



PRESS RELEASE

Further enquiries:

Northbank Communications Ltd
Dr Douglas Pretsell or Sue Charles
Tel: +44 (0)20 7886 8150
d.pretsell@northbankcommunications.com
s.charles@northbankcommunications.com

PowderMed Ltd
Dr Clive Dix
Tel: +44 (0)1865 501 549
clive.dix@powdermed.com

LUDWIG INSTITUTE FOR CANCER RESEARCH AND POWDERMED INITIATE A PHASE I CLINICAL TRIAL FOR A NOVEL THERAPEUTIC CANCER VACCINE

Phase I clinical trial of therapeutic cancer vaccine commences in New York, in patients with non-small cell lung cancer (NSCLC), using PowderMed's novel DNA-on-Gold technology

Oxford, UK, 17th September 2004 – PowderMed Ltd (PowderMed), a company focusing on the development of therapeutic DNA vaccines, in collaboration with its partner, the Ludwig Institute for Cancer Research (LICR), have announced that they have initiated a Phase I trial of a novel therapeutic DNA cancer vaccine that uses DNA encoding for the NY-ESO-1 tumour specific antigen and the Particle Mediated Epidermal Delivery (PMED™) technology owned by PowderMed.

The trial, being carried out at the Weill Medical College of Cornell University in New York, will be conducted in patients with non-small cell lung cancer (NSCLC) and will recruit up to 18 patients with NSCLC stages IIIA, IIIB or IV. This clinical trial forms part of the Cancer Vaccine Collaboration (CVC), which is an innovative clinical research program designed and directed by LICR and the Cancer Research Institute in New York.

DNA vaccines offer a promising new therapeutic intervention for a wide range of cancers. By stimulating the immune system to produce cytotoxic T-cells and antibodies specifically directed against cancer cells, these vaccines direct the immune system to attack and control or even remove the cancerous tissue. The therapeutic DNA vaccine being developed by PowderMed and LICR elicits an immune response that targets cells expressing the NY-ESO-1 cancer antigen on their surface. NY-ESO-1, discovered and patented by LICR, is expressed by many different types of human tumours and it is one of the most highly immunogenic tumour antigens discovered to date, eliciting both cellular and humoral immune responses, a combination that is best suited to attack tumours. Such characteristics make vaccines based upon NY-ESO-1 potentially useful for treating a sizeable percentage of cancer sufferers.

Dr Clive Dix, CEO of PowderMed, said:

“When we launched PowderMed in May of this year we indicated that five of our programmes would enter clinical development before the end of 2005. This trial is our first step towards that commitment, but is also our first step in demonstrating why the PowderMed technology is ideal for cancer therapy.”

PowderMed's therapeutic vaccines use the company's proprietary PowderJect® DNA particle mediated epidermal delivery (PMED) technology, which uses DNA bound to microscopic gold particles that are propelled at high speed into the skin. PMED is particularly well suited for therapeutic vaccines, which require the induction of both humoral and cellular immunity.

Commenting on the clinical trial, Dr. Eric Hoffman, the Director of LICR's Office of Clinical Trials Management, said:

"The goal of this CVC trial is to evaluate the ability of NY-ESO-1 DNA formulated on gold particles to induce an antigen-specific immune response. We consider the PMED technology to have great potential as a means of safely and effectively delivering cancer antigens".

- ends -

NOTES FOR EDITORS

1. **About PowderMed Ltd – www.powdermed.com**

PowderMed Ltd, a leader in the development of therapeutic DNA vaccines, based in Oxford, UK, was launched in May 2004 as a management spin out of the PowderJect therapeutic DNA vaccine programmes, previously owned by Chiron Vaccines. The Company has the rights to the PowderJect® DNA -particle mediated epidermal delivery (PMED) technology which it plans to use, in the first instance, in the development of therapeutic vaccines in the areas of chronic viral diseases and cancer. PowderMed has five preclinical lead programmes targeting genital herpes, hepatitis B, genital warts, HIV/AIDS (partnered with GSK) and lung cancer (partnered with Ludwig Institute for Cancer Research).

2. **About the Ludwig Institute for Cancer Research – www.licr.org**

The Ludwig Institute for Cancer Research (LICR) is the largest international academic institute dedicated to understanding and controlling cancer. With ten Branches in seven countries, and numerous Affiliates and Clinical Trial Centers in many others, the scientific network that is LICR quite literally covers the globe. The uniqueness of LICR lies not only in its size and scale, but also in its philosophy and ability to drive its results from the laboratory into the clinic. LICR has developed an impressive portfolio of reagents, knowledge, expertise and intellectual property, and has also assembled the personnel, facilities, and practices necessary to patent, clinically evaluate, license, and thus translate, the most promising aspects of its own laboratory research into cancer therapies.

