

# Phynova Group

April 2008

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**Index: Aim**

**Sector: Healthcare**

## Key points

- Structure of both the operations and the organisation strengthened
- Drug development program moving forward on track
- £1.4m cash at year end, bolstered by subsequent equity placement
- Subject to financing, Group's potential not reflected in current share levels

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# Phynova Group



## Phynova Group

PYN.L

Date:	09-04-08
Share price p	43
52 week High/Low p	60/42
Issued share cap m	20
Market cap £m	9

[www.phynova.com](http://www.phynova.com)

Company Description: Phynova Group Plc (PYN) is a UK-based, semi-virtual pharmaceutical development company focused on the discovery and development of plant-derived prescription drugs for the treatment of viral and bacterial infections, metabolic diseases and cancer.

## FY2007 YEAR-END RESULTS AND UPDATE

The year reported has seen all aspects of the business further developed and strengthened:

- Over the last 12 months Phynova has moved forward with the development of its 6 drug candidates, including the successful completion of the Phase I/II clinical trial of PYN17. On the back of positive results generated by other projects the Company has started negotiations with a number of interested parties for both product development collaborations and out-licensing agreements. In some cases commercial due diligence is already in progress which suggests that news flow in the coming months will be particularly strong.
- The Company has strengthened the Board of Directors and Senior Management team by appointing a Chairman and new senior staff. Access to investors has been increased with the Company's shares now traded on the AIM, the PLUS-Market (since November) and, from April 16 2008 onwards, the US International PrimeQX platform as well.
- Phynova's fiscal year ended in line with expectations. Pre-tax losses widened to £2.9m (FY2006: £1.6m), EPS -15.1p (FY2006: 13.1p) and the period ended with cash resources of £1.4m (FY2006: £2m). We expect losses to increase further in 2008 as PYN17 commences a Phase IIb clinical trial in the US. Another two drug candidates, depending on the timing of the regulators' response, *could* be entering the clinic in 2008. Post-period the Company successfully raised over £1.1 from existing and new investors but we foresee additional funds being required in 2008.
- We do not envisage Phynova becoming profitable until FY2009 when the first revenues should be generated from initial up-front payments, generating a positive EPS. We don't discount, however, the possibility of some deals arriving early, during 2008. As we mentioned in our previous report (*June 2007*), the current status of the portfolio development makes an *exact* current valuation all but impossible. Nonetheless, we see sound reasons for **Phynova to trade at more than twice the current share price** as awareness of its potential grows from the visibility that positive clinical and pre-clinical results can bring.

Phynova is quoted on AIM and investors should be aware that share traded on AIM are subject to lighter due diligence than shares quoted on the main market and are therefore more likely to carry a higher degree of risk than main market companies.

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## FY 2007 - OVERVIEW

Phynova ended the 2007 fiscal year in line with expectations. R&D and administration expenses increased by 48.4% and 87.9% respectively, creating pre-tax losses of £2.9m (FY2006: £1.6m) and negative EPS 15.1p (FY2006: 13.6p).

Total R&D expense for the year came to just over £1m (FY2006: £499k) reflecting the progress made in the development of the pipeline and in particular the completion of Phase I/II clinical trials for PYN17. We expect this amount to increase substantially in 2008 and 2009; PYN17 will start a Phase IIb efficacy and safety trial in the US which will involve over 230 patients; two drug candidates are expected to enter the clinic in the UK (PYN22) and in China (PYN9) possibly this calendar year; and PYN6 in 2009. Exact timing is dependent on the regulators' responses.

In 2007 Phynova's business structure has grown its infrastructure via the increased involvement of existing consultants and the hiring of new ones. During the period the Board of Directors was strengthened with the appointment of a new Chairman, and a number of senior managerial staff. Within the administration expense payroll more than doubled during the period to £949k from £410k the previous year.

FY2007 also represented Phynova's first full year as a public Company. The completion of the Botanic Century acquisition, the establishment of Phynova China Ltd. and the drive in marketing activities have been all contributory factors to the increase in operating costs that totalled £1.9m (FY2006: £1m).

