

**DE NOVO CLASSIFICATION REQUEST FOR  
STANZA**

**REGULATORY INFORMATION**

FDA identifies this generic type of device as:

**Computerized behavioral therapy device for the treatment of fibromyalgia symptoms.** A computerized behavioral therapy device for the treatment of fibromyalgia symptoms is a prescription only device intended to provide a computerized version of a behavioral therapy for the treatment of fibromyalgia symptoms.

**NEW REGULATION NUMBER:** 21 CFR 882.5804

**CLASSIFICATION:** Class II

**PRODUCT CODE:** QWI

**BACKGROUND**

**DEVICE NAME:** Stanza

**SUBMISSION NUMBER:** DEN220083

**DATE OF DE NOVO:** November 21, 2022

**CONTACT:** Swing Therapeutics, Inc.  
548 Market Street #63989  
San Francisco, CA 94104

**INDICATIONS FOR USE**

Stanza is a prescription digital therapeutic that provides Acceptance and Commitment Therapy, a form of Cognitive Behavioral Therapy, and is indicated for the treatment of fibromyalgia symptoms in adult patients.

**LIMITATIONS**

The sale, distribution, and use of the Stanza are restricted to prescription use in accordance with 21 CFR 801.109.

The device is contraindicated for use by patients who have severe, untreated depression and patients who are at risk of harming themselves.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS.

### **DEVICE DESCRIPTION**

Stanza is a prescription-only smartphone-based digital therapy that delivers a self-guided program of Acceptance and Commitment Therapy (ACT), a form of Cognitive Behavioral Therapy (CBT), for patients with fibromyalgia.

Stanza is designed to be a 12-week treatment, followed by open access to the program materials for a period of time. Stanza contains 42 unique daily sessions, organized into 8 chapters, which comprise the core program. Once the core program is completed, patients have access to reinforcement sessions, organized into playlists, to strengthen the skill building and reinforce the core program.

To use Stanza, patients first download Stanza from the Apple App store or Google Play store and then securely log in and are authorized. Patients go through a brief tutorial of Stanza's major features and exit the tutorial onto the Today page, which is a patient's home base for the treatment program.

The core program is organized into eight chapters (Table 1). Each of the eight chapters are intended to train the patient on the core ACT skills: Acceptance, Values, Mindfulness, Defusion, Self-as-Context, and Willingness/Committed Action.

**Table 1: Stanza Program Organization**

<b>Chapter</b>	<b>Session Number</b>	<b>Title</b>	<b>ACT Skill</b>
1	1-6	Dropping the rope	Acceptance
2	7-11	Identifying your values	Values
3	12-15	Finding your rhythm	Acceptance, Willingness
4	16-21	You are not your thoughts	Defusion, Mindfulness
5	22-26	Thoughts are not facts	Defusion, Mindfulness
6	27-31	Moving with fibro	Willingness / Committed Action
7	32-36	Daily mindfulness	Mindfulness and Self-as-Context
8	37-42	Living your values	Willingness / Committed Action

A summary of each skill is copied below from the submission.

ACT Skill	Description
Acceptance	Acceptance is taught as an alternative to avoidance. It involves approaching unwanted, yet often uncontrollable experiences with openness and present moment awareness. Acceptance skills teach patients how to resist avoiding activities or stimuli that evoke unwanted feelings, and instead approach and experience them when they align with the patient’s values. For example, fibromyalgia patients are encouraged to let go of the struggle with pain and engage in activities they may have previously avoided.
Values	Values refer to personally held beliefs about who the patient wants to be and what provides them meaning in life. Patients identify their personal values, which are used throughout the therapy as motivation and ongoing treatment targets. Values are not goals that can be accomplished; rather values act as a compass to help the patient make choices that enrich their life. Patients are guided to take actions that align with who they want to be and how they envision their life being meaningful.
Defusion	Defusion skills help patients change the way they interact with or relate to their thoughts, emotions, and urges. This is taught via methods of de-identifying with unhelpful cognitions and unwanted experiences and observing these experiences rather than letting them dictate actions. Defusion is used as a skill to facilitate values-based action as an alternative to fusion-based action (e.g., emotion-driven or avoidance-driven behaviors).
Self as Context	Self-as-Context enables patients to experience a separation between observed thoughts and feelings and the patient themselves. This skill helps patients learn to observe their experiences and thoughtfully respond, rather than quickly react, to symptoms or unhelpful beliefs about themselves. It supports patients in building stronger mindfulness skills to observe and choose which experiences to respond to and which to let go of.
Mindfulness	Mindfulness is present moment awareness without judgment. It enables patients to be more aware and focused on difficult or negative thoughts and feelings. This allows for such thoughts and feelings to have less of an impact and influence over the patient. Mindfulness is taught through a variety of meditations in the program.
Willingness/ Committed Action	Committed action is a step-by-step process which allows the patient to honor their identified values, even in the presence of obstacles or unwanted discomfort, because they enrich the patient’s life in personally meaningful ways.

