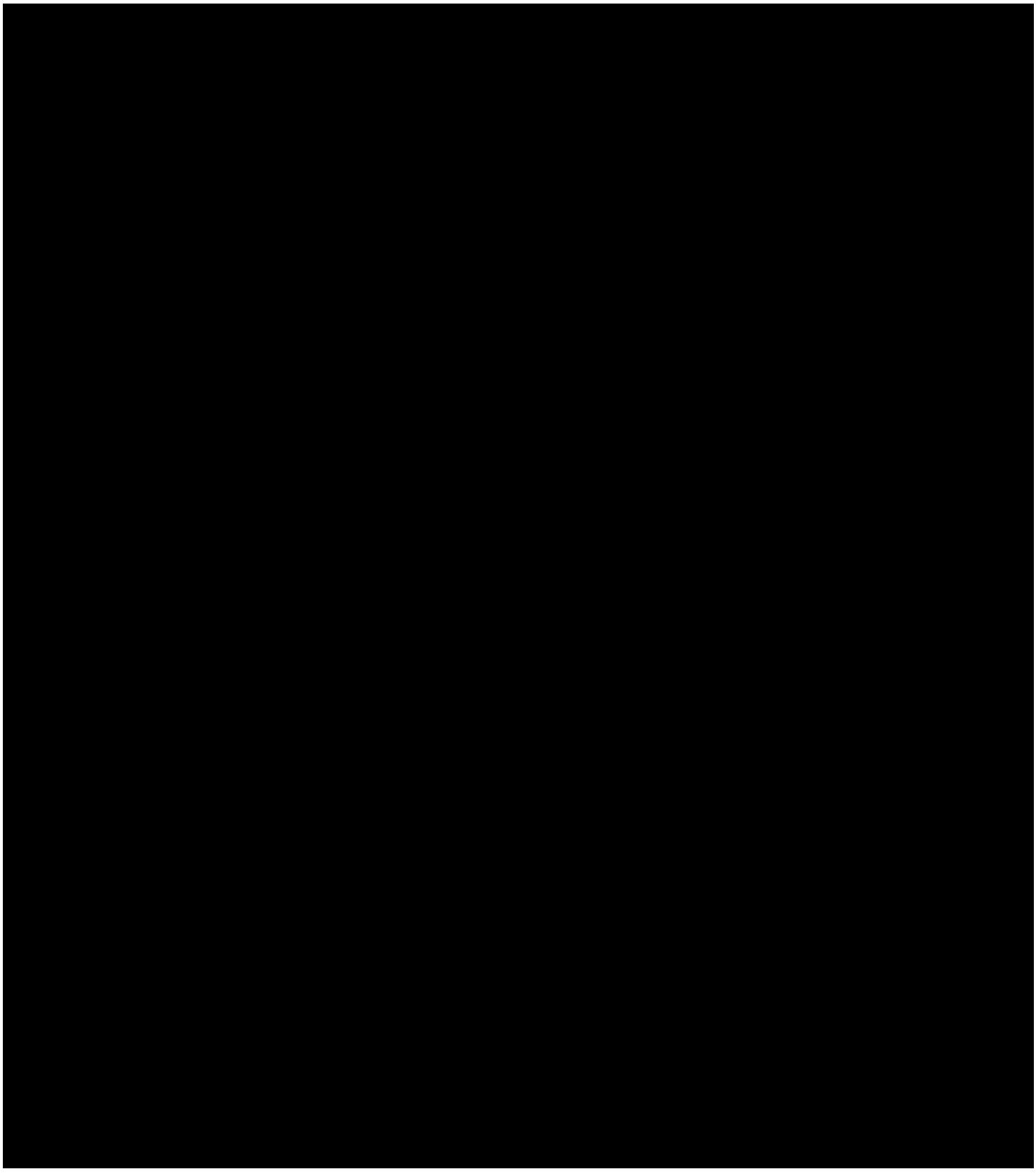
1.1 SYNOPSIS

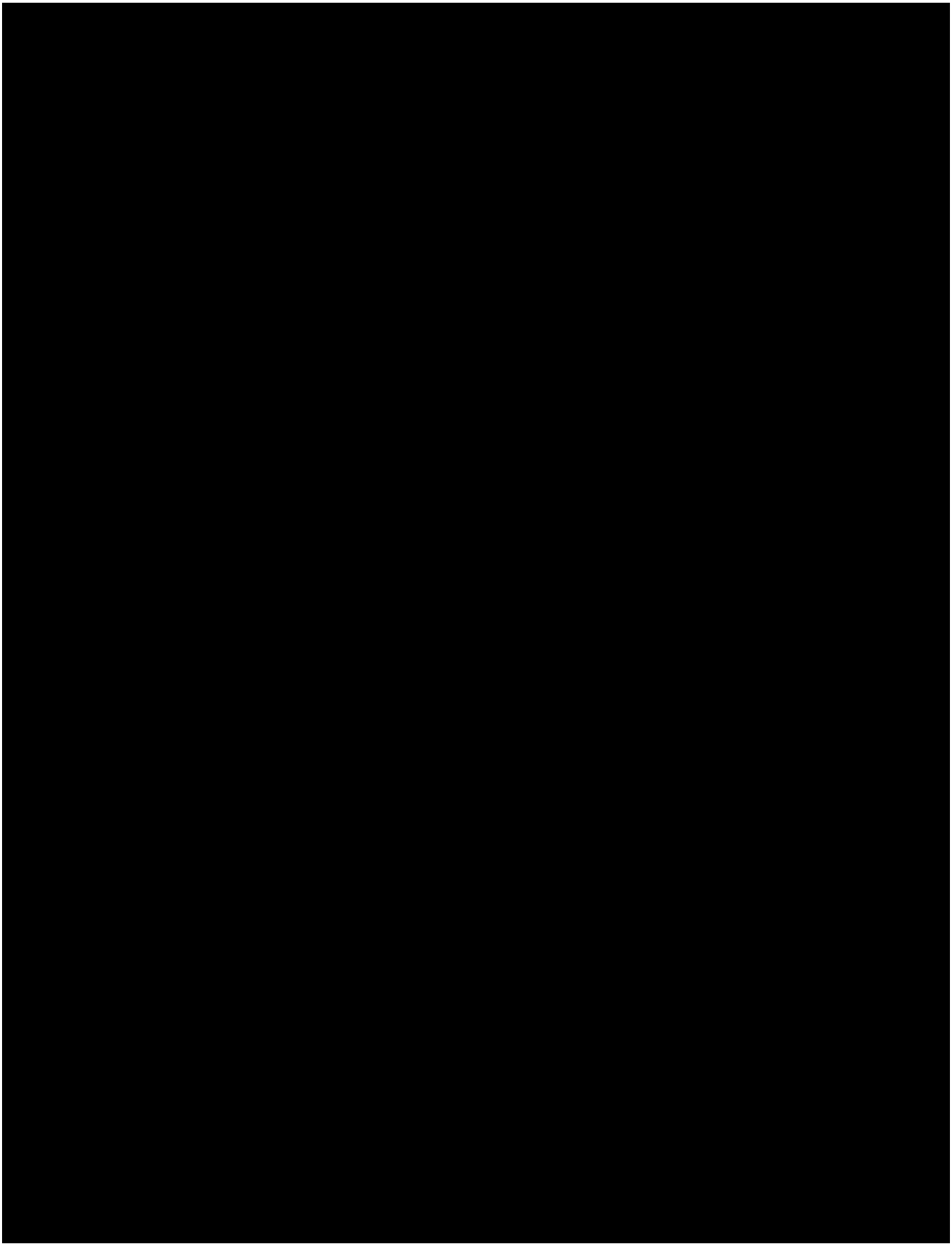
Title:	A Prospective, Randomized, Double-Blinded, Placebo-Controlled Trial of DaxibotulinumtoxinA for Injection for the Management of Plantar Fasciitis
Study Description:	Treatment with DaxibotulinumtoxinA for Injection (Daxi for Injection) of plantar fascia and plantar muscles combined with transient and selective partial paralysis of gastrocnemius/soleus complex (dysfunction) and a simple home program and inexpensive splinting will ameliorate signs and symptoms of plantar fasciitis; will improve function, and will optimize health related quality of life.
Objectives:	Primary Objective: • To compare the safety and efficacy of DaxibotulinumtoxinA for Injection versus placebo for managing plantar fasciitis [redacted]
[redacted]	[redacted]
Study Population:	Male and female adult subjects who have plantar fasciitis that has not responded to conservative treatment modalities.
Phase:	2
Description of Sites/Facilities Enrolling Participants:	Up to 5 sites in the United States (US) will participate in the study. Approximately 60 subjects will be enrolled.
[redacted]	[redacted]

[redacted]

Study Duration: Approximately eight (8) months

Participant Duration: The study duration for each participant is up to approximately five (5) months (up to four [4] weeks for Screening, a single day of Treatment, and up to 16 weeks of Follow-up).





