

## Identification of WAC-224, a Novel Anticancer Quinolone as a Human Topoisomerase II Inhibitor

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Topoisomerase II inhibitors, such as Anthracyclines, are an important class of chemotherapeutic agents, which are employed for the treatment in multiple types of cancers including acute myeloid leukemia (AML). However, the therapeutic applications of Anthracyclines are limited because of a cumulative cardiotoxicity and an efflux-mediated drug resistance. WAC-224 is a novel anticancer quinolone derivative targeting human topoisomerase II and has the superior characteristics in potency and safety both *in vitro* and *in vivo* compared with Vosaroxin (QINPREZO<sup>®</sup>, formerly SNS-595), which showed lower potential for cardiotoxicity in the clinical trials. In our evaluations, WAC-224 had higher selectivity for cancer cells versus normal cells in its antiproliferative activity; the IC<sub>50</sub> value was 1.4 nM for MV4-11 AML cell line versus > 50 μM for MRC-5 normal cell line. WAC-224 also showed the potent *in vitro* activity against multi drug-resistant cell lines such as MES-SA/Dx-5. Additionally, *in vivo* murine xenograft studies confirmed the potent therapeutic effects of WAC-224 for therapy of different types of cancers including multi-drug resistant one. These results suggest that WAC-224 is a potentially effective therapeutic agent for leukemia and multi-drug resistant cancers.