



synairgen plc

Annual Report and Accounts 2006

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Synaigen is a drug discovery company focused on identifying and out-licensing new pharmaceutical products which address the underlying causes of asthma and chronic obstructive pulmonary disease

## Highlights

for the year ended 30 June 2006

### Financial highlights

- Turnover for the year: £82k (year ended 30 June 2005: £202k)
- Research and development expenditure for the year: £1,069k (2005: £557k)
- Retained loss for the year: £1,042k (2005: loss of £610k)
- Cash at 30 June 2006 of £7.5 million (2005: £8.7 million)

### Operational highlights

- Commencement of Phase I clinical trial in lead proprietary programme in inhaled interferon beta ('IFNβ')
- Second indication for IFNβ in COPD identified
- Proteomics research programme commenced
- Collaboration extended with undisclosed North American biotechnology company (post period-end)
- In-licensing of interferon lambda intellectual property (post period-end)



# Chairman's Statement

## Overview

Synairgen is a drug discovery company focused on researching treatments to address the underlying causes of asthma and chronic obstructive pulmonary disease ('COPD') through proprietary and collaborative programmes. Situated within the University of Southampton's School of Medicine, our work consists of a mix of proprietary research conducted in our leased laboratories by our own staff and research carried out by the University's scientists, sponsored and assisted by Synairgen's staff and specific resources.

A key theme in the commercial market, evidenced by transactions executed during the year, is the increasing need amongst the major pharmaceutical and biotechnology companies to fill development pipelines and we have continued to see significant relationships formed through licence and acquisition of promising intellectual property and collaborative research programmes from independent discovery and biotechnology companies.

Three years from its formation around a renowned team of professors based at the University of Southampton's School of Medicine, Synairgen has created for itself a potentially significant stake in new intellectual property in the field of respiratory research. This has come both through our proprietary research programmes and through our share of collaborative research. Our purpose in this phase has been, and continues to be, to build the value of the Company by creating, and adding value to, intellectual property in our area of expertise with a view to realising that value through licensing and collaborative development programmes.

Our scientific expertise lies in the fields of severe asthma and COPD, where there are significant unmet clinical needs and large target markets. During the year under review we have reviewed more opportunities than we have the resources to fulfil and have therefore re-visited our criteria for undertaking collaborative projects to limit them to those where there is scope for generating potentially valuable intellectual property for the Company. We have therefore ceased to undertake pure fee for service work.

During the year we have made good progress. Our lead proprietary programme for inhaled interferon beta has progressed well into its Phase I clinical trial. We have signalled a second indication for our interferon programme in the treatment of COPD, the fourth leading cause of death worldwide. Post period-end, we have further strengthened our interferon programme by in-licensing related intellectual property regarding a related interferon from Imperial Innovations. We have established discussions with potentially interested partners for this important programme.

Our research into the failure of the lung's self defence mechanism ('barrier function') and the associated proteomics research has continued to yield promising opportunities which will be pursued in subsequent periods, some by Synairgen alone and others in collaboration with research partners. To this end, we are delighted to have extended our initial programme with one significant unnamed collaboration partner with whom we have been working for some two years and uncovered potentially significant avenues for further research.

## Board

In April 2006 David Norwood resigned as a non-executive director in order to devote more time to IP Group plc and the Board appointed Dr Bruce Campbell as his replacement. On behalf of the Board I would like to thank David for his help and the enthusiastic support he has shown for Synairgen since its formation in late 2003. Bruce is non-executive Chairman of Proximagen Neuroscience plc and Chief Scientific Officer of IP Group plc. He has significant international experience in pharmaceutical drug development.

## Outlook

The last year has seen Synairgen add significantly to its intellectual property portfolio. The opportunities we have created so far have significant potential value over the coming years and the progress of our focused research programmes is promising.

**Simon Shaw**  
Chairman



# Managing Director's Report

This has been a year of good progress for Synairgen in our mission to generate out-licensable drug discoveries in the fields of asthma and COPD. Synairgen's business model is to research these areas, add value to our discoveries by utilising our *in vitro* testing platform of human disease, or by conducting early stage clinical trials, and ultimately out-license them to pharmaceutical or biotechnology companies.

During the year we progressed our inhaled interferon beta ('IFN $\beta$ ') programme into the clinic and produced preliminary data suggesting there is a place for inhaled IFN $\beta$  for the treatment of COPD. We have continued to evaluate two candidate growth factors capable of improving the lung's "barrier function" in asthma and in December 2005 we commenced our proteomics programme.

After the year-end, in July 2006, we in-licensed intellectual property relating to interferon lambda from Imperial Innovations, further enhancing our interferon programme. Following successful completion of the first phase of our joint discovery collaboration with the undisclosed North American biotechnology company, we have extended this programme.

## Inhaled IFN $\beta$ Asthma

Synairgen is developing inhaled IFN $\beta$  as a therapy to prevent or treat exacerbations of asthma caused by the common cold, principally the rhinovirus ('RV').

RVs cause up to 80% of asthma exacerbations. Severe asthma exacerbations will often lead to unscheduled use of healthcare resources. In the United States there are 1.9 million emergency department visits due to asthma per year and \$4.1 billion is spent every year on unplanned physician visits and hospitalisations. Current treatments depend on the use of steroids and  $\beta$ -agonist bronchodilators with actions on the symptoms of worsening asthma as opposed to the underlying causes. These treatments are inadequate, particularly in the severe asthmatic population and there is a large unmet and costly clinical need for an effective therapy.

Using human *in vitro* models, IFN $\beta$  has been shown to return to normal the asthmatic epithelium's protective response against RVs, by significantly lowering the amount of virus replication and ensuing tissue damage, thereby helping to fight infection in the lungs. Synairgen is developing an inhaled formulation for use in asthma. Synairgen intends to progress this

opportunity in the clinic towards a proof of concept Phase IIa clinical trial. We commenced a Phase I study in November designed to establish safety in allergic individuals without asthma and this study has now been extended to optimise aerosol delivery. Injectable IFN $\beta$  is already a well-established multiple sclerosis therapy marketed by Biogen Idec, Schering AG, and Serono/Pfizer.

## COPD

In our view, the common cold could potentially pose a greater risk to COPD patients than influenza, and is reported to be a major factor behind the worsening of COPD symptoms and resultant hospitalisations. At the American Thoracic Society meeting in May, we presented preliminary data showing that RV is 100 times more toxic to epithelial cells from smokers than non-smokers, which may help explain the occupancy of hospital beds by COPD patients during the common cold season. Our studies showed that COPD cells were able to eliminate RV when IFN $\beta$  was applied to the cultures *in vitro*.

## Interferon lambda

In August 2006 Prof. Johnston of Imperial College, and consultant to Synairgen, published a paper in Nature Medicine describing a deficiency of interferon lambda when cells from asthmatics were exposed to RV. Synairgen has licensed intellectual property relating to interferon lambda from Imperial Innovations, adding to our IP coverage in this area.

## Out-licensing

Synairgen is seeking to out-license its IFN $\beta$  programmes for both COPD and asthma any time up to or around completion of the Phase IIa proof of concept study and we have begun actively to engage with a number of potentially interested parties.

## Barrier Function

The epithelial cellular barrier in the lungs of asthma sufferers has been likened to a chronic wound and is known to be 'leaky'. This failure in barrier function may allow allergens, pollutants and viruses to penetrate through the epithelium into the underlying tissue. Synairgen scientists have been testing various growth factors to see if they can restore this protective barrier function. Two lead compounds have been identified; one is manufactured as a medicinal product and the other is a proprietary product for Synairgen.

# Managing Director's Report (continued)

## Proteomics

Proteomics is a technology being applied by Synairgen to identify individual protein differences between non-asthmatic and asthmatic cell populations. The proteomics programme commenced in December 2005 and although this is a new research programme, it has already identified several asthma-related candidate proteins. Over the next year Synairgen will identify and validate which of these individual proteins may constitute 'drugable', patentable targets for development and out-licensing.

## Staff

In order to meet the needs of our proprietary and collaborative programmes we have increased our number of research and clinical staff from 10 to 16 during the year.

## Post year-end

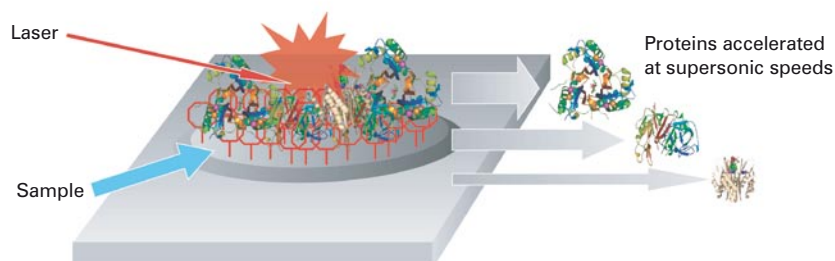
As announced in August 2006, we have in-licensed intellectual property relating to interferon lambda. In addition, the drug discovery collaboration with our unidentified biotechnology partner has been extended to enhance the power of the first round of experiments. We continue to develop new opportunities through our links to the research capability of the Company's Founders and have identified and assisted the University of Southampton with some early research into new discoveries in our field. Some of these appear very promising at this early stage.

## Outlook

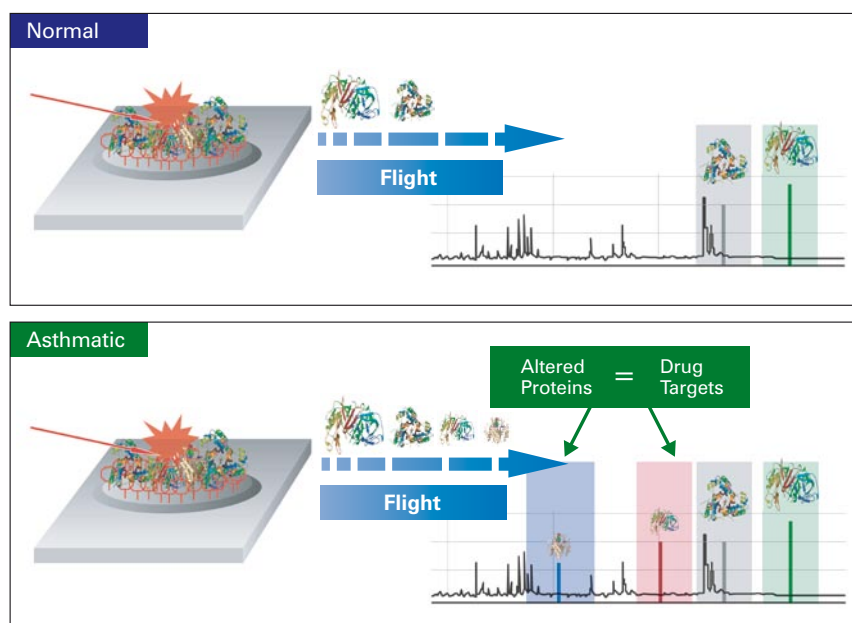
Over the next six to twelve months, we look forward to updating the market as to our progress in our IFN $\lambda$  clinical programme as well as developments in respect of potential partners. We anticipate that our growth factor compound will be validated *in vitro* and prepared for pre-clinical development. We will also continue to liaise with potential out-licensing partners for all of our programmes.