The year ended with cash resources of £1.4m (FY2006: £2m).

### Post period

In March, Phynova raised £1.1m by placing 2.75m new ordinary shares at 40p with existing and new private investors. These funds will be partly used to fund the PYN17 Phase IIb clinical trial, but with an estimated administration overheads burn rate of around £150k a month, we expect the Company to come back to the market for additional funding in 2008.

Since November 2007, Phynova's shares have been traded on both AIM and the PLUS-Market under the same trading symbol. In April 2008, Phynova's shares will be also traded in the US on the US International OTCQX platform (*International PrimeQX tier*) under the symbol PHNVY. The Company has established a sponsored level one ADR (American Depositary Receipt) and will issue ADRs in respect of up to 25% of its issued share capital and each ADR will represent 10 ordinary Phynova shares.

The International OTCQX is a new trading platform that provides a cost effective approach for non-US companies already listed on a qualified international exchange to establish a presence in the US securities market. As long as an OTCQX-traded company complies with the regulatory environment of its primary exchange, there is no need for the Company to adhere to the SEC registration and reporting rules, as it falls within the exemption set in SEC Rule 12g3-2(b).

*Shares traded in the  
UK and in the US*

**Table 1: Profit & Loss**

<b>Year-end September (£ '000)</b>	<b>2005A</b>	<b>2006A</b>	<b>2007A</b>	<b>2008E</b>	<b>2009E</b>
Revenues	0.0	0.0	0.0	0.0	6,600.0
COGS	0.0	0.0	0.0	0.0	0.0
Gross profit	0.0	0.0	0.0	0.0	6,600.0
R&D	243.3	497.8	1,027.0	3,000.0	4,100.0
Administration expense	363.4	1,034.1	1,943.3	1,950.0	1,950.0
AiM Listing	0.0	131.8	0.0	0.0	0.0
	606.7	1,663.7	2,971.0	4,950.0	6,050.0
Share of operating loss in associated undertaking	-	-	58,652		
<b>EBIT</b>	<b>-606.7</b>	<b>-1,663.7</b>	<b>-3,029.4</b>	<b>-4,950.0</b>	<b>550.0</b>
Interest receivable	0.0	24.7	87.2	42.8	27.9
Interest payable	0.0	1.4	3.6	3.0	2.0
Net interest	0.0	23.3	83.6	39.8	25.9
<b>Pre-tax loss/income</b>	<b>-606.7</b>	<b>-1,640.4</b>	<b>-2,945.8</b>	<b>-4,910.2</b>	<b>575.9</b>
<b>Taxation on ordinary activities</b>			<b>93.1</b>		
<b>Net loss/income</b>	<b>-606.7</b>	<b>-1,640.4</b>	<b>-2,852.7</b>	<b>-4,910.2</b>	<b>1,184.0</b>
EPS	-8.7	-13.6	-15.1	-20.0	2.3
Weighted Av. no. of shares	6,953	12,028	18,855	24,536	24,536

ED estimates

**Table 2: Balance sheet**

<b>Year-end September (£ '000)</b>	<b>2005A</b>	<b>2006A</b>	<b>2007A</b>	<b>2008E</b>	<b>2009E</b>
Fixed assets	2.2	7.6	547.6	500.6	504.9
Current Assets	233.5	2,232.4	1,845.5	1,836.8	2,518.5
Current Liabilities	217.1	206.5	374.8	572.7	682.7
Net Current Assets	16.4	2,025.8	1,470.7	1,264.1	1,835.7
<b>TOTAL NET ASSETS</b>	<b>-217.5</b>	<b>1,662.2</b>	<b>1,674.9</b>	<b>1,414.7</b>	<b>1,990.6</b>

