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Phytopharm



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SUPPL

**Phytopharm plc**  
**Fast Track designation granted by the FDA for ALS drug candidate Myogane™**

**GODMANCHESTER, CAMBRIDGESHIRE, UK (November 9th 2004)**—Phytopharm plc (PYM: London Stock Exchange; NASDAQ: PHYOF) (“Phytopharm”) announces today that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to its drug candidate PYM50018 (Myogane™) for the treatment of amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease).

The Fast Track program is designed to expedite the review of drug candidates for the treatment of patients with serious or life-threatening diseases with unmet medical needs for new therapeutic approaches. The Fast Track designation allows a company to file a New Drug Application (NDA) on a rolling basis as data become available and to request the evaluation of studies using surrogate endpoints. This permits the FDA to review the filing as it is received and can lead to a decrease in the typical review period.

Myogane is a patented, orally active, neuroprotective and neuroregenerative compound. In pre-clinical models, Myogane has been observed to protect against neuronal damage, increase neurite outgrowth, reverse oxidative damage and reverse neuronal apoptosis *in vitro*. When administered orally to a transgenic pre-clinical model of ALS, Myogane delays the loss of muscle strength and extends survival time.

In April 2004, Phytopharm announced the successful completion of a phase I clinical study to evaluate the safety, tolerability and pharmacokinetic profile of Myogane. This study was conducted under an investigational new drug (IND) application filed with the FDA. A repeat dose phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetic profile of Myogane in healthy volunteers is expected to commence in the first half of 2005.

Commenting on today’s announcement, Richard Dixey, Chief Executive of Phytopharm, said: “This is an important step in the development of Myogane and may help us bring this potentially promising drug to patients more quickly.”

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## NOTES TO EDITORS

### **Phytopharm plc**

Phytopharm is a pharmaceutical company specialising in the discovery and development of novel therapeutic agents in neurodegeneration, obesity, inflammation and dermatology. It has lead products in development for Alzheimer's disease, obesity and Amyotrophic Lateral Sclerosis. The Company's strategy is to develop first-in-class drug products through Phase II testing, then to secure pharmaceutical partners for late-stage development, sales and marketing. Cogane™ is in a Phase II trial as a potential therapy to reverse neurodegeneration in the brain of patients with Alzheimer's disease. Myogane™ is in Phase I testing as a neuroregenerative agent for treating ALS, an always-fatal disease, and has received Orphan Drug designation. Phytopharm is also developing a product for the dietary control of obesity within the P57 program. The Company has preclinical programs in several other disease areas including eczema, asthma and metabolic disease. Further, there are two marketed products: Phytopica™ for canine skin disorders, and Zanthofen™ for canine joint disorders.

### **Amyotrophic Lateral Sclerosis**

ALS is the most common motor neurone disease resulting from progressive degeneration of both upper and lower motor neurones which lead to severe muscle weakness and wasting, followed by paralysis and death, generally caused by respiratory failure. It is estimated that as many as 30,000 Americans may have the disease at any given time with 5,000 new cases diagnosed each year (source: ALS Association). For the families of ALS 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). Thus, there is an urgent need for the development of new and more effective therapies for this devastating condition.

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

This press release may contain forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933 and Section 21E of the U.S. Securities Exchange Act of 1934 with respect to the financial condition, results and business achievements/performance of Phytopharm and certain of the plans and objectives of its management. These statements are statements that are not historical facts. Words such as "should", "expects", "anticipates", "estimates", "believes" or similar expressions, as they relate to Phytopharm, are intended to identify forward-looking statements. By their nature, forward-looking statements involve risk and uncertainty because they reflect Phytopharm's current expectations and assumptions as to future events and circumstances that may not prove accurate. There is no guarantee that the expected events, trends or results will actually occur. Any changes in such assumptions or expectations could cause actual results to differ materially from current expectations.