Each daily Session may include the following types of interactive activities:

- A lesson to build an ACT skill
- A guided audio awareness activity

- A journaling activity to help patients reflect on incorporating ACT skills in their daily lives
- Self-guided pacing or exercise activity to help patients gradually increase their activity level and physical functioning

#### Third-party Components and Accessories:

The subject device is a mobile medical application (MMA) intended to be accessed via any patient's smartphone and downloaded from the Apple App Store or Google Play Store. No accessories are included for this system and a phone is not provided by the sponsor.

### NONCLINICAL/BENCH STUDIES

#### SOFTWARE

The submission contained all the elements of software documentation corresponding to a "Moderate" level of concern, as outlined in the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices", issued May 11, 2005 (<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices>). Adequate documentation describing the software, firmware, software specifications, architecture design, software development environment, traceability, revision level history, unresolved anomalies and cybersecurity provides the foundation that the software will operate in a manner as described in the specifications. A hazard analysis was performed to characterize software risks including device malfunction and measurement related errors. The submission included verification and validation (V&V) testing to address the hazards presented by the device with satisfactory result. The submission included a breakdown of each hazard and how the collective hazards are mitigated as well as the impact of the hazard before and after mitigation. The sponsor includes all mitigation techniques, and the analysis is in accordance with ISO 14971. The device level of concern matches the acceptability of the hazards identified by the sponsor and no gaps were identified in their risk analysis.

### SUMMARY OF CLINICAL INFORMATION

#### **Overview**

The sponsor provided the following clinical evidence for Stanza's safety and effectiveness: a pivotal randomized control trial (RCT) (PROSPER-FM), a pilot RCT (SMART-FM), and an ongoing real-world evidence (RWE) trial (REACT-FM), representing data from 211 patients meeting the 2016 : American College of Rheumatology (ACR) criteria for fibromyalgia.

#### **Subject Selection**

Subject selection was identical across all clinical studies.

#### Inclusion Criteria

Eligible participants included patients aged 22 to 75 years with primary fibromyalgia meeting the requirements as defined by the 2016 American College of Rheumatology Preliminary Diagnostic Criteria, a mean baseline FIQ-R total score  $\geq 35$  and  $\leq 80$ , and a

mean baseline score  $\geq 4$  and  $\leq 9$  on the 11-point FIQ-R pain intensity items with no score  $> 9$

Participants were allowed to continue ongoing permitted medications, provided the dose and regimen was stable for 30 days prior to screening and would remain stable throughout the study period.

Permitted concomitant medications included non-steroidal anti-inflammatory drugs (NSAIDs), triptans, ergotamines, and antidepressants, as well as FDA approved FM medications.

#### Exclusion Criteria

Exclusion criteria included lifetime history of bipolar or other psychotic disorders, those already receiving psychotherapy, at increased risk of suicide, and medical conditions or medications that could endanger the patient or interfere with the evaluation of the study device's safety and efficacy.

#### PROSPER-FM Study

The PROSPER-FM study was a multicenter, randomized, active-controlled, non-significant risk device study to evaluate the safety and effectiveness at 12 weeks of daily therapy with Stanza in participants with fibromyalgia (FM). Up to 300 eligible subjects were planned to be recruited from up to 30 North American sites and randomized in a 1:1 fashion to treatment with either the Digital ACT (Stanza) or the Digital Symptom Tracker (ST).