ED estimates

**Table 3: Cash Flow**

<b>Year-end September (£ '000)</b>	<b>2005A</b>	<b>2006A</b>	<b>2007A</b>	<b>2008E</b>	<b>2009E</b>
Cash flow from Operations	-453.6	-1,586.4	-2,847.4	-4,749.7	-20.3
Cash Flow from Investing	-0.7	15.4	-524.9	29.5	14.4
Net cash flow before financing	<b>-454.3</b>	<b>-1,571.0</b>	<b>-3,372.3</b>	<b>-4,720.2</b>	<b>-5.8</b>
Net cash flow from financing	429.2	3,520.2	2,821.1	4,700.0	0.0
<b>Change in liquid funds</b>	<b>-25.1</b>	<b>1,949.2</b>	<b>-551.3</b>	<b>-20.2</b>	<b>-5.8</b>
Cash at beginning of the period	53.9	28.8	1,978.0	1,426.7	1,406.5
<b>Cash at the end of the period</b>	<b>28.8</b>	<b>1,978.0</b>	<b>1,426.7</b>	<b>1,406.5</b>	<b>1,400.7</b>

ED estimates

**Table 4: Forward Events (calendar)**

<b>DATE</b>	<b>DESCRIPTION</b>
H12008	PYN17 – Phase IIb clinical trial expected to start in the US
H2 2008	PYN18 - Completion of <i>in-vitro</i> studies
H2 2008	PYN22 - Start of clinical trial
H2 2008	PYN9 – Start clinical trial in China
2008/2009	Possible out-licensing agreements
H2 2009	PYN 17 – Preliminary Phase IIb clinical results
H2 2009	PYN18 - Completion of <i>in-vivo</i> studies
Q4 2009/Q1 2010	Completion PYN9 clinical trials in China
Sometime in 2009	PYN6 – Starting clinical trials

## DEVELOPMENT PROGRAMMES

Phynova has made significant progress in the development of its 6 drug candidates and all of them seem to be within the planned development timeline.

These products are at a differentiated development stage ranging from pre-clinical to Phase IIb. They consist of a combination of i) existing therapeutic compounds, derived from **botanical medicines** that have a proven track record of effectiveness and safety in clinical settings in China (but not through the Western regulatory approval process) and ii) novel phytochemical compounds. These drug candidates have been acquired or in-licensed through a combination of joint-ventures, collaboration agreements with Chinese scientific organisations or in-licensing, as indicated in the table below.

Table 5: Development Status				
Project's code	Targeted therapeutic area	Development stage	Available treatments	Origin
PYN17	Symptoms associated with CHC	completed Phase I/II in the US	<b>Limited, Safety/tolerability issues</b>	*ONP
PYN18	Anti-viral HCV & Dengue fever virus	Pre-clinical	<b>No specific treatment for Dengue fever</b>	In-house development
PYN22	Obesity: non-alcoholic fatty liver disease (NAFLD)	Advanced pre-clinical	<b>No specific treatment</b>	Chongqing Institute
PYN6	Anti-bacterial(Acne & MRSA)	Pre-clinical	<b>Limited treatment for MRSA</b>	Botanic Century
PYN7	Cancer	Pre-clinical	<b>Limited, safety issues</b>	Co-development with HKJCICM
PYN9	Post-operative ileus	Advanced pre-clinical	<b>Limited</b>	Botanic Century

Company's Data

\*Oxford Natural Products Ltd.

Two of the six drug candidates have been developed by **Botanic Century (Beijing) Co. Ltd. (Botanic Century)**, Phynova's 45% owned subsidiary, an independent young pharmaceutical R&D organisation focused on the development of botanical formulations for the pharmaceutical industry and looking to expand its services to include fast growing sectors such as functional foods and beverages, nutraceuticals and cosmeceuticals. There is an increasingly marked shift in these sectors towards the use of natural plant-based extracts with multi-functional active ingredients that have specifications close to those of pharmaceutical ingredients.

The Company has a flexible business model that allow them not only to widen their customer base, but also to provide a broad range of R&D services within CHM (Chinese Herbal Medicine) from product design and process development to batch manufacturing, including regulatory filing, giving them the characteristics of a "one-stop-shop" organisation.

Since its formation in 2003, Botanic Century has been involved in the development of nine botanical compounds for third parties as a CRO (Clinical Research Organisation), started the development of five proprietary products, one of which is expected to enter the clinic in 2008 and has in-licensed Phynova's treatment for hepatitis C virus, PYN18, for the Chinese market.