###



# Phytopharm

## Phytopharm Announces Preliminary results for the year ended 31 August 2004

**GODMANCHESTER, CAMBRIDGESHIRE, UK (December 3, 2004)** Phytopharm plc (PYM: London Stock Exchange; NASDAQ: PHYOF) ("Phytopharm" or the "Group") today announces its preliminary results for the year ended 31 August 2004.

### Highlights

- Commencement of Phase II study of novel Alzheimer's disease treatment, Cogane™, 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) with marketing partner
- UK launch of Zanthofen™ with marketing partner for canine joint disorders (Programme P54v)
- Successful placing of new shares to raise £6.3 million after expenses
- Successful completion of Phase I study for novel motor neurone disease (ALS) treatment, Myogane™, under US Investigational New Drug application (Programme P59)
- Completion of level I ADR programme and stated intention to list on NASDAQ
- Orphan drug designation granted by the U.S. Food and Drug Administration (FDA) for Myogane™ (Programme P59)
- Fast Track designation granted by the FDA for Myogane™ (Programme P59)

Dr Richard Dixey, Chief Executive of Phytopharm, said: '*Phytopharm has made excellent progress in its development of novel therapeutics, as evidenced by the achievement of so many of our goals during the past financial year. We are confident that the year ahead will hold many more achievements.*'

#### Enquiries:

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**A presentation for analysts will be held at Financial Dynamics, Holborn Gate, 26 Southampton Buildings London WC2A 1PB at 9:30am today.**

***www.phytopharm.com***

## **Operational Review**

**Phytopharm** is a pharmaceutical company specialising in the discovery and development of novel therapeutic agents for neurodegeneration, obesity and metabolic disease, dermatology and inflammation. The Company's strategy is to develop first-in-class products through Phase II clinical testing and then secure pharmaceutical partners for late stage development, sales and marketing. The current status of our products, each at different stages of development, is described below.

### **Neurodegeneration**

The neurodegeneration programmes include Alzheimer's disease (**P58**), Parkinson's disease (**P63**) and amyotrophic lateral sclerosis (**P59**), a motor neurone disease.

Our lead product, **Cogane**<sup>TM</sup> (coded PYM50028) is being developed for Alzheimer's and Parkinson's disease. In pre-clinical studies, PYM50028 was shown to be neuroprotective and reverse both the decrease of a neuronal growth factor 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 Cogane<sup>TM</sup> after once-daily oral administration over three months. The effects of Cogane<sup>TM</sup> on memory, concentration and executive function will be evaluated during the study, which is expected to report at the end of 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 Cogane<sup>TM</sup>. This milestone was paid following receipt by Yamanouchi of the results of the Phase Ib study of Cogane<sup>TM</sup>.

Our second lead product, **Myogane**<sup>TM</sup> (coded PYM50018) is being developed for amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease). ALS is the most common motor neurone disease and results from progressive degeneration of both upper and lower motor neurones and is usually fatal within five years. In pre-clinical models, PYM50018 was seen to protect against neuronal damage, increase neurite outgrowth, and reverse oxidative damage and neuronal apoptosis *in vitro*. When administered orally in a transgenic pre-clinical model of ALS, PYM50018 also delayed the loss of muscle strength and extended survival time.

In April 2004, Phytopharm announced the successful completion of a Phase I clinical study to evaluate the safety, tolerability and pharmacokinetic profile of Myogane<sup>TM</sup>. This study was

conducted under an investigational new drug (IND) application filed with the United States Food and Drug Administration (FDA) and confirmed that the product was well absorbed with a good safety profile. A repeat dose Phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetic profile of Myogane™ in healthy volunteers is expected to commence in the Q2 2005.