2 INTRODUCTION

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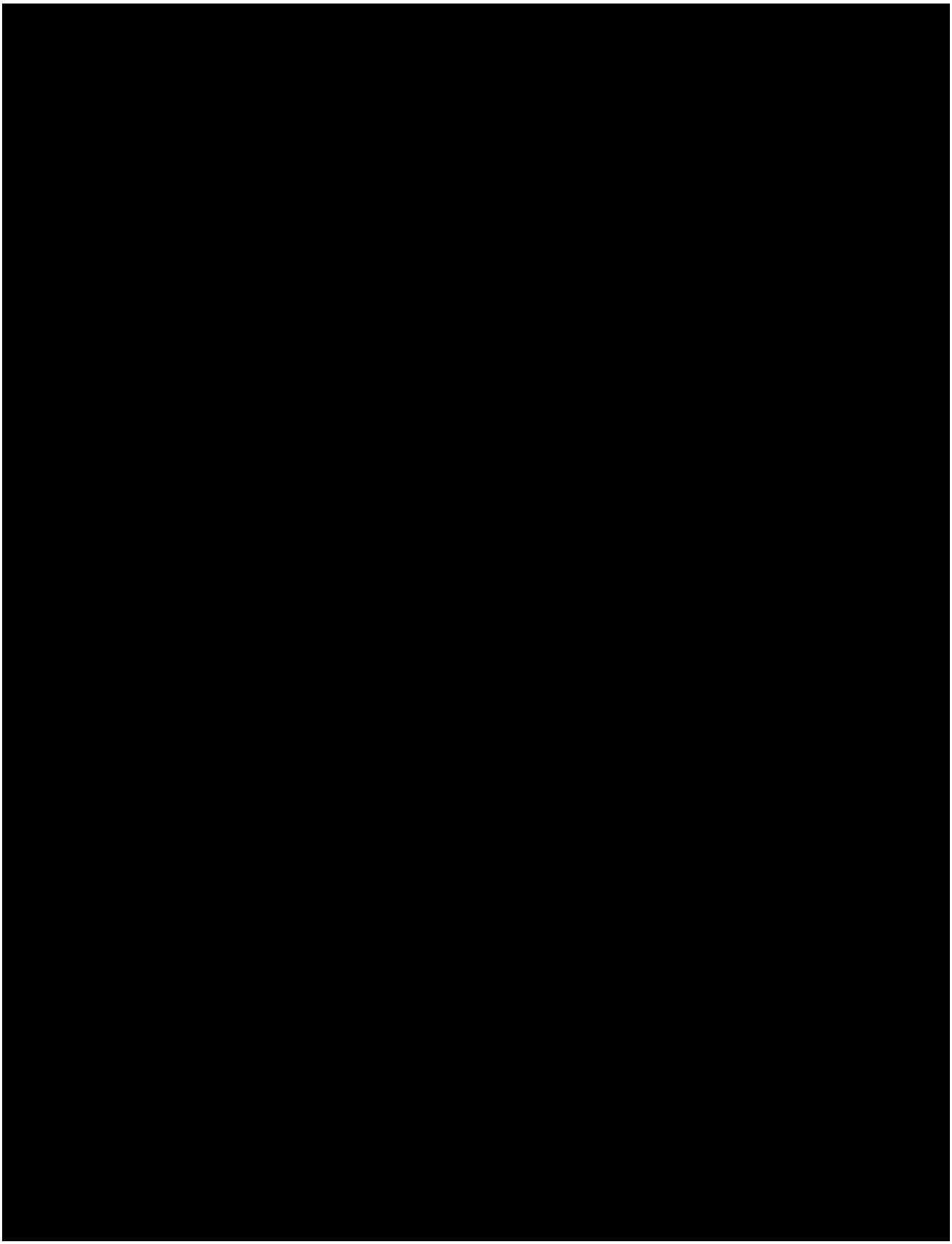
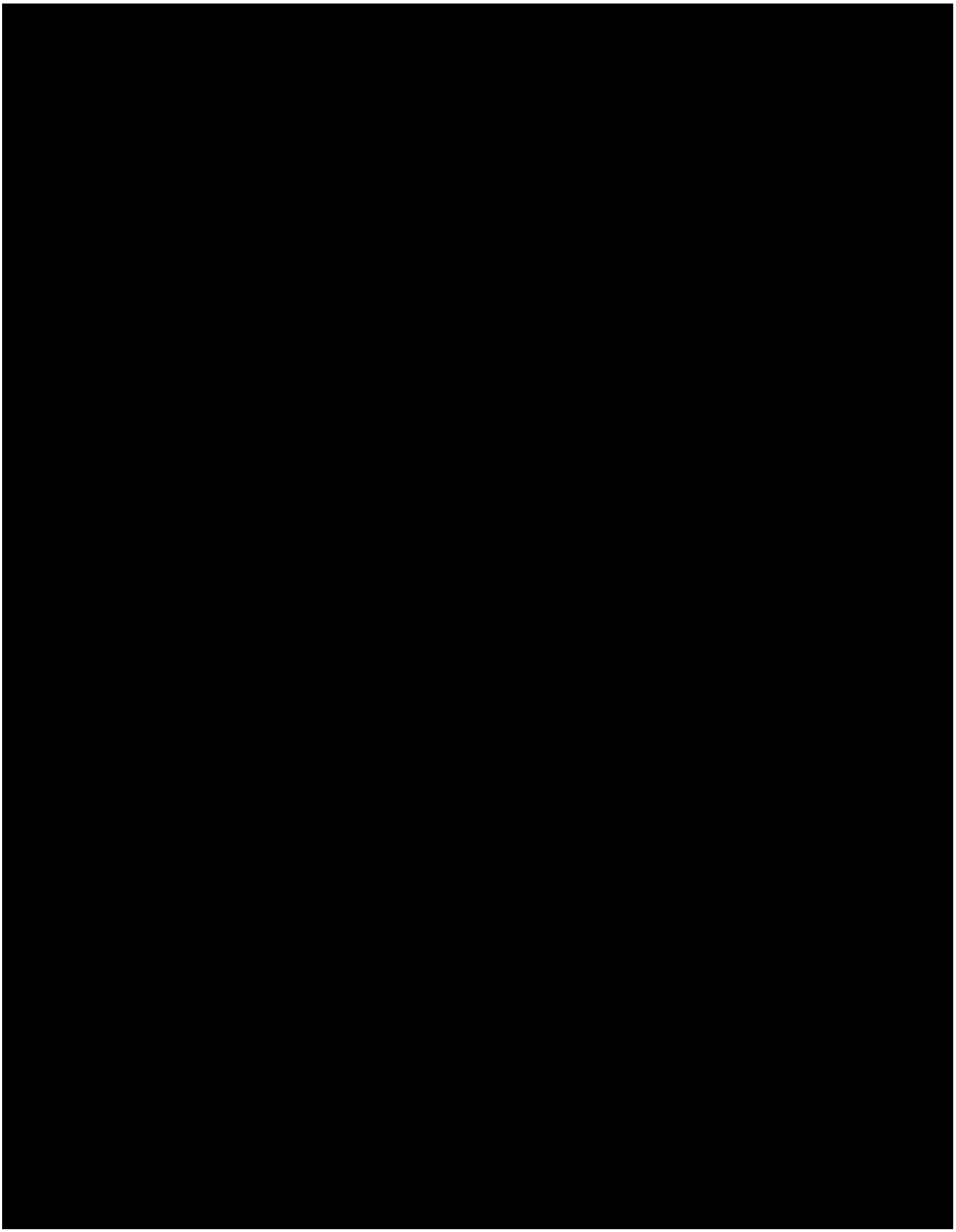
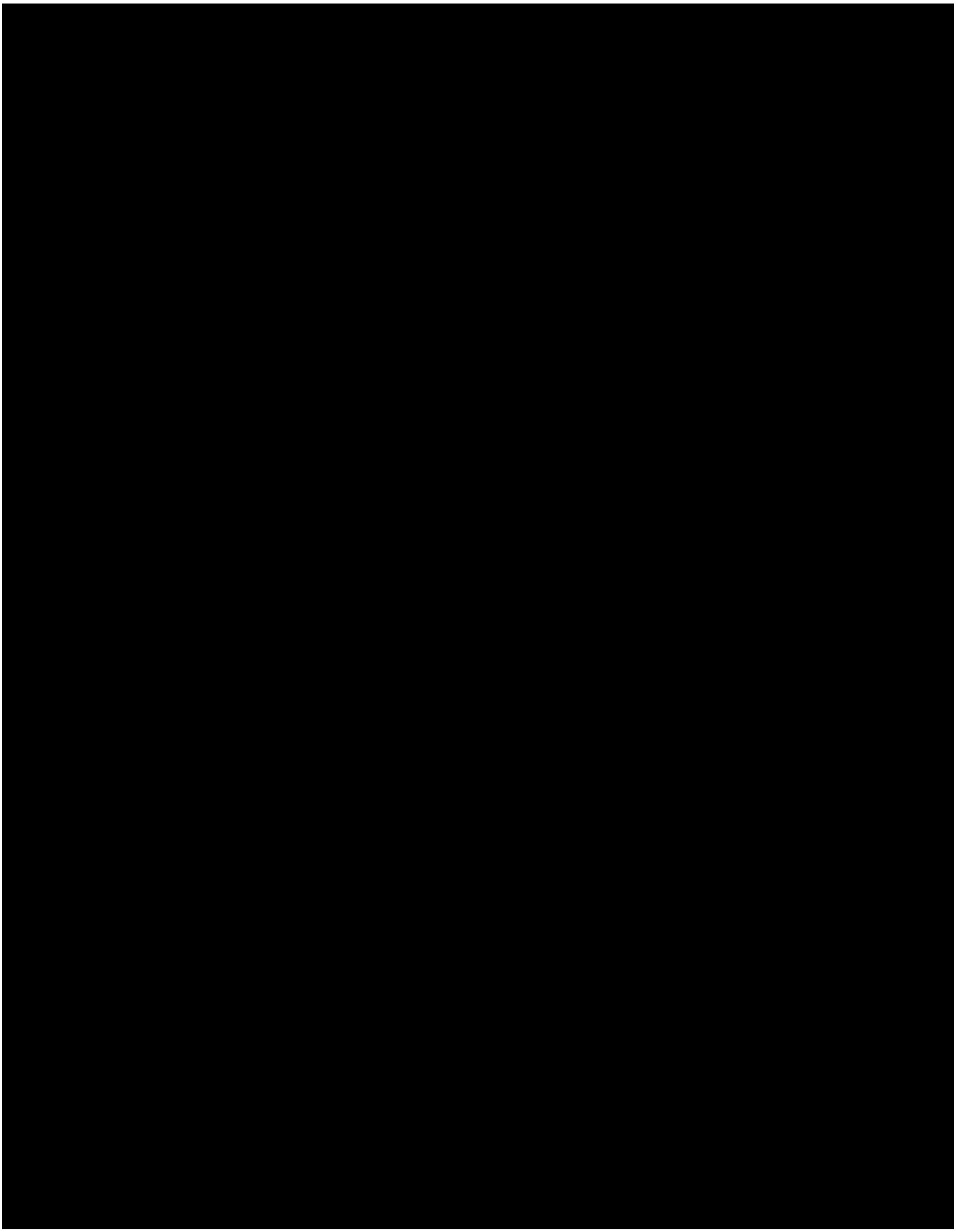
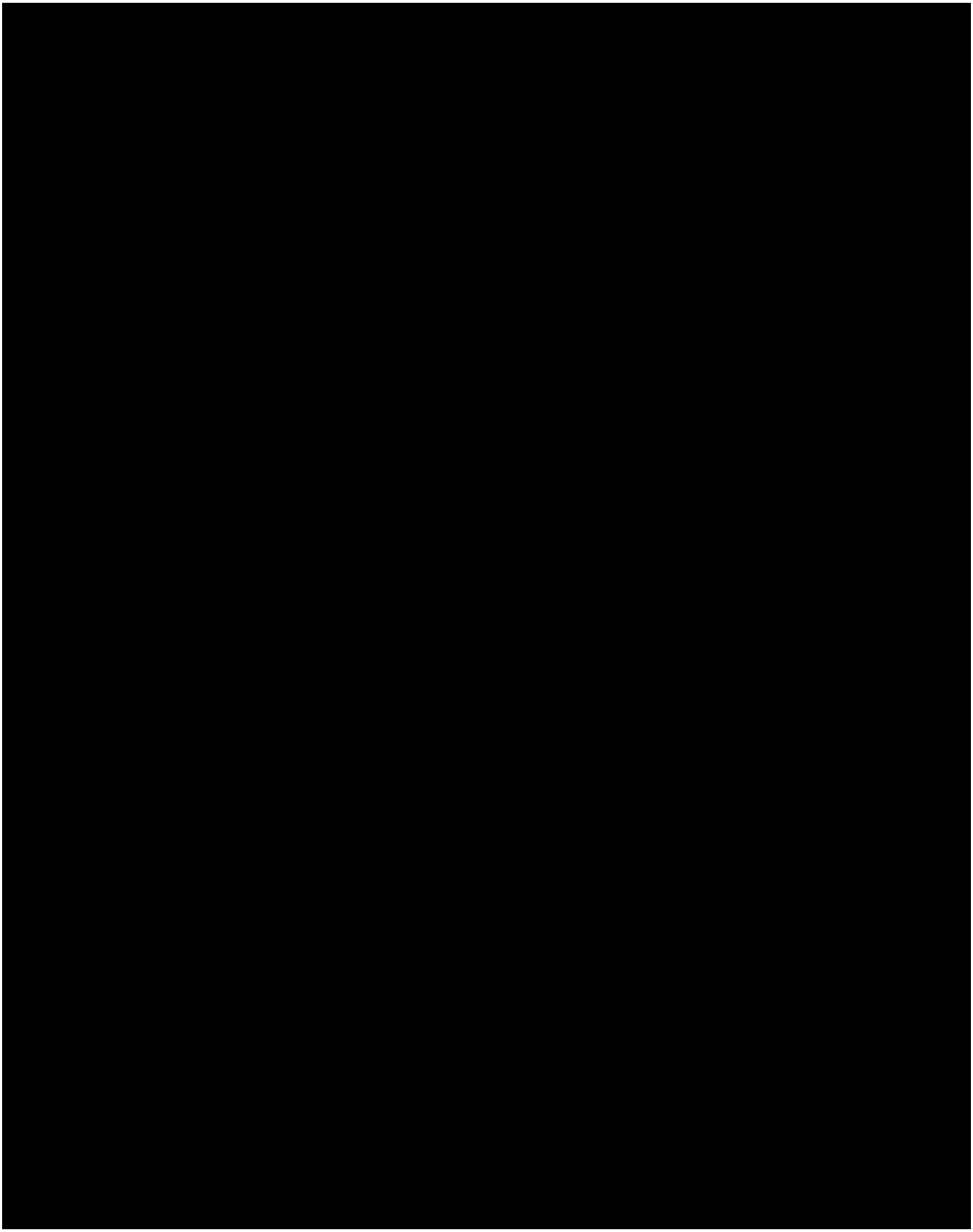
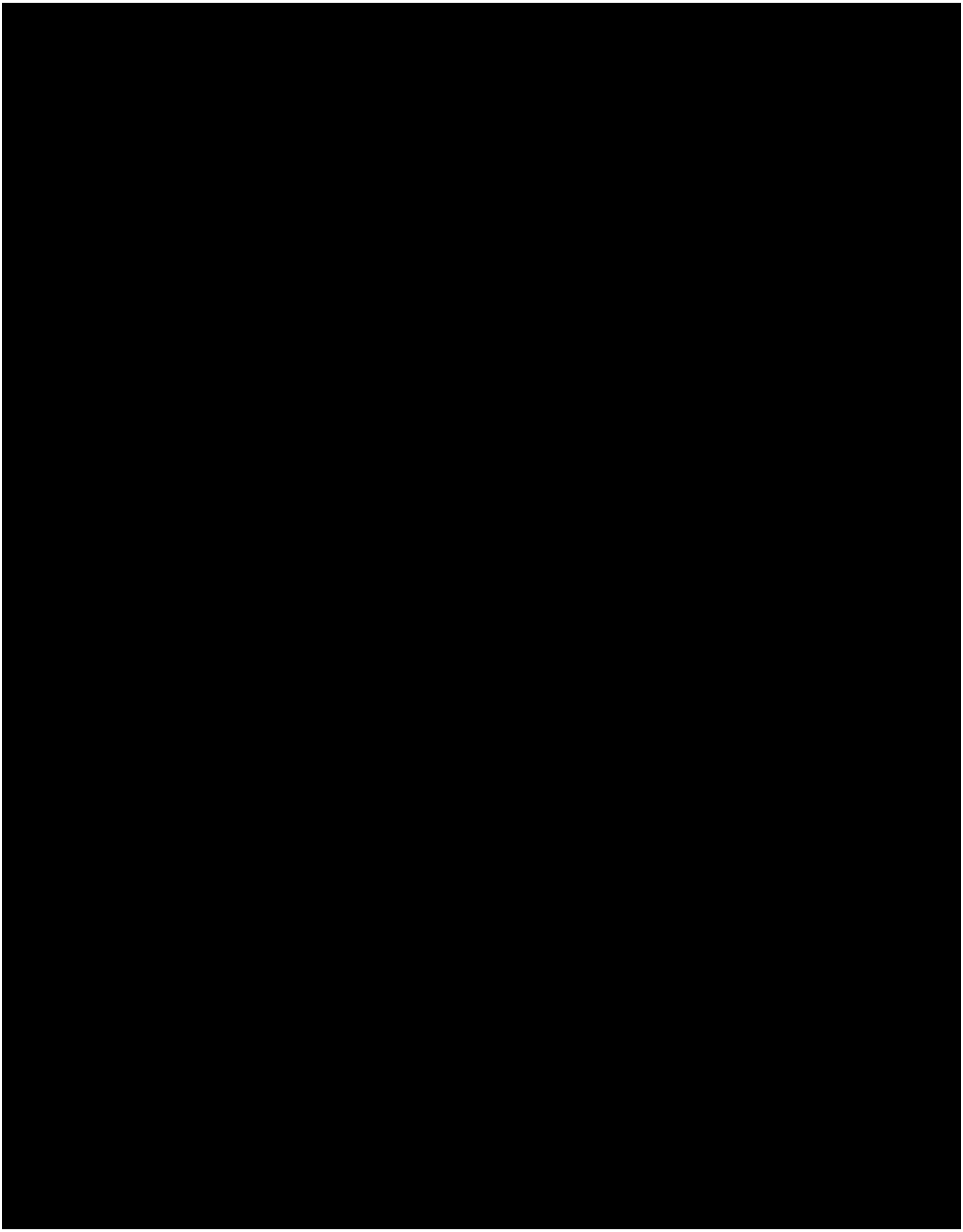










