COMPASS Pathways announces publication of phase 2b study of COMP360 psilocybin therapy for treatment-resistant depression in The New England Journal of Medicine

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After a single 25mg dose of COMP360 psilocybin therapy, approximately 30% of patients with

treatment-resistant depression (TRD) were in remission at week 3

Sustained response seen through week 12 in twice the number of TRD patients that received 25mg dose vs 1mg

Phase 3 pivotal programme expected to commence in 2022

LONDON, Nov. 03, 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 *The New England Journal of Medicine (NEJM)*, the world's leading peer-reviewed medical journal, has published the positive results from its phase 2b trial of COMP360 psilocybin therapy for treatment-resistant depression (TRD) - the largest study of its kind.

The objective of the randomised, controlled, double-blind phase 2b study was to understand the efficacy and safety of a single dose of investigational COMP360 psilocybin (25mg or 10mg), compared to 1mg, in patients with TRD. After a single 25mg dose of COMP360 psilocybin, in combination with psychological support, 29.1% of participants with TRD were in remission by week 3 ($p<0.002$) - this is higher than the response rates seen for equivalent lines of treatment in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study*, a large prospective clinical trial of major depressive disorder conducted to determine the effectiveness of different treatments for depression.

"The publication of our COMP360 psilocybin therapy study in the most prestigious peer-reviewed medical journal in the world is a proud moment for everyone involved," said Dr Guy Goodwin, Chief Medical Officer, COMPASS Pathways. "We saw positive results in a particularly difficult to treat group of patients, and the highest dose of COMP360 psilocybin had the greatest impact on people's depression. This suggests that COMP360 psilocybin has a true pharmacological effect, a finding that is critical for it to be recognised as a new treatment option in the future. We look forward to starting our phase 3 programme later this year, moving us closer to providing COMP360 psilocybin with psychological support for patients who desperately need it."

Further detail: phase 2b study synopsis

In the phase 2b trial, 233 patients with TRD received either 1mg, 10mg or 25mg COMP360 psilocybin, in conjunction with psychological support from specially trained therapists.

- **Rapid reduction in symptoms:** Approximately 30% of patients in the 25mg group were in remission at week 3 (29.1%). This is higher than the response rates seen for equivalent lines of treatment in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, a large prospective clinical trial of major depressive disorder conducted to determine the effectiveness of different treatments for depression
    - Patients who received a single 25mg dose of COMP360 psilocybin, in combination with psychological support, experienced a highly statistically significant, rapid reduction in symptoms of depression after three weeks: the difference between the 25mg group and 1mg group was -6.6 on the MADRS** depression scale at week 3, $p<0.001$
- **Sustained response:** Double the number of patients who received a 25mg dose had a sustained response at week 12, compared to those who received 1mg (20.3% of patients in the 25mg group vs 10.1% in the 1mg group)
- **Well-tolerated:** 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
- **Safety monitoring:** Suicidal ideation and intentional self-injury were seen in all treatment groups, as is common in TRD studies. Most 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

Scott Aaronson, MD, Chief Science Officer of the Institute for Advanced Diagnostics and Therapeutics, Sheppard Pratt Health System, and a Principal Investigator on the trial, said, "Over 100 million people around the world suffer with treatment-resistant depression, and haven't found relief from existing therapies. With every new treatment, the chance of responding decreases significantly, and patients become even more hopeless. Yet in this study, a substantial number of patients in the 25mg group experienced improvement in their symptoms of depression, with the effects lasting for up to three months. I'm proud to have been part of this important study and to see the results recognised today by such a respected journal."

Data from the phase 2b trial was announced in November and December 2021, and presented at the American Psychiatric Association annual meeting in New Orleans in May 2022. COMPASS Pathways presented the design of its phase 3 clinical programme on 12 October 2022 and plans to commence by the end of the year.

*Sinyor M, Schaffer A, Levitt A. The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Trial: A Review. The Canadian Journal of Psychiatry. 2010;55(3):126-135. doi:10.1177/070674371005500303
**MADRS = Montgomery-Åsberg Depression Rating Scale, a diagnostic questionnaire used to measure the severity of depression. A higher score indicates more severe depression.
Response = ≥50% decrease in MADRS total score from baseline; remission = MADRS total score ≤10; sustained response = patients meeting the MADRS response criteria from week 3 and at all subsequent visits until week 12.

About treatment-resistant depression (TRD)

More than 320 million people globally suffer with major depressive disorder (MDD)[1], the leading cause of disability worldwide and one of the fastest growing mental health illnesses[2]. About a third of these patients – 100 million people – aren't helped by existing therapies and suffer with treatment-resistant depression (TRD)[3]. As many as 30% of these attempt suicide at least once during their lifetime[4,5]. 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[6]. 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 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[7].

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 depression, COMPASS’s expectations for the timing of its pivotal phase 3 programme and the potential for the pivotal phase III programme or other trials to support regulatory filings and approvals, 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.

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Videos accompanying this announcement are available at:

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