Study Protocol and Statistical Analysis Plan

Official Title: Safety and Efficacy of an Accelerated, Rectangular Waveform rTMS Protocol in Treatment of Adults With Major Depressive Disorder

NCT Number: NCT06772987
Sponsor Protocol Number: CL-NQ-2024-01
Sponsor: NeuroQore, Inc.

Document: Clinical Study Protocol, Version 6.0
Document Date: 14 October 2024

Note: The statistical analysis plan is contained within the protocol (Statistical Considerations section); no separate SAP document was prepared.

NQ TMS for MDD Therapy using

1 Day x 3 Sessions Protocol for Adult Patients

Protocol No: CL-NQ-2024-01

Principal Investigator: [redacted]

Sponsor: NeuroQore, Inc.

Version Number: v.6.0

14 OCT 2024

Investigator Signature: [investigator signature and date redacted]

Date:

Pages 2?4 (Table of Contents, Statement of Compliance) omitted ? not relevant to results

1. PROTOCOL SUMMARY

1.1 Synopsis

Title:	Safety and efficacy of an accelerated, rectangular waveform rTMS protocol in treatment of adults with Major Depressive Disorder.
Study Description:	This single center, open label study will evaluate the safety and efficacy of accelerating the delivery of the NeuroQore TMS system's rectangular waveform rTMS protocol for the treatment of adults aged 22-85 with Major Depressive Disorder. Currently cleared protocol with the FDA (the Standard of Care Protocol) is one 19-min treatment session a day for 5 days/week for 6 weeks. The accelerated protocol will involve the same 19-min treatment session offered three times in a single day, with no additional treatment sessions.
Objectives:	<u>Primary</u> 1. To assess the efficacy of the NeuroQore TMS system, with accelerated delivery, in the treatment of adults with major depressive disorder as measured by a change in MADRS score 24 hours and 7 days after the treatment end. 2. To compare the safety profile of the accelerated delivery protocol to the historical safety profile of the Standard of Care protocol.
Endpoints:	**Primary** • Change in MADRS score from baseline to 24 hours and 7 days post treatment. • Number and type of adverse events. **Secondary** • Change in PHQ-9 score from baseline to 24 hours and 7 days post treatment.
Study Population:	Men and women 22-85 with major depressive disorder that have failed one medication in the current episode.
Description of Study Intervention:	NeuroQore TMS System includes (1) a pulse generator, (2) a magnetic coil, (3) a coil cooler, and (4) a chair with a headpiece. It has been cleared for clinical use (K232688) by the FDA for the treatment of Major Depressive Disorder (MDD) using a 19-min Standard of Care protocol. Treatment during this study will be administered according to this protocol and following the instructions in the device user manual. Personalized stimulation targets will be produced from participants' structural MRI via the proprietary targeting generation component of the NeuroQore TMS system. Only personnel trained and certified by NeuroQore will be permitted to administer treatment. All session and device information will be captured on appropriate data collection forms.

Study Duration:	The study is anticipated to last up to 6 months including enrollment and follow-up. Individual participant duration in the study will be 1 day of treatment, 24-hour and 7-day follow-up.
Study Site:	Los Gatos Treatment Center (LGTC) 4850 Union Avenue, San Jose, CA 95124
Inclusion Criteria:	1. Males or females aged 22-85. 2. Current diagnosis of major depressive disorder according to the criteria defined in the current Diagnosis and Statistical Manual of Mental Disorders (DSM-V) without psychotic features. 3. Failed to receive satisfactory improvement from prior antidepressant medication in the current episode. 4. MADRS score $\geq$ 20 at baseline and immediately prior to the day of treatment. 5. Agrees to adhere to the study treatment and follow-up schedule. 6. Willingness to remain on stable medications during rTMS therapy. 7. Fluent in English.
Exclusion Criteria:	1. Any medical conditions that would preclude the use of rTMS to treat depression. 2. Any conditions that would prevent the ability to undergo MRI testing. 3. Pregnancy as determined by serum/urine pregnancy test 4. History of epilepsy, seizure(s), or a seizure disorder as determined by the principal investigator based on a medical history obtained from the patient and/or others authorized to provide such history, combined with a brief screening instrument. 5. Active substance abuse 6. Diagnosis of bipolar or psychotic disorder 7. Considered to be at moderate-high risk of suicide according to the C-SSRS assessment (i.e., Answers YES to Question 3 and NO to Question 6; or answers YES to Question 4, 5, or 6) 8. As determined by the Principal Investigator, subjects with cognitive impairment according to either the medical history obtained from the patient and/or a reliable secondary source, or the results of the Montreal Cognitive Assessment (MoCA) performed during screening.

