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Phase II Clinical Trial Is First for Drug Known to Unblock Death Receptors Vital to Destruction of Cancer Cells

Marshall Edwards Inc. Begins Trial of Phenoxodiol at Yale University School of Medicine for Women with Ovarian Cancer

(December 10, 2002 -- Washington, D.C.) U.S. pharmaceutical company, Marshall Edwards, Inc. (LSE-AIM: MSH), today announced an important advance for its anti-cancer drug, phenoxodiol, with the establishment at Yale University School of Medicine of a Phase II clinical trial in women with recurrent ovarian and fallopian cancers.

Phenoxodiol will be assessed for its ability to halt the growth or to shrink tumors in women with ovarian or fallopian cancer who have failed other forms of chemotherapy. Phenoxodiol will be the only anti-cancer drug to be used in these women.

The trial is part of a multi-center, multi-national study. Yale University is the only U.S. site participating in this trial. Thomas Rutherford, M.D., Ph.D., Associate Professor of Gynecologic Oncology and Gil Mor, M.D., Associate Professor of Obstetrics and Gynecology will lead the trial.

A total of approximately forty women who have already failed other forms of chemotherapy will be enrolled in the trial in the first instance. Patients will receive phenoxodiol by intravenous injection on two consecutive days per week for a treatment cycle lasting 12 weeks. The clinical end-points will include tumor mass, tumor markers, and one-year survival.

"We have had particularly exciting results with phenoxodiol in the laboratory, finding that phenoxodiol was able to induce cell death in ovarian cancer cells that proved to be resistant to the effects of all other drugs, including those presently in use for the treatment of ovarian

cancer," said Dr. Mor. "We have good evidence as to why this is happening, and we look forward to seeing the drug tested in women with this difficult form of cancer."

"In Yale laboratories, we could not find another compound as promising as phenoxodiol for this form of cancer," said Dr. Rutherford. "We look forward to seeing how the compound will work in our patients."

Dr. Graham Kelly, Executive Chairman of Marshall Edwards Inc, stated that the significance of this phase II trial is that phenoxodiol is the first drug in Phase II trials that switches off production within cancer cells of the main anti-apoptotic proteins, FLIP and XIAP. These proteins have been identified recently as being critically important to the ongoing survival of many forms of human cancer, including ovarian cancer. The targeting of these proteins by drug therapy has become a major focus of oncologists.

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

Phenoxodiol Regulates Death Receptor Activity

Phenoxodiol is a pan-acting anti-cancer drug. That is, it is active against all forms of human cancer tested to date, and it kills cancer cells by inducing apoptosis (programmed cell death). It does this by allowing activation of the death receptors, a characteristic that researchers at Yale described earlier this year.

The death receptors are a family of proteins on the surface of all cells that, when activated, lead immediately to the death of the cell. These receptors (Fas, TNFR1, DR3, TRAIL) are activated by the immune system and trigger the cell to self-destruct through a process of auto-digestion, or apoptosis. The death receptors and apoptosis are important to our health, allowing the body's immune system to kill a cell whenever it is damaged or when it is required to die as part of normal tissue remodeling.

Normal cells prevent accidental triggering of this mechanism by producing blocking proteins (known as anti-apoptosis proteins such as FLIP and XIAP) that block low level activation of the death receptors. A damaged cell normally shuts off production of these anti-apoptosis proteins, thereby allowing the immune system to trigger apoptosis by contacting the death receptors.

Cancer cells resist this process by producing large amounts of blocking proteins such as FLIP. In this way, cancer cells are protected from the body's attempts to destroy the cancer cells. Switching off the production of these blocking proteins in cancer cells leads immediately to their death. For this reason, these blocking proteins have become recognized as an important new target for a new generation of anti-cancer drugs. However, the challenge has been how to knock out production of proteins such as FLIP and XIAP in cancer cells without having a similar effect in non-cancer cells.

Research conducted at Dr. Mor's laboratories at Yale University School of Medicine confirmed phenoxodiol as the first drug to achieve this outcome. Phenoxodiol potently switches off the production of anti-apoptotic proteins in human cancer cells in a highly

selective manner. In the laboratory, phenoxodiol is highly effective at killing ovarian cancer cells that are resistant to the killing effects of all other known anti-cancer drugs.

Five Phase I Trials Completed, Excellent Safety Profile

Phenoxodiol has been used in a total of 65 patients in Phase I trials worldwide. These trials have involved patients with end-stage solid cancers that have become refractory to standard chemotherapy. The drug has exhibited a highly satisfactory safety profile, with no side-effects attributed to the drug. A number of patients have been reported by the clinicians to have exhibited anti- tumor responses.

Ovarian Cancer is a Major Cause of Death

Ovarian cancer (including fallopian cancer) is the fourth leading cause of cancer-related death in women in the United States. It is the leading cause of cancer death from gynecologic malignancies. In 2002, it is estimated that 23,300 new cases will be diagnosed in the United States and 13,900 deaths will occurⁱ. One out of one hundred women will die from ovarian cancer. The high mortality is largely related to the absence of early symptoms. Approximately 80 percent of patients are diagnosed in advanced stages of the disease. Even in properly diagnosed patients with stage I or II disease, the five year survival ranges from 50 to 90 percent depending on the degree of tumor differentiation. Patients will respond to initial chemotherapy in 80 to 90 percent of cases, yet less than 10 to 15 percent will remain in remission. Advances in treatment have led to improved five-year survival, approaching 45 percent, however there have been no advances made in overall survival.

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.

More information on phenoxodiol can be found at www.novogen.com and www.marshalledwardsinc.com.

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ⁱ Anonymous, 2002. CA Cancer J Clin 52: 23-47