

Depression Expertise Exceeds Milestone Expectations and Leads to FDA Approval

Labopharm, headquartered in Laval, Canada, is an emerging leader in optimizing the performance of existing small molecule drugs using its proprietary controlled-release technologies. Based on the success of its lead product, a unique once-daily formulation of tramadol, the company has developed a novel formulation of the drug, trazodone, for the treatment of major depressive disorder (MDD) in adults.

The market for antidepressants is very large. Annual sales in the U.S. alone are in excess of \$11 billion. Yet one of the biggest challenges of conducting a depression trial is patient compliance. Multiple Phase III trials often must be conducted before a sponsor will produce a successful drug.

As a mid-sized specialty pharmaceutical company, Labopharm has limited resources, making multiple Phase III trials impractical. Therefore, this Phase III trazodone trial was critical for the company, making the selection of the right CRO partner pivotal.

It was important for Olga Uresandi, Director Clinical Operations, to work with a CRO that had proven expertise with MDD protocols.

After a thorough search, Uresandi and her team met with INC Research, [a therapeutically focused CRO](#) that specializes in providing clinical trial services to support Phase I through Phase IV studies. It was clear from the start that INC Research had vast mental-health clinical research experience and brought access to the type of specialty MDD private practice investigative sites that were required for this study.

“INC Research had a very refreshing approach to managing clinical trials. During our initial meetings, we didn’t get a sales pitch about the company, but rather a discussion of the science. Their team was very skilled at listening and understood our needs very quickly,” said Uresandi. “INC Research’s reputation in the market and the synergy we felt with their team was very reassuring.”

Study Description

An eight-week randomized, double-blind, two-arm, multi-centre study in patients with unipolar major depressive disorder (MDD) demonstrated the efficacy of Labopharm’s novel formulation of anti-depressant as a treatment for MDD.

Study Objective

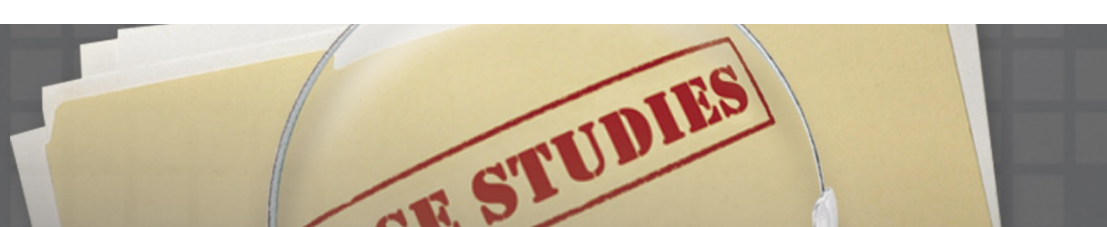
The primary efficacy endpoint of the study was to compare the change in the Hamilton Rating Scale for Depression (HAM-D-17) total score from baseline to the end of the study in the treated group versus the placebo group.

Study Challenges

Recruit and retain major depressive disorder patients from 38 sites in U.S. and Canada and meet aggressive timelines.

Study Results

- Met First Patient First Visit milestone
- Completed First Patient Randomized 1 week earlier than target
- Randomized 412 patients 1.5 months ahead of schedule
- Completed database lock 11 weeks ahead of schedule
- FDA approval within about 18 months of submission



Uresandi also liked having her INC Research project management team based in INC Research's Canadian office in [Toronto](#) for a more seamless extension of Labopharm's internal team.

Reduce Variability, Maintain Flexibility with The Trusted Process®

[The Trusted Process](#) is a series of phases, created and perfected by INC Research, that proactively led Labopharm through this critical Phase III clinical trial with repeatable and measurable methodology. As a result, INC Research was able to minimize trial risk factors and trial variability, yet maintain the flexibility to meet Labopharm's needs.

PlanActivation®

During the PlanActivation phase, led by Dr. Michael Gibertini, PhD, the Executive Vice President of CNS at INC Research, the team provided valuable recommendations on how Labopharm should conduct its protocol and set the right expectations on milestones throughout the process based on long-standing relationships with psychiatric sites and specific experience with this indication.

