Epilepsy is one of the most common neurological diseases in the world. It is estimated that approximately 65 million people in the world, i.e. approximately 1% of the population, suffer from epilepsy. Currently, the number of people suffering from the active form of epilepsy is around 5-10 people in 1,000. Active form of epilepsy is defined as at least one seizure episode in the last five years. In Poland, the number of patients with epilepsy varies between 300-400 thousand. Epileptics are at an increased risk of death (about 1.6 - 4.1 times higher compared to the general population) which is associated with epileptic seizures, epileptic state, suicide or sudden unexpected death in epilepsy (SUDEP).

Treating epilepsy is primarily based on properly selected pharmacotherapy. Currently used drugs do not have the ability to inhibit epileptogenesis, they only show a symptomatic effect. The first-line treatment of epilepsy is the use of so-called classic antiepileptic drugs. According to statistics they are effective, giving a full control of seizures, in about 60% patients with epilepsy. Also polytherapy turned out to be effective in the next 20% cases. Unfortunately, nearly 30% of patients suffer from drug-resistant epilepsy (MRE). New drugs available on the pharmaceutical market, such as gabapentin, pregabalin, rufinamide, lamotrigine, vigabatrin, topiramate or felbamate are characterized by better pharmacokinetics and fewer side effects compared to classical antiepileptic drugs, and slightly increased effectiveness in treatment-resistant epilepsy. A serious problem associated with drug resistance is higher mortality rate in patients with drug-resistant epilepsy in comparison with other patients with epilepsy. Recurrent epileptic seizures increase secondary epileptogenesis, which increases the frequency of seizures. Frequent generalized seizures have numerous medical and social consequences, e.g. increased risk of injuries and fractures, progressive memory disorders, progressive cognitive impairment, and increased risk of mental disorders. The social consequences of drug-resistant epilepsy include social stigmatization, job loss, costs of treatment of co-morbidities and complications of epilepsy and costs of long-term institutional care.

The aim of this project is to characterize a group of 1,2,4-triazole-3-thione derivatives as potential anti-epileptic drugs acting on the cause of epilepsy. In the project, a comprehensive comparative analysis of transcriptome profiles between a group of control mice and a group of mice receiving the selected 1,2,4-triazole-3-thione derivative will be performed. The results of the transcriptomic analysis will allow for the selection of mRNA biomarkers with the highest expression, which will allow for the analysis of the molecular effects of the tested compound. The deposition sites of the selected drug-candidate and its impact on the functional parameters of internal organs will also be determined. The interaction risk of the selected 1,2,4-triazole-3-thione derivative with substances metabolized by the cytochrome P450 system will also be investigated. The research will employ modern techniques of spectrometric imaging (MALDI MSI) as well as new generation genetic techniques (expression microarrays).

The expected results will allow for more precise characterization of 1,2,4-triazole-3-thione derivatives with respect to their potential application in pharmacotherapy of epilepsy including drug-resistant epilepsy, which would show new possible directions of research into antiepileptic drugs.