



Commencement of Clinical Study of Cogane™ in Patients with Parkinson's disease

GODMANCHESTER, Cambridgeshire, UK, 20 April 2009, Phytopharm plc today announces the commencement of a safety, tolerability and pharmacokinetic (PK) study of its orally active neurotrophic factor inducer PYM50028 (Cogane™), which will involve both healthy volunteers and patients with Parkinson's disease (PD). This follows approval from the Medicines and Healthcare Products Regulatory Agency (MHRA) and Research Ethics Committee to commence recruitment for the UK study.

In pre-clinical models, Cogane™ reverses the changes in the area of the brain involved in Parkinson's disease by inducing the body's own production of proteins known as neurotrophic factors. In particular, one of these factors known as "GDNF" has been shown to be particularly effective in re-growing damaged nerves. Since GDNF is a protein it cannot be given orally (in pill or liquid form) because it is degraded in the stomach and intestine, and also does not readily cross the blood-brain barrier. GDNF can work only when injected into or when produced inside the brain. Direct injection of GDNF into the area of the brain involved in Parkinson's disease has shown substantial beneficial effects in small-scale clinical studies but requires highly complex and difficult surgical procedures. Cogane™, which can be taken orally, readily crosses the blood-brain barrier and stimulates the release of GDNF in the brain and therefore has the potential to overcome many of the difficulties associated with GDNF administration.

The current study, to be conducted on a part residential, part out-patient basis, will employ a randomised, double-blind, multiple dose-ascending, placebo-controlled design to evaluate the safety, tolerability and PK profile of a new oral solution formulation of Cogane™ when taken for up to 28 days at various dose levels. In total, 18 healthy male and female volunteers and up to 18 male and female patients with PD aged between 40-80 years, are planned to be enrolled with doses being escalated sequentially following a safety review at each dose level.

The primary objective of this study is to confirm the safety and tolerability of Cogane™ in healthy subjects and PD patients when administered at these dose levels for up to 28 days, the secondary objective being to determine the plasma PK profile of Cogane™ in these subjects.

Significantly, the range of doses to be administered in this study has been selected to target plasma levels of Cogane™ equating to therapeutically relevant concentrations in preclinical disease models. The PK data from this study should facilitate dose selection for a Phase IIb proof-of-concept study in PD patients.

Mr Sandy Morrison, Interim CEO of Phytopharm, commented: "Pre-clinical studies with Cogane™ have been highly encouraging in reversing the changes in the area of the brain involved in Parkinson's disease. We are very pleased to have commenced this safety, tolerability and pharmacokinetic study of Cogane™ and look forward to reporting the results of this trial and continuing the development of an orally administered product that can stimulate production of GDNF in the brain, thus overcoming the difficult surgical problems associated with direct GDNF injection into the brain."

Dosing of the first group of enrolled subjects has commenced with enrolment expected to be completed in Q3 of this year and the results reported in Q4.

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Notes to Editors

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Phytopharm plc

Phytopharm is a pharmaceutical development and functional food company. Our products are developed from medicinal plants, thereby reducing the development risk, cost and time to market. As a virtual company, Phytopharm's model is centred on a lean cash burn with all laboratory, manufacturing and clinical work out-sourced to specialists, while core competencies such as strategy and management are maintained in-house. Close collaboration with charitable organisations enhances our interaction with Key Opinion Leaders and accelerates our development programmes increasing their value.

Cogane™

Cogane™ (PYM50028) is a novel non-peptide, orally bioavailable neurotrophic factor inducer that readily crosses the blood brain barrier. In pre-clinical studies, Cogane™ stimulates the release of neuronal growth factors such as GDNF, increases neurite outgrowth and *protects* against neuronal degeneration. Importantly, Cogane™ also *reverses* the decrease of GDNF and *reverses* dopaminergic neuronal degeneration observed *in vitro* and *in vivo*. When administered orally to pre-clinical models of Parkinson's disease, Cogane™ reverses the loss of dopaminergic neurones.

The Michael J. Fox Foundation

The Michael J. Fox Foundation funding is supporting our preclinical studies to determine the optimal dosing requirements for Cogane™ and is being carried out by Dr Jonathan Brotchie, a Senior Scientist at the Toronto Western Hospital and part of the University Health Network (UHN) in Toronto, Canada. Dr Brotchie is a recognised expert in the field of Parkinson's disease. Founded in 2000, The Michael J. Fox Foundation for Parkinson's Research is dedicated to ensuring the development of a cure for Parkinson's disease within this decade through an aggressively funded research agenda. The Foundation has funded \$112 million in research to date. More information on the Foundation is available at www.michaeljfox.org.

Parkinson's disease

Parkinson's disease is a movement disorder characterised by muscle rigidity, tremor, a slowing of physical movement (bradykinesia) and, in extreme cases, a loss of physical movement (akinesia). The primary symptoms are the result of altered signalling of an area of the brain, *the striatum*, responsible for the control of movement. This is caused by degeneration of dopaminergic neurones between the *striatum* and the *substantia nigra* part of the brain leading to insufficient formation and action of dopamine. Parkinson's disease is therefore termed a neurodegenerative disease. The disease is slow in onset and the appearance of symptoms reflects the gradual loss of dopaminergic neurones.

The prevalence of the disease is estimated to be 100 to 200 per 100,000 population (Source: Datamonitor). In the US alone, there are estimated to be one million patients with diagnosed Parkinson's disease with associated healthcare costs to the economy of \$25 billion (Source: Northwest Parkinson's Foundation submission to US Congress). Parkinson's disease can affect people of any age, though the incidence is higher in older people. Individuals will experience varying combinations of the symptoms, each with differing degrees of severity. The cause of Parkinson's disease in the majority of

cases is unknown (idiopathic Parkinson's disease), though some cases have been found to have a hereditary component (familial Parkinson's disease) and possible mechanisms include oxidative damage of nerve cells coupled with loss of neurotrophic factors. Neurotrophic factors such as GDNF are essential for the survival and maintenance of nerve cells and provide protection against toxic insults, however as proteins, their utility as pharmacological treatments are limited (Source: Michael J. Fox Foundation for Parkinson's Research).

At present, there is no cure for Parkinson's disease, but a variety of medications provide relief from the symptoms, usually by dopamine replacement therapy either by L-DOPA, which is converted to dopamine in the *striatum*, or by dopamine agonists which act on the dopamine receptors to restore normal motor function (control of movement). However, both treatments cause either less dopamine to be released by the brain or the dopamine receptors to become progressively less sensitive, thereby eventually increasing the symptoms of the underlying Parkinson's disease. There is an urgent need for the development of new approaches to this debilitating condition and non-peptide orally bioavailable neurotrophic factor inducers which readily cross the blood brain barrier represent an important new therapeutic approach.

For further information about Phytopharm please see our website at <http://www.phytopharm.com>