Request for Copy of Published Material

Enclosure:

- POSTER: Meyer C, Zhang Z, Cochran J, et al. Presented at Psych Congress, September 17-21, 2025; San Diego, CA, USA.

Assessment of Efficacy Outcomes Based on Treatment Adherence to Rejoyn (CT-152), a Digital Therapeutic for Patients With Major Depressive Disorder, During the Mirai Trial

Chip Meyer[1]; Zhen Zhang[1]; Jeffrey Cochran[1]; Jessica Ash[1]; Brian Rothman[1]; Tarolyn Carlton[1]; Caitlin A. Stamatis[1]; Shaheen E Lakhan[2]; Daniel Carpenter[3]; Ainslie Forbes[1]

[1]Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA; [2]Click Therapeutics, Inc., New York, NY, USA; [3]Otsuka Precision Health, Inc., Princeton, NJ, USA

Poster presented at the
38th Psych Congress 2025
September 17–21, San Diego, CA, USA

Scan the QR code to receive a PDF of the poster

Introduction

- Rejoyn® (CT-152) is the first US Food and Drug Administration-authorized prescription digital therapeutic (DTx) adjunct to antidepressant medication for patients with major depressive disorder (MDD).[1]
- Literature reports on the completion of DTx regimens in clinical trials are generally low (one review found that 56% of participants completed the protocol-recommended course and 44% completed the full round of therapy).[2]
- The pivotal remote Mirai trial (NCT04770285) was designed to collect data on adherence and engagement in addition to safety and efficacy.
  - In the Mirai trial, the Rejoyn group showed high adherence, with an associated benefit on the Montgomery–Åsberg Depression Rating Scale (MADRS) for participants who completed more sessions.[1,2]
- Although the MADRS is frequently used for measuring depression efficacy outcomes in clinical trials, this scale is not as easily interpreted in clinical practice.[3,4]
  - Previous analyses have suggested that Rejoyn may show similar benefits on a range of scales, including the Patient Health Questionnaire 9-Item (PHQ-9).[1,5]
  - The PHQ-9 is more commonly used in routine clinical practice to evaluate depression symptom severity and may help to interpret the Mirai adherence and engagement outcomes in the context of clinical practice.[6]

Objective

- This post hoc analysis assessed the effect of participant adherence on the efficacy of Rejoyn versus the sham app in reducing depression symptoms as measured by the PHQ-9 total score, an assessment commonly used in clinical practice.

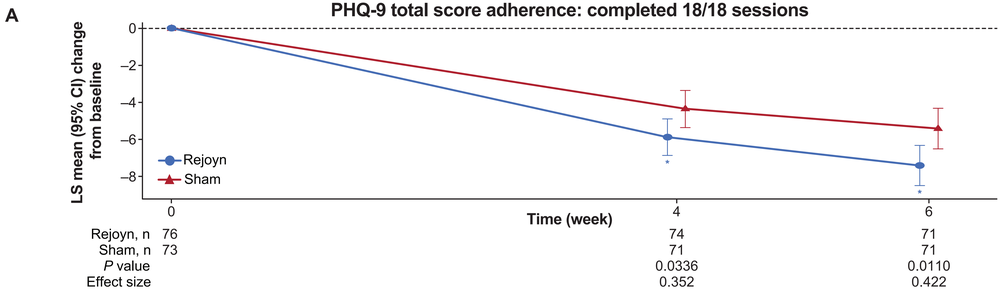
Methods

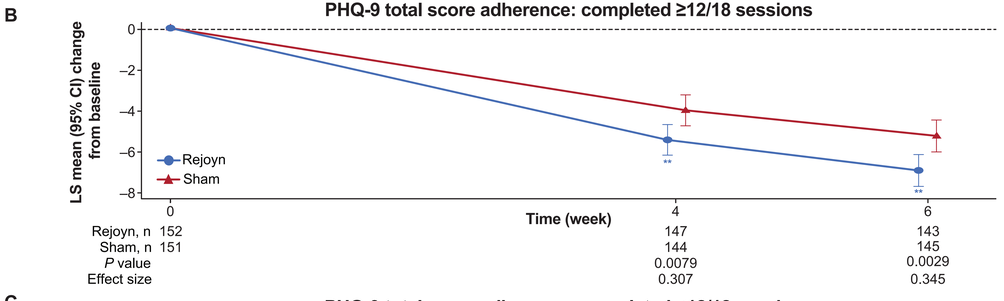
- Adults aged 22–64 years with a primary diagnosis of MDD (based on the criteria in the Diagnostic and Statistical Manual of Mental Disorders [DSM], Fifth Edition) and inadequate response to current antidepressant medication participated in the Phase 3 multicenter, randomized, blinded, sham-controlled, remote Mirai study with a 6-week intervention period and 4-week extension.[7]
- Participants were randomly assigned 1:1 to either treatment with Rejoyn or sham.[7]
  - Delivered via a smartphone app, Rejoyn includes 3 components:[7]
    1. Cognitive-emotional training exercises (Emotional Faces Memory Task [EFMT])
    2. Brief cognitive-behavioral therapy (CBT)-based lessons to reinforce and apply therapeutic skills
    3. Personalized text messages
  - The control group received a sham app that included a Shapes Memory Task (SMT), which is a working-memory task designed to match the EFMT for time, attention, and participant expectation of therapeutic effect, but which is not intended to be therapeutic and does not contain the CBT-based lessons.[7]
  - All participants continued their current antidepressant medication, and both groups received supportive text messages to encourage treatment completion, along with weekly adherence follow-ups during the trial.[1,7]
- Per Mirai protocol, a participant was defined as adherent if they completed ≥12/18 total sessions of Rejoyn or sham, respectively.[1,7]
  - In this analysis, adherence groups were defined as those who completed <12/18, ≥12/18, and 18/18 sessions.
- We assessed the effect of Rejoyn treatment based on participant adherence using the PHQ-9, a 9-item scale comprised of the 9 DSM criteria for depression. The scale is typically completed by the patient. Each item is rated from 0 (not at all) to 3 (nearly every day) for a maximum score of 27, with higher scores indicating more severe depression.[6]
- Change in PHQ-9 total score was assessed for each adherence group via mixed-effects model for repeated measures with model terms: treatment, visit, treatment by visit interaction, and baseline by visit interaction for Rejoyn versus sham groups.
  - Change from baseline at Week 6 in PHQ-9 total score was assessed for all participants who received ≥1 treatment session, a baseline MADRS assessment, and ≥1 post-baseline MADRS assessment.
  - *P* values for post hoc analyses were not adjusted for multiplicity, and were not intended for hypothesis testing, and are provided to help interpret findings. Effect size is reported as Cohen's *d* (small: 0.20 to <0.50, medium: 0.50 to <0.80, large: ≥0.80).

