PowderMed’s Therapeutic DNA Vaccine for Chronic Hepatitis B Enters Phase I Clinical Trials in Patients

Oxford, UK, 29 March 2006 …PowderMed, the immunotherapeutics company focused on the development and manufacture of DNA-based vaccines for viral diseases and cancer, has announced that its dual-antigen encoding immunotherapeutic for Hepatitis B (HBV) has received US IND approval together with approval from the Singapore, Hong Kong and Taiwanese Regulatory Authorities and has entered Phase I Clinical Trials. The study will primarily evaluate the safety and tolerability of the HBV immunotherapeutic, pdpSC18, administered by PMED™, PowderMed’s needle-free delivery technology, in patients with chronic hepatitis B infection, both in combination with lamivudine and as monotherapy. Additionally, assessments of immunogenicity and clinical response will be made.

Worldwide HBV affects 350 million people and there are no commercially available therapeutic vaccines for the treatment of chronic HBV infection. Chronic infection occurs in 98% of newborn children infected by vertical transmission from the mother (the most common means of transmission in Asia-Pacific), and in 5% of individuals infected after 2 years of age. About 25% of these patients will progress to cirrhosis and 20% of this subgroup will develop hepatocellular carcinoma – one of the most common cancers worldwide.

Welcoming this study and the potential for a novel therapeutic vaccine to HBV, Dr Antonio Bertoletti, of the Center for Molecular Medicine, Singapore, said:

“Patients with chronic hepatitis B show a state of relative hypo-responsiveness of HBV-specific T cells compared with that demonstrated in patients who control the virus replication after acute infection. Therapeutic induction and/or activation of the T-cell response for HBV core and surface proteins may have the potential to control infection. It has been shown that Hepatitis B surface (HBsAg) and core antigen (HBCAg) induces envelope-and core specific CD4+ and CD8+ T-cell responses and that the response against the Hepatitis B core antigen (HBCAg), is often associated with viral control. The combination of these two genes in PowderMed’s pdpSC18 HBV therapeutic DNA vaccine, thus provides a potential mechanism to both clear the virus via the CD8+ response and to overcome unresponsiveness in chronically infected patients via the CD4+ response.”

This Phase I, First Time in Human Study will enrol patients at seven sites in SE Asia (Singapore, Taiwan, Hong Kong) and the USA. Since the immunological response and hepatic tolerability of the hepatitis B immunotherapeutic would be expected to differ considerably between non-infected subjects and subjects with active hepatitis B disease, the Phase I clinical study will enrol subjects with active hepatitis B disease in order to specifically address both safety and immunogenicity in the most predictive manner possible. Each subject will participate in the study for a period of up to 27 weeks, plus a 4-week run-in and screening period. Allowing for the planned safety reviews between dosing cohorts and a 4-month recruitment window, results can be expected during 2007.

Commenting on the trial, Dr John Beadle, PowderMed’s Chief Medical Officer, said:

“Given the limitations of the currently available treatment regimens for chronic Hepatitis B, a regimen, either as a monotherapy or combination, that could provide enhanced clearance of virus, seroconversion, a reduction in resistant strains or a reduction in post-treatment
exacerbations of hepatitis would be highly desirable. The concept of a novel DNA therapeutic vaccine to boost the immune response to the virus and promote viral clearance is thus an attractive and timely novel therapeutic strategy in an area of substantial unmet medical need.”

Phase I clinical trials of a prophylactic DNA Vaccine containing only the HBsAg gene (pPWRG7128) in 95 subjects, showed that vaccination via PMED™ was generally well tolerated both locally and systemically, and resulted in seroprotective levels of antibodies and measurable cell-mediated immune responses.

NOTES FOR EDITORS


PowderMed is a private immunotherapeutic company based in Oxford, UK. The Company is focused on the clinical development and manufacture of therapeutic and prophylactic DNA-based vaccines for viral diseases and cancer. The company has 4 clinical and 3 pre-clinical stage projects. The lead clinical programme has shown positive Phase I results in the treatment and prevention of human influenza. This technology is uniquely and easily adaptable to treat avian flu and to address the pandemic threat. PowderMed also has a product for the treatment of genital herpes in Phase I trials, and two partnered Phase I programmes in Cancer (Ludwig Institute for Cancer Research) and HIV/AIDS (Glaxo SmithKline). PowderMed vaccines are delivered using PMED™ (Particle mediated epidermal delivery), a needle-free, painless delivery system that requires minimal medical training, allows self-administration and requires no refrigeration for stockpiling. Specifically, PowderMed’s technology delivers DNA to the epidermal layer of the skin where it is presented to the cells of the immune network, thereby creating immunity and thus facilitating both treatment and prevention of disease.

The Company has a highly experienced management team that has a combined 160 years of experience, with Rolf Stahel as the chair of the board. The Company has sufficient funds through to the end of 2006 having raised £20 million in venture financing to date, with an additional £5 million available from its existing investor syndicate that comprises Abingworth Management, Advent Venture Partners, Isis College Fund, Oxford Bioscience Partners and SV Life Sciences.

2. PowderJect® 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 of 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 DNA-based vaccines.

3. Chronic Hepatitis B in Man

Hepatitis B virus (HBV) is responsible for the most common form of parenterally transmitted viral hepatitis. Approximately 350 million people worldwide are persistent carriers of the virus. 75 percent of all carriers are of Asian origin and the disease is endemic in these regions. It is a major cause of acute and chronic infections of the liver with significant associated morbidity and mortality. HBV is a non-cytopathic virus and liver injury is mainly mediated by the host immune
response against virus-infected liver cells and by the production of inflammatory cytokines. A vigorous T cell response is believed to be responsible for the elimination of the hepatitis B virus.

There are no commercially available therapeutic vaccines for the treatment of chronic HBV infection. Treatment for chronic hepatitis B infection is limited to immunomodulators (Interferon alpha (IFN-α)) and antiviral agents.

Immunisation seeks to exploit the adaptive immune response either by inducing protective immune responses prior to infection (prophylactic immunisation) or by representing antigenic components of persistent infectious organisms to revitalise immune responses that are insufficient to effect clearance of the pathogen (therapeutic immunisation).

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