Psychedelics

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INNOVATORS & IDEAS: RESEARCH LEADER

Stephen Ross: Psychedelic-assisted therapies for difficult-to-treat psychiatric and medical disorders

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Professor Stephen Ross is a prominent faculty member in the Departments of Psychiatry and Child and Adolescent Psychiatry at the New York University (NYU) Grossman School of Medicine who has transformed the landscape of psychedelic research since 2006. In this Genomic Press Interview, Dr. Ross reveals how as co-director of the NYU Langone Center for Psychedelic Medicine and director of its research training program, he has spearheaded groundbreaking clinical trials demonstrating the remarkable efficacy of psilocybin-assisted psychotherapy for treating existential distress in advanced cancer patients, alcohol use disorder, and major depressive disorder. His 2016 landmark study showing rapid, substantial, and enduring improvements in cancer-related anxiety and depression following single-dose psilocybin treatment garnered global attention with 1.7 billion media views. It rejuvenated a dormant field of psychiatric research. Despite early career warnings that psychedelic research was "a road to nowhere," Dr. Ross persevered to secure the first National Cancer Institute grant for psychedelic research in over 50 years, establishing NYU as a pioneering institution in psychedelic medicine. Throughout his 25-year career at NYU, he has balanced research innovation with clinical leadership, directing Bellevue Hospital's substance abuse division for 12 years, receiving numerous teaching awards, and maintaining a compassion-driven approach inspired by early experiences with hospice care. His current research extends beyond psychiatry into pain management, early-stage cancer interventions, and the potential anti-inflammatory properties of psychedelics, reflecting his commitment to developing novel therapeutics for conditions with substantial unmet needs and public health burden.

Part 1: Stephen Ross - Life and Career

the pivotal moments that first kindled your passion for science?

I was born in South Africa and moved to Los Angeles with my family when I was 7. Inspired by my parents and a black African woman who took care of me in South Africa, as far back as I can remember, I wanted to pursue a career in medicine to help others. On a track to be a cardiothoracic surgeon, the experiences of family members of mine motivated me to pursue a clinical and research career in psychiatry and addiction medicine. As a teenager, I spent several summers accompanying my mom, a hospice volunteer worker. This had a profound impact on me and taught me the importance of helping people die with psychological, emotional, and spiri-

Could you give us a glimpse into your personal history, emphasizing

clinical research in end-of-life care.

I went into medicine to help people. Early in my career, that would entail helping one person at a time in my psychiatric practice. Inspired by mentors at Bellevue Hospital, my focus evolved. I developed a desire to

tual well-being. This experience inspired me later in my career to pursue

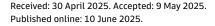


Figure 1. Stephen Ross, MD, New York University School of Medicine, USA.

pursue clinical leadership that allowed me to help groups of people at a time. This culminated in me directing the substance abuse division at Bellevue Hospital for 12 years, overseeing a range of inpatient and outpatient programs that cared for thousands of patients annually. This experience galvanized my passion to pursue clinical research as a tool to help people on a larger scale by developing novel therapeutics to treat neuropsychiatric disorders where there is a substantial unmet need and public health burden.

Please share with us what initially piqued your interest in your favorite research or professional focus area.

My interest in psychedelic clinical research began serendipitously one day in 2006 when my supervisor at the time, Dr Jeffrey Guss, walked into my office and asked me what I knew about the history of psychedelic research in psychiatry. I told him that I did not know what he was talking about and was unaware that psychedelics had ever been a significant part of psychiatry. Stimulated by our conversation, I was shocked to find out that, hidden in plain sight, psychedelics were extensively studied in psychiatry from the 1950s to the 1970s in the US and internationally with over 40,000 participants and over 1,000 articles published. Nowhere in my training, from medical school to general psychiatry residency to addiction fellowship training, did I ever hear about this exciting and significant part of psychiatric history. My interest was further piqued when I found out that the most promising therapeutic targets of psychedelic-assisted therapies (mostly with LSD) were alcohol use disorder as well as depression, anxiety, and existential distress in advanced cancer-since these were areas of interest to me. I came to understand that the promise of psychedelic therapy ended when the drugs escaped from the lab in the 1960s, were used extensively by the general public in unsafe settings, leading to serious adverse outcomes, and ultimately leading to this class of drugs becoming







illegal with the passage of the Controlled Substances Act of 1970. This prohibition effectively ended the promise of the first wave of psychedelic research so extensively that it was absent from all of my education and training. Soon after, Jeffrey Guss, MD, Anthony Bossis, PhD, and I formed the NYU Psychedelic Research Group in 2006 with the goal of starting a program of clinical research at NYU exploring the therapeutic potential of psychedelic-assisted psychotherapies. Our group was one of the first psychedelic research programs that helped spark the second wave of psychedelic research over the last 25 years.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

