## Reg. No: 2021/41/N/NZ7/01181; Principal Investigator: mgr Marcin Konrad Jakubiec

Epilepsy is one of the most common neurological disorders, with frequency of occurrence about 1-2% in population. It is a disease with an extremely complicated and multifactorial pathomechanism. Clinically, it manifests as spontaneous and recurrent seizures resulting from abnormal brain bioelectrical activity. Despite the fact that currently the treatment has a large amount of newer and newer preparations, pharmacotherapy does not always bring the desired effect. Patients who have seizures that do not efficiently respond to currently available anticonvulsant drugs are claimed to have drug resistant epilepsy. Drug resistance of epilepsy has recently become a serious clinical problem, as it affects up to 40% of patients. Uncontrolled seizures significantly reduce the quality of life of patients and may contribute to an increased risk of psychosocial disorders, psychiatric and medical complications, and in extreme cases may lead to premature death. Currently, antiseizure drugs are used as monotherapy or in combination therapy (polytherapy) to control seizures in patients with drug resistant epilepsy. The main advantages of monotherapy are reduced risk of drug interactions, side effects and lower costs. Nevertheless, most patients require at least two drugs. Therefore, therapy with application of multifunctional molecule, which use a single chemical capable of simultaneous interaction with different molecular targets, appears to be a promising approach, potentially eliminating the problems of polytherapy such as differences in pharmacokinetics, numerous side effects, and an increased risk of drug-drug interactions. Considering the above facts, the further search for new multifunctional anticonvulsants effective in various types of epilepsy, especially in drug resistant epilepsy, is fully justified. Additionally, neuropathic pain is another serious neurological disorder and affects 7-10% of the general population. It is worth mentioning that only 50% of patients manage to reduce neuropathic pain by 30–50%. Interestingly, currently antiseizure drugs, apart from antidepressants, are the most commonly used drugs in the pharmacotherapy of neuropathic pain. It is postulated that this pharmacological group is suitable for the treatment of neuropathic pain, e.g. through a complex mechanism of action. Considering the above facts, the search for new substances with unique analgesic properties in the group of potential antiseizure drugs is fully justified.

The main aim of the presented project is to obtain a series of original compounds characterized by broad activity in animal models of seizures. These molecules can be considered as potential candidates for the treatment of various types of epilepsy, including tonic-clonic seizures, focal seizures and the aforementioned drug resistant epilepsy. Taking into consideration the similarities in the pathophysiology of epilepsy and neuropathic pain, it is postulated that the proposed substances may also act as potent analgesics. Therefore, another aim of the project is to identify the active substance in animal models of pain.

The project results can significantly contribute to the development of a new chemical class of multifunctional antiseizure drugs, effective especially in drug resistant epilepsy (but also in other types of epilepsy, e.g. generalized tonic-clonic seizures as well as focal seizures) and in neuropathic pain; hopefully with a satisfactory safety profile in both *in vivo* and *in vitro* studies. It should be emphasized, that the multifunctional compounds can be effective especially in the treatment of neurological diseases with high drug resistance, such as the aforementioned epilepsy and neuropathic pain.