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# Phytopharm plc

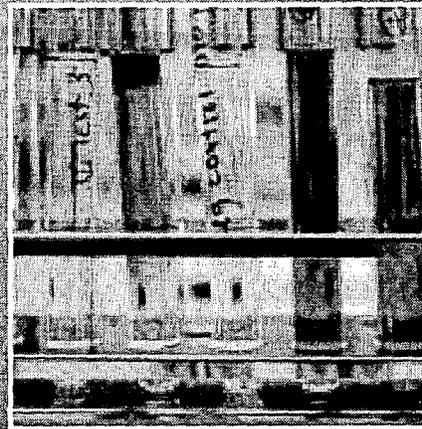
Annual report & accounts  
for the year ended 31 August 2001

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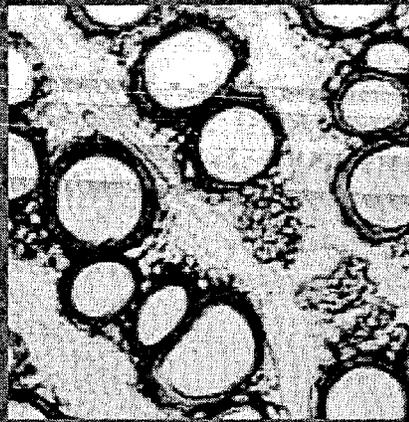
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CORPORATE FINANCE

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Phytopharm is an established drug discovery specialist. It takes both simple and complex extracts and single chemicals derived from plant sources into development. Building on strong clinical anecdotes the Company has developed a portfolio of drug discovery platforms with 10 products in development.



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# Highlights



Successful completion of proof of principle clinical study in obesity (P57)

Initiation of repeat dose study in age related cognitive impairment (P58)

Extension of neuronal degeneration platform into Parkinson's disease (P63)

Establishment of large scale manufacture for canine eczema (P7v)

Completion of phase IIa study in cancer chemo-prevention (P54)

Completion of phase II study in canine arthritis (P54v)

Initiation of phase II study in inflammatory bowel disease (P54)

# Phytopharm at a glance

The first botanical  
pharmaceutical company

## Our business model

**Phytopharm** is an established drug discovery specialist with a proven record in developing plant extracts as candidates for full pharmaceutical development. We are committed to the discovery and development of medicines for the treatment of poorly understood, difficult to treat diseases. Plants produce an astonishing array of novel phytochemicals. Many of these have marked biological activity, and are found within traditional medicines. We manufacture these phytochemical extracts, known as Botanicals, and take them into full pharmaceutical development.

## Out-licensing collaborations

**Phytopharm** seeks licensing partners for development and commercialisation of its products following phase IIa or 'proof of principle' clinical evaluation and development of a scalable manufacturing process. Multinational partners are sought, with milestones paid on completion of agreed clinical targets, submission of regulatory documents and royalties paid on sales.

## Therapeutic focus

There are **four platforms** in full development within Phytopharm:-

- Metabolic
- Neural and muscular degeneration
- Inflammation
- Dermatology

In addition, Phytopharm continues to conduct early evaluation programmes across a wide range of therapeutic areas.

## Phytopharm's strategy

**Botanicals** lie at the heart of Phytopharm's development strategy. The Botanical development path enables the rapid evaluation of plant extracts for chronic and poorly understood diseases; the generation of insights into their mode of action; the development of screens based on this data to isolate and patent the active molecules responsible, and the synthesis of derivatives of such molecules to offer multiple additional product candidates. Therapeutic areas in which these phases are complete are called drug discovery platforms.

## Intellectual property

**Intellectual property** can be generated at all stages of the Botanical development process. Patents protect formulations that demonstrate clinical activity, screens based upon novel modes of action discovered in the clinic as well as novel natural and semi-synthetic molecules. Phytopharm has now developed over 20 separate patent families, which are being prosecuted worldwide.

## Drug discovery platforms

**Platforms** form the basis for families of product opportunities that exploit the same mode of action. Products range in chemical complexity from mixtures with limited chemical identification to products in which the chemical composition is fully identified. In the latter case such products are single chemical entities and their development follows the conventional pharmaceutical path. They differ from conventional products only in that they have been discovered using the Botanical approach to drug discovery.

# Chairman's statement



The essence of Phytopharm's activities is to utilise the skills of specialists as partners around a nucleus of Phytopharm expertise.

I have reported before that due to the nature of a drug development company, and of Phytopharm in particular, a major concern of non-executive directors is to ensure that costs and associated budgetary disciplines are closely controlled. The importance of cost control is emphasised this year as continuing growth generated by maturing major projects has led to an increase in expenditure on research and development of 19% whilst staff numbers increased by a modest 5%. This most positive development testifies to the orderly management of the company and the soundness of our basic strategy.

As the business grows, the demands of day to day management increases and so during the year we appointed Dr Daryl Rees as Chief Operating Officer to ensure effective consolidation and direction of our operational activities. This has enabled Dr Richard Dixey, our Chief Executive, to continue to seek and evaluate those strategic developments that are important to our future growth.

Phytopharm is, of course, an international operator with interests and responsibilities in many countries. We are increasingly aware of our environmental and corporate social responsibilities and the need to show we meet the guidelines for Socially Responsible Investment. No business welcomes additional bureaucratic involvement in their activities but our aim has always been to manage the business within the highest social, environmental and pharmaceutical standards. We have achieved a good grading on the FTSE4Good Indices. Next year we begin formally reporting our performance against the associated guidelines to better communicate our commitment to our environmental and corporate social responsibilities.

Your company has made impressive progress over the last year due to the dedication and hard work of the talented people who work for you. As you know the essence of Phytopharm's activities is to utilise the skills of specialists as partners around a nucleus of Phytopharm expertise.

This requires very special management skills to work successfully and over the years Phytopharm people have achieved such ability, which lies at the heart of the business's success. In addition to Board operations and general contact with the business the non-executive directors form both the Audit and Remuneration Committee and are therefore in a position to monitor important aspects of the Company. There has been steady progress throughout the year both within the operational and corporate governance aspects of the business and the additional funds raised in November 2000 puts Phytopharm in an excellent position to maintain growth in the underlying value of the business.

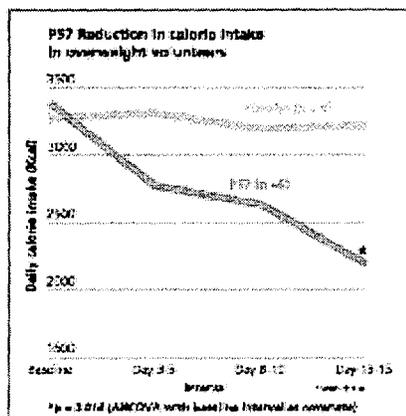
I am happy to report that Phytopharm is in good health and we may all expect a positive future.

Gordon Stevens  
Chairman

# Chief Executive's review

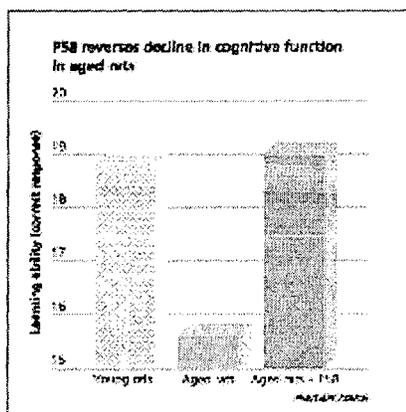


Phytopharm's core competence in the development of new molecules discovered from nature is now firmly established.



Phytopharm's core competence in the development of new molecules discovered from nature is now firmly established, and our business is moving forward vigorously in developing the expertise to manufacture these products on a commercial scale.

Running a drug development business is about managing risks, and our portfolio approach gives us multiple opportunities for success. This year we have taken the decision to focus on the products that are generated by our platforms, where we have established novel modes of action and identified active molecules of interest. These platforms cover the major therapeutic categories of obesity and metabolic disease, neural and muscular degeneration, inflammation and dermatology. However, behind these platforms Phytopharm continues to conduct early evaluation programmes across a wide range of therapeutic areas.

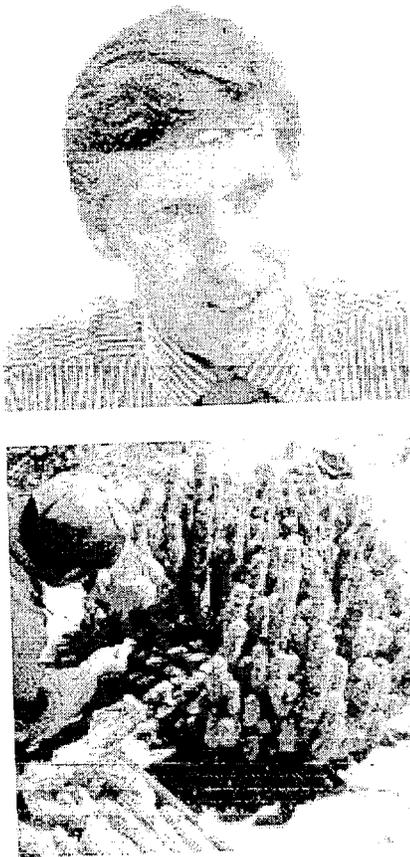


Phytopharm continues to operate a low cost early evaluation process. This enables the Company to conduct clinical studies on a wide range of products of potential therapeutic and commercial value. Inevitably, some of these studies are not successful. Last year we reported that P45, our product for alopecia androgenica failed to demonstrate a statistically significant improvement in hair re-growth when compared with placebo. Clinical studies in this condition are difficult to evaluate and as such the future of our work in alopecia is now under review.

Whilst it is disappointing to report early stage failures, there are an additional four projects under investigation in our early stage portfolio and thirty projects currently awaiting review. The further growth of our business depends on this activity, and early project evaluation continues to play a vital role in the future development and success of Phytopharm.

Dr Richard Dixey  
Chief Executive Officer

# Operational review



**The obesity platform**, which encompasses metabolic syndrome, has generated product **P57** which is focussed on obesity and obese onset diabetes. The platform comprises the patented use of three plant species, their mode of action and 17 related active molecules.

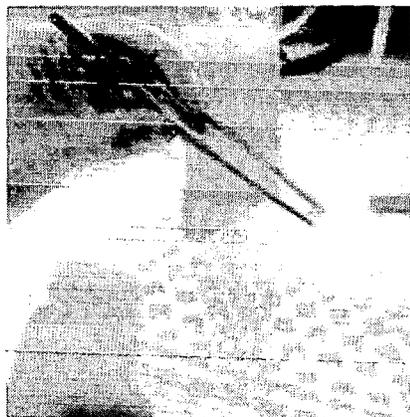
Licensed to Pfizer Inc in 1998, we announced in December 2001 the successful completion of the 'proof of principle' clinical study for this orally administered agent. In this three-stage study the safety, tolerability, pharmacokinetic profile and effects of P57 on daily calorie intake were studied in overweight volunteers. Pharmacokinetic data confirmed the systemic absorption of the active constituents of P57 in the single and repeat dose stages. In the last phase of this controlled study, overweight subjects were dosed for 15 days with P57 or placebo. The results of this study were positive and confirmed proof of principle. We saw a statistically significant reduction in the average daily calorie intake of the P57 group compared with the placebo group ( $p=0.014$ ). Data also indicated a statistically significant reduction in body fat content in the P57 group compared with the placebo group at the completion of dosing ( $p=0.035$ ). No serious adverse effects were experienced by any of the subjects, and the safety data are consistent with a satisfactory emerging safety profile. This study is the fruit of a substantial research programme which we have been conducting in collaboration with Pfizer over the past three years. With predictive drug screens and a clear cut demonstration of the potential of this novel approach for the treatment of obesity, we now have the foundation for the substantial body of work required to carry this project forward to commercialisation.

**The neural and muscular degeneration platform**, which includes Alzheimer's disease, involves the patented use of four plant species, their mode of action, drug screens and a library of seven families of novel semi-synthetic compounds. Several lines of research are now progressing in parallel, including studies at the cutting edge of proteomics. The picture that is emerging is very encouraging. Not only does the research pursued by Phytopharm demonstrate that these novel molecules have the potential to reverse the age related decline in neuronal receptor expression in the brain, but they also produce powerful protective effects on these cells. This work has enabled Phytopharm to develop a series of laboratory based screens that mimic these important observations, and has guided the development of semi-synthetic analogues of the original plant based materials. This has enabled us to combine efficacy in the laboratory screening models with the potential for manufacture at a large scale. Three separate products coded P58, P59 and P63 are now in development focussed on the reversal of age related cognitive impairment and Alzheimer's disease, neuromuscular degeneration and Parkinson's disease respectively.

Manufacture of the lead candidate for age related cognitive impairment and Alzheimer's disease, **P58**, has been successfully scaled up to kilogram quantities. A series of pre-clinical toxicology studies has now been completed, and we announced the commencement of an extended clinical programme of repeat dosing in the elderly in November 2001. The results of the seven day phase of this study will lead to a one-month placebo controlled study in Q2 2002, and the commencement of a full phase II study in the autumn of that year. In the meantime, the programme for Parkinson's disease, **P63**, should enter the clinical phase in the second half of the year. Pre-clinical work has demonstrated that P63 is a powerful protective agent against neurodegeneration that is characteristic of Parkinson's disease.

## The neural and muscular degeneration platform, which includes Alzheimer's disease, involves the patented use of four plant species, their mode of action, drug screens and a library of seven families of novel semi-synthetic compounds

**The inflammation platform** comprises a novel, third generation non steroidal anti-inflammatory drug (NSAID) family characterised by their potent inhibition of NFkB, the gene activator for a wide range of enzymes central to inflammation. The lead candidate, a patented formulation with a novel mode of action, is in clinical evaluation for the treatment of inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. The ongoing phase II study to evaluate the safety and efficacy of **P54** for the treatment of steroid dependent inflammatory bowel disease is due to complete in Q2 2002.



Earlier in the year we also reported the results of a dose escalation study in patients with advanced colorectal cancer. The results of this small study suggest that **P54** may possess cancer chemotherapeutic as well as chemopreventive efficacy and confirmed that **P54** may have a role in the prevention of colon cancer.

There is also potential for the use of compounds that reduce the expression of inflammatory enzymes in the companion animal market. In July 2001 we announced the completion of a double-blind placebo controlled trial using **P54v** in canine osteoarthritis in which 61 dogs with osteoarthritis of the hip or elbow were recruited by the University of Bristol Veterinary School. At the end of the treatment period the investigator

reported that 56% of the dogs were 'better' or 'much better' after being treated with **P54** compared to 26% of those treated with placebo ( $p=0.047$ ). The treatment was generally well tolerated with no serious adverse events recorded. These results have enabled us actively to pursue commercialisation of **P54v** in the veterinary market.

A further programme arising out of this platform, codenamed **P61**, has continued to generate novel semi-synthetic molecules for the treatment of disorders of the digestive tract. Pre-clinical work has demonstrated that these molecules inhibit intestinal spasm in a model of irritable bowel syndrome. The lead candidate will enter development in the second half of next year.

Finally, the **dermatology platform** comprises the patented use of five plants with a novel mode of action for the treatment of eczema.

One product arising from the platform, **P7v**, has been the subject of Phase II evaluation in companion animals. This is the largest ever published study in canine atopy and the results were reported in Q4 last year. Mode of action work over the year has established that the product has a dual mechanism of action and targets both the allergic and the inflammatory



components of eczema to alleviate the condition. Pharmaceutical development of the product has continued through the year and we are now manufacturing tonne quantities of material to GMP standards through a relationship with an experienced botanical manufacturer. Discussions with potential partners are now advancing concerning the further development and commercialisation of this product.

Efforts to develop a scalable version of the active compound emerging from this platform, coded **P55**, are continuing. We hope to be able to announce the final specification of a dosage form during the course of 2002.

Dr Daryl Rees  
Chief Operating Officer

# Product portfolio

Drug discovery platform	Product code	Indication
<b>Metabolic diseases</b>	P57	Obesity and metabolic syndrome
<b>Neural and muscular degeneration</b>	P58	Alzheimer's disease
	P59	Neuromuscular degeneration
	P63	Parkinson's disease
<b>Dermatology</b>	P1	Refractory atopic eczema
	P7v	Canine atopic dermatitis
	P55	Eczema
<b>Inflammation</b>	P54	Inflammatory bowel disease and colon cancer chemoprevention
	P54v	Canine arthritides
	P61	Inflammation and bowel disorders

## Projects under review

### Phytopharm has four early phase projects under evaluation

Phytopharm benefits from a multi product and varied portfolio. This diversifies the risks inherent to the drug development process. Phytopharm is building on its strengths with four drug discovery platforms firmly established and a portfolio of ten products now in development. In addition, the Company continues to evaluate a large number of early phase projects.

#### Metabolic syndrome

The World Health Organisation has stated that "Obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected health problems of our time with an impact on health that could well prove to be as great as that of smoking".

It has been estimated that obesity affects at least 39 million Americans: more than one quarter of all adults and about one in five children. Each year, obesity causes 300,000 excess deaths in the USA alone. Obesity exacerbates stroke, atherosclerosis, cardiovascular disease, diabetes and cancer - five of the leading causes of death in the industrialised world.

Type II diabetes is an increasing problem across the world, exacerbated by the increase in obesity and an ageing population. Obesity can lead to high blood pressure and eventually to heart disease and other cardiovascular complications.

P57 is unique in having genuine appetite suppressant activity and recent clinical results have proved 'proof of principle' for this compound in treating obesity.

#### Neural and muscular degenerative diseases

Dementia including Alzheimer's disease is a major emerging market in the West. There are currently 12 million cases worldwide and this is likely to grow to 22 million by 2025 according to the Alzheimer's Association. Alzheimer's disease is now the 8th leading cause of death in people aged over 65 in the USA. With the ageing baby boomer population this market is likely to grow dramatically.

The majority of drugs used to treat dementias have focussed on correcting imbalances in brain chemistry. The clinical improvements are not dramatic and only relatively small transient improvements in cognitive function have been observed. There is therefore a lack of effective

disease modifying therapies available.

Phytopharm has identified a novel treatment, P58, for dementias including Alzheimer's disease and reversal of age-related cognitive dysfunction. The mode of action is totally novel with extensive patent cover in grant and pending for use of plant extracts and semi-synthetic derivatives. Furthermore, an extensive research programme is ongoing to support a patent covering screens based on the mode of action that lies behind this established drug discovery platform.

By restoring the loss of receptors associated with ageing processes, P58 has applications in a wide range of cognitive dysfunctions including Alzheimer's disease and other neurological disorders.

The mode of action of other novel chemicals arising out of this platform suggests a potential treatment for Parkinson's disease. Early work on prevention of neurodegeneration has progressed well. P63 molecules have been shown to be neuroprotective, providing encouraging evidence not only for Parkinson's disease but also other neurodegenerative disorders. We anticipate that a phase I programme will commence during 2002. A further early phase

Mode of action	Stage of development
Not released	Phase IIa reported
Reverses age related declines in acetylcholine receptor density in brain tissue	Phase Ib in progress
Reverses decline in receptors in neuromuscular junction	Pre-clinical
Neuroprotective	Pre-clinical
Down regulates CD23 expression in the skin	Phase III reported
Inhibits inflammatory and allergic cytokines IL2 and IL4	Phase II reported
Inhibits inflammatory and allergic cytokines IL2 and IL4	Pre-clinical
Inhibition of NFkB induction, upstream of inflammatory enzymes (including COX-II and iNOS)	Phase II in progress
Inhibition of NFkB induction	Phase IIa reported
Inhibition of NFkB induction and anti-spasmodic	Pre-clinical

programme is in development for age related loss of neuromuscular receptors. Initial preclinical work indicates that P59 molecules are effective in reversing this process.

#### Inflammation

Inflammatory conditions of the digestive tract represent a major and poorly treated class of diseases. P54 represents a novel and well-tolerated third generation NSAID for managing inflammatory bowel disease and colorectal tumour prevention. P54 has the potential as a novel anti-inflammatory product and as such, it offers a global commercial opportunity in a growing market. The mode of action, evidence of clinical activity, apparent wide safety index and simple oral administration provide the potential for a significant therapeutic advance.

P54 also represents an opportunity in the companion animal osteoarthritis market, which has considerable unmet needs and where therapy by dietary supplementation is growing.

P61 is a semi-synthetic derivative of the active components of the P54 product, which may also have applications in the treatment of irritable bowel syndrome due to its marked antispasmodic activity.

#### Dermatology

Canine atopic dermatitis is a common problem affecting 15% of dogs, the principal symptom being pruritis (itching) initially round the face, front legs and later over the trunk.

Atopy is often seasonal and caused by an allergic response to either inhaled or percutaneously absorbed allergens such as pollens, grasses, weed and moulds. It can also be hereditary, but often, as with human eczema, the exact cause is unknown.

P7v is a non-steroidal, oral treatment for the management of canine atopic dermatitis derived from the P1 product.

P7v specifically inhibits the allergic and inflammatory phases of atopy without the detrimental effects associated with corticosteroids or immune modifying therapies.

The product offers the potential for a meaningful advance in the management of this common veterinary problem. Preclinical efforts are focused on an active fraction, P55, derived from the component plants of P7. P55 has exhibited a significant increase in activity over P7. Further patenting and derivatisation activity is ongoing.

#### Early stage product evaluation

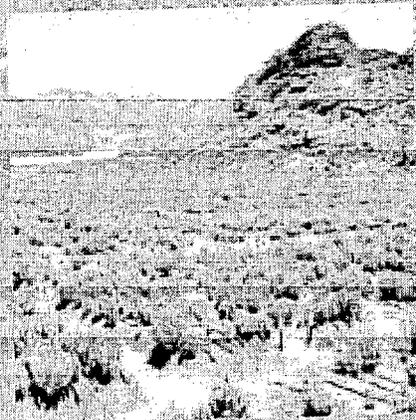
In addition to the four product platforms discussed above, Phytopharm has a number of early stage products currently under investigation which may generate further product platforms. Phytopharm also has a number of product leads generated from our network of partners currently under evaluation.

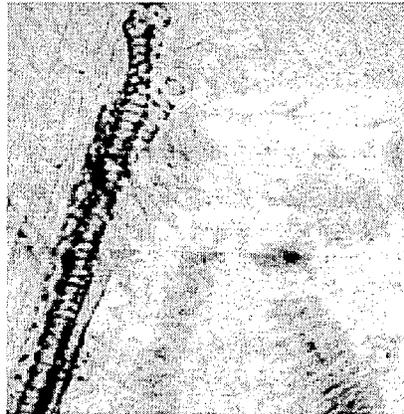
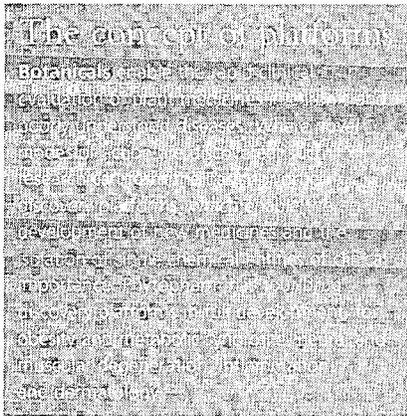
# Botanicals

The development advantage

## Definition of Botanical

Phytopharm has a proven record in developing plant extracts as candidates for full pharmaceutical development. The United States Food and Drug Administration (FDA) defines these medicinal plant extracts, manufactured to international pharmaceutical standards, as Botanicals. The Botanical development path allows early clinical evaluation programmes to be undertaken at low cost, the discovery of novel modes of action and the potential for early income generation.





## Phytopharm continues to deliver...

Using the Botanical paradigm, we continue to deliver:-

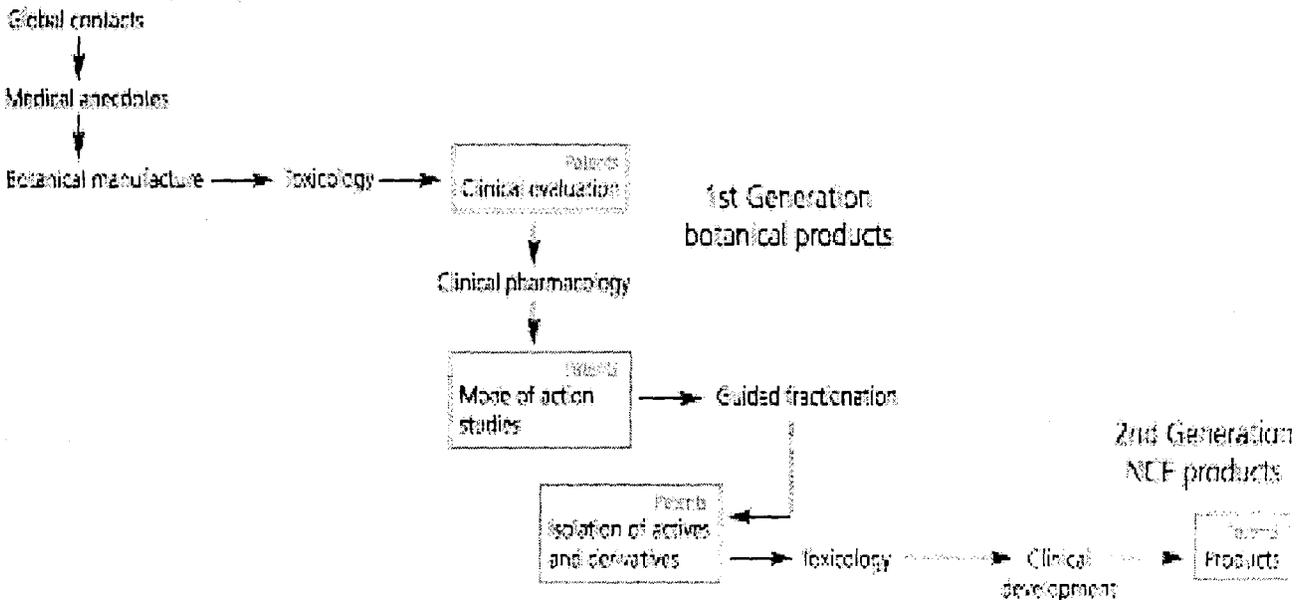
- novel compounds
- novel modes of action and screens
- patents
- development candidates and
- proof of principle in the clinic.

# Botanicals – the development advantage

## Conventional phytochemical development path



## Botanical development path



# Corporate issues



Phytopharm is a semi-virtual organisation of 34 employees. Although significantly smaller than most pharmaceutical companies we still encounter many similar corporate aspects in our day to day operations. The Board is conscious of its responsibilities not just to shareholders and employees but also our wider ethical, social and environmental responsibilities.

## Employees

Our policy is to attract and develop the best people at all levels and encourage them to use their skills and capabilities to the maximum advantage of the business. The majority of our employees are senior scientists with significant pharmaceutical experience who manage the business through a network of academic, industry and contract relationships. The Board recognises the need to grow the business responsibly and therefore offers equal opportunities to all without discrimination.

## Share schemes

Phytopharm encourages employees to be involved at all levels of the business through its participatory environment. We ensure our employees benefit from the success of the business and one key element of this is our share option scheme. Every employee's contribution to the growth of the business is recognised and rewarded by annual awards of share options.

## Environmental

Phytopharm prides itself on being in the vanguard of companies promoting the development of medicines that are produced in an environmentally aware manner. We recognise that protecting the environment is a primary corporate responsibility and that environmental matters are not just the responsibility of the Board but also an area in which each employee, each corporate partner and each contractor has a contribution to make. Phytopharm encourages all involved in its operations to act in an environmentally responsible manner under the principles of the British Standards Institute ISO 14001 'Environmental Management Systems'.

## Biodiversity treaty

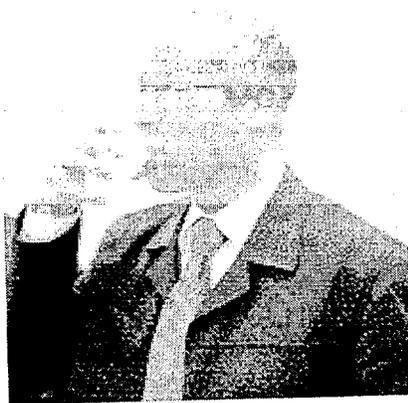
It is our policy to address the many issues biodiversity raises in research and prospecting in countries where plant diversity is abundant. We embrace the principles of the Biodiversity Treaty by supporting farmers in developing countries, by transfer of knowledge and skills and by establishing fair commercial arrangements.





#### Social accountability

It is our policy to address the growing concern among consumers regarding labour conditions around the world. Social Accountability International has developed a standard, SA 8000, that outlines acceptable working terms and conditions and a system for independently verifying compliance. Phytopharm is committed to this standard and endeavours to ensure that it and its contractors comply with the standard and national law, and to respect the international policies and their interpretation. Phytopharm achieves this by raising awareness and promoting SA8000 amongst employees, partners, suppliers and contractors. Assessment of standards is through audit and improvement plans are implemented to raise the level of compliance where appropriate.



#### Quality

As a responsible pharmaceutical company our focus is to develop prescription pharmaceuticals to current international quality guidelines to meet the increasingly high regulatory standards. Phytopharm's operations comply with the following guidelines and by doing so we are committed to meeting the highest principles.

#### Good Agricultural Practice (GAP)

The principles of Good Agricultural Practice are applied to the growing and primary processing of plants. As well as providing a framework for efficient production of quality crops, GAP serves to minimise environmental impact, maintain biodiversity and promote sustainable production. Phytopharm promotes synergy between its operations and contractors by agreeing procedures for growing the crop that incorporate the concepts of GAP and local practice. Compliance is monitored by making routine visits to the growing and primary processing areas and by documented adherence to the written procedures.



#### Good Manufacturing and Laboratory Practice (GMP and GLP)

Adherence to GMP and GLP by contractors involved in each stage of the manufacture, packaging and analysis of products obtained from plants is mandatory if products are to be granted a Marketing Authorisation (MA) by Regulatory Authorities. Manufacturing in accordance with these processes ensures product safety and efficacy to the patient. Phytopharm incorporates these requirements into their commercial contracts and associated technical agreements as well as working practices. Contractors used are audited to ensure compliance.

#### Good Clinical Practice (GCP)

GCP guidelines provide an international ethical and scientific standard for designing, conducting, recording and reporting trials that involve the willing participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well being of trial subjects are protected and that the clinical trial data is credible. Phytopharm conducts in house studies in accordance with these principles and uses consultants and contractors who operate within the standard. Compliance is established by auditing data and premises.

# Financial review



## Results of operations

Turnover of £1.5m for the year (2000: £2.1m) comprises development income under the licence and development agreement with Pfizer Inc for P57, the Group's appetite suppressant. The reduction in turnover this year arises as the previous year's figure included a milestone of £0.63m for the completion of Phase I dose ranging studies earned under the Pfizer agreement. After allowing for this, the development income has remained consistent for the last two years at £1.5m as the project progressed into a multistage Phase IIa clinical study at the year end.

The cost of sales of £0.31m in the previous year represents the proportion of the milestone income from Pfizer due to the CSR from whom the Group originally licensed the product P57.

Overall operating expenses for the year of £5.01m are 19% higher than the previous year, an increase of £0.79m. Within those totals expenditure on research and development rose by 19% (£0.64m) to £4.03m, with administration costs also increasing by 19% to £0.97m. The increase in research and development expenditure is due to increased expenditure across the Group's portfolio of products other than P57 where expenditure remained at a similar level to the previous year. Expenditure on P57 is anticipated to increase in the coming year following the successful completion of the multistage study announced in December 2001. Within the rest of the portfolio, expenditure on P58, the Group's treatment for age related

dementias, has increased significantly as the project progresses into the clinic and larger scale manufacturing processes are developed. The increase in administrative overheads arises from a strengthening of the business development and corporate elements of the business introduced during the previous year.

Interest income during the year of £0.67m is significantly higher this year (2000: £0.28m) following the fund raising in November 2000 (see below). The tax credit of £0.22m (2000: £nil) arose as the Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund.

The increase in interest income and the tax credit have more than offset the reduction in turnover and enabled the Group to increase operating expenditure by £0.79m or 19%, while limiting the increase in the overall loss for the year by £0.47m or 22% to £2.65m.

## Balance sheet

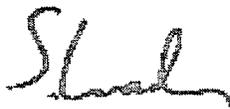
The net assets at the end of the year of £13.09m show a considerable increase over the previous year end figure of £4.76m due to the proceeds of the share issue in November 2000 which raised net proceeds of £10.8m. The working capital of the Group comprises 98% (2000: 96%) of the net asset value and the bulk of this is held as cash, either on hand or on term deposits.

The Group has a small investment in fixed assets of £0.28m at the year end which has not changed significantly over the year. The fixed asset levels are low as the Group contracts out its research requirements and therefore does not need to finance its own laboratory facilities. Short term creditors at the year end were £1.05m and are 23% more than the previous year. This is as expected and is primarily due to higher levels of expenditure in the year ended 31 August 2001 as noted above.

#### **Financing**

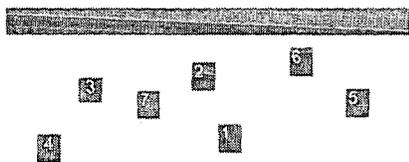
Overall, after allowing for the share issue in November 2000 and the exercise of options during the year, the Group utilised £2.71m of working capital during 2001 (2000: £2.22m). This is equivalent to an average of £226,000 per month (2000: £185,000) during the year. Excluding the effects of the tax credit received this year (£18,700 per month) and the net milestone in the previous year (£26,200 per month), the average monthly working capital consumption figure over the current year of £245,000 has increased by £34,000 per month when compared to £211,000 per month for the previous year. The increase in expenditure was planned following the Group's fundraising and is in accordance with the Group's policy of tight control of overheads and careful allocation of resources between projects.

The additional working capital raised during the year has strengthened the Group's balance sheet significantly and the directors anticipate this will allow the Group to fully develop the P58 platform to maximise its licensing potential while continuing development within the rest of the portfolio.



Dr Simon Charles Loach  
**Chief Financial Officer and  
Company Secretary**

# Directors and Advisers



## Registered office

Corpus Christi House, 9 West Street,  
Godmanchester, Cambridgeshire PE29 2HY

## Company number

3131723

## Registrars

Capita IRG plc  
Bourne House, 34 Beckenham Road,  
Kent BR3 4TU

## Auditors

PricewaterhouseCoopers  
Abacus House, Castle Park,  
Cambridge CB3 0AN

## Solicitors

Nicholson Graham & Jones  
110 Cannon Street, London EC4N 6AR

## Financial public relations consultants

Financial Dynamics  
30 Furnival Street, London EC4A 1JE

## Bankers

Bank of Scotland  
41 South Gyle Crescent,  
Edinburgh EH12 9XD

## Financial advisers

N M Rothschild & Sons Ltd  
New Court, St Swithins Lane,  
London EC4P 4DU

## Stockbrokers

WestLB Panmure Ltd  
Woodgate Exchange, 25 Basinghall Street,  
London EC2V 5HA

## 1. Dr R P Dixey

Chief Executive Officer

Dr Richard Dixey (aged 49) has a BA (Hons) in physiological sciences (Oxford, 1973), a PhD in biophysics (London, 1984) and an MSc in history and philosophy of science (London, 1988). He founded the Bioelectronic Research Unit at St Bartholomew's Hospital, London in 1979 and became its director in 1984. In 1990 he became a founding director of Phytopharm Limited and its vice chairman in 1992. In 1994 he became chief executive officer of the company and led its flotation as Phytopharm plc in 1996. In 1989 he founded Chakra Limited, an investment company, of which he remains a director.

## 2. Dr S C Loach

Chief Financial Officer

Dr Simon Loach (aged 45) has an MA (Cantab) in engineering (1978) and a PhD in civil engineering (Nottingham 1986). He qualified as a chartered accountant in 1990 with Coopers & Lybrand Deloitte. He was appointed as chief financial officer of Phytopharm in February 1996. Prior to that he was financial controller of Ethical Holdings plc. Before joining Coopers & Lybrand in 1987 he worked for Ove Arup and Partners as a geotechnical engineer.

## 3. Dr D D Rees

Chief Operating Officer

Dr Daryl Rees (aged 40) joined Phytopharm in June 1999 from University College London where he was a Senior Lecturer in Clinical Pharmacology. Prior to this Dr Rees gained 10 years experience in the discovery and clinical development of medicines as a Senior Scientist at Wellcome and was part of a multi-disciplinary team involved in the discovery of the L-arginine-NO pathway. He is an Honorary Senior Lecturer in the Department of Medicine at University College London, a former Editor of the British Journal of Pharmacology, and is Chairman of Huntingdon Local Research Ethics Committee.

## 4. Ms J E Allan

Director of Resource and Planning

Ms Jayne Allan (aged 38) has an MRSC and a CChem from Kingston upon Hull University (1988) and a diploma in clinical science from Cardiff University. She is a member of the Royal Society of Chemistry. Prior to joining Phytopharm in 1991 she worked for Reckitt and Colman Pharmaceuticals Limited as a senior clinical research associate.

## 5. Mr G K G Stevens

Non-Executive Chairman

Mr Gordon Stevens MA (Oxon) (aged 75) retired in 1996 as non-executive chairman of WPP plc, the international marketing services group, and as non-executive chairman of Scholl plc, the international foot and leg care company. Prior to those responsibilities his career had been with Unilever plc in international marketing and management where he served on the boards of Unilever plc and Unilever N.V. for twelve years. He was appointed as non-executive chairman on 3 May 1997.

## 6. Dr P M Whitney

Non-Executive Deputy Chairman

Dr Paul Whitney (aged 53) has a BSc (Hons) in chemistry (Aston, 1969), a PhD in physical chemistry (Aston, 1972) and an MBA (Cranfield, 1980). From 1996 to 1998 he was chief executive of Sunlife Asset Management Limited. Prior to that he was chief executive of NatWest Investment Management Limited and managing director of NatWest Asset Managers Limited. He is currently chairman and chief executive of Parallel Ventures Managers Limited. He was appointed as non-executive deputy chairman of the company on 1 April 1996.

## 7. Dr T H Flanagan

Non-Executive Director

Dr Trevor Flanagan (aged 64) has a BSc (Hons) in biochemistry (Cardiff, 1960) and a PhD in biochemistry (Cardiff, 1963). From 1963 to 1978 he worked at ICI Pharmaceuticals Limited in research project management and as a licensing manager. From 1978 to 1986 he worked for Synthelabo and was responsible for international project management and global regulatory affairs. In 1986 he joined Wellcome Foundation where he was strategic business manager for all therapeutic areas except anti-infectives. In 1995 he established his own pharmaceutical consultancy. He was appointed a non-executive director of the company on 1 April 1996.

# Directors' report

for the year ended 31 August 2001

The directors present their report and the audited financial statements for the year ended 31 August 2001.

## Principal activities

The principal activities of the group remain as last year, and are the investigation and development of medicines derived from plant origins.

## Review of the business

Development of the group's portfolio of products has progressed satisfactorily during the year. In particular the three stage clinical study on P57, the group's appetite suppressant, has shown encouraging results and since the year end P58, the group's treatment for age related dementias, commenced a multistage clinical trial which is anticipated to report the middle of next year. A full review of the business and future developments is given in the Operational review on page 6 and the Financial review on page 14.

The directors are satisfied with the year end position and this, together with the placing in November 2000, leaves the group in a strong position for the coming year.

## Dividends

The directors do not recommend a dividend for the year ended 31 August 2001.

## Group research and development activities

The group is heavily committed to research and development activities in order to continue its work in the field of plant based prescription medicines. Such development costs are written off as they are incurred and the charge for the year is shown in note 3 to the financial statements.

## Directors

The directors of the company, all of whom have been directors for the whole of the year, except as noted below, are as follows:

Dr R P Dixey  
Dr S C Loach  
Dr P M Whitney  
Dr T H Flanagan  
Mr G K G Stevens  
Ms J E Allan  
Dr D D Rees (appointed 22 September 2000)

There were no contracts of significance with the company or any of its subsidiaries subsisting during or at the end of the financial year in which a director of the company was materially interested.

The interests of directors in the shares and share options of the company at 31 August 2001 are disclosed in the Report of the board on remuneration on pages 19 to 22.

## Substantial shareholdings

The directors have been advised of the following substantial holdings in the company's issued share capital:

Name of shareholder	% holding
Chakra Ltd	20.8
Standard Life Investments	5.1
M & G Asset Management Ltd (Prudential Holdings plc)	5.0
Brian Whittle Associates Ltd	4.2

Save for the above, the company has not been notified, as at 19 December 2001, of any material interest of 3% or more or any non-material interest exceeding 10% of the issued share capital of the company.

## Employees

The group's policy towards its employees is detailed on page 12.

## Directors' report continued

for the year ended 31 August 2001

### **Creditor payment policy**

The group's current policy concerning the payment of the majority of its trade creditors is to follow the CBI's Prompt Payers Code (copies are available from the CBI, Centre Point, 103 New Oxford Street, London WC1A 1DU). For other suppliers, the group's policy is to:

- a) agree the terms of payment with those suppliers when negotiating the terms of each transaction;
- b) ensure that those suppliers are made aware of the terms of payment by inclusion of the relevant terms in contracts; and
- c) pay in accordance with its contractual and other legal obligations.

The payment policy applies to all payments to creditors for revenue and capital supplies of goods and services without exception. The average credit period (expressed as creditor days) taken during the year was 28 days (2000: 39 days) for the group and 3 days (2000: 13 days) for the company.

### **Impact of the Euro**

The group does not anticipate any immediate impact on its business practices as a result of the introduction of the Euro.

### **Environment**

Details of the group's policy towards the environment is detailed on page 12.

### **Charitable donations**

During the year the group made charitable donations of £210 (2000: £890).

### **Auditors**

A resolution to reappoint PricewaterhouseCoopers as auditors to the company will be proposed at the next annual general meeting.

### **By order of the board**

#### **Dr S C Loach**

Company Secretary  
19 December 2001

# Report of the board on remuneration

The remuneration committee is comprised exclusively of non-executive directors. They are as follows:

Dr P M Whitney (chairman)

Mr G K G Stevens

Dr T H Flanagan

The company's remuneration committee decides the remuneration policy that applies to executive directors and all of the group's employees including other senior management.

## Remuneration of non-executive directors

The non-executive directors each receive a fee for their services, which is agreed by the board following recommendation by the chairman with the assistance of independent advice concerning comparable organisations and appointments.

Neither the chairman nor the other non-executive directors receive any pension or other benefits from the company.

## Remuneration policy for executive directors

The company's remuneration policy for executive directors is to:

- a) have regard to the directors' experience and the nature and complexity of their work and due regard to directors' remuneration in comparable companies in order to pay a competitive salary that attracts and retains management of the highest quality;
- b) link individual remuneration packages to the group's long-term performance through the award of share options and incentive schemes;
- c) provide post retirement benefits through the group's pension schemes; and
- d) provide employment related benefits including the provision of a company car, life assurance, insurance relating to the directors' duties and medical insurance.

## Salaries and benefits

The remuneration committee meets as required in order to consider and set the annual salaries for executive directors, having regard to personal performance and independently compiled salary survey information. The group operates a performance related bonus scheme for executive directors, senior managers and all other staff. The bonus for each individual depends on the group achieving performance targets and on the performance of the individual. The bonus is paid through a small cash element with the majority awarded in share options. The performance targets for the group are derived from the annual budget and are agreed by the board and remuneration committee when the board approves the budget.

## Share option schemes

The company operates two share option schemes, both of which are open to all members of staff. The first scheme is an Inland Revenue approved scheme, while the second scheme is an unapproved scheme. Options which become exercisable after three years (basic options) may be granted under either scheme while options which become exercisable after five years (super options) may only be granted under the unapproved scheme. All options are subject to exercise criteria which are currently based on share price performance, which the directors consider most appropriate at this stage of the company's development where income streams have not stabilised and the group has not yet made a profit. There are three exercise criteria, two for the basic options and one for the super options. All grants to employees and directors are split equally between basic options and super options. The grant in basic options is also split equally between the two basic option criteria. The criteria for the basic options are that the increase in the share price must exceed one and a half times or twice the increase in the FTSE All share index while that for the super options must have exceeded one and a half times the increase in the FT Pharmaceuticals Index. All criteria are based on the values at the date of grant and all options are granted at market value.

## Pensions

All the executive directors have money purchase pension schemes to which the company contributes 8% of basic salary.

## Contracts of service

The executive directors have contracts of service which can be terminated by the company with a notice period of one year in the case of Dr R P Dixey, six months in the case of Dr S C Loach and Dr D D Rees and three months in the case of Ms J E Allan. In addition, all executive directors have agreed to retire on attaining the age of 65. The contracts for service for the non-executive directors cannot be terminated by the company, although they can be terminated on not less than 90 days notice by the non-executive director. In addition, one third of all directors are required under the Articles of Association to resign and offer themselves for re-election at each annual general meeting.

## Report of the board on remuneration continued

### Directors' detailed emoluments

Details of individual directors' emoluments for the year are as follows:

	2001					2000	
	Salary & fees £	Bonus £	Benefits £	Pension contributions £	Total £	Total £	Pension contributions £
<b>Executive</b>							
Dr R P Dixey	145,527	4,439	10,593	11,642	172,201	163,148	10,838
Dr S C Loach	79,199	1,948	14,018	6,336	101,501	94,997	6,181
Ms J E Allan	62,789	1,624	17,536	5,023	86,972	62,286	3,700
Dr D Rees*	73,965	2,438	15,765	5,917	98,085	-	-
	<b>361,480</b>	<b>10,449</b>	<b>57,912</b>	<b>28,918</b>	<b>458,759</b>	<b>320,431</b>	<b>20,719</b>
<b>Non-executive</b>							
Mr G K G Stevens	30,000	-	-	-	30,000	30,000	-
Dr P M Whitney	15,000	-	-	-	15,000	15,000	-
Dr T H Flanagan	15,000	-	-	-	15,000	15,000	-
	<b>60,000</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>60,000</b>	<b>60,000</b>	<b>-</b>
<b>Total</b>	<b>421,480</b>	<b>10,449</b>	<b>57,912</b>	<b>28,918</b>	<b>518,759</b>	<b>380,431</b>	<b>20,719</b>

\*From appointment on 22 September 2000

No director waived emoluments in respect of the year ended 31 August 2001 (2000: £nil).

The table below shows gains made by individual directors from the exercise of share options. The gains are calculated as at the exercise date, although the shares may have been retained.

	Number of options	Market value	2001 £	2000 £
		on exercise £		
Dr R P Dixey	-	-	-	3,055,025
Dr S C Loach	17,555	6.06	73,513	433,563
	17,555		73,513	3,488,588

### Directors' interests in shares

The interests of the directors in the shares of the company at 31 August 2001 were:

	Ordinary shares of 1 pence	
	31 August 2001	31 August 2000
Dr R P Dixey*	166,500	111,500
Dr S C Loach	5,000	5,000
Mr G K G Stevens	7,750	7,750
Dr T H Flanagan	1,000	1,000

All directors' interests are beneficially held.

\*In addition to these shares, Dr R P Dixey has a beneficial interest in 7,932,000 (2000: 7,932,000) ordinary shares of 1 pence each by virtue of holding 50% of the issued share capital of Chakra Limited, which owns 7,932,000 shares in Phytopharm plc.

Apart from the interests disclosed above no directors were interested at any time in the year in the share capital of the company or other group companies.

There has been no change in the interests set out above between 31 August 2001 and 19 December 2001.

## Report of the board on remuneration continued

### Directors' interests in share options

Details of options over shares of the company held by directors are set out below:

	At 31 August 2000	Number of options			At 31 August 2001	Note*	Exercise price	Date from which exercisable	Expiry Date
		Held prior to Appointment	granted during the year	Exercised in the year					
Dr R P Dixey	126,600	-	-	-	<b>126,600</b>	4	£1.925	24 Apr 01	23 Apr 03
	72,223	-	-	-	<b>72,223</b>	2b	45p	7 Dec 00	6 Dec 04
	72,222	-	-	-	<b>72,222</b>	3b	45p	7 Dec 00	6 Dec 04
	144,444	-	-	-	<b>144,444</b>	4	45p	7 Dec 02	6 Dec 04
	8,564	-	-	-	<b>8,564</b>	2b	£3.89	15 Dec 02	16 Dec 06
	8,563	-	-	-	<b>8,563</b>	3b	£3.89	15 Dec 02	16 Dec 06
	17,127	-	-	-	<b>17,127</b>	4	£3.89	15 Dec 04	16 Dec 08
	-	-	8,555	-	<b>8,555</b>	2b	£6.575	8 Dec 03	7 Dec 07
	-	-	8,555	-	<b>8,555</b>	3b	£6.575	8 Dec 03	7 Dec 07
	-	-	17,110	-	<b>17,110</b>	4	£6.575	8 Dec 05	7 Dec 07
	<b>449,743</b>	-	<b>34,220</b>	-	<b>483,963</b>				
Dr S C Loach	75,000	-	-	-	<b>75,000</b>	1	26.25p	17 Apr 99	16 Apr 03
	17,000	-	-	17,000	-	2a	£1.925	24 Apr 99	23 Apr 06
	18,200	-	-	-	<b>18,200</b>	2b	£1.925	24 Apr 99	23 Apr 03
	39,900	-	-	-	<b>39,900</b>	3b	£1.925	24 Apr 99	23 Apr 03
	107,900	-	-	-	<b>107,900</b>	4	£1.925	24 Apr 01	23 Apr 03
	555	-	-	555	-	2a	45p	7 Dec 00	6 Dec 07
	37,363	-	-	-	<b>37,363</b>	2b	45p	7 Dec 00	6 Dec 04
	37,916	-	-	-	<b>37,916</b>	3b	45p	7 Dec 00	6 Dec 04
	75,833	-	-	-	<b>75,833</b>	4	45p	7 Dec 02	6 Dec 04
	4,885	-	-	-	<b>4,885</b>	2b	£3.89	15 Dec 02	16 Dec 06
	4,884	-	-	-	<b>4,884</b>	3b	£3.89	15 Dec 02	16 Dec 06
	9,768	-	-	-	<b>9,768</b>	4	£3.89	15 Dec 04	16 Dec 08
	-	-	1,518	-	<b>1,518</b>	2b	£6.575	8 Dec 03	7 Dec 07
	-	-	1,518	-	<b>1,518</b>	3b	£6.575	8 Dec 03	7 Dec 07
	-	-	3,036	-	<b>3,036</b>	4	£6.575	8 Dec 05	7 Dec 07
	<b>429,204</b>	-	<b>6,072</b>	<b>17,555</b>	<b>417,721</b>				
Ms J E Allan	8,000	-	-	-	<b>8,000</b>	2a	£1.925	24 Apr 99	23 Apr 06
	8,000	-	-	-	<b>8,000</b>	3a	£1.925	24 Apr 99	23 Apr 06
	18,000	-	-	-	<b>18,000</b>	4	£1.925	24 Apr 01	23 Apr 03
	4,444	-	-	-	<b>4,444</b>	2a	45p	7 Dec 00	6 Dec 07
	17,301	-	-	-	<b>17,301</b>	2b	45p	7 Dec 00	6 Dec 04
	21,744	-	-	-	<b>21,744</b>	3b	45p	7 Dec 00	6 Dec 04
	43,489	-	-	-	<b>43,489</b>	4	45p	7 Dec 02	6 Dec 04
	18,750	-	-	-	<b>18,750</b>	2b	£3.89	15 Dec 02	14 Dec 06
	18,750	-	-	-	<b>18,750</b>	3b	£3.89	15 Dec 02	14 Dec 06
	37,500	-	-	-	<b>37,500</b>	4	£3.89	15 Dec 04	16 Dec 08
	-	-	2,019	-	<b>2,019</b>	2b	£6.575	8 Dec 03	7 Dec 07
	-	-	2,019	-	<b>2,019</b>	3b	£6.575	8 Dec 03	7 Dec 07
	-	-	7,984	-	<b>7,984</b>	4	£6.575	8 Dec 05	7 Dec 07
	<b>195,978</b>	-	<b>12,022</b>	-	<b>208,000</b>				

## Report of the board on remuneration continued

### Directors' interests in share options continued

	At 31 August 2000	Held prior to Appointment	Number of options granted during the year	Exercised in the year	At 31 August 2001	Note*	Exercise price	Date from which exercisable	Expiry Date
Dr D D Rees	-	13,043	-	-	<b>13,043</b>	2a	£2.30	24 Jun 02	23 Jun 09
	-	6,957	-	-	<b>6,957</b>	2b	£2.30	24 Jun 02	23 Jun 06
	-	20,000	-	-	<b>20,000</b>	3b	£2.30	24 Jun 02	23 Jun 06
	-	40,000	-	-	<b>40,000</b>	4	£2.30	24 Jun 04	23 Jun 06
	-	10,000	-	-	<b>10,000</b>	2b	£3.89	16 Dec 02	15 Dec 06
	-	10,000	-	-	<b>10,000</b>	3b	£3.89	16 Dec 02	15 Dec 06
	-	20,000	-	-	<b>20,000</b>	4	£3.89	16 Dec 04	15 Dec 06
	-	-	5,704	-	<b>5,704</b>	2b	£6.575	8 Dec 03	7 Dec 07
	-	-	5,703	-	<b>5,703</b>	3b	£6.575	8 Dec 03	7 Dec 07
	-	-	11,406	-	<b>11,406</b>	4	£6.575	8 Dec 05	7 Dec 07
	-	-	7,500	-	<b>7,500</b>	2b	£4.60	2 Aug 04	1 Aug 08
	-	-	7,500	-	<b>7,500</b>	3b	£4.60	2 Aug 04	1 Aug 08
	-	-	15,000	-	<b>15,000</b>	4	£4.60	2 Aug 06	1 Aug 08
	-	120,000	52,813	-	<b>172,813</b>				
<b>Total</b>	<b>1,074,925</b>	<b>120,000</b>	<b>105,127</b>	<b>17,555</b>	<b>1,282,497</b>				

\*Further details of the terms of the share option schemes are contained in note 21 to the financial statements under the note reference in the above table.

Options granted at 26.25 pence and which are exercisable from 17 April 1999 were granted prior to the company's flotation on 25 April 1996. The remaining options have been granted under the options schemes established at the time of the flotation. All options granted under these schemes are subject to performance criteria, details of which are given in note 21 to the financial statements.

The company has no long term incentive plans.

The market price of the company's shares at the end of the financial year was 465.5 pence (31 August 2000: 591.5 pence) and the range of market prices during the year was between 347.5 pence and 880 pence.

### On behalf of the board

**Dr P M Whitney**

Chairman of the remuneration committee  
19 December 2001

# Corporate governance

## **The Combined Code**

The directors are accountable to shareholders for the good corporate governance of the group and seek to uphold and report on compliance with current best practice in Corporate Governance.

In accordance with the Combined Code on Corporate Governance appended by the Financial Services Authority to the Listing Rules, this Corporate Governance report and the Report of the board on remuneration sets out how the principles of good governance described in the Combined Code have been applied to the group throughout the financial year.

## **The board of directors**

The board is chaired by Mr G K G Stevens and meets for regular business six times a year. In addition, further meetings are held if circumstances require. The board has agreed a schedule of items that are specifically reserved for its consideration. The board is responsible for the overall direction and strategy of the group and for securing the optimum performance from group assets.

Dr T H Flanagan was appointed senior non-executive director on 30 October 2001. He replaced Mr G K G Stevens as the senior non-executive, in order to bring the company into compliance with provision A.2.1 of the Combined Code.

The board of directors consists of four executive and three non-executive directors following the appointment of Dr D D Rees as an executive director on 22 September 2000. Biographies of the directors are set out on page 16. None of the non-executive directors are involved in the day to day running of the group's business and, after reviewing their respective shareholdings and business interests notified to the company, the board considers that they are independent of the company. Details of the directors' shareholdings are shown on page 20.

The board has established procedures to allow individual directors to seek independent professional advice at the company's expense for the furtherance of their duties, and all directors have access to the services of the company secretary. Newly appointed directors receive a comprehensive introduction to the group's business as well as information on their responsibilities and role as a director of the company.

The board has established the following committees:

### *Audit committee*

The audit committee comprises Dr P M Whitney, Dr T H Flanagan and Mr G K G Stevens and is chaired by Dr P M Whitney. It meets as required and assists the board in ensuring that the group's published financial statements give a true and fair view and in securing reliable internal financial information for decision making. It also reviews the suitability and effectiveness of the group's internal controls. The committee reviews the findings of the external auditors and reviews key accounting policies and judgements. The group has a Quality Assurance manager but does not have an internal financial audit function. The board considers that this is appropriate at this time given the size of the group.

### *Remuneration committee*

The remuneration committee comprises Dr P M Whitney, Dr T H Flanagan and Mr G K G Stevens and is chaired by Dr P M Whitney. It meets as required and is responsible for making recommendations to the board on remuneration policy for all members of staff and executive directors. The policy recommendations include setting salary scales, and approving the format and range of incentive payments and share option grants to all staff. Remuneration of non-executive directors is under the control of the executive directors.

The directors have not considered it necessary to establish a nomination committee due to the small size of the board. In the event that the board wishes to appoint a director from outside the group then the board will consider establishing a nomination committee.

## **Relationship with shareholders**

The company is committed to maintaining good relations with its shareholders and reports formally to shareholders on a six monthly basis through the provision of interim and annual reports. In addition, the company keeps shareholders informed of significant events for the group during the year by issuing press releases. The company also maintains communication by making presentations during the year to institutional shareholders on request and to all shareholders through the company's website [www.phytopharm.co.uk](http://www.phytopharm.co.uk). This contains information on all of the group's products and all financial reports and press releases issued by the company. Details of the current share price and historic share price performance are also included.

## Corporate governance continued

### Annual general meetings

The principal forum for discussion with shareholders is the annual general meeting. Formal notification together with an explanation of each proposed resolution is sent to shareholders at least twenty working days in advance of the meeting. At the meeting the board provides a summary of the year's events after which all the directors are available to answer questions from shareholders. During the meeting all shareholders present are informed of the proxy votes cast for and against each resolution.

### Internal controls

The board acknowledges that it is responsible for the group's system of internal control and for regularly reviewing its effectiveness. However, the board acknowledges that such a system can only provide reasonable and not absolute assurance against material misstatement or loss, as it is designed to manage rather than eliminate the risk of failure to achieve business objectives.

The key procedures that the board have established are designed to provide effective internal controls within the group and comply with the Internal Control Guidance for Directors on the Combined Code issued by the Institute of Chartered Accountants in England and Wales. There is an ongoing process for identifying and managing significant risks faced by the group which has been in place throughout the year.

The group's key internal control procedures include the following:

### Control environment

The group's control environment is the responsibility of the group's directors and managers at all levels. The group's organisational structure has clear lines of reporting and responsibility. Regular project reviews are held to review progress against plan for each project. These groups report monthly to a management group comprising the executive directors and key senior managers to compare progress against plan for the business as a whole. Overall control of the business rests with the board of directors.

### Risk identification and evaluation

Regular assessments of ongoing risks facing the business are undertaken as part of the project reviews and monthly management group meetings in the key areas such as management of working capital, compliance, legal and operational issues.

### Operational controls

*Manufacturing.* All supplies of pharmaceutical products manufactured on behalf of Phytopharm are produced in accordance with Good Manufacturing Practice (GMP) which ensures that the products are manufactured consistently to the appropriate quality standards. The company also has a number of plantations operating under Good Agricultural Practice (GAP) to ensure that raw material supply is consistently controlled and of appropriate quality.

*Pre-clinical studies.* Key pre-clinical studies to determine the safety and efficacy of new products are conducted in accordance with Good Laboratory Practice (GLP) at contractors who operate under those regulations. Each contractor is visited by our Quality Assurance auditor to assess compliance with GLP prior to commencing studies.

*Clinical studies.* All clinical studies carried out by the group are in accordance with Good Clinical Practice. This ensures that the health and well being of the subjects is carefully monitored during the study and that the data gathered is complete and reliable. These procedures are subject to audit, either by our Quality Assurance manager or a third party.

### Financial controls

*Financial reporting.* Budgets and long term forecasts are prepared biannually and allow management to monitor the key business and financial risks. Further more frequent forecasts are prepared if circumstances require. The budgets are reviewed and approved by the board prior to adoption by the company. Management accounts are prepared on a monthly basis and performance against budget is analysed in detail and reported on monthly.

*Control procedure.* The group has established detailed policies, and accounting and administrative procedures are in place covering all significant areas and key systems, including formal authorisation procedures for the transfer of funds, capital expenditure and recruitment. Any commitment of expenditure requires documentary approval which is subject to prescribed limits of authority. Any major expenditure or commitment including the appointment of senior members of staff requires board approval.

### Compliance

The group has established series of standard operating procedures (SOPs) covering the operations of the business, including the operation of review meetings and the dissemination of information externally to the business. These SOPs are designed to ensure compliance with the agreed internal procedures of the group and external regulations where appropriate. All SOPs are reviewed on a regular basis and updated where necessary by the relevant group or department under the control of the Quality Assurance manager.

## Corporate governance continued

### **Going concern**

The directors have a reasonable expectation that the group and the company have adequate resources to continue in operational existence for the foreseeable future. For this reason, they continue to adopt the going concern basis in preparing the group's financial statements.

### **Statement of directors' responsibilities**

*The directors are required under the Companies Act 1985 to prepare financial statements for each financial year that give a true and fair view of the state of affairs of the company and the group as at the end of the financial year and of the profit or loss of the group for the financial year.*

The directors confirm that, in preparing these financial statements, the group has used appropriate accounting policies, applied them consistently and where necessary made reasonable and prudent estimates and judgements. The directors also confirm that all applicable accounting standards have been followed subject to any explanations and material departures disclosed in the notes to the financial statements.

Under the Companies Act 1985 the directors are also responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the company and the group and enable them to ensure that the financial statements comply with the Companies Act 1985. They are also responsible for safeguarding the assets of the company and the group and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The directors' are responsible for the maintenance and integrity of the company's website. Uncertainty regarding legal requirements for the preparation and dissemination of financial statements is compounded as information published on the internet is accessible in many countries with differing legal requirements relating to this.

### **Statement of compliance**

The board has carried out a review of its corporate governance procedures during the year and is pleased to confirm that the group complies with the provisions of the Combined Code with the following exceptions:

Provision A.2.1 recommends that a senior independent non-executive director be nominated, other than the chairman. Until 30 October 2001 the company was not in compliance with this provision as the senior non-executive was also the chairman. With effect from 30 October 2001 this matter has been addressed and the company is now in a position of compliance.

Provision A.6.1 recommends that non-executive directors should be appointed for specified terms subject to re-election and to Companies Act provisions relating to the removal of a director. The service contracts for the non-executive directors are not fixed term, and can only be terminated by the non-executive director on giving 90 days notice or by the shareholders in general meeting. The board consider this to be satisfactory and are of the opinion that, in certain circumstances, the ability of the company to remove non-executive directors from office may be counterproductive.

### **By order of the board**

**Dr S C Loach**

Company Secretary

19 December 2001

# Independent auditors' report to the members of Phytopharm plc

We have audited the financial statements which comprise the consolidated profit and loss account, the consolidated and company balance sheets, the consolidated cash flow statement and the related notes.

## **Respective responsibilities of directors and auditors**

The directors' responsibilities for preparing the annual report and the financial statements in accordance with applicable United Kingdom law and accounting standards are set out in the statement of directors' responsibilities.

