CLINICAL STUDY PROTOCOL

IND - 145417

A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia

ABP-19000

Sponsor:	Aeon Biopharma, Inc. [redacted]
Sponsor Contact:	[redacted]
Medical Monitor:	[redacted]
Version of Protocol:	Version 2.1
Date of Protocol:	13 May 2021 18 March 2020 (Version 1.0) 26 August 2020 (Version 1.1) 19 November 2020 (Version 2.0)

CONFIDENTIAL

The study will be conducted according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guideline E6 (R2): Good Clinical Practice (GCP).

Protocol Approval – Sponsor Signatory

Study Title	A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia
Protocol Number	ABP-19000
Protocol Date and Version	13May 2021; Version 2.1

Protocol accepted and approved by:

Vice President, Technical Operations and Regulatory

[redacted]

Signature

14 May 2021

Date

Protocol Approval – Principal/Coordinating Investigator

Study Title A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia

Protocol Number ABP-19000

Protocol Date and Version 13 May 2021; Version 2.1

Protocol accepted and approved by:

Principal/Coordinating Investigators

[redacted]

Signature

5/17/2021
Date

[redacted]

Signature

5/20/2021
Date

Protocol Approval – Lead Statistician

Study Title	A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia
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Protocol Date and Version	13 May 2021; Version 2.1

Protocol accepted and approved by:

Lead Statistician

[redacted]

Signature

Date

Protocol Approval – Medical Monitor

Study Title	A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia
Protocol Number	ABP-19000
Protocol Date and Version	13 May 2021; Version 2.1

Protocol accepted and approved by:

Medical Monitor

[redacted]

I approve this document
18 May 2021 09:56:25 -04:00

DocuSign

Signature

Date

Declaration of Investigator

I have read and understood all sections of the protocol entitled "A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia" and the accompanying investigator's brochure.

I agree to supervise all aspects of the protocol and to conduct the clinical investigation in accordance with the Final Protocol Version 2.1, dated 13 May 2021, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guideline E6(R2): Good Clinical Practice and all applicable government regulations. I will not make changes to the protocol before consulting with Aeon Biopharma, Inc. or implement protocol changes without independent ethics committee approval except to eliminate an immediate risk to patients. I agree to administer investigational study drug only to patients under my personal supervision or the supervision of a subinvestigator.

I will not supply the investigational study drug to any person not authorized to receive it. Confidentiality will be protected. Patient identity will not be disclosed to third parties or appear in any study reports or publications.

I will not disclose information regarding this clinical investigation or publish results of the investigation without authorization from Aeon Biopharma, Inc.

_____ _____

Signature of Principal Investigator Date

_____

Printed Name of Principal Investigator

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Protocol Synopsis

Protocol Number:	ABP-19000
Title:	A Phase 2, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Intramuscular ABP-450 (prabotulinumtoxinA) Injection for the Treatment of Cervical Dystonia
Sponsor:	Aeon Biopharma, Inc. [redacted]
Study Phase:	2
Study Sites:	Approximate number of total sites in the United States: 42
Indication:	Cervical dystonia
Rationale:	Cervical dystonia (spasmodic torticollis) is the most common form of focal dystonia, affecting the neck and shoulder muscles. Cervical dystonia is characterized by abnormal head and neck posture and involuntary head and neck movements. It is often associated with neck and shoulder pain. Botulinum toxin A is considered first-line therapy for cervical dystonia, helping to improve pain, posture, and disability. ABP-450 (prabotulinumtoxinA) is a toxin produced by *Clostridium botulinum*. It blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. Blocking the release of acetylcholine plays a role in relaxing muscles by reducing muscle activity. [redacted]

[redacted]

[redacted]

This Phase 2, multicenter, randomized, double-blind, active- and placebo-controlled study aims to demonstrate the safety and efficacy of ABP-450 doses (low, medium, and high) compared with placebo in patients with cervical dystonia. The current Phase 2 study will help to determine appropriate doses of ABP-450 in this study population.

Objectives:

Primary Objective

- To demonstrate the safety of a single treatment of ABP-450 (low, medium, or high dose) compared with placebo in the treatment of cervical dystonia

Secondary Objective

- To demonstrate the efficacy of a single treatment of ABP-450 (low, medium, or high dose) at Week 4 compared with placebo in the treatment of cervical dystonia

Estimands:

Primary Estimand

- Proportion of patients who would develop treatment-related serious adverse events (SAEs) during the first 20 weeks of a single treatment cycle when dosed with:
    - Placebo;
    - Low-dose ABP-450 (150 units);
    - Medium-dose ABP-450 (250 units);
    - High-dose ABP-450 (350 units); or

- Any ABP-450 dose.

Treatment-related SAEs are counted during a single treatment cycle (up to 20 weeks and prior to administering any further treatment) and irrespective of change in background treatment or low doses that were below the set low-dose amount (ie, below 150 units) or high doses that were above the set high-dose amount (ie, above 350 units).

Secondary Estimands

- Mean difference in change in Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. This is the hypothetical estimand, assuming no change in background treatment or further treatment before Week 4 and administration of treatment with the correct dose amount.
- Mean difference in change in the subscale scores of the TWSTRS (disability, severity, and pain) from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. This is the hypothetical estimand assuming no change in background treatment or further treatment before Week 4 and administration of treatment with the correct dose amount.
- Mean difference in change in scores on the Clinical Global Impression of Severity, Patient Global Impression of Severity, Clinical Global Impression of Change, and Patient Global Impression of Change from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. This is the hypothetical estimand, assuming no change in background treatment or further treatment before Week 4

and administration of treatment with the correct dose amount.

For all estimands, the target population is patients diagnosed with cervical dystonia who have not had previous treatment with botulinum toxin within the last 16 weeks, are receiving stable doses of treatment for focal dystonia (eg, anticholinergics and benzodiazepines), and who meet the inclusion/exclusion criteria.

Study Population:

Inclusion Criteria

Each patient must meet all of the following criteria to be enrolled in this study:

1. Male or female patients between 18 and 75 years of age (inclusive)

[redacted]

4. [redacted]

[redacted]

6. Provided written informed consent to participate in the study.

7. Stated willingness to comply with all study procedures, including attendance at the study center for all study visits as scheduled and have technological capabilities to have tele visits with video capabilities

Exclusion Criteria

Patients who meet any of the following criteria will be excluded from the study:

9. [redacted]

Study Design:

This is a Phase 2, multicenter, randomized, double-blind, placebo-controlled study of ABP-450 purified neurotoxin complex for the treatment of cervical dystonia.

Both previously treated patients and those who have never been exposed to botulinum toxin (naïve patients) will be eligible. Pre-treated patients must be stable responders who are receiving no more than 300 units of botulinum toxin type A or 750 units abobotulinumtoxinA. The last injection for those previously treated should be at least 16 weeks prior to treatment in ABP-19000. Botulinum toxin–naïve patients are defined as those not receiving treatment with a botulinum toxin in the head or neck.

Patients will be randomly assigned (ratio of 1:1:1:1) into 1 of 4 treatment arms: ABP-450 low dose (150 units), ABP-450 medium dose (250 units), ABP-450 high dose (350 units), or placebo. The investigator will be blinded to the dose level. The doses will be prepared to the same volume using appropriate dilution as per the dose level. The volume injected will be equivalent across the doses and placebo. To ensure balance across the treatment groups, randomization will be stratified by previous treatment with BOTOX® (BOTOX® naïve vs. previously treated with BOTOX® within 4-12 months prior to baseline). The safety and efficacy of the three dose cohorts of ABP-450 or placebo will be evaluated over a maximum of 20 weeks. At the completion of the Phase 2 study, all patients, irrespective of treatment group, will have the option to receive treatment with ABP-450 by rolling over into an open-label extension (OLE) study (ABP-19002). [redacted]

[redacted]

Estimated Study Duration:

Estimated duration of the study will be approximately 21 weeks, including 1 week of Screening. Patients will be followed up to 20 weeks after the initial treatment.

Safety Assessments:

Safety will be evaluated by frequency, severity, and duration of any adverse reactions. Adverse events will be assessed at each office visit and telephone contact.

[redacted]

Study Drug, Dosage, and Route of Administration:

Study drug is a *Clostridium botulinum* toxin type A

- Investigational study drug vials contain 100 units of lyophilized ABP-450
- Placebo vials contain sodium chloride for injection, USP, 0.9%, preservative-free

The dose to be administered to patients in the study will range between 150 units and 350 units.

Active Treatment Arms	Dose
ABP-450 low dose	150 units
ABP-450 medium dose	250 units
ABP-450 high dose	350 units

[redacted]

The dose should be divided among the affected muscles. Dosing in initial sessions should be tailored to the individual patient based on the patient's head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history. The use of electromyographic guidance or ultrasound imaging should be left to the PI.