**Richard Marsden**  
Managing Director

## Proteomics enables the identification of protein differences between disease states



The 'time of flight' varies according to the mass of the protein, and allows different proteins to be detected. The diagrams below illustrate a comparison between the normal and asthmatic proteome



# Financial Review

The Financial Review should be read in conjunction with the financial statements and the notes thereto on pages 24 to 37. These financial statements have been compiled under UK Generally Accepted Accounting Practice ('UK GAAP') and comprise the consolidated financial statements of the Company and Synairgen Research Limited (together the 'Group').

## Profit and loss account

Revenue for the year ended 30 June 2006 was £82k (year ended 30 June 2005: £202k). The reduction in revenue from the prior year follows the Group's decision to cease undertaking pure fee for service activity which does not offer intellectual property upside and concentrate its resources on proprietary projects. The operating loss for the year was £1,673k (2005: loss of £908k), in line with our expectations. Research and development expenditure increased from £557k to £1,069k as the Group commenced its Phase I clinical trial on the IFN $\beta$  project and broadened its investment into the barrier function and proteomic programmes. During the year the number of research and clinical staff has increased from 10 to 16. The increase in other administrative costs from £418k to £671k reflects the full-year effect of both the additional senior management personnel recruited at the time of the IPO in October 2004 and the ongoing costs of being an AIM-quoted company. Interest receivable increased from £298k to £376k on account of the IPO funds raised. In July 2006, post year-end, the Group received a payment of £89k in full settlement of its research and development tax credit claim in respect of the year ended 30 June 2005. This amount and an amount of £166k in respect of the year ended 30 June 2006 have been recognised in this year's profit and loss account. The retained loss for the year was £1,042k (2005: loss of £610k) and the loss per share was 4.80p (2005: loss of 3.26p).

## Balance sheet and cash flow

At 30 June 2006, net assets amounted to £7.8 million (30 June 2005: £8.8 million) including cash and deposit balances of £7.5 million (2005: £8.7 million).

The principal elements of the £1.2 million decrease (2005: £8.3 million increase) in cash and deposit balances were:

- operating cash outflow of £1,530k (2005: £840k outflow);
- capital expenditure of £52k (2005: £60k);
- interest received of £397k (2005: £196k); and
- share issues (net of expenses) £nil (2005: £8,980k)

Capital expenditure comprised investment of £35k in laboratory and IT equipment and £17k on patent and licence costs.

## Treasury policy and financial risk management

The Group follows a risk-averse policy of treasury management. Sterling deposits are held with one or more approved UK-based financial institutions. The Group's primary treasury objective is to minimise exposure to potential capital losses whilst at the same time securing prevailing market rates.

### Interest rate risk

The Group's cash held in current bank accounts is subject to the risk of fluctuating base rates. The majority of the Group's financial assets are placed on fixed interest deposits. The interest rate profile of financial assets is illustrated in Note 17 to the financial statements.

### Currency risk

The Group is exposed to US dollar currency exposure as some of its revenues are denominated in this currency. The Group does not routinely hedge against this currency exposure.

## Adoption of International Financial Reporting Standards ('IFRS')

IFRS adoption becomes mandatory for AIM-quoted companies for periods beginning on or after 1 January 2007. The Company has reviewed as to when it should adopt IFRS and has decided to defer adoption until 1 July 2007 when accounting practice under certain standards has become clearer and custom and practice amongst smaller quoted companies in respect of the adoption of IFRS has emerged.

**John Ward**  
Finance Director



# Scientific Review

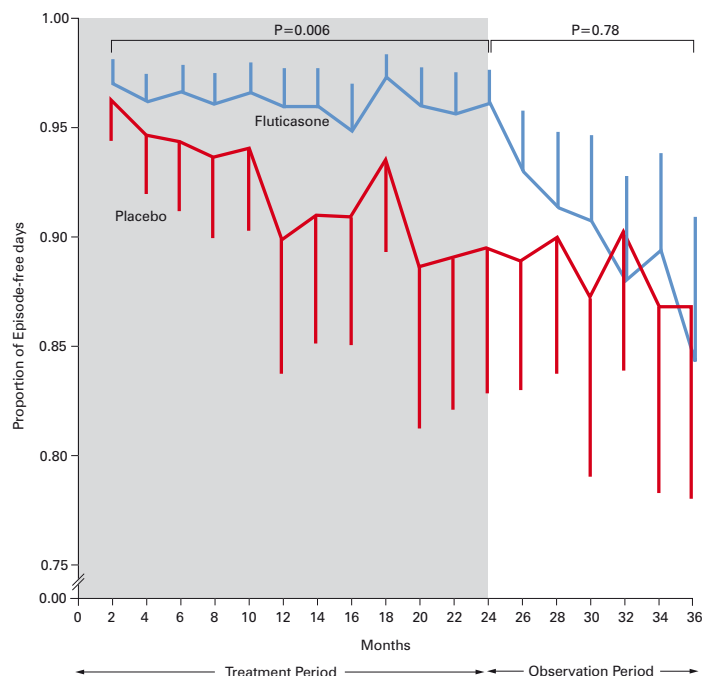
## The need for new asthma therapies

A recent survey undertaken by the British Lung and Asthma Information Agency, The Burden of Lung Disease (2nd Edition)<sup>1</sup>, has emphasised the importance of respiratory disease as a major cause of mortality and morbidity worldwide, with asthma, chronic obstructive pulmonary disease ('COPD') and associated infection accounting for most of this. When compared with other complex disorders, those affecting the lung continue to create challenges for effective therapy, especially in relation to agents that treat the causes rather than simply suppressing symptoms. In the case of asthma, focusing on treatments that relax airway smooth muscle such as the long and short acting  $\beta_2$ -adrenoceptor agonists or anti-inflammatory drugs that suppress inflammation has resulted in all asthma being treated in much the same way – ever increasing doses of these drugs in combination are being used to manage the disease in proportion to disease severity. This strategy has achieved good control of patients with mild-moderate disease, but according to international surveys of asthma patients there still remains a substantial unmet clinical need fuelled by the need to take drugs

with systemic side effects (such as oral steroids) especially at high doses. More recently concerns have been expressed over the safety of long acting  $\beta_2$ -agonists<sup>2</sup>, further emphasising the need for asthma treatments which are closer to the origins of the disease.

## Inflammation is not asthma

A clear understanding of the importance of airway inflammation in causing airway dysfunction in asthma has, by implication, led to the concept that if inflammation is sufficiently suppressed early in the course of the disease then this will influence its natural history. However, two large longitudinal studies of asthma in school children<sup>3,4</sup> and two very recent two year studies in infants at risk of asthma<sup>5,6</sup> have failed to show any long term benefit on the course of asthma despite suppression of symptoms (Guilbert et al<sup>5</sup> Figure 1, shown below). Thus, while current asthma therapy is adequate for controlling asthma in patients with mild to moderate disease, there exists no cure – patients with asthma need to take their controller therapy regularly and indefinitely.



**Figure 1:** Long term steroid use in children suppresses inflammation and symptoms but does not alter the course of the disease.

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Medical Society

## Bimonthly Proportion of Episode-free Days during the Two-Year Treatment Period and the Observation Period.

Fluticasone treatment, as compared with placebo, did not increase the proportion of episode-free days during the observation year (86.8 percent vs. 85.9 percent,  $P=0.78$ ), but during the two-year treatment period (shaded area) it significantly increased the proportion of episode-free days (93.2 percent vs. 88.4 percent,  $P=0.006$ ). The proportions of episode-free days in the fluticasone group and the placebo group were 97 percent and 96 percent, respectively, during the first two months of the treatment period; 96 percent and 89 percent during the last two months of the treatment period; and 84 percent and 87 percent during the last two months of the observation year — results that demonstrate an increase in the frequency of asthma-like symptoms over time. The two study groups were compared by analysis of covariance at each two-month interval. P values are for the comparison between the groups at each interval. Vertical bars represent 95 percent confidence intervals.

## Scientific Review (continued)

### Allergy is not asthma

The concept that asthma is solely an allergic disorder has led investigators and the pharmaceutical industry to develop allergen/antigen challenge tests as a primary screen for potential anti-asthma therapeutic activity. While this led to the identification of drugs such as sodium cromoglicate and nedocromil sodium, these proved to be of very limited efficacy and have not been developed further into more active interventions<sup>7</sup>. Similarly, allergen-specific immunotherapy, while effective in treating allergic rhinitis and insect venom allergy, has been disappointing as a treatment for asthma and is not recommended<sup>8</sup>. There is increasing evidence that while an important trigger of asthma, allergen exposure alone is insufficient to cause the disease. Atopy (the genetic risk for developing allergy) occurs in up to 40% of the population and yet asthma affects only 7-10%.

### Is an abnormal epithelium the cause of asthma?

There is mounting evidence to incriminate a range of other environmental factors in increasing the risk of developing asthma that include maternal and early life exposure to tobacco smoke, certain drugs and foods that reduce anti-oxidant defences (e.g. paracetamol), and virus infections<sup>9,10</sup>. For all these to operate as susceptibility factors in the origins of this disease, the primary defect is likely to lie in the airway epithelium that lies at the interface between the external inhaled environment and the airway tissue. Most asthma symptoms in preschool children were controlled by the use of inhaled corticosteroids, except for unplanned physician visits and hospitalisations. Most of these events are thought to be caused by respiratory viruses that infect the epithelium. Abnormality in the epithelium also helps explain why the majority of the novel asthma susceptibility genes that have been identified by positional cloning are epithelial in origin.

### Symptom Control and Impulse-Oscillometric Outcomes during the Treatment and Observation Periods.\*

Variable	End of 2-Year Treatment Period			End of 1-Year Observation Period		
	Fluticasone	Placebo	P Value	Fluticasone	Placebo	P Value
Exacerbations requiring a course of systemic corticosteroid — no./100 child-yr (95% CI)	57.4 (49.0–67.3)	89.4 (78.3–102.2)	<0.001	85.5 (70.9–103.2)	82.5 (68.0–100.1)	0.78
<b>Unscheduled physician visits — no./100 child-yr (95% CI)</b>	<b>79.0 (68.7–90.7)</b>	<b>83.9 (73.3–96.1)</b>	<b>0.51</b>	<b>108.1 (90.6–129)</b>	<b>88.0 (72.2–107.1)</b>	<b>0.11</b>
<b>Hospitalizations — no./100 child-yr (95% CI)</b>	<b>1.05 (0.34–3.25)</b>	<b>1.76 (0.73–4.23)</b>	<b>0.47</b>	<b>0.76 (0.11–5.38)</b>	<b>1.54 (0.39–6.15)</b>	<b>0.55</b>
Bronchodilator use — mean no. of days/yr (95% CI)†	14.4 (10.8–18.0)	18.0 (14.4–21.6)	0.07	18.0 (14.4–21.6)	18.0 (14.4–21.6)	0.73
Montelukast use — mean no. of days/yr (95% CI)†	11.4 (9.3–13.7)	24.2 (20.5–27.9)	<0.001	22.2 (18.3–27.3)	25.8 (21.3–31.2)	0.22
Montelukast use for ≥2 mo — no./total no. (%)	14/143 (9.8)	30/142 (21.1)	0.008	21/132 (15.9)	24/130 (18.5)	0.61
Supplemental use of fluticasone — mean no. of days/yr (95% CI)†	8.3 (6.8–10.4)	17.6 (14.9–20.9)	<0.001	20.1 (16.5–24.6)	27.0 (22.5–32.7)	0.007
At least 2 mo of open-label inhaled-corticosteroid use — no./total no. (%)	10/143 (7.0)	19/142 (13.4)	0.08	24/132 (18.2)	25/130 (19.2)	0.86
Reactance at 5 Hz at end of period — kPa/liter/sec	–0.39±0.12	–0.44±0.14	0.008	–0.38±0.12	–0.38±0.12	0.83
Resistance at 5 Hz at end of period — kPa/liter/sec	1.01±0.20	1.05±0.20	0.09	0.95±0.19	0.94±0.19	0.61

Exacerbations caused by respiratory virus?

