

MICROBIOTIX, INC. RECEIVES NIAID PARTNERSHIPS FOR BIODEFENSE VIRAL PATHOGENS GRANT TO DISCOVER NOVEL THERAPEUTICS TARGETING EBOLA HEMORRHAGIC FEVER VIRUS.

July 1, 2010. Microbiotix, Inc, a privately held biotechnology company, announced today that it was awarded a Partnerships for Biodefense Viral Pathogens R01 grant from the National Institutes of Health/NIAID. The grant, entitled “Developing small molecule therapeutics for Ebola hemorrhagic fever virus” provides five years of support to discover and develop small molecule therapeutic agents against Ebola virus to respond to natural outbreaks of Ebola virus infection and to counter potential acts of bioterrorism.

Ebola virus (EBOV) causes periodic outbreaks of severe viral hemorrhagic fever in Africa with high mortality rates in infected patients. EBOV is classified as a Category A bioweapons agent by the Centers for Disease Control and Prevention (CDC) because of its highly infectious nature. Currently, no FDA approved vaccines or antiviral drugs are effective against EBOV infections. Moreover, rapid progression of EBOV infection will offer little opportunity for developing acquired immunity in an infected population. Therefore, there is a critical need for development of effective antivirals to respond to an EBOV outbreak or bioterrorist attack. EBOV infection is initiated by the fusion between viral and host cell membranes, which is mediated by the viral envelope glycoprotein (GP). This selective interaction between EBOV-GP and host cell surface receptor molecules is essential for the initiation and establishment of the infection. Blocking of EBOV entry will lead to suppression of viral infectivity early in its life cycle. Our goal is to develop small molecule inhibitors of EBOV infection that can be used either prophylactically to a potentially EBOV exposed population or therapeutically during the post-infection period. In preliminary studies of this project, we have identified eight EBOV entry inhibitors of different chemotypes, which are active against infectious EBOV ($IC_{50} \leq 20 \mu M$) and have high selectivity indices. The potential inhibitors and their derivatives will be further optimized and characterized by medicinal chemistry to increase their anti-EBOV potency ($IC_{50} < 1 \mu M$), and selectivity indices ($SI > 10$). In addition, we will continue to screen a large number of molecules in a search for inhibitors with higher selectivity to provide new entry points for chemical optimization. The major milestone of this proposal is to select 2-3 EBOV entry inhibitor candidates that will be advanced to Investigational New Drug (IND) enabling toxicology and safety pharmacology studies.

The aims of the research program are as follows: 1. Screen compound libraries to identify selective noncytotoxic inhibitors of EBOV entry; 2. Optimize the potency and selectivity of hit compounds and validate their antiviral activities; 3. Determine the mechanism of action (MOA) of the initial hit series and prioritize screening hits; 4. Identify EBOV inhibitors with *in vitro* ADME properties suitable for i.v. and oral dosing; and 5. Evaluate EBOV inhibitors in a guinea pig model of EBOV infection.

Arnab Basu, Ph.D., Senior Scientist 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.