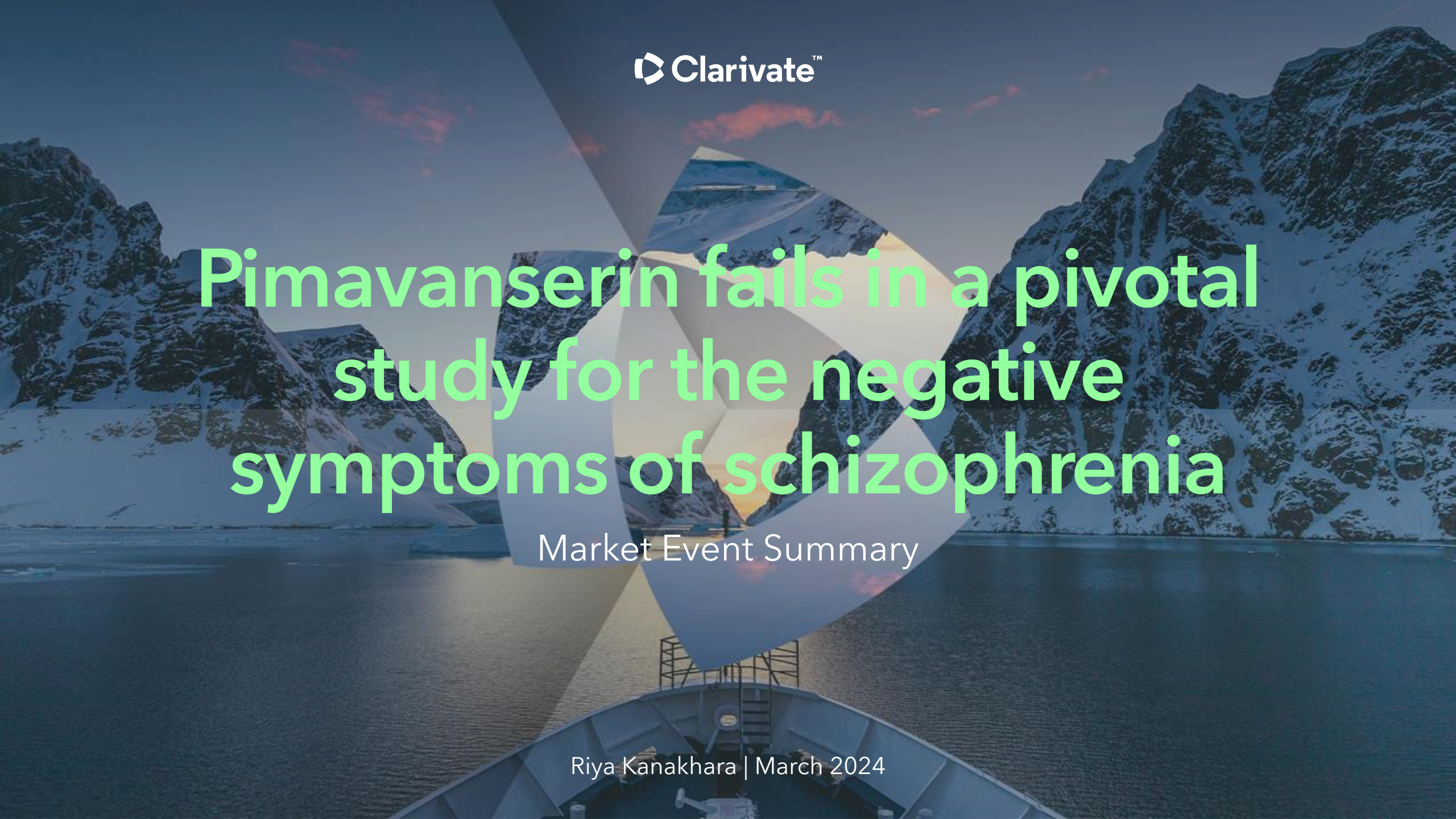

Pimavanserin fails in a pivotal study for the negative symptoms of schizophrenia

Market Event Summary

Riya Kanakhara | March 2024

Pimavanserin fails in a pivotal study for the negative symptoms of schizophrenia

Background

Acadia Pharmaceuticals markets pimavanserin (Nuplazid) in the United States to treat hallucinations and delusions associated with PD psychosis. Pimavanserin—an inverse agonist and antagonist at 5-HT2A receptors and, to a lesser extent, 5-HT2C receptors—was in Phase 3 development (ADVANCE-2 study) as an adjunctive therapy to antipsychotics for patients with the negative symptoms of schizophrenia.