In July 2004, we announced that the FDA had granted orphan drug designation to Myogane™ for the treatment of ALS. Orphan drug designation can be granted by the FDA for treatments that may provide significant benefit to patients with serious, life-threatening diseases that affect less than 200,000 people in the United States. The Orphan Drug Act was created by the United States Congress to provide assistance and incentives for sponsors to develop drugs judged to be of potential benefit for a qualifying disease. Orphan drug designation qualifies a product for possible financial incentives, including seven years of marketing exclusivity upon FDA approval, and the potential of an expedited approval. In addition to market exclusivity, orphan drug status provides possible tax incentives for a company's investment in US clinical research.

In November 2004, Phytopharm announced that the FDA had granted Fast Track designation to Myogane™ for the treatment of ALS. The Fast Track programme is designed to expedite the review of drug candidates for the treatment of patients with serious or life-threatening diseases where there is an unmet medical need for new therapeutic approaches. Having a Fast Track designation allows a company to file a New Drug Application (NDA) on a rolling basis as data becomes available. This enables the FDA to review the filing as it is received, rather than waiting for the entire document prior to commencing the review process. With a Fast Track designation, there is often the opportunity for more frequent interactions with the FDA and the option of requesting evaluation of studies using surrogate endpoints. In addition, there may be the possibility of a priority review, which could decrease the typical review period.

### **Obesity and metabolic disease**

Our obesity programme (P57) includes an extract of *Hoodia gordonii* for the dietary control of obesity, which contains a novel appetite suppressant that reduces caloric intake in overweight subjects, as demonstrated in our double-blind, placebo-controlled clinical study announced in December 2001. In June 2004, Phytopharm initiated a substantial increase in its agronomy programme for the cultivation of the raw material and optimised the process for making extracts from the plant, with emphasis on the inclusion of the material into products including meal replacement products for controlling obesity. The US market for meal replacement products was estimated to be worth in excess of \$1.2 billion in 2002. As advanced discussions are on-going with a licensing partner in this area, the Company can make no further comment.

Phytopharm has also developed screens that appear to be predictive of appetite suppressant activity to evaluate pharmaceutical development candidates in our metabolic disease programme (P64).

### **Dermatology**

The dermatology programmes include products for canine skin disorders (P7v) and human eczema (P55). These products have a dual mode of action that targets both the allergic and inflammatory components of skin disorders.

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 March, 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 90,000 affected animals in the UK, the canine dermatology market is estimated to be potentially worth £10 million in the UK and £100 million worldwide. Phytopica™ is recognised by consultant veterinarians as a potential first line, premium price product. Following the UK launch to registered veterinary dermatologists, Phytopharm is now seeking global partners to market Phytopica™ in other territories.

### **Inflammation**

Finally, the inflammation programmes include products for canine joint disorders (**P54v**) and human inflammatory disorders, including asthma (**P61**). These products are characterised by their inhibition of a wide range of enzymes central to chronic inflammation.

In June 2004, we announced the UK launch of **Zanthofen™** (coded PYM50014) for the maintenance of canine joint mobility. Pre-clinical studies have demonstrated that the components of Zanthofen™ have beneficial properties that help maintain joint mobility. In our previously reported placebo-controlled clinical study, two months' administration of Zanthofen™ components demonstrated a statistically significant improvement in canine joint mobility as determined by veterinarians and this was associated with a good safety profile. Zanthofen™ is now available to veterinarians across the UK and distributed and marketed by Genitrix Ltd, a UK based veterinary product company.

Good progress has been made in developing novel synthetic molecules intended to result in a pharmaceutical prescription medicine for the treatment of inflammatory disorders, including asthma (**P61**). Pre-clinical work has demonstrated that these molecules have anti-inflammatory and antispasmodic effects. We anticipate that further proof of concept studies using these compounds in pre-clinical models of asthma will be investigated in 2005.

### **Financial Review**

Phytopharm has core expertise in all aspects of drug development and subcontracts all laboratory work to specialists in the field all over the world, while retaining full control over the direction of the pharmaceutical development process. As a result, Phytopharm has lower fixed overheads, access to the latest research techniques and a lower development cost structure.

