March 22, 2024

Neuronetics, Inc.
Robin Fatzinger, RAC
Sr. Director, Regulatory & Medical Affairs
3222 Phoenixville Pike
Malvern, PA 19355

Re: K231926
Trade/Device Name: NeuroStar Advanced Therapy System
Regulation Number: 21 CFR 882.5805
Regulation Name: Repetitive transcranial magnetic stimulation system
Regulatory Class: Class II
Product Code: OBP
Dated: February 23, 2024
Received: February 23, 2024

Dear Robin Fatzinger:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Robert Kang -S

for Pamela Scott, MS
Assistant Director
DHT5B: Division of Neuromodulation
and Physical Medicine Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K231926

Device Name

NeuroStar Advanced Therapy System

Indications for Use *(Describe)*

NeuroStar Advanced Therapy is indicated as an adjunct for the treatment of Major Depressive Disorder (MDD) in adolescent patients (age 15-21).

Type of Use *(Select one or both, as applicable)*

☑ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510k Summary

510(k) Number:	K231926
Date Prepared:	21 March 2024
Applicant:	Neuronetics, Inc. 3222 Phoenixville Pike Malvern, PA 19355
Primary Contact:	Robin Fatzinger, RAC AVP, Regulatory and Medical Affairs Phone: 610-981-4027 Email: robin.fatzinger@neurostar.com
Secondary Contact:	Cory Anderson Sr. VP, R&D and Clinical Phone: Email: cory.anderson@neurostar.com
Device Trade Names:	NeuroStar, NeuroStar TMS Therapy System, NeuroStar Advanced Therapy System, NeuroStar Advanced Therapy for Mental Health
Device Common Name:	Transcranial Magnetic Stimulator
Classification:	21 CFR 882.5805
Product Code:	OBP
Predicate Devices:	Primary Predicate - NeuroStar Advanced Therapy System: K230029 Reference Predicates - NeuroStar Advanced Therapy System: K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230

Device Description

The NeuroStar Advanced Therapy System is a transcranial magnetic stimulation device. Specifically, it is a computerized, electromechanical medical device that produces and delivers non-invasive magnetic fields to induce electrical currents targeting specific regions of the cerebral cortex. Transcranial magnetic stimulation (TMS) is a non-invasive technique used to apply brief magnetic pulses to the brain. The pulses are administered by passing high currents through an electromagnetic coil placed adjacent to a patient's scalp. The pulses induce an electric field in the underlying brain tissue. When the induced field is above a certain threshold and is directed in an appropriate orientation relative the brain's neuronal pathway, localized axonal depolarizations are produced, thus activating neurons in the targeted brain region.

The NeuroStar System consists of a combination of hardware, software, disposable, and consumable supplies, which are required for the operation of the system. The basic configuration includes the following components:

- Mobile Console
- System Software
- Treatment Chair
- Head Support System
- MT Cap
- D-Tect MT Accessory
- TrakStar Data Management

Indications for Use:

NeuroStar Advanced Therapy is indicated as an adjunct for the treatment of Major Depressive Disorder (MDD) in adolescent patients (15-21).

Technological Characteristics and Substantial Equivalence:

NeuroStar TMS Therapy system has previously obtained FDA clearance for treatment of major depressive disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode (K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230).

Neuronetics has provided real-world clinical data that provides evidence that when used as an adjunct, NeuroStar Advanced Therapy has the same safety and efficacy profile in the adolescent population (15-21) as in the adult population and therefore the subject device is substantially equivalent to the predicate device that was cleared under K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230. Neuronetics has implemented minor labeling changes to update the indications for use and clinical summaries. None of these changes alter the technical specifications for the subject device.

The components of and mechanisms of operation for the subject device are identical to the previously cleared predicate device, NeuroStar Advanced Therapy System (K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230). The performance characteristics, including the

Electrical and Magnetic Field Distribution testing are the same as the previously cleared NeuroStar Advanced Therapy System. The subject device has the following similarities to the predicate NeuroStar Advanced Therapy System:

- Principles of operation
- Design for delivery of Transcranial Magnetic Stimulation (TMS)
- Materials
- Stimulation parameters (frequency, train duration, inter-train interval, number of trains, number of pulses, and total duration

The proposed changes for the NeuroStar Advanced Therapy System are limited to labeling updates, specifically for the NeuroStar Advanced Therapy System to be used as an adjunct for the treatment of Major Depressive Disorder (MDD) in adolescent patients (15-21). The proposed change is supported by information submitted in this premarket notification and with the following rationale:

- The subject device is substantially equivalent to the FDA-cleared Primary Predicate Device, NeuroStar Advanced Therapy System, cleared by FDA under K230029. The subject device is also substantially equivalent to the Reference Predicate Devices previously cleared by FDA under K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230.
- The subject device changes remain limited to labeling revisions, in support of the adjunct treatment of adolescent patients (15 -21). No other changes are made to the device or product labeling.

Clinical data has been provided to support the substantial equivalence of the subject NeuroStar Advanced Therapy System in terms of safety and effectiveness for the expanded patient population. Therefore, the NeuroStar TMS Therapy System with the proposed changes to the product labeling is substantially equivalent to the and predicate device.

Non-Clinical Testing:
There have been no changes to the hardware or software of the subject device and therefore no non-clinical testing was required.

Performance Standards:

The NeuroStar Advanced Therapy System has been previously tested and conforms with the following standards:

- ISO 13485:2016
- IEC60601-1
- IEC60601-1-2

Additionally, the contents of this 510(k) complies with the FDA Guidance Document: *"Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation (rTMS) Systems - Guidance for Industry and Food and Drug Administration Staff"*. Prior non-clinical performance testing of the components of NeuroStar Advanced Therapy System was conducted as required according to the standards listed above. All system components have been previously cleared by the FDA.

Clinical Performance Data:

Clinical performance data was provided to support the safety and effectiveness of the NeuroStar Advanced Therapy System device for use as an adjunct for the treatment of Major Depressive Disorder (MDD) in adolescent patients (15-21).

The clinical performance data was based on a large-scale analysis of real-world data (RWD) of 1,169 patients, as well as a literature review.

Evidence of Safety and Efficacy in the Use of TMS as an Adjunctive Treatment for Adolescent Patients with MDD: Real-World Data

A large-scale retrospective analysis of real-world data (RWD) derived from the TrakStar registry data of 1,169 per protocol adolescent patients (age 12-21) who received the standard NeuroStar treatment protocol for MDD over a span of 15 years, beginning in 2008. This RWD was collected from patients across 347 TMS centers in the US. These 1,169 patient records were analyzed to determine the difference in measures of depression (PHQ-9 scores) over a pre-post TMS treatment interval of 6 weeks. (TrakStar (2023) Adolescent Study).

