Results from CONVOKE: A Phase 3 RCT Evaluating a First-in-class Digital Therapeutic for Experiential Negative Symptoms of Schizophrenia in Adults

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Introduction

1 NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

- Negative symptoms of schizophrenia are associated with poor outcomes and long-term disability[1]
- There are no FDA-approved pharmacological treatments specifically indicated for negative symptoms[2]

2 DIGITAL THERAPEUTICS

- Digital therapeutics (DTx) are evidence-based software programs that deliver medical interventions digitally to treat diseases and are validated through clinical trials
- People living with schizophrenia generally use mobile devices at rates comparable to the overall population[3,4]

3 CT-155/ BI 3972080

- CT-155/BI 3972080 (CT-155) is an investigational DTx being developed to treat experiential negative symptoms (ENS) adjunctive to standard-of-care antipsychotic medication[5,6]
- Its development was informed by patients during clinical learning studies using earlier versions of the app[5,6]
- CT-155 integrates multiple evidence-based psychosocial treatment components[6]

Aim

To evaluate the effectiveness and safety of CT-155 for negative symptoms of schizophrenia

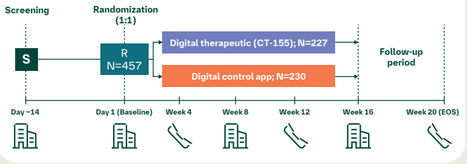
Methods

Study design

In-person visit · Remote visit

Phase 3 · Multicenter · Randomized · Double-blind · Parallel-group, controlled · 16-week

CONVOKE (NCT05838625) was a Phase 3, multicenter, randomized, double-blind, parallel-group, controlled, 16-week trial conducted between March 2023 and July 2025 across 66 clinical sites in the US



Further details are available in the published study protocol.[5]
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Key inclusion criteria

- ≥18 years of age
- Primary diagnosis of schizophrenia present for ≥6 months prior to screening
- Stable dose of antipsychotic medication(s) for ≥12 weeks prior to randomization
- Average score of ≥2 (moderate to severe) in at least 2 of the 3 CAINS-MAP domains (social, work, or recreational)
- Sole user of smartphone with regular internet access

Key exclusion criteria:

- Treated with >2 antipsychotic medications (including >2 dosage forms)
- Currently or in the last 3 months receiving psychotherapy or cognitive remediation
- Current DSM-5 diagnosis other than schizophrenia
- Moderate or severe positive symptoms

Outcomes

Primary effectiveness endpoint

- Change from baseline to Week 16 in ENS using CAINS-MAP total score
  - Administered by a centralized blinded rater team to avoid any potential bias

CAINS-MAP

- CAINS is a second generation, semi-structured clinician-rated instrument recommended by experts, designed to comprehensively assess negative symptoms of schizophrenia with strong reliability and validity[7–9]
- CAINS items are scored on a 5-point scale; higher scores indicate greater negative symptom severity

Other endpoints

- **Secondary effectiveness endpoints:** included change from baseline to Week 16 in PANSS positive subscale score
- **Exploratory endpoints:** included key engagement and adherence metrics
- **Safety:**
  - Frequency and severity of AEs, serious AEs, relationship of AEs to study treatment (assessed over the 20-week study period), and discontinuations due to AEs and serious AEs
  - Incidence of suicidal ideation and behavior, monitored using C-SSRS

Statistical analyses

- The study was powered to detect an effect size of Cohen's *d*=0.35 at 90% power with an assumption of 20% early termination, resulting in 432 participants (~216 per arm)
- All baseline demographics and characteristics, effectiveness, and engagement analyses were performed with the ITT set (all uniquely randomized participants)
- Safety was analyzed in the safety set (all randomized participants who signed consent, activated either CT-155 or digital control, and completed at least 1 available daily activity during the active period)
- The primary and secondary endpoints were analyzed using mixed models repeated measures

Results

Baseline demographics and clinical characteristics

- Baseline demographics and clinical characteristics were balanced across both arms (**Table 1**)

