April 22, 2024

Curio Digital Therapeutics Inc.
Shailja Dixit
CEO
100 Outlook Drive, 2nd Floor
Princeton, New Jersey 08540-7814

Re: K223515
Trade/Device Name: MamaLift Plus
Regulation Number: 21 CFR 882.5801
Regulation Name: Computerized behavioral therapy device for psychiatric disorders
Regulatory Class: Class II
Product Code: SAP
Dated: February 14, 2024
Received: February 14, 2024

Dear Shailja Dixit:

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
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)*
K223515

Device Name
MamaLift Plus

Indications for Use *(Describe)*
MamaLift Plus is a prescription-only digital therapeutic intended to provide neurobehavioral interventions to patients 22 years of age and older, as an adjunct to clinician-managed outpatient care. MamaLift Plus treats mild to moderate postpartum depression by improving a patient's symptoms of depression.

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.

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510(k) Summary

MamaLift Plus
Submission Number: K223515

Submitter:
Curio Digital Therapeutics, Inc.
100 Overlook Drive, Floor 2
Princeton, NJ 08540-7814
Phone: 267-629-9674
Contact person: Shailja Dixit

Date Prepared: April 18, 2024

Name of Device: MamaLift Plus™
Common or Usual Name: Prescription Digital Therapeutic for Postpartum Depression
Regulation Number: 21 CFR 882.5801
Regulation Name: Computerized Behavioral Therapy Device for Psychiatric Disorders
Product Code: SAP
Product Code Name: Computerized behavioral therapy device for depressive disorders.
Regulatory Class: II

Predicate Device: Somryst™ (K191716) by Pear Therapeutics Inc., a cognitive behavioral therapy for insomnia (CBT-I) via a mobile application).
Trade/Device Name: Somryst
Regulation Number: 21 CFR 882.5801
Regulation Name: Computerized Behavioral Therapy Device for Psychiatric Disorders
Product Code: QVO
Product Code Name: Computerized behavioral therapy device for insomnia
Regulatory Class: Class II

Device Description:
MamaLift Plus is a digital therapy designed to treat symptoms of postpartum depression by delivering evidence-based therapeutic components of Cognitive Behavioral Therapy (CBT) via software on a mobile application (smartphone or tablet). MamaLift Plus is indicated as a behavioral health intervention for patients 22 years of age and older with mild to moderate symptoms of depression by improving their symptoms of depression. As with face- to-face CBT, MamaLift Plus uses personalized cognitive restructuring as the main therapeutic component to improve the symptoms of postpartum depression. This element is mapped onto standard, evidence-based CBT interventions that are developed for and provided by a therapist in a face-to-face care setting with a patient. The content is conveyed via a sequence of eight self-guided and interactive treatment modules daily over a period of eight to nine weeks sequentially.

Patients are encouraged to complete all eight modules of the MamaLift Plus application at the rate of one module per week. However, the entire program can last up to 9 weeks, inclusive of the baseline and post-treatment assessment periods. Full engagement by prescribing clinicians and their support staff facilitates effective use by patients of the prescribed treatment and their continued use in conjunction with ongoing monitoring by the clinician.

The content of MamaLift Plus is delivered through a variety of features which include text, personalized goal setting, graphical feedback based on inputted symptoms, animations, and illustrations to enrich comprehension, quizzes to test and enhance user knowledge, video vignettes to promote user identification with material, and video-based expert explanations. Periodic notifications or "nudges" are also sent to increase user engagement and encourage program adherence. Additional features of MamaLift Plus include a daily tracker in which patients can self- monitor and record standardized sleep parameters (e.g., sleep and naps), self-reports of perceived Sleep Quality, and self-reports of perceived Energy Level. In addition, MamaLift Plus offers a daily mood tracker and activity tracker. The application provides personalized cognitive restructuring guidance based on the individual's beliefs, context, and attitudes.

To facilitate its use as an adjunct to outpatient standard of care conducted under the supervision of a qualified health care provider, MamaLift Plus includes a clinician dashboard. The clinician facing dashboard summarizes patient use of the mobile application during the treatment period thereby enabling the clinician to assess and monitor their patient's progress throughout the therapeutic period. Clinical data collected via the patient interface, including self-reports of depressive symptoms/moods, and sleep data, are also displayed via the clinician dashboard. (All data are encrypted and compliant with data privacy and patient confidentiality requirements of the Health Insurance Portability and Accountability Act.) These features are intended to support the clinician and enable patient follow up, engagement and communication of healthcare decisions. This facilitates treatment adherence and achievement of optimal patient outcomes. These are critical components that demonstrate the effectiveness of MamaLift Plus.