Following 'proof of principle' or Phase II clinical evaluation, Phytopharm seeks licensing partners for the development and commercialisation of its products. Multinational partners are sought, with milestones receivable on completion of agreed targets, submission of regulatory documents and royalties receivable on sales. Agreements are negotiated by reference to each product's market potential, stage of development, and the robustness of the data generated. Phytopharm's current commercialisation partners are Yamanouchi Pharmaceutical Co. Ltd for PYM50028 and Genitrix Limited for Zanthofen™.

Phytopharm aims to reduce investors' risk by the parallel development of the original plant-based products for early marketing; for example, Hoodia extract as a human functional food and Phytopica™ as a companion animal health product to generate early revenue that can assist in funding the development of the Group's major pharmaceutical products.

The Group's principal activity since the foundation of its predecessor (Phytopharm Limited) in 1990 has been pharmaceutical research and product development. The Group has made losses since its initial public offering in 1996. As at 31 August 2004, Phytopharm's accumulated losses were £33 million (2003: £27 million).

The Group's losses fluctuate from year to year principally due to the commencement or termination of collaborative research and development agreements, the timing of milestone payments, the level of interest income and variations in the level of expenditures relating to research and clinical development programmes. Phytopharm expects to incur continued losses and not to achieve sustainable profitability while its lead pharmaceutical products are still in development, subject to the terms of any product licensing agreements in the intervening years. Phytopharm continues to incur the greater part of its costs on personnel and external contract costs needed to support the research and development of pharmaceutical products, including expenses related to the filing, defence and enforcement of patent and other intellectual property rights.]

### **Turnover**

Revenues for the year ended 31 August 2004 were £1.07 million (2003: £2.43 million). The revenues for 2004 result from and include a milestone payment of £1 million, on which £0.1 million has been paid in respect of Japanese withholding taxes, derived from the licence agreement on PYM50028 with Yamanouchi (signed May 2003), revenue of £0.05 million from the development work conducted for Yamanouchi and £0.02 million from the sales of Phytopica™ and Zanthofen™. All revenues derived from Yamanouchi referred to in this document are subject to 10% withholding tax, so that the cash received is 90% of the revenue. This will continue until Phytopharm is profitable, when the Group expects to be able to recover the withholding tax.

### **Operating expenses**

#### **Research and development expenses**

Phytopharm subcontracts all laboratory work to third party specialists. The research and development expenses include the reimbursement of the costs incurred by the third party subcontractors and the overhead (including the relevant staff costs) of Phytopharm allocated to research and development activities.

Research and development expenses were £6.35 million (2003: £7.23 million). Expenditure was dominated by the commencement of the PYM50028 Phase IIa clinical trial in Alzheimer's disease. Expenses were also incurred by the successful completion of the PYM50018 Phase Ia clinical trial in motor neurone disease and the PYM00217 Phase IIb clinical trial in canine atopic dermatitis. Additional expenses included the commencement of the agronomy programme for the dietary control of obesity product and the marketing of Phytopica™.

#### **Administrative expenses**

Administrative expenses comprised mainly the costs incurred in respect of the employees in the finance, business development and secretarial departments. Administrative expenses were £1.71 million (2003: £1.15 million). The increased costs reflect the additional administrative support required for the growing research and development activity, the share option compensation charge and US financial compliance costs.

## **Net interest receivable**

Net interest receivable comprises mainly the interest income generated from cash invested in short-term deposits. Net interest income was £0.24 million (2003: £0.28 million). The change over the year was due to changing short-term deposits as the Group utilised the cash of £10.8 million raised from the equity financing in November 2000, and £6.3 million raised from another equity financing in February 2004, and also changing interest rates during the year.

## **Taxation**

There were no corporation tax charges for the period under review due to the incidence of tax losses. The tax credit on the loss on ordinary activities was £0.53 million (2003: £0.38 million). The tax credit has been offset by a 10% withholding tax on the income from Yamanouchi.