Our responsibility is to audit the financial statements in accordance with relevant legal and regulatory requirements, United Kingdom Auditing Standards issued by the Auditing Practices Board and the Listing Rules of the Financial Services Authority.

We report to you our opinion as to whether the financial statements give a true and fair view and are properly prepared in accordance with the Companies Act 1985. We also report to you if, in our opinion, the directors' report is not consistent with the financial statements, if the company has not kept proper accounting records, if we have not received all the information and explanations we require for our audit, or if information specified by law or the Listing Rules regarding directors' remuneration and transactions is not disclosed.

We read the other information contained in the annual report and consider the implications for our report if we become aware of any apparent misstatements or material inconsistencies with the financial statements. The other information comprises only the Directors' report, Chairman's statement, Chief Executive's review, Operational review, Financial review, Corporate governance and the Report of the board on remuneration.

We review whether the Corporate governance statement reflects the company's compliance with the seven provisions of the Combined Code specified for our review by the Listing Rules, and we report if it does not. We are not required to consider whether the board's statements on internal control cover all risks and controls, or to form an opinion on the effectiveness of the company's or group's corporate governance procedures or its risk and control procedures.

## **Basis of audit opinion**

We conducted our audit in accordance with Auditing Standards issued by the Auditing Practices Board. An audit includes examination, on a test basis, of evidence relevant to the amounts and disclosures in the financial statements. It also includes an assessment of the significant estimates and judgements made by the directors in the preparation of the financial statements, and of whether the accounting policies are appropriate to the company's circumstances, consistently applied and adequately disclosed.

We planned and performed our audit so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or other irregularity or error. In forming our opinion we also evaluated the overall adequacy of the presentation of information in the financial statements.

## **Opinion**

In our opinion the financial statements give a true and fair view of the state of affairs of the company and the group at 31 August 2001 and of the loss and cash flows of the group for the year then ended and have been properly prepared in accordance with the Companies Act 1985.

## **PricewaterhouseCoopers**

### **Chartered Accountants and Registered Auditors**

Cambridge, 19 December 2001

# Consolidated profit and loss account

for the year ended 31 August 2001

	Notes	2001 £	2000 £
<b>Turnover</b>	2	<b>1,471,226</b>	2,077,817
Cost of sales	3	–	(313,923)
<b>Gross profit</b>		<b>1,471,226</b>	1,763,894
Net operating expenses	3	<b>(5,006,104)</b>	(4,212,724)
<b>Operating loss</b>		<b>(3,534,878)</b>	(2,448,830)
Interest receivable and similar income		<b>665,560</b>	274,917
Interest payable and similar charges	6	<b>(8,022)</b>	(9,309)
<b>Loss on ordinary activities before taxation</b>	7	<b>(2,877,340)</b>	(2,183,222)
Tax on loss on ordinary activities	8	<b>224,193</b>	–
<b>Loss for the financial year</b>	22	<b>(2,653,147)</b>	(2,183,222)
Basic and diluted loss per ordinary share (pence)	10	<b>(7.1)</b>	(6.3)
IIMR loss per share (pence)	10	<b>(7.1)</b>	(6.3)

All revenues and expenses shown above were generated from continuing operations.

The group has no recognised gains or losses other than those included in the losses above, and therefore no separate statement of total recognised gains and losses has been presented.

There is no difference between the loss on ordinary activities before taxation and the loss for the year stated above, and historical cost equivalents.

## Reconciliation of movements in shareholders' funds

for the year ended 31 August 2001

	2001 £	2000 £
Loss for the financial year	<b>(2,653,147)</b>	(2,183,222)
New share capital issued	<b>11,213,383</b>	4,998,578
Expenses of share issue	<b>(228,706)</b>	(116,365)
Net increase in shareholders' funds	<b>8,331,530</b>	2,698,991
Opening shareholders' funds	<b>4,760,016</b>	2,061,025
<b>Closing shareholders' funds</b>	<b>13,091,546</b>	4,760,016

# Consolidated and company balance sheets

at 31 August 2001

	Notes	Group		Company	
		2001 £	2000 £	2001 £	2000 £
<b>Fixed assets</b>					
Tangible assets	11	246,959	254,943	–	–
Investments	12	30,098	30,098	235,898	235,898
		<b>277,057</b>	<b>285,041</b>	<b>235,898</b>	<b>235,898</b>
<b>Current assets</b>					
Debtors: amounts falling due after one year	13	–	–	18,341,712	15,188,877
Debtors: amounts falling due within one year	13	368,579	103,707	23,206	31,934
Cash held on deposit as short term investments	14	12,668,172	4,527,897	12,668,172	4,527,897
Cash at bank and in hand		854,125	791,722	703,464	807,788
		<b>13,890,876</b>	<b>5,423,326</b>	<b>31,736,554</b>	<b>20,556,496</b>
<b>Creditors: amounts falling due within one year</b>	15	<b>1,045,810</b>	<b>853,565</b>	<b>75,049</b>	<b>149,493</b>
<b>Net current assets</b>		<b>12,845,066</b>	<b>4,569,761</b>	<b>31,661,505</b>	<b>20,407,003</b>
<b>Total assets less current liabilities</b>		<b>13,122,123</b>	<b>4,854,802</b>	<b>31,897,403</b>	<b>20,642,901</b>
<b>Creditors: amounts falling due after more than one year</b>	16	<b>14,318</b>	<b>63,786</b>	–	–
<b>Provisions for liabilities and charges</b>	17	<b>16,259</b>	<b>31,000</b>	–	<b>31,000</b>
<b>Net assets</b>		<b>13,091,546</b>	<b>4,760,016</b>	<b>31,897,403</b>	<b>20,611,901</b>
<b>Capital and reserves</b>					
Called up share capital	20	381,918	361,467	381,918	361,467
Share premium account	22	31,252,629	20,288,403	30,757,222	19,792,996
Merger reserve	22	(204,211)	(204,211)	–	–
Profit and loss account	22	(18,338,790)	(15,685,643)	758,263	457,438
<b>Equity shareholders' funds</b>		<b>13,091,546</b>	<b>4,760,016</b>	<b>31,897,403</b>	<b>20,611,901</b>

The financial statements comprising the consolidated profit and loss account, consolidated and company balance sheets, consolidated cash flow statement and related notes, were approved by the board of directors on 19 December 2001 and were signed on its behalf by:

**Dr S C Loach**  
Chief Financial Officer

# Consolidated cash flow statement

for the year ended 31 August 2001

	Notes	2001 £	2000 £
<b>Net cash outflow from continuing operating activities</b>	25	<b>(3,273,174)</b>	<b>(2,458,225)</b>
<b>Returns on investments and servicing of finance</b>			
Interest received		665,560	264,599
Interest paid on finance leases		(8,022)	(9,309)
<b>Net cash inflow from returns on investments and servicing of finance</b>		<b>657,538</b>	<b>255,290</b>
<b>Taxation</b>			
UK corporation tax paid		-	-
<b>Capital expenditure and financial investment</b>			
Purchase of fixed asset investments		-	(30,098)
Purchase of tangible fixed assets		(128,027)	(102,427)
Sale of tangible fixed assets		13,650	13,460
<b>Net cash outflow for capital expenditure</b>		<b>(114,377)</b>	<b>(119,065)</b>
<b>Cash outflow before use of liquid resources and financing</b>		<b>(2,730,013)</b>	<b>(2,322,000)</b>
<b>Management of liquid resources</b>			
Increase in cash held on short-term deposit	24	(8,140,275)	(2,519,185)
<b>Financing</b>			
Proceeds from exercise of share options		183,264	611,235
Proceeds from issue of share capital		11,030,119	4,387,343
Expenses of issue of share capital		(228,706)	(116,365)
Repayment of principal under finance leases		(51,986)	(66,806)
<b>Net cash inflow from financing</b>		<b>10,932,691</b>	<b>4,815,407</b>
<b>Increase/(decrease) in net cash</b>	24	<b>62,403</b>	<b>(25,778)</b>

## Reconciliation to net cash

for the year ended 31 August 2001

	2001 £	2000 £
Net cash at 1 September	791,722	817,500
Increase/(decrease) in net cash	62,403	(25,778)
<b>Net cash at 31 August</b>	<b>854,125</b>	<b>791,722</b>

# Notes to the financial statements

for the year ended 31 August 2001

## 1 Principal accounting policies

These financial statements have been prepared in accordance with applicable Accounting Standards in the United Kingdom. A summary of the more important group accounting policies, which have been applied consistently and which the directors consider to be the most appropriate, is set out below. The financial statements are prepared in accordance with the historical cost convention.

### Basis of consolidation

On 3 April 1996 the group structure was reorganised and a new holding company established by way of a share exchange. This has been accounted for as a merger in the consolidated accounts, and all transactions within the group have been eliminated.

The acquisition by the company's subsidiary, Phytotech Limited (formerly Phytopharm Limited), of Phytodevelopments Limited on 21 March 1996 has been accounted for as a merger in the consolidated financial statements, and all transactions between the two companies have been eliminated.

### Changes in presentation of financial statements

Financial Reporting Standard number 17, "Retirement benefits", and Financial reporting Standard number 18, "Accounting Policies", came into effect for these financial statements but have not resulted in any changes in presentation.

### Comparative figures

The comparative figures for creditors and provisions have been re-presented to show the national insurance liability as a provision rather than as an accrual, in accordance with the provision of Urgent Issues Task Force Abstract 25 ("National Insurance contributions on share options gains"). The effect of this re-presentation is the creation of a provision of £31,000 and an equal reduction across creditors falling due within one year.

### Financial instruments

The Group's financial instruments comprise cash and short term investments, trade debtors and trade creditors that arise directly from operations and finance leases. All financial instruments are carried at cost.

### Tangible fixed assets

The cost of tangible fixed assets is their purchase cost, together with any incidental expenses of acquisition.

Depreciation is calculated so as to write off the cost of tangible fixed assets, less their estimated residual values, on a straight line basis over the expected useful economic lives of the assets concerned. The principal rates used for this purpose are:

Plant and machinery	20%
Computer equipment	33%
Fixtures and fittings	20%
Motor vehicles	25%

Leasehold improvements are amortised over the length of the lease.

### Research and development expenditure

Expenditure on research and development is written off as incurred.

### Finance and operating leases

Costs in respect of operating leases are charged on a straight line basis over the lease term. Where fixed assets are financed by leasing agreements, which transfer to the company substantially all the benefits and risks of ownership, the assets are treated as if they had been purchased outright and included in tangible fixed assets. The capital element of the leasing commitments is shown as obligations under finance leases. The lease rentals are treated as consisting of capital and interest elements. The capital element is applied to reduce the outstanding obligations and the interest element is charged against profit in proportion to the reducing capital element outstanding. Assets held under finance leases are depreciated over the shorter of the lease term and the useful lives of equivalent owned assets.

### Foreign currencies

Assets and liabilities expressed in foreign currencies are translated into sterling at rates of exchange ruling at the end of the financial year. Foreign exchange differences are taken to the profit and loss account in the year in which they arise.

# Notes to the financial statements continued

for the year ended 31 August 2001

## 1 Principal accounting policies continued

### Turnover

Turnover, which excludes value added tax, represents the invoiced value of goods and services supplied.

Amounts received or receivable under research and development contracts and collaborative research agreements are recognised as turnover when earned. Amounts received or receivable in respect of licence fees or milestone payments are recognised as turnover when the licence rights are granted or the specific conditions stipulated in the licence agreement have been satisfied.

### Cost of sales

Cost of sales comprises the proportion of milestone and royalty income earned by the group and due to third parties under licence agreements and the direct cost of goods sold. All research and development costs, whether funded by third parties under licence and development agreements or not, are included within operating expenses and classified as research and development costs.

### Deferred taxation

Tax deferred or accelerated is accounted for in respect of all material timing differences to the extent that it is probable that a liability or asset will crystallise.

### Pension costs

The group contributes between five and eight percent of employees' gross salary costs to defined contribution money purchase schemes. Employees may opt out of the State scheme if they wish. The pension costs charged against profit represent the amount of contributions payable to the pension schemes in respect of the accounting period.

The group provides no other post retirement benefits to its employees.

### Provisions

In accordance with the provisions of Urgent Issues Task Force Abstract 25 ('National Insurance Contributions on Share options'), a provision is made based on the current employer's National Insurance rate applied to the difference between the market value of the shares under option and the option exercise price at the balance sheet date. The provision is charged to the profit and loss account over the period in which the share options vest.

## 2 Analysis of turnover

	2001	2000
	£	£
<b>By business activity</b>		
Licensing and development	1,471,226	2,077,817
<b>Destination by geographical area</b>		
North America	1,471,226	2,077,817

All turnover originated in the United Kingdom.

## 3 Cost of sales and other operating income and expenses

	2001	2000
	£	£
Cost of sales	-	313,923
Gross profit	1,471,226	1,763,894
Research and development expenditure	4,033,188	3,393,862
Administrative expenses	972,916	818,862
Operating expenses	5,006,104	4,212,724
Operating loss	(3,534,878)	(2,448,830)

## Notes to the financial statements continued

for the year ended 31 August 2001

### 4 Directors' emoluments

	2001	2000
	£	£
Aggregate emoluments	489,841	359,712
Contributions to money purchase pension schemes	28,918	20,719
	<b>518,759</b>	<b>380,431</b>

Detailed disclosures of directors' individual remuneration and share options are given in the report of the board on remuneration on pages 19 to 22.

Four directors (2000: three) have retirement benefits accruing to them from money purchase pension schemes in respect of qualifying services.

Fees and other emoluments (excluding pension contributions) payable to the highest paid director are as follows:

	2001	2000
	£	£
Aggregate emoluments	160,559	152,310
Contributions to money purchase pension schemes	11,642	10,838
	<b>172,201</b>	<b>163,148</b>

### 5 Employee information

At 31 August 2001 the group employed 34 (2000: 29) persons (including executive directors). The average monthly number of persons (including executive directors) employed during the year was:

	2001	2000
	Number	Number
Administration	7	8
Research and development	24	21
	<b>31</b>	<b>29</b>

	2001	2000
	£	£
<b>Staff costs (for the above persons):</b>		
Wages and salaries	1,179,919	1,006,595
Social security costs	124,662	149,244
Other pension costs	73,751	62,236
	<b>1,378,332</b>	<b>1,218,075</b>

On the 1 February 2001 all contracts of employment were transferred from the holding company to the company's subsidiary, Phytotech Limited. This allows Phytotech Limited to reclaim corporation tax relief on research and development expenditure as described in Note 8. The terms and conditions of employment remained unchanged.

### 6 Interest payable and similar charges

	2001	2000
	£	£
On finance leases	8,022	9,309

## Notes to the financial statements continued

for the year ended 31 August 2001

### 7 Loss on ordinary activities before taxation

	2001	2000
	£	£
Loss on ordinary activities before taxation is stated after charging/(crediting):		
Depreciation charge for the year:		
Tangible owned fixed assets	80,199	67,196
Tangible assets held under finance leases	51,598	51,826
Profit on disposal of fixed assets	(9,436)	(8,946)
Auditors' remuneration for audit (company £12,500)	20,500	18,500
Auditors' remuneration for non-audit work	5,975	6,720
Operating lease charges:		
Plant and machinery	13,005	9,840
Other assets	80,300	86,800

### 8 Tax on loss on ordinary activities

	2001	2000
	£	£
United Kingdom		
Corporation tax credit at 24%	224,193	-

There is no corporation tax charge because of the incidence of tax losses (2000: £nil). The group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby a company may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

### 9 Profit for the financial year

As permitted by section 230 of the Companies Act 1985, the parent company's profit and loss account has not been included in these financial statements. The parent company's profit for the year to 31 August 2001 was £300,825 (2000: £47,590).

### 10 Loss per ordinary share

The calculation of basic and diluted earnings per share on the net basis is based on the loss on ordinary activities after taxation, namely £2,653,147 (2000: £2,183,222) and on 37,609,090 (2000: 34,923,482) ordinary shares, being the weighted average number of ordinary shares in issue and ranking for dividend during the year. The group has no dilutive potential ordinary shares in issue.

A further measure of earnings per share has been recommended by the Institute of Investment Management and Research (the 'IIMR') for adoption by financial analysts. This measure, known as headline earnings, adjusts standard earnings per share to eliminate capital items only, rather than all exceptional items. IIMR headline loss per share amounted to 7.1p (2000: 6.3p) as set out below:

	2001	2000
	pence per share	pence per share
Loss per share	(7.1)	(6.3)
IIMR adjustments		
Profit/(loss) on sale of tangible fixed assets	-	-
IIMR loss per share	(7.1)	(6.3)

## Notes to the financial statements continued

for the year ended 31 August 2001

### 11 Tangible fixed assets

Group	Short leasehold £	Computer equipment £	Motor vehicles £	Plant and machinery £	Fixtures and fittings £	Total £
<b>Cost</b>						
At 1 September 2000	3,363	175,209	282,227	17,185	95,956	573,940
Additions	-	55,384	62,244	3,325	7,074	128,027
Disposals	-	-	(56,023)	-	-	(56,023)
<b>At 31 August 2001</b>	<b>3,363</b>	<b>230,593</b>	<b>288,448</b>	<b>20,510</b>	<b>103,030</b>	<b>645,944</b>
<b>Depreciation</b>						
At 1 September 2000	3,363	112,060	121,507	14,924	67,143	318,997
Charge for year	-	40,608	70,901	1,560	18,728	131,797
Disposals	-	-	(51,809)	-	-	(51,809)
<b>At 31 August 2001</b>	<b>3,363</b>	<b>152,668</b>	<b>140,599</b>	<b>16,484</b>	<b>85,871</b>	<b>398,985</b>
<b>Net book value</b>						
<b>At 31 August 2001</b>	<b>-</b>	<b>77,925</b>	<b>147,849</b>	<b>4,026</b>	<b>17,159</b>	<b>246,959</b>
Net book value						
At 31 August 2000	-	63,149	160,720	2,261	28,813	254,943

The net book values of tangible fixed assets held under finance leases and hire purchase contracts included in the above figures are as follows:

	2001 £	2000 £
Motor vehicles	82,148	137,959

### Company

The Company has no tangible fixed assets.

## Notes to the financial statements continued

for the year ended 31 August 2001

### 12 Fixed asset investments

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
<b>Shares in group undertakings</b>				
<b>At 1 September and 31 August</b>	-	-	205,800	205,800
<b>Other investments</b>				
At 1 September	30,098	-	30,098	-
Additions	-	30,098	-	30,098
<b>At 31 August</b>	<b>30,098</b>	<b>30,098</b>	<b>30,098</b>	<b>30,098</b>
<b>Total fixed asset investments</b>	<b>30,098</b>	<b>30,098</b>	<b>235,898</b>	<b>235,898</b>

### Interests in group undertakings

Name of undertaking	Country of incorporation	Description of shares held	Proportion of voting rights and nominal value of issued shares held by	
			Group	Company
			%	%
Phytotech Limited	England and Wales	Ordinary 10 pence shares	100	100
Phytodevelopments Limited	England and Wales	Ordinary £1 shares	100	-

Both the above companies have been included in these financial statements and operated principally in their country of incorporation or registration.

The principal business activities of these subsidiary undertakings are:

Phytotech Limited – research and development of plant based medicines

Phytodevelopments Limited – dormant

### Other investments

Name of undertaking	Country of incorporation	Description of shares held	Proportion of voting rights and nominal value of issued shares held by	
			Group	Company
			%	%
Tumkur Chemicals Limited	India	Equity shares of Rs 10/-	10	10

### 13 Debtors

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
<b>Amounts falling due after one year</b>				
Amounts owed from group undertakings	-	-	18,341,712	15,188,877
<b>Amounts falling due within one year</b>				
Other debtors	105,588	42,615	14,202	4,194
Corporation tax recoverable	224,209	16	-	-
Prepayments and accrued income	38,782	61,076	9,004	27,740
	<b>368,579</b>	<b>103,707</b>	<b>23,206</b>	<b>31,934</b>
	<b>368,579</b>	<b>103,707</b>	<b>18,364,918</b>	<b>15,220,811</b>

## Notes to the financial statements continued

for the year ended 31 August 2001

### 14 Cash held on deposit as short term investments

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
Cash held on deposit as short term investments	<b>12,668,172</b>	4,527,897	<b>12,668,172</b>	4,527,897

The company holds its excess cash reserves on a combination of fixed term money market deposits and deposit accounts. At 31 August 2001 and 31 August 2000 these did not exceed three months in duration.

### 15 Creditors: amounts falling due within one year

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
Obligations under finance leases	<b>49,468</b>	51,986	-	-
Trade creditors	<b>380,375</b>	159,622	<b>2,686</b>	6,402
Other creditors including taxation and social security	<b>44,678</b>	70,156	<b>563</b>	67,941
Accruals and deferred income	<b>571,289</b>	571,801	<b>71,800</b>	75,150
	<b>1,045,810</b>	853,565	<b>75,049</b>	149,493

Included within other creditors for the group is an amount of £3,370 (2000: £3,924) relating to pension creditors.

### 16 Creditors: amounts falling due after more than one year

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
Obligations under finance leases	<b>14,318</b>	63,786	-	-

### Finance leases

The net finance lease obligations to which the group is committed are:

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
In one year or less	<b>52,402</b>	58,999	-	-
Between one and two years	<b>14,810</b>	52,402	-	-
Between two and five years	-	14,810	-	-
	<b>67,212</b>	126,211	-	-
Less: interest	<b>3,426</b>	10,439	-	-
	<b>63,786</b>	115,772	-	-

## Notes to the financial statements continued

for the year ended 31 August 2001

### 17 Provisions for liabilities and charges

#### Provision for employer's national insurance on share option gains

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
At 1 September	31,000	–	31,000	–
Transferred to subsidiary company	–	–	(31,000)	–
(Credited)/charged to profit and loss account	(14,741)	31,000	–	31,000
At 31 August	16,259	31,000	–	31,000

As stated in Note 5 the company's employees were transferred to Phytotech Limited, the company's subsidiary. The liability for employer's national insurance on share option gains has also been transferred to Phytotech Limited.

#### Deferred taxation

No deferred taxation has been provided in the financial statements. The analysis of unprovided deferred tax assets is as follows:

	Group		Company	
	2001	2000	2001	2000
	£	£	£	£
<b>Amount unprovided</b>				
Tax effect of timing differences:				
Excess of tax allowances over depreciation	182,372	93,745	–	–
Accumulated losses	4,995,000	4,500,000	–	–
Other	1,073	3,612	138	3,612
	5,178,445	4,597,357	138	3,612

### 18 Financial instruments

The group's objectives in using financial instruments are to maximise the returns of funds held on deposit, to conserve cash resources by entering financing arrangements for the acquisition of major capital assets, to minimise exchange rate risk where appropriate, and to generate additional cash resources through the issue of shares when market conditions are appropriate.

These objectives, policies and strategies are consistent with those of previous years. The balance sheet positions at 31 August 2001 and 2000 are not representative of the positions throughout the year as cash and short-term investments fluctuate considerably depending on when fund raising activities have occurred.

Short term debtors and creditors have been excluded from the following disclosures as permitted by the Financial Reporting Standard 13 "Derivatives and other financial instruments".

#### Interest rate risk profile of the group's financial assets

With the exception of a nominal amount held in US Dollars and South African Rand the group held all cash, bank and deposits in Sterling accounts with UK banks. Interest rates on deposit accounts are floating and are based on LIBID, while interest rates on term deposits are fixed for the duration of deposit and earned interest between 5.00% and 6.00% in the year ended 31 August 2001.

The group holds a small investment as disclosed in note 12. The directors are of the opinion that the fair value of this investment is not materially different from cost.

#### Interest rate risk profile of the group's financial liabilities

The group's liabilities, other than short term creditors, which are excluded as above, were all in Sterling at fixed rates of interest and were in respect of lease agreements for the purchase of capital assets. The maturity profile and amounts outstanding are disclosed in Note 16. The weighted average interest rate and period remaining on liabilities at 31 August 2001 was 8% and 1.2 years (2000: 8% and 2.1 years).

#### Currency risk profile

The group had no significant commitments in foreign currencies throughout the year.

## Notes to the financial statements continued

for the year ended 31 August 2001

### 18 Financial instruments continued

#### Borrowing facilities

The group had no borrowing facilities at 31 August 2001 (2000: £nil).

#### Fair values

There is no material difference between the fair value and the carrying values of the financial instruments referred to above, because of the short maturity period of these financial instruments.

#### Credit risk

The financial instruments that subject the group to a potential credit risk comprise principally of cash and short term investments. The group's policy is to minimise this risk by placing these deposits with institutions with a recognised high rating, or with one of the major clearing banks.

### 19 Pension and similar obligations

The group operates a number of defined contribution pension schemes for employees. The assets of the schemes are held separately from those of the group in independently administered funds. The pension cost represents contributions paid and payable by the group to the funds and amounted to £73,751 (2000: £62,236).

### 20 Called-up share capital

	2001	2000
	£	£
<b>Authorised</b>		
50,000,000 (2000: 50,000,000) ordinary shares of 1p each	500,000	500,000
<b>Allotted, called-up and fully paid</b>		
38,191,815 (2000: 36,146,676) ordinary shares of 1p each	381,918	361,467

On the 29 November 2000 the company issued 1,764,819 ordinary 1p shares for gross proceeds of £11,030,119 to provide the company with additional working capital.

### 21 Options and warrants in shares of Phytopharm plc

#### Options

Options have been granted for 1p ordinary shares as follows:

	2001	2000
	Number	Number
At 1 September	2,224,097	3,266,839
Granted during the year	278,848	607,991
Exercised during the year	(280,320)	(1,246,411)
Lapsed during the year	(98,530)	(404,322)
<b>At 31 August</b>	<b>2,124,095</b>	<b>2,224,097</b>

At the 31 August 2001 the outstanding share options are shown below. These have been analysed according to the exercise criteria detailed below.

Number outstanding 31/8/01	Note	Date granted	Exercise price	Option exercisable from	Option exercisable to	Currently exercisable
81,000	1	17/4/96	26.25p	18/4/99	16/4/03	81,000

## Notes to the financial statements continued

for the year ended 31 August 2001

### 21 Options and warrants in shares of Phytopharm plc continued

Number outstanding 31/8/01	Note	Date granted	Exercise price	Option exercisable from	Option exercisable to	Currently exercisable
15,000	2a	24/04/96	£1.925	25/04/99	23/04/06	15,000
18,200	2b	24/04/96	£1.925	25/04/99	23/04/03	18,200
4,444	2a	06/12/97	45p	07/12/00	05/12/07	4,444
126,887	2b	06/12/97	45p	07/12/00	05/12/04	126,887
13,043	2a	23/06/99	£2.30	24/06/02	22/06/09	–
6,957	2b	23/06/99	£2.30	24/06/02	22/06/06	–
5,000	2a	02/08/99	£2.24	03/08/02	01/08/09	–
12,987	2a	20/09/99	£2.31	21/09/02	19/09/09	–
7,013	2b	20/09/99	£2.31	21/09/02	19/09/06	–
7,500	2a	06/12/99	£2.915	07/12/02	05/12/09	–
16,158	2a	15/12/99	£3.89	16/12/02	14/12/09	–
45,846	2b	15/12/99	£3.89	16/12/02	14/12/06	–
3,138	2a	18/01/00	£4.78	19/01/03	17/01/10	–
1,029	2b	18/01/00	£4.78	19/01/03	17/01/07	–
3,352	2a	17/04/00	£4.475	18/04/03	16/04/10	–
1,648	2b	17/04/00	£4.475	18/04/03	16/04/07	–
3,571	2a	20/04/00	£4.20	21/04/03	19/04/10	–
5,179	2b	20/04/00	£4.20	21/04/03	19/04/07	–
2,500	2a	02/05/00	£4.40	03/05/03	01/05/10	–
3,247	2a	05/06/00	£4.62	06/06/03	04/06/10	–
16,753	2b	05/06/00	£4.62	06/06/03	04/06/07	–
3,135	2a	12/06/00	£4.785	13/06/03	11/06/10	–
1,865	2b	12/06/00	£4.785	13/06/03	11/06/07	–
2,671	2a	23/08/00	£5.615	24/08/03	22/08/10	–
2,329	2b	23/08/00	£5.615	24/08/03	22/08/07	–
2,306	2a	09/09/00	£6.505	10/09/03	08/09/10	–
819	2b	09/09/00	£6.505	10/09/03	08/09/07	–
2,177	2a	18/09/00	£6.89	19/09/03	17/09/10	–
2,073	2b	18/09/00	£6.89	19/09/03	17/09/07	–
2,016	2a	09/10/00	£7.44	10/10/03	08/10/10	–
3,609	2b	09/10/00	£7.44	10/10/03	08/10/07	–
7,710	2a	07/12/00	£6.575	08/12/03	06/12/10	–
32,323	2b	07/12/00	£6.575	08/12/03	06/12/07	–
1,115	2a	20/01/01	£7.40	21/01/04	19/01/11	–
1,473	2a	07/03/01	£6.00	08/03/04	06/03/11	–
1,440	2a	30/07/01	£4.60	31/07/04	29/07/11	–
495	2a	30/07/01	£4.60	31/07/04	29/07/11	–
7,500	2b	01/08/01	£4.60	02/08/04	31/07/08	–
740	2a	14/08/01	£4.725	15/08/04	13/08/11	–
2,938	2a	21/08/01	£4.68	22/08/04	20/08/11	–
<b>398,186</b>						<b>164,531</b>

## Notes to the financial statements continued

for the year ended 31 August 2001

### 21 Options and warrants in shares of Phytopharm plc continued

Number outstanding 31/8/01	Note	Date granted	Exercise price	Option exercisable from	Option exercisable to	Currently exercisable
15,000	3a	24/04/96	£1.925	25/04/99	23/04/06	15,000
39,900	3b	24/04/96	£1.925	25/04/99	23/04/03	39,900
131,882	3b	06/12/97	45p	07/12/00	05/12/04	131,882
20,000	3b	23/06/99	£2.30	24/06/02	22/06/06	-
5,000	3a	02/08/99	£2.24	03/08/02	01/08/09	-
20,000	3b	20/09/99	£2.31	21/09/02	19/09/06	-
2,791	3a	06/12/99	£2.92	07/12/02	05/12/09	-
4,709	3b	06/12/99	£2.92	07/12/02	05/12/06	-
10,378	3a	15/12/99	£3.89	16/12/02	14/12/09	-
51,614	3b	15/12/99	£3.89	16/12/02	14/12/06	-
3,138	3a	18/01/00	£4.78	19/01/03	17/01/10	-
1,028	3b	18/01/00	£4.78	19/01/03	17/01/07	-
3,351	3a	17/04/00	£4.48	18/04/03	16/04/10	-
1,649	3b	17/04/00	£4.48	18/04/03	16/04/07	-
3,571	3a	20/04/00	£4.20	21/04/03	19/04/10	-
5,179	3b	20/04/00	£4.20	21/04/03	19/04/07	-
2,500	3a	02/05/00	£4.40	03/05/03	01/05/10	-
3,246	3a	05/06/00	£4.62	06/06/03	04/06/10	-
16,754	3b	05/06/00	£4.62	06/06/03	04/06/07	-
3,134	3a	12/06/00	£4.79	13/06/03	11/06/10	-
1,866	3b	12/06/00	£4.79	13/06/03	11/06/07	-
2,671	3a	23/08/00	£5.62	24/08/03	22/08/10	-
2,329	3b	23/08/00	£5.62	24/08/03	22/08/07	-
2,305	3a	09/09/00	£6.51	10/09/03	08/09/10	-
820	3b	09/09/00	£6.51	10/09/03	08/09/07	-
2,177	3a	18/09/00	£6.89	19/09/03	17/09/10	-
2,073	3b	18/09/00	£6.89	19/09/03	17/09/07	-
2,016	3a	09/10/00	£7.44	10/10/03	08/10/10	-
3,609	3b	09/10/00	£7.44	10/10/03	08/10/07	-
7,703	3a	07/12/00	£6.58	08/12/03	06/12/10	-
32,319	3b	07/12/00	£6.58	08/12/03	06/12/07	-
1,115	3a	20/01/01	£7.40	21/01/04	19/01/11	-
1,473	3a	07/03/01	£6.00	08/03/04	06/03/11	-
1,440	3a	30/07/01	£4.60	31/07/04	29/07/11	-
494	3a	30/07/01	£4.60	31/07/04	29/07/11	-
7,500	3b	01/08/01	£4.60	02/08/04	31/07/08	-
741	3a	14/08/01	£4.73	15/08/04	13/08/11	-
2,937	3a	21/08/01	£4.68	22/08/04	20/08/11	-
<b>420,412</b>						<b>186,782</b>

## Notes to the financial statements continued

for the year ended 31 August 2001

### 21 Options and warrants in shares of Phytopharm plc continued

Number outstanding 31/8/01	Note	Date granted	Exercise price	Option exercisable from	Option exercisable to	Currently exercisable
276,500	4	24/04/96	£1.925	25/04/01	23/04/03	276,500
10,000	4	10/10/97	99.5p	11/10/02	09/10/04	-
470,114	4	06/12/97	45p	07/12/02	05/12/04	-
40,000	4	23/06/99	£2.30	24/06/04	22/06/06	-
10,000	4	02/08/99	£2.24	03/08/04	01/08/06	-
40,000	4	20/09/99	£2.31	21/09/04	19/09/06	-
15,000	4	06/12/99	£2.915	07/12/04	05/12/06	-
123,991	4	15/12/99	£3.89	16/12/04	14/12/06	-
5,000	4	18/01/00	£4.78	19/01/05	17/01/07	-
10,000	4	17/04/00	£4.475	18/04/05	16/04/07	-
17,500	4	20/04/00	£4.20	21/04/05	19/04/07	-
5,000	4	02/05/00	£4.40	03/05/05	01/05/07	-
40,000	4	05/06/00	£4.62	06/06/05	04/06/07	-
10,000	4	12/06/00	£4.785	13/06/05	11/06/07	-
10,000	4	23/08/00	£5.615	24/08/05	22/08/07	-
6,250	4	09/09/00	£6.505	10/09/05	08/09/07	-
8,500	4	18/09/00	£6.89	19/09/05	17/09/07	-
11,250	4	09/10/00	£7.44	10/10/05	08/10/07	-
83,993	4	07/12/00	£6.575	08/12/05	06/12/07	-
2,229	4	20/01/01	£7.40	21/01/06	19/01/08	-
2,945	4	07/03/01	£6.00	08/03/06	06/03/08	-
2,880	4	30/07/01	£4.60	31/07/06	29/07/08	-
989	4	30/07/01	£4.60	31/07/06	29/07/08	-
15,000	4	01/08/01	£4.60	02/08/06	31/07/08	-
1,481	4	14/08/01	£4.725	15/08/06	13/08/08	-
5,875	4	21/08/01	£4.68	22/08/06	20/08/08	-
1,224,497						276,500

#### Note

- 1 These options vest in tranches of one third on each of the first, second and third anniversaries of the date of grant. The options are exercisable between three and seven years from the date of grant.
- 2a These options vest in tranches of one third on each of the first, second and third anniversaries of the date of grant, and have been granted under a scheme approved by the Inland Revenue. Each option is subject to the following condition which must be satisfied before it can be exercised, namely that the increase between an amount equal to 91% of the option price for those options granted on 24 April 1996 or the option price for later grants and the middle market quotation of a share on a date falling no earlier than the third anniversary of the date of grant of that option shall be at least one and a half times the increase over the period from the date of grant to such date in the FT Actuaries All Share Index. The options remain exercisable for ten years from the date of grant.
- 2b These options vest and must satisfy the same conditions as under note 2a above. However, these options remain exercisable for seven years from the date of grant and have not been submitted to the Inland Revenue for approval.
- 3a These options vest in tranches of one third on each of the first, second and third anniversaries of the date of grant and have been granted under a scheme approved by the Inland Revenue. Each option is subject to the following condition which must be satisfied before it can be exercised, namely that the increase between an amount equal to 91% of the option price for those options granted on 24 April 1996 or the option price for later grants and the middle market quotation of a share on a date falling no earlier than the third anniversary of the date of grant of that option shall be at least two times the increase over the period from the date of grant to such date in the FT Actuaries All Share Index. The options remain exercisable for ten years from the date of grant.
- 3b These options vest and must satisfy the same conditions as under note 3a above. However, these options remain exercisable for seven years from the date of grant and have not been submitted to the Inland Revenue for approval.

## Notes to the financial statements continued

for the year ended 31 August 2001

### 21 Options and warrants in shares of Phytopharm plc continued

- 4 These options vest in tranches of one fifth on each of the first, second, third, fourth and fifth anniversaries of the date of grant. Each option is subject to the following condition which must be satisfied before it can be exercised, namely that the increase between an amount equal to 91% of the option price for those options granted on 24 April 1996 or the option price for later grants and the middle market quotation of a share on a date falling no earlier than the fifth anniversary of the date of grant of that option shall be at least one and a half times the increase over the period from the date of grant to such date in the Pharmaceuticals Index as published by the Financial Times as a constituent part of the FT Actuaries All Share Index. The options remain exercisable for seven years from the date of grant.

#### Warrants

On 19 July 1996 the group entered into an option and evaluation agreement with a third party for the evaluation of certain patented treatments. On 20 May 1998 the group exercised its option under the agreement and the third party assigned the patent rights, intellectual property and knowhow to the group to enable it to continue development of these products. As part of the consideration the group issued 50,000 share warrants at an exercise price of £1.01 per warrant. These warrants were exercised during the year ended 31 August 2000.

Under the terms of this agreement a further 300,000 warrants are issuable dependent on certain development milestones for the product being successfully achieved. These warrants, if issued, will be at a subscription price of £1.01 per share and will be exercisable for a period of four years from the date of issue.

### 22 Share premium account and reserves

#### Group

	Share premium account £	Merger reserve £	Profit and loss account £
At 1 September 2000	20,288,403	(204,211)	(15,685,643)
Premium on new share issue	11,192,932	-	-
Expenses of share issue	(228,706)	-	-
Loss for the financial year	-	-	(2,653,147)
<b>At 31 August 2001</b>	<b>31,252,629</b>	<b>(204,211)</b>	<b>(18,338,790)</b>

#### Company

	Share premium account £	Profit and loss account £
At 1 September 2000	19,792,996	457,438
Premium on new share issue	11,192,932	-
Expenses of share issue	(228,706)	-
Retained profit for the year	-	300,825
<b>At 31 August 2001</b>	<b>30,757,222</b>	<b>758,263</b>

### 23 Reconciliation of net cash flow to movement in net funds

	2001		2000	
	£	£	£	£
Increase/(decrease) in cash in the period	62,403		(25,778)	
Cash outflow from decrease in debt	51,986		66,806	
Increase in liquid resources	8,140,275		2,519,185	
Change in net funds resulting from cashflows	<b>8,254,664</b>		2,560,213	
Other non-cash items				
New finance leases		-		(65,747)
Movement in net funds in the year	<b>8,254,664</b>		2,494,466	
Net funds at 1 September	<b>5,203,847</b>		2,709,381	
Net funds at 31 August	<b>13,458,511</b>		5,203,847	

## Notes to the financial statements continued

for the year ended 31 August 2001

### 24 Analysis of net funds

	At 1 September 2000	Cashflow	Other non-cash changes	At 31 August 2001
	£	£	£	£
Cash at bank and in hand	791,722	62,403	-	854,125
	791,722	62,403	-	854,125
Finance leases	(115,772)	51,986	-	(63,786)
	675,950	114,389	-	790,339
Current asset investment	4,527,897	8,140,275	-	12,668,172
	5,203,847	8,254,664	-	13,458,511

### 25 Reconciliation of operating loss to net cash outflow from operating activities

	2001	2000
	£	£
<b>Continuing activities</b>		
Operating loss	(3,534,878)	(2,448,830)
Depreciation on tangible fixed assets	131,797	119,022
Profit on disposal of fixed assets	(9,436)	(8,946)
Decrease in trade debtors	-	2,200
(Increase)/decrease in other debtors	(62,973)	49,326
Decrease in prepayments and accrued income	22,294	18,467
Increase/(decrease) in trade creditors	220,753	(289,348)
(Decrease)/increase in other taxation and social security	(25,478)	21,169
(Decrease)/increase in accruals and deferred income	(512)	47,715
(Decrease)/increase in provision for employer's national insurance on share option gains	(14,741)	31,000
<b>Net cash outflow from continuing operating activities</b>	<b>(3,273,174)</b>	<b>(2,458,225)</b>

### 26 Major non-cash transactions

During the year the company entered into finance lease arrangements in respect of fixed assets with a total capital value at the inception of the leases of £nil (2000: £65,747).

### 27 Capital commitments

There were no capital commitments for fixed assets contracted for at 31 August 2001 (2000: £nil).

### 28 Contingent liabilities

There were no contingent liabilities at 31 August 2001 (2000: £nil).

## Notes to the financial statements continued

for the year ended 31 August 2001

### 29 Financial commitments

At 31 August 2001 there were the following annual commitments under non-cancellable operating leases:

#### Group

	2001		2000	
	Land and buildings	Other	Land and buildings	Other
	£	£	£	£
Expiring within one year	56,800	3,720	–	876
Expiring between two and five years inclusive	–	9,452	56,800	12,739
Expiring in over five years	–	–	–	–
	<b>56,800</b>	<b>13,172</b>	56,800	13,615

#### Company

	2001		2000	
	Land and buildings	Other	Land and buildings	Other
	£	£	£	£
Expiring within one year	56,800	–	–	–
Expiring between two and five years inclusive	–	–	56,800	–
Expiring in over five years	–	–	–	–
	<b>56,800</b>	–	56,800	–

### 30 Related party transactions

The group has taken advantage of the exemption available under FRS 8 not to disclose transactions between group companies.



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5 May 2004

Phytopharm plc

Interim results for the period to 29 February 2004

Phytopharm plc today announces interim results for the six-month period to 29 February 2004.

Highlights

- Commencement of Phase II study of novel Alzheimer's disease treatment under a UK Clinical Trial Exemption certificate (Programme P58)
- Second milestone received from Yamanouchi Pharmaceutical Co., Ltd. (Yamanouchi) following evaluation of Phase I data (Programme P58)
- Positive results from European multi-centre study in canine atopic dermatitis (Programme P7v)
- UK launch of Phytopica™ for canine skin disorders (Programme P7v)
- Agreement with Genitrix to launch canine joint disorders product (Programme P54v)
- Successful placing of new shares to raise £6.3 million after expenses
- Successful completion of Phase I study of novel motor neurone disease treatment under US Investigational New Drug application (Programme P59)

Dr Richard Dixey, Chief Executive of Phytopharm, said: *'Phytopharm is now in a position to benefit from income arising from both licensees and product sales. With a stronger balance sheet and major products in the clinic, we look forward to the next period with confidence.'*

Enquiries:

**Phytopharm plc**

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**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

A presentation for analysts will be held at Financial Dynamics, Holborn Gate, 26 Southampton Buildings London WC2A 1PB at 9:30am today. A recording of the analyst presentation will be available from 5pm on 5 May 2004, please call Mo Noonan on 020 7269 7116 for further details.

[www.phytopharm.co.uk](http://www.phytopharm.co.uk)

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## **Operational Review**

Phytopharm is focused on developing novel pharmaceutical products based on clinical data generated from medicinal plant extracts. Such research can identify important and innovative platforms for drug discovery that include libraries of compounds, biological targets and associated clinical and pre-clinical data. These platforms create drug development programmes aimed at target diseases, leading to multiple licensing opportunities for specific compounds within those programmes. The current status of the four platforms within Phytopharm, each at different stages of development, is described below.

### **Neurodegeneration**

The neurodegeneration platform includes programmes for Alzheimer's disease (**P58**), Parkinson's disease (**P63**) and amyotrophic lateral sclerosis (**P59**), a motor neurone disease. Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform. These molecules, which have a novel mechanism of action, are potential disease modifiers and are expected to offer a real therapeutic advance in these conditions, where there is a high unmet medical need.

The lead compound from the Alzheimer's and Parkinson's disease programmes is coded PYM50028. In pre-clinical studies, PYM50028 has been shown to be neuroprotective and to reverse both the decrease of neuronal growth factors and the neuronal degeneration observed in the ageing brain. Importantly, this product has also been shown to restore levels of proteins that are altered in the ageing brain, returning them to levels observed in the young, causing beneficial outgrowth and branching of neurites.

In December 2003, we announced that we had been granted clearance by the Medicines and Healthcare Products Regulatory Agency (MHRA) to commence a Phase II 'proof of concept' clinical study in Alzheimer's disease under a clinical trial exemption (CTX) certificate. The Phase II study utilises a randomised, double-blind, placebo-controlled design to evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after once daily oral administration over three months. The effects of PYM50028 on memory, concentration and executive function will be evaluated during the study. The study is expected to report in Q1 2005.

In January 2004, we announced that we had received a milestone of approximately \$2 million from Yamanouchi Pharmaceutical Co., Ltd., a leading Japanese pharmaceutical company and our partner for the P58 programme. This milestone was paid following receipt by Yamanouchi of the results of the Phase Ib study of PYM50028.

The lead compound arising from the motor neurone disease programme (**P59**), which targets amyotrophic lateral sclerosis (ALS), is coded PYM50018. Pre-clinical work has demonstrated that PYM50018 is a potent neuroprotective agent, reverses neurodegeneration in spinal motor neurones and improves survival and muscle strength to a greater extent than standard treatment in superoxide dismutase 1 (SOD1) mice, a model of ALS.

In December 2003, we announced that we had been granted clearance by the US Food and Drug Administration to commence a Phase I clinical study under an investigational new drug (IND) application to evaluate the safety, tolerability and pharmacokinetic profile of PYM50018 for amyotrophic lateral sclerosis. The results of this study were reported in April 2004 and confirmed that the product was well absorbed with a good safety profile. Work is now underway in preparation for a Phase Ib clinical study with this product, which should commence in Q4 2004.

### **Metabolic disease**

The metabolic disease platform is focused on obesity, obese-onset diabetes and metabolic disease. This platform comprises the patented use of three plant species, their mode of action

and related active molecules. Programme **P57** contains a novel appetite suppressant product that has been shown to reduce calorific intake in overweight subjects, as demonstrated in a double-blind, placebo-controlled clinical study that was announced by Phytopharm in December 2001. Since August 2003, Phytopharm has focussed on the development of P57 for use as a product for the dietary control of obesity. Active discussions are underway with a number of potential licensing partners in this area. Following the successful raising of £6.3 million through the issuing of new shares in February 2004, Phytopharm has initiated a substantial increase in its agronomy programme for cultivating the raw material and has optimised product characteristics, which should enable the company to be able to produce an estimated 200 million product units in 2007.

Phytopharm has also developed screens that are predictive of appetite suppressant activity that can be used to evaluate other compounds. Good progress has been made in understanding the structural activity relationships of our compounds and in the development of synthetic molecules that will form the basis of a further licensing opportunity. This programme (**P64**) is focused on the development of pharmaceutical prescription products for the treatment of obesity and metabolic disease, both of which are recognised as high risk factors for cardiovascular disease.

### **Dermatology**

The dermatology platform includes a programme concerning the use of plant extracts with a novel mode of action for the treatment of canine skin disorders (**P7v**). A programme aimed at human eczema is also emerging from this platform. Coded **P55**, steady progress has been made in developing a dosage form suitable for use in man. These products have a dual mode of action that targets both the allergic and inflammatory components of eczema.

In February 2004, we announced positive results from a European multi-centre study in canine atopic dermatitis with our three-plant product, coded PYM00217. This randomised, double-blind, placebo-controlled study in 120 dogs was conducted by 14 veterinary dermatologists in the UK and France. The study confirmed that the optimal daily dose of PYM00217 is 200 mg/kg and that the product is palatable, well tolerated and has a good overall safety profile. By the end of the 12-week dosing period there was a statistically significant reduction (-23%) in the mean Canine Atopic Dermatitis Extent and Severity Index (CADESI) score for the 200 mg/kg group ( $p < 0.01$ ). This study also demonstrated that the benefit of PYM00217 was most evident in the more severe cases (i.e., baseline CADESI greater than 50). A greater than 20% reduction in baseline score was observed for 64% of the dogs in the 200 mg/kg group compared with only 25% of cases in the placebo group ( $p < 0.05$ ).

Following the success of this study, we launched PYM00217 with the brand name Phytopica™ for the UK market on 31<sup>st</sup> March 2004, after the period end at a special symposium at the British Veterinary Dermatology Study Group's Spring meeting in Birmingham. Canine dermatological disorders are well recognised by veterinarians to be a major problem in small animal practice, with an estimated 15% of the global dog population affected by skin conditions due to allergy (Muller & Kirk's Small Animal Dermatology, 6<sup>th</sup> Ed, 2000). With around 900,000 affected animals in the UK, the canine dermatology market is estimated to be potentially worth £10 million in the UK and £100 million worldwide.

As the company's first product launch, this is a landmark event for Phytopharm. Phytopica™ is recognised by consultant veterinarians as a potential first line, premium price product. Following this UK launch to registered veterinary dermatologists, Phytopharm is now seeking global partners to market Phytopica™ in other territories.

### **Inflammation**

Finally, the inflammation platform includes a programme containing a family of novel, third generation, non-steroidal anti-inflammatory drugs ("NSAIDs") characterised by their

inhibition of a wide range of enzymes central to chronic inflammation (**P54v**). The lead product, coded PYM50014, is manufactured from two related Asian plant species.

In November 2003, we entered into a distribution, sales and marketing agreement with Genitrix Ltd, one of the UK's fastest growing veterinary products companies, to launch PYM50014 for canine joint disorders. Under the terms of the agreement, Phytopharm and Genitrix will each receive 50% of the total sales revenues of PYM50014 after deduction of manufacturing costs. Genitrix will be responsible for distribution, sales and marketing, but no deductions from the total sales revenues will be made for these activities. Phytopharm has also retained the right to co-market the product with Genitrix.

Large-scale manufacture of PYM50014 has been completed to GMP standards and the product launch to veterinarians across the UK is anticipated in Q2 2004.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This has given rise to a new programme (**P61**) that is intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders, including asthma. We anticipate the lead candidate will be ready to enter development at the end of 2004.

#### **Statement of Prospects**

In our Annual Report 2003, we wrote that Phytopharm had reached a turning point, and that the challenges that began in 2003 should bear demonstrable fruit in 2004 in terms of income from both licensing and product sales. We have now achieved two cash positive events. We received a milestone from Yamanouchi Pharmaceutical Co. concerning our P58 programme in Alzheimer's disease and after the end of the period launched our first product, Phytopica<sup>TM</sup> (**P7v**), for canine skin disorders. In addition, to strengthen our balance sheet further, we successfully raised £6.5 million from shareholders. Our portfolio continues to mature, such that we have two additional programmes, P57 for the dietary control of obesity and P59 for motor neurone disease, that are attracting substantial interest from potential licensees. We also anticipate that our other veterinary product for canine joint disorders (**P54v**) will be launched in the coming weeks.

Progress so far has been very satisfying, and we look forward to a period of sustained corporate development and financial progress.

**Dr Richard Dixey**  
**Chief Executive**

**4 May 2004**

## Financial review

	Six months ended 29 February 2004 £m	Six months ended 31 August 2003 £m	Six months ended 28 February 2003 £m	Year ended 31 August 2003 £m
Turnover	1.05	2.01	0.42	2.43
Research & development	2.59	4.00	3.23	7.23
Administrative Costs	0.59	0.65	0.51	1.15
Interest income	0.07	0.12	0.16	0.27
Net tax recoverable	0.21	0.11	0.27	0.38
Loss for period	(1.86)	(2.42)	(2.88)	(5.30)
Loss per share (p)	(4.8)	(6.2)	(7.5)	(13.7)
Working Capital	9.45	4.93	7.24	4.93

### Summary

Financial performance for the first six months to 29 February 2004 has been influenced by two main events: the second milestone payment from Yamanouchi for PYM50028 in January 2004 and the successful fund raising of a net total of £6.3 million in February 2004. The Group's investment in research and development continues to grow in line with the progress of our four development platforms, in particular, programmes P58, P59, P57, P7v and P54v, resulting in the consumption of significant cash resources.

### Turnover

Revenues of £1.05 million for the first six months of FY2004 (H1 2003: £0.42 million, H2 2003: £2.01 million) comprised principally a £1 million milestone payment from Yamanouchi Pharmaceutical Co., Ltd., following receipt by Yamanouchi of the results of the Phase Ib study of PYM50028.

### Expenses

Research and development remained our most significant investment, totalling £2.59 million or 82% of total operating costs, a decrease of 19% (H1 2003: £3.23 million, H2 2003: £4.00 million). This expenditure is mainly attributable to the successful progress of the P58 programme which is in clinical trials and to a lesser extent the now successfully completed PYM00217 (P7v) clinical trial. The research and development activity required administrative support of £0.59 million (H1 2003: £0.51 million, H2 2003: £0.65 million). This period's total operating expenses were £3.18 million, a decrease of 15% (H1 2003: £3.74 million, H2 2003: £4.65 million), in line with the budget.

### Interest and Tax

Interest income of £0.07 million was lower this period (H1 2003: £0.16 million, H2 2003: £0.12 million), due to a combination of lower average cash balances and lower interest rates, and represents an average return of 2.1% on the cash balances throughout the period. The net tax recoverable of £0.21 million was also lower this period (H1 2003: £0.27 million, H2 2003: £0.11 million), despite a similar research and development corporation tax credit to the previous period, due to the payment of a 10% Japanese withholding tax deducted from the Yamanouchi income earlier in the year.

### Liquidity and Capital Resources

At 29 February 2004 the Group had cash and liquid resources of £9.07 million, £3.45 million higher than at the start of the financial year, following the successful fund raising in February 2004.

The fixed asset base remained low at £0.17 million from the start of the six month period as research and development activities are contracted out so that the Group does not need to finance its own laboratory facilities. Debtors of £1.12 million are 2.6% higher than at the start of the period, comprising principally research and development tax credits. Creditors of £0.94 million are 48% lower than at the start of the period, comprising mainly trade creditors and accruals.

Working capital at 29 February 2004 was £9.4 million. The Group utilised £1.8 million of working capital during H1 2004, excluding the fundraising which occurred at the end of the period, which is equivalent to around £301,000 per month. This expenditure is in line with the Group's business plan and is a consequence of the P58 programme maturing.

The loss for the period was £1.86 million, which is a reduction of £1.02 million from the loss reported in H1 2003. This improvement was a result of a combination of an increase in turnover of £0.63 million and decreases in net tax recoverable of £0.06 million, interest income of £0.09 million and operating expenses of £0.55 million. Overall the results for the period were very gratifying and within budget.

**Dr Wang Chong**

**4 May 2004**

## **Independent review report to Phytopharm plc**

### **Introduction**

We have been instructed by the company to review the financial information which comprises the consolidated profit and loss account, the consolidated balance sheet, the reconciliation of movements in group shareholders' funds and the consolidated cashflow statement and the related notes. We have read the other information contained in the interim report and considered whether it contains any apparent misstatements or material inconsistencies with the financial information.

### **Directors' responsibilities**

The interim report, including the financial information contained therein, is the responsibility of, and has been approved by the directors. The directors are responsible for preparing the interim report in accordance with the Listing Rules of the Financial Services Authority which require that the accounting policies and presentation applied to the interim figures should be consistent with those applied in preparing the preceding annual accounts except where any changes, and the reasons for them, are disclosed.

### **Review work performed**

We conducted our review in accordance with guidance contained in Bulletin 1999/4 issued by the Auditing Practices Board for use in the United Kingdom. A review consists principally of making enquiries of company management and applying analytical procedures to the financial information and underlying financial data and, based thereon, assessing whether the accounting policies and presentation have been consistently applied unless otherwise disclosed. A review excludes audit procedures such as tests of controls and verification of assets, liabilities and transactions. It is substantially less in scope than an audit performed in accordance with United Kingdom Auditing Standards and therefore provides a lower level of assurance than an audit. Accordingly we do not express an audit opinion on the financial information. This report, including the conclusion, has been prepared for and only for the company for the purpose of the Listing Rules of the Financial Services Authority and for no other purpose. We do not, in producing this report, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

### **Review conclusion**

On the basis of our review we are not aware of any material modifications that should be made to the financial information as presented for the six months ended 29 February 2004.

PricewaterhouseCoopers LLP  
Chartered Accountants  
Cambridge  
4 May 2004

## Unaudited consolidated profit and loss account for six months ended 29 February 2004

	Notes	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
Turnover	2	1,052,360	420,000	2,426,654
Other operating expenses	3	(3,184,923)	(3,735,536)	(8,380,956)
<b>Operating loss</b>		<b>(2,132,563)</b>	<b>(3,315,536)</b>	<b>(5,954,302)</b>
Interest receivable and similar income		69,693	156,963	277,336
Interest payable and similar charges		-	(268)	(4,451)
<b>Loss on ordinary activities before taxation</b>		<b>(2,062,870)</b>	<b>(3,158,841)</b>	<b>(5,681,417)</b>
Tax on loss on ordinary activities	4	205,434	274,341	378,099
<b>Loss for the period</b>	6	<b>(1,857,436)</b>	<b>(2,884,500)</b>	<b>(5,303,318)</b>
Basic and fully diluted loss per share (pence)	5	(4.8)	(7.5)	(13.7)
IIMR loss per share (pence)	5	(4.8)	(7.5)	(13.7)

## Unaudited reconciliation of movements in Group shareholders' funds for the six months ended 29 February 2004

	Notes	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
Loss for the period		(1,857,436)	(2,884,500)	(5,303,318)
New share capital issued		6,517,429	20,155	84,060
Expenses of share capital issued		(163,721)	-	-
Share option compensation charge		27,340	10,000	31,470
Net increase in shareholders' funds		4,523,612	(2,854,345)	(5,187,788)
Opening shareholders' funds		5,096,884	10,284,672	10,284,672
<b>Closing shareholders' funds</b>		<b>9,620,496</b>	<b>7,430,327</b>	<b>5,096,884</b>

## Unaudited consolidated balance sheet at 29 February 2004

	Notes	Unaudited At 29 Feb 2004 £	Unaudited At 28 Feb 2003 £	Audited At 31 Aug 2003 £
<b>Fixed assets</b>				
Tangible assets		<u>171,675</u>	<u>190,415</u>	<u>161,925</u>
		171,675	190,415	161,925
<b>Current assets</b>				
Stocks		195,820	-	42,751
Debtors		1,122,908	1,801,726	1,094,549
Cash held on deposit as short term investments		2,541,243	6,524,725	5,131,552
Cash at bank and in hand		<u>6,526,875</u>	<u>60,406</u>	<u>481,603</u>
		10,386,846	8,386,857	6,750,455
Creditors: amounts falling due within one year		<u>(938,025)</u>	<u>(1,146,945)</u>	<u>(1,815,496)</u>
		9,448,821	7,239,912	4,934,959
<b>Net current assets</b>		<u>9,448,821</u>	<u>7,239,912</u>	<u>4,934,959</u>
<b>Total assets less current liabilities</b>		<u>9,620,496</u>	<u>7,430,327</u>	<u>5,096,884</u>
<b>Net assets</b>		<u>9,620,496</u>	<u>7,430,327</u>	<u>5,096,884</u>
<b>Capital and reserves</b>				
Called up share capital		427,433	386,553	387,852
Share premium account	6	38,122,526	31,745,796	31,808,399
Merger reserve	6	(204,211)	(204,211)	(204,211)
Profit and loss account	6	<u>(28,725,252)</u>	<u>(24,497,811)</u>	<u>(26,895,156)</u>
<b>Equity shareholders' funds</b>		<u>9,620,496</u>	<u>7,430,327</u>	<u>5,096,884</u>

## Unaudited consolidated cash flow statement for the six months ended 29 February 2004

	Notes	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
<b>Net cash outflow from continuing operating activities</b>		<b>(3,095,843)</b>	<b>(2,748,491)</b>	<b>(3,938,176)</b>
<b>Returns on investment and servicing of finance</b>				
Interest received		69,693	156,963	277,336
Interest paid on finance leases		-	(269)	(321)
Other interest paid		-	-	(4,130)
<b>Net cash inflow from returns on investment and servicing of finance</b>		<b>69,693</b>	<b>156,694</b>	<b>272,885</b>
<b>Taxation</b>				
UK corporation tax credit received		277,600	-	276,954
Foreign taxation paid		(100,000)	-	(200,000)
<b>Net cash inflow from taxation</b>		<b>177,600</b>	<b>-</b>	<b>76,954</b>
<b>Capital expenditure and financial investment</b>				
Purchase of tangible fixed assets		(59,945)	(37,349)	(85,547)
Proceeds on sale of tangible fixed assets		9,750	46,166	57,467
<b>Net cash (outflow)/inflow for capital expenditure</b>		<b>(50,195)</b>	<b>8,817</b>	<b>(28,080)</b>
<b>Cash outflow before use of liquid resources</b>		<b>(2,898,745)</b>	<b>(2,582,980)</b>	<b>(3,616,417)</b>
<b>Management of liquid resources</b>				
Decrease in cash held on short term deposit		2,590,309	2,306,533	3,699,707
<b>Financing</b>				
Proceeds from exercise of share options		33,367	19,709	84,060
Proceeds from issue of share capital		6,484,062	448	-
Expenses of share capital issue		(163,721)	-	-
Repayment of principal under finance leases		-	(5,829)	(8,271)
<b>Net cash inflow from financing</b>		<b>6,353,708</b>	<b>14,328</b>	<b>75,789</b>
<b>Increase/(decrease) in cash</b>		<b>6,045,272</b>	<b>(262,119)</b>	<b>159,079</b>

## Reconciliation of operating loss to net cash outflow from operating activities

	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
<b>Continuing activities</b>			
Operating loss	(2,132,563)	(3,315,536)	(5,954,302)
Depreciation on tangible fixed assets	45,168	56,875	105,978
(Profit)/loss on disposal of fixed assets	(4,723)	(15,132)	1,152
Increase in stocks	(153,069)	-	(42,751)
(Increase)/decrease in debtors	(525)	1,316,009	2,049,990
Decrease in creditors	(877,471)	(800,707)	(129,713)
Share option compensation charge	27,340	10,000	31,470
<b>Net cash outflow from continuing operating activities</b>	<b>(3,095,843)</b>	<b>(2,748,491)</b>	<b>(3,938,176)</b>

## Notes to the interim report

### 1. Preparation of Interim Statements

The interim results have been prepared in accordance with the accounting policies set out in the Group's 2003 annual report and are unaudited. The information set out in this interim report for the six months to 29 February 2004 does not comprise statutory accounts within the meaning of the Companies Act 1985.

The figures for the year ended 31 August 2003 are abridged from the Group's statutory accounts for that year, which received an unqualified auditors' report and have been filed with the Registrar of Companies.

### 2. Turnover

	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
<b>By business activity</b>			
Licensing and development	<u>1,052,360</u>	<u>420,000</u>	<u>2,426,654</u>

### 3. Other Operating Expenses

Other operating expenses comprise:

	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
Research and development expenditure	2,597,986	3,226,908	7,227,930
Administrative expenditure	<u>586,937</u>	<u>508,628</u>	<u>1,153,026</u>
	<u>3,184,923</u>	<u>3,735,536</u>	<u>8,380,956</u>

### 4. Tax on Loss on Ordinary Activities

	Unaudited Six months ended 29 Feb 2004 £	Unaudited Six months ended 28 Feb 2003 £	Audited Year ended 31 Aug 2003 £
<b>Current tax</b>			
UK corporation tax credit on loss for period	305,434	274,341	578,099
Foreign tax	<u>(100,000)</u>	<u>-</u>	<u>(200,000)</u>
Corporation tax credit at 24%	<u>205,434</u>	<u>274,341</u>	<u>378,099</u>

Foreign tax related to 10% Japanese withholding tax.

