

### НПАК «ПАМ»

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### NP AC PAM

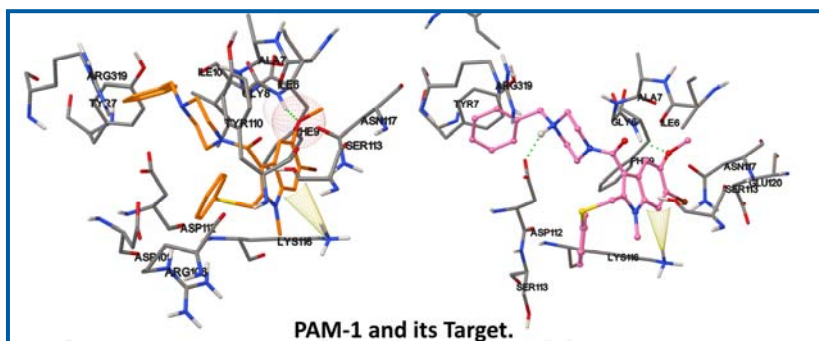
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Dear colleagues,

Finally, the winter has come to an end. The early morning is full of birds' songs, the snow has mostly disappeared. Although the soil is still cold, everything around is pleasant. The spring has come!

At the beginning of the month the [permission to perform the phase I clinical trial was received for PAM-1: "A Novel Compound with Antiviral Activity Against Influenza and Other Acute Respiratory Infection Viruses"](#). An open non-randomized study is planned to evaluate the safety, tolerability and pharmacokinetics of single repeated administration of the drug in doses of 50 and 100 mg by healthy volunteers.

The compound was developed in cooperation with a team of chemists from the Medical Radiological Research Center of the Russian Ministry of Health.



PAM-1 acts at the early stages of influenza virus 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 preclinical studies also revealed interferon-inducing

properties of PAM-1 and its ability to increase the resistance of the organism against different viral infections.

The studies suggest that the new substance PAM-1 is **28 times less toxic** than its closest analogue. The therapeutic index of PAM-1 **exceeds 40**.

The experiments showed that PAM-1 lacks strain specificity. The drug candidate effectively inhibited the viral reproduction of influenza A and B viruses, including those resistant to main groups of anti-influenza drugs: rimantadine-resistant strains and oseltamivir-resistant viruses, pandemic 2009 *H1N1* influenza virus, as well as pathogenic avian *H5N1* influenza viruses, isolated in Russia.

The preclinical trials were carried out in the following leading Russian scientific centers: 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.

PAM-1 is protected by Russian and foreign patents. European patent is validated in many countries of the European Union. Patent applications are being examined in the Eurasian Patent Office, Indian Patent Office, and in other countries. The object of protection is the active substance, its therapeutic indication, methods of preparation, final dosage forms and pharmaceutical compositions thereof. For the territory of the Russian Federation the licensing rights to the molecule have been transferred to a large Russian pharmaceutical company. We are ready to organize cooperation on this project for all other territories.

This month was also marked by active studies of PAM-3 "Oxygen Carrier". We will be happy to present you the detailed information about this project in our next letter.

Sincerely yours,  
Rakhim ROZIEV, MD, Ph.D.