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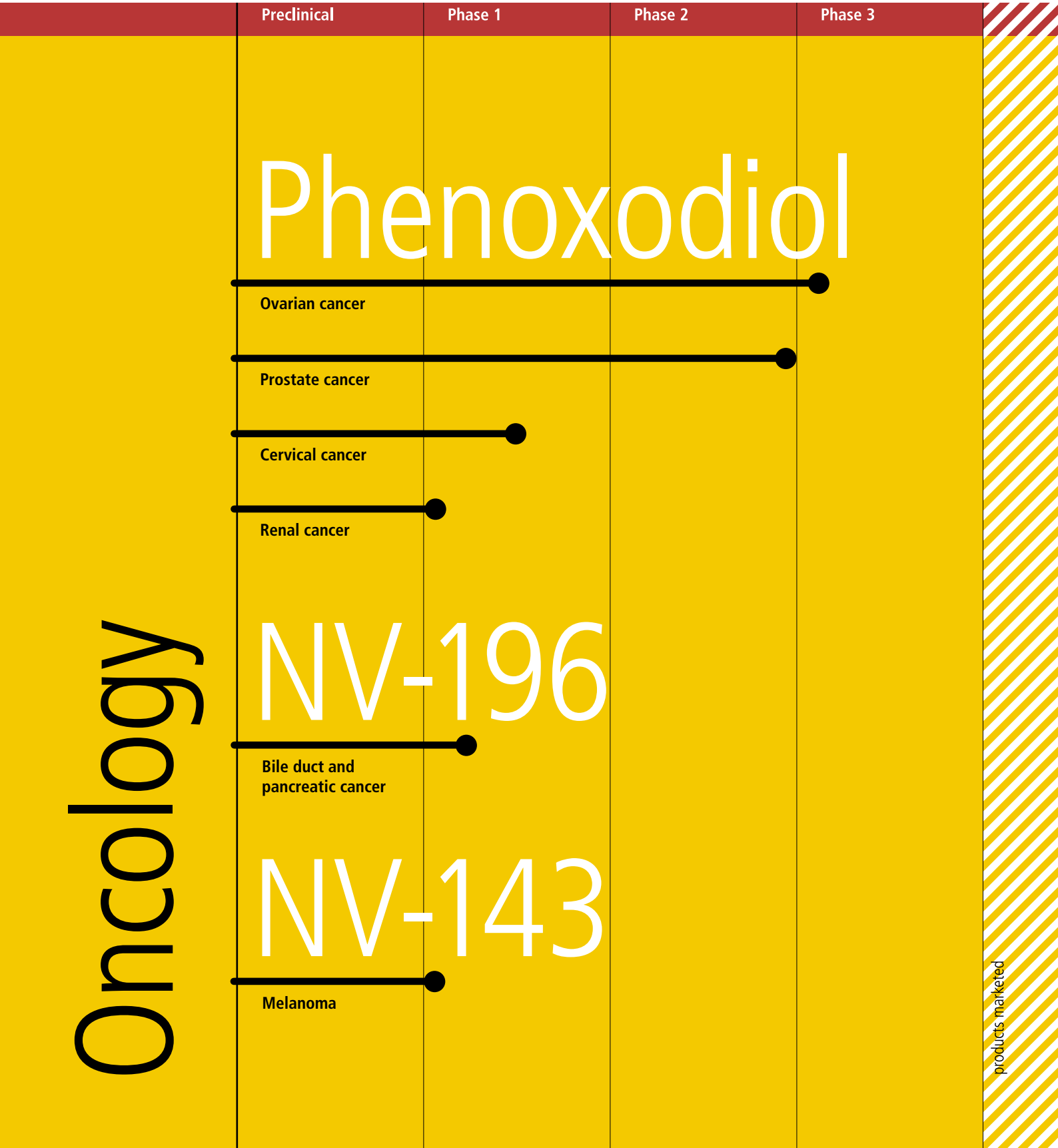
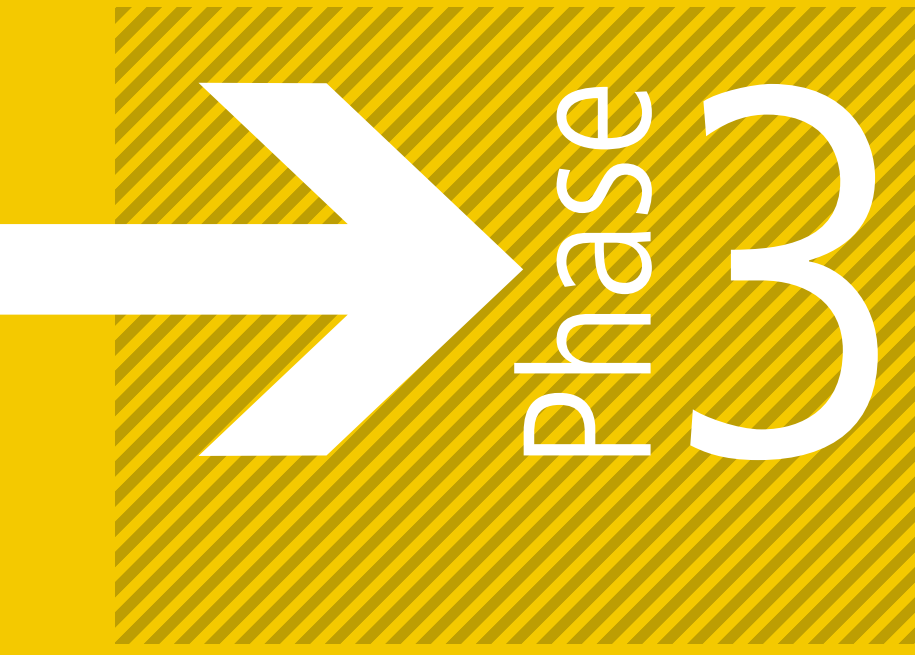
MARSHALL EDWARDS INC



