COMP360 psilocybin therapy shows potential in open-label study in type II bipolar disorder presented at ACNP

December 8, 2022

12 out of 14 patients went into remission for three months following a single 25mg dose of COMP360 psilocybin therapy, in an independent investigator-initiated, exploratory open-label study of type II bipolar disorder

New data from COMPASS' phase 2b trial, also presented at ACNP, validate potential of COMP360 psilocybin therapy in treatment-resistant depression

LONDON, Dec. 08, 2022 (GLOBE NEWSWIRE) -- COMPASS Pathways plc (Nasdaq: CMPS) ("COMPASS"), a mental health care company dedicated to accelerating patient access to evidence-based innovation in mental health, today announced that new positive data demonstrating the potential of COMP360 psilocybin therapy in depression have been presented at the Annual Meeting of the American College of Neuropsychopharmacology (ACNP). The results were presented from an investigator-initiated, exploratory open-label study of investigational COMP360 psilocybin therapy in type II bipolar disorder and a mechanistic analysis of the phase 2b trial of COMP360 psilocybin therapy in treatment-resistant depression (TRD).

Type II bipolar disorder
Positive early signals have been presented in a poster from an open-label pilot study, which investigated the safety and efficacy of a single 25mg dose of COMP360 psilocybin therapy in participants with type II bipolar disorder depression.[1] The study, run by Dr Scott Aaronson at Sheppard Pratt Baltimore, found that 86% (12 out of 14) of the participants met response and remission criteria for the Montgomery-Åsberg Depression Rating Scale (MADRS) at 12 weeks after COMP360 psilocybin therapy. There was no increase in the suicidality score based on the MADRS, no manic symptoms and no unexpected adverse events or difficulties with the dosing sessions reported throughout the study.

"Type II bipolar disorder can have a huge impact on people's lives, as well as their loved ones, and is extremely difficult to treat. It is really encouraging to have seen 12 of 14 participants go into remission lasting three months, following just a single dose of 25mg of COMP360 psilocybin therapy. These findings now need to be validated in larger studies," said Scott Aaronson, MD, Chief Science Officer, Institute for Advanced Diagnostics and Therapeutics, Sheppard Pratt.

Treatment-resistant depression (TRD)
New data from the recently published phase 2b trial of COMP360 psilocybin therapy, also presented at ACNP, further demonstrated its potential in treatment-resistant depression, and how it may work:[2,3]

- **Mechanism of action validated:** experiencing emotional breakthrough* and specific aspects of the subjective psychedelic experience** predicted reductions in depression severity three weeks after receiving COMP360 psilocybin therapy. The relationship between positive psychedelic experience and treatment response was seen for all three doses studied.
- **Effect of higher dose:** whilst both the 10mg and 25mg dose of COMP360 psilocybin produced a subjective psychedelic experience, the 25mg dose was significantly better at reducing depressive symptoms compared to a 1mg dose, whereas the 10mg dose was not found to be significantly better than 1mg.
- **Psychological support:** the therapeutic alliance between the participant and therapist did not predict improvement in symptoms of depression, suggesting that COMP360 psilocybin may provide greater therapeutic effect via its pharmacological action. This hypothesis will be tested further in COMPASS' phase 3 programme.

Dr David Feifel, Principal Investigator in the COMPASS phase 2b study at Kadima Neuropsychiatry Institute, La Jolla, California, said, "The positive results published in the *New England Journal of Medicine* showed the efficacy of COMP360 psilocybin in treatment-resistant depression, and now these new findings are providing insights on how that antidepressant effect may be produced. This new analysis suggests that positive psychedelic experiences facilitate emotional breakthrough which may change thought patterns in people with depression."