There is no corporation tax charge because of the incidence of tax losses. The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound of actual spend.

### 5. Loss Per Share

The loss per share is based on losses of £1,857,436 and 38,882,416 ordinary shares, being the weighted average number of shares in issue during the period. The Institute of Investment Management and Research (the 'IIMR') earnings per share figures exclude gains and losses from disposals of fixed assets during the period.

6. Share Premium Account and Reserves

	Share Premium Account £	Merger Reserve £	Profit and Loss Account £
At 1 September 2003	31,808,399	(204,211)	(26,895,156)
Premium on new share issue	6,477,848	-	-
Expense of share issue	(163,721)	-	-
Share option compensation charge	-	-	27,340
Loss for the period	-	-	(1,857,436)
<b>At 29 February 2004</b>	<b><u>38,122,526</u></b>	<b><u>(204,211)</u></b>	<b><u>(28,725,252)</u></b>

1 May 2003

**Phytopharm plc**

**Interim results for the period to 28 February 2003**

Phytopharm plc today announces interim results for the six-month period to 28 February 2003.

**Announced Today (see separate press release)**

- Yamanouchi Pharma Co Ltd licenses compound PYM50028 from neurodegeneration platform
  - \$33 million of potential milestones for Alzheimer's indication (P58)
  - Royalties payable on product sales
- Yamanouchi takes options for Parkinson's disease, Lewy body dementia, vascular dementia and mild cognitive impairment (P63)
  - Payments based on relative market size of indications to Alzheimer's disease
  - Royalties payable on product sales
- Licence and option to Yamanouchi relate to Japan and other Asian territories representing some 15% of the world market

**Period Highlights**

- Commencement of Phase I clinical study in Parkinson's disease (P63)
- Positive first six-month update received from Pfizer on progress of obesity programme (P57)
- Good pre-clinical progress on semi-synthetic appetite suppressant programme (P64)
- Good clinical progress on veterinary products (P7v and P54v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"Phytopharm has met a key strategic objective in entering its agreement with Yamanouchi. The Phase II development of a lead compound from the neurodegeneration platform now joins a lead compound from the metabolic disease platform in being fully funded by a multinational licensing partner. Furthermore, this has been achieved in a manner that has retained considerable value within the Company."*

*Enquiries:*

**Phytopharm plc**  
Dr Richard Dixey, Chief Executive

Today: 07867 782000  
Thereafter: 01480 437697  
Mobile: 07867 782000

**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113

A presentation for analysts will be held at Nomura International plc, 1 St Martin's-le-Grand, London EC1A 4NP at 9:30am today. Coffee will be available from 9.15am. A webcast of the analyst presentation will be available from Friday 2 May on the Company's website:

*www.phytopharm.co.uk*

## Operational Review

Phytopharm is focused on generating novel pharmaceutical products based on clinical data generated from medicinal plant extracts. Such research can lead to important and innovative platforms for drug discovery that include libraries of compounds, biological targets and associated clinical and pre-clinical data. This data in turn leads to drug development programmes aimed at target diseases, and creates multiple licensing opportunities for specific compounds within those programmes. The four platforms being developed within Phytopharm, each at different stages of development, are described below.

The metabolic disease platform is focused on obesity, obese onset diabetes and metabolic syndrome. In August 1998, Phytopharm licensed a programme coded as **P57** from within this platform to Pfizer Inc ("Pfizer"). This programme comprises the patented use of three plant species, their mode of action and related active molecules.

In March 2003, Phytopharm announced that it had received the first six monthly progress report from Pfizer concerning the ongoing development of P57. This followed the announcement in July 2002 that Pfizer was taking responsibility for the development of the programme, under the terms of the Licence and Royalty agreement entered between Pfizer and Phytopharm in August 1998. Programme P57 contains a novel appetite suppressant that has been shown to reduce calorific intake in overweight subjects, as demonstrated in a double blind placebo controlled clinical study that was announced by Phytopharm in December 2001.

The first six monthly report from Pfizer summarised the steps they have taken to continue the development of P57. A committee within Pfizer has been formed to oversee the project, which is a key development in its further progress. Work has now commenced in preparation for a double-blind, placebo-controlled residential study to clinically validate the appetite suppression mechanism and to assess the safety of a simplified low dose botanical mixture.

Phytopharm has developed screens that are predictive of appetite suppressant activity and good progress has been made in understanding the structure activity relationships and in the development of synthetic molecules that will form the basis of a further licensing opportunity. This new programme (**P64**) is focussed on the development of separate pharmaceutical prescription products for the treatment of obesity and metabolic syndrome.

The neurodegeneration platform has been extended from a programme for Alzheimer's disease (**P58**) to include programmes for Parkinson's (**P63**) and motor neurone disease (**P59**). Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform. These molecules, which have a novel mechanism of action, are potential disease modifiers and should offer a real therapeutic advance in a serious prevalent condition where there is a high unmet medical need.

A series of pre-clinical toxicology studies has now been successfully completed in advance of the forthcoming Phase II clinical study in Alzheimer's disease and other dementias using a lead compound from the Alzheimer's programme, coded PYM50028. This study is expected to commence recruitment in Q2 2003. In pre-clinical studies, PYM50028 was demonstrated to be neuroprotective, to reverse the decrease of neuronal growth factors and to reverse neuronal degeneration observed in the ageing brain. Importantly, this product restores levels of proteins that are altered in the ageing brain, returning them to levels seen in the young, causing beneficial outgrowth and branching of neurites and restoring the levels of muscarinic acetylcholine receptors.

In January 2003, we announced the start of a Phase I clinical study using a new formulation of PYM50028 to evaluate the safety, tolerability and pharmacokinetic profile for Parkinson's disease. We anticipate that the results will be reported during Q2 2003.

The programme for motor neurone disease (P59) contains different compounds and is progressing well. Pre-clinical work has demonstrated that P59 is a potent neuroprotective agent, reverses neurodegeneration in spinal motor neurones and improves survival to a greater extent than standard treatment in superoxide dismutase 1 (SOD1) mice, a model of motor neurone disease such as amyotrophic lateral sclerosis (ALS). A Phase I clinical study is planned for Q4 2003.

The inflammation platform contains a programme containing a family of novel, third generation non-steroidal anti-inflammatory drugs ("NSAID") characterised by their inhibition of a wide range of enzymes central to chronic inflammation (P54).

There is potential to use these compounds to reduce the expression of inflammatory enzymes in the companion animal market. The results of our double-blind placebo controlled trial using P54v in canine osteoarthritis have enabled us to actively pursue commercialisation of P54v in the veterinary market, and a potential partner is currently assessing the product in a field trial. Large-scale manufacture of P54v has been completed to GMP with a view to commercialisation.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This has given rise to a new programme (P61) that is intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders and also has potential in the treatment of asthma. The lead candidate will enter development towards the end of this year.

Finally, the dermatology platform comprises a programme concerning the use of extracts of plants with a novel mode of action for the treatment of canine atopic dermatitis (P7v). These products have a dual mode of action that targets both the allergic and the inflammatory components of dermatitis.

Last year, we announced the commencement of a European multi-centre study in canine atopic dermatitis with a three plant botanical product. This randomised, double-blind, placebo-controlled study is being conducted by specialist veterinary dermatologists and will determine the optimal dose for future commercialisation of the product. The study is expected to report in Q4 2003.

Phytopharm has completed the pharmaceutical development of P7v and is now able to manufacture tonne-scale quantities of material to GMP standards. Discussions with potential partners are now advancing with regard to the further development and commercialisation of this product for early next year.

A new programme aimed at eczema is also emerging from this platform. Coded P55, steady progress in developing a dosage form suitable for use in man has been made.

### **Statement of prospects**

Whereas programmes within both the metabolic disease and neurodegeneration platforms have major pharmaceutical partners funding the development of lead products, the lead products in the arthritis (P54v) and dermatitis programmes (P7v) are being aimed at veterinary markets to generate early revenue. All four platforms offer considerable upside and the potential for near-term income.

With regard to the neurodegeneration platform, further substantial licensing activity for the compound licensed to Yamanouchi can be anticipated following the Phase II trial currently planned to complete by Q4 2004. Territories representing 85% of the world market are still available following the agreement announced today. Furthermore, the large library of compounds within the platform has the potential to deliver additional licensing partnerships.

A different compound from the platform now forms the basis of the extremely encouraging P59 programme, which is addressing motor neurone disease. The expansion of the neurodegeneration platform into further disease modalities such as the neuropathies secondary to diabetes and cancer can also be anticipated.

With regard to the metabolic disease platform, not only is Pfizer fully funding the development of the lead extract for obesity within the P57 programme, but Phytopharm now has the potential of further licensing of the compound library being developed within the P64 programme, which uses different chemical forms to address the same novel mode of action. A similar situation exists with regard to the inflammation and dermatology platforms. Although lead compounds within the P7v and P54v programmes are being targeted at the veterinary market, both platforms contain libraries of compounds and data with substantial and unlicensed pharmaceutical upside. We anticipate further good progress across each of our platforms during the second half of the year.

**Dr Richard Dixey**  
**Chief Executive**

**30 April 2003**

## Financial review

	Six months ended		Year to	
	28 February	31 August	28 February	31 August
	2003	2002	2002	2002
	£000	£000	£000	£000
Turnover	420	1,627	1,087	2,714
Research & development	3,227	3,291	2,712	6,003
Administrative costs	509	538	486	1,024
Interest receivable	157	211	267	478
Corporation tax credit	274	276	278	554
Loss for period	(2,885)	(1,717)	(1,568)	(3,285)
Loss per share (p)	(7.5)	(4.5)	(4.1)	(8.5)
Working capital	7,240	10,044	11,744	10,044

### Comparison between the six-month periods ended February 2003 and August 2002

Turnover for the six months to February 2003 of £420,000 (six months to August 2002: £1,627,000) consists of development income received from Pfizer Inc for P57, the Group's appetite suppressant product. This represents the completion of the development income receivable from Pfizer under this stage of the development of P57. In July 2002, Phytopharm announced that Pfizer will now progress development of P57 under the terms of the existing licensing and royalty agreement, under which Phytopharm will receive milestone payments as the project progresses and royalties on sales.

Research and development expenditure of £3,227,000 for this six-month period has remained at approximately the same level as the previous six-month period to August 2002 (£3,291,000). However, the level of expenditure on both the P58 platform and on P64 has increased this half year in preparation for the Phase II study in Alzheimer's disease, which is due to commence later this year, and on the identification of active molecules for P64.

Administrative costs for the six months to February 2003 of £509,000 have reduced from £538,000 in the previous six month period, a decline of 5% over the period. This is principally because the half year to August 2002 included some one-off costs relating to the annual report for the year end.

Interest income has declined from £211,000 for the six months to August 2002 to £157,000 reflecting the lower average cash balances over the six months to February 2003.

The research and development tax credit for the six months to February 2003 is similar to that for the period to August 2002 as it has been limited by the level of employee taxes paid during the period.

Overall, the loss for the six months to February 2003 is £2,885,000 (six months to August 2002: £1,717,000), an increase of 68%. This reflects the reduction in turnover and was anticipated following the announcement in July 2002 regarding P57 noted above.

## **Comparison between the six month periods ended February 2003 and February 2002**

Turnover for the six months to February 2003 of £420,000 has declined by 61% over the corresponding period last year following the announcement in July 2002 that Pfizer was progressing the development of P57 as noted above.

Research and development expenditure of £3,227,000 for the period represents an increase of 19% or £515,000 over the corresponding period last year. Significant increases in development expenditure on P58 as the development phase has moved through Phase I towards Phase II have more than offset the reduction in expenditure on P57, and expenditure has also been committed to P64 in the current six month period.

Administrative costs have increased marginally by £23,000 or 5% from £486,000 in the six months to February 2002 to £509,000 in the current six month period, representing a general overall increase.

Interest income has declined from £267,000 in the six month period to February 2002 to £157,000 for the current six month period, mainly as a result of lower average cash balances during the current period.

The research and development tax credit of £274,000 for the current period is similar to that for the corresponding period last year, again because it has been restricted to the level of employee taxes paid during each period.

Overall the loss for the current period of £2,885,000 is £1,317,000 greater than the corresponding period last year due to a decrease in turnover resulting from Pfizer progressing development of P57 directly, and increased research and development costs as the portfolio in general matures and P58 in particular moves through the clinic from Phase I towards Phase II.

### **Balance sheet**

The net assets at 28 February 2003 were £7,430,000, which was £2,855,000 lower than at the start of the period. This comprises the loss for the period of £2,885,000 offset by a small increase in share capital arising from the exercise of share options and a charge for the performance share award.

The fixed assets remain low at £190,000, a reduction of £51,000 over the period, as the company subcontracts its research and development and has no need to maintain its own laboratory facilities. Fixed assets comprise mainly motor vehicles and computer equipment.

Debtors at 28 February 2003 of £1,802,000 were lower than at the start of the period by £1,041,000 due to receipts from Pfizer under the development agreement for P57, the final instalment of which is included in debtors at 28 February 2003. Also included in debtors is the research and development tax credit for the year to August 2002.

Creditors at 28 February 2003 of £1,147,000 are £806,000 less than at the start of the period. This is due to a reduction in trade creditors and accruals and deferred income. Trade creditors and accruals are lower at the end of the February 2003 compared to August 2002, although the level of expenditure in each of the six month periods was similar due to a combination of phasing of individual projects and invoicing from contractors. There was also no deferred income at the end of February 2003. The Group has no long-term creditors.

### **Financing**

At the end of February, the Group had working capital of £7,240,000, representing 97% of the total assets of the group (28 February 2002: 98%) as the Group had a low level of fixed assets and no long term creditors. Over the six month period, the Group utilised £2,824,000 of working capital excluding the proceeds from share issues (six months to August 2002:

£1,744,000), which represents a monthly average of £471,000 (six months to August 2002: £291,000). This increase in net expenditure was in line with the Group's expectations for the period and was due to the reduction in development income in the current period.

The licence agreement announced today with Yamanouchi for P58 in Japan and other Asian countries provides a milestone stream over the next two years, which we anticipate will be sufficient to finance the Group until the forecast completion of the Phase II study in Alzheimer's disease and subsequent licence of P58 for the rest of the world.

**Dr Simon Loach**  
**Chief Financial Officer**  
**30 April 2003**

## **Independent review report to Phytopharm plc**

### **Introduction**

We have been instructed by the company to review the financial information which comprises the consolidated profit and loss account, the consolidated balance sheet and the consolidated cashflow statement and the related notes. We have read the other information contained in the interim report and considered whether it contains any apparent misstatements or material inconsistencies with the financial information.

### **Directors' responsibilities**

The interim report, including the financial information contained therein, is the responsibility of, and has been approved by the directors. The directors are responsible for preparing the interim report in accordance with the Listing Rules of the Financial Services Authority which require that the accounting policies and presentation applied to the interim figures should be consistent with those applied in preparing the preceding annual accounts except where any changes, and the reasons for them, are disclosed.

### **Review work performed**

We conducted our review in accordance with guidance contained in Bulletin 1999/4 issued by the Auditing Practices Board for use in the United Kingdom. A review consists principally of making enquiries of company management and applying analytical procedures to the financial information and underlying financial data and, based thereon, assessing whether the accounting policies and presentation have been consistently applied unless otherwise disclosed. A review excludes audit procedures such as tests of controls and verification of assets, liabilities and transactions. It is substantially less in scope than an audit performed in accordance with United Kingdom Auditing Standards and therefore provides a lower level of assurance than an audit. Accordingly we do not express an audit opinion on the financial information. This report, including the conclusion, has been prepared for and only for the company for the purpose of the Listing Rules of the Financial Services Authority and for no other purpose. We do not, in producing this report, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

### **Review conclusion**

On the basis of our review we are not aware of any material modifications that should be made to the financial information as presented for the six months ended 28 February 2003.

PricewaterhouseCoopers LLP  
Chartered Accountants  
Cambridge  
30 April 2003

## Unaudited consolidated profit and loss account for six months ended 28 February 2003

	Notes	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
<b>Turnover</b>	2	420	1,087	2,714
Other operating expenses	3	(3,736)	(3,198)	(7,027)
<b>Operating loss</b>		<b>(3,316)</b>	<b>(2,111)</b>	<b>(4,313)</b>
Interest receivable and similar income		157	267	478
Interest payable and similar charges		-	(2)	(4)
<b>Loss on ordinary activities before taxation</b>		<b>(3,159)</b>	<b>(1,846)</b>	<b>(3,839)</b>
Tax on loss on ordinary activities	4	274	278	554
<b>Loss for the period</b>	6	<b>(2,885)</b>	<b>(1,568)</b>	<b>(3,285)</b>
Basic and fully diluted loss per share (pence)	5	(7.5)	(4.1)	(8.5)
IIMR loss per share (pence)	5	(7.5)	(4.1)	(8.4)

## Unaudited consolidated balance sheet at 28 February 2003

	Notes	At 28 Feb 2003 £000	At 28 Feb 2002 £000	At 31 Aug 2002 £000
<b>Fixed assets</b>				
Tangible assets		190	226	241
Investments		-	30	-
		<b>190</b>	<b>256</b>	<b>241</b>
<b>Current assets</b>				
Debtors		1,802	901	2,843
Cash held on deposit as short term investments		6,525	11,427	8,831
Cash at bank and in hand		60	830	323
		<b>8,387</b>	<b>13,158</b>	<b>11,997</b>
Creditors: amounts falling due within one year		(1,147)	(1,414)	(1,953)
<b>Net current assets</b>		<b>7,240</b>	<b>11,744</b>	<b>10,044</b>
<b>Total assets less current liabilities</b>		<b>7,430</b>	<b>12,000</b>	<b>10,285</b>
Creditors: amounts falling due after more than a year		-	(3)	-
<b>Provision for liabilities and charges</b>		<b>-</b>	<b>(39)</b>	<b>-</b>
<b>Net assets</b>		<b>7,430</b>	<b>11,958</b>	<b>10,285</b>
<b>Capital and reserves</b>				
Called up share capital		387	386	386
Share premium account	6	31,745	31,682	31,726
Merger reserve	6	(204)	(204)	(204)
Profit and loss account	6	(24,498)	(19,906)	(21,623)
<b>Equity shareholders' funds</b>		<b>7,430</b>	<b>11,958</b>	<b>10,285</b>

## Unaudited consolidated cash flow statement for the six months ended 28 February 2003

	Notes	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
<b>Net cash outflow from continuing operating activities</b>		<b>(2,749)</b>	<b>(2,124)</b>	<b>(5,361)</b>
<b>Returns on investment and servicing of finance</b>				
Interest received		157	267	478
Interest paid on finance leases		-	(2)	(4)
<b>Net cash inflow from returns on investment and servicing of finance</b>		<b>157</b>	<b>265</b>	<b>474</b>
<b>Taxation</b>				
UK corporation tax credit		-	224	224
<b>Capital expenditure and financial investment</b>				
Purchase of tangible fixed assets		(37)	(43)	(140)
Proceeds on sale of tangible fixed assets		46	-	13
<b>Net cash inflow/(outflow) for capital expenditure</b>		<b>9</b>	<b>(43)</b>	<b>(127)</b>
<b>Cash outflow before use of liquid resources</b>		<b>(2,583)</b>	<b>(1,678)</b>	<b>(4,790)</b>
<b>Management of liquid resources</b>				
Decrease in cash held on short term deposit		2,306	1,241	3,837
<b>Financing</b>				
Proceeds from exercise of share options		20	434	478
Repayment of principal under finance leases		(6)	(21)	(56)
<b>Net cash inflow from financing</b>		<b>14</b>	<b>413</b>	<b>422</b>
<b>Decrease in cash</b>		<b>(263)</b>	<b>(24)</b>	<b>(531)</b>

### Reconciliation of operating loss to net cash outflow from operating activities

	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
<b>Continuing activities</b>			
Operating loss	(3,316)	(2,111)	(4,313)
Depreciation on tangible fixed assets	57	64	124
(Profit)/loss on disposal of fixed assets	(15)	-	9
Decrease/(increase) in debtors	1,315	(478)	(2,144)
(Decrease)/increase in creditors	(800)	378	949

Share option compensation charge (Note 7)	10	-	-
Provision for impairment of value in fixed asset investments	-	-	30
Increase/(decrease) in provision for employer's national insurance on share option gains	-	23	(16)
<b>Net cash outflow from continuing operating activities</b>	<b><u>(2,749)</u></b>	<b><u>(2,124)</u></b>	<b><u>(5,361)</u></b>

## Notes to the interim report

### 1. Preparation of Interim Statements

The interim results have been prepared in accordance with the accounting policies set out in the Group's 2002 annual report and are unaudited. The information set out in this interim report for the six months to 28 February 2003 does not comprise statutory accounts within the meaning of the Companies Act 1985.

The figures for the year ended 31 August 2002 are abridged from the Group's statutory accounts for that year, which received an unqualified auditor's report and have been filed with the Registrar of Companies.

### 2. Turnover

	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
<b>By business activity</b>			
Licensing and development	<u>420</u>	<u>1,087</u>	<u>2,714</u>

### 3. Other Operating Expenses

Other operating expenses comprise:

	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
Research and development expenditure	3,227	2,712	6,003
Administrative expenditure	<u>509</u>	<u>486</u>	<u>1,024</u>
	<u>3,736</u>	<u>3,198</u>	<u>7,027</u>

### 4. Tax on Loss on Ordinary Activities

	Six months ended 28 Feb 2003 £000	Six months ended 28 Feb 2002 £000	Year ended 31 Aug 2002 £000
<b>United Kingdom</b>			
Corporation tax credit at 24%	<u>274</u>	<u>278</u>	<u>554</u>

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

### 5. Loss Per Share

The loss per share is based on losses of £2,885,000 and 38,628,101 ordinary shares, being the weighted average number of shares in issue during the period. The Institute of Investment Management and Research (the 'IIMR') earnings per share figures exclude gains and losses from disposals of fixed assets during the period.

### 6. Share Premium Account and Reserves

	Share Premium Account £000	Merger Reserve £000	Profit and Loss Account £000
At 1 September 2002	31,726	(204)	(21,623)
Premium on new share issue	19	-	-
Reversal of share option compensation charge (Note 7)	-	-	10
Loss for the period	<u>-</u>	<u>-</u>	<u>(2,885)</u>

At 28 February 2003

31,745

(204)

(24,498)

**7. Performance share award**

On 6 December 2002 the Remuneration Committee made a performance share award of 300,000 ordinary shares at par to Dr D D Rees. The Remuneration Committee considered that there was considerable risk of Dr Rees leaving the company as his existing share option awards were at option prices significantly in excess of the current share price and this performance share award was granted, as permitted by Chapter 13.13A of the Listing Rules, to retain the services of Dr Rees. The award is subject to performance conditions and the benefits are not pensionable. The performance conditions are based on total shareholder return (TSR) over a three year period (with no retesting opportunities) when compared to a peer group comprising 27 other UK listed biotech and pharmaceutical companies for 200,000 shares and compared to the FTSE SmallCap index for the remaining 100,000. In each case 25% of the shares awarded will vest for median performance against the comparator group rising prorata to 100% for upper decile and above performance. None of the shares awarded will vest for below median performance. TSR is considered by the Remuneration Committee to be the most robust method of measuring company performance over the period. The terms of the awards will not be amended to the benefit of Dr Rees without seeking shareholder approval.

At the 28 February 2003 the company has calculated a compensation charge of £10,000 for the difference between the market value and share award price after adjustment for the likelihood of satisfying the performance criteria.



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## Interim results for the period to 28 February 2002

Phytopharm plc today announces interim results for the six month period to 28 February 2002.

### Highlights

- Opening of a new botanical supplies unit in South Africa to expand manufacturing capacity (P57)
- Discussions with Pfizer continue on obesity and metabolic syndrome (P57)
- Completion of 7 day repeat dose study in age related cognitive impairment (P58)
- Initiation of 28 day repeat dose study in age related cognitive impairment (P58)
- Evidence of neuroprotective effect in pre-clinical models of Parkinson's disease (P63)
- Establishment of large scale manufacture for inflammatory bowel disease (P54)
- Commencement of European multi-centre study in canine atopic dermatitis (P7v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"This has been a successful half year for Phytopharm. Sustained clinical progress has been underpinned by a strong performance in both preclinical evaluation and manufacture."*

### Enquiries:

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**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113



## Operational Review

The obesity platform, which encompasses metabolic syndrome, gives rise to programme **P57** which is focussed on obesity, obese onset diabetes and metabolic disorders. The platform comprises the patented use of three plant species, their mode of action and 17 related active molecules.

Licensed to Pfizer Inc in 1998, we remain in discussions with Pfizer concerning the future development plans for this novel appetite suppressant. This follows the successful completion of the 'proof of principle' clinical study for this orally administered agent that demonstrated a statistically significant reduction in the average daily calorie intake and reduction in body fat content of the treatment group compared with the placebo group at the completion of 15 day dosing.

In March 2002 we announced the opening of a new botanical supplies unit in South Africa to substantially expand the manufacturing capacity for P57 in support of the further development of the product. The new facility will expand the capacity for processing the raw materials by 300 percent and a programme to process substantial quantities of plant material is now underway.

The neural and muscular degeneration platform, which includes Alzheimer's and Parkinson's disease, involves the patented use of four plant species, their mode of action, drug screens and a library of 7 families of novel semi-synthetic compounds. Several lines of research are now progressing in parallel, indicating that these molecules are disease modifying agents with a similar profile to oestrogen. This work has enabled Phytopharm to develop a series of screening models that mimic these important observations, and has guided the development of semi-synthetic analogues of the original plant based materials with the potential for manufacture at a large scale. These modified oestrogen molecules (MOMs) are devoid of adverse feminising and cell proliferative effects but act by reversing the age related decline in neuronal receptor expression in the brain as well as producing powerful protective effects on these cells.

Three separate programmes coded P58, P59 and P63 are in development focussed on the reversal of age related cognitive impairment and Alzheimer's disease, neuromuscular degeneration and Parkinson's disease respectively.

Manufacture of a compound arising from **P58**, the programme for age related cognitive impairment and Alzheimer's disease, has been successfully completed to GMP in kilogram quantities. A series of pre-clinical toxicology studies has now been completed, and we announced the completion of a 7 day clinical programme of repeat dosing in the elderly in April 2002. The results enabled the commencement of a one-month placebo controlled study in elderly subjects also announced in April 2002. This stage of the study will utilise a randomised, double-blind, placebo controlled design, and will enrol 30 healthy subjects aged 55 years and older. Results will be reported during the third quarter of 2002, and will be used to determine the design for a three-month, phase II study that will commence during Q1, 2003. In the meantime, a product from the programme for Parkinson's disease (**P63**) should enter the clinical phase in Q4 2002. Pre-clinical work has demonstrated that P63 is a potent protective agent against neurodegeneration *in vitro* and stimulates the release of brain-derived neurotrophic factor (BDNF). Furthermore, P63 derived products reverse the loss of dopamine receptors in the brain and have powerful neuroprotective effects in models of Parkinson's disease *in vivo*.

The inflammation platform includes a family of novel, third generation non steroidal anti-inflammatory drugs (NSAID) characterised by their potent inhibition of NFkB, the gene activator for a wide range of enzymes central to chronic inflammation. The lead candidate, a

patented formulation with a novel mode of action, is in clinical evaluation for the treatment of inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. The ongoing phase II study to evaluate the safety and efficacy of **P54** for the treatment of steroid dependent inflammatory bowel disease is due to complete in June 2002.

There is also potential for the use of compounds that reduce the expression of inflammatory enzymes in the companion animal market. The results last year of our double-blind placebo controlled trial using **P54v** in canine osteoarthritis have enabled us actively to pursue commercialisation of **P54v** in the veterinary market. Large scale manufacture of **P54** is currently ongoing in preparation for commercialisation.

A further programme arising out of this platform, codenamed **P61**, has continued to generate novel semi-synthetic molecules for the treatment of disorders of the digestive tract, in particular irritable bowel syndrome (IBS). Pre-clinical work has demonstrated that these molecules have powerful inhibitory effects on intestinal spasm in a model of irritable bowel syndrome in addition to their anti-inflammatory effects. Importantly these molecules inhibit both histamine and serotonin induced intestinal spasms. The lead candidate will enter development in the second half of next year.

Finally, the dermatology platform comprises the patented use of five plants with a novel mode of action for the treatment of eczema. In March we announced the commencement of a European multi-centre study in canine atopic dermatitis (**P7v**). This randomised, double-blind, placebo controlled study will be conducted by specialist veterinary dermatologists located in France and the United Kingdom. The study will determine the optimal dose for future commercialisation of the product, which consists of granules presented in a foil sachet. The study is expected to complete in Q4 2002 and will be reported in Q1 2003.

Mode of action work continues to demonstrate the dual mechanism of action of the product targeting both the allergic and the inflammatory components of eczema to alleviate the condition. Over the period we completed the pharmaceutical development of the product and we are now able to manufacture tonne quantities of material to GMP standards.

Discussions with potential partners are now advancing concerning the further development and commercialisation of this product.

Efforts to develop a scalable version of the active compound emerging from this programme, coded **P55**, are continuing. We hope to be able to announce the final specification of a dosage form by the end of 2002.

Dr Richard Dixey  
Chief Executive  
8 May 2002

## Financial review

	Six months ended			Year to
	28 February	31 August	28 February	31 August
	2002	2001	2001	2001
	£000	£000	£000	£000
Turnover	1,087	789	682	1,471
Research & development	(2,712)	(2,150)	(1,883)	(4,033)
Administrative costs	(486)	(523)	(450)	(973)
Interest receivable	267	384	282	666
Corporation tax credit	278	195	29	224
Loss for period	(1,568)	(1,308)	(1,345)	(2,653)
Loss per share (p)	(4.1)	(3.4)	(3.6)	(7.1)
Working capital	11,744	12,845	14,111	12,845

### Comparison between the six month periods ended February 2002 and August 2001

Turnover, representing development income under the Group's licence and development agreement with Pfizer Inc for P57, increased by 38% to £1,087,000 for the six months to 28 February 2002 as P57 successfully completed the proof of principle phase of clinical development.

Overall operating expenses for the first six months of financial year 2002 were £3,198,000, an increase of 20% over the previous 6 months. Within operating expenses research and development expenditure increased by 26%, due to a combination of the increased expenditure on P57 noted above and also to increased spend on the rest of the portfolio, most particularly on the P58 platform which entered the clinical phase in this last six months. Expenditure on administrative costs declined by 7% to £486,000 for the six months to February 2002 mainly because the previous six months included non recurring costs such as relocation and year end costs such as the cost of production of the annual report.

Interest receivable for the six months to February 2002 was £267,000, a fall of 30% on the previous 6 months due to the fall in interest rates and lower average cash balances for the period. The research and development tax credit increased by 43% to £278,000 for the period to February 2002 due to the increased level of research and development.

The net effect of the above was an increase in the loss for the period of 20% to £1,568,000, which was in line with expectations.

### Comparison between the six month periods ended February 2002 and February 2001

Turnover for the six months to February 2002 has increased by 59% to £1,087,000 compared to the corresponding period last year due to increased activity on project P57. This was

mainly due to the proof of principle clinical phase which was successfully completed and reported in the period.

Research and development costs for the period to February 2002 are 44% higher than the corresponding period last year at £2,712,000 due to the increased activity on project P57 noted above and also increased spend on the rest of the portfolio. Administrative costs to February 2002 have increased by 8% to £486,000 compared to the corresponding period last year. Overall overheads for the period to February 2002 are 37% higher than for the corresponding period last year.

Interest receivable for the six months to February 2002 is £267,000 and is 5% less than the corresponding period last year. This is caused principally by lower average interest rates over the current period. The research and development tax credit available for the six months to February 2002 was £278,000. The group was eligible for the research and development tax credit from 1 February 2001, so the tax credit of £29,000 for the corresponding period last year represented only one month.

The loss for the six months to February 2002 of £1,568,000 was 17% higher than the loss for the six months to February 2001, which was in-line with expectations.

### **Balance sheet**

The net assets of the group at 28 February 2002 were £11,958,000 and are £1,134,000 lower than at the start of the period. This decrease comprises the loss of £1,568,000 offset by an increase in share capital and premium of £434,000 arising from the exercise of share options. Fixed assets remain relatively low at £226,000, a reduction of £21,000 since August 2001, as the company subcontracts out its research and development requirements to specialist contractors and has no need to maintain its own laboratory facilities.

Debtors of £901,000 are £307,000 higher than at February 2001. This increase comprises mainly the increase in the research and development tax credit available of £249,000, with the balance representing research and development income due under the licence and development agreement for P57. The debtors at the end of August 2001 did not include any development income.

Short term creditors at the end of February 2002 were £1,414,000 and were £296,000 higher than at the end of February 2001 which is as expected from the higher levels of expenditure in the period. The provisions for liabilities and charges represent the potential liability of the group to Employer's National Insurance on the gains arising on the exercise of share options, which will become exercisable in future.

### **Financing**

At 28 February 2002 working capital was £11,744,000 and comprised 98% (28 February 2001: 98%) of net assets. During the six months to 28 February 2002 the group utilised £1,535,000 of working capital after allowing for the exercise of share options, which equates to £256,000 per month. However, if the research and development tax credit is excluded this increases to £270,000 per month. The average working capital usage, excluding the tax credit, for the six months to August 2001 was £248,000 while that for the six months to February 2001 was £231,000. These increases in working capital usage are in line with the group's forecasts and arise principally as the projects within the group's portfolio develop towards the clinical phase, particularly the P58 platform for neuromuscular degeneration.

The current level of working capital and expenditure rates provide the company with over three years working capital and will, in line with current plans, allow the group to complete the first phase IIa 'proof of concept' studies of the P58 platform under its own resources in order to maximise value to the group when the product is out licensed.

Dr Simon Loach  
Chief Financial Officer  
8 May 2002

## **Independent review report to Phytopharm plc**

### **Introduction**

We have been instructed by the company to review the financial information set out on pages 7 to 9. We have read the other information contained in the interim report and considered whether it contains any apparent misstatements or material inconsistencies with the financial information.

### **Directors' responsibilities**

The interim report, including the financial information contained therein, is the responsibility of, and has been approved by the directors. The directors are responsible for preparing the interim report in accordance with the Listing Rules of the Financial Services Authority which require that the accounting policies and presentation applied to the interim figures should be consistent with those applied in preparing the preceding annual accounts except where any changes, and the reasons for them, are disclosed.

### **Review work performed**

We conducted our review in accordance with guidance contained in Bulletin 1999/4 issued by the Auditing Practices Board for use in the United Kingdom. A review consists principally of making enquiries of group management and applying analytical procedures to the financial information and underlying financial data and, based thereon, assessing whether the accounting policies and presentation have been consistently applied unless otherwise disclosed. A review excludes audit procedures such as tests of controls and verification of assets, liabilities and transactions. It is substantially less in scope than an audit performed in accordance with United Kingdom Auditing Standards and therefore provides a lower level of assurance than an audit. Accordingly we do not express an audit opinion on the financial information.

### **Review conclusion**

On the basis of our review we are not aware of any material modifications that should be made to the financial information as presented for the six months ended 28 February 2002.

PricewaterhouseCoopers  
Chartered Accountants  
Cambridge  
Date 8 May 2002

### **Notes:**

- (a) *The maintenance and integrity of the Phytopharm plc website is the responsibility of the directors; the work carried out by the auditors does not involve consideration of these matters and, accordingly, the auditors accept no responsibility for any changes that may have occurred to the interim report since it was initially presented on the website.*
- (b) *Legislation in the United Kingdom governing the preparation and dissemination of financial information may differ from legislation in other jurisdictions.*

## Unaudited consolidated profit and loss account for six months ended 28 February 2002

	Notes	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
<b>Turnover</b>	2	1,087	682	1,471
Other operating expenses	3	<u>(3,198)</u>	<u>(2,333)</u>	<u>(5,006)</u>
<b>Operating loss</b>		<b>(2,111)</b>	<b>(1,651)</b>	<b>(3,535)</b>
Interest receivable and similar income		267	282	666
Interest payable and similar charges		<u>(2)</u>	<u>(5)</u>	<u>(8)</u>
<b>Loss on ordinary activities before taxation</b>		<b>(1,846)</b>	<b>(1,374)</b>	<b>(2,877)</b>
Tax on loss on ordinary activities	4	<u>278</u>	<u>29</u>	<u>224</u>
<b>Loss for the period</b>	6	<b><u>(1,568)</u></b>	<b><u>(1,345)</u></b>	<b><u>(2,653)</u></b>
Basic and fully diluted loss per share (pence)	5	(4.1)	(3.6)	(7.1)
IIMR loss per share (pence)	5	(4.1)	(3.6)	(7.1)

## Unaudited consolidated balance sheets at 28 February 2002

	Notes	At 28 Feb 2002 £000	At 28 Feb 2001 £000	At 31 Aug 2001 £000
<b>Fixed assets</b>				
Tangible assets		226	277	247
Investments		<u>30</u>	<u>30</u>	<u>30</u>
		256	307	277
<b>Current assets</b>				
Debtors		901	594	369
Cash held on deposit as short term investments		11,427	14,591	12,668
Cash at bank and in hand		<u>830</u>	<u>44</u>	<u>854</u>
		13,158	15,229	13,891
<b>Creditors: amounts falling due within one year</b>		<b>(1,414)</b>	<b>(1,118)</b>	<b>(1,046)</b>
<b>Net current assets</b>		<b>11,744</b>	<b>14,111</b>	<b>12,845</b>
<b>Total assets less current liabilities</b>		<b>12,000</b>	<b>14,418</b>	<b>13,122</b>
<b>Creditors: amounts falling due after more than one year</b>		<b>(3)</b>	<b>(42)</b>	<b>(14)</b>
<b>Provision for liabilities and charges</b>		<b>(39)</b>	<b>(33)</b>	<b>(16)</b>
<b>Net assets</b>		<b><u>11,958</u></b>	<b><u>14,343</u></b>	<b><u>13,092</u></b>
<b>Capital and reserves</b>				
Called up share capital		386	381	382
Share premium account	6	31,682	31,196	31,252
Merger reserve	6	(204)	(204)	(204)
Profit and loss account	6	<u>(19,906)</u>	<u>(17,030)</u>	<u>(18,338)</u>
<b>Equity shareholders' funds</b>		<b><u>11,958</u></b>	<b><u>14,343</u></b>	<b><u>13,092</u></b>

**Unaudited consolidated cash flow statement for the six months ended 28 February 2002**

	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
<b>Net cash outflow from continuing operating activities</b>	<b>(2,124)</b>	<b>(1,789)</b>	<b>(3,273)</b>
<b>Returns on investment and servicing of finance</b>			
Interest received	267	296	666
Interest paid on finance leases	(2)	(5)	(8)
<b>Net cash inflow from returns on investment and servicing of finance</b>	<b>265</b>	<b>291</b>	<b>658</b>
<b>Taxation</b>			
UK corporation tax credit	224	-	-
<b>Capital expenditure and financial investment</b>			
Purchase of tangible fixed assets	(43)	(89)	(128)
Proceeds on sale of tangible fixed assets	-	4	13
<b>Net cash outflow for capital expenditure</b>	<b>(43)</b>	<b>(85)</b>	<b>(115)</b>
<b>Cash outflow before use of liquid resources</b>	<b>(1,678)</b>	<b>(1,583)</b>	<b>(2,730)</b>
<b>Management of liquid resources</b>			
Decrease/(increase) in cash held on short term deposit	1,241	(10,063)	(8,140)
<b>Financing</b>			
Proceeds from exercise of share options	434	127	183
Proceeds from issue of share capital	-	11,030	11,030
Expenses of issue of share capital	-	(229)	(229)
Repayment of principal under finance leases	(21)	(30)	(52)
<b>Net cash inflow from financing</b>	<b>413</b>	<b>10,898</b>	<b>10,932</b>
<b>(Decrease)/increase in cash</b>	<b>(24)</b>	<b>(748)</b>	<b>62</b>

**Reconciliation of operating loss to net cash outflow from operating activities**

	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
<b>Continuing activities</b>			
Operating loss	(2,111)	(1,651)	(3,535)
Depreciation on tangible fixed assets	64	64	132
Profit on disposal of fixed assets	-	(1)	(9)
Increase in debtors	(478)	(476)	(41)
Increase in creditors	378	273	195

Increase/(decrease) in provision for employer's national insurance on share option gains	23	2	(15)
<b>Net cash outflow from continuing operating activities</b>	<u>(2,124)</u>	<u>(1,789)</u>	<u>(3,273)</u>

## Notes to the interim report

### 1. Preparation of Interim Statements

The interim results have been prepared in accordance with the accounting policies set out in the Group's 2001 annual report and are unaudited. The information set out in this interim report for the six months to 28 February 2002 does not comprise statutory accounts within the meaning of the Companies Act 1985.

The figures for the year ended 31 August 2001 are abridged from the Group's statutory accounts for that year which received an unqualified auditor's report and have been filed with the Registrar of Companies.

### 2. Turnover

	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
<b>By business activity</b>			
Licensing and development	<u>1,087</u>	<u>682</u>	<u>1,471</u>

### 3. Other Operating Expenses

Other operating expenses comprise:

	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
Research and development expenditure	2,712	1,883	4,033
Administrative expenditure	<u>486</u>	<u>450</u>	<u>973</u>
	<u>3,198</u>	<u>2,333</u>	<u>5,006</u>

### 4. Tax on loss on ordinary activities

	Six months ended 28 Feb 2002 £000	Six months ended 28 Feb 2001 £000	Year ended 31 Aug 2001 £000
<b>United Kingdom</b>			
Corporation tax credit at 24%	<u>278</u>	<u>29</u>	<u>224</u>

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

### 5. Loss Per Share

The loss per share is based on losses of £1,568,000 and 38,363,467 ordinary shares, being the weighted average number of shares in issue during the period. The IIMR earnings per share figures exclude gains and losses from disposals of fixed assets during the period.

### 6. Share Premium Account and Reserves

	Share premium account £000	Merger reserve £000	Profit and loss account £000
At 1 September 2001	31,252	(204)	(18,338)
Premium on new share issue	430	-	-
Loss for the period	<u>-</u>	<u>-</u>	<u>(1,568)</u>

9 December 2003

### **Preliminary results for the year ended 31 August 2003**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm" or the "Group") today announces its preliminary results for the year ended 31 August 2003.

#### **Announced today**

- Commencement of Phase II study of novel Alzheimer's disease treatment under the terms of a UK Clinical Trial Exemption certificate (Programme P58, see separate press release).

#### **Highlights**

- Commencement of Phase I study of novel motor neurone disease treatment under US Investigational New Drug application (Programme P59)
- Successful completion of 28-day Phase I repeat dose study in novel Parkinson's disease treatment (Programme P63)
- Second milestone due from Yamanouchi Pharmaceutical Co., Ltd. ("Yamanouchi") following evaluation of Phase I data (Programmes P58 and P63)
- Return of rights and licensing progress in programme for the dietary control of obesity (Programme P57)
- Licence and Option agreement with Yamanouchi for development and commercialisation of PYM50028 in Japan and other Asian countries (Programmes P58 and P63)
- First milestone of \$3 million paid by Yamanouchi
- Appointment of marketing partner and launch programme for novel treatment for canine osteoarthritis (Programme P54v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"We have met all our deliverables for 2003 and have made strong progress. We expect 2004 to continue in a similar vein, with significant cash flows coming into the company from milestones and the launch of our veterinary products."*

*Enquiries:*

**Phytopharm plc**  
Dr Richard Dixey, Chief Executive

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Thereafter: 01480 437697  
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**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113

*Phytopharm has updated its website from 9 December 2003*  
**[www.phytopharm.com](http://www.phytopharm.com)**

## Operational review

Phytopharm is focused on developing novel pharmaceutical products based on clinical data generated from medicinal plant extracts. Such research can identify important and innovative platforms for drug discovery that include libraries of compounds, biological targets and associated clinical and pre-clinical data. This data creates drug development programmes aimed at target diseases, and leads to multiple licensing opportunities for specific compounds within those programmes. The current status of the four platforms being developed within Phytopharm, each at different stages of development, are described below.

Platform	Programme	Indication	Mode of Action	Development stage
Neuro-degeneration	P58	Alzheimer's disease/dementia	Reverse age related decline in memory	Phase II in progress
	P59	Motor neurone disease (ALS)	Neuroregenerative	Phase I in progress
	P63	Parkinson's disease	Neuroregenerative	Phase Ib completed
Metabolic disease	P57	Dietary control of obesity	Direct action on satiety centre	Phase IIa reported
	P64	Obesity and metabolic syndrome	Direct action on satiety centre	Pre-clinical
Dermatology	P7v	Canine atopic dermatitis	Inhibits allergic and inflammatory cytokines	Pre-launch
	P55	Eczema	Inhibits allergic and inflammatory cytokines	Pre-clinical
Inflammation	P54v	Canine osteoarthritis	Inhibits induction of inflammatory enzymes	Pre-launch
	P61	Asthma and other inflammatory disorders	Anti-inflammatory and anti-spasmodic	Pre-clinical

### Platform 1: Neurodegeneration

The neurodegeneration platform has been extended from a programme for Alzheimer's disease (P58) to include programmes for Parkinson's (P63) and motor neurone disease, including amyotrophic lateral sclerosis (P59). Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform. These molecules, which have a novel mechanism of action, are potential disease modifiers and are expected to offer a real therapeutic advance in these conditions where there is a high unmet medical need.

The lead compound from the Alzheimer's and Parkinson's disease programme is coded PYM50028. In pre-clinical studies, PYM50028 has been shown to be neuroprotective and to reverse both the decrease of neuronal growth factors and the neuronal degeneration observed in the ageing brain. Importantly, this product was also observed to restore levels of proteins that are altered in the ageing brain, returning them to levels observed in the young, causing beneficial outgrowth and branching of neurites. Key events during the year were the following:

- In January 2003, we announced the start of a Phase I randomised, double-blind, placebo-controlled clinical study using a new formulation of PYM50028 to evaluate the safety, tolerability and pharmacokinetic profile for Alzheimer's and Parkinson's disease. This data is a key component in understanding how PYM50028 is absorbed by man.
- In May 2003, Phytopharm signed a licensing agreement with the leading Japanese pharmaceutical company, Yamanouchi Pharmaceutical Co., Ltd., for the development and commercialisation of PYM50028. Under the agreement, Yamanouchi acquired an exclusive licence to develop, manufacture and market PYM50028 for the treatment of Alzheimer's disease in Japan and some other Asian countries, which [together] represent some 15% of the world market. Phytopharm received \$3 million upon signing of the agreement, with a further five milestones totalling \$17 million potentially payable over the next eighteen months, subject to the achievement of specific objectives. In total, Phytopharm is entitled to \$33 million of licence fees and potential milestone payments with respect to the Alzheimer's indication (of which \$3 million had been received by the year end), as well as receiving royalties on sales of PYM50028.
- Yamanouchi also acquired the option to licence PYM50028 for the additional indications of Parkinson's disease, Lewy body dementia, vascular dementia and mild cognitive impairment, for which Phytopharm will be entitled to receive potential additional licence fees and milestones. These further fees and milestones are based on each indication's market potential relative to the Alzheimer's indication. Phytopharm will also receive royalties on sales of PYM50028 by Yamanouchi for all indications developed.
- In May 2003 we announced the successful completion of the safety, tolerability and pharmacokinetics of single and repeated oral dosing of PYM50028 administered over 7 days to healthy subjects aged over 50 years.
- In June 2003 we announced that we had entered into an agreement with the Oxford Project to Investigate Memory and Ageing (OPTIMA) regarding the clinical development of PYM50028. Under the joint leadership of Professor David Smith (Project Leader, OPTIMA) and Professor Robin Jacoby (Principal Investigator), OPTIMA will enroll patients with memory impairment into the Phase II proof of principle study.
- In November 2003 we announced the successful completion of the Phase Ib stage of the study in which thirty healthy men and women aged 50 years and older were enrolled and randomly allocated to receive either PYM50028 or placebo once daily for 28 days. Results indicated that the product has absorption and pharmacokinetic characteristics suitable for once-daily dosing and is well tolerated with a good emergent safety profile.
- In November 2003 the Phase Ib data was submitted to Yamanouchi, the results of which are the subject of the second milestone payable under the licence agreement announced on 1 May 2003 between Yamanouchi and Phytopharm for marketing of PYM50028 in Japan and some other Asian countries. This payment is due imminently.

- In December 2003, we announced that we had been granted clearance by the Medicines and Healthcare Products Regulatory Agency (MHRA) to commence a Phase II 'proof of concept' clinical study in Alzheimer's disease patients under a clinical trial exemption (CTX) certificate, that was granted following a review of all the manufacturing, safety, pharmacological and clinical data generated by Phytopharm concerning PYM50028. The Phase II study utilises a randomised, double-blind, placebo-controlled design to evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after once daily oral administration over three months. The effects of PYM50028 on memory, concentration and executive function will be evaluated during the study. The study is expected to report in Q1 2005.

The lead compound arising from the motor neurone disease programme, which targets amyotrophic lateral sclerosis (ALS), (**P59**) is coded PYM50018. Pre-clinical work has demonstrated that PYM50018 is a potent neuroprotective agent, reverses neurodegeneration in spinal motor neurones and improves survival to a greater extent than standard treatment in superoxide dismutase 1 (SOD1) mice, a model of ALS.

In December 2003, we announced that **P59** had been granted clearance by the USA Food and Drug Administration to commence a Phase I clinical study under an investigational new drug (IND) application, to evaluate the safety, tolerability and pharmacokinetic profile of PYM50018 for amyotrophic lateral sclerosis. We anticipate that the results will be reported at the end of Q2 2004.

#### **Platform 2: Metabolic disease**

The metabolic disease platform is focused on obesity, obese-onset diabetes and metabolic disease. This platform comprises the patented use of three plant species, their mode of action and related active molecules. Programme **P57** contains a novel appetite suppressant product that has been shown to reduce calorific intake in overweight subjects, as demonstrated in a double-blind-placebo controlled clinical study that was announced by Phytopharm in December 2001.

In March 2003, Phytopharm announced that it had received the first six monthly progress report from Pfizer Inc. ("Pfizer") concerning the ongoing development of programme **P57**. This followed the announcement in July 2002 that Pfizer was taking responsibility for the development of the programme, under the terms of the Licence and Royalty agreement entered into between Pfizer and Phytopharm in August 1998.

In July 2003, Phytopharm announced that it had received notice from Pfizer that it was discontinuing clinical development of **P57** and returning the rights to the company. Pfizer stated that in a changing environment for discovery and development of new medicines, it continually reviews its pipeline of potential new therapies. Following the closure of the Natureceuticals group within Pfizer, the company determined that the development of **P57** might be best achieved by another organisation. Pfizer also stated that the positive clinical data of **P57** in patients generated to date encourages further study of this natural material as a therapy for obesity.

As a consequence, Phytopharm is now free to Licence **P57** to other parties. This has now created an opportunity to extend the **P57** programme into the dietary control of obesity with multiple licensing opportunities. This licensing programme is progressing vigorously, with detailed development plans in discussion with potential partners.

Phytopharm has also developed screens that are predictive of appetite suppressant activity that can be used to evaluate other compounds. Good progress has been made in understanding the structural activity relationships of our compounds and in the development of synthetic molecules that form the basis of a further licensing opportunity. This new programme (**P64**) is focused on the development of pharmaceutical prescription products for the treatment of obesity and metabolic disease.

### **Platform 3: Dermatology**

The dermatology platform comprises a programme concerning the use of extracts of plants with a novel mode of action for the treatment of canine atopic dermatitis (P7v). These products have a dual mode of action that targets both the allergic and inflammatory components of dermatitis.

In November 2003, we completed a European multi-centre study in canine atopic dermatitis with a three plant product, coded PYM00217. This randomised, double-blind, placebo-controlled study was conducted by specialist veterinary dermatologists to determine the optimal dose for future commercialisation of the product. The study is expected to report in Q1 2004.

Phytopharm has completed the pharmaceutical development of PYM00217 and is now able to manufacture tonne-scale quantities of material to Good Manufacturing Practice (GMP) standards. Commercialisation and launch of this product is well underway for early 2004.

A programme aimed at human eczema is also emerging from this platform. Coded P55, steady progress has been made in developing a dosage form suitable for use in man.

### **Platform 4: Inflammation**

Finally, the inflammation platform contains a programme containing a family of novel, third generation, non-steroidal anti-inflammatory drugs ("NSAID") characterised by their inhibition of a wide range of enzymes central to chronic inflammation (P54v).

The results of a double-blind, placebo-controlled trial of our product, coded PYM50014, in canine osteoarthritis have enabled us to actively pursue commercialisation and enter a licence and distribution agreement in the companion animal market. Large-scale manufacture of PYM50014 has been completed to GMP standards and the product will be launched in Q1 2004.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This has given rise to a new programme (P61) that is intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders including asthma. The lead candidate will enter development towards the end of 2004.

### **Statement of prospects**

We enter the coming year with considerable optimism. We are anticipating a number of cash positive events in the year: including significant milestones from Yamanouchi concerning our P58 programme in Alzheimer's disease and two product launches, for our veterinary product P7v in canine atopic dermatitis and P54v in canine osteoarthritis. In addition to this, the maturity of our portfolio means that we have three additional programmes, P57 and P64 in obesity and P59 in motor neurone disease, that are attracting substantial interest from licencees. Along with the key clinical data for P58 emerging in the first quarter of 2005, a product where 85% of the world territories remain unlicensed, the progress in our portfolio means that we are looking forward to a period of sustained progress.

### **Financial Review**

#### **Summary**

Financial performance for the fiscal year ended 31 August 2003 has been influenced by two main events: the licensing of PYM50028 to Yamanouchi in May 2003 and the transfer of the P57 development activities to Pfizer in December 2002. The Group's investment in research and development continues to grow in line with the continuing progress of our four development platforms, in particular, the P58, P63 and P7v programmes, resulting in the consumption of significant cash resources. However, the Group anticipates potential milestone payments of up to \$17 million from Yamanouchi over the next 18 months.

## Turnover

Revenues of £2.43 million for the year (2002: £2.71m) comprised a £2 million milestone payment from Yamanouchi, for the exclusive licence to develop, manufacture and market PYM50028 for the treatment of Alzheimer's disease in Japan and some other Asian countries, and £0.42 million in development income from Pfizer for P57, the Group's appetite suppressant. Revenues were lower this year following the transfer of the P57 development work to Pfizer in December 2002.

## Expenses

Research and development remained our most significant investment, totalling £7.23 million or 86% of total operating costs, an increase of 20% (2002: £6.00 million). This is largely due to the successful progress of the P58 programme which is in clinical trials and to a lesser extent the ongoing P7v clinical trial. The rise in research and development activity required additional administrative support, which is reflected in the higher administration costs of £1.16 million, an increase of 13% (2002: £1.02 million). This year's total operating expenses were £8.38 million, a rise of 19% (2002: £7.03 million), in line with budget.

## Interest and Tax

Interest income of £0.28 million was lower this year (2002: £0.48 million), due to a combination of lower average cash balances and lower interest rates, and represents an average return of 3.8% on the cash balances throughout the year. The net tax recoverable of £0.38 million was also lower this year (2002: £0.55 million), despite a similar research and development corporation tax credit to the previous year, due to the payment of a 10% Japanese withholding tax deducted from the Yamanouchi income earlier in the year.

## Liquidity and Capital Resources

At 31 August 2003 the Group had cash and liquid resources of £5.61 million, £3.54 million lower than at the start of the year.

The fixed asset base remained low at £0.16 million (2002: £0.24 million) as research and development activities are contracted out so that the Group does not need to finance its own laboratory facilities. Debtors of £1.09 million (2002: £2.84 million) comprised principally research and development tax credits. Creditors of £1.82 million (2002: £1.95 million) comprise mainly trade creditors and accruals.

Working capital at 31 August 2003 was £4.93 million. The Group utilised £5.11 million of working capital during 2003, which is equivalent to £426,000 per month. This expenditure is in line with the Group's business plan and is a consequence of the P58 programme maturing.

A combination of decreases in turnover of £0.29 million, interest income of £0.20 million, and a net tax recoverable of £0.18 million, together with an increase in operating expenses of £1.36 million, resulted in an increase in the loss for the year of £2.02 million to £5.31 million. Overall the results for the year were better than anticipated and within the budget.

## PHYTOPHARM PLC

### Consolidated Profit and Loss Account for the year ended 31 August 2003

Notes	2003 Unaudited £'000	2002 Audited £'000
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<b>Turnover</b>	2	<b>2,427</b>	2,714
		<hr/>	<hr/>
<b>Gross profit</b>		<b>2,427</b>	2,714
Other operating expenses	3	<b>(8,381)</b>	(7,027)
		<hr/>	<hr/>
<b>Operating loss</b>		<b>(5,954)</b>	(4,313)
Interest receivable and similar income		277	478
Interest payable and similar charges		(4)	(4)
		<hr/>	<hr/>
<b>Loss on ordinary activities before taxation</b>		<b>(5,681)</b>	(3,839)
		<hr/>	<hr/>
Tax on loss on ordinary activities	4	<b>378</b>	554
		<hr/>	<hr/>
<b>Loss for the year</b>	6	<b>(5,303)</b>	(3,285)
		<b>=====</b>	<b>=====</b>
Basic fully diluted loss per ordinary share (pence)	5	<b>(13.7)</b>	(8.5)
IIMR loss per share (pence)	5	<b>(13.7)</b>	(8.4)

All revenue and expenses shown above were generated from continuing operations.

The Group has no recognised gains or losses for the financial year other than those disclosed above.

PHYTOPHARM PLC

Consolidated Balance Sheet at 31 August 2003

	Notes	2003 Unaudited £'000	2002 Audited £'000
<b>Fixed assets</b>			
Tangible assets		162	241
<b>Current assets</b>			
Stocks		43	-
Debtors		1,094	2,843
Cash held on deposit as short term investments		5,131	8,831
Cash at bank and in hand		482	323
		<hr/>	<hr/>
		6,750	11,997
<b>Creditors: amounts falling due within one year</b>		<b>(1,815)</b>	<b>(1,953)</b>
		<hr/>	<hr/>
<b>Net current assets</b>		<b>4,935</b>	<b>10,044</b>
		<hr/>	<hr/>
<b>Total assets less current liabilities</b>		<b>5,097</b>	<b>10,285</b>
		<hr/>	<hr/>
<b>Net assets</b>		<b>5,097</b>	<b>10,285</b>
		=====	=====
<b>Capital and reserves</b>			
Called up share capital		388	386
Share premium account	6	31,808	31,726
Merger reserve	6	(204)	(204)
Profit and loss account	6	(26,895)	(21,623)
		<hr/>	<hr/>
<b>Equity shareholders' funds</b>		<b>5,097</b>	<b>10,285</b>
		=====	=====

PHYTOPHARM PLC

Consolidated Cash Flow Statement for the year ended 31 August 2003

	Notes	2003 Unaudited £'000	2002 Audited £'000
<b>Net cash outflow from continuing operating activities</b>	7	<b>(3,938)</b>	<b>(5,362)</b>
<b>Returns on investment and servicing of finance</b>			
Interest received		277	478
Interest paid on finance leases		-	(4)
Other interest paid		(4)	-
		<b>273</b>	<b>474</b>
<b>Taxation</b>			
UK corporation tax received		277	224
Foreign taxation paid		(200)	-
		<b>77</b>	<b>224</b>
<b>Capital expenditure and financial investment</b>			
Purchase of tangible fixed assets		(85)	(140)
Proceeds on sale of tangible fixed assets		57	13
		<b>(28)</b>	<b>(127)</b>
<b>Cash outflow before use of liquid resources and financing</b>		<b>(3,616)</b>	<b>(4,791)</b>
<b>Management of liquid resources</b>			
Decrease in cash held on short term deposit		3,700	3,837
<b>Financing</b>			
Proceeds from exercise of share options		83	478
Repayment of principal under finance leases		(8)	(56)
<b>Net cash inflow from financing</b>		<b>75</b>	<b>422</b>
<b>Increase/(Decrease) in cash in the year</b>		<b>159</b>	<b>(532)</b>

## Notes to the preliminary announcement

### 1. Basis of preparation

These financial statements have been prepared in accordance with the accounting policies set out in the annual report of the Group for the year ended 31 August 2002.

The figures shown for the year to 31 August 2003 represent unaudited abridged financial statements and have not as yet been delivered to the Registrar of Companies. The comparative figures for the year to 31 August 2002 have been taken from, but do not constitute, the Group's financial statements for that financial year. Those financial statements have been reported on by the Group's auditors and delivered to the Registrar of Companies. The report of the auditors was unqualified and did not contain a statement under s237 (2) or (3) of the Companies Act 1985.

### 2. Turnover

	2003 Unaudited £'000	2002 Audited £'000
<b>By business activity</b>		
Licensing and development	2,427 =====	2,714 =====

All turnover arose in the United Kingdom.

### 3. Other operating expenses

Other operating expenses comprise:

	2003 Unaudited £'000	2002 Audited £'000
<b>Continuing operations</b>		
Research and development	7,228	6,003
Administrative expenses	1,153	1,024
	<u>8,381</u> =====	<u>7,027</u> =====

### 4. Tax on loss on ordinary activities

	2003 Unaudited £'000	2002 Audited £'000
<b>United Kingdom</b>		
Corporation tax credit	578	554
<b>Foreign Taxation</b>		
Withholding tax suffered	(200)	-
	<u>378</u> =====	<u>554</u> =====

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses

incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

#### 5. Loss per share

The basic undiluted loss per share is based on losses of £5,303,318 (2002: loss of £3,284,518) and ordinary shares of 38,671,689 (2002: 38,480,633), being the weighted average number of shares in issue during the period. The IIMR earnings per share figure excludes gains and losses on disposals of fixed assets during the year.

#### 6. Share premium account and reserves

	Share premium account	Merger reserve	Profit and loss account
	<i>Unaudited</i> £'000	<i>Unaudited</i> £'000	<i>Unaudited</i> £'000
At 1 September 2002	31,726	(204)	(21,623)
Premium on issue of shares	82	-	-
Loss for the year	-	-	(5,303)
Share option compensation charge	-	-	31
<b>At 31 August 2003</b>	<u>31,808</u>	<u>(204)</u>	<u>(26,895)</u>

#### 7. Reconciliation of operating loss to net cash outflow from operating activities

	2003 Unaudited £'000	2002 Audited £'000
<b>Continuing activities</b>		
Operating loss	(5,954)	(4,313)
Depreciation on tangible fixed assets	106	124
Loss on disposal of fixed assets	1	9
(Increase) in stocks	(43)	-
Decrease/(Increase) in debtors	2,051	(2,145)
(Decrease)/Increase in creditors	(130)	949
Provision for impairment of value in fixed asset investments	-	30
Decrease in provision for employers National Insurance on share option gains	-	(16)
Increase in provision for share option compensation charge	31	-
<b>Net cash outflow from continuing activities</b>	<u>(3,938)</u>	<u>(5,362)</u>



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CORPORATE FINANCE  
5 December 2002

### Preliminary results for the year ended 31 August 2002

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm or the "Group" today announces its preliminary results for the year ended 31 August 2002.