Indications for use:
MamaLift Plus™ is a prescription-only digital therapeutic intended to provide neurobehavioral interventions to patients 22 years of age and older, as an adjunct to clinician-managed outpatient care. MamaLift Plus treats mild to moderate postpartum depression by improving a patient's symptoms of depression.

Substantial Equivalence Comparison:
The table below compares the intended use and technological characteristics of MamaLift Plus and the predicate device.

Technological Characteristics Comparison

Item	**Subject Device MamaLift Plus**	**Proposed Predicate Device (**K191716**)** Somryst	**Comparison**
Medical Device Type	Software as a Medical Device (SaMD)	Software as a Medical Device (SaMD)	Same
Product Code Name	Computerized behavioral therapy device for depressive disorders.	Computerized behavioral therapy device for insomnia	Similar, therapies for different conditions
Regulation Number	21 CFR 882.5801	21 CFR 882.5801	Same
Regulation Name	Computerized Behavioral Therapy Device for Psychiatric Disorders	Computerized behavioral therapy device for psychiatric disorders	Same
Product Code	SAP	QVO	Similar

Device Type	Class II	Class II	Same
Software Architecture	Patient facing mobile application, clinician facing dashboard, backend services.	Patient facing mobile application, clinician facing dashboard, backend services.	Same
Mechanism of Action	Cognitive Behavioral Therapy (for Post partum depression)	Cognitive Behavioral Therapy (for Insomnia).	Similar, therapies for different conditions only.
Software Content	Text, video, and audio content.	Text, video, and audio content.	Same
Therapy Duration	8-9 weeks	9 weeks	Similar, 0 to 1 week less duration in subject device
Intended Environments	Health care settings or home	Health care settings or home	Same
Target Population	Female patients 22 years of age and older diagnosed with post partum depression currently enrolled in outpatient treatment under the supervision of a clinician	Patients 22 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician	Similar, one is gender based
User Interface	Software application that requires users to log in, go through modules of therapeutic content (text, video, audio), interact with the device, and receive notifications to increase engagement and encourage program adherence.	Software application that requires users to log in, go through modules of therapeutic content (text, video, audio), interact with the device (through quizzes, videos, reporting sleep and mood, etc.), and receive notifications to increase engagement and encourage program adherence.	Similar, interactions tailored for different conditions.
Mobile Platform	Smartphones, tablets (iOS and Android).	Smartphones, tablets (iOS and Android).	Same

The subject and predicate device implement similar device technologies with similar architectures and software content in the intended environments. In addition, both MamaLift Plus and Somryst are computerized behavioral therapy devices for psychiatric disorders regulated under 21 CFR 882.5801. The products deliver digitized cognitive behavioral therapy and are deployed through mobile applications for smart devices. They both have a sequence of content modules with similar behavioral treatment techniques, software architecture, and are prescription devices.

MamaLift Plus and Somryst are both intended to be used by patients 22 years of age or older, however, MamaLift Plus is solely to be used by those diagnosed with post-partum depression. The Mechanism

of Action and User Interface are similar for both devices but tailored for different therapeutic conditions.

Non-Clinical Performance Data:
Testing to support the safety and performance of MamaLift Plus can be summarized as follows:

- Human factors testing for functionality and usability as per recommendations of the 2016 guidance document *Applying Human Factors and Usability Engineering to Medical Devices*
- Functional and Software verifications and validation testing as per recommendations of 2019 FDA Policy for *Device Software Functions: Guidance for Industry and Food and Drug Administration Staff*
- Matrix Traceability testing as per recommendations of 2019 FDA Policy for *Device Software Functions: Guidance for Industry and Food and Drug Administration Staff*
- Cybersecurity per recommendations of FDA's April 8, 2022, draft guidance entitled Cybersecurity in *Medical Devices: Quality System Considerations and Content of Premarket Submissions for supporting its premarket submission.*

Clinical Performance Data:
Performance to assess safety and efficacy in MamaLift Plus was addressed as per the 2017 *FDA Policy for Software as a Medical Device (SaMD): Clinical Evaluation Guidance for Industry and Food and Drug Administration Staff*.