An additional 1,006 (45%) adolescent patients in the TrakStar database were not included due to insufficient available data. When compared for average age, gender distribution, type of site at which the patient was treated, and the U.S. geographical location of the sites, there were no statistically significant differences found between the two groups.

Eligible subjects in the TrakStar patient database were selected for analysis according to the following protocol-specified selection criteria.

Inclusion Criteria

- Primary diagnosis of Major Depressive Disorder (MDD), according to DSM-4/ICD-9 or DSM-5/ICD-19 criteria applicable on the date treatment with NeuroStar Advanced Therapy begins.
- 12 to 21 years of age.
- Male or female.
- Treatment with NeuroStar Advanced Therapy.
- Treatment start-date of November 1, 2008, or later.
- Treatment end date on or before the date on which the retrospective study sample is extracted from the TrakStar database.
- *Per Protocol Subjects:* Subject received a course of a minimum of 20 treatments with NeuroStar Advanced Therapy.
- *Intent to Treat (ITT) Subjects:* Subject received at least one treatment with NeuroStar Advanced Therapy.
- Treatment with NeuroStar Advanced Therapy to the left dorsolateral prefrontal cortex (DLPFC) only.
- Treatment with NeuroStar Advanced Therapy according to standardized NeuroStar Advanced Therapy treatment protocols of DASH and/or Standard as per the original clinical study that supported FDA clearance of NeuroStar Advanced Therapy to reduce depression in adults suffering from MDD.

- Each of GAD-7 and PHQ-9 scores available at each of pre-treatment (defined as the closest score available within 7 days prior to administration of the first treatment) and post-treatment (defined as the closest score available within ± 7 days of the date of the last treatment) evaluations for the single NeuroStar Advanced Therapy course.
- Subjects with moderate or greater depression prior to NeuroStar Advanced Therapy (pre-treatment), defined as a score on the Physician Health Questionnaire-9 (PHQ-9) ≥ 10 within 7 days prior to the first treatment.
- Subjects with moderate or greater anxiety symptoms prior to NeuroStar Advanced Therapy (pre-treatment), defined as a score on the Generalized Anxiety Disorder-7 (GAD-7) ≥ 10 within 7 days prior to the first treatment.

Exclusion Criteria
- Gap in NeuroStar Advanced Therapy treatment due to COVID of > 14 continuous days, where applicable.
- More than one DLPFC treatment session on the same day.

Patients included in this RWD study had a primary diagnosis of MDD, had received at least 20 treatments with NeuroStar Advanced Therapy to the left dorsolateral prefrontal cortex (DLPFC) and were required to exhibit baseline moderate or greater depression, defined as a score on the Physician Health Questionnaire-9 (PHQ-9) ≥ 10. The mean patient age was 19.2 years (min.12, max. 21), and 60.8% were female.

The primary endpoint was defined as the proportion of the per protocol population that met the Individual Success Criteria. The primary endpoint was met as 77.8% (95% CI: 72.8%, 83.0%) of the primary per protocol analysis population met the Individual Subject Success Criteria, with the lower limit of the 95% confidence interval exceeding the pre-established Overall Study Success Criteria of a minimum 50% by 22.79%. This proportion was found to be statistically significant at $p<0.0001$. The mean change in PHQ-9 scores from baseline to endpoint was -10.0 ± 6.6 and 30.0% attained remission of MDD symptoms defined as post-treatment PHQ-9 of <5. Due to the smaller number of patients, aged 12 - 14 years old (n=10), the final cleared indication for adolescents is age 15 – 21 years old.

A graphical representation of the per protocol change in PHQ-9 category of depression severity rating from pre-treatment to post-treatment is provided in Figure 1 below.

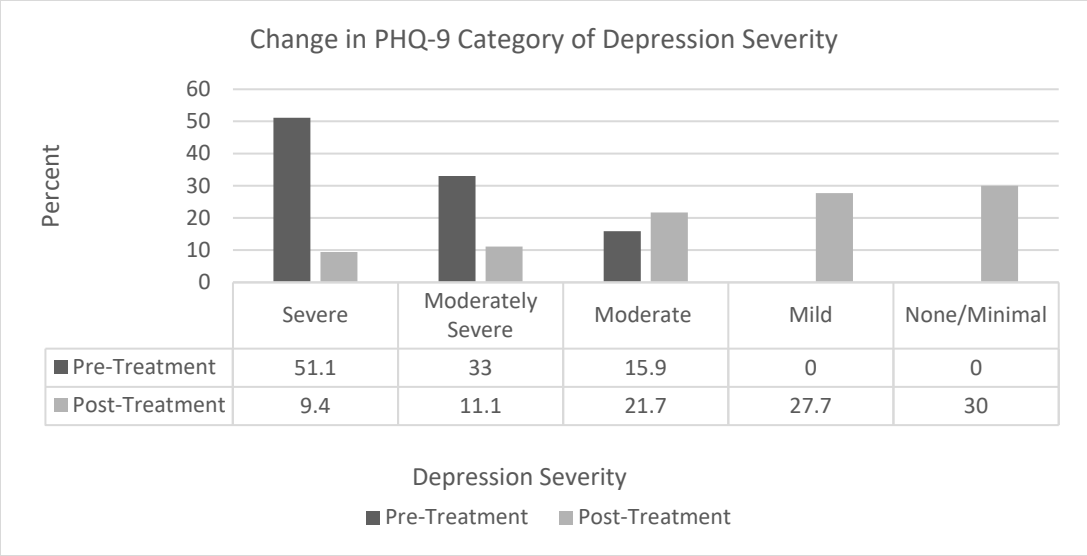

Figure 1. Change in PHQ-9

Literature Review

A systematic literature search was performed to identify all available applicable published research evaluating use of TMS therapy for the intended patient population of adolescents to enable a thorough descriptive evaluation of findings. The systematic literature search was opened to identification of available published literature inclusive of randomized controlled trials, open-label trials, and retrospective studies.

Literature Search Methodology

Goal: The systematic literature search was intended to identify and collate all available applicable and relevant published research evaluating use of TMS Therapy to treat adolescent patients for the symptoms of depression, with a focus on published research evaluating application of the NeuroStar device and other figure 8 coil technology devices to perform a thorough descriptive analysis of current findings of available relevant literature.

Selection Criteria: The parameters for the literature search, as listed below, were intentionally pre-determined to be broad to capture all potentially relevant literature:

- *Study Treatment*: NeuroStar Therapy per standard protocol (left DLPFC) or rTMS Therapy with a figure 8 coil over the left DLPFC comparable to NeuroStar Therapy.
- *Patient/Subject Population*: Adolescents covering the age range of 12 to 21 years, inclusive, who received treatment for symptoms of depression and/or anxiety.
- *Outcome Assessments*:
  - An outcome measure of depression, any scale (mandatory)
  - An outcome measure of anxiety, any scale (preferred)
- *Review Timeline*: November 2008 to January 2024
- *Search Terms:*
  - Device: transcranial magnetic stimulation, TMS, rTMS, NeuroStar, Neuronetics, Figure 8 coil.
  - Condition: depression, depressive disorder, MDD, major depressive disorder, depressive

episode,
- Population: adolescent, teen, teenager, child, children, childhood, young adult.
- Indication: antidepressant, antidepressant therapy, antidepressant medication, depression medication, Escitalopram, Lexapro, Fluoxetine, Prozac, selective serotonin reuptake inhibitors, SSRI.