[redacted]

[redacted]

Sample Size:

Fifteen patients will be randomly assigned to each of four treatment arms (placebo, ABP-450 low dose, ABP-450 medium dose, and ABP-450 high dose) using a 1:1:1:1 ratio and therefore requiring a total of 60 patients. [redacted]

Statistical Methods:

The proportion of patients with treatment-related SAEs up to Week 20 and the end of a single treatment cycle will be

summarized separately for ABP-450 (all doses together and separately) and placebo.

[redacted]

Treatment-related SAEs will be counted if they start prior to administering any further treatment irrespective of change to background treatment or low doses that were below the set low-dose amount (ie, below 150 units) or high doses that were above the set high-dose amount (ie, above 350 units).

[redacted]

Version and Date of Protocol: Version 2.0 dated 19 November 2020

List of Abbreviations

Abbreviation	Definition
ABP-450	prabotulinumtoxinA / Jeuveau (prabotulinumtoxinA-xvfs)
AE	adverse event
ANCOVA	analysis of covariance
BOTOX®	onabotulinumtoxinA
Dysport®	abobotulinumtoxinA
CFR	Code of Federal Regulations
CGI-C	Clinical Global Impression of Change
CGI-S	Clinical Global Impression of Severity
CSR	clinical study report
C-SSRS	Columbia–Suicide Severity Rating Scale
ECG	electrocardiogram
eCRF	electronic case report form
EMG	electromyographic
EOS	end of study
FAS	Full Analysis Set
FDA	United States Food and Drug Administration
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
GCP	Good Clinical Practice
HbA1c	hemoglobin A1c
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	independent ethics committee

Abbreviation	Definition
IRB	institutional review board
IRT	interactive response technology
MedDRA	Medical Dictionary for Regulatory Activities
mFAS	Modified Full Analysis Set
OLE	open-label extension
PGI-C	Patient Global Impression of Change
PGI-S	Patient Global Impression of Severity
PI	principal investigator
PPS	Per-Protocol Analysis Set
SAE	serious adverse event
SAP	statistical analysis plan
SUSAR	suspected unexpected serious adverse reaction
TWSTRS	Toronto Western Spasmodic Torticollis Rating Scale

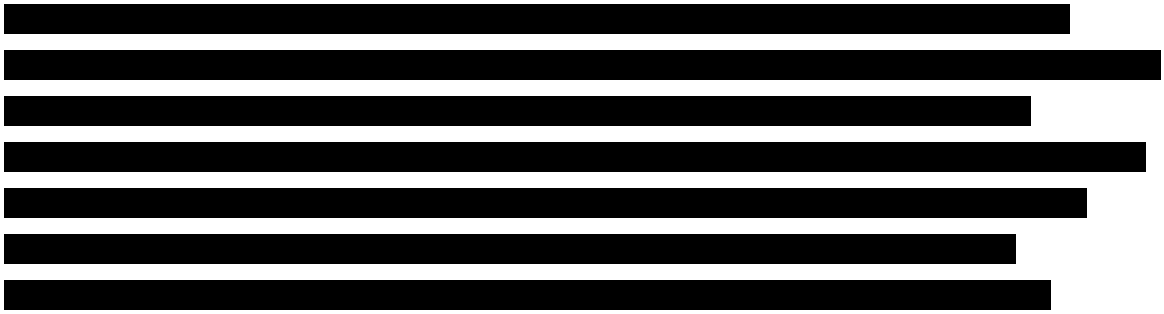
1 Introduction

Cervical dystonia (spasmodic torticollis) is the most common form of focal dystonia, affecting the neck and shoulder muscles (Defazio 2004, Mittal 2019). Cervical dystonia is characterized by abnormal head and neck posture and involuntary head and neck movements. It is often associated with neck and shoulder pain.

Botulinum toxin A is considered first-line therapy for cervical dystonia, helping to improve pain, posture, and disability (Comella 2011, Simpson 2016, Mittal 2019). ABP-450 (prabotulinumtoxinA) is a toxin produced by *Clostridium botulinum*. It blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. Blocking the release of acetylcholine plays a role in relaxing muscles by reducing muscle activity.

[redacted]

PrabotulinumtoxinA was evaluated in multiple non-clinical safety and toxicological tests to determine the pharmacologic and safety profile of the product in complying with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines/requirements for biologic products. [redacted]



PrabotulinumtoxinA has also been found to be non-inferior to onabotulinumtoxinA (BOTOX®) for the treatment of moderate to severe glabellar lines in adult patients and for upper limb spasticity in stroke patients (Nam 2015, Rzany 2019). The doses of ABP-450 used in the Phase 3 study for upper limb spasticity were similar to the doses of BOTOX® used (no significant differences were seen between the two groups) (Nam 2015).

This Phase 2, multicenter, randomized, double-blind, active- and placebo-controlled study aims to demonstrate the safety and efficacy of ABP-450 doses (low, medium, and high) compared with placebo in patients with cervical dystonia. The current Phase 2 study will help to determine appropriate doses of ABP-450 in this study population.

Clostridium botulinum toxins have become the standard of care for the treatment of patients with cervical dystonia. In addition to onabotulinumtoxinA, abobotulinumtoxinA, incobotulinumtoxinA, and rimabotulinumtoxinB have been approved for the treatment of patients with cervical dystonia. Even though these toxin products have been approved for the treatment of cervical dystonia and are the standard of care in patients with this condition, they do have significant risks associated with their use in these patients. The labels for all these products carry prominent warnings concerning their side effects, such as dysphagia and even death, if they are not carefully administered and the patient monitored while under treatment. Even so, the benefit for all these products is greater than the risks and that is why these products are the standard of care.

Clinical development of drugs has been impacted by the ongoing COVID-19 pandemic. The current study aims to implement several adjustments or mitigations to allow the study to continue despite pandemic-related disruption. To prioritize patient and site staff safety, several planned office visits have been converted to tele visits to allow the required data collection to meet the study objectives.

2 Study Objectives and Estimands

2.1 Study Objectives

2.1.1 Primary Objective

- To demonstrate the safety of a single treatment of ABP-450 (low, medium, or high dose) compared with placebo in the treatment of cervical dystonia

2.1.2 Secondary Objective

- To demonstrate the efficacy of a single treatment of ABP-450 (low, medium, or high dose) at Week 4 compared with placebo in the treatment of cervical dystonia

2.2 Study Estimands

2.2.1 Target Population

For all estimands, the target population is patients diagnosed with cervical dystonia. The patients are expected to:

- Have not had previous treatment with a botulinum toxin within the last 16 weeks;
- Be receiving stable doses of treatment for focal dystonia (eg, anticholinergics and benzodiazepines); and
- Meet the inclusion/exclusion criteria.

2.2.2 Primary Estimand

- Proportion of patients who would develop treatment-related serious adverse events (SAEs) during the first 20 weeks of a single treatment cycle when dosed with:
    - Placebo;
    - Low-dose ABP-450 (150 units);
    - Medium-dose ABP-450 (250 units);
    - High-dose ABP-450 (350 units); or
    - Any ABP-450 dose.

Treatment-related SAEs are counted during a single treatment cycle (up to 20 weeks and prior to administering any further treatment) and irrespective of change in background treatment or low doses that were below the set low-dose amount (ie, below 150 units) or high doses that were above the set high-dose amount (ie, above 350 units).

2.2.3 Secondary Estimands

- Mean difference in change in Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. [redacted]
- Mean difference in change in the subscale scores of the TWSTRS (disability, severity, and pain) from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. [redacted]
- Mean difference in change in scores on the Clinical Global Impression of Severity (CGI-S), Patient Global Impression of Severity (PGI-S), Clinical Global Impression of Change (CGI-C), and Patient Global Impression of Change (PGI-C) from baseline to Week 4 for each of low, medium, and high doses of ABP-450 compared with placebo. [redacted]

3 Investigational Plan

3.1 Study Design

This is a Phase 2, multicenter, randomized, double-blind, placebo-controlled study of ABP-450 purified neurotoxin complex for the treatment of cervical dystonia.

Both previously treated patients and those who have never been exposed to botulinum toxin (naïve patients) will be eligible. Pre-treated patients must be stable responders who are receiving no more than 300 units of botulinum toxin type A or 750 units abobotulinumtoxinA. The last injection for those previously treated should be at least 16 weeks prior to treatment in ABP-19000. Botulinum toxin–naïve patients are defined as those not receiving treatment with a botulinum toxin in the head or neck.

