An Exploratory Randomized Controlled Trial of Participant Satisfaction with the BUILD Mobile Application

NCT05948670

September 8, 2023

Protocol Number:	**W-DISC-001**
NCT Number:	**NCT05948670**
Date	**8/SEP/2023**

W-DISC-001

An Exploratory Randomized Controlled Trial of Participant Satisfaction with the BUILD Mobile Application

Document Type: Clinical Trial Protocol

Clinical Trial Phase: Phase I/II

Version Number: 1.1

CLINICAL STUDY PROTOCOL

An Exploratory Randomized Controlled Trial of Participant Satisfaction with the BUILD Mobile Application

Protocol Number	**W-DISC-001**
Investigational Product	**DISC-MVP**
Sponsor	**Woebot Health** **535 Mission Street, 14th Floor** **San Francisco, CA 94105**
Principal Investigator	**Tim Campellone, PhD** **tim_campellone@woebothealth.com**
Version	**1.1**
Date	**8/SEP/2023**

This study will be performed in compliance with the principles of Good Clinical Practice.

Protocol Version and Amendment Tracking

Version	Date	Brief Summary of Changes
1.0/	**22/MAY/2023**	**Original Protocol**
1.1	**8/SEP/2023**	**Minor changes to study protocol. Reformatted mobile app name from Build to BUILD. Updated Day 1 to be defined as the date of randomization. Made explicit reference to Lindus Health as the recruitment vendor and study platform manager. Added clarifying language regarding the language detection protocol and subsequent transcript review process. Updated titles for the SAC members.**

Confidentiality Statement

Protocol Signature Page | Sponsor

This protocol has been reviewed and approved by the representative(s) listed below. Any modification of the protocol must be agreed upon by the Sponsor and the investigator and must be documented in writing.

Woebot Health Representative(s):

_____ _____

[Principal Investigator or Sponsor Signature] [Signatory Date]

_____

[Name and Title of Signatory]

Protocol Signature Page | Principal Investigator

I have read this protocol, which has been agreed by Woebot Health, and given approval/favorable opinion by the institutional review board, and I agree that it contains all necessary details for my staff and I to conduct this study as described. I will provide copies of the protocol and any amendments to all study personnel under my supervision and provide access to all information provided by Woebot Health or their specified designees. I will discuss the material with the study personnel to ensure that they are fully informed about the study.

I understand that information contained in or pertaining to this protocol is confidential and should not be disclosed, other than to those directly involved in the execution or the ethical review of the study, without written authorization from Woebot Health. It is, however, permissible to provide information to a participant in order to obtain consent.

I agree to conduct this study according to this protocol and to comply with its requirements, participant to ethical and safety considerations and guidelines, and to conduct the study in accordance with the Declaration of Helsinki, International Council for Harmonisation guidelines on Good Clinical Practice, and applicable regional regulatory requirements.

I agree to comply with the procedures described for data recording and reporting and to permit monitoring and auditing by Woebot Health and inspection by the appropriate regulatory authorities.

I agree to make my participants' study records available to Woebot Health personnel, their representatives, and relevant regulatory authorities in order to verify data that I have entered in the case report forms. I will retain the study-related essential documents until Woebot Health indicates that they are no longer needed. I am aware of my responsibilities as an investigator as provided by Woebot Health.

I understand that Woebot Health may decide to suspend or prematurely terminate the study at any time for whatever reason; such a decision will be communicated to me in writing. Conversely, should I decide to withdraw from execution of the study, I will communicate my intention immediately in writing to Woebot Health.

_____	_____
[Principal Investigator Signature]	[Date]
_____	_____
[Name and Title]	[Site]

Protocol Synopsis

Protocol Number:	**W-DISC-001**
Full Title:	**An Exploratory Randomized Controlled Trial of Participant Satisfaction with the BUILD Mobile Application**
Abbreviated Title:	**Participant Satisfaction with the BUILD Mobile Application**
Sponsor:	**Woebot Health**
Study Type:	**Product learning**
Number of Participants:	**~165 (150 complete)**
Number of Sites:	**1**
Study Objective:	**The overarching goal of this study is to explore satisfaction with a version of Woebot that leverages Large Language Models (LLMs) to recreate core therapeutic experiences. As a benchmark for understanding the relative performance, this LLM MVP of Woebot will be compared against a version of Woebot that does not use LLMs.**
Primary Aim and Endpoint:	**Aim: To explore user satisfaction with the DISC-MVP** **Endpoints: Client Satisfaction Questionnaire for both treatment groups.**
Secondary Aims and Endpoints:	**Aim: To explore user satisfaction with DISC-MVP for users with mild symptomatology or above (PHQ-8 or GAD-7 >= 5).** **Endpoint: Client Satisfaction Questionnaire for both treatment groups.**
[redacted]	[redacted]

	[redacted]
Study Design:	**Randomized controlled trial**
Study Duration:	**2 week intervention period**
Target Population:	**Adults with or without clinical symptoms**
Key Inclusion Criteria:	**1. Be 18+ years of age and older (no upper limit)** **2. Own or have regular access to a smartphone with a recent operating system installed (Android: 0S 8.0 or higher, Apple: iOS 13.0 or higher) with reliable Wi-Fi access or sufficient data plan to engage with assigned treatment condition for the duration of the study** **3. Available and committed to engage with the program and complete assessments for a 2-week duration** **4. Able to read and write in English** **5. Participants must have primary residence in the United States**
Key Exclusion Criteria:	**1. Current suicidal ideation with a plan and/or intent or a suicide attempt within the past 12 months** **2. Previous Woebot use**
Study Conditions:	**DISC-MVP**

	DISC-CON
Test Device:	**DISC-MVP**
Control Device:	**DISC-CON**
Statistical Methods:	**Descriptive statistics will be reported for study measures for each study arm as well as the total sample. Summary reports will be presented for all time periods independently.** [redacted]
Protocol Version and Date:	**1.1 (8/SEP/2023)**
Keywords:	**digital mental health intervention, chatbot, conversational agent, relational agent, natural language processing, artificial intelligence**