Uresandi was very pleased with how responsive the INC Research team was right from the beginning, particularly when it came to contract negotiations. If the clinical trial services agreement is held up in negotiations, other critical start-up steps are also held up. "The set-up process and contract work was smooth and painless. INC Research offers the flexibility that other large CROs just can't match," she said.

QuickStart®

During the dedicated two-day meeting, a robust patient recruitment and retention strategy was developed and proactively implemented to support each site's individual advertising and recruitment plans. The 30 U.S. sites that were targeted for trial were a mixture of research and academic sites with leading investigators and key opinion leaders in the field of anxiety and depression. QuickStart Camp helped solidify the partnership and sense of camaraderie between Labopharm and INC Research.

ProgramAccelerate®

In addition to study management for the U.S. sites, INC Research's project management and monitoring team worked closely with the sites to develop and implement study and site-specific recruitment and retention plans. The success of the study was mainly due to proactive planning of key enrollment strategies detailing patient recruitment and retention during the QuickStart camp.

Sites were provided advertising funds to support their specific advertising and recruitment plans and the project team worked with the sites to track and monitor these plans on a weekly and monthly basis. The result of this close oversight and interaction with the sites was a more efficient and successful enrollment of the required number of patients.

"We felt that ad campaigns are a tremendous drain of resources with not a lot of return on investment. However, the INC Research team coached us on the pros and cons of an ad budget for this indication and within our timeframes. We were happy we took their advice as the success of patient recruitment speaks for itself," added Uresandi.





The monitoring team also served an integral role in ensuring the investigators were motivated and focused on the quality of the data, and that patient enrollment met the strict protocol inclusion/exclusion criteria. The site staff performed regular follow-ups with patients and provided excellent patient care and attention by the investigators to retain the enrolled patients in the studies. With close oversight and collaborative interaction with the sites, this was the most rapid enrolling study to-date for INC Research's Psychiatry division:

- First Patient First Visit – Met this major milestone after a 2-month initial FDA review of the study.
- First Patient Randomized – One week after first patient screened. Original target was to have First Patient randomized 2 weeks after first patient screened.
- Total Enrollment – Randomized 412 patients in 3.5 months, 1.5 months ahead of target schedule. Original contract called for randomizing 380 patients in 5 months.

QualityFinish®

With all milestones met at or ahead of original targets, database lock occurred 11 weeks ahead of schedule.

At that time, Dr. Gibertini provided critical consultation in the preparation of the analysis and FDA submission. He was a co-author of the research results that appeared in *Psychopharmacology Bulletin* and was co-presenter of the poster at the 2009 Institute on Psychiatric Services (IPS) conference titled, *A Novel Contramid-based Reformulation of Trazodone in Major Depressive Disorder: Characteristics of Antidepressant Response*.

Results

About a year and a half after submission, Labopharm received FDA product approval for its novel once-daily formulation of the antidepressant trazodone for the treatment of major depressive disorder (MDD) in adults.

"INC Research lived up to its reputation in managing studies in the depression arena. They quickly became a seamless part of our team, which translated into a very efficient and effective study that helped our ultimate objective of FDA approval," said Uresandi.

INC Research is well versed in the means and nuances of psychiatric drug research. With an expansive group of in-house central nervous system (CNS) professionals, our team represents a vast store of mental health research expertise that extends around the globe and across the spectrum of psychiatric indications, including depression, anxiety, addiction, ADD/ADHD, bipolar disorder, panic disorder, smoking cessation, and schizophrenia. Our team has conducted nearly 100 Phase I through IV psychiatric trials with more than 1,500 investigative sites and 17,000 psychiatric patients. Through our [Trusted Process](#) methodology for conducting clinical trials, we guide each study toward the desired endpoint of providing clear and reliable data.

For more information on our CNS expertise, please visit www.incresearch.com/Therapeutic or call 919-876-9300.