### Period highlights

- Future development programme agreed with Pfizer on obesity and metabolic syndrome (P57)
- Opening of a new botanical supplies unit in South Africa to expand manufacturing capacity (P57)
- Phytopharm's own novel synthetic programme for obesity initiated (P64)
- Successful completion of 28 day Phase I repeat dose study in age-related cognitive impairment (P58)
- Evidence of neuroprotective effect in pre-clinical models of Parkinson's disease (P63)
- Survival benefit demonstrated in pre-clinical models of motor neurone disease (P59)
- Completion of Phase II study in inflammatory bowel disease (P54)
- Commencement of European multi-centre study in canine atopic dermatitis (P7v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"Phytopharm's focus on its four key platforms has allowed the Group to generate strong intellectual property and to move into related disease processes with new chemical forms. In addition to the eight products we had in development at the beginning of the year, two further projects have entered full development during 2002. We continue to generate strong product progress within tightly controlled operational costs and are on target to meet all our deliverables during 2003."*

### Enquiries:

**Phytopharm plc**  
Dr Richard Dixey, Chief Executive

Today: 07867 782000  
Thereafter: 01480 437697  
Mobile 07867 782000

**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113

*Phytopharm has updated its website from 5 December 2002  
[www.phytopharm.co.uk](http://www.phytopharm.co.uk)*

### **Business model**

Phytopharm develops a portfolio of products that have emerged from a well-established research base. Its expertise in manufacturing controlled plant extracts (botanicals) enables it to initiate early clinical evaluations and base substantial research platforms on the emergent clinical data. These platforms are not only novel, but allow the Group to generate strong intellectual property and to move into related disease processes with new chemical forms.

Phytopharm invests shareholders' funds in developing its portfolio, and remains a well-funded Group with over two years working capital at current burn rates. Once product development programmes have reached a substantive stage, the Group seeks pharmaceutical partners who pay for options to market products based on intellectual property owned by Phytopharm. These option agreements involve substantial payments to the Group, comprising the reimbursement of further development costs, the payment of milestones as key phases are completed, and royalties on eventual product sales. These payments are negotiated by reference to the size of the eventual market, the stage of development of the product concerned and the strength of the data generated.

With its small central overhead, Phytopharm offers the potential of sustained profitability once its main products have been licensed in this manner, even if royalty income arising from sales of such products is some years off. Furthermore, the botanical approach also enables the parallel development of products for early marketing in the companion animal market, thereby balancing early revenue generators with major pharmaceutical products.

### **Operational Review**

The metabolic disorders platform is focussed on obesity, obese onset diabetes and metabolic syndrome. Licensed to Pfizer Inc in 1998, the **P57** platform comprises the patented use of three plant species, their mode of action and 17 related active molecules.

In March 2002, Phytopharm announced the opening of a new botanical supplies unit in South Africa to substantially expand the manufacturing capacity for P57 in support of the further development of the product. The new facility expands the capacity for processing the raw materials by 300 per cent and a programme to process substantial quantities of plant material has been successfully undertaken.

In July 2002, Phytopharm announced the future development programme with Pfizer. The agreement followed the successful demonstration of proof of principle in man that was announced in December 2001. Pfizer will now progress the P57 development programme concerning extracts of medicinal plants under the ongoing terms of the Licence and Royalty Agreement announced between Pfizer and Phytopharm in 1998. This programme is intended to result in the development of a botanical prescription pharmaceutical for the treatment of obesity and metabolic syndrome.

Phytopharm has now developed screens that are predictive of appetite suppressant activity. This has enabled the development of synthetic molecules that will form the basis of a further licensing opportunity. This programme (**P64**) is intended to result in the development of a pharmaceutical prescription product for the treatment of obesity and metabolic syndrome.

The neurodegeneration platform has been extended to include Alzheimer's, Parkinson's and motor neurone disease. Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform that share this activity. These molecules are actively neuroprotective and stimulate the release of neuronal growth factors. Several lines of research are now progressing in parallel, indicating that these molecules actively reverse the neurodegenerative process. This novel mode of action has established a platform for the development of a number of potentially important therapeutic

approaches to diseases including those associated with ageing, such as memory impairment and dementia. This work has enabled Phytopharm to develop a series of screening models that mimic these important observations, and has guided the development of semi-synthetic analogues of the original plant based materials.

A series of preclinical toxicology studies has now been completed on a compound arising from the **P58** programme, for age-related cognitive impairment, including memory loss, dementia and Alzheimer's disease. In April 2002 Phytopharm announced the completion of a 7-day clinical programme of repeat dosing in the elderly. The successful completion of the final stage of a 28-day repeat dose clinical study was announced in October 2002. The results indicated that the product was well tolerated with a good emergent safety profile. A battery of 10 computerised cognitive function tests was also performed on days 1, 14 and 28 to optimise the cognitive endpoints for further clinical studies. These data have been evaluated for subject variability and consistency and have led to a study design, which centres on verbal memory performance including delayed word recall and overall quality of memory. These parameters will be the focus of the cognitive assessments to be conducted in the forthcoming phase II clinical study in 2003.

Manufacture of a compound from the programme for Parkinson's disease (**P63**) has been successfully completed to GMP in multi-kilogram quantities. This product is planned to enter the clinical phase in Q1 2003. Pre-clinical work has demonstrated that P63 is a potent protective agent against neurodegeneration *in vitro* and stimulates the release of neurotrophic factors, which have been shown to reverse Parkinson's disease. Furthermore, we have shown that P63 derived products reverse the loss of dopamine receptors in the brain and have powerful neuroprotective effects in models of Parkinson's disease *in vivo*.

The programme for motor neurone disease (**P59**) has progressed well. Pre-clinical work has demonstrated that P59 improves survival to a greater extent than standard treatment in Progressive Motor Neuropathy (*pnn*) mice, a model of motor neurone disease (amyotrophic lateral sclerosis; ALS).

The inflammation platform consists of a patented combination of two medicinal plants (**P54**), and includes a family of novel, third generation non steroidal anti-inflammatory drugs ("NSAID") characterised by their inhibition of a wide range of enzymes central to chronic inflammation (**P61**).

In August 2002 Phytopharm announced the results of a Phase IIa study investigating the safety and efficacy of the oral product, **P54**, in inflammatory bowel disease. The study was conducted at Addenbrooke's Hospital, Cambridge, UK and utilised a double-blind placebo-controlled design. All twenty-seven patients had clinically stable disease, but were dependent on chronic treatment with oral prednisolone (5 – 30 mg / day). Faecal calprotectin (a biomarker of disease activity released by inflammatory cells into the bowel) was determined in each subject at the start of the study. For patients with a baseline calprotectin level below 450 milligrammes per litre, all the patients in the P54 group were able to withdraw from steroid therapy. By contrast, in the placebo group less than half of the patients in this category were able to discontinue steroids without relapse. The study indicated that the P54 product, which is derived from the turmeric family, may play a role in reducing steroid dependency in patients with less severe forms of bowel disease. Treatment with P54 was generally very well tolerated and there were no safety concerns that caused any changes of dosing regimen.

There is also potential for the use of compounds that reduce the expression of inflammatory enzymes in the companion animal market. The results last year of our double-blind placebo controlled trial using **P54v** in canine osteoarthritis have enabled the Group to actively pursue

commercialisation of P54v in the veterinary market. Large-scale manufacture of P54 is currently ongoing with a view to commercialisation.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This programme is intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders and irritable bowel syndrome. The lead candidate, **P61**, will enter development in the second half of 2003.

Finally, the dermatology platform comprises the patented use of five plants with a novel mode of action for the treatment of eczema. These products have a dual mode of action that targets both the allergic and the inflammatory components of eczema.

In March 2002 Phytopharm announced the commencement of a European multi-centre study in canine atopic dermatitis with **P7v**, a three plant botanical product. This randomised, double blind, placebo controlled study is being conducted by specialist veterinary dermatologists and will determine the optimal dose for future commercialisation of the product. In total, one hundred and twenty dogs with perennial atopic dermatitis are being randomly allocated to one of four dose groups. The owners add the appropriate dose of either P7v or the matching placebo product to their dogs' food once daily for 12 weeks. The response to dosing will be assessed by changes in the canine atopic dermatitis extent and severity index (CADESI), severity of pruritus, the incidence of secondary skin infection and the overall response reported by both the veterinarians and dog owners. The study is expected to report in Q4 2003.

Over the period Phytopharm completed the pharmaceutical development of the product and is now able to manufacture tonne quantities of material to GMP standards. Discussions with potential partners are now advancing with regard to the further development and commercialisation of this product.

Methods to develop a scalable version of the active compound emerging from this programme, coded **P55**, are being developed for use in the treatment of dermatitis and eczema in humans.

### **Licensing progress**

Discussions under confidentiality agreements are in progress on products from all four platforms owned and developed by Phytopharm. Such discussions can be lengthy, and involve substantial due diligence and assessment on the part of potential licensees. Nonetheless, significant progress is being made on the neurodegeneration platform (P58) and the opportunity presented by the new chemical forms within the obesity platform (P64) is also generating substantial interest. With Pfizer's stated intention to progress the P57 product and commercial quantities of both veterinary products (P54v and P7v) becoming available during 2003, Phytopharm looks forward to the coming year with confidence.

## Financial Review

### *Results of operations*

Turnover of £2.7m for the year (2001: £1.5m) comprises development income under the licence and development agreement with Pfizer Inc for P57, the Group's appetite suppressant. The turnover is higher this year as it includes reimbursement of the 'proof of concept' clinical study completed at the end of 2001 and further manufacturing and other work to prepare for the next clinical study.

Overall operating expenses for the year of £7.03m are £2.02m higher than the previous year, an increase of 40%. Within those totals expenditure on research and development rose by 49% (£1.97m) to £6m, with administration costs also increasing by 5% to £1.02m. The increase in research and development expenditure is due to increased expenditure across the Group's portfolio of products, particularly the P58 platform and P7v with the completion of the multistage Phase I clinical study in P58 and the commencement of the multicentre clinical study in P7v. Expenditure on P57 also increased this year with the completion of the clinical study as noted above.

Interest income during the year of £0.48m is lower this year (2001: £0.67m) due to a combination of lower average cash balances during the current year and lower interest rates. The tax credit of £0.55m (2001: £0.22m) arose as the Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund. The increase in the tax credit is due in part to the higher levels of research and development expenditure this year compared to last and because the tax credit was limited to seven months research and development expenditure in the previous year.

The increase in turnover of £1.24m and the increase in the tax credit this year of £0.33m have partially offset the increase in research and development expenditure of £1.97m to give a net increase in the loss for the year of £0.63m or 24% to £3.29m. Overall the results for the year were as anticipated and were within budget.

### *Balance sheet*

The net assets at the end of the year of £10.29m show a reduction of £2.81m over the figure at the start of the year. This represents the loss for the year of £3.29m offset by £0.48m arising from the exercise of share options. The net asset level at the year-end was in line with expectations. The working capital of the Group comprises 98% (2001: 98%) of the net asset value and the bulk of this is held as cash, either on hand or on term deposits.

The fixed asset base of the Group remains low at £0.24m (2001: £0.25m) as the Group contracts out its research requirements and therefore does not need to finance its own laboratory facilities.

Debtors of £2.84m (2001: £0.37m) comprise principally income due under the licence agreement with Pfizer for P57 and the research and development tax credit. As announced on 30<sup>th</sup> July 2002 Pfizer will now progress the P57 development programme under the terms of the existing milestone and royalty agreement, which includes up to \$32m in milestone payments as well as royalties on sales of P57 by Pfizer, and the debtor from Pfizer at the year end completes reimbursement of this stage of the project. There was no income due under the licence agreement for P57 at the end of the previous year as this fell between the regular reimbursement dates.

Short-term creditors at the year-end were £1.95m and are 87% higher (£0.91m) than the previous year. Included within this figure is an additional £0.31m of deferred income with the balance comprising higher trade creditors and accruals. The increase in trade creditors and accruals arises due to higher than average monthly expenditure in July and August 2002.

#### *Financing*

Working capital at 31 August 2002 was £10.04m compared to £12.85m at the end of the previous year. Overall, after allowing for the exercise of options during the year, the Group utilised £3.28m of working capital during 2002 (2001: £2.68m). This is equivalent to an average of £273,000 per month (2001: £223,000) during the year. The average expenditure over the second half of the year was £291,000 (2001: £220,000), which represents an increase of £35,000 per month over the first six months of the year. Both the increase in expenditure over the previous year and the increase in the second half of this year were in accordance with the Group's plan and arise principally as the P58 platform matures and moves through Phase I towards Phase II clinical studies which are anticipated to start in 2003. The Group continues to maintain close control over expenditure, particularly the administrative side of the business, while continuing to develop a wide portfolio of products.

**PHYTOPHARM PLC**

**Consolidated Profit and Loss Account for the year ended 31 August 2002**

	Notes	2002 Unaudited £'000	2001 Audited £'000
<b>Turnover</b>	2	2,714	1,471
<b>Gross profit</b>		2,714	1,471
Other operating expenses	3	(7,027)	(5,006)
<b>Operating loss</b>		(4,313)	(3,535)
Interest receivable and similar income		478	666
Interest payable and similar charges		(4)	(8)
<b>Loss on ordinary activities before taxation</b>		(3,839)	(2,877)
Tax on loss on ordinary activities	4	554	224
<b>Loss for the year</b>		<u>(3,285)</u>	<u>(2,653)</u>
Basic fully diluted loss per ordinary share (pence)	5	(8.5)	(7.1)
IIMR loss per share (pence)	5	(8.4)	(7.1)

All revenue and expenses shown above were generated from continuing operations.

The Group has no recognised gains or losses for the financial year other than those disclosed above.

## PHYTOPHARM PLC

### Consolidated Balance Sheet at 31 August 2002

	Notes	2002 Unaudited £'000	2001 Audited £'000
<b>Fixed assets</b>			
Tangible assets		241	247
Investments		-	30
		241	277
<b>Current assets</b>			
Debtors		2,843	369
Cash held on deposit as short term investments		8,831	12,668
Cash at bank and in hand		323	854
		11,997	13,891
<b>Creditors: amounts falling due within one year</b>		<b>(1,953)</b>	<b>(1,046)</b>
<b>Net current assets</b>		<b>10,044</b>	<b>12,845</b>
<b>Total assets less current liabilities</b>		<b>10,285</b>	<b>13,122</b>
<b>Creditors: amounts falling due after more than one year</b>		-	(14)
<b>Provisions for liabilities and charges</b>		-	(16)
<b>Net assets</b>		<b>10,285</b>	<b>13,092</b>
<b>Capital and reserves</b>			
Called up share capital		386	382
Share premium account	6	31,726	31,252
Merger reserve	6	(204)	(204)
Profit and loss account	6	(21,623)	(18,338)
<b>Equity shareholders' funds</b>		<b>10,285</b>	<b>13,092</b>

**PHYTOPHARM PLC**

**Consolidated Cash Flow Statement for the year ended 31 August 2002**

	Notes	2002 Unaudited £'000	2001 Audited £'000
<b>Net cash outflow from continuing operating activities</b>	7	(5,361)	(3,273)
<b>Returns on investment and servicing of finance</b>		-----	-----
Interest received		478	666
Interest paid on finance leases		(4)	(8)
		-----	-----
		474	658
<b>Taxation</b>		-----	-----
UK corporation tax received		224	-
<b>Capital expenditure and financial investment</b>		-----	-----
Purchase of fixed asset investments		-	-
Purchase of tangible fixed assets		(140)	(128)
Proceeds on sale of tangible fixed assets		13	13
		-----	-----
		(127)	(115)
<b>Cash outflow before use of liquid resources and financing</b>		-----	-----
		(4,790)	(2,730)
<b>Management of liquid resources</b>		-----	-----
Decrease/(increase) in cash held on short term deposit		3,837	(8,140)
<b>Financing</b>		-----	-----
Proceeds from exercise of share options		478	183
Proceeds from issue of share capital		-	11,030
Expenses of issue of share capital		-	(229)
Repayment of principal under finance leases		(56)	(52)
		-----	-----
<b>Net cash inflow from financing</b>		422	10,932
		-----	-----
<b>(Decrease)/increase in cash in the year</b>		(531)	62
		=====	=====

## Notes to the preliminary announcement

### 1. Basis of preparation

These financial statements have been prepared in accordance with the accounting policies set out in the annual report of the Group for the year ended 31 August 2001, together with the following:

#### Basis of extraction

The figures shown for the year to 31 August 2002 represent unaudited abridged financial statements and have not as yet been delivered to the Registrar of Companies. The comparative figures for the year to 31 August 2001 have been taken from, but do not constitute, the Group's financial statements for that financial year. Those financial statements have been reported on by the Group's auditors and delivered to the Registrar of Companies. The report of the auditors was unqualified and did not contain a statement under s237 (2) or (3) of the Companies Act 1985.

### 2. Turnover

	2002 Unaudited £'000	2001 Audited £'000
<b>By business activity</b>		
Licensing and development	2,714	1,471

All turnover arose in the United Kingdom.

### 3. Other operating expenses

Other operating expenses comprise:

	2002 Unaudited £'000	2001 Audited £'000
<b>Continuing operations</b>		
Research and development	6,003	4,033
Administrative expenses	1,024	973
	<u>7,027</u>	<u>5,006</u>

### 4. Tax on loss on ordinary activities

	2002 Unaudited £'000	2001 Audited £'000
<b>United Kingdom</b>		
Corporation tax credit at 24%	554	224

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

## 5. Loss per share

The basic undiluted loss per share is based on losses of £3,284,517 (2001: loss of £2,653,147) and ordinary shares of 38,480,633 (2001: 37,609,090), being the weighted average number of shares in issue during the period. The IIMR earnings per share figure excludes gains and losses on disposals of fixed assets during the year.

## 6. Share premium account and reserves

	Share premium account Unaudited £'000	Merger Reserve Unaudited £'000	Profit and loss account Unaudited £'000
At 1 September 2001	31,252	(204)	(18,338)
Premium on issue of shares	474	-	-
Loss for the year	-	-	(3,285)
<b>At 31 August 2002</b>	<b>31,726</b>	<b>(204)</b>	<b>(21,623)</b>

## 7. Reconciliation of operating loss to net cash outflow from operating activities

	2002 Unaudited £'000	2001 Audited £'000
<b>Continuing activities</b>		
Operating loss	(4,313)	(3,535)
Depreciation on tangible fixed assets	124	132
Profit on disposal of fixed assets	9	(9)
(Increase)/decrease in debtors	(2,144)	(41)
Increase/(decrease) in creditors	949	195
Provision for impairment of value in fixed asset investments	30	-
(Decrease)/increase in provision for employer's national insurance on share option gains	(16)	(15)
<b>Net cash outflow from continuing activities</b>	<b>(5,361)</b>	<b>(3,273)</b>

5 December 2001

**Preliminary results for the year ended 31 August 2001**

Phytopharm plc today announces its preliminary results for the year ended 31 August 2001.

**Announced today**

- Successful completion of proof of principle clinical study of P57 for obesity (see separate press release)

**Period highlights**

- Initiation of repeat dose study in age related cognitive impairment (P58)
- Extension of neuronal degeneration platform into Parkinson's disease (P63)
- Establishment of large scale manufacture for canine eczema (P7v)
- Completion of phase IIa study in cancer chemo-prevention (P54)
- Completion of phase II study in canine arthritis (P54v)
- Initiation of phase II study in inflammatory bowel disease (P54)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"This has been a successful year for Phytopharm. Novel product opportunities are emerging from our drug discovery platforms in obesity, neural and muscular degeneration, dermatitis and inflammation as we continue to make good progress in the clinic, and we are now moving forward to manufacture these products on a commercial scale."*

*Enquiries:*

**Phytopharm plc**  
Dr Richard Dixey, Chief Executive

Today: 0207 638 4010  
Thereafter: 01480 437697  
Mobile 07867 782000

**Financial Dynamics**  
David Yates / Fiona Noblet

Tel: 0207 831 3113

*Phytopharm has updated its website from 5 December 2001*  
[www.phytopharm.co.uk](http://www.phytopharm.co.uk)

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CORPORATE FINANCE

## Chief Executive's Review

Phytopharm's core competence in the development of new molecules discovered from nature is now firmly established, and our business is moving forward vigorously in developing the expertise to manufacture these products on a commercial scale.

Running a drug development business is about managing risks, and our portfolio approach gives us multiple opportunities for success. This year we have taken the decision to focus on the products that are generated by our platforms, where we have established novel modes of action and identified active molecules of interest. These platforms cover the major therapeutic categories of obesity and metabolic disease, neural and muscular degeneration, inflammatory disease and dermatology. However, behind these platforms Phytopharm continues to conduct early evaluation programmes across a wide range of therapeutic areas.

## Operational Review

The obesity platform, which encompasses metabolic syndrome, gives rise to product **P57** which is focussed on obesity and obese onset diabetes. The platform comprises the patented use of three plant species, their mode of action and 17 related active molecules.

Licensed to Pfizer Inc in 1998, we announced today the successful completion of the 'proof of principle' clinical study for this orally administered agent. In this three-stage study the safety, tolerability, pharmacokinetic profile and effects of P57 on daily calorie intake were studied in overweight volunteers. Pharmacokinetic data confirmed the systemic absorption of the active constituents of P57 in the single and repeat dose stages. In the last phase of this controlled study, overweight subjects were dosed for 15 days with P57 or placebo. The results of this study were positive and confirmed proof of principle. We saw a statistically significant reduction in the average daily calorie intake of the P57 group compared with the placebo group ( $p=0.014$ ). Data also indicated a statistically significant reduction in body fat content in the P57 group compared with the placebo group at the completion of dosing ( $p=0.035$ ). No serious adverse effects were experienced by any of the subjects, and the safety data are consistent with a satisfactory emerging safety profile. This study is the fruit of a substantial research programme which we have been conducting in collaboration with Pfizer over the past three years. With predictive drug screens in operation and a clear cut demonstration of the potential of this novel approach to the treatment of obesity, we now have the basis for the substantial body of work required to carry this project forward to commercialisation.

The neural and muscular degeneration platform, which includes Alzheimer's disease, involves the patented use of four plant species, their mode of action, drug screens and a library of 7 families of novel semi-synthetic compounds. Several lines of research are now progressing in parallel, including studies at the cutting edge of proteomics. The picture that is emerging is very encouraging. Not only does the research pursued by Phytopharm demonstrate that these novel molecules have the potential to reverse the age related decline in neuronal receptor expression in the brain, but they also produce powerful protective effects on these cells. This work has enabled Phytopharm to develop a series of laboratory based screens that mimic these important observations, and has guided the development of semi-synthetic analogues of the original plant based materials which combine efficacy in the laboratory screening models with the potential for manufacture at a large scale. Three separate products coded P58, P59 and P63 are now in development focussed on the reversal of age related cognitive impairment and Alzheimer's disease, neuromuscular degeneration and Parkinson's disease respectively.

Manufacture of the lead candidate for age related cognitive impairment and Alzheimer's disease, **P58**, has been successfully scaled up to kilogram quantities. A series of pre-clinical toxicology studies has now been completed, and we announced the commencement of an extended clinical programme of repeat dosing in the elderly in November 2001. The results of the seven day phase of this study will lead to a one-month placebo controlled study in Q2 2002, and the commencement of a full phase II study in the autumn of that year. In the meantime, the programme for Parkinson's disease (**P63**) should enter the clinical phase in the second half of the year. Pre-clinical work has demonstrated that **P63** is a powerful protective agent against neurodegeneration that is characteristic of Parkinson's disease.

The inflammation platform comprises a novel, third generation non steroidal anti-inflammatory drug (NSAID) family characterised by their potent inhibition of the enzyme NFkB, the gene activator for a wide range of enzymes central to chronic inflammation. The lead candidate, a patented formulation with a novel mode of action, is in clinical evaluation for the treatment of inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. The ongoing phase II study to evaluate the safety and efficacy of **P54** for the treatment of steroid dependent inflammatory bowel disease is due to complete in Q2 2002.

Earlier in the year we also reported the results of a dose escalation study in patients with advanced colorectal cancer. The results of this small study suggest that **P54** may possess cancer chemotherapeutic as well as chemopreventive efficacy and confirmed that **P54** may have a role in the prevention of colon cancer.

There is also potential for the use of compounds that reduce the expression of inflammatory enzymes in the companion animal market. In July 2001 we announced the completion of a double-blind placebo controlled trial using **P54v** in canine osteoarthritis in which 61 dogs with osteoarthritis of the hip or elbow were recruited by the University of Bristol Veterinary School. At the end of the treatment period the investigator reported that 56% of the dogs were 'better' or 'much better' after being treated with **P54** compared to 26% of those treated with placebo ( $p=0.047$ ). The treatment was generally well tolerated with no serious adverse events recorded. These results have enabled us actively to pursue commercialisation of **P54v** in the veterinary market.

A further programme arising out of this platform, codenamed **P61**, has continued to generate novel semi-synthetic molecules for the treatment of disorders of the digestive tract. Pre-clinical work has demonstrated that these molecules inhibit intestinal spasm in a model of irritable bowel syndrome. The lead candidate will enter development in the second half of next year.

Finally, the dermatology platform comprises the patented use of five plants with a novel mode of action for the treatment of eczema. One product arising from the platform, **P7v**, has been the subject of Phase II evaluation in companion animals. This is the largest ever published study in canine atopy and the results were reported in Q4 last year. Mode of action work over the year has established that the product has a dual mechanism of action and targets both the allergic and the inflammatory components of eczema to alleviate the condition. Pharmaceutical development of the product has continued through the year and we are now manufacturing tonne quantities of material to GMP standards through a relationship with an experienced botanical manufacturer.

Discussions with potential partners are now advancing concerning the further development and commercialisation of this product.

Efforts to develop a scalable version of the active compound emerging from this platform, coded **P55**, are continuing. We hope to be able to announce the final specification of a dosage form during the course of 2002.

#### Early stage product evaluation

Phytopharm continues to operate a low cost early evaluation process. This enables the Company to conduct clinical studies on a wide range of products of potential therapeutic and commercial value. Inevitably, some of these studies are not successful. Last year we reported that **P45**, our product for alopecia androgenica failed to demonstrate a statistically significant improvement in hair re-growth when compared with placebo. We extended the study to examine this potential treatment for autoimmune alopecia, with inconclusive results. The future of our work in alopecia is now under review. Whilst it is disappointing to report early stage failures, there are an additional four projects under investigation in our early stage portfolio and thirty projects currently awaiting review. The further growth of our business arises from this activity, and it continues to play an important role in the development of new opportunities across the business.

#### **Financial Review**

##### *Results of operations*

Turnover of £1.5m for the year (2000: £2.1m) comprises development income under the licence and development agreement with Pfizer Inc for **P57**, the Group's appetite suppressant. The reduction in turnover this year arises as the previous year's figure included a milestone of £0.63m for the completion of Phase I dose ranging studies earned under the Pfizer agreement. After allowing for this, the development income has remained consistent for the last two years at £1.5m as the project progressed into a multistage Phase IIa clinical study at the year end.

The cost of sales of £0.31m in the previous year represents the proportion of the milestone income from Pfizer due to the CSIR from whom the Group originally licensed the product **P57**.

Overall operating expenses for the year of £5.01m are 19% higher than the previous year, an increase of £0.79m. Within those totals expenditure on research and development rose by 19% (£0.64m) to £4.03m, with administration costs also increasing by 19% to £0.97m. The increase in research and development expenditure is due to increased expenditure across the Group's portfolio of products other than **P57** where expenditure remained at a similar level to the previous year. Expenditure on **P57** is anticipated to increase in the coming year following the successful completion of the multistage study announced in December 2001. Within the rest of the portfolio, expenditure on **P58**, the Group's treatment for age related dementias, has increased significantly as the project progresses into the clinic and larger scale manufacturing processes are developed. The increase in administrative overheads arises from a strengthening of the business development and corporate elements of the business introduced during the previous year.

Interest income during the year of £0.67m is significantly higher this year (2000: £0.28m) following the fund raising in November 2000 (see below). The tax credit of £0.22m (2000: £nil) arose as the Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund.

The increase in interest income and the tax credit have more than offset the reduction in turnover and enabled the Group to increase operating expenditure by £0.79m or 19%, while limiting the increase in the overall loss for the year by £0.47m or 22% to £2.65m.

#### *Balance sheet*

The net assets at the end of the year of £13.09m show a considerable increase over the previous year end figure of £4.76m due to the proceeds of the share issue in November 2000 which raised net proceeds of £10.8m. The working capital of the Group comprises 98% (2000: 96%) of the net asset value and the bulk of this is held as cash, either on hand or on term deposits.

The Group has a small investment in fixed assets of £0.28m at the year end which has not changed significantly over the year. The fixed asset levels are low as the Group contracts out its research requirements and therefore does not need to finance its own laboratory facilities.

Short term creditors at the year end were £1.05m and are 23% more than the previous year. This is as expected and is primarily due to higher levels of expenditure in the year ended 31 August 2001 as noted above.

#### *Financing*

Overall, after allowing for the share issue in November 2000 and the exercise of options during the year, the Group utilised £2.71m of working capital during 2001 (2000: £2.22m). This is equivalent to an average of £226,000 per month (2000: £185,000) during the year. Excluding the effects of the tax credit received this year (£18,700 per month) and the net milestone in the previous year (£26,200 per month), the average monthly working capital consumption figure over the current year of £245,000 has increased by £34,000 per month when compared to £211,000 per month for the previous year. The increase in expenditure was planned following the Group's fundraising and is in accordance with the Group's policy of tight control of overheads and careful allocation of resources between projects.

The additional working capital raised during the year has strengthened the Group's balance sheet significantly and the directors anticipate this will allow the Group to fully develop the P58 platform to maximise its licensing potential while continuing development within the rest of the portfolio.

Dr Richard Dixey  
Chief Executive  
5 December 2001

**PHYTOPHARM PLC**

**Consolidated Profit and Loss Account for the year ended 31 August 2001**

	Notes	2001 Unaudited £'000	2000 Audited £'000
<b>Turnover</b>	2	1,471	2,078
Cost of sales		-	(314)
<b>Gross profit</b>		1,471	1,764
Other operating expenses	3	(5,006)	(4,213)
<b>Operating loss</b>		(3,535)	(2,449)
Interest receivable and similar income		666	275
Interest payable and similar charges		(8)	(9)
<b>Loss on ordinary activities before taxation</b>		(2,877)	(2,183)
Tax on loss on ordinary activities	4	224	-
<b>Loss for the year</b>		(2,653)	(2,183)
Basic fully diluted loss per ordinary share (pence)	5	(7.1)	(6.3)
IIMR loss per share (pence)	5	(7.1)	(6.3)

All revenue and expenses shown above were generated from continuing operations.

The Group has no recognised gains or losses for the financial year other than those disclosed above.

## PHYTOPHARM PLC

### Consolidated Balance Sheet at 31 August 2001

	Notes	2001 Unaudited £'000	2000 Audited £'000
<b>Fixed assets</b>			
Tangible assets		247	255
Investments		30	30
		277	285
<b>Current assets</b>			
Debtors		369	103
Cash held on deposit as short term investments		12,668	4,528
Cash at bank and in hand		854	792
		13,891	5,423
<b>Creditors: amounts falling due within one year</b>		(1,046)	(853)
<b>Net current assets</b>		12,845	4,570
<b>Total assets less current liabilities</b>		13,122	4,855
<b>Creditors: amounts falling due after more than one year</b>		(14)	(64)
<b>Provisions for liabilities and charges</b>		(16)	(31)
<b>Net assets</b>		13,092	4,760
<b>Capital and reserves</b>			
Called up share capital		382	361
Share premium account	6	31,252	20,288
Merger reserve	6	(204)	(204)
Profit and loss account	6	(18,338)	(15,685)
<b>Equity shareholders' funds</b>		13,092	4,760

## PHYTOPHARM PLC

### Consolidated Cash Flow Statement for the year ended 31 August 2001

	Notes	2001 Unaudited £'000	2000 Audited £'000
<b>Net cash outflow from continuing operating activities</b>	7	(3,273)	(2,458)
<hr/>			
<b>Returns on investment and servicing of finance</b>			
Interest received		666	264
Interest paid on finance leases		(8)	(9)
		<hr/>	<hr/>
		658	255
<hr/>			
<b>Taxation</b>			
UK corporation tax paid		-	-
<hr/>			
<b>Capital expenditure and financial investment</b>			
Purchase of fixed asset investments		-	(30)
Purchase of tangible fixed assets		(128)	(102)
Proceeds on sale of tangible fixed assets		13	13
		<hr/>	<hr/>
		(115)	(119)
<hr/>			
<b>Cash outflow before use of liquid resources and financing</b>		(2,730)	(2,322)
<hr/>			
<b>Management of liquid resources</b>			
Increase in cash held on short term deposit		(8,140)	(2,519)
<hr/>			
<b>Financing</b>			
Proceeds from exercise of share options		183	611
Proceeds from issue of share capital		11,030	4,387
Expenses of issue of share capital		(229)	(116)
Repayment of principal under finance leases		(52)	(67)
		<hr/>	<hr/>
<b>Net cash inflow from financing</b>		10,932	4,815
<hr/>			
<b>Increase/(decrease) in cash in the year</b>		<u>62</u>	<u>(26)</u>

## Notes to the preliminary announcement

### 1. Basis of preparation

These financial statements have been prepared in accordance with the accounting policies set out in the annual report of the Group for the year ended 31 August 2000, together with the following:

#### Basis of extraction

The figures shown for the year to 31 August 2001 represent unaudited abridged financial statements and have not as yet been delivered to the Registrar of Companies. The comparative figures for the year to 31 August 2000 have been taken from, but do not constitute, the Group's financial statements for that financial year. Those financial statements have been reported on by the Group's auditors and delivered to the Registrar of Companies. The report of the auditors was unqualified and did not contain a statement under s237 (2) or (3) of the Companies Act 1985.

### 2. Turnover

	2001 Unaudited £'000	2000 Audited £'000
<b>By business activity</b>		
Licensing and development	1,471	2,078

All turnover arose in the United Kingdom.

### 3. Other operating expenses

Other operating expenses comprise:

	2001 Unaudited £'000	2000 Audited £'000
<b>Continuing operations</b>		
Research and development	4,033	3,394
Administrative expenses	973	819
	<u>5,006</u>	<u>4,213</u>

### 4. Tax on loss on ordinary activities

	2001 Unaudited £'000	2000 Audited £'000
<b>United Kingdom</b>		
Corporation tax credit at 24%	224	-

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

## 5. Loss per share

The basic undiluted loss per share is based on losses of £2,653,147 (2000: loss of £2,183,222) and ordinary shares of 37,609,090 (2000: 34,923,482), being the weighted average number of shares in issue during the period. The IIMR earnings per share figure excludes gains and losses on disposals of fixed assets during the year.

## 6. Share premium account and reserves

	Share premium account Unaudited £'000	Merger Reserve Unaudited £'000	Profit and loss account Unaudited £'000
At 1 September 2000	20,288	(204)	(15,685)
Premium on issue of shares	11,193	-	-
Expenses of share issue	(229)	-	-
Loss for the year	-	-	(2,653)
<b>At 31 August 2001</b>	<b><u>31,252</u></b>	<b><u>(204)</u></b>	<b><u>(18,338)</u></b>

## 7. Reconciliation of operating loss to net cash outflow from operating activities

	2001 Unaudited £'000	2000 Audited £'000
<b>Continuing activities</b>		
Operating loss	(3,535)	(2,449)
Depreciation on tangible fixed assets	132	119
Profit on disposal of fixed assets	(9)	(9)
(Increase)/decrease in debtors	(41)	70
Increase/(decrease) in creditors	195	(220)
(Decrease)/increase in provision for employer's national insurance on share option gains	(15)	31
<b>Net cash outflow from continuing activities</b>	<b><u>(3,273)</u></b>	<b><u>(2,458)</u></b>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Director Shareholding
Released	15:54 6 May 2004
Number	3833Y

RNS Number:3833Y  
Phytopharm PLC  
6 May 2004

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

DR R P DIXEY

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2 ABOVE

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2 ABOVE

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

AS 2 ABOVE

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003

7) Number of shares/amount of stock acquired

8) Percentage of issued Class

9) Number of shares/amount

10

of stock disposed

- 10) Percentage of issued Class  
(any treasury shares held by company should not be taken into account when calculating percentage)
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
5 MAY 2004
- 18) Period during which or date on which exercisable  
6 MAY 2007 TO 5 MAY 2014 SUBJECT TO PERFORMANCE CRITERIA
- 19) Total amount paid (if any) for grant of the option  
~~NIL~~
- 20) Description of shares or debentures involved: class, number.  
20,000 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES
- 21) Exercise price (if fixed at time of grant) or indication that price  
is to be fixed at time of exercise  
185 PENCE
- 22) Total number of shares or debentures over which options held  
following this notification  
615,509
- 23) Any additional information  
PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO  
COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT.

NO OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND 100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATE VESTING BETWEEN MEDIAN AND UPPER DECILE PERFORMANCE. FOR 13,334 OPTIONS THE COMPARATOR GROUP COMPRISES 19 OTHER UK LISTED BIOTECH COMPANIES AND FOR 6,666 OPTIONS THE COMPARATOR GROUP IS THE FTSE SMALL CAP INDEX

24) Name of contact and telephone number for queries

25) Name and signature of authorised company official responsible for making this notification

DR G W CHONG

Date of Notification

6 MAY 2004

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641,318
- 23) Any additional information

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165,932
- 23) Any additional information  
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Date of Notification DR G W CHONG  
6 MAY 2004

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 Headline      Research Update  
 Released      07:00 28 Apr 2004  
 Number        0524Y

28 April 2004

**Phytopharm plc**

**Successful completion of phase I clinical study of novel treatment for motor neurone disease**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the successful completion of a phase I clinical study to evaluate the safety, tolerability and pharmacokinetic profile of PYM50018, its patented, orally active, synthetic neuroprotective and neuroregenerative product. This is the lead compound within the P59 programme under development for the treatment of amyotrophic lateral sclerosis (ALS, the most prevalent form of motor neurone disease).

This residential clinical study was conducted under an investigational new drug (IND) application filed with the US Food and Drug Administration (FDA). It utilised a randomised, double blind, placebo controlled design to evaluate the safety, tolerability and pharmacokinetic profile of single oral doses of PYM50018. The dose level was escalated across four groups of eight healthy adult male subjects (an additional two subjects in each group were randomly allocated to receive placebo).

All of the subjects tolerated their allocated dose without any significant safety issues. The pharmacokinetic profile determined for each dose group confirmed that the product is bioavailable after oral administration. There was generally a linear relationship between dose, peak plasma concentration and exposure.

These results will support the future conduct of a phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetic profile of PYM50018 associated with repeated daily dosing.

Approximately 350,000 patients suffer from ALS worldwide, of which 50% die within 18 months of diagnosis. For the families of these patients the burden of providing supportive care is exceedingly high, and it is estimated that in the advanced stage of the disease supportive care can cost an average of \$200,000 per year (source: International Alliance of ALS Associations). Treatment with the only drug currently indicated for ALS typically increases the average survival time by only three months (source Datamonitor). There is an urgent need for the development of new and more effective therapies for this devastating condition.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "We continue to make strong progress in the development of this potentially important medicine."

-ENDS-

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive	Tel:	01480 437697
	Mobile:	07867 782000
Dr Wang Chong, Chief Financial Officer	Tel:	01480 437697
	Mobile:	07876 684223

**Financial Dynamics**

David Yates / Ben Atwell	Tel:	0207 831 3113
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**BACKGROUND INFORMATION**

### Phytopharm plc

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms for metabolic disease, neurodegeneration, inflammation and dermatology.

ALS is a fatal neurodegenerative disease that most commonly strikes people between 40 and 60 years of age. The underlying cause of ALS is unknown, although approximately 5-10% of cases appear to be of familial origin. It is characterized by progressive loss of both lower (spinal cord and brainstem) and upper (cerebral cortex) motor neurones, which leads to severe muscle weakness and wasting, followed by paralysis and death, generally caused by respiratory failure.

Phytopharm has developed a large group of patented compounds whose properties provide a platform for the development of novel therapeutic approaches for neurodegenerative disorders. PYM50018 has potent neuroprotective effects that have been demonstrated using various pre-clinical models. Specifically, PYM50018 has been observed to protect against neuronal damage, increase neurite outgrowth, reverse oxidative damage and reverse neuronal apoptosis *in vitro*. When administered orally to SOD1-G93A mice, a model of ALS, PYM50018 delays the loss of muscle strength and extends survival time. These features make PYM50018 a promising medicine for the treatment of ALS.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects that are in the early phase of evaluation.

More information concerning Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.co.uk>.

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Notice of Results
Released	10:40 27 Apr 2004
Number	0335Y

27 April 2004

**Phytopharm plc**

Phytopharm plc will be announcing its interim results for the six months ended 28 February 2004 on Wednesday, 5 May 2004.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	13:38 20 Apr 2004
Number	8024X

RNS Number:8024X  
Phytopharm PLC  
20 April 2004

Re: Notification of Major Interests in Shares

The Company received notification on 19 April 2004 from HBOS plc that HBOS plc has a material interest (for the purposes of Sections 208 and 209 of the Act) in 1,736,654 Ordinary shares of 1p. This represents 4.06% of the issued share capital. Details of the interest are set out below:

HDSL Nominees Limited	9
HSBC Global Custody Nominees (UK) Ltd a/c 823733	30,596
HSBC Global Custody Nominees (UK) Ltd a/c 823721	35,930
HSBC Global Custody Nominees (UK) Ltd a/c 823587	310,987
HSBC Global Custody Nominees (UK) Ltd a/c 823575	434,448
HSBC Global Custody Nominees (UK) Ltd a/c 823496	924,684

This information is provided by RNS  
The company news service from the London Stock Exchange

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	13:35 20 Apr 2004
Number	8023X

RNS Number:8023X  
Phytopharm PLC  
20 April 2004

Re: Notification of Major Interests in Shares

The Company received notification on 19 April 2004 from AMVESCAP plc that following the purchase of 30,000 Ordinary shares on 16th April 2004, INVESCO Perpetual UK Investment Series ICVC is the beneficial owner of 4,699,974 Ordinary Shares of 1p each representing 11.06%. The shares are registered in the name of Vidacos Nominees Limited.

This information is provided by RNS  
The company news service from the London Stock Exchange

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Product Launch
Released	07:00 31 Mar 2004
Number	1209X

31 March 2004

**Phytopharm plc**

**Launch of first product in UK**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the launch in the UK of Phytopica™, its lead veterinary dermatology product from the P7v programme.

Phytopica™ has been the subject of two successful clinical trials in canine dermatology and enjoys strong support from consultant veterinarians in the UK. Launched today at a special symposium at the British Veterinary Dermatology Study Group in Birmingham, it has been recognised as a potential first line, premium price product and will be marketed to registered UK veterinary dermatologists. Following the UK launch, Phytopharm will be seeking global partners to market Phytopica™ in other territories.

Phytopica™ is presented as a granulated extract which is simply sprinkled on food. Due to the product's palatability, canine compliance has been excellent, with over 97% compliance in clinical studies. Derived from three Asian plants, the product is the subject of granted patents in the UK, Europe and the USA, and is pending in other territories worldwide.

Canine dermatological disorders are well recognised by veterinarians to be a major problem in small animal practice, with an estimated 15% of the global dog population affected by skin conditions due to allergy (Muller & Kirk's Small Animal Dermatology, 6<sup>th</sup> Ed, 2000). With around 900,000 affected animals in the UK, the value of the canine dermatology market is potentially worth £10 million in the UK and £100 million worldwide.

Dr Wang Chong, Chief Financial Officer of Phytopharm, said: "Although Phytopharm's focus is on human pharmaceuticals, this first product launch is a landmark for the company. Phytopica™ has been enthusiastically supported by veterinary dermatologists and we look forward to a strong sales performance."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Wang Chong, Chief Financial Officer

Tel: 01480 437697

Mobile: 07876 684223

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

More information on Phytopica™ can be found on its website at: <http://www.phytopica.com>

## BACKGROUND INFORMATION

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

Phytopharm announced on 6<sup>th</sup> February 2004 positive results from a 120 dog European multi-centre, randomised, double-blind, placebo-controlled study of P7v for canine atopic dermatitis, conducted by 14 veterinary dermatologists in the UK and France. This study confirmed that the optimal daily dose of P7v is 200 mg/kg and that the product is palatable, well tolerated and has a good overall safety profile. By the end of the 12-week dosing period there was a statistically significant reduction (-23%) in the mean Canine Atopic Dermatitis Extent and Severity Index (CADESI) score for the 200 mg/kg group ( $p < 0.01$ ). This study also demonstrated that the benefit of P7v was most evident in the more severe cases (baseline CADESI greater than 50). A greater than 20% reduction in baseline score was observed for 64% of the dogs in the 200 mg/kg group compared with only 25% of cases in the placebo group ( $p < 0.05$ ).

A previous clinical study reported by Phytopharm on 5<sup>th</sup> October 2000 demonstrated the benefit of the product in treating canine atopic dermatitis at a dose of 200mg/kg. Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information on Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Additional Listing
Released	07:00 16 Mar 2004
Number	5241W

### Phytopharm plc (the "Company")

16 March 2004

#### Additional Listing

Application has been made to the UK Listing Authority and London Stock Exchange for a block listing of 400,000 new ordinary shares of 1 penny each (the "Shares") of the Company to trade on the London Stock Exchange and to be admitted to the Official List upon issuance.

These Shares will, upon issue, rank pari passu with the Company's existing ordinary shares. The Shares are being reserved under a block listing and will be issued pursuant to the exercise of options and subject to the rules of the Company's 1996 Unapproved Discretionary Share Option Scheme.

Theses shares will nor be allotted immediately but as and when the scheme rules allow.  
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Company	Phytopharm PLC
TIDM	PYM
Headline	Statement re Placing
Released	07:00 25 Feb 2004
Number	7909V

25 February 2004

Not for release, publication or distribution in, or into, the United States, Canada, Australia or Japan

**Phytopharm plc  
Placing raises £6.5 million**

Phytopharm plc ("Phytopharm" or the "Company") today announces that it has raised approximately £6.5 million before expenses (£6.3 million after expenses) through a placing of new shares. The placing was oversubscribed and the proceeds will be used to strengthen the Company's balance sheet and continue the development of its products.

Phytopharm's lead programmes in development are P57 for obesity and P58 for Alzheimer's disease. The Company is currently in discussions with a number of potential partners to progress the development of P57 for the dietary control of obesity. A substantial expansion of the raw material production capacity is underway. Phytopharm continues to develop its other lead development programme P58 with its partner Yamanouchi. A product from this programme (PYM50028) entered Phase II studies in December 2003 and is expected to report initial safety results in the second half of 2004, following which the Company anticipates receiving further milestone payments from Yamanouchi. Phytopharm also has two programmes, P7v for canine atopic dermatitis and P54v for canine arthritis, with products that are anticipated to launch in the UK during the first half of 2004.

The placing of 3,882,218 new ordinary shares of 1 penny each represents 9.99 per cent of the Company's issued share capital prior to the placing. The new shares have been placed with a range of institutional investors by Nomura International plc and Canaccord Capital (Europe) Ltd at a placing price of 167 pence per share. The placing price represents a discount of approximately 7.2 per cent to the closing middle market price on the London Stock Exchange on 24 February 2004. This placing was undertaken pursuant to a resolution of shareholders at the Company's Annual General Meeting on 23 February 2004 which approved the disapplication of shareholders' pre-emption rights in relation to 10 per cent of the then issued share capital of the Company.

Application will be made today for the new shares to be admitted to the Official List and to trading on the London Stock Exchange. The placing is conditional on admission, which is expected to become effective on 1 March 2004. When issued, the new shares will rank pari passu in all respects with the Company's existing ordinary shares. Following the placing, Phytopharm will have a total of 42,743,269 ordinary shares in issue.

**Enquiries:**

<b>Phytopharm plc</b>	Tel: +44 (0)1480 437 697
Dr. Richard Dixey, Chief Executive Officer	
Dr Wang Chong, Chief Financial Officer	

<b>Nomura International plc</b>	Tel: +44 (0)20 7521 2000
---------------------------------	--------------------------

David Rasouly  
John Milad

**Financial Dynamics**  
David Yates  
Ben Atwell

Tel: +44 (0)20 7831 3113

## BACKGROUND INFORMATION

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Appointment of Joint Broker
Released	07:01 25 Feb 2004
Number	7911V

**Phytopharm plc  
Appointment of Joint Broker**

Phytopharm plc today announces that it has appointed Canaccord Capital (Europe) Ltd as the company's joint stockbroker.

Enquiries:

**Phytopharm**

Dr Richard Dixey, Chief Executive Officer  
Dr Wang Chong, Chief Financial Officer

Tel: +44 (0)1480 437697

**Canaccord Capital (Europe) Ltd**

Mr Paul Reynolds, Chief Operating Officer  
Mr Neil Johnson, Managing Director Corporate Finance

Tel: +44 (0)20 7518 2777

**Financial Dynamics**

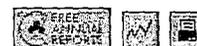
David Yates / Ben Atwell

Tel: +44 (0)20 7831 3113

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Company	Phytopharm PLC
TIDM	PYM
Headline	AGM Statement
Released	10:52 24 Feb 2004
Number	7520V

24 February 2004

### Phytopharm plc AGM Results

The board of Phytopharm plc announces that at its Annual General Meeting held yesterday all the resolutions put to the meeting were duly passed.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 6 Feb 2004
Number	0865V

6 February 2004

**Phytopharm plc  
Positive results from European multi-centre study in canine atopic dermatitis  
UK launch expected H1 2004**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the results from a European multi-centre study of P7v, its patented botanical product for canine atopic dermatitis.

This randomised, double-blind, placebo-controlled study was conducted by 14 veterinary dermatologists located in the UK and France. The aim of the study was to determine the optimal dose for commercialisation of the product, which consists of granules presented in a foil sachet. One hundred and twenty dogs with perennial atopic dermatitis were randomly allocated to receive either 100 mg/kg, 200 mg/kg (the dose used in an earlier study), 400 mg/kg or a matching placebo, which was added to their food once daily.

The response was assessed using the Canine Atopic Dermatitis Extent and Severity Index (CADESI), which was scored by the supervising vets. By the end of the 12-week dosing period there was a statistically significant reduction (-23%) in the mean CADESI score for the 200 mg/kg group (p<0.01). This study also demonstrated that the benefit of P7v was most evident in the more severe cases (baseline CADESI greater than 50). A greater than 20% reduction in baseline score was observed for 64% of the dogs in the 200 mg/kg group compared with only 25% of cases in the placebo group (p<0.05). Although there was a trend to improvement in the other treatment groups, this was not statistically significant.

This study confirms that the optimal daily dose of P7v is 200 mg/kg and that the product is palatable, well tolerated and has a good overall safety profile.

Canine atopic dermatitis affects 15% of dogs. The 2002 canine atopic dermatitis market was estimated to be around £10 million in the UK and £200 million worldwide.

Professor David Lloyd, Chair of Veterinary Dermatology, Royal Veterinary College, commented: "Canine atopic dermatitis is a major problem in small animal practice. The promising results from this study suggest that P7v could provide a safe and effective first line therapy for many dogs with this challenging condition."

Dr Richard Dixey, Chief Executive of Phytopharm, said: "We anticipate the first commercialisation of this product during H1 2004 and will announce details of the launch programme shortly."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

Dr Wang Chong, Chief Financial Officer

Tel: 01480 437697

Mobile: 07876 684223

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

## BACKGROUND INFORMATION

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

P7v contains a proprietary blend of three standardised plant extracts with a unique mode of action that specifically inhibits the allergic and inflammatory phases associated with atopic dermatitis. A previous clinical study reported by Phytopharm on October 5<sup>th</sup> 2000 demonstrated the benefit of the product in treating canine atopic dermatitis at a dose of 200mg/kg. The aim of the current study was to confirm that this dose was optimal, enabling the launch of the product for this challenging condition.

P7v has a good overall safety profile without the detrimental side effects associated with steroids or immunosuppressants. In the study, only three cases (one that received 200 mg/kg and two that received 400 mg/kg) were withdrawn due to adverse gastrointestinal effects and only two dogs refused to eat the medicated food.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at <http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 21 Jan 2004
Number	4611U

21 January 2004

**Phytopharm plc**

**Receives second milestone from its collaboration with Yamanouchi Pharmaceutical Co Ltd in Alzheimer's disease**

Phytopharm plc (PYM: London Stock Exchange) announces today that it has received a milestone of \$2M from Yamanouchi Pharmaceutical Co., Ltd., the leading Japanese pharmaceutical company. This milestone was paid following receipt by Yamanouchi of the results of the phase I study of its orally active, synthetic, neuroprotective and neuroregenerative product, PYM50028, which is under development as a treatment for Alzheimer's disease.

This data was also considered by the UK Medicines and Healthcare Products Regulatory Agency, which granted a clinical trial exemption (CTX) certificate on December 9<sup>th</sup> 2003 enabling Phytopharm to commence a Phase II study in the UK with the material.

On 1 May 2003, Phytopharm entered a licensing agreement with Yamanouchi for the development and commercialisation of PYM50028 in Japan and other Asian territories. A total potential milestone stream of \$33 million is payable during the course of development of the product, and Phytopharm has now received two milestones amounting to \$5 million from this total. A further \$15 million is potentially payable over the next 18 months.

Dr Richard Dixey, Chief Executive of Phytopharm, said: *"We continue to make strong progress in the development of this potentially important medicine."*

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.



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Company	Phytopharm PLC
TIDM	PYM
Headline	Director Shareholding
Released	18:23 6 Jan 2004
Number	9265T

RNS Number:9265T  
Phytopharm PLC  
6 January 2004

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

- 1) NAME OF COMPANY  
  
PHYTOPHARM PLC
  
- 2) NAME OF DIRECTOR  
  
DR R P DIXEY
  
- 3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest  
  
AS 2 ABOVE
  
- 4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)  
  
AS 2 ABOVE
  
- 5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)  
  
AS 2 ABOVE
  
- 6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary  
  
GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003
  
- 7) Number of shares/amount of stock acquired

- 8) Percentage of issued Class
- 9) Number of shares/amount  
of stock disposed
- 10) Percentage of issued Class  
(any treasury shares held by company should not be taken into account when  
calculating percentage)
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
9 DECEMBER 2003
- 18) Period during which or date on which exercisable  
10 DECEMBER 2006 TO 9 DECEMBER 2013 SUBJECT TO PERFORMANCE CRITERIA
- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
51,249 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES
- 21) Exercise price (if fixed at time of grant) or indication that price  
is to be fixed at time of exercise

212.5 PENCE

- 22) Total number of shares or debentures over which options held following this notification

595,509

- 23) Any additional information

PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT. NO OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND 100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATE VESTING BETWEEN MEDIAN AND UPPER DECILE PERFORMANCE. FOR 34,168 OPTIONS THE COMPARATOR GROUP COMPRISES 19 OTHER UK LISTED BIOTECH COMPANIES, AND FOR 17,081 OPTIONS THE COMPARATOR GROUP IS THE FTSE SMALL CAP INDEX

- 24) Name of contact and telephone number for queries

DR G W CHONG  
1480 437697

- 25) Name and signature of authorised company official responsible for making this notification

Date of Notification 6 JANUARY 2004

#### SCHEDULE 11

#### NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

- 1) NAME OF COMPANY

PHYTOPHARM PLC

- 2) NAME OF DIRECTOR

DR D D REES

- 3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of a non-beneficial interest

AS 2 ABOVE

- 4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2 ABOVE

- 5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

AS 2 ABOVE

- 6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003

- 7) Number of shares/amount of stock acquired
- 8) Percentage of issued Class
- 9) Number of shares/amount of stock disposed
- 10) Percentage of issued Class  
(any treasury shares held by company should not be taken into account when calculating percentage)
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
9 DECEMBER 2003
- 18) Period during which or date on which exercisable  
10 DECEMBER 2006 TO 9 DECEMBER 2013 SUBJECT TO PERFORMANCE CRITERIA

- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
62,304 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES
- 21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise  
212.5 PENCE
- 22) Total number of shares or debentures over which options held following this notification  
621,318
- 23) Any additional information  
PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT. NO OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND 100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATE VESTING BETWEEN MEDIAN AND UPPER DECILE PERFORMANCE. FOR 41,538 OPTIONS THE COMPARATOR GROUP COMPRISES 19 OTHER UK LISTED BIOTECH COMPANIES, AND FOR 20,766 OPTIONS THE COMPARATOR GROUP IS THE FTSE SMALL CAP INDEX
- 24) Name of contact and telephone number for queries  
DR G W CHONG  
1480 437697
- 25) Name and signature of authorised company official responsible for making this notification  
Date of Notification 6 JANUARY 2004

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

- 1) NAME OF COMPANY  
PHYTOPHARM PLC
- 2) NAME OF DIRECTOR  
DR G W CHONG
- 3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2 ABOVE

- 4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2 ABOVE

- 5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

AS 2 ABOVE

- 6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003

- 7) Number of shares/amount of stock acquired
- 8) Percentage of issued Class
- 9) Number of shares/amount of stock disposed
- 10) Percentage of issued Class  
(any treasury shares held by company should not be taken into account when calculating percentage)
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE

COMPLETE THE FOLLOWING BOXES

17) Date of grant

9 DECEMBER 2003

18) Period during which or date on which exercisable

10 DECEMBER 2006 TO 9 DECEMBER 2013 SUBJECT TO PERFORMANCE CRITERIA

19) Total amount paid (if any) for grant of the option

NIL

20) Description of shares or debentures involved: class, number.

35,124 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES

21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise

212.5 PENCE

22) Total number of shares or debentures over which options held following this notification

145,932

23) Any additional information

PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT. NO OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND 100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATE VESTING BETWEEN MEDIAN AND UPPER DECILE PERFORMANCE. FOR 23,418 OPTIONS THE COMPARATOR GROUP COMPRISES 19 OTHER UK LISTED BIOTECH COMPANIES, AND FOR 11,706 OPTIONS THE COMPARATOR GROUP IS THE FTSE SMALL CAP INDEX

24) Name of contact and telephone number for queries

DR G W CHONG  
1480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification 6 JANUARY 2004

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	14:22 19 Dec 2003
Number	4969T

RNS Number:4969T  
Phytopharm PLC  
19 December 2003

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: PHYTOPHARM PLC
  
2. NAME OF SCHEME: THE PHYTOPHARM 1996 UNAPPROVED DISCRETIONARY SHARE OPTION SCHEME
  
3. PERIOD OF RETURN: FROM: 11 JUNE 2003 TO: 10 DECEMBER 2003
  
4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD: 260,000 ORDINARY SHARES OF 1 PENCE
  
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: 127,024 ORDINARY SHARES OF 1 PENCE
  
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 132,976 ORDINARY SHARES OF 1 PENCE
  
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: 260,000 ORDINARY SHARES OF 1 PENCE ON 10TH DECEMBER 2001

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,805,218 ORDINARY SHARES OF 1 PENCE AT 10 DECEMBER 2003

CONTACT FOR QUERIES

NAME: DR G W CHONG

TELEPHONE: 01480 437697

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 9 Dec 2003
Number	0160T

9 December 2003

**Phytopharm plc**

**Commences phase II proof of principle study in Alzheimer's disease**

Phytopharm plc (PYM: London Stock Exchange) announces today the start of a phase II proof of principle clinical study of its orally active, synthetic, neuroprotective and neuroregenerative product, PYM50028, which is under development as a treatment for Alzheimer's disease. The study will be conducted in the UK under the terms of a clinical trial exemption (CTX) certificate, which has been granted by the Medicines and Healthcare Products Regulatory Agency.

This study will utilise a randomised, double-blind, placebo-controlled design to evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after once daily oral administration to patients with Alzheimer's disease. Approximately 200 patients will be enrolled and randomly allocated to receive either PYM50028 or placebo (1:1 ratio) during a three month dosing period.

The effects of treatment with PYM50028 on memory, concentration and executive function will be evaluated during the study. These cognitive domains, which are particularly impaired in patients with Alzheimer's disease, will be assessed using the Hopkin's verbal learning test and a computerised neuropsychological test system.

Recruitment of patients for the study is expected to be completed by Q3 2004, with a final report available Q1 2005. An interim safety analysis will be conducted after the first 60 patients have been treated. The data will be reviewed by an independent consultant physician, who will provide Phytopharm with a summary report of the findings. This is expected to be available by Q3 2004.

There are no treatments currently available with the potential to reverse Alzheimer's disease. The global annual market for Alzheimer's disease is estimated to be worth in excess of \$2.5 billion (source: Datamonitor); it is also estimated that in the US, the total annual cost burden for Alzheimer's disease exceeds \$100 billion (source: US Alzheimer's Association).

On 1 May 2003, Phytopharm entered a licensing agreement with Yamanouchi Pharmaceutical Co., Ltd., a leading Japanese pharmaceutical company, for the development and commercialisation of PYM50028 in Japan and other Asian territories.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "*The progression of PYM50028 into this phase II trial is an important milestone for Phytopharm. We will progress this study vigorously over the coming year.*"

-ENDS-

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**NOTES TO EDITORS**

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

PYM50028 arose from research into the activity of an Asian medicinal plant. In pre-clinical studies, this synthetic chemical has been shown to be neuroprotective, to reverse the decrease of neuronal growth factors and to reverse neuronal degeneration observed in the ageing brain. Importantly, this product was observed to restore levels of proteins that are altered in the ageing brain, returning them to levels seen in the young and causing beneficial neurite outgrowth and branching. PYM50028 thereby offers the potential of disease modification in poorly treated but prevalent neurodegenerative conditions such as Alzheimer's disease. The neurodegeneration platform, from which PYM50028 has been developed, is protected by nine global patent families and contains a library of related chemical compounds that share this mode of action.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Final Results
Released	07:00 9 Dec 2003
Number	0173T

9 December 2003

**Preliminary results for the year ended 31 August 2003**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm" or the "Group") today announces its preliminary results for the year ended 31 August 2003.

**Announced today**

- Commencement of Phase II study of novel Alzheimer's disease treatment under the terms of a UK Clinical Trial Exemption certificate (Programme P58, see separate press release).

**Highlights**

- Commencement of Phase I study of novel motor neurone disease treatment under US Investigational New Drug application (Programme P59)
- Successful completion of 28-day Phase I repeat dose study in novel Parkinson's disease treatment (Programme P63)
- Second milestone due from Yamanouchi Pharmaceutical Co., Ltd. ("Yamanouchi") following evaluation of Phase I data (Programmes P58 and P63)
- Return of rights and licensing progress in programme for the dietary control of obesity (Programme P57)
- Licence and Option agreement with Yamanouchi for development and commercialisation of PYM50028 in Japan and other Asian countries (Programmes P58 and P63)
- First milestone of \$3 million paid by Yamanouchi
- Appointment of marketing partner and launch programme for novel treatment for canine osteoarthritis (Programme P54v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"We have met all our deliverables for 2003 and have made strong progress. We expect 2004 to continue in a similar vein, with significant cash flows coming into the company from milestones and the launch of our veterinary products."*

Enquiries:

Phytopharm plc

Today:

07867 782000

Dr Richard Dixey, Chief Executive

Thereafter: 01480 437697

Mobile 07867 782000

**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113

*Phytopharm has updated its website from 9 December 2003  
www.phytopharm.com*

## Operational review

Phytopharm is focused on developing novel pharmaceutical products based on clinical data generated from medicinal plant extracts. Such research can identify important and innovative platforms for drug discovery that include libraries of compounds, biological targets and associated clinical and pre-clinical data. This data creates drug development programmes aimed at target diseases, and leads to multiple licensing opportunities for specific compounds within those programmes. The current status of the four platforms being developed within Phytopharm, each at different stages of development, are described below.

