

MARSHALL EDWARDS INC RELEASE  
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## ONCOGENE PUBLISHES PHENOXODIOL DATA

### ***Yale Researchers Find Phenoxodiol Overwhelmingly Effective for Treating Chemo-Resistant Ovarian Cancer Cells; Data Published in Nature Publishing's Oncogene***

(Washington, D.C. April 30, 2003 – 7:01pm EST) -- Phenoxodiol, a synthetic anti-cancer drug manufactured by Novogen, has been found in laboratory studies to induce cell death in 100 percent of ovarian cancer cells, including those cells resistant to conventional agents such as paclitaxel and carboplatin. The tests were conducted on human cell lines at Yale University School of Medicine.

The drug works by altering a signal pathway in cancerous cells that otherwise does not allow unhealthy cells to die. These findings indicate that the drug could be successful at treating other cancer types as well. The study is published in the May 1 issue (Volume 22:17) of Oncogene, published by The Nature Publishing Group, and funded in part by a grant from the National Cancer Institute.

A phase II trial using phenoxodiol is underway at Yale University, for women with chemo-resistant ovarian cancer. Phenoxodiol is supplied by Marshall Edwards Inc. (LSE-AIM: MSH), a subsidiary of Novogen, Limited, Sydney, Australia.

Five phase I human trials with phenoxodiol are complete and show few if any side effects. Preliminary results of a trial conducted at the Cleveland Clinic found that over half of the 10 patients tested on the experimental drug showed some response. Each of these patients had different types of advanced cancer that did not respond to chemotherapy.

In the published study, the Yale research team determined that phenoxodiol induces cell death in primary ovarian cancer cells by inducing apoptosis, and that it restores the sensitivity of ovarian cancer cells to "Fas-mediated" apoptosis, one of the main death receptors for cancer cells that is otherwise turned off in ovarian cancer cells.

"For years Yale researchers have studied cells of women with chemo-resistant ovarian cancer," said Graham Kelly, PhD., Executive Chairman, Marshall Edwards, Inc. "They used these samples to predict which chemotherapy agents are most likely to work on which particular women. So when phenoxodiol was tested, they were surprised to see that our compound kills all ovarian cancer cells, regardless of their resistance to chemo agents."

Gil Mor, M.D., associate professor, department of obstetrics and gynecology, Yale School of Medicine, believes this is accomplished because phenoxodiol interrupts two key signaling pathways of cells, known by researchers as FLIP and XIAP, which in turn regulate the survival of ovarian cancer cells. Phenoxodiol stops FLIP and XIAP from inhibiting cell death.

The researchers also tested phenoxodiol in mice and found that when dosed at 20mg/kg every day for six days there was a three-fold reduction in tumor mass compared to a control group. No side-effects were noted.

In the laboratory at Yale, the researchers treated petri dishes with ovarian cancer cell lines with phenoxodiol, and found a significant decrease in cell viability in all the ovarian cancer cell cultures.

Ovarian cancer is the most lethal gynecological malignancy and is the fifth leading cause of all cancer deaths in women. Although the initial response to chemotherapy is greater than 80 percent, the majority of ovarian cancer ultimately recurs due to resistance to chemotherapy.

"Phenoxodiol may unlock a mystery that has been plaguing cancer researchers – how to get a cancer cell to die when it for some reason has been programmed to live," said Dr. Mor M.D. "Apoptosis, or cell death, happens to cells in our bodies all of the time – and that's good – because all cells must eventually die and be replaced.

"But when it doesn't happen to cancer cells, that's when problems occur. A key objective in cancer therapy is to restore sensitivity to apoptosis. It's our hope that phenoxodiol does that," said Dr. Mor.

Under U.S. law, a new drug cannot be marketed until it has been investigated in clinical trials. After the results of these trials are submitted in a new drug application to the FDA, the FDA must approve the drug as safe and effective before marketing can take place.

Novogen (NASDAQ: NVGN) is a world leader in the research and development of drugs derived from its phenolic technology platform. The company manages its international research and development programs utilizing the expertise

and clinical research capabilities of universities and hospitals in the U.S., Australia and other key international locations. The oncology compound phenoxodiol is being developed by the Company's listed subsidiary Marshall Edwards Inc. (LSE-AIM: MSH).

More information on phenoxodiol and on the Company can be found at [www.marshalledwardsinc.com](http://www.marshalledwardsinc.com) and [www.novogen.com](http://www.novogen.com).

Marshall Edwards Inc. is listed on the London Stock Exchange's Alternative Investment Market (MSH) and is 95 per cent owned by ASX and NASDAQ-listed Novogen Limited (ASX: NRT, NASDAQ: NVGN)

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