- *Search Sources:* The pre-determined sources searched per the above selection criteria were the following:

  - PubMed
  - Medline
  - Embase
  - Central
  - Google Scholar

Tables 1 and 2 summarize the studies from the literature search.

Table 1. Summary of Published Randomized Controlled Studies

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (between groups)</th></tr>
<tr>
<td>Ren and Pu (2022)</td>
<td>• RCT:
• Active: Active TMS + Sertraline vs.
• Control: Sertraline only

• Active TMS: LDLPFC; 10 Hz; 90%MT; 2,000 pulses per session; 4 weeks

• Sertraline:
– 8 - 12 yrs.: 25mg/d
– 12 – 18 yrs.: 50 mg/d</td>
<td>• Age (yrs.): 8-18</td>
<td>107</td>
<td>• HAMD-24</td>
<td>Mean change in scores on the HAMD-24 from baseline to endpoint (week 4) for each of the control and active treatment groups, and the significance of the difference in the change between the two groups is shown below.
<table>
<tr><th>HAMD-24</th><th>Baseline</th><th>Week 4</th><th>Mean Change</th></tr>
<tr><td>Active TMS + antidepressant</td><td>55.32 ± 6.35</td><td>15.33 ± 2.03</td><td>-39.87 (p<0.0001)</td></tr>
<tr><td>Antidepressant only</td><td>55.25 ± 5.89</td><td>36.75 ±3.76</td><td>-18.50 (p<0.0001)</td></tr>
</table>
The 21.27-point difference in the mean change in HAMD-24 Total score at endpoint relative to baseline in favor of active over control was statistically significant at p<0.005 at end of week 4.
HAMD-24 % reductions at week 4 relative to baseline are shown below for each of the study groups:
<table>
<tr><th>HAMD-24</th><th>Active TMS + antidepressant</th><th>Antidepressant only</th></tr>
<tr><td>≥75% reduction</td><td>16%</td><td>11%</td></tr>
<tr><td>≥50% reduction</td><td>16%</td><td>13%</td></tr>
<tr><td>≥25% reduction</td><td>13%</td><td>15%</td></tr>
<tr><td><25% (no improvement)</td><td>5%</td><td>11%</td></tr>
</table>
Conclusion: HAMD-24 total depression scores decreased significantly for both the active and control treatment groups at week 8 relative to baseline. The finding of a significant decrease for the control group is not surprising; however, given that the subjects in this study were not taking any medication prior to study entry, and therefore a treatment effect component of medication implementation was to be expected. However, the 21.37-point difference in depression improvement in favor of the active group is supportive of the enhanced effect of TMS as an adjunct to antidepressant therapy. Note there was no sham device to account for a potential device placebo effect.</td>
<td>HAMD-24
-7.15
CI [-8.21, -6.08]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (between groups)</th></tr>
<tr>
<td>Chen. et al. (2022)</td>
<td>• Prospective RCT
• Active: rTMS:
- left DLPFC
- 90% MT
- 60 trains of 4 secs on and 15 secs off
- 10 Hz
- 2400 pulses
- 5 days/week for 2 weeks + sertraline 50mg daily for 4 weeks
• Control: sertraline 50mg daily for 4 weeks</td>
<td>• MDD:
– First episode
• Age (yrs):
– Active: Mean ± SD: 14.65 ± 2.34
Range: 12-18
– Control: Mean ± SD: 15.39 ± 2.44
Range: 12-18
• Gender:
– Active: 85% female
Control: 78% female</td>
<td>Total: 97
Active: 48
Control: 49</td>
<td>• HAM-D
• CDRS-R</td>
<td>Mean change in scores on the respective scales from baseline to endpoint (week 4) for each of the control and active treatment groups, and the significance of the difference in the change between the two groups is shown below for the HAM-D and CDRS-R.
<table>
<tr><th></th><th>Active</th><th>Control</th><th>Change</th></tr>
<tr><td>HAM-D</td><td>-10.54</td><td>-6.27</td><td>p < 0.001</td></tr>
<tr><td>CDRS-R</td><td>-27.73</td><td>-4.23</td><td>p < 0.001</td></tr>
</table>
Conclusion: Mean decreases in depression scores were statistically significantly greater for subjects in the active than in the control group, supporting the that active TMS as an adjunct to medication is superior to medication alone according to two distinct depression measures. There were no reported adverse events in this study with the exception of transient pain at the treatment site. Note there was no sham device to account for a potential device placebo effect.</td>
<td><u>HAM-D</u>
-2.555
CI: [-3.137, -1.973]</td>
</tr>
<tr>
<td>Lu et al. (2020)</td>
<td>• RCT:
• Active: Sertraline + active TMS vs.
• Control: Sertraline + sham TMS
• Active TMS: LDLPFC 10 Hz 80% MT for 2 weeks.
• Sertraline: Started at 25 mg/day and titrated to effect to max of 100-150 mg/day.</td>
<td>• Age (yrs.): 12 – 18
• Subjects were medication-free prior to study start and experiencing their first depressive episode,</td>
<td>116</td>
<td>• HAMD-24</td>
<td>Mean change in scores on the HAMD-24 from baseline to endpoint (for each of the control and active treatment groups, and the significance of the difference in the change within each group is shown below.
<table>
<tr><th>HAMD-24</th><th>Baseline</th><th>Endpoint</th><th>Mean Change</th></tr>
<tr><td>Active TMS + Sertraline</td><td>27.12 ± 3.24</td><td>13.02 ± 3.63</td><td>-14.10 (p<0.0001)</td></tr>
<tr><td>Sham TMS + Sertraline</td><td>26.67 ± 3.45</td><td>19.57 ± 3.96</td><td>-7.10 (p<0.0001)</td></tr>
</table>
Conclusion: HAMD-24 total depression scores decreased significantly for both the active and sham treatment groups. The finding of a significant decrease for the sham group is not surprising; however, given that the subjects in this study were not taking any medication prior to study entry. However, the 7-point difference in depression improvement in favor of the active group was statistically significant at p<0.0001, clearly demonstrating and supporting the enhanced effect of TMS as an adjunct to antidepressant therapy over antidepressant therapy alone.</td>
<td>HAMD-24
-4.028
CI: [-4.825,-3.232]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (between groups)</th></tr>
<tr>
<td>Qui et al. (2021)</td>
<td>• RCT:
• Active: Active TMS + Sertraline/ aripiprazole vs.
• Control: Sertraline/ aripiprazole only