Setbacks in schizophrenia

In March 2024, Acadia announced that, in the ADVANCE-2 study, pimavanserin failed to demonstrate significant improvement versus placebo on the primary endpoint: the change from baseline to week 26 on NSA-16 total score. Earlier, the drug was studied in Phase 3 for partially responding schizophrenia (ENHANCE-1 study); however, it failed to show significant improvement in the PANSS total score versus placebo. The negative trial results in both of the lucrative patient segments in these studies mark an end to the drug's prospects in schizophrenia.

Clinical results for the negative symptoms of schizophrenia

Phase 3 (ADVANCE-2): Pimavanserin 34 mg + background antipsychotic vs. placebo + background antipsychotic

- Change from baseline to week 26 on NSA-16 total score: -11.8 vs. -11.1, P = 0.4825, effect size = 0.07
- AE rate: 30.4% vs. 40.3%; pimavanserin was well tolerated

Phase 2 (ADVANCE): Pimavanserin (10-34 mg) + background antipsychotic vs. placebo + background antipsychotic

- Change from baseline to week 26 on NSA-16 total score: -10.4 vs. -8.5, P = 0.043, effect size = 0.21; greater efficacy occurred with the 34 mg dose: -11.6 vs. -8.5, P = 0.0065, effect size = 0.34
- No treatment effect on the PSP scale
- AE rate: 39.8% vs. 35.1%; pimavanserin was well tolerated

Market impact

Clarivate estimates that, in the G7 markets, about 60% of diagnosed schizophrenia patients have significant negative symptoms. However, no drug is specifically approved to manage this symptom domain, with some current antipsychotics having limited efficacy in managing negative symptoms.

With the Phase 3 failure of pimavanserin reported in March 2024, followed by the FDA's rejection of Minerva Neurosciences' roluperidone earlier in 2024, the unmet need for novel and efficacious drugs for the negative symptoms of schizophrenia will remain unfulfilled in the near future.

Clarivate research suggests that multiple opportunities exist in this patient segment; psychiatrists will highly value efficacious therapies specifically approved for the treatment of negative symptoms in schizophrenia patients, particularly therapies that demonstrate improvement in both negative symptoms and patient functioning.

AE = Adverse event; G7 = United States, EU5, and Japan; NSA-16 = Negative Symptom Assessment-16; PANSS = Positive and Negative Syndrome Scale; PD = Parkinson's disease; PSP = Personal and Social Performance.