Dr Guy Goodwin, Chief Medical Officer, COMPASS Pathways, added, "These studies provide further evidence to support COMP360 psilocybin therapy's potential for difficult-to-treat depression. Psilocybin binds to serotonin receptors in the brain, and by allowing different brain regions to connect and communicate more easily than usual, it produces a profound psychedelic experience. This experience is driven by drug dose and correlates with the effect on depressive symptoms. Psychological support is focused on safety, which facilitates the psychedelic experience, but does not directly drive the effect on depression: it is not a psychotherapy."

COMPASS Pathways is running the world's first phase 3 programme of COMP360 psilocybin therapy in treatment-resistant depression – for more information please click here.

*Measured by the Emotional Breakthrough Inventory, a validated scale which assesses emotional experience.

**Aspects including oceanic boundlessness, visual restructuralisation, and auditory alterations – as measured by the Five-Dimensional Altered States of Consciousness questionnaire.

About treatment-resistant depression (TRD)

More than 320 million people globally suffer with major depressive disorder (MDD)[4], the leading cause of disability worldwide and one of the fastest growing mental health illnesses[5]. About a third of these patients – 100 million people – aren't helped by existing therapies and suffer with treatment-resistant depression (TRD)[6]. As many as 30% of these attempt suicide at least once during their lifetime[7,8]. TRD carries two to three times the medical costs of a non-TRD MDD patient, and patients with TRD have a higher all-cause mortality compared with non-TRD MDD patients[9]. The TRD population is by definition more difficult to treat and more likely to relapse than patients with major depressive disorder. In 2018, COMPASS received FDA Breakthrough Therapy designation for its COMP360 psilocybin therapy for TRD.

About type II bipolar disorder

Bipolar disorders are a complex group of severe and chronic disorders affecting approximately 40 million people globally[10,11]. Bipolar I disorder (BP-I) and bipolar II disorder (BP-II) are some of the major forms of bipolar disorders[12.] While both involve shifts in mood, energy, activity levels and concentration, they differ in the intensity of manic episodes and the prevalence of major depressive episodes[9]. Bipolar disorders are associated with high levels of functional impairment, morbidity, mortality, and an increased risk of suicide[13]. In fact, they have the highest rate of suicide of all psychiatric conditions which is about 30 times that of the general population[14].

About COMP360 psilocybin therapy

COMP360 is our proprietary stabilised, high-purity polymorphic crystalline synthesised formulation of psilocybin. Psilocybin acts on serotonin 2a receptors in the brain. It's believed that acting on this receptor may make the brain work with greater flexibility, allowing regions to connect and communicate more easily. Connections underlying unhealthy brain states, such as TRD, may reconnect in a healthier way after the drug effects have worn off[15].

About the COMP360 psilocybin therapy phase 2b study

This randomised, controlled, multicentre, double-blind phase 2b trial is the largest psilocybin therapy clinical trial ever conducted, with 233 patients from 10 countries in North America and Europe. 94% of the patients had no prior experience with psilocybin. The objective of the trial was to find the appropriate dose for a larger, pivotal phase 3 programme, which COMPASS expects to begin in 2022.

The trial assessed the safety and efficacy of COMP360 psilocybin therapy at three doses: 1mg, 10mg, 25mg. A total of 233 patients enrolled in the study and were randomised and blinded into three arms comprising 79 patients for each of the 25mg and 1mg doses, and 75 patients for the 10mg dose. Patients were followed up for 12 weeks. The trial used the Montgomery-Åsberg depression rating scale (MADRS), a widely used and accepted scale for assessing depression; assessments were made by an independent, blinded rater. The primary endpoint was the change in the MADRS total score from baseline to week 3.

COMP360 psilocybin was generally well-tolerated. On the day of COMP360 administration, headache, nausea, and dizziness were the most common adverse events where a dose-related increase in incidence was evident**.** Suicidal ideation and intentional self-injury were seen in all treatment groups (as is regularly observed in a TRD population). The majority of cases occurred more than a week after the COMP360 psilocybin session. There was no mean worsening of suicidal ideation scores on the MADRS scale in any treatment group. Suicidal behaviours were reported at least one month after COMP360 administration for three non-responders in the 25mg arm.