**Figure 2.** Most asthma symptoms in pre-school children were controlled by the use of inhaled corticosteroids, except for unplanned physician visits and hospitalisations. Most of these events are thought to be caused by respiratory viruses.

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\* Plus-minus values are means±SD. SDs were estimated from the regression model. Means have been adjusted for age at randomization, sex, race or ethnic group (non-Hispanic white vs. all other), center, aeroallergen skin-test reactivity (yes vs. no), duration of symptoms at baseline, severity of symptoms at baseline, percentage eosinophils at baseline, and eczema at baseline (yes vs. no). CI denotes confidence interval.

† Values are based on annualized two-week recall data based on parents' reports. In addition, values reported for the two-year treatment period have been annualized for comparison with values reported for the one-year observation period.

# Scientific Review (continued)

## Respiratory viruses and the asthma exacerbation

The rapid and unexpected worsening of asthma is one of the major concerns to those who suffer from this disease and yet there are no specific treatments<sup>11</sup>. If the exacerbation is caused by sudden allergen exposure, then corticosteroids are effective, however the majority of exacerbations are caused by respiratory virus infections with the common cold viruses such as rhinovirus being the most common<sup>12,13</sup>. Furthermore Guilbert et al<sup>5</sup> showed that whilst steroids could suppress daily symptoms and inflammation steroids had no effect on the unplanned physician visits and hospitalisations, most of these visits are thought to be due to respiratory virus infections (Guilbert et al<sup>5</sup>, Figure 2 opposite).

## Why are asthmatics not able to eliminate the rhinovirus from the lungs?

While it was known that asthmatic patients were more susceptible to developing lower airway symptoms with common colds, the reason for this was, until recently, a mystery. The Founders' discovery that, in asthma, the airway epithelium is deficient in its capacity to eliminate rhinovirus infection due to a deficiency in the capacity to generate the powerful cytokine, interferon- $\beta$  has provided a new therapeutic opportunity to prevent and treat this important component of asthma<sup>14</sup>.

## The need for new COPD therapies

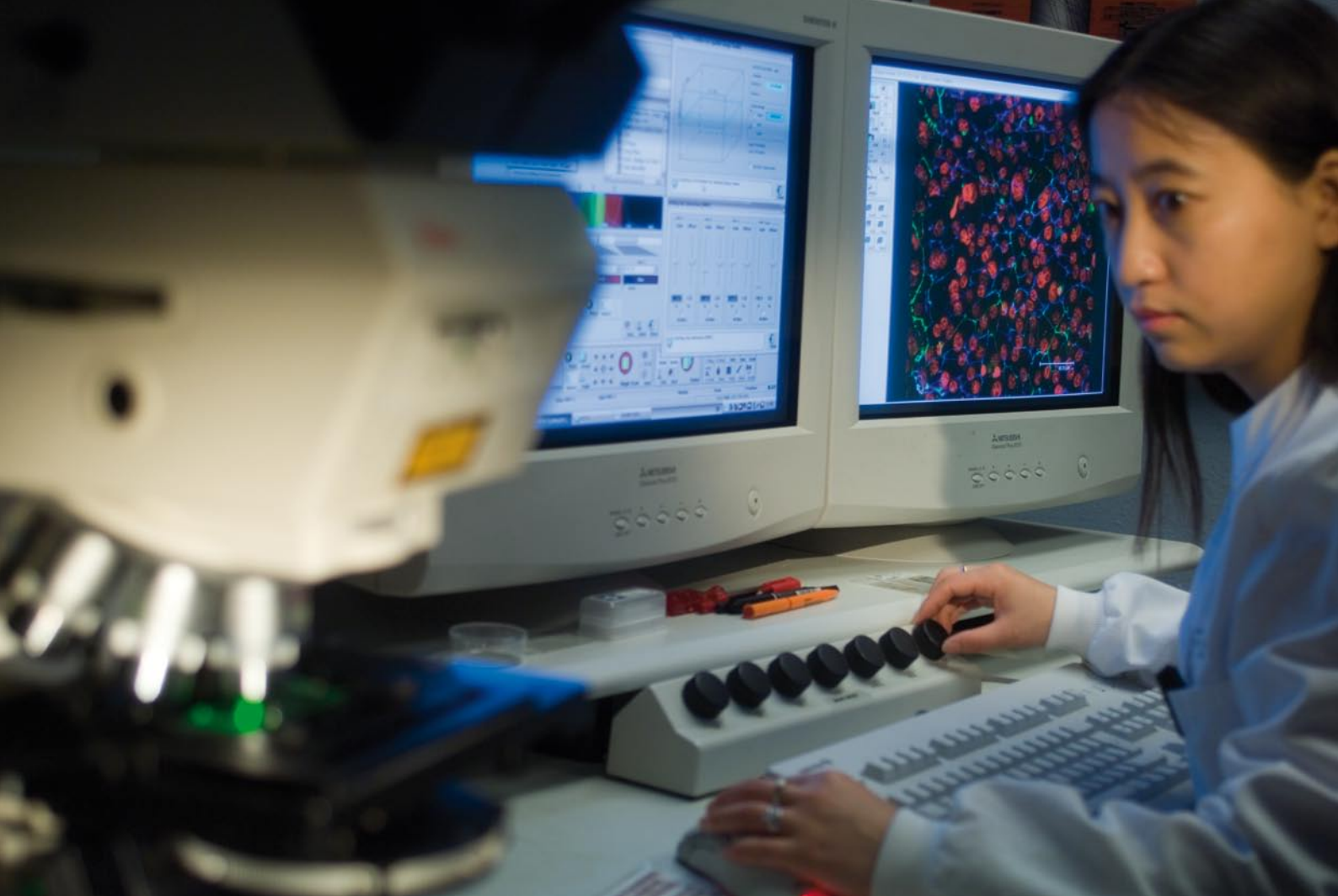
At present there are no treatments that affect the course of COPD, current treatment relying on anti-cholinergic bronchodilators, xanthines and long acting  $\beta_2$ -agonists; corticosteroids are of limited use<sup>15</sup>. As in asthma, the major difficulty in COPD is the exacerbation in which virus infections play a key role in rendering the airways vulnerable to secondary bacterial infection<sup>16</sup>. As in asthma, Synairgen has found that epithelial cells from patients with a long history of tobacco smoking or with COPD when compared to those from non-smokers, are highly sensitive to the effect of rhinovirus infection with increased cytotoxic cell death and minimal interferon- $\beta$  production. Since infection is the major health burden in smokers and especially those with impaired baseline lung function as occurs in COPD, replacing the missing interferon as an essential component of the lung's innate immune response has important therapeutic potential to prevent the winter exacerbations that carry so much of the morbidity and mortality of this disease<sup>1</sup>.

## Drug discovery models for asthma and COPD

For many years animal models of allergen sensitisation and challenge have been used to screen new chemical entities for potential anti-asthma activity, but despite the identification of many agents that were effective in these models, none have translated into new drugs when trialled in asthmatic patients other than those predicted from the known mechanisms of the acute allergic response e.g. leukotriene receptor antagonists (montelukast, zafirlukast) and the anti-IgE monoclonal antibody, omalizumab (Xolair®). Initially promising targets that have emerged from animal studies have been prostaglandins, platelet activating factor, bradykinin, neuropeptides, anti-allergic agents, anti-IL-5 to name but a few. One is left to conclude that such models do not recapitulate the chronic aspects of asthma such as airway remodelling nor the very many environmental factors that lead to deterioration in control. Most importantly, they do not model the underlying genetic differences that predispose certain people for the development of asthma. Immortalised human cell lines have also been used as tools to screen for anti-asthma activity, but because the cell machinery that controls cell regulation has been interfered with in the immortalisation process, any abnormality that involves subtle changes in cell control linked to asthma will be masked. Indeed, the variation in cell functions that characterise responses of primary cells is the aspect that creates a state of susceptibility.

## Synairgen's models of the human diseased epithelium

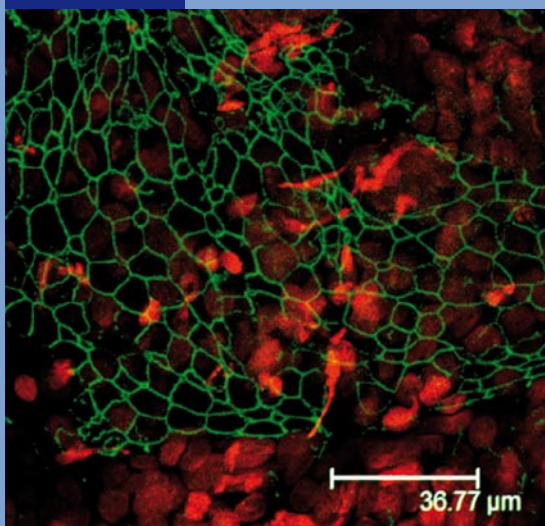
Recognising the urgent need for new approaches to the treatment and prevention of these common airway diseases, Synairgen has created an *in vitro* tissue engineering platform which has provided the basis for the discoveries described above. Epithelial cells obtained at fiberoptic bronchoscopy by brushing the airways of healthy volunteers, or those with asthma or COPD, are cultured *in vitro* as confluent monolayers or differentiated at an air-liquid interface so that the cells form an intact epithelium with ciliated and mucus-secreting cells, as found in the airways. Crucially, cells derived from diseased epithelia will carry those susceptibility genes that contribute to altered epithelial function in asthma or COPD.