3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To compare the safety and efficacy of DaxibotulinumtoxinA for Injection versus placebo for managing plantar fasciitis	• Reduction in the visual analog scale (VAS) for pain for the foot at Week 8	Clinically relevant outcome measure for this indication
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]

4 STUDY DESIGN

4.1 OVERALL DESIGN

The study is designed as a prospective, randomized, placebo-controlled, double-blinded clinical trial to compare DaxibotulinumtoxinA for Injection and placebo injections for the management of plantar fasciitis signs and symptoms.

4.5 DURATION OF TRIAL

The study duration for each participant is up to approximately five (5) months (up to four [4] weeks for Screening, a single Injection day, and up to 16 weeks of Follow-up).

[redacted]

4.7 END OF STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed all visits of the study including the last visit or the last scheduled procedure shown in Section 1.3, Schedule of Assessments.

The end of the study is defined as completion of the last visit or procedure shown in the SoA in the trial globally.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

All subjects must meet the following inclusion criteria:

1. Written informed consent, including authorization to release health information
2. Male or female subjects 18 to 65 years of age with diagnosis of unilateral plantar fasciitis by physical examination and/or ultrasonography
3. Unilateral plantar fasciitis as defined as no symptoms or signs in the contralateral foot and no sought medical attention in the contralateral foot within three (3) months of diagnosis
4. Persistent heel pain for more than three (3) months (such as pain with walking, pain interfering with quality of life, pain > 45/100 on the VAS for pain in the morning)

[redacted]

[redacted]

Subjects will not be enrolled if they meet any of the following exclusion criteria:

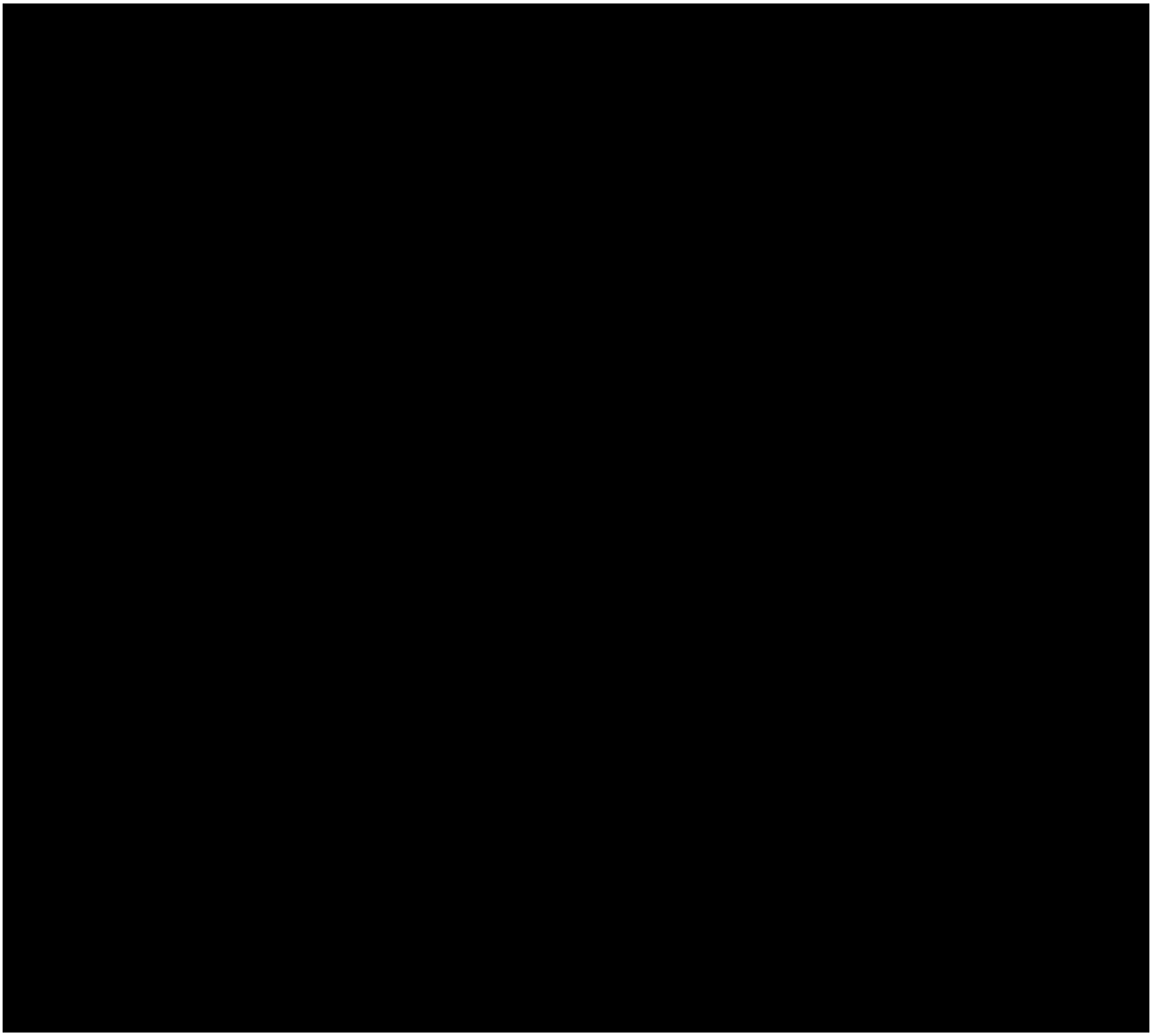
1. Previous injections of botulinum toxins in the lower extremities or feet
2. Entrapment of the posterior tibial, lateral plantar, or medial plantar nerve (local nerve entrapment)
3. Fixed hindfoot varus
4. Posterior tibial tendon dysfunction
5. Severe pes planus
6. Midfoot collapse
7. Significant talar or navicular callus
8. Tarsal coalition or rigid flatfoot
9. Systemic disease associated with foot pain
10. Sciatica
11. Severe osteoarthritis of the forefoot, midfoot, or ankle

12. Use of antibiotics that may interfere with neuromuscular junction function, for example, aminoglycoside antibiotics (e.g., gentamicin sulfate, fradiomycin sulfate), polypeptide antibiotics (e.g., polymixin B sulfate), tetracycline antibiotics, and lincomycin antibiotics, except for those contained in topical antimicrobials, three (3) days prior to treatment and three (3) days post-treatment
13. Peripheral vascular disease
14. Rheumatoid arthritis
15. Insulin dependent diabetes mellitus
16. Previous surgery on the midfoot or hindfoot
17. Hypertonicity
18. Neuromuscular disease
19. Systemic muscle weakness
20. Fibromyalgia
21. Allergy or hypersensitivity to any components of the study treatments
22. Comorbidities that confound the evaluation of the feet

[redacted]

5.3 LIFESTYLE CONSIDERATIONS

[redacted]



5.4 SCREEN FAILURES

A screen failure subject will be a person from whom informed consent is obtained and is documented in writing (i.e., subject signs an informed consent form), but who does not meet the study eligibility requirements.

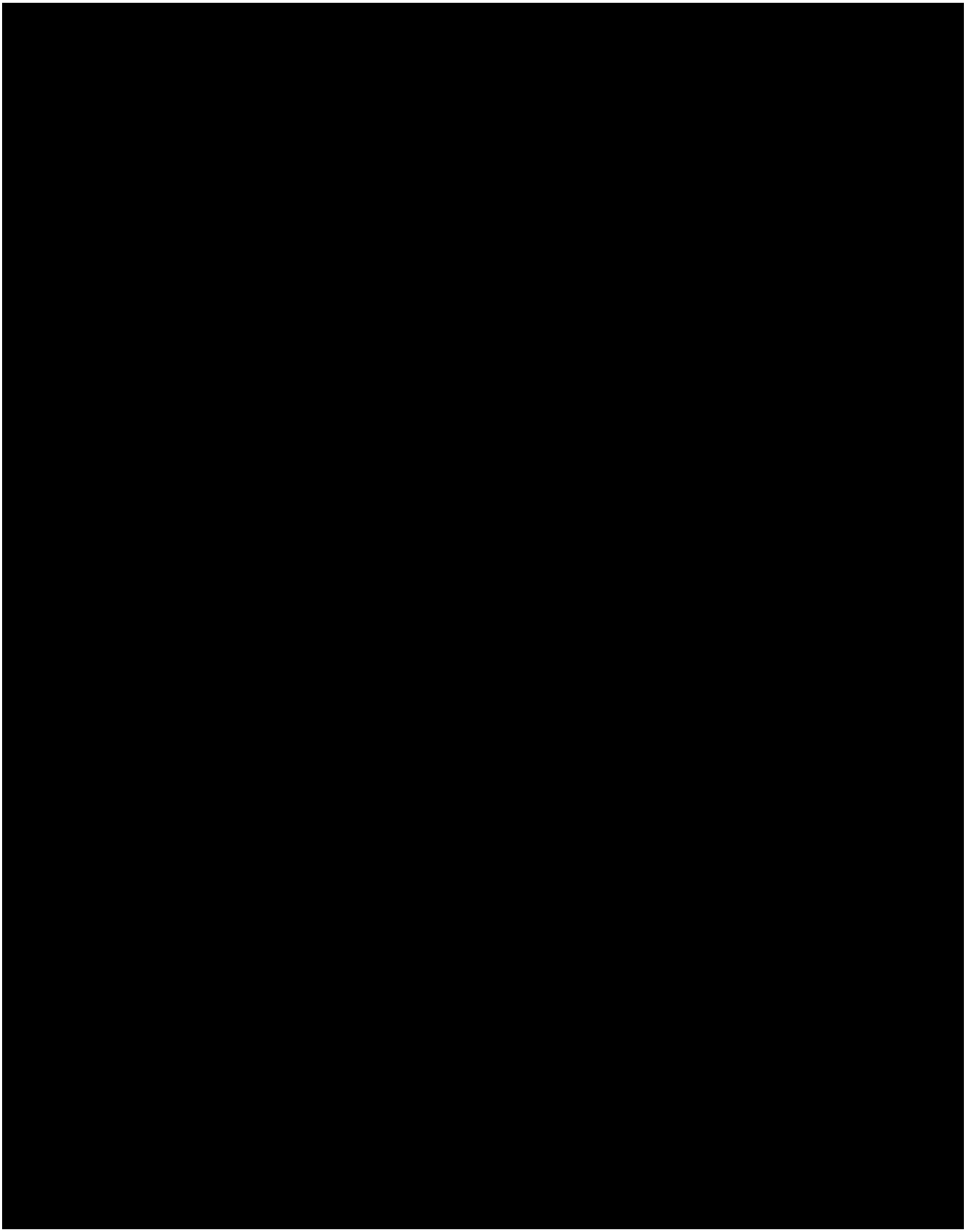
5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