## **Liquidity and capital resources**

Since Phytopharm's initial public offering, cash expenditures have exceeded revenues. Phytopharm has financed its research and development operations primarily through:

- an initial public offering of ordinary shares in 1996
- ordinary share offerings in November 1998, October 2000, December 2001 and February 2004
- revenue generated from collaborative arrangements.

The net cash outflow from operating activities for the year ended 31 August 2004 was £6.83 million (2003: £3.94 million) resulting principally from the operating losses incurred by the Group during the year. The increase in net cash used by operating activities compared to the previous year reflects the significant expenses incurred in conducting a Phase IIa clinical trial in Alzheimer's disease. Phytopharm incurred operating losses of £7.00 million (2003: £5.95 million), principally as a result of costs incurred in performing research and development and from general and administrative costs associated with the Group's operations.

Phytopharm's net cash outflow for capital expenditure was £103,000 (2003: £28,000). The capital expenditure is primarily for office and administrative facilities. There was no cash outflow for acquisitions during these periods.

Phytopharm's net cash inflow from financing activities was £6.37 million (2003: £75,000) following the equity financing in February 2004. The net cash inflow in 2003 primarily resulted from the proceeds from the exercise of the share options.

Phytopharm had cash and short-term deposits of £5.43 million at 31 August 2004 (2003: £5.61 million). The decrease in cash and short term deposits mainly reflected the net cash used by operating activities. Phytopharm invested funds that were surplus to its requirements in highly liquid short-term deposits and has not borrowed funds during the financial year. Phytopharm had working capital of £5.11 million at 31 August 2004 (2003: £4.94 million). The Group utilised £6.15 million of working capital during 2004, which is equivalent to £512,000 per month. This expenditure is in line with the Group's business plan.

Overall the results for the year were within the budget. Phytopharm has raised a net total of £33 million since the float in 1996. As at 31 August 2004, a net total of £28 million has been invested by shareholders in developing Phytopharm and its product opportunities.

## PHYTOPHARM PLC

### Consolidated Profit and Loss Account for the year ended 31 August 2004

	Notes	<b>2004</b> <b>Unaudited</b> <b>£'000</b>	2003 Audited £'000
<b>Turnover</b>	2	<b>1,072</b>	2,427
Cost of sales		<b>(10)</b>	-
		<hr/>	<hr/>
<b>Gross profit</b>		<b>1,062</b>	2,427
Other operating expenses	3	<b>(8,058)</b>	(8,381)
		<hr/>	<hr/>
<b>Operating loss</b>		<b>(6,996)</b>	(5,954)
Interest receivable and similar income		<b>239</b>	277
Interest payable and similar charges		-	(4)
		<hr/>	<hr/>
<b>Loss on ordinary activities before taxation</b>		<b>(6,757)</b>	(5,681)
		<hr/>	<hr/>
Tax on loss on ordinary activities	4	<b>531</b>	378
		<hr/>	<hr/>
<b>Loss for the year</b>	6	<b>(6,226)</b>	(5,303)
		<hr/> <hr/>	<hr/> <hr/>
Basic fully diluted loss per ordinary share (pence)	5	<b>(15.3)</b>	(13.7)

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 2004**

	Notes	2004 Unaudited £'000	2003 Audited £'000
<b>Fixed assets</b>			
Tangible assets		178	162
<b>Current assets</b>			
Stocks		350	43
Debtors falling due after one year		614	-
Debtors falling due within one year		978	1,094
Cash held on deposit as short term investments		5,237	5,131
Cash at bank and in hand		194	482
		7,373	6,750
<b>Creditors: amounts falling due within one year</b>		(2,259)	(1,815)
<b>Net current assets</b>		5,114	4,935
<b>Total assets less current liabilities</b>		5,292	5,097
<b>Net assets</b>		5,292	5,097
<b>Capital and reserves</b>			
Called up share capital		427	388
Share premium account	6	38,135	31,808
Merger reserve	6	(204)	(204)
Profit and loss account	6	(33,066)	(26,895)
<b>Equity shareholders' funds</b>		5,292	5,097

