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Docs Lead 'Reviva' in Schizophrenia Drug

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Not all scientists want to spend their lives in a lab. Laxminarayan Bhat was bitten by the entrepreneurial bug, and his desire to speed up drug development without sacrificing quality became the impetus for Reviva Pharmaceuticals Inc., which he founded in 2006.

With 15 years of experience in drug discovery and development under his belt, including tenure at Xenoport Inc. and Aryx Therapeutics Inc., and more than 20 patents in his name, Bhat was exposed to a variety of therapeutic areas, including central nervous system (CNS) and metabolic diseases and cancer, so he didn't limit his vision to developing one or two compounds.

The plan was to advance multiple compounds to proof of concept by applying chemical genomics to clinically validated targets to shorten the discovery timetable.

"Often, people have the notion that if you go for a novel target you come up with a good drug," Bhat told *BioWorld Today*. "I don't believe in that concept."

Rather than applying new chemical entities to new targets and failing in clinical development or encountering troubling side effects, as some biotechs are willing to do, "we want to discover a new chemical entity for an existing target," he said. "As a small company, we want a high success rate, and then we should be able to develop a safe and efficacious drug in a much quicker time."

Bhat also took an unconventional route to financing the company, based in San Jose, Calif.

"Obviously, starting a pharmaceutical company requires a large amount of capital, like any other entrepreneurship, and it was difficult to raise money," he admitted.

Too, "no matter how fascinating your idea, at the end of the day, you have to listen to the people who put dollars in the company," Bhat added. "And those people are not necessarily savvy with respect to the technology."

Eschewing venture capital (VC), Bhat sought out medical doctors in fields of interest, raising small amounts of money every six months for two years while acquiring assets and advancing them through the discovery process. By 2008, the company had proof-of-concept data for four programs and was ready to file the first investigational new drug (IND) application for its lead drug, RP5063, in schizophrenia.

"At the time, we had the option to go to VCs or raise the money again from high net worth individuals," Bhat said. "We met with a handful of existing investors, and they understood the need and potential of this technology. They realized we efficiently managed their money and that investing again in this company would give them higher returns."

The schizophrenia IND was approved by the FDA in October 2010, and the company moved the compound, RP5063, into a U.S. Phase I study two months later. The dopamine-serotonin stabilizer is designed with partial agonist activity at the dopamine D2, D3 and D4 receptors and the serotonin 5-HT1A and 5-HT2A receptors, and antagonist activity at the serotonin 5-HT6 and 5-HT7 receptors.

The initial human study was completed in September 2011. In March 2012, the company began enrolling patients in a Phase II study of RP5063 at one U.S. site, one site in Eastern Europe and multiple sites in India and Southeast Asia. The 234-patient REFRESH study was designed to assess the drug's efficacy, safety and tolerability.

Earlier this year, Reviva reported the Phase II top-line data showing broad efficacy across the Positive and Negative Syndrome Scale total scores, as well as Positive, Negative and General Psychopathology subscales. RP5063 also showed efficacy in the Clinical Global Impression Severity Scale, and the compound was well tolerated.

Weight gain, a major side effect of many antipsychotic drugs, concerns many schizophrenia patients, who typically are diagnosed in their 20s and 30s, Bhat pointed out.

"With our drug, RP5063, so far in the Phase II trial, we've seen a very good safety profile, with no weight gain and no metabolic, cardiac or movement side effects, in addition to good efficacy," he said.

Reviva plans to begin enrolling the Phase III trial of RP5063 by early next year. If all goes well, a new drug

application in schizophrenia could be submitted to the FDA in late 2015, followed by filings in most global markets.

In the meantime, the company's pipeline includes six additional programs spanning CNS, cardiovascular, metabolic and inflammatory indications.

The company has filed 80 patents and received 20 approvals. RP5063, which may also have applications in major depressive disorder, bipolar disorder, psychosis related to Parkinson's and Alzheimer's diseases, Tourette's syndrome, autism and attention deficit hyperactivity disorder, has patent protection through at least September 2030.

Although Reviva is engaged in potential partnering discussions and hopes to out-license at least RP5063, current investors "are very happy with the outcome" of the Phase II trial and willing to invest additional funds for the Phase III trial, which will move forward with or without a partnering deal, according to Bhat. ■