



Dear colleagues,

Finally, the spring has come. The fresh light wind and warm sun are outside. The spring sun, however, comes along with viral respiratory diseases.

This month we would like to tell you about our progress achieved for the project PAM-1: "A Novel Compound with Antiviral Activity Against Influenza and Other Acute Respiratory Infection Viruses".

The studies of this molecule began in 2004. We are pleased to inform you that during the development of this project, the following leading Russian scientific centers became our partners: the Federal State Budgetary Institution "Medical Radiological Research Center" (FSBI MRRC), I. Mechnikov Research Institute of Vaccines and Sera of Russian Academy of Medical Sciences, Federal State Institution D.I. Ivanovsky Institute of Virology, and FSBI "Russian Cardiology Research and Production Complex" (FSBI "RCRPC") of the Russian Ministry of Health.

According to the results of investigations, PAM-1 acts at the early stages of influenza A and B viruses' reproduction and inhibits the fusion of virus envelope with the cellular membranes, preventing the penetration of the virus into the cell. PAM-1 targets a surface protein of the influenza virus, called hemagglutinin (HA). By interacting with HA of influenza virus, the compound inhibits the low pH induced conformational changes of this protein and thereby prevents the fusion processes between the viral envelope and the endosomal membrane. The challenge with lethal mouse-adapted A/Aichi/2/69 (H3N2) virus revealed the efficacy of PAM-1 in small doses of 10 and 20 mg/kg. Our compound reduced the mortality rate by 50-60%, twicely increased the mean survival day and completely protected from weight loss. Our studies also revealed interferon-inducing properties of PAM-1.

At present, the preclinical studies have completed, the pharmacologic substance has been registered, the final dosage form is prepared for registration. In order to gain the permission to conduct the phase 1 clinical trial, the PAM-1 drug registration dossier is planned to be filed to the Ministry of Health in April 2014.

The clinical trial of the drug PAM-9 "Radio- and Chemoprotector, Adjuvant of Radiation/Chemotherapy", which we have mentioned about in our previous letter, continued this month. The phase 1 clinical trial revealed no evidence of adverse events. The clinical part has ended. Pharmacokinetic analysis of samples are currently completing.

This month was also marked by the studies of the mechanism of action of PAM-10 - the drug candidate for the treatment and prevention of metabolic syndrome.

We will be happy to present you the detailed information about this project in our next letter.

Sincerely yours,

Rakhimdjhan Roziev, MD, Ph.D.