Table of Contents

Schedule of Events

Visit Weeks/Days	Screening Period *Screening / Baseline* *Day -6 to Day 1*	Treatment Period *Week 1* *Day 3 (+2)*	Treatment Period *Week 2 (EOS/ET)* *Day 14 (+6)*
Informed Consent	X		
Eligibility Confirmation (Inclusion/Exclusion)	X		
Demographics	X		
Psychiatric History	X		
Prior & Concomitant Medications/Therapy	X		X
[redacted]	[redacted]		
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]		[redacted]
Participant Identity Verification [a]	X		
Randomization	X		
Register within the Study Application	X		
CSQ-8 [b]			X
[redacted]		[redacted]	[redacted]
[redacted]		[redacted]	[redacted]
[redacted]		[redacted]	[redacted]
[redacted]			[redacted]
Assessment of AE/SAEs			X
App Engagement Metrics (collected throughout study)			X
Termination of App Access			X

[a] Video call with designated study team member **[b] Self-Report Clinical Assessment**

EOS = End of Study

CSQ-8 = Client Satisfaction Questionnaire; [redacted]

Participants will have up to one week from the time of providing informed consent to complete all screening and baseline tasks including registering for the study application. Participants will not be withdrawn for failing to register for the app. Date of randomization will be considered Day 1.

1. Introduction

1.1 Background

Conversational agents (also known as chatbots) create an interactive experience through a sustained dialogue with a user. To date, the vast majority of these agents use rule-based logic that enables pre-written responses to be served up in response to user inputs (either free-text or button presses). The nature of these interactions can limit how personalized any conversation can be as responses are not based on understanding of the full nature of the content a user is expressing. Large Language Models (LLMs) provide the opportunity to better understand natural language and generate responses based on this understanding. As such, LLMs may enable more naturalistic conversations with personalized responses based on a fuller understanding of the intent expressed in a user's statement.

1.2 Study Rationale

The overarching goal of this study is to explore the feasibility and acceptability of a Minimally Viable Product (MVP) of Woebot, a natural language powered relational agent, that leverages LLMs to augment core therapeutic experiences. In a previous study, results demonstrated that Woebot is able to establish levels of therapeutic bond equivalent to those of a human mental health professional[1]. Here, this study is looking to explore how integrating LLMs into Woebot impacts both the user experience of Woebot as well as the therapeutic bond that drives the relational agent mechanism of behavior change.

1.3 Investigational Device

Woebot is an automated relational agent based on researched and scientifically validated psychotherapies, primarily CBT, and accessible via iOS and Android applications. [redacted]

The Woebot LLM MVP (referred to as MVP moving forward) is a minimal version of Woebot [redacted]

[redacted]

[redacted]

[redacted] the MVP will be compared against a version of Woebot that contains the same scope of features, but does not use LLMs. For safety, both the MVP and control will use the established Language Detection Protocol (see section 8.5.2 for more details).

2. Objectives

2.1 Primary Aim

- To explore user satisfaction with the DISC-MVP
    - Endpoint:
        - Client Satisfaction Questionnaire (CSQ-8) for both treatment groups

2.2 Secondary Aim

- To explore user satisfaction with the DISC-MVP for users with mild symptomatology or above (i.e., baseline PHQ-8 or GAD-7 >=5)
    - Endpoint: CSQ-8 for both treatment groups.

[redacted]

3. Study Design

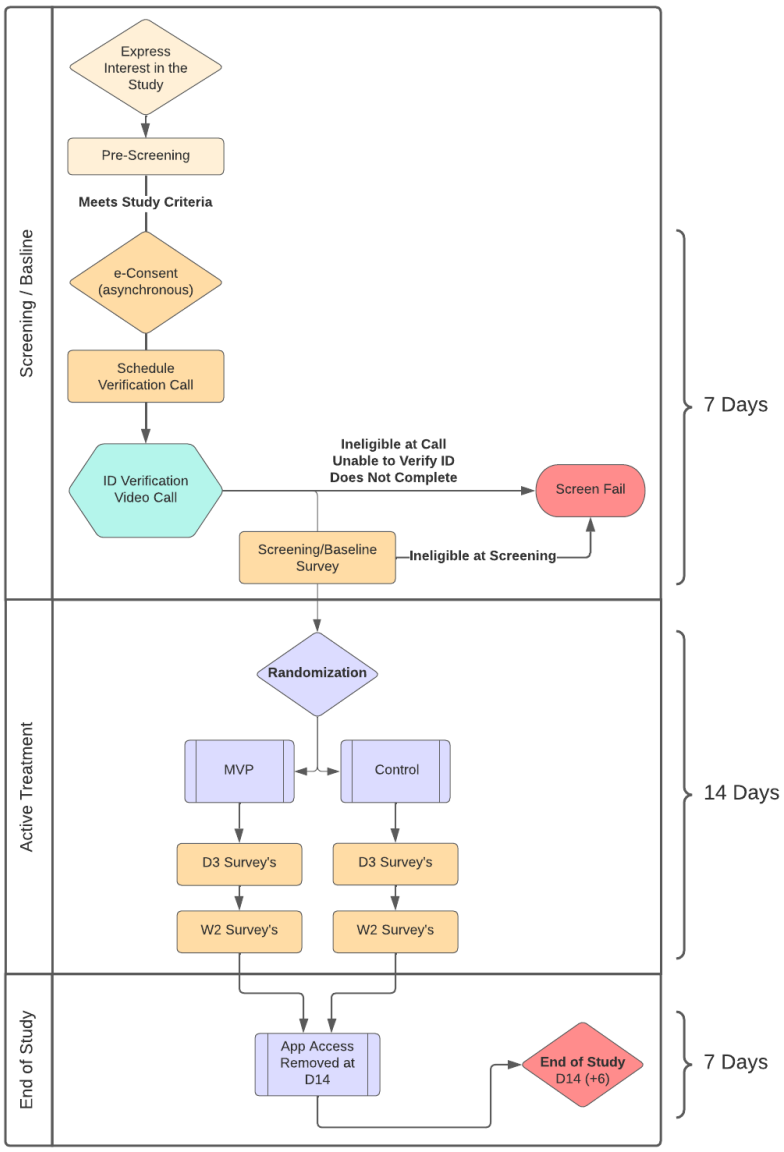
3.1 Description of Trial Design

This study is a double-blind, randomized controlled trial (RCT) exploring user satisfaction with an augmented version of Woebot and a previous version of Woebot among a sample of adults. Participants who consent and meet study eligibility criteria will be randomized 1:1 into one of the 2 arms. Study participation is up to 4 weeks in total, including a 1 week screening/baseline phase followed by a 2 week active intervention phase, and 1 week to complete the final study survey.

