August 12, 2026

Definium Therapeutics Announces Positive Topline Results from Phase 3 Voyage Study of DT120 ODT in Generalized Anxiety Disorder

Study met primary and all key secondary efficacy endpoints

Participants receiving DT120 ODT achieved a statistically significant reduction in Hamilton Anxiety Rating Scale (HAM-A) score, with a placebo-adjusted change of 5.4 points from baseline at Week 12 ($p<0.0001$, Cohen's $d=0.81$)

DT120 ODT was generally well tolerated, with a safety profile consistent with prior clinical experience

Company to host webcast today at 8:00 am EDT

NEW YORK--(BUSINESS WIRE)-- Definium Therapeutics, Inc. (Nasdaq: DFTX) ("Definium" or the "Company"), a late-stage clinical biopharmaceutical company developing a new generation of therapeutics intended to address underlying causes of psychiatric and neurological disorders, today announced positive topline results from Voyage, its first Phase 3 study of DT120 (lysergide) Orally Disintegrating Tablet (ODT) 100 µg in adults with generalized anxiety disorder (GAD). The results mark the Company's second positive DT120 ODT Phase 3 readout, following the positive Emerge results in major depressive disorder (MDD) announced in June.

Voyage met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement from baseline compared with placebo, as measured by the change in HAM-A total score at Week 12. The Least Squares (LS) mean change from baseline in HAM-A total score at Week 12 in participants who received DT120 ODT 100 µg was -11.6 compared with -6.2 for participants who received placebo, an LS mean difference of -5.4 points ($p<0.0001$), corresponding to a standardized effect size of $d=0.81$. Efficacy was rapid, with changes seen as early as Day 2 and sustained at all post-baseline timepoints in Part A.

"The unprecedented efficacy demonstrated in Voyage should raise the bar for what patients and clinicians expect from GAD treatments and reinforces our belief that DT120 has the potential to redefine care for the millions of patients in need," said Rob Barrow, Chief Executive Officer of Definium Therapeutics. "Importantly, the consistent, large effect size we've now observed across three studies underscores the potential of DT120 to transform psychiatry and usher in a new era of mental health care. With our Panorama topline results in GAD expected in September, we remain focused on bringing this potential new treatment to patients as quickly as possible. We are deeply grateful to the patients, investigators, site personnel, and our team whose commitment made this milestone possible."

DT120 ODT was generally well tolerated, with treatment-emergent adverse events mild to moderate in severity, transient, and predominantly occurring on the day of dosing in Part A. No new safety signals were identified, including no suicidality signal or suicidal behavior.

On the day of dosing, participants were assessed hourly beginning at hour 5 post-dose on a structured end-of-session checklist (EoSC). The average time to meeting EoSC criteria was 6.4 hours for participants receiving DT120 ODT in Part A, with a median of 6.1 hours and 92% of participants meeting the EoSC criteria by hour 8.

“GAD affects approximately 26 million adults in the United States, and when left untreated, can cause chronic, pervasive, and debilitating symptoms that can seriously impact a person’s daily life. It is one of the most undertreated conditions in psychiatry,” said Brian Barnett, MD, Vice Chair of Psychiatry at Cleveland Clinic, and a Voyage principal investigator. “Despite the burden of the disorder, the last new FDA-approved treatment for this condition was nearly two decades ago, and many of the patients I see have not found relief despite trying multiple therapies. A single-dose treatment option delivering meaningful benefits for 12 weeks is a promising step forward not found in today’s therapies. If approved, it could give patients and their physicians a treatment option that works through an entirely different mechanism than anything currently used in clinical practice.”

Highlights from Voyage Topline Results

The mean baseline HAM-A score at study entry was 28.4 in the DT120 ODT treatment group (n=107) and 27.4 in the placebo group (n=107).

Primary Endpoint	DT120 ODT 100 µg	Placebo ODT	Placebo-Adjusted Difference
HAM-A: LS mean change at Week 12	-11.6	-6.2	-5.4 (p<.0001)
Key Secondary Endpoints			
CGI-S: LS mean change at Week 12	-1.0	-0.4	-0.6 (p<.0001)
HAM-A: LS mean change at Week 1	-11.9	-4.2	-7.7 (p<.0001)
CGI-S: LS mean change at Day 2	-1.0	-0.2	-0.8 (p<.0001)
Other Secondary Endpoints			
HAM-A: response rate (≥50%) at Week 12	43%	16%	27% (p<0.0001)
HAM-A: remission rate (≤7) at Week 12	14%	4%	10% (p=0.0222)
HAM-A: mild or better (<16) at Week 12	51%	23%	28% (p<0.0001)

HAM-A = Hamilton Anxiety Rating Scale; CGI-S = Clinical Global Impression-Severity Scale; LS = least squares; LS mean difference = difference in LS means of change from baseline between DT120 and placebo groups

Webcast Details

Definium Therapeutics management will host a webcast at 8:00 a.m. EDT today to review the Phase 3 Voyage study topline results. Listeners can register for the webcast via this link. Analysts wishing to participate in the question-and-answer session should use this link. A replay of the webcast will be available via the Investor Relations section of the Definium Therapeutics website, ir.definiumtx.com, and archived for at least 30 days after the webcast. Those who plan on participating are advised to join 15 minutes prior to the start time.