**Photograph above:** Use of confocal microscopy to measure tight junction formation

## Tight junctions are disrupted in asthmatic tissue

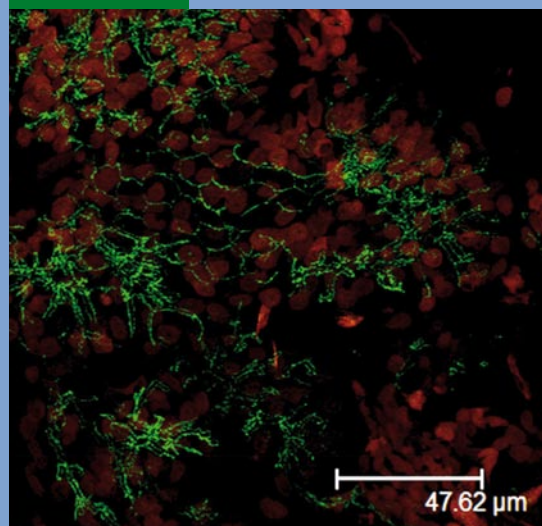
### Normal



Normal bronchial biopsy showing intact tight junction protein formation (stained in green)

**Green**    epithelial tight junction protein  
**Red**     cell nuclei

### Asthmatic



In contrast, an asthmatic bronchial biopsy showing disrupted tight junction formation (stained in green)



# Scientific Review (continued)

## Application of these model systems

The monolayer culture model has revealed the interferon- $\beta$  deficiencies in asthma, smokers and COPD while the latter has enabled us to uncover an abnormality that we believe maybe fundamental to the asthmatic airways' vulnerability to multiple environmental insults. Apart from being able to defend itself against virus and bacterial infections, a key function of the epithelium is to act as a physical barrier to exclude inhaled particles and other injurious agents from penetrating into the airway tissue, a function provided by a complex series of proteins called tight junctions that form a seal at the apex of the epithelial columnar cells.

In asthma, the capacity of the differentiated epithelium to form intact fully functional tight junctions is seriously impaired and is further weakened in the presence of airway pollutants, biologically active allergens and virus infection. In living asthmatic patients, the permeability of the airway epithelium to agents such as Te99m-DTPA when inhaled is also increased<sup>16,17</sup>. An exciting discovery that Synairgen has been working on is the capacity of certain growth factors that include Epidermal Growth Factor to restore the tight junctions to normal. Again, a novel therapeutic opportunity has been identified using a modified growth factor as a therapeutic agent to improve the barrier function of the epithelium in asthma.

## Drug discovery platform

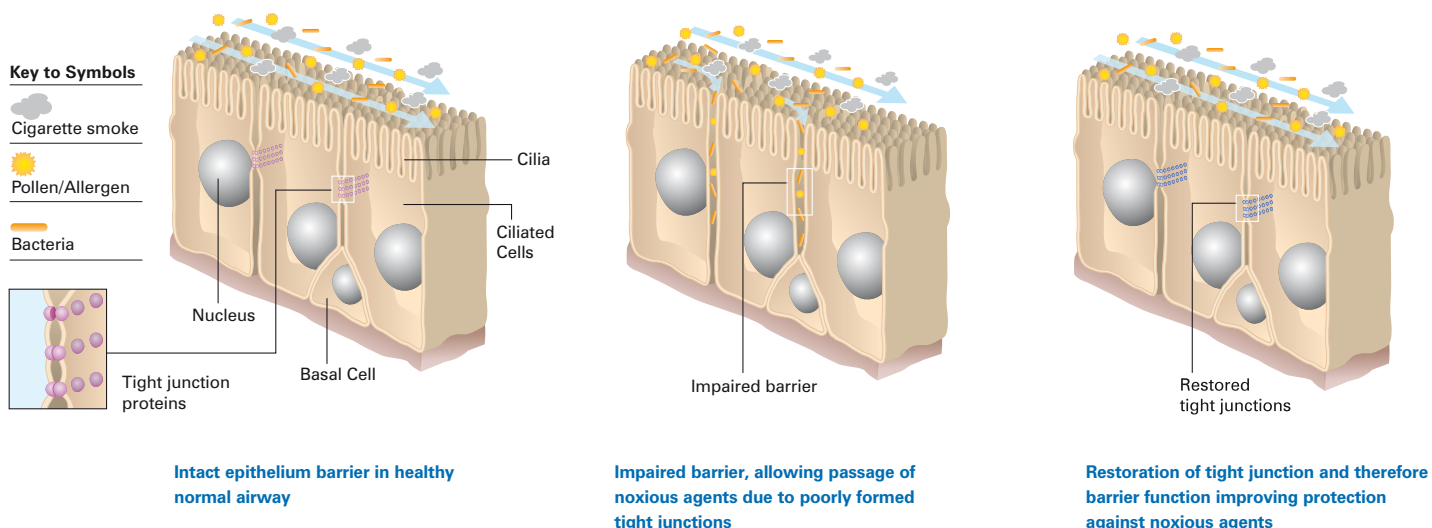
Cells obtained from diseased airways maintain their phenotype and either alone or when challenged with environmental insults known to be associated with asthma can be used to

look for biochemical abnormalities that are disease-specific. Thus, we are also able to use these epithelial cultures to apply proteomic-based and gene-based technologies to mine further this "rich seam" of therapeutic targets close to the origins of asthma. These technologies enable sets of genes or proteins that may be different between disease and normal tissues to be identified in the form of a "fingerprint" and therefore provide opportunities for identifying unique disease targets.

## Parallels with other epithelium-based diseases – skin

Asthma is not the only disorder in which breakdown of barrier function predisposes to an allergic disorder. The recent discovery that filaggrin a candidate gene on chromosome 1 for the genetic skin disorder ichthyosis vulgaris with loss of function polymorphisms leading to lack of formation of the superficial protective layer of the skin, also strongly predispose to atopic dermatitis (eczema)<sup>18</sup> suggests that reduced barrier function is implicated in this common allergic skin disorder<sup>19</sup>. Filaggrin is involved in the formation of an impermeable surface layer in the skin, a breakdown of which renders the skin more susceptible to allergen penetration and subsequent immunological sensitisation, a characteristic feature of atopic dermatitis. The recent finding that the loss of function variants of the filaggrin gene also predisposes to asthma in association with eczema<sup>18</sup> reinforces the idea that a breakdown in barrier function is an important component of asthma.

## Barrier function





# Scientific Review (continued)

## Parallels with other epithelium-based diseases – gastro intestinal

An important theme that underpins our drug discovery programme at Synairgen is the identification of therapies that increase the resistance of the lung to the many insults it receives in susceptible subjects. This approach embraces the concept of tissue injury and repair as being fundamental to the origins and progression of asthma and COPD. These “chronic wound” scenarios move the debate about disease causation away from inflammation as being primary, to it being a component part of the chronic wound created by aberrant responses to the inhaled environment<sup>20</sup>. Evidence in support of this concept has come from the recent success of growth factors such as EGF in not only preventing and reversing mucosal ulceration in ulcerative colitis, a form of inflammatory bowel disease<sup>21</sup>, but also reversing inflammation and tissue remodelling.

## Conclusion

Thus in asthma and COPD, treatments directed at increasing the airway epithelium’s resistance to injury are likely to have far reaching effects on multiple aspects of the pathology and functional impairment associated with these complex disorders. We believe this is a fundamental difference in Synairgen’s approach to these diseases when compared with the more traditional inflammation-based hypotheses. After all, if airway inflammation was the underlying primary cause of these diseases then with the £ billions that have been spent on discovery programmes in asthma and COPD, why has there not been more to show in terms of novel therapies? One answer is that the working hypotheses that have been the entire focus of this research is only part of the story and targets higher up the cascade need to be found. We believe that by recapitulating the disease phenotypes in tissue culture, such targets are being found and others will be discovered.

## Professor Stephen Holgate

Founder and non-executive director

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## Directors

### **Simon Shaw**

Non-executive Chairman (aged 41)

Simon Shaw joined Synairgen as executive Chairman on its inception in June 2003 and became non-executive Chairman in October of that year. He is currently Chief Financial Officer of Gyrus Group PLC, having previously been Chief Operating Officer of Profile Therapeutics plc between 1998 and 2003. Between 1991 and 1997 he was a corporate financier, latterly at Hambros Bank Limited. He is a chartered accountant. Simon is a member of the techMARK Advisory Group of the London Stock Exchange, which advises the Exchange on matters of Technology and Mediscience.



### **Richard Marsden**

Managing Director (aged 39)

Richard Marsden joined Synairgen in a consulting role as General Manager in November 2003 and was appointed to the Board as Managing Director in June 2004. Between 1998 and 2003 he worked as Projects Manager and Cystic Fibrosis Business Development Manager at Profile Therapeutics plc, where he managed the Cystic Fibrosis business and played a major role in the development of its proprietary pharmaceutical unit, Profile Pharma Limited. Prior to this, he worked for Zimmer Limited, Genentech (UK) Limited and Roche Products Limited.



### **John Ward**

Finance Director (aged 45)

John Ward joined Synairgen in October 2004 as Finance Director. From December 1999 to July 2004 he was Chief Financial Officer and Company Secretary of Profile Therapeutics plc and was appointed to the Profile Therapeutics board in March 2003. From 1996 to 1999 he was Finance Director of Rapid Deployment Group Limited, the UK holding company for the healthcare operations of Ventiv Health, Inc. Prior to joining Rapid Deployment he was a Director of Corporate Finance at Price Waterhouse. He is a chartered accountant.



### **Dr Bruce Campbell**

Non-executive Director (aged 61)

Bruce Campbell joined Synairgen as a non-executive Director in April 2006. He is currently non-executive Chairman of Proximagen Neuroscience plc and Chief Scientific Officer of IP Group plc. Formerly he was Senior VP



of International Development at Neurocrine Biosciences, Inc. ('Neurocrine'). Prior to joining Neurocrine he worked for 27 years at Servier (United Kingdom), latterly as Scientific Director. In addition, he has also been a director and European Chairman of the Drug Information Association and a member of the European ICH Safety Working Party. He is a visiting Professor in Pharmacology at King's College, London.

### **Prof. Stephen Holgate**

Non-executive Director (aged 59)

Stephen Holgate is a co-founder of Synairgen and was appointed a non-executive director in June 2003. After qualifying in Medicine at Charing Cross Hospital Medical School, London he has pursued an academic career leading to his appointment in 1987 to his current position as Medical Research Council Clinical Professor of Immunopharmacology at the University of Southampton. His research interests have been largely focused on the cellular and molecular mechanisms of asthma that has involved use of both epidemiological and genetic approaches. He has published over 800 papers in peer-reviewed literature and is co-editor of Clinical and Experimental Allergy. He has been Visiting Professor at Vanderbilt, Wake Forest, Harvard, Yale, Chicago, Rochester, McMaster, Toronto, Vancouver (UCB), Pittsburgh and Edmonton Universities. He is currently Chairman of the Science Council's Science in Health Group, Chairman of the MRC's Evaluation Committee, a member of the Royal Commission on Environmental Pollution and a scientific board member or advisor to eleven companies, including Amgen and Novartis.

### **Susan Sundstrom**

Non-executive Director (aged 49)

Susan Sundstrom joined Synairgen as a non-executive director in June 2003. She is Director, Lifescience Enterprise of the University of Southampton's Technology Transfer group. Previously, her career includes twenty years with AstraZeneca where she held a wide range of international commercial positions, encompassing general management and global business development. Susan graduated from the London Business School and Wharton MBA programme with distinction and is a director of a number of private companies spun out from the University of Southampton.

Photographs in order of text: top to bottom.

# Directors' Report

The directors present their report and the audited financial statements for Synairgen plc (the 'Company') and its subsidiary (together the 'Group') for the year ended 30 June 2006. This report includes the Corporate Governance Statement and the Directors' Remuneration Report on pages 16 to 22.