1.2 Schedule of Activities (SoA)

‘	Baseline	Treatment Day (Before Treatment)	Treatment Day (After 3rd Treatment)	24 hours post-treatment	7 days post-treatment
Consent	X				
Assessment of I/E criteria	X	X			
Demographics, medical history, concomitant medications	X				
C-SSRS	X	X	X	X	X
YMRS	X	X	X	X	X
MoCA*	X				
MADRS	X	X	X	X	X
PHQ-9 (participant)	X	X	X	X	X
rTMS/Safety evaluation	X				
MRI	X				
Motor Threshold		X			
NeuroQore TMS Accelerated Protocol Session		X			
Adverse Event Assessment		X	X	X	X

* MoCA assessment will be performed only for patients aged 65 and older, and in patients below age 65 suspected of having cognitive impairment.

[Section 2 Introduction / Background redacted ? not relevant to results]

Pages 8?13 (Section 2.2 Risk/Benefit Assessment ? literature review) omitted ? not relevant to results

Participants in this study will be subjected to only a one-day MDD treatment, compared to a more commonly used 6-weeks therapy for MDD treatment, thus greatly reducing the logistical burden of completing the therapy regime.

It is also possible that subjects will not derive benefit from participation in the trial.

3. OBJECTIVES AND ENDPOINTS

3.1 Objectives

The study will assess the safety and efficacy of the NeuroQore TMS system, with accelerated delivery, in the treatment of adults with major depressive disorder as measured by a change in MADRS score at 24 hours and 7 days after treatment.

3.2 Endpoints

3.2.1 Primary Endpoint

1. Change in MADRS score from baseline to immediately post treatment, 24 hours and 7 days post-treatment.
2. Number and type of adverse events (Adverse Event Assessment) from baseline to immediately post-treatment, 24 hours post-treatment 7 days post-treatment.

3.2.2 Secondary Endpoints

1. Change in PHQ-9 score from baseline to immediately post-treatment, 24 hours post-treatment 7 days post-treatment.

4. STUDY DESIGN

4.1 Overall Design & Rationale

This single-center trial is designed to evaluate the safety and efficacy of an accelerated protocol in the treatment of adults with major depressive disorder who have failed one medication in the current episode.

Adults aged 22-85 will be enrolled and treated with NeuroQore's TMS system using a neuro-navigation system utilizing MRI to identify individualized target area for stimulation.

The trial visits will be conducted as outlined in section 1.2 Schedule of Activities and section 8.

The primary endpoint, Montgomery Åsberg Depression Rating Scale (MADRS), is a standardized, validated assessment of depression symptoms using ten items administered by a trained clinician. The MADRS score will be obtained at baseline, at the end of the sole treatment day and at 24 hours and 7 days post-treatment.

Other secondary analyses will include the participant's self-assessment of depression, captured via the administration of the Patient Health Questionnaire (PHQ9) at the same cadence as the MADRS.

4.2 End of Study Definition

The study may be terminated early in the event of unanticipated adverse events that may pose further risks to subjects as determined by the Principal Investigator in conjunction with the study sponsor, or by the IRB. The Principal Investigator in conjunction with the sponsor may terminate the study early if its interim analysis indicates that the study has definitively met its statistical criteria for success or will definitively fail to meet its statistical criteria for success. Such a decision will be promptly communicated to the IRB.