Patients will be randomly assigned (ratio of 1:1:1:1) into 1 of 4 treatment arms: ABP-450 low dose (150 units), ABP-450 medium dose (250 units), ABP-450 high dose (350 units), or placebo. The investigator will be blinded to the dose level. The doses will be prepared to the same volume using appropriate dilution as per the dose level. The volume injected will be equivalent across the doses and placebo. To ensure balance across the treatment groups, randomization will be stratified by previous treatment with BOTOX® (BOTOX® naïve vs. previously treated with BOTOX® within 4-12 months prior to baseline). The safety and efficacy of the three dose cohorts of ABP-450 or placebo will be evaluated over a maximum of 20 weeks. At the completion of the Phase 2 study, all patients, irrespective of treatment group, will have the option to receive treatment with ABP-450 by rolling over into an open-label extension (OLE) study (ABP-19002). [redacted]

This study will evaluate the safety and efficacy of ABP-450 or placebo over a maximum of 20 weeks. The primary objective will include evaluation of the safety of a single treatment of ABP-450 (low, medium, or high dose) compared with placebo. The secondary objective will include evaluation of the efficacy of a single treatment of ABP-450 (low, medium, or high dose) compared with placebo at Week 4.

[redacted]

3.1.1 Rationale for Study Design

[redacted]

[redacted]

3.1.2 Conduct of the Study During the COVID-19 Pandemic

Coronavirus Disease 2019 (COVID-19) is a viral illness caused by the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) and has impacted most of the countries across the globe. It was declared as a global public health emergency by the World Health Organization on 30 January 2020. This pandemic is recognized to have impacted the conduct of clinical trials of medical products in various ways.

The safety and well-being of patients and site staff is of paramount importance during the COVID-19 pandemic. Measures will be implemented during the study to reduce the chance that study drug will be administered to patients who are infected with SARS-CoV-2.

Testing for COVID-19 will be performed as required by the individual sites in case deemed necessary by the PI as per institutional standards. If a patient tests positive, study visits will be delayed until the patient recovers. The investigator will provide the patients with guidance of further clinical care for their SARS-CoV-2 infection. If the result is indeterminate, the PCR testing may need to be repeated as per institutional standards.

Other potential measures will be taken to assure the safety and welfare of patients, maintaining compliance with GCP, and minimizing risks to trial integrity during the COVID-19 pandemic, such as tele visits. Any other potential measures or changes will be handled according to the regulations.

Any events of COVID-19, including asymptomatic and symptomatic SARS-CoV-2 infection (i.e., COVID-19), are to be reported as AEs per Section 6.2.1. [redacted]

All the measures taken in relation to COVID-19 will be reported to the regulatory authorities as appropriate.

[redacted]

4 Patient Selection and Withdrawal Criteria

4.1 Selection of Study Population

Approximately 60 patients will be enrolled at approximately 42 sites in the United States. Patients will be assigned to investigational study drug only if they meet all of the inclusion criteria and none of the exclusion criteria. Patients who fail their initial Screening will be allowed to present for rescreening once, if approved in advance by the medical monitor (see Section 4.1.3).

4.1.1 Inclusion Criteria

Each patient must meet all of the following criteria to be enrolled in this study:

1. Male or female patients between 18 and 75 years of age (inclusive)
2. [redacted]
6. Provided written informed consent to being treated for cervical dystonia with ABP-450
7. Stated willingness to comply with all study procedures, including attendance at the study center for all study visits as scheduled and have technological capabilities to have tele visits

4.1.2 Exclusion Criteria

Patients who meet any of the following criteria will be excluded from the study:

[redacted]

12. Participation in another interventional study during participation in this study

13. Pregnant or lactating females, or females of child-bearing potential not willing to use an acceptable method of contraception (ie, intrauterine device, barrier methods with spermicide, or abstinence)
14. For pre-treated patients only: The patient's most recent injection with botulinum toxin exceeding the number of units specified as follows (Dashtipour 2016):
    - OnabotulinumtoxinA (BOTOX®): >300 units
    - IncobotulinumtoxinA (Xeomin®): >300 units
    - AbobotulinumtoxinA (Dysport®): >750 units

4.1.3 Rescreening

A screen failure is a patient who has given informed consent and failed to meet all of the inclusion criteria and/or met at least one of the exclusion criteria and has not been randomized (eg, due to a viral or other active infection, or repeat laboratory test result outside of reference range). Patients who fail their initial Screening will be allowed to present for rescreening once, if approved in advance by the medical monitor. Rescreen requests must be discussed with the medical monitor prior to rescreening the patient, including what has changed about the patient's medical status.

Patients who present for rescreening will be assigned a new Screening number. The investigator or designee will record rescreening data on the source document and the appropriate eCRF. Details for rescreening procedures will be provided in the IRT manual.

4.2 Withdrawal of Patients from the Study

Estimated duration of the study will be approximately 21 weeks, including 1 week of Screening. Patients will be followed up to 20 weeks after the initial treatment.

4.2.1 Reasons for Withdrawal/Discontinuation

Patients may withdraw from the study at any time and for any reason without prejudice to their future medical care by the investigator or at the study site. Every effort should be made to keep patients in the study. The reasons for patients not completing the study will be recorded. A patient may be withdrawn from the study for any of the following reasons:

1. The patient does not meet the protocol inclusion or exclusion criteria at the baseline visit.
2. [redacted]

[redacted]

9. The patient withdraws consent.

The investigator will also withdraw a patient if Aeon Biopharma terminates the study. Upon occurrence of a serious or intolerable AE, the investigator will confer with the sponsor. If a patient is discontinued because of an AE, the event will be followed until it is resolved.

4.2.2 Handling of Withdrawals

Patients are free to withdraw from the study or investigational study drug at any time upon their request. Patient participation in the study may be stopped at any time at the discretion of the investigator or at the request of the sponsor.

[redacted]

It is vital to obtain follow-up data on any patient withdrawn because of an AE or SAE. In every case, efforts must be made to undertake protocol-specified, safety, follow-up procedures.

4.2.3 Replacements

Patients who discontinue prematurely from the study will not be replaced.

5 Study Treatments

5.1 Method of Assigning Patients to Treatment Groups

Patients will be randomly assigned at the baseline visit (Visit 2) to receive ABP-450 low dose (150 units), ABP-450 medium dose (250 units), ABP-450 high dose (350 units), or placebo using a 1:1:1:1 allocation ratio. To ensure balance across the treatment groups, randomization will be stratified by previous treatment with BOTOX® (BOTOX® naïve vs. previously treated with BOTOX® within 4-12 months prior to baseline).

5.2 Treatments Administered

Investigational study drug is a *Clostridium botulinum* toxin type A

- Investigational study drug vials contain 100 units of lyophilized ABP-450
- Placebo vials contain sodium chloride for injection, USP, 0.9%, preservative-free

The dose to be administered to patients in the study will range between 150 units and 350 units.

Active Treatment Arms	Dose
ABP-450 low dose	150 units
ABP-450 medium dose	250 units
ABP-450 high dose	350 units

[redacted]

5.3 Identity of Investigational Product

ABP-450 is lyophilized powder packed in vials containing 100 units. Placebo will be sodium chloride for injection, USP, 0.9%, preservative-free (from the same lot that is used for reconstitution of the toxin[s]).

[redacted]

The following drug supplies will be used in the study:

Product	Supplied as:
ABP-450	100 units of lyophilized powder packed in 10-mL vials
Placebo	Sodium chloride injection, USP, 0.9%, preservative-free, 10-mL vials

5.4 Management of Clinical Supplies

5.4.1 Investigational Study Drug Packaging and Storage

[redacted]

5.4.2 Test Article Accountability

The investigator will maintain accurate records of receipt of all test articles, including dates of receipt. In addition, accurate records will be kept regarding when and how much test article is dispensed and used by each patient in the study. Reasons for departure from the expected dispensing regimen must also be recorded. At the completion of the study, to satisfy

regulatory requirements regarding drug accountability, all investigational study drugs will be reconciled and retained or destroyed according to applicable regulations.

5.4.3 Other Supplies

[redacted]

5.5 Overdose Management

An overdose is any dose of investigational study drug given to a patient or taken by a patient that exceeds the dose described in the protocol. [redacted] Overdoses without signs or symptoms do not need to be recorded as AEs; in case of any AEs associated with the overdose, these should be reported on relevant AE/SAE sections in the eCRF.

5.5.1 Treatment of Overdose

Treatment of suspected overdose of investigational study drugs should include investigational study drug discontinuation and implementation of appropriate supportive measures.

5.6 Blinding

The investigator will be blinded to the dose level. The volume injected will be equivalent across the doses and placebo. To ensure blinding, an appropriate and protocol-trained person at each site, such as a study nurse or other designee, will reconstitute investigational product vials in a manner blinded to the investigator and patient. [redacted] The designated person will then fill the syringe with the investigational product and give the filled syringe in a blinded fashion to the investigator. Appropriate spatial separation is required to ensure blinding. Blinding for the initial phase will be maintained throughout the study until the final assessment for the final patient has been entered into the database and the database lock has been performed.

5.6.1 Breaking the Blind

A patient's treatment assignment will not be broken until the end of the study unless medical treatment of the patient depends on knowing the study treatment the patient received. In the event that the blind needs to be broken because of a medical emergency, the investigator may unblind an individual patient's treatment allocation.