## Principal activities

Synairgen plc is the holding company for Synairgen Research Limited, a drug discovery company focused on identifying the underlying causes of, and discovering new treatments for, asthma and chronic obstructive pulmonary disease ('COPD').

## Review of the business and future developments

A review of the business and future developments is included in the Chairman's Statement, the Managing Director's Report, the Financial Review and the Scientific Review set out on pages 3 to 12.

## Research and development

During the year, the Group has invested £1,069,000 (2005: £557,000) in research and development activities and a review of this expenditure is included in the Managing Director's Report.

## Key performance indicators

The Board considers that the most important key performance indicators ('KPIs') are non-financial and relate to the progress of the scientific programmes which are discussed in the Managing Director's Report. The most

important financial KPIs are the cash position and the operating loss of the Group. At 30 June 2006 cash and deposit balances amounted to some £7.5 million and were above budgeted levels. The operating loss for the year was also favourable to the budgeted loss for the year.

## Principal risks and uncertainties

The Board considers that the principal risks and uncertainties facing the Group may be summarised as follows:

- Failure to generate innovative discoveries;
- Discoveries do not complete clinical trials and regulatory approval process;
- Patent applications do not succeed;
- Failure to secure out-licensing agreements;
- Loss of research facilities and/or biobank through natural disaster; and
- Loss of key staff.

## Results and dividends

The Group's loss for the year after taxation amounted to £1,042,000 (2005: loss of £610,000). A Financial Review is set out on page 6. The directors do not propose the payment of a dividend.

## Financial instruments

The Group's use of financial instruments is discussed in the Financial Review on page 6 and in note 17 to the financial statements.

## Substantial shareholdings

As at 15 September 2006, the Company had been advised of the following shareholders with interests of 3% or more in its ordinary share capital:

Name of shareholder	Number of ordinary shares	% of share capital
IP2IPO Limited and IP2IPO Management Limited	6,640,000	30.6%
Southampton Asset Management Limited	3,600,000	16.6%
Lansdowne Partners Limited Partnership	1,950,000	9.0%
Tudor BVI Global Portfolio Limited and Tudor Proprietary Trading LLC	850,000	3.9%
Prof. S. Holgate (i)	835,323	3.9%
Prof. D. Davies	833,300	3.8%
Prof. R. Djukanovic	833,300	3.8%
Invesco English and International Trust plc	655,250	3.0%

(i) Prof. Stephen Holgate's shareholding includes 1,923 shares owned by his wife, Elizabeth Holgate.

# Directors' Report (continued)

## Directors

The directors of the Company during the year were:

### Executive directors:

Richard Marsden  
John Ward

### Non-executive directors:

Simon Shaw  
Dr Bruce Campbell (appointed 11 April 2006)  
Prof. Stephen Holgate  
David Norwood (resigned 11 April 2006)  
Susan Sundstrom

In accordance with the Company's Articles of Association, which require that each director appointed to the Board since the previous Annual General Meeting and one third of the remaining directors shall retire from office, at the Annual General Meeting on 15 November 2006 Dr Bruce Campbell, Richard Marsden and Prof. Stephen Holgate will retire and, being eligible, offer themselves for re-appointment.

### Directors' interests in ordinary shares

The directors, who held office at 30 June 2006, had the following interests in the ordinary shares of the Company:

	30 June 2006 No. of shares	1 July 2005 No. of shares
John Ward	7,692	7,692
Simon Shaw	15,400	15,400
Prof. Stephen Holgate	835,323	835,323

Between 30 June 2006 and the date of this report there has been no change in the interests of directors in shares or share options as disclosed in this annual report.

### Directors' remuneration and share options

Details of directors' remuneration and share options are given in the Directors' Remuneration Report on pages 19 to 22.

## Directors' and officers' liability insurance

Insurance cover has been arranged in respect of the personal liabilities which may be incurred by directors and officers of the Group during the course of their service with the Group.

## Payment of creditors

It is the policy of the Group and the Company that payments to suppliers are made in accordance with those terms and conditions agreed between the Group and its suppliers, provided that all trading terms and conditions have been complied with. At 30 June 2006 the Company had an average of 6 days' purchases outstanding in trade creditors (2005: 37 days' purchases).

## Charitable and political donations

The Group made no charitable or political donations during the year (2005: nil).

## Disabled employees

The Group gives every consideration to applications for employment from disabled persons where the requirements of the job may be adequately covered by a handicapped or disabled person. Should any employee become disabled, every practical effort is made to provide continued employment.

## Annual general meeting ('AGM')

The AGM will be held at 12 noon on 15 November 2006 at Stringer Saul LLP, 17 Hanover Square, London W1S 1HU.

## Auditors

All of the current directors have taken all the steps that they ought to have taken to make themselves aware of any information needed by the Company's auditors for the purposes of their audit and to establish that the auditors are aware of that information. The directors are not aware of any relevant audit information of which the auditors are unaware.

A resolution to re-appoint BDO Stoy Hayward LLP as auditors will be put to members at the AGM.

By order of the Board

## John Ward

Company Secretary  
15 September 2006

# Corporate Governance Statement

The Board is accountable to the Company's shareholders for good corporate governance and it is the objective of the Board to attain a high standard of corporate governance. As an AIM-quoted company full compliance with The Principles of Good Governance and Code of Best Practice (2003) (the 'Combined Code') is not a formal obligation. The Company has not sought to comply with the full provisions of the Combined Code, however it has sought to adopt the provisions that are appropriate to its size and organisation and establish frameworks for the achievement of this objective. This statement sets out the corporate governance procedures that are in place.

## Board of directors

On 30 June 2006 the Board of directors (the 'Board') consisted of a non-executive Chairman (Simon Shaw), two executive directors (Richard Marsden and John Ward), and three non-executive directors (Dr Bruce Campbell, Prof. Stephen Holgate and Susan Sundstrom). Brief details about the directors are given on page 13. The responsibilities of the non-executive Chairman and the Managing Director are clearly divided. The non-executive directors bring relevant experience from different backgrounds and receive a fixed fee for their services and reimbursement of reasonable expenses incurred in attending meetings.

The Board retains full and effective control of the Group. This includes responsibility for determining the Group's strategy and for approving budgets and business plans to fulfil this strategy. The full Board meets regularly and during the year ended 30 June 2006 met seven times, with each member attending as follows:

Name	Number of meetings held whilst a Board member	Number of meetings attended
Simon Shaw	7	7
Richard Marsden	7	7
John Ward	7	7
Dr Bruce Campbell	2	2
Prof. Stephen Holgate	7	5
Susan Sundstrom	7	7
David Norwood	5	1

It is the duty of the Chairman to ensure that all directors are properly briefed on issues arising at Board meetings. Prior to each Board meeting, directors are sent an agenda and Board papers for each agenda item to be discussed. Additional information is provided, when requested by the Board or individual directors.

The Company Secretary is responsible to the Board for ensuring that Board procedures are followed and that the applicable rules and regulations are complied with. All directors have access to the advice and services of the Company Secretary, and independent professional advice, if required, at the Company's expense. Removal of the Company Secretary would be a matter for the Board.

As appropriate, the Board has delegated certain responsibilities to Board committees.

## Audit Committee

The Audit Committee currently comprises Simon Shaw (Chairman) and Dr Bruce Campbell. Whilst it is not normal in larger companies for the Chairman of the Company to chair the Audit Committee, the Company considers it appropriate for Simon Shaw to be Chairman as he is considered to have the most significant, recent and relevant financial experience of the non-executive directors.

The committee has primary responsibility for ensuring that the financial performance of the Group is properly measured and reported on, reviewing the interim financial information and annual financial statements before they are submitted to the Board. The committee also reviews, and reports on, reports from the Group's auditors relating to the Group's accounting controls. It makes recommendations to the Board on the appointment of auditors and the audit fee. The committee monitors the scope, results and cost-effectiveness of the audit. It has unrestricted access to the Group's auditors. In certain circumstances it is permitted by the Board for the auditors to supply non-audit services (in the provision of tax advice, or on specific projects where they can add value). The committee has approved and monitored the application of this policy in order to safeguard auditor objectivity and independence. The Group does not have an internal audit function, but the Board considers that this is appropriate, given the size of the Group. The committee keeps this matter under review annually.



# Corporate Governance Statement (continued)

## Remuneration and Nomination Committee

The Remuneration and Nomination Committee currently comprises Susan Sundstrom (Chairman) and Simon Shaw. It is responsible for making recommendations to the Board on remuneration policy for executive directors and the terms of their service contracts, with the aim of ensuring that their remuneration, including any share options and other awards, is based on their own performance and that of the Group generally. The committee administers the Long-Term Incentive Plan and the staff share option scheme and approves grants under both schemes. It also advises on the remuneration policy for the Group's employees. The committee is responsible for all senior appointments that are made within the Group. During the year the Committee has met three times.

## Investor relations

The directors seek to build a mutual understanding of objectives between the Company and its shareholders by meetings with major institutional investors and analysts after the Company's preliminary announcement of its year-end results and its interim results. The Company also maintains investor relations pages on its website ([www.synairgen.com](http://www.synairgen.com)) to increase the amount of information available to investors.

There is an opportunity at the Annual General Meeting for individual shareholders to question the Chairman, the Chairmen of the Audit and Remuneration and Nomination committees, and the executive directors. Notice of the meeting is sent to shareholders at least 20 working days before the meeting. Shareholders are given the opportunity to vote on each separate issue. The Company counts all proxy votes and will indicate the level of proxies lodged on each resolution, after it has been dealt with by a show of hands. Details of the resolutions and explanations thereto are shown with the notice on pages 38 and 39. This year's meeting will be held at 12 noon on 15 November 2006 at Stringer Saul LLP, 17 Hanover Square, London W1S 1HU.

## Internal control

The directors are responsible for establishing and maintaining the Group's system of internal control and reviewing its effectiveness. The system of internal control is designed to manage, rather than eliminate, the risk of failure to achieve business objectives and can only provide reasonable but not absolute assurance against material misstatement or loss.

The main features of the internal control system are as follows:

- a control environment exists through the close management of the business by the executive directors. The Group has a defined organisational structure with delineated approval limits. Controls are implemented and monitored by personnel with the necessary qualifications and experience;
- a list of matters reserved for board approval;
- monthly management reporting and analysis of variances;
- financial risks for each major transaction are identified and evaluated by the Board;
- standard financial controls operate to ensure that the assets of the Group are safeguarded and that proper accounting records are maintained; and
- an on-going risk management process exists, which identifies key risks against business objectives.

# Corporate Governance Statement (continued)

## Statement of directors' responsibilities

The directors are responsible for preparing the Annual Report and the financial statements in accordance with applicable law and United Kingdom Generally Accepted Accounting Practice.

Company law requires the directors to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the Company and of the Group and of the profit or loss of the Group for that period. In preparing these financial statements, the directors are required to:

- select suitable accounting policies and then apply them consistently;
- make judgments and estimates that are reasonable and prudent;
- state whether applicable accounting standards have been followed, subject to any material departures disclosed and explained in the financial statements;
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the Company and the Group will continue in business.