5. STUDY POPULATION

5.1 Inclusion Criteria

All subjects are required to meet the following inclusion criteria in order to be considered eligible for participation in this study:

1. Males or females aged 22-85.
2. Current diagnosis of major depressive disorder according to the criteria defined in the current Diagnosis and Statistical Manual of Mental Disorders (DSM-V) without psychotic features.
3. Failed to receive satisfactory improvement from prior antidepressant medication in the current episode.
4. MADRS score $\geq$ 20 at baseline and immediately prior to the day of treatment.
5. Agrees to adhere to the study treatment and follow-up schedule.
6. Willingness to remain on stable medications during rTMS therapy.
7. Fluent in English.

5.2 Exclusion Criteria

Subjects will be excluded from participating in this trial if they meet any of the following exclusion criteria:

1. Any medical conditions that would preclude the use of rTMS to treat depression.
2. Any conditions that would prevent the ability to undergo MRI testing.
3. Pregnancy as determined by serum/urine pregnancy test
4. History of epilepsy, seizure(s), or a seizure disorder as determined by the principal investigator based on a medical history obtained from the patient and/or others authorized to provide such history, combined with a brief screening instrument.
5. Active substance abuse
6. Diagnosis of bipolar or psychotic disorder
7. Considered to be at moderate-high risk of suicide according to the C-SSRS assessment (i.e., Answers YES to Question 3 and NO to Question 6; or answers YES to Question 4, 5, or 6)
8. As determined by the Principal Investigator, subjects with cognitive impairment according to either the medical history obtained from the patient and/or a reliable secondary source, or the results of the Montreal Cognitive Assessment (MoCA) performed during screening.

5.3 Lifestyle Considerations

The study requires participants to be treated with rTMS stimulation for a single day. Participants will need to remain on-site during treatment.

5.4 Strategies for Recruitment and Retention

Subjects will be recruited from the existing patient population from the single clinic (LGTC) participating in this study and from the local community through community outreach or IRB approved social media campaigns or similar.

Subjects will be provided the entire treatment on a single day over a period of few hours. Staff will be dedicated to setting treatment expectations with trial participants during the consent process to aid with retention. During the follow-up period, clinic visits, including the exit visit and on-site visits, are not required. Study site staff will remain in contact with participants for the 7-day assessment to assess depression status and adverse events.

Participants who are unresponsive to follow-up attempts will be contacted a minimum of three times through their preferred communication medium, email, text, or courier mail to minimize attrition.

6. STUDY INTERVENTION

NeuroQore TMS System includes (1) a pulse generator, (2) a magnetic coil, (3) a coil cooler, and (4) a chair with a headpiece. Details of the equipment are in the NeuroQore TMS system user manual and video.

Treatment will be administered according to the protocol and device manual. Personalized stimulation targets will be produced from participants' structural MRI via the proprietary targeting generation component of the NeuroQore TMS system.

Only personnel trained and certified by NeuroQore will be permitted to administer treatment. All session and device information will be captured on appropriate data collection forms.

6.1 Device Description

Before administering rTMS using NeuroQore TMS System, each participant's resting motor threshold will be determined by visualizing the thumb twitch at the lowest TMS intensity sufficient to induce movement. Utilizing the pre-treatment MRI, an individualized target for stimulating the L-DLPFC (dorsolateral prefrontal cortex) will be created, utilizing the most commonly used MNI (Montreal Neurological Institute) target coordinates (x = -38, y = 44, z = 26) to identify the L- DLPFC for each individual. The treatment coil will then be positioned over the target using a neuronavigation system to ensure that the coil center is accurately aligned with the x, y, z coordinates after retransformation from MNI space into the individual's anatomical space. The coil's orientation and tilt are optimized to minimize the distance between the center of the coil and the center of the target for precise stimulation. The target coordinates, overlaid on the T1-weighted anatomical MRI, will be provided to the principal investigator for review to ensure accuracy and correctness before treatment.

