

## Product Candidates

Our programs are focused on the development of novel medicines for the treatment of hepatitis C virus (HCV) infection, Avian Flu Viruses.

The present invention provides a method of treatment and prophylaxis for viral diseases, comprising an inorganic, antimony-containing compound. More specifically, the invention provides a method of treating viral diseases by administering to a subject in need thereof a material comprising antimony silicates .

The material of the present invention, a highly effective sorbent, suppresses the infectious activity of a variety of viruses by blocking the initial stages of viral replication in cells infected by the virus. The prepared material, through its sorbent properties, also neutralizes thermostable and thermolabile protein toxins. Because the finer formulation comprising the material of the present invention may also be injected intravenously, it can be used to rapidly bind blood-borne endotoxins, exotoxins, and products of incomplete toxin breakdown, thus facilitating their elimination from the body.

A comprehensive array of non clinical studies has been completed with BOV-23. The range of antiviral activity was initially studied in vitro against a panel of infectious virus lines such as HCV, HIV and type A avian flu (H5N1). Confirmatory studies for in vivo antiviral activity were then conducted using murine models infected with type A avian flu (H5N1), type A influenza and specially designed HCV persistence mice models. BOV-23 was administered intraperitoneally (IP) as well as via intravenous (IV) and oral (PO) injection during these studies.

The findings of this pioneering studies were confirmed at the Laboratory of Hepatitis Research, Center for Biologics Evaluation and Research, Food and Drug Administration (Bethesda, Maryland) in early 2000.

### AVIAN FLU H5N1

Scientists are increasingly worried that the H5N1 strain of Avian Flu will mutate into a form easily passed between humans, triggering a global pandemic. H5N1 infection, viral sepsis leading to major organ failure is often the cause of death. At present, only one antiviral, Oseltamivir (Tamiflu) is known to offer some level of effectiveness against the H5N1 strain of Avian Flu. However, Tamiflu is indicated as a treatment for normal household varieties of influenza if administered within 48 hours of first symptoms. The treatment window for an ultra-virulent H5N1 strain is likely to narrow considerably.

Reports already indicate the potency of Tamiflu against the avian flu virus is reduced,

when taken after 24 hours of the first symptoms of the disease. H5N1 resistance to

Tamiflu is already being reported in Southeast Asia. The antiviral effect of BOV-23 was tested in vitro against H5N1 using cytopathic effect assay in porcine embryo kidney cells (PEKC) cells and determination of the 50% tissue culture infectious dose (TCID<sub>50</sub>) analyzed according to Reed-Muench accumulative titration method. The study revealed that BOV-23 was able to inactivate H5N1 infectivity in highly sensitive PEKC cultures. BOV-23 at 1.5 mg/mL has suppressed H5N1 viral infectivity by 10,000 fold and the complete suppression was achieved at 3.1 mg/mL (Table 2). Different fractions of 3 mg/ml water suspension of BOV-23 and the serial dilutions maintained antiviral activity at a high level.

Based on these findings and favorable long half-life, oral bioavailability, low toxicity profiles, we believe that BOV-23 is a promising candidate oral drug to be used in therapy for treating type A avian flu H5N1 infection.

### HCV

The anti HCV effect of BOV-23 was tested against HCV-1b strain using an in vitro and in vivo models established by Professors, Dr. Peter G. Deryabin at D.I.Ivanovsky Institute of Virology of Russian Academy of Medical Sciences, Moscow, Russia. The primary mouse brain cell culture (SMBC), the most sensitive cell cultures for the cytopathogenic HCV-1b variant [2,3] was selected. It was shown that HCV is very pathogenic for cells of different origin: primary chick embryo fibroblasts (CEF), porcine embryo kidney cells (PEKC), hamster kidney cells (BHK-21), green monkey kidney cells (Vero) and lymphoblastoid cell line.

HCV can induce both acute and chronic infection after infecting of porcine embryo kidney cells by cytopathogenic HCV variant isolated from infected SMBC. Cytopathogenic virus variants isolated from above mentioned cells have been identified as HCV using various serological tests in which polyclonal and monoclonal HCV- specific antibodies were used. RNA of HCV variants isolated have been identified also by RT PCR with primers to HCV core and "NTR regions and sequencing analysis.

The findings of this pioneering studies were confirmed at the Laboratory of Hepatitis Research, Center for Biologics Evaluation and Research, Food and Drug Administration (Bethesda, Maryland) in early 2000.