*A combination of **existing and novel** therapeutic compounds*

*One-stop-shop R&D platform*

*CRO and proprietary drug development activities*

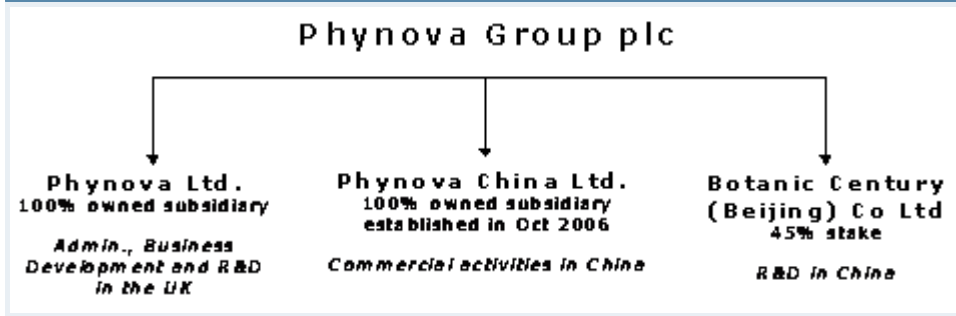
*Investigational process  
of existing drugs*

Botanic Century’s scientists have extensive experience and expertise in both CHM’s pharmacopeia and Western pharmacology. Over time they have built a ‘herbarium’ of around 300 medicinal plants specimens that have a record of safety and efficacy and relative suppliers in China. This is a particularly valuable tool for internal research but also, given the increasing demand for plant-derived phyto-medicines, provides a service to those manufacturers looking to widen their sourcing of plant extracts or seeking plant identification services outside the proprietary herbarium.

The methodology for the investigation of CHM as a source of new drugs includes (*but is not limited to*) the pharmacological screening of the plant preparation(s) followed by a bioassay-guided fractionation, which leads to the isolation of the pure active plant constituent(s). The *in-vivo* testing of the compound(s) consents the establishment of the claimed pharmacological activity. Once the activity has been confirmed, a corresponding *in-vitro* method is developed for the monitoring of the activity during the purification of the active constituent(s). The next step is the development of the plant preparation’s standardisation or the commencement of the structure activity relationship studies by partial or total synthesis of the active substance(s) to optimise the efficacy, safety and bioavailability profiles in *in-vivo* studies. This process requires a multi-disciplinary research team, which comprises pharmacognosists, microbiologists and biochemists depending on the kind of test models used during the screening process. The procedure just described is an example of the R&D activities and services provided by Botanic Century’s at their phytochemistry laboratories located in the Zhong-Guan-Cun Life Science Park near Beijing.

Through this joint-venture Phynova has been able to access new drugs candidates, R&D facilities and expertise, and a presence in mainland China. Also, as Botanic Century expands its commercial operations Phynova is set to benefit from the increased revenue generation. We expect Phynova to exercise its option to increase its stake in Botanic Century as soon as the terms of the agreement will allow them to do so. Two of the original founders hold 33% and 22% stakes respectively.

**Figure 1: Organisational structure**



*Company Data*

Phynova’s commercial strategy is seeking to out-license its drug candidates to pharmaceutical companies, once Phase II has been completed or earlier should the opportunity arise, in exchange for upfront fees, milestones and royalty payments. The cash flow generated will help to fund drug development and reduce the investment risk in the Company.

## R&D PIPELINE IN DETAIL

### PYN17 - Symptoms associated with Chronic Hepatitis C (CHC)

PYN17 is initially being developed as an oral **stand-alone** therapy for the treatment of symptoms and liver inflammation associated with (CHC) and could also be developed as a **combination therapy** to be used with peg-interferon and ribavirin, as well as a treatment to prevent the progression of liver fibrosis associated with a number of viral, metabolic and drug induced disorders. This is the only treatment undergoing clinical development addressing the debilitating symptoms, impaired quality of life and liver inflammation caused by CHC.

