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Is Psychedelic–Mediated Therapy a Possibility or Just a Dream? Turning Clinical Success Into Real–World Practice

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The development of psychedelic drugs to be used in conjunction with traditional therapies is gaining more media coverage and momentum by the day. Clinical trials, permissive legislation, and scientific research are converging to legitimize these once-stigmatized substances, prompting companies to address this new and rapidly growing body of research. Investors, too, are paying close attention, looking to back innovators whose therapies can make the leap from clinical trial success to something clinicians can work with in the real world. This article explores some of the emerging regulatory, legal, and practical challenges companies are facing.

Psychedelic Pharmacotherapy, Traditional Psychotherapy, and Digital Therapeutics

Currently, ketamine is the only legally available psychedelic medicine for certain forms of treatment-resistant depression, such as post-traumatic stress disorder (PTSD); however, alternative therapies could be in the offing. For example, in May 2021, the Multidisciplinary Association for Psychedelic Studies (MAPS) published a Phase 3 clinical trial with methylenedioxymethamphetamine (MDMA)-mediated therapy for the treatment of PTSD. The clinical trial results found that 63% of patients who completed the trial no longer qualified for a clinical diagnosis of PTSD.

MDMA is a designated Schedule I drug under the Controlled Substances Act;[1] nonetheless, MDMA-mediated therapy for PTSD was granted breakthrough therapy designation by the U.S. Food and Drug Administration (FDA), which shortens the lengthy review process for regulatory approval.

For the moment, however, ketamine stands alone among the psychedelic medicines that are legally available, and because of this, companies are entering the field with products that would assist clinicians utilizing ketamine-mediated psychotherapy. These include medical software that supplements clinical care by preparing patients for a session, monitoring and guiding patients through the treatment, and—after the treatment sessions with the clinician (in the integration phase)—helping patients integrate their experiences derived from the ketamine administration. A typical course of treatment could involve a preparatory session with the therapist, followed by administration of the psychedelic, whereby the clinician would monitor the patient's responses and environment over the course of a few hours.

Following this administration, traditional therapy practices come into play to treat the underlying cause of depression where patients would participate in psychotherapy sessions to integrate their psychedelic experience. The integration sessions vary from person to person and could take place over the course of weeks or months since patients seek integration care for different reasons. The integration aspect of psychedelic-mediated therapy lends itself to tools developed to personalize a patient's journey toward wellness as well as guide clinicians on how best to guide and treat a patient's mental health condition.

One pathway for offering a psychedelic-mediated therapy tool is through a mental health digital platform. Such a platform would provide health professionals data on patients, psychedelic protocols, and procedures.

The Importance of FDA Certification for SaMD Platforms

Any robust Software as a Medical Device (SaMD) solution associated with psychedelic drug development must address an interconnected web of regulatory and legal issues that bear directly on the ability of innovations to reach the market and their subsequent valuations. FDA certification is among a handful that innovator companies—and their investors—need to keep top of mind.

Securing FDA authorization would likely be helpful in persuading patients in the robustness and legitimacy of psychedelic-mediated therapy, understanding that meeting regulatory standards will garner trust in utilizing this new tool. Certification potentially opens the door to products being prescribed by a health care practitioner and covered by insurance.

Naturally, the potential for insurance coverage enhances the commercial profile of SaMD products; however, it also comes with the inevitable requirement that insurance companies will require concrete, real-world, evidence-based data that this new form of therapy is efficacious. If consistent results with this new form of therapy are observed, there will be even more evidence to support the justification of insurance payment for psychedelic-mediated therapy.

The regulatory obstacles for entities seeking SaMD pre-certification can be daunting. The FDA's regulation of SaMD that incorporates technologies based on artificial intelligence (AI) and machine learning (ML) is currently under development. For example, the FDA proposes to introduce guidance detailing a "Predetermined Change Control Plan," which identifies the aspects of the software that are intended to change from the software learning process, and how the software will learn and change based on inputs. As the FDA is still developing its strategy, there is a great deal of ambiguity, such as anticipating modifications in a given software application.

