

Clinical Data To Test Phase III Tandem Of Vilazodone, Marker

By Aaron Lorenzo
Washington Editor

Further expanding its business into molecular diagnostics, Clinical Data Inc. is soon to begin the first of two Phase III trials to test the depression compound vilazodone in combination with a companion biomarker.

"It's really a question of being at the forefront of a brand new opportunity as we see it, in identifying the right drug for the right patient at the right dosage," said President and CEO Israel Stein. "This is where we're at and what we believe in for the future, not only for ourselves, but in the whole practice of medicine."

As part of the double-blinded, placebo-controlled study, Clinical Data will identify biomarkers for response to vilazodone and use them to develop a test to screen for patients likely to benefit from the drug. No such predictivetests are available, and should this approach work, it could pay off in more ways than one.

"We're now in the molecular diagnostics sphere," Israel said, "and the primary reason for looking at it is the difference in growth opportunities between classical diagnostics, which is on the order of 3, 4 or 5 percent, and the opportunities in molecular diagnostics, which are far greater than that."

The Newton, Mass.-based company, which previously focused on diagnostics and instruments for physicians' offices, hospital and small- to medium-sized labs, said about half of depressed patients don't achieve satisfactory results with current first-line treatment options, and there are 17 million Americans suffering from depressive illness, according to data from the U.S. Surgeon General's office.

One estimate suggests treating depressive illness generated antidepressant sales in excess of \$9.75 billion in 2004.

So Clinical Data, which grew toward molecular diagnostics through last year's all-stock acquisitions of Genaissance Pharmaceuticals Inc. and Icoria Inc., hopes to help physicians match their patients with effective treatments. The buyout of New Haven, Conn.-based Genaissance was valued at about \$56 million, and the purchase of Research Triangle Park, N.C.-based Icoria cost about \$12.5 million. (See BioWorld Today, June 22, 2005, and Sept. 21, 2005.)

A "track record" of mining for associations between biomarker and drugs "fits very well" with Clinical Data's prior focus, said Carol Reed, the company's chief medical officer.

Previously, she was Genaissance's vice president of medical affairs. Clinical Data expects to have initial results by the middle of next year and hopes to file a new drug application by the end of 2008.

While its goal is not limited to creating a fixed drug diagnostic combination product, Reed said the company believes it is the first "to publicly talk about concurrent development of a drug and test" to screen for responders in the field of depression. As a result, vilazodone could find users in a similar fashion to the breast cancer drug Herceptin (trastuzumab, from Genentech Inc.), which is most effective in patients whose tumors overexpress the HER2 protein.

The safety and efficacy study will enroll about 400 adult patients with major depressive disorder at eight U.S. centers. Potential biomarkers will be examined for each of them, and the genetic analysis will be performed at the company's facilities where it already performs similar services for drug development firms.

Randomization will begin next month, and while Reed declined to specify the study's primary endpoints, she said efficacy measures would include ratings scales standard to depression trials. In previous studies with positive controls – Prozac (fluoxetine) and Celexa (citalopram) – vilazodone failed to demonstrate significant efficacy against placebo, although the company said its effectiveness was comparable to that of the controls.

The second efficacy trial will follow a design based largely on findings from the first. It is likely to begin in the second half of next year.

At least one long-term safety study, for which a design has yet to receive FDA clearance, will be required as part of the pivotal program prior to filing for approval, and the company hopes that subjects from both of its two planned efficacy trials will participate in the long-term safety studies.

Labeled a dual serotonergic antidepressant, vilazodone is both a selective serotonin reuptake inhibitor (SSRI) and a 5HT1A partial agonist. The company said it has an acceptable safety profile, based on 15 Phase I and five Phase II trials involving a total of 369 healthy subjects and 1,163 depressed patients.

"This would be marketed as a drug that's clearly differentiated from other first-line treatments for depression in that there is accompanying genetic information to assist physicians in identifying patients most likely to respond," Reed said. "The intent, certainly, is to discover those response markers as we take the drugs through the pivotal studies."

Stein added that Clinical Data hopes that biomarkers uncovered in the coming vilazodone studies will apply to other drugs of the same class, in addition to those unique to the drug. Genaissance acquired exclusive worldwide rights to develop and commercialize vilazodone from Merck KGaA, of Darmstadt, Germany, in a deal with undisclosed terms. (See BioWorld Today, Sept. 24, 2004.)

Apart from its drug development plans for vilazodone, Clinical Data is moving forward with similar research into safety biomarkers for the schizophrenia drug clozapine. A longtime generic compound, it is associated with a white blood cell-reducing condition

called agranulocytosis, so the company's efforts are focused on developing screens for patients' predisposition to that condition.

"Ultimately, it will be efficacy markers or safety markers that we will be able to identify for a number of drugs and a number of classes of drugs," Stein said. In addition to its research into central nervous system disorders is a focus on cardiovascular disease, with a marketed clinical diagnostic test called Familion for inherited cardiac channelopathies.

Clinical Data also markets pharmacogenomics and molecular services to the pharmaceutical, biotech, clinical, academic, government and agricultural marketplaces. On Thursday, its shares (NASDAQ:CLDA) gained \$1.23 to close at \$22.22.