

TSL-1502

Overview

DNA is damaged all the time but when they are damaged beyond a certain point, the cell will die. In order to repair DNA damage, the body uses tumor suppressor genes such as BRCA and other proteins such as Poly-ADP Ribose Polymerase (PARP) to fix the damaged DNA. The tumor suppressor gene is defective in cancer and the cancer cells can only be repaired by using PARP. By inhibiting PARP with medications such as PARP Inhibitors, apoptosis will be induced in cancer cells due to damaged DNA and the growth of the tumor will be obstructed.

The initial clinical testing of PARP inhibitors began nearly a decade ago, following the discovery that these agents in vitro had heightened anticancer activity in cancer cells that harbored BRCA mutations compared to BRCA wild-type cancer cells with intact DNA repair. Research proved that fault in either of BRCA 1 and BRCA 2 genes have an increased risk of certain types of cancer such as breast cancer, ovarian cancer, and prostate cancer. Cells are less likely to repair themselves if there is a fault in either one or both genes. Blocking PARP with a PARP inhibitor showed impressive results in preventing the proliferation of cancer cells by interfering with their DNA repair mechanism and killing them, thus resulting in a therapeutic outcome.

Product Description

Compared with current FDA approved PARP Inhibitors, TSL-1502 is a pro-drug and its metabolite TSL-1502M has higher localized concentration at cancer sites with more potency, thus, our preclinical studies demonstrated that TSL-1502's anticancer activity is superior to competitor(s) while having a much wider therapeutic window.

Safety and Efficacy

TSL-1502M, active metabolite of TSL-1502, inhibited PARP1/PARP2 enzymes with a lower IC50 value than that of the reference competitor. TSL-1502 did not have significant inhibitory effect on PARP enzymes. TSL-1502M inhibited PARP activity in breast cancer cell with IC50 value lower than that of the reference competitor. In single dose oral toxicity studies, TSL-1502 was orally administered to animals and no significant adverse side effects were noted for TSL-1502 in the animal studies on the cardiovascular, nervous, and respiratory systems in the rat and dog models at beyond human equivalent dose.

Developmental Stage

TSL-1502 is a small molecule drug, ready for clinical investigation (INDs) under both Chinese FDA (cFDA) and US FDA regulations. A clinical phase I open labeled dose-escalation study is currently being conducted in patients with advanced solid tumor in China under cFDA regulation to evaluate the safety, tolerability, and pharmacokinetics, and an IND was granted a green light by the US FDA in April 2019. A phase II clinical trial will be managed and conducted in the USA. TSL-1502 is positioned to have strong PCT patent protections. Patents cover chemical structure, chiral auxiliary structures, crystal form, synthesize methods, and all potential indications.

Available for out-license or co-development.