Participants will be recruited and enrolled into the study by Lindus Health . All remaining data collection and study monitoring will be managed through the Citrus decentralized trial platform managed by Lindus Health and by designated Woebot Health study personnel.

Self-report survey assessments will be administered to all participants at Screening/Baseline, Day 3, and Week 2. Members of the study team may contact participants through the Citrus platform via phone/sms and/or email to remind participants to complete study activities.

3.1.2 Participant Journey Flowchart



[redacted]

3.3 Participant Assignment, Randomization, and Blinding

3.3.1 Participant Assignment

Following confirmation of eligibility, participants will be randomly assigned to one of the two treatment groups.

3.3.2 Randomization

Randomization into the treatment arms will be 1:1 with no additional stratification by group demographics. The study may over enroll in order to meet 75 completed participants in each treatment arm. Participants will be considered randomized once they complete all of their screening and baseline activities including surveys, their identity has been verified, and eligibility has been confirmed (e.g., checked for duplicate registrations).

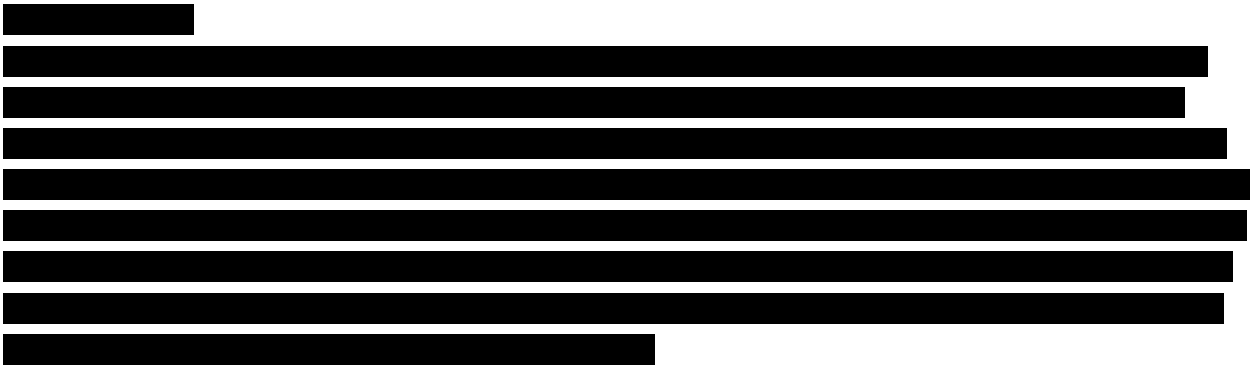
3.3.3 Blinding and Unblinding

Participants will be blinded to their assigned treatment group. The primary research associate and project manager remain unblinded. Every effort will be made to keep a majority of the research staff blinded including study PI (unless there is a safety event which would require them to become unblinded for follow-up) and those conducting study analyses.

4. Trial Intervention

4.1 Study Conditions

Both treatment conditions will be available through a bespoke study app called the 'Build' app and will be made available exclusively for study participants through unique access codes.



[redacted]

4.3 Trial Intervention Compliance

Trial intervention compliance will not be monitored in this study and participants will not be removed from the study for failing to register and/or not regularly engaging with their assigned treatment. Instead, intervention compliance will be assessed post study during analysis. Compliance may be defined as opening the app at least once per week for a minimum of 50% of weeks (1 of 2) during the intervention period.

[redacted]

5. Study Population

Participants will be recruited through the Lindus Health CitrusRecruit network which utilizes a combination of participant sources including but not limited to existing patient databases, primary care networks, and targeted social media campaigns. Those interested in participating will be invited to complete a survey to confirm they meet the pre-screening criteria (excluding questions about suicidal ideation and attempt) and be presented with the opportunity to independently review and electronically sign the study consent form. Upon signing the consent form, participants will be asked to schedule a video call during which a designated member of the virtual site team will verify the participants identity. After successful completion of the verification call, participants will be provided with a secure link to complete the screening/baseline survey. Participants will be asked questions about their current suicidal ideation with plan and/or intent as well as an attempt in the past 12 months. People who do not meet study criteria based on suicidal ideation/attempt will be notified that they may benefit from a level of care beyond the scope of the study and that if they feel they are in need of immediate medical care they should contact 911 or go to their nearest emergency room and reach out to someone they trust that can help them stay safe. Additional resources will also be provided electronically. If a participant endorses

presence of current suicidal plan and/or intent, the study PI will attempt to follow-up with the participant (up to three times). See Section 8.5.1 of this protocol for more details.

Approximately ~165 adults will be randomized for this study to ensure a final sample of 150 completers (e.g., randomized and completed all study activities through Week 2; assuming a 10% attrition rate).

5.1 Selection of Study Population

5.1.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Be 18+ years of age and older
2. Own or have regular access to a smartphone with a recent operating system installed (Android: 0S 8.0 or higher, Apple: iOS 13.0 or higher) with reliable Wi-Fi access or sufficient data plan to engage with assigned treatment condition for the duration of the study
3. Available and committed to engage with the program and complete assessments for a 2-week duration
4. Able to read and write in English
5. Participants must have primary residence in the United States

5.1.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Current suicidal ideation with a plan and/or intent or a suicide attempt within the past 12 months
2. Previous Woebot use

5.2 Screen Failures

Participants who sign study consent and do not meet inclusion/exclusion criteria at Screening, will be considered a Screen Failure. Participants will be notified that they did not meet eligibility criteria and provided with a set of resources. Re-screens will not be permitted in this study. De-identified participant ID numbers assigned to participants who screen fail will not be reused.

5.3 Withdrawal of Participants from the Study

If a participant decides to withdraw consent from the study, they will be removed from future study activities and any data collected before withdrawal may be retained and used in study analyses. In addition, a participant may be withdrawn by the investigator if the participant violates the study plan, or for administrative and/or other safety reasons.

Discontinuation of study treatment for a participant occurs when study treatment is stopped earlier than the protocol planned duration and can be initiated by either the participant or the investigator. The investigator must discontinue study treatment for a given participant if he/she believes that continuation would negatively impact the participant's well-being. Involvement in the study is strictly voluntary. Participants have the right to withdraw from the study at any time for any reason, without any reprisal.

