Psilocybin administration to healthy participants: safety and feasibility in a placebo-controlled study

James Rucker,1 Allan Young,1 Catherine Bird,1 Aster Daniel,2 Molly Lennard-Jones,1 Lindsey Marwood,2 Kristina Grace Posadas,2 Frederick Reinholdt,1 Francesco Saldarini,3 Susan Stansfield,1 Sam Williams,1 Neil Weston,1 Hans Eriksson,1 Ekaterina Malievskaia3
1South London and Maudsley NHS Foundation Trust and Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, UK; 2Clinical Research Facility, King’s College Hospital, London, UK; 3COMPASS Pathways Ltd, London, UK

Background
Treatment-resistant depression remains a significant current medical need. From a population health perspective, a recent meta-analysis with 1101 studies and 100,000 participants showed that the evidence for treatment-resistant depression is poor, with remission rates of less than 15%. A major challenge is the development of new therapeutics; drugs that can be prescribed on a generic basis are immaterial unless they are effective. Psilocybin (Psilocybe semilanceata, or magic mushroom), a mushroom that contains a class of indolealkylamines that are classified as hallucinogens (psilocybin, psilocin, and other derivatives such as 10-methoxymethylecgonine), has re-emerged as a potential treatment for depression, anxiety, and other psychological conditions.

Methods
Study design
A phase 1, open-label, double-blind, placebo-controlled study to evaluate the efficacy of 25mg and 10mg psilocybin (pilot studies) compared with placebo in healthy participants, conducted at the Clinical Research Facility, King’s College Hospital, London, UK.

Participants
Participants were aged 18–65 years, healthy, and without any psychiatric diagnosis or recent (within 1 year) psychiatric medication. The study was approved by an independent ethics committee (LREC 08/H0102/010). Participants were self-selected from a database of volunteers, with the aim of recruiting 50 participants. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study was registered with ClinicalTrials.gov (NCT01762281).

Results
Participant disposition and demographics
Figure 1 presents participant disposition.

Adverse events
511 AEs were reported throughout the 12-week duration of the study. 25% of all AEs were reported in the 25mg psilocybin group. AEs were categorized by treatment arm: 208 (95.9%) in the 25mg psilocybin arm, 188 (92.6%) in the 10mg psilocybin arm, and 87 (45.8%) in the placebo arm (reported by 89.7% of participants).

Table 1. Adverse events by treatment and severity

Conclusions
Psilocybin (Psilocybin COMP360) was well tolerated in healthy participants and results support further investigation of simultaneous 1:1 therapeutic administration.