• Active TMS: LDLPFC 10 Hz 6 weeks 80%MT

• sertraline: 25 – 100 mg/d
• aripiprazole from 2mg/d to 5mg/d (for patients with psychotic symptoms).</td>
<td>• Age (yrs.): 13 – 19.
• HAMD-24 ≥ 35
• First onset, unipolar depressive episode
• No prior anti-depressants, antipsychotics, or ECT therapy.</td>
<td>100</td>
<td>• HAMD-24</td>
<td>Mean change in scores on the HAMD-24 from baseline to endpoint (week 8) for each of the control and active treatment groups, and the significance of the difference in the change within each group is shown below.
<table>
<tr><th>HAMD-24</th><th>Baseline</th><th>Week 8</th><th>Mean Change</th></tr>
<tr><td>Active TMS + antidepressant</td><td>43.00 ± 2.96</td><td>7.86 ± 1.60</td><td>-35.14 (p<0.0001)</td></tr>
<tr><td>Antidepressant only</td><td>44.10 ± 2.85</td><td>13.00 ± 1.59</td><td>-31.10 (p<0.0001)</td></tr>
</table>
HAMD-24 % reductions at week 8 relative to baseline are shown below.
<table>
<tr><th>HAMD-24</th><th>Active TMS + antidepressant</th><th>Antidepressant only</th></tr>
<tr><td>≥75% reduction</td><td>21%</td><td>15%</td></tr>
<tr><td>≥50% reduction</td><td>19%</td><td>12%</td></tr>
<tr><td>≥25% reduction</td><td>11%</td><td>7%</td></tr>
<tr><td><25% (no improvement)</td><td>3%</td><td>12%</td></tr>
</table>
Conclusion: HAMD-24 total depression scores decreased significantly for both the active and control treatment groups at week 8 relative to baseline, although the magnitude of the change was greater for the active group relative to control. The finding of a significant decrease for the control group is not surprising; however, given that the subjects in this study were not taking any medication prior to study entry. However, the 4-point difference in depression improvement in favor of the active group clearly demonstrates and supports the enhanced effect of TMS as an adjunct to antidepressant therapy over antidepressant therapy alone. Note there was no sham device to account for a potential device placebo effect.</td>
<td>HAMD-24
-2.01
CI [-2.49, -1.54]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (between groups)</th></tr>
<tr>
<td>Pan, F. et al. (2020)</td>
<td>• Prospective, double-blind RCT.
• Subjects randomized to escitalopram oxalate (10mg/d) in combination with either active or sham rTMS.
• Left-sided DLPFC based on MRI data.
• rTMS treatment for 7 continuous days
• 120 trains of 5 s duration
• 10 Hz w/ inter-train intervals of 15 s
• 100% resting MT
• Total 6,000 pulses per session</td>
<td>• Treatment naïve MDD patients with suicidal ideation
• Age (yrs)
Active
18.14±3.94
Sham
21.43±6.79
• Gender (M/F)
Active
2/19
Sham
5/16</td>
<td>42
Active: 21
Control: 21</td>
<td>• HAMD-24
• MADRS
• Beck Scale for Suicide Ideation (BSI)
• Wisconsin Card Sorting Test (WCST)
• Continuous Performance Test (CPT)
• Stroop Color-Word Test (SCWT)</td>
<td>Mean change in scores on each of the HAMD-24, MADRS, and BSI for each of the active and sham control study groups from baseline to endpoint (Day 7) is shown in the table below.
<table>
<tr><th></th><th>Active TMS + escitalopram (n=21)</th><th>Sham TMS + escitalopram (n=21)</th><th>F</th><th>p</th></tr>
<tr><td colspan="5">HAMD-24</td></tr>
<tr><td>Baseline mean scores</td><td>38.33±7.93</td><td>35.76 ± 8.85</td><td>0.992</td><td>0.327</td></tr>
<tr><td>Baseline to Day 7 Change</td><td>-19.19±8.72</td><td>-4.48±6.27</td><td>36.682</td><td><0.001</td></tr>
<tr><td colspan="5">MADRS</td></tr>
<tr><td>Baseline mean scores</td><td>37.14±7.18</td><td>36.43±4.87</td><td>0.377</td><td>0.708</td></tr>
<tr><td>Baseline to Day 7 Change</td><td>-19.67±9.22</td><td>-4.33±6.53</td><td>37.997</td><td><0.001</td></tr>
<tr><td colspan="5">BSI</td></tr>
<tr><td>Baseline mean scores</td><td>19±5.94</td><td>21.48±5.91</td><td>-1.354</td><td>0.183</td></tr>
<tr><td>Baseline to Day 7 Change</td><td>-14.76±7.22</td><td>-4.71±5.30</td><td>37.553</td><td><0.001</td></tr>
</table>
Conclusion: Statistically significant decreases in depression ratings were attained for each of the HAMD-24, MADRS, and BSI assessment scales following 7 continuous days of treatment with Active rTMS + escitalopram versus Sham rTMS + escitalopram (p<0.0001) with no serious adverse events noted. Two adolescents displayed symptoms of hypomania after day 4 of treatment and were excluded from completing the study; however, It could not definitely be determined whether the hypomania was related to the TMS treatment, the escitalopram, or the combination therapy. Mild, transient adverse reactions, such as headache and tiredness, occurred in only 4 subjects. The findings of this RCT clearly demonstrate and provide additional support for the enhanced effect of TMS as an adjunct to antidepressant therapy over antidepressant therapy alone.</td>
<td>HAMD-24
-2.117 (Large)
CI [-2.878, -1.356]</td>
</tr>
</table>