Table 10. rTMS Parameters

Pulse Type	Rectangular biphasic
Applicator	[redacted]
Pulse Width	~300us
Location	Left DLPFC
% of Motor Threshold	120%
Frequency	10Hz
Train Duration	4s
Inter-train Interval	11s
Number of trains	75
Session time	18.8 minutes
Time in-between each session	60 minutes
Number of pulses per session	3,000
Number of sessions per day	3
Number of days	1
Total number of treatment sessions	3
Total number of pulses	9,000

A physician will always be on-site during rTMS administration to provide seizure management if required. Treatment will be discontinued if the patient has a significant adverse event or asks to stop the treatment for any reason. The participant may be withdrawn from participation by the PI if a risk to the participant's safety is questioned.

[device photograph redacted ? confidential]

Pages 18?19 (Sections 6.2?6.6: device handling, bias, compliance, concomitant therapy, seizure management procedures) omitted ? operational / confidential; not relevant to results

Item	Planned Response
	• Ongoing monitoring of participants for signs of increased seizure risk throughout the study

7. STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/ WITHDRAWAL

7.1 Discontinuation of Study Intervention

All participants will be treated with the NeuroQore TMS system three times on a single day.

7.2 Participant Discontinuation/ Withdrawal from Study

Subjects may voluntarily withdraw from the study at any time for any reason. In addition, the site investigator may withdraw the subject due to any reason determined by the site investigator to be in the best interest of the subject.

If a participant is withdrawn from the trial early, the study staff will attempt to collect all data from assessments normally completed at the study exit visit. Study staff will document the resolution or continuation of any adverse events reported during the trial.

7.3 Lost to Follow-Up

A subject will be considered lost to follow-up if he or she fails to participate in the 24 hours and/or 7 days follow-up assessment for MADRS score and is unable to be contacted by the study site staff. A subject may also be considered lost to follow-up if he or she fails to complete the 24 hours and/or 7 days follow-up self-assessment of PHQ9 score.

The following actions should be taken if a subject fails to continue participation in the study:

- The site will attempt to contact the subject and reschedule the missed participation, counsel the subject on the importance of maintaining the assigned schedule, and ascertain whether the subject wishes to and/or should continue in the study.
- Before a subject is deemed lost to follow-up, the site investigator will try to regain contact with the subject (where possible, 3 telephone calls/texts/emails). These contact attempts should be documented in the subject's medical record or study file.
- Should the subject continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1 Study Procedures

Baseline: approximately 3 hours

- Consent
- Confirmation of eligibility
- Collection of medical history, including medications
    - MRI and rTMS safety evaluation

- C-SSRS
- YMRS
- MoCA
- MADRS
- PHQ-9
- MRI

Treatment: 3 times/day x 1 day, approximately 4 hours

- Motor threshold determination
- Treatment
  - 18.8 minutes of stimulation
  - 60 minutes of rest
- C-SSRS (after 3rd treatment)
- YMRS (after 3rd treatment)
- MADRS (after the 3rd treatment)
- PHQ-9 (after the 3rd treatment)
- Adverse events (after the 3rd treatment)

24 hours Follow-Up: approximately 1 hour

- C-SSRS
- YMRS
- MADRS
- PHQ-9
- Adverse events

7 Days Follow-Up: approximately 1 hour

- C-SSRS
- YMRS
- MADRS
- PHQ-9
- Adverse events

Moment of Enrollment

Subjects are considered enrolled in the trial after they provide informed consent, after all inclusion/ exclusion criteria have been met, and after they received at least one stimulation from the NeuroQore TMS system.

8.2 Efficacy Assessments

Stimulation efficacy will be evaluated using the Montgomery Åsberg Depression Rating Scale (MADRS) and PHQ-9. The MADRS is a standardized, validated assessment of depression symptoms consisting of ten items (Montgomery & Asberg, 1979) administered by a trained, clinician. The results will be entered directly into the case report forms by the administering clinician. If a participant remits from depression (MADRS score $\leq$ 6) during the first week of trial participation, they will be considered to have achieved remission. Individual successful response to stimulation is achieved if a participant's MADRS score at 7 days post-treatment is 50% or lower than their

MADRS score was at the study entry. Study successful response is achieved if at least 50% of the participants meet individual success criteria.