Participants should be discontinued from the study if any of the following occur:

1. It is discovered that the participant shared app images/screenshots publicly
2. The participant withdraws consent to participate in the study
3. The participant develops an illness that would interfere with their continued participation in the study
4. The participant has an SAE rated as Grade 3 (severe) or higher (see Section 8.3.2)
5. The participant is noncompliant with treatment schedule, study procedures, in the opinion of the investigator and per the protocol, where applicable
6. The PI, Sponsor, IRB, or regulatory agency requests withdrawal of the participant
7. Any other reason relating to the participant's safety or integrity of the study data as determined by the Safety Assessment Committee (SAC)

Participants who withdraw or are withdrawn from the study may be replaced. Participants who withdraw or are withdrawn from the study cannot subsequently rejoin the study.

If a participant withdraws or is withdrawn from the study for reasons related to safety, the study Sponsor-Investigator and SAC will be informed immediately.

If the participant withdraws consent for disclosure of further information, the Sponsor-Investigator may retain and continue to use any collected data before such a withdrawal of consent.

Although a participant is not obliged to give a reason for withdrawing from a study, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the participant's rights.

6. Study Assessments and Procedures

All assessments, and their corresponding administration points, are listed in Table 1.

6.1 Screening/Baseline Assessments and Procedures

6.1.1 Demographic Questions

In an effort to ensure equitable access and representation as well as assess clinical efficacy in diverse populations, Woebot Health has researched current best practices and language around demographic data collection, and developed a health equity demographic battery. The demographic battery consists of age, biological sex, gender identity, sexual orientation, race, ethnicity, education, marital status, employment status, living situation, able bodiedness, physical health conditions, and health insurance status.

6.1.2 Psychiatric History

Participants will be asked to complete questions about their history of diagnosed mental health disorders.

6.1.3 Concomitant Medication and Therapy

Participants will be asked to complete questions evaluating whether they are currently seeing a mental health professional (i.e., therapist, social worker), whether they are currently taking any psychotropic medications, as well as satisfaction with concurrent mental health treatment.

[redacted]

6.1.5 Eligibility Verification Call

After signing the study eICF, participants will be asked to schedule an eligibility verification video call with a member of the decentralized study team. During this call the designated member of the study team will ask the participant to verify their identity (e.g., show a government issued ID), confirm their contact information and DOB.

6.2 Efficacy Assessments and Procedures

6.2.1 Satisfaction

<u>The Client Satisfaction Questionnaire (CSQ-8)</u>

The CSQ-8 is an 8-item measure used to assess client's satisfaction with treatment on a 4-point scale (1 = "very dissatisfied" to 4 = "very satisfied"). Example questions include, "how would you rate the quality of service you received?" and "did you get the kind of service you wanted?" Total sums range from 8-32, with high scores indicating greater satisfaction with Woebot. The CSQ-8 has been widely disseminated and considered both valid and reliable (α ranges = .83-.93).[2]

[redacted]

[redacted]

Safety Assessments

Safety events will be captured through participant spontaneous report, in-app content, and via a self-report assessment of Adverse Events (AE) collected at the Week 2/EOS visit. See Section 8.5 for further detail.

7. Study Stopping Rules

Study procedures will be stopped if the Sponsor-Investigator, in discussion with the SAC and/or IRB as applicable, determines that the number and/or severity of AEs justify putting the study on hold.

The study may resume following the safety review, if the Sponsor-Investigator agrees it is safe to proceed.

The Sponsor-Investigator may initiate study closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

7.1 Early Study Termination

The study can be terminated by the Sponsor-Investigator at any time. Reasons for early termination include:

- Study recruitment or retention is too low for the study to provide meaningful results
- Unanticipated, significant, or unacceptable safety risk to participants enrolled in the study
- Decision based on recommendations from Sponsor-Investigator and SAC after review of safety and efficacy data

- Discontinuation of study if Sponsor-Investigator, in collaboration with study team members and SAC, determine from planned analyses that the app is not efficacious or if there are safety concerns.

In making the decision to terminate, the Sponsor-Investigator and SAC will always consider the participants' welfare and safety. Should early termination be necessary, participants must be contacted as soon as possible to conduct EOS assessments, if willing, and treated as a prematurely withdrawn participant. Additional procedures may be provided to ensure that adequate consideration is given to the protection of the participant's interests. The Sponsor-Investigator will be responsible for informing Institutional Review Boards (IRB) of the early termination of the trial.

8. Data and Safety Monitoring

8.1 Risk and Benefit Assessment

8.1.1 Risks

Given that the research aims to enroll participants into a low-risk intervention, we do not anticipate that participation in the study will be associated with elevated risk. [redacted] The overall evaluation of risk is that it is low.

8.1.2 Procedures for minimizing risk

Misunderstanding the Capabilities of the Application

The 'Build' app is not intended to be a crisis service, however there is the potential that participants may misunderstand the limitations of the app. To mitigate this risk, the study will provide clear information on the capabilities of the app, intended use, and limitations of the app at consent, randomization, and key points throughout. Resources are also accessible within the app as well as will be sent to the participant in the event that they are requested.

Data Breach

All study data are gathered on either a HIPAA-compliant web platform that resides behind Woebot Health security firewalls or via HIPAA-compliant online platforms, thus actual risk from data breach for study data is low. Research material obtained from human subjects will include self-report questionnaires and conversations and engagement data within the 'Build' app. All data obtained via Woebot will be encrypted and stored on Amazon Web Services (AWS) and/or Google Cloud Platform; Woebot Health data gathering and storage procedures are compliant with both HIPAA and the European Union's General Data Protection Regulation. Only members of the research team will have access to identifiable study data. De-identified data will be accessible to the product development team (designers, user researchers, and product managers) as well as the research team.

Potential Upset due to Study Procedures

Foreseeable risks to participants include the possibility that some assessment questions and/or treatment procedures may be upsetting to participants. Experience with similar populations has indicated that the risk of emotional upset during the assessments is low and if it occurred, the upset would likely be temporary and not be serious in nature. Such risks will be minimized by the thoughtful

selection of questionnaires. Participants will also be informed that they may withdraw from the study at any time and if requested, appropriate resources will be provided.

There is also a potential risk for upset upon discontinued access to the study intervention at end of treatment/study (Week 2). Participants are informed during the consent process and are reminded at onboarding of how long they will have access to the intervention for. Return to care and other resources are provided upon removing access to the 'Build' app.

Participants can refuse and withdraw from participation at any time. If they withdraw consent from the study, they will no longer have access to the study treatments.