Table 2. Supportive Single-Arm Studies from the Literature

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Wall, C. et al. (2016)</td>
<td>• Open-label, single-arm.
• Left-sided DLPFC rTMS Therapy per standard treatment protocol.
• 120% MT
• 10 Hz
• ITI: 26s
• duration: 4s
• 3,000 pulses
• 30 sessions, 5/wk over 6-8 wks.</td>
<td>• TRMDD
• Age (yrs):
– Mean ± SD: 15.9 ± 1.1
– Range: 13.9-17.4
60% male</td>
<td>10</td>
<td>• Children's Depression Rating Scale-Revised (CDRS-R)
• Quick Inventory of Depressive Symptomatology–- Adolescent (17 Item) – Self Report (QIDS-A17-SR)
Clinical Global Impression's Scale – Severity (CGI-S)</td>
<td>Change in mean assessment scores from baseline to treatment end (30 days) and from baseline to 6-months post-treatment were statistically significant for all measures:
<table>
<tr><th></th><th>CDRS-R</th><th>QIDS-A17-SR</th><th>CGI-S</th></tr>
<tr><td>30 days</td><td>-21.1 (p<0.005)</td><td>-4.0 (p<0.05)</td><td>-2.0 (p<0.005)</td></tr>
<tr><td>6 months</td><td>-23.0 (p<0.05)</td><td>-5.7 (p<0.05)</td><td>-2.4 (p<0.005)</td></tr>
</table>
Conclusion: TMS treatment resulted in statistically significant improvements in depression for this group of adolescents that was sustained through 6 months post-treatment, supporting the long-term efficacy of TMS Therapy as an adjunct to antidepressant therapy for the treatment of depressive symptoms in the adolescent patient population. Furthermore, there were no adverse events or tolerability issues with the treatment reported for any subject.</td>
<td>-1.671 (Large)
[-2.597,-0.745]</td>
</tr>
<tr>
<td>Wall, C. et al. (2011)</td>
<td>• Open-label, single-arm.
• Left-sided DLPFC rTMS Therapy per standard NeuroStar treatment protocol.
• 120% MT
• 10 Hz
• ITI: 26s
• duration: 4s
• 3,000 pulses
• 30 sessions, 5/wk over 6-8 wks.</td>
<td>• MDD
• Age (yrs):
– Mean ± SD: 16.5 ± 1.18
• Range: 14.6-17.887.5% female (7 of 8 subjects)</td>
<td>8</td>
<td>• CDRS-R
• QIDS-A17-SR
• CGI-S–</td>
<td>Change in mean assessment scores from baseline to treatment end (30 days) and from baseline to 6-months post-treatment were statistically significant for all measures:
<table>
<tr><th></th><th>CDRS-R</th><th>QIDS-A17-SR</th><th>CGI-S</th></tr>
<tr><td>30 days</td><td>-33.3±7.3 (p<0.005)</td><td>-6.4±2.8 (p<0.001)</td><td>-2.3±1.0 (p<0.001)</td></tr>
<tr><td>6 months</td><td>-33.1±3.8 (p<0.0001)</td><td>-7.6±2.1 (p<0.0001)</td><td>-2.7±1.0 (p<0.001)</td></tr>
</table>
Conclusion: TMS treatment resulted in statistically significant improvements in depression for this group of adolescents that were sustained through 6 months post-treatment, supporting the long-term efficacy of TMS Therapy as an adjunct to antidepressant therapy for the treatment of depressive symptoms in the adolescent patient population. Additionally, TMS treatment was well tolerated by the subjects, and no serious adverse events occurred. Of special note, three (3) of the subjects reported suicidal ideation at baseline which improved during the treatment course.</td>
<td>-4.243
[-6.411, -2.075]</td>
</tr>
</table>

Study	Study Design and Treatment	Population	Sample Size	Outcome Measure(s)	Study Results	Effect Size Hedges' g (within group)
Dhami. et al. (2019)	• Open-label, single-arm. • iTBS left DLPFC • cTBS right DLPFC–-80% MT • 10 sessions over 2 weeks	• MDD single or recurrent • Mean ATHF 3.0 ± 2.2 • Age (yrs): – Mean ± SD: 20.9 ± 2.6 – Range: 16-24 • 50% male / 50% female	20	• CDRS-R • HRSD-17 • Beck Depression Inventory (BDI-II) • Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q) •	Primary efficacy assessment of the change in mean rating from baseline to treatment end (2 weeks) on the HDRS-17 was found to be statistically significant, as with all other secondary assessments. Mean change and significance of the change for all study assessments at treatment end (2 weeks) relative to baseline: • HDRS-17: M -8.90 ($p < 0.0001$) • BDI-II: -13.1 ($p<0.005$) • Q-LES-I: -38.35 ($p<0.0005$) • CDRS-R: -25.3 ($p<0.05$) **Conclusion:** TMS therapy in adolescents with one or more failed medications in the current treatment episode resulted in statistically significant improvements in depression and quality of life.	-1.965 [-2.705, -1.225]

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Zhang, T. et al. (2019)</td>
<td>• Open label: 3-arm (Adolescents, Adults, and Older Adults)
• Left DLPFC
• 120% MT
• 10 Hz
• ITI: 12s
• 2,400 pulses
20 sessions, 4/wks</td>
<td>• Mood and anxiety disorders.
• Baseline score inclusion criteria
–HAM-D: ≥ 14
– HAM-A ≥ 10
<u>Adolescents</u>:
• n=42
• Age (yrs):
- Mean ± SD: 14.6 ± 2.0
- Range: 10-17
- 69% female
<u>Adults</u>:
• n=27
• Age (yrs):
- Mean ± SD: 39.3 ± 13.1
- Range: 18-59
- 56% male
<u>Older Adults</u>:
• n=48
• Age (yrs):
- Mean ± SD: 71.7 ± 7.1
- Range: 60-80
- 56% female</td>
<td>42</td>
<td>• Hamilton Depression Rating Scale (HAM-D)</td>
<td>Outcome assessments occurred after 2 weeks (mid-treatment) and 4 weeks (end of treatment) relative to baseline for the following, with results shown in the table below:
• HAM-D Treatment Response (TR), defined as ≥ 50% decrease in total score.
• HAM-D Remission Rates (RR), defined as endpoint score <7, .
<table>
<tr><th>HAM-D</th><th>Adolescent 2wk/4wk</th><th>Adult 2wk/4wk</th><th>Older Adult 2wk/4wk</th></tr>
<tr><td>TR</td><td>71%/100%</td><td>50%/100%</td><td>43.7%/76.2%</td></tr>
<tr><td>RR</td><td>48.4%/86.7%</td><td>34.6%/53.8%</td><td>8.3%/33.3%</td></tr>
</table>
Conclusion: While all age groups demonstrated improvement in depression symptoms following rTMS therapy, subjects in the adolescent group demonstrated statistically significant superior outcomes to those of subjects in each of the adult and older groups at both 2 week and 4 week assessments. There were no serious adverse events reported throughout the study duration. Only transient mild headache and musculoskeletal discomfort were noted.</td>
<td>-2.073 (Large)
[-2.607, -1.540]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Zhang, T. et al. (2020)</td>
<td>• Open label
• Left or Right DLPFC
• 120% MT
• 10 Hz or 1 Hz
• ITI: 12s
• 2,400 pulses
20 sessions, 4/wks</td>
<td>• Anxiety disorders.
• Baseline score inclusion criteria
–HAM-D: ≥ 14
– HAM-A ≥ 10
<u>Adolescents</u>:
• n=42
• Age (yrs):
- Mean ± SD: 15.2 ± 1.6
- 57% female
<u>Adults</u>:
• n=35
• Age (yrs):
- Mean ± SD: 44.6 ± 12.6
- 60% female
<u>Older Adults</u>:
• n=70
• Age (yrs):
- Mean ± SD: 71.4 ± 6.8
- 56% female</td>
<td>42</td>
<td>HAMD-17</td>
<td>Primary assessment occurred at 4 weeks post-treatment relative to baseline.
<table><tr><th></th><th>Baseline</th><th>Week 4</th><th>Change</th></tr><tr><td>HAM-D</td><td>14.31 ± 5.60</td><td>3.23 ± 1.74</td><td>F = 61.470,
p < 0.001</td></tr></table>
Conclusion: All age groups demonstrated improvement in depression and anxiety symptoms with rTMS, but subjects in the Adolescent group demonstrated statistically significant superior outcomes to those of subjects in each of the Adult and Older Groups, respectively. Furthermore, there was only one adverse event in the adolescent group which was mild and transient (dizziness).</td>
<td>-2.191
[-2.746, -1.636]</td>
</tr>
</table>