The PHQ-9 is a standardized, validated, participant-administered instrument commonly used by clinicians to screen for and monitor depression. Participants will receive a secure link to the PHQ-9 and instructions on how to complete it during the trial. The PHQ-9 score is used to track participant self-assessment. These scores will be analyzed using the same method and criteria listed above for MADRS scores, and will be used for secondary assessment of the study efficacy.

8.3 Safety Assessments

Safety will be evaluated during the intervention period (day of stimulation) by collecting adverse events (AEs), serious adverse events (SAEs), and unanticipated adverse device effects (UADEs). Adverse events will also be collected at all follow-up assessments for the duration of the trial.

8.4 Adverse Events and Serious Adverse Events

8.4.1 Definitions

An Adverse Event (AE) is defined as any unwanted medical occurrence, whether or not related to the investigational device.

A Serious Adverse Event (SAE) is any untoward medical occurrence in a subject that:

- Led to a death;
- Led to a serious deterioration in the health of the subject that:
    - resulted in a life-threatening illness or injury;
    - resulted in a permanent impairment of a body structure or a body function;
    - required in-subject hospitalization or prolongation of existing hospitalization;
    - resulted in medical or surgical intervention to prevent permanent impairment to body structure or body function;
- Led to fetal distress, fetal death or a congenital abnormality or birth defect.

A planned hospitalization for a previously identified disease/condition is not considered an SAE.

An Adverse Device Effect (ADE) is any untoward and unintended response to a medical device. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device, as well as any event that is a result of user error.

If an SAE is determined to be probably or definitely related to the device and has not been previously anticipated, the clinical finding would be classified as an unanticipated adverse device effect (UADE). An UADE is defined as "any serious adverse effect on health or safety or any life threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects."

8.4.2 Classification of an Adverse Event / Serious Adverse Event

Severity

The severity of the adverse event will be categorized by the site investigator as follows:

Mild:	*Events require minimal or no treatment and do not interfere with the subject's daily activities.*
Moderate:	*Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.*
Severe:	*Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious."*

Relationship to Study Intervention

The relationship of the adverse event to the device will be categorized by the site investigator as follows:

Not Related:	*The event is due to an underlying, concurrent, or new illness or effect of another device, drug or intervention and is not related to the device.*
Related:	*The event has a temporal relationship to the use of the device, and an alternative etiology is less likely; or the event can be attributed to the use of the device.*

8.4.3 Time Period and Frequency for Event Assessment and Follow-Up

AEs will be assessed during study treatment, prior to each treatment session, and at the end of the day. The temporal association to active treatment will be recorded in the case report forms to accurately attribute any adverse event to stimulation therapy. All related AEs should be followed until the event is resolved or judged to be chronically stable or the subject has completed participation in the trial. The investigational site will provide relevant follow-up information to the study sponsor upon request.

8.4.4 Adverse Event and Serious Adverse Event Reporting

All AEs, including all SAEs, will be monitored from enrollment through discharge from this study. All AEs must be recorded in the patient chart. A description of the event, including the start date, resolution date where applicable, action taken, and outcome, should be provided along with the site investigator's assessment of the relationship between the AE and the study device.

All SAEs, including UADEs, must be reported to the study sponsor as soon as possible after the site investigator becomes aware of the event and to the respective IRB per their reporting requirements. Completion of the appropriate case report form (CRF) in the

electronic data capture (EDC) system will satisfy the requirement to notify the sponsor. If EDC entry is not possible for any reason, the investigator must notify the sponsor by submitting an email to [redacted] or by calling [redacted].

The investigator will provide any supporting information about the event to the sponsor upon request.

The sponsor will report individual Adverse Events to the FDA using the eMDR process.

