



## PRESS RELEASE

**P1vital establishes pre-competitive consortium in  
CNS Experimental Medicine with AstraZeneca, GlaxoSmithKline,  
Lundbeck, Organon – part of Schering-Plough and Wyeth  
*£4 million investment accelerates research into mental illness***

Oxford, UK, 8 January 2008. – P1vital Limited (“P1vital”) announces that it has entered into a consortium agreement with AstraZeneca Pharmaceuticals LP, GlaxoSmithKline, Lundbeck, Organon – part of Schering-Plough and Wyeth to establish and validate healthy volunteer CNS Experimental Medicine models.

Under the agreement P1vital and its consortium partners will fund a series of studies over a period of three years to establish the sensitivity of healthy volunteer CNS Experimental Medicine models and to validate their ability to detect the efficacy of novel compounds. The studies will be carried out by P1vital in collaboration with five internationally renowned academic clinical psychopharmacology groups in the UK based at the University of Bristol, Cardiff University, the Institute of Psychiatry, the University of Manchester and the University of Oxford. The objective of the studies is to validate existing healthy volunteer models and to develop novel models in the areas of anxiety, cognitive disorders, depression and schizophrenia. The initial studies will validate new surrogate biomarkers for positive, negative and cognitive deficits in schizophrenia. In depression, the consortium will validate an “at risk” group (dysphoric volunteers) using a recently established emotional test battery as a surrogate population for depressed patients. In cognitive disorders, studies will focus on two recently developed virtual reality models and examine their utility for the early detection of cognitive deficits in Mild Cognitive Impairment (MCI) and schizophrenia. Studies will also investigate the potential efficacy of antidepressant drugs in treating anxiety disorders using an experimental model of anxiety.

Dr Colin Dourish, Chief Executive of P1vital commented:

"The consortium agreement combines the expertise of the P1vital, Pharma and academic clinical research teams in a highly innovative approach to the development of new treatments for psychiatric disorders."

Dr Gerry Dawson, Chief Scientific Officer at P1vital commented:

"We already have in place an agreed research programme and have established an excellent rapport between the clinical research teams which will enable the consortium to get off to a flying start."



Dr Gersham Dent, Director of Discovery Medicine at AstraZeneca commented:

"AstraZeneca is pleased to be a member of the P1vital Consortium because we have great hopes that it will help AstraZeneca bring innovative medical treatment to patients that suffer from psychiatric disorders".

Dr Robert Alexander, Vice President, Psychiatry Clinical Pharmacology and Discovery Medicine at GlaxoSmithKline commented:

"The GSK Psychiatry Centre of Excellence for Drug Discovery is committed to the development of innovative treatments for psychiatric disorders. We are therefore excited to join the P1vital Consortium in their efforts to develop validated translational approaches which we believe will aid in the development of our compounds."

Dr Anders Gersel Pedersen, Senior Vice President for Development at Lundbeck commented:

"By combining expertise from several academic and Pharma units in the P1vital Consortium we strengthen the efforts in developing new models and methods that will optimise clinical drug development and in the end be to the benefit of patients."

***This news release contains forward-looking statements that reflect the Company's current expectation regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the uncertainties relating to the development of new medicines and the regulatory process.***

***– ends –***



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## Notes to Editors

### **CNS Experimental Medicine and Drug Development for Psychiatric Disorders**

The principal cause of compound failure in clinical development is insufficient efficacy and safety (accounting for approximately 30% and 20% respectively of all failures). This is a particular problem in CNS drug development which has a lower than average chance of success due to the poor translation from preclinical models to clinical efficacy. Experimental or translational medicine (defined as the 'Investigation undertaken in human beings to identify mechanisms of pathophysiology or disease, or to test the validity and importance of new discoveries or treatments, relating where appropriate to model systems') aims to address this problem and currently has a very high priority in both academic and industrial arenas.

In the preclinical arena both academia and industry have contributed to a significant increase in fundamental knowledge, new experimental techniques and, indeed, whole new classes of candidate compounds for the treatment of psychiatric disorders. However, clinical translation of these findings to benefit patients has to date been very limited. Almost all of the medicines we think of as new, atypical antipsychotics for example, were conceived as refinements of previous treatments. The failure, to date, to translate the innovations of molecular biology to the clinical arena has been disappointing. For example, preclinical and early clinical studies with novel putative antidepressants have often identified promising trends that have not been confirmed by the results of subsequent Phase 3 studies. Unfortunately, placebo controlled trials are difficult to conduct in patients with the type and degree of depression that most requires pharmacologic intervention. What remains are populations for study in which placebo response rates are high thereby confounding detection of positive treatment effects. Attempts to compensate for poor signal detection by increasing sample size has often led only to very expensive failed trials. Thus, there is a growing gap for many Pharma companies between their pre-clinical portfolio and willingness to invest in such large scale clinical studies.

Moreover, despite the very large existing global market for CNS drugs, the spiralling costs of drug development (including lost opportunity costs) are beginning to discourage investment in this very important therapeutic area. Even for "me too/me better" drugs the average cost of development is currently estimated to be in excess of \$1000 million. In the absence of any clear successes, it is very difficult to calculate the costs of development for truly novel CNS drugs, a fact which can have a chilling effect on those in some pharmaceutical companies who must decide on whether to risk the unknown. Consequently, both the lack of translation from promising preclinical data to clinical efficacy and the rising cost of drug development have highlighted an evident gap between pre-clinical promise and failure in large scale clinical trials. In addition, this has occurred at a time when the number of compounds entering the clinic has quadrupled due to the introduction of robotic screening technology some 5-10 years ago. Initially, this huge increase in research productivity moved the bottlenecks in drug discovery from screening to preclinical toxicology. More recently as capacity in preclinical toxicology was increased the bottleneck has moved further downstream to early clinical development where the lack of predictive efficacy screening assays is now clearly evident.