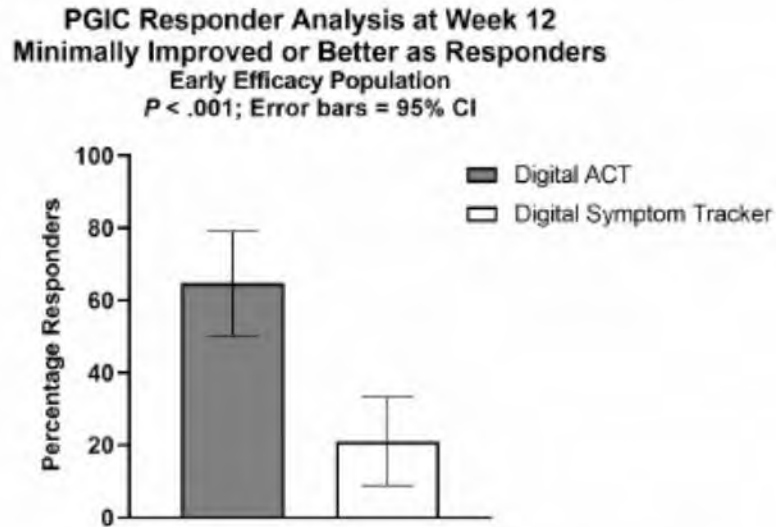
The provided results for the PROSPER-FM study were based on the pre-specified interim look which occurred when first 90 randomized subjects completed 12-week follow-up by October 10, 2022. At the interim look, 44 subjects were randomized to the digital ACT arm and 46 were randomized to the digital ST arm.

The primary efficacy endpoint was the difference between the Stanza Digital ACT Arm (ACT Arm) and the Digital Symptom Tracker application arm (DST Arm) in the Patient Global Impression of Change (PGIC) assessment at Week 12. Participants were randomized at a 1:1 ratio to treatment with either ACT or DST. Digital ACT arm participants were asked to complete an ACT-based program consisting of 42 core sessions, with a goal of completing 5-7 sessions per week. Through the DST application, DST Arm participants were prompted throughout their 12-week participation period to answer daily questions focused on symptoms and related functioning. DST Arm participants also had access to digital fibromyalgia educational resources provided by the app. All participants were required to complete weekly Patient Reported Outcomes (PROs) as well as 6 study visits performed in clinic or via telehealth (phone or videoconferencing). Safety assessments were conducted in clinic or via videoconference at the Screening (C1), Baseline (C2), and Week 12 (C6) visits, and via phone or videoconferencing at the Week 2 (C3), Week 4 (C4), and Week 8 (C5) visits. At interim, a total of 159 participants were screened at 13 study sites with the 90 randomized participants comprising the early efficacy and early safety populations. The primary analysis of the primary endpoint at interim evaluated the early efficacy population and dichotomized the 7-point PGIC scale into responders and non-responders

using “Very Much Improved,” “Much Improved,” and “Minimally Improved” as responders and all other responses as non-responders.

The results of primary endpoint analyses at interim indicate treatment with Stanza Digital ACT resulted in improved fibromyalgia management as compared to treatment with the Digital Symptom Tracker comparator. At Week 12, 64.7% of ACT arm participants reported improvement on the Patient Global Impression of Change versus 21.0% of Digital Symptom Tracker arm participants (Fig. 1).

**Figure 1 PGIC Responder Analysis at Week 12**



There were no device-related adverse events observed in this study, and safety assessments and observations were comparable across intervention groups (Table 2). In total, 17 participants reported one or more treatment emergent adverse events (TEAEs); none were attributed to the device, nor resulted in study discontinuation. All TEAEs were classified as mild or moderate and most were attributed to respiratory ailments or sickness that developed during the course of treatment. The study device did not negatively impact participant psychological status.

**Table 2: Summary of Adverse Events**

Summary of Adverse Events, Early Safety Population			
<i>Adverse Events, n (%):</i>	<i>Digital ACT (N=44)</i>	<i>Digital Symptom Tracker (N=46)</i>	<i>Total (N=90)</i>
Participants with $\geq 1$ device-related AE	0 (0)	0 (0)	0 (0)
Participants with $\geq 1$ TEAE <sup>1</sup>	10 (22.7)	7 (15.2)	17 (18.9)
Participants with $\geq 1$ AE	10 (22.7)	9 (19.6)	19 (21.1)
Participants with $\geq 1$ TEAE by severity <sup>2</sup>			
Mild	6 (13.6)	2 (4.3)	8 (8.9)
Moderate	4 (9.1)	5 (10.9)	9 (10.0)
Participants with $\geq 1$ AE leading to study withdrawal	0 (0)	0 (0)	0 (0)
Participants with $\geq 1$ SAE	0 (0)	0 (0)	0 (0)
Participants with $\geq 1$ UADE	0 (0)	0 (0)	0 (0)

ACT, Acceptance and Commitment Therapy; AE, adverse event; SAE, serious adverse event; TEAE, treatment emergent adverse event; UADE, unanticipated adverse device event.