Platform	Programme	Indication	Mode of Action	Development stage
Neuro-degeneration	P58	Alzheimer's disease/dementia	Reverse age related decline in memory	Phase II in progress
	P59	Motor neurone disease (ALS)	Neuroregenerative	Phase I in progress
	P63	Parkinson's disease	Neuroregenerative	Phase Ib completed
Metabolic disease	P57	Dietary control of obesity	Direct action on satiety centre	Phase IIa reported
	P64	Obesity and metabolic syndrome	Direct action on satiety centre	Pre-clinical
Dermatology	P7v	Canine atopic dermatitis	Inhibits allergic and inflammatory cytokines	Pre-launch
	P55	Eczema	Inhibits allergic and inflammatory cytokines	Pre-clinical
Inflammation	P54v	Canine osteoarthritis	Inhibits induction of inflammatory enzymes	Pre-launch
	P61	Asthma and other inflammatory disorders	Anti-inflammatory and anti-spasmodic	Pre-clinical

### Platform 1: Neurodegeneration

The neurodegeneration platform has been extended from a programme for Alzheimer's disease (P58) to include programmes for Parkinson's (P63) and motor neurone disease, including amyotrophic

lateral sclerosis (P59). Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform. These molecules, which have a novel mechanism of action, are potential disease modifiers and are expected to offer a real therapeutic advance in these conditions where there is a high unmet medical need.

The lead compound from the Alzheimer's and Parkinson's disease programme is coded PYM50028. In pre-clinical studies, PYM50028 has been shown to be neuroprotective and to reverse both the decrease of neuronal growth factors and the neuronal degeneration observed in the ageing brain. Importantly, this product was also observed to restore levels of proteins that are altered in the ageing brain, returning them to levels observed in the young, causing beneficial outgrowth and branching of neurites. Key events during the year were the following:

- In January 2003, we announced the start of a Phase I randomised, double-blind, placebo-controlled clinical study using a new formulation of PYM50028 to evaluate the safety, tolerability and pharmacokinetic profile for Alzheimer's and Parkinson's disease. This data is a key component in understanding how PYM50028 is absorbed by man.
- In May 2003, Phytopharm signed a licensing agreement with the leading Japanese pharmaceutical company, Yamanouchi Pharmaceutical Co., Ltd., for the development and commercialisation of PYM50028. Under the agreement, Yamanouchi acquired an exclusive licence to develop, manufacture and market PYM50028 for the treatment of Alzheimer's disease in Japan and some other Asian countries, which together represent some 15% of the world market. Phytopharm received \$3 million upon signing of the agreement, with a further five milestones totalling \$17 million potentially payable over the next eighteen months, subject to the achievement of specific objectives. In total, Phytopharm is entitled to \$33 million of licence fees and potential milestone payments with respect to the Alzheimer's indication (of which \$3 million had been received by the year end), as well as receiving royalties on sales of PYM50028.
- Yamanouchi also acquired the option to licence PYM50028 for the additional indications of Parkinson's disease, Lewy body dementia, vascular dementia and mild cognitive impairment, for which Phytopharm will be entitled to receive potential additional licence fees and milestones. These further fees and milestones are based on each indication's market potential relative to the Alzheimer's indication. Phytopharm will also receive royalties on sales of PYM50028 by Yamanouchi for all indications developed.
- In May 2003 we announced the successful completion of the safety, tolerability and pharmacokinetics of single and repeated oral dosing of PYM50028 administered over 7 days to healthy subjects aged over 50 years.
- In June 2003 we announced that we had entered into an agreement with the Oxford Project to Investigate Memory and Ageing (OPTIMA) regarding the clinical development of PYM50028. Under the joint leadership of Professor David Smith (Project Leader, OPTIMA) and Professor Robin Jacoby (Principal Investigator), OPTIMA will enroll patients with memory impairment into the Phase II proof of principle study.
- In November 2003 we announced the successful completion of the Phase Ib stage of the study in which thirty healthy men and women aged 50 years and older were enrolled and randomly allocated to receive either PYM50028 or placebo once daily for 28 days. Results indicated that the product has absorption and pharmacokinetic characteristics suitable for once-daily dosing and is well tolerated with a good emergent safety profile.
- In November 2003 the Phase Ib data was submitted to Yamanouchi, the results of which are the subject of the second milestone payable under the licence agreement announced on 1 May 2003 between Yamanouchi and Phytopharm for marketing of PYM50028 in Japan and some other Asian countries. This payment is due imminently.
- In December 2003, we announced that we had been granted clearance by the Medicines and

Healthcare Products Regulatory Agency (MHRA) to commence a Phase II 'proof of concept' clinical study in Alzheimer's disease patients under a clinical trial exemption (CTX) certificate, that was granted following a review of all the manufacturing, safety, pharmacological and clinical data generated by Phytopharm concerning PYM50028. The Phase II study utilises a randomised, double-blind, placebo-controlled design to evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after once daily oral administration over three months. The effects of PYM50028 on memory, concentration and executive function will be evaluated during the study. The study is expected to report in Q1 2005.

The lead compound arising from the motor neurone disease programme, which targets amyotrophic lateral sclerosis (ALS), (P59) is coded PYM50018. Pre-clinical work has demonstrated that PYM50018 is a potent neuroprotective agent, reverses neurodegeneration in spinal motor neurones and improves survival to a greater extent than standard treatment in superoxide dismutase 1 (SOD1) mice, a model of ALS.

In December 2003, we announced that P59 had been granted clearance by the USA Food and Drug Administration to commence a Phase I clinical study under an investigational new drug (IND) application, to evaluate the safety, tolerability and pharmacokinetic profile of PYM50018 for amyotrophic lateral sclerosis. We anticipate that the results will be reported at the end of Q2 2004.

### **Platform 2: Metabolic disease**

The metabolic disease platform is focused on obesity, obese-onset diabetes and metabolic disease. This platform comprises the patented use of three plant species, their mode of action and related active molecules. Programme P57 contains a novel appetite suppressant product that has been shown to reduce calorific intake in overweight subjects, as demonstrated in a double-blind-placebo controlled clinical study that was announced by Phytopharm in December 2001.

In March 2003, Phytopharm announced that it had received the first six monthly progress report from Pfizer Inc. ("Pfizer") concerning the ongoing development of programme P57. This followed the announcement in July 2002 that Pfizer was taking responsibility for the development of the programme, under the terms of the Licence and Royalty agreement entered into between Pfizer and Phytopharm in August 1998.

In July 2003, Phytopharm announced that it had received notice from Pfizer that it was discontinuing clinical development of P57 and returning the rights to the company. Pfizer stated that in a changing environment for discovery and development of new medicines, it continually reviews its pipeline of potential new therapies. Following the closure of the Natureceuticals group within Pfizer, the company determined that the development of P57 might be best achieved by another organisation. Pfizer also stated that the positive clinical data of P57 in patients generated to date encourages further study of this natural material as a therapy for obesity.

As a consequence, Phytopharm is now free to Licence P57 to other parties. This has now created an opportunity to extend the P57 programme into the dietary control of obesity with multiple licensing opportunities. This licensing programme is progressing vigorously, with detailed development plans in discussion with potential partners.

Phytopharm has also developed screens that are predictive of appetite suppressant activity that can be used to evaluate other compounds. Good progress has been made in understanding the structural activity relationships of our compounds and in the development of synthetic molecules that form the basis of a further licensing opportunity. This new programme (P64) is focused on the development of pharmaceutical prescription products for the treatment of obesity and metabolic disease.

### **Platform 3: Dermatology**

The dermatology platform comprises a programme concerning the use of extracts of plants with a novel mode of action for the treatment of canine atopic dermatitis (P7v). These products have a dual mode of action that targets both the allergic and inflammatory components of dermatitis.

In November 2003, we completed a European multi-centre study in canine atopic dermatitis with a three plant product, coded PYM00217. This randomised, double-blind, placebo-controlled study was conducted by specialist veterinary dermatologists to determine the optimal dose for future commercialisation of the product. The study is expected to report in Q1 2004.

Phytopharm has completed the pharmaceutical development of PYM00217 and is now able to manufacture tonne-scale quantities of material to Good Manufacturing Practice (GMP) standards. Commercialisation and launch of this product is well underway for early 2004.

A programme aimed at human eczema is also emerging from this platform. Coded P55, steady progress has been made in developing a dosage form suitable for use in man.

#### **Platform 4: Inflammation**

Finally, the inflammation platform contains a programme containing a family of novel, third generation, non-steroidal anti-inflammatory drugs ("NSAID") characterised by their inhibition of a wide range of enzymes central to chronic inflammation (P54v).

The results of a double-blind, placebo-controlled trial of our product, coded PYM50014, in canine osteoarthritis have enabled us to actively pursue commercialisation and enter a licence and distribution agreement in the companion animal market. Large-scale manufacture of PYM50014 has been completed to GMP standards and the product will be launched in Q1 2004.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This has given rise to a new programme (P61) that is intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders including asthma. The lead candidate will enter development towards the end of 2004.

#### **Statement of prospects**

We enter the coming year with considerable optimism. We are anticipating a number of cash positive events in the year: including significant milestones from Yamanouchi concerning our P58 programme in Alzheimer's disease and two product launches, for our veterinary product P7v in canine atopic dermatitis and P54v in canine osteoarthritis. In addition to this, the maturity of our portfolio means that we have three additional programmes, P57 and P64 in obesity and P59 in motor neurone disease, that are attracting substantial interest from licencees. Along with the key clinical data for P58 emerging in the first quarter of 2005, a product where 85% of the world territories remain unlicensed, the progress in our portfolio means that we are looking forward to a period of sustained progress.

#### **Financial Review**

##### **Summary**

Financial performance for the fiscal year ended 31 August 2003 has been influenced by two main events: the licensing of PYM50028 to Yamanouchi in May 2003 and the transfer of the P57 development activities to Pfizer in December 2002. The Group's investment in research and development continues to grow in line with the continuing progress of our four development platforms, in particular, the P58, P63 and P7v programmes, resulting in the consumption of significant cash resources. However, the Group anticipates potential milestone payments of up to

\$17 million from Yamanouchi over the next 18 months.

## Turnover

Revenues of £2.43 million for the year (2002: £2.71m) comprised a £2 million milestone payment from Yamanouchi, for the exclusive licence to develop, manufacture and market PYM50028 for the treatment of Alzheimer's disease in Japan and some other Asian countries, and £0.42 million in development income from Pfizer for P57, the Group's appetite suppressant. Revenues were lower this year following the transfer of the P57 development work to Pfizer in December 2002.

## Expenses

Research and development remained our most significant investment, totalling £7.23 million or 86% of total operating costs, an increase of 20% (2002: £6.00 million). This is largely due to the successful progress of the P58 programme which is in clinical trials and to a lesser extent the ongoing P7v clinical trial. The rise in research and development activity required additional administrative support, which is reflected in the higher administration costs of £1.16 million, an increase of 13% (2002: £1.02 million). This year's total operating expenses were £8.38 million, a rise of 19% (2002: £7.03 million), in line with budget.

## Interest and Tax

Interest income of £0.28 million was lower this year (2002: £0.48 million), due to a combination of lower average cash balances and lower interest rates, and represents an average return of 3.8% on the cash balances throughout the year. The net tax recoverable of £0.38 million was also lower this year (2002: £0.55 million), despite a similar research and development corporation tax credit to the previous year, due to the payment of a 10% Japanese withholding tax deducted from the Yamanouchi income earlier in the year.

## Liquidity and Capital Resources

At 31 August 2003 the Group had cash and liquid resources of £5.61 million, £3.54 million lower than at the start of the year.

The fixed asset base remained low at £0.16 million (2002: £0.24 million) as research and development activities are contracted out so that the Group does not need to finance its own laboratory facilities. Debtors of £1.09 million (2002: £2.84 million) comprised principally research and development tax credits. Creditors of £1.82 million (2002: £1.95 million) comprise mainly trade creditors and accruals.

Working capital at 31 August 2003 was £4.93 million. The Group utilised £5.11 million of working capital during 2003, which is equivalent to £426,000 per month. This expenditure is in line with the Group's business plan and is a consequence of the P58 programme maturing.

A combination of decreases in turnover of £0.29 million, interest income of £0.20 million, and a net tax recoverable of £0.18 million, together with an increase in operating expenses of £1.36 million, resulted in an increase in the loss for the year of £2.02 million to £5.31 million. Overall the results for the year were better than anticipated and within the budget.

## Consolidated Profit and Loss Account for the year ended 31 August 2003

Notes	2003	2002
	Unaudited	Audited
	£'000	£'000

<b>Turnover</b>	2	2,427	2,714
		<hr/>	<hr/>
<b>Gross profit</b>		2,427	2,714
Other operating expenses	3	(8,381)	(7,027)
		<hr/>	<hr/>
<b>Operating loss</b>		(5,954)	(4,313)
Interest receivable and similar income		277	478
Interest payable and similar charges		(4)	(4)
		<hr/>	<hr/>
<b>Loss on ordinary activities before taxation</b>		(5,681)	(3,839)
Tax on loss on ordinary activities	4	378	554
		<hr/>	<hr/>
<b>Loss for the year</b>	6	<u>(5,303)</u>	<u>(3,285)</u>
Basic fully diluted loss per ordinary share (pence)	5	(13.7)	(8.5)
IMR loss per share (pence)	5	(13.7)	(8.4)

All revenue and expenses shown above were generated from continuing operations.

The Group has no recognised gains or losses for the financial year other than those disclosed above.

#### Consolidated Balance Sheet at 31 August 2003

	Notes	2003 Unaudited £'000	2002 Audited £'000
<b>Fixed assets</b>			
Tangible assets		162	241
<b>Current assets</b>			
Stocks		43	-
Debtors		1,094	2,843
Cash held on deposit as short term investments		5,131	8,831
Cash at bank and in hand		482	323
		<hr/>	<hr/>
		6,750	11,997
<b>Creditors: amounts falling due within one</b>		<b>(1,815)</b>	<b>(1,953)</b>

year			
<b>Net current assets</b>		<b>4,935</b>	<b>10,044</b>
<b>Total assets less current liabilities</b>		<b>5,097</b>	<b>10,285</b>
<b>Net assets</b>		<b>5,097</b>	<b>10,285</b>
<b>Capital and reserves</b>			
Called up share capital		388	386
Share premium account	6	31,808	31,726
Merger reserve	6	(204)	(204)
Profit and loss account	6	(26,895)	(21,623)
<b>Equity shareholders' funds</b>		<b>5,097</b>	<b>10,285</b>

**Consolidated Cash Flow Statement for the year ended 31 August 2003**

	Notes	2003 Unaudited £'000	2002 Audited £'000
<b>Net cash outflow from continuing operating activities</b>	7	<b>(3,938)</b>	<b>(5,362)</b>
<b>Returns on investment and servicing of finance</b>			
Interest received		277	478
Interest paid on finance leases		-	(4)
Other interest paid		(4)	-
		<b>273</b>	<b>474</b>
<b>Taxation</b>			
UK corporation tax received		277	224
Foreign taxation paid		(200)	-
		<b>77</b>	<b>224</b>
<b>Capital expenditure and financial investment</b>			
Purchase of tangible fixed assets		(85)	(140)
Proceeds on sale of tangible fixed assets		57	13
		<b>(28)</b>	<b>(127)</b>

<b>Cash outflow before use of liquid resources and financing</b>	<u>(3,616)</u>	<u>(4,791)</u>
<b>Management of liquid resources</b>		
Decrease in cash held on short term deposit	3,700	3,837
<b>Financing</b>		
Proceeds from exercise of share options	83	478
Repayment of principal under finance leases	(8)	(56)
<b>Net cash inflow from financing</b>	<u>75</u>	<u>422</u>
Increase/(decrease) in cash in the year	<u>159</u>	<u>(532)</u>

## Notes to the preliminary announcement

### 1. Basis of preparation

These financial statements have been prepared in accordance with the accounting policies set out in the annual report of the Group for the year ended 31 August 2002.

The figures shown for the year to 31 August 2003 represent unaudited abridged financial statements and have not as yet been delivered to the Registrar of Companies. The comparative figures for the year to 31 August 2002 have been taken from, but do not constitute, the Group's financial statements for that financial year. Those financial statements have been reported on by the Group's auditors and delivered to the Registrar of Companies. The report of the auditors was unqualified and did not contain a statement under s237 (2) or (3) of the Companies Act 1985.

### 2. Turnover

	2003 Unaudited £'000	2002 Audited £'000
<b>By business activity</b>		
Licensing and development	<u>2,427</u>	<u>2,714</u>

All turnover arose in the United Kingdom.

### 3. Other operating expenses

Other operating expenses comprise:

	2003 Unaudited £'000	2002 Audited £'000
<b>Continuing operations</b>		
Research and development	7,228	6,003
Administrative expenses	1,153	1,024

	<u>8,381</u>	<u>7,027</u>
<b>4. Tax on loss on ordinary activities</b>		
	<b>2003</b>	<b>2002</b>
	<b>Unaudited</b>	<b>Audited</b>
	<b>£'000</b>	<b>£'000</b>
<b>United Kingdom</b>		
Corporation tax credit	578	554
<b>Foreign Taxation</b>		
Withholding tax suffered	(200)	-
	<u>378</u>	<u>554</u>

The Group has taken advantage of the Research and Development corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund at the rate of 24 pence in the pound.

#### 5. Loss per share

The basic undiluted loss per share is based on losses of £5,303,318 (2002: loss of £3,284,518) and ordinary shares of 38,671,689 (2002: 38,480,633), being the weighted average number of shares in issue during the period. The IIMR earnings per share figure excludes gains and losses on disposals of fixed assets during the year.

#### 6. Share premium account and reserves

	Share premium account <i>Unaudited</i> £'000	Merger reserve <i>Unaudited</i> £'000	Profit and loss account <i>Unaudited</i> £'000
At 1 September 2002	31,726	(204)	(21,623)
Premium on issue of shares	82	-	-
Loss for the year	-	-	(5,303)
Share option compensation charge	-	-	31
<b>At 31 August 2003</b>	<u>31,808</u>	<u>(204)</u>	<u>(26,895)</u>

#### 7. Reconciliation of operating loss to net cash outflow from operating activities

	<b>2003</b>	<b>2002</b>
	<b>Unaudited</b>	<b>Audited</b>
	<b>£'000</b>	<b>£'000</b>
<b>Continuing activities</b>		
Operating loss	(5,954)	(4,313)
Depreciation on tangible fixed assets	106	124
Loss on disposal of fixed assets	1	9
(Increase) in stocks	(43)	-

Decrease/(increase) in debtors	2,051	(2,145)
(Decrease)/Increase in creditors	(130)	949
Provision for impairment of value in fixed asset investments	-	30
Decrease in provision for employers National Insurance on share option gains	-	(16)
Increase in provision for share option compensation charge	31	-
<b>Net cash outflow from continuing activities</b>	<b>(3,938)</b>	<b>(5,362)</b>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 3 Dec 2003
Number	7823S

3 December 2003

**Phytopharm plc**

**Commences phase I clinical study of treatment for motor neurone disease**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today that it has been granted clearance by the US Food and Drug Administration to commence a phase I clinical study, under an investigational new drug (IND) application, to evaluate its patented oral product, PYM50018, which is the lead compound within the P59 programme for amyotrophic lateral sclerosis (ALS, the most prevalent form of motor neurone disease).

This residential clinical study will utilise a randomised, double blind, placebo-controlled design. It will evaluate the safety, tolerability and pharmacokinetic profile of single oral doses of PYM50018 that will be escalated across four groups of eight healthy adult subjects. Each group will be assigned a different dose level. It is expected that the results will be reported during the second quarter of 2004.

Approximately 350,000 patients suffer from ALS world wide, of which 50% die within 18 months of diagnosis. The financial cost to families of patients is exceedingly high, and it is estimated that in the advanced stage, care can cost an average of \$200,000 per year (source: International Alliance of ALS Associations). Current therapy with the only agent indicated for the treatment of this condition increases average survival by only three months (source Datamonitor). There is an urgent need for the development of new approaches to this devastating condition.

Phytopharm has developed a large group of patented compounds whose properties provide a platform for the development of novel therapeutic approaches for neurodegenerative disorders. PYM50018 has potent neuroprotective effects that have been demonstrated using various pre-clinical models. Specifically, PYM50018 has been observed to protect against neuronal damage, increase neurite outgrowth, reverse oxidative damage and reverse neuronal apoptosis *in vitro*. When administered orally to SOD1-G93A mice, a model of ALS, PYM50018 delays the loss of muscle strength and extends survival time. These features make PYM50018 a promising medicine for the treatment of ALS.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "*This is the second compound from our neurodegeneration library to enter the clinic, and it is very gratifying to be able to advance this potentially important medicine.*"

-ENDS-

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

## NOTES TO EDITORS

### Phytopharm plc

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neurodegeneration, inflammation and dermatitis.

ALS is a fatal neurodegenerative disease that most commonly strikes people between 40 and 60 years of age. The underlying cause of ALS is unknown, although approximately 5-10% of cases appear to be of familial origin. It is characterized by progressive loss of both lower (spinal cord and brainstem) and upper (cerebral cortex) motor neurones, which leads to severe muscle weakness and wasting, followed by paralysis and death, generally caused by respiratory failure.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects that are in the early phase of evaluation.

More information concerning Phytopharm's activities can be found on its web site at <http://www.phytopharm.co.uk>.

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Other Announcements from this Company

Send to a Friend



Company Phytopharm PLC  
 TIDM PYM  
 Headline Holding(s) in Company  
 Released 14:09 28 Nov 2003  
 Number 6090S

RNS Number:6090S  
 Phytopharm PLC  
 27 November 2003

Re: Notification of Major Interests in Shares

The Company received notification on 27th November 2003 from AMVESCAP PLC concerning the realignment of interests in the Company's shares. Following the recent conversion of unit trusts to ICVCs, AMVESCAP ceased to be interested, within the meaning of Sections 203 and 208 of the Act, in 6,238,803 ordinary shares. Immediately following this transaction, AMVESCAP had a notifiable interest in 4,002,059 (10.3%) shares. The breakdown of AMVESCAP's registered holders are set out below:

Registered Holder	Number of Shares
Bank of New York Nominees Limited	618,918
Chase Nominees Limited	342,000
Vidacos Nominees Limited	1,309,764
HSBC Nominees Limited	1,514,427
Northern Trust Nominees Limited	210,000
CM Investment Nominees Limited	6,950

Immediately following the same transaction, the ICVC and registered holder named below had a notifiable interest in the following number of shares:

ICVC	Registered Holder	Number of Shares	%
INVESCO Perpetual UK Investment Series	Vidacos Nominees Limited	5,406,647	13.9

AMVESCAP's aggregate holding remains unchanged at 10,240,862 shares (26.4%) as disclosed on 2 June 2003, following transfers between the funds under its management.

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 The company news service from the London Stock Exchange

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	12:25 27 Nov 2003
Number	5660S

RNS Number:5660S  
Phytopharm PLC  
27 November 2003

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: PHYTOPHARM PLC
2. NAME OF SCHEME: THE PHYTOPHARM 1996 UNAPPROVED DISCRETIONARY SHARE OPTION SCHEME
3. PERIOD OF RETURN: FROM: 1ST MAY 2003 TO: 31ST OCTOBER 2003
4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME 42,871 ORDINARY SHARES OF 1 PENCE  
AT END OF THE LAST PERIOD:
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: 42,871 ORDINARY SHARES OF 1 PENCE
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: NIL ORDINARY SHARES OF 1 PENCE
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES) 260,000 ORDINARY SHARES OF 1 PENCE  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: ON 18TH MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD  
IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,805,218 ORDINARY SHARES OF 1 PENCE AT 31 OCTOBER 2003

CONTACT FOR QUERIES

NAME: DR G W CHONG  
TELEPHONE: 01480 437697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: PHYTOPHARM PLC
  
2. NAME OF SCHEME: THE PHYTOPHARM
  
3. PERIOD OF RETURN: FROM: 1ST MAY 2003 TO: 31 OCTOBER 2003
  
4. NUMBER AND CLASS OF SHARES (S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME 159,660 ORDINARY SHARES OF 1 PENCE  
AT END OF THE LAST PERIOD:
  
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: NIL
  
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 159,660 ORDINARY SHARES OF 1 PENCE
  
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES) 400,000 ORDINARY SHARES OF 1 PENCE  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: ON 18TH MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD  
IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,805,218 ORDINARY SHARES OF 1 PENCE AT 31 OCTOBER 2003

CONTACT FOR QUERIES

NAME: DR G W CHONG  
TELEPHONE: 01480 437697

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The company news service from the London Stock Exchange

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Company	Phytopharm PLC
TIDM	PYM
Headline	Re Agreement
Released	07:00 26 Nov 2003
Number	4927S

26 November 2003

**Phytopharm enters agreement with Genitrix to launch canine osteoarthritis product**

Phytopharm plc (PYM: London Stock Exchange) announces today that it has entered into a distribution, sales and marketing agreement with Genitrix Ltd, one of the UK's fastest growing veterinary products companies, to launch its product PYM50014 for the maintenance of canine joint mobility. Both partners anticipate that PYM50014 will be launched in Q1 2004 and will be available from veterinarians across the UK.

PYM50014 is the lead compound within Phytopharm's P54 research programme. The product has novel non-steroidal anti-inflammatory properties and is manufactured from two related tropical plant species. In July 2001, Phytopharm announced the results of a placebo-controlled trial of PYM50014 in canine osteoarthritis, in which a statistically significant improvement in joint mobility was reported by veterinarians following two months treatment with the product.

Under the terms of the agreement, Phytopharm and Genitrix will each receive 50% of the total sales revenues of PYM50014 after deduction of manufacturing costs. Genitrix will be responsible for distribution, sales and marketing, but no deductions from the total sales revenues will be made for these activities. Phytopharm has also retained the right to co-market the product with Genitrix.

Canine osteoarthritis is a chronic and progressive inflammatory disease mainly affecting the synovial joints, causing pain, joint swelling and stiffness with loss of function. It is estimated that canine osteoarthritis affects 20% of the canine population over one year old, which is equivalent to around 1.2 million animals in the UK. Current treatment consists of a variety of steroidal and non-steroidal anti-inflammatory drugs (NSAIDS) which can have adverse side effects, and corticosteroids are not recommended for long-term use. The market for canine osteoarthritis and joint stiffness is currently estimated to be in excess of \$20m in the UK, and over \$80m in the USA (source: American Veterinary Medical Association).

Howard Wilder, Managing Director of Genitrix, said: "PYM50014 has an interesting and important profile that will complement our range of products for the companion animal market. We look forward to our ongoing collaboration with Phytopharm."

Commenting on today's announcement, Richard Dixey, Chief Executive of Phytopharm, said: "Genitrix is an excellent partner for the distribution, sales and marketing of PYM50014 in the UK. We look forward to launching the product in the UK next year and also hope to announce further marketing partners for other territories in due course."

-ENDS-

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

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Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

**Genitrix Ltd**

Howard Wilder, Managing Director

Tel: 01403 734555

NOTES TO EDITORS

**Genitrix Ltd**

Genitrix Animal Health and Nutrition is one of the UK's fastest growing veterinary products companies operating in the UK ethical companion animal and equine markets. In addition, Genitrix has a growing export business to Western and Central Europe.

The Genitrix product line comprises a number of nutritional as well as pharmaceutical specialities including licensed veterinary medicinal products for equine lameness, anti-infectives for birds and drugs for gastro-intestinal disorders in dogs. Through its Xenex range, Genitrix was also the first veterinary company to introduce insect control products for the rapidly expanding small mammal market. Genitrix aims to be the largest independent veterinary drug company in the UK.

More information concerning Genitrix can be found on its web site at  
<http://www.genitrix.co.uk>

**Phytopharm plc**

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

Research into PYM50014, including human and canine clinical studies, suggests that it is a third generation non-steroidal anti-inflammatory drug (NSAID), which achieves a significant reduction in inflammation by inhibiting several inflammatory enzymes, including inducible COX II and NOS. This may result in fewer gastrointestinal or circulatory side effects that are associated with the first and second generation NSAID products. In a clinical trial reported in July 2001, investigators reported that 56% of the dogs were 'better' or 'much better' after being treated with PYM50014 compared to 26% of those treated with placebo (p=0.047). The owners' assessment of response also favoured PYM50014 (60%) compared with placebo (38%). The treatment was well tolerated. No serious adverse side effects were observed.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Notice of Results
Released	07:00 21 Nov 2003
Number	3296S

21 November 2003

### Phytopharm plc

Phytopharm plc will be announcing its preliminary results for the year ended 31 August 2003 on Tuesday 9 December 2003.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 3 Nov 2003
Number	5528R

3 November 2003

**Phytopharm plc**

**Successful completion of phase Ib study in Alzheimer's and Parkinson's product**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the successful completion of a phase Ib clinical study of its orally active synthetic neuroprotective and neuroregenerative product, PYM50028, which is under development as a treatment for a range of neurological disorders, including Alzheimer's and Parkinson's diseases (programmes P58 and P63, respectively).

This study utilised a randomised, double blind, placebo controlled design to examine the safety, tolerability, pharmacokinetics and cognitive effects of PYM50028. Thirty healthy men and women aged 50 years and older were enrolled and randomly allocated to receive either PYM50028 or placebo once daily for 28 days. Results indicate that the product has absorption and pharmacokinetic characteristics suitable for once-daily dosing and is well tolerated with a good emergent safety profile. A phase II clinical study in Alzheimer's patients is now anticipated to begin shortly, during which PYM50028 will be compared with placebo over a three-month dosing period.

The phase Ib data have now been submitted to Yamanouchi Pharmaceutical Co Ltd ("Yamanouchi"), the results of which are the subject of the second milestone payable under the licence agreement announced on 1 May 2003 between Yamanouchi and Phytopharm for marketing of PYM50028 in Japan and some other Asian countries. A total of \$33 million in milestones was specified in the agreement, subject to the achievement of specific objectives, of which \$17 million will be potentially payable to Phytopharm over the next 18 months. Phytopharm will also receive royalties on the sale of PYM50028 by Yamanouchi.

Dr Richard Dixey, Chief Executive of Phytopharm, said: 'We are making rapid progress in the development of PYM50028 and are encouraged with the dosing profile of this product.'

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

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Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

PYM50028 arose from research into the activity of an Asian medicinal plant. In pre-clinical studies, this synthetic chemical has been shown to be neuroprotective, to reverse the decrease of neuronal growth factors and to reverse neuronal degeneration observed in the ageing brain. Importantly, this product was observed to restore levels of proteins that are altered in the ageing brain, returning them to levels seen in the young and causing beneficial neurite outgrowth and branching. PYM50028 thereby offers the potential of disease modification in poorly treated but prevalent neurodegenerative conditions such as Alzheimer's and Parkinson's diseases. The neurodegeneration platform, from which PYM50028 has been developed, is protected by nine global patent families and contains a library of related chemical compounds that share this mode of action.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at <http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	18:32 19 Sep 2003
Number	9971P

RNS Number:9971P  
 Phytopharm PLC  
 19 September 2003

The Company received notification on 19 September from RAB Capital Ltd that RAB Capital currently holds 1,303,982 shares, representing 3.4% of the issued share capital, registered in the name of Morstan Nominees Ltd.

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 The company news service from the London Stock Exchange

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	10:21 19 Aug 2003
Number	81420

RNS Number:81420  
 Phytopharm PLC  
 19 August 2003

Re: Notification of Major Interests in Shares

The Company received notification on 13 August from AMVESCAP PLC that AMVESCAP's overall holding has remained at 26%, as disclosed on 2 June 2003, following transfers between funds under its management. The notifiable change in holdings is that on 8 August 2003, INVESCO Perpetual Income Fund sold 310,000 shares and now holds 3,869,362 shares (9.98%) registered in the name of Vidacos Nominees Limited.

AMVESCAP's current aggregate holding is 10,240,862 shares (26.41%).

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	15:00 30 Jul 2003
Number	14350

30 July 2003

**Phytopharm plc**

**Pfizer returns rights of P57**

Phytopharm announced today that it has received notice from Pfizer that it will discontinue clinical development of P57 for the treatment of obesity and return the rights to the company. P57 is a novel appetite suppressant that has been shown to reduce caloric intake in overweight subjects, as announced by Phytopharm in December 2001.

In a changing environment for discovery and development of new medicines, Pfizer continually reviews its pipeline of potential new therapies. Following the closure of the Natureceuticals group within Pfizer, the company has determined that the development of P57 might be best achieved by another organization. As a consequence, Phytopharm is now free to license P57 to other parties.

The company also stated that clinical data of P57 in patients encourage further study of the natural material as a therapy for obesity.

Dr Richard Dixey, Chief Executive of Phytopharm, commented: "We have enjoyed our relationship with Pfizer over the past five years, during which a considerable body of clinical and pre-clinical data has been generated within the P57 program. We will now take further steps to build on this substantial foundation and seek other partners for this exciting opportunity."

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

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**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

There will be a conference call for analysts at 4pm this afternoon. For details, please call Mo Noonan on 0207 831 3113.

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome,

neurodegeneration, inflammation and dermatitis.

P57 is a novel appetite suppressant containing extracts derived from a South African plant. Under an agreement announced on August 24<sup>th</sup> 1998, Pfizer acquired an exclusive worldwide licence to develop and market P57.

Phytopharm is developing ten products based on its four drug discovery platforms of which five are in the clinic and five are in pre-clinical development. There are also a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	18:34 9 Jul 2003
Number	3808N

RNS Number: 3808N  
Phytopharm PLC  
9 July 2003

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: Phytopharm plc
2. NAME OF SCHEME: The Phytopharm 1996 Unapproved Discretionary Share Option Scheme
3. PERIOD OF RETURN: FROM: 11th December 2002 TO: 10th June 2003
4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD: 260,000 Ordinary Shares of 1 pence
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: nil Ordinary Shares of 1 pence
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 260,000 Ordinary shares of 1 pence
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: 260,000 Ordinary Shares of 1 pence on 10th December 2001

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,770,913 ORDINARY SHARES OF 1 PENCE AT 3RD JULY 2003

CONTACT FOR QUERIES

NAME: Dr W CHONG

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Company	Phytopharm PLC
TIDM	PYM
Headline	Board Change
Released	08:00 8 Jul 2003
Number	2716N

8 July 2003

**Phytopharm plc**

**Appointment of Finance Director**

Phytopharm plc (PYM: London Stock Exchange) (“Phytopharm”), the Botanical pharmaceutical company, announces today that Dr Wang Chong has been appointed Chief Financial Officer with immediate effect. Dr Chong, who was appointed to Phytopharm as Commercial Director in April 2003, replaces Dr Simon Loach who is leaving the company to pursue other interests.

Dr Chong is a physician with over 19 years of experience in the healthcare industry. His previous positions include CEO of Osmetech plc and leader of UK Healthcare Initiatives at management consultants, Arthur D. Little Inc from 1996 to 1999, where he was involved in developing corporate and global commercial strategy at Glaxo Wellcome plc and SmithKline Beecham plc. He holds a medical degree from King’s College School of Medicine and Dentistry, London, an MBA from London Business School, and is an Affiliate of the Securities Institute.

Dr Richard Dixey, Chief Executive of Phytopharm said: “Since joining the company, Phytopharm has benefited from Wang’s considerable commercial and financial expertise. We welcome him to the Board and thank Simon for his substantial contribution to the company.”

**Phytopharm plc**

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**Financial Dynamics**

Ben Atwell

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**Notes to Editors**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatology.

More information concerning Phytopharm’s activities can be found on its web site at

<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Re Agreement
Released	07:00 23 Jun 2003
Number	6035M

23 June 2003

Collaboration with OPTIMA (University of Oxford)  
to Advance the Development of PYM50028 as a Treatment for Dementia

Phytopharm plc (PYM: London Stock Exchange) announces today that it has entered into an agreement with the Oxford Project to Investigate Memory and Ageing (OPTIMA) regarding the clinical development of PYM50028, its novel oral treatment for dementias including Alzheimer's disease. Under the joint leadership of Professor David Smith (Project Leader, OPTIMA) and Professor Robin Jacoby (Principal Investigator), OPTIMA will enrol patients with memory impairment into the Phase II proof of principle study, which is expected to commence dosing in Q4 2003.

The study will utilise a randomised, double blind, placebo controlled design, and evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after repeated oral administration to patients with dementia. An interim safety analysis will be conducted during Q2 2004 and the study should complete by Q4 2004.

OPTIMA was founded in 1988 as part of University of Oxford's Department of Pharmacology and has since enrolled over 800 normal and cognitively impaired elderly people. Regular assessment of these volunteers has enabled the assembly of a unique and growing database of psychological, neurological, biochemical and anatomical information about the effects of ageing and cognitive impairment. The database of information enables better understanding of the key events that may trigger dementia and insights into novel approaches, such as PYM50028, to prevent and treat this devastating condition.

Today's agreement follows Phytopharm's announcement on May 1<sup>st</sup> 2003, that the Company had signed a licensing agreement with Yamanouchi Pharmaceutical Co., Ltd., a leading Japanese pharmaceutical company, for the development and commercialisation of PYM50028 in Japan and other Asian territories.

Professor David Smith, Professor of Pharmacology and Project Leader, OPTIMA, said: "PYM50028 displays an important array of pharmacological properties that are relevant to the treatment of Alzheimer's disease. Neurodegeneration plays a central role in the pathology of dementia and agents with the ability to reverse this process represent a potentially significant therapeutic advance."

Commenting on today's announcement, Richard Dixey, Chief Executive of Phytopharm, said: "OPTIMA is an excellent partner for the recruitment and evaluation of PYM50028 in patients with dementia. Their proven clinical investigative capabilities and expertise in the field provides Phytopharm with an important advantage in ensuring the rapid clinical development of this innovative therapeutic agent."

-ENDS-

Enquiries:

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Financial Dynamics

David Yates / Ben Atwell

Tel: 0207 831 3113

OPTIMA

Professor David Smith

Tel: 01865 271883

## NOTES TO EDITORS

The Oxford Project to Investigate Memory and Ageing (OPTIMA)

OPTIMA is one of the UK's leading centres for the study of dementia and has pioneered the use of neuroimaging as a diagnostic aid and for following the progression of Alzheimer's disease. Its cohort of more than 800 subjects is unique in the world for the detailed longitudinal data covering clinical assessment, neuropsychology, neuroimaging, biochemistry and genetics.

More information concerning OPTIMA can be found on its web site at

<http://www.pharm.ox.ac.uk/optima.htm>

Phytopharm plc

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PYM50028 arose from research into the activity of an Asian medicinal plant. In pre-clinical studies, this synthetic chemical is neuroprotective, reverses the decrease of neuronal growth factors and reverses neuronal degeneration observed in the ageing brain. Importantly, this product restores levels of proteins that are altered in the ageing brain, returning them to levels seen in the young, causing beneficial neurite outgrowth and branching. PYM50028 thereby offers the potential of disease modification in poorly treated but prevalent neurodegenerative conditions such as Alzheimer's and Parkinson's disease. The neurodegeneration platform, from which PYM50028 has been developed, is protected by nine global patent families and contains a library of related chemical compounds that share this mode of action.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at

<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	16:38 5 Jun 2003
Number	9796L

RNS Number:9796L  
Phytopharm PLC  
5 June 2003

Phytopharm PLC (the 'Company')

5 June 2003

Notification of major interests in shares

The Company received notification today from HBOS PLC ('HBOS') that HBOS and its subsidiary companies have an interest in 1,172,818 Ordinary 1p Shares. This represents 3.03% of the issued share capital of the Company. Details of that interest, together with a breakdown between registered holders, are set out below:-

HSBC Global Custody Nominees (UK) Ltd	1,171,408
JP Morgan Chase Bank, Luxembourg	1,410

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The company news service from the London Stock Exchange

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	10:19 3 Jun 2003
Number	8418L

RNS Number:8418L  
Phytopharm PLC  
3 June 2003

Phytopharm PLC (the 'Company')

3 June 2003

Notification of major interests in shares

The Company received notification on 2 June 2003 from AMVESCAP PLC ('AMVESCAP') and subsidiary companies on behalf of discretionary clients that, following the purchase of 350,000 shares on 30 May 2003. AMVESCAP has an interest within the meaning of Part VI of the Act in 10,113,882 Ordinary 1p Shares. This represents 26.16% of the issued share capital. Details of that interest, together with a breakdown between registered holders (as required by Section 202(3) of the Act), are set out below:-

Vidacos Nominees Limited	7,719,657
HSBC Nominees Limited	1,297,539
Bank of New York Nominees Limited	551,511
Chase Nominees Limited	337,617
Northern Trust Nominees Limited	200,608
CM Investment Nominees Limited	6,950

None of these shares are beneficially owned by AMVESCAP. Subsidiary companies of AMVESCAP have a large number of portfolio management clients for whom they act as investment manager and investment advisor, and by virtue of Section 203 of the Companies Act 1985 AMVESCAP is deemed to have the same interest in the shares.

The above holding includes 4,137,411 shares representing 10.70% held by INVESCO Perpetual Income Fund and 1,341,006 shares representing 3.47% held by INVESCO Perpetual UK Growth Fund, both registered in the name of Vidacos Nominees Limited.

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<b>Company</b>	Phytopharm PLC
<b>TIDM</b>	PYM
<b>Headline</b>	Holding(s) in Company
<b>Released</b>	16:36 2 Jun 2003
<b>Number</b>	8189L

RNS Number:8189L  
 Phytopharm PLC  
 2 June 2003

Phytopharm PLC (the 'Company')

#### Notification of major interests in shares

The Company received notification on 30 May 2003 from AMVESCAP PLC (AMVESCAP) and subsidiary companies on behalf of discretionary clients that following the purchase of 537,020 shares on 29 May 2003 AMVESCAP has an interest within the meaning of Part VI of the Act in 9,763,882 Ordinary 1p Shares. This represents 25.25% of the issued share capital. Details of that interest, together with a breakdown between registered holders (as required by Section 202(3) of the Act), are set out below:-

Vidacos Nominees Limited	7,474,588
HSBC Nominees Limited	1,278,555
Bank of New York Nominees Limited	503,533
Chase Nominees Limited	325,536
Northern Trust Nominees Limited	174,720
CM Investment Nominees Limited	6,950

None of these shares are beneficially owned by AMVESCAP. Subsidiary companies of AMVESCAP have a large number of portfolio management clients for whom they act as investment manager and investment advisor and by virtue of Section 203 of the Companies Act 1985 AMVESCAP is deemed to have the same interest in the shares.

The above holding includes 4,021,780 shares representing 10.40% held by INVESCO Perpetual Income Fund and 1,296,134 shares representing 3.35% held by INVESCO Perpetual UK Growth Fund, both registered in the name of Vidacos Nominees Limited.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	12:40 21 May 2003
Number	3760L

RNS Number:3760L  
Phytopharm PLC  
21 May 2003

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: Phytopharm plc
2. NAME OF SCHEME: The Phytopharm 1996 Unapproved Discretionary Share Option Scheme
3. PERIOD OF RETURN: FROM: 1st November 2002 TO: 30th April 2003
4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD: 87,664 Ordinary Shares of 1 pence
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: 43,793 Ordinary Shares of 1 pence
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 43,871 Ordinary shares of 1 pence
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: 260,000 Ordinary Shares of 1 pence on 18th May 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,655,323 ORDINARY SHARES OF 1 PENCE AT 30TH APRIL 2003

CONTACT FOR QUERIES

NAME: Dr S C Loach  
TELEPHONE: 01480 437 697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY: Phytopharm plc

2. NAME OF SCHEME: The Phytopharm 1996 Company Share Option Plan
3. PERIOD OF RETURN: FROM: 1st November 2002 TO: 30th April 2003
4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD: 159,660 Ordinary Shares of 1 pence
5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: Nil
6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 159,660 Ordinary shares of 1 pence
7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION: 400,000 Ordinary Shares of 1  
pence on 18th May 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD  
IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,655,323 ORDINARY SHARES OF 1 PENCE AT 30TH APRIL  
2003

CONTACT FOR QUERIES

NAME: Dr S C Loach  
TELEPHONE: 01480 437 697

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	18:05 20 May 2003
Number	3538L

Phytopharm PLC

Phytopharm PLC (the 'Company')

20 May 2003

Notification of major interests in shares

The Company received notification on 19 May 2003 from AMVESCAP PLC (AMVESCAP) and subsidiary companies on behalf of discretionary clients that following the purchase of 140,000 shares on 16 May 2003 AMVESCAP has an interest within the meaning of Part VI of the Act in 8,935,434 Ordinary 1p Shares. This represents 23.11% of the issued share capital. Details of that interest, together with a breakdown between registered holders (as required by Section 202(3) of the Act), are set out below:-

Vidacos Nominees Limited	6,823,567
HSBC Nominees Limited	1,249,427
Bank of New York Nominees Limited	369,918
Chase Nominees Limited	292,000
Northern Trust Nominees Limited	135,000
Mellon Bank Pittsburgh Nominees	58,572
CM Investment Nominees Limited	6,950

None of these shares are beneficially owned by AMVESCAP. Subsidiary companies of AMVESCAP have a large number of portfolio management clients for whom they act as investment manager and investment advisor and by virtue of Section 203 of the Companies Act 1985 AMVESCAP is deemed to have the same interest in the shares.

The above holding includes 3,844,362 shares representing 9.94% held by INVESCO Perpetual Income Fund and registered in the name of Vidacos Nominees Limited.  
END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 20 May 2003
Number	2974L

20 May 2003

**Phytopharm plc**

**Successful completion of phase I clinical study of treatment for Parkinson's disease**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the successful completion of a phase I clinical study to evaluate the safety, tolerability and pharmacokinetic profile of its orally active synthetic neuroprotective and neuroregenerative product, PYM50028, which is under development as a treatment for a series of neurological disorders, including Parkinson's disease (programme P63).

The residential study was conducted in two stages, each utilising a double-blind, placebo-controlled design. The first stage evaluated the safety, tolerability and pharmacokinetics of single oral doses escalated across four groups of eight healthy subjects. The second stage assessed the safety, tolerability and pharmacokinetics of repeated oral dosing administered over 7 days to three groups of eight healthy subjects aged over 50 years.

These two stages have now been successfully completed. The data indicate that PYM50028 is very well tolerated, with a good emergent safety profile and a linear pharmacokinetic relationship between dose and systemic exposure.

The phase I study results have now enabled Phytopharm to receive approval for a 28-day randomised, double-blind, and placebo-controlled study that will enrol 30 healthy subjects aged over 50 years. This study will assess the safety, tolerability, pharmacokinetics and cognitive effects of two dose levels of PYM50028 administered for 28 days. The study will start immediately and results will be reported during the third quarter of 2003.

As announced on 1 May 2003, Yamanouchi Pharmaceutical Co Ltd. has acquired an option to license PYM50028 for a number of indications, including Parkinson's disease, pursuant to which Phytopharm will receive licence fees, milestones and royalties on sales in Japan and certain other Asian countries.

Dr Richard Dixey, Chief Executive of Phytopharm, said: 'the onset of neuronal degeneration underlies both Parkinson's and Alzheimer's diseases as well as many of the peripheral neuropathies. PYM50028 offers the potential of directly reversing this process and significantly advancing the treatment of these devastating conditions.'

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

## NOTES TO EDITORS

### Phytopharm plc

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. These plant-based medicines, manufactured to pharmaceutical standards, can be clinically evaluated in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic disease, neurodegeneration, inflammation and dermatitis.

Neurodegenerative disorders such as Parkinson's disease are chronic, progressive conditions that predominantly affect the middle aged and elderly, causing severe disability and premature death. In the US market alone, there are estimated to be one million patients with diagnosed Parkinson's disease and a further two million undiagnosed, with associated health care costs to the economy of \$10 billion (source: AHP submission to US Congress).

Despite substantial progress in our understanding of these conditions over recent years, in most cases the underlying cause(s) remain unknown. The currently available drug therapies can provide symptomatic improvement and in some cases may delay disease progression to a modest extent. The medical, social and economic impact of these diseases is increasing, particularly in the developed world, due to the ageing population.

Phytopharm is developing nine programmes based on its four drug discovery platforms alongside a number of other projects in early evaluation.

More information concerning Phytopharm's activities can be found on its web site at  
<http://www.phytopharm.com>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Acquisition of Shares
Released	15:19 7 May 2003
Number	8062K

RNS Number:8062K  
Phytopharm PLC  
07 May 2003

Phytopharm PLC

Phytopharm PLC (the 'Company')

7 May 2003

Notification of major interests in shares

The Company received notification on 6 May 2003 from RAB Capital Ltd, informing it that as a result of acting as investment manager for a number of commingled funds RAB Capital Ltd has acquired 1,603,500 ordinary shares in Phytopharm plc. This represents 4.2% of the issued share capital. RAB Capital Ltd does not act as custodian for its clients and the shares are held in the name of Morstan Nominees Ltd.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Director Shareholding
Released	14:47 7 May 2003
Number	7889K

RNS Number:7889K  
Phytopharm PLC  
7 May 2003

#### DEALINGS BY DIRECTORS

1) NAME OF COMPANY  
PHYTOPHARM PLC

2) NAME OF DIRECTOR  
DR R P DIXEY

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest  
AS 2 ABOVE

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)  
AS 2 ABOVE

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)  
AS 2 ABOVE

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary  
GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003

7) Number of shares/amount of stock acquired

8) ( % )  
of issued Class

9) Number of shares/amount of stock disposed

10) ( %)  
of issued Class

11) Class of security

12) Price per share

13) Date of transaction

14) Date company informed

15) Total holding following this notification

16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

17) Date of grant  
2 MAY 2003

18) Period during which or date on which exercisable  
FROM 3 MAY 2006 TO 2 MAY 2013 SUBJECT TO PERFORMANCE CRITERIA

19) Total amount paid (if any) for grant of the option  
NIL

20) Description of shares or debentures involved: class, number.  
48,649 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES

21) Exercise price (if fixed at time of grant) or indication that price  
is to be fixed at time of exercise  
142.5 PENCE

22) Total number of shares or debentures over which options held  
following this notification  
544,260 ORDINARY SHARES

23) Any additional information  
PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO  
COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT. NO  
OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND  
100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATA VESTING BETWEEN MEDIAN AND

UPPER DECILE PERFORMANCE. FOR 32,433 OPTIONS THE COMPARATOR GROUP COMPRISES 27 OTHER UK LISTED BIOTECH COMPANIES, AND FOR 16,216 OPTIONS THE COMPARATOR GROUP IS THE FTSE SMALL CAP INDEX.

24) Name of contact and telephone number for queries  
DR S C LOACH - 01480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification            7 MAY 2003

#### DEALINGS BY DIRECTORS

1) NAME OF COMPANY  
PHYTOPHARM PLC

2) NAME OF DIRECTOR  
DR D D REES

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest  
AS 2 ABOVE

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)  
AS 2 ABOVE

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)  
AS 2 ABOVE

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary  
GRANT OF SHARE OPTIONS UNDER THE PHYTOPHARM SHARE OPTION PLAN 2003

7) Number of shares/amount of stock acquired

8) ( % )  
of issued Class

9) Number of shares/amount of stock disposed

- 10) ( %)  
of issued Class
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
2 MAY 2003
- 18) Period during which or date on which exercisable  
FROM 3 MAY 2006 TO 2 MAY 2013 SUBJECT TO PERFORMANCE CRITERIA
- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
33,342 PHYTOPHARM PLC ORDINARY 1 PENCE SHARES
- 21) Exercise price (if fixed at time of grant) or indication that price  
is to be fixed at time of exercise  
142.5 PENCE
- 22) Total number of shares or debentures over which options held  
following this notification  
559,014 ORDINARY SHARES
- 23) Any additional information  
PERFORMANCE CRITERIA ARE BASED ON TOTAL SHAREHOLDER RETURN COMPARED TO  
COMPARATOR GROUPS AT THE THIRD, FOURTH AND FIFTH ANNIVERSARIES OF GRANT. NO  
OPTIONS VEST FOR BELOW MEDIAN PERFORMANCE, 25% VEST FOR MEDIAN PERFORMANCE AND  
100% VEST FOR UPPER DECILE AND ABOVE WITH PRORATA VESTING BETWEEN MEDIAN AND  
UPPER DECILE PERFORMANCE. FOR 22,228 OPTIONS THE COMPARATOR GROUP COMPRISED 27  
OTHER UK LISTED BIOTECH COMPANIES, AND FOR 11,114 OPTIONS THE COMPARATOR GROUP  
IS THE FTSE SMALL CAP INDEX.

24) Name of contact and telephone number for queries  
DR S C LOACH - 01480 437697

25) Name and signature of authorised company official responsible for  
making this notification

Date of Notification            7 MAY 2003

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Company	Phytopharm PLC
TIDM	PYM
Headline	Re Agreement
Released	07:00 1 May 2003
Number	6050K

1 May 2003

**Collaboration with Yamanouchi  
to Develop and Commercialise Alzheimer's Drug (PYM50028)**

*First Drug Licensed from Phytopharm's P58 Neurodegeneration Platform*

Phytopharm plc (PYM: London Stock Exchange) announces today that it has signed a licensing agreement with the leading Japanese pharmaceutical company, Yamanouchi Pharmaceutical Co., Ltd., for the development and commercialisation of PYM50028, a synthetic neuroprotective and neuroregenerative agent that has been selected from the library of compounds within the company's P58 discovery platform. The initial target indication licensed by Yamanouchi is Alzheimer's disease. Yamanouchi also receives options to develop the product for additional indications, as detailed below.

Under this agreement, Yamanouchi has acquired an exclusive licence to develop, manufacture and market PYM50028 for the treatment of Alzheimer's disease in Japan and some other Asian countries. Phytopharm will receive \$3 million immediately, followed by a further five milestones totalling \$17 million payable over the next two years, subject to the achievement of specific objectives. In total, Phytopharm is entitled to \$33 million of licence fees and potential milestone payments with respect to the Alzheimer's indication.

Yamanouchi has also acquired the option to license PYM50028 for the additional indications of Parkinson's disease, Lewy body dementia, vascular dementia and mild cognitive impairment, for which Phytopharm will receive additional licence fees and milestones. Further details of these fees and milestones are based on each indication's market potential relative to the Alzheimer's indication but are not further disclosed.

Phytopharm will also receive royalties on sales of PYM50028 by Yamanouchi for all indications developed.

Phytopharm will continue to develop PYM50028 in other territories as a prescription drug for neurodegenerative conditions including Alzheimer's, Parkinson's, vascular dementia and mild cognitive impairment. After an extensive programme of pre-clinical development, the product is planned to enter Phase II clinical trials for Alzheimer's disease in the second half of 2003. Phytopharm and Yamanouchi will share all data pertaining to PYM50028, with Phytopharm retaining the right to use the data generated to seek licensees for other territories in due course.

The markets licensed to Yamanouchi under this agreement constitute approximately 15% of the world pharmaceutical market (source: IMS). The global annual market for Alzheimer's and Parkinson's disease is estimated to be worth in excess of \$3 billion (source: Cognos and Pharmasource); it is also estimated that in the US, the total annual cost burden for Alzheimer's disease exceeds \$100 billion (Source: US Alzheimer's Association).

Commenting on the agreement, Dr Toichi Takenaka, President & Chief Executive Officer of Yamanouchi stated: "We look forward to working with Phytopharm to develop PYM50028, a novel product having the potential to make a significant impact within the CNS marketplace. This

collaboration not only demonstrates our enthusiasm for Phytopharm's discovery but also reflects the commitment of Yamanouchi to identify and develop important medicines for neurodegenerative conditions such as Alzheimer's disease. This is a distressing disease without effective treatment, whose prevalence is growing rapidly in Japan."

Commenting on today's announcement, Richard Dixey, Chief Executive of Phytopharm, said: "We are delighted to be working with Yamanouchi which is one of the leading Japanese pharmaceutical companies with an outstanding record of achievement in research led innovation. In addition to this agreement being strongly cash positive for Phytopharm, it confirms the true potential of both PYM50028 and the P58 platform, as well as the company's strategy of seeking a Japanese partner for this exciting product."

- ENDS -

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

**A presentation for analysts will be held at Nomura International plc, 1 St Martin's-le-Grand, London EC1A 4NP at 9:30am today. Coffee will be available from 9.15am. A webcast of the analyst presentation will be available from Friday 2 May on the Company's website:**

*[www.phytopharm.co.uk](http://www.phytopharm.co.uk)*

NOTES TO EDITORS

**Phytopharm plc**

Phytopharm is a leading company in the development of **Botanical pharmaceuticals**. Botanicals, extracts of medicinal plants manufactured to pharmaceutical standards, enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome and obesity, neurodegeneration, inflammation and dermatitis, and is developing libraries of synthetic chemical compounds based this research.

PYM50028 has arisen from research into the activity of an Asian medicinal plant. In pre-clinical studies using a variety of models, this single chemical, synthetic product has been demonstrated to be neuroprotective, to reverse the decrease of neuronal growth factors and to reverse neuronal degeneration observed in the ageing brain. Importantly, this product restores levels of proteins that are altered in the ageing brain, returning them to levels seen in the young, causing beneficial outgrowth and branching of neurites and restoring the levels of muscarinic acetylcholine and dopaminergic receptors. PYM50028 thereby offers the potential of disease modification in poorly treated but prevalent neurodegenerative conditions such as Alzheimer's and Parkinson's disease. The P58 research platform, from which PYM50028 has been developed, is protected by nine global patent families and contains a library of related chemical compounds that share this activity.

**Yamanouchi Pharmaceutical Co., Ltd.**

Yamanouchi Pharmaceutical Co., Ltd., established in 1923 and headquartered in Tokyo, Japan, is a leading pharmaceutical company in Japan. Yamanouchi is expanding its business base to Europe, the United States and Asia and employs about 9,000 people worldwide. As a research-based developer, manufacturer and marketer, Yamanouchi has introduced several world-class drugs to the international market, including the H2 antagonist, famotidine; the calcium antagonist, nifedipine; and tamsulosin, a treatment for functional symptoms of benign prostatic hyperplasia.

More information concerning Yamanouchi can be found on its Web site at <http://www.yamanouchi.com>

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<b>Company</b>	Phytopharm PLC
<b>TIDM</b>	PYM
<b>Headline</b>	Appointment
<b>Released</b>	07:00 14 Apr 2003
<b>Number</b>	9854J

14 April 2003

**Phytopharm plc**

**Appointment of Commercial Director**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today that Dr Wang Chong has joined the company's senior management team as Commercial Director. Dr Chong will be responsible for the overall management of in- and out-licensing and commercial development of Phytopharm's product pipeline.

Dr Wang Chong is a physician with over 19 years of experience in the healthcare industry. His previous positions have included Biotechnology Analyst at Canaccord Capital, CEO of Osmetech plc, a UK based healthcare diagnostics company from 1999 to 2001 and leader of UK Healthcare Initiatives at Arthur D. Little Inc from 1996 to 1999, in which role he had responsibility for developing corporate and global commercial strategy at Glaxo Wellcome plc and SmithKline Beecham plc. He holds a medical degree from King's College School of Medicine and Dentistry, London, and an MBA from London Business School.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "Wang is an important addition to our management team here at Phytopharm, and brings considerable experience and expertise in the development of licensing partnerships and the commercialisation of products."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697  
Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

## NOTES TO EDITORS

### Phytopharm plc

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neurodegeneration, inflammation and dermatitis.

Phytopharm is developing ten products based on its four drug discovery platforms of which five are in the clinic and five are in pre-clinical development. There are also a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Notice of Results
Released	15:04 8 Apr 2003
Number	7826J

8 April 2003

### Phytopharm plc

Phytopharm plc will be announcing its interim results for the six months ended 28 February 2003 on Thursday 1 May 2003.

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<b>Company</b>	Phytopharm PLC
<b>TIDM</b>	PYM
<b>Headline</b>	Holding(s) in Company
<b>Released</b>	07:00 14 Mar 2003
<b>Number</b>	72311

Phytopharm PLC (the "Company")  
14 March 2003

#### Notification of major interests in shares

The Company received notification on 13 March 2003 from Standard Life Investments, informing it that as a result of a disposal of 1,516,766 ordinary shares on 12 March 2003 on behalf of Standard Life Group, this decreased the total shares held as a material interest to 11,839 shares, being below 3% of the issued shares of that class.

The remaining 11,839 shares are registered in the name of Stanlife Nominees Limited.

END

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Send to a Friend



Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 12 Mar 2003
Number	60131

12 March 2003

**Phytopharm plc**

**Update on development programme for Appetite Suppressant P57**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today that it has received the first six monthly progress report from Pfizer Inc ("Pfizer") concerning the ongoing development of its appetite suppressant P57. This follows the announcement in July 2002 that Pfizer was taking responsibility for the development of the product, under the terms of the Licence and Royalty agreement entered between Pfizer and Phytopharm in August 1998. P57 is a novel appetite suppressant that has been shown to reduce caloric intake in overweight subjects, as announced by Phytopharm in December 2001.

The first six monthly report from Pfizer summarises the steps they have taken to continue the development of P57. A committee within Pfizer has been formed to oversee the project, and work has commenced in preparation for a double blind, placebo-controlled residential study to clinically validate the appetite suppression mechanism and to assess the safety of a simplified low dose botanical mixture.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "The P57 project continues to make satisfactory progress in the capable hands of the Pfizer team. We look forward to further updates in due course."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neurodegeneration, inflammation and dermatitis.

P57 is a novel appetite suppressant containing extracts derived from a South African plant. Under an agreement announced on August 24<sup>th</sup> 1998, Pfizer has acquired an exclusive worldwide licence to develop and market P57. Phytopharm will receive up to \$32 million in licence fees and milestone payments based upon the achievement of specific objectives. Phytopharm will also receive royalties on sales of P57 by Pfizer.

Phytopharm is developing ten products based on its four drug discovery platforms of which five are in the clinic and five are in pre-clinical development. There are also a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Appt: Broker & Joint Adviser
Released	07:00 26 Feb 2003
Number	9716H

26 February 2003

**Phytopharm plc**

**Appointment of Broker and Joint Financial Adviser**

Phytopharm plc, the UK-based, LSE listed botanical pharmaceuticals company, announces today the appointment of Nomura International plc as its broker and joint financial adviser, with immediate effect.

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates /

Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

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Neurodegenerative disorders such as Parkinson's disease are chronic, progressive conditions that predominantly affect the middle aged and elderly, causing severe disability and premature death. In the US market alone, there are estimated to be one million patients with diagnosed Parkinson's disease and a further two million undiagnosed, with a cost to the economy of \$10 billion in associated health care costs (source: AHP submission to US Congress).

