



*Partnering With the Immune System
to Prolong Human Health*

A novel approach to treating chronic viral infections

ViroStatics Overview

ViroStatics is a Bio-pharmaceutical company that is developing, and plans to partner for commercialization, novel, first-in-class oral therapies for the treatment of chronic viral infectious diseases. These new products incorporate the latest discoveries in the fields of virology, immunology and pharmacology for a totally new approach (ie, a “paradigm shift”) to the treatment of global diseases representing untapped, multibillion dollar/euro markets. ViroStatics has brought the concept, which stems from the Company’s founder’s work at the National Institutes of Health (NIH), to clinical proof of concept. The Company is headquartered in Sassari, Sardinia (Italy) with research laboratories in Porto Conte, Sardinia and operational offices in Princeton, New Jersey (USA).

The unmet medical need: Immune system hyperactivation

The immune system is the first line of defense providing protection against infectious diseases. One key step in the immune system response is the activation of T cells that allows the immune system to mount a successful offensive against the invading pathogen. However, if the pathogen is not cleared (chronic disease), or even with pharmacological viral suppression, a well-documented **hyperactivation of the immune system** can persist. This hyperactivation leads to a continuous cycle of excessive T cell **hyperproliferation** (with subsequent cell death) and **inflammation**. Left unchecked, this vicious cycle can eventually cause more damage than the infection itself.

Paradoxically, immune system hyperactivation occurs the most rapidly and to the greatest extent in HIV/AIDS, even when the virus has been suppressed to undetectable levels. In HIV, this uncontrolled immune system hyperactivation ultimately results in immune exhaustion, accelerated senescence (aging), cardiovascular and other organ diseases, and, in HIV disease, the onset of the Acquired Immunodeficiency Syndrome (AIDS). Advances in HIV drug therapy today allow the majority of infected individuals to reduce the amount of virus in their bloodstreams to undetectable levels. Despite this therapeutic “success,” those being treated for HIV still progress to AIDS and suffer a reduced life expectancy due to a number of diseases resulting from uncontrolled immune system hyperactivation. Very importantly, immune hyperactivation is not unique to HIV infections but also appears to be a hallmark for other chronic infections such as human cytomegalovirus (HCMV).

Therefore, there is an **unmet need for new drugs that reduce immune system hyperactivation**, beginning with HIV/AIDS and **extending to other chronic viral infectious diseases**.

The solution: A new drug class being developed by ViroStatics

ViroStatics is designing new oral therapies that go beyond simply reducing the amount of virus in a virally infected individual’s bloodstream to returning immune system activation to normal levels. HIV/AIDS represents the ideal viral disease to begin with. Although the Company’s initial efforts address significant unmet medical needs in the global HIV pandemic, the ViroStatics philosophy of “*partnering with the immune system to improve human health*” can be expanded to novel therapeutics to treat other chronic and life-threatening viral infections.

ViroStatics is first mover in its field. The Company’s lead candidates are novel antiviral compounds for the treatment of HIV/AIDS known as **AntiViral-HyperActivation Limiting Therapeutics (AV-HALTs)**. By their unique dual mechanism of action, AV-HALTs are expected not only to reduce the amount of HIV virus in an individual’s bloodstream, but also to improve or prevent cardiovascular, inflammatory and metabolic disorders, tumors, and premature aging that continue to plague those living with HIV despite otherwise successful antiviral therapy.

Human proof of concept achieved with VS411

ViroStatics successfully established the human Proof of Concept for this new class of antiviral/immune protective agents using its two-drug **first-generation AV-HALT, VS411**. In a multinational Phase 2a study, VS411 demonstrated significant anti-HIV activity in only 28 days with a median 1.47 log₁₀ viral load reduction in antiretroviral-naïve subjects while simultaneously generating rapid, significant reductions in several key biomarkers of immune system hyperactivation.

The next step: Second-generation, single-molecule AV-HALTs

Having successfully proven the AV-HALT concept with the two-drug VS411, ViroStatics is now focused exclusively on **the development of the second-generation of AV-HALTs**. As the first-mover in the new science of AV-HALTs, ViroStatics scientists have established a proprietary screening methodology to rapidly identify small molecule compounds containing *both* AV and HALT activities. Using human data from the VS411 Phase 2a study as a comparator to bridge *in vitro* screening with predicted clinical results, the Company has identified product candidates from two in-house compound libraries that display the appropriate combination of antiviral (AV) and anti-inflammatory (HALT) activities **in a single molecule**.

The expertise and know-how of the highly experienced ViroStatics team is unique. Trade secrets and patents protect both the Company's compounds and screening technology. This puts ViroStatics in an advantageous position to complement its promising in-house second-generation AV-HALT program through parallel collaborations with other companies to identify later-stage compounds with the appropriate mechanisms of action that could be in-licensed to **accelerate the development of the first commercial second-generation AV-HALT**. In this regard, ViroStatics is actively engaged in AV-HALT screening and in-licensing discussions with a number of companies.

A new science with roots in the NIH

The concept that led to the ViroStatics AV-HALTs was established in 1993 by Dr. Franco Lori while working with Dr. Robert Gallo – *the co-discoverer of the HIV virus* – at the National Institutes of Health (NIH). In 1994, Dr. Lori established the **Research Institute for Genetic and Human Therapies (RIGHT)** where he raised more than \$ 20 million in non-dilutive grants to further refine the AV-HALT concept over the next 10 years in laboratories located in Maryland, Washington, DC and Italy.

Since 2005, ViroStatics has continued its AV-HALT research and development in Europe. Today, ViroStatics is headquartered in Sardinia, Italy with the Company's research laboratories located in a state-of-the-art research park, *Porto Conte Ricerche*, near Sassari while our Princeton, New Jersey office is located in the middle of the USA's "Pharmaceutical Corridor."

Business model

The Company's Business model calls for the development of novel AV-HALT product candidates from discovery through receiving an Investigational New Drug (IND) application from the US Food and Drug Administration (FDA). At that time, ViroStatics will out-license the lead AV-HALT products to one or more pharmaceutical companies with antiviral franchises for further development and registration in exchange for upfront cash, milestone payments and royalties.

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