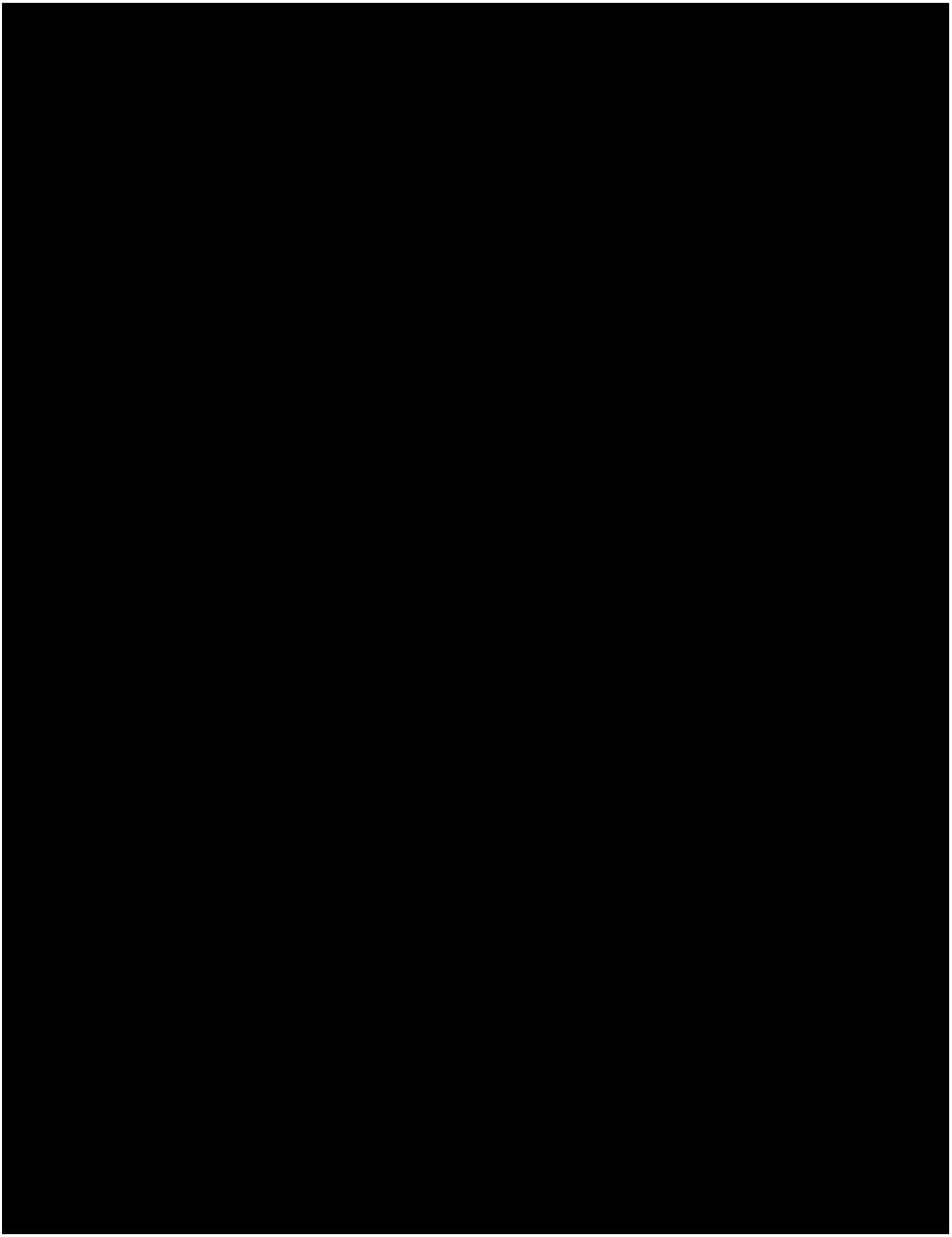
Adult male and female subjects who have been diagnosed with plantar fasciitis that have not responded to conservative treatment modalities for three (3) months as per the PI's discretion will be enrolled in these clinical trials.

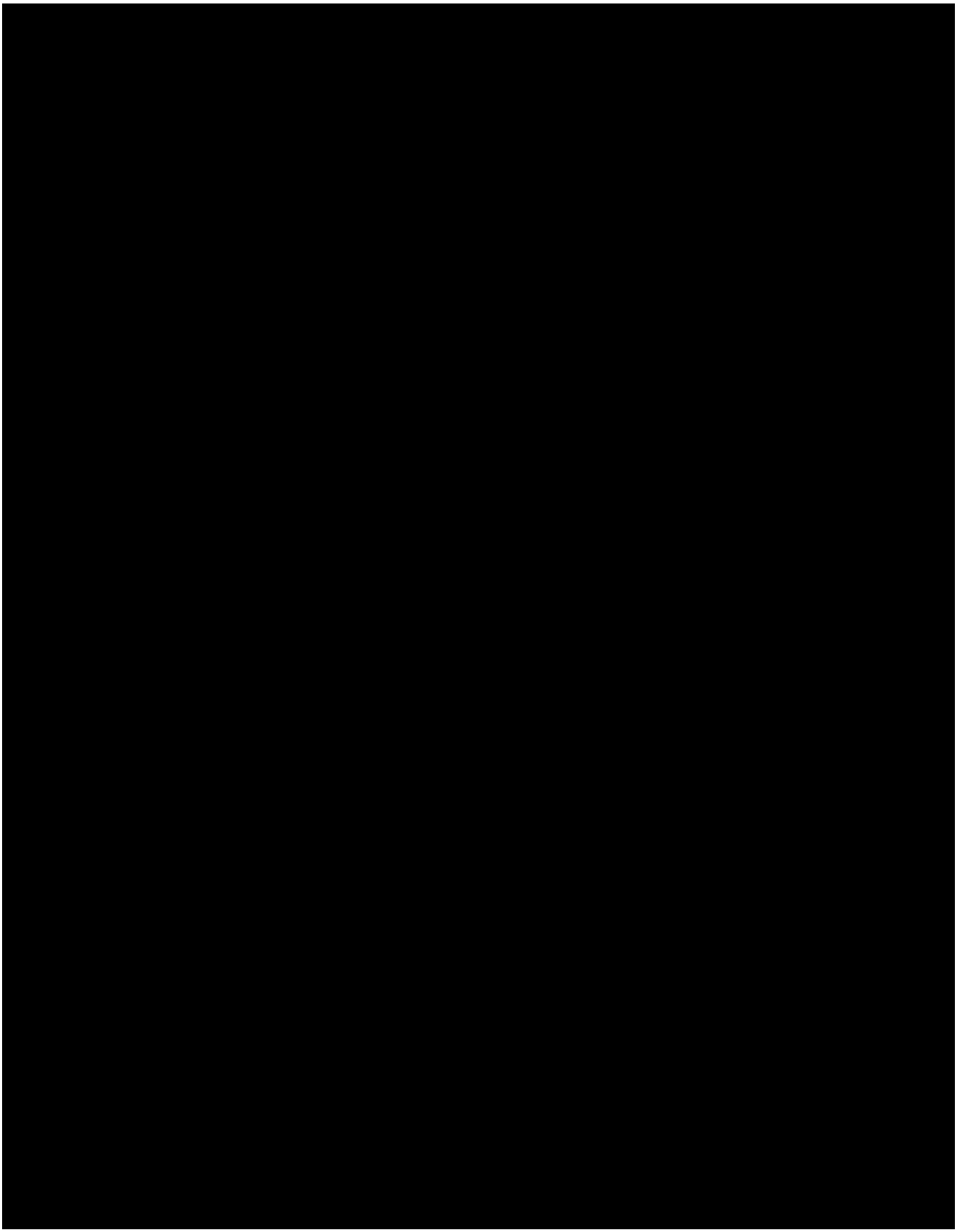
All subjects who present with plantar fasciitis who meet the study inclusion/exclusion criteria found in Sections 5.1 and 5.2 will be asked to participate in the study. If subjects agree to participate and provide informed consent, they will be enrolled in the study and randomized to one (1) of the two (2) study treatments, DaxibotulinumtoxinA for Injection or placebo.

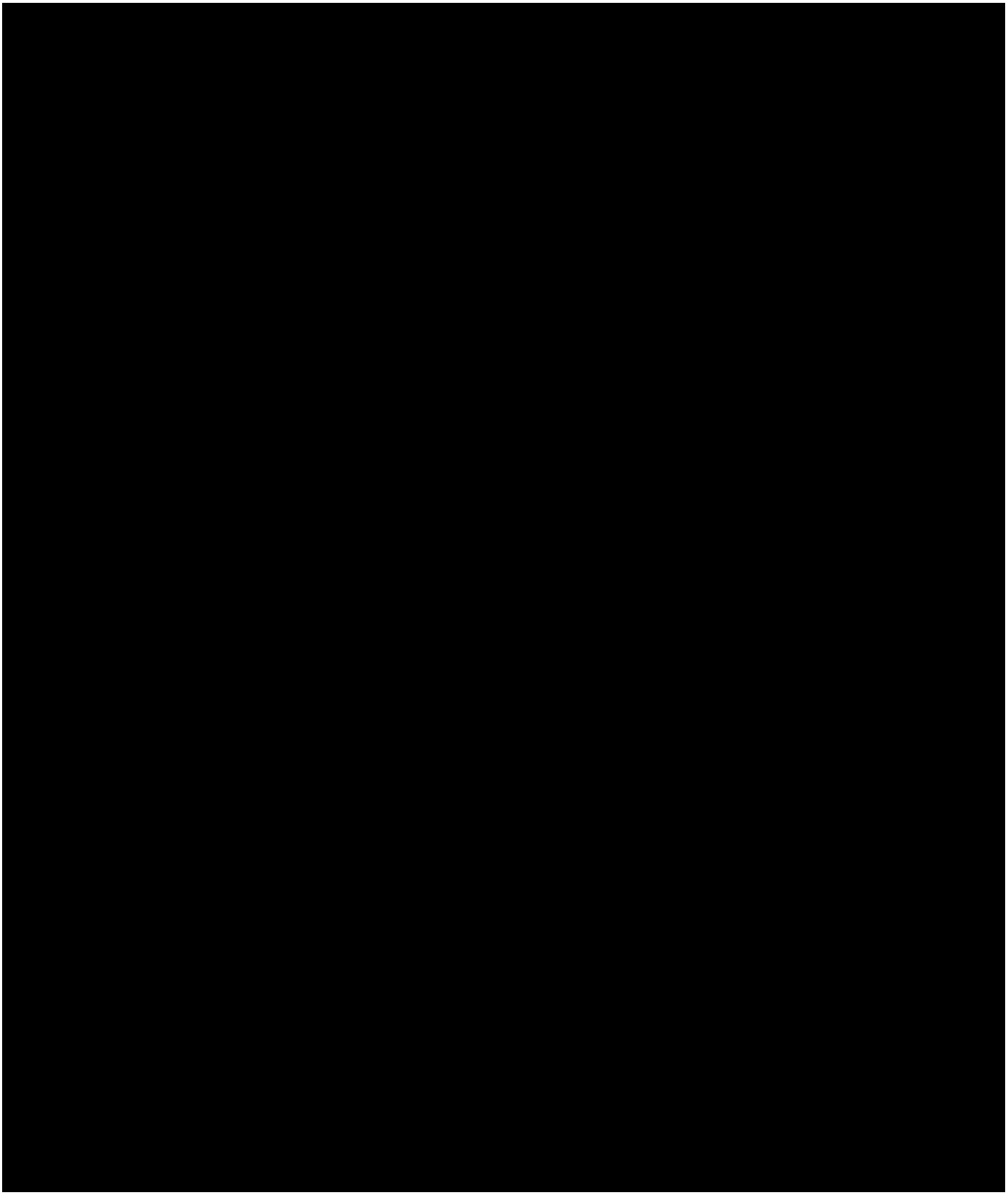
Sites selected are those known to have a patient population being treated for plantar fasciitis. Selected sites will also receive referrals of potential subjects for this study via their respective physician network as appropriate. Subject recruiting materials is provided to all sites. In addition, selected Clinical Research Organization (CRO) is supporting sites in managing subject recruitment.

