



The sunny summer has ended. The fall has come, being accompanied by its incredibly beautiful leaves of different shades, clean air, and sunshower. Autumn represents a new lease of life: new projects, goals, plans. This is the time when a good summer holiday results in fresh mind, interesting ideas and readiness to immerse ourselves in work and research.

It is our pleasure to present to your kind attention a new project PAM-28 "Autism Spectrum Disorders Treatment Drug".

Active studies of this compound started 5 months ago. During this time the acute toxicity of the compound at different ways of administration was determined, and lack of mutagenic activity was established.

For the moment, there is no known cure for autism. The treatment and education approaches that are used today can address some of the challenges associated with the condition, assuring optimal adaptation of autistic children to the environment, and a more adequate mental evolution.

In experiments on specially developed experimental models of autism in animals, PAM-28 demonstrated the ability to:

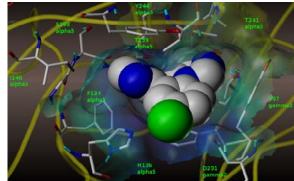
- improve long-term memory during spatial skills reproduction;
- reduce anxiety and restore behavioral health;
- contribute to a more rapid adaptation to social and non-social signals during their re-presentment.

Based on PAM-28's structure, an effect over brain was presumed. This idea was confirmed during in vivo experiments. Drugs with nootropic and neuroprotective activity are commonly used to treat autism spectrum disorders. That is why during the preliminary efficacy studies PAM-28 was compared to Phenibut, a drug used to treat low-grade anxiety, mild sleep disorders, and certain mood disorders. Antiamnesic activity of the compound PAM-28 in dose 5 mg/kg was higher than that of the drug of comparison in a 10-fold higher dose (50 mg/kg).

During August the documents for <u>phase II clinical studies</u> of PAM-9 "Radio- and Chemoprotector, Adjuvant of Radio- and Chemotherapy" were filed to the Ministry of Health.

Permission to conduct <u>phase Ib clinical trial</u> of PAM-8 "A Compound for the Reproductive Function Recovery" was gained in August. The mentioned clinical study is planned for October-December 2014. The screening of volunteers has already started.

Preclinical research of PAM-14 "An Anticancer Compound" continue. We would be happy to provide you with more details on this project in our next letter.



Docking results of PAM-28 to ligand binding domain of its presumable biotarget

Sincerely yours, Roziev R.

ΠAM-12