Study	Study Design and Treatment	Population	Sample Size	Outcome Measure(s)	Study Results	Effect Size Hedges' g (within group)
MacMaster, F. et al. (2019)	• Open-label, single-arm. • Left-sided DLPFC • 120% MT • 10 Hz • ITI: 26s • 75 trains • 3,000 pulses • 15 sessions, 5/wk for 3 wks.	• Moderate – severe TRMDD • Age (yrs): – Mean ± SD: 17.57 ± 1.98 – Range: 13-21 53% male	32	• HAM-D • CDRS • Beck Depression inventory (BDI)	Primary assessment at treatment end relative to baseline: • HAM-D TR: > 50% decrease in score: 56% • HAM-D RR: Endpoint score ≤ 7: 44% • Mean change in HAM-D from baseline to endpoint: -10.87 ($p < 0.0001$) Additional outcomes were also statistically significant for baseline to endpoint change: • CDRS: -13.64 ($p<0.0001$) • BDI: -13.90 ($p<0.0001$) **Conclusion:** 3 measures of depression each demonstrated statistically significant improvement post-treatment relative to baseline. There were only mild to moderate adverse events reported which were self-limiting (headache and neck pain) with no serious adverse events reported.	-1.779 CI [-2.331, -1.228]

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Rosenich, et al. (2019)</td>
<td>• Retrospective, comparative
• rTMS
• Right unilateral (n=8) or bilateral (n=4) DLPFC
• 110% MT
• 1 Hz and/or 10 Hz
• 900-2,400 pulses
• 18 sessions, 3/wk for 6 wks.</td>
<td>• MDD
• Failed ≥ 1 med (53% failed ≥5 meds)
• Age (yrs):
– Mean ± SD: 20.69 ± 2.55
– Range: 17-25
• 53% female</td>
<td>15</td>
<td>• HAM-D
• Montgomery-Asperg Depression Rating Scale (MADRS)
Zung Self-Rating Depression Scale</td>
<td>The results of this retrospective analysis were compared to the results of a previous retrospective analysis conducted on 229 adult patients aged 26 to 82 years treated with the identical TMS protocol at the same site. The findings revealed both statistically significant changes on all assessment tools for the currently evaluated adolescent group and no difference in findings between the adolescent and the adult group. Mean change in scores from baseline to end of treatment for each treatment group is shown below.
<table>
<tr><th></th><th>HAM-D</th><th>MADRS</th><th>Zung</th></tr>
<tr><td>Adolescent (n=15)</td><td>-7.27*</td><td>-9.43ł</td><td>-9.44ł</td></tr>
<tr><td>Adult (n=229)</td><td>-7.90</td><td>-9.70</td><td>-9.74</td></tr>
</table>
* significant at p<0.0001
ł significant at p<0.01

Below is a comparison of the response rate, partial response rate and remission rate on the HAM-D for the current adolescent and comparative adult treatment populations. Rates are defined as follows:
• Full response (FR): > 50% decrease in score
• Partial response (PR): 25% - 50% decrease in score
• Remission (REM): HAM-D Total score at endpoint <7
<table>
<tr><th>HAM-D</th><th>Adolescent (n=15)</th><th>Adult (n=229)</th></tr>
<tr><td>FR</td><td>40.0%</td><td>39.7%</td></tr>
<tr><td>PR</td><td>86.7%</td><td>64.4%</td></tr>
<tr><td>REM</td><td>13.3%</td><td>27.5%</td></tr>
</table>
Conclusion: 3 measures of depression demonstrated statistically significant improvements in post-treatment scores for 15 adolescents with MDD treated with TMS. Furthermore, the findings were consistent with those for a group of adult patients with MDD who were treated at the same facility using the same treatment protocol. This indicates that TMS therapy is equally effective on adolescents as it is on adults when used as an adjunctive therapy to antidepressants. There were no serious adverse events and only mild and transient side effects such as discomfort at the treatment site, headache, and tiredness following treatment.</td>
<td>-1.150
[-1.781, -0.519]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Shere, SS. et al. (2021)</td>
<td>• Open-label, single-arm.
• iTBS left DLPFC
• cTBS right DLPF– -80% MT
– 1,800 pulses
• 1 session per day for 10 consecutive days.</td>
<td>• Adolescents with depression:
– 84% unipolar
– 8% recurrent depressive disorder
– 8% bipolar
– Add-on therapy
• Age (yrs):
16.22 Mean ± SD:8 ± 1.20
– Range:12-18</td>
<td>26</td>
<td>• CDRS-R
• Brief Psychiatric Rating Scale for Children (BPRS-C)
Children's Global Assessment Scale (CGAS)</td>
<td>Of the 26 adolescents enrolled in the study, 23 completed all 10 sessions and were available for the 12w follow up. Mean change is scored on the respective scales from baseline to endpoint (end of treatment) as shown below. Two subjects with bipolar disorder at baseline experienced affective switches during treatment: one after 3 treatments and the other after 10. The subject experiencing affective switch after 3 treatments withdrew from the study and is not included in the data below.
<table>
<tr><th></th><th>CDRS-R</th><th>BPRS-C</th><th>CGAS</th></tr>
<tr><td>10 days*</td><td>-26.7±11.2 (p<0.01)</td><td>-9.72±5.15 (p<0.01)</td><td>15.2±9.1 (p<0.01)</td></tr>
<tr><td>12 weeks*</td><td>-29.3±14.0 (p<0.01)</td><td>-</td><td>25.6±12.01 (p<0.01)</td></tr>
</table>
* Change relative to baseline