About COMPASS Pathways

COMPASS Pathways plc (Nasdaq: CMPS) is a mental health care company dedicated to accelerating patient access to evidence-based innovation in mental health. Our focus is on improving the lives of those who are suffering with mental health challenges and who are not helped by current treatments. We are pioneering the development of a new model of psilocybin therapy, in which our proprietary formulation of synthetic psilocybin, COMP360, is administered in conjunction with psychological support. COMP360 has been designated a Breakthrough Therapy by the US Food and Drug Administration (FDA) and has received Innovative Licensing and Access Pathway (ILAP) designation in the UK for treatment-resistant depression (TRD). We have completed a phase 2b clinical trial of psilocybin therapy for TRD, in 22 sites across Europe and North America and we are preparing to commence a phase 3 programme by the end of 2022. This was the largest randomised, controlled, double-blind psilocybin therapy clinical trial ever conducted, and our topline data showed a statistically significant ($p<0.001$) and clinically relevant improvement in depressive symptom severity after three weeks for patients who received a single high dose of COMP360 psilocybin with psychological support. We are also running phase 2 clinical trials of COMP360 psilocybin therapy for post-traumatic stress disorder (PTSD) and anorexia nervosa. COMPASS is headquartered in London, UK, with offices in New York and San Francisco in the US. Our vision is a world of mental wellbeing. www.compasspathways.com

Availability of other information about COMPASS Pathways

Investors and others should note that we communicate with our investors and the public using our website (www.compasspathways.com), our investor relations website (ir.compasspathways.com), and on social media (LinkedIn), including but not limited to investor presentations and investor fact sheets, US Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that we post on these channels and websites could be deemed to be material information. As a result, we encourage investors, the media, and others interested in us to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on our investor relations website and may include additional social media channels. The contents of our website or these channels, or any other website that may be accessed from our website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

Forward-looking statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. In some cases, forward-looking statements can be identified by terminology such as “may”, “might”, “will”, “could”, “would”, “should”, “expect”, “intend”, “plan”, “objective”, “believe”, “contemplate”, “estimate”, “potential”, “continue” and “ongoing,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Forward-looking statements include express or implied statements relating to, among other things, the safety or efficacy of COMP360 psilocybin therapy as a treatment for treatment-resistant depression or bipolar II depression, COMPASS’s ability to secure regulatory approval for COMP360 psilocybin therapy, COMPASS’s business strategy and goals, including its ability to launch and commercialise COMP360 psilocybin therapy, COMPASS’s ability to continue to advance its research or develop plans to bring COMP360 psilocybin therapy to patients, including COMP360, and COMPASS’s expectations regarding the benefits of its COMP360 psilocybin therapy. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond COMPASS’s control and which could cause actual results, levels of activity, performance or achievements to differ materially from those expressed or implied by these forward-looking statements.

These risks, uncertainties, and other factors include, among others: clinical development is lengthy and uncertain, and therefore our clinical trials may be delayed or terminated, or may never advance to a regulatory filing or support regulatory approval; and those risks and uncertainties described under the heading “Risk Factors” in COMPASS’ most recent annual report on Form 10-K or quarterly report on Form 10-Q and in other reports we have filed with the U.S. Securities and Exchange Commission (“SEC”), which are available on the SEC’s website at www.sec.gov. Except as required by law, COMPASS disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on COMPASS’s current expectations and speak only as of the date hereof.