The directors are responsible for keeping proper accounting records that disclose with reasonable accuracy at any time the financial position of the Company 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 Group and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The financial statements are published on the Company's website in accordance with legislation in the United Kingdom governing the preparation and dissemination of financial statements. However, the information published on the internet is accessible in many countries with different jurisdictions. The maintenance and integrity of the Company's website is the responsibility of the directors. The directors' responsibility also extends to the ongoing integrity of the financial statements therein.

## Going concern

The directors have prepared and reviewed financial forecasts. After due consideration of these forecasts and current cash resources, the directors consider that the Company and the Group have adequate financial resources to continue in operational existence for the foreseeable future (being a period of at least twelve months from the date of this report), and for this reason the accounts have been prepared on a going concern basis.

**Simon Shaw**  
Chairman

# Directors' Remuneration Report

## Remuneration Committee

The Company's remuneration policy is the responsibility of the Remuneration and Nomination Committee (the 'Committee'), which was established in October 2004. The composition and terms of reference of the Committee is outlined in the Corporate Governance Statement on page 17.

The Committee, which is required to meet at least twice a year, met three times during the year ended 30 June 2006.

During the year, the Committee has been advised on executive director remuneration, including the formation of the Long-Term Incentive Plan, by its retained independent remuneration adviser, New Bridge Street Consultants LLP. No other advice has been provided to the Group by this firm during the year.

## Remuneration policy

### (i) Executive remuneration

The Committee has a duty to establish a remuneration policy which will enable it to attract and retain individuals of the highest calibre to run the Group. Its policy is to ensure that executive remuneration packages are appropriate given performance, scale of responsibility, experience and consideration of the remuneration packages for similar executive positions in companies it considers are comparable. Packages are structured to motivate executives to achieve the highest level of performance in line with the best interests of shareholders.

Executive remuneration currently comprises a base salary, an annual performance-related bonus, a pension contribution to the executive director's individual money purchase scheme (at 9% of base salary), family private health cover, permanent health and life assurance. Salaries and benefits are reviewed annually in July, taking into account Group and individual performance, external benchmark information and internal relativities.

Executive directors are also rewarded for improvements in the performance of the Group sustained over a period of years in the form of Long-Term Incentive Plan share awards granted on a discretionary basis by the Committee.

### (ii) Chairman and non-executive director remuneration

Currently, each of the non-executive directors receives a fixed fee for service, which covers preparation for and attendance at meetings of the full Board and committees thereof. The executive directors are responsible for setting the level of non-executive remuneration. The non-executive directors are also reimbursed for all reasonable expenses incurred in attending meetings. With the exception of Simon Shaw's options, which were granted at the inception of the Company when he was the founding executive, the non-executive directors have not been granted options and have not participated in any other incentive schemes. However the Board would consider such participation for a non-executive director if appropriate.

### (iii) Equity-based incentive schemes

The Committee strongly believes that equity-based incentive schemes increase the focus of employees in improving Group performance, whilst at the same time providing a strong incentive for retaining and attracting individuals of a high calibre.

## Long-Term Incentive Plan

As reported in the 2005 Remuneration Report, the Committee undertook a review of long-term incentive arrangements for senior executives during the first half of 2005 and concluded that a Long-Term Incentive Plan, comprising conditional (performance-related) share awards (technically structured as nominal cost options pursuant to which participants must pay 1p per share on the exercise of their awards), should be introduced as the primary long-term incentive vehicle for executive directors. A resolution to adopt the Synairgen Long-Term Incentive Plan (the 'LTIP') was approved at the 2005 Annual General Meeting. Under the LTIP, senior executives may be granted an award which will normally vest if demanding performance conditions are achieved over a three-year period and if the grantee remains an employee of the Group.

# Directors' Remuneration Report (continued)

In November 2005 Richard Marsden and John Ward were granted awards over shares worth 50% and 150% of base salary respectively. Future grants under the LTIP in any financial year are capped at a maximum of 100% of base salary. Executive directors are expected to retain no fewer than 50% of shares acquired upon vesting of awards under the LTIP, net of taxes, until such time as, in combination with any other shares the executives may have acquired, they hold shares with a value equivalent to 100% of base salary.

All awards will lapse at the end of the applicable performance period to the extent that the applicable performance criteria conditions have not been satisfied with no opportunity for retesting. In the event of a good leaver event or a change of control of the Company, the LTIP awards may vest early, but only to the extent that, in the opinion of the Committee, the performance conditions have been satisfied at that time. The awards will generally also be subject to a time pro-rated reduction to reflect the reduced period of time between the grant of the awards and the time of vesting although this reduction may not be applied in certain cases.

## Performance conditions for the 2005 LTIP awards

The awards granted in November 2005 year will vest if the total shareholder return ('TSR') of the Company over the three year period exceeds the increase in the techMARK mediscience™ index over the same period and the following TSR rates are achieved:

Percentage annual rate of TSR over the performance period	Vesting percentage of total number of shares subject to award
20% (73% compound over three years)	25%
25% (95% compound over three years)	35%
30% (120% compound over three years)	60%
35% (146% compound over three years)	100%
Performance between the steps	Pro-rata on a straight-line basis

The base TSR assumes a share price of 130p, being the IPO price.

## (iv) Service contracts and letters of appointment

The executive directors have entered into service agreements which can be terminated on six months' notice by either party.

The Chairman and non-executive directors have entered into letters of appointment for an initial fixed period of twelve months, which renew automatically for a further twelve month period on the anniversary of commencement. The appointment can be terminated on three months' notice by either party.

# Directors' Remuneration Report (continued)

## Directors' remuneration

The aggregate remuneration received by directors who served during the year ended 30 June 2006 was as follows:

£000	Note	Salary/fee 2006	Benefits 2006	Bonus 2006	Total (excl. pension) 2006	Pension 2006	Total (incl. pension) 2006	Total (excl. pension) 2005	Pension 2005	Total (incl. pension) 2005
<b>Executive directors</b>										
Richard Marsden	(i)	108	1	8	117	10	127	104	8	112
John Ward		90	1	8	99	8	107	63	4	67
<b>Non-executive directors</b>										
Simon Shaw		25	–	–	25	–	25	28	–	28
Dr Bruce Campbell	(ii)	1	–	–	1	–	1	–	–	–
Prof. Stephen Holgate	(iii)	5	–	–	5	–	5	3	–	3
Susan Sundstrom	(iv)	5	–	–	5	–	5	3	–	3
<b>Former directors</b>										
David Norwood	(v)	4	–	–	4	–	4	3	–	3
<b>Total</b>		<b>238</b>	<b>2</b>	<b>16</b>	<b>256</b>	<b>18</b>	<b>274</b>	<b>204</b>	<b>12</b>	<b>216</b>

(i) Richard Marsden was the highest paid director during the years ended 30 June 2005 and 2006.

(ii) Dr Bruce Campbell was appointed a director of the Company on 11 April 2006. This amount was paid to IP2IPO Limited for the services of Dr Bruce Campbell.

(iii) In addition to this fee for his services as a director, Prof. Holgate received consultancy fees and expenses amounting to £15,000 (2005: £16,000) as disclosed in Note 21 to the financial statements.

(iv) This amount was paid to the University of Southampton for the services of Susan Sundstrom.

(v) David Norwood resigned as a director of the Company on 11 April 2006. This amount was paid to IP2IPO Limited for the services of David Norwood.

## Directors' interests in share options

The interests of directors in share options over ordinary shares during the year were as follows:

Date of grant	At 1 July 2005	Granted during the year	At 30 June 2006	Exercise price	Earliest exercise date	Expiry date
<b>Richard Marsden</b>						
15 November 2005	–	43,829	<b>43,829</b>	1p	15 Nov 2008	14 Nov 2009
<b>John Ward</b>						
15 November 2005	–	105,191	<b>105,191</b>	1p	15 Nov 2008	14 Nov 2009

The options awarded under the LTIP will only vest if the performance conditions outlined above are met.



# Directors' Remuneration Report (continued)

## Other options granted on or before the IPO

Date of grant	At 1 July 2005	Granted during the year	At 30 June 2006	Exercise price	Earliest exercise date	Expiry date
<b>Simon Shaw</b>						
11 October 2004	420,000	–	<b>420,000</b>	1p	11 Oct 2004	10 Oct 2014
	280,000	–	<b>280,000</b>	1p	26 Oct 2004	10 Oct 2014
<b>Richard Marsden</b>						
11 October 2004	280,000	–	<b>280,000</b>	10p	11 Oct 2004	10 Oct 2014
11 October 2004	140,000	–	<b>140,000</b>	10p	30 June 2005	10 Oct 2014
26 October 2004	140,000	–	<b>140,000</b>	130p	30 June 2006	25 Oct 2014
26 October 2004	140,000	–	<b>140,000</b>	130p	30 June 2006	25 Oct 2014
<b>John Ward</b>						
26 October 2004	140,000	–	<b>140,000</b>	130p	30 June 2005	25 Oct 2014
26 October 2004	140,000	–	<b>140,000</b>	130p	30 June 2006	25 Oct 2014

The vesting and exercise of these other options is subject to the relevant option holder continuing to be an employee or director of a company in the same Group as the Company at the relevant time. There are no further performance criteria.

There were no other options granted to directors or which were exercised or lapsed during the year.

The mid-market price of the Company's shares at 30 June 2006 was 107p. During the year then ended the mid-market price ranged from 105p to 128.5p. On 15 September 2006 the closing price was 87.5p.

By order of the Board

**Susan Sundstrom**

Chairman of the Remuneration and Nomination Committee  
15 September 2006

# Independent Auditors' Report to the shareholders of Synairgen plc

We have audited the group and parent company financial statements (the 'financial statements') of Synairgen plc for the year ended 30 June 2006 which comprise the Consolidated Profit and Loss Account, the Consolidated and Company Balance Sheets, the Consolidated Cash Flow Statement and the related notes. These financial statements have been prepared under the accounting policies set out therein.

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

The directors' responsibilities for preparing the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice) 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 and International Standards on Auditing (UK and Ireland).

We report to you our opinion as to whether the financial statements give a true and fair view and have been properly prepared in accordance with the Companies Act 1985 and whether the information given in the Directors' Report is consistent with those financial statements. We also report to you if, in our opinion, 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 regarding directors' remuneration and other transactions is not disclosed.

We read other information contained in the Annual Report and consider whether it is consistent with the audited financial statements. The other information comprises only the Chairman's Statement, the Managing Director's Report, the Financial Review, the Scientific Review, the Directors' Report, the Corporate Governance Statement and the Directors' Remuneration Report. We consider the implications for our report if we become aware of any apparent misstatements or material inconsistencies with the financial statements. Our responsibilities do not extend to any other information.

Our report has been prepared pursuant to the requirements of the Companies Act 1985 and for no other purpose. No person is entitled to rely on this report unless such a person is a person

entitled to rely upon this report by virtue of and for the purpose of the Companies Act 1985 or has been expressly authorised to do so by our prior written consent. Save as above, we do not accept responsibility for this report to any other person or for any other purpose and we hereby expressly disclaim any and all such liability.