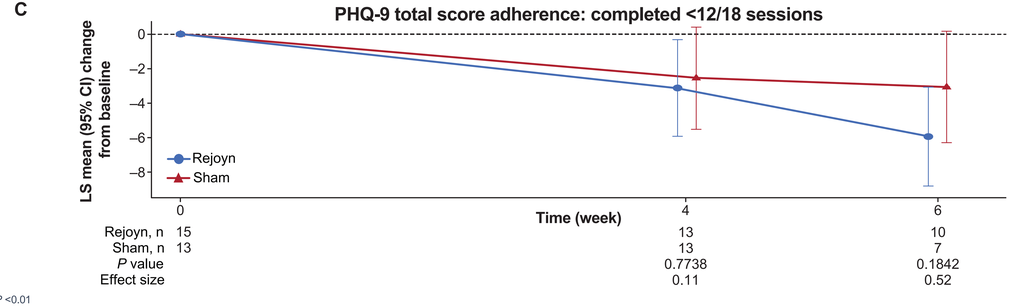
Results

- Participants (N=386) were randomly assigned to Rejoyn (n=194; overall, 165 completed the trial) or sham (n=192; overall, 164 completed the trial).
  - Of these participants, 354 had received ≥1 treatment session, a baseline MADRS assessment, and ≥1 post-treatment MADRS assessment.
  - For the adherence groups:
    - For those who completed <12/18 sessions, 15 were assigned Rejoyn and 13 were assigned sham.
    - For those who completed ≥12/18, 152 were assigned Rejoyn and 151 were assigned sham.
    - For those who completed all 18/18 sessions, 76 were assigned Rejoyn and 73 were assigned sham.
- Rejoyn was favored over sham on the PHQ-9 overall, with nominal significance for those who completed 18/18 sessions (between-group difference: −2.0, *P* <0.05, *d*=0.422) and ≥12/18 sessions (protocol-defined adherence; between-group difference: −1.7, *P* <0.01, *d*=0.345) (**Figure 1A** and **Figure 1B**).
  - Numerically, Rejoyn was also favored over sham for those who did not complete the protocol-defined number of sessions (<12/18) to meet the definition of adherence (**Figure 1C**).
  - However, for those who completed <12/18 sessions, nominal significance was not reached and the number of participants (n) was very small (n=10 for Rejoyn and n=7 for sham at Week 6).

Figure 1. Change from baseline on the PHQ-9 for those who completed all 18/18 sessions (A), ≥12/18 sessions (B), and <12/18 sessions for Rejoyn versus sham (C).







*P <0.05; **P <0.01

CI, confidence interval; LS, least-squares; PHQ-9, Patient Health Questionnaire 9-Item.

CONCLUSIONS

Greater improvement on the PHQ-9 total score for participants who completed more sessions of Rejoyn was consistent with prior primary and supporting post hoc analyses on the MADRS.

- Although overall adherence was high, the trend toward increasing improvement in PHQ-9 scores with increasing adherence may suggest a dose-response relationship, where greater adherence with the therapeutic regimen yields greater clinical benefit.

These findings support the consistency of Rejoyn treatment efficacy in alleviating symptoms of depression between different scales for depression symptoms, including for scales that are used frequently in real-world practice, such as the PHQ-9.

Findings further reinforce the importance of adherence and engagement with the Rejoyn treatment regimen for maximizing therapeutic benefit.

References

1. Rothman B et al. *J Affect Disord*. 2025;388:119409.
2. Forbes A et al. *J Med Internet Res*. 2023;25:e43727.
3. Katzman MA et al. *J Affect Disord*. 2022;316:201–208.
4. Byrne D et al. *J Affect Disord*. 2025;368:584–590.
5. Zhang Z et al. Presented at the Psych Congress Elevate 2025; Las Vegas, NV, USA. Abstract 15.
6. Kroenke K et al. *J Gen Intern Med*. 2001;16:606–613.
7. Rothman B et al. *JMIR Res Protoc*. 2024;13:356960.

Funding

This study was funded by Otsuka Pharmaceutical Development & Commercialization, Inc. Click Therapeutics, Inc. was a co-development collaborator.

Acknowledgments

Medical writing support was provided by George Pellegrino, MD, PhD, of Oxford PharmaGenesis Inc., Wilmington, DE, USA, and was funded by Otsuka Pharmaceutical Development & Commercialization, Inc.

At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

Disclosures

CM, **ZZ**, **JC**, **JA**, **BR**, **TC**, **CAS**, and **AF** employees: Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA. DC employee: Otsuka Precision Health, Inc., Princeton, NJ, USA. **SEL** employee: Click Therapeutics, Inc., New York, NY, USA.