3. **PowderJect® DNA particle mediated epidermal delivery (PMED™) technology**

Using the PowderJect device, DNA precipitated onto microscopic gold particles, is propelled by pressurised helium gas at near supersonic speeds into the epidermis. The microscopic gold particles (mean particle diameter 1 - 3 microns) are used as the carrier because they have the appropriate size and density needed to deliver the DNA directly into the immunologically active antigen presenting cells (APCs) of the epidermis. These cells have a mean diameter 20 microns and thus the microscopic gold can easily enter the cell. Studies have shown that once inside the nuclei of APCs, the DNA elutes off the gold and becomes transcriptionally active, producing the encoded protein that when presented by the APCs to lymphocytes, triggers strong T-cell mediated immune responses. It is this ability of PMED to produce a robust and reproducible T-cell mediated immune response to a broad range of viral

and cancer antigens, that provides PowderMed with its unique competitive advantage in the field of therapeutic vaccines.

4. Therapeutic vaccines

Therapeutic vaccines are a new class of product, which harness the immune system in order to produce a therapeutic effect. The PowderJect technology has previously been tested in the clinic as a vaccine for prophylaxis against Hepatitis B but will be used by PowderMed in the development of therapeutic vaccines for chronic viral diseases and, in the present instance, cancer.

5. Non-Small Cell Lung Cancer

Lung cancer is the leading cause of cancer-related deaths. There are 177,000 new cases of lung cancer per year in the United States. Despite continuous development of chemotherapeutic agents, the five-year survival of patients with lung cancer remains at only 13%.

Over 80% of lung tumors are non-small cell lung cancer (NSCLC) and only 30% of patients with the diagnosis of NSCLC are surgical candidates. The remaining 70% are considered unresectable due either to locally advanced (stages IIIA or IIIB) or metastatic (stage IV) disease. Thus, while surgery currently offers the only hope for cure, few patients are amenable to such treatment. While complete resection for early stage NSCLC is possible, patients nonetheless face a high rate of recurrence. The recurrence rate for stage I disease is as high as 40%.

6. A therapeutic vaccine targeting NY-ESO-1

PowderMed has produced a DNA Plasmid (pPJV7611), which encodes the NY-ESO-1 protein. PPJV7611 is precipitated onto the surface of gold particles 1 to 3 μ M in diameter and will be administered to patients by particle mediated epidermal delivery (PMED).

NY-ESO-1 antigen, which was discovered by LICR, is expressed in a range of human cancers, including melanoma, breast cancer, prostate cancer, lung cancer, ovarian cancer and bladder cancer. NY-ESO-1 shows restricted expression in normal tissues, with high-levels found only in the germ line cells in testis. Since germ line cells do not carry HLA molecules on their surface they cannot present antigens to T cells.

To date, over 100 patients with NY-ESO-1 expressing tumors have received NY-ESO-1 vaccination using various formulations. This clinical data has established an extensive safety profile for NY-ESO-1, with toxicities limited to Grade 1 or 2 injection site reactions or flu-like symptoms, e.g., fever, malaise, etc. Vaccination with these agents has generated or enhanced NY-ESO-1 specific antibodies and CD8+ T-cells in the majority of patients whose serum and/or^{TT} blood has been subjected to standardised immune monitoring.

7. Phase I Clinical trial in Non-Small Cell Lung Cancer (NSCLC) patients

Phase I clinical trials are the first trials of a drug in humans. They are usually short term trials in a small number of individuals designed to evaluate preliminary safety of a compound in the human. In the present trial, up to 18 patients with NSCLC stages IIIA, IIIB or IV expressing either NY-ESO-1 or LAGE-1 (an antigen closely related to NY-ESO-1) will have the vaccine administered via PMED on three occasions over a twelve-week period. Over that time the vaccine's safety will be assessed in the patients through blood tests and an assessment of likely adverse drug reactions.

8. The Cancer Vaccine Collaborative

The Cancer Vaccine Collaborative (CVC) is a partnership between two not-for-profit academic institutions, the Cancer Research Institute and the Ludwig Institute for Cancer Research, which has developed an unparalleled programme that conducts a systematic analysis in humans comparing immunological approaches to the creation of therapeutic cancer vaccines through a coordinated global effort. This clinical trial forms part of the CVC. Unlike conventional, stand-alone trials—where data from one trial are often incomparable to data from another because of the number of uncontrolled variables between the two—investigators for the CVC will use standardised tests to evaluate different ways to deliver the same vaccine agent, the antigen NY-ESO-1. This standardised methodology and data collection will allow for direct comparison with other trials in the CVC and help the researchers understand why certain vaccine strategies might result in a more robust immune response while others might not.

9. The Cancer Research Institute

Since its inception in 1953, the Cancer Research Institute (CRI) has had a singular mission—to foster research that will yield an understanding of the immune system and its response to cancer, with the ultimate goal of developing immunological methods for the control and prevention of the disease. To accomplish these goals, CRI supports scientists at all stages of their careers and funds every step of the research process, from basic laboratory studies to clinical trials testing novel immunotherapies. Guided by a Scientific Advisory Council, which includes 4 Nobel Prize winners and 24 members of the National Academy of Sciences, CRI awards fellowships and grants to scientists around the world. Additionally, the Institute has more recently taken on a new leadership role in the areas of preclinical and clinical research by serving as the integrating force and facilitator of collaborations among leading experts. CRI has thus become a catalyst for accelerating the development of cancer vaccines and antibody therapies.