8.1.3 Benefits

When evaluating the risks and benefits of the proposed study, it is believed that risks are relatively minimal when compared to the potential [redacted] benefits that subjects are likely to receive. The benefits of receiving Woebot include potentially improving mood (anxiety, stress, and/or depression), acquiring practical psychotherapeutic skills (from cognitive behavioral therapy, dialectical behavior therapy, and mindfulness), and receiving psychoeducation about mental health.

Participants who improve mood may derive additional benefits should said mood improvements be associated with other psychological improvements such as interpersonal or occupational functioning. Study of the effectiveness of this intervention will also benefit society more generally by providing data on the utility of Woebot t.

8.2 Adverse Events

8.2.1 Definitions

Adverse Event (AE): An AE is any unanticipated medical occurrence in a clinical study participant using an investigational product or from study procedures that does not necessarily have a causal relationship with this product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.

Serious Adverse Event (SAE): Any SAE is any AE that meets any of the following criteria:

- Results in *death*
- Is *life-threatening*
- Requires inpatient *hospitalization* or prolongation of existing hospitalization
- Results in persistent or significant *disability/incapacity*
- Is a *congenital anomaly/birth defect*
- Is an *important medical event* that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

Unanticipated Problem (UAP): A UAP is an incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e., not described in study-related documents such as the IRB- or IEC-approved protocol or consent form)
- Related or possibly related to participation in the research (i.e., 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)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

An individual AE observed during the conduct of a study may be considered an unanticipated study problem involving risk to human subjects, and reported to the IRB, only if it is unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant and, usually, safety-related change in the protocol such as revising the inclusion/exclusion criteria or including a new monitoring requirement or informed consent). Investigators should report possible UAP to the Sponsor and the Sponsor will make a determination for the UAP in the context of the study and any change to the study.

Adverse Device Effect (ADE): Any adverse event related to the use of an investigational medical device. This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. This also includes any event that is a result of a use error or intentional misuse.

Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on the health or safety, or any life-threatening problem or death caused by or associated with a device which was not previously identified in nature, severity or degree of incidence in the protocol, Instructions for Use, Summary of Previous Studies Document, or other sources of information for the investigational product. Additionally, a UADE is any other unanticipated serious problem associated with the investigational device that relates to the rights, safety, or welfare of subjects.

UADEs will include events meeting either A or B as stated below:

A. Events meeting ALL of the following criteria:

- Not included in the list of Anticipated Events (refer to protocol section 8.2.2)
- Related (possibly, probably, or definitely) to the investigational device per the site principal investigator
- Serious (meets any of the SAE criteria)

B. Any other unanticipated serious problem associated with the investigational device that relates to the rights, safety, or welfare of participants.

Device Deficiencies: Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. The reporting of a Device Deficiency is a Product Complaint.

Product Complaints: Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

8.2.2 Previously Noted Adverse Device Effects

Any ADE that is not identified in nature, severity, or is not listed below is considered unanticipated:

- There are no known ADEs at the time of writing this protocol.

8.3 Assessment of Adverse Events

Due to the low-risk profile of this study, adverse and serious adverse events are not anticipated. The investigator will be alert to any complaints or adverse reactions that arise and will take appropriate steps to alleviate the difficulties as soon as possible.

Existing disclaimers that the 'Build' app is not intended for crisis management will be presented in the ICF and at onboarding. Adverse events (AEs) will be assessed via:

1) Spontaneous participant self reports communicated outside of the 'Build' app
2) Direct participant self reports collected via the Week 2 survey at EOS
3) Language Detection Protocol (e.g., helplines feature)
4) Upon review of select conversations/transcripts with Woebot

All potential AE/SAE triggers described above will follow a predetermined safety protocol as outlined in a Safety Management Plan (SMP). In the event of a suspected AE, the Principal Investigator would be immediately alerted, and unblinded if indicated, as well as provided with all available clinical and other details of the event. Based on the initial report, appropriate steps would be taken to gather further information from the participant as needed, address the AE/SAE, and complete reporting requirements. The study team will make every effort to follow-up with the participant within 3 business days of the initial report.

8.3.1 Time Frame

Collection of AEs and SAEs will begin at ICF signature, and will continue through End of Study (EOS) at Week 2.

8.3.2 AE Severity

Investigators will grade the severity of all AEs using the Common Terminology Criteria for Adverse Events (CTCAE). If possible, investigators should report event terms that reflect a single, unifying diagnosis rather than individual signs or symptoms (e.g., "influenza" instead of "coughing, body aches, fever;" and "anemia" rather than "low hemoglobin").

If an AE term is not listed in the CTCAE criteria, a corresponding grading is to be performed by the investigator based on his/her best medical judgment as follows:

- **Mild (Grade 1):** asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- **Moderate (Grade 2):** minimal, local, or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living (ADL)
- **Severe (Grade 3):** medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care ADL
- **Life-threatening (Grade 4):** life-threatening consequences; urgent intervention indicated
- **Fatal (Grade 5):** death related to an AE

8.3.3 AE Causality

An event's relatedness to the investigational device will be determined by the Principal Investigator and classified under the following causality ratings:

- **Non-related:** There is no evidence of any causal relationship.
- **Related:** There is clear evidence of a casual relationship between the device and event; all other explanations have been ruled out.

8.4 Documenting and Reporting AE and SAEs

The designated study team will report an event to the Sponsor-Investigator within 24 hours of awareness. The investigator should make every attempt to obtain as much information as possible and must assess the relationship of the event to the study device and complete the AE/SAE assessment form. It is understood that more may be learned about the event after the initial report and this information may and should be updated as collected.

Any event that the sponsor determines is/are reportable to the IRB will be made within 5 working days of when the Sponsor-Investigator makes that determination. If it should be determined that an event presents an unreasonable risk to all participants, the study or parts of the study presenting that risk will be terminated as soon as possible.

8.5 Safety Monitoring

8.5.1 Safety Procedures At Screening

Study participants will be asked to self-report on recent suicidal thoughts including current suicidal ideation with plan and/or intent as well as attempts in the past 12 months. Responses are not monitored in real time. Participants who endorse having a current suicidal plan and/or intent or an attempt in the past 12 months will be excluded from the study. Participants will be notified that:

- They may benefit from a level of care beyond the scope of the study and investigational treatment.
- They should call 9-1-1 or go to their local emergency room and reach out to someone they trust and can help them stay safe if they feel they are in crisis or in need of medical attention.
- Will be electronically provided with a list of resources.