Conclusion: Depression and overall behavioral health assessments improved significantly for the population of adolescents treated in this study with theta burst TMS therapy as an add-on treatment to existing medication. Adverse events were mainly mild and transient in the MDD cohort. Additionally, cognitive function tests showed significant improvement.</td>
<td>-2.262 [-2.981, -1.543]</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Study Design and Treatment</th><th>Population</th><th>Sample Size</th><th>Outcome Measure(s)</th><th>Study Results</th><th>Effect Size Hedges' g (within group)</th></tr>
<tr>
<td>Bloch, Y. et al. (2008)</td>
<td>• Open label
• DLPFC
• rTMS
- 80% MT
- 2 s trains of 5 s duration
- 10 Hz
- ITT of 58 s
- 20 mins / session
• 1 session per day for 14 consecutive days.</td>
<td>• MDD:
– Failed 2+ meds
– Failed 1+ psychotherapy
• Age (yrs):
– Mean ± SD: 17.22 ± 0.83
– Range:16-18
• 78% female</td>
<td>9</td>
<td>• CDRS-R
• BDI-II
• CGIS
• Suicidal Ideation Questionnaire (SIQ)
• Cambridge Neuropsychological Test</td>
<td>Nine adolescents with severe resistant depression were enrolled in this study. Subjects included those with a history of childhood sexual trauma, PTSD, substance abuse, eating disorder, borderline personality disorder, ADHD, OCD, and prior suicide attempts. Two subjects had previously been treated with ECT with partial response. Mean change is scored on the respective scales from baseline to endpoint (one-month post-treatment) as shown below.
<table>
<tr><th>CDRS-R</th><th>BDI</th><th>CGI-S</th><th>SIQ</th></tr>
<tr><td>-16.6</td><td>-12.1</td><td>-2.0</td><td>-12.0</td></tr>
</table>
In consideration of the study primary efficacy measure of a 30% reduction on the CDRS-R, 3 patients were responders, and 2 remained in clinical remission at 1-year post-treatment. There were no serious adverse events and only mild side effects (5 of 9 reported mild headache). Furthermore, negative cognitive changes were not observed.</td>
<td>-1.166
[-1.964, -0.367]</td>
</tr>
</table>

Summary

In summary, the large real-world data set from the TrakStar database and available published data demonstrates substantially equivalent treatment effect of TMS therapy as an adjunct to antidepressant therapy over antidepressant therapy alone in reducing depression in adolescents that is consistent within and across all studies based on a total of 1,812 adolescents. Furthermore, the authors of the 14 studies concluded that TMS is well tolerated and safe for adolescents.

Table 3: Substantial Equivalence Comparison

	Subject Device **NeuroStar Advanced Therapy System** **K231926**	**Primary Predicate Device** **NeuroStar Advanced Therapy System** **K230029** **Reference Devices** **NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	**Explanation of Differences**
Indications for Use	NeuroStar Advanced Therapy is indicated as an adjunct for the treatment of Major Depressive Disorder (MDD) in adolescent patients (15-21).	NeuroStar Advanced Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.	Adding adolescent patients (15 and older) as an adjunct treatment for MDD to the IFU. Clinical data provided demonstrates that the subject device is safe and effective for the treatment of adolescent patients and that there are no new risks associated with the expanded indication.
Intended Use	Major Depressive Disorder (MDD)	Major Depressive Disorder (MDD)	No Difference
Anatomical Sites	Left dorsolateral prefrontal cortex	Left dorsolateral prefrontal cortex	No Difference
Target Population	Adolescent patients age 15-21	Adult Patients	Adding adolescent patients (15 and older) as an adjunct treatment for MDD to the IFU. Clinical data provided demonstrates that the subject device is safe and effective for the treatment of adolescent patients and that there are no new risks associated with the expanded indication.
Clinical Setting	Inpatient and outpatient settings including physician's offices and clinics, hospitals, and general medical/surgical hospitals	Inpatient and outpatient settings including physician's offices and clinics, hospitals, and general medical/surgical hospitals	No Difference

	Subject Device	Primary Predicate Device NeuroStar Advanced Therapy System K230029	Explanation of Differences
	NeuroStar Advanced Therapy System K231926	**Reference Devices NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	
Materials	Standard materials commonly used in the manufacture of electrical medical devices	Standard materials commonly used in the manufacture of electrical medical devices	No Difference
Biocompatibility	Patient-contacting device components use standard materials compliant with ISO 10993-1 that are commonly used in consumer products and medical device applications	Patient-contacting device components use standard materials compliant with ISO 10993-1 that are commonly used in consumer products and medical device applications	No Difference
Energy Source	Power console with magnetic coil for delivery for magnetic energy	Power console with magnetic coil for delivery for magnetic energy	No Difference
Electrical Safety & EMC	IEC 60601-1 compliant IEC 60601-1-2 compliant	IEC 60601-1 compliant IEC 60601-1-2 compliant	No Difference
Communication with TrakStar	Wireless (Wi-fi) and Ethernet cable	Wireless (Wi-fi) and Ethernet cable	No Difference
Sterility	No parts of the device, accessories or components are required to be sterilized	No parts of the device, accessories or components are required to be sterilized	No Difference
Coil Type	Ferromagnetic Iron core Internal cooling fan	Ferromagnetic Iron core Internal cooling fan	No Difference
Coil Positioning System	Integrated into Head Support System Laser-aided coil placement	Integrated into Head Support System Laser-aided coil placement	No Difference

	Subject Device	Primary Predicate Device NeuroStar Advanced Therapy System K230029	Explanation of Differences
	NeuroStar Advanced Therapy System K231926	**Reference Devices NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	
Treatment Schedule	5 days per week for 6 weeks with taper over 3 weeks (3 sessions first week, 2 sessions second week and 1 session third week) for total of 36 treatment sessions	5 days per week for 6 weeks with taper over 3 weeks (3 sessions first week, 2 sessions second week and 1 session third week) for total of 36 treatment sessions	No Difference
Device Components	• Mobile Console • Ferromagnetic Coil for delivering treatment • Head Support System for coil positioning • MT Cap for coil positioning • D-Tect™ MT Accessory for MT location and level determination • Multi-use disposable for contact sensing and magnetic field quality control • Single-use treatment pack including disposable hygienic barriers and coil positioning head strap for use with the standard 5 cm method • Single-use treatment pack including disposable hygienic barriers and head strap for use with the Beam F3 method for determining treatment location and coil positioning • TrakStar System for recording patient data	• Mobile Console • Ferromagnetic Coil for delivering treatment • Head Support System for coil positioning • MT Cap for coil positioning • D-Tect™ MT Accessory for MT location and level determination • Multi-use disposable for contact sensing and magnetic field quality control • Single-use treatment pack including disposable hygienic barriers and coil positioning head strap for use with the standard 5 cm method • Single-use treatment pack including disposable hygienic barriers and head strap for use with the Beam F3 method for determining treatment location and coil positioning • TrakStar System for recording patient data	No Difference
%MT Range	25% to 140% MT	25% to 140% MT	No Difference