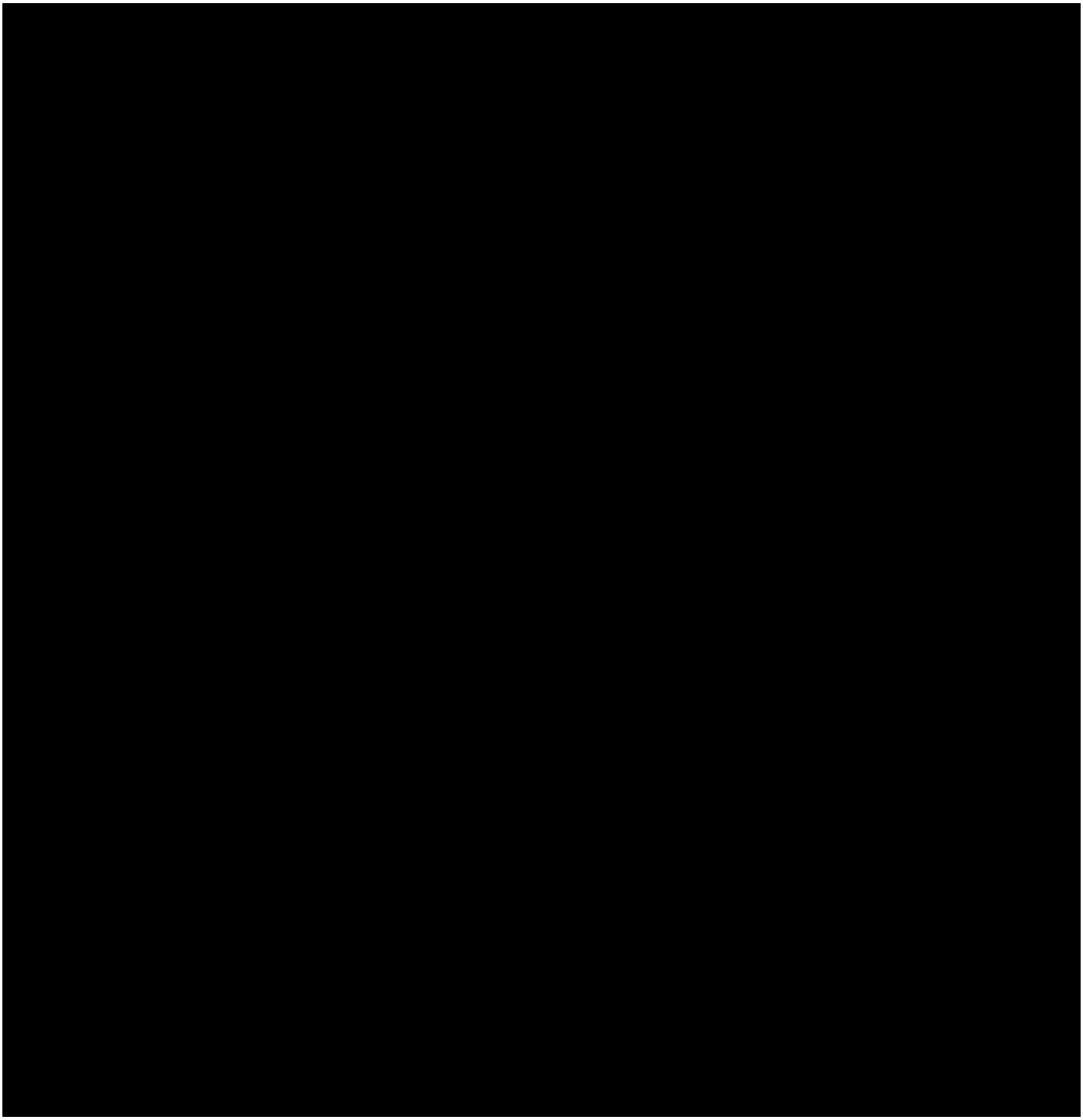
Subject retention will include regular study visits with the Investigator and site staff. A minimal acceptable stipend is provided to enrolled subjects for travel and time. Selected CRO will also work with Sponsor in developing an appropriate subject retention plan.











6.6 CONCOMITANT THERAPY

Concomitant medications are any prescription or over-the-counter preparations used by subjects during participation in the trial. Use of concomitant medications will be recorded on the Concomitant Medications case report form (CRF) beginning at the Screening Visit until the Week 16/Early Termination visit. The dose and dosing regimen of all prescription and non-prescription therapies and medications, including herbs, vitamins, or other nutritional supplements administered will be documented.

Standardized home therapy program including Achilles tendon and plantar fascia stretching exercises and night splints will also be recorded throughout the study.

6.6.1 RESCUE MEDICINE

The Sponsor will not allow any type of rescue medication in this clinical study for the treatment of plantar fasciitis. Subject(s) may withdraw from the study at any time if rescue medication is required.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

Study subjects will receive a one (1) time only treatment for this study. Discontinuation of study treatment is not applicable. However, subjects may choose to discontinue their participation in the follow-up phase at any time. Refer to Early Discontinuation/Withdrawal Procedures, Section 7.2, for more details.

If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the Investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

7.2 EARLY DISCONTINUATION/WITHDRAWAL PROCEDURES

A subject may voluntarily withdraw from study participation at any time. If the subject withdraws consent and discontinues from the trial, the Investigator will attempt to determine the reason for discontinuation and record the reason in the subject's trial records and on the case report form (CRF). If a subject withdraws consent because of an AE, that AE should be indicated as the reason for withdrawal. In the event of early discontinuation, (i.e., prior to the Final Evaluation) and whenever possible, the subject should be asked to return to the trial center to complete the assessments specified in the Week 16/Early Termination visit. Subjects who withdraw from the trial will not be replaced.

If at any time during the trial, the Investigator determines that it is not in the best interest of the subject to continue, the subject will be discontinued from participation. The Investigator can discontinue a subject from study participation at any time if medically necessary or if the subject has failed to follow trial procedures or to keep follow-up appointments. Appropriate documentation in the subject's trial record and CRF regarding the reason for discontinuation must be completed. Prior to discontinuing a subject from study participation, the Investigator will discuss his/her intentions with the Medical Monitor or designee.

All subjects who fail to return to the trial center for the required follow-up visits will be contacted by phone to determine the reason(s) why the subject failed to return for the necessary visit or elected to discontinue from the trial. If a subject is unreachable by telephone after a minimum of two (2) documented attempts (one [1] attempt on two [2] different days), a registered letter will be sent requesting that contact be made with the Investigator.

Revance has the right to terminate or to stop the trial at any time. Should this be necessary, both Revance and the Investigator will ensure that proper study discontinuation procedures are completed

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to return for scheduled study visits and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant and reschedule the missed visit(s) and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the Investigator or designee will make every effort to regain contact with the participant (where possible, three (3) telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 STUDY ASSESSMENTS

All clinical laboratory assessments will be conducted locally at the clinical site facilities.

8.1.1 SCREENING VISIT

Subjects presenting with heel pain will be examined to verify the diagnosis of plantar fasciitis. Then, subjects with plantar fasciitis will be screened to determine if they meet the study eligibility criteria. Prospective study participants will be informed of the study, and the requirements for study participation will be explained to them. Subject informed consent must be obtained prior to conducting screening procedures. Refer to Section 1.3 Schedule of Assessments, for activities to be performed.

After the informed consent is obtained, the following procedures will be completed:

- Physical examination
- Foot and Ankle Examination of both feet (including range or motion and motor strength)
- Collect vital signs (blood pressure [BP], pulse, temperature), weight, and height
- Collect blood samples for clinical laboratory (chemistry, hematology, urinalysis), [redacted]
- Collect ECG if not done within the last six (6) months
- Collect X-rays if not done within the last six (6) months
- Collect concomitant medications/therapies, medical history information
- VAS for pain for the foot to be completed by subject

The Foot and Ankle Examination is developed by Dr. L. Andrew Koman at Wake Forest Baptist Medical Center (WFBMC) to document a visual inspection of the foot as well as a thorough foot examination.

Results from clinical laboratory tests and cardiologist-interpreted ECG must be obtained, reviewed, and signed by the Investigator. Any abnormal results must be determined to be not clinically significant by the Investigator prior to randomization. Any WOCBP having a positive pregnancy test pre-treatment will not be treated.

8.1.2 INJECTION VISIT

The following procedures will be completed **pre-treatment**:

- Physical examination
- [redacted]
- Collect vital signs (blood pressure [BP], pulse, temperature) and weight
- [redacted]
- [redacted]
- [redacted]
  - [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Confirm subject eligibility.

[redacted]

- [redacted]
- [redacted]

[redacted]

8.1.3 FOLLOW-UP VISITS

Subjects will be evaluated five (5) times after their injection at Weeks 1, 2, 4, 8, and 16 or any time subjects terminate prematurely. Acceptable study visit windows can be ±3 days. The following procedures will be completed at each follow-up visits:

- [redacted]
- [redacted]
- Collect vital signs (blood pressure [BP], pulse, temperature) and weight
- [redacted]
- [redacted]
- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- [redacted]
- Collect concomitant medications/therapies and adverse event(s)

Variation from Scheduled Visit Days

To allow for scheduling flexibility, limited variation will be permitted from the specified time of each visit as in table shown below.

Allowed Variation from Scheduled Visit Days

Scheduled Visit	Allowed Variation
Weeks 1, 2, 4, 8, 16	+/- 3 days

8.2 EFFICACY ASSESSMENTS

Visual Analog Scale (VAS) for Pain: The pain VAS is a continuous scale self-completed by the respondent comprised of a horizontal (HVAS) or vertical (VVAS) line, usually 10 centimeters (100 mm) in length, anchored by two (2) verbal descriptors, one (1) for each symptom extreme. Instructions, time period for reporting, and verbal descriptor anchors have varied widely in the literature depending on intended use of the scale.

For pain intensity, the scale is most commonly anchored by "no pain" (score of 0) and "pain as bad as it could be" or "worst imaginable pain" (score of 100 [100-mm scale]). The respondent is asked to place a line perpendicular to the VAS line at the point that represents their pain intensity. (http://onlinelibrary.wiley.com/doi/10.1002/acr.20543/full)

American Orthopaedic Foot and Ankle Score (AOFAS): The American Academy of Orthopaedic Surgeons developed several musculoskeletal outcomes instruments to collect subject based data to use to assess the effectiveness of treatments and to study the clinical outcomes of the treatments. The AOFAS foot and ankle questionnaire was designed for use in subjects 18 years old and older. This questionnaire documents subject assessments of foot and ankle conditions and improvements resulting from treatments. Disability indices for the lower limb core, global foot and ankle function, and shoe comfort can be evaluated using this instrument. The questionnaire requires about 10 minutes to complete.

Foot and Ankle Disability Index (FADI): The FADI contains 34 questions divided into two (2) subscales: the Foot and Ankle Disability Index and the Foot Ankle Disability Index Sport (Martin, 1999). Each of the questions is scored using a five-point Likert Scale from 0 (unable to do) to 4 (no difficulty at all). The FADI was designed to collect information from subjects regarding their functional limitations related to their feet and ankles. The FADI Sports module is a population specific subscale designed for athletes. The questionnaire requires five (5) to seven (7) minutes to complete.