As soon as possible, the investigator should first contact the medical monitor to discuss the medical emergency and the reason for revealing the actual treatment received by that patient. The treatment assignment will be unblinded through IRT. Reasons for treatment unblinding must be clearly explained and justified in the eCRF. The date on which the code was broken along with the identity of the person responsible must also be documented.

5.7 Treatment Compliance

Patient compliance will be determined by capturing the precise dose administered and the time and date of dosing in the source document and the dosage administration eCRF. Delays in dosing and the reason for any delay in dosing is to be recorded on the dosage administration eCRF.

5.8 Prior and Concomitant Therapy

Use of all concomitant medications will be recorded in the patient's eCRF. The minimum requirement is that drug name, dose, and dates of administration are to be recorded. This will include all prescription drugs, herbal products, vitamins, minerals, and over-the-counter medications. Any changes in concomitant medications also will be recorded in the patient's eCRF.

Any concomitant medication deemed necessary for the welfare of the patient during the study may be given at the discretion of the investigator. However, it is the responsibility of the investigator to ensure that details regarding the medication are recorded in full in the eCRF.

6 Study Assessments and Procedures

Before performing any study procedures, all potential patients will sign an informed consent form (ICF). Patients will have the opportunity to have any questions answered before signing the ICF. The investigator must address all questions raised by the patient. The investigator or designee will also sign the ICF.

6.1 Study Visits

Estimated duration of the study is approximately 21 weeks, including 1 week of Screening.

The schedule of assessments is detailed in Section 13.1.

[redacted]

[redacted]

6.2 Safety Assessments

Safety will be evaluated by frequency, severity, and duration of any adverse reactions. Adverse events will be assessed at each office visit and telephone contact.

[redacted]

6.2.1 Adverse Events

6.2.1.1 Definitions of Adverse Events

The investigator is responsible for reporting all AEs that are observed or reported during the study, regardless of their relationship to investigational study drugs. The investigator will query the patient for changes since last visit and ask about the patient's ability to swallow.

An AE is defined as any untoward medical occurrence in a patient enrolled into this study regardless of its causal relationship to investigational study drugs. Patients will be instructed to contact the investigator at any time after randomization if any symptoms develop.

A treatment-emergent AE is defined as any event not present before exposure to investigational study drugs or any event already present that worsens in either intensity or frequency after exposure to investigational study drugs.

6.2.1.2 Serious Adverse Events

An SAE is defined as any event that

- Results in death
- Is immediately life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect

[redacted]

6.2.1.3 Eliciting and Documenting Adverse Events

Adverse events will be assessed from the time the patient signs the ICF until exit from the study (20 weeks after initial treatment).

Serious AEs that occur more than 90 days after the last dose of investigational study drug and the patient has exited the study need not be reported unless the investigator considers them related to investigational study drug.

At every study visit, patients will be asked a standard non-leading question to elicit any medically related changes in their well-being. They will also be asked if they have been hospitalized, had any accidents, used any new medications, or changed concomitant medication regimens (both prescription and over-the-counter medications).

In addition to patient observations, AEs identified from any study data (eg, laboratory values, physical examination findings, ECG changes) or identified from review of other documents that are relevant to patient safety will be documented on the AE page in the eCRF.

6.2.1.4 Reporting Adverse Events

All AEs reported or observed during the study will be recorded on the AE page in the eCRF. Information to be collected includes the following:

- Drug treatment
- Dose
- Event term
- Time of onset
- Investigator-specified assessment of severity and relationship to investigational study drugs
- Time of resolution of the event
- Seriousness
- Any required treatment or evaluations
- Outcome

Adverse events resulting from concurrent illnesses, reactions to concurrent illnesses, reactions to concurrent medications, or progression of disease states must also be reported. All AEs will be followed to adequate resolution. The Medical Dictionary for Regulatory Activities (MedDRA) will be used to code all AEs.

Any medical condition that is present at the time that the patient is screened but does not deteriorate should not be reported as an AE. However, if it deteriorates at any time after Screening visit, it should be recorded as an AE.

6.2.1.5 Reporting Serious Adverse Events

[redacted]

The sponsor or its designee is responsible for reporting relevant SAEs to the competent authority, other applicable regulatory authorities, and participating investigators, in accordance with the ICH guidelines and/or local regulatory requirements.

The sponsor is responsible for reporting unexpected fatal or life-threatening events associated with the use of the investigational study drugs (expedited reports) to the regulatory agencies and competent authorities by telephone or fax within 7 calendar days after being notified of the event. The sponsor should report other relevant SAEs associated with the use of the investigational study drugs to the appropriate competent authorities (according to local guidelines), investigators, and the institutional review board (IRB) by a written safety report within 15 calendar days of notification.

6.2.1.6 Suspected Unexpected Serious Adverse Reactions and Non-Serious Adverse Events of Special Interest

The sponsor will promptly evaluate all suspected unexpected serious adverse reactions (SUSARs) and non-serious AEs of special interest against cumulative investigational study drug experience to identify and expeditiously communicate possible new safety findings to investigators, IRBs/independent ethics committees (IECs), and applicable health authorities based on applicable legislation.

[redacted]

[redacted]

6.2.1.7 Assessment of Severity

The severity, or intensity, of an AE refers to the extent to which an AE affects the patient's daily activities. The intensity of the AE will be rated as mild, moderate, or severe using the following criteria:

Mild: An event usually transient in nature and generally not interfering with normal activities.

Moderate: An AE that is sufficiently discomforting to interfere with normal activities.

Severe: An AE that is incapacitating and prevents normal activities.

Changes in the severity of an AE should be documented to allow an assessment of the duration of the event at each level of intensity to be performed. AEs characterized as intermittent do not require documentation of onset and duration of each episode.

6.2.1.8 Assessment of Causality

The investigator's assessment of an AE's relationship to investigational study drugs is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported.

The relationship or association of the test article in causing or contributing to the AE will be characterized using the following classification and criteria:

Unrelated: This relationship suggests that there is no association between the investigational study drugs and the reported event.

Possible: This relationship suggests that treatment with the investigational study drugs caused or contributed to the AE, ie, the event follows a reasonable temporal sequence from the time of drug administration or follows a known response pattern to the investigational study drugs, but could also have been produced by other factors.

Probable: This relationship suggests that a reasonable temporal sequence of the event with drug administration exists and, based upon the known pharmacological action of the drug, known or previously reported adverse reactions to the drug or class of drugs, or judgment based on the investigator's clinical experience,

[redacted]

the association of the event with the investigational study drugs seems likely. The event disappears or decreases on cessation or reduction of the dose of investigational study drugs.

Definite: This relationship suggests that a definite causal relationship exists between drug administration and the AE, and other conditions (concurrent illness, progression/expression of disease state, or concurrent medication reaction) do not appear to explain the event. The event reappears or worsens if the investigational study drug is re-administered.

6.2.1.9 Follow-Up of Patients Reporting Adverse Events

All AEs must be reported in detail on the appropriate page in the eCRF and followed to satisfactory resolution, until the investigator deems the event to be chronic or not clinically significant, or until the patient is considered to be stable.

[redacted]

[redacted]

6.3 Efficacy Assessments

6.3.1 TWSTRS Scale

Most studies leading to the approval of currently available botulinum neurotoxins have used the TWSTRS scale as the primary efficacy measure (Espay 2018, Fernandez 2013). The standard TWSTRS is a comprehensive scale that comprises three subsets to assess motor severity, pain, and disability (Comella 2016). The motor severity subscale consists of 10 items, with variable scaling and weighting. It also includes a disability subscale with 7 items and a pain scale with 3 items. The total score is the sum of each of the subscales. [redacted]

6.3.2 PGI-C and CGI-C Scales

The PGI-C enables the patient to rate changes in their perception of their general health status over the duration of the assessment via a 7-point scale ranging from “very much improved” to “very much worse” (Fischer 1999). For this study, a 5-point generic PGI-C scale ranging from “much better” to “much worse” was used (FDA 2018). Similarly, the CGI-C is a 7-point scale ranging from “very much improved” to “very much worse” (Guy 1976) based on the physician’s perception of the patient’s health status. Detailed descriptions of the CGI-C and PGI-C are provided in Appendix 13.4 and Appendix 13.6, respectively.

6.3.3 PGI-S and CGI-S Scales

The PGI-S is a 1-item global index that enables the patient to rate their impression of disease severity via a 4-point scale ranging from "normal" to "severely ill" (Guy 1976). The appropriateness of the PGI-S scale used depends on the context of use (eg, patient population) (FDA 2018). For this study, a 5-point generic PGI-S scale ranging from "none" to "very severe" was used. Similarly, the CGI-S enables the clinician to rate the severity of the patient's illness, relative to their past experience with patients who have the same diagnosis, on a 7-point scale ranging from "normal" to "among the most extremely ill patients" (Guy 1976). Detailed descriptions of the PGI-S and CGI-S are provided in Appendix 13.4 and Appendix 13.5, respectively.