Participants who endorse current suicidal ideation with a plan and/or intent will also be notified that a member of the study team will attempt to follow-up with them. Three attempts will be made by the Study PI to contact participants with the third being by email and efforts/resolution will be documented in accordance with the study protocol. The study team will make every effort to follow-up with the participant within 3 business days of the initial report.

8.5.2 Unscheduled Visits

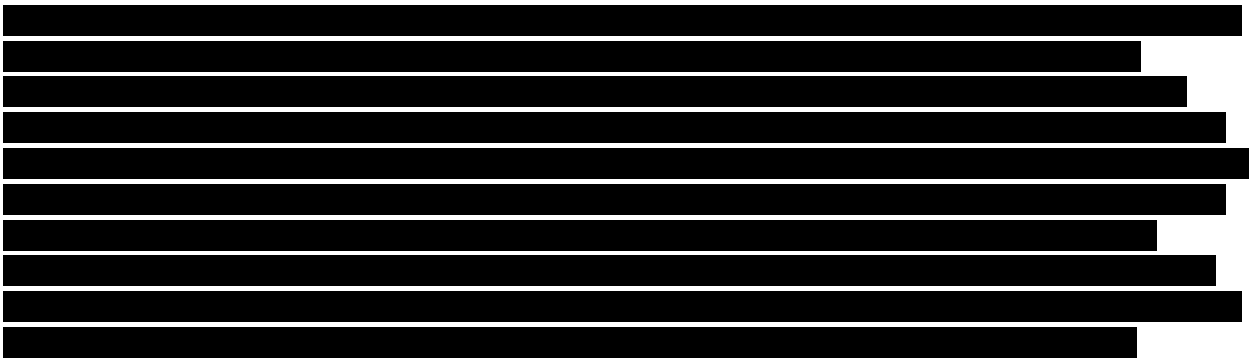
Study participants are welcome to initiate contact anytime throughout the duration of the study. If the contact is attributable to safety reasons or if the study team learns about a suspected safety event at any time, then an Unscheduled Visit would ensue, wherein the qualified study personnel would attempt to follow-up with the participant, and if it is determined that they are in immediate risk for hurting themselves or others, appropriate steps would be taken.

8.5.3 Week 2/EOS Safety Event Self-Report

Study participants will be asked to self-report on potential safety events at the Week 2 / EOS timepoint. Questions will explicitly ask about changes since starting the study (about 2 weeks ago) in their (1) mental and/or physical health, (2) any new thoughts about ending their life including new intent/plan/or attempts, and (3) any worsening of symptoms that led to changes in their medical care including medications taken for a psychiatric condition and/or therapy. Information gathered through this survey will be used to inform the need for follow-up, AE/SAE/UADE determination, and resolution.

8.5.4 Language Detection Protocol (LDP)

In addition to the onboarding screens re-stating that Woebot is not a crisis service, Woebot has a Language Detection Protocol (LDP), developed by Woebot Health. The LDP is available and operates the same regardless of assigned intervention group. The purpose of the LDP is to detect potentially concerning topics within participant-input free-text and will be enacted for all participants regardless of treatment condition. Upon detection of any concerning topics, LDP initiates a conversation to remind the participant of the application's limitations of services and offer a resource list which includes readily accessible support channels. If a possible mention of concerning topics is detected, the participant is reminded of the limitations of services (which they will have already seen in both the informed consent and well as Woebot's onboarding screens) as well as offered a list of external-to-application resources, specifically contact information, that were thoughtfully curated in consultation with suicide prevention experts. This resource list includes emergency contact phone numbers, and suicide ideation and domestic violence hotline information.



[redacted]

8.6 Safety Assessment Committee (SAC)

The SAC is the formal WH committee charged with responsibility for the review and evaluation of previous as well as accumulating data from clinical studies of WH devices, to assess safety, perform signal confirmation and risk assessment, assess the risk-benefit associated with study continuation, efficacy and other trial conduct issues such as scientific merit, and to develop recommendations so as to ensure safety across studies and minimize risk for subjects.The SAC members will include the following individuals:

1. Independent Medical Safety Expert, who will serve as the SAC Chair;
2. A Clinical Development Lead;
3. a Medical Lead;
4. a Regulatory Lead;
5. a Device Vigilance Lead

Validated, accurate and interpretable data are to be provided to the SAC, as requested. Data files to be used for SAC analyses will undergo established data review/QC procedures to the extent possible and critical fields will be identified. The Sponsor must ensure that data is of sufficient quality to support the performance of safety surveillance and confirm the assessment of causality associated with the event(s), the associated WH application and confirmation of reportability.

The SAC will determine whether any missing data will significantly impact the safety assessment and will direct the necessary actions to address missing data.

8.6.1 Risk and Quality Tolerance Limits

Perceived risks and quality tolerance limits (QTLs) will be identified and documented before the study start.

The Sponsor will review risk control measures periodically to ascertain whether the implemented quality management activities remain effective and relevant. The quality management approach and any important deviations from the predefined QTLs (and remedial actions adopted) will be described in the clinical study report (CSR).

8.7 Quality Control and Quality Assurance

The Sponsor maintains a robust Quality Management System (QMS) that includes all activities involved in quality assurance and quality control per 21 CFR 820, to ensure compliance with written SOPs as well as applicable global/local GCP regulations and ICH Guidelines.

Audits of investigator sites, vendors, and Sponsor systems are performed by auditors, independent from those involved in conducting, monitoring, or performing quality control of the clinical trial. The clinical audit process uses a knowledge/risk-based approach.

Audits are conducted to assess 21 CFR 820 and GCP compliance with global and local regulatory requirements, protocols and internal SOPs and are performed according to specified Sponsor processes.

9. Statistical Analysis

9.1 General Methodology

Descriptive statistics will be reported for study measures for each study arm as well as the total sample. Summary reports will be presented for all time periods independently, as well as for relevant change scores from Baseline to Week-2 EOT. For continuous variables that are normally distributed the mean and standard deviation will be reported, for non-normal data the median and interquartile range (IQR) will be reported. Frequencies and percentages will be reported for categorical variables.