US Pivotal Study Design

The indication for use is supported by the results from the SuMMER (Supporting Maternal Mental health & Emotional Regulation), a pivotal, remote, sham controlled, randomized study that enrolled 141 participants in the 33 states of USA: 4 states with the largest enrolments are California, New York, Florida, and Texas. The patients were recruited using online-ads (Google Ads, Facebook Ads, Reddit Ads) and social media (Instagram Ads).

The participants were randomized in a 2:1 ratio to the treatment arm (CDT001, MamaLift Plus plus treatment as usual (TAU)) or sham control arm (CDP002, Digital Placebo arm plus TAU). The study was powered to enroll 210 US subjects in total (140 in CDT001 and 70 in CDT002). The protocol allowed for an interim analysis to meet the cutoff date for an FDA response. A total of 141 subjects were enrolled when the study was stopped for this purpose. Sponsor chose a 2:1 ratio for the following reasons: increased exposure to active arm, more data in active arm, and to facilitate recruitment and retention. The study sample size was planned to have 80% power for the primary endpoint for a 2:1 randomization scheme. The randomization was stratified by "New Mother" status (Yes/No).

Assessments were scheduled for week 4 and week 8 (end of study). There was no planned follow-up after the week 8 assessment.

US Pivotal Study Population

The study enrolled female patients from 18 to 50 years who gave birth within 3 months prior to the enrollment, had an EPDS score at baseline between 13-19 (inclusive) and a confirmatory clinical diagnosis of PPD that was confirmed by licensed behavioral health therapist or medical professional.
Only those participants were included who answered "0/Never" or "1/Hardly Ever" to the self-harm question (question number 10) on the EPDS questionnaire.

Key exclusion criteria included patients who were diagnosed with serious mental illness (SMIs) as defined by psychotic symptoms or treatment-resistant depression; severe depression (which includes participants hospitalized for depression or currently using more than 2 medications for depression at the same time); or cognitive impairment.

Participants were randomly assigned to one of two arms: treatment device plus treatment as usual (TAU) or sham control plus TAU. Participants were allowed to continue with TAU in both arms. The sham control mimicked the features, functionality, and user experience of the treatment. It was designed to appear and feel similar to the treatment, but without the therapeutic or active ingredients that would induce the intended physiological or psychological effects. Specifically, the most important difference between participants in the two arms was that participants in sham control app did not receive any CBT content. Sham control content paralleled the treatment arm with regards to frequency of engaging with the app and the relative "workload" in each arm was similar.

Analysis Populations

The Intent to Treat Analysis Set (ITT) included all randomized participants who started at least 1 module. ITT participants with no post-baseline EPDS assessment were classified as non-responders.

Full Analysis Set (FAS) is a subset of the ITT and included all participants randomized in the study who started at least 1 module and provided a post-baseline (either Week 4 or end of treatment) EPDS assessment. This population was used for primary effectiveness analyses. For participants with no week 8 EPDS assessment in ITT and FAS, their week 4 EPDS value was used.

Evaluable Population (EP) population is a subset of the FAS and included all participants who completed their baseline and end of treatment EPDS assessments.

The sample sizes for the 3 analysis sets are shown in Table 2. A small number of participants (5 in treatment and 6 in sham control) did not provide any post-baseline EPDS assessment. Missing rates are 5.3% and 13.0% for the treatment and control arms, respectively.

Table 2: Participant Disposition

Analysis Set	MamaLift Plus (CDT001)	Sham Control (CDP002)
Intent to Treat (ITT)	95	46
Full Analysis Set (FAS)	90	40
Evaluable Set (EP)	78	38

Socio-demographic baseline characteristics of the ITT population are presented in Table 3. The two groups are comparable in age (32.39 vs 30.74 years), marital status (76.8% vs 82.6% married/living together) and educational level (68.4% vs 80% higher education). Approximately two-thirds (63.1% vs 67.3%) of the women were first time mothers in each of the study arms.