The Patient Reported Outcomes Measurement Information System (PROMIS): The PROMIS is a system of highly reliable, precise measures of subject–reported health status for physical, mental, and social well–being (http://www.nihpromis.org/). PROMIS tools measure what subjects are able to do and how they feel by asking questions. PROMIS measures can be used across a wide variety of chronic diseases and conditions in clinical studies of the effectiveness of treatment.

Plantar fasciitis pain and disability scale (PFPS): The PFPS is a survey that includes a series of key questions that relate to symptoms and control questions for plantar fasciitis (https://faoj.files.wordpress.com/2009/05/pain scale for plantar fasciiits.pdf). The PFPS also includes the VAS for pain and questions to measure the effect the pain has on their activities of daily living. This survey was designed to create a more descriptive, exclusive analysis for plantar fasciitis and has been shown to effectively discriminate pain that is unique to plantar fasciitis versus heel pain caused by other foot pathologies.

8.3 SAFETY AND OTHER ASSESSMENTS

Physical examination: A full physical examination, in addition to vital signs, including neurological examination of the face, general appearance, skin, neck (including thyroid), eyes, ears, nose, throat, heart, lungs, abdomen, lymph nodes, and extremities will be conducted at Screening and pre-treatment at the Injection visit. At visits post-treatment, the physical examination may be abbreviated, as deemed medically appropriate at the discretion of the Investigator. Significant physical examination findings that are present prior to investigational product administration are to be included on the Medical History page.

Significant physical examination findings which meet the definition of an adverse event will be recorded on the adverse event page post-treatment.

Pregnancy Testing: All WOCBP will have a SPT at the Screening and at Week 16/Early Termination visits and UPT at Injection visit pre-treatment. If any result is positive prior to treatment, the subject will not be allowed to participate. The results of the UPTs for WOCBP will be evaluated at the trial center.

WOCBP must use an effective method of birth control during the course of the trial, such as the oral contraceptive pill, injection, implant, patch, vaginal ring, intrauterine coil, intrauterine device, tubal ligation, barrier method used WITH an additional form of contraception (e.g., sponge, spermicide or condom), abstinence, no heterosexual intercourse, or has a vasectomized partner. A female is considered to be of childbearing potential UNLESS she is post-menopausal (no menses for 12 consecutive months) or without a uterus and/or both ovaries.

Before enrolling WOCBP in this clinical trial, Investigator must review guidelines about study participation for WOCBP. The topics should generally include:

- Informed consent document
- Pregnancy prevention information
- Risks to unborn child(ren)
- Any drug interactions with hormonal contraceptives
- Contraceptives in current use
- Guidelines for the follow-up of a reported pregnancy

Prior to study enrollment, WOCBP must be advised of the importance of avoiding pregnancy during participation in this clinical trial and the potential risk factors for an unintentional pregnancy. The subject must sign the informed consent document stating that the above-mentioned risk factors and the consequences were discussed with her.

Height, Weight, Vital Signs: Height will be collected only at the Screening visit. Weight and vital signs (i.e., body temperature, respiration rate, sitting radial pulse rate, and sitting systolic and diastolic blood pressures) will be obtained at the Screening, Injection Visit (pre- and post-treatment), Weeks 1, 2, 4, 8, and 16/Early Termination visits and at any visit where signs or symptoms of botulinum toxicity is reported.

12-Lead Electrocardiograms (ECGs): At Screening, Week 2, and Week 16/Early Termination, a single standard supine 12-lead ECG will be obtained after a subject has rested quietly for at least 10 minutes. The ECG data will be submitted to a central reader for measurement. Instructions for the collection, transmission, and archiving of the ECG data is outlined in the ECG central reader manual. The analyzed ECG data will be reviewed and signed by the Investigator.

X-rays: X-rays of the affected foot is collected at Screening or prior to Injection visit. This procedure is to be done at individual study site. If subject(s) have had X-ray done within six (6) months prior to the

Injection visit, this procedure is not required. Records of the X-ray is to be collected and kept with the subject's study information.

Biological specimen collection and laboratory evaluations: As outlined in the Clinical Laboratory Tests table below, non-fasting samples for hematology, chemistry, and urinalysis will be collected at Screening, Week 2, and at Week 16/Early Termination visits. [redacted] will be collected at Screening and Week 16/Early Termination visits. [redacted] Blood and urine will be collected using applicable safety precautions and will be processed according to the local clinical laboratory's instructions.

Clinical Laboratory Tests

Hematology	Chemistry	Urinalysis	Additional Tests
Hemoglobin	Glucose	Specific gravity	[redacted]
Hematocrit	Total bilirubin	pH	
Leukocyte count (total)	Alanine aminotransferase	Glucose	
Leukocyte count (differential)	Aspartate aminotransferase	Protein	
Red blood cell count	Alkaline phosphatase	Blood	
Platelet count	Blood urea nitrogen	Bilirubin	
	Pregnancy (WOCBP at Screening)	Ketones	
	Sodium		
	Potassium		
	Chloride		
	CO2		
	Creatinine		
	Calcium		
	Protein		

[redacted]

It is the Investigator's responsibility to review the results of all laboratory tests as they become available. For each laboratory test result outside the reference range, the Investigator must ascertain if the abnormal lab result is a clinically significant result for that individual subject. Likewise, if laboratory tests are taken at follow-up visits, the Investigator must ascertain if this is an abnormal and clinically significant change pre-treatment for that individual subject. The Investigator may repeat the laboratory test or request additional tests to verify the results of the original laboratory test. The Investigator must sign and date all written laboratory results (e.g., urinalysis, hematology, chemistry, and pregnancy tests) and note Not Clinically Significant (NCS) or Clinically Significant (CS) for each out of range laboratory value. Toxicity grading for laboratory results is standardized using the FDA's "Guidance for Industry: Toxicity Grading Scale for Health Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials" dated September 2007. If a laboratory value is determined to be a clinically significant result for that subject, this may be considered an AE to be assessed according to severity. Refer to Section 8.4 for further information.

[redacted]

Injection Site Evaluation: The injection sites will be evaluated at Injection Visit (Day 0) pre- and post-treatment (to determine if there is an immediate reaction to the investigational product), follow-up visits (Weeks 1, 2, 4, 8 and 16 or Early Termination visit, if applicable. The assessment will be done as a global evaluation of the injection sites.

Injection Site Evaluation

Assessment Descriptor	Present?	
	Yes	No
Erythema		
Edema		
Burning or Stinging (sensation as described by subject)		
Itching (sensation as described by subject)		
Bruising		
Drainage		

Foot and Ankle Examination: Examination for the foot includes ankle, toe, and subtalar range of motion, foot motor strength, location of pain, and examination of the heel fat pad and Tinel's sign will be done at Screening, pre-treatment Injection, Weeks 1, 2, 4, 8, and 16/Early Termination visits. The presence of toe deformities, bunions, ulcers, and/or sores will be documented. The feet will be examined for signs of swelling, pitting edema, infection, or vascular abnormalities (refer to *Appendix A*).

Assessment of adverse events: Adverse Events (AEs) will be graded as mild, moderate, or severe as defined in Section 8.4.3 of this protocol.

AEs will be evaluated at the Injection visit post-treatment, follow-up Weeks 1, 2, 4, 8, and 16 or Early Termination visits, if applicable. Section 8.4.5 outlines the procedures for recording and reporting AEs.

Adverse events will be reported by the Sponsor in accordance with "21CRF part 312.32 and Guidance for Industry and Investigators: Safety Reporting Requirements." The Investigator will report any serious adverse events (SAEs) to the IRB.

[redacted]

8.4 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.4.1 DEFINITION OF ADVERSE EVENTS (AE)

For this protocol, an **adverse event (AE)** is any untoward medical occurrence (e.g., sign, symptom, disease, syndrome, intercurrent illness, clinically significant abnormal laboratory finding, injury or

accident) that emerges or worsens following administration of investigational product and until the end of trial participation that may not necessarily have a causal relationship to the administration of the investigational product. An AE can therefore be any unfavorable and/or unintended sign (including a clinically significant abnormal laboratory result), symptom, or disease temporally associated with the use of an investigational product, whether or not considered related to the investigational product. A treatment-emergent AE is one that occurs after any period of exposure to treatment.

Pre-existing conditions, which increase in frequency or severity or a change in nature as a consequence of an investigational product use will also be considered an adverse event.

An unexpected AE is an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

Any clinically significant change in the study safety evaluations, (e.g., vital signs, laboratory results, ECG, injection site evaluation, physical/neurological examinations, etc.) post-treatment must be reported as an AE.

8.4.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

A **serious adverse event (SAE)** is any untoward medical occurrence that results in any of the following outcomes:

- Death
- Life-threatening, (i.e., the subject was, in the opinion of the Investigator, at immediate risk of death from the event as it occurred. It does not apply to an AE that hypothetically might have caused death if it were more severe)
- Persistent or significant disability/incapacity or substantial disruption of the subject's ability to carry out normal life functions
- Requires in-patient hospitalization or prolongs hospitalization (i.e., a prolonged hospitalization beyond the expected length of stay; hospitalizations for elective medical/surgical procedures, scheduled treatments, or routine check-ups are not SAEs by this criterion)
- Congenital anomaly/birth defect (i.e., an adverse outcome in a child or fetus of a subject exposed to the molecule or investigational product before conception or during pregnancy)
- Does not meet any of the above serious criteria but based upon appropriate medical judgement may jeopardize the subject or may require medical or surgical intervention to prevent one (1) of the outcomes listed above (i.e., is a significant or important medical event)

8.4.3 CLASSIFICATION OF AN ADVERSE EVENT

8.4.3.1 SEVERITY OF EVENT

The Investigator is responsible for evaluating all AEs and determining the severity of the event. Severity will be categorized as mild, moderate or severe according to the following definitions:

- **Mild:** Event may be noticeable to subject; does not influence daily activities; usually does not require intervention
- **Moderate:** Event may be of sufficient severity to make subject uncomfortable; performance of daily activities may be influenced; intervention may be needed

- **Severe:** Event may cause severe discomfort; usually interferes with daily activities; subject may not be able to continue in the trial; treatment or other intervention usually needed

8.4.3.2 RELATIONSHIP TO STUDY INTERVENTION

Relationship of an AE to investigational product will be assessed as follows:

- **Definite:** There is a clinically plausible time sequence between the onset of the AE and the administration of investigational product; when the event responds to withdrawal of investigational product and/or recurs with re-administration of investigational product
- **Probable:** There is a clinically plausible time sequence between the onset of the AE and the administration of investigational product; the AE is unlikely to be caused by the concurrent/underlying illness, other drugs or procedures
- **Possible:** There may or may not be a clinically plausible time sequence between the onset of the AE and the administration of investigational product and a cause cannot be ruled out
- **Unrelated:** There is not a temporal or causal relationship to investigational product administration

8.4.3.3 EXPECTEDNESS

The Medical Monitor and Sponsor will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention. Expectedness is further defined in the Investigator's Brochure (IB) under Anticipated Risks and Side Effects. The list of AEs found in the IB can be considered to be expected AEs.

8.4.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The Investigator or study staff will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the Investigator or study staff will inquire about the occurrence of

AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.4.5 ADVERSE EVENT REPORTING

The Investigator will assess subjects post-treatment and at each subsequent trial visit for the occurrence of AEs. In order to avoid bias in eliciting AEs, subjects should be asked the following non leading question: "How have you felt since your last visit?" All AEs (serious and non-serious) reported by the subject must be recorded on the source documents and CRFs.

In addition, an Investigator must report an SAE to Revance within **24 hours** of their awareness of the event according to the procedure outlined below. All fatal or life-threatening SAEs should be telephoned to Revance or the authorized representative as soon as the Investigator learns of the event.

8.4.6 SERIOUS ADVERSE EVENT REPORTING

An Investigator must report an SAE to Revance or the designated CRO's authorized representative within **24 hours** of their awareness of the event:

1. Complete and return an SAE Form with all information known to date; including the Investigator's assessment of causality.
2. If the event is fatal or life-threatening, telephone Revance or the authorized representative as soon as the Investigator learns of the event.
3. Obtain and maintain all pertinent medical records (discharge summary, autopsy report, etc.) and medical judgments of medical personnel who assisted in subject's treatment and follow-up.
4. Provide follow-up information to Revance or the authorized representative.