9. STATISTICAL CONSIDERATIONS

9.1 Samples Size Determination

A sample size of 50 participants is estimated to have 90% power in demonstrating the targeted efficacy detailed in section 8.2 above. This estimation is based on the following:

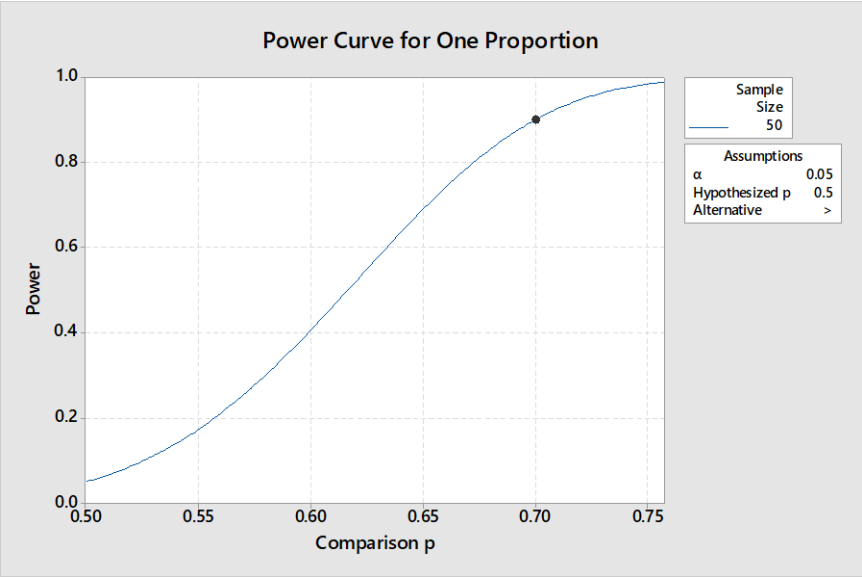
If 70% or higher number of participants exhibit 50% reduction in MADRS score, we can conclude with 95% confidence (p = 0.05) that the efficacy target of 50% participants showing 50% reduction in MADRS score is achieved, as detailed here:

Power and Sample Size

Test for One Proportion
Testing p = 0.5 (versus > 0.5)
α = 0.05

Results

Comparison p	Sample Size	Target Power	Actual Power
0.7	50	0.9	0.901715



The sample size of 50 will also give this study the sensitivity to detect with 95% confidence (p = 0.05) and 90% power if the Mean MADRS score of all participants lowers by as little as 2.1. This estimation is based on the following:

Participants pre-treatment MADRS scores: 20 to 50, with a mean of 35 and variation range of 30

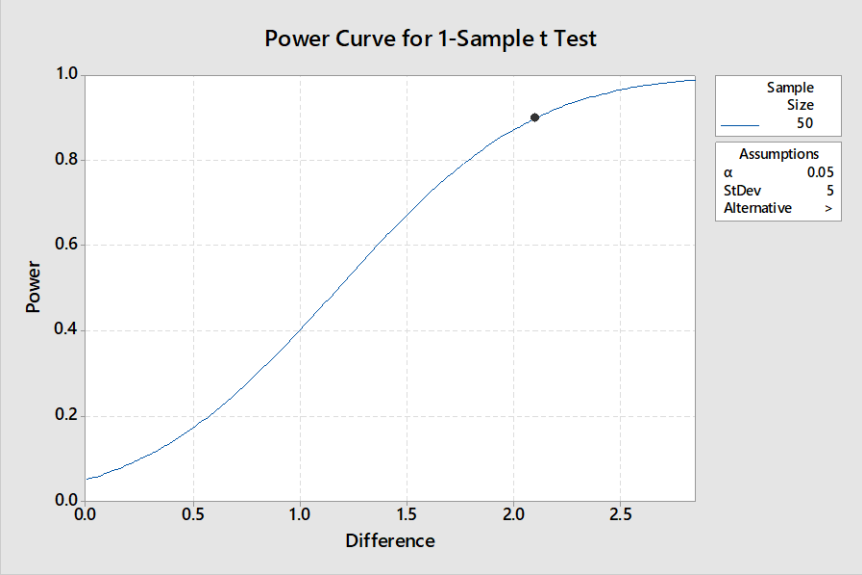
Standard deviation of participants' MADRS scores: 5 (1/6th of the variation range, indicating that 99% of participants fall within this range)

Power and Sample Size

1-Sample t Test
Testing mean = null (versus > null)
Calculating power for mean = null + difference
α = 0.05 Assumed standard deviation = 5

Results

Sample Size	Power	Difference
50	0.9	2.09854



9.2 Populations for Analyses

All enrolled subjects who successfully complete the study regime, including the treatment sessions and the follow-up assessments, and who are not disqualified for other reasons will be included in the analysis.