9.2 Analysis Sets

Primary and secondary analyses will be completed on two sets of data - the full intent-to-treat sample of anyone randomized with available survey data, as well as a per-protocol sample (i.e., registered for app, completed all assessment timepoints, no protocol deviations, etc).

9.3 Sample Size Determination

Given that this study is for internal exploratory purposes and is relying on descriptive statistics for analyses, no power analyses were conducted. The N of 165 with a 10% attrition rate was determined based on the necessary N for meaningful internal learning.

10. Statistical Methods

10.1 Primary Endpoint

10.1.1 Aim
To explore satisfaction with the DISC-MVP among a group of adults with or without clinical symptoms.

10.1.2 Hypothesis
Participants in the DISC-MVP arm and the DISC-CON arm will have descriptively similar levels of satisfaction.

10.1.3 Endpoints
User satisfaction will be measured by:

- Client Satisfaction Questionnaire (CSQ-8)

10.1.4 Analysis Plan
Statistical analysis will be descriptive. The total scale score from the CSQ-8 will be summarized continuously for both treatment groups as well as overall.

10.2 Secondary Endpoint

10.2.1 Aim
To explore satisfaction with the DISC-MVP among a group of adults with at least mild baseline symptomatology.

10.2.2 Hypothesis
Participants with mild symptomatology and above in both the DISC-MVP arm and the DISC-CON arm will have descriptively similar levels of satisfaction.

10.2.3 Endpoints
User satisfaction will be measured by:

- CSQ-8

10.2.4 Analysis Plan
Statistical analysis will be descriptive. Analyses will be restricted to users in each group that had a score of 5 or above on the PHQ-8 and/or the GAD-7 at baseline. The total scale score from the CSQ-8 will be summarized continuously for both treatment groups as well as overall.

[redacted]

[redacted]

10.4 Safety Endpoints

10.4.1 Aims and Endpoints

The relative safety of DISC-MVP against a historical control will be investigated as an exploratory aim and measured through:

[redacted]

- Frequency of AE/SAE/UADEs
    - Spontaneous participant report of safety events that are determined to be an AE/SAE/UADE
    - Direct participant self-report of safety events at the Week 2, end of study, survey that are determined to be an AE/SAE/UADE
    - Number of transcript reviews that detect safety events that are determined to be an AE/SAE/UADE

10.4.2 Analysis of Safety

To observe and describe upon the utilization and outcomes of the safety procedures utilized within this study (e.g., [redacted] AE/SAEs and device relatedness). For each safety endpoint, n(%) will be reported.

10.5 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized overall and separately for each study arm. Continuous variables will be summarized using tables of descriptive statistics, with normally distributed variables summarized by mean and standard deviation and non-normal data summarized by median and interquartile range (IQR). Categorical and ordinal variables will be described using frequencies and percentages.

10.6 Handling of Missing Values

Frequencies of missing values will be indicated in all descriptive tables, and no imputation or other statistical manipulation will be used for missing values.

11. Ethics and Responsibilities

11.1 Good Clinical Practice

This study will be conducted in accordance with the Note for Guidance on GCP ICH Harmonised Tripartite Guideline E6 (R1)/Integrated Addendum E6 (R2); US FDA Code of Federal Regulation (CFR) (Title 21 Parts 50, 56, 312); the general guidelines indicated in the Declaration of Helsinki; and all applicable regulatory requirements.

11.2 Institutional Review Board

The final study protocol, including the final version of the ICF, must be approved, or given a favorable opinion in writing from the IRBs as appropriate. A written approval from the IRB is required for any study protocol amendment(s), ICF updates, participant recruitment procedures (e.g., advertisements), and any written information to be provided to participants and a statement from IRB to ensure compliance with GCP requirements (if applicable). The investigator is required to sign a protocol signature page confirming their agreement to conduct the study in accordance with the document and all of the instructions and procedures found in this protocol and to give access to all relevant data and records to Sponsor monitors, auditors, Sponsor Quality assurance representatives, designated agents of Sponsor, IRBs, and regulatory authorities as required.

The IRB approval must identify the protocol version as well as the documents reviewed. Any amendments to the protocol will require IRB approval before the implementation of the changes made to the study, except for changes necessary to eliminate an immediate hazard to the study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB
- Notifying the IRB of SAEs or other significant safety findings as required by IRB procedures

- Providing oversight of the conduct of the study at the site and adherence to the requirements of all applicable regulations
- Promptly reporting deviations from, or changes to, the protocol to eliminate immediate hazards to the study participants

11.3 Informed Consent

In obtaining and documenting consent via an Electronic Informed Consent Form (eICF), the investigator should comply with the applicable regulatory requirement(s) and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the study, the investigator should have the IRB's written approval/favorable opinion of the eICF and any other pertinent information to be provided to participants.

- Following completion of pre-screening, participants will be provided with a link to the eICF where they will have the opportunity to independently review and determine whether they are interested in participating.
- Participants will be provided with contact information for the study team whom they can reach out to with any questions prior to signing the eICF.
- Participants are informed that their participation is voluntary, and consent can be withdrawn at any point.
- Participants will be required to sign a statement of informed consent that meets the requirements of US FDA CFR Title 21 Part 50, local regulations, ICH guidelines, HIPAA requirements in the US, and the IRB or study site.
- Prior to a participant's participation in the study, the eICF should be signed and personally dated by the participant.
- An electronic copy of the signed eICF will be retained by the study team.
- A copy of the eICF and any other pertinent information must be provided to the participant.
- If the eICF is revised, the revised eICF must have received the IRB's approval/favorable opinion in advance of its use. Participants must be informed of the changes to the eICF and must re-consent to the most current version during their participation in the study if the IRB confirms the change requires re-consent. The participant should be informed in a timely manner if new information becomes available that may be relevant to the participant's willingness to continue participation in the study. The communication of this information should be documented.

12. Records Management

All clinical study information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification. This principle applies to all records referenced in this protocol, irrespective of the type of media used. All records will be collected and maintained via secure and approved online platforms.

Details regarding eCRF access and handling are detailed in the "Electronic Case Report Form Completion and Data Management" section.

Any contact with the participant via telephone or other means that provides significant clinical information is to be documented and maintained as part of the study record. Information from the study records and other source documents is to be promptly entered into the appropriate section of the eCRF.

Changes to information in the study record and other source documents will be electronically tracked. If the reason for the change is not apparent, a brief explanation for the change is to be written adjacent to the change.

The lead biostatician will write a data management plan, which will be finalized prior to performing any data validation.