All SAEs will be followed until satisfactory resolution or until the Investigator deems the event to be chronic or the participant is stable. Other supporting documentation of the event may be requested by the Data Coordinating Center (DCC)/study sponsor and should be provided as soon as possible.

The study sponsor will be responsible for notifying the Food and Drug Administration (FDA) of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible, but in no case later than 7 calendar days after the sponsor's initial receipt of the information. In addition, the sponsor must notify FDA and all participating investigators in an Investigational New Drug (IND) safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting.

Regulatory authorities, IRBs/IEC, and Investigators will be notified of SAEs in accordance with applicable regulations and requirements (e.g., GCPs, ICH Guidelines, national regulations and local requirements).

8.4.7 REPORTING EVENTS TO PARTICIPANTS

Revance will disclose clinical trial data to individuals, to investigators at clinical sites, and publicly as aggregate summaries, in accordance to Regulatory and local legal requirements.

8.4.8 FOLLOW-UP OF NON-SERIOUS ADVERSE EVENTS

Non-serious AEs that are identified during the last scheduled trial visit (or early discontinuation, if applicable) must be recorded on the AE CRF as ongoing.

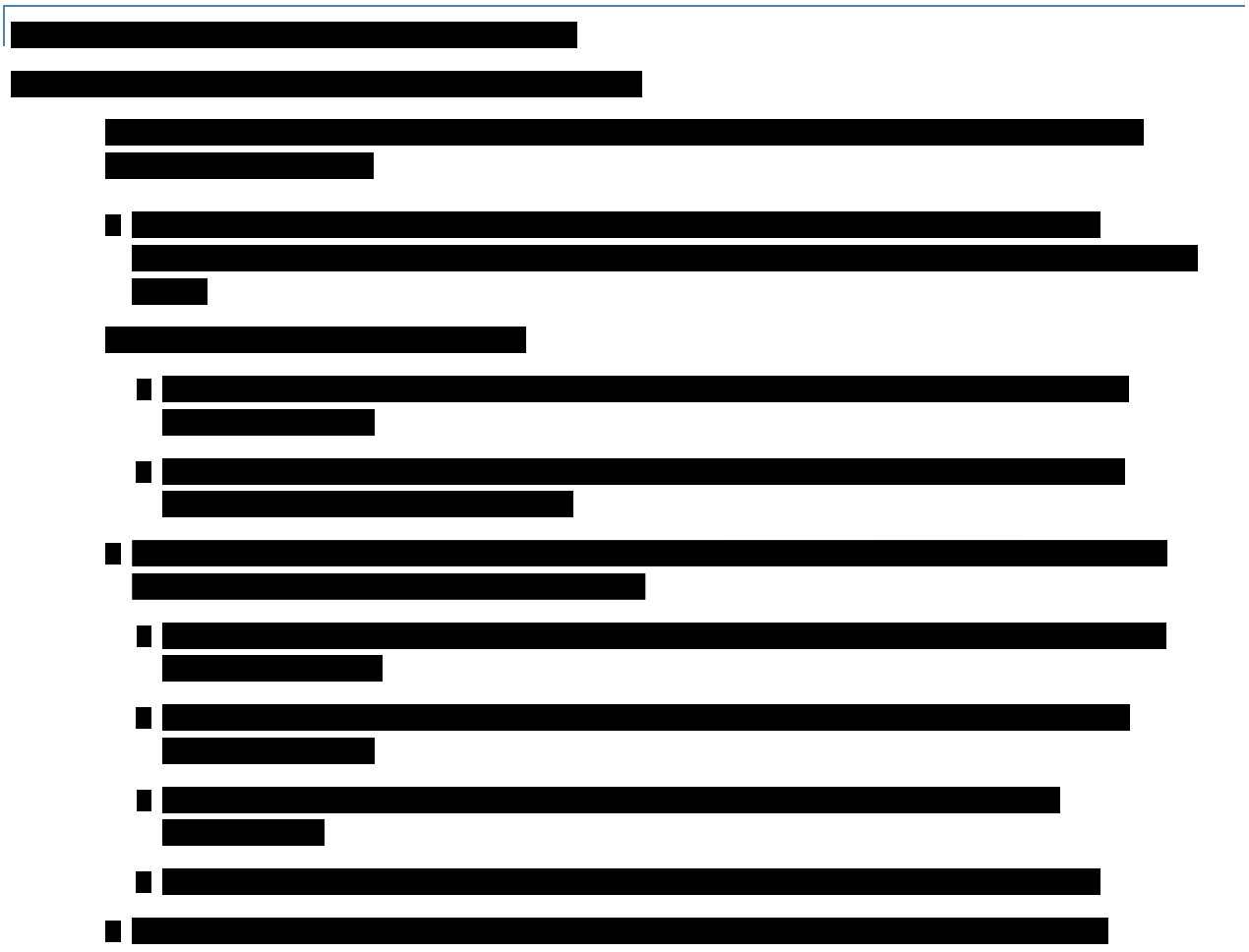
Any clinically significant abnormal test results, e.g., laboratory findings, at the Week 16/Early Termination visit should be followed to resolution or until determined by the Investigator to be stabilized. Repeat tests may be indicated to establish this.

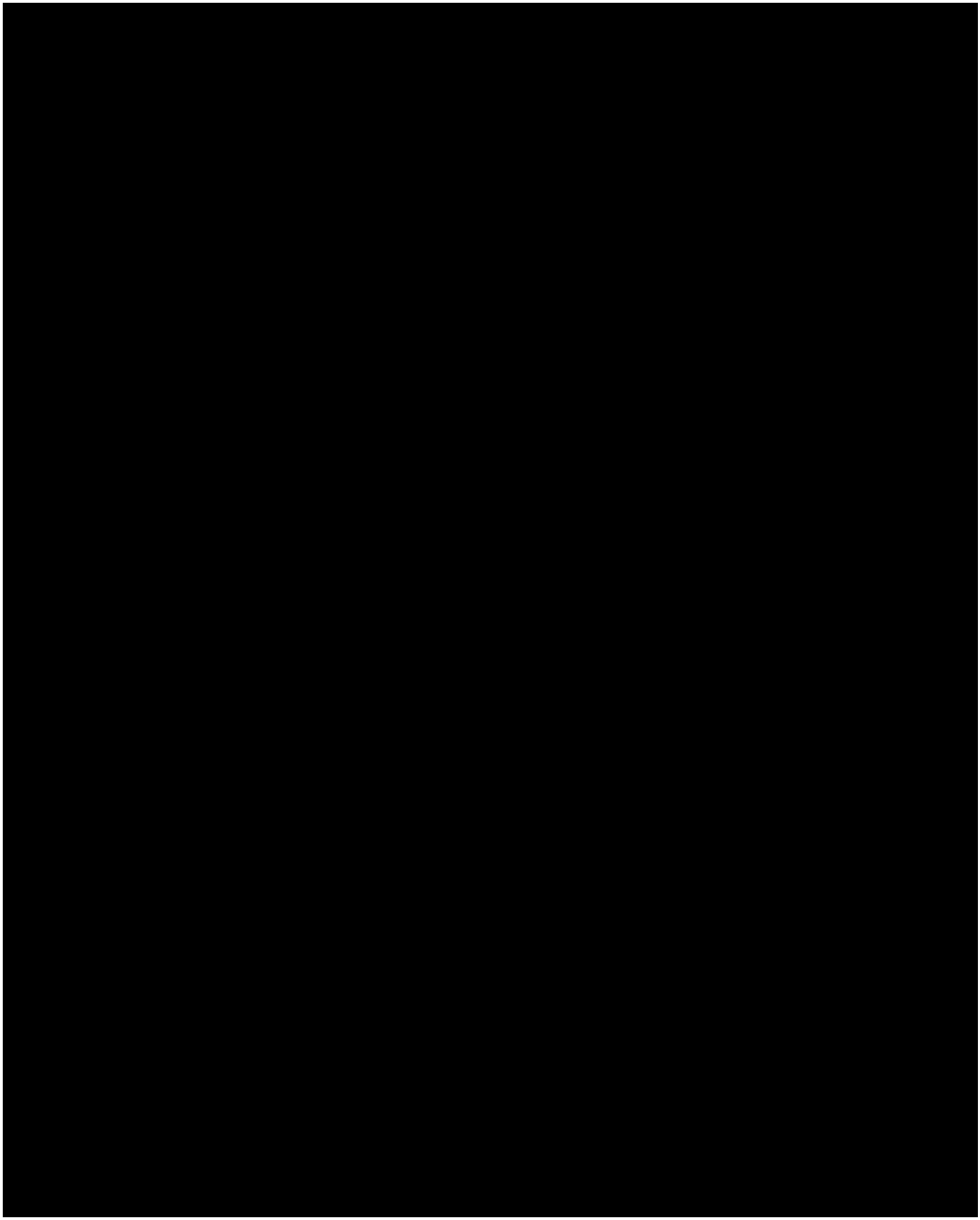
If a subject has any clinically significant, trial-related abnormalities at the end of the trial, the Medical Monitor should be notified and every effort made by the Investigator to arrange follow up evaluations at appropriate intervals to document the course of the abnormalities.

8.4.9 FOLLOW-UP OF POST TRIAL SERIOUS ADVERSE EVENTS

SAEs that are identified on the last scheduled contact (or early discontinuation, if applicable) must be recorded on the AE CRF page and reported to the CRO and Revance according to the reporting procedures outlined in Section 8.4.6. This may include unresolved previously reported SAEs, or new SAEs. The Investigator should follow these SAEs until the events are resolved, or the subject is lost to follow-up. The Investigator should continue to report any significant follow-up information to the Medical Monitor, Revance, and the IRB/IEC up to the point the event has been resolved. Resolution means the subject has returned to the baseline state of health, or the Investigator does not expect any further improvement or worsening of the subject's condition.

Any new SAEs reported by the subject to the Investigator that occur after the last scheduled contact and are determined by the Investigator to be reasonably associated with the administration of investigational product should be reported to Revance and the IRB/IEC.





8.4.11 REPORTING OF PREGNANCY

During the trial, all WOCBP should be instructed to contact the Investigator immediately (within 24 hours) if they suspect they might be pregnant (e.g., missed or late menstrual cycle). The Investigator must immediately notify Revance or designated Contract Research Organization (CRO) of any female subject who becomes pregnant any time during study participation, record the information on the Pregnancy Notification Form and send the form to the CRO. The site will be asked to follow-up with the subject periodically during the pregnancy for ongoing health and safety information through term, as applicable. Subjects will remain on the trial.

8.5 UNANTICIPATED ADVERSE EVENTS

8.5.1 DEFINITION OF UNANTICIPATED ADVERSE EVENTS

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

Revance will comply with these criteria for reporting Unanticipated Adverse Events.

8.5.2 UNANTICIPATED ADVERSE EVENT REPORTING

The Investigator will report unanticipated Adverse Events to the reviewing Institutional Review Board (IRB) and the Sponsor. The unanticipated adverse event report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an unanticipated adverse event;
- A description of any changes to the protocol by the Sponsor or other corrective actions that have been taken or are proposed in response to the unanticipated adverse event.
- The Sponsor will update the IB or provide Dear Doctor letter should these actions be deemed required.

To satisfy the requirement for prompt reporting, unanticipated adverse events will be reported using the following timeline:

- Unanticipated adverse events that are fatal and life-threatening serious adverse events (SAEs) will be reported to the IRB and to the Sponsor within seven (7) days of the Investigator becoming aware of the event.
- Any other unanticipated adverse events that are SAEs will be reported to the IRB and to the Sponsor within 15 days of the Investigator becoming aware of the problem.
- All unanticipated adverse events that non-serious AEs are not required to be reported to the IRB or to the Sponsor.
- All unanticipated serious adverse events should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) if applicable.

8.5.3 REPORTING UNANTICIPATED ADVERSE EVENTS TO PARTICIPANTS

Revance will disclose clinical trial data to individuals, to investigators at clinical sites, and publicly as aggregate summaries, in accordance to Regulatory and local legal requirements.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESIS

Treatment with DaxibotulinumtoxinA for Injection of plantar fascia and plantar muscles combined with transient and selective partial paralysis of gastrocnemius/soleus complex (dysfunction) and a simple home program and inexpensive splinting will ameliorate signs and symptoms of plantar fasciitis; will improve function, and will optimize health related quality of life.

