TINA strategia

Therapy Insights and Analytics
Navigate Healthcare with Strategic Vision

Navigating the Future: The Promises and Pitfalls of Emerging Drugs for Major Depressive Disorder

Executive insights
September 2025

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CONTEXT

Although the demand for antidepressants and antipsychotics for major depressive disorder (MDD) has increased with the rising diagnosed prevalence of MDD in the G7 markets, few innovative treatments (e.g., Spravato [an NMDA receptor modulator]) have entered clinical practice for MDD over the past decade. Driven by the rising prevalence and multiple areas of unmet need, MDD is one of the key psychiatric indications with a diverse and very active clinical pipeline. This Executive Insights report explores the rapidly evolving landscape of emerging drugs for MDD, from psychedelic-assisted therapies to other novel treatments. It critically examines the scientific promise of these treatments, the regulatory and ethical challenges they face, and the broader implications for mental health care in the 21st century.

INTRODUCTION

Major Depressive Disorder (MDD) remains one of the most pervasive and debilitating mental health conditions worldwide. In the United States alone, post-COVID-19 pandemic estimates suggest that more than 15% of adults have experienced depressive symptoms in the past year—a staggering rise from pre-COVID levels. Antidepressants' consumption analysis and findings from interviewed psychiatrists point to the increases in both the diagnosis and drug-treated MDD populations, driven by the increasing awareness of the condition. We advise drug marketers and developers to update their forecast models in MDD based on the latest epidemiology estimates for the condition.

Despite the availability of multiple therapies, a significant portion of MDD patients continue to suffer from residual symptoms and treatment-resistant depression (TRD), prompting an urgent need for novel therapies that are faster-acting, more effective, and better tolerated. Given the lucrative commercial opportunity (e.g., the blockbuster sales potential for Spravato and Auvelity), multiple psychedelic-based therapies are in early to mid-phases of development for TRD. In addition, several agents with novel mechanisms of action are targeting niche patient segments in MDD. In 2025, we conducted interviews with 15 key opinion leaders (KOLs) in the G7 for our 'Epi & Markets' offering related to MDD to understand the potential for emerging therapies. Here, we summarize the key findings regarding the potential advantages and drawbacks of the leading novel emerging therapies in MDD.

Novel Late-Phase Emerging Therapies in MDD

ET (class; phase; developer)	Target patients	Potential advantages	Target patients
COMP360 (Psychedelic; Phase 3; COMPASS Pathways)	• TRD • TRD patients with comorbid PTSD	• Once or twice a year dosing • Positive efficacy with a single dose in TRD • Rapid onset of action • First-in-class • Monotherapy • Enthusiasm among interviewed psychiatrists in the United States and Europe	• Modest efficacy in the single-dose Phase 3 study • Expected challenges in regulatory approvals • Stigma with psychedelic use and potential for abuse/misuse • Logistic burden for psychotherapy, training, and post-administration patient monitoring
Seltorexant (Orexin-2 receptor antagonist; Phase 3; J&J)	3L+MDD patients with comorbid insomnia	• Devoid of weight gain—the side- effect commonly observed with mirtazapine • Better efficacy and safety data versus quetiapine XR in Phase 2 • No signs of addiction/ withdrawal, unlike BZDs	• Combination therapy with another antidepressant; therefore, polypharmacy will not be reduced in MDD patients with comorbid insomnia • Likely DEA scheduling
Azetukalner (Kv7 potassium channels opener; Phase 3; Xenon Pharma)	3L+ MDD patients with residual anhedonia; MDD patients with comorbid focal onset or tonic-clonic epilepsy	• Monotherapy for MDD patients with unresolved anhedonia after early-line antidepressants • Low incidence of sexual dysfunction and weight gain	• Long-term safety concerns were expressed by some KOLs because of the agent's mechanism of action. • Modest efficacy improvements in Phase 2
Navacaprant (Kappa opioid receptor antagonist; Phase 3; Neumora Therapeutics)	3L+ MDD patients; residual anhedonia	Monotherapy for MDD patients with unresolved anhedonia after early-line antidepressants	Did not beat placebo in efficacy improvements in a Phase 3 study
Solriamfetol (Dopamine and norepinephrine reuptake inhibitor; Phase 3 planned; Axsome Therapeutics)	MDD with severe excessive daytime sleepiness	• Safety profile • Targets a niche population in MDD	• Mixed efficacy results in Phase 2 • Competition from generically available psychostimulants
Osavampator (AMPA potentiator; Phase 3; Neurocrine Biosciences)	3L+ MDD patients who are inadequate responders	• Robust antidepressant response in a Phase 2 study • The fixed-dose approach in Phase 3 might address the dose- ranging variability in efficacy outcomes	Combination therapy with another antidepressant; therefore, polypharmacy will not be reduced in MDD patients

Please note that the above table contains a partial list of emerging therapies in MDD with blockbuster peak-year sales potential. For the complete list, please refer to our 'Epi & Markets' report in MDD.