Table 1. Demographics and clinical characteristics

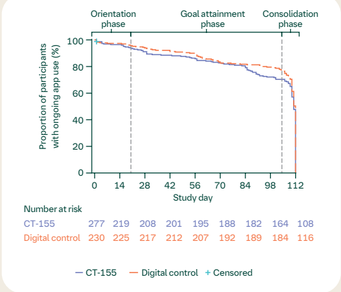
	CT-155 (n=227)	Digital control (n=230)	Overall (n=457)
Age, years, mean (SD)	46.2 (12.44)	45.3 (12.50)	45.8 (12.46)
Sex, male, n (%)	142 (62.6)	135 (58.7)	277 (60.6)
Race, Black or African American, n (%)	125 (55.1)	119 (51.7)	244 (53.4)
Race, White, n (%)	88 (38.8)	93 (40.4)	181 (39.6)
Ethnicity, Hispanic or Latino, n (%)	62 (27.3)	65 (28.3)	127 (27.8)
Ethnicity, Not Hispanic or Latino, n (%)	165 (72.7)	161 (70.0)	326 (71.3)
Living/housing status, living with family, n (%)[a]	110 (48.5)	118 (51.3)	228 (49.9)
Living/housing status, living on own, n (%)	71 (31.3)	68 (29.6)	139 (30.4)
Employment status, unemployed, n (%)	175 (77.1)	192 (83.5)	367 (80.3)
Employment status, employed, n (%)	35 (15.4)	30 (13.0)	65 (14.2)
CAINS-MAP total score, mean (SD)	26.0 (6.11)	26.6 (5.95)	26.3 (6.04)
PANSS positive subscale score, mean (SD)	15.0 (3.95)	15.2 (3.90)	15.1 (3.92)
Time since diagnosis, median (IQR)	15.3 (6.7, 28.4)	14.5 (7.0, 24.4)	14.8 (6.9, 26.1)
Number of antipsychotics used at baseline, n (%)			
1	193 (85.0)	209 (90.9)	402 (88.0)
2	33 (14.5)	21 (9.1)	54 (11.8)
Class of antipsychotics at baseline, n (%)			
First generation[b]	19 (8.4)	19 (8.3)	38 (8.3)
Second generation[c]	207 (91.2)	211 (91.7)	418 (91.5)

[a]Includes those living with their family or spouse/partner. [b]Includes patients who took first-generation antipsychotics regardless of whether they also took second-generation antipsychotics. [c]Includes patients who only took second-generation antipsychotics.

Engagement

- Participants retention was high across both arms (**Figure 1**), with most participants remaining active in CT-155 or digital control through to the end of the goal attainment phase at Week 15 (CT-155: 70.4% [160/227]; digital control: 76.5% [176/230])

Figure 1. Kaplan–Meier retention analysis



Retention was assessed with Kaplan–Meier analysis, where the time-to-event was the last recorded day of app use. Participant retention was assessed over the 16-week active period, consisting of a 3-week orientation phase, a 12-week goal attainment phase, and a 1-week consolidation phase.[6] Dashed vertical lines mark phase transitions.

- Participant engagement and adherence was high (**Table 2**)

Table 2. Key engagement and adherence metrics

Variable	CT-155 (n=227)	Digital control (n=230)
Engagement: Number of days the app was used Median (range)	76.0 (0–112)	92.0 (1–112)
Adherence: Number of days with at least 1 completed activity Median (range)	75.0 (0–112)	91.0 (0–112)

- Median (IQR) daily study app exposure was 8 (6, 11) minutes with CT-155 compared with 2 (1, 3) minutes for the digital control

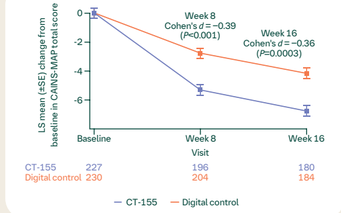
Safety

- Serious AEs were reported for 3 participants (1.3%) in the CT-155 arm and 5 participants (2.2%) in the digital control arm; none were treatment related (**Table 3**)
- There was no meaningful emergence or increase in suicidal ideation or behavior