Despite substantial progress in our understanding of these conditions over recent years, in most cases the underlying cause(s) remain unknown. The currently available drug therapies can provide symptomatic improvement and in some cases may delay disease progression to a modest extent. The medical, social and economic impact of these diseases is increasing, particularly in the developed world, due to the ageing population.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its web site at

<http://www.phytopharm.co.uk>

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	11:48 25 Feb 2003
Number	9307H

Phytopharm PLC ("the Company")

#### Notification of Major Interests in Shares

The Company received a notification today from Standard Life Investments Limited, informing it that following a sale of 29,577 shares on the 24 February 2003, its resultant material interest is 1,528,408 shares representing 3.954% of the issued share capital of the company.

25 February 2003

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Result of AGM
Released	18:16 24 Feb 2003
Number	9049H

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm" or "the Company")  
24 February 2003

Company number 3131723

#### Results of AGM

Phytopharm is pleased to announce that at the Annual General Meeting of the Company held on 24 February 2003 all of the resolutions proposed were duly passed. A copy of those resolutions other than Ordinary Business has been submitted to the UK Listing Authority and will shortly be available for inspection at the UK Listing Authority's document viewing facility, which is situated at:

Financial Services Authority  
25 The North Colonnade  
Canary Wharf  
London  
E14 5HS

Enquiries:

Phytopharm plc 01480 437697  
Dr S C Loach

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	09:59 28 Jan 2003
Number	6999G

Phytopharm PLC ("the Company")

#### Notification of Major Interests in Shares

The Company received a notification on 27 January 2003 from Legal & General Investment Management Limited, informing it that they currently have an interest in 1,261,357 shares, representing 3.26% of the issued ordinary share capital of the Company.

The shares are registered in the name of HSBC Global Custody Nominees (UK) Ltd.

28 January 2003

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Director Shareholding
Released	17:50 20 Jan 2003
Number	4047G

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

1) Name of company

Phytopharm PLC

2) Name of director

Dr Richard Dixey

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of a non-beneficial interest

As in 2 above

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them (if notified)

As in 2 above

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

As in 2 above

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

Purchase of Equities

7) Number of shares/amount of stock acquired

88,575

8) Percentage of issued class

0.23%

9) Number of shares/amount of stock disposed

n/a

10) Percentage of issued class

n/a

11) Class of security

Ordinary 1p shares

12) Price per share

100p

13) Date of transaction

20<sup>th</sup> January 2003

14) Date company informed

20<sup>th</sup> January 2003

15) Total holding following this notification

255,075

16) Total percentage holding of issued class following this notification

0.66%

If a director has been granted options by the company please complete the following boxes

17) Date of grant

18) Period during which or date on which exercisable

19) Total amount paid (if any) for grant of the option

20) Description of shares or debentures involved: class, number

21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise

22) Total number of shares or debentures over which options held following this notification

23) Any additional information

24) Name of contact and telephone number for queries

S. Loach 01480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification.....20<sup>th</sup> January 2003.....

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Company	Phytopharm PLC
TIDM	PYM
Headline	Phase I Clinical Trials
Released	07:00 20 Jan 2003
Number	3559G

20 January 2003

**Phytopharm plc**

**Commences phase I clinical study of treatment for Parkinson's disease**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the start of a phase I clinical study to evaluate the safety, tolerability and pharmacokinetic profile of its patented oral product, P63, which is under development as a treatment for neurodegenerative disorders, including Parkinson's disease.

This residential study will be conducted in two stages, each utilising a double blind, placebo-controlled design. The first stage will evaluate the safety, tolerability and pharmacokinetics of single oral doses that will be escalated across four groups of eight healthy subjects. The second stage will assess the safety, tolerability and pharmacokinetics of repeated oral dosing administered over 7 days to three groups of eight healthy subjects aged over 50 years. Each group will be assigned a different dose level. It is expected that the results will be reported during the second quarter of 2003.

Phytopharm has developed a large group of patented compounds whose properties form a platform for the development of novel therapeutic approaches for neurodegenerative disorders. These properties include the restoration of neuronal growth factors, the increase in neuronal interconnections, the reversal of neuronal receptor decline including dopamine receptors, and protection against the effects of a neurotoxin that causes symptoms similar to Parkinson's disease in man.

Dr Richard Dixey, Chief Executive of Phytopharm, said: 'The onset of neuronal degeneration underlies Parkinson's, Alzheimer's disease and many other peripheral neuropathies. This product arising from our family of 60 patented compounds offers the potential of directly reversing this process, and significantly advancing the treatment of these devastating conditions.'

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates /

Tel: 0207 831 3113

Ben Atwell

## NOTES TO EDITORS

### Phytopharm plc

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neurodegeneration, inflammation and dermatitis.

Neurodegenerative disorders such as Parkinson's disease are chronic, progressive conditions that predominantly affect the middle aged and elderly, causing severe disability and premature death. In the US market alone, there are estimated to be one million patients with diagnosed Parkinson's disease and a further two million undiagnosed, with a cost to the economy of \$10 billion in associated health care costs (source: AHP submission to US Congress).

Despite substantial progress in our understanding of these conditions over recent years, in most cases the underlying cause(s) remain unknown. The currently available drug therapies can provide symptomatic improvement and in some cases may delay disease progression to a modest extent. The medical, social and economic impact of these diseases is increasing, particularly in the developed world, due to the ageing population.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its web site at <http://www.phytopharm.co.uk>.

END

[Company website](http://www.phytopharm.co.uk)

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	14:22 19 Dec 2002
Number	3420F

RNS Number:3420F  
Phytopharm PLC  
19 December 2002

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

Phytopharm plc

2. NAME OF SCHEME:

The Phytopharm 1996 Unapproved Discretionary Share Option Scheme

3. PERIOD OF RETURN: FROM: 11th June 2002 TO: 10th December 2002

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD:

260,000 Ordinary Shares of 1 pence

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

nil Ordinary Shares of 1 pence

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD:

260,000 Ordinary shares of 1 pence

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION:

260,000 Ordinary Shares of 1 pence on 10th December 2001

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD  
IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,655,323 ORDINARY SHARES OF 1 PENCE AT 10TH DECEMBER  
2002

CONTACT FOR QUERIES

NAME: Dr S C Loach

TELEPHONE: 01480 437 697

This information is provided by RNS  
The company news service from the London Stock Exchange

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Director Shareholding  
 Released: 16:50 6 Dec 2002  
 Number: 8071E

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

1	Name of Company
	Phytopharm PLC
2	Name of Director
	DR R P Dixey
3	Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of a non-beneficial interest
	As 2 above
4	Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them (if notified)
	As 2 above
5	Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)
	As 2 above
6	Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary
	Grant of Options. (see box 17)
	If a director has been granted options by the company please complete the following boxes
17	Date of grant
	6 December 2002
18	Period during which or date on which exercisable
	49,491 from 7 December 2005 to 6 December 2009 49,490 from 7 December 2007 to 6 December 2009
19	Total amount paid (if any) for grant of the option
	Nil

20	Description of shares or debentures involved: class, number
	98,981 Ordinary 1 pence shares
21	Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise
	£1.165
22	Total number of shares or debentures over which options held following this notification
	622,211
23	Any additional information
24	Name of contact and telephone number for queries
	S Loach 01480 437697
25	Name and signature of authorised company official responsible for making this notification
	S Loach
26	Date of Notification
	6 December 2002

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Director Shareholding  
 Released: 16:46 6 Dec 2002  
 Number: 8056E

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

1	Name of Company
	Phytopharm PLC
2	Name of Director
	DR S C Loach
3	Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of a non-beneficial interest
	As 2 above
4	Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them (if notified)
	As 2 above
5	Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)
	As 2 above
6	Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary
	Grant of Options (see box 17)
	If a director has been granted options by the company please complete the following boxes
17	Date of grant
	6 December 2002
18	Period during which or date on which exercisable
	5,855 from 7 December 2005 to 6 December 2009
	5,854 from 7 December 2007 to 6 December 2009
19	Total amount paid (if any) for grant of the option
	Nil

20	Description of shares or debentures involved: class, number
	11,709 Ordinary 1 pence shares
21	Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise
	£1.165
22	Total number of shares or debentures over which options held following this notification
	146,152
23	Any additional information
24	Name of contact and telephone number for queries
	S Loach 01480 437697
25	Name and signature of authorised company official responsible for making this notification
	S Loach
26	Date of Notification
	6 December 2002

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Company      Phytopharm PLC  
 TIDM        PYM  
 Headline    Director Shareholding  
 Released    16:27 6 Dec 2002  
 Number      8025E

SCHEDULE 11

NOTIFICATION OF INTERESTS OF DIRECTORS AND CONNECTED PERSONS

1	Name of Company
	PHYTOPHARM PLC
2	Name of Director
	Dr D D REES
3	Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of a non-beneficial interest
	As 2 above
4	Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them (if notified)
	As 2 above
5	Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)
	As 2 above
6	Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary
	Grant of a single performance share award to Dr D D Rees to secure his retention under Listing Rule 13.13A. The award is over up to 300,000 ordinary shares at par, vesting from 6 December 2005 and lapsing on 5 June 2006 and is subject satisfaction of demanding total shareholder return performance criteria.
7	Number of shares/amount of Stock acquired
8	Percentage of issued class

9	Number of shares/amount of stock disposed
10	Percentage of issued class
11	Class of security
	Ordinary 1 Pence
12	Price per share
	Par
13	Date of transaction
	6 December 2002
14	Date company informed
	6 December 2002
15	Total holding following this notification
	Nil
16	Total percentage holding of issued class following this notification
	Nil
	If a director has been granted options by the company please complete the following boxes
17	Date of grant
18	Period during which or date on which exercisable
19	Total amount paid (if any) for grant of the option
20	Description of shares or debentures involved: class, number
21	Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise
22	Total number of shares or debentures over which options held following this notification
23	Any additional information

24	Name of contact and telephone number for queries
	S Loach 01480 437697
25	Name and signature of authorised company official responsible for making this notification
	S Loach
26	Date of Notification
	6 December 2002

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Company	Phytopharm PLC
TIDM	PYM
Headline	Final Results
Released	07:00 5 Dec 2002
Number	6895E

**5 December 2002**

Preliminary results for the year ended 31 August 2002

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm or the "Group") today announces its preliminary results for the year ended 31 August 2002.

Period highlights

- Future development programme agreed with Pfizer on obesity and metabolic syndrome (P57)
- Opening of a new botanical supplies unit in South Africa to expand manufacturing capacity (P57)
- Phytopharm's own novel synthetic programme for obesity initiated (P64)
- Successful completion of 28 day Phase I repeat dose study in age-related cognitive impairment (P58)
- Evidence of neuroprotective effect in pre-clinical models of Parkinson's disease (P63)
- Survival benefit demonstrated in pre-clinical models of motor neurone disease (P59)
- Completion of Phase II study in inflammatory bowel disease (P54)
- Commencement of European multi-centre study in canine atopic dermatitis (P7v)

Dr Richard Dixey, Chief Executive of Phytopharm, said:

*"Phytopharm's focus on its four key platforms has allowed the Group to generate strong intellectual property and to move into related disease processes with new chemical forms. In addition to the eight products we had in development at the beginning of the year, two further projects have entered full development during 2002. We continue to generate strong product progress within tightly controlled operational costs and are on target to meet all our deliverables during 2003."*

Enquiries:

**Phytopharm plc**  
Dr Richard Dixey, Chief Executive

Today: 07867 782000  
Thereafter: 01480 437697  
Mobile: 07867 782000

**Financial Dynamics**  
David Yates / Ben Atwell

Tel: 0207 831 3113

Phytopharm has updated its website from 5 December 2002; [www.phytopharm.co.uk](http://www.phytopharm.co.uk)

#### Business Model

Phytopharm develops a portfolio of products that have emerged from a well-established research base. Its expertise in manufacturing controlled plant extracts (botanicals) enables it to initiate early clinical evaluations and base substantial research platforms on the emergent clinical data. These platforms are not only novel, but allow the Group to generate strong intellectual property and to move into related disease processes with new chemical forms.

Phytopharm invests shareholders' funds in developing its portfolio, and remains a well-funded Group with over two years working capital at current burn rates. Once product development programmes have reached a substantive stage, the Group seeks pharmaceutical partners who pay for options to market products based on intellectual property owned by Phytopharm. These option agreements involve substantial payments to the Group, comprising the reimbursement of further development costs, the payment of milestones as key phases are completed, and royalties on eventual product sales. These payments are negotiated by reference to the size of the eventual market, the stage of development of the product concerned and the strength of the data generated.

With its small central overhead, Phytopharm offers the potential of sustained profitability once its main products have been licensed in this manner, even if royalty income arising from sales of such products is some years off. Furthermore, the botanical approach also enables the parallel development of products for early marketing in the companion animal market, thereby balancing early revenue generators with major pharmaceutical products.

#### Operational Review

The metabolic disorders platform is focussed on obesity, obese onset diabetes and metabolic syndrome. Licensed to Pfizer Inc in 1998, the **P57** platform comprises the patented use of three plant species, their mode of action and 17 related active molecules.

In March 2002, Phytopharm announced the opening of a new botanical supplies unit in South Africa to substantially expand the manufacturing capacity for P57 in support of the further development of the product. The new facility expands the capacity for processing the raw materials by 300 per cent and a programme to process substantial quantities of plant material has been successfully undertaken.

In July 2002, Phytopharm announced the future development programme with Pfizer. The agreement followed the successful demonstration of proof of principle in man that was announced in December 2001. Pfizer will now progress the P57 development programme concerning extracts of medicinal plants under the ongoing terms of the Licence and Royalty Agreement announced between Pfizer and Phytopharm in 1998. This programme is intended to result in the development of a botanical prescription pharmaceutical for the treatment of obesity and metabolic syndrome.

Phytopharm has now developed screens that are predictive of appetite suppressant activity. This has enabled the development of synthetic molecules that will form the basis of a further licensing opportunity. This programme (**P64**) is intended to result in the development of a pharmaceutical prescription product for the treatment of obesity and metabolic syndrome.

The neurodegeneration platform has been extended to include Alzheimer's, Parkinson's and motor neurone disease. Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform that share this activity. These molecules are actively neuroprotective and stimulate the release of neuronal growth factors. Several lines of research are now progressing in parallel, indicating that these molecules actively reverse the neurodegenerative process. This novel mode of action has established a platform for the development of a number of potentially important therapeutic approaches to diseases including those associated with ageing, such as memory impairment and dementia. This work has enabled

Phytopharm to develop a series of screening models that mimic these important observations, and has guided the development of semi-synthetic analogues of the original plant based materials.

A series of preclinical toxicology studies has now been completed on a compound arising from the **P58** programme, for age-related cognitive impairment, including memory loss, dementia and Alzheimer's disease. In April 2002 Phytopharm announced the completion of a 7-day clinical programme of repeat dosing in the elderly. The successful completion of the final stage of a 28-day repeat dose clinical study was announced in October 2002. The results indicated that the product was well tolerated with a good emergent safety profile. A battery of 10 computerised cognitive function tests was also performed on days 1, 14 and 28 to optimise the cognitive endpoints for further clinical studies. These data have been evaluated for subject variability and consistency and have led to a study design, which centres on verbal memory performance including delayed word recall and overall quality of memory. These parameters will be the focus of the cognitive assessments to be conducted in the forthcoming phase II clinical study in 2003.

Manufacture of a compound from the programme for Parkinson's disease (**P63**) has been successfully completed to GMP in multi-kilogram quantities. This product is planned to enter the clinical phase in Q1 2003. Pre-clinical work has demonstrated that P63 is a potent protective agent against neurodegeneration in vitro and stimulates the release of neurotrophic factors, which have been shown to reverse Parkinson's disease. Furthermore, we have shown that P63 derived products reverse the loss of dopamine receptors in the brain and have powerful neuroprotective effects in models of Parkinson's disease in vivo.

The programme for motor neurone disease (**P59**) has progressed well. Pre-clinical work has demonstrated that P59 improves survival to a greater extent than standard treatment in Progressive Motor Neuropathy (pnm) mice, a model of motor neurone disease (amyotrophic lateral sclerosis; ALS).

The inflammation platform consists of a patented combination of two medicinal plants (**P54**), and includes a family of novel, third generation non steroidal anti-inflammatory drugs ("NSAID") characterised by their inhibition of a wide range of enzymes central to chronic inflammation (**P61**).

In August 2002 Phytopharm announced the results of a Phase IIa study investigating the safety and efficacy of the oral product, **P54**, in inflammatory bowel disease. The study was conducted at Addenbrooke's Hospital, Cambridge, UK and utilised a double-blind placebo-controlled design. All twenty-seven patients had clinically stable disease, but were dependent on chronic treatment with oral prednisolone (5 – 30 mg / day). Faecal calprotectin (a biomarker of disease activity released by inflammatory cells into the bowel) was determined in each subject at the start of the study. For patients with a baseline calprotectin level below 450 milligrammes per litre, all the patients in the P54 group were able to withdraw from steroid therapy. By contrast, in the placebo group less than half of the patients in this category were able to discontinue steroids without relapse. The study indicated that the P54 product, which is derived from the turmeric family, may play a role in reducing steroid dependency in patients with less severe forms of bowel disease. Treatment with P54 was generally very well tolerated and there were no safety concerns that caused any changes of dosing regimen.

There is also potential for the use of compounds that reduce the expression of inflammatory enzymes in the companion animal market. The results last year of our double-blind placebo controlled trial using **P54v** in canine osteoarthritis have enabled the Group to actively pursue commercialisation of P54v in the veterinary market. Large-scale manufacture of P54 is currently ongoing with a view to commercialisation.

Research into the mode of action of this platform has continued to generate novel synthetic molecules. Pre-clinical work has demonstrated that these molecules have powerful anti-inflammatory and antispasmodic effects. This programme is intended to result in a pharmaceutical

prescription medicine for the treatment of inflammatory disorders and irritable bowel syndrome. The lead candidate, **P61**, will enter development in the second half of 2003.

Finally, the dermatology platform comprises the patented use of five plants with a novel mode of action for the treatment of eczema. These products have a dual mode of action that targets both the allergic and the inflammatory components of eczema.

In March 2002 Phytopharm announced the commencement of a European multi-centre study in canine atopic dermatitis with **P7v**, a three plant botanical product. This randomised, double blind, placebo controlled study is being conducted by specialist veterinary dermatologists and will determine the optimal dose for future commercialisation of the product. In total, one hundred and twenty dogs with perennial atopic dermatitis are being randomly allocated to one of four dose groups. The owners add the appropriate dose of either **P7v** or the matching placebo product to their dogs' food once daily for 12 weeks. The response to dosing will be assessed by changes in the canine atopic dermatitis extent and severity index (CADESI), severity of pruritus, the incidence of secondary skin infection and the overall response reported by both the veterinarians and dog owners. The study is expected to report in Q4 2003.

Over the period Phytopharm completed the pharmaceutical development of the product and is now able to manufacture tonne quantities of material to GMP standards. Discussions with potential partners are now advancing with regard to the further development and commercialisation of this product.

Methods to develop a scalable version of the active compound emerging from this programme, coded **P55**, are being developed for use in the treatment of dermatitis and eczema in humans.

#### Licensing progress

Discussions under confidentiality agreements are in progress on products from all four platforms owned and developed by Phytopharm. Such discussions can be lengthy, and involve substantial due diligence and assessment on the part of potential licensees. Nonetheless, significant progress is being made on the neurodegeneration platform (**P58**) and the opportunity presented by the new chemical forms within the obesity platform (**P64**) is also generating substantial interest. With Pfizer's stated intention to progress the **P57** product and commercial quantities of both veterinary products (**P54v** and **P7v**) becoming available during 2003, Phytopharm looks forward to the coming year with confidence.

#### Financial Review

##### Results of operations

Turnover of £2.7m for the year (2001: £1.5m) comprises development income under the licence and development agreement with Pfizer Inc for **P57**, the Group's appetite suppressant. The turnover is higher this year as it includes reimbursement of the 'proof of concept' clinical study completed at the end of 2001 and further manufacturing and other work to prepare for the next clinical study.

Overall operating expenses for the year of £7.03m are £2.02m higher than the previous year, an increase of 40%. Within those totals expenditure on research and development rose by 49% (£1.97m) to £6m, with administration costs also increasing by 5% to £1.02m. The increase in research and development expenditure is due to increased expenditure across the Group's portfolio of products, particularly the **P58** platform and **P7v** with the completion of the multistage Phase I clinical study in **P58** and the commencement of the multicentre clinical study in **P7v**. Expenditure on **P57** also increased this year with the completion of the clinical study as noted above.

Interest income during the year of £0.48m is lower this year (2001: £0.67m) due to a combination of lower average cash balances during the current year and lower interest rates. The tax credit of £0.55m (2001: £0.22m) arose as the Group has taken advantage of the Research and Development

corporation tax credits introduced in the Finance Act 2000 whereby the Group may surrender corporation tax losses incurred on research and development expenditure for a corporation tax refund. The increase in the tax credit is due in part to the higher levels of research and development expenditure this year compared to last and because the tax credit was limited to seven months research and development expenditure in the previous year.

The increase in turnover of £1.24m and the increase in the tax credit this year of £0.33m have partially offset the increase in research and development expenditure of £1.97m to give a net increase in the loss for the year of £0.63m or 24% to £3.29m. Overall the results for the year were as anticipated and were within budget.

#### Balance sheet

The net assets at the end of the year of £10.29m show a reduction of £2.81m over the figure at the start of the year. This represents the loss for the year of £3.29m offset by £0.48m arising from the exercise of share options. The net asset level at the year-end was in line with expectations. The working capital of the Group comprises 98% (2001: 98%) of the net asset value and the bulk of this is held as cash, either on hand or on term deposits.

The fixed asset base of the Group remains low at £0.24m (2001: £0.25m) as the Group contracts out its research requirements and therefore does not need to finance its own laboratory facilities.

Debtors of £2.84m (2001: £0.37m) comprise principally income due under the licence agreement with Pfizer for P57 and the research and development tax credit. As announced on 30<sup>th</sup> July 2002 Pfizer will now progress the P57 development programme under the terms of the existing milestone and royalty agreement, which includes up to \$32m in milestone payments as well as royalties on sales of P57 by Pfizer, and the debtor from Pfizer at the year end completes reimbursement of this stage of the project. There was no income due under the licence agreement for P57 at the end of the previous year as this fell between the regular reimbursement dates.

Short-term creditors at the year-end were £1.95m and are 87% higher (£0.91m) than the previous year. Included within this figure is an additional £0.31m of deferred income with the balance comprising higher trade creditors and accruals. The increase in trade creditors and accruals arises due to higher than average monthly expenditure in July and August 2002.

#### Financing

Working capital at 31 August 2002 was £10.04m compared to £12.85m at the end of the previous year. Overall, after allowing for the exercise of options during the year, the Group utilised £3.28m of working capital during 2002 (2001: £2.68m). This is equivalent to an average of £273,000 per month (2001: £223,000) during the year. The average expenditure over the second half of the year was £291,000 (2001: £220,000), which represents an increase of £35,000 per month over the first six months of the year. Both the increase in expenditure over the previous year and the increase in the second half of this year were in accordance with the Group's plan and arise principally as the P58 platform matures and moves through Phase I towards Phase II clinical studies which are anticipated to start in 2003. The Group continues to maintain close control over expenditure, particularly the administrative side of the business, while continuing to develop a wide portfolio of products.

#### Consolidated Profit and Loss Account for the year ended 31 August 2002

	Notes	2002 Unaudited £'000	2001 Audited £'000
Turnover	2	2,714	1,471

<b>Gross profit</b>		<b>2,714</b>	<b>1,471</b>
Other operating expenses	3	<b>(7,027)</b>	<b>(5,006)</b>
<b>Operating loss</b>		<b>(4,313)</b>	<b>(3,535)</b>
Interest receivable and similar income		<b>478</b>	<b>666</b>
Interest payable and similar charges		<b>(4)</b>	<b>(8)</b>
<b>Loss on ordinary activities before taxation</b>		<b>(3,839)</b>	<b>(2,877)</b>
Tax on loss on ordinary activities	4	<b>554</b>	<b>224</b>
<b>Loss for the year</b>		<b>(3,285)</b>	<b>(2,653)</b>
Basic fully diluted loss per ordinary share (pence)	5	<b>(8.5)</b>	<b>(7.1)</b>
HMR loss per share (pence)	5	<b>(8.4)</b>	<b>(7.1)</b>

All revenue and expenses shown above were generated from continuing operations.

The Group has no recognised gains or losses for the financial year other than those disclosed above.

#### Consolidated Balance Sheet at 31 August 2002

	Notes	2002 Unaudited £'000	2001 Audited £'000
<b>Fixed assets</b>			
Tangible assets			

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Company	Phytopharm PLC
TIDM	PYM
Headline	Notice of Results
Released	16:47 20 Nov 2002
Number	0754E

20 November 2002

**Phytopharm plc**

Phytopharm plc will be announcing its preliminary results for the year ended 31 August 2002 on Thursday 5 December 2002.

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Blocklisting Interim Review
Released	16:32 20 Nov 2002
Number	0695E

RNS Number: 0695E  
Phytopharm PLC  
20 November 2002

#### BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM 1996 COMPANY SHARE OPTION PLAN

3. PERIOD OF RETURN: FROM: 1st MAY 2002 TO: 31st OCTOBER 2002

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME

AT END OF THE LAST PERIOD: 166,372 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

6,712 ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD:

159,660 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)

ORIGINALLY LISTED AND THE DATE OF ADMISSION: 400,000 ORDINARY SHARES OF  
1 PENCE ON 18th MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,610,530 ORDINARY SHARES OF 1 PENCE AT 31 OCTOBER 2002

CONTACT FOR QUERIES

NAME: Dr S C LOACH

TELEPHONE: 01480 437697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM 1996 UNAPPROVED DISCRETIONARY SHARE OPTION SCHEME

3. PERIOD OF RETURN: FROM: 1st MAY 2002 TO: 31st OCTOBER 2002

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME

AT END OF THE LAST PERIOD: 106,312 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

18,648 ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED

AT END OF PERIOD: 87,664 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)

ORIGINALLY LISTED AND THE DATE OF ADMISSION: 260,000 ORDINARY SHARES OF  
1 PENCE ON 18th MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER  
FOR US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,610,530 ORDINARY SHARES OF 1 PENCE AT 31 OCTOBER 2002

CONTACT FOR QUERIES

NAME: DR S C LOACH

TELEPHONE: 01480 437697

This information is provided by RNS  
The company news service from the London Stock Exchange

END

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Holding(s) in Company  
 Released: 17:40 18 Oct 2002  
 Number: 7081C

Phytopharm PLC ( the "Company" )

Notification of Major Interests in Shares

The Company received a notification today from AMVESCAP PLC, informing it that following a purchase of 375,000 shares on 17 October 2002 , AMVESCAP PLC and subsidiary companies on behalf of discretionary clients have a non beneficial interest in 5,985,228 ordinary 1p shares, representing 15.50% of the issued ordinary share capital of the Company.

The Shares are registered in the following names:

Vidacos Nominees Limited		4,760,419
HSBC Nominees Limited		704,455
Chase Nominees Limited		192,000
Bank of New York Nominees Ltd		184,782
Northern Trust Nominees Limited		85,000
Mellon Bank Pittsburgh Nominees		58,572

In addition the Company received a notification today from AMVESCAP PLC, informing it that, INVESCO Perpetual Income Fund has an interest in 2,460,296 ordinary 1p shares, representing 6.37% of the issued ordinary share capital of the Company. The shares are registered in the name of Vidacos Nominees Limited.

18 October, 2002

END

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Holding(s) in Company  
 Released: 17:18 15 Oct 2002  
 Number: 5275C

Phytopharm PLC ( the "Company")

Notification of Major Interests in Shares

The Company received a notification today from AMVESCAP PLC, informing it that following a purchase of 500,000 shares on 14 October 2002, AMVESCAP PLC and subsidiary companies on behalf of discretionary clients have a non beneficial interest in 5,610,228 ordinary 1p shares, representing 14.53% of the issued ordinary share capital of the Company.

The Shares are registered in the following names:

Vidacos Nominees Limited	4,402,834
HSBC Nominees Limited	692,016
Chase Nominees Limited	192,000
Bank of New York Nominees Ltd	179,806
Northern Trust Nominees Limited	85,000
Mellon Bank Pittsburgh Nominees	58,572

In addition the Company received a notification today from AMVESCAP PLC, informing it that, INVESCO Perpetual Income Fund has an interest in 2,117,072 ordinary 1p shares, representing 5.48% of the issued ordinary share capital of the Company. The shares are registered in the name of Vidacos Nominees Limited.

15 October, 2002

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	15:36 15 Oct 2002
Number	5171C

Phytopharm PLC ( the "Company" )

#### Notification of Major Interests in Shares

The Company received a notification on 11 October 2002 from AMVESCAP PLC, informing it that, INVESCO Perpetual Income Fund has an interest in 1,659,440 ordinary 1p shares, representing 4.3% of the issued ordinary share capital of the Company. The shares are registered in the name of Vidacos Nominees Limited.

15 October, 2002

END

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Company	Phytopharm PLC
TIDM	PYM
Headline	Holding(s) in Company
Released	12:36 14 Oct 2002
Number	4330C

Phytopharm PLC (or "the Company")

**Notification of Major Interests in Shares**

The Company received a notification on 11 October 2002 from Standard Life Investments Limited, informing it that following a disposal of 160,180 shares on the 10 October 2002, its resultant notifiable interest is 1,797,298 shares representing 4.655% of the issued share capital of the Company.

14 October, 2002

WestLB Panmure Limited

END

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Holding(s) in Company  
 Released: 12:34 14 Oct 2002  
 Number: 4328C

Phytopharm PLC ( the "Company" )

Notification of Major Interests in Shares

The Company received a notification on 11 October 2002 from AMVESCAP PLC, informing it that following a purchase of 775,000 shares on 10 October 2002 , AMVESCAP PLC and subsidiary companies on behalf of discretionary clients have a non beneficial interest in 5,110,228 ordinary 1p shares, representing 13.24% of the issued ordinary share capital of the Company.

The Shares are registered in the following names:

Vidacos Nominees Limited		3,926,054
HSBC Nominees Limited		675,430
Chase Nominees Limited		192,000
Bank of New York Nominees Ltd		173,172
Northern Trust Nominees Limited		85,000
Mellon Bank Pittsburgh Nominees		58,572

14 October, 2002

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 3 Oct 2002
Number	0077C

3<sup>rd</sup> October 2002

**Phytopharm plc**

**Successful completion of 28 day repeat dose clinical study of dementia treatment P58**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the successful completion of the final stage of a repeat dose clinical study for P58 which is under development as an oral treatment for age-related cognitive dysfunction, which typically presents as memory loss and dementia, including Alzheimer's disease.

This stage of the study utilised a randomised, double blind, placebo controlled design to examine the safety, tolerability and pharmacokinetics of P58. Thirty healthy men and women aged 55 years and older were enrolled and randomly allocated to receive either P58 or placebo once daily for 28 days. Results indicate that the product was well tolerated with a good emergent safety profile. The pharmacokinetic data confirm biologically active concentrations of P58 in the systemic circulation after oral dosing. A battery of 10 computerised cognitive function tests was also performed on days 1, 14 and 28 to optimise the cognitive endpoints for further clinical studies. These data have been evaluated for subject variability and consistency and have led to a study design which centres on verbal memory performance including delayed word recall and overall quality of memory. These parameters will be the main focus of the cognitive assessments to be conducted in the forthcoming phase II clinical study, during which two doses of P58 will be compared with placebo over a three month dosing period. Enrolment of subjects with memory impairment for this study will commence during Q1, 2003.

P58 is actively neuroprotective, stimulates the release of neuronal growth factors and reverses the loss of neuronal receptors in the ageing brain. This novel mode of action has established a platform for the development of a number of potentially important therapeutic approaches to diseases associated with ageing, including memory impairment and dementia. Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform that share this activity.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "We have made excellent progress in defining the mode of action of the P58 platform and can now finalise the design of the phase II proof of principle study that will commence enrolment of up to 150 subjects during the winter and is expected to run for a year."

-ENDS-

Enquiries:

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

## NOTES TO EDITORS

### Phytopharm plc

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neurodegeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

The adult brain contains approximately two trillion neurones, each of which have some 100,000 receptors on their surface. These receptors are replaced every two months in healthy cells. It has been estimated that during the process of ageing, people progressively lose more than 20 percent of these receptors, resulting in a gradual decline in cognitive performance.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

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Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Holding(s) in Company  
 Released: 17:20 27 Sep 2002  
 Number: 7954B

Phytopharm PLC ( the "Company" )

Notification of Major Interests in Shares

The Company received a notification today from AMVESCAP PLC, informing it that following a purchase of 100,000 shares on 26 September 2002 , AMVESCAP PLC and subsidiary companies on behalf of discretionary clients have a non beneficial interest in 4,335,228 ordinary 1p shares, representing 11.23% of the issued ordinary share capital of the Company.

The Shares are registered in the following names:

Vidacos Nominees Limited		3,187,045
HSBC Nominees Limited		649,722
Chase Nominees Limited		192,000
Bank of New York Nominees Ltd		162,889
Northern Trust Nominees Limited		85,000
Mellon Bank Pittsburgh Nominees		58,572

27 September 2002

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Company	Phytopharm PLC
TIDM	PYM
Headline	Research Update
Released	07:00 23 Aug 2002
Number	3133A

23 August 2002

**Phytopharm plc**

**Clinical Study Results of P54 for Inflammatory Bowel Disease**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the results of a Phase IIa study to investigate the safety and efficacy of its patented oral product P54 in inflammatory bowel disease. The study indicated that P54, which is derived from the turmeric family, may play a role in reducing steroid dependency in patients with less severe forms of bowel disease.

The study was conducted at Addenbrooke's Hospital, Cambridge, UK, and utilised a double-blind placebo-controlled parallel group design. Twenty-seven patients with steroid-dependent ulcerative colitis (n=16) or Crohn's disease (n=11) were recruited. All recruits had clinically stable disease, but were dependent on chronic treatment with oral prednisolone (5 – 30 mg / day). The patients were randomly assigned to receive either P54 or placebo for up to 16 weeks. During this period their dose of steroid was incrementally reduced every 2 weeks (if clinically appropriate) until it had either been discontinued or their symptoms of bowel disease recurred. The primary objective of the study was to assess whether or not treatment with P54 could reduce the dose of steroid required to maintain disease remission in patients with steroid-dependent inflammatory bowel disease.

Faecal calprotectin (a biomarker of disease activity released by inflammatory cells into the bowel) was determined in each subject at the start of the study. Taking the data from all patients there was a 45% reduction in steroid dose achieved by the P54 group with a similar result in the placebo group. However, for patients with a baseline calprotectin level below 450 mg l<sup>-1</sup>, all the patients in the P54 group were able to withdraw from steroid therapy. By contrast, in the placebo group only 44 % of patients in this category were able to discontinue steroids without relapse.

Treatment with P54 was generally very well tolerated. There were no safety concerns that caused any changes of dosing regimen, although a few patients reported minor side effects such as eructation and altered taste sensation.

The lead investigator Dr John Hunter commented: 'There is a pressing need for new, more effective treatments for inflammatory bowel disease. In this study all the patients involved suffered from refractory, corticosteroid-dependent disease. Although there was no overall benefit for patients taking P54, we saw dramatic improvements in some, who managed to come off steroids completely. It may well be that P54 will have a valuable role in less severe cases. Further studies would be of value'.

Dr Richard Dixey, Chief Executive of Phytopharm, said: 'This small study indicates that P54

may well be of benefit to some patients with refractory bowel disease. We will be announcing our next steps concerning this project in the near future'.

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697  
07867 782000

**Financial Dynamics**

Jonathan Birt / Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm's business is to take both simple and complex mixtures derived from plant sources into full pharmaceutical development. The US Food and Drug Administration call such medicinal products 'Botanicals'. Botanical products are whole or partially purified extracts of medicinal plants in which the chemical composition is not fully characterised. Apart from being a new sector in the pharmaceutical market, botanicals also act as an enabling technology to discover single chemical entities of clinical importance from plant sources.

Phytopharm is the leading company in the development of **botanical pharmaceuticals**. It has developed a portfolio of 11 such products, nine of which are in the clinical evaluation phase. These products have been targeted in the five therapeutic categories of anti-inflammatory treatments, neurological disorders, dermatology, cancer and metabolic diseases.

**P54**

P54 is a patented non-steroidal anti-inflammatory drug manufactured from two related species from the turmeric family, *Curcuma Longa* and *Curcuma Xanthoriza*. The drug works by inhibiting the production of the pro-inflammatory enzyme, cyclo-oxygenase 2 (COX-2), which is known to be increased in both inflammatory diseases and certain cancers, including those affecting the lung, breast, prostate and bowel.

**Inflammatory bowel disease**

Inflammatory bowel disease (Crohn's disease and ulcerative colitis), is characterised by chronic inflammation of the gastrointestinal tract, which in the case of ulcerative colitis is limited to the large bowel. The causes of these chronic debilitating illnesses are currently unknown. The typical symptoms include malaise, cramping abdominal pain and diarrhoea. Affected patients usually require long-term medical management, which can often include the need for major surgery. Systemic steroids are commonly used to treat inflammatory bowel disease, both in the short term to treat an acute relapse and in more severe cases for sustained periods to maintain disease remission. Steroids are powerful anti-inflammatory drugs that are associated with highly undesirable side effects, particularly if given at high doses for prolonged periods of time.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

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Company	Phytopharm PLC
TIDM	PYM
Headline	Re Agreement
Released	07:15 30 Jul 2002
Number	2739Z

30 July 2002

**Phytopharm plc**

**Future development of P57**

Phytopharm plc ("Phytopharm") announces today that it has agreed with Pfizer Inc, ("Pfizer") the future development programme for P57, Phytopharm's novel appetite suppressant for the treatment of obesity and metabolic syndrome. The agreement follows the successful demonstration of proof of principle in man that was announced in December 2001.

The agreement is in two parts:

- Pfizer will now progress the P57 development programme concerning extracts of medicinal plants under the ongoing terms of the Licence and Royalty Agreement announced between Pfizer and Phytopharm in 1998. This programme is intended to result in the development of a botanical prescription pharmaceutical for the treatment of obesity and metabolic syndrome. Under the terms of this agreement, Phytopharm will receive up to \$32 million in milestone payments as well as royalties on sales of P57 by Pfizer. Phytopharm will additionally receive \$2.8 million funding as part of this agreement.
- Phytopharm will develop semi-synthetic versions of the active molecules discovered in the P57 programme and will be free to seek other partners to commercialise these products.

Commenting on these arrangements, Dr Richard Dixey, Chief Executive of Phytopharm, stated: "This is a very positive development for Phytopharm with substantial potential upside. With Pfizer progressing the botanical opportunity, Phytopharm will concentrate its efforts on the development of semi-synthetic molecules, offering the possibility of two different milestone and income streams emerging from the P57 platform. With over two years' working capital the Company remains well funded to progress this expanded platform. "

END

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive Officer	Tel:	01480 437697
	Mobile:	07867 782000

**Financial Dynamics**

Ben Atwell / Jonathan Birt	Tel:	0207 831 3113
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**NOTES TO EDITORS**

## Phytopharm plc

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for obesity and metabolic syndrome, neural and muscular degeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

Obesity is a global problem which affects more than 100 million people seriously enough to warrant medical intervention. It is a direct causal contributor to the pathophysiology of many diseases and exacerbates numerous others. Among these are five of the leading causes of death in the industrialised world: stroke, atherosclerosis, cardiovascular disease, diabetes and cancer. According to the World Health Organisation (WHO), obesity accounts for tens of billions of pounds in direct healthcare costs worldwide. A panel of experts convened by WHO stated on 12 June 1997 that 'obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time. It has an impact on health, which may well prove to be as great as that of smoking' (World Health Organisation).

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

END

[Company website](#)

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Full Text Announcement

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Other Announcements from this Company ▶

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Company	Phytopharm PLC
TIDM	PYM
Headline	Statement re. Press Comment
Released	07:17 22 Jul 2002
Number	9206Y

22 July 2002

**Phytopharm plc**

**P57 update in response to press speculation**

Further to recent press speculation, Phytopharm plc (the "Company") confirms that it is continuing with negotiations regarding the P57 development programme with Pfizer Inc following the demonstration of proof of principle for the project that was announced in December of 2001.

The Company will make a further announcement in due course

END

*Enquiries:*

**Phytopharm plc**

Dr Daryl Rees, Chief Operating Officer

Tel: 01480 437697

**Financial Dynamics**

Ben Atwell

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for obesity and metabolic syndrome, neural and muscular degeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

P57 is a novel appetite suppressant containing extracts derived from a South African plant. Under an agreement announced on August 24<sup>th</sup> 1998, Pfizer has acquired an exclusive worldwide licence to develop and market P57. Phytopharm will receive up to \$32 million in licence fees and milestone payments based upon the achievement of specific objectives.

Phytopharm will also receive royalties on sales of P57 by Pfizer.

Obesity is a global problem which affects more than 100 million people seriously enough to warrant medical intervention. It is a direct causal contributor to the pathophysiology of many diseases and exacerbates numerous others. Among these are five of the leading causes of death in the industrialised world: stroke, atherosclerosis, cardiovascular disease, diabetes and cancer. According to the World Health Organisation (WHO), obesity accounts for tens of billions of pounds in direct healthcare costs worldwide. A panel of experts convened by WHO stated on 12 June 1997 that 'obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time. It has an impact on health, which may well prove to be as great as that of smoking' QUOTE "(World Health Organisation, 1997)" (World Health Organisation, 1997).

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

END

[Company website](#)

Close

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Full Text Announcement

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Other Announcements from this Company

Send to a Friend



Company: Phytopharm PLC  
 TIDM: PYM  
 Headline: Blocklisting Interim Review  
 Released: 17:23 14 Jun 2002  
 Number: 3009X

**SCHEDULE 5**

**BLOCK LISTING SIX MONTHLY RETURN**

To: Listing Applications

UK Listing Authority

Financial Services Authority

25, The North Colonnade

Canary Wharf

London, E14 5HS

AVS No:

Please ensure the entries on this return are typed

1.	Name of company Phytopharm plc	
2.	Name of scheme The Phytopharm Share Option Scheme	
3.	Period of return: From 1 November 2001 to 30 April 2002	
4.	Number and class of share(s) (amount of stock/debt security) not issued under scheme	81,000 Ordinary Shares of 1 pence
5.	Number of shares issued/allotted under scheme during period:	81,000 Ordinary Shares of 1 pence
6.	Balance under scheme not yet issued/allotted at end of period	nil Ordinary Shares of 1 pence
7.	Number and class of share(s) (amount of stock/debt securities) originally listed and the date of admission;	1,407,000 Ordinary Shares of 1 pence on 14 <sup>th</sup> April 1999

Please confirm total number of shares in issue at the end of the period in order for us to update our records

Total shares in issue 38,585,170 Ordinary Shares of 1 pence at 30 April 2002

Contact for queries:	Address:
Name: Dr S C Loach	Corpus Christi House
Telephone: 01480 437697	9 West Stree Godmanchester Huntingdon Cambs PE29 2HY

Person making return

Name: Dr S C Loach

Position: Chief Financial Officer and Company Secretary

Signature: S C Loach

### SCHEDULE 5

### BLOCK LISTING SIX MONTHLY RETURN

To: Listing Applications

UK Listing Authority

Financial Services Authority

25, The North Colonnade

Canary Wharf

London, E14 5HS

AVS No:

Please ensure the entries on this return are typed

1.	Name of company	Phytopharm plc
2.	Name of scheme	The Phytopharm 1996 Unapproved Discretionary Share Option Scheme
3.	Period of return:	From 1 <sup>st</sup> November 2001 to 30 <sup>th</sup> April 2002
4.	Number and class of share(s) (amount of stock/debt security) not issued under scheme	138,223 Ordinary Shares of 1 pence
5.	Number of shares issued/allotted under scheme during period:	138,223 Ordinary Shares of 1 pence

6.	Balance under scheme not yet issued/allotted at end of period	nil Ordinary Shares of 1 pence
7.	Number and class of share(s) (amount of stock/debt securities) originally listed and the date of admission;	341,200 Ordinary Shares of 1 pence on 14 <sup>th</sup> April 1999
Please confirm total number of shares in issue at the end of the period in order for us to update our records		
Total shares in issue 38,585,170 Ordinary Shares of 1 pence at 30 April 2002		
Contact for queries:		Address:
Name: Dr S C Loach		Corpus Christi House
Telephone: 01480 437697		9 West Street
		Godmanchester
		Huntingdon
		Cambs PE29 2HY

Person making return

Name: Dr S C Loach

Position: Chief Financial Officer and Company Secretary

Signature: S C Loach

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Financial Services Authority

25, The North Colonnade

Canary Wharf

London, E14 5HS

AVS No:

Please ensure the entries on this return are typed

1.	Name of company Phytopharm plc
----	--------------------------------

2.	Name of scheme The Phytopharm 1996 Company Share Option Plan	
3.	Period of return: From 1 <sup>st</sup> November 2001 to 30 <sup>th</sup> April 2002	
4.	Number and class of share(s) (amount of stock/debt security) not issued under scheme	186,816 Ordinary Shares of 1 pence
5.	Number of shares issued/allotted under scheme during period:	20,444 Ordinary Shares of 1 pence
6.	Balance under scheme not yet issued/allotted at end of period	166,372 Ordinary Shares of 1 pence
7.	Number and class of share(s) (amount of stock/debt securities) originally listed and the date of admission;	400,000 Ordinary Shares of 1 pence on 18 <sup>th</sup> May 2000
Please confirm total number of shares in issue at the end of the period in order for us to update our records		
Total shares in issue 38,585,170 Ordinary Shares of 1 pence at 30 April 2002		
Contact for queries:	Address:	
Name: Dr S C Loach	Corpus Christi House	
Telephone: 01480 437697	9 West Street	
	Godmanchester	
	Huntingdon	
	Cams PE29 2HY	

Person making return

Name: Dr S C Loach

Position: Chief Financial Officer and Company Secretary

Signature: S C Loach

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Financial Services Authority

25, The North Colonnade

Canary Wharf

London, E14 5HS

AVS No:

Please ensure the entries on this return are typed

1.	Name of company <i>Phytopharm plc</i>	
2.	Name of scheme <i>The Phytopharm 1996 Unapproved Discretionary Share Option Scheme</i>	
3.	Period of return: From 1 <sup>st</sup> November 2001 to 30 <sup>th</sup> April 2002	
4.	Number and class of share(s) (amount of stock/debt security) not issued under scheme	260,000 Ordinary Shares of 1 pence
5.	Number of shares issued/allotted under scheme during period:	153,688 Ordinary Shares of 1 pence
6.	Balance under scheme not yet issued/allotted at end of period	106,312 Ordinary Shares of 1 pence
7.	Number and class of share(s) (amount of stock/debt securities) originally listed and the date of admission;	260,000 Ordinary Shares of 1 pence on 18 <sup>th</sup> May 2000
Please confirm total number of shares in issue at the end of the period in order for us to update our records		
Total shares in issue 38,585,170 Ordinary Shares of 1 pence at 30 April 2002		
Contact for queries:	Address:	
Name: Dr S C Loach	Corpus Christi House	
Telephone: 01480 437697	9 West Street	
	Godmanchester	
	Huntingdon	
	Cams PE29 2HY	

Person making return

Name: Dr S C Loach

Position: Chief Financial Officer and Company Secretary

Signature: S C Loach

## SCHEDULE 5

## BLOCK LISTING SIX MONTHLY RETURN

To: Listing Applications

UK Listing Authority

Financial Services Authority

25, The North Colonnade

Canary Wharf

London, E14 5HS

AVS No:
---------

Please ensure the entries on this return are typed

1.	Name of company <i>Phytopharm plc</i>	
2.	Name of scheme <i>The Phytopharm 1996 Unapproved Discretionary Share Option Scheme</i>	
3.	Period of return: <i>From 11<sup>th</sup> December 2001 to 10<sup>th</sup> June 2002</i>	
4.	Number and class of share(s) (amount of stock/debt security) not issued under scheme	<i>260,000 Ordinary Shares of 1 pence</i>
5.	Number of shares issued/allotted under scheme during period:	<i>nil Ordinary Shares of 1 pence</i>
6.	Balance under scheme not yet issued/allotted at end of period	<i>260,000 Ordinary Shares of 1 pence</i>
7.	Number and class of share(s) (amount of stock/debt securities) originally listed and the date of admission;	<i>260,000 Ordinary Shares of 1 pence on 10<sup>th</sup> December 2001</i>
<p>Please confirm total number of shares in issue at the end of the period in order for us to update our records</p> <p><i>Total shares in issue 38,610,530 Ordinary Shares of 1 pence at 13<sup>th</sup> June 2002</i></p>		
<p>Contact for queries:</p> <hr/> <p>Name: <i>Dr S C Loach</i></p> <hr/> <p>Telephone: <i>01480 437697</i></p>		<p>Address:</p> <p><i>Corpus Christi House</i></p> <p><i>9 West Street</i></p> <p><i>Godmanchester</i></p> <p><i>Huntingdon</i></p> <p><i>Cambs PE29 2HY</i></p>

Person making return

Name: Dr S C Loach

Position: Chief Financial Officer and Company Secretary

Signature: S C Loach

END

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## Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 13:54  
To: Zoe McGowan



pic19072.pcx (4 KB)pic06270.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 13:53 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC May 21, 2002  
Tuesday  
moved to file:  
pic19072.pcx)

708-709 Phytopharm PLC - Director Shareholding

Source: XR: Extel RNS RDS 21/05/2002 11:57

RNS Number:2073W  
Phytopharm PLC  
21 May 2002

### DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

DR DARYL REES

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2 ABOVE

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2 ABOVE

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non

discretionary

- 7) Number of shares/amount of stock acquired
- 8) (N/A %) of issued Class
- 9) Number of shares/amount of stock disposed
- 10) ( N/A %) of issued Class
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
21 MAY 2002
- 18) Period during which or date on which exercisable  
26,429 FROM 22 MAY 2005 TO 20 MAY 2009  
26,430 FROM 22 MAY 2007 TO 20 MAY 2009
- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
52,859 ORDINARY 1 PENCE
- 21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise

#1.775

22) Total number of shares or debentures over which options held following this notification

225,672

23) Any additional information

24) Name of contact and telephone number for queries

S LOACH 01480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification DR S LOACH

This information is provided by RNS  
The company news service from the London Stock Exchange

END

RDSFFLFLLEBEBBD .

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Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic06270.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 13:53  
To: Zoe McGowan



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Information

(Embedded image Issuer Name: PHYTOPHARM PLC May 1, 2002  
Wednesday  
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pic29168.pcx)

262-263 Phytopharm PLC - Notice of Results

Source: XR: Extel RNS NOR 01/05/2002 09:20

RNS Number:3541V  
Phytopharm PLC  
1 May 2002

1 May 2002

Phytopharm plc

Phytopharm plc will be announcing its interim results for the six months ended 28  
February 2002 on Thursday 9 May 2002.

This information is provided by RNS  
The company news service from the London Stock Exchange

END

NORUAUKRURRVRRR

XRviaNewsEDGE

Tickers: PYM

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Zoe McGowan

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pic27140.pcx (4 KB)pic22894.pcx (2 KB)

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Information

(Embedded image Issuer Name: PHYTOPHARM PLC April 30, 2002  
Tuesday  
moved to file:  
pic27140.pcx)

1076-1077 Phytopharm PLC - Holding(s) in Company

Source: XR: Extel RNS HOL 30/04/2002 15:03

RNS Number:3145V  
Phytopharm PLC  
30 April 2002

Phytopharm PLC ( "the Company")

Notification of Major Interests in Shares

The Company received a notification today from M&G Investment Management Limited,  
informing it that Prudential plc, and certain of its subsidiary companies have a  
notifiable interest in  
1,547,189 ordinary shares, representing 4.01% of the issued ordinary share capital of  
the Company.

30 April 2002

This information is provided by RNS  
The company news service from the London Stock Exchange

END

HOLEBLFXLZBBBBX

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Tickers: PYM PRU

Prohibited Period Start:

FORWARDED PERIOD END:

(Embedded image moved to file: pic22894.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

22 April 2002

**Phytopharm plc**

**Commencement of 28 day repeat dose clinical study of dementia treatment P58 and completion of first stage**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the commencement of the final stage of a clinical study to evaluate the safety, tolerability, pharmacokinetic profile and effect on cognitive performance of its oral treatment P58. P58 is under development as a treatment for age-related cognitive dysfunction, which typically presents as memory loss and dementia, including Alzheimer's disease.

The first stage of the study evaluated the safety, tolerability and pharmacokinetics of once daily dosing for up to 7 days in healthy volunteers aged 55 years and older. This stage has now been completed and the data indicate that P58 is well tolerated.

The second and final stage will examine the safety, tolerability, pharmacokinetics and cognitive effects of a daily dose of P58 administered for 28 days. This stage of the study will utilise a randomised, double-blind, placebo controlled design, and will enrol 30 healthy subjects aged 55 years and older. Results will be reported during the third quarter of 2002, and will be used to determine the design for a three-month, phase II study that will commence during Q1, 2003.

The adult brain contains approximately two trillion nerve cells, each of which have some 100,000 receptors on their surface. These receptors are replaced every two months in healthy cells. It has been estimated that during the process of ageing, people progressively lose more than 20 percent of these receptors, resulting in a gradual decline in cognitive performance. Measurable reductions in both memory and cognitive performance can be detected in healthy subjects over the age of 55.

P58 acts by reversing this loss of nerve cell receptors in the ageing brain, as well as actively protecting the nerve cells themselves. This novel mode of action has established a platform for the development of a number of potentially important therapeutic approaches to diseases associated with ageing, including memory impairment and dementia. Phytopharm has now developed a total of nine patent families to protect the large group of related chemical compounds within this platform that share this activity.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "P58 has enormous promise in both protecting brain cells from the effects of ageing and in reversing the underlying degenerative processes. A 28 day dosing period is a short period for the full effects of the treatment to become manifest, but the data gathered from the cognitive testing will be instructive in finalising the design for the three month phase II study that will commence during the winter."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neural and muscular degeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its Web site at  
<http://www.phytopharm.co.uk>.

11 April 2002

**Phytopharm plc**

**Opens new manufacturing unit in South Africa**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today that it has completed the installation of a new botanical supplies unit in South Africa to substantially expand the manufacturing capacity for its appetite suppressant P57 in support of the further development of the product.

P57 is derived from an extract of Hoodia Gordonii, a South African succulent plant. It was licensed in June 1997 by Phytopharm from the CSIR (Council for Scientific and Industrial Research) in South Africa. In August 1998, an exclusive world-wide licensing agreement was signed with Pfizer Inc for the development and global commercialisation of P57 as an oral prescription drug to treat obesity.

The successful completion of the proof of principle clinical study for P57 was announced in December 2001. This study used raw materials manufactured in the existing unit in South Africa. The new facility will expand the capacity for processing the raw materials by 300 percent and a programme to process tonne quantities of plant material is now underway.

Commenting on the announcement, Dr Richard Dixey, Chief Executive of Phytopharm said: "Phytopharm continues to make strong progress in the development of P57, as well as other products we hope to develop in our long term collaboration with the CSIR."

The US market for treating obesity is estimated to be worth in excess of \$3 billion, with annual costs relating to obesity-related diseases exceeding \$75 billion (source IMS).

- Ends -

*Enquiries:*

**Phytopharm plc**  
Dr Richard Dixey

Tel: 01480 437697  
Mobile: 07867 782000

**Financial Dynamics**  
Fiona Noblet

Tel: 0207 831 3113

## NOTES TO EDITORS

### **Phytopharm plc**

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More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>

5 April 2002

## **Phytopharm plc**

### **Retirement of Director**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces that Ms Jayne Allan stands down today from the Board of Directors (the "Board") as Director of Resource and Planning to spend more time with her young family. Ms Allan has worked for the business for over 10 years and was appointed to the Board in October 1999.

Dr Richard Dixey, Chief Executive Officer, commented: "Jayne has made a substantial contribution to the development of Phytopharm. We all thank her for her efforts on behalf of the company and wish her well in the future."

#### *Enquiries:*

##### **Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

##### **Financial Dynamics**

David Yates

Tel: 0207 831 3113

## **NOTES TO EDITORS**

### **Phytopharm plc**

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More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>

20 March 2002

**Phytopharm plc**

**Commences European multi-centre study of P7v in canine atopic dermatitis**

Phytopharm plc (PYM: London Stock Exchange) (“Phytopharm”) announces today the start of a European multi-centre study of P7v, its novel, patented botanical product for the treatment of canine atopic dermatitis (canine “eczema”).

This randomised, double blind, placebo controlled study will be conducted by specialist veterinary dermatologists located in France and the United Kingdom. The study will determine the optimal dose for future commercialisation of the product, which consists of granules presented in a foil sachet. One hundred and twenty dogs with perennial atopic dermatitis will be randomly allocated to one of four dose groups. The owners will add the appropriate dose of either P7v or the matching placebo product to their dogs’ food once daily for 12 weeks.

The response to dosing will be assessed by changes in the canine atopic dermatitis extent and severity index (CADESI), severity of pruritus, the incidence of secondary skin infection and the overall response reported by both the veterinarians and dog owners. The study is expected to complete in Q4 2002 and will be reported in Q1 2003.

The global market for health and nutrition products used by dogs and cats is estimated to be worth \$2.21 billion annually (Vivash-Jones Consultants-1999). There are approximately 95 million dogs in the US, Europe and Japan. As a condition, atopic dermatitis is the largest disease segment believed to affect up to 15% of the entire canine population with 80% of those affected having perennial signs of the condition (Muller & Kirk’s Small Animal Dermatology, 6th Edition).

Dr Richard Dixey, Chief Executive of Phytopharm, said: “There is a requirement for new therapies that are effective and well-tolerated for the treatment of canine eczema as there are few presently available. I am encouraged by our good progress with this product which addresses a potentially substantial market.”

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates

Tel: 0207 831 3113

## NOTES TO EDITORS

### **Phytopharm plc**

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Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:31  
To: Zoe McGowan



pic27753.pcx (4 KB)pic14945.pcx (2 KB)

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(Embedded image Issuer Name: PHYTOPHARM PLC January 29, 2002  
Tuesday  
moved to file:  
pic27753.pcx)

4542-4550 Phytopharm PLC - Annual Report and Accounts

Source: XR: Extel RNS ACS 29/01/2002 11:59

6499Q  
RNS Number:6499Q  
Phytopharm PLC  
29 January 2002

Annual Report and Accounts 2001

A Copy of the above document has been submitted to the UK Listing Authority, and will shortly be available for inspection at the UK Listing Authority's Document Viewing Facility, which is situated at:

Financial Services Authority  
25 The North Colonnade  
Canary Wharf  
London  
E14 5HS

Tel. no. (0)20 7676 1000

(Documents will usually be available for inspection within six normal business hours of this notice being given).

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Tickers: PYM

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Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

**Zoe McGowan**

---

**From:** akubiak@londonstockexchange.com  
**Sent:** 25 May 2004 09:31  
**To:** Zoe McGowan



pic31780.pcx (4 KB) pic11963.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:30 ----- RNS Information

(Embedded image Issuer Name: PHYTOPHARM PLC December 10, 2001  
Monday  
moved to file:  
pic31780.pcx)

4811-4818 Phytopharm PLC - Director Shareholding

Source: XR: Extel RNS RDS 10/12/2001 16:09

45050  
RNS Number:45050  
Phytopharm PLC  
10 December 2001

DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

Ms J E ALLAN

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

DIRECTOR ONLY

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

EXERCISE OF OPTION AND MARKET SALE

7) Number of shares/amount of stock acquired

77489

8) (0.20%)  
of issued Class

9) Number of shares/amount of stock disposed

77,489

10) (0.20%)  
of issued Class

11) Class of security

ORDINARY

12) Price per share

NO.	BOUGHT	SOLD
43,489	#0.45	#5.20
34,000	#1.925	#5.45

13) Date of transaction

7 DEC 01  
10 DEC 01

14) Date company informed

10 DEC 01

15) Total holding following this notification

NIL

16) Total percentage holding of issued class following this notification

NIL

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

17) Date of grant

18) Period during which or date on which exercisable

19) Total amount paid (if any) for grant of the option

20) Description of shares or debentures involved: class, number.

- 21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise
- 22) Total number of shares or debentures over which options held following this notification
- 23) Any additional information
- 24) Name of contact and telephone number for queries
- 25) Name and signature of authorised company official responsible for making this notification

Date of Notification 10 DEC 2001

END  
RDSQBLFFFLBBFBK

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic11963.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:31  
To: Zoe McGowan



pic22355.pcx (4 KB)pic24767.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:30 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC December 7, 2001  
Friday  
moved to file:  
pic22355.pcx)

4202-4221 Phytopharm PLC - Director Shareholding

Source: XR: Extel RNS RDS 07/12/2001 17:51

39370  
RNS Number:39370  
Phytopharm PLC  
7 December 2001

DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

MS J.E. ALLAN

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

- 6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary
- 7) Number of shares/amount of stock acquired
- 8) (N/A %)  
of issued Class
- 9) Number of shares/amount of stock disposed
- 10) ( N/A %)  
of issued Class
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
6 DECEMBER 2001
- 18) Period during which or date on which exercisable  
5497 7 DEC 2004 - 5 DEC 2008  
5497 7 DEC 2006 - 5 DEC 2008
- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
10,994 ORDINARY 1 PENCE
- 21) Exercise price (if fixed at time of grant) or indication that price

is to be fixed at time of exercise

#4.775

22) Total number of shares or debentures over which options held following this notification

218994

23) Any additional information

24) Name of contact and telephone number for queries

S. LOACH 01480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification 7 DECEMBER 2001

#### DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

DR R.P. DIXEY

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

7) Number of shares/amount of stock acquired

8) (N/A %)  
of issued Class

9) Number of shares/amount of stock disposed

10) ( N/A %)
of issued Class

11) Class of security

12) Price per share

13) Date of transaction

14) Date company informed

15) Total holding following this notification

16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE
COMPLETE THE FOLLOWING BOXES

17) Date of grant

6 DECEMBER 2001

18) Period during which or date on which exercisable

19,633 7 DEC 2004 - 5 DEC 2008
19,634 7 DEC 2006 - 5 DEC 2008

19) Total amount paid (if any) for grant of the option

NIL

20) Description of shares or debentures involved: class, number.

39,267 ORDINARY 1 PENCE

21) Exercise price (if fixed at time of grant) or indication that price
is to be fixed at time of exercise

#4.775

22) Total number of shares or debentures over which options held
following this notification

523,230

23) Any additional information

24) Name of contact and telephone number for queries

S. LOACH 01480 437697

25) Name and signature of authorised company official responsible for

making this notification

Date of Notification 7 DECEMBER 2001

DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

DR S.C. LOACH

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

DIRECTOR ONLY

6) Please state the nature of the transaction. For PEP transactions please indicate whether general/single co PEP and if discretionary/non discretionary

EXERCISE OF OPTION AND MARKET SALE

7) Number of shares/amount of stock acquired

300,000

8) (0.78%)  
of issued Class

9) Number of shares/amount of stock disposed

300,000

10) (0.78%)  
of issued Class

11) Class of security

ORDINARY

12) Price per share

BOUGHT 75,000 AT #0.2625  
149,721 AT #1.925  
75,279 AT #0.45

SOLD #5.35

13) Date of transaction

7 DEC 2001

14) Date company informed

7 DEC 2001

15) Total holding following this notification

0.01%

16) Total percentage holding of issued class following this notification

0.01%

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

17) Date of grant

6 DECEMBER 2001

18) Period during which or date on which exercisable

8,361 7 DEC 2004 - 5 DEC 2008

8,361 7 DEC 2006 - 5 DEC 2008

19) Total amount paid (if any) for grant of the option

NIL

20) Description of shares or debentures involved: class, number.