Table 3: Socio-demographic characteristics (ITT)

	MamaLift Plus (CDT001) N= 95	Sham Control (CDP002) N=46
Age	32.39 (5.54)	30.74 (5.54)
Marital status		
Married/living together	73 (76.8%)	38 (82.6%)
Educational level		
Until High school	25 (26.3%)	7 (15.2%)
Higher education	65 (68.4%)	36 (80.0%)
Other or Unknown	5 (5.3%)	3 (4.8%)
New Mom		
Yes	60 (63.1%)	31 (67.3%)
Region (USA)		
California	12 (12.6%)	8 (17.4%)
New York	10 (10.5%)	6 (13%)
Texas	12 (12.6%)	3 (6.5%)
Florida	7 (7.4%)	2 (4.3%)
All other States	54 (56.8%)	27 (58.7%)

Effectiveness Endpoints

Primary Endpoint: The primary end point of the study was "4 or more points improvement in the Edinburgh Postpartum Depression Scale (EPDS)." The 4-point improvement is considered a clinically meaningful improvement.

Key Secondary Endpoint: Improvement of EPDS below the threshold (< 13). EPDS score of below 13 is considered below the threshold of diagnosable postpartum depression.

Results in ITT and FAS Population

Results in the ITT indicate that a greater proportion of the participants treated with MamaLift Plus plus TAU (CDT001) achieved improvement (4+ points is defined as clinically meaningful) compared to the sham plus TAU control group (86.3% vs 23.9%). The comparison between the 2 arms is significant with a p-value < 0.0001.

Similar results are observed in the FAS population and are consistent as shown in Table 4.

The key secondary endpoint of improving to below an EPDS of 13 at a post-baseline assessment showed

that a greater proportion of participants in the MamaLift Plus plus TAU arm achieved this compared to the sham plus TAU control arm in both ITT and FAS with, the corresponding p-values being significant (< 0.0001). [Table 4]

Table 4: Responder analysis for ITT and FAS Population

Population		MamaLift Plus (CDT001) N= 95	Sham Control (CDP002) N= 46	p-value
ITT	Primary Endpoint: Improvement of 4+ points	82 (86.3%)	11 (23.9)	< 0.0001
	Secondary Endpoint: Improvement to < 13 EPDS	79 (83.2%)	15 (32.6)	< 0.0001
		MamaLift Plus (CDT001) N= 90	Sham Control (CDP002) N= 40	p-value
FAS	Primary Endpoint: Improvement of 4+ points	82 (91.1%)	11 (27.5%)	< 0.0001
	Secondary Endpoint: Improvement to < 13 EPDS	79 (87.7%)	15 (37.5%)	< 0.0001

Effectiveness by Antidepressant Medication Use

Further analysis was done to understand the effectiveness while using anti-depressant medication by the participants in the two arms. Out of a total of 141 participants, 111 participants (78.7%) did not take any antidepressant medication during the study period. In the treatment plus TAU arm, 83.2% (79/95) were not on anti-depressants while the corresponding percentage in the sham plus TAU control arm 69.6% (32/46).

Response rates for the ITT population (taking and not taking antidepressant medication) are in favor of the MamaLift Plus plus TAU 5(CDT001) arm.

These results for population "Not taking antidepressant Medication Use" are provided in Table 5a and for population taking anti-depressant medication is shown in Table 5b.
It is noted that even though the percentage of anti-depressant usage is greater in the sham control arm (30% vs 17%), the effect size remains consistent and in favor (93.8% vs 21.4%) of the active arm indicating that there was no impact of anti-depressives.

Table 5a: Primary Endpoint Results for Participants Not taking antidepressant medication

	MamaLift Plus (CDT001) (N=79)	Sham Control (CDP002) (N=32)
All moms	67 (84.8%)	8 (25%)
New mom= Yes	44/52 (84.6%)	6/23 (26.1%)

New mom= No	23/27 (85.2%)	2/9 (22.2%)

Table 5b: Primary Endpoint Results for Participants Taking Antidepressant Medication

	MamaLift Plus (CDT001) (N=16)	Sham Control (CDP002) (N=14)
All moms	15 (93.8%)	3 (21.4%)
New mom= Yes	7/8 (87.5%)	2/8 (25%)
New mom= No	8/8 (100%)	1/6 (16.7%)

Subgroup Analysis: A key subgroup was defined by "New Mother (Mom)" status. Approximately 2/3 of all participants were mothers for the first time. Results for the primary endpoint are provided by "New Mother" status in Table 6. The findings in each subgroup strata are consistent with the overall treatment arm results and are in favor of the MamaLift Plus plus TAU treatment.