The FDA's procedures for authorizing SaMD must ensure that devices deliver safe and effective software functionality that improves the quality of care that patients receive. SaMD that drive treatment decisions garner greater scrutiny by the FDA. Given the level of regulation and many gray areas, SaMD developers may consider releasing software products in two or more phases with an initial release that features "lower-risk" functionality, followed by a later release with information and data acquisition features geared more toward driving treatment decisions.

Developers need to be aware of potential issues with software that utilizes AI and ML-based technologies. As AI/ML-based systems are known to train on historical datasets, they are vulnerable to bias. In particular, critics in the psychedelic-mediated therapy field have echoed concerns of race, ethnicity, and socio-economic status limiting access to such therapies and how such patients are historically underrepresented. Developers in this space should consider a method for identifying and eliminating bias in their protocols being optimized by AI. Other challenges for developers include implementing Good Machine Learning Practice to describe a set of AI/ML best

practices (e.g., data management, feature extraction, training, interpretability, evaluation, and documentation) in this emerging industry.

Intellectual Property Rights & SaMD Platforms

One of the great benefits of SaMD platforms is the ability to collect, synthesize, and transform datasets into formatted and usable information that is capable of point-of-use customization. SaMD platforms that aggregate data need to carefully consider intellectual property law implications. First movers in SaMD development could gain a significant market advantage by securing and asserting IP rights; conversely, follow-on market participants would need to monitor the evolving IP landscape to ensure that product development does not infringe recently patented processes.

Determining whether medical protocols and therapeutic methods will be granted patent protection is a developing area and may prove to be an obstacle to overcome in the development of digital therapies; however, the introduction of these technologies also hold out the possibility of completely transforming patient care. After all, under current practice most of the data is lost when patients leave the therapy session. Methods for capturing and using that data are likely to optimize therapeutic outcomes, and with that possibility comes the promise of enormous market potential.

Data Privacy Challenges to Consider

Digital health developers will need to implement proper transfer protocols of data to ensure protection of Protected Health Information (PHI) and compliance with privacy laws such as the Health Insurance Portability and Accountability Act (HIPAA), General Data Protection Regulation (GDPR), and applicable state privacy laws. Ownership of any data being generated is also an important consideration. Many developers plan to seek consent for a patient's health data and anonymize all data before using it as part of a database. Each developer will need to consider whether their procedures provide for adequate compliance in light of the changing legal landscape regarding privacy under HIPAA, GDPR, and applicable state privacy law.

Vulnerability to enforcement actions by the Federal Trade Commission (FTC) also requires analysis. The FTC has authority to enforce a variety of sector-specific laws affecting consumers. The FTC can obtain civil monetary penalties for violations of certain privacy statutes and rules. Further, the FTC enforces the EU-U.S. Privacy Shield Framework, which provides a legal mechanism for companies to transfer personal data from the European Union to the United States. The Framework helps protect consumers' privacy and security through an agreed-upon set of Privacy Shield Principles, which can be enforced by the FTC. The FTC also serves as a privacy enforcement authority in the Asia-Pacific Economic Cooperation Cross-Border Privacy Rules (APEC CBPR) System. The APEC CBPR System is a voluntary, enforceable code of conduct designed to enhance the privacy and security of consumers' personal information transferred among the United States and other APEC members.

Conclusion

Bold, visionary treatment modalities are likely needed to push psychedelic medicine out of the research lab and into the marketplace. While somewhat murky and under development, the legal and regulatory framework for these drugs—as well as associated products and services—need not be merely a source of risk. There are also opportunities for market participants who understand how the regulatory system works. Regulation is not just a barrier to entry; it can also serve as a moat for companies that have the sophistication and wherewithal to work within the system.

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[1] Psychedelic compounds have psychoactive properties and are the subject of intense research and study, including clinical trials, for the treatment of a multitude of mental health conditions. Most psychedelics are in Schedule I of the Controlled Substances Act, which imposes significant restrictions on their use in research. Schedule I substances by definition are those that have "no currently accepted medical use in treatment in the United States," and "lack . . . accepted safety for use . . . under medical supervision."