CONCLUSION

While Spravato has found commercial success in the U.S. market, its adoption has been gradual, and it currently holds a limited share of the treatment-resistant MDD patient population. In contrast, the newer NMDA receptor modulator, Auvelity, is anticipated to achieve blockbuster sales more rapidly, although it is likely to capture only a modest share of patients. These insights reveal that even capturing a small segment of MDD patients—those who do not respond well to traditional antidepressants and experience lingering symptoms—can still lead to significant commercial success for a new drug in this market. To enhance commercial viability, a new medication must address the limitations associated with Spravato, such as challenges related to administration and monitoring requirements, as well as the shortcomings of Auvelity, which did not demonstrate superiority over another antidepressant in clinical trials. Furthermore, successfully targeting the right patient segments is crucial, especially given the competitive landscape of established generics across various classes of antidepressants and the complexities associated with payer systems.

REFERENCES

1. Epi & Markets content: Disease Landscape, Market Sizing and Forecast (2024-2034) in MDD (publishing in October 2025)
2. EpiSage content: Detailed epidemiology Insights in MDD (2020-2040) (publishing in October 2025)

AUTHOR

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For more insights like these, please contact us for our following Market Assessment report offerings in MDD:

Epi & Markets:

This report provides a comprehensive analysis of the current and evolving disease landscape, including market sizing and forecasts for the G7 from 2024 to 2034. Supported by expert interviews, epidemiological data, and real-time drug pipeline intelligence, this report equips you with the strategic insights necessary to succeed in the MDD space.

Key Questions Answered:

- What's the size of the prevalent, diagnosed and treated populations?
- What percentage of MDD patients experience residual symptoms (e.g., anxiety, insomnia, anhedonia, excessive daytime sleepiness, pain) after early-line treatments?
- Which comorbidities in MDD patients are of clinical significance for psychiatrists?
- What is the current and forecasted market size? How will the key pipeline agents shape the future of this therapy market?
- What unmet needs and opportunities exist? What are the requirements for commercial success?
- What are the market access forces that will drive and influence treatment selection?
- What strategies should drug developers follow to minimize late-phase trial failures in MDD? What are the key learnings from Spravato's commercialization?

Salient features:

Epidemiology-based 10-year forecasts, segmented by drug class, drugs, and country

Customizable and user-friendly market forecast model

Patient funnels, clearly indicating target patient pools

Expert opinions from 15 in-depth interviews to enable decision-making

Utilize industry-leading data sources

Comprehensive market dynamics

EpiSage:

This report provides a comprehensive analysis of epidemiology for the G8+ markets from 2020 to 2040. Supported by peer-reviewed literature, data from patient registries, real-world insights, primary market research, and validated bottom-up methodology, this report equips you with the much-needed epidemiology insights in MDD to support portfolio, clinical trial, launch, and other critical planning decisions.

Key Questions Answered:

- How can we quickly gauge the potential addressable patients for my asset?
- Of all people with MDD, how many people in each country have been formally diagnosed and drug-treated?
- What are the various patient subsegments with high unmet needs?
- What is the in-depth view of MDD patients with breakout data on age, sex, race/ethnicity, etc.?
- How will the prevalent and other populations evolve in the future? What factors will affect the epidemiology over the forecast period?

Salient features:

Global, country, and region-level coverage

Customizable and user-friendly epidemiology forecast model

Patient funnels, clearly indicating target patient pools

Utilize relevant latest data sources

Interactive epidemiology dashboard

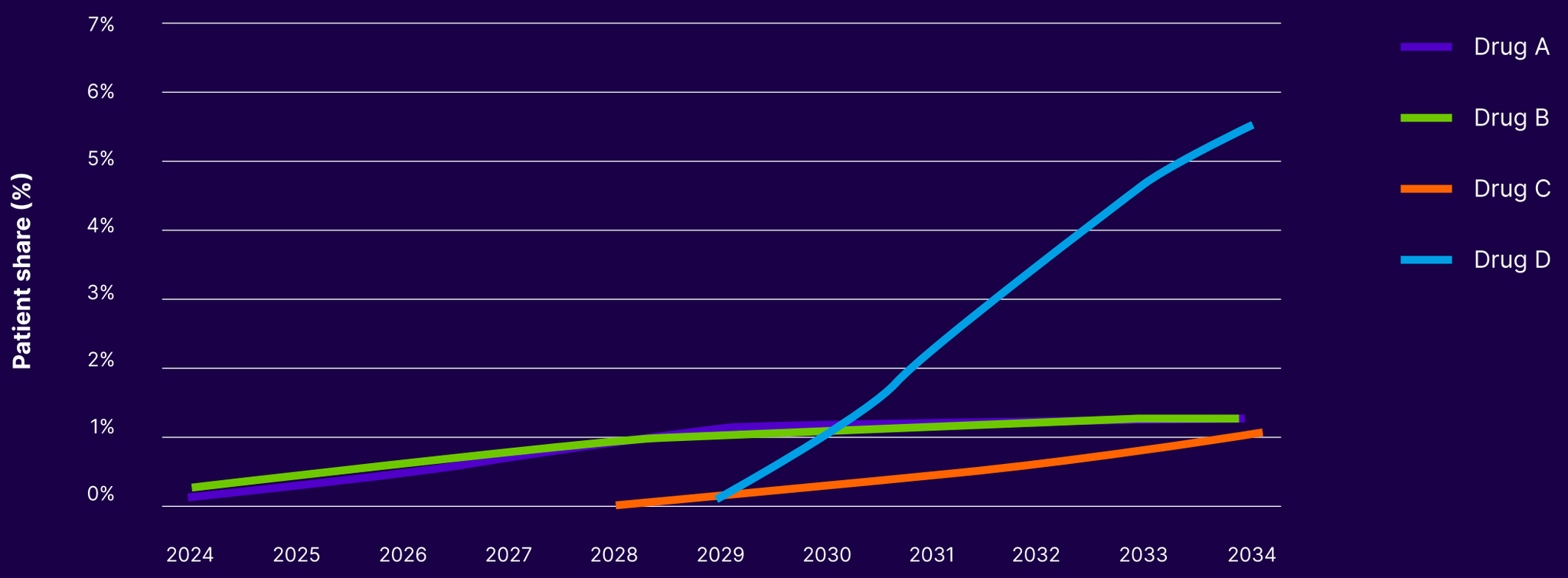
Transparent and validated methodology and assumptions, with proprietary models

About TINA Strategia

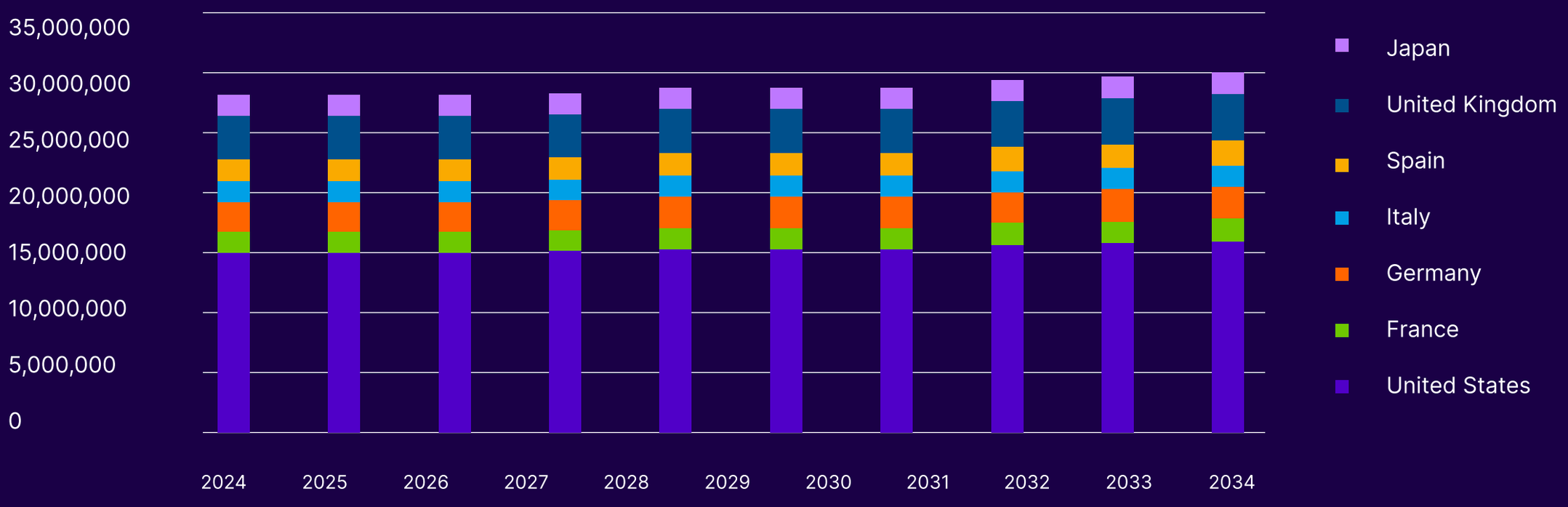
TINA stands for Therapy Insights & Analytics. We provide strategic insights and advanced analytics to life sciences and healthcare companies, helping them make informed decisions. Our Market Assessment reports, including ‘Epi & Markets’ and ‘EpiSage,’ are highly valued by our clients for their depth, accuracy, and relevance, among other offerings.

Get the much-needed market insights and epidemiology-based forecast models for MDD.

Patient share by drug 2024 to 2034



Drug-treated patients, by country 2024-2034



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