Table 6: Primary endpoint (change of 4+ points) analysis for subgroup of "New Mom" women (FAS Population)

	MamaLift Plus (CDT001) N = 90	Sham Control (CDP002) N = 40
New Mom = YES (N = 84)	51/56 (91.1%)	8 /28 (28.6%)
New Mom = NO (N = 46)	31/34 (91.2%)	3/12 (25%)

Results in the Evaluable Population (EP)

Responder analysis for improvement of 4 or more points in the EPDS scale and for improving EPDS below the threshold (< 13) in the Evaluable (participants who completed their baseline and End of study EPDS assessments) population are presented in Table 7. A total of 116 participants completed the study and provided week 8 EPDS assessments.

Table 7: Responder analysis for the Evaluable Population

	MamaLift Plus (CDT001) N = 78	Sham Control (CDP002) N = 38
Primary Endpoint: Change of 4+ points	70/78 (89.7%)	11/38 (28.9%)
Key Secondary: Change to < 13 EPDS	69/78 (88.5%)	14/38 (36.8%)

The results in the Evaluable population are consistent with those observed in the FAS and in favor of MamaLift Plus treatment arm.

Subgroup Analysis of "new mom"

Table 8 presents responder analysis for improvement of 4 or more points and for improving below the threshold (< 13) in a subset of women who are New Mom, i.e., gave birth to their first child. Results are consistent with the FAS population.

Table 8: Primary endpoint (change of 4+ points) analysis for subgroup of New Mom women (Evaluable Population)

	MamaLift Plus (CDT001) N = 78	Sham Control (CDP002) N = 38
New Mom = YES	43/48 (89.6%)	8/28 (28.6%)
New Mom = NO	27/30 (90%)	3/10 (30%)

Summary of Effectiveness Results

Use of MamaLift Plus can result in improvements in the symptoms of depression for patients, as measured by Edinburgh Postnatal Depression Score (EPDS). The long-term benefit of treatment with MamaLift Plus plus TAU on recurrent depression has not been evaluated in studies lasting beyond eight weeks. The ability of MamaLift Plus to prevent potential depression relapse or recurrent depressive episodes after treatment discontinuation has not been studied.

There are blinding concerns, a blinding assessment was not conducted. Note, the study coordinator performing the randomization and assigning the MamaLift Plus or Sham App was unblinded.

Further, participants were allowed to continue with treatment as usual (TAU). Treatment as usual was untracked, participants were allowed to continue with TAU; however, TAU was not followed or tracked to determine what it entailed and if it was applied consistently between the two groups. Sponsor did collect use of anti-depressives at baseline and end of study.

There was no multiplicity adjustment for the interim analysis. Only two-thirds of planned subjects were enrolled. However, after applying plausible multiplicity adjustment, the statistical conclusion remains the same.

Of the 141 enrolled participants, 11(8%) did not complete a post-baseline EPDS assessment. Missing rates are 5.3% and 13.0% for the treatment and control arms, respectively. Missing data handling was not mentioned in the protocol.

Participants with no post baseline EPDS assessments (missing both week 4 and week 8 assessments) were considered as non-responders in ITT analysis. For participants with no week 8 EPDS assessments, their week 4 EPDS were imputed as week 8 EPDS.

This last observation carried forward method is not optimal but even the worst-case imputation may not change the statistical conclusion.

Summary Results from the MamaLift Plus Pivotal Study conducted in the US are shown in the table below (ITT population).

	MamaLift Plus (CDT001) N= 95	Sham Control (CDP002) N=46	p-value
Improvement of 4+	82 (86.3%)	11 (23.9%)	<0.0001

Points			
Change to <13 EPDS	79 (83.2%)	15 (32.6%)	<0.0001

This pivotal clinical trial was powered to demonstrate effectiveness of MamaLift Plus versus a sham control with a 2:1 randomization. The study sample size was planned to have 80% power for the primary endpoint for a 2:1 randomization scheme. The results for the primary and secondary endpoint in the overall study population as well as the subgroup (New Mom, Anti-depressive use) analyses were all in favor of MamaLift plus arm.