Phenoxodiol

FDA approval granted under Special Protocol Assessment (SPA) scheme to commence Phase 3 trial for ovarian cancer.

The first therapeutic indication being sought for phenoxodiol is as a chemosensitiser for carboplatin in patients with ovarian cancer that has become refractory or resistant to at least two lines of platinum therapy. The compound demonstrated efficacy in this setting in Phase 2 studies which led to phenoxodiol being granted Fast Track Approval status by the FDA in 2004. This offers the opportunity for the drug to be assessed for Accelerated Approval during its pivotal study. Accelerated Approval can occur following an interim analysis early in the study where evidence of efficacy based on an agreed surrogate endpoint (approved under the SPA scheme) can lead to the drug being granted marketing approval, while the Sponsor continues to study the drug to provide proof that the drug leads to a survival benefit.



A 15 month odyssey

The Phase 3 OVATURE study has undergone considerable progress towards initiation over the past 15 months. MSHL has worked closely with the FDA on the OVATURE Study. The company retains the services of the Health Care division of one of the largest law firms in the US to advise on regulatory matters, including helping to guide the regulatory strategy and to co-ordinate the liaison with the FDA.

Mindful of the fact that a number of pivotal drug studies by other companies over the past 2 years have received criticism by the FDA for their inadequate design, MSHL has sought to design this pivotal study in a way that is compatible with the latest FDA guidelines. This is always challenging because of the inevitable shift in official thinking over time as different clinical studies conclude and yield data that varies from the unexpected to the contentious. There are few absolutes in the oncology field, each set of data being considered on its own merits, and often the cause of considerable debate between the sponsor and the agency.

The design of this pivotal study has been an exhaustive process that commenced with the appointment of a Steering Committee (comprising sponsor representatives and respected oncologists), which then consulted with senior oncologists from the UK and US who had agreed to participate in OVATURE and to be Principal Investigators for their hospitals. Overseeing the whole design process and liaising with the FDA, is the company's Washington-based legal and regulatory representatives.