PHYTOPHARM PLC

Consolidated Cash Flow Statement for the year ended 31 August 2004

	Notes	2004 Unaudited £'000	2003 Audited £'000
<b>Net cash outflow from continuing operating activities</b>	7	(6,826)	(3,938)
<b>Returns on investment and servicing of finance</b>			
Interest received		239	277
Other interest paid		-	(4)
		<u>239</u>	<u>273</u>
<b>Taxation</b>			
UK corporation tax received		856	277
Foreign taxation paid		(100)	(200)
		<u>756</u>	<u>77</u>
<b>Capital expenditure and financial investment</b>			
Purchase of tangible fixed assets		(117)	(85)
Proceeds on sale of tangible fixed assets		14	57
Advances to suppliers		(614)	-
		<u>(717)</u>	<u>(28)</u>
<b>Cash outflow before use of liquid resources and financing</b>		<u>(6,548)</u>	<u>(3,616)</u>
<b>Management of liquid resources</b>			
Decrease in cash held on short term deposit		(106)	3,700
<b>Financing</b>			
Proceeds from exercise of share options		37	83
Proceeds from issue of share capital		6,483	-
Expenses of issue of share capital		(154)	-
Repayment of principal under finance leases		-	(8)
		<u>6,366</u>	<u>75</u>
<b>Net cash inflow from financing</b>		<u>6,366</u>	<u>75</u>
<b>(Decrease)/increase in cash in the year</b>		<u><u>(288)</u></u>	<u><u>159</u></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 2003.

The figures shown for the year to 31 August 2004 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 2003 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

	2004 Unaudited £'000	2003 Audited £'000
Licensing and development	1,052	2,427
Product sales	20	-
	<u>1,072</u>	<u>2,427</u>

### 3. Other operating expenses

	2004 Unaudited £'000	2003 Audited £'000
Research and development	6,347	7,228
Administrative expenses	1,711	1,153
	<u>8,058</u>	<u>8,381</u>

### 4. Tax on loss on ordinary activities

	2004 Unaudited £'000	2003 Audited £'000
<b>United Kingdom</b>		
Corporation tax credit	631	578
<b>Foreign Taxation</b>		
Withholding tax suffered	(100)	(200)
	<u>531</u>	<u>378</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 the loss on ordinary activities of £6,226,130 (2003: loss of £5,303,318) and on 40,820,636 (2003: 38,671,689) ordinary shares, being the weighted average number of shares in issue during the period

The Company has no dilutive potential ordinary shares in issue because it is loss making.

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. There are no material adjustments in respect of this measure

## 6. Share premium account and reserves

	Share premium account Unaudited £'000	Merger reserve Unaudited £'000	Profit and loss account Unaudited £'000
At 1 September 2003	31,808	(204)	(26,895)
Premium on issue of shares	6,481	-	-
Expenses of new share issue	(154)	-	-
Loss for the year	-	-	(6,226)
Share option compensation charge	-	-	55
<b>At 31 August 2004</b>	<u><u>38,135</u></u>	<u><u>(204)</u></u>	<u><u>(33,066)</u></u>

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

	2004 Unaudited £'000	2003 Audited £'000
<b>Continuing activities</b>		
Operating loss	(6,996)	(5,954)
Depreciation on tangible fixed assets	93	106
(Gain)/loss on disposal of fixed assets	(6)	1
(Increase) in stocks	(308)	(43)
(Increase)/decrease in debtors	(108)	2,051
Increase/(decrease) in creditors	444	(130)
Increase in provision for share option compensation charge	55	31
<b>Net cash outflow from continuing operating activities</b>	<u><u>(6,826)</u></u>	<u><u>(3,938)</u></u>

