Since 1967, the first epidemic of Ebola virus (EBOV) infection, frequently occurring outbreaks of hemorrhagic fever are characterized higher and higher mortality rate. Symptoms of infection begins with flu like symptoms and progress rapidly to the final stage of hemorrhagic fever which are characterized by multisystem manifestations including gastrointestinal (vomiting, diarrhea), respiratory (breath shortness, chest pain), vascular (hypotension, edema, bleeding) and neurologic (confusion, coma) symptoms. Direct contact, contact with body fluids or with contaminated clothes or lines of an infected primate leads to the transmission of the virus. The unpredictable onset, simplicity of transmission, fast progression of disease, high fatality and lack of approved effective vaccine or therapy make the Ebola virus classified as a one of the most dangerous bioterrorism agents. Therefore the developing of specific treatment is necessary. The most specific part of EBOV lifecycle is entry to the host cell, where Niemann-Pick C1 protein (NPC1) plays an important role allowing the release of RNA into the cytoplasm and initiate replication. To prevent infection and effectively block the spreading of virus at an early stage, inhibition of NPC1 is necessary. Therefore, the main aim of this project is to design and search for new NPC1 inhibitors.

The primary scientific objective of the project is to develop the theoretical tools in a form of virtual screening cascade allowing for the prioritization of chemical compounds in terms of their potential inhibitory activity against NPC1. The protocol will consist of several subsequent steps (prefiltering, pharmacophore mapping, docking protocol ADMETox filter, clustering, visual inspection) which select the most valuable structures. The protocol will be applied for evaluation of virtual combinatorial library of compounds (created within this project) and selection for the synthesis (at Institute of Organic Chemistry and Analytical Chemistry in Orleans, ICOA) or purchasing (from commercial databases of organic compounds) the most promising structures.

At least one scientific publication in journal from the Master Journal List will be notable effects of the research. In addition, the project results will be presented at both international and national conferences and Medicinal Chemistry Department will be the first scientific center in Poland involved in the search of anti EBOV agents. The implementation of the program will also enhance the candidate experience in management of independent scientific project. .