The compound is a novel formulation consisting of four botanical extracts derived from three Chinese plant species and one Western plant species. Individually they have been used to treat a range of liver diseases in Asia and Europe so have a long history of safety with very little, or no, toxicity. The pharmaceutical grade raw material is commercially available and supplied by two manufacturers.

PYN 17 successfully completed a Phase I/II clinical trial confirming safety and tolerability and validated the findings of an earlier study conducted in London. Details of the clinical trial and results are shown in the table below.

**Table 6: PYN 17 - Phase I/II US clinical trial design and results**

Design	<ul style="list-style-type: none"> <li>● Double-blind, randomised, placebo controlled</li> <li>● Multi-centre: 5 hepatology centres in the US (2 in Colorado, 2 in North Carolina and 1 in Florida)</li> <li>● Single dose twice a day oral administration (25mg sachet)</li> <li>● 4 weeks treatment</li> <li>● 39 patients enrolled (2:1 PYN17:placebo randomisation), 38 patients completed the study</li> </ul>
End points	<ul style="list-style-type: none"> <li>● Safety and efficacy (adverse events, fatigue, health related Quality of Life (HRQoL), vitality and ALT levels)</li> </ul> <p>Monitored through well validated tests, including careful reporting of adverse events, HRQoL and fatigue scores and liver function tests to assess patients' response and alleviation of the symptoms and liver inflammation associated with the disease</p>
Patient Group	<ul style="list-style-type: none"> <li>● Patients suffering with CHC, who have not responded to pegylated interferon and ribavirin or are not suitable for such treatment typically on account of the side effects and risks associated with these treatments</li> </ul>
Comments	<ul style="list-style-type: none"> <li>● No serious adverse events were reported</li> <li>● The group treated with PYN17, 11/26 (42.3%) patients reported adverse events of some kind during treatment against 10/13 (76.9%) in the group receiving placebo</li> <li>● For drug-related adverse events, the incidence was 6/26 (23.1%) on PYN17 compared with 3/13 (23.1%) on placebo</li> </ul>

#### Company Data

The Phase IIb clinical trial is expected to start sometime in H1 2008. The study involving a three month treatment period is a randomised, double-blind, placebo-controlled, multi-centre trial, including over 230 CHC patients. The primary objective of the trial is to evaluate the efficacy and safety of three dose levels of PYN17 in improving the symptoms, impaired HRQoL and liver inflammation associated with CHC. Results expected in H2 2009.

*Dual development opportunity*

*4 botanical extracts of Chinese and Western origin*

*Completed Phase IIa*

*Phase IIb results expected in H2 2009*

## About CHC symptoms

CHC is the most common liver disease currently seen in clinical practice. The incubation period, from the time of exposure to the virus until the onset of the disease, is 1 to 6 months. Early symptoms include poor appetite, nausea, aching muscles and joints, abdominal pain and light fever. Patients going onto develop chronic disease (around 80%) experience fatigue, reduced vitality, abdominal discomfort below the right ribs and aching muscles and joints, although not all patients develop obvious symptoms. HCV can be present for as long as 20 years without presenting any further problems. In other patients, however, CHC can lead to long-term disability, cirrhosis of the liver, liver cancer and liver failure requiring transplantation. In many patients, symptoms increase as the disease progresses, particularly with the development of cirrhosis, liver failure and liver cancer, although in some patients symptoms develop quite late in the progression of the disease.

## Statistical data

Since its discovery and characterisation in 1989 HCV has become a global health issue. It is one of the 10 leading causes of infectious disease deaths worldwide with an estimated 250,000 reported deaths per annum. Recent data from the WHO (World Health Organisation) shows 170m individuals chronically infected with the virus and 3 to 4m are newly infected each year. There are geographic differences in the prevalence of the disease. In Europe, prevalence varies from 0.01% up to 5% population. In Africa rates of up to 51% have been reported, Egypt alone has an infection rate of 22% due to the use of contaminated glass syringes in a nationwide schistosomiasis campaign. The highest prevalence has been reported in Asia and Africa, whereas the prevalence of the disease is lower in industrialised countries like North America, Northern and Western Europe.