## **Kaufman, Ross (Shld-NY-CP/Intl)**

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**From:** Lippert/Heilshorn & Associates, Inc. [etang@lhai.com]  
**Sent:** Thursday, January 20, 2005 8:02 AM  
**To:** Kaufman, Ross (Shld-NY-CP/Intl)  
**Subject:** Phytopharm plc News

Phytopharm Announces Results of Interim Data Review for Phase II Proof of Principle Study in Alzheimer's Disease

Preliminary Results of Completed Study Expected Fourth Quarter 2005

GODMANCHESTER, Cambridgeshire, U.K.--Jan. 20, 2005--Phytopharm plc (LSE:PYM) (OTC:PHYOF) (OTC:PHYOY) ("Phytopharm") announces today the outcome of a scheduled interim data review for the ongoing phase II proof of principle clinical study of PYM50028 (Cogane(TM)). The compound is an orally active, synthetic, neuroprotective and neuroregenerative product that is under development as a treatment for Alzheimer's disease. The study is being conducted in the UK under the terms of a clinical trial authorization (CTA), which has been granted by the Medicines and Healthcare products Regulatory Agency (MHRA).

This randomized, double-blind, placebo-controlled study is designed to evaluate the safety, efficacy and pharmacokinetic profile of PYM50028 after once daily oral administration for 12 weeks to patients with Alzheimer's disease. In accordance with the protocol, an interim review was conducted after the first 60 subjects completed the study. The objectives of this review were to evaluate the emergent safety profile of the study and to re-estimate the total number of subjects required to measure the efficacy of PYM50028 on cognitive performance.

The safety review was conducted by an independent consultant physician, who was provided with blinded data for each of the two treatment groups. He concluded that "the data obtained to date indicate that the study medication is not associated with any safety concerns." Therefore, the study will continue with no changes to the safety monitoring.

The sample size re-assessment was conducted by an independent statistician, who reported that the sample size for the study should be increased from 200 to 238 subjects. Phytopharm is seeking regulatory and ethics approval for this amendment.

Subject recruitment for the study is expected to be completed during the second quarter of 2005, with preliminary results still anticipated to be available in the fourth quarter of 2005.

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

Dr. Richard Dixey, Chief Executive of Phytopharm, said: "We are encouraged by the emerging safety profile of Cogane(TM) and look forward to completing the study by the end of the year. With more than 4.5 million people thought to be suffering from Alzheimer's disease in the U.S., and similar prevalence in other major markets, Cogane(TM) addresses a major opportunity where there is a clear need for improved medication."

### NOTES TO EDITORS

Alzheimer's disease

Alzheimer's disease is a neurodegenerative disorder that mainly affects the elderly and is characterized by a progressive loss of learning ability and memory. Alzheimer's disease is thought to affect 4.5 million Americans, and it is believed that this number will continue to grow to approximately 16 million by 2050 (Source:

Alzheimer's Association). Several factors have been proposed to play a role in the underlying neurodegeneration, including the excessive formation of beta-amyloid, glutamate and a decrease in neurotrophic factors in the brain.

In pre-clinical studies, the synthetic chemical PYM50028 has been shown to be neuroprotective against beta-amyloid and glutamate damage, to reverse the decrease of neuronal growth factors and to reverse neuronal degeneration observed in the aging brain. Importantly, this product restores levels of proteins that are altered in the aging brain, returning them to levels observed in the young and causing beneficial neurite outgrowth and branching. In addition, PYM50028 restores the learning and memory ability in Alzheimer's disease models and thereby offers the potential to reverse the symptoms of 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 U.S., the total annual cost burden for Alzheimer's disease exceeds \$100 billion (source: U.S. Alzheimer's Association).

#### Phytopharm plc

Phytopharm is focused on the research and development of novel pharmaceutical and functional food products based on clinical and pre-clinical data generated from medicinal plant extracts. The Company has seven development programs in four disease areas: neurodegeneration, obesity and metabolic disease, dermatology and inflammation and has a portfolio of two marketed veterinary products.

