June 22, 2026

Definium Therapeutics Announces Positive Topline Results from Phase 3 Emerge Study of DT120 Orally Disintegrating Tablet (ODT) in Major Depressive Disorder

Study met primary and all key secondary efficacy endpoints

8.1 point Montgomery-Åsberg Depression Rating Scale (MADRS) placebo-adjusted change from baseline at Week 6 for the primary endpoint (p<0.0001)

7.3 point MADRS placebo-adjusted change from baseline at Week 12, a secondary endpoint (p<0.0001)

DT120 ODT was generally well tolerated with no serious adverse events or suicidality signal

Company to host webcast today at 8:00 a.m. EDT

NEW YORK--(BUSINESS WIRE)-- Definium Therapeutics, Inc. (“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 Emerge, its first randomized, double-blind, placebo-controlled Phase 3 study evaluating a single dose of DT120 (lysergide) ODT 100 µg in adults with major depressive disorder (MDD).

Emerge met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement from baseline compared with placebo, as measured by the change in MADRS total score at week 6. The Least Squares (LS) mean change from baseline in MADRS total score at Week 6 in participants who received DT120 ODT 100 µg was -13.3 compared with -5.2 for patients who received placebo, a LS mean difference of -8.1 points (p<0.0001). Beyond the primary endpoint, the effect was rapid with a placebo-adjusted LS mean reduction in MADRS total score at Week 1 of -14.2 (p<0.0001) and durable with a placebo-adjusted LS mean reduction in MADRS total score of -7.3 at Week 12 (p<0.0001).

“The Emerge topline results represent unprecedented and highly differentiated efficacy, demonstrating that a single dose of DT120 ODT can deliver rapid, robust, and durable relief in MDD,” said Rob Barrow, Chief Executive Officer of Definium Therapeutics. “As the first of our Phase 3 studies to report results, Emerge marks a major milestone in our development program and strengthens our confidence in DT120 as a potential best-in-class treatment for mental health disorders. These findings could support a fundamentally new approach to treating MDD for patients and providers who continue to face the limitations of existing treatment options. We are deeply grateful to the patients and investigators who participated in this trial. Grounded in decades of scientific research, these results bring us one step

closer to potentially delivering a transformative new treatment option as we advance toward FDA submission."

DT120 ODT was generally well tolerated with 99% of treatment-emergent adverse events mild to moderate in severity, transient, and predominantly occurring on the day of dosing. No new safety signals were identified, including no increase in suicidal ideation or behavior, and discontinuation rates were low and comparable between treatment groups. On the day of dosing, participants were assessed hourly from hours 5 to 8 on a structured end of session checklist (EoSC). The average time to meeting EoSC criteria was 5.8 hours for participants receiving DT120 ODT in Part A, with a median of 5.1 hours and 100% of participants meeting the EoSC criteria by hour 8.

"Many patients with MDD aren't helped by existing treatments, often experiencing partial responses, frequent medication changes, and long-term side effects," said John Sonnenberg, Ph.D., Emerge principal investigator, clinical psychologist, founder of Uptown Research Institute, and faculty member at Northwestern University Feinberg School of Medicine. "The Emerge topline results demonstrate that a single dose of DT120 ODT can produce a meaningful and durable benefit for people with depression. Importantly, these results stand apart from existing treatments, representing a potentially new paradigm for the management of major depression."

Highlights from Emerge Topline Results

The mean baseline MADRS score at study entry was 35.0 in the DT120 ODT treatment group (n=75) and 34.0 in the placebo ODT group (n=74).

Endpoint	DT120 ODT 100 µg	Placebo ODT	Placebo-Adjusted Difference
MADRS: LS mean change at Week 6*	-13.3	-5.2	-8.1 (p<0.0001)
MADRS: LS mean change at Week 12**	-11.0	-3.6	-7.3 (p<0.0001)
MADRS: LS mean change at Week 1**	-17.6	-3.4	-14.2 (p<0.0001)
CGI-S: LS mean change at Week 6**	-1.2	-0.3	-0.9 (p<0.0001)
CGI-S: LS mean change at Week 12**	-1.0	-0.3	-0.7 (p<0.0001)
CGI-S: LS mean change at Day 2**	-1.0	-0.1	-0.9 (p<0.0001)
MADRS: response rate (≥50%) at Week 6***	35%	7%	28% (p<0.001)
MADRS: remission rate (≤12) at Week 6***	24%	3%	21% (p<0.01)

* Pre-specified primary endpoint
** Pre-specified key secondary endpoint
*** Pre-specified secondary endpoint
CGI-S = Clinical Global Impressions – 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 Emerge 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 Emerge

Emerge 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

participants with major depressive disorder (MDD). The study consists of a 12-week double-blind phase (Part A) followed by a 40-week open-label extension phase (Part B) during which participants may be eligible to receive DT120 ODT based on symptom severity.

The study enrolled 149 participants aged 18 to 74 years across 20 sites with a DSM-5-confirmed diagnosis of MDD, a Montgomery-Åsberg Depression Rating Scale (MADRS) total score of at least 26, and a Clinical Global Impression–Severity (CGI-S) score of at least 4 at screening and baseline.