16,722 ORDINARY 1 PENCE

21) Exercise price (if fixed at time of grant) or indication that price  
is to be fixed at time of exercise

#4.775

22) Total number of shares or debentures over which options held  
following this notification

134,443

23) Any additional information

24) Name of contact and telephone number for queries

S. LOACH 01480 437697

25) Name and signature of authorised company official responsible for  
making this notification

Date of Notification 7 DECEMBER 2001

END

RDSDDLFBFLBEFBEF

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic24767.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

**Zoe McGowan**

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:30  
To: Zoe McGowan



pic15573.pcx (4 KB)pic05097.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:30 ----- RNS Information

(Embedded image Issuer Name: PHYTOPHARM PLC December 7, 2001  
Friday  
moved to file:  
pic15573.pcx)

2992-2994 Phytopharm PLC - Additional Listing

Source: XR: Extel RNS LIS 07/12/2001 14:33

36840  
RNS Number:36840  
Phytopharm PLC  
7 December 2001

Phytopharm plc

Application has been made to the UK Listing Authority and to the London Stock Exchange for a Block Listing of 260,000 ordinary shares of 1p each to be admitted to the Official List.

These shares, ranking pari passu in all respects with the existing shares in issue, will be allotted pursuant to the exercise of options and to the rules of the Phytopharm 1996 Unapproved Discretionary Share Option Scheme.

These shares will not be allotted immediately but as and when the scheme rules allow.

7 December, 2001

WestLB Panmure Limited

END

LISDKOKNBDDNBK

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic05097.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

**Zoe McGowan**

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:30  
To: Zoe McGowan



pic05097.pcx (4 KB)pic18636.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:29 ----- RNS Information

(Embedded image Issuer Name: PHYTOPHARM PLC December 6, 2001  
moved to file: Primary Issuer: PHYTOPHARM PLC  
Thursday  
pic05097.pcx) Related Issuers: Prudential PLC

4844-4846 Phytopharm PLC - Holding in Company

Source: XR: Extel RNS HOL 06/12/2001 15:10

30210---1Prudential PLC----  
RNS Number:30210  
Phytopharm PLC  
6 December 2001

Phytopharm PLC ( the "Company")

Notification of Major Interests in Shares

The Company received a notification yesterday from M&G Investment Management Limited, informing them that as at the close of business on 4th December 2001, Prudential plc, and certain of its subsidiary companies have a notifiable interest of 1,901,189 ordinary shares, representing 4.978% of the issued ordinary share capital of the Company.

6th December, 2001

WestLB Panmure Limited

END

HOLDKAKDPBDDKKBK

XRviaNewsEDGE

Tickers: PYM PRU

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic18636.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

December 5th 2001

## Phytopharm plc

### Successful Completion of Proof of Principle Clinical Study of P57 for Obesity

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the successful completion of the third and final stage of its proof of principle clinical study of P57. The objectives of this stage of the study included the evaluation of the safety, tolerability, pharmacokinetic profile and effect on calorie intake of P57. This is a patented product which is under development as an appetite suppressant for the treatment of obesity and related conditions.

This stage of the study used a double-blind, randomised, placebo-controlled design. Nineteen overweight but otherwise healthy male volunteers were randomly allocated to receive either P57 or placebo twice daily for 15 days. Eighteen subjects completed the study (nine subjects in each of the P57 and placebo groups). Assessments recorded during the study included daily calorie intake, body weight and body fat content. The primary endpoint compared the average daily calorie intake between the groups for the last three days of dosing. Blood samples were also obtained for routine analysis of safety parameters and pharmacokinetic profiling of this orally administered agent.

Preliminary data indicate that there was a statistically significant reduction in the average daily calorie intake of the P57 group compared with the placebo group ( $p=0.014$ ). Preliminary data also indicate a statistically significant reduction in body fat content in the P57 group compared with the placebo group at the completion of dosing ( $p=0.035$ ). No serious adverse effects were experienced by any of the subjects, and the safety data are consistent with a satisfactory overall safety profile. The pharmacokinetic data confirm that the systemic exposure to biologically active constituents of P57 was consistent with the observed clinical effects.

Obesity is a global problem which affects more than 100 million people seriously enough to warrant medical intervention. It is a direct causal contributor to the pathophysiology of many diseases and exacerbates numerous others. Among these are five of the leading causes of death in the industrialised world: stroke, atherosclerosis, cardiovascular disease, diabetes and cancer. According to the World Health Organisation (WHO), obesity accounts for tens of billions of pounds in direct healthcare costs worldwide. A panel of experts convened by WHO stated on 12 June 1997 that 'obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time. It has an impact on health, which may well prove to be as great as that of smoking' (World Health Organisation, 1997).

Dr Richard Dixey, Chief Executive of Phytopharm, said: 'This study demonstrates proof of principle for P57. The data are very encouraging and provide a foundation for the substantial body of work that now needs to be done to carry the project forward to commercialisation'.

#### *Enquiries:*

#### **Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

#### **Financial Dynamics**

David Yates

Tel: 0207 831 3113

## NOTES TO EDITORS

### **Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for obesity and metabolic syndrome, neural and muscular degeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

P57 is a novel appetite suppressant containing extracts derived from a South African plant. Under an agreement announced on August 24<sup>th</sup> 1998, Pfizer has acquired an exclusive worldwide licence to develop and market P57. Phytopharm will receive up to \$32 million in licence fees and milestone payments based upon the achievement of specific objectives. Phytopharm will also receive royalties on sales of P57 by Pfizer.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

## Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:29  
To: Zoe McGowan



pic09877.pcx (4 KB)pic10519.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:29 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC December 4, 2001  
Tuesday  
moved to file:  
pic09877.pcx)

2791-2804 Phytopharm PLC - Blocklisting Interim Review

Source: XR: Extel RNS BLR 03/12/2001 18:32

12250  
RNS Number:12250  
Phytopharm PLC  
3 December 2001

### BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM 1996 UNAPPROVED DISCRETIONARY SHARE OPTION SCHEME

3. PERIOD OF RETURN: FROM: 1ST MAY 2001 TO: 31ST OCTOBER 2001

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME

AT END OF THE LAST PERIOD: 260,000 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

NIL ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD:

260,000 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION:

260,000 ORDINARY SHARES OF 1 PENCE ON 18TH  
MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR  
US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,191,815 ORDINARY  
SHARES OF 1 PENCE

CONTACT FOR QUERIES

NAME: DR S C LOACH

TELEPHONE: 01480 437697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM 1996 COMPANY SHARE OPTION SCHEME

3. PERIOD OF RETURN: FROM: 1ST MAY 2001 TO: 31ST OCTOBER 2001

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD:

195,260 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

8,444 ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD:

186,816 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION:

400,000 ORDINARY SHARES OF 1 PENCE ON 18TH  
MAY 2000

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR  
US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,191,815 ORDINARY  
SHARES OF 1 PENCE

CONTACT FOR QUERIES

NAME: DR S C LOACH

TELEPHONE:

01480 437697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM 1996 UNAPPROVED DISCRETIONARY SHARE OPTION SCHEME

3. PERIOD OF RETURN: FROM: 1ST MAY 2001 TO: 31ST OCTOBER 2001

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME

AT END OF THE LAST PERIOD: 196,573 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD:

58,350 ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD:

138,223 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)

ORIGINALLY LISTED AND THE DATE OF ADMISSION:

341,200 ORDINARY SHARES OF 1 PENCE ON 14TH  
APRIL 1999

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR  
US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,191,815 ORDINARY  
SHARES OF 1 PENCE

CONTACT FOR QUERIES

NAME: DR S C LOACH

TELEPHONE: 01480 437697

BLOCKLISTING SIX MONTHLY REVIEW

1. NAME OF COMPANY:

PHYTOPHARM PLC

2. NAME OF SCHEME:

THE PHYTOPHARM SHARE OPTION SCHEME

3. PERIOD OF RETURN: FROM: 1ST MAY 2001 TO: 31ST OCTOBER 2001

4. NUMBER AND CLASS OF SHARES(S)  
(AMOUNT OF STOCK/DEBT SECURITY)  
NOT ISSUED UNDER SCHEME  
AT END OF THE LAST PERIOD: 81,000 ORDINARY SHARES OF 1 PENCE

5. NUMBER OF SHARES ISSUED/ALLOTTED  
UNDER SCHEME DURING PERIOD: NIL ORDINARY SHARES OF 1 PENCE

6. BALANCE UNDER SCHEME NOT YET ISSUED/ALLOTTED  
AT END OF PERIOD: 81,000 ORDINARY SHARES OF 1 PENCE

7. NUMBER AND CLASS OF SHARE(S)  
(AMOUNT OF STOCK/DEBT SECURITIES)  
ORIGINALLY LISTED AND THE DATE OF ADMISSION:  
1,407,000 ORDINARY SHARES OF 1 PENCE ON 14TH  
APRIL 1999

PLEASE CONFIRM TOTAL NUMBER OF SHARES IN ISSUE AT THE END OF THE PERIOD IN ORDER FOR  
US TO UPDATE OUR RECORDS.

TOTAL SHARES IN ISSUE 38,191,815 ORDINARY  
SHARES OF 1 PENCE

CONTACT FOR QUERIES

NAME: DR S C LOACH

TELEPHONE: 01480 437697

END  
BLRUOOWRAURURAA

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic10519.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:29  
To: Zoe McGowan



pic09865.pcx (4 KB)pic25046.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:29 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC November 8,  
2001  
moved to file:  
Thursday  
pic09865.pcx)

4973-4974 Phytopharm PLC - Notice of Results

Source: XR: Extel RNS NOR 08/11/2001 16:58

8654M.  
RNS Number:8654M  
Phytopharm PLC  
8 November 2001

8 November 2001

Phytopharm plc

Phytopharm plc will be announcing its preliminary results for the year ended 31  
August 2001 on Wednesday 5 December 2001.

END

NORUWVNRAWRARAA

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic25046.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

8 November 2001

**Phytopharm plc**

**Commences repeat dose clinical study of dementia treatment, P58**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the start of a clinical study to evaluate the safety, tolerability, pharmacokinetic profile and effect on cognitive performance of its oral product, P58. This product is under development as a treatment for age-related cognitive dysfunction, which typically presents as memory loss, dementia and Alzheimer's disease.

This residential study will recruit healthy volunteers aged over 55 years in two parts, each utilising a double blind, placebo-controlled design. The first part will evaluate the safety, tolerability and pharmacokinetics of repeated dosing for 7 days in three groups of eight subjects at escalating dose. The data obtained from the first part will be used to determine the dose for the second part of the study. The second part will determine the tolerability, safety, pharmacokinetics and effects on cognitive performance of repeated dosing for 28 days in up to 40 patients at a single dose level. Final results will be reported during the second quarter of 2002.

The adult brain contains approximately two trillion nerve cells, each of which have some 100,000 receptors on their surface. It has been estimated that from the age of 40 people progressively lose more than 20 percent of these receptors, resulting in a gradual decline in cognitive performance. P58 acts by reversing this loss of nerve cell receptors in the ageing brain. This totally novel mode of action provides a platform for the development of a number of potentially important therapeutic approaches to diseases associated with ageing, including memory loss and dementia. P58 is derived from one of a family of phytochemicals found in a traditional Asian "tonic" for the elderly that has previously been shown to offer significant benefits to those with dementia. Phytopharm has now developed a total of seven patent families to protect a large family of related chemical compounds that share this activity.

A substantial programme of research is also in progress to determine the action of this family of molecules at the level of gene expression, and further patents concerning their mode of action are also in preparation. Based on the emergent data, it is now anticipated that a second family of molecules, coded P63, will commence clinical evaluation as a potential treatment for Parkinson's disease during 2002.

Dr Richard Dixey, Chief Executive of Phytopharm, said: "The product platform exemplified by P58 offers tremendous potential in a range of neuro-degenerative diseases related to ageing. The two-stage study initiated today will enable Phytopharm to optimise the design of a three-month phase II study for P58, planned to start in the third quarter of 2002. Furthermore, we anticipate the emergence of further indications from the platform alongside the programmes in Dementia and Parkinson's disease."

-ENDS-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates / Sophie Pender Cudlip

Tel: 0207 831 3113

**NOTES TO EDITORS**

**Phytopharm plc**

Phytopharm is the leading company in the development of **Botanical pharmaceuticals**. Botanicals enable the rapid clinical evaluation of plant medicines in chronic and poorly understood diseases. Where novel modes of action are discovered, such research can form the basis for drug discovery platforms, which enable the development of new medicines and the isolation of single chemical entities of clinical importance. Phytopharm has four drug discovery platforms in full development, for metabolic syndrome, neural and muscular degeneration, inflammation and dermatitis.

Phytopharm is developing nine products based on its four drug discovery platforms alongside a number of other projects in early evaluation phase.

More information concerning Phytopharm's activities can be found on its Web site at

<http://www.phytopharm.co.uk>.

Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:29  
To: Zoe McGowan



pic29872.pcx (4 KB)pic03640.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:28 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC October 31,  
2001  
moved to file:  
Wednesday  
pic29872.pcx)

5177-5179 Phytopharm PLC - Holding in Company

Source: XR: Extel RNS HOL 31/10/2001 17:07

4486M  
RNS Number:4486M  
Phytopharm PLC  
31 October 2001

Phytopharm PLC (or "the Company")

Notification of Major Interests in Shares

Phytopharm PLC received a notification today from Standard Life Investments Limited, informing the Company that it sold 1,315,123 shares on the 24 October 2001 and purchased 1,315,123 shares on the 25 October 2001. Its resultant notifiable interest therefore remains unchanged.

These shares form part of today's announcement by HSBC Investment Bank plc

31 October, 2001

WestLB Panmure Limited

END

HOLDKDKKOBDDOKN

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic03640.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

Zoe McGowan

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From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:29  
To: Zoe McGowan



pic19008.pcx (4 KB) pic17987.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:28 ----- RNS Information

(Embedded image Issuer Name: PHYTOPHARM PLC October 31, 2001  
moved to file: Primary Issuer: PHYTOPHARM PLC  
Wednesday  
pic19008.pcx) Related Issuers: HSBC Holdings PLC

735-738 Phytopharm PLC - Holding in Company

Source: XR: Extel RNS HOL 30/10/2001 18:32

3842M---1HSBC Holdings PLC----  
RNS Number:3842M  
Phytopharm PLC  
30 October 2001

Phytopharm PLC ("the Company")

Notification of Major Interests in Shares

The Company received the following notification from HSBC Investment Bank plc on the 29 October 2001

"Dear Sirs

Part VI Companies Act 1985

We hereby notify you in accordance with Part VI Companies Act 1985 ("the Act") that HSBC Investment Bank plc was as at close of business on 24 October 2001 interested in 1,334,663 ordinary shares of Phytopharm PLC ("the Shares"). Of these interests, 9,352 were interests of a kind described in S.208(5) of the Act

We further notify you that as at close of business on 25 October 2001, HSBC Investment Bank plc no longer had a notifiable interest in the Shares.

HSBC Investment Bank Holdings plc as HSBC Investment Bank plc's parent and HSBC Holdings plc, our ultimate parent company, were also interested, and are no longer interested by virtue of S.203 of the Act in all of the above mentioned Shares."

30 October, 2001

END

HOLDKKKNFBDDDBKN

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Tickers: PYM HSBA

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic17987.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
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Zoe McGowan

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From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:28  
To: Zoe McGowan



pic08792.pcx (4 KB)pic17943.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:28 ----- RNS  
Information

(Embedded image Issuer Name: PHYTOPHARM PLC September 19,  
2001  
moved to file:  
Wednesday  
pic08792.pcx)

3338-3340 Phytopharm PLC - Response to press comment

Source: XR: Extel RNS SPC 19/09/2001 09:38

2467K  
RNS Number:2467K  
Phytopharm PLC  
19 September 2001

19 September 2001

Phytopharm PLC

Response to press comment

Phytopharm plc ("Phytopharm") notes the article in today's issue of The Independent newspaper which refers to Phytopharm being "poised to issue some negative news" regarding one of its drugs.  
Phytopharm wishes to make it absolutely clear that the story is entirely without foundation. It also wishes to point out that The Independent made no attempt to make contact with the Company regarding the veracity of this unfounded rumour.

Enquiries

Phytopharm plc

Richard Dixey, Chief Executive

Tel: 07867 782 000

END

SPCEANNNFDPFEEE

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic17943.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
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**Zoe McGowan**

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**From:** akubiak@londonstockexchange.com  
**Sent:** 25 May 2004 09:28  
**To:** Zoe McGowan



pic32209.pcx (4 KB)pic24221.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:27 ----- RNS Information

(Embedded image Issuer Name: PHYTOPHARM PLC August 2, 2001  
Thursday  
moved to file:  
pic32209.pcx)

5059-5065 Phytopharm PLC - Director Shareholding

Source: XR: Extel RNS RDS 02/08/2001 10:06

9095H  
RNS Number:9095H  
Phytopharm PLC  
2 August 2001

DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

DR D D REES

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

AS 2

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

6) Please state the nature of the transaction. For PEP transactions

please indicate whether general/single co PEP and if discretionary/non discretionary

- 7) Number of shares/amount of stock acquired
- 8) (N/A %)  
of issued Class
- 9) Number of shares/amount of stock disposed
- 10) ( N/A %)  
of issued Class
- 11) Class of security
- 12) Price per share
- 13) Date of transaction
- 14) Date company informed
- 15) Total holding following this notification
- 16) Total percentage holding of issued class following this notification

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE COMPLETE THE FOLLOWING BOXES

- 17) Date of grant  
1 AUGUST 2001
- 18) Period during which or date on which exercisable  
15,000 2 AUGUST 04 - 31 JULY 2008  
15,000 2 AUGUST 06 - 31 JULY 2008
- 19) Total amount paid (if any) for grant of the option  
NIL
- 20) Description of shares or debentures involved: class, number.  
30,000 ORDINARY 1 PENCE
- 21) Exercise price (if fixed at time of grant) or indication that price is to be fixed at time of exercise

#4.60

22) Total number of shares or debentures over which options held following this notification

172,813

23) Any additional information

OPTIONS SUBJECT TO SHARE PRICE PERFORMANCE CRITERIA

24) Name of contact and telephone number for queries

DR S LOACH  
01480 437697

25) Name and signature of authorised company official responsible for making this notification

Date of Notification 2 AUGUST 2001

END

RDSBLLFBFVBBBBQ

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic24221.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

Zoe McGowan

---

From: akubiak@londonstockexchange.com  
Sent: 25 May 2004 09:28  
To: Zoe McGowan



pic00353.pcx (4 KB)pic11586.pcx (2 KB)

----- Forwarded by Andrew Kubiak/TOWER/LondonStockEx on 25/05/2004 09:27 ----- RNS Information

{Embedded image Issuer Name: PHYTOPHARM PLC August 1, 2001  
Wednesday  
moved to file;  
pic00353.pcx}

5093-5100 Phytopharm PLC - Director Shareholding

Source: XR: Extel RNS RDS 01/08/2001 14:05

8637H  
RNS Number:8637H  
Phytopharm PLC  
1 August 2001

DEALINGS BY DIRECTORS

1) NAME OF COMPANY

PHYTOPHARM PLC

2) NAME OF DIRECTOR

Dr A P DIXEY

3) Please state whether notification indicates that it is in respect of holding of the shareholder named in 2 above or in respect of a non-beneficial interest or in the case of an individual holder if it is a holding of that person's spouse or children under the age of 18 or in respect of an non-beneficial interest

DIRECTOR

4) Name of the registered holder(s) and, if more than one holder, the number of shares held by each of them. (If notified)

AS 2

5) Please state whether notification relates to a person(s) connected with the Director named in 2 above and identify the connected person(s)

DIRECTOR

6) Please state the nature of the transaction. For PEP transactions

please indicate whether general/single co PEP and if discretionary/non discretionary

MARKET PURCHASE

7) Number of shares/amount of stock acquired

55,000

8) ( 0.14% )  
of issued Class

9) Number of shares/amount of stock disposed

10) ( N/A % )  
of issued Class

11) Class of security

ORDINARY

12) Price per share

#4.65

13) Date of transaction

1 AUGUST 2001

14) Date company informed

1 AUGUST 01

15) Total holding following this notification

BENEFICIAL HOLDING OF 8,098,500  
AS 166,500 DIRECTLY AND 7,932,000 HELD BY CHAKRA LTD OF WHICH  
Dr DIXEY OWNS 50%

16) Total percentage holding of issued class following this notification

21.23%

IF A DIRECTOR HAS BEEN GRANTED OPTIONS BY THE COMPANY PLEASE  
COMPLETE THE FOLLOWING BOXES

17) Date of grant

18) Period during which or date on which exercisable

19) Total amount paid (if any) for grant of the option

20) Description of shares or debentures involved: class, number.

21) Exercise price (if fixed at time of grant) or indication that price

is to be fixed at time of exercise

22) Total number of shares or debentures over which options held following this notification

23) Any additional information

24) Name of contact and telephone number for queries

SIMON LOACH

25) Name and signature of authorised company official responsible for making this notification

Date of Notification 1 AUGUST 2001

END

RDSZFLFBFVBBBBBE

XRviaNewsEDGE

Tickers: PYM

Prohibited Period Start:

Prohibited Period End:

(Embedded image moved to file: pic11586.pcx)

Andrew Kubiak  
Manager, RNS Customer Services  
020 7797 3497  
akubiak@londonstockexchange.com

31 July 2001

## Phytopharm plc

### Results of P54 trial in canine osteoarthritis

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces today the results of a randomised, double blind, placebo-controlled study of its natural anti-inflammatory product P54 for the treatment of canine osteoarthritis (OA). P54 is a patented non-steroidal anti-inflammatory drug (NSAID) manufactured from 2 related plant species.

Canine OA is a chronic inflammatory disease, which mainly affects the synovial joints, causing pain, joint swelling and stiffness with loss of function. A variety of steroidal and non-steroidal anti-inflammatory drugs have been used to treat dogs with OA although all are associated with adverse effects. There is a clear need for effective and better tolerated products for the treatment of canine OA.

A total of 61 dogs with osteoarthritis of the hip or elbow (confirmed by radiography) were entered into the study, which was conducted by the Department of Clinical Veterinary Science, University of Bristol Veterinary School, UK. Fifty-four dogs were randomly allocated to receive twice daily treatment with either P54 (n=25) or placebo (inactive) therapy (n=29) for up to 8 weeks. The investigating veterinary surgeon and the owners were not aware of which treatment was given to each dog.

The outcome measures included force plate analysis (peak vertical force and vertical impulse), clinical assessment of lameness, pain on joint manipulation and the owners' and investigator's overall assessment of response.

According to the measures of peak vertical force and vertical impulse, there was no detectable difference in outcome between the 2 groups ( $p > 0.05$ ). The changes from baseline for the clinical assessments of lameness and pain on joint manipulation were similar in both groups.

At the end of the treatment period the investigator reported that 56% of the dogs were 'better' or 'much better' after being treated with P54 compared to only 26% of those treated with placebo ( $p = 0.047$ ). The owners' assessment of response also favoured P54 (60%) compared with placebo (38%). The treatment was generally well tolerated with no serious adverse events recorded. The most common reported side effect was malodour of the animals' coat.

Commenting on the results, Dr John Innes said: 'Evaluation of treatments for canine OA is difficult. Although we were unable to demonstrate a treatment effect using gait analysis, there is a suggestion from the investigator's and owners' assessments that some aspects of OA may have been improved'.

Dr Richard Dixey, Chief Executive, added: 'We are cautiously optimistic about the results of this study and are examining options for the development and commercialisation of the product'.

ENDS

Phytopharm plc      Tel: 01480 437697

Richard Dixey, Chief Executive

Financial Dynamics Tel: 0207 831 3113

David Yates / Sophie Pender-Cudlip

## NOTES TO EDITORS

Phytopharm plc

Phytopharm's business is to take both simple and complex mixtures derived from plant sources into full pharmaceutical development. The US Food and Drug Administration call such medicinal products 'Botanicals'. Botanical products are whole or partially purified extracts of medicinal plants in which the chemical composition is not fully characterised. Apart from being a new sector in the pharmaceutical market, Botanicals also act as an enabling technology to discover single chemical entities of clinical importance from plant sources.

Phytopharm is the leading company in the development of **botanical pharmaceuticals**. It has developed a portfolio of 11 such products, nine of which are in the clinical evaluation phase. These products have been targeted in the five therapeutic categories of anti-inflammatory treatments, neurological disorders, dermatology, cancer and metabolic diseases. In 1997, Phytopharm was granted an Investigational New Drug (IND) approval in the US. The guidelines for the registration of botanical products have recently been published by the FDA.

P54 is a novel anti-inflammatory agent containing extracts derived from two related tropical plants. Components of the product have been shown to have activity in reducing the production of the inflammatory enzyme COX2 in the joints and gut. This activity is consistent with its apparent efficacy in treating Arthritis, Crohn's disease and as a cancer chemo-preventive agent.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

# # #

July 5th 2001

**Phytopharm plc**

**Proof of Principle Clinical Study of P57 for Obesity – Successful Completion of Second Stage**

Phytopharm plc (PYM: London Stock Exchange) (“Phytopharm”) announces today the successful completion of the second stage of its clinical study of P57 for obesity. The objectives of this stage of the study include evaluation of the safety, tolerability and pharmacokinetic profile of P57, a patented oral product licensed to Pfizer Inc., which is under development as an appetite suppressant for the treatment of obesity.

This second stage used a double-blind, randomised, placebo-controlled design to evaluate the safety, tolerability and pharmacokinetics of repeated dosing with either P57 or placebo given to eighteen subjects over 5 days. Three groups of six overweight but otherwise healthy male volunteers were administered either P57 or placebo daily at ascending doses.

Pharmacokinetic data confirm that there was systemic exposure to biologically active constituents of P57. No serious adverse effects were experienced by any of the subjects. The study will now proceed to the third stage.

The third and final stage of the study has been designed to assess the safety, tolerability, pharmacokinetics and effects on daily calorie intake of P57 compared to placebo when administered repeatedly over at least 10 days to healthy, overweight volunteers.

Obesity is a global problem, which affects more than 100 million people seriously enough to warrant medical intervention. It is a direct causal contributor to the pathophysiology of many diseases and exacerbates numerous others. Among these are five of the leading causes of death in the industrialised world: stroke, atherosclerosis, cardiovascular disease, diabetes and cancer. According to the World Health Organisation (WHO), obesity accounts for tens of billions of pounds in direct healthcare costs worldwide. A panel of experts convened by WHO stated on 12 June 1997 that ‘obesity’s impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time. It has an impact on health, which may well prove to be as great as that of smoking’ (World Health Organisation, 1997).

Dr Richard Dixey, Chief Executive of Phytopharm, said: ‘We are very encouraged by the results of the second stage of the study and await the completion in early November of the third and final stage of this proof of principle study’.

- ENDS -

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates

Tel: 0207 831 3113

## NOTES TO EDITORS

### **Phytopharm plc**

Phytopharm's business is to take both simple and complex mixtures derived from plant sources into full pharmaceutical development. The US Food and Drug Administration call such medicinal products 'Botanicals'. Botanical products are whole or partially purified extracts of medicinal plants in which the chemical composition is not fully characterised. Apart from being a new sector in the pharmaceutical market, Botanicals also act as an enabling technology to discover single chemical entities of clinical importance from plant sources.

Phytopharm is the leading company in the development of **botanical pharmaceuticals**. It has developed a portfolio of 12 such products, nine of which are in the clinical evaluation phase. These products have been targeted in the five therapeutic categories of anti-inflammatory treatments, neurological disorders, dermatology, cancer and metabolic diseases.

P57 is a novel appetite suppressant containing extracts derived from a South African plant. Under an agreement announced on August 24<sup>th</sup> 1998, Pfizer has acquired an exclusive worldwide licence to develop and market P57. Phytopharm will receive up to \$32 million in licence fees and milestone payments based upon the achievement of specific objectives. Phytopharm will also receive royalties on sales of P57 by Pfizer.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

June 11 2001

**Phytopharm plc**

**Appointment of Chief Operating Officer**

Phytopharm plc (PYM: London Stock Exchange) ("Phytopharm") announces the appointment today of Dr Daryl Rees as Chief Operating Officer for the Company. In this executive role he will have responsibility for the conduct of Phytopharm's research and development programmes as well as direct responsibility for the Company's manufacturing operations worldwide.

Dr Rees joined the Company in 1999 and was appointed to the Board in September 2000 as Chief Scientific Officer. Prior to this Dr Rees gained 10 years experience in the discovery and clinical development of medicines as a Senior Scientist at Wellcome and was part of a multi-disciplinary team involved in the discovery of the L-arginine-NO pathway. He is an Honorary Senior Lecturer in the Department of Medicine at University College London, a former Editor of the *British Journal of Pharmacology* and is Chairman of Huntingdon Local Research Ethics Committee.

Commenting on his appointment, Richard Dixey, Chief Executive of Phytopharm, said: "Daryl has made a tremendous contribution to the ongoing success of Phytopharm. As the Company matures, I am very happy to have a senior executive of such high calibre to manage both our research and development programmes and our expanding manufacturing operations."

-END-

*Enquiries:*

**Phytopharm plc**

Dr Richard Dixey, Chief Executive

Tel: 01480 437697

Mobile: 07867 782000

**Financial Dynamics**

David Yates

Tel: 0207 831 3113

## NOTES TO EDITORS

### **Phytopharm plc**

Phytopharm's business is to take both simple and complex mixtures derived from plant sources into full pharmaceutical development. The US Food and Drug Administration call such medicinal products 'Botanicals'. Botanical products are whole or partially purified extracts of medicinal plants in which the chemical composition is not fully characterised. Apart from being a new sector in the pharmaceutical market, Botanicals also act as an enabling technology to discover single chemical entities of clinical importance from plant sources.

Phytopharm is the leading company in the development of **botanical pharmaceuticals**. It has developed a portfolio of 12 such products, nine of which are in the clinical evaluation phase. These products have been targeted in the five therapeutic categories of anti-inflammatory treatments, neurological disorders, dermatology, cancer and metabolic diseases.

More information concerning Phytopharm's activities can be found on its Web site at <http://www.phytopharm.co.uk>.

The Companies Acts 1985 and 1989

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PUBLIC COMPANY LIMITED BY SHARES

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ARTICLES OF ASSOCIATION  
of  
PHYTOPHARM PLC

Adopted by special resolution passed on 18th April 1996  
Amended by special resolution passed on 17 February 2000

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**PRELIMINARY**

1. No regulations contained in any statute concerning companies, or in any statutory instrument or other subordinate legislation made under any such statute, shall apply as regulations or articles of the Company.

**INTERPRETATION**

2. In these Articles (if not inconsistent with the subject or context):  
(A) The words standing in the first column of the table next hereinafter contained shall bear the meanings set opposite to them respectively in the second column thereof

<u>Words</u>	<u>Meanings</u>
the Act	the Companies Act 1985 including any statutory modification or re-enactment thereof for the time being in force
these Articles	these articles of association as from time to time altered

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2001 JUN -3 AM 11:03  
OFFICE OF INTEGRATED  
CORPORATE INFORMATION

dividend	dividend and/or bonus
month	calendar month
Office	the registered office of the Company
paid up	paid up or credited as paid up
the Register	the register of members of the Company
Seal	the common seal of the Company
the Statutes	the Act and every other statute for the time being in force concerning companies and affecting the Company
the Stock Exchange	the London Stock Exchange Limited
the United Kingdom	Great Britain and Northern Ireland
year	calendar year

(B) The expressions "debenture" and "debenture-holder" shall include "debenture stock" and "debenture stockholder".

The expression "Secretary" shall include any person appointed by the Directors to perform any of the duties of the Secretary of the Company and where two or more persons are appointed to act as joint secretaries shall include any one of those persons.

An act which is expressed to require the sanction of or to be effected by an "ordinary resolution" may be sanctioned by or effected by a special or extraordinary resolution.

Words importing the singular number shall include the plural and vice versa.

Words importing the masculine gender shall include the feminine gender.

References to writing include references to any method of representing or reproducing words in a legible and non-transitory form.

Save as aforesaid any words or expressions defined in the Statutes shall (if not inconsistent with the subject or context) bear the same meanings in these Articles but excluding any statutory modification thereof not in force at the date of adoption of these Articles as the articles of association of the Company.

Any reference in these Articles to any provision in any enactment shall where applicable be construed as a reference to the same as for the time being modified or re-enacted whether before or after the date hereof.

The headings are inserted for convenience only and shall not affect the construction of these Articles.

### SHARE CAPITAL

3. The capital of the Company at the date of adoption of these Articles as the articles of association of the Company is £500,000 divided into 50,000,000 Ordinary Shares of 1p each.
  
4. Without prejudice to any special rights previously conferred on the holders of any shares or class of shares for the time being issued and subject to the provisions of the Statutes, any share in the Company may be issued with such preferred, deferred or other special rights, or such restrictions, whether in regard to dividend, capital, transfer, voting or otherwise, as the Company may from time to time by ordinary resolution determine (or, failing any such determination, as the Directors may determine) and the Company may issue any shares which are to be redeemed or are liable to be redeemed at the option of the Company or the shareholder on such terms and in such manner as may be provided by these Articles. Any share may be issued in certificated or uncertificated form and converted from certificated form into uncertificated form and vice versa in accordance with the Statutes or any subordinate legislation made from time to time under the Statutes and the Directors shall have power to implement any arrangements they think fit in respect of shares in certificated form or uncertificated form and for the conversion of shares in certificated into uncertificated form and vice versa which accord with the Statutes or such subordinate legislation.

5. Subject to the provisions of the Statutes and these Articles, all unissued shares of the Company (whether forming part of the existing or any increased capital) shall be at the disposal of the Directors who may allot, grant options over, offer or otherwise deal with or dispose of them to such persons at such times and generally on such terms and conditions as they may determine but so that no share shall be issued at a discount.
6. Subject to the provisions of the Statutes and without prejudice to any special rights previously conferred on the holders of any shares or class of shares for the time being in issue the Company may, with the sanction of an ordinary resolution of the Company purchase its own shares including any redeemable shares. The Directors are unconditionally authorised to exercise the power of the Company to purchase its own shares (including any redeemable shares) pursuant to this Article.
7. No share in the Company (other than a share allotted in pursuance of an employees' share scheme) shall be allotted except as paid up in money or money's worth at least as to one-quarter of the nominal value of the share and whole of any premium on it.
8. The Company may exercise the powers of paying commissions conferred by the Statutes. The Company may also on any issue of shares pay such brokerage as may be lawful.
9. Except as required by law, no person shall be recognised by the Company as holding any share upon any trust, and the Company shall not be bound by or compelled in any way to recognise (even when having notice thereof) any equitable, contingent, future or partial interest in any share, or any interest in any fractional part of a share, or (except only as by these Articles or by law otherwise provided) any other right in respect of any share, except an absolute right to the entirety thereof in the registered holder.

#### VARIATION OF RIGHTS

10. (A) Whenever the share capital of the Company is divided into different classes of shares, the special rights attached to any class may, subject to the provisions of the Statutes, be varied or abrogated either with the consent in writing

of the holders of three-fourths in nominal amount of the issued shares of the class or with the sanction of an extraordinary resolution passed at a separate general meeting of the holders of the shares of the class (but not otherwise) and may be so varied or abrogated either whilst the Company is a going concern or during or in contemplation of a winding up. To every such separate general meeting all the provisions of these Articles as for the time being in force relating to general meetings of the Company and to the proceedings thereat shall mutatis mutandis apply, except that (a) the necessary quorum (other than at an adjourned meeting) shall be two persons at least holding or representing by proxy one third in nominal amount of the issued shares of the class, and at an adjourned meeting shall be one person holding shares of the class in question or his proxy, (b) any holder of shares of the class present in person or by proxy may demand a poll and (c) a Director shall be entitled to notice thereof and to attend and speak thereat. The foregoing provisions of this Article shall apply to the variation or abrogation of the special rights attached to some only of the shares of such class as if the shares concerned and the remaining shares of such class formed separate classes, or to any scheme for the distribution (though not in accordance with legal rights) of assets in money or in kind in or before liquidation, or to any contract for the sale or disposal of the whole or any part of the Company's property or business determining the way in which as between the several classes of shareholders the purchase considerations shall be distributed, and generally to any alteration, contract, compromise or arrangement which the persons voting thereon could, if sui juris and holding all the shares of the class, consent to or enter into, and such resolution shall be binding upon all holders of shares of the class.

(B) Save as otherwise provided in these Articles, the special rights attached to any class of shares having preferential rights shall not unless otherwise expressly provided by the terms of issue thereof be deemed to be varied or abrogated by the creation or issue of further shares ranking as regards participation in the profits or assets of the Company or voting in some or all respects *pari passu* therewith but in no respect in priority thereto, or by any reduction of the capital paid up thereon, or by any purchase by the Company of its own shares.

### ALTERATION OF SHARE CAPITAL

11. The Company may from time to time by ordinary resolution increase its capital by such sum to be divided into shares of such amounts as the resolution shall prescribe. All new shares shall, save in so far as may be otherwise provided by the terms of issue thereof, be subject to the provisions of these Articles with reference to allotment, payment of calls, lien, transfer, transmission, forfeiture and otherwise.
12. (A) The Company may from time to time by ordinary resolution :-
- (i) consolidate and divide all or any of its share capital into shares of a larger amount than its existing shares;
  - (ii) cancel any shares which, at the date of the passing of the resolution, have not been taken, or agreed to be taken, by any person and diminish the amount of its capital by the amount of the shares so cancelled; and
  - (iii) sub-divide its shares, or any of them, into shares of smaller amount than is fixed by the Memorandum of Association provided that in the sub-division the proportion between the amount paid and the amount, if any, unpaid on each reduced share shall be the same as it was in the case of the share from which the reduced share is derived, and so that the resolution whereby any share is sub-divided may determine that, as between the holders of the shares resulting from such sub-division, one or more of the shares may, as compared with the others, have any such preferred, deferred or other special rights, or be subject to any such restrictions, as the Company has power to attach to unissued or new shares.
- (B) Upon any consolidation of fully paid shares into shares of larger amount, the Directors may settle any difficulty which may arise with regard thereto and in particular may as between the holders of shares so consolidated determine which shares are consolidated into each consolidated share and in the case of any shares registered in the name of one holder (or joint holders) being consolidated with shares registered in the name of another holder (or joint holders) may make such arrangements for the allocation, acceptance or sale of the consolidated share and for the distribution to the persons entitled thereto of any monies received in respect thereof as may be thought fit and

for the purpose of giving effect thereto may appoint some person to transfer the consolidated share or any fractions thereof and to receive the purchase price thereof (and any transfer executed in pursuance thereof shall be effective and after such transfer has been registered no person shall be entitled to question its validity), and may in each case where the number of shares held by any holder is not an exact multiple of the number of shares to be consolidated into a single share issue to each holder credited as fully paid up by way of capitalisation the minimum number of shares required to round up his holding to such a multiple (such issue being deemed to have been effected immediately prior to consolidation) and the amount required to pay up such shares shall be appropriated at their discretion from any of the sums standing to the credit of any of the Company's reserve accounts (including share premium account and capital redemption reserve fund) or to the credit of profit and loss account and capitalised by applying the same in paying up such shares.

13. The Company may by special resolution reduce its share capital or any capital redemption reserve fund or share premium account in any manner and with and subject to any incident authorised and consent required by law.

#### **SHARE CERTIFICATES AND TITLE TO SHARES**

14. Title to any shares may be evidenced otherwise than by a definitive share certificate in accordance with the Statutes or any subordinate legislation made from time to time under the Statutes and the Directors shall have power to implement any arrangements they think fit for such evidencing which accord with the Statutes or such subordinate legislation. The Company shall enter on the Register, in respect of all shares registered in the name of each holder, how many of such shares are in certificated form and uncertificated form respectively.
15. Every person whose name is entered as a member in the Register in respect of any shares of any class in certificated form (except a person in respect of whom the Company is not by law required to issue a share certificate) shall be entitled without payment to a certificate therefor, upon the issue thereof within one month after allotment (or such other period as the terms of issue shall provide), and upon

the transfer thereof in the case of fully paid shares within one month after lodgement of transfer and in the case of partly paid shares within two months after lodgement of transfer and in the case of conversion thereof from uncertificated to certificated form within two months of the date of conversion. The Company shall not be bound to register more than four persons as the joint holders of a share and in the case of a share held jointly by several persons the Company shall not be bound to issue more than one certificate therefor and delivery of a certificate to any one of such persons shall be sufficient delivery to all.

16. Every definitive certificate for shares shall be issued under the Seal (or an official seal kept under section 40 of the Act or, in the case of shares on a branch register, an official seal for use in the relevant territory). Every such certificate shall specify the number and class of shares to which it relates and the amount paid up thereon. No certificate shall be issued representing shares of more than one class.

17. Where a member transfers part only of the shares comprised in a share certificate the old certificate shall be cancelled and a new certificate for the balance of such shares issued in lieu without charge.

18. (A) Any two or more certificates representing shares of any one class held by any member may at his request be cancelled and a single new certificate for such shares issued in lieu upon payment of such charge as the Directors may from time to time determine.

(B) If any member shall surrender for cancellation a share certificate representing shares held by him and request the Company to issue in lieu two or more share certificates representing such shares in such proportions as may be specified, the Directors may, if they think fit, comply with such request upon payment of such charge as the Directors may from time to time determine.

(C) If a share certificate shall be damaged or defaced or alleged to have been lost, stolen or destroyed a new certificate representing the same shares may be issued to the holder upon request subject to delivery up of the old certificate or (if alleged to have been lost, stolen or destroyed) compliance with such conditions as to evidence and indemnity and (in either case) the payment of any exceptional out-of-pocket expenses of the Company in connection with the request as the Directors may think fit. Subject as aforesaid no charge

will be made for a new share certificate issued to replace one that has been damaged, lost or destroyed.

(D) In the case of shares held jointly by several persons any such request may be made by any one of the joint holders except where the certificate is alleged to be lost, stolen or destroyed.

#### CALLS ON SHARES

19. The Directors may from time to time make calls upon the members in respect of any monies unpaid on their shares and not by the terms of issue thereof made payable at fixed times. Each member shall (subject to receiving at least fourteen days' notice specifying the time or times and place of payment) pay to or as directed by the Company at the time or times and place so specified the amount called on his shares. A call may be wholly or in part revoked or postponed as the Directors may determine.
20. A call shall be deemed to have been made at the time when the resolution of the Directors authorising the call was passed and may be made payable by instalments.
21. The joint holders of a share shall be jointly and severally liable to pay all calls in respect thereof. A person upon whom a call is made shall remain liable for calls made upon him, notwithstanding the subsequent transfer of the shares on which the call was made.
22. If a sum called in respect of a share is not paid before or on the day appointed for payment thereof, the person from whom the sum is due shall pay interest on the sum from the day appointed for payment thereof to the time of actual payment at such rate (not exceeding twenty per cent per annum) as the Directors determine, together with all expenses that may have been incurred by the Company by reason of such non-payment, but the Directors shall be at liberty in any case or cases to waive payment of such interest and expenses wholly or in part.
23. Any sum (whether on account of the nominal value of the share or by way of premium) which by the terms of issue of a share becomes payable upon allotment or at a fixed date shall for all the purposes of these Articles be deemed to be a call

duly made and payable on the date on which by the terms of issue the same becomes payable. In the case of non-payment all the relevant provisions of these Articles as to payment of interest and expenses, forfeiture or otherwise shall apply as if such sum had become payable by virtue of a call duly made and notified.

24. The Directors may on the issue of shares differentiate between the holders as to the amount of calls to be paid and the times of payment.
25. The Directors may if they think fit receive from any member willing to advance the same all or any part of the monies (whether on account of the nominal value of the shares or by way of premium) uncalled and unpaid upon the shares held by him and such payment in advance of call shall extinguish pro tanto the liability upon the shares in respect of which it is made and upon the money so received (until and to the extent that the same would but for such advance become payable) the Company may pay interest at such rate as the member paying such sum and the Directors agree upon but any such advance payment shall not entitle the holder of the share to participate in respect of such amount in any dividend.

#### **FORFEITURE AND LIEN**

26. If a member fails to pay in full any call or instalment of a call on the day appointed for payment thereof, the Directors may at any time thereafter serve a notice on him requiring payment of so much of the call or instalment as is unpaid together with any interest and expenses which may have accrued or been incurred.
27. The notice shall name a further day (not being less than fourteen days from the date of service of the notice) on or before which and the place where the payment required by the notice is to be made, and shall state that in the event of non-payment in accordance therewith the shares on which the call was made will be liable to be forfeited.
28. If the requirements of any such notice as aforesaid are not complied with, any share in respect of which such notice has been given may at any time thereafter, before payment of all calls and interest and expenses due in respect thereof has been made, be forfeited by a resolution of the Directors to that effect. Such forfeiture shall include all dividends declared and other monies payable in

respect of the forfeited share and not actually paid before forfeiture. The Directors may accept a surrender of any share liable to be forfeited.

29. Subject to the provisions of the Statutes, a share so forfeited or surrendered shall be deemed to be the property of the Company and may be sold, re-allotted or otherwise disposed of either to the person who was before such forfeiture or surrender the holder thereof or entitled thereto or to any other person upon such terms and in such manner as the Directors think fit, and at any time before a sale, re-allotment or disposal the forfeiture or surrender may be cancelled on such terms as the Directors think fit. The Directors may, if necessary, authorise some person to transfer a forfeited or surrendered share to any such other person as aforesaid. Any share not disposed of in accordance with this Article within a period of three years from the date of its forfeiture or surrender shall, at the expiry of that period, be cancelled in accordance with the Statutes.
30. A member whose shares have been forfeited or surrendered shall cease to be a member in respect of the shares but shall notwithstanding the forfeiture or surrender remain liable to pay to the Company all monies which at the date of forfeiture or surrender were presently payable by him to the Company in respect of the shares with interest thereon at twenty per cent per annum (or such lower rate as the Directors may approve) from the date of forfeiture or surrender until payment, but the Directors may waive payment of such interest either wholly or in part. The Directors may enforce payment, without any allowance for the value of the shares at the time of forfeiture or surrender.
31. The Company shall have a first and paramount lien on every share (not being a fully paid share) for all monies payable (whether presently or not) in respect of such share. The Company's lien on a share shall extend to all dividends or other monies payable thereon or in respect thereof. The Directors may waive any lien which has arisen and may resolve that any share shall for some limited period be exempt wholly or partially from the provisions of this Article.
32. Subject to the provisions of the Statutes, the Company may sell in such manner as the Directors think fit any share on which the Company has a lien, but no sale shall be made unless the period for the payment or discharge of some part

at least of the debt or liability in respect of which the lien exists shall have actually arrived nor until the expiration of fourteen days after a notice in writing stating and demanding payment or discharge thereof and giving notice of intention to sell in default shall have been given to the holder for the time being of the share or the person entitled thereto by reason of his death or bankruptcy.

33. The net proceeds of such sale after payment of the cost of such sale shall be applied in or towards payment or satisfaction of the debts or liabilities in respect whereof the lien exists so far as the same are presently payable and any residue shall (subject to a like lien for debts or liabilities the period for the payment or discharge of which has not actually arrived as existed upon the shares prior to the sale) be paid to the person entitled to the shares at the time of the sale. For giving effect to any such sale the Directors may authorise some person to transfer the shares sold to the purchaser.

34. A statutory declaration in writing that the declarant is a Director or the Secretary and that a share has been duly forfeited or surrendered or sold to satisfy a lien of the Company on a date stated in the declaration shall be conclusive evidence of the facts therein stated as against all persons claiming to be entitled to the share. Such declaration and the receipt of the Company for the consideration (if any) given for the share on the sale, re-allotment or disposal thereof together with the share certificate delivered to a purchaser or allottee thereof shall (subject to the execution of a transfer if the same be required) constitute a good title to the share and the person to whom the share is sold, re-allotted or disposed of shall be registered as the holder of the share and shall not be bound to see to the application of the purchase money (if any) nor shall his title to the share be affected by any irregularity or invalidity in the proceedings in reference to the forfeiture, surrender, sale, re-allotment or disposal of the share.

#### TRANSFER OF SHARES

35. Shares in uncertificated form may be transferred otherwise than by a written instrument in accordance with the Statutes or any subordinate legislation made from time to time under the Statutes and the Directors shall have power to implement any arrangements they think fit for such transfer which accord with the Statutes or such subordinate legislation.

36. Transfers of shares in certificated form may be effected by transfers in writing in any usual or common form or in any other form acceptable to the Directors and may be under hand only. The instrument of transfer shall be signed by or on behalf of the transferor and (except in the case of fully paid shares) by or on behalf of the transferee. The transferor shall remain the holder of the shares concerned until the name of the transferee is entered in the Register in respect thereof.
37. The registration of transfers may be suspended at such times and for such periods as the Directors may from time to time determine either generally or in respect of any class of shares. The Register shall not be closed and registration suspended for more than thirty days in any year.
38. The Directors may in their absolute discretion and without assigning any reason therefor decline to register any transfer in favour of more than four persons jointly and any transfer which is in respect of more than one class of share. The Directors may decline to register any transfer of shares which are not fully paid provided that dealings in such shares are not prevented from taking place on an open and proper basis.
39. The Directors may decline to recognise any instrument of transfer unless the instrument of transfer is deposited at the Office, duly stamped, accompanied by the relevant share certificate(s) (except where no certificate shall have been issued therefore) and such other evidence as the Directors may reasonably require to show the right of the transferor to make the transfer and, if the instrument of transfer is executed by some other person on his behalf, the authority of that person so to do.
40. If the Directors refuse to register a transfer they shall within two months after the date on which the transfer was lodged with or notified to the Company send to the transferee notice of the refusal.
41. The Company shall be entitled to destroy all instruments of transfer which have been registered at any time after the expiration of six years from the date of registration thereof and all dividend mandates and notifications of change of address

at any time after the expiration of two years from the date of recording thereof and all share certificates which have been cancelled at any time after the expiration of one year from the date of cancellation thereof and any other document on the basis of which any entry in the Register is made at any time after the expiry of six years from the date an entry in the Register was first made in respect of it, and it shall conclusively be presumed in favour of the Company that every entry in the register purporting to have been made on basis of an instrument of transfer or other document so destroyed was duly and properly made and every instrument of transfer so destroyed was a valid and effective instrument duly and properly registered and every share certificate so destroyed was a valid and effective certificate duly and properly cancelled and every other document hereinbefore mentioned so destroyed was a valid and effective document in accordance with the recorded particulars thereof in the books or records of the Company. Provided always that :-

(A) the provisions aforesaid shall apply only to the destruction of a document in good faith and without notice of any claim (regardless of the parties thereto) to which the document might be relevant;

(B) nothing herein contained shall be construed as imposing upon the Company any liability in respect of the destruction of any such document earlier than as aforesaid or in any other circumstances which would not attach to the Company in the absence of this Article; and

(C) references herein to the destruction of any document include references to the disposal thereof in any manner.

42. No fee will be charged by the Company in respect of the registration of any instrument of transfer, probate, letters of administration, certificate of marriage or death, stop notice, power of attorney or other document relating to or affecting the title to any shares or otherwise for making any entry in the Register affecting the title to any shares.

43. Nothing in these Articles shall preclude the Directors from recognising a renunciation of the allotment of any share by the allottee in favour of some other person, and the Directors may accord to any allottee of a share a right to effect such renunciation upon and subject to such terms and conditions as they may think fit.

### TRANSMISSION OF SHARES

44. In the case of the death of a shareholder the survivors or survivor where the deceased was a joint holder and the executors or administrators of the deceased where he was a sole or only surviving holder, shall be the only persons recognised by the Company as having any title to his interest in the shares, but nothing in this Article shall release the estate of a deceased holder (whether sole or joint) from any liability in respect of any share held by him.
45. Any person becoming entitled to a share in consequence of the death or bankruptcy of a member or of his becoming a patient within the meaning of the Mental Health Act 1983 (or the equivalent of bankruptcy or of becoming such patient under the laws of any competent jurisdiction) may (subject as hereinafter provided) upon supplying to the Company such evidence as the Directors may reasonably require to show his title to the share either require to be registered himself as a holder of the share by giving to the Company notice in writing to that effect or transfer such share to some other person. All the limitations, restrictions and provisions of these Articles relating to the right to transfer and the registration of transfers of shares shall be applicable to any such notice or transfer as aforesaid as if the event giving rise thereto had not occurred and the notice or transfer were a transfer executed by such member.
46. Save as otherwise provided by or in accordance with these Articles, a person becoming entitled to a share in consequence of the death or bankruptcy of a member (or the equivalent of bankruptcy under the laws of any competent jurisdiction) shall upon supplying to the Company such evidence as the Directors may reasonably require to show his title to the share be entitled to the same dividends and other advantages as those to which he would be entitled if he were the registered holder of the share, but he shall not be entitled in respect thereof to exercise any right conferred by membership in relation to meetings of the Company until he shall have been registered as a member in respect of the share. Provided always that the Directors may at any time give notice requiring such person to elect either to be registered himself or to transfer the share, and if within sixty days the notice is not complied with, such person (but only in the case of a share which is fully paid up) shall be deemed to have elected to be registered as a member in respect thereof and the Directors may cause him to be registered accordingly. Where two or more

persons are jointly entitled by transmission to a share they shall for the purposes of these Articles be treated as if they were joint holders of such share registered in the order in which their names have been supplied to the Company or such other order as the person requiring to be registered may by notice in writing to the Company have prescribed at that time.

#### SUSPENSION OF RIGHTS ATTACHING TO SHARES

47. Where the holder of any shares, or any other person appearing to be interested in those shares, fails to comply within fourteen days with a notice in respect of such shares under any provisions of the Statutes regarding disclosure of interests in shares (a "statutory notice"), the Directors may give the holder of those shares a further notice (a "restriction notice") to the effect that from the service of the restriction notice those shares (the "restricted shares") shall be subject to some or all of the following restrictions:

(A) that the restricted shares shall not confer on the holder any right to attend or vote at any general meeting of the Company or at any separate general meeting of the holders of any class of shares in the Company;

(B) that the Directors may withhold payment of all or any part of any dividend (including shares issued in lieu of dividend) on the restricted shares; and

(C) that the Directors may decline to register a transfer of the restricted shares or any of them unless such a transfer is pursuant to an arm' length sale; provided that, where the restricted shares comprise less than 0.25% of the shares of any class, the restriction notice shall only impose the restrictions set out in paragraph (A) above.

48. A restriction notice shall cease to apply to any restricted shares on the expiry of seven days from the earlier of:

(A) receipt by the Company of notice that such restricted shares have been sold to a third party pursuant to an arm's length sale; and

(B) due compliance, to the satisfaction of the Company, with the statutory notice given in respect of such restricted shares.

49. Any new shares issued in right of any shares subject to a restriction notice shall also be subject to the restriction notice.

50. In this Article:

(A) "arm's length sale" means a sale of the entire interest in the shares the subject of the sale on a recognised investment exchange or on acceptance of a takeover offer or pursuant to any other sale which is in the reasonable opinion of the Directors at arm's length;

(B) a person shall be treated as appearing to be interested in any shares if information given in response to a statutory notice fails to establish the identities of those interested in the shares and if (after taking into account the information given in response to any other statutory notice) the Company knows or has reasonable cause to believe that the person in question is or may be interested in the shares; and

(C) reference to a person having failed to comply with a statutory notice includes reference to him having failed or refused to give all or any part of the information required by such notice and reference to his having given information which he knows to be false in a material particular or having recklessly given information which is false in a material particular.

#### SALE OF SHARES BY COMPANY

51. The Company shall be entitled to sell at the best price reasonably obtainable any share of a member or any share to which a person is entitled by transmission if and provided that:-

(A) for a period of twelve years during which at least three dividends have been paid by the Company no cheque or warrant sent by the Company through the post in a pre-paid letter addressed to the member or to the person entitled by transmission to the share at his address on the Register or other the last known address given by the member or the person entitled by transmission to which cheques and warrants are to be sent has been cashed and so far as any director of the Company at the end of such period is then aware no communication has been received by the Company from the member or the person entitled by transmission; and

(B) the Company has at the expiration of the said period of twelve years by advertisement in a national daily newspaper and in a newspaper circulating in the area in which the address referred to in paragraph (A) of this Article is located given notice of its intention to sell such share; and

(C) the Company has not during the further period of three months after the date of publication of the advertisements (or of the later of the two advertisements to be published if they are not published on the same day) and prior to the exercise of the power

of sale received any communication from the member or person entitled by transmission; and

(D) the Company has first given notice in writing to the Quotations Department of the Stock Exchange of its intention to sell such share.

To give effect to any such sale the Company may appoint any person to execute as transferor an instrument of transfer of such share and such instrument of transfer shall be as effective as if it had been executed by the registered holder of or person entitled by the transmission to such share. The Company shall account to the member or other person entitled to such share for the net proceeds of such sale by carrying all monies in respect thereof to a separate account which shall be a permanent debt of the Company and the Company shall be deemed to be a debtor and not a trustee in respect thereof for such member or other person. Monies carried to such separate account may either be employed in the business of the Company or investments (other than shares of the Company or its holding company if any) as the Directors may from time to time think fit.

#### GENERAL MEETINGS

52. The Company shall comply with the provisions of the Statutes regarding the holding of annual general meetings. Subject to such provisions the annual general meeting shall be held at such time and place as may be determined by the Directors.

53. All other general meetings shall be called extraordinary general meetings. The Directors may whenever they think fit, and shall on requisition in accordance with the Statutes, convene an extraordinary general meeting to be held at such time and place as the Directors may determine.

#### NOTICE OF GENERAL MEETINGS

54. An annual general meeting and any general meeting at which it is proposed to pass a special resolution or (save as provided by the Statutes) a resolution of which special notice has been given to the Company, or a resolution appointing a person as a Director, shall be called by twenty-one days' notice in writing at least, and any other general meeting by fourteen day's notice in writing at least (exclusive in either case of the day on which it is served or deemed to be served and of the day for which it is given) given in manner hereinafter mentioned to all members other than such as by or by virtue of these Articles are not entitled to receive such notices from the Company, to the Directors and to the Auditors. Provided that a

general meeting notwithstanding that it has been called by a shorter notice than that specified above shall be deemed to have been duly called if it is so agreed:-

(A) in the case of an annual general meeting by all the members entitled to attend and vote thereat; and

(B) in the case of an extraordinary general meeting by a majority in number of the members having a right to attend and vote thereat, being a majority together holding not less than 95 per cent in nominal value of the shares giving that right.

Provided also that the accidental omission to give notice of a meeting or (in cases where instruments of proxy are sent out with the notice) the accidental omission to send such instrument of proxy to, or the non-receipt of notice of a meeting or such instrument of proxy by, any person entitled thereto shall not invalidate the proceedings at any general meeting.

55. (A) Every notice calling a general meeting shall specify the place and the day and hour of the meeting, and there shall appear with reasonable prominence in every such notice a statement to the effect that a member entitled to attend and vote is entitled to appoint one or more proxies to attend and, on a poll, vote instead of him and that a proxy need not be a member of the Company.

(B) In the case of an annual general meeting the notice shall also specify the meeting as such.

(C) In the case of any general meeting at which business other than routine business is to be transacted the notice shall specify the general nature of such business; and if any resolution is to be proposed as an extraordinary resolution or as a special resolution, the notice shall contain a statement to that effect.

56. Routine business shall mean and include only business transacted at an annual general meeting of the following classes, that is to say:-

(A) declaring dividends;

(B) considering and adopting the accounts, the reports of the Directors and Auditors and other documents required to be annexed to the accounts;

(C) appointing or re-appointing Directors to fill vacancies arising at the meeting on retirement by rotation or otherwise;

(D) re-appointing the retiring Auditors unless they were last appointed otherwise than by the Company in general meeting; and

(E) fixing the remuneration of the Auditors or determining the manner in which such remuneration is to be fixed.

57. The Directors shall on the requisition of members in accordance with the provisions of the Statutes, but subject as therein provided:-

(A) give to the members entitled to receive notice of the next annual general meeting notice of any resolution which may properly be moved and is intended to be moved at that meeting;

(B) circulate to the members entitled to have notice of the next annual general meeting any statement of not more than one thousand words with respect to the matter referred to in any proposed resolution or the business to be dealt with at that meeting.

58. Any member present, either personally or by proxy, at any meeting of the Company shall for all purposes be deemed to have received due notice of such meeting and, where requisite, of the purposes for which such meeting was convened.

#### **PROCEEDINGS AT GENERAL MEETINGS**

59. No business shall be transacted at any general meeting unless a quorum is present at the time when the meeting proceeds to business. Three members present in person or by proxy shall be a quorum for all purposes.

60. The chairman of the Directors, failing whom a deputy chairman (to be chosen, if there be more than one, by agreement amongst them or, failing agreement, by lot) shall preside as chairman at a general meeting. If there be no such chairman or deputy chairman, or if at any meeting none be present within five minutes after the time appointed for holding the meeting or none be willing to act, the Directors present shall choose one of their number or, if no Director be present or if all the Directors present decline to take the chair, the members present shall choose one of their number to be chairman of the meeting.

61. If within fifteen minutes from the time appointed for a general meeting (or such longer period as the chairman of the meeting may think fit to allow) a quorum is not present, the meeting, if convened on the requisition of members, shall be dissolved. In any other case it shall stand adjourned to the same day in the next week, at the same time and place, or to such day and at such time and place as the

chairman of the meeting may determine, and if at such adjourned meeting a quorum is not present within such period from the time appointed for holding the meeting, the members present in person or by proxy, not being less than two, shall be a quorum.

62. The chairman of the meeting may at any time without the consent of the meeting adjourn any general meeting (whether or not it has commenced or a quorum is present) either sine die or to another time or place where it appears to him that the members wishing to attend cannot conveniently be accommodated in the place appointed for the meeting or that the conduct of persons present prevents or is likely to prevent the orderly continuation of business or that an adjournment is otherwise necessary so that the business of the meeting may be properly conducted. In addition the chairman of the meeting may with the consent of any general meeting at which a quorum is present (and shall if so directed by the meeting) adjourn the meeting from time to time (or sine die) and from place to place, but no business shall be transacted at any adjourned meeting except business which might lawfully have been transacted at the meeting from which the adjournment took place. Where a meeting is adjourned sine die, the time and place for the adjourned meeting shall be fixed by the Directors.
63. When a meeting is adjourned for thirty days or more or sine die not less than seven days' notice of the adjourned meeting (exclusive of the day on which it is served or deemed to be served and of the day for which it is given) shall be given as in the case of the original meeting, but it shall not be necessary to specify in such notice the nature of the business to be transacted at the adjourned meeting. Save as aforesaid, it shall not be necessary to give any notice of an adjournment or of the business to be transacted at an adjourned meeting.
64. (A) In the case of any general meeting the Directors may, notwithstanding the specification in the notice of the place of the general meeting (the "principal place") at which the chairman of the meeting shall preside, make arrangements for simultaneous attendance and participation at other places by members and proxies entitled to attend the general meeting but excluded from the principal place under the provisions of this Article.

