Health Business

Analysis: AIDS virus attacked inside & out

By ED SUSMAN

DENVER, Feb. 6 (UPI) -- Researchers unveiled Monday a host of experimental drugs designed to target different mechanisms of human immunodeficiency virus (HIV) - the virus that causes AIDS.

At the premier U.S. meeting of scientists engaged in fighting the disease - first recognized 25 years ago - that has infected more than one million Americans and 39 million others around the world, scientists described several new products in development.

The drug furthest down the road to clinical use, PA-457, dramatically wiped out about 95 percent of the circulating virus by itself, said Patrick Smith, assistant professor of pharmacy at the State University of New York at Buffalo.

Smith and colleagues administered the oral drug, known as a maturation inhibitor to 24 patients in studies designed to see how the drug works in the body and to measure its impact on the virus.

In his report at the 13th Conference on Retroviruses and Opportunistic Infections in Denver, Smith said the potent drug has a 72-hour half-life that would make once-daily dosing practical. He also said the drug was well-tolerated.

Smith said that PA-457, being developed by Panacos, Watertown, Mass., prevents the virus from sending infectious material into the blood stream - the final step in the virus life-cycle.

In addition, Pfizer Global Research is developing a maturation inhibitor that appears to target only that crucial last phase of development in spewing virions into the bloodstream.

Wade Blair, senior virologist at Pfizer said that the researchers identified UK-201844 after running more than a million compounds through a high throughput screening system.

Remarkably, he said in his presentation, the compound was restricted in its actions to the final stages of HIV development. It didn't prevent the virus from entering the cells or running through the various steps that lead to further production.

But in laboratory tests UK-201844 just stopped the last stage of the HIV life-cycle.

"We have learned in the past that drugs from various classes all work better when combined with other treatments," Mario Stevenson, professor of molecular medicine at the University of Massachusetts, Worcester, told United Press International.

He said that to prevent the virus from getting around maturation inhibitors, multiple drugs will be required. "We need to suppress the replication of HIV enough that it can't mutate enough to develop a defense for the new drug," he said.

Two other drugs, called entry inhibitors, are designed to prevent the virus from fusing with other cells at the start of the infection process. The first fusion inhibitor, enfuvirtide (Fuzeon), is the first injectable

antiretroviral drug.

The new drugs,TRI-1144 and TRI-999, said Mary Delmedico, a researcher for Trimeris in Morrisville, NC, appear to be between 100 to 150 times more potent than Fuzeon in fighting HIV infection.

She said that in laboratory tests the "sons of Fuzeon" are able to inhibit proliferation of the virus even when the virus has mutations that make it resistant to Fuzeon.

"These drugs also have a very long half-life," she said, "which may make them candidates for once-a-week dosing." Fuzeon patients now inject themselves twice a day with the drug.

"We are quite happy with these early results," she said. Delmedico said researchers are working on a delayed release formula for the drugs as well as alternate delivery systems such as inhaled or through-the-skin patches instead of injections.

Also, researchers at Gilead Sciences in Foster City, Calif., are working on a new nucleoside reverse transcriptase inhibitor that would be able to overcome numerous HIV mutations that make most drugs in the class ineffective.

The nucleoside analogs were the first anti-AIDS drugs, with the first AZT or zidovudine being approved in 1986.

Since 1996, the nucleoside analogs are the backbone of most combination treatments.

Thomas Chilar, a researcher with Gilead, said the new drug GS9148, not only appears in laboratory tests to overcome HIV resistance, it also appears to be have a long half-life -- which reduces its dosing needs -- and it does not appear to cause damage to normal cells' DNA.

Other researchers presented data on yet more treatments in the anti-HIV pipeline, including a zinc finger nuclease that disrupts co-receptors on the virus, inhibiting their replication cycles.

Japanese researchers reported on early development of agents that specifically target other less-common HIV receptors.