About Voyage

Voyage is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of a single 100 µg dose of DT120 ODT versus placebo in adults with generalized anxiety disorder (GAD). The study consists of a 12-week double-blind period (Part A) followed by a 40-week open-label extension (Part B), during which

participants may be eligible to receive up to four additional doses of DT120 ODT based on symptom severity.

The study enrolled 214 participants aged 18 to 74 years across approximately 35 sites in the United States with a DSM-5-confirmed diagnosis of GAD, based on clinical assessment and the Mini-International Neuropsychiatric Interview (MINI), and a Hamilton Anxiety Rating Scale (HAM-A) total score of at least 20 at screening and baseline.

The primary endpoint is change from baseline in HAM-A total score at Week 12. Key secondary multiplicity-controlled endpoints are change from baseline in Clinical Global Impression-Severity (CGI-S) scale score at Week 12, change from baseline in HAM-A total score at Week 1, and change from baseline in CGI-S score at Day 2.

Voyage is one of two pivotal Phase 3 studies in GAD. Panorama, the second Phase 3 study in GAD, is aligned with Voyage, but includes a low-dose 50 µg dose arm. Participants will be randomized 2:1:2 to receive DT120 ODT 100 µg, DT120 ODT 50 µg, or placebo. The 50 µg arm is intended to confound participants' ability to accurately assess the dose condition to which they have been randomized. This approach continues to build on the Company's Phase 2b study of DT120 in GAD, which the Company believes demonstrated that DT120's clinical activity is not attributable to functional unblinding and aligns with FDA guidance on the use of complementary designs across the Company's DT120 clinical development program. The primary endpoint of Panorama is change from baseline in HAM-A total score at Week 12 between DT120 ODT 100 µg and placebo.

About Generalized Anxiety Disorder (GAD)

GAD is one of the most common psychiatric disorders, affecting approximately 26 million U.S. adults.[1,2] People with GAD experience constant, overwhelming worry that is hard to control. Common symptoms include fatigue, muscle tension, trouble concentrating, and difficulty sleeping.[3] GAD is associated with the development of other chronic physical illnesses, as well as depression, other anxiety disorders, and trauma-related conditions. Together, these issues can seriously impact a person's daily life, including substantial functional, economic, and quality-of-life burdens, and are associated with increased healthcare utilization and costs.[4,5,6] Despite the significant personal and societal burden of GAD, there has been little innovation in the treatment of GAD in the past several decades, with the last new drug approval occurring in 2007.[7]

About DT120 (lysergide) Orally Disintegrating Tablet (ODT)

DT120 ODT is an ergoline derivative belonging to the group of classic serotonergic psychedelics, which acts as a partial agonist at serotonin-2A (5-HT2A) receptors. DT120 ODT is Definium's proprietary and pharmaceutically optimized formulation of LSD. DT120 ODT is an advanced formulation incorporating Catalent's Zydis® ODT fast-dissolve technology, designed to deliver several unique advantages, including faster absorption and onset of transient cognitive, perceptual, and affective changes, improved bioavailability, and a lower incidence of gastrointestinal side effects. Definium is developing DT120 ODT, the tartrate salt form of lysergide, for generalized anxiety disorder (GAD), major depressive disorder (MDD), and posttraumatic stress disorder (PTSD), and is exploring its potential applications in other serious brain health disorders. DT120 has received Breakthrough Therapy designation from the FDA for GAD. Definium maintains a strong foundation to protect and extend the long-term value of the DT120 ODT franchise through a multi-layered

intellectual property strategy spanning composition, formulation, and methods-of-use patents.

About Lysergide (LSD)

Lysergide (LSD) is one of the most extensively studied psychopharmaceuticals in history, with over 1,000 published reports.[8] First synthesized in 1938 by Swiss chemist Albert Hofmann in his search for active principles from ergot fungus, its profound psychological effects were discovered in 1943, which transformed psychiatric research.[8] LSD, a definitional classic psychedelic, temporarily alters perception, cognition, and emotion, is physiologically safe, non-addictive, and is not associated with withdrawal.[8] While its precise mechanism of action in the treatment of psychiatric illness is unknown, its acute perceptual, cognitive, and affective effects are mediated by agonism of the serotonin 5-hydroxytryptamine 2A (5-HT2A) receptor, and mechanistic hypotheses suggest that it causes sustained increases in neuroplasticity in a variety of brain regions.[9,10]

About Definium Therapeutics

The mission of Definium Therapeutics is to forge a new era of psychiatry by applying scientific rigor to psychedelics, with the goal of developing accessible treatments that unlock healing at scale. Guided by a recognition that patients deserve more than better, Definium is relentlessly advancing a new generation of therapeutics intended to address underlying causes of psychiatric and neurological disorders. By turning evidence into impact, Definium aims to change the trajectory of today’s mental health care crisis and enable a healthier future. Headquartered in New York, Definium Therapeutics trades on Nasdaq under the symbol DFTX.