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

This press release may contain forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933 and Section 21E of the U.S. Securities Exchange Act of 1934 with respect to the financial condition, results and business achievements/performance of Phytopharm and certain of the plans and objectives of its management. These statements are statements that are not historical facts. Words such as "should," "expects," "anticipates," "estimates," "believes" or similar expressions, as they relate to Phytopharm, are intended to identify forward-looking statements. By their nature, forward-looking statements involve risk and uncertainty because they reflect Phytopharm's current expectations and assumptions as to future events and circumstances that may not prove accurate. There is no guarantee that the expected events, trends or results will actually occur. Any changes in such assumptions or expectations could cause actual results to differ materially from current expectations.

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**From:** Lippert/Heilshorn & Associates, Inc. [etang@lhai.com]  
**Sent:** Wednesday, December 15, 2004 7:36 AM  
**To:** Kaufman, Ross (Shld-NY-CP/Intl)  
**Subject:** Phytopharm plc News

Phytopharm and Unilever Enter into a Licence and Joint Development Agreement for Hoodia Gordonii Extract

Agreement includes provisions for substantial milestone payments, stage payments and royalties

GODMANCHESTER, United Kingdom--Dec. 15, 2004--Phytopharm plc (NASDAQ:PHYOF)(LSE:PYM) ("Phytopharm") announced today that it has granted an exclusive global licence to its Hoodia gordonii extract to Unilever plc, the global consumer products company and owner of a number of the world's leading brands.

As part of the agreement, Unilever will commit to initial payments totalling approximately GBP 6.5 million (\$12.5 million) out of a potential total of GBP 21 million (\$40 million) in payments to Phytopharm. In addition Phytopharm will receive an undisclosed royalty on sales of all products containing the extract.

The extract of Hoodia gordonii, a South African plant, was licensed exclusively by Phytopharm from the South African Council for Scientific and Industrial Research (CSIR) in 1997. Phytopharm has been actively developing the extract for incorporation into weight loss products.

Unilever and Phytopharm will collaborate on a five stage research and development programme of safety and efficacy studies with a view to bringing new products to market. Unilever will also manage a separate agronomy programme and will support the international patent programme for the products.

Obesity has reached epidemic proportions globally, with more than 1 billion adults overweight -- at least 300 million of them clinically obese -- and is a major contributor to the global burden of chronic disease and disability (Source: World Health Organisation).

Commenting on today's announcement, Dr. Richard Dixey, Chief Executive Officer of Phytopharm, said: "We are delighted to enter into this agreement with the global leader in weight management products. Our partnership with Unilever supports the development of this product with milestones and a fully funded programme and we look forward to generating royalty income from our partner's globally recognised brands."

A conference call for analysts and investors will be held at 8.30am today. Please call Mo Noonan on 020 7269 7116 for details.

### NOTES TO EDITORS

#### Unilever

Unilever is one of the world's largest consumer products companies with annual sales of \$48.4 billion in 2003. It produces and markets a wide range of foods and home and personal care products including Becel, Bertolli, Birds Eye, Blue Band, Country Crock, Findus, Flora Pro-Activ, Heart, Hellmann's, Iglo, Knorr, Lipton, Rama, and SlimFast. Unilever operates in more than 100 countries around the globe and employs approximately 230,000 people.

#### CSIR

The CSIR is the largest public Research and Development organisation in Africa. It has a turnover of US\$150 million and a staff complement of approximately 2500 specialist scientists,

engineers, technologists and support staff who undertake broadly-based, market-driven research and development for the benefit of the commercial market place, as well as urban and rural communities in South Africa and the region. In 2003, the CSIR entered a benefit sharing agreement with the South African San Council, who represent the peoples whose traditional use led to the investigation of the Hoodia plant.

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