## Available treatments

Antiviral drugs such as pegylated interferon (sub-cutaneous injection), taken alone or in combination with ribavarin (oral) can be used for the treatment of patients with CHC, but the cost of treatment is very high. Treatment with interferon alone is effective in about 10% to 20% of patients. Interferon combined with ribavarin is effective in roughly up to 50% of patients. Ribavarin does not appear to be effective when used alone. Both these drugs, however, are associated with unpleasant and serious side effects. Compliance and side effects represent considerable issues for practitioners and patients alike. Global market size estimated to be around US\$10bn by 2010

## PYN 18 – Anti-viral for the treatment of CHC & Dengue Fever (DF)

PYN18 is an *in-house* discovery and contains a highly purified active fraction in common with PYN17. Phynova filed a patent for HCV in 2006 and one for Dengue fever in 2007. Dengue Fever is a tropical, mosquito-borne disease for which there is **no specific treatment available or vaccine**, only supportive therapy. The only way to stop the virus is to contain the mosquito population.

The preliminary screening for HCV and DF has been conducted in Imperial College in the UK and at the Siriraj Hospital in Bangkok. Confirmatory work for both HCV and DF has been also done at the Rega Institute in Belgium. The in-vitro studies

*170m individuals infected*

*250,000 deaths per annum*

*3 to 4m new cases each*

*Compliance and side-effect represent considerable issues with existing treatment modalities*

*No specific treatment available for Dengue fever*

*Confirmatory work done in Belgium*

could be completed in H2 2008 and the *in-vivo* in H2 2009. New patent applications have been filed and PYN18 has attracted interest from several companies in the antiviral field.

Phynova is seeking an early development **out-licensing deal** for these two compounds and the management have confirmed that a considerable level of interest has been shown by a number of large pharmaceuticals companies for the PYN18-Dengue Fever.

## About Dengue Fever

Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) are infectious diseases transmitted to humans by the *Aedes aegypti* mosquito and are characterised by sudden fever, severe headache, muscle and joint pain, rashes and in certain severe cases hemorrhagic episodes. There are four closely related strains each sufficiently different to cause no cross-protection and epidemics by multiple strains. Dengue Fever is the second largest tropical disease and often found in urban areas of developed tropical nations like Singapore.

## Statistical data

There are about 40 million cases of DF and several hundred thousand cases of DHF globally each year. In 2007 according to the Pan American Health Organisation 630,356 cases were reported in Latin America, most in Brazil (559,954 DEN1, 2 and 3 serotypes ([www.paho.org](http://www.paho.org))), Venezuela and Colombia, with 12,147 cases of DHF and 183 deaths, 25 of which in the Dominican Republic alone. Mexico struggled with the alarming increase in the deadly hemorrhagic form of dengue, which accounted for roughly one in four cases. Figures from South East Asia are not any better:

- Singapore has reported more than 6,000 cases and 8 deaths at the end of September 2007;
- In the Philippines about 19,000 people have been stricken with the disease so far and 190 have died. Death toll is 4.6% down when compared to the same period in 2006 according to the Department of Health.
- The incidence in Vietnam has risen by almost 50% in both reported cases (68,000) and death toll (60) in 2007.

In the first three months of 2008 the Brazilian health authorities have reported 406 cases of DHF, with 34 deaths nationally and constitute a significant increase in the number of cases in several states This constitutes a significant increase in the number of cases in several states compared to the same period in 2007: Amazonas (9.8 times), Rondônia (5.3 times), Sergipe (4.7 times), Bahia (3.4 times), Rio Grande do Norte (2.8 times), Pará (2.5 times), and Rio de Janeiro (2.2 times). DEN 2 and DEN 3 are the circulating serotypes.

