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ViroStatics Demonstrates Clinical Proof of Concept for Dual Antiviral Anti-Hyperactivation AV-HALT Drugs

Phase 2 Study Results in HIV-infected Individuals Presented at the Conference on Retroviruses and Opportunistic Infections

Boston, MA – March 1, 2011 – An analysis of immune markers measured in a sub-study of ViroStatics’ proof-of-concept Phase 2a trial showed that VS411 was able to reduce immune activation while producing a median 1.5 log₁₀ reduction in viral load. VS411 is a first-generation AV-HALT (antiviral-hyperactivation limiting therapeutic) designed to reduce both viral load and the state of chronic activation that exists in HIV-infected individuals. This analysis was presented today at the 18th Conference on Retroviruses and Opportunistic Infections.

Results were obtained from 32 HIV-infected individuals enrolled in a Phase 2a study who were randomized to receive one of several escalating once-daily doses of oral VS411 for 28 days. In addition to antiviral activity and safety, several immune markers were assessed, including the surface activation markers, CD38 and HLA-DR; Ki-67, a cell surface protein indicative of cell replication; and PD-1, a marker of cell exhaustion after chronic activation. Rapid and statistically significant reductions were measured in each of the above immune markers.

“These reductions in activation are similar to the effect of several years of suppressive antiretroviral therapy and were accomplished in only one month. This indicates the potency of the anti-hyperactivation component of our strategy,” Franco Lori, MD, chief executive officer of ViroStatics, commented. “Notably, this effect was generated without completely suppressing HIV, suggesting that VS411 was able to specifically target the immune system hyperactivation.”

The median decrease in HIV viral loads at day 28 was 1.5 log₁₀, with HIV levels falling below the level of detection (<50 copies/mL) in only two subjects. The median CD4⁺ cell increase was 108 cells/mm³. At day 28, the percentage of CD4⁺ and CD8⁺ T cells expressing the activation markers CD38 and HLA-DR had decreased 28.9% and 34.4%, respectively. Elevations of these markers are indicative of HIV infection and its progression to AIDS.

At day 28, significant declines were also detected in Ki-67, a protein expressed on T cells that is up-regulated during cell proliferation. Declining Ki-67 expression suggests a decrease in T-cell proliferation and, therefore, a reduction in immune system hyperactivation. Likewise, declines were observed for PD-1, a receptor that is up-regulated on the surface of exhausted T cells.

“T-cell exhaustion,” which results when the immune system has become unable to replenish the pool of CD4⁺ T cells that are lost during active HIV infection, is a main contributor to the progression of HIV infection to AIDS. Reduction of PD-1 expression suggests a restoration of normal T-cell function. No significant adverse changes in blood chemistry were observed in the course of the trial, nor were there any signs of drug resistance.

“Current HIV/AIDS treatments have been successful in reducing viral loads, in many cases to undetectable levels,” said Elly T. Katabira, MB ChB, FRCP, lead investigator and professor of medicine at Makerere University in Uganda. “However, we will never be able to address the entire disease state without reducing the chronic immune hyperactivation that exists in HIV-infected individuals and the resulting destruction of CD4⁺ T cells.”

Poster Title: Prompt, Significant Reduction of Activation and Proliferation Markers in CD4⁺ and CD8⁺ T Cell Subsets Despite Incomplete Viral Suppression: Proof-of-Concept for AV-HALTs: New Class of Anti-HIV Therapeutics Inhibiting Both HIV Replication and Immune Activation.

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Date/Time: March 1, 2011 at 2:00 – 4:00

Location: Poster #381 (Abstract #H-109)

Immune Activation and HIV

Immune activation is necessary for the body to defend against diseases. When white blood cells become activated, their metabolism dramatically increases so that they can locate the site of infection, produce substances that kill invading microbes, and send chemical signals that mobilize more cells. They also rapidly replicate to expand the activated cell pool. During HIV infection, the immune response proves ineffective, leading to a state of chronic activation that exhausts the immune system and is now believed to be one of the driving forces leading to AIDS. Even when potent HIV therapies reduce HIV to below detectable levels, the immune system’s level of activation does not return to normal. This persistent activation may lead to a number of diseases, including those of the heart, kidney and central nervous system. The growing recognition of “accelerated aging” in persons on successful antiretroviral therapy has led to a search for new ways to calm the immune system while controlling HIV.

About VS411 and Novel AV-HALT

VS411 is an antiviral-hyperactivation limiting therapeutic (AV-HALT) designed to simultaneously manage HIV infection and immune dysfunction. VS411 is a fixed-dose combination of the cell activation-limiting agent hydroxycarbamide and a slow-release form of the antiretroviral didanosine. While these two agents are associated with toxicity at higher doses, they have demonstrated a manageable safety profile at the relatively low doses used in VS411.

Due to the adverse safety profiles associated with hydroxycarbamide and didanosine, ViroStatics will not advance VS411 into further clinical development. Rather, the Company has identified

several candidates from two families of inhibitory compounds that have major roles in cell signaling and activation that combine the antiviral and anti-hyperactivation properties in a single molecule. ViroStatics is currently evaluating these compounds for candidate selection in advance of preclinical testing.

About ViroStatics

ViroStatics, a biopharmaceutical company with operations in Sassari, Italy, and Princeton, NJ, was founded in 2005 as a spin-off of the Research Institute for Genetic and Human Therapy (RIGHT), located in Cambridge, MA. ViroStatics is focused on the discovery and development of novel therapeutics to address significant medical needs in HIV/AIDS, chronic infections and related fields.

NOTE:

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