9.2 SAMPLE SIZE DETERMINATION

With a total of 60 subjects (30 per group) and assuming a drop-out rate of no more than 20%, [redacted]

9.3 POPULATIONS FOR ANALYSES

Approximately 60 subjects, 18-65 years of age, will be randomized in a 1:1 ratio to receive injections of either active (DaxibotulinumtoxinA for Injection) or placebo. [redacted]

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

All evaluable efficacy data will be included in the analysis following the intent-to-treat (ITT) principle. All subjects who received the study treatment (DaxibotulinumtoxinA for Injection or placebo) will comprise the modified-ITT population and will be grouped according to each subject's randomization assignment. The primary analysis will focus on the reduction from baseline in the VAS for pain at eight (8) weeks with missing data imputed by the last available value prior to the visit with missing value, that is, the last-observation-carried-forward (LOCF) approach. Analysis of covariate (ANCOVA) model including treatment group as a factor and baseline pain score as a covariate will be used.

Reductions from baseline VAS for pain for the foot over time up to eight (8) weeks will also be analyzed using a statistical method that handles repeated measures such as a generalized linear model (GLM) including treatment group, time (visit) and the treatment-visit interaction term as factors and the baseline VAS for pain as a covariates. For other secondary and exploratory efficacy outcome measures, appropriate statistical models (e.g., ANCOVA or GLM for continuous variables, and chi-squared/Fisher's

exact test or logistic regression for dichotomy or categorical variables) adjusting for relevant covariates will be employed to evaluate the treatment effect.

As a sensitivity analysis to check the impact of major protocol violations to study results, the primary and secondary efficacy outcome measures will also be analyzed on data from all subjects in per-protocol (PP) population, which consists of subjects in the modified-ITT population who do not have any major protocol violations. To check the robustness of results using the LOCF approach, different methods (such as observed data only or multiple imputation) may be employed to handle missing data when appropriate.

As an exploratory analysis, proportion of subjects achieving certain status defined by some efficacy assessments (e.g., having a reduction in the VAS for pain by a certain clinical meaning cut-point) will also be compared between treatment groups.

Safety data from all subjects who received study treatment will be summarized with subjects being grouped based on the treatment each subject actually received.

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

The primary endpoint is:

- Reduction in the visual analog scale (VAS) for pain for the foot at Week 8

Analysis of the primary efficacy endpoint is fully defined in the statistical analysis plan.

[redacted]

[redacted]

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 INFORMED CONSENT AND AUTHORIZATION TO RELEASE HEALTH INFORMATION

Written informed consent will be obtained from all subjects before any study-related procedures (including any screening procedures) are performed. The Investigator may discuss the trial and the possibility for entry with a potential subject without first obtaining consent. However, a subject wishing to participate must give written informed consent prior to any study-related procedures being conducted, including those performed solely for the purpose of determining eligibility for study participation, and including withdrawal from current medication (if required prior to study entry). The Investigator has both the ethical and legal responsibility to ensure that each subject being considered for inclusion in this trial has been given a full explanation of the procedures and expectations for study participation.

The site-specific informed consent must be forwarded to Revance for approval prior to submission to an Institutional Review Board (IRB)/Independent Ethics Committee (IEC) that is registered with the US Department of Health and Human Services (HHS) or applicable health authority. Each subject will sign the consent form that has been approved by the same IRB/IEC that was responsible for protocol approval. Each informed consent document must adhere to the ethical principles stated in the Declaration of Helsinki and will include the elements required by FDA regulations in 21 CFR Part 50, as well as the elements required by the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guideline, and applicable federal and local regulatory requirements. The consent form must also include a statement that Revance, their designees, and auditing regulatory agencies will have direct access to the subject's records and medical history for study related purposes.

Once the appropriate essential information has been provided to the subject and fully explained by the Investigator (or a qualified designee) and it is felt that the subject understands the implications and risks of participating in the trial, the IRB/IEC approved consent document shall be signed and dated by both the subject and the person obtaining consent (Investigator or designee), and by any other parties required by the IRB/IEC or other regulatory authorities. The subject will be given a copy of the signed informed consent document with the original kept on file by the Investigator. All of the above activities must be completed before any study related procedures are conducted (including any screening study procedures).

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The Investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The

participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.]

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigators, the Investigational New Drug (IND) sponsor and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or Food and Drug Administration (FDA).

[redacted]

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[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	

10.1.6 SAFETY MONITORING/DATA MANAGEMENT COMMITTEE

An independent Data Management Committee (DMC) will be appointed to review safety data during the study. Details of the composition and scope of the committee's mandate will be presented in a DMC Charter document. Following recruitment of all subjects, the DMC will evaluate all safety data available at timepoints specified in the Charter, and will make appropriate recommendations.

10.1.7 MONITORING, COMPLIANCE, AND QUALITY

All aspects of the trial will be monitored by Revance or authorized representatives of Revance according to Good Clinical Practices (GCP) and Standard Operating Procedures (SOPs) for compliance with applicable government regulations, (i.e., Informed Consent Regulations and Institutional Review Board regulations). [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

10.1.9.1.1 DATA COLLECTION

For this trial, all protocol-specified data recorded in the source documents will be entered on the CRFs from the source documents. Subject assessments will be completed by the individual subjects directly on the corresponding CRFs. In addition to signature confirmation that a subject meets the study eligibility criteria, upon each subject's completion of the trial, the Investigator will sign a statement indicating that all pages of the subject's case report have been reviewed. Signature stamps and "per signatures" are not acceptable.

It is Revance's policy that the trial data be verifiable with the source data that necessitates access to all original recordings, laboratory reports, and other records for each subject. The Investigator must therefore

agree to allow access to subjects' records, and source data must be made available for all trial data. Subjects (or their legal representatives) must also allow access to their medical records. Subjects will be informed of the importance of increased record access and permission granted by signature on the informed consent document prior to Screening.

Checks will be performed to ensure the quality, consistency, and completeness of the data. Instances of missing or un-interpretable data will be resolved with the Investigator or Study Coordinator. Data queries will be sent to the trial center. Site personnel will be responsible for providing resolutions to the data queries and for correcting the CRFs, as appropriate. All unused Revance source documents and binders must be returned to Revance upon completion of the trial.

The Investigator must keep written or electronic source documents for every subject participating in the clinical trial. The subject file that identifies the study in which the subject is participating must include the subject's available demographic and medical information including:

- Date of birth
- Sex
- Race
- Ethnicity
- Medical history
- Comorbid conditions
- Concomitant therapies/medication
- Study visit dates
- Performed examinations, evaluations, and clinical findings
- Investigational product administration
- AEs, SAEs, or pregnancy (as applicable)

Additionally, any other documents with source data, especially original printouts of data that were generated by technical equipment must be included in the subject's source document (e.g., laboratory value listings). All these documents must have at least the subject's initials, trial number, and the date of the evaluation.

The data recorded during the course of the trial will be documented in the CRF and/or the trial-specific forms. Before or at study termination, all data must be forwarded to Revance. The data will then be recorded, evaluated, and stored in anonymous form in accordance with data-protection regulations.

Subjects will authorize the use of their protected health information during the informed consent process in accordance with the applicable privacy requirements. Subjects who deny permission to use and disclose protected health information will not be eligible to participate in the trial. The Investigator will ensure that the trial documents forwarded to Revance, and any other documents, contain no mention of subject names.

Any amendments and corrections necessary will be undertaken in both the source documents and CRFs (as appropriate) and countersigned by the Investigator, or documented designee, stating the date of the amendment/correction. Errors must remain legible and may not be deleted with correction aids. The

Investigator must state his/her reason for the correction of any data. In the case of missing data/remarks, the entry spaces provided in the CRF should be cancelled out so as to avoid unnecessary follow-up inquiries.

Regulatory authorities, the IRB/IEC and/or the Revance's Quality Assurance group (or designee) may request access to all source documents, CRFs, and other trial documentation for on-site audit or inspection. The Investigator must guarantee direct access to these documents. CRFs will be kept by Revance or an authorized designee in a secured area. Clinical data will be recorded in a computer format for subsequent statistical analyses. Data files will be stored on electronic media with a final master data file kept by Revance after descriptive and statistical analyses and reports have been generated and are complete.

10.1.9.1.2 FILE MANAGEMENT AT THE TRIAL CENTER

It is the responsibility of the Investigator to ensure that the trial center file is maintained in accordance with ICH Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, Section 8 – Essential Documents for the Conduct of a Clinical Trial. Documentation is subject to inspection by the sponsor and relevant regulatory agencies.

10.1.9.2 RECORDS RETENTION AT THE TRIAL CENTER

It is a sponsor requirement that all Investigators participating in clinical studies maintain detailed clinical data for one (1) of the following periods:

- Country-specific requirements, or
- A period of at least two (2) years following the last approval of a marketing application approved by a Regulatory Authority in an ICH region or until there are no pending or contemplated marketing applications in an ICH region, or,
- A period of two (2) years after Revance notifies the Investigator that the data will not be submitted for review by any Regulatory Authority

10.1.9.3 TREATMENT OF MISSING DATA

Some data elements will be missing in this study due to subjects who withdraw from the study, subjects who are lost to follow-up, or subjects who do not complete all study visits. The completion status of each subject will be documented (e.g., completed protocol, withdrew from study, lost to follow-up, etc.). All reasonable efforts will be made by the study staff to maintain contact with the study participants during their participation in the study. The study coordinator will attempt to contact any subjects who are lost to follow-up. For subjects who are unwilling to return to clinic for follow-up, the study coordinator will attempt to contact them and to collect study data from them during a telephone call or by forms sent to them through the mail.

10.1.10 PROTOCOL DEVIATIONS

This trial will be conducted as described in this protocol, except for an emergency situation in which the protection, safety, and well-being of the subject requires immediate intervention, based on the judgment of the Investigator (or a responsible, appropriately trained professional designated by the Investigator). In the event of a significant deviation from the protocol due to an emergency, accident, or mistake, the Investigator or designee must contact Revance at the earliest possible time by telephone. This will allow

an early joint decision regarding the subject's continuation in the trial. This decision will be documented by the Investigator and the Sponsor.

[redacted]

[redacted]

10.2 ADDITIONAL CONSIDERATIONS

10.2.1 ETHICS AND RESPONSIBILITY

This trial must be conducted in compliance with the protocol, the ICH Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance and the applicable regulatory requirements. Investigators must submit all essential regulatory documentation, as required by local and national regulations (including approval of the protocol and informed consent form by an HHS-registered IRB/IEC) to Revance before investigational product will be shipped to the study site.

[redacted]

[redacted]

10.3 ABBREVIATIONS

AE	Adverse Event
ANCOVA	Analysis of Covariance
AOFAS	American Orthopaedic Foot and Ankle Score
BoNTA	Botulinum Toxin Type A
BP	Blood Pressure
CFR	Code of Federal Regulations
cm	Centimeter
CRF	Case Report Form
CS	Clinical Significant
DMC	Data Management Committee
EC	Ethics Committee
ECG	Electrocardiogram
FADI	Foot and Ankle Disability Index
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HHS	Health and Human Services
HR	Heart Rate
IB	Investigator's Brochure
ICH	International Council for Harmonisation
IM	Intramuscular(ly)
in	Inch
IND	Investigational New Drug Application
IRB	Institutional Review Board
ITT	Intention-To-Treat
kDA	Kilodalton
MedDRA	Medical Dictionary for Regulatory Activities
mL	Milliliter
mm	Millimeter
msec	Millisecond
NCS	Not Clinically Significant
ng	Nanogram
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PFPS	Plantar Fasciitis Pain and Disability Scale
PP	Per Protocol
PROMIS	Patient Reported Outcome Measurement Information System
QT	Measurement of time between start of the q wave and the end of the t wave in the heart's electrical conduction
QTc	Corrected QT interval; represents electrical systole
Revance	Revance Therapeutics, Inc.
RT002	DaxibotulinumtoxinA for Injection
RTP004	Revance absorption enhance peptide
SAE	Serious Adverse Event
SC	Subcutaneous

SoA	Schedule of Assessments
SOP	Standard Operating Procedure
SPT	Serum Pregnancy Test
TdP	Torsade de Pointe
U	Units (botulinum toxin)
UA	Urinalysis
UPT	Urine Pregnancy Test
US	United States of America
VAS	Visual Analog Scale
WFBMC	Wake Forest Baptist Medical Center
WOCBP	Women of Child-Bearing Potential