About the Author

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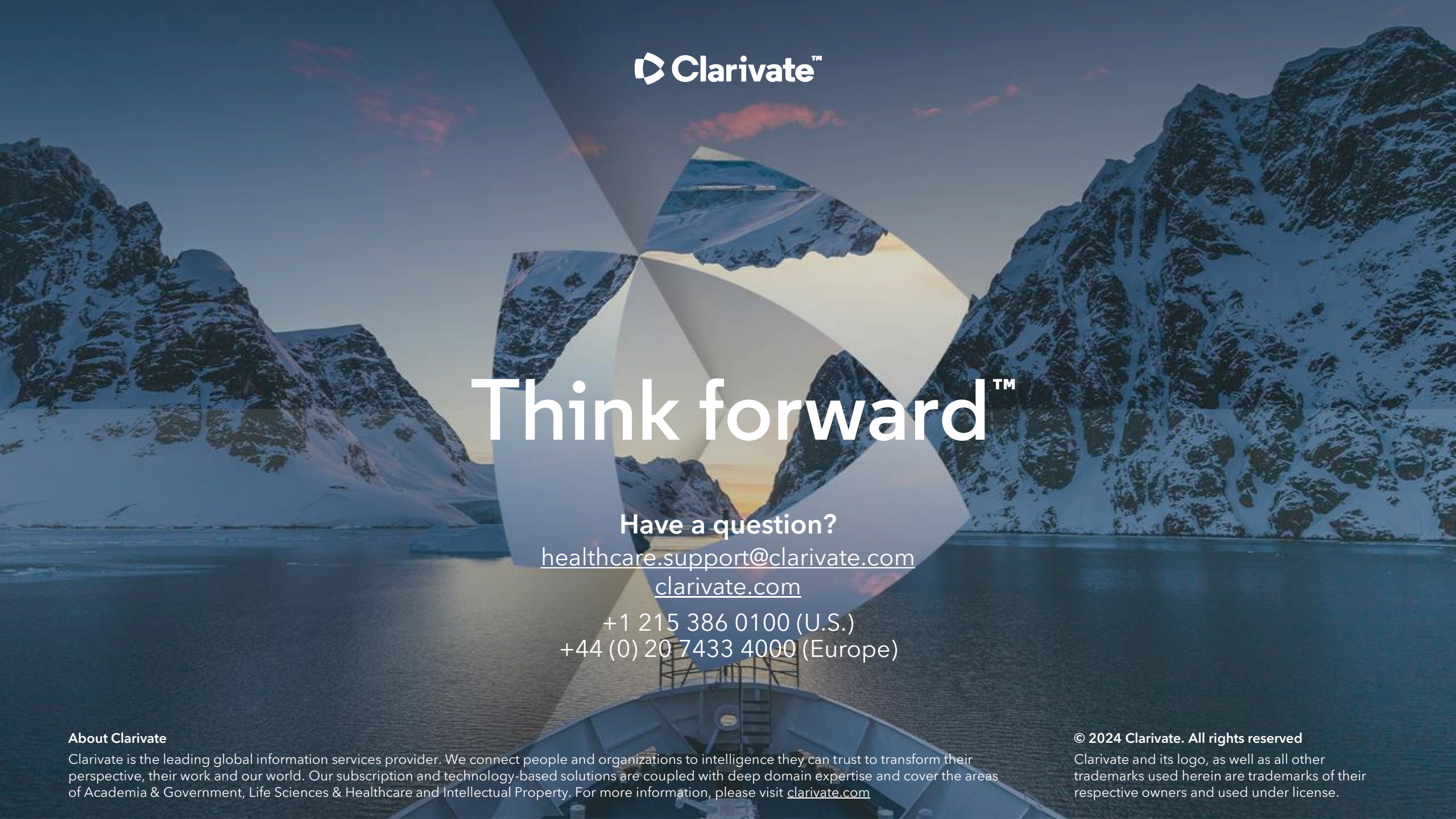
Clarivate coverage of schizophrenia

- Disease Landscape & Forecast: Schizophrenia (G7), providing comprehensive market intelligence insights
- Epidemiology: diagnosed incidence and prevalence data for various schizophrenia population segments across the G7 markets
- Current Treatment: Detailed, Expanded Analysis (EU), exploring the prescribing trends among EU psychiatrists
- Current Treatment: Treatment Algorithms | Schizophrenia (US), exploring U.S. prescribing trends via claims data analysis
- Unmet Need: Schizophrenia (Positive Symptoms, Negative Symptoms, Cognitive Impairment) (US/EU), including an Excel-based Target Product Profile Simulator
- Access & Reimbursement: Schizophrenia (US), providing insights on the impact of payer policies on prescribing behavior in schizophrenia
- Special Topics: Novel Drugs in Psychiatry (US), examining U.S. psychiatrists' perception of key late-phase drugs in MDD, cognitive impairment in schizophrenia, and PTSD

Author Bio

Ms. Kanakhara has substantial experience in market research and has produced competitive intelligence reports in multiple therapy areas, including oncology, ophthalmology, neurology, and psychiatry. She has also prepared post-conference reports for organizations such as the American Academy of Neurology. She holds a bachelor's degree in biotechnology from Amity University in India.



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