6.3.4 C-SSRS

The C-SSRS was developed by the United States Food and Drug Administration (FDA) in 2012 for measuring suicidal ideation and behavior in clinical trials (Posner 2011). The C-SSRS was designed to distinguish the domains of suicidal ideation and suicidal behavior. Four constructs are measured. The first is the severity of ideation (hereafter referred to as the "severity subscale"), which is rated on a 5-point ordinal scale in which 1=wish to be dead, 2=non-specific active suicidal thoughts, 3=suicidal thoughts with methods, 4=suicidal intent, and 5=suicidal intent with plan. The second is the intensity of ideation subscale (hereafter referred to as the "intensity subscale"), which comprises five items, each rated on a 5-point ordinal scale: frequency, duration, controllability, deterrents, and reason for ideation. The third is the behavior subscale, which is rated on a nominal scale that includes actual, aborted, and interrupted attempts; preparatory behavior; and non-suicidal self-injurious behavior. The fourth is the lethality subscale, which assesses actual attempts; actual lethality is rated on a 6-point ordinal scale, and if actual lethality is zero, potential lethality of attempts is rated on a 3-point ordinal scale (Posner 2011). A detailed description is provided in Appendix 13.7.

6.3.5 Dysphagia Score

[redacted]

6.4 Safety Monitoring Committee

The medical monitor and sponsor will hold monthly reviews of all AEs; consequently, an independent Safety Committee will not be formed for this study.

6.5 Pregnancy

[redacted]

6.6 Laboratory Analyses

Any abnormal laboratory test results [redacted] including those that worsen from baseline or are felt to be clinically significant in the medical and scientific judgment of the investigator, are to be recorded as AEs or SAEs.

[redacted]

However, any clinically significant safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the patient's condition, are not to be reported as AEs or SAEs.

6.7 Sample Collections

Site personnel will collect blood samples at the visits specified in Section 6.1. These samples will be processed at the site and shipped same day to a central laboratory, as specified in the laboratory manual. [redacted]

7 Statistical Considerations

This section briefly describes statistical and analytical methods to be used for the study. A statistical analysis plan (SAP) will provide details of the statistical methods and definitions for the analysis of efficacy and safety data. To preserve the integrity of the statistical analysis and study conclusions, the SAP will be finalized before database lock.

7.1 Estimands

[redacted]

7.2 Sample Size Calculations

Fifteen patients will be randomly assigned to each of four treatment arms (placebo, ABP-450 low dose, ABP-450 medium dose, and ABP-450 high dose) using a 1:1:1:1 ratio and therefore requiring a total of 60 patients. [redacted]

7.3 Analysis Sets

The following analysis sets will be used in the statistical analyses.

Full Analysis Set (FAS): The FAS will consist of all patients who received investigational study drug. All analyses using the FAS will group patients according to randomized treatment.

Modified Full Analysis Set (mFAS): The mFAS will consist of all patients in the FAS, but will exclude data points after patients have a significant change to their "stable" background medication, receive a dose outside of the set dose amounts, or receive further treatment. All analyses using the mFAS will group patients according to randomized treatment.

Per-Protocol Analysis Set (PPS): The PPS will consist of all patients in the FAS who received placebo or ABP-450 (according to the set dose amount), but will exclude all patients who

discontinued the study prior to Week 4 or had significant protocol violations affecting evaluation of the primary endpoint. All analyses using the PPS will group patients according to actual treatment received.

Safety Analysis Set: The Safety Analysis Set will consist of all patients who received any investigational study drug. All analyses using the Safety Analysis Set will group patients according to treatment actually received.

7.4 Description of Subgroups to be Analyzed

No subgroup analyses are planned.

7.5 Statistical Analysis Methodology

[redacted] Variables will generally be summarized using number of observations, mean, SD, median, minimum, maximum, and missing data (for continuous variables) and using frequencies, percentages, and missing data (for categorical variables). Data will be listed in data listings.

Details of the statistical analyses, methods, and data conventions are described in the SAP.

[redacted]

7.5.1 Analysis of Primary Estimand

The proportion of patients with treatment-related SAEs up to Week 20 and the end of a single treatment cycle will be summarized separately for ABP-450 (all doses together and separately) and placebo.

[redacted]

Treatment-related SAEs will be counted if they start prior to administering any further treatment irrespective of change to background treatment or low doses that were below the set low-dose amount (ie, below 150 units) or high doses that were above the set high-dose amount (ie, above 350 units).

7.5.2 Analysis of Secondary Estimands

The analysis of the first secondary efficacy estimand is based on the comparison of least square means [redacted]

[redacted]

7.5.3 Safety Analyses

The incidence of treatment-emergent AEs for the Safety Analysis Set will be summarized by treatment group. Adverse events will be coded using MedDRA to classify events under primary system organ class and preferred term. [redacted]

7.5.4 Other Analyses

Summary statistical analyses will be provided by treatment group for demographics, background characteristics, medical history, and physical examination results.

7.5.5 Interim Analyses

No interim analyses are planned.

8 Data Quality Assurance

The sponsor or its designee will perform the quality assurance and quality control activities of this study, including regular monitoring visits to study sites and meeting with site personnel. However, the investigator generating the data will be responsible for the accuracy, completeness, and reliability of the study data presented to the sponsor.

8.1 Data Management

As part of the responsibilities assumed by participating in the study, the investigator agrees to maintain adequate case histories for the patients treated as part of the research under this protocol. The investigator agrees to maintain accurate eCRFs and source documentation as part of the case histories. These source documents may include laboratory reports and [redacted]

[redacted]

All eCRF information is to be filled in. If an item is not available or is not applicable, this fact should be indicated. Blank spaces should not be present unless otherwise directed. A correction to source documentation should be made by striking through the incorrect entry with a single line, and the corrected information should be entered adjacent to the deleted item. The correction must be initialed and dated by the person making the correction.

Investigative site personnel will enter patient data into an electronic data capture system. The analysis data sets will be a combination of these data and data from other sources (eg, laboratory data).

Clinical data management will be performed in accordance with applicable Aeon Biopharma standards and data cleaning procedures to ensure the integrity of the data, eg, removing errors and inconsistencies in the data. Adverse event terms will be coded using MedDRA, an internal validated medical dictionary, and concomitant medications will be coded using the World Health Organization Drug Dictionary.

[redacted]

9 Ethics

9.1 Independent Ethics Committee or Institutional Review Board

Federal regulations and the ICH guidelines require that approval be obtained from an IRB/IEC before participation of human patients in research studies. Before study onset, the protocol, informed consent, advertisements to be used for the recruitment of study patients, and any other written information regarding this study to be provided to the patient must be approved by the IRB/IEC. Documentation of all IRB/IEC approvals and of the IRB/IEC compliance with ICH harmonised tripartite guideline E6(R2): Good Clinical Practice (GCP) will be maintained by the site and will be available for review by the sponsor or its designee.

All IRB/IEC approvals should be signed by the IRB/IEC chairman or designee and must identify the IRB/IEC name and address, the clinical protocol by title or protocol number or both, and the date of approval or the date a favorable opinion was granted.

The investigator is responsible for providing written summaries of the progress and status of the study at intervals not exceeding 1 year or otherwise specified by the IRB/IEC. The investigator must promptly supply the sponsor or its designee, the IRB/IEC, and, where applicable, the institution with written reports on any changes significantly affecting the conduct of the study or increasing the risk to patients.

9.2 Ethical Conduct of the Study

The study will be performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki, ICH GCP, the protocol, and all applicable regulations.

9.3 Patient Information and Consent

A written informed consent in compliance with United States Title 21 Code of Federal Regulations (CFR) Part 50 shall be obtained from each patient before entering the study or performing any study procedure. An informed consent template may be provided by the sponsor to investigative sites. If any institution-specific modifications to study-related procedures are proposed or made by the site, the consent should be reviewed by the sponsor or its designee or both before IRB/IEC submission. Once reviewed, the consent will be submitted by the investigator to his or her IRB/IEC for review and approval before the start of the study. If the ICF is revised during the course of the study, all active participating patients must sign the revised form.

Before recruitment and enrollment, each prospective patient will be given a full explanation of the study and be allowed to read the approved ICF. Once the investigator is assured that

the patient understands the implications of participating in the study, the patient will be asked to give consent to participate in the study by signing the ICF.

The investigator shall retain the signed original ICF(s) and give a copy of the signed original form to the patient.

10 Investigator's Obligations

The following administrative items are meant to guide the investigator in the conduct of the study but may be subject to change based on industry and government standard operating procedures, working practice documents, or guidelines. Administrative changes will be reported to the IRB/IEC but will not result in protocol amendments.

10.1 Confidentiality

All laboratory specimens, evaluation forms, reports, and other records will be identified in a manner designed to maintain patient confidentiality. All records will be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the patient, except as necessary for monitoring and auditing by the sponsor, its designee, the FDA, or the IRB/IEC.