Enquiries

Media: Amy Lawrence, amy@compasspathways.com, +44 7813 777 919
Investors: Stephen Schultz, stephen.schultz@compasspathways.com, +1 401 290 7324

References:

[1] An Open Label Study of the Safety and Efficacy of COMP360 (COMPASS Pathways Proprietary Synthetic Psilocybin) in Participants with Type II Bipolar Disorder (BP-II) Depression.
[2] Dose-dependent acute subjective psychedelic effects following COMP360 psilocybin across three clinical studies and its relationship to therapeutic response [poster]. Presented at the Annual Meeting of the American College of Neuropsychopharmacology; December 4-7, 2022; Phoenix, Arizona. Available at: https://compasspathways.com/wp-content/uploads/2022/11/COMPASS_ACNP_DoseDependentEffects.pdf
[3] Predicting depression outcomes through the influence of therapeutic alliance and the psychedelic experience using path modeling in a phase IIb randomized controlled trial of COMP360 psilocybin therapy [poster]. Presented at the Annual Meeting of the American College of Neuropsychopharmacology; December 4-7, 2022; Phoenix, Arizona. Available at: https://compasspathways.com/wp-content/uploads/2022/11/COMPASS_ACNP_PathAnalysis.pdf
[4] WHO (2017). Depression and Other Common Mental Disorders Global Health Estimates [Online]. Available at: https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf [Accessed November 2022]
[5] WHO (2012). Depression: A Global Crisis [Online]. Available at: https://www.wfmh.org/2012DOCS/WMHDay%202012%20SMALL%20FILE%20FINAL.pdf [Accessed November 2022]
[6] Al-harbi. (2012). Treatment-resistant depression: therapeutic trends, challenges, and future directions. Patient Preference and Adherence, 369. https://doi.org/10.2147/ppa.s29716
[7] Bergfeld, I. O., Mantione, M., Figee, M., Schuurman, P. R., Lok, A., & Denys, D. (2018). Treatment-resistant depression and suicidality. Journal of Affective Disorders, 235, 362–367. https://doi.org/10.1016/j.jad.2018.04.016
[8] Dong, M., Lu, L., Zhang, L., Zhang, Q., Ungvari, G. S., Ng, C. H., Yuan, Z., Xiang, Y., Wang, G., & Xiang, Y.-T. (2019). Prevalence of suicide attempts in bipolar disorder: a systematic review and meta-analysis of observational studies. Epidemiology and Psychiatric Sciences, 29. https://doi.org/10.1017/s2045796019000593
[9] Li, G., Fife, D., Wang, G., Sheehan, J. J., Bodén, R., Brandt, L., Brenner, P., Reutfors, J., & DiBernardo, A. (2019). All-cause mortality in patients with treatment-resistant depression: a cohort study in the US population. Annals of General Psychiatry, 18(1). https://doi.org/10.1186/s12991-019-0248-0
[10] McIntyre, R. S., Berk, M., Brietzke, E., Goldstein, B. I., López-Jaramillo, C., Kessing, L. V., Malhi, G. S., Nierenberg, A. A., Rosenblat, J. D., Majeed, A., Vieta, E., Vinberg, M., Young, A. H., & Mansur, R. B. (2020). Bipolar disorders. The Lancet, 396(10265), 1841–1856. https://doi.org/10.1016/s0140-6736(20)31544-0
[11] WHO (2022). Mental disorders [Online]. Available at: https://www.who.int/news-room/fact-sheets/detail/mental-disorders
[12] National Institute of Mental Health. (2020, Jan.). Bipolar Disorder. https://www.nimh.nih.gov/health/topics/bipolar-disorder/index.shtml[13] Munoli, R. N., Praharaj, S. K., & Sharma, P. S. V. N. (2014). Co-morbidity in Bipolar Disorder: A Retrospective Study. Indian Journal of Psychological Medicine, 36(3), 270–275. https://doi.org/10.4103/0253-7176.135377
[14] Miller, J. N., & Black, D. W. (2020). Bipolar Disorder and Suicide: a Review. Current Psychiatry Reports, 22(2). https://doi.org/10.1007/s11920-020-1130-0
[15] Carhart-Harris, R. L., & Friston, K. J. (2019). REBUS and the Anarchic Brain: Toward a Unified Model of the Brain Action of Psychedelics. Pharmacological Reviews, 71(3), 316–344. https://doi.org/10.1124/pr.118.017160