It is increasingly recognised that the introduction of experimental and translational medicine models at the interface between Phase 1 and Phase 2 clinical trials is potentially a significant step forward for CNS drug development. Such studies bridge the gap between animal and human studies and have the potential to accelerate clinical trials by providing rapid Go/No-Go decisions. The studies can use volunteers or small patient groups but importantly employ experimental design in a laboratory setting to introduce rigour and harder endpoints for measurement.

While this strategy commands a broad consensus, the tactics to enable its development are in their infancy. If, using their own limited resources, any one pharmaceutical company were to attempt to develop and validate experimental medicine models as effective decision making tools for the development of new drug treatments, progress would be slow and very expensive. The fragmentation implied by this analysis is counter-productive at a fragile stage in the development of this new approach. Moreover, expertise in experimental medicine resides largely in clinical academic centres of excellence that have access to volunteers and patients to develop such models. P1vital's solution is to initiate a coordinated effort across academia and industry by establishing a pre-competitive consortium to develop technology in this key area of clinical drug development. The advantage to companies that join the consortium is that new technology is developed more rapidly than could be achieved using in-house resources alone and at a fraction of the cost. Thus, there is the efficiency of scale, coordination and funding that a pre-competitive consortium brings. An additional advantage is the increased interaction between industry and academic scientists and the intangible benefit that accrues when each group achieves a better understanding of the others needs and a reduction of the potentially very high cost of standardisation across clinical study sites. Furthermore, the consortium will increase the employment of academic clinical research facilities that exist around the UK and offer important training and development opportunities for young scientists interested in clinical pharmacology research, who need to acquire the necessary skills to develop the area of experimental and translational medicine to reach its full potential. The funding of a large scale project of this kind has required significant investment from P1vital's Pharma partners. However, the ability and expertise to achieve the objectives has been harnessed and the consortium has the potential to achieve international success which will provide both scientific insight and economic benefit. Ultimately, the healthcare benefit to society is likely to be acceleration of the launch of new and more efficacious treatments for psychiatric disorders.

### **P1vital**

P1vital is a clinical research company that specialises in CNS Experimental Medicine. The company has established a high quality CNS clinical research organisation in the UK based on a unique range of Experimental Medicine models of psychiatric disorders and obesity. The founders, Dr Dourish (CEO) and Dr Dawson (CSO) are both experienced Pharma scientists who recognised the need for pharmaceutical companies to make more rapid and effective decisions in Phase 1 and Phase 2 clinical development of drugs for CNS disorders. The company was incorporated in October 2004 and has its' Head Office at the University of Oxford, Department of Psychiatry in the Warneford Hospital. P1vital has established a UK network of university hospitals and clinical research facilities and an Advisory Panel of internationally renowned psychopharmacologists and psychiatrists.



**P1vital's** clinical trials are managed by experienced physicians and scientists to a standard that is acceptable to the Pharma industry for early decision making. **P1vital** has synergistically combined its' CNS drug discovery and development expertise with the strong clinical science base in the UK to create a worldwide centre of excellence for the refinement and validation of CNS Experimental Medicine models. **P1vital's** Experimental Medicine models enable their pharmaceutical company clients to focus and accelerate their CNS clinical development programmes. For company information please visit [www.p1vital.com](http://www.p1vital.com).

#### **AstraZeneca**

AstraZeneca is a major international healthcare business engaged in the research, development, manufacture and marketing of prescription pharmaceuticals and the supply of healthcare services. It is one of the world's leading pharmaceutical companies with healthcare sales of \$26.47 billion and leading positions in sales of gastrointestinal, cardiovascular, neuroscience, respiratory, oncology and infection products. AstraZeneca is listed in the Dow Jones Sustainability Index (Global) as well as the FTSE4 Good Index.

#### **GlaxoSmithKline**

GlaxoSmithKline is one of the world's leading research-based pharmaceutical and healthcare companies and is committed to improving the quality of human life by enabling people to do more, feel better, and live longer. For company information visit [www.gsk.com](http://www.gsk.com).

#### **Lundbeck**

H. Lundbeck A/S is an international pharmaceutical company engaged in the research and development, production, marketing and sale of drugs for the treatment of psychiatric and neurological disorders. In 2006, the company's revenue was DKK 9.2 billion (approximately EUR 1.2 billion or USD 1.6 billion). The number of employees is approximately 5,300 globally. For further information, please visit [www.lundbeck.com](http://www.lundbeck.com).

#### **Schering-Plough**

As of November 2007, Organon is part of Schering-Plough, an innovation-driven, science-centered global health care company. Through its own biopharmaceutical research and collaborations with partners, Schering-Plough creates therapies that help save and improve lives around the world. The company applies its research-and-development platform to human prescription and consumer products as well as to animal health products. In November 2007, Schering-Plough acquired Organon BioSciences, with its Organon human health and Intervet animal health businesses, marking a pivotal step in the company's ongoing transformation. Schering-Plough's vision is to "Earn Trust, Every Day" with the doctors, patients, customers and other stakeholders served by its approximately 50,000 people around the world. The company is based in Kenilworth, N.J., and its Website is [www.schering-plough.com](http://www.schering-plough.com)



### **Wyeth Pharmaceuticals**

Wyeth Pharmaceuticals, a division of Wyeth, has leading products in the areas of women's health care, infectious disease, gastrointestinal health, central nervous system, inflammation, transplantation, haemophilia, oncology, vaccines and nutritional products. Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing and marketing of pharmaceuticals, vaccines, biotechnology products and non-prescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare and Fort Dodge Animal Health.