In conclusion, prodrugs SB 9001 and SB 9002-1 have been developed as orally bioavailable analogs of SB 9000, a novel anti-HBV agent.

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Characterization of Influenza Virus Clinical Isolates Obtained During Clinical Study of Arbidol

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An antiviral drug arbidol has been widely used in Russia now. Clinical trials and experience of using of this drug in the clinic have shown arbidol to be effective in preventing and treating influenzas A and B and well tolerated by patients. Our aim was to monitor the arbidol susceptibility of clinical isolates obtained in group of patients treated for influenza. Arbidol-resistant mutants were obtained by 15 passages of virus in MDCK cells in the presence of increasing from 5 to 20 μg/ml drug concentrations. Resistance of mutants was confirmed in cell ELISA and plaque activity assays and by haemolysis tests. To determine the molecular basis of arbidolresistance, the HA genes of the wild-type and arbidol-resistant mutants were sequenced. All mutants had amino acid substitutions only in the HA2 subunit, but at different positions. Paired isolates ($n = 25$) obtained from patients before and during therapy with arbidol (3×200 mg for 5 days) were studied for susceptibility to arbidol using ELISA-cell assay in MDCK cells. All isolates were equally sensitive to arbidol with IC50 falling in the range of 7.0–12.5 μg/ml and similar to IC_{50} previously observed for laboratory and clinical isolates. Two matched pairs of isolates of two patients from whom we were able to obtain days 4 and 5 samples were chosen for sequence analysis. No amino acid changes that had previously been identified in vitro as being involved with reduction of susceptibility to arbidol were observed. In our clinical study, it was shown that no arbidol resistance had emerged during 5 days of therapy of acute influenza infection.

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Preclinical Development of A New Class of Orally Active Drug Candidates for the Treatment of RSV Infections

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Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia in children under 1 year of age and is a leading cause of severe lower respiratory infections in infants and young children. It has been estimated in some U.S. communities that between 50% and 80% of bronchiolitis hospitalizations from November through April are due to RSV disease.

Prophylactic antibodies such as Synagis® (palivizumab) effectively reduce the incidence and severity of RSV disease in high-risk pediatric populations but the only antiviral treatment available for patients with RSV disease is ribavirin, a nucleoside analog with suboptimal clinical efficacy and safety profile.

We have developed a novel, potent class of small-molecule, orally available candidates that specifically target the RSV fusion glycoprotein. Representatives of this imidazoisoindolone class of fusion inhibitors are orally bioavailable in multiple species and have demonstrated efficacy in rodent models. They represent promising candidates for advancement into clinical trials for RSV.

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Carbohydrate-Binding Agents (CBAs) Potently Inhibit HIV Infection In Human Primary Monocytes/Macrophages and Efficiently Prevent Viral Capture and Subsequent Transmission to CD+4 T Lymphocytes

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Macrophages (M/M) are recognized as an important cellular target of HIV, and a crucial virus reservoir, producing and releasing large amounts of infectious viral particles for a long period of time. Moreover, productively infected M/M can interact with $CD4^+$ T-lymphocytes and transfer the virus to these cells. Carbohydrate-binding agents (CBAs) have been recently proposed as innovative anti-HIV compounds selectively targeting the glycans of the HIV-1 envelope glycoprotein gp120. Short pre-exposure of HIV-1 to CBAs prevents the DC-SIGN-expressing B-lymphoblast Raji cells (Raji/DC-SIGN) to efficiently bind HIV-1 and no syncytia formation occurs upon subsequent co-cultivation with CD4+ T-lymphocyte C8166 cells. Thus, the mannose-specific (i.e. the plant lectins HHA,