Safety:

Adverse event assessment was conducted by a) monitoring reserve key words in the App and b) by an increase in EPDS score of more than 4 points. No serious adverse events (SAE) were reported during the study.

Adverse Events (AEs) were monitored in the treatment group and the sham control arm via a journal function using a free text option. AEs were not tracked via direct questioning in either group. A total of 4 AEs were identified, triaged, and documented in the study, 2 in active arm and 2 in sham control arm.

Of the 4 AEs, 2 AEs were identified via use of reserve keywords and both were in the active arm. As per the protocol, participant use of specific keywords in the applications triggered an alert to the study staff.
Remaining 2 AE were identified based on EPDS scores increasing by 4 or more points from baseline and both were in the sham control arm. After a joint evaluation by investigator and participant clinicians, these participants continued in the study.

Details on the 2 participants that were identified with AEs by usage of reserve key words are provided below. The reserve key words are presented in italics.

Participant 1: AE was identified as a result of usage of reserve key words in response to structured questionnaire in the App.

> Question 1 - First, describe a recent situation or trigger that made you feel sad, angry, or fearful. Answer –" We watched a movie last night and the man's wife died a long time before he did. This had me thinking all night about how I didn't want to die and leave my daughter without a mom or my partner alone."
>
> Question 2 - Next, describe the automatic thought(s) that popped up in your mind. This should be the raw, unedited version of what you were thinking, without any rationale (purely the thoughts). Answer – "I am going to die. YY won't have a mom. XX parents are going to raise her. XX is going to love someone else and forget about me." (names have been deleted to protect patient privacy).
>
> Question 3 - What is the emotion you went through? Use a scale from 0-10 to state the intensity. Answer - Anxious-8 Sad-10

Resolution: The medical monitor and PI were notified via email. PI notified the participant's clinical care provider and the participant continued in the study.

Participant 2: Patient entered the following text in response to the question below.

Question1-Describe your worries: “I worry that I am going to harm or be inpatient with my son as we learn more about his developmental needs.” (as entered by the participant)

Resolution: PI was notified by email and the case was escalated to Medical Monitor via email. PI notified the participant’s clinical care provider and the participant continued in the study.

Details on the 2 AEs that were identified via increase in EPDS scores by 4 or more points from baseline.

Participant 3: AE was identified as a result of an increase in EPDS score of 4 points from baseline to endline (Baseline EPDS =16 & Week 8 =20).
Resolution: PI notified the participant’s clinical care provider and the participant continued in the study.

Participant 4: AE was identified as a result of an increase in EPDS score of 4 points from baseline to endline (Baseline EPDS=15 & Week 8 EPDS=19).
Resolution: PI notified the participant’s clinical care provider and the participant continued in the study.

Therapeutic benefit from the use of MamaLift Plus plus TAU is only possible for patients if they follow the instructions and practice the exercises and strategies provided in the program. Treatment results may vary for patients.

Conclusions:
MamaLift Plus™ and its predicate, Somryst™, both are computerized behavioral therapy devices intended for patients with psychiatric disorders. The differences in their indications for use are due to differences in the primary psychiatric diagnosis of the patient populations in whom the device was studied and for whom the device is intended: Postpartum Depression (MamaLift Plus) and Insomnia (Somryst). MamaLift Plus and Somryst have similar technological characteristics, including digital delivery of behavioral therapy through a smartphone application and therapeutic content that addresses a psychiatric disorder. Differences in content delivery sequence and therapy duration are due to the different intended patient populations specific to MamaLift Plus and Somryst (Postpartum Depression vs Insomnia, respectively).
Software testing and documentation demonstrate that the device effectively implements the behavioral therapy model. The pivotal clinical trial shows that MamaLift Plus has demonstrated safety and effectiveness for the target population, consistent with the predicate device's special controls on clinical validation. These data reasonably demonstrate that the differences between MamaLift Plus and the predicate device do not raise new safety and effectiveness questions. MamaLift Plus is substantially equivalent to the predicate device. MamaLift Plus meets all special controls per the regulatory requirements regarding clinical data, software, and labeling for a computerized behavioral therapy device for psychiatric disorders (21 CFR 882.5801). Given the positive benefit-to-risk ratio, these data support a 510(k) clearance for MamaLift Plus as a treatment option for those suffering from mild to moderate Postpartum Depression.