The primary endpoint is change from baseline in the MADRS total score at Week 6. Key secondary endpoints are change from baseline in CGI-S score at Week 6, Week 12 and Day 2 and change from baseline in MADRS total score at Week 12 and Week 1.

Emerge is one of two pivotal Phase 3 studies in MDD. Ascend, the second Phase 3 study in MDD, is aligned with Emerge, but includes a low dose arm and is also conducted in two parts: Part A, a 12-week, randomized, double-blind, placebo-controlled, parallel-group period; and Part B, a 40-week extension period during which participants will be eligible for open-label treatment with DT120 ODT based on symptom severity. 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 generalized anxiety disorder (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 Ascend is change from baseline in MADRS total score at Week 6 between DT120 ODT 100 µg and placebo.

About Major Depressive Disorder (MDD)

Major Depressive Disorder (MDD) is the second-most common mental health disorder in the U.S., with over 21 million adults experiencing a major depressive episode (MDE) each year.[1,2] This disorder, a leading cause of disability worldwide,[3] brings persistent feelings of worthlessness, fatigue, and recurrent thoughts of death[4] while increasing long-term mortality risk by 40%.[5] MDD also carries a $326 billion annual economic burden in the U.S., driven by healthcare costs and lost productivity.[6] The MDD treatment paradigm is characterized by critical unmet needs, including fewer than one-third of patients reaching remission with first-line treatments,[7] onset of clinical activity that takes weeks to months,[8,9] poor tolerability,[10,11] and frequent switching, augmentation, and discontinuation of pharmacotherapy.[12]

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), 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.[13] 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.[13] LSD, a definitional classic psychedelic, temporarily alters perception, cognition, and emotion, is physiologically safe, non-addictive, and isn't associated with withdrawal.[13] 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.[14,15]

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 (including the anticipated topline readouts for the Voyage, Panorama, and Ascend studies), 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 ("FDA") or other regulatory approvals; the Company's beliefs regarding potential benefits of its product candidates; the Company's belief that DT 120 ODT can deliver rapid, robust, and durable relief for people living with MDD; the Company's belief that DT120 ODT could be a best-in-class treatment for mental health disorders; the Company's belief that the results from its Phase 3 Emerge Study of DT120 ODT could support a fundamentally new approach to

treating MDD and a transformative new treatment option; the ability of DT120 ODT to be a potentially new paradigm for the management of major depression; and the potential for psychedelics as a class of treatment options in psychiatry. 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 Report on Form 10-Q for the fiscal quarter ended March 31, 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. National Institute of Mental Health (NIMH). "Major Depression: Prevalence of Major Depressive Episode Among Adults." Updated 2024.
2. Substance Abuse and Mental Health Services Administration (SAMHSA). "2023 National Survey on Drug Use and Health (NSDUH)."
3. World Health Organization (WHO). "Depression Fact Sheet." Updated 2023.
4. American Psychiatric Association. "Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)." 2013.
5. Cuijpers, P., et al. "Long-Term Mortality Risk in Depression: A 20-Year Follow-Up Study." JAMA Psychiatry, 2023.
6. Greenberg, P. E., et al. "The Economic Burden of Adults with Major Depressive Disorder in the United States (2020)." Journal of Clinical Psychiatry, 2024.
7. Rush, A. J., et al. "Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report." American Journal of Psychiatry, 2006.
8. APA. Practice Guideline for the Treatment of Patients with Major Depressive Disorder. Published 2010.

9. Alemi F, Min H, et al. Effectiveness of common antidepressants: A post market release study. eClinicalMedicine. 2021;41.
10. Cipriani A, et al. Comparative Efficacy and acceptability of 21 antidepressant drugs for the Acute Treatment of Adults with Major Depressive Disorder: A Systematic Review and Network Meta-analysis. Lancet. 2018;391(10128):1357-66.
11. Braund TA, Tillman G, et al. Antidepressant Side Effects and Their Impact on Treatment Outcome in People with Major Depressive Disorder: An Ispot-D Report. Transl Psychiatry. 2021;11(1):417.
12. Zhu L, Ferries E, et al. Economic Burden and Antidepressant Treatment Patterns Among Patients with Major Depressive Disorder in the United States. J Manag Care Spec Pharm. 2022 Nov;28(11-a Suppl): S2-S13.
13. Nichols, DE. “Psychedelics.” Pharmacological Reviews, 2016;68(2): 264–355.
14. Passie, T, Halpern, JH, Stichtenoth, DO, et al. “The Pharmacology of Lysergic Acid Diethylamide: A Review.” CNS Neuroscience & Therapeutics. 2008;14:295–314.
15. Liechti, ME. “Modern clinical research on LSD.” Neuropsychopharmacology. 2017;42: 2114–2127.

View source version on businesswire.com:
https://www.businesswire.com/news/home/20260622572802/en/

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

Media:
media@definiumtx.com

Source: Definium Therapeutics, Inc.