<sup>1</sup>TEAEs are AEs that either commenced following initiation of study treatment or were present prior to study device use but increased in frequency or severity following initiation of study device use.

<sup>2</sup>Participants were counted only once at the worst severity.

### SMART-FM Study

The SMART-FM was a multicenter, randomized-controlled, non-significant risk pilot study to assess the effect size between the Tempo Digital Acceptance and Commitment Therapy (ACT) arm and the Tempo Digital Symptom Tracker (ST) arm over 12 weeks of therapy. Here the Tempo ACT device is the previous version of Stanza. Up to 150 eligible subjects with diagnosis of fibromyalgia (FM) was planned to be enrolled from up to 10 North American sites.

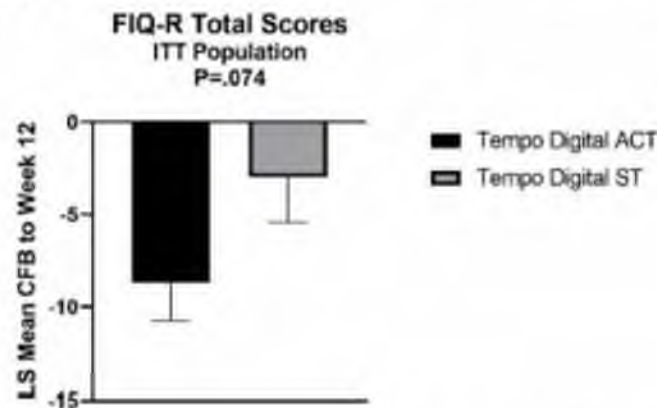
This was a parallel group study designed to investigate the safety and efficacy of the self-guided smartphone-based Tempo<sup>1</sup> Digital ACT and Tempo Digital Symptom Tracker apps for the management of fibromyalgia symptoms. Participants received treatment-as-usual

<sup>1</sup> Please note that the Stanza device was previously referred to as “Tempo”. The only difference between the tested device and the final device is the name. Therefore, all supporting documents and clinical evidence are still applicable and representative of the Stanza device.

(TAU) plus daily interaction with either 1) one of three Tempo Digital ACT versions, or 2) one of two Tempo Digital symptom tracker versions for 12 weeks. The study was performed with 2 cohorts in and were randomized at a 1:1 ratio into Tempo Digital ACT (Group A) and Tempo Digital ST (Group S) arms similar to the PROSPER-FM Study. The primary effect size assessment was the difference between the Tempo Digital ACT arm and the Tempo Digital ST arm in mean change from baseline to Week 12 in Revised Fibromyalgia Impact Questionnaire (FIQ-R) total scores analyzed in the intent to treat patient population. A total of 106 participants were screened and 67 participants were enrolled. All enrolled participants were randomized and included in the safety and intention-to-treat (ITT) populations.

The combined results of primary endpoint analyses indicate the Tempo Digital ACT treatment resulted in improved fibromyalgia symptom management as compared to treatment with the Tempo Digital ST control. The between-arm effect size for the primary endpoint of change from baseline to Week 12 in FIQ-R total scores in the intent-to-treat population was 0.44, corresponding to a least square mean score difference of  $-5.7$ . The CFB to Week 12 LS mean score change in FIQ-R total scores was  $-8.7$  (SE, 2.03) for the Tempo Digital ACT group and  $-3.0$  (SE, 2.40) for the Tempo Digital ST group (Fig. 2).

**Figure 2 FIQ-R Total Scores: Least-Squares Mean Change from Baseline to Week 12, Intention -to Treat Population**



The SMART-FM trial shared a similar safety profile with that of PROSPER-FM. There were no device-related Adverse Events observed. In total, 15 AEs were reported throughout the study period; none were attributed to the study treatment, and none resulted in study discontinuation (Table 3). The treatment did not negatively impact participant psychological status as assessed by the Beck Depression Inventory I and II (BDI-II) and Columbia Suicide Severity Rating Scale (C-SSRS) instruments.