(B) Such arrangements for simultaneous attendance at the meeting may include arrangements regarding the level of attendance aforesaid at the other places provided that they shall operate so that any members and proxies excluded from attendance at the principal place are able to attend at one of the other places. For the purpose of all other provisions of these Articles any such meeting shall be treated as being held and taking place at the principal place.

(C) The Directors may, for the purpose of facilitating the organisation and administration of any general meeting to which such arrangements apply, from time to time make arrangements, whether involving the issue of tickets (on a basis intended to afford to all members and proxies entitled to attend the meeting an equal opportunity of being admitted to the principal place) or the imposition of some random means of selection or otherwise as they shall in their absolute discretion consider to be appropriate, and may from time to time vary any such arrangements or make new arrangements in their place and the entitlement of any member or proxy to attend a general meeting at the principal place shall be subject to such arrangements as may be for the time being in force whether stated in the notice convening the meeting to apply to that meeting or notified to the members concerned subsequent to the notice convening the meeting.

65. The Directors may direct that members or proxies wishing to attend any general meeting should submit to such searches or other security arrangements or restrictions as the Directors shall consider appropriate in the circumstances and shall be entitled in their absolute discretion to refuse entry to such general meeting to any member or proxy who fails to submit to such searches or otherwise to comply with such security arrangements or restrictions.

66. (A) At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is (before or on the declaration of the result of the show of hands) demanded by either:-

- (i) the chairman of the meeting; or
- (ii) not less than two members present in person or by proxy and entitled to vote; or
- (iii) a member or members present in person or by proxy and representing not less than one-tenth of the total voting rights of all the members having the right to vote at the meeting; or

(iv) a member or members present in person or by proxy and holding shares conferring a right to vote at the meeting being shares on which an aggregate sum has been paid up equal to not less than one-tenth of the total sum paid up on all the shares conferring the right.

(B) A demand for a poll may be withdrawn only with the consent of the meeting. Unless a poll is so demanded (and the demand is not withdrawn) a declaration by the chairman of the meeting that a resolution has been carried, or carried unanimously, or by a particular majority, or lost, and an entry to that effect in the minute book, shall be conclusive evidence of that fact without proof of the number or proportion of the votes recorded for or against such resolution.

67. (A) If a poll is duly demanded (and the demand is not withdrawn) it shall be taken in such manner (including the use of ballot or voting papers or tickets) as the chairman of the meeting may direct, and the result of the poll shall be deemed to be the resolution of the meeting at which the poll was demanded. The chairman of the meeting may (and if so directed by the meeting shall) appoint scrutineers and may adjourn the meeting to some place and time fixed by him for the purpose of declaring the result of the poll.

(B) A poll demanded on the election of a chairman or on a question of adjournment shall be taken forthwith. A poll demanded on any other question shall be taken either immediately or at such subsequent time (not being more than thirty days from the date of the meeting) and place as the chairman may direct. No notice need be given of a poll not taken immediately. The demand for a poll shall not prevent the continuance of the meeting for the transaction of any business other than the question on which the poll has been demanded.

68. In the case of an equality of votes, whether on a show of hands or on a poll, the chairman of the meeting at which the show of hands takes place or at which the poll is demanded shall be entitled to a second or casting vote.

69. If an amendment shall be proposed to any resolution under consideration but shall in good faith be ruled out of order by the chairman of the meeting, the proceedings on the substantive resolution shall not be invalidated by any error in such ruling. In the case of a resolution duly proposed as a special or extraordinary

resolution no amendments thereto (other than a mere clerical amendment to correct a patent error) may in any event be considered or voted upon.

70. If any votes shall be counted which ought not to have been counted, or might have been rejected, the error shall not vitiate the result of the voting unless it is pointed out at the same meeting, or at any adjournment thereof, and not in that case unless it shall in the opinion of the chairman of the meeting be of sufficient magnitude to affect the result of the voting.

### VOTES OF MEMBERS

71. Subject to any special rights or restrictions as to voting attached by or by virtue of these Articles to any shares or any class of shares, on a show of hands every member who is present in person shall have one vote and on a poll every member who is present in person or by proxy shall have one vote for every share of which he is the holder.

72. In the case of joint holders of a share the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders and for this purpose seniority shall be determined by the order in which names stand in the Register in respect of the joint holding.

73. Where in England or elsewhere a receiver or other person (by whatever name called) has been appointed by any court claiming jurisdiction in that behalf to exercise power with respect to the property or affairs of any member on the ground (however formulated) of mental disorder, the Directors may in their absolute discretion, upon or subject to production of such evidence as they may require, permit such receiver or other person to vote in person or by proxy on behalf of such member at any general meeting.

74. No member shall, unless the Directors otherwise determine, be entitled to be present or to vote at any general meeting either in person or by proxy or upon any poll or to exercise any other right conferred by membership in relation to meetings of the Company in respect of any shares held by him if any call or other sum presently payable by him to the Company in respect of those shares remains unpaid.

75. No objection shall be raised as to the admissibility of any vote except at the meeting or adjourned meeting or poll at which the vote objected to is or may be given or tendered and every vote not disallowed at such meeting shall be valid for all purposes. Any such objection shall be referred to the chairman of the meeting whose decision shall be final and conclusive.

76. On a poll votes may be given either personally or by proxy and a person entitled to more than one vote need not use all his votes or cast all his votes in the same way.

### PROXIES

77. A proxy need not be a member of the Company. A member may appoint more than one proxy in respect of the same meeting or poll provided that the instrument appointing the proxy shall specify the number of shares in respect of which the proxy is appointed and only one proxy shall be appointed in respect of any one share. When two or more valid but differing appointments of proxy are executed in respect of the same share for use at the same meeting, the one which is last executed shall be treated as replacing and revoking the others as regards that share. If the Company is unable to determine which was last executed none of them shall be treated as valid in respect of that share.

78. An instrument appointing a proxy shall be in writing in any usual or common form or in any other form which the Directors may accept and:-

(A) in the case of an individual shall be signed by the appointor or by his attorney; and

(B) in the case of a corporation shall be either given under its common seal or signed on its behalf by an attorney or a duly authorised officer of the corporation.

The Directors may, but shall not be bound to, require evidence of the authority of any such attorney or officer. The signature on such instrument need not be witnessed.

79. An instrument appointing a proxy, together with the power of attorney or other authority (if any) under which it is signed or a copy thereof authenticated in a manner acceptable to the Directors, must be left at such place or one of such places (if any) as may be specified for that purpose in or with the notice convening the meeting or in any instrument of proxy sent out by the Company in relation to the meeting (or, if no place is so specified, at the Office) not less than forty eight hours before the time appointed for the holding of the meeting or adjourned meeting or for the taking of the poll at which it is to

be used, and in default shall not be treated as valid, but the Directors may waive compliance with this provision in their discretion. An instrument of proxy relating to more than one meeting (including any adjournment thereof) having once been so left for the purposes of any meeting shall not require again to be delivered in relation to any subsequent meeting to which it relates. No instrument appointing a proxy shall be valid after the expiration of twelve months from the date named in it as the date of its signature, except at an adjourned meeting or on a poll demanded at a meeting or an adjourned meeting in cases where the meeting was originally held within twelve months from such date.

80. An instrument appointing a proxy shall be deemed to include the right to demand or join in demanding a poll and shall, unless the contrary is stated thereon, be valid as well for any adjournment of the meeting as for the meeting to which it relates.

81. A vote cast by proxy shall not be invalidated by the previous death or insanity of the principal or by the revocation of the appointment of the proxy or of the authority under which the appointment was made or by the transfer of the share in respect of which the proxy was given provided that no intimation in writing of such death, insanity or revocation shall have been received by the Company at the Office or that no transfer as aforesaid shall have been registered by the Company at least three hours before the commencement of the meeting or adjourned meeting or the time appointed for the taking of the poll at which the vote is cast.

82. The Directors may at the expense of the Company send, by post or otherwise, to members instruments of proxy (with or without provision for their return prepaid) for use at any general meeting or at any meeting of any class of members of the Company in such form as the Directors may determine. If for the purpose of any meeting invitations to appoint as proxy a person, or one of a number of persons, specified in the invitations are issued at the Company's expense they shall be issued to all (and not to some only) of the members entitled to be sent notice of the meeting and to vote thereat by proxy.

#### **CORPORATIONS ACTING BY REPRESENTATIVES**

83. Any corporation which is a member of the Company may by resolution of its directors or other governing body authorise such person as it thinks fit to act as its representative at any meeting of the Company or of any class of members of the Company. The person so authorised shall be entitled to exercise the same powers on behalf of such

corporation as the corporation could exercise if it were an individual member of the Company and such corporation shall for the purposes of these Articles be deemed to be present in person at any such meeting if a person so authorised is present thereat.

#### DIRECTORS

84. Subject as hereinafter provided the number of Directors shall not be less than two nor more than 12. The Company may by ordinary resolution from time to time vary the minimum or maximum number of Directors.

85. The Directors shall be entitled to ordinary remuneration at such rate as the Directors may from time to time determine, not exceeding £150,000 per annum in aggregate or such higher sum as the Company may from time to time by ordinary resolution determine, divisible in such proportions and in such manner as the Directors may from time to time determine. Such remuneration shall accrue from day to day.

86. The Directors may repay to any Director all such reasonable expenses as he may incur in attending and returning from meetings of the Directors or of any committee of the Directors or general meetings or class meetings or otherwise in or about the business of the Company.

87. Any Director who is appointed to any executive office or who serves on any committee or who otherwise performs services which in the opinion of the Directors are outside the scope of the ordinary duties of a Director may be paid such extra remuneration by way of salary, commission, bonus or otherwise (whether expressed to be exclusive or inclusive of his remuneration (if any) under these Articles) as the Directors may determine.

88. The Directors shall have power to pay and agree to pay pensions or other retirement, superannuation, death or disability benefits to (or to any person in respect of) any Director or ex-Director of the Company or any other company in which the Company is or may have been or may become interested, and for the purpose of providing any such pensions or other benefits to contribute to any scheme or fund or to pay premiums.

89. A Director or intending Director (including an alternate Director) may contract or be interested in any contract or arrangement with the Company or any other company in which the Company is or may have been or may become interested and hold any office or

place of profit (other than the office of auditor of the Company or any subsidiary undertaking thereof) under the Company or any such other company and he (or any firm of which he is a member) may act in a professional capacity for the Company or any such other company and (save as otherwise agreed) may retain for his own absolute use and benefit all emoluments, dividends, profits, benefits and other advantages accruing to him therefrom.

90. (A) Subject to the provisions of the Statutes, the Directors may from time to time appoint one or more of their body to be holder of any executive office (including, where considered appropriate, the office of chairman or deputy chairman) on such terms and for such period as they may determine and, without prejudice to any claim for damages under any contract entered into in any particular case, may at any time revoke any such appointment.

(B) The appointment of any Director to the office of chairman or deputy chairman or managing or joint managing or deputy or assistant managing director shall automatically terminate if he ceases to be a Director, but without prejudice to any claim by either the Company or the Director for damages for breach of any contract between him and the Company.

(C) The appointment of any Director to any other executive office shall not automatically terminate if he ceases from any cause to be a Director, unless the contract or resolution under which he holds office shall expressly state otherwise, in which event such termination shall be without prejudice to any claim by either the Company or the Director for damages for breach of any contract between him and the Company.

#### APPOINTMENT AND RETIREMENT OF DIRECTORS

91. Unless and until otherwise determined by the Company by ordinary resolution, either generally or in any particular case, any provisions of the Statutes which, subject to the provisions of these Articles, would have the effect of rendering any person ineligible for appointment as a Director or liable to vacate office as a Director on account of his having reached any specified age or of requiring special notice or any other special formality in connection with the appointment of any Director over a specified age, shall not apply to the Company. Where the Directors convene any general meeting of the Company at which, to the knowledge of the Directors, a person will be proposed for appointment or reappointment as a Director who at the date for which the meeting is convened will have attained the age of seventy years or more, the Directors shall give notice of his age in years in the notice

convening the meeting or in any document accompanying the notice and shall give an explanation in such notice or document of why it is felt appropriate that such person be appointed or retained as a Director.

92. A Director and an alternate Director shall not require a share qualification but nevertheless shall be entitled to attend and speak at any general meeting of the Company and at any separate meeting of the holders of any class of shares in the Company.

93. Subject to Article 94 below, at each Annual General Meeting one-third of the Directors for the time being (or, if their number is not a multiple of three, the number nearest to but not less than one-third) shall retire from office by rotation, provided that no director appointed by the Directors since the last annual general meeting shall be taken into account in determining the number of directors to retire. In any event all directors shall offer themselves for re-election on at least one occasion in every period of three years, such period being calculated from the date of their appointment or last re-election as the case may be.<sup>1</sup>

94. The Directors to retire by rotation shall include (so far as necessary to obtain the number required) any Director who wishes to retire and not to offer himself for re-election. Any further Directors so to retire shall be those of the other Directors subject to retirement by rotation who have been longest in office since their last re-election or appointment and so that as between persons who became or were last re-elected Directors on the same day, those to retire shall (unless they otherwise agree among themselves) be determined by lot.

95. A retiring Director shall be eligible for re-election. The Company at the meeting at which a Director retires under any provisions of these Articles may by ordinary resolution fill up the office being vacated by electing thereto the retiring Director or some other person eligible for appointment. In default the retiring Director shall be deemed to have been re-elected except in any of the following cases : -

(A) where at such meeting it is expressly resolved not to fill up such office or a resolution for the re-election of such Director is put to the meeting and lost;

(B) where such Director has given notice in writing to the Company that he is unwilling to be re-elected; or

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<sup>1</sup> Amended by a special resolution of the Company on 17 February 2000

(C) where the default is due to the moving of a resolution in contravention of the next following Article.

96. The retirement shall not have effect until the conclusion of the meeting except where a resolution is passed to elect some other person in the place of the retiring Director or a resolution for his re-election is put to the meeting and lost and accordingly a retiring Director who is re-elected or deemed to have been re-elected (and his alternate, if any) will continue in office without break.

97. The Company may in accordance with and subject to the provisions of the Statutes by ordinary resolution of which special notice has been given remove any Director from office notwithstanding any provision of these Articles or of any agreement between the Company and such Director, but without prejudice to any claim he may have for damages for breach of any such agreement, and appoint another person in place of a Director so removed from office. Any person so appointed shall be treated for the purpose of determining the time at which he or any other Director is to retire by rotation as if he had become a Director on the day on which the Director in whose place he is appointed was last elected a Director. In default of such appointment the vacancy arising upon the removal of a Director from office may be filled as a casual vacancy.

98. The Company may by ordinary resolution and the Directors shall have power at any time and from time to time to appoint any person to be a Director either to fill a casual vacancy or as an additional Director, but so that the total number of Directors shall not at any time exceed the maximum number (if any) fixed by or in accordance with these Articles. Any Director so appointed by the Directors shall hold office only until the next annual general meeting and shall then be eligible for re-election but shall not be taken into account in determining the number of Directors who are to retire by rotation at such meeting.

99. A resolution for the appointment of two or more persons as Directors by a single resolution shall not be moved at any general meeting unless a resolution that it shall be so moved has first been agreed to by the meeting without any vote being given against it; and any resolution moved in contravention of this provision shall be void.

100. No person other than a Director retiring at the meeting shall, unless recommended by the Directors for election, be eligible for appointment as a Director at any general meeting unless not less than seven nor more than forty-two clear days before the day appointed for the meeting there shall have been left at the Office notice in writing signed by some member (other than the person to be proposed) duly qualified to attend and vote at the meeting for which such notice is given of his intention to propose such person for election and also notice in writing signed by the person to be proposed of his willingness to be elected.

101. The office of a Director shall be vacated in any of the following events, namely :-

- (A) if he shall become prohibited by law from acting as a Director;
- (B) if he shall resign in writing under his hand left at the Office or if he shall tender his resignation and the Directors shall resolve to accept the same;
- (C) if he shall become bankrupt or shall make any arrangement with or compound with his creditors generally;
- (D) if he is, or may be, suffering from mental disorder and either :-
  - (v) he is admitted to hospital in pursuance of an application for admission for treatment under the Mental Health Act 1983 or, in Scotland, an application for admission under the Mental Health (Scotland) Act 1960, or
  - (vi) an order is made by a Court having jurisdiction (whether in the United Kingdom or elsewhere) in matters concerning mental disorder for his detention or for the appointment of a receiver, curator bonis or other person to exercise powers with respect to his property or affairs;
- (E) if he shall be absent from meetings of the Directors for six months without leave (and his alternate Director, if any, shall not during such period have attended in his stead) and the Directors shall resolve that his office be vacated;
- (F) if when there are at least three Directors he shall be requested in writing by all his co-Directors to resign; or
- (G) at any annual general meeting after he shall have attained the age of sixty-five unless during the four months preceding that annual general meeting he be requested by resolution of the Directors to continue in office.; or
- (H) if any contract with the Company relating to his appointment as a Director or to any executive office is terminated by the Company, unless the Directors resolve that he should continue in office as a Director.

### ALTERNATE DIRECTORS

102. (A) Any Director may at any time by writing under his hand deposited at the Office, or delivered at a meeting of the Directors, appoint any person to be his alternate Director and may in like manner at any time terminate such appointment. Such appointment, unless previously approved by the Directors or appointing another Director as an alternate, shall have effect only upon and subject to being so approved.

(B) The appointment of an alternate Director shall terminate on the happening of any event which if he were a Director would cause him to vacate such office or if his appointor ceases to be a Director.

(C) An alternate Director shall (except when absent from the United Kingdom) be entitled to be given notice of meetings of the Directors of which his appointor is not given notice due to his appointor's absence from the United Kingdom or of which his appointor shall have requested, in writing under the appointor's hand deposited at the Office or delivered at a meeting of the Directors, that he be given notice either generally or in any particular case or cases.

(D) An alternate Director shall be entitled to attend and vote as a Director at any meeting of the Directors at which the Director appointing him is not personally present and generally at such meeting to perform all functions of his appointor as a Director and for the purposes of the proceedings at such meeting the provisions of these Articles shall apply as if he were a Director. If his appointor is for the time being absent from the United Kingdom or temporarily unable to act through ill-health or disability his signature to any resolution in writing of the Directors shall be as effective as the signature of his appointor. To such extent as the Directors may from time to time determine in relation to any committee of the Directors the provisions of paragraphs (C) and (D) of this Article shall also apply to any meeting of any such committee of which his appointor is a member. An alternate Director shall not (save as aforesaid) have power to act as a Director nor shall he be deemed to be a Director for the purposes of these Articles.

(E) An alternate Director shall be an officer of the Company and shall alone be responsible to the Company for his own acts and defaults and he shall not be deemed an agent of or for the Director appointing him. An alternate Director may be interested in contracts, arrangements and other proposals, may be repaid expenses by the Company and shall be entitled to be indemnified by the Company to the same extent as if he were a Director, but he shall not be entitled to receive from the Company in respect of his appointment as alternate Director any remuneration except only such proportion (if any) of

the remuneration otherwise payable to his appointor as such appointor may by notice in writing to the Company from time to time direct.

(F) Where an alternate Director is the alternate of more than one Director and attends a meeting of the Directors or a meeting of a committee of the Directors which the Directors have determined he is entitled to attend in his capacity as an alternate, he shall in the absence of more than one appointor have a separate vote for each appointor for whom he is attending; if he is himself a Director his vote or votes as an alternate Director shall be in addition to his own vote as a Director.

### PROCEEDINGS OF DIRECTORS

103. The Directors may meet together for the despatch of business, adjourn and otherwise regulate their meetings as they think fit. Questions arising at any meeting shall be determined by a majority of votes. In the case of an equality of votes the chairman of the meeting shall have a second or casting vote. A Director may, and the Secretary on the requisition of a Director shall, at any time summon a meeting of the Directors. Any Director may waive notice of any meeting and any such waiver may be retrospective.

104. A Director who is unable to attend any meeting of the Directors and has not appointed an alternate Director may authorise any other Director to vote for him at that meeting, and in that event the Director so authorised shall have a vote for each Director by whom he is so authorised, in addition to his own vote. Any such authority may be in writing or by cable, telex, radiogram or telegram, which must be produced at the meeting at which the same is to be used, and left with the Secretary for filing.

105. All or any of the Directors may participate in a meeting of the Directors by any lawful means including by means of a conference telephone or any communication equipment which allows all persons participating in the meeting to hear and speak to each other at the same time. A person so participating shall be deemed to be present in person at the meeting and shall be entitled to vote and be counted in the quorum accordingly. Such a meeting shall be deemed to take place where the largest group of those participating is assembled or, if there is no such group, where the chairman of the meeting then is.

106. The quorum necessary for the transaction of the business of the Directors may be fixed by the Directors and unless so fixed at any other number shall be two. For the purposes of this Article an alternate Director shall be counted in a quorum, but so that not

less than two individuals shall constitute the quorum. A meeting of the Directors at which a quorum is present shall be competent to exercise all powers and discretions for the time being exercisable by the Directors.

107. A Director who is in any way, whether directly or indirectly, interested in a contract or proposed contract or any other arrangement or proposed arrangement with the Company shall declare the nature and extent of his interest.

108. (A) Save as provided in this Article, a Director shall not vote in respect of any contract or arrangement or any other proposal whatsoever in which he has an interest which (together with any interest of any person connected with him) is to his knowledge a material interest otherwise than by virtue of his interests in shares or debentures or other securities of or otherwise in or through the Company. A Director shall not be counted in the quorum at a meeting in relation to any resolution on which he is debarred from voting.

(B) A Director shall (in the absence of some other material interest than is indicated below) be entitled to vote (and be counted in the quorum) in respect of any resolution concerning any of the following matters, namely:-

(i) the giving of any security, guarantee or indemnity in respect of money lent or obligations incurred by him or by any other person at the request of or the benefit of the Company or any of its subsidiary undertakings;

(ii) the giving of any security, guarantee or indemnity in respect of a debt or obligation of the Company or any of its subsidiary undertakings for which he himself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;

(iii) where the Company or any of its subsidiary undertakings is offering securities in which offer the Director is or may be entitled to participate as a holder of securities or in the underwriting or sub-underwriting of which the Director is to participate;

(iv) another company in which he and any persons connected with him do not to his knowledge hold an interest in shares (as that term is used in sections 198 to 211 of the Act) representing one per cent or more of either any class of the equity share capital, or the voting rights, in such company;

(v) an arrangement for the benefit of the employees of the Company or any of its subsidiary undertakings which does not award him any privilege or benefit not generally awarded to the employees to whom such arrangement relates; or

(vi) insurance which the Company proposes to maintain or purchase for the benefit of Directors or for the benefit of persons including Directors.

(C) Where proposals are under consideration concerning the appointment (including fixing or varying the terms of appointment) of two or more Directors to offices or employments with the Company or any company in which the Company is interested, such proposals may be divided and considered in relation to each Director separately and in such case each of the Directors concerned (if not debarred from voting under the proviso to paragraph (B)(iv) of this Article) shall be entitled to vote (and be counted in the quorum) in respect of each resolution except that concerning his own appointment.

(D) If any question shall arise at any meeting as to the materiality of a Director's interest or as to the entitlement of any Director to vote and such question is not resolved by his voluntarily agreeing to abstain from voting, such question shall be referred to the chairman of the meeting and his ruling in relation to any Director other than himself shall be final and conclusive, except in a case where the nature or extent of the interests of the Director concerned has not been fully disclosed.

109. The continuing Directors may act notwithstanding any vacancy in their number, but if and so long as the number of Directors is reduced below the minimum number fixed by or in accordance with these Articles the continuing Directors or Director may act for the purpose of filling up such vacancies or of summoning general meetings of the Company, but not for any other purpose. If there be no Directors or Director able or willing to act, then any two members may summon a general meeting for the purpose of appointing Directors.

110. The Directors may elect a chairman and, if thought fit, one or more deputy chairmen and determine the period for which each is to hold office. The chairman, failing whom a deputy chairman (to be chosen, if there be more than one, by agreement amongst them or failing agreement by lot), shall preside at all meetings of the Directors, but if no chairman or deputy chairman shall have been elected, or if at any meeting none be present within five minutes after the time appointed for holding the meeting or none be willing to act, the Directors present may choose one of their number to be chairman of the meeting.

111. A resolution in writing signed by, or by the alternate Directors of, all the Directors who are or whose alternate Directors are for the time being in the United Kingdom shall be as effective as a resolution passed at a meeting of the Directors duly convened and held

and may consist of several documents in the like form, each signed by one or more of the Directors; any such resolution may be signed by an alternate Director in place of his appointor if his appointor is for the time being absent from the United Kingdom or temporarily unable to act through ill-health or disability.

### **BORROWING POWERS**

112. (A) Subject as hereinafter provided the Directors may exercise all the powers of the Company to borrow money, and to mortgage or charge its undertaking, property and uncalled capital or any part thereof and, subject to the provisions of section 80 of the Act, to issue debentures and other securities whether outright or as collateral security for any debt, liability or obligation of the Company or of any third party.

(B) The Directors shall restrict the borrowings of the Company and exercise all voting and other rights or powers of control exercisable by the Company at general meetings of its subsidiary undertakings (if any) so as to secure (so far, as regards subsidiary undertakings, as by such exercise they can secure) that the aggregate amount for the time being remaining undischarged of all monies borrowed by the Group (which expression means the Company and its subsidiary undertakings for the time being) shall not (excluding intra-Group borrowings) at any time without the previous sanction of an ordinary resolution of the Company exceed a sum equal to two and a half (2.5) times the adjusted total of capital and reserves.

(C) For the purpose of this Article:-

(i) The following shall (unless otherwise taken into account) be deemed to constitute monies borrowed:-

- (a) the principal amount outstanding in respect of any debenture notwithstanding that the same may have been issued in whole or in part for a consideration other than cash;
- (b) the principal amount outstanding in respect of any debenture of any member of the Group which is not beneficially owned within the Group;
- (c) the principal amount outstanding under any bill accepted by any member of the Group and not beneficially owned within the Group or under any acceptance credit opened on behalf of or in favour of any member of the Group other than by another member of the Group (not being an amount

outstanding in respect of the purchase of goods in the ordinary course of trading;

- (d) the nominal amount of the issued and paid-up preference share capital of any subsidiary undertaking of the Company not beneficially owned within the Group;
- (e) the nominal amount of any issued share capital and the principal amount of any monies borrowed (not being issued share capital or monies borrowed beneficially owned within the Group) the redemption or repayment whereof is guaranteed or secured by the Company or by any of its subsidiary undertakings; and
- (f) any fixed or minimum premium payable on final redemption or repayment of any debentures or other monies borrowed or share capital in addition to the principal or nominal amount thereof.

(ii) Monies borrowed for the purpose of and actually applied within six months in repaying the whole or any part of other monies borrowed by the Group and for the time being outstanding shall not pending their application for such purpose be deemed to be monies borrowed.

(iii) Monies borrowed from bankers or others for the purpose of financing any contract up to an amount not exceeding that part of the price receivable under the contract which is guaranteed or insured by the Export Credit Guarantees Department or any other institution or body carrying on a similar business shall be deemed not to be monies borrowed.

(D) For the purposes of this Article:-

- (i) The adjusted total of capital and reserves means:-
  - (a) the nominal amount of the issued and paid up or credited as paid up share capital for the time being of the Company; and
  - (b) the amount standing to the credit of the consolidated reserves of the Group including share premium account and capital redemption reserve fund (if any) and the amount standing to the credit of the consolidated profit and loss account,

all as shown in a consolidation of the most recent audited balance sheets of the Company and its subsidiary undertakings available at the date the calculation falls to be made but after:-

- (a) adjusting as may be necessary in respect of any variation in such paid up share capital and reserves since the dates of such balance sheets but so far as profit and loss account is concerned only to take account of (I) any distribution (otherwise than within the Group) paid, recommended or declared and not (A) already provided for as a liability in such balance sheets or (B) being a normal preference or interim dividend payable out of profits since earned and (II) any provision made other than out of profits since earned,
- (b) excluding any sum set aside for taxation (other than deferred taxation),
- (c) excluding a sum equal to the book value of goodwill other than goodwill arising upon such consolidation (the amount of which so far as previously written off to be written back); and
- (d) deducting if not already deducted any debit balance on profit and loss account.

(ii) Share capital allotted shall be treated as issued and any share capital already called up or payable at any future date within the following twelve months shall be treated as already paid up and if the Company proposes to issue any shares for cash and the issue of such shares has been underwritten then such shares shall be deemed to have been issued and the subscription monies (including any premium) payable in respect thereof within the following twelve months shall be deemed to have been paid up.

(iii) In calculating the adjusted total of capital and reserves any adjustments may be made that the Auditors may certify in their opinion to be appropriate, including in particular adjustments to provide for the carrying into effect of any transaction for the purposes of or in connection with which it requires to be calculated.

(iv) The certificate of the Auditors as to the amount of the adjusted total of capital and reserves at any time shall be conclusive and binding upon all concerned.

(E) No person dealing with the Company or any of its subsidiaries shall by reason of the foregoing provisions of this Article be concerned to see or inquire whether this limit is observed, and no debt incurred or security given in excess of such limit shall

be invalid or ineffectual unless the lender or the recipient of the security had at the time when the debt was incurred or security given express notice that the limit hereby imposed had been or would thereby be exceeded.

#### GENERAL POWERS OF DIRECTORS

113. The business of the Company shall be managed by the Directors, who may exercise all such powers of the Company as are not by the Statutes or by these Articles required to be exercised by the Company in general meeting, subject nevertheless to any regulations of these Articles, to the provisions of the Statutes and to such regulations, being not inconsistent with the aforesaid regulations or provisions, as may be prescribed by special resolution of the Company, but no regulation so made by the Company shall invalidate any prior act of the Directors which would have been valid if such regulation had not been made. The general powers given by this Article shall not be limited or restricted by any special authority or power given to the Directors by any other Article.

114. The Directors may delegate any of their powers to committees consisting of such person or persons (whether Directors or not) upon such terms and conditions and with such restrictions as they think fit provided that the majority of the members of the committee are Directors. Any such delegation (which may include authority to sub-delegate all or any of the powers so delegated) may be collateral with, or to the exclusion of, the powers which are the subject of the delegation (or sub-delegation). Any committees so formed shall in the exercise of the powers so delegated conform to any regulations which may from time to time be imposed by the Directors and any or all of the powers so delegated may be altered, waived, withdrawn or revoked by the Directors.

115. The meetings and proceedings of any such committee consisting of two or more members shall be governed by the provisions of these Articles regulating the meetings and proceedings of the Directors (including, without limitation, provisions relating to written resolutions), so far as the same are applicable and are not superseded by any regulations made by the Directors under the last preceding Article.

116. The Directors delegate any of their powers to any Director upon such terms and conditions and with such restrictions as they think fit. Any such delegation (which may include authority to sub-delegate all or any of the powers so delegated) may be collateral with, or to the exclusion of, the powers which are the subject of the delegation (or sub-delegation). Any or all of the powers so delegated may be altered, waived, withdrawn or revoked by the Directors.

117. The Directors may establish any local boards or agencies for managing any of the affairs of the Company, either in the United Kingdom or elsewhere, and may appoint any persons to be members of such local boards, or any managers or agents, and may fix their remuneration, and may delegate to any local board, manager or agent any of the powers, authorities and discretions vested in the Directors, with power to sub-delegate, and may authorise the members of any local boards, or any of them, to fill any vacancies therein, and to act notwithstanding vacancies, and any such appointment or delegation may be made upon such terms and subject to such conditions as the Directors may think fit, and the Directors may remove any person so appointed, and may annul or vary any such delegation, but no person dealing in good faith and without notice of any annulment or variation shall be affected thereby.

118. The Directors may from time to time and at any time by power of attorney or otherwise appoint any company, firm or person or any fluctuating body of persons, whether nominated directly or indirectly by the Directors, to be the attorney or attorneys of the Company for such purposes and with such powers, authorities and discretions (not exceeding those vested in or exercisable by the Directors under these Articles) and for such period and subject to such conditions as they may think fit, and any such power of attorney may contain such provisions for the protection and convenience of persons dealing with any such attorney as the Directors may think fit, and may also authorise any such attorney to sub-delegate all or any of the powers, authorities and discretions vested in him. The Directors may revoke or vary the appointment but no person dealing in good faith with the Company and without notice of the revocation or variation shall be affected by it.

119. Any power of the Directors to delegate any of their powers under these Articles (and the power to sub-delegate any of such powers) shall be effective in relation to the powers, authorities and discretions of the Directors generally and shall not be limited by the fact that in certain articles, but not in others, express reference is made to particular powers,

authorities or discretions being exercised by the Directors or by a committee of the Directors.

120. All acts done by or in pursuance of a resolution of any meeting of the Directors, or of a committee of Directors, or by any person acting as a Director or alternate Director or as a member of a committee, shall as regards all persons dealing in good faith with the Company, notwithstanding that there was some defect in the appointment or continuance in office of any such Director or alternate Director, or person acting as aforesaid, or that they or any of them were disqualified or had vacated office, or were not entitled to vote, be as valid as if every such person had been duly appointed and was qualified and had continued to be a Director or alternate Director and had been entitled to vote.

121. The Directors may from time to time appoint any person to an office or employment having a designation or title including the word "Director" or attach to any existing office or employment with the Company such a designation or title. The inclusion of the word "Director" in the designation or title of any office or employment with the Company shall not imply that the holder thereof is a Director of the Company nor shall such holder thereby be empowered in any respect to act as a Director of the Company or be deemed to be a Director for any of the purposes of these Articles or the Statutes.

122. Subject to and to the extent permitted by the Statutes, the Company, or the Directors on behalf of the Company, may cause to be kept in any territory a branch register of members resident in such territory, and the Directors may make and vary such regulations as they may think fit regarding the keeping of any such register.

123. All cheques, promissory notes, drafts, bills of exchange and other negotiable or transferable instruments, and all receipts for monies paid to the Company, shall be signed, drawn, accepted, endorsed or otherwise executed, as the case may be, in such manner as the Directors shall from time to time determine.

124. If any uncalled capital of the Company is included in or charged by any mortgage or other security, the Directors may delegate to the person in whose favour such mortgage or security is executed, or to any other person in trust for him, the power to make calls on the members in respect of such uncalled capital, and to sue in the name of the Company or otherwise for the recovering of monies becoming due in respect of calls so made and to

give valid receipts for such monies, and the power so delegated shall subsist during the continuance of the mortgage or security, notwithstanding any change of Directors, and shall be assignable if expressed so to be.

125. A register of Directors' interests shall be kept in accordance with the Statutes and shall be open to the inspection of any member or holder of debentures of the Company or of any other person authorised by the Statutes between the hours 10 am and noon on each day during which the same is bound to be open for inspection pursuant to the Statutes. The register shall also be produced at the commencement of each annual general meeting and shall remain open and accessible during the continuance of the meeting to any person attending the meeting.

#### SECRETARY

126. (A) The Secretary shall be qualified in accordance with the provisions of the Statutes and shall be appointed by the Directors on such terms and for such period as they may think fit. The Secretary may at any time be removed from office by the Directors, but without prejudice to any claim for damages for breach of any contract between him and the Company.

(B) Any provision of the Statutes or of these Articles requiring or authorising a thing to be done by or to a Director and the Secretary shall not be satisfied by its being done by or to the same person acting both as Director and as, or in the place of, the Secretary.

#### THE SEAL

127. (A) The Directors shall provide for the safe custody of the Seal, which shall only be used by the authority of the Directors or of a committee of the Directors authorised by the Directors in that behalf, and every instrument to which the Seal shall be affixed shall (subject to the provisions of paragraph (B) of this Article and to sub-Sections 185(3) and (4) of the Act) be signed by a Director and shall be countersigned by a second Director or by the Secretary or some other person appointed by the Directors for the purpose and in favour of any purchaser or other person dealing with the Company in good faith and relying thereon such signatures shall be exclusive evidence of the fact that the Seal has been properly affixed.

(B) The Directors may determine that the signature and countersignature of certificates for shares, debentures or other securities of the Company or any class thereof

shall be dispensed with or affixed by some method or system of mechanical signature or that the certificates shall bear the names of the Company's issuing agents.

128. The Company may exercise the powers conferred by the Statutes with regard to having an official seal for use abroad and such powers shall be vested in the Directors.

#### **AUTHENTICATION OF DOCUMENTS**

129. Any Director or the Secretary or any person appointed by the Directors for the purpose shall have power to authenticate any documents affecting the constitution of the Company and any resolutions passed by the Company or the Directors or any committee of the Directors, and any books, records, documents and accounts relating to the business of the Company, and to certify copies thereof or extracts therefrom as true copies or extracts; and where any books, records, documents or accounts are elsewhere than at the Office the local manager or other officer of the Company having the custody thereof shall be deemed to be a person appointed by the Directors as aforesaid. A document purporting to be a copy of a resolution, or an extract from the minutes of a meeting of the Company or of the Directors or any committee of the Directors which is certified as aforesaid shall be conclusive evidence in favour of all persons dealing with the Company in good faith and relying thereon that such resolution has been duly passed or, as the case may be, that such minutes are or extract is true and accurate record of proceedings at a duly constituted meeting.

#### **DIVIDENDS**

130. The Company may by ordinary resolution declare dividends and fix the time for payment thereof, but no dividend shall be payable except out of profits of the Company available for distribution in accordance with the Statutes or in excess of the amount, or at any earlier date than, recommended by the Directors.

131. Unless and to the extent that the rights attached to any shares or the terms of issue thereof otherwise provide, dividends may be declared or paid in any currency.

132. Unless and to the extent that the rights attached to any shares or the terms of issue thereof otherwise provide, all dividends shall (as regards any shares not fully paid throughout the period in respect of which the dividend is paid) be apportioned and paid pro rata according to the amounts paid on the shares during any portion or portions of the

period in respect of which the dividend is paid. For the purposes of this Article no amount paid on a share in advance of call shall be treated as paid on the share.

133. Subject to the provisions of the Statutes, if and so far as in the opinion of the Directors the profits of the Company justify such payments, the Directors may pay the fixed dividend on any class of shares carrying a fixed dividend expressed to be payable on fixed dates on the half-yearly or other dates prescribed for the payment thereof and may also from time to time pay interim dividends of such amounts and on such dates and in respect of such periods as they think fit. A resolution of the Directors declaring any such dividend shall (once published with their authority) be irrevocable and have the same effect as if such dividend had been declared upon the recommendation of the Directors by an ordinary resolution of the Company. Provided the Directors act bona fide they shall not incur any responsibility to the holders of shares conferring a preference for any damage they may suffer by reason of the payment of any interim dividend on any shares having deferred or non-preferred rights.

134. Subject to the provisions of the Statutes, where any asset, business or property is bought by the Company as from a past date the profits and losses thereof as from such date may at the discretion of the Directors in whole or in part be carried to revenue account and treated for all purposes as profits or losses of the Company. Subject as aforesaid, if any shares or securities are purchased cum dividend or interest, such dividend or interest may at the discretion of the Directors be treated as revenue, and it shall not be obligatory to capitalise the same or any part thereof.

135. No dividend or other monies payable on or in respect of a share shall bear interest as against the Company.

136. The Directors may retain any dividend or other monies payable on or in respect of any share :-

(A) on which the Company has a lien, and may apply the same in or towards satisfaction of the debts, liabilities, or engagements in respect of which the lien exists;

(B) in respect of which any person is under the provisions as to the transmission of shares hereinbefore contained entitled to become a member, or which any person is under those provisions entitled to transfer, until such person shall become a member in respect of such shares or shall transfer the same; or

(C) in accordance with a restriction notice served under Article 47.

137. The Company may cease to send any cheque or warrant through the post for any dividend or other monies payable on or in respect of any share if in respect of at least two consecutive dividends payable on those shares the cheques or warrants have been returned undelivered or remain uncashed, or the cheque or warrant in respect of any one dividend has been returned undelivered or remains uncashed and reasonable enquiries have failed to establish any new address of the holder, but may recommence sending cheques or warrants in respect of dividends payable on those shares if the holder or person entitled thereto requests such recommencement in writing.

138. All unclaimed dividends or other monies payable on or in respect of a share may be invested or otherwise made use of by the Directors for the benefit of the Company until claimed. The payment by the Directors of any such dividend or other monies into a separate account shall not constitute the Company a trustee in respect thereof and any dividend unclaimed after a period of twelve years from the date of declaration of such dividend or the date on which such dividend became due for payment shall be forfeited and shall revert to the Company, but the Directors may at their discretion pay any such dividend or such other monies or some part thereof to a person who would have been entitled thereto had the same not reverted to the Company.

139. The Company may upon the recommendation of the Directors by ordinary resolution direct payment of a dividend in whole or in part by the distribution of specific assets (and in particular of paid up shares or debentures of any other company) and the Directors shall give effect to such resolution, and where any difficulty arises in regard to such distribution, the Directors may settle the same as they think expedient and in particular may issue fractional certificates and fix the value for distribution of such specific assets or any part thereof and may determine that cash payments shall be made to any members upon the footing of the value so fixed in order to adjust the rights of all parties and may vest any such specific assets in trustees as may seem expedient to the Directors, and generally may make such arrangements for the allotment, acceptance and sale of such specific assets or fractional certificates or any part thereof and otherwise as they think fit.

140. Any dividend or other monies payable in cash on or in respect of a share may be paid by cheque or warrant sent through the post to or left at the registered address of the

member or person entitled thereto (or, if two or more persons are registered as joint holders of the share or are entitled thereto in consequence of the death or bankruptcy of the holder, to any one of such persons) or to such person and such address as such member or person may by writing direct. Every such cheque or warrant shall be made payable to the order of the person to whom it is sent or to such persons as the holder or joint holders or person or persons entitled to the share in consequence of the death or bankruptcy of the holder may by writing direct and payment of the cheque or warrant by the banker upon whom it is drawn shall be a good discharge to the Company. Every such cheque or warrant shall be sent at the risk of the person entitled to the monies represented thereby.

141. If two or more persons are registered as joint holders of any share, or are entitled jointly to a share in consequence of the death or bankruptcy of the holder, any one of them may give effectual receipts for any dividend or other monies payable or property distributable on or in respect of the share.

#### **RESERVES**

142. The Directors may from time to time set aside out of the profits of the Company and carry to reserve such sums as they think proper which, at the discretion of the Directors, shall be applicable for any purpose to which the profits of the Company may properly be applied and pending such application may either be employed in the business of the Company or be invested. The Directors may from time to time designate the reserves or any part thereof for such purposes or in such manner as they think fit. The Directors may also without placing the same to reserve carry forward any profits.

#### **CAPITALISATION OF RESERVES**

143. The Company may upon the recommendation of the Directors by ordinary resolution resolve to capitalise any sum standing to the credit of any of the Company's reserve accounts (including share premium account and capital redemption reserve fund) or any sum standing to the credit of profit and loss account (provided that such sum be not available and required for paying the dividends on any shares carrying a fixed cumulative preferential dividend) and authorise the Directors to appropriate the sum resolved to be capitalised to the holders of shares in the proportions in which such sum would have been divisible amongst them had the same been a distribution of profits by way of dividend on the shares and to apply such sum on their behalf either in or towards paying up the amounts (if any) for the time being unpaid on any shares held by them respectively or in or towards paying

up in full unissued shares or debentures of the Company of a nominal amount equal to such sum, such shares or debentures to be allotted and distributed credited as fully paid up to and amongst them in the proportion aforesaid or partly in one way and partly in the other. Provided that any sum standing to the credit of share premium account or capital redemption reserve fund and any other undistributable reserves shall only be applied in or towards the paying up of unissued shares to be allotted as fully paid.

144. Subject to approval by the Company in general meeting the Directors may, in respect of any dividend declared or proposed to be declared at that general meeting or any time prior to the next following annual general meeting, determine and announce, prior to or contemporaneously with their announcement of the dividend in question that ordinary shareholders will be entitled to elect to receive in lieu of such dividend (or part thereof) an allotment of additional ordinary shares credited as fully paid. In any such case the following provisions shall apply:-

(A) The basis of allotment shall be determined by the Directors so that, as nearly as may be considered convenient, the value (calculated by reference to the average quotation) of the additional ordinary shares (including any fractional entitlement) to be allotted in lieu of any amount of dividend shall equal such amount. For such purposes the "average quotation" of an ordinary share shall be the average of the means of quotations on the Stock Exchange, as shown in the Daily Official List, on each of the first five business days on which the ordinary shares are quoted ex the relevant dividend.

(B) The Directors shall give notice in writing to the ordinary shareholders of the right of election accorded to them and shall send with or following such notice forms of election and specify the procedure to be followed and the place at which and the latest date and time by which duly completed forms of election must be lodged in order to be effective.

(C) The dividend (or that part of the dividend in respect of which a right of election has been accorded) shall not be payable on ordinary shares in respect whereof the share election has been duly exercised ("the elected ordinary shares"), and in lieu thereof additional shares shall be allotted to the holders of the elected ordinary shares on the basis of allotment determined as aforesaid and for such purpose the Directors shall capitalise, out of such of the sums standing to the credit of reserves (including any share premium account or capital redemption reserve fund) or profit and loss account as the Directors may determine a sum equal to the aggregate nominal amount of additional ordinary shares to be

allotted on such basis and apply the same in paying up in full the appropriate number of unissued ordinary shares on such basis.

(D) The additional ordinary shares so allotted shall rank *pari passu* in all respects with the fully paid ordinary shares then in issue save only as regards participation in the relevant dividend (or share election in lieu).

(E) The Directors may on any occasion determine that rights of election shall not be made available to any ordinary shareholders with registered addresses in any territory where in the absence of a registration statement or other special formalities the circulation of an offer of rights of election would or might be unlawful, and in such event the provisions aforesaid shall be read and construed subject to such determination.

145. Whenever such a resolution as aforesaid shall have been passed, the Directors shall make all appropriations and applications of the sum resolved to be capitalised thereby and all allotments and issues of fully paid shares or debentures (if any) and generally shall do all acts and things required to give effect thereto, with full power to the Directors to make such provisions as they think fit for the case of shares or debentures becoming distributable in fractions (including provisions whereby the benefit of fractional entitlements accrues to the Company rather than to the members concerned) and also to authorise any person to enter on behalf of all the members interested into an agreement with the Company providing for the allotment to them respectively, credited as fully paid, of any further shares or debentures to which they may be entitled upon such capitalisation, or (as the case may require) for the payment by the Company on their behalf, by the application thereto of their respective interests in such capitalised sum, of the amounts or any part of the amounts remaining unpaid on their existing shares and for matters incidental thereto and any agreement made under any such authority shall be effective and binding on all concerned.

#### RECORD DATES

146. Notwithstanding any other provision of these Articles, the Company or the Directors may fix any date as the record date for any dividend, distribution, offer, allotment or issue and such record date may be on or any time before or after any date on which the dividend, distribution, offer, allotment or issue is declared, paid or made.

#### MINUTES AND BOOKS

147. The Directors shall cause minutes to be made in books to be provided for the purpose:-

- (A) of all appointments of officers made by the Directors;
  - (B) of the names of the Directors present at each meeting of Directors and of any committee of Directors;
  - (C) of all resolutions and proceedings at all meetings of the Company and of any class of members of the Company and of the Directors and of committees of Directors.
- Any such minutes if purporting to be signed by the chairman of the meeting at which the proceedings took place, or by the chairman of the next following meeting, shall be sufficient evidence without any further proof of the facts therein stated.

148. Any register, index, minute book, book of account or other book required by these Articles or the Statutes to be kept by or on behalf of the Company may be kept either by making entries in bound books or by recording them in any other manner. In any case in which bound books are not used, the Directors shall take adequate precautions for guarding against falsification and for facilitating its discovery.

149. Any register, index, minute book, book of account or other book or document of the Company shall always be open to the inspection of the officers of the Company. Subject as aforesaid no member of the Company or other person shall have any right of inspecting any book or document of the Company except as conferred by the Statutes or as ordered by a Court of competent jurisdiction or as authorised by the Directors and the Directors shall (subject to the provisions of the Statutes) determine at what times and under what conditions any such right may be exercised.

#### ACCOUNTS

150. Accounting records sufficient to show and explain the Company's transactions and otherwise complying with the Statutes shall be kept at the Office, or at such other place within Great Britain as the Directors think fit.

151. The Directors shall from time to time in accordance with the provisions of the Statutes cause to be prepared and to be laid before a general meeting of the Company such profit and loss accounts, balance sheets, group accounts (if any) and reports as may be necessary.

152. A printed copy of the Directors' report accompanied by the balance sheet and profit and loss account and Auditor's report which is to be laid before a general meeting of the

Company (including every document required by law to be attached or annexed thereto) shall not less than twenty-one days before the date of the meeting be sent to every member of, and every holder of debentures of, the Company and to every other person who is entitled to receive notices of meetings from the Company under the provisions of the Statutes or of these Articles. Provided that this Article shall not require a copy of such documents to be sent to more than one of joint holders or to any person who is not entitled to receive notices of meetings and of whose address the Company is not aware, but any member or holder of debentures to whom a copy of such documents has not been sent shall be entitled to receive a copy free of charge on application at the Office. The requirements of this Article shall be deemed to be satisfied in relation to any member by sending to that member, where permitted by the Statutes, a summary financial statement prepared in the form and containing the information prescribed by the Statutes. No accidental non-compliance with the provisions of this Article shall invalidate the proceedings at the meeting.

153. Every account of the Company when audited and approved by the Company in general meeting shall be conclusive except as regards any error discovered therein within three months next after the approval thereof. Whenever such an error is discovered within that period, the account shall forthwith be corrected and thereupon shall be conclusive.

#### AUDITORS

154. Auditors shall be appointed and their duties, powers, rights and remuneration regulated in accordance with the provisions of the Statutes.

155. Subject to the provisions of the Statutes, all acts done by persons acting as Auditors shall, as regards all persons dealing in good faith with the Company, be valid, notwithstanding that there was some defect in their appointment or that they were at the time of their appointment not qualified for appointment.

156. The Auditors shall be entitled to attend any general meeting and to receive all notices of and other communications relating to any general meeting which any member is entitled to receive, and to be heard at any general meeting on any part of the business of the meeting which concerns them as Auditors.

#### NOTICES

157. Any notice or document (including a share certificate) may be served on or delivered to any member by the Company either personally, or by sending it through the post in a prepaid letter or leaving it in a letter addressed to such member at his registered address or (if he has no registered address within the United Kingdom) to the address, if any, within the United Kingdom supplied by him to the Company as his address for the service of notices. Where a notice or other document is sent by post, service or delivery shall be deemed to be effected at the expiration of twenty-four hours (or, where second class mail is employed, forty-eight hours) after the time when the letter containing the same is posted and in proving such service or delivery it shall be sufficient to prove that such letter was properly addressed, stamped and posted.

158. In respect of joint holdings all notices shall be given to the joint holder with a registered address or other address for service in the United Kingdom whose name stands first in the Register and notice so given shall be sufficient notice to all the joint holders of that joint holding.

159. Any notice or document delivered or sent by post to or left at the registered address of any member in pursuance of these Articles shall, notwithstanding that such member be then dead or bankrupt, and whether or not the Company has notice of his death or bankruptcy, be deemed to have been duly served or delivered in respect of any share registered in the name of such member as sole or joint holder, provided that where a person entitled to a share in consequence of the death or bankruptcy of a member has supplied to the Company evidence to show his title to the share and an address within the United Kingdom for the service of notices, any notice or document to which the member but for his death or bankruptcy would be entitled shall be served on or delivered to such person in like manner as a member, and shall for all purposes be deemed a sufficient service or delivery of such notice or document on all persons interested (whether jointly with or as claiming through or under him) in the share.

160. Every person who by operation of law, transfer or other means whatsoever shall become entitled to any share shall be bound by any notice or document in respect of such share which previously to his name and address being entered in the Register as the holder thereof shall have been served on or delivered to a person from or through whom he derives his title to such share provided that the provisions of this Article shall not apply to any notice given under Article 47 or the provisions of the Statutes referred to therein.

161. A member who (having no registered address within the United Kingdom) has not supplied to the Company an address within the United Kingdom for the service of notices shall not be entitled to receive notices from the Company.

162. If at any time by reason of the suspension or curtailment of postal services within the United Kingdom or any part thereof the Company is unable effectively to convene a general meeting by notices sent through the post, a general meeting may be convened by a notice advertised in two national daily newspapers published on the same date and such notice shall be deemed to have been duly served on all members entitled thereto at noon on the day when the advertisement appears. In any such case the Company shall send confirmatory copies of the notice by post if, at least forty-eight hours prior to the meeting, the posting of notices to addresses throughout the United Kingdom again becomes practicable.

163. Any notice required to be given by the Company to the members, or any of them, and not provided for by or pursuant to these Articles shall be sufficiently given if given by advertisement which shall be inserted once in at least one national daily newspaper, and in such case shall be deemed to have been given at noon on the day on which the advertisement first appears.

164. Nothing in these Articles shall affect any requirement of the Statutes that any particular offer, notice or other document be served in any particular manner.

#### WINDING UP

165. The Directors shall have power in the name and on behalf of the Company to present a petition to the Court for the Company to be wound up.

166. If the Company shall be wound up (whether the liquidation is voluntary, under supervision, or by the Court) the liquidator may, with the authority of an extraordinary resolution, divide amongst the members in specie the whole or any part of the assets of the Company (whether or not the assets shall consist of property of one kind or shall consist of properties of different kinds) and may for such purpose set such value as he deems fair upon any one or more class or classes of property and may subject to any special rights attached to any shares or the terms of issue thereof determine how such division shall be carried out as between the members or different classes of members. The liquidator may,

with the like authority, vest any part of the assets in trustees upon such trusts for the benefit of members as the liquidator with the like authority shall think fit, and the liquidation of the Company may be closed and the Company dissolved, but so that no contributory shall be compelled to accept any shares or other property in respect of which there is a liability.

#### INDEMNITY AND INSURANCE

167. Subject to the provisions of and so far as may be permitted by the Statutes, every Director, Secretary or other officer of the Company shall be entitled to be indemnified by the Company against all costs, charges, losses, expenses and liabilities incurred by him in the execution and discharge of his duties or in relation thereto including any liability incurred by him in defending any proceedings, civil or criminal, which relate to anything done or omitted or alleged to have been done or omitted by him as an officer or employee of the Company and in which judgement is given in his favour, or the proceedings otherwise disposed of without any finding or admission of any material breach of duty on his part, or in which he is acquitted or in connection with any application under any statute for relief from liability in respect of any such act or omission in which relief is granted by the Court.

168. The Directors shall have the power to purchase and maintain insurance for, or for the benefit of, any persons who are, or were at any time, Directors, officers or employees of the Company or of any other company in which the Company has any interest, whether direct or indirect, or who are, or were, at any time trustees of any pension fund or employees' share scheme, or any other scheme or arrangement principally for the benefit of employees, in which employees of the Company, or of any such other company, are interested; including (without prejudice to the generality of the foregoing) insurance against any liability incurred by such persons in respect of any act or omission in the actual or purported execution or discharge of their duties, or in the exercise of their powers, or otherwise in relation to their duties, powers or offices in relation to the Company, or any such other company, or any such pension fund, employees' share scheme or other scheme or arrangement.

THE COMPANIES ACTS 1985 to 1989

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A PUBLIC COMPANY LIMITED BY SHARES

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MEMORANDUM OF ASSOCIATION

of

PHYTOPHARM PLC

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1. The name of the Company is PHYTOPHARM PLC.\*
2. The Company is to be a public company.
3. The Registered Office of the Company will be situated in England and Wales.
4. The objects for which the Company is established are :-
  - (A) To carry on business as a general commercial company.
  - (B) To carry on the business of a holding company and to acquire by purchase, exchange, subscription or otherwise and to hold the whole or any part of the shares, stocks, debentures and other securities and interests of and in any corporations, companies, associations or firms for the time being engaged, concerned or interested in any industry, trade or business and to promote the beneficial co-operation of any such companies, associations or firms as well with one another as with the Company and to exercise in respect of such investments and holdings all the rights, powers and privileges of ownership including the right to vote thereon.
  - (C) (i) To carry on all or any of the businesses of importers and

\* By a special resolution passed on 26th February 1996 the Company's name was changed from Lawnhale PLC to Phytopharm PLC

exporters and manufacturers of and dealers in human and veterinary medicines and prophylactics, animal feeding stuffs, nutritional supplements and additions, salts, acids, alkalis, drugs, pharmaceutical, chemical and surgical compounds, materials, substances and instruments, dressings, syringes and accessories, disinfectants, fertilisers, pesticides, cleaning materials, chemists sundries, agricultural sprays, horticultural and agricultural chemicals and requisites.

- (li) To carry on the business of chemists, pharmacists, druggists, drysalters, oil and colour men, importers, exporters, and manufacturers of and dealers in pharmaceutical, medicinal, chemical, industrial, and other preparations and articles, herbal remedies, fertilisers, compounds, cements, oils, paints, resins, pigments and varnishes, drugs, dyeware, paint and colour grinders, makers of and dealers in proprietary articles of all kinds.
- (D) To carry on any other business which in the opinion of the Company, may be capable of being conveniently or profitably carried on in connection with or subsidiary to any other business of the Company and is calculated to enhance the value of the Company's property.
- (E) To purchase or by any other means acquire freehold, leasehold or any other property for any estate or interest whatever, movable or immovable or any interest in such property, and to sell, lease, let on hire, develop such property, or otherwise turn the same to the advantage of the Company.
- (F) To apply for, register or by other means acquire any patents, patent rights, brevets d'invention, licences, trademarks, concessions and inventions and to use and turn to account the same or to develop, sell or assign the same or grant licences or privileges in respect thereof or otherwise turn the same to the advantage of the Company.

- (G) To build, reconstruct or generally maintain buildings and works of all kinds, whether or not these are situate on the property of the Company.
- (H) To invest and deal with the monies of the Company in such shares or upon such securities and in such manner as from time to time may be determined.
- (I) To enter into arrangements for joint workings in business or amalgamate with or enter into any partnership or arrangement for sharing profits, union of interests, reciprocal concession or co-operation with any company, firm or person carrying on or proposing to carry on any business within the objects of this Company or which is capable of being carried on so as directly or indirectly to benefit the Company.
- (J) To purchase or otherwise acquire, take over and undertake all or any part of the business, property, liabilities and transactions of any person, firm or company carrying on any business the carrying on of which is calculated to benefit this Company or to advance its interests, or possessed of property suitable for the purposes of the Company.
- (K) To sell, improve, manage, develop, turn to account, let on rent or royalty or share of profits or otherwise, grant licences or easements or other rights in or over, or in any other manner deal with or dispose of the undertaking and all of any of the property and assets for the time being of the Company for such consideration as the Company may think fit.
- (L) To subscribe for, take, purchase or otherwise acquire either for cash, shares or debentures in this Company or any other consideration any other company or business which, in the opinion of the Company, may be carried on so as directly or indirectly to benefit the Company.

- (M) To sell or otherwise dispose of the whole or any part of the business or property of the Company for any consideration, shares or debentures as the Company may think fit.
- (N) To lend and advance money or give credit on any terms and with or without security to any company, firm or person (including without prejudice to the generality of the foregoing any holding company, subsidiary or fellow subsidiary of, or any other company associated in any way with, the Company), to enter into guarantees, contracts of indemnity and suretyships of all kinds, to receive money on deposit or loan upon any terms, and to secure or guarantee in any manner and upon any terms the payment of any sum of money or the performance of any obligation by any company, firm or person (including without prejudice to the generality of the foregoing any such holding company, subsidiary, fellow subsidiary or associated company as aforesaid).
- (O) To borrow or raise money in any manner and to secure the repayment of any money borrowed raised, or owing by mortgage, charge, standard security, lien or other security upon the whole or any part of the Company's property or assets (whether present or future), including its uncalled capital and also by a similar mortgage, charge, standard security, lien or security to secure and guarantee the performance by the Company of any obligation or liability it may undertake or which may become binding on it.
- (P) To draw, make, accept, endorse, discount, negotiate, execute and issue cheques, bills of exchange, promissory notes, bills of lading, warrants, debentures and other negotiable or transferable instruments.
- (Q) To apply for, promote, and obtain any Act of Parliament, order or licence of the Department of Trade or other authority for enabling the Company to carry any of its objects into effect, or for effecting any modification of the Company's constitution, or for any other purpose which may seem calculated directly or indirectly to promote the

Company's interests, and to oppose any proceedings or applications which may seem calculated directly or indirectly to prejudice the Company's interests.

- (R) To support and subscribe to any funds and to subscribe to or assist in the promotion of any charitable, benevolent or public purpose or object for the benefit of the Company or its employees, directors or other officers past or present and to grant pensions to such persons or their dependants.
- (S) To distribute among the members of the Company in kind any property of the Company of whatever nature.
- (T) To purchase and/or maintain for any director, officer or employee of the Company or any company which is or was a subsidiary of or otherwise associated with the company insurance against any liability which by virtue of any law would attach to him in respect of any negligence, default, breach of duty or breach of trust of which he may be guilty in relation to the Company or any such other company.
- (U) To pay all or any expenses in connection with the promotion, formation and incorporation of the Company, or to contract with any company, firm or person to pay the same, and to pay commission to brokers and others for underwriting, placing, selling, or guaranteeing the subscription of any shares or other securities of the Company.
- (V) To do all or any of the above things in any part of the world, and either as principals, agents, trustees, contractors or otherwise and either alone or in conjunction with others, and either by or through agents, sub-contractors, trustees or otherwise.
- (W) To do all such other things as may be deemed incidental or conducive to the attainment of the Company's objects or any of them.

None of the objects set forth in any sub-clause of this Clause shall be restrictively construed but the widest interpretation shall be given to each such object, and none of such objects shall, except where the context expressly so requires, be in any way limited or restricted by reference to or inference from any other object or objects set forth in any sub-clause or by reference to or interference from the terms of any other sub-clause of this Clause, or by reference to or inference from the name of the Company.

5. The liability of the Members is limited.
6. The share capital of the Company is £50,000 divided into 50,000 shares of £1.00 each.\*

\* By a resolution passed on 26th February 1996, the authorised share capital of the Company was increased to £500,000 divided into 500,000 shares of £1.00 each.

By a resolution passed on 18th April 1996 conditionally on a placing agreement to be made between the Company and others becoming unconditional in all respects and not being terminated prior to admission of the ordinary shares of 1p each in the capital of the Company issued and to be issued to the Official List of the London Stock Exchange Limited ("Admission") and Admission becoming effective not later than 25th April 1996, each ordinary share of £1 in the capital of the Company was sub-divided into 100 ordinary shares of 1p each.

We, the subscribers of this Memorandum of Association, wish to be formed into a Company pursuant to this Memorandum, and we agree to take the number of Shares shown opposite our respective names.

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NAMES AND ADDRESSES OF SUBSCRIBERS	Number of Shares taken by each Subscriber
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HALLMARK SECRETARIES LIMITED 120 East Road London N1 6AA	ONE
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HALLMARK REGISTRARS LIMITED 120 East Road London N1 6AA	ONE
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Dated the 1st November 1995

Witness to the above signatories:-

DAVID ORDISH  
120 East Road  
London N1 6AA

The Companies Acts 1985 to 1989  
A Public Company Limited by Shares