CAINS-MAP

- At Week 16, CT-155 was associated with a statistically significant improvement in CAINS-MAP total score vs digital control (**Figure 2**)

Figure 2. Primary endpoint of change from baseline to Week 16 in CAINS-MAP total score



PANSS positive subscale

- Change in positive symptom severity (assessed using PANSS positive subscale) at Week 16 was not significantly different between arms (*P*=0.7900; LS mean difference [95% CI]: 0.1 [−0.57 to 0.75]), indicating that participants' positive symptoms remained stable over the study period. This suggests that the improvement of ENS was not due to changes in positive symptoms

Table 3. Summary of adverse events

Category, n (%)	CT-155 (n=228)		Digital control (n=231)	
	Event, m	Participant, n (%)	Event, m	Participant, n (%)
Any AE	29	19 (8.3)	39	31 (13.4)
Any serious AE	3	3 (1.3)	6	5 (2.2)
Any serious AE related to study treatment	0	0	0	0
Any TEAE	26	18 (7.9)	35	27 (11.7)
Mild	15	11 (4.8)	16	16 (6.9)
Moderate	10	9 (3.9)	17	11 (4.8)
Severe	1	1 (0.4)	2	2 (0.9)
Any serious TEAE	2	2 (0.9)	6	5 (2.2)
Any serious TEAE related to study treatment	0	0	0	0
Any TEAE leading to study discontinuation	0	0	2	2 (0.9)

Key Conclusions

- CONVOKE is the first controlled trial to demonstrate statistically significant improvement in experiential negative symptoms using an investigational DTx (Cohen's *d*, −0.36; *P*=0.0003)
- Retention (70.4% and 76.5%) and engagement (76 days and 92 days) was high in both the CT-155 and digital control arms, respectively, reflecting that the study included an appropriate digital control
- These data show that CT-155 can be an effective, well-tolerated, first-in-class, patient-centered treatment option adjunctive to antipsychotic medications for people with schizophrenia

Additional Conclusions

- Limitations: Participants were required to be on stable antipsychotic medication dose for ≥12 weeks (excluded individuals with recent diagnoses or newly initiated treatment), own a smartphone and have internet access (potential selection bias), and no recent psychotherapy
- ENSPIRUS, a prospective cohort study, is currently underway to determine efficacy and safety of CT-155 in a broader population in a real-world-like setting (NCT06791122)

References

1. Correll CU, Schooler NR. *Neuropsychiatr Dis Treat* 2020;16:519–34. **2.** U.S. National Library of Medicine. DailyMed search: "schizophrenia" AND "negative symptoms" in Indications and Usage. 2025. https://dailymed.nlm.nih.gov/dailymed/search.cfm?adv=1&labeltype=human&query=34067-9%3A%28negative+symptoms%29+AND+34067-9%3A%28schizophrenia%29+. [Accessed October 2025]. **3.** Gay K, et al. *JMIR Ment Health* 2016;3(2):e15. **4.** Naslund JA, et al. *Psychiatr Rehabil J* 2016;39(4):364–7. **5.** Goenjian H, et al. *Schizophrenia* 2025;11(1):120. **6.** Lakhan SE, et al. *JMIR Res Protoc* 2025;14:e81293. **7.** Kring AM, et al. *Am J Psychiatry* 2013;170(2):165–72. **8.** Blanchard JJ, et al. *Schizophr Res* 2017;185:137–43. **9.** Marder SR, Fenton W. Schizophr Res 2004;72(1):5–9.

Disclosures

These data were previously presented in an oral presentation at the 38th European College of Neuropsychopharmacology Congress (ECNP; October 11–October 14, 2025).

The PANSS positive subscale result and Table 2 are analyses beyond those reported in the accepted NEI abstract.