## **Basis of audit opinion**

We conducted our audit in accordance with International Standards on Auditing (UK and Ireland) 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 judgments made by the directors in the preparation of the financial statements, and of whether the accounting policies are appropriate to the group's and 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 group financial statements give a true and fair view, in accordance with United Kingdom Generally Accepted Accounting Practice, of the state of the group's affairs as at 30 June 2006 and of its loss for the year then ended;
- the parent company financial statements give a true and fair view, in accordance with United Kingdom Generally Accepted Accounting Practice, of the state of the parent company's affairs as at 30 June 2006;
- the financial statements have been properly prepared in accordance with the Companies Act 1985; and
- the information given in the Directors' Report is consistent with the financial statements.

## **BDO STOY HAYWARD LLP**

Chartered Accountants and Registered Auditors  
Southampton  
15 September 2006

# Consolidated Profit and Loss Account

for the year ended 30 June

	Notes	2006 £000	Proforma 2005 £000
Turnover	2	82	202
Cost of sales		(15)	(135)
<b>Gross profit</b>		<b>67</b>	<b>67</b>
Administrative expenses			
Research and development expenditure		(1,069)	(557)
Other		(671)	(418)
<b>Total</b>		<b>(1,740)</b>	<b>(975)</b>
<b>Operating loss</b>	3	<b>(1,673)</b>	<b>(908)</b>
Bank interest receivable		376	298
<b>Loss on ordinary activities before taxation</b>		<b>(1,297)</b>	<b>(610)</b>
Tax on loss on ordinary activities	5	255	–
<b>Loss on ordinary activities after taxation and retained loss for the year</b>	19	<b>(1,042)</b>	<b>(610)</b>
<b>Loss per ordinary share</b>			
Basic and diluted loss per share (pence)	6	<b>(4.80)p</b>	(3.26)p

There are no recognised gains and losses other than the loss above and therefore no separate statement of total recognised gains and losses has been presented.

All amounts relate to continuing activities.

# Consolidated Balance Sheet

as at 30 June

	Notes	2006 £000	2005 £000
<b>Fixed assets</b>			
Intangible assets	8	36	21
Tangible assets	9	157	154
		<b>193</b>	<b>175</b>
<b>Current assets</b>			
Stocks	11	68	55
Debtors	12	423	325
Investments: short-term deposits		7,464	8,605
Cash at bank and in hand		33	78
		<b>7,988</b>	<b>9,063</b>
<b>Creditors: amounts falling due within one year</b>	13	<b>(334)</b>	<b>(398)</b>
<b>Net current assets</b>		<b>7,654</b>	<b>8,665</b>
<b>Total assets less current liabilities</b>		<b>7,847</b>	<b>8,840</b>
<b>Creditors: amounts falling due after more than one year</b>	14	<b>(10)</b>	<b>–</b>
<b>Net assets</b>		<b>7,837</b>	<b>8,840</b>
<b>Capital and reserves</b>			
Called up share capital	18	217	217
Share premium account	19	8,903	8,903
Merger reserve	19	483	483
Profit and loss account	19	(1,766)	(763)
<b>Shareholders' funds</b>	19	<b>7,837</b>	<b>8,840</b>

The financial statements on pages 24 to 37 were approved and authorised for issue by the Board of directors on 15 September 2006 and signed on its behalf by:

**Richard Marsden** Director

**John Ward** Director

# Company Balance Sheet

as at 30 June

	Notes	2006 £000	2005 £000
<b>Fixed assets</b>			
Investments	10	<b>1,877</b>	575
<b>Current assets</b>			
Debtors	12	<b>95</b>	121
Investments: short-term deposits		<b>7,464</b>	8,605
Cash at bank and in hand		<b>6</b>	28
		<b>7,565</b>	8,754
<b>Creditors: amounts falling due within one year</b>	13	<b>(34)</b>	(71)
<b>Net current assets</b>		<b>7,531</b>	8,683
<b>Total assets less current liabilities</b>		<b>9,408</b>	9,258
<b>Capital and reserves</b>			
Called up share capital	18	<b>217</b>	217
Share premium account	19	<b>8,903</b>	8,903
Profit and loss account	19	<b>288</b>	138
<b>Shareholders' funds</b>	19	<b>9,408</b>	9,258

The financial statements on pages 24 to 37 were approved and authorised for issue by the Board of directors on 15 September 2006 and signed on its behalf by:

**Richard Marsden** Director

**John Ward** Director



# Consolidated Cash Flow Statement

for the year ended 30 June

	Notes	2006 £000	Proforma 2005 £000
Net cash outflow from operating activities	20(i)	(1,530)	(840)
Returns on investments and servicing of finance			
Interest received		397	196
Capital expenditure and financial investment			
Purchase of intangible fixed assets		(17)	(18)
Purchase of tangible fixed assets		(35)	(42)
Net cash outflow from capital expenditure		(52)	(60)
Net cash outflow before management of liquid resources and financing		(1,185)	(704)
Management of liquid resources			
Decrease/(Increase) in short-term deposits		1,141	(8,255)
Financing			
Repayment of capital element of finance leases and hire purchase contracts		(1)	–
Issues of ordinary share capital		–	77
Share premium received on share issues		–	9,923
Share issue costs		–	1,020
Cash (outflow)/inflow from financing		(1)	8,980
(Decrease)/Increase in cash	20(iii)	(45)	21

# Notes to the Financial Statements

for the year ended 30 June 2006

## 1. Accounting policies

### Accounting convention and basis of consolidation

The consolidated financial statements have been prepared under the historical cost convention, in accordance with the Companies Act 1985 and applicable UK accounting standards. The consolidated financial statements incorporate the financial statements of the Company and its subsidiary undertaking for the year ended 30 June 2006. Comparative figures are for the year ended 30 June 2005 on the basis set out in the following paragraph.

Synairgen plc was incorporated on 16 September 2004 and 2 ordinary shares of 1p each were issued. On 11 October 2004 Synairgen plc acquired the entire issued share capital of Synairgen Research Limited by issuing 13,999,998 ordinary shares of 1p each on the basis of issuing 100 shares for each ordinary share of 1p each held in Synairgen Research Limited. The directors have accounted for this group reconstruction using the merger accounting principles as set out in Financial Reporting Standard 6. Accordingly proforma financial information has been prepared to show the position as if Synairgen plc had been in existence and the parent of Synairgen Research Limited throughout the prior period. The proforma information has been compiled by taking the results of Synairgen Research Limited before the restructuring and adjusting for the capital structure of the new group.

A summary of the material accounting policies which have been applied consistently throughout the year is set out below.

### Turnover

Turnover is stated net of value added tax and is recognised when products or services are supplied, except in respect of long-term contracts where turnover represents the sales value of work done in the year and is calculated as that proportion of total contract value which costs incurred to date bear to total expected costs for that contract.

### Research and development

Expenditure on pure and applied research is charged to the profit and loss account in the year in which it is incurred.

Development costs are charged to the profit and loss account in the year of expenditure, unless individual projects satisfy all of the following criteria:

- the project is clearly defined and related expenditure is separately identifiable;
- the project is technically feasible and commercially viable;
- current and future costs are expected to be exceeded by future sales; and
- adequate resources exist for the project to be completed.

Any capitalised amounts are subsequently amortised over the directors' estimate of their useful economic life.

### Intangible fixed assets

Intangible assets are stated at cost less amortisation. Patent and licence costs are amortised over the directors' estimate of their useful lives.

### Tangible fixed assets

Tangible fixed assets are stated at cost less depreciation. Depreciation is provided on a straight-line basis at rates calculated to write off the cost of fixed assets, less their estimated residual value over their expected useful lives, which are as follows:

Computer equipment: 3 years

Laboratory and clinical equipment: 5 years

The carrying values of tangible fixed assets are reviewed for impairment if events or changes in circumstances indicate that the carrying value may not be recoverable.

### Fixed asset investments

Investments in subsidiaries are held in the Company financial statements at cost less provision for impairment.

### Stocks

Stocks are stated at the lower of cost and net realisable value.

### Finance and operating leases

Assets acquired under finance leases are included in fixed assets and are depreciated over the shorter of the lease period or their expected economic useful lives. The capital elements of the leasing commitments are 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 to the profit and loss account so as to give a constant periodic rate of charge on the remaining balance outstanding at the end of each accounting period. Costs in respect of operating leases are charged to the profit and loss account on a straight-line basis over the term of the lease.

### Deferred taxation

Deferred tax balances are recognised in respect of all timing differences that have originated but not reversed by the balance sheet date except that the recognition of deferred tax assets is limited to the extent that the Group anticipates making sufficient taxable profits in the future to absorb the reversal of the underlying timing differences.

Deferred tax balances are not discounted.

### Foreign currencies

Foreign currency transactions are translated at the rates ruling when they occurred. Foreign currency monetary assets and liabilities are translated at the rate of exchange ruling at the balance sheet date. Any differences are taken to the profit and loss account.

### Financial instruments

The Group's policies in relation to financial instruments are set out in Note 17. The Group has taken advantage of the exemption allowed under Financial Reporting Standard 13 'Derivatives and Financial Instruments', and excluded short-term debtors and creditors under financial instruments other than the disclosures required in respect of currency risk.

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## Pensions

The Group operates a defined contribution stakeholder pension scheme and contributes to certain employees' personal pension plans. The pension charge to the profit and loss account represents the amounts payable by the Group in respect of the year.

at the date of grant and the option exercise price in accordance with UITF Abstract 17 (revised 2003) 'Employee Share Schemes'. The credit entry for this charge is taken to the profit and loss reserve and reported in the reconciliation of movements in shareholders' funds.

## Share-based employee remuneration

When shares and share options are awarded to employees a charge is made to the profit and loss account based on the difference between the market value of the Company's shares

## 2. Turnover

All turnover is generated within the United Kingdom from continuing activities and is stated net of value added tax.

The Group operates in one area of activity, namely drug discovery. Turnover by destination to third parties is analysed as follows:

Geographical area	2006 £000	Proforma 2005 £000
United States of America	77	125
United Kingdom	–	5
Rest of the world	5	72
	<b>82</b>	<b>202</b>

## 3. Operating loss

This is arrived at after charging:

	2006 £000	Proforma 2005 £000
Depreciation and amortisation	48	34
Auditors' remuneration:		
Audit services	15	15
Non-audit services (i)	13	20

(i) For the year ended 30 June 2005, in addition to the fees of £20,000 for non-audit services, which represent tax compliance and other advisory work and have been charged to the profit and loss account, a further £93,000 was paid to the auditors for their work in relation to the initial public offering, which has been offset against the share premium account.

## 4. Staff costs

The average monthly number of employees (including executive directors) was:

	Group 2006	Proforma Group 2005	Company 2006	Company 2005
Research	11	6	–	–
Administration	3	2	2	2
	<b>14</b>	<b>8</b>	<b>2</b>	<b>2</b>

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 4. Staff costs (continued)

Their aggregate remuneration comprised:

	Group 2006 £000	Proforma Group 2005 £000	Company 2006 £000	Company 2005 £000
Wages and salaries	503	315	–	–
Social security costs	57	32	–	–
Other pension costs	33	20	–	–
	<b>593</b>	<b>367</b>	<b>–</b>	<b>–</b>

The Company's costs in respect of the two executive directors are recharged in full to Synairgen Research Limited.