The investigator and all employees and coworkers involved with this study may not disclose or use for any purpose other than performance of the study any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

10.2 Financial Disclosure and Obligations

Investigators are required to provide financial disclosure information to allow the sponsor to submit the complete and accurate certification or disclosure statements required under 21 CFR 54. In addition, the investigator must provide to the sponsor a commitment to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

Neither the sponsor nor [redacted] is financially responsible for further testing or treatment of any medical condition that may be detected during the Screening process. In addition, in the absence of specific arrangements, neither the sponsor nor [redacted] is financially responsible for further treatment of the patient's disease.

10.3 Investigator Documentation

Prior to beginning the study, the investigator will be asked to comply with ICH E6(R2) 8.2 and Title 21 of the CFR by providing the following essential documents, including but not limited to:

- IRB/IEC approval
- Original investigator-signed investigator agreement page of the protocol
- Form FDA 1572, fully executed, and all updates on a new fully executed Form FDA 1572
- Curriculum vitae for the investigator and each subinvestigator listed on Form FDA 1572
- Financial disclosure information to allow the sponsor to submit complete and accurate certification or disclosure statements required under 21 CFR 54. In addition, the investigators must provide to the sponsor a commitment to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year after the completion of the study
- IRB/IEC-approved informed consent, samples of site advertisements for recruitment for this study, and any other written information regarding this study that is to be provided to the patient
- Laboratory certifications and normal ranges for any local laboratories used by the site, in accordance with 42 CFR 493

10.4 Study Conduct

The investigator agrees that the study will be conducted according to the principles of ICH E6(R2). The investigator will conduct all aspects of this study in accordance with all national, state, and local laws or regulations. Study information from this protocol will be posted on publicly available clinical trial registers before enrollment of patients begins.

10.5 Adherence to Protocol

The investigator agrees to conduct the study as outlined in this protocol in accordance with ICH E6(R2) and all applicable guidelines and regulations.

10.6 Adverse Events and Study Report Requirements

By participating in this study, the investigator agrees to submit reports of SAEs to the sponsor and/or IRB/IEC according to the timeline and method outlined in the protocol. In addition, the investigator agrees to submit annual reports to the study site IRB/IEC as appropriate.

10.7 Investigator's Final Report

Upon completion of the study, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB/IEC with a summary of the study's outcome and the sponsor and regulatory authorities with any reports required.

10.8 Records Retention

Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational study drug. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

10.9 Publications

After completion of the study, the data may be considered for reporting at a scientific meeting or for publication in a scientific journal. In these cases, the sponsor will be responsible for these activities and will work with the investigators to determine how the manuscript is written and edited, the number and order of authors, the publication to which it will be submitted, and other related issues. The sponsor has final approval authority over all such issues.

Data are the property of the sponsor and cannot be published without prior authorization from the sponsor, but data and publication thereof will not be unduly withheld.

11 Study Management

The administrative structure will include a scientific steering committee and event adjudication committee.

The scientific steering committee, composed of key opinion leaders who are expert in the treatment of patients with cervical dystonia, will consult with the sponsor on the design of the study protocol, review the data, and analyze the data incorporated into the final study report.

11.1 Monitoring

11.1.1 External Data Monitoring Committee

No data monitoring committee is planned for this study.

11.1.2 Monitoring of the Study

The clinical monitor, as a representative of the sponsor, has the obligation to follow the study closely. [redacted]

11.1.3 Inspection of Records

Investigators and institutions involved in the study will permit study-related monitoring, audits, IRB/IEC review, and regulatory inspections by providing direct access to all study records. [redacted]

11.2 Management of Protocol Amendments and Deviations

11.2.1 Modification of the Protocol

Any changes in this research activity, except those necessary to remove an apparent, immediate hazard to the patient, must be reviewed and approved by the sponsor or its

designee. Amendments to the protocol must be submitted in writing to the investigator's IRB/IEC for approval before patients can be enrolled into an amended protocol.

11.2.2 Protocol Deviations

The investigator or designee must document and explain in the patient's source documentation any deviation from the approved protocol. [redacted]

11.3 Study Termination

Although Aeon Biopharma has every intention of completing the study, Aeon Biopharma reserves the right to discontinue the study at any time for clinical or administrative reasons.

The end of the study is defined as the date on which the last patient completes the EOS visit (20 weeks after initial treatment), patient withdrawal (for any reason), or study discontinuation by the sponsor.

11.4 Final Report

Whether the study is completed or prematurely terminated, the sponsor will ensure that the clinical study reports (CSRs) are prepared and provided to the regulatory agencies as required by the applicable regulatory requirements. The sponsor will also ensure that the CSRs in marketing applications meet the standards of the ICH harmonised tripartite guideline E3: Structure and Content of Clinical Study Reports.

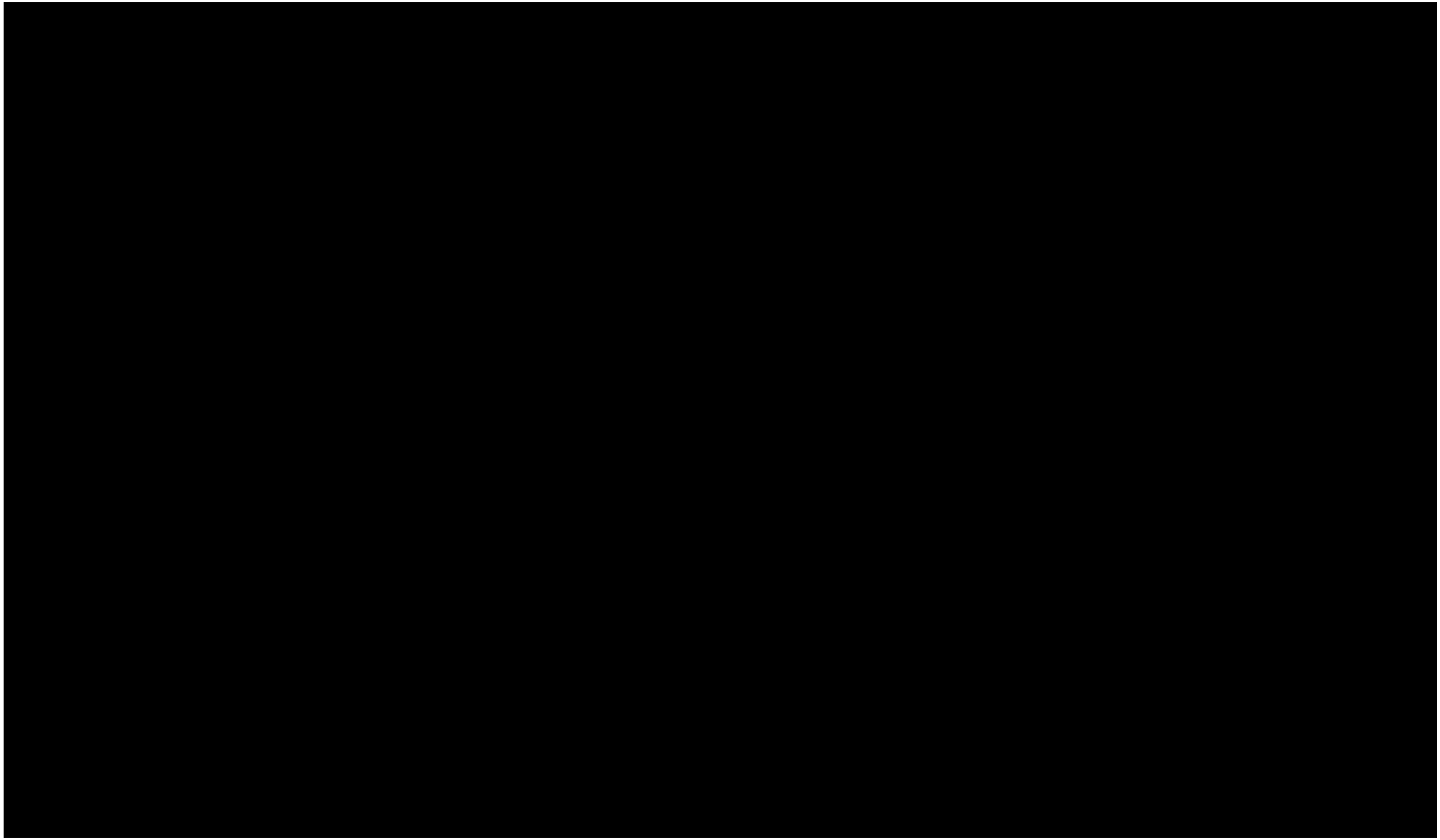
Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the CSR. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results.

Upon completion of the CSR, the sponsor will provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study patients, as appropriate. The study results will be posted on publicly available clinical trial registers.

