COMPASS Pathways announces positive outcome of 25mg COMP360 psilocybin therapy as adjunct to SSRI antidepressants in open-label treatment-resistant depression study

December 13, 2021

- **Patients taking COMP360 psilocybin with concomitant SSRIs showed comparable treatment outcomes to patients withdrawn from their SSRI therapy in COMPASS's phase IIb trial**
- **All patients tolerated COMP360 psilocybin therapy well**

London, UK – 13 December 2021

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 the results from its exploratory study of COMP360 psilocybin therapy in conjunction with SSRI use. This single-arm open label study of 19 patients taking concomitant SSRI therapy with COMP360 psilocybin therapy using a single dose of 25mg saw comparable treatment outcomes to patients in COMPASS's phase IIb trial where patients were withdrawn from their SSRI prior to COMP360 psilocybin therapy.

"The results of this study challenge the widely-held belief that the use of SSRI medication together with psilocybin could interfere with psilocybin's therapeutic effect. Our findings provide a strong signal that COMP360 psilocybin therapy could be an adjunctive treatment to SSRI antidepressants as well as a monotherapy. For some patients with treatment-resistant depression, withdrawal is a difficult step even though, by definition, 'treatment-resistant' means that those antidepressants are not working. This is exactly why we conduct rigorous research to help guide our clinical trial design - including addressing barriers to adoption of COMP360 therapy," stated Guy Goodwin, COMPASS Pathways' Chief Medical Officer. "We are now looking forward to meeting with the FDA early in the new year in light of these new data to finalise our plans for the phase III programme, which we expect to begin in Q3 2022."

Study result

This open-label study included 19 patients from clinical sites in Ireland and the United States. The majority of patients were female (68.4%) and the average age was 42 years. The primary endpoint was the change in baseline MADRS[1] total score at 3 weeks in patients having 25mg COMP360 psilocybin therapy given in augmentation with their existing SSRI antidepressant regimen. In the study, 8 of the 19 patients (42.1%) were responders1 at week 3 (compared with 36.7% at week 3 in the phase IIb trial) and all 8 were also remitters[1]. The mean reduction from baseline observed in MADRS total score was 14.9 at week 3 (compared with a 12.0 mean reduction in MADRS in the phase IIb trial). There was a rapid response from day 2 to week 3 after COMP360 therapy, which is also consistent with the phase IIb result. The baseline MADRS score of patients entering the study was 31.7, representing moderate to severe depression. MADRS scores were assessed by blinded independent raters at baseline, on the day following COMP360 psilocybin therapy, and at weeks 1, 2 and 3. Patients were then invited to participate in COMPASS's long-term follow-up study which also includes patients from the phase IIb trial.

COMP360 psilocybin therapy using a 25mg dose also showed overall signals of improvement in most other measures including improvement in anxiety, clinician and self-rated depressive symptoms, and positive and negative affect.

25mg COMP360 psilocybin therapy was generally well-tolerated when it was administered simultaneously with the patient's SSRI treatment. There were no treatment-emergent adverse events (TEAEs) classed as serious (life threatening, leading to disabilities, hospitalisation or in general medically significant) and no TEAEs related to suicidal ideation or behaviour or intentional self-injury.

COMPASS is now preparing for a meeting with the FDA in early 2022 and this result will be included in that discussion. COMPASS expects to finalise a phase III programme design with the FDA and anticipates commencing that programme in Q3 2022. As a reminder, COMPASS has Breakthrough Therapy designation with the FDA.

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Notes to editors:

About treatment-resistant depression (TRD)

More than 320 million people globally suffer with major depressive disorder (MDD)[2], the leading cause of disability worldwide and one of the fastest growing mental health illnesses[3]. About a third of these patients - 100 million people - aren't helped by existing therapies and suffer with treatment-resistant depression (TRD)[4]. As many as 30% of these attempt suicide at least once during their lifetime[5,6]. 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[7]. 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 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), for treatment-resistant depression (TRD), and we have completed a phase IIb clinical trial of psilocybin therapy for TRD, in 22 sites across Europe and North America. 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 a phase II clinical trial of COMP360 psilocybin therapy for post-traumatic stress disorder (PTSD). 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”, “anticipate”, “believe”, “contemplate”, “estimate”, “predict”, “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 III programme and the potential for that or other trials to support regulatory filings and approvals, COMPASS’s business strategy and goals, the future accessibility of COMP360 psilocybin therapy, COMPASS’s ability to continue to advance its research, including COMP360, COMPASS’s expectations regarding the benefits of its psilocybin therapy, including COMP360 and COMPASS’s ability to advance new psychedelic compounds in other areas of unmet mental health need. 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: preclinical research and clinical development is lengthy and uncertain, and therefore our preclinical studies and clinical trials may be delayed or terminated, or may never advance to or in the clinic; and those risks and uncertainties described under the heading “Risk Factors” in COMPASS’s annual report on Form 20-F filed with the US Securities and Exchange Commission (SEC) on 9 March 2021 and in subsequent filings made by COMPASS with the 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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[1]MADRS = Montgomery-Åsberg Depression Rating Scale; response = ≥50% decrease in MADRS total score from baseline; remission = MADRS total score ≤10

[2] 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 21 October 2021]

[3] WHO (2012). Depression: A Global Crisis [Online]. Available at: https://www.who.int/mental_health/management/depression/wfmh_paper_depression_wmhd_2012.pdf [Accessed 21 October 2021]

[4] Al-Harbi KS. Treatment-resistant depression: therapeutic trends, challenges, and future directions. Patient Preference and Adherence. 2012; 6: 369–388.

[5] Bergfeld IO, Mantione M, Figee M, Schuurman PR, Lok A, Denys D. Treatment-resistant depression and suicidality. Journal of Affective Disorders. 2018;235:362-367

[6] Dong M, Lu L, Zhang L, et al. Prevalence of suicide attempts in bipolar disorder: a systematic review and meta-analysis of observational studies. Epidemiology and Psychiatric Sciences. 2020;29:e63

[7] Gang L, Fife D, Wong G, Sheehan JJ, et al. All-cause mortality in patients with treatment-resistant depression: a cohort study in the US population. Annuals of General Psychiatry. 2019; 18:23.