Pursuant to a meeting with the FDA in late 2004, a study design was selected that was finally ratified by a meeting of 20 international oncologists in Florida in April 2005. That design was duly submitted to the FDA for its approval under the IND (Investigational New Drug) scheme in May 2005, a default scheme where a trial can start unless blocked by the FDA for reasons such as safety concerns. That submission coincided with the completion by another major pharmaceutical company of a large study of an anti-cancer drug for use in late-stage lung cancer patients. The FDA had earlier granted Accelerated Approval status on the basis of an apparent delay in tumour progression but a continuation of the study failed in the FDA's view to provide ultimately any overall survival benefit. The rescinding by the FDA of regulatory approval for that drug in that particular indication is the subject of ongoing discussion.

A major consequence of this experience was to cause the FDA to review its policy concerning Accelerated Approval, an entirely unanticipated outcome, but one which obliged MSHL to undertake a major re-design of the OVATURE study. A new design subsequently was discussed with the FDA, using a design that involved a novel approach by which reversal of chemoresistance could be tested. However, MSHL considered it prudent to test this novel, highly stringent approach in a pilot study using a small group of patients with late-stage ovarian cancer. Sufficient data subsequently was generated by that pilot study to allow the re-designed protocol to be lodged with the FDA in November 2005.

That protocol has now been agreed between MSHL and the FDA and will provide the basis for two determinations by the FDA – the first being consideration for Accelerated Approval following the interim analysis, and the second being consideration for New Drug Approval status following the final analysis. Based on this agreement OVATURE will now proceed, with patient enrolment commencing in Q306.

In the meantime MSHL, along with the Contract Research Organisation retained for project management, has used the available time to establish the trial infrastructure and to select and appoint hospital sites within the US, Europe, UK and Australia.

The ability to manufacture the considerable quantity of drug product required for a Phase 3 clinical trial also has been developed in this interim period.

Joint study with Sanofi-Aventis and Yale University enrolling patients.

The following study is currently enrolling patients at Yale-New Haven Hospital, Connecticut, USA: **'A Randomized Placebo-Controlled Phase Ib/IIa Safety, Tolerability and Efficacy Study of Oral Phenoxodiol in Combination with Docetaxel versus Docetaxel Alone in Patients with Recurrent Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer.'**

The purpose of this study is to test the ability of phenoxodiol to restore sensitivity to docetaxel (Taxotere™, Sanofi-Aventis) in patients who have failed prior taxane therapy. This follows on from laboratory studies at Yale which showed that phenoxodiol had a potent ability to reverse resistance in ovarian cancer cells to docetaxel. Sixty (60) patients will be randomised to either docetaxel alone or a combination of docetaxel and phenoxodiol.

The objectives of this study are as follows:

Primary objective:
- to determine the safety and tolerability of combination therapy of oral phenoxodiol + docetaxel in patients with recurrent ovarian cancer.

Secondary objective:
- to determine the effect of phenoxodiol on the toxicity of docetaxel using a weekly treatment regimen;
- to determine if combination therapy of phenoxodiol + docetaxel is more efficacious than docetaxel therapy alone;
- to determine if combination therapy of phenoxodiol + docetaxel affects blood levels of either drug;
- to determine phenotypic differences in the tumor cells of 'responders' and 'non-responders.'

Cervical Cancer

Phenoxodiol proves to have anti-cancer effect in cervical cancer.

The following study is enrolling patients at Yale-New Haven Hospital, USA, and shortly at other US hospitals: '**Phase Ib study of Neoadjuvant Use of Oral Phenoxodiol in Patients with Primary Diagnosis of Squamous Cell Carcinoma or Adenocarcinoma of the Cervix, Vagina or Vulva.**'

There are two main reasons for conducting this study. The first is to provide incontrovertible, biological evidence that the oral dosage form of phenoxodiol exerts an anti-tumour effect when used as a mono-therapy, and to determine the most effective dose. The nature of these types of gynaecological malignancies is conducive to this objective. In this study, women with a primary diagnosis of cancer of the cervix, vagina or vulva are receiving daily phenoxodiol therapy at one of three doses for up to 28 days prior to surgical resection of the cancer. This is known as a neoadjuvant treatment trial, where a drug is added to normal surgical management in order to evaluate the drug's effectiveness without disturbing normal management of the cancer. In this case, each patient has granted permission for investi-gators to gain access to the tumour both before phenoxodiol commences and at the time of surgical resection. The effect of phenoxodiol therapy on tumour size, rate of tumour cell death, and the level of phenoxodiol within the cancer are all being measured.