12 References

[redacted]

[redacted]



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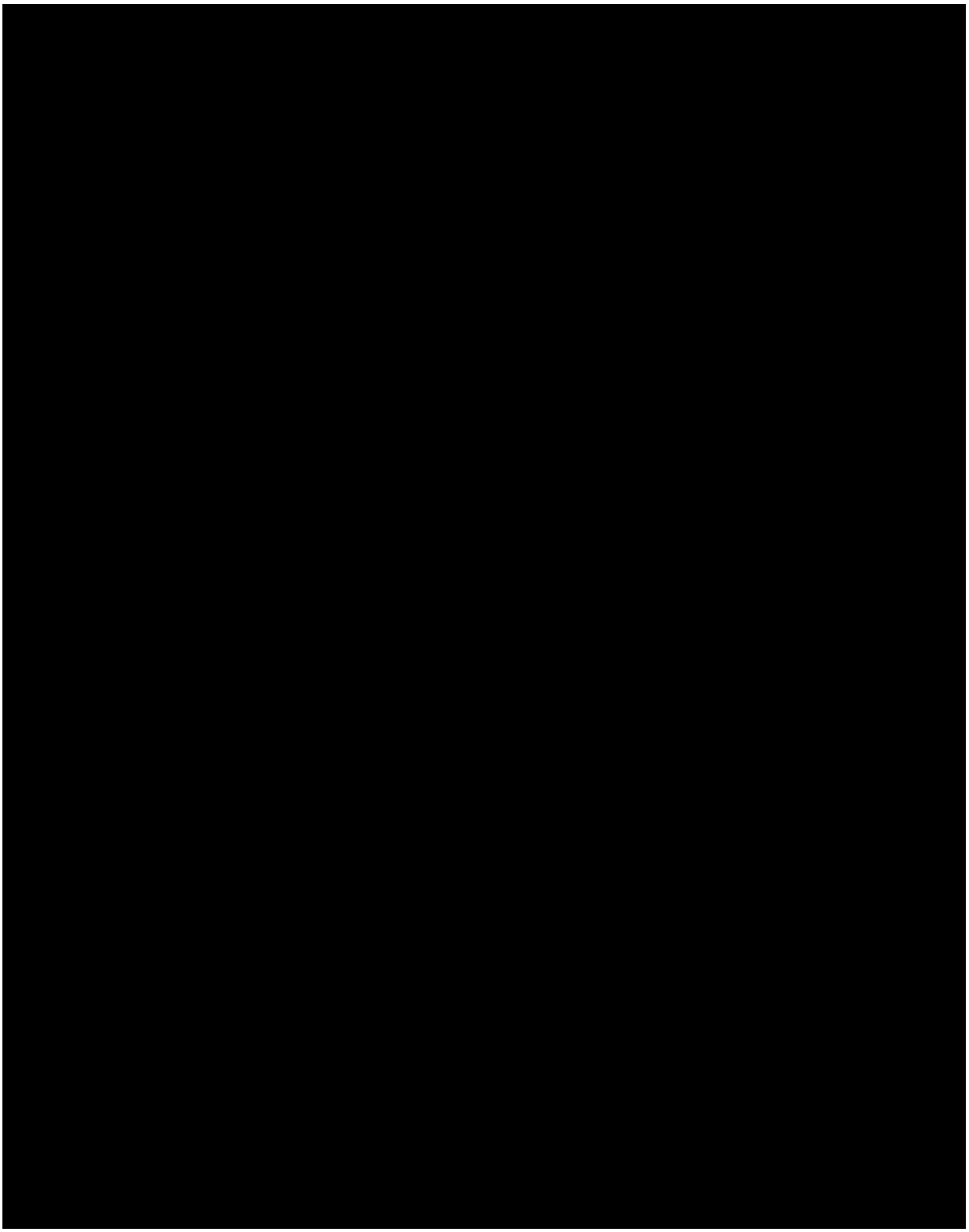
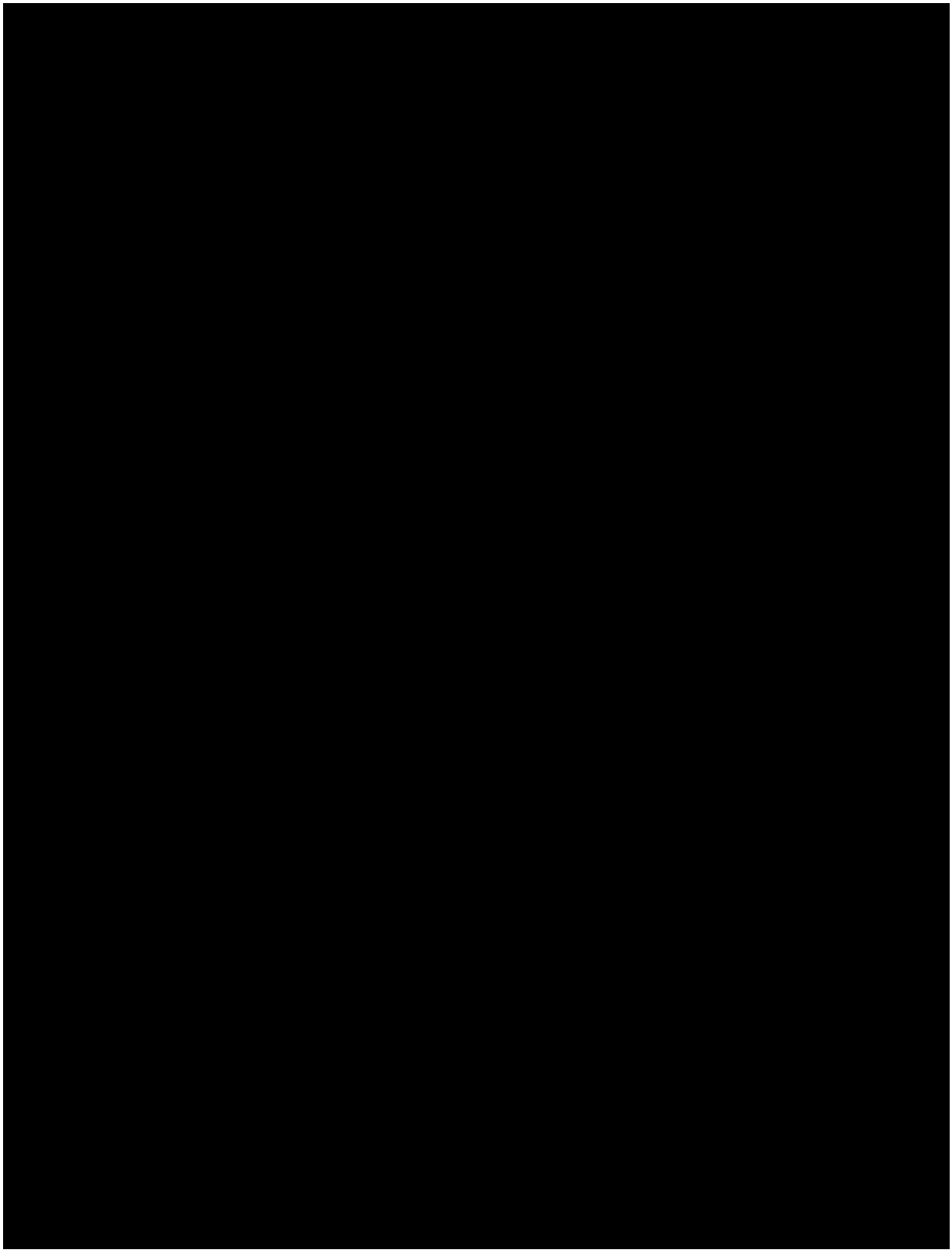
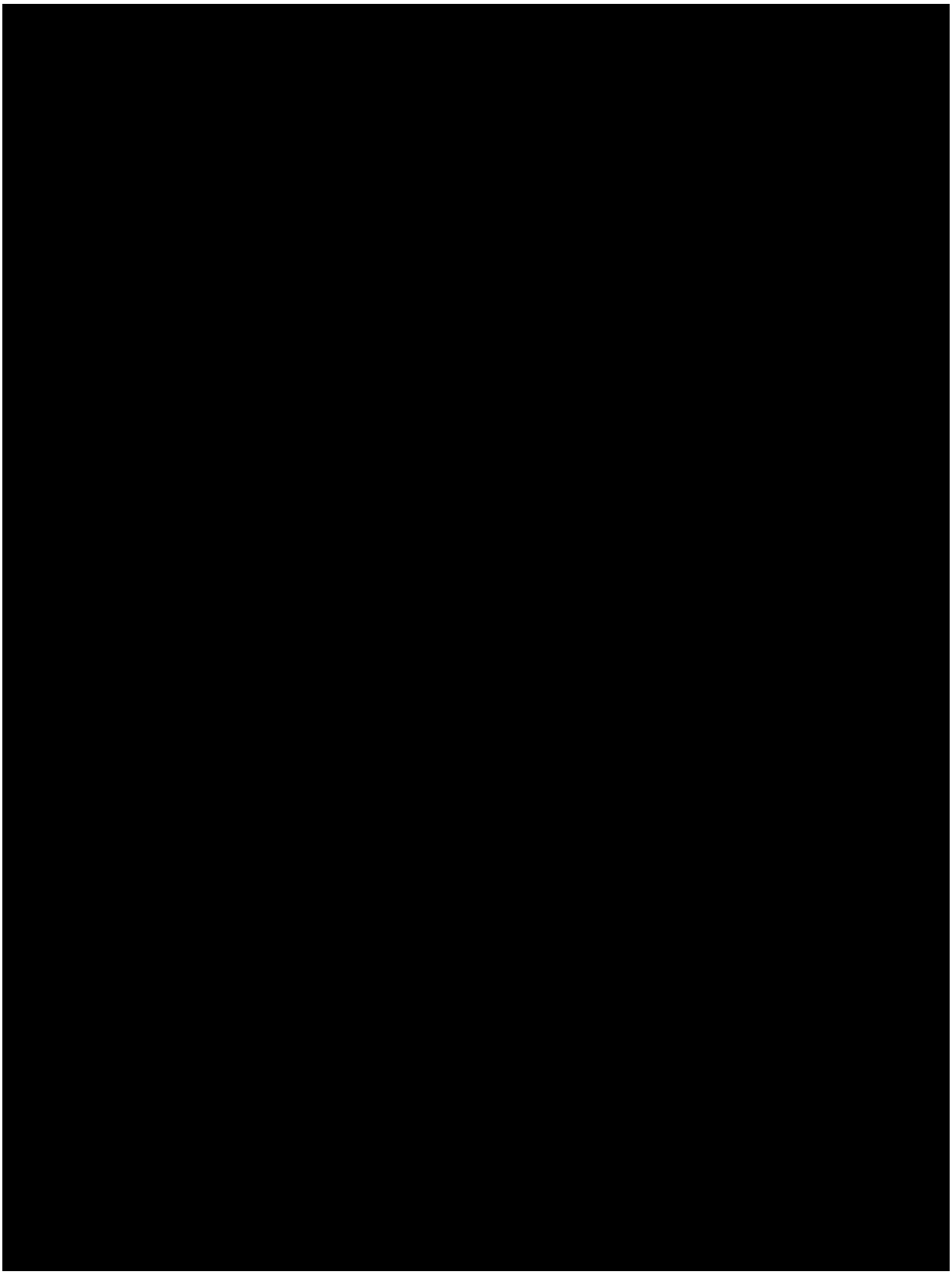
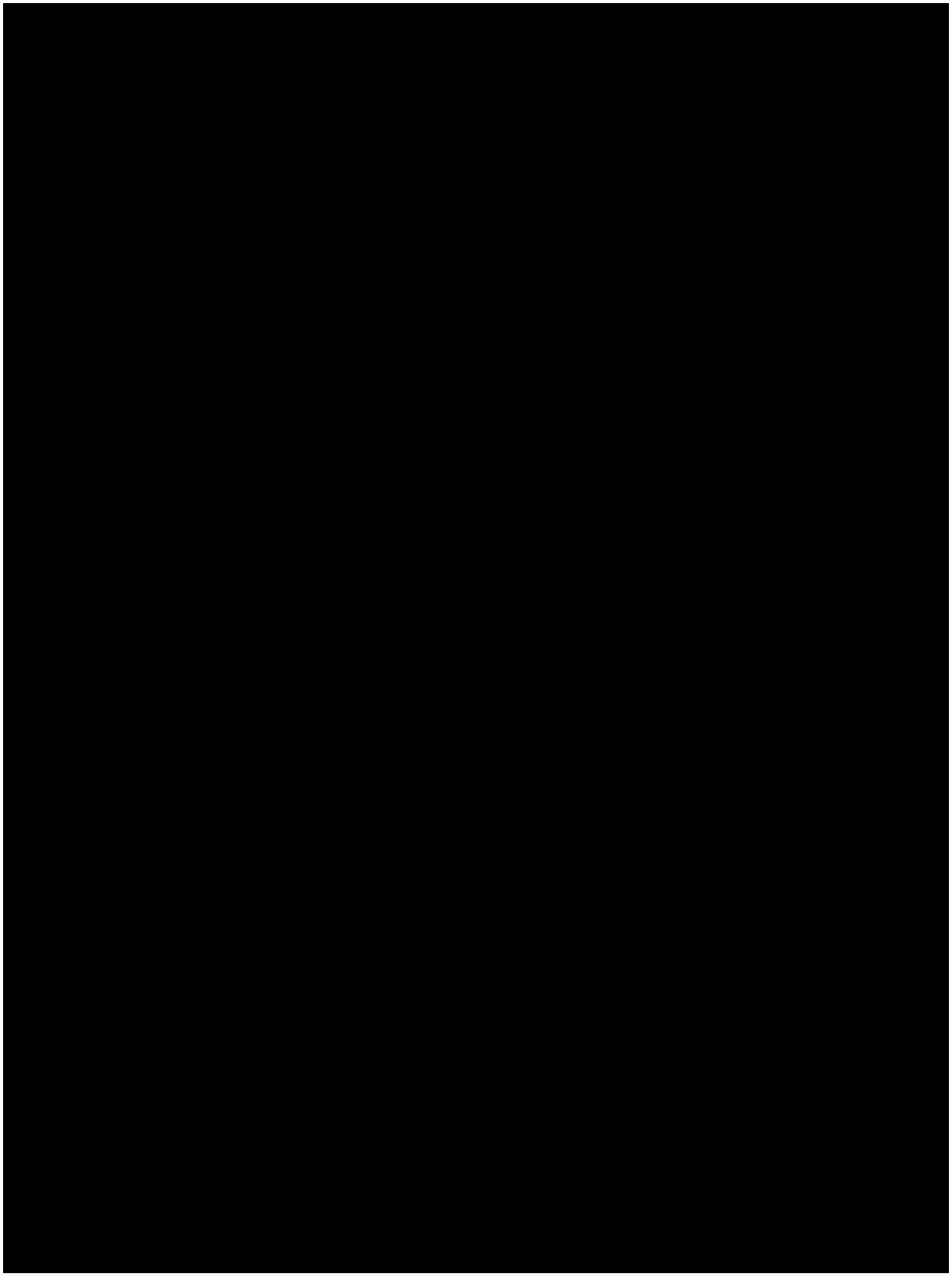
13.2 TWSTRS Scale





