UC San Diego
MOORES CANCER CENTER
An NCI-designated Comprehensive Cancer Center

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"IND enabling studies of LT-415 a novel chemotherapeutic agent with a unique target"

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This project is founded on the identification of a new class of cancer drug leads called the seriniquinones discovered by Dr. Fenical at SIO as part of a program to identify novel types of chemotherapeutic agents. The seriniquinones were found to be highly potent in a cytotoxicity screen, and subsequent chemical characterization disclosed that they are completely new chemotypes. Structure-activity studies have now nominated LT-415 as a lead compound for development. LT-415 is of particular interest for several reasons. First, inhibits a completely new target in the cell, a protein called dermicidin, that is involved in malignant progression and metastasis, but which is not targeted by any other existing cancer drug. Second, dermicidin is highly expressed in melanomas and breast cancers, and testing to date has shown that LT-415 is very effective against the B16 melanoma in vivo. Third, LT-415 is very potent; it is effective against melanoma at the 10 nM level. Fourth, LT-415 does not produce toxicity in murine models at doses that are effective at inhibiting tumor growth. Fifth, LT-415 is a small molecule with chemical characteristics that make it very attractive as a drug. Sixth, LT-415 shows clear selectivity in the NCI-60 cell line panel. Seventh, the seriniquinone discovery, as well as numerous synthetic derivatives, has been protected by US patents and now form the foundation for transition to IND and subsequent development. Taken together, these features make LT-415 a very interesting candidate for development. The overall goal of this project is to advance LT-415 through several of the key steps needed to secure an IND for this molecule. It is our hypothesis that LT-415 will have the efficacy, pharmacokinetic toxicology characteristics needed for and IND and that it will eventually be shown to have clinical activity through a completely novel mechanism of interaction with dermcidin.