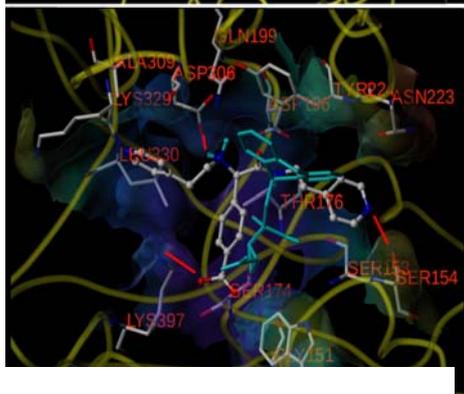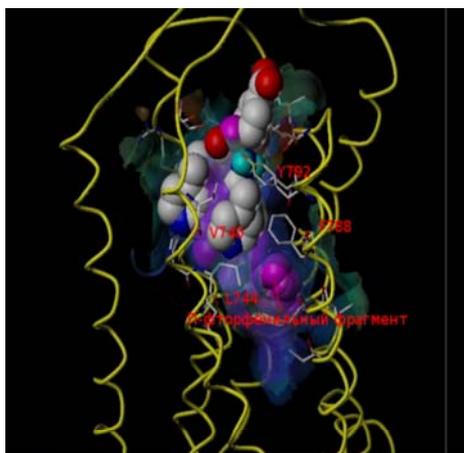Dear friends and colleagues,
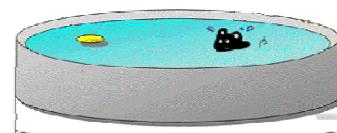It is our pleasure to share our news with you.

This month we are glad to present to your kind attention our project PAM-12 "Memory Recovery and Consolidation Compound Efficient for Treatment of Alzheimer's Type Dementia".

Neurodegenerative diseases are currently becoming more prevalent because of demographic processes. The most frequent cause of dementia in the elderly and senile age is Alzheimer's disease (AD). Each five-year period AD incidence doubles for people elder than 60 years old. To date, unfortunately, no effective treatment for Alzheimer's disease is known. There are no drugs that can suppress the development of the disease-associated pathological processes. Alzheimer's disease is characterized by a gradual, steady development of memory disorders, followed by the decay of intelligence and mental activity.

Morris Maze.

PAM-12 reveals antiamnesic action, improves long-term spatial memory, enhances locomotor activity, reduces mild neurological dysfunctions and is capable of correcting the lack of attention. According to the data of the preclinical studies of this compound, PAM-12 removed cognitive deficits developed in the rat model of Alzheimer's disease, as evidenced by a statistically significant decrease (1.8 fold) of the percentage of animals with amnesia. Toxicological study of the compound showed its low toxicity (LD_{50} is more than 4 g / kg) and lack of mutagenic effect.

The specific pharmacological activity of PAM-12 was studied by intraperitoneal and oral administration of different doses of the drug to rats with a model of sporadic Alzheimer's disease.

The functional efficacy studies were carried out using a range of tests. To evaluate spatial learning and memory, for example, the Morris water maze test was performed. The neurological deficits in aged rats were assessed with the use of McGrow scale and Pole test. The method of amnesia induced by maximal electroshock was also applied.

PAM-12 interacts with metabotropic glutamate receptor 5 (mGluR5) thus enhancing cognitive functions, such as education, memory formation, consolidation and retrieval. The compound/ biotarget interaction was assessed through molecular modeling. The docking results allow us planning the future studies that would clear up the precise mechanism of action.

Pam-12 is in the active phase of preclinical research, that is estimated to result in recommending this drug for first-in-men clinical trial. The compound is expected to be efficient as a cognition enhancer and memory recovery in patients suffering from Alzheimer's disease.

Docking results to ligand binding domain (shown in blue on the lower picture) and transmembrane domain (on the top picture) mGluR5 receptor of negative allosteric modulator.

Pole Test.

This month was also marked by active work on the project PAM-28 "Compound for the Treatment of Autism-Associated Behavioral Anomalies"
We would be happy to provide you more details on this project in our next letter.

Sincerely yours,
Roziev Rakhim.