9.3 Statistical Analyses

9.3.1 General Approach

This study aims to compare the efficacy of the NeuroQore TMS system with an accelerated delivery protocol in the treatment of adults with major depressive disorder as measured by a change in MADRS score pre- and post-treatment. The pre-treatment score will be measured within a 24-hour period preceding the treatment. The post-treatment score will be at 24 hours and 7 days after the treatment. MADRS score is in the range of 0 to 60 and thus lends itself to both attribute and variable data analysis. Lowering of the score indicates efficacy of the treatment. This lowering can be assessed in attribute fashion (whether the targeted lowering was achieved or not) as well as in variable fashion (lower bound of the % lowering achieved at 95% confidence).

9.3.2 Analysis of the Primary Efficacy Endpoint

Attribute Analysis:

- Actual % change in MADRS score of each participant will be calculated.
- % of participants exceeding 50% drop in MADRS score will be determined.
- % of participants exceeding 70% drop in MADRS score will be determined.
- If either 70% or more of participants show 50% or more drop in MADRS score, or if 50% or more participants show 70% or more drop in MADRS score, it will be concluded with 95% confidence ($p = 0.05$) that the targeted efficiency of 50% participants recording 50% drop in MADRS score is achieved.

Variable Analysis:

- Pre- and post-treatment MADRS score values will be assessed for normality or alternate distributions.
- 95% confidence range of pre- and post-treatment MADRS score will be calculated and reported.
- 95% confidence lower bound in the mean value drop (minimum drop) of the MADRS score for the study population will be calculated and reported.
- Actual % change in MADRS score of each participant will be calculated and assessed for normality or alternate distributions.
- 95% confidence lower bound in the % change (minimum % drop) of the MADRS score for the study population will be calculated and reported.

9.3.3 Analysis of the Secondary Endpoints

For reference purpose only, the PHQ-9 scores will be analyzed in the exact same manner as the MADRS scores. They will not be used for formal assessment of whether the study efficacy criteria were met or not.

9.3.4 Additional Analyses

Any statistical outliers encountered in the MADRS or PHQ-9 data will be investigated. If a justifiable and assignable cause is identified, then such outliers will be excluded and statistical analyses of sections 9.3.2 and 9.3.3 will be repeated without the outliers.

9.3.5 Safety Analyses

Qualitative assessment of the adverse events encountered during the study period will be summarized.

9.3.6 Baseline Descriptive Statistics

Minimum number of participants to be enrolled in the study = 50

Pre-treatment MADRS score for each participant >= 20

Estimated Range of Pre-treatment MADRS score of participants = 20 to 50 with mean of 35

9.3.7 Planned Interim Analyses

Multiple interim analyses are planned as data for each set of 20 new enrollees become available. These analyses are intended to determine if the study needs to be terminated earlier as a result of extremely favorable or unfavorable data. They will involve the exact same data analysis and assessment described in section 9.3.2.

If these interim analyses determine that the study has already achieved its statistical criteria of 95% confidence (p = 0.05) of success (50% of participants showing 50% drop in MADRS score), then the study may be terminated before all planned participants are enrolled.

If these interim analyses determine that the study will not be able to achieve its statistical criteria of 95% confidence (p = 0.05) of success (50% of participants showing 50% drop in MADRS score) even if continued to completion, then the study may be terminated before all planned participants are enrolled.

[Section 10 Supporting Documentation and Operational Considerations redacted ? not relevant to results]

Pages 28?33 (Section 10 operational and regulatory considerations, abbreviations, amendment history, references) omitted ? not relevant to results