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

01 May 2012. Microbiotix, Inc, a privately held biotechnology company, announced today that it was awarded a Phase II Small Business Innovation Research (SBIR) grant from the National Institutes of Health/NIAID. The SBIR Phase II grant entitled, "Novel Methylenecyclopropane Analogs as Anti-Human Herpesvirus 6 and 8 Agents" provides three years of support to develop a novel series of purine nucleoside analogs as broad spectrum anti-herpes agents.

The overall goal of the project is to develop a single agent active against all herpes viruses for use in the immunocompromised patient population. The primary objective of this SBIR Phase II proposal is to evaluate a limited number of the most potent MCPNs in murine toxicity, PK/PD, and efficacy (HSV/CMV/VZV) models to identify a final broad-spectrum anti-herpesvirus preclinical candidate, and backup compound, to advance into IND-enabling rat GLP toxicology and safety pharmacology studies.

The human *herpesviridae* family contains eight members divided into three subfamilies, designated alpha, beta and gamma. The alphaherpesviruses include herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2) and varicella zoster virus (VZV). The betaherpesviruses include human cytomegalovirus (HCMV), two variants of human herpesvirus 6 (HHV-6A, HHV-6B), and human herpesvirus 7 (HHV-7). The gammaherpesviruses include Epstein-Barr virus (EBV) and human herpesvirus 8 (HHV-8). Herpesvirus infections are commonly acquired, and many present major health concerns, especially among immunocompromised patient populations (e.g., transplant recipients, AIDS patients, and the elderly). Because of the narrow spectrum of current therapeutics, emergence of resistant virus strains, and the limiting toxicities of current treatment options, there is a definite need for new agents that are effective and safe for treating herpesvirus infections, particularly those caused by drug-resistant virus strains in the immunocompromised patient. We have previously identified the methylenecyclopropane nucleosides (MCPNs) as potent inhibitors of HCMV, HHV-6 and HHV-8. The original goal of the SBIR Phase I proposal was to identify new MCPN analogs with even greater anti-HHV6/8 potency and efficacy, while maintaining HCMV activity. We have exceeded that SBIR Phase I goal, and have now identified novel MCPN analogs with a very unusual, broad anti-herpes spectrum of activity that includes the alpha-, beta- and gamma-herpesviruses, including ACV resistant strains. To our knowledge, this broad spectrum activity has not been seen with existing anti-herpesvirus agents. The primary objective of this SBIR Phase II proposal is to evaluate a limited number of the most potent MCPNs in murine toxicity, PK/PD, and efficacy (HSV/CMV/VZV) in animal models to identify a final broad-spectrum anti-herpesvirus preclinical candidate, and backup compound, to advance into IND enabling rat GLP toxicology and safety pharmacology studies.

The aims of this research program are as follows: (1) Evaluate and prioritize novel MCPN anti-herpesvirus compounds based upon favorable *in vitro* "drug-like" ADME properties.; (2) Scale-up MCPNs and evaluate toxicity, PK/PD and anti-herpesvirus efficacy *in vivo*.; (3) Investigate the broad-spectrum anti-herpesvirus mechanism of action (MOA) of the new MCPNs and assess their efficacy against drug-resistant strains of HCMV and HSV-1; (4) Conduct preclinical rat GLP toxicology, pharmacokinetics (PK), genetic toxicology and safety pharmacology studies using the final MCPN preclinical candidate.

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.