According to the Rio's Secretary of State for Health, Sérgio Côrtes, Rio de Janeiro state alone has reported 58,000 cases of dengue fever (DF) and 245 cases of DHF (21 deaths) with the state capital reporting 36,600 cases and 67 deaths. A change in the age distribution of severe cases has been observed: of the 2,116 patients hospitalized, 53% were children under the age of 14 years. There have been 20 reported deaths due to DHF, 8 due to Dengue Shock Syndrome (DSS) and 19 due to DF with complications. More than 50% of the deaths have occurred among children aged 2–13 years. The number of deaths suggests a more severe

*Incidence*

*Worst outbreak in recent memory*

evolution of clinical illness than expected. A neighbouring country, Paraguay, actually declared a related state of emergency on 25 February 2008.

## **PYN22 – Non-Alcoholic Fatty Liver Disease (NAFLD)**

PYN22 has been in-licensed from the Chongqing Institute of Ecological Materia Medica Co. Ltd. This compound contains a highly purified active fraction from one plant extract. PYN22 is in an advanced pre-clinical development stage and the data emerging from the studies carried out so far show that PYN22 reduces blood lipids and body fat and appears to reduce insulin resistance.

Phynova is preparing a regulatory dossier and if everything goes according to plan PYN22 could be in the clinic sometime in 2008 in the UK. Also, the management has confirmed that they are in licensing discussions with several interested parties and entering in commercial due diligences. A patent has been filed in the UK.

### **About NAFLD**

NAFLD is a liver disorder defined as a significant lipid deposition in patients without a history of excessive alcohol ingestion. The pathophysiological mechanism underlying NAFLD is currently unknown, although the close link with obesity, a growing problem that has reached epidemic levels in the U.S and other industrialised nations, has suggested a role for insulin resistance. In severe cases of NAFLD the disease spectrum includes nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and liver failure. **Currently there is no specific treatment for NAFLD and the size of the global market is estimated to be c. US\$1bn.**

## **PYN6 – Anti-bacterial**

PYN6 is being co-developed with Botanic Century as an anti-bacterial treatment for MRSA and acne. This compound contains a highly purified active fraction from one plant extract and is in a pre-clinical development stage, expected to be in the clinic sometime in 2009.

Pre-clinical studies have been conducted in collaboration with the University of East London have demonstrated a high degree of bacterial inhibition against 30 common strains of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from London's teaching hospitals. Inhibition was demonstrated against all of the strains of MRSA that were tested, using levels of PYN6 that were some tenfold less than that typically needed to achieve inhibition with mupirocin, the topical antibiotic currently routinely used for treatment of skin infections involving MRSA. Very importantly no resistance was observed even after prolonged culture of numerous MRSA strains with PYN6. The compound also showed significant activity against *Propionibacterium acnes*, the organism that causes acne.

Formulation studies to develop a topical gel, cream or ointment containing PYN6 as active ingredient are ongoing and Phynova in active discussions with several dermatological companies regarding future development options and commercialisation possibilities.

*Possibly in the clinic in 2008*

*Possibly in the clinic in 2009*

*Started formulation studies*

## About MRSA

MRSA (Methicillin Resistant *Staphylococcus aureus*) is commonly referred to as the 'superbug'. It's estimated that one in three healthy people carry the bacteria on their skin, in their noses or in the back of their throats. Infection happens if the bacteria enter the body through a cut, a graze or any break in the skin, either accidentally or deliberately (i.e. drip or surgery). MRSA is treatable but the resistance of the MRSA bacteria to certain types of antibiotics makes treatment more difficult. Most strains of MRSA can be treated with the antibiotics vancomycin and teicoplanin given by injection or through an intravenous drip. **Long-term, targeted treatment is not currently available and the global market size is estimated at around US\$1bn.**

## About Acne

Acne is a skin condition typically affecting the skin of the face, back, neck, chest and arms of adolescents and the severity of the condition can vary from minor inflammatory lesions to frank fibrosis. Most people affected are aged between 12 and 25. However, men and women in their 30s and 40s can also suffer with acne. There are many treatments available to help deal with the condition, but none have proved very effective. Global market size is expected to be over US\$2bn by 2010.

## PYN9 – Post-Operative Ileus (POI)

Botanic Century is developing PYN9 for the Chinese market with Phynova retaining the exclusive global rights.