**Table 2: Treatment-Emergent Adverse Events (TEAEs) Reported During the 12-week treatment Period**

<b>TEAEs Reported During Study Treatment Period, Safety Population</b>		
<i>Treatment-Emergent Adverse Event:</i>	<i>Tempo Digital ACT (N=39)</i>	<i>Tempo Digital ST (N = 28)</i>
Any TEAE, n (%)	10 (25.6)	5 (17.9)
Anxiety, n (%)	1 (2.6)	0 (0)
Broken foot, n (%)	1 (2.6)	0 (0)
Cellulitis in face, n (%)	0 (0)	1 (3.6)
COVID-19 infection, n (%)	0 (0)	2 (7.1)
Exacerbation of FM pain, n (%)	1 (2.6)	0 (0)
Exacerbation of gastroparesis, n (%)	1 (2.6)	0 (0)
Fever, n (%)	1 (2.6)	0 (0)
Headache, n (%)	1 (2.6)	0 (0)
Left side rib contusions, n (%)	1 (2.6)	0 (0)
Post-COVID-19 vaccination syndrome, n (%)	1 (2.6)	0 (0)
Sinus infection, n (%)	0 (0)	1 (3.6)
Urinary tract infection, n (%)	0 (0)	1 (3.6)
Vertigo, n (%)	1 (2.6)	0 (0)
Worsening anemia, n (%)	1 (2.6)	0 (0)

ACT = acceptance and commitment therapy; COVID-19 = coronavirus disease-2019; ST = symptom tracker; TEAE = treatment-emergent adverse event.

#### REACT-FM STUDY

The “Real-World Evidence from Smartphone-Based Acceptance and Commitment Therapy in Fibromyalgia (REACT-FM)” Trial is a virtual, single-arm investigation intended to assess the effectiveness of the Stanza in a real-world setting with reduced trial visit activity with clinical study staff. The trial is currently under execution. An ongoing assessment was performed on the first 95 enrolled patients in the REACT-FM trial.

All participants who have completed the end of treatment outcome data collection were analyzed (N=54, completer analysis). 77.8% of total participants were considered “responders” to the treatment as defined by participants who scored “Very Much Improved,” “Much Improved,” and “Minimally Improved” on the dichotomized the 7-point PGIC scale (Table 4). Furthermore, 59.35% of participants reported clinically meaningful improvement on FIQ-R ( $\geq 20\%$  improvement), which is greater than that observed for the PROSPER-FM interim analysis (42.7%) and the SMART-FM study (40.5%).

**Table 4: Summary of Effectiveness Results for REACT-FM Study**

<b>Measures</b>	<b>Stanza (N=54)</b>
PGIC Responder	77.8%
PGIC Continuous	2.7 $\pm$ 1.0
FIQ-R total, CFB to Week 12	-17.0 $\pm$ 16.3
FIQ-R Responder ( $\geq 20\%$ Improvement on FIQ-R total)	59.3%
FIQ-R Function, CFB to Week 12	-14.4 $\pm$ 15.5
FIQ-R Impact, CFB to Week 12	-7.9 $\pm$ 5.1
FIQ-R Symptoms, CFB to Week 12	-14.2 $\pm$ 15.6

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

**LABELING**

The labeling is sufficient and satisfies the requirements of 21 CFR § 801.109 Prescription devices.

The labeling provides information to users describing the clinical data showing the safety and effectiveness of the Stanza device in the intended patient population. It also includes instructions for operating the device and navigating the user interface. Appropriate warnings and precautions are included to avoid hazardous situations and ensure safe use of the device as intended.

### **RISKS TO HEALTH**

The table below identifies the risks to health that may be associated with use of the computerized behavioral therapy device for the treatment of fibromyalgia symptoms and the measures necessary to mitigate these risks.

<b>Risks to Health</b>	<b>Mitigation Measures</b>
Worsening of condition due to device providing ineffective treatment	Clinical data Labeling
Delayed access to treatment due to device software failure	Software verification, validation, and hazard analysis
Ineffective treatment due to use error/ improper use of device	Labeling

### **SPECIAL CONTROLS**

In combination with the general controls of the FD&C Act, the computerized behavioral therapy device for treatment of fibromyalgia symptoms is subject to the following special controls:

- (1) Clinical data must demonstrate that the device performs as intended under the anticipated conditions of use and include the following:
  - (i) Evaluation of improvement in the symptoms of fibromyalgia; and
  - (ii) Evaluation of relevant adverse events.
- (2) Software verification, validation, and hazard analysis must demonstrate that the device performs as intended.
- (3) Physician and patient labeling must include the following
  - (i) Recommended treatment regimes, including frequency and duration of use; and
  - (ii) A summary of the clinical data for the device, including a discussion of adverse events.

