

Koronis Rebounds From Setback, Seeks New Funds For HIV Drug Trial

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Koronis Pharmaceuticals Inc. has rebounded from a setback that nearly doomed its effort to develop a novel HIV therapy. But now it faces another hurdle: securing funds to push the drug through new clinical studies.

Three years ago Koronis suspended a Phase IIa study of a drug that causes mutations to build up rapidly in the HIV genome, eventually leading the virus to collapse. This approach contrasts with existing drugs, which inhibit viral enzymes or block the virus from infecting cells. Today, patients take multiple drugs to suppress the virus, but resistance can ultimately develop to one or more of the medicines.

While these drugs have turned a lethal condition into a manageable one, the problem of HIV infection remains large. More than 33 million people are living with HIV, and 2.6 million are newly infected each year, according to a 2009 World Health Organization report.

Instead of suppressing the virus, like existing drugs, Koronis aims to make it disappear. But in June 2008, while its clinical study was ongoing and recruiting more patients, Koronis found in a lab test that its therapy was not ablating the virus as it had in previous experiments. In earlier test-tube studies, it had reduced the virus to below detectable levels, according to the company.

Though the medicine was well-tolerated by patients, Koronis elected to suspend the study after seeing the new lab test results. Since the product, KP-1461, works in a new way, the company decided to err on the side of patient safety, said Mark Fromhold, vice president, manufacturing and business development.

Koronis stopped accepting new people into the study, which had sought to enroll a total of 27 subjects, but it did manage to treat 13 patients for 124 days, the duration of treatment called for in the trial.

Though these patients said they felt better, Koronis nonetheless found that the drug was not reducing viral load, or the amount of virus in the blood. Though a drop in viral load was not a primary clinical endpoint of this study, the company monitored this because it is the gold standard for determining clinical efficacy of an HIV drug, according to Fromhold.

"The wisdom on the street was the drug didn't work, game over," said Donald J. Elmer, interim chief executive of Koronis and managing general partner of Pacific Horizon Ventures, the company's largest shareholder.

Elmer and other company executives saw it differently. Since their product works

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through a novel mechanism, it should not be judged the same way as viral-suppressing medicines, they argue. While existing drugs reduce viral load quickly, they are not a cure, Elmer said.

"The world tends to look at HIV drugs through the lens of today's suppressive mechanisms, and there's an implicit assumption that activity occurs quickly," Elmer said. "This drug, because of its novelty, should not be evaluated according to today's suppressive mechanisms."

The Food and Drug Administration limited the duration of the Phase IIa trial to 124 days because Koronis had not yet completed long-term animal-toxicology studies. But since the drug is new, it was hard to predict when it would have an effect on viral load in humans, according to the company.

After suspending the study, Koronis redid lab tests to see if it could reproduce the results that had led it to move the drug into humans. The tests reconfirmed its earlier research, according to Koronis, which is based in Seattle.

Koronis also sequenced the viral genomes of 10 patients who took part in the Phase IIa study. This work showed that the drug was increasing mutations in the virus's genetic material at the rate that would have been predicted given the company's lab research. Koronis published the results in the Public Library of Science in January.

All this led Koronis to conclude that KP-1461 has potential to help patients if they take the drug for more than 124 days.

"We're quite confident that the mechanism is working as intended," Elmer said. "We simply have to administer it for a longer period of time."

Koronis, which has raised \$44 million from Pacific Horizon, Asset Management Co., Johnson & Johnson Development Corp., and others, now seeks funds to run a new Phase II study.

The company, which plans to submit a protocol for the study to the FDA for approval this year, expects this new Phase II trial to last at least 48 weeks, which is standard length for an HIV trial, said Fromhold.

Unlike the last trial, which tested "salvage" patients who were out of other options, Koronis aims to recruit people who are also receiving existing drugs to see if KP-1461 can have an additive effect, Fromhold said. Preliminary data suggest that KP-1461-treated virus becomes progressively more sensitive to today's antiretroviral drugs, he said.

Koronis estimates that it would need about \$15 million more to complete a new Phase II study, Fromhold said. It is considering its options, which include raising a new financing or striking a corporate partnership.