MICROBIOTIX, INC. RECEIVES SBIR PHASE I GRANT TO DEVELOP INHIBITORS TARGETING HUMAN HERPESVIRUS 6 AND 8

11 February 2009. Microbiotix, Inc, a privately held biotechnology company, announced today that it was awarded a Phase I Small Business Innovation Research (SBIR) grant from the National Institutes of Health/NIAID. The SBIR Phase I grant entitled, "Novel Methylenecyclopropane Analogs as Anti-Human Herpesviurs 6 and 8 Agents" provides two years of support to develop a novel series of purine nucleoside analogs for therapeutic efficacy against emerging infectious disease agents HHV-6 and HHV-8.

There is an unmet medical need for new agents that are effective and safe for treating beta-herpesvirus and gamma-herpesvirus related emerging infections. The overall goal of this research program is to develop novel therapies for the emerging infectious disease agents HHV-6 and HHV-8 by applying medicinal chemistry structure activity relationship (SAR) approaches to improve the potency of a class of anti-HCMV inhibitors, the methylenecyclopropanes (MP).

A new series of purine nucleoside analogs, the MPs, have been shown to be promising antiviral agents with a very unusual spectrum of activity that includes the beta- and gamma-herpeviruses. Such a broad spectrum of activity has not been seen with existing anti-herpes agents. The first generation of MP compounds were biosteric analogs of acyclovir with the C-O-C moiety replaced by the MP moiety. A second generation of MP analogues, the 2,2-bis-hydroxymethyl series, exhibited very good activity against HCMV. In both cases, the Z- and E-isomers were generated, with the Z isomers demonstrating the best overall potency. A limited number of analogs of both the first and second generation of MP's have exhibited some of the most potent inhibition of HHV-6 and HHV-8 replication so far identified. Proven medicinal chemistry structure activity relationship (SAR) approaches will be used to improve the potency of the MP compound series against HHV-6 and HHV-8. The specific objective of this research program is to chemically optimize the MP series of compounds to improve the potency against HHV-6 and HHV-8. Lead MP compounds should also maintain activity against HCMV and will also be useful for treating these infections. There is no good antiviral drug with this unique profile. Suitable lead compounds will exhibit excellent HHV-6 and HHV-8 inhibitory activity (IC_{50} <1μM) with minimum cytotoxicity in primary HEL299 cells (CC_{50} >100μM). Data generated in these studies will further justify their future evaluation in animal studies, which will be used to identify a clinical candidate and support a subsequent application for Phase I/II HHV-6/-8 human clinical studies.

The aims of this research program are as follows: (1) Conduct a medicinal chemistry structure activity relationship (SAR) study to improve the potency of the methylenecyclopropane compounds against human herpesviruses-6 and -8; (2) Evaluate antiviral activity of the new methylenecyclopropane analogs against HHV-6 and HHV-8; (3) Investigate the mechanism of action of the new methylenecyclopropane compounds against human herpesviruses-6 and -8.

Terry Bowlin, Ph.D., CEO, will serve as the Principal Investigator of the grant.

About Microbiotix

Founded in 1998, Microbiotix, Inc. is a product-focused biopharmaceutical company engaged in the research and development of novel, small-molecule, anti-infective drugs that address commercially significant medical markets. The company currently has several active research programs in the fields of anti-bacterial and anti-viral discovery, with three compound series in pre-clinical development. More information can be found on the company's web site, www.microbiotix.com.