### **BENEFIT/RISK DETERMINATION**

The probable risks of the Stanza device were established with data collected in nonclinical studies (e.g., software testing) as well as data collected in the clinical trials described above and are generally well understood. Specifically,

- a. The results of the nonclinical testing demonstrated that the Stanza device performed as per specifications and the results did not raise concerns regarding risks to the patients.
- b. There were no serious adverse events reported in the studies.
- c. The indications for use and labeling (i.e., description of clinical study results) will guide physicians towards prescribing Stanza to treat the patient population demonstrated to be most responsive to the therapy.

- d. Patient populations that were not demonstrated to be responsive to therapy with the device are described in the labeling to aid in physician prescribing.

Furthermore, no device-related AEs or SAEs were recorded during all three studies. All AEs that occurred during the treatment period were classified as mild or moderate. Thus, Stanza raised no additional safety concerns during treatment.

The probable benefits of the device are also based on data collected in the clinical studies as described above. The clinical evidence from the PROSPER-FM, SMART-FM, and REACT-FM analyses collectively demonstrates the robust and clinically meaningful benefit of Stanza for improvement in the symptoms of fibromyalgia with no observed risk (device-related adverse events). The PROSPER-FM and SMART-FM results demonstrated that treatment with the Stanza device resulted in significantly superior PGIC response rates compared to an active control. Response on the FIQ-R was clinically meaningful as well, with over 40% of Stanza treated patients demonstrating a  $\geq 20\%$  improvement from baseline on the FIQ-R total score across all studies. The observed results in the REACT-FM real world evidence study were also consistent with the results from the PROSPER-FM and SMART-FM studies, demonstrating the effectiveness of Stanza in a real-world population. In addition to demonstrating a statistically significant improvement in PGIC scores, Stanza also showed numerically greater improvement in all secondary and exploratory endpoints of the PROSPER-FM pivotal study, further supporting that Stanza can provide a beneficial contribution to a patient's fibromyalgia symptoms and overall quality of life.

Sources of uncertainty in the benefits include the use of an imperfect comparator in the control arm. However, the sponsor provided additional clarification in the user manual to fully describe the control arm in the device labeling. Additionally, the clinical data showed a greater improvement in the Stanza treatment group compared to the control group.

#### Patient Perspectives

Patient perspectives considered for the Stanza included information provided by the sponsor about patient reported outcomes (PROs) that assess patients' impressions about the treatment effectiveness and disease impact. Specifically, the sponsor includes the following PROs as part of their submission; Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue Short Form 6a score; Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance- Short Form 6a score; PIPS (Psychological Inflexibility in Pain Scale) total score and fusion and avoidance subscales; Committed Action Questionnaire (CAQ-8); Mean mHealth App Usability Questionnaire (MAUQ) Modules E and I for Standalone mHealth Apps Used by participants; and the Beck Depression Inventory (BDI-II)

Compared to the Active Control arm, the Stanza arm exhibited greater improvement trending towards significance ( $p = 0.027$ ) on committed action, a key ACT process (CAQ-8). Additional improvements on clinically relevant symptoms of fibromyalgia patients<sup>11</sup> numerically favored the Stanza group and approached significance, including fatigue (PROMIS Fatigue, T-score, effect size of 0.38), sleep (PROMIS Sleep, T-score, effect size of 0.39), and depressed mood (BDI-II, effect size of 0.28). Specifically, the Stanza group exhibited an average post-treatment improvement of 3.1 and 2.7 points on the PROMIS Fatigue and Sleep T-score, respectively.

### Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for the Stanza device for the following indications statement:

Stanza is a prescription digital therapeutic that provides Acceptance and Commitment Therapy, a form of Cognitive Behavioral Therapy, and is indicated for the treatment of fibromyalgia symptoms in adult patients.

The Stanza provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

### CONCLUSION

The De Novo request for the Stanza is granted and the device is classified under the following:

Product Code: QWI

Device Type: Computerized behavioral therapy device for the treatment of fibromyalgia symptoms

Class: II

Regulation: 21 CFR 882.5804

### REFERENCE

Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken)*. May 2010;62(5):600-10.