

## SYNERGISTIC COMBINATION AGENT FOR CANCER THERAPY

### SUMMARY

The Nanotechnology Characterization Laboratory of the Frederick National Laboratory for Biomedical Research seeks parties interested in collaborative research to co-develop a ceramide and vinca alkaloid combination therapy for treatment of cancer.

### REFERENCE NUMBER

E-007-2011

### PRODUCT TYPE

- Therapeutics

### KEYWORDS

- ceramide
- vinca alkaloid
- autophagy
- cytotoxicity

### COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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### DESCRIPTION OF TECHNOLOGY

Work by the Nanotechnology Characterization Laboratory (NCL), a joint initiative of NCI, NIST, and the FDA, has led to the discovery of a novel combination chemotherapy. This combination is shown to have synergistic effects on cytotoxicity to cancer cells in vitro, and to cause a substantial decrease in tumor growth in preclinical tumor models in vivo. Combination therapy using these agents may enhance the response rate of different cancers to these drugs and may significantly reduce side effects by permitting a lower therapeutic dose to be administered.

SAIC Frederick's Nanotechnology Characterization Laboratory seeks parties interested in collaborative research to co-develop a ceramide and vinca alkaloid combination therapy for treatment of cancer. Potential commercial applications include cancer treatment, especially for cancers sensitive to treatment with vinca alkaloids such as breast cancer, testicular cancer, head and neck cancer, Hodgkin's

lymphoma, and non-small cell lung cancer.

The instant invention relates to a novel combination of ceramide and vinca alkaloids, which synergistically decrease cancer cell growth without increasing the toxicity profile compared to the individual drugs. The drug combination has been rigorously evaluated in both in vitro and in vivo models of cancer, and a dose range-finding toxicology study has been conducted in rodents.

This combination induces cell death via a novel mechanism (induction of autophagy with simultaneous blockade of autophagy flux). This mechanism appears to impart selectivity of the therapy to cancer cells.

#### Development Status:

- The drug combination has been evaluated in both human hepatocarcinoma models (in vitro cell culture assays) and human colon cancer models (in vivo mouse xenografts).
- Additional in vivo studies with other cancer types and early stage preclinical toxicology studies are being planned.

#### POTENTIAL COMMERCIAL APPLICATIONS

- Treatment for cancers such as breast cancer, testicular cancer, head and neck cancer, Hodgkin's lymphoma, and non-small cell lung cancer

#### COMPETITIVE ADVANTAGES

- Vinca alkaloids alone at therapeutic doses produce the standard side effects of cancer chemotherapy.
- The vinca alkaloid-ceramide combination can be administered at lower doses with comparable efficacy and may allow for more frequent dosing (metronomic dosing).
- The novel mechanism of action of this combination appears to be selective to cancer cells.

#### INVENTOR(S)

[Stephan Stern](#) (NCI)

#### DEVELOPMENT STAGE

- Pre-clinical (in vivo)

#### PATENT STATUS

- **U.S. Filed:** U.S. Provisional Patent Application No. 61/451,925 filed March 11, 2011
- **Foreign Filed:** PCT Application No. PCT/US2012/028567 filed March 9, 2012

#### THERAPEUTIC AREA

- Cancer/Neoplasm