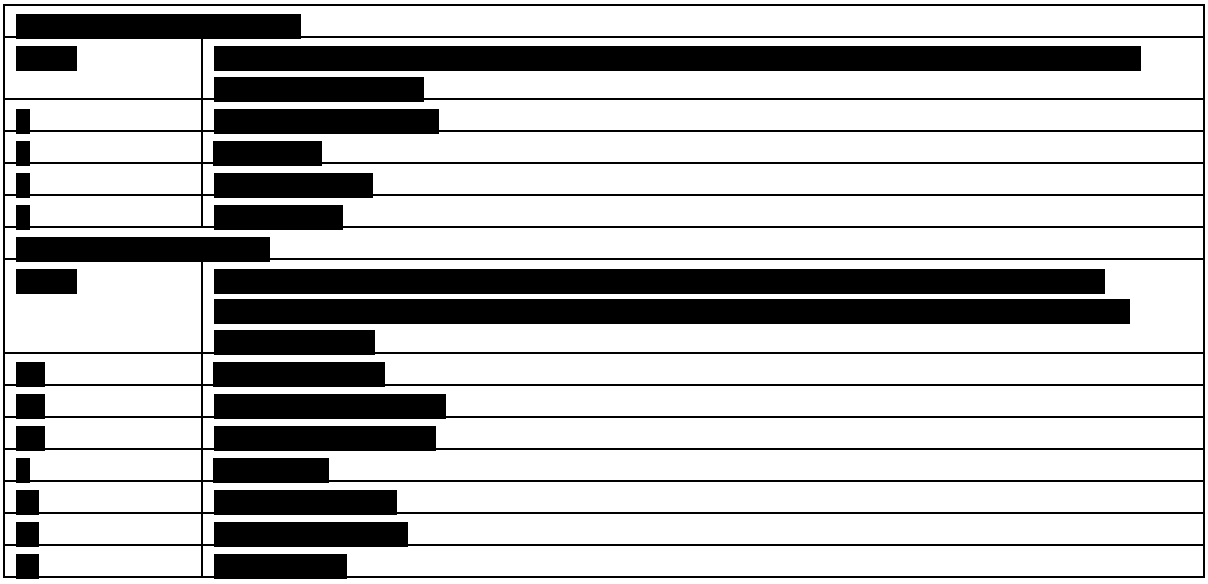




13.3 Dysphagia Severity Scale

[redacted]

13.4 CGI-S and CGI-C Scales



13.5 PGI-S Scale

13.6 PGI-C Scale

13.7 C-SSRS Scale