All the pre-clinical trials have been conducted in China following the Chinese regulatory procedures. An IND application as been filed with the SFDA and approval is still pending. Phynova's management remains confident that PYN9 will be in the clinic sometime in 2008 in China. Three clinical trials have been scheduled over a 2-year period with completion expected in late 2009 or early 2010. Initial IP will be filed with the Chinese patent office and international filing will follow through PCT (Patent Cooperation Treaty).

On the basis of the positive *in-vivo* motility preclinical data carried out by Botanic Century, Phynova is planning to continue the preclinical and clinical development of PYN9, particularly as there is currently no effective treatment available and very few products in development. Phynova is preparing a preclinical development plan for Europe and the Company is already in commercial due diligence with a mid cap speciality pharma company from Europe.

## About POI

PYN is being developed for the treatment of Post-Operative Ileus (POI), a transient impairment of bowel mobility usually considered an inevitable response to surgery and one of the most common causes of prolonged hospital stay following abdominal surgery. It is believed that POI also occurs as a result of the use of opioids. Current treatment modalities include the avoidance of opiates and when possible the use of epidural local anaesthetics. Other potentially effective treatments include early enteral feeding and less invasive surgical procedures. **No targeted pharmacological treatment is currently available.**

*Pending approval of  
IND by SFDA*

### Drug in development (late development stage) for POI’s treatment

- **Entereg® (alvimopan)** is a first-in-class small molecule, peripherally-acting mu opioid receptor (PAM-OR) antagonist designed to block the adverse side effects of opioid analgesics on the GI tract without blocking their analgesic effects. The development of this product was recently stopped due to the occurrence of serious side effects including heart attacks and cancer in Phase III trials.

### PYN7 – Anti-cancer

PYN17 is being developed in collaboration with the Institute of Cancer Studies in Birmingham. It is based on products used in China for the treatment of different cancers and contains extracts from one plant. Although in early development stage, from the initial screening it appears active in a number of solid tumour cell based assays. PYN7 could be used in combination with existing cancer treatments to treat a number of common cancers with a high prevalence and high-unmet medical need. IP is being created.

## PATENTS

Phynova has three granted patents in the UK and several international applications, whereas Botanic Century has filed two patents covering the Chinese territory and one under the Patent Cooperation Treaty (PCT). The Company intends to increase patent protection as discoveries are made during the course of their activities, which include research programmes, acquisitions and future manufacturing activities. The same strategy will be applied to trademarks and design rights.

**Table 7: Patents**

Title	Status
Botanical drug or dietary supplement	Granted
Plant based medicament for the treatment of Hepatitis C	Pending
Extracts of Scutellaria for the treatment of SARS	Granted
Extracts of Scutellaria for the treatment of RSV	Granted

*Company Data and UK Patent Office*

**Table 8 : Trade marks**

Description	Trade Mark Ref. No	Status	Registration date
PHYNOVA	2417807	Registered	3rd November 2006
Phynova	2417819	Registered	3rd November 2006
Device only	2433905	Registered	21st September 2006

*Company Data and UK Patent Office*

**Table 9:2006-2007 Historic news**

	<b>Description</b>
<b>2007</b>	
Dec-07	Preliminary pre-clinical data for PYN6
Nov-07	Preliminary data for PYN17 Phase I/II PYN shares admitted to trading on PLUS-Market
Sep-07	Completed patient enrolment for PYN17
May-07	Nominated for an industry award Launched Chinese website Started US Phase IIa clinical trial for PYN17
Mar-07	Appointment of Director of Business Development
Feb-07	Signed a cancer treatment collaboration with the HKJCICM
Jan-07	FDA approved IND for PYN17 (CHC) Appointment of Chairman
<b>2006</b>	
Nov-06	Completed the acquisition and received the approval from the Chinese Authorities for an initial 45% stake in Botanic Century
Oct-06	Established Phynova China Ltd.
Sep-06	Raised c.£2.5m in a second round of financing
Aug-06	UK Patent Office granted key patent for PYN 17 covering HCV programme
Jul-06	Filed two patents applications covering PYN22 (obesity) and PYN18 (HCV)

*Company Data*

I certify that this report represents my own opinions  
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