Details of directors' emoluments, pensions and share options are set out in the Directors' Remuneration Report on pages 19 to 22.

## 5. Tax on loss on ordinary activities

There is a taxation credit of £255,000 for the year (2005: £nil), analysed as follows:

	2006 £000	Proforma 2005 £000
<b>Current tax</b>		
UK corporation tax on profits of the period	(166)	–
Adjustment in respect of prior periods	(89)	–
	<b>(255)</b>	<b>–</b>

The tax assessed on the loss on ordinary activities for the year is different to the standard rate of corporation tax in the UK of 30%. The differences are reconciled below:

	2006 £000	Proforma 2005 £000
Loss on ordinary activities before tax	(1,297)	(610)
Loss on ordinary activities before tax multiplied by the standard rate of corporation tax in the UK	(389)	(183)
Effects of:		
Expenses not deductible for tax purposes	1	5
Fixed asset timing differences	7	(1)
Enhanced research & development relief	(104)	(51)
Variable rates on tax losses surrendered for research & development tax credit	145	–
Losses carried forward	174	230
Over provision in respect of previous periods	(89)	–
<b>Group tax credit for the current year</b>	<b>(255)</b>	<b>–</b>

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 6. Loss per ordinary share

	2006	Proforma 2005
Loss on ordinary activities after taxation (£000)	(1,042)	(610)
Weighted average number of ordinary shares in issue	21,692,308	18,730,993

The loss attributable to ordinary shareholders and weighted average number of ordinary shares for the purpose of calculating the diluted earnings per ordinary share are identical to those used for basic earnings per share. This is because the exercise of share options would have the effect of reducing the loss per ordinary share and is therefore not dilutive under the terms of Financial Reporting Standard 22. At 30 June 2006 there were 1,946,594 options outstanding (30 June 2005: 1,813,500 options outstanding). The comparative figures are proforma based on the number of shares that would have been in issue had the capital structure of the new parent company always been in place.

## 7. Profit attributable to members of the parent company

As permitted by Section 230 of the Companies Act 1985, the Company's profit and loss account has not been included in these financial statements. The profit dealt with in the financial statements of the parent company was £150,000 (2005: £138,000).

## 8. Intangible fixed assets

Group	Patent & licence costs £000
<b>Cost</b>	
At 1 July 2005	22
Additions	17
<b>At 30 June 2006</b>	<b>39</b>
<b>Amortisation</b>	
At 1 July 2005	1
Provided for the year	2
<b>At 30 June 2006</b>	<b>3</b>
<b>Net book amount at 30 June 2006</b>	<b>36</b>
Net book amount at 30 June 2005	21

## 9. Tangible fixed assets

Group	Computer equipment £000	Laboratory and clinical equipment £000	Total £000
<b>Cost</b>			
At 1 July 2005	17	172	189
Additions	24	25	49
<b>At 30 June 2006</b>	<b>41</b>	<b>197</b>	<b>238</b>
<b>Depreciation</b>			
At 1 July 2005	2	33	35
Provided for the year	11	35	46
<b>At 30 June 2006</b>	<b>13</b>	<b>68</b>	<b>81</b>
<b>Net book value at 30 June 2006</b>	<b>28</b>	<b>129</b>	<b>157</b>
Net book value at 30 June 2005	15	139	154

Included within laboratory and clinical equipment at 30 June 2006 are assets under hire purchase contracts at a cost of £14,000 (30 June 2005: £nil) and net book value of £14,000 (30 June 2005: £nil).

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 10. Investments

Company	Investment in subsidiary undertaking £000	Loan to subsidiary undertaking £000	Total £000
At 1 July 2005	140	435	575
Additions	–	1,302	1,302
<b>At 30 June 2006</b>	<b>140</b>	<b>1,737</b>	<b>1,877</b>

Subsidiary undertakings included in the consolidated group accounts:

Name of company	Country of incorporation	Proportion of voting rights and ordinary share capital held	Nature of business
Synairgen Research Limited	England	100%	Drug discovery

## 11. Stocks

Group	2006 £000	2005 £000
Raw materials	60	55
Finished goods	8	–
	<b>68</b>	<b>55</b>

## 12. Debtors

	Group 2006 £000	Group 2005 £000	Company 2006 £000	Company 2005 £000
Trade debtors	–	119	–	–
Corporation tax recoverable	255	–	–	–
Other tax and social security	29	28	5	13
Prepayments and accrued income	139	178	90	108
	<b>423</b>	<b>325</b>	<b>95</b>	<b>121</b>

All amounts fall due for payment within one year.

## 13. Creditors: amounts falling due within one year

	Group 2006 £000	Group 2005 £000	Company 2006 £000	Company 2005 £000
Obligations under finance leases and hire purchase contracts (note 15)	3	–	–	–
Trade creditors	108	95	3	10
Amounts due to group undertakings	–	–	5	20
Other tax and social security	22	18	–	12
Other creditors	6	1	–	–
Accruals and deferred income	195	284	26	29
	<b>334</b>	<b>398</b>	<b>34</b>	<b>71</b>



# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 14. Creditors: amounts falling due after more than one year

Group	2006 £000	2005 £000
Obligations under finance leases and hire purchase contracts (note 15)	10	—

## 15. Obligations under finance leases and hire purchase contracts

Group	2006 £000	2005 £000
Amounts payable:		
Within one year	4	—
In one to two years	3	—
In two to five years	9	—
	16	—
Less finance charges allocated to future periods	(3)	—
	13	—

## 16. Deferred taxation

### Recognised deferred taxation

Group	2006 £000	Proforma 2005 £000
Accelerated capital allowances	39	44
Trading losses	(39)	(44)
Charge for the year	—	—

### Unrecognised deferred taxation

The Group has an unrecognised deferred tax asset of £312,000 at 30 June 2006 (2005: £291,000), representing trading losses carried forward which are available for offset against future profits of the Group. The full utilisation of these losses in the foreseeable future is uncertain and no deferred tax asset has therefore been recognised.

The movement on the unrecognised deferred tax asset comprises the following:

	2006 £000
Unrecognised deferred tax asset at 1 July 2005	(291)
Movement in current year	(21)
Unrecognised deferred tax asset at 30 June 2006	(312)

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 17. Financial instruments

An explanation of the Group's objectives, policies and strategies for financial instruments can be found in the Financial Review on page 6.

Other than short-term debtors and creditors that arise directly from operations, the Group's financial instruments comprise cash and hire purchase finance. The fair value is not materially different to their book values. The objective of holding financial instruments is to have access to finance for the Group's operations and manage related risks. The main risks arising from holding these instruments are liquidity, interest rate risk and currency risk.

### Interest rate risk

Interest rate risk profile of financial liabilities and assets, excluding short-term debtors:

Group	Fixed rate financial liabilities 2006 £000	Floating rate financial assets 2006 £000	Fixed rate financial liabilities 2005 £000	Floating rate financial assets 2005 £000
Sterling	13	7,497	–	8,683

Fixed rate financial liabilities comprises a hire purchase contract, which expires in 2010 and has a weighted average interest rate of 8.26%. The maturity profile is detailed in note 15. There is no material difference between the carrying amount and the fair value of the financial liabilities.

Floating-rate financial assets comprise cash on deposit and cash at bank. There is no difference between the carrying amount and the fair value of the financial assets.

Short-term deposits are placed with banks for periods of up to six months and, in accordance with Financial Reporting Standard 13, are categorised as floating-rate financial assets. Contracts in place at 30 June 2006 had a weighted average period to maturity of 92 days and a weighted average annualised rate of interest of 4.61%.

### Liquidity risk

The Group's policy is to maintain adequate cash resources to meet liabilities as they fall due. Cash balances are placed on deposit for varying periods with reputable banking institutions to ensure there is limited risk of capital loss. The Group does not maintain an overdraft facility.

### Currency risk

The Group is exposed to US dollar currency exposures as some of its revenues are denominated in this currency. The Group does not routinely hedge against these currency exposures.

At 30 June 2006 the Group had trade debtors of £nil (2005: £24,000) denominated in US dollars and £nil (2005: £49,000) denominated in Canadian dollars.

## 18. Called up share capital and share options

Authorised	2006 £000		2005 £000	
Equity				
Ordinary shares of 1p each	1,000		1,000	
Issued, called up, allotted and fully paid	2006 Number	2005 Number	2006 £000	2005 £000
Equity				
Ordinary shares of 1p each	21,692,308	21,692,308	217	217

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 18. Called up share capital and share options (continued)

### Options

At 30 June 2006 there were options outstanding over 1,946,594 un-issued ordinary shares, equivalent to 9.0% of the issued share capital, as follows:

Date of Grant	Ordinary shares under option at 30 June 2006	Earliest exercise date	Latest exercise date	Exercise price
11 October 2004	420,000	11 October 2004	10 October 2014	1p
11 October 2004	280,000	26 October 2004	10 October 2014	1p
11 October 2004	280,000	11 October 2004	10 October 2014	10p
11 October 2004	140,000	30 June 2005	10 October 2014	10p
26 October 2004	140,000	30 June 2005	25 October 2014	130p
26 October 2004	280,000	30 June 2006	25 October 2014	130p
26 October 2004	140,000	30 June 2007	25 October 2014	130p
26 October 2004	70,000	26 October 2007	25 October 2014	130p
12 May 2005	28,000	12 May 2008	11 May 2015	136.5p
15 November 2005	149,020	15 November 2008	14 November 2009	1p
15 November 2005	19,574	15 November 2008	14 November 2015	117.5p
	<b>1,946,594</b>			

The earliest and latest exercise dates, as set out above, assume continuing employment by option-holders.

## 19. Reconciliation of movements in reserves and shareholders' funds

Group	Share capital £000	Share premium account £000	Merger reserve £000	Profit and loss account £000	Shareholders' funds £000
At 1 July 2004	113	—	510	(153)	470
Issue of ordinary shares	104	9,923	(27)	—	10,000
Share issue costs	—	(1,020)	—	—	(1,020)
Loss for the year	—	—	—	(610)	(610)
At 30 June 2005	217	8,903	483	(763)	8,840
Loss for the year	—	—	—	(1,042)	(1,042)
Reversal of UITF 17 charge	—	—	—	39	39
At 30 June 2006	<b>217</b>	<b>8,903</b>	<b>483</b>	<b>(1,766)</b>	<b>7,837</b>

The issue of 140,000 1p ordinary shares by Synairgen Research Limited prior to its acquisition by Synairgen plc has been restated to reflect the 100 for 1 share for share exchange which was effected in October 2004. In accordance with the principles of merger accounting, the difference between the nominal value of the shares issued in the share exchange and sum of the amounts standing to the issued share capital and share premium accounts has been taken to a merger reserve.

Company	Share capital £000	Share premium account £000	Profit and loss account £000	Shareholders' funds £000
At 16 September 2004	—	—	—	—
Issue of ordinary shares	217	9,923	—	10,140
Share issue costs	—	(1,020)	—	(1,020)
