NEWS RELEASE

COMPASS Pathways presents largest ever study of psilocybin therapy, at American Psychiatric Association annual meeting

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Positive data from phase IIb study shows potential of COMP360 psilocybin therapy in treatment-resistant depression

London, UK – 23 May 2022

COMPASS Pathways plc (Nasdaq: CMPS) ("COMPASS"), a mental health care company dedicated to accelerating patient access to evidence-based innovation in mental health, today presented positive data from the largest randomised, controlled, double-blind study of psilocybin therapy ever completed, at the American Psychiatric Association annual meeting in New Orleans*. The study showed that a single 25mg dose of COMP360 psilocybin, in combination with psychological support, was associated with a highly statistically significant reduction in depressive symptoms after three weeks ($p<0.001$), with a rapid and durable response for up to 12 weeks.

The randomised, controlled, double-blind phase IIb clinical trial was designed to understand the efficacy and safety of a single dose of investigational COMP360 psilocybin (25mg or 10mg), compared to 1mg in patients with treatment-resistant depression (TRD). 233 patients with TRD received either 1mg, 10mg or 25mg COMP360 psilocybin, in conjunction with psychological support from specially trained therapists. Symptoms of depression were assessed using the Montgomery-Åsberg depression rating scale (MADRS)**, a widely used and accepted scale for assessing depression; the MADRS assessments were made by an independent, blinded rater.

Key results:

- Depression symptoms: patients who received a 25mg dose of COMP360 psilocybin with psychological support experienced a highly statistically significant reduction in symptoms of depression after three weeks: the difference between 25mg group and 1mg group was -6.6 on the MADRS* depression scale at week 3, $p<0.001$.
- Durability: double the number of patients who received 25mg 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).
- Tolerability: COMP360 psilocybin was generally well-tolerated. On the day of COMP360 administration, headache, nausea, and dizziness were the only adverse events where a dose-related increase in incidence was evident and there were no clinically significant differences between dose group in vital signs or clinical laboratory tests observed during the study.
- Adverse events: In this study suicidal ideation and intentional self-injury were seen in all treatment groups (as is regularly observed in a TRD population), and the majority occurred more than a week after the psilocybin session. There was no mean worsening of suicidal ideation scores in any treatment group. Suicidal behaviours were reported at least 1 month after COMP360 administration for 3 non-responders in the 25mg arm.

David J Hellerstein MD, a Principal Investigator on the trial and Professor of Clinical Psychiatry at the Columbia University Irving Medical Center, said: “Treatment-resistant depression is one of the biggest challenges we face in psychiatry, and chances of success decreases with each treatment that a patient tries. It’s rare to see such positive outcomes of clinical trials in this disease area, which is why these results are so significant. I hope this represents a major step in finding new options for people living with treatment-resistant depression.”

Dr Guy Goodwin, Chief Medical Officer, COMPASS Pathways, said, “Our mission is all about developing mental health innovations through scientific evidence, which is why we’re so honoured to present the largest study of its kind at the APA. In this study, a significant number of patients experienced improvement in their symptoms of depression after just a single dose of 25mg psilocybin with psychological support, with effects lasting for up to three months of the study. We now need to continue our research to understand if this can be replicated in even larger trials.”

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*The safety and efficacy of COMP360 psilocybin therapy in treatment-resistant depression: Results from a phase IIb randomized controlled trial. Guy M. Goodwin, Susan C. Stansfield, David J. Hellerstein, Allan H. Young, Ekaterina Malievskaia. APA: Abstract Number: 5301 Session Title: Poster Session 6

**MADRS = Montgomery-Åsberg Depression Rating Scale; 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 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 the COMP360 psilocybin therapy phase IIb study

This randomised, controlled, multicentre, double-blind phase IIb 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 III 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.

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 business strategy and goals, including its ability to launch and commercialise products, COMPASS’s ability to continue to advance its research or develop plans to bring its product candidates to patients, including COMP360, and COMPASS’s expectations regarding the benefits of its 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: 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 10-K filed with the US Securities and Exchange Commission (SEC) on 24 February 2022 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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Video accompanying this announcement is available at:
https://www.youtube.com/embed/k4EerZeZJHM