The company has already reported on the results from women who have completed the 2 lower doses of 50mg and 200mg phenoxodiol per dose. Radiology has confirmed that as little as 28 days of phenoxodiol therapy has been sufficient to halt tumour growth in many cases and in some cases even to lead to tumour shrinkage.

Prostate Cancer

Marshall Edwards, Inc. is also committed to the development of phenoxodiol as a treatment for prostate cancer. Following the successful completion of a Phase 2 study where phenoxodiol was used as a second-line therapy in men with hormone-refractory prostate cancer, the company currently is engaged in collaboration with urologists internationally in the development of a clinical program where phenoxodiol will be evaluated both as a monotherapy in early-stage prostate cancer and as a chemo-sensitiser for standard therapy in late-stage prostate cancer. A Prostate Cancer Steering committee has been established to advise the company on this program, and the company anticipates being able to inform shareholders during 2006 of the details of this program.

Phase 2 Complete

At the 200 mg dose, all of the 8 patients showed stable disease over this period, with 2 of the 8 patients showing a 19% and 20% reduction in the diameter of their tumour. It has also been shown that phenoxodiol accumulates in the tumour tissue, indicating that the oral dosage form is a suitable, bioavailable form of this drug.

While the use of phenoxodiol to treat these gynae-cological tumours is of considerable clinical interest in offering a prospective therapeutic option, the primary interest in testing this form of cancer relates to the second objective in conducting this study which is to test the place for phenoxodiol in early-stage or even pre-malignant cancer. Testing that hypothesis requires a form of cancer which is readily diagnosed early, and where the course of the disease is readily followed. Cervical cancer is one such cancer, where PAP smears and colposcopy are able first to diagnose and then to track the course of this disease. This opportunity is possible also because of the safety of phenoxodiol, making chemotherapy in patients with very early-stage cancer feasible.

NV-196

A novel and potentially new anti-cancer drug with a highly selective tumour-killing effect.