12.1 Source Documentation

Source documents will be collected electronically. Source documents contain the results of original observations and activities of this research study. They are the original records in which raw data are first recorded. Source documents include, but are not limited to screening logs, consent forms, and recorded data from automated instruments.

The investigator/study personnel should maintain adequate and accurate source documents and study records that include all pertinent observations on each of the study participants. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

All source documents from this study are to be maintained by the investigator and made available for inspection by authorized persons. The investigator will provide direct access to source documents/data for study-related monitoring, audits, IRB review, and regulatory inspections. The Sponsor-Investigator should verify that each participant has consented, in writing, to direct access to his/her original study records for study-related monitoring, audit, IRB review, and regulatory inspection.

12.2 Case Report Form Completion and Data Management

Access to the eCRF will be strictly password protected and limited to personnel directly participating in the study. Data should be entered into the eCRF completely by authorized site personnel (e.g., investigators and the study coordinator). The eCRF must be completed as soon as possible (no later than 5 business days) after any participant evaluation or communication. Changes to the eCRF will be electronically tracked.

Data will be entered/loaded into a validated online platform. Computerized data cleaning checks will be used in addition to manual review to check for discrepancies and to ensure consistency of the data.

12.3 Study Files and Record Retention

All data derived from the study will remain the property of the Sponsor-Investigator. The Sponsor-Investigator assumes accountability for actions delegated to other individuals (e.g., CRO, other study personnel).

Records must be retained in accordance with the current ICH Guidelines on GCP. All essential study documents, including records of participants, source documents, and eCRFs must be kept on file.

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 until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. However, essential documents may be retained for a longer period if required by the applicable regulatory requirements or by agreement with the Sponsor. The Sponsor is responsible for informing the investigator when these documents need no longer be retained.

The investigator is not to dispose of any records relevant to this study without written permission from the Sponsor and is to provide the Sponsor the opportunity to collect such records. The investigator shall take responsibility for maintaining adequate and accurate hard copy source documents, if utilized, of all observations and data generated during this study. Such documentation is subject to inspection by the Sponsor, its representatives, and regulatory authorities.

If an investigator moves, withdraws from a study, or retires, the responsibility for maintaining the records may be transferred to another person who will accept responsibility. Notice of transfer must be made to and agreed by the Sponsor.

13. Auditing and Monitoring

Quality control will occur at each stage of data handling to ensure that all data are reliable and have been processed correctly. The Sponsor-Investigator should ensure oversight of any study-related duties and functions carried out on its behalf, including study-related duties and functions that are subcontracted to another party by the Sponsor's contracted vendors or other study personnel.

The eCRFs should be completed in a timely manner and on an ongoing basis to allow regular review by the study monitor or designee.

Details describing the strategy, responsibilities, and requirements of the study monitoring are provided in the study monitoring plan.

The purpose of an audit is to assess whether ethics, regulatory, and quality requirements are being fulfilled. The Sponsor or its representative may conduct audits including, but not limited to, presence of required documents, the informed consent process, and comparison of eCRFs with source documents. Government regulatory authorities may also conduct an inspection during or after the study. All study records must be available for audit. The Sponsor-Investigator must agree to participate with audits conducted at a convenient time in a reasonable manner.

13.1 Protocol Adherence and Deviations

The investigator and study personnel should conduct the study in compliance with the protocol and should use continuous vigilance to identify and report protocol deviations.

A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol that may be on the part of the investigator, site personnel, or the participant.

Protocol Violations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a participant's rights, safety, or well-being. For example, important protocol deviations may include enrolling participants in violation of key eligibility criteria designed to ensure a specific participant population or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the study.

The investigator should not implement any deviation from the protocol without agreement from the Sponsor and prior review and approval from the IRB of an amendment, except where necessary to eliminate an immediate hazard to a study participant, or when the change involves only logistical or administrative aspects of the study, such as a change in a monitor or telephone number.

In the event of an important protocol deviation, the investigator will report the deviation to the SAC, as described in the SMP, and will come to an agreement as to whether the participant should be withdrawn from the study due to the important protocol deviation.

14. Amendments

Protocol modifications, except those intended to reduce immediate risk to study participants, may be made only by the Sponsor. A protocol change intended to eliminate an apparent immediate hazard to participants should be implemented immediately.

Any permanent change to the protocol must be handled as a protocol amendment. The written amendment must be submitted to the IRB, and the investigator must await approval before implementing the changes. The Sponsor will submit protocol amendments to the appropriate regulatory authorities for approval.

The current version of the ICF will require similar modification if the IRB, investigator, and/or Sponsor, judge the amendment to the protocol to substantially change the study design and/or increase the potential risk to the participant and/or impact the participant's involvement as a study participant. In such cases, the ICF will be renewed for enrolled participants before their continued participation in the study.

15. Study Start and Termination

The study start date is the date on which the first participant provides informed consent.

The end of the study is defined as the last participant’s last assessment.

Both the Sponsor and the investigator reserve the right to terminate the study or the participation in the study at an investigator’s site at any time. In terminating the study, the Sponsor and the investigator will assure that adequate consideration is given to the protection of the participants’ interests.

If the study is prematurely terminated or suspended for any reason, the Sponsor-Investigator or designated study personnel should promptly inform the study participants and should assure

appropriate therapy and follow-up for the participants. Where required by the applicable regulatory requirements, the IRB, and other entities involved in the study should be informed promptly and be provided with a detailed written explanation of the termination or suspension.

16. Confidentiality

All information generated in this study is considered highly confidential and must not be disclosed to any person or entity not directly involved with the study unless prior written consent is gained from the Sponsor. However, authorized regulatory officials, IRB personnel, the Sponsor and its authorized representatives are allowed full access to the records.

All study participants must be informed that their personal study-related data will be used by the Sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant, who will be required to give consent for their data to be used as described in the ICF. Participants must be informed that their medical records may be examined by auditors or other authorized personnel appointed by the Sponsor, by appropriate IRB members, and by inspectors from regulatory authorities.

Identification of participants and eCRFs shall be by unique participant identification numbers (such as screening or randomization number) only. All personal identifiers according to applicable regulations (e.g., name, phone number) must be redacted permanently by the site personnel and replaced with the participant ’s unique identification number in all records and data before transfer to the Sponsor (or designee).

All personal details will be treated as confidential by the investigator and study team members.

17. References

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