CS, OB, and **AS** are employees of Click Therapeutics, Inc. **SEL** was an employee of Click Therapeutics, Inc at the time of the study and is also affiliated with Boricua Bio, San Juan, PR, USA, Neurocentrx Pharma, Edinburgh, UK, Franelle Pharma, Minneapolis, MN, USA, Morehouse School of Medicine, Atlanta, GA, USA, and Western University of Health Sciences, Pomona, CA, USA. **CDC** and **CvdG** are employees of Boehringer Ingelheim International GmbH. **AP** and **WT** are employees of Boehringer Ingelheim Pharmaceuticals, Inc. **AP** is also affiliated with King's College London, London, UK, Boston University, Boston, MA, USA, and the University of Washington, Seattle, WA, USA. **FD** has received research grant funding from Boehringer Ingelheim and was a site investigator on the CONVOKE study. **RSK** is a consultant for Boehringer Ingelheim, BMS, and Alkermes, and was a site investigator on the CONVOKE study. **JPL** is also affiliated with the Department of Psychiatry, Grossman School of Medicine, NY, and receives research funding from Avanir, BMS, Alto, Neurocrine, and Roche. **JPL** is also a consultant to Newron, receives royalties for the Sci-PANSS, and was a site investigator on the CONVOKE study. **JWF** was a site investigator on the CONVOKE Study, and is also affiliated with the Morsani College of Medicine, University of South Florida, Tampa, FL, USA. **GM** has served as a consultant to AbbVie, Acadia, Akili, Alkermes, Angelini, Axsome, Aytu, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Cerevel, Corium, Eisai, Intracellular, Ironshore, Johnson & Johnson, Liva Nova, Lumos Labs, Lundbeck, Neurocrine, Noven, Otsuka, Redax, Relmada, Revibe, Roche, Sage, Sirona, Sky Therapeutics, Sunovion, Supernus, Takeda, Teva, and Tris Pharma; has received research support from AbbVie, Acadia, Alkermes, Akili, Alto Therapeutics, Avanir, Axsome, Bristol Myers Squibb, Boehringer Ingelheim, Cingulate, Click Therapeutics, Corium, Emalex, Idorsia, Intracellular, Johnson & Johnson, Karuna, Lumos Labs, Medgenics, Neurocrine, NLS Pharma, Redax, Relmada, Roche, Sage, Sirtsei, Sumitomo, Sunovion, Supernus, Takeda, and Teva; and has participated in speaker's bureaus for AbbVie, Alkermes, Angelini, Axsome, Bristol Myers Squibb, Corium, Intracellular, Ironshore, Johnson & Johnson, Lundbeck, Neurocrine, Noven, Otsuka, Sunovion, Supernus, Takeda, Teva, and Tris Pharma. **JT** has received research support from Otsuka in the past 3 years. **GS** is one of the original developers of the Brief Negative Symptom Scale (BNSS) and receives royalties and consultation fees from WCG in connection with commercial use of the BNSS and other professional activities; these fees are donated to the Brain and Behavior Research Foundation. **GS** has also received honoraria and travel support from WCG for training pharmaceutical company raters on the BNSS, and has consulted for and/or been on the speaker's bureau for Minerva Neurosciences, Acadia, Lundbeck, Sunovion, Boehringer Ingelheim, Otsuka, and Johnson & Johnson pharmaceutical companies.

Abbreviations

AE, adverse event; CAINS, Clinical Assessment Interview for Negative Symptoms; CAINS-MAP, Clinical Assessment Interview for Negative Symptoms, Motivation and Pleasure subscale; CI, confidence interval; C-SSRS, Columbia-Suicide Severity Rating Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, fifth edition; DTx, digital therapeutics; ENS, experiential negative symptoms; EOS, end of study; FDA, Food and Drug Administration; ITT, intention-to-treat; IQR, interquartile range; LS, least squares; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event; US, United States.

Key contributors

WT, AP, SEL, and **OB** had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: **AP, SEL, CS, AS, CvdG,** and **CDC**. Acquisition, analysis, or interpretation of data: All authors. Critical review of the poster for important intellectual content: All authors. Statistical analysis: **AP, WT,** and **OB**. Obtained funding: **AP, SEL, AS, CvdG,** and **CDC**. Administrative, technical, or material support: **AP, SEL, FD, RSK, JPL, JWF, AS,** and **CDC**. Supervision: **AP, SEL, WT, FD, RSK, JPL, JWF, AS, CvdG,** and **CDC**.

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