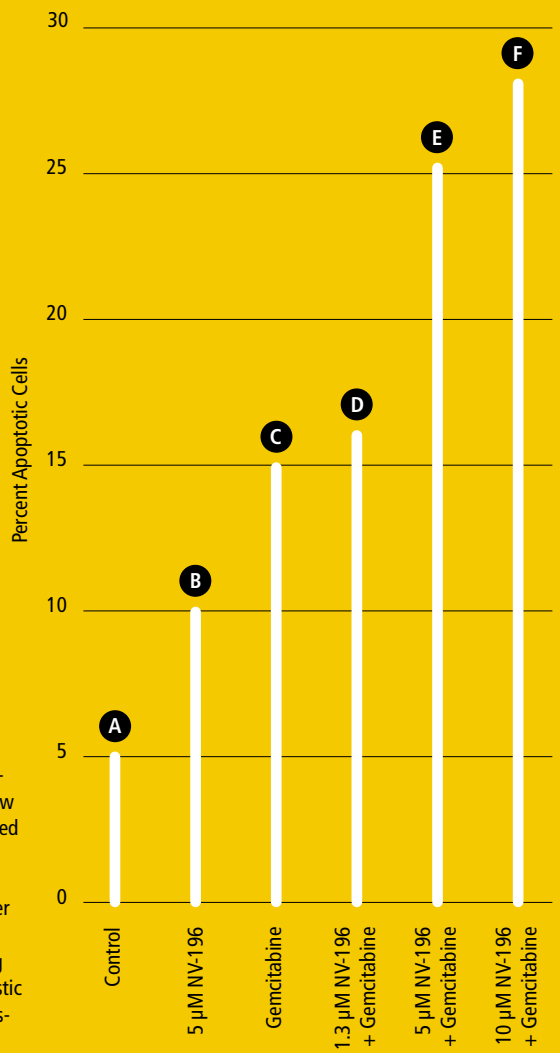


Figure 1. The percent of pancreatic cancer cells which die by apoptosis (programmed cell death) as a result of treatment with gemcitabine, NV-196 or a combination of both drugs. Untreated cells (A) display very low levels of apoptosis, but increased cell death is observed when cells are treated with NV-196 (B) or gemcitabine (C). However a combination of both drugs is more effective than either drug alone (D, E, F) and this synergistic effect is magnified with increasing doses of NV-196.

NV-196 is the second drug in the oncology pipeline to enter the clinic. Closely related structurally to phenoxodiol, and sharing the ability of phenoxodiol to kill a wide range of cancer cells and to reverse resistance in those cells to standard anti-cancer drugs, NV-196 has a substantially different biological profile, marking it a highly attractive new drug candidate.

The clinical development program for NV-196 currently is planned to focus on its use as an orally-delivered, chemosensitising agent, intended for use in conjunction with standard chemotoxic anti-cancer drugs for the treatment of pancreatic cancer, cholangiocarcinoma (cancer of the bile duct), and possibly malignant melanoma.

The differential effect of NV-196 compared to phenoxodiol is thought to be associated with its ability to kill cancer cells via the TRAIL family of death receptors, compared to the Fas death receptor, the main pathway through which phenoxodiol induces tumour cell death. The differential effect of NV-196 and phenoxodiol on a tumour cell's death receptor mechanisms is thought to account for the drug's substantially greater activity against pancreatic cancer, cholangiocarcinoma, and melanoma.

In common with phenoxodiol, the tumour-killing effect of NV-196 is highly selective, with little effect on non-tumour cells. The safety of NV-196 has been confirmed in animals at what is expected to be therapeutically effective doses. An initial Phase Ia study has been conducted in a small number of cancer patients, confirming that oral NV-196 is absorbed, and showing that short-term dosing with NV-196 is without toxicity.

The promising potential of NV-196 in pancreatic cancer is demonstrated by its effect *in vitro* in pancreatic cancer cell lines that are highly resistant to the drug gemcitabine, the standard therapy for patients with advanced pancreatic cancer. In the example shown in Figure 1, NV-196 is able to kill MIAPaCa-2 pancreatic cancer cells on its own and to chemo-sensitise the ability of gemcitabine to kill these particularly chemo-resistant cells. Similar results have been achieved with cholangiocarcinoma cells, also notoriously chemoresistant, and for which there are no approved chemotherapies.

NV-196 shows significant promise as a selective radiosensitiser.

On the basis of impressive preclinical data NV-196 will be tested initially in patients with pancreatic cancer and cholangiocarcinoma, both of which show poor sensitivity to standard chemotoxic drugs and which carry a poor prognosis when diagnosed in late-stage. In addition, having in mind *in vitro* activity of NV-196 against a broad range of cancer cells, its application to other cancer indications will continue to be evaluated.

The next step in the clinical program is to conduct Phase I studies intended to define the safety and efficacy of NV-196 when given over sustained periods of time to patients with solid cancers. That will define the dose to be taken into Phase II trials in combination with gemcitabine in patients with pancreatic cancer and cholangiocarcinoma.

Pancreatic cancer and cholangiocarcinoma usually are diagnosed at a late stage, are usually inoperable (approximately 15% and 20% of patients, respectively, undergo surgery) and have a very poor survival rate. Pancreatic cancer is the fourth most common cause of cancer-related mortality with the death rate >98%. According to the American Cancer Society, an estimated 33,730 new cases of pancreatic cancer are expected to occur in the US in 2006 and about 4,000 people in the US will develop bile duct cancer each year.

