# PHARMACEUTICAL COMPOSITION COMPRISING A PRMT5 INHIBITOR AND AN EGFR INHIBITOR

## TECHNICAL FIELD

The present disclosure belongs to the field of medicine, and specifically relates to a pharmaceutical composition comprising a PRMT5 inhibitor and an EGFR inhibitor.

## BACKGROUND

Cancer is among the leading causes of death worldwide. Popular treatments, such as chemotherapy and immunotherapy, are limited in that their cytotoxic effects are not restricted to cancer cells and can also cause adverse side effects in normal tissues.

PRMT5 is a type II arginine methyltransferase that regulates important cellular functions, including cell cycle progression, apoptosis, and the DNA damage response, by symmetrically dimethylating proteins involved in transcription and signal transduction. However, data from genome-wide genetic perturbation screens using shRNA revealed a selective requirement for PRMT5 activity in MTAP-deleted cancer cell lines (Kruykov et al., 2016; Marjon et al., 2016, and Markarov et al., 2016). The accumulation of MTA caused by MTAP deletion in these cell lines partially inhibits PRMT5, making these cells selectively sensitive to additional PRMT5 inhibition.

Certain PRMT5 inhibitors have been developed, but they do not show selectivity for MTAP-deleted cancer cell lines. This lack of selectivity could be explained by the inhibitors' mechanism of action, as they are either SAM-uncompetitive or SAM-competitive inhibitors and therefore independent of MTAP (Kruykov et al., 2016; Marjon et al., 2016, and Markarov et al., 2016).

By using inhibitors that bind PRMT5 non-competitively or cooperatively with MTA, selectivity for MTAP-deleted/MTA-accumulating cells can be improved. PRMT5 inhibitors