	Subject Device	Primary Predicate Device NeuroStar Advanced Therapy System K230029	Explanation of Differences
	NeuroStar Advanced Therapy System **K231926**	**Reference Devices** **NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	
Pulses per Second (PPS) Range	For treatment: 1 to 30 PPS For MT determination: 0.1-0.3 PPS	For treatment: 1 to 30 PPS For MT determination: 0.1-0.3 PPS	No Difference
Induced Electrical Field at 2 cm at 1.0 SMT	135 V/m (Nominal)	135 V/m (Nominal)	No Difference
Pulse Type	Biphasic Sinusoid	Biphasic Sinusoid	No Difference
Pulse Width	185 µS (Nominal)	185 µS (Nominal)	No Difference
Treatment Protocols	**Standard Treatment:** **Level:** 120% MT with allowable adjustments **Repetition Rate:** 10 PPS **Stimulation Time:** 4 s **Inter-train Interval:** As low as 11 s **Session Duration:** As low as 18.75 min **Pulses per Session:** 3000 **Sessions per Week:** 5	**Standard Treatment:** **Level:** 120% MT with allowable adjustments **Repetition Rate:** 10 PPS **Stimulation Time:** 4 s **Inter-train Interval:** As low as 11 s **Session Duration:** As low as 18.75 min **Pulses per Session:** 3000 **Sessions per Week:** 5	No Difference
	NeuroBurst Treatment: **Level:** 80-120% MT with allowable adjustments **Stimulation Time:** 2 s **Inter-train Interval:** 8 s **Pulses per Burst:** 3 **Interpulse Interval:** 20 ms **Session Duration:** 3.3 min **Pulses per Session:** 600	**NeuroBurst Treatment:** **Level:** 80-120% MT with allowable adjustments **Stimulation Time:** 2 s **Inter-train Interval:** 8 s **Pulses per Burst:** 3 **Interpulse Interval:** 20 ms **Session Duration:** 3.3 min **Pulses per Session:** 600	

	Subject Device	Primary Predicate Device NeuroStar Advanced Therapy System K230029	Explanation of Differences
	NeuroStar Advanced Therapy System **K231926**	**Reference Devices** **NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	
	Bursts per Second: 5 **Amplitude:** 0.22-2.08 SMT (≤5% drop)	**Bursts per Second:** 5 **Amplitude:** 0.22-2.08 SMT (≤5% drop)	
Treatment Level Range	**Standard Treatment:** 0.22 to 2.08 SMT Calibrated linear output	**Standard Treatment:** 0.22 to 2.08 SMT Calibrated linear output	No Difference
	NeuroBurst Treatment: 0.22 to 1.9 SMT 80-120% MT ≤5% drop	**NeuroBurst Treatment:** 0.22 to 1.9 SMT 80-120% MT ≤5% drop	
Stimulation Time Pulse Train Duration Range	**Standard Treatment:** 1 PPS: 1 to 600 s >1 PPS: 1 to 20 s	**Standard Treatment:** 1 PPS: 1 to 600 s >1 PPS: 1 to 20 s	No Difference
	NeuroBurst Treatment: 1 to 10 s	**NeuroBurst Treatment:** 1 to 10 s	
Inter-train Interval Range	**Standard Treatment:** 1 PPS: 0 to 600 s >1 PPS: 10 to 60 s	**Standard Treatment:** 1 PPS: 0 to 600 s >1 PPS: 10 to 60 s	No Difference
	NeuroBurst Treatment: 1 to 60 s	**NeuroBurst Treatment:** 1 to 60 s	
Pulses per Treatment Session	**Standard Treatment:** Nominal: 3000 Maximum: 5000	**Standard Treatment:** Nominal: 3000 Maximum: 5000	No Difference

	Subject Device	Primary Predicate Device NeuroStar Advanced Therapy System K230029	Explanation of Differences
	NeuroStar Advanced Therapy System **K231926**	**Reference Devices** **NeuroStar Advanced Therapy System** K083538, K130233, K133408, K160703, K161519, K201158, K213543, and K222230	
	NeuroBurst Treatment: Nominal: 600 Maximum: 2000	**NeuroBurst Treatment:** Nominal: 600 Maximum: 2000	
Pulses per Burst (PPB)	**NeuroBurst Treatment:** 1 to 5	**NeuroBurst Treatment:** 1 to 5	No Difference
Interpulse Interval	**NeuroBurst Treatment:** 20 to 2000 ms	**NeuroBurst Treatment:** 20 to 2000 ms	No Difference
Bursts per Second (BPS)	**NeuroBurst Treatment:** 0.1 to 20.0 Hz	**NeuroBurst Treatment:** 0.1 to 20.0 Hz	No Difference

	Treatment parameters		Treatment parameters		
	Magnetic Field Intensity	120%	Magnetic Field Intensity	120%	No Difference
	Repetition Rate	10 Hz	Repetition Rate	10 Hz	No Difference
	Train Duration	4 sec	Train Duration	4 sec	No Difference
	Inter-Train-Interval	11-26 secs	Inter-Train-Interval	11-26 secs	No Difference
Energy Delivered and Performance	Number of Trains	75	Number of Trains	75	No Difference
	Number of Pulses	3000	Number of Pulses	3000	No Difference
	Treatment Duration	18.75 min	Treatment Duration	18.75 min	No Difference
	Treatment area of brain to be stimulated: Left Dorsolateral Prefrontal Cortex		Treatment area of brain to be stimulated: Left Dorsolateral Prefrontal Cortex		No Difference
	Output Stimulation Parameters Available Stimulation Intensity in terms of Standard Motor Threshold (SMT) units		Output Stimulation Parameters: Available Stimulation Intensity in terms of Standard Motor Threshold (SMT) units		No Difference
	Range: .22 – 2.08 Waveform: Biphasic		Range: .22 – 2.08 Waveform: Biphasic		No Difference

Design	The system consists of: 1. Mobile console 2. System software with GUI 3. Treatment chair 4. Head support system 5. Coil positioning system 6. Same Coil for both MT and treatment 7. Coil fixture 8. Data management system	The system consists of: 1. Mobile console 2. System software with GUI 3. Treatment chair 4. Head support system 5. Coil positioning system 6. Same Coil for both MT and treatment 7. Coil fixture 8. Data management system	No Difference
Coil	Biphasic Figure 8 Coil with Ferromagnetic Core	Biphasic Figure 8 Coil with Ferromagnetic Core	No Difference
Cooling	Air cooled. Used for both MT determination and treatment	Air cooled. Used for both MT determination and treatment	No Difference
Quality & Risk Standards	Company complies with ISO 13485:2016 and ISO 14971	Company complies with ISO 13485:2016 and ISO 14971	No Difference
Electrical Safety & Electromagnetic Compatibility	Complies with IEC60601-1 and IEC60601-1-2	Complies with IEC60601-1 v. 3.1, and IEC60601-1-2	No Difference

Conclusion:

The NeuroStar Advanced Therapy System has the same intended use, principles of operation, and technological characteristics as the predicate device. Clinical performance data demonstrates that the subject device is as safe and effective as the predicate device when used for its intended purpose as an adjunct to treat major depressive disorder in adolescents (15-21). Thus, the NeuroStar Advanced Therapy System is substantially equivalent to the predicate device.