Radiosensitisation refers to the ability to enhance the killing effect of radiotherapy on cancer cells. Procedures used range from hyperthermia, to lowering the oxygen tension, to drugs. Each of these modalities has produced a modest increase in the effectiveness of the radiotherapy at best, but in each case has had the unwanted consequence of enhancing the side effects of the radiotherapy as a result of their non-specificity.

NV-196 has proven in the laboratory to be a potent radio-sensitiser in certain tumour cell types, and to achieve this effect selectively, that is, without any effect on non-tumour cells (Figure 2). In conjunction with a number of different radiobiology research institutes around the world, Novogen currently is active in further exploring the potential for NV-196 to be a selective radiosensitiser in a range of cancers where radiation is standard therapy, including cancer of the breast, lung, and head and neck.

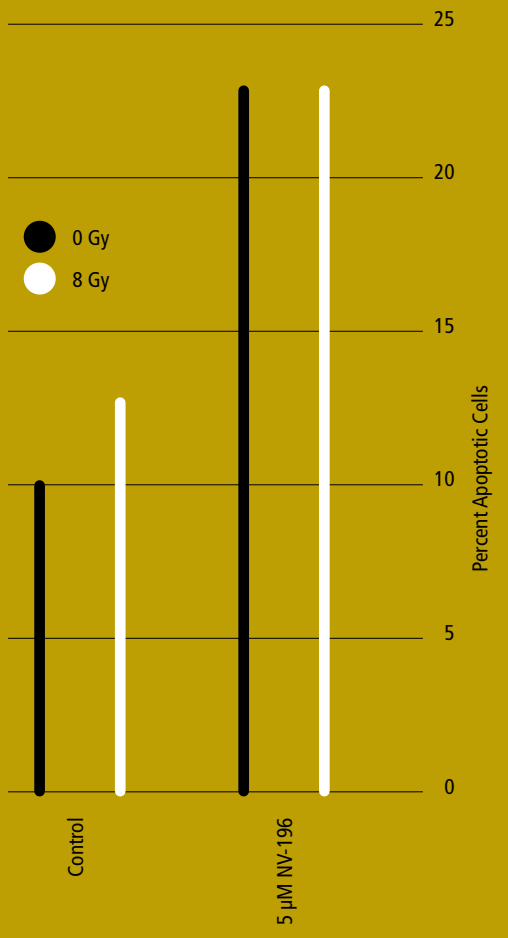


Figure 2. The percentage of pancreatic cancer cells entering apoptosis as a result of radiotherapy at each of two doses of radiation (0 Gy and 8 Gy) is enhanced by pre-treatment of cells with NV-196.

NV-143

NV-143 is a companion molecule to NV-196 being co-developed for the treatment of malignant melanoma.

In preliminary laboratory screening studies, NV-143 was identified as a candidate for product development because if its broad activity against cancer cells representative of melanoma, glioma, prostate, ovarian, breast and lung cancer, but like phenoxodiol and NV-196, NV-143 does not exhibit toxicity against normal cells.

NV-143 has been shown to have especially potent activity against melanoma both in vitro and in mice. Studies have also been performed to assess the ability of NV-143 to chemosensitize melanoma cells to those drugs used in the clinic to treat melanoma (such as platinum derivatives and decarbazine). These studies have indicated that NV-143 is able to synergistically chemosensitize melanoma cancer cells to these drugs.

Melanoma is a cancer that begins in skin melanocytes, most often appearing on the trunk of fair-skinned men and on the lower legs of fair-skinned women, but it can appear other places as well. Melanoma is much less common than basal cell and squamous cell skin cancers, but it is far more serious. While melanomas are almost always curable in early stages, the cells spread to other parts of the body, and metastatic disease is highly aggressive and difficult to treat with conventional therapies.

Melanoma accounts for about 4% of skin cancer cases, but it causes most skin cancer deaths. The number of new cases of melanoma in the United States is on the rise. The American Cancer Society estimates that in 2006 there will be 62,190 new cases of melanoma and about 7,910 people will die of the disease.

The pre-clinical development of NV-143 will progress to provide information on the mechanisms of action and to obtain toxicology data sufficient to enable human clinical studies to be performed.