Forward-Looking Statements

Certain statements in this news release related to the Company constitute "forward-looking information" within the meaning of applicable securities laws and are prospective in nature. Forward-looking information is not based on historical facts, but rather on current expectations and projections about future events and are therefore subject to risks and uncertainties which could cause actual results to differ materially from the future results expressed or implied by the forward-looking statements. These statements generally can be identified by the use of forward-looking words such as "will", "may", "should", "could", "intend", "estimate", "plan", "anticipate", "expect", "believe", "potential" or "continue", or the negative thereof or similar variations. Forward-looking information in this news release includes, but is not limited to, statements regarding the anticipated design, timing, progress and results of the Company's investigational programs for DT120 ODT for the treatment of generalized anxiety disorder, major depressive disorder and posttraumatic stress disorder; the success and timing of the Company's development activities; the likelihood of success of any clinical trials or of obtaining U.S. Food and Drug Administration or other regulatory approvals; the Company's beliefs regarding potential benefits of its product candidates; the Company's belief that DT120 ODT has the potential to transform psychiatry and usher in a new era of mental health care; and the ability of DT120 ODT to redefine care for the millions of patients in need. There are numerous risks and uncertainties that could cause actual results and the Company's plans and objectives to differ materially from those expressed in the forward-looking information, including history of negative cash flows; limited operating history; incurrence of future losses; availability of additional capital; compliance with laws and regulations; legislative and regulatory developments, including decisions by the Drug

Enforcement Administration and states to reschedule any of the Company's product candidates, if approved, containing Schedule I controlled substances, before they may be legally marketed in the U.S.; difficulty associated with research and development; risks associated with clinical studies or studies; heightened regulatory scrutiny; early stage product development; clinical study risks; regulatory approval processes; novelty of the psychedelic inspired medicines industry; ability to maintain effective patent rights and other intellectual property protection for the Company's product candidates, the Company's expectations regarding the size of the eligible patient populations for its lead product candidates, if approved and commercialized; the Company's ability to identify third-party treatment sites to conduct its trials and its ability to identify and train appropriate qualified healthcare practitioners to administer its treatments; the pricing, coverage and reimbursement of the Company's lead product candidates, if approved and commercialized; the rate and degree of market acceptance and clinical utility of the Company's lead product candidates, in particular, and controlled substances, in general as well as those risk factors discussed or referred to herein and the risks, uncertainties and other factors described in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2025 and its Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2026 and June 30, 2026, under headings such as "Special Note Regarding Forward-Looking Statements," and "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other filings and furnishings made by the Company with the securities regulatory authorities in all provinces and territories of Canada which are available under the Company's profile on SEDAR+ at www.sedarplus.ca and with the U.S. Securities and Exchange Commission on EDGAR at www.sec.gov. Except as required by law, the Company undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events, changes in expectations or otherwise.

References

1. Ringeisen, H., et al. (2023). Mental and substance use disorders prevalence study (MDPS): Findings report. RTI International and current U.S. Census data and internal company estimates.
2. Ferries, E., et al. The Prevalence and Burden of Generalized Anxiety Disorder in the United States Healthcare System: Real-World Prevalence and Incidence from 2020-2023. *Journal of Mood and Anxiety Disorders*. 2026;13.
3. Patriquin, M. A., & Mathew, S. J. (2017). The neurobiological mechanisms of generalized anxiety disorder and chronic stress. *Chronic Stress*. Mar 2017;1:1-10.
4. Barrera, T. L., & Norton, P. J. (2009). Quality of life impairment in generalized anxiety disorder, social phobia, and panic disorder. *Journal of Anxiety Disorders*. 2009;23(8):1086–1090.
5. Armbrecht, E., Shah, R., Poorman, G. W., et al. (2021). Economic and humanistic burden associated with depression and anxiety among adults with non-communicable chronic diseases (NCCDs) in the United States. *Journal of Multidisciplinary Healthcare*. 2021;14;887–896.
6. Newman, M. G., Llera, S. J., Erickson, T. M., Przeworski, A., & Castonguay, L. G. (2013). Worry and generalized anxiety disorder: A review and theoretical synthesis of evidence on nature, etiology, mechanisms, and treatment. *Annual Review of Clinical Psychology*, 2013;9:275–297.
7. U.S. Food and Drug Administration. (2007, August 9). FDA approves Cymbalta for treatment of generalized anxiety disorder [Press release]. https://investor.lilly.com/static-files/499f0aa3-281f-49f4-9655-049aae179593.
8. Nichols, DE. “Psychedelics.” Pharmacological Reviews. 2016;68(2):264-355.
9. Passie, T, Halpern, JH, Stichtenoth, DO, et al. “The Pharmacology of Lysergic Acid Diethylamide: A Review.” CNS Neuroscience & Therapeutics. 2008;14:295-314.
10. Liechti, ME. “Modern clinical research on LSD.” Neuropsychopharmacology. 2017;42:2114-2127.

View source version on businesswire.com:
https://www.businesswire.com/news/home/20260812579720/en/

Investors:
Gitanjali Jain
VP, Head of Investor Relations
ir@definiumtx.com

Media:
media@definiumtx.com

Source: Definium Therapeutics, Inc.