In 2021, along with my colleague Dr Michael Bogenschutz, we established the NYU Langone Center for Psychedelic Medicine, one of the first centers of psychedelic research to be established in the US, after receiving a \$10M philanthropic gift. I am co-director of CPM and director of the center's research training program. The mission of CPM is to develop novel psychedelic therapies for some of the most difficult-to-treat conditions in psychiatry and medicine. Although psychedelic research to date has been concentrated within the field of psychiatry, the CPM seeks to expand this focus through the pursuit of promising clinical applications across health-related disciplines in medicine. As an example, we are actively researching psychedelics as a treatment for various pain and inflammatory conditions. Our pre-clinical branch investigates mechanisms by which psychedelics impact physical and mental health, and we have developed a training program for research scientists interested in careers in psychedelic medicine.

After forming the NYU Psychedelic Research Group in 2006 with several colleagues, we embarked on a pilot randomized controlled trial (RCT) assessing the safety and efficacy of single-dose psilocybin-assisted psychotherapy (PAP) to treat anxiety, depression, and existential distress associated with advanced cancer. We published our findings in 2016 and found that PAP produced rapid, substantial, and sustained (e.g., 6.5 months) improvements in anxiety and depressive symptoms associated with cancer. We also found that the intervention reduced existential distress and improved quality of life. Approximately 75% of the participants rated the psilocybin experience as one of their life's most spiritual, meaningful, and memorable experiences. This publication was considered a landmark in the field of psychiatry and psychedelic medicine. It was covered extensively internationally, was one of the biggest news stories in medicine in 2016-2017, garnering approximately 1.7 billion views, and was featured on the front page of the New York Times on 1 December 2016. It has been cited approximately 2000 times since its publication and is credited as one of the key events re-opening the field of psychedelic clinical research. I was shocked at the results of this trial, not expecting such rapid and robust clinical responses. This had a profound impact on me, especially since I learned almost nothing about palliative care during my medical training, and it reminded me of my positive experiences as a teenager witnessing people dying with peace and well-being in a hospice in Los Angeles. The findings from this trial emboldened me to pursue clinical research further using psychedelic therapies to help people with advanced cancer and other serious medical illnesses experiencing clinically significant psychiatric and existential distress. Attempting to replicate the findings of our pilot trial, along with colleagues, in 2022, we were awarded an RO1 from the National Cancer Institute to conduct the largest clinical trial of psychedelics to treat advanced cancer-related emotional and spiritual distress to date. This was the first grant ever given by NCI, one of the first awarded by NIH in over 50 years for psychedelic clinical research, and signaled an openness of NIH to reconsider funding this novel area of therapeutics. If in the future, psilocybin or other psychedelics were approved and prescribable medications in people with serious medical illnesses, such as advanced cancer, to be used in the context of psychotherapeutic platforms, it could be a significant development that opens up a pathway for clinical dissemination and public health impact internationally. Examples of care delivery settings would likely include cancer centers, palliative care programs, and hospices.

Towards the end of our pilot RCT of PAP in advanced cancer, as an addiction psychiatrist, I decided to tack in the direction of researching PAP to treat substance use disorders. This was the most promising area of clinical research during the first wave of psychedelic research, with data from 5 RCTs suggesting the efficacy of single-dose LSD-assisted therapy to treat alcohol use disorder (AUD). Teaming up with my colleague Dr Michael Bogenschutz, who was recruited to NYU in 2015, we conducted the first RCT assessing the efficacy of a two-dose psilocybin administration regimen, combined with psychotherapy, to treat AUD. Of all substance use disorders, AUD arguably represents the greatest public health threat in the US and globally when factoring in prevalence, preventable death, premature death, disability, healthcare/societal costs, adverse medical and neuropsychiatric complications, unintentional injuries, and its significant causal link to suicidal and violent behaviors. Current treatment approaches are limited in effectiveness. In 2022, we published our findings in JAMA Psychiatry that PAP produced rapid, robust, and sustained (e.g., 8 months) decreases in the percentage of heavy drinking days. This publication was covered internationally in the media and recognized as the pivotal psychedelic medicine breakthrough in 2022. Psychedelic therapies for substance use disorders are one of the most promising areas of clinical research with psychedelics. If larger trials continue to demonstrate safety and efficacy, it potentially opens up a pathway for clinical dissemination, including inpatient and outpatient SUD treatment programs.

Our pilot RCT of PAP in advanced cancer-related anxiety and depression was the first RCT to demonstrate that psilocybin produced rapidly acting and sustained (e.g., weeks to months) anti-depressant effects from single-dose administration. This led several biotech companies to invest in developing psilocybin therapy as a treatment for major depressive disorder (MDD), with two companies having received breakthrough status from the US FDA for this approach. I was a senior author on a phase 2, multi-center trial published in JAMA in 2023 that demonstrated that single-dose PAP in MDD is safe and produces rapid, clinically significant, and sustained (up to 6 weeks) reductions in depressive symptoms and functional disability. Several biotech companies are finishing up phase 3 trials of psilocybin therapy for MDD, with converging data suggesting safety and efficacy. This is the leading edge of psilocybin drug development and potentially opens up a pathway for psilocybin to become an FDA-approved and prescribable treatment for MDD within a few years. This could represent a paradigmatic shift and breakthrough in the therapeutics of MDD, arguably the most disabling brain-based illness in the world.

What is a decision or choice that seemed like a mistake at the time but ended up being valuable or transformative for your career or life?

My decision to pursue a research career in psychedelic medicine seemed like a big mistake in 2006 when I first started. Several of my research mentors told me that it was a terrible idea due to the intense societal and governmental stigma associated with the long shadow of the prohibition against psychedelics after the first wave of psychedelic research was shut down in the early 1970s. I was told that it was a road to nowhere, a career killer, and an area that would never again attract federal funding. Intrigued by the areas of psychedelic clinical research that appeared promising, such as addiction and end-of-life care, and perhaps being young and naïve in my career, I decided to keep putting one foot in front of the other and kept going. It was very challenging at first, but I slowly and meticulously worked through all of the roadblocks and barriers. Our first study with PAP in advanced cancer took a decade to complete, but the experience completely transformed my career and set me on a path to continue to focus on psychedelics as novel therapies for some of the most intractable conditions in psychiatry and medicine.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?

Habits: obsessive focus on achieving a goal; diligence; resilience-learning from and finding opportunities in the face of setbacks or failure; going deep into a topic.



Values: Finding meaning and purpose in helping others; working collaboratively with others and the power of group dynamics in fostering scientific creativity and innovation; the vital importance of ethical treatment of research participants.

Please tell us more about your current scholarly focal points within your chosen field of science.

Within my field of psychedelic psychiatry and medicine, I have several main areas of scholarly interest focusing on the treatment of difficult-totreat disorders in psychiatry and medicine including: psychiatric and existential distress in advanced cancer and other serious medical illnesses; mood disorders such as MDD; substance use disorders, personality disorders, PTSD, and chronic pain. I am particularly active in the area of psychedelic therapeutics for cancer and other serious medical illnesses. I am more than halfway through my current NCI RO1 assessing the safety and efficacy of PAP to treat anxiety, depression, and existential distress in advanced cancer. Tacking from studying psychedelics in advanced cancer towards earlier staged cancers with substantial psychiatric morbidity, I am hoping shortly to begin a pilot RCT of PAP, funded by NCI, to treat clinically significant fear of recurrence in women with early-stage breast cancer. I am also the site PI of a biotech-funded multi-center clinical trial assessing the safety and efficacy of a short-acting novel psychedelic to treat adjustment disorder in cancer and other serious medical illnesses, which represents an extension of work I have done with PAP in cancer. I am also expanding my research focus on psychedelics to target chronic pain. I have developed a concept that I have submitted to NIH, picking up from work conducted in the 1960s, of an RCT of LSD-assisted therapy to treat metastatic cancer-induced bone pain. I am also focused on research with psychedelic therapies for MDD, being part of a phase 3 multicenter RCT (site PI) of psilocybin therapy for MDD, as well as a phase 2 multi-center RCT (site PI) of a short-acting novel psychedelic to treat post-partum MDD. I plan to continue my focus on psychedelic therapeutics for substance use disorders soon.

Apart from my clinical research with psychedelics as therapies for psychiatric and medical conditions, I was Principal Investigator (PI) of a study administering psilocybin to healthy volunteers, namely religious professionals. This RCT was conducted in conjunction with colleagues at Johns Hopkins. It was a follow-up to the famous Good Friday Experiment, conducted in 1962 by Walter Pahnke, that suggested that single-dose psilocybin administration to divinity students in a group setting, as compared to active placebo, produced mystical experiences and was associated with increased positive changes in attitudes and behavior at 6-month and 25-year follow-up. The study, published in May 2025 (DOI: 10.1089/ psymed.2023.0044), found that in population of psychedelic-naïve clergy from various major world religions, psilocybin administration was safe and increased multiple domains of overall psychological well-being including positive changes in religious attitudes, including increased tolerance of other religions, and behavior as well as their vocation as a religious leader.

What impact do you hope to achieve in your field by focusing on specific research topics?

My goal is to continue to conduct rigorous clinical trial research with psychedelics to determine if they are safe and efficacious. My focus has been on research PAP as a novel treatment for three areas within psychiatry and medicine where there is a substantial unmet need and public health burden: major depressive disorder, existential distress in advanced cancer and other serious medical illnesses, and alcohol addiction. I approach these efforts with equipoise and neutrality, not knowing the outcome. Suppose the research continues to demonstrate safety and efficacy. In that case, I hope there is a process, in particular drug development with the FDA, that puts the interventions on track to be translated into clinical care to impact the lives of as many people as possible positively.

What do you most enjoy in your capacity as an academic or research leader?

I love the opportunity to delve deeply into a topic with the ultimate goal of helping as many people as possible. I also greatly enjoy the opportunity to

mentor junior scientists and see them grow and flourish in their research careers, with the ultimate goal of translating their passion for science into alleviating suffering.

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that you feel strongly devoted to?

Within my field of psychedelic medicine, both historically and currently, the response of the press, general culture, and even the scientific community has tended towards hyperbolic responses, ranging from unbridled enthusiasm that psychedelics are a cure all for all ailments to beliefs that they are so harmful and dangerous that they need to be prohibited. I hope that through rigorous, unbiased, and meticulous scientific study, the truth about psychedelic therapies emerges so that we can develop a rationale and clear-eyed view of their therapeutic potential and risks.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?

In my leisure time, I love spending time with my wife and our two beautiful Boston Terriers. My favorite hobbies are travel, hiking, eating, and sailing.

Part 2: Stephen Ross – Selected questions from the Proust Questionnaire¹

What is your most marked characteristic? Compassion towards others.

Among your talents, which one(s) give(s) you a competitive edge?

I am doggedly determined to achieve my objectives, never give up, and have always been able to be resilient, find opportunities, and grow in the face of adversity and failure.

If you could change one thing about yourself, what would it be? I would like to be less anxious and fearful.

What is your current state of mind?

I feel a sense of stability and happiness that I have not experienced since childhood. I credit this to my amazing wife and our beautiful dogs, as well as being blessed by having two loving parents, a wonderful brother, and an extended network of supportive family members, friends, and work colleagues.

What is your idea of perfect happiness?

Snuggling in bed with my wife and our two dogs.

¹In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust's handwritten answers were auctioned off for \$130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.





Figure 2. Dr. Stephen Ross sailing on the Hudson River with his two Boston Terriers, one of his favorite leisure activities. In the background is the Hudson River Park's pier 40, with its 'I want to thank you' mural by Stephen Powers, an internationally recognized contemporary artist, Fulbright scholar and local resident.

When and where were you happiest? And why were so happy then?

I am most happy currently. See 'what is your current state of mind' question.

What is your greatest fear?

Despite dedicating myself to helping people with serious medical illnesses who have a fear of dying, I am very fearful of sickness and death.

What is your greatest regret?

When I was younger, I was a star athlete in soccer and baseball. In my midteens, I decided that I needed to focus all of my efforts on academics and felt that there was no room for anything else, and so I stopped all of my organized sports activities that I loved. I regret this decision and wish I could have balanced academics and sports at the time.

What are you most proud of?

I am most proud of the clinical care I have provided to my patients, some of whom I have treated for approximately a quarter century.

What do you consider your greatest achievement?

My greatest achievement is reducing the suffering of others through my work as a physician and researcher.

What or who is your greatest passion?

I love sailing (see Fig. 2). It reminds me a lot of research filled with endless complexities, depth, and opportunities to learn and grow. I love the euphoria and calm I get after sailing for several hours on a beautiful sunny day with great wind.

What is your favorite occupation (or activity)?

I love being a clinical psychiatrist and find the work meaningful, rewarding, humbling, and sacred.

What is your greatest extravagance?

I am a foodie and love eating amazing food, abundant in New York City, with my wife.

What is your most treasured possession?

My sailboat.

Where would you most like to live?

Besides New York City, where I have lived for the past 30 years, I would most like to live in Hawaii or Italy.

What is the quality you most admire in people?

The quality I most admire in people is kindness.

What is the trait you most dislike in people?

The trait I most dislike in people is a mix of hatred and cruelty.

What do you most value in your friends?

What I most value in my friends is the long-term bonds of mutual care and respect that we have formed, some of which I have known all of my life.

Which living person do you most admire?

My wife, Adriane Giebel, is the kindest, sweetest, most beautiful, intelligent, and loving person I know.

Who are your heroes in real life?

My parents are my heroes. I feel so lucky to have two of the most loving, supportive, and kind parents a child could ever ask for. They instilled in me the values of hard work, resilience, compassion, and service to others. My parents have been together for close to 60 years, and their love and bond have been a source of inspiration to me my entire life.

If you could have dinner with any historical figure, who would it be and why?

I love Carl Sagan because he has a special talent for explaining the complexities of astrophysics in a way that is understandable to those of us who are not astrophysicists.

Who are your favorite writers?

Sigmund Freud, Carl Jung, and Victor Frankl.

What aphorism or motto best encapsulates your life philosophy?

"Our greatest glory is not in never falling, but in rising every time we fall." — Confucius

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> > Stephen Ross¹ D



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