- 1. The <u>CNBC news story</u> "Peter Thiel-backed psychedelic start-up's shares pop in Wall Street debut" describes the huge investor interest in a start-up company based on psychedelic pharmaceuticals (note that Peter Thiel's father is a CWRU alum, with his degree in chemical engineering). The webpage also includes a video interview with the founder of the start-up company. Please read the article and watch the video, and then answer the following questions.
- (A) What types of illnesses is the company aiming to treat, and what recent discoveries regarding psychedelic compounds have caused investor interest in psychedelic therapies to grow? Treating mental health issues (e.g. anxiety, depression, PTSD, brain injuries, schizophrenia) is the company's main goal. Recent studies of MDMA reveal its efficacy in treating post-traumatic stress disorder, and psilocybin has recently been seen treating drug-resistant depression. Johns Hopkins University, Yale University, the University of California, Berkeley, and the Icahn School of Medicine have all contributed to these studies, further legitimizing the field and heightening interest among investors.
- (B) What is the major regulatory/legal hurdle that must be overcome before the treatment can be used?

They are currently illegal in the West. They are aiming to bring them back into the MEDICAL world, so during therapy or during hospital visits. To make them legal for these applications, they must battle the Schedule 1 drug classification (no accepted medical use and a high potential for abuse) of psychedelics in the United States, undergo rigorous clinical trials, and get approval from the FDA.

- 2. This journal article presents a research study on the medical use of psychedelic pharmaceuticals. Please read the first page of this article, and answer the following questions.
- (A) Where was the study carried out and what year was the paper published? The study was carried out at the Center for Psychedelic and Consciousness Research in the Department of Psychiatry and Behavioral Sciences at the John Hopkins University School of Medicine. It was published in the Journal of Psychopharmacology in 2022.
- (B) What was the disease being addressed, and what was the treatment that was being studied (was it just administering a drug, or was there more to it?)

 They were treating Major Depressive Disorder (MDD). The treatment was having patients assigned to a treatment condition where they received two doses of psilocybin with supportive psychotherapy. This study took place over a 12 month period.
- (C) What was the key finding from this study?

They found that there were no serious adverse events related to psilocybin in the long-term follow-up period. Participants reported increased ratings of personal meaning, spiritual experience, and mystical experience but did not predict improvements in depression. The study's findings "demonstrate that the substantial antidepressant effects of psilocybin-assisted therapy may be durable at least through 12 months following acute intervention in some patients."

(D) The first paragraph of pg 157 addresses a potential issue with the medical use of psychedelic pharmaceuticals. What is this issue, what did this paper find in regard to this issue and how did this finding relate to previous findings in regard to this issue?

The issue they brought up is patients' desire to use psilocybin outside of the research setting. They seem to be concerned about opening this door up to people, who may then seek out the drug in a less than legal setting. This paper's study found that none of their participants reported any psilocybin or psychedelic drug use during the follow-up period. This contrasts a previous study in which 5 of 19 total participants reported the use of psilocybin outside of the research setting by the end of that study's 6-month follow-up period.

(E) Read the declaration of conflicting interests on pg 157. One of the authors of the article may be working in an ethical "gray area". Which author is this, why is this author in an ethical gray area, and how might this affect how one should trust the findings of this article?

Matthew W Johnson (MWJ) has multiple financial and advisory relationships with companies involved in psychedelic drug development. This results in an ethical gray area, as the author is driven by these companies to produce positive results, but should be performing this study from a neutral, unbiased, and scientific point of view. MWJ's financial relationships are benefited by positive conclusions, so readers should be very critical of the data presented and the methods

used. While disclosures like this increase transparency, they do not eliminate bias, so conclusions and findings should be viewed with caution.

- 3. This patent covers some of the intellectual property pertaining to the current interest in psychedelic pharmaceuticals. Please read the Abstract and Column 1 (first column of text after the figures), and answer the following questions.
- (A) A patent must be for one of the following: a process, machine, manufacture, or composition of matter. Which category of invention is this patent, and how do you know this? This patent seems to be most directed towards composition of matter, but an argument for manufacturing can be made as well. In terms of composition of matter, the 'Background' section clearly emphasizes the synthesis of the drug, discussing how this new process is efficient for batch productions of psilocybin and its intermediates. Due to the discussion of chemical compounds and synthesis techniques/analysis, this patent falls most aptly under composition of matter. One might argue for manufacture, as this parent relates to large-scale production of psilocybin, but this production requires an altered synthesis process, and hence composition of matter seems most fitting.
- (B) Who owns the patent, and how do you know this? As discussed in lecture, the Assignee is the one who owns the patent. While there are multiple investors, the assignee is the ultimate owner. In this case, it is listed as COMPASS Pathways Limited, London (GB).

- 4. This article is a first-hand account of how psychedelic mushrooms were first "discovered" by westerners. Please read this article, and answer the following questions.
- (A) The author says he made a "cultural discovery of importance" what was this discovery? The author's significant cultural discovery was the ritual use of hallucinogenic mushrooms by the indigenous people of Huautla, Mexico. He was the first outsider to partake in the ceremony led by the indigenous priestess María Sabina.
- (B) Who was Maria, and what was her role in regard to this "cultural discovery"? María Sabina was a "priestess of the rite" who guided the author through the sacred mushroom ritual. She was the key figure who introduced him to the traditional use of psilocybin mushrooms for spiritual and healing purposes.
- (C) The author questions whether he should have suppressed his discovery. Does the author follow a consequentialist, deontological or a virtue ethics approach (and why)? The author takes a consequentialist approach to his discovery. This is because he reflects on the unintended negative effects of his revelation (commercial exploitation). He expresses regret, indicating that he evaluates his actions based on their outcomes rather than adhering to an absolute moral rule (deontology) or focusing on personal virtue. He believes his actions should be judged by their long-term impact, which aligns with consequentialist reasoning.

- 5. This <u>article</u> is a first-hand account of the scientific discovery of the active component in psychedelic mushrooms. Please read the section "Teonanácatl, the 'sacred mushroom' of the Aztecs" in the article "Teonanácatl and Ololiuqui, two ancient magic drugs of Mexico.", and then answer the following questions.
- (A) Psilocybin is the active chemical in the mushrooms—how does this article say that the chemical was discovered, and by whom?

Use of Psilocybin is dated back to the Indians of Mexico, who consumed the mushrooms and hence Psilocybin for feasts, religious ceremonies, social events, and through witchdoctors. Mycologist Roger Heim is reported to have first identified and classified these mushrooms as part of the genus Psilocybe. Psilocybin was discovered chemically by Albert Hoffman (the author) through chemical analysis of the mushroom material in the Pharmaceutical Chemical Research Laboratories of Sandoz Ltd. in Basle.

(B) Who was used for the first human testing of the extracted psilocybin, and what was this person's relationship to the scientist who first extracted psilocybin?

The first human test was the author of this article, Albert Hoffman. He took thirty-two dried specimens of Psilocybe mexicana weighing 2.4 g to settle whether or not the mushrooms were still psychoactive after testing and extraction. So, the first test was performed by the author who is the one who first extracted the chemical.

(C) Upload a picture of the chemical structure of psilocybin

Psilocybin
= 4-phosphoryloxy-N,N-dimethyltryptamine

(D) Psilocybin can be obtained by extraction from mushrooms, but also by another method which is "much more rational than obtaining it from the mushrooms". What is this other method?

Synthesis. Being a chemical, the synthesis of psilocybin is most likely doable. Hoffman studied synthesis techniques for producing synthetic psilocybin, leading to him reporting that "the synthetic production of psilocybin is much more rational than obtaining it from the mushrooms".

6. This journal article addresses the ethics of patents covering psilocybin-based pharmaceuticals. Please read this article and answer the following questions.

(A) What is the ethical concern brought up by the authors?

The ethical concern raised by the authors is that the commercialization and patenting of psilocybin-based treatments have occurred without recognition of the indigenous Mazatec communities who have traditionally used these mushrooms for centuries. Furthermore, the financial benefits from introducing these methods into the medical sphere will not be shared with the 'founding' communities.

- (B) The authors discuss Psilocybe semilanceata, which is native to Europe. Why do the authors feel that the situation with Psilocybe semilanceata strengthens their argument? They believe that this example strengthens the argument because there was no reported evidence of people being interested in the medical properties of these mushrooms, while the Mazatec were interested primarily in medicinal use. This supports their argument that the Mazatec played a fundamental role in bringing psilocybin to medicinal attention and deserve recognition and compensation.
- (C) Do the authors appear to follow a consequentialist, deontological or a virtue ethics approach as they consider this question, and what is your reasoning for this answer? The authors appear to follow a deontological approach, as their argument is centered on the inherent rights of the Mazatec people rather than the consequences of psilocybin commercialization. They emphasize the indigenous people's right to protect, preserve, and develop their traditional medical practices. This contrasts a consequentialist approach which would praise such developments as the ultimate benefit would be for society. They also are more in line with rights and obligations than virtues or moral character, so they wouldn't necessarily follow a virtue ethics approach either.

(D) Describe your view on this ethical concern.

My view aligns with the author's perspective. Time and time again, influential and overpowering forces have taken advantage of indigenous peoples without giving them any recognition or fair compensation. While medical advancements in psilocybin research could bring significant benefits to mental health treatment (as discussed in previous questions), this progress should not come at the expense of the indigenous communities. It is for this reason that I also take a deontological approach, as these indigenous peoples have a right to the knowledge that they have curated across generations. If we are to commercialize such treatments in the medical sphere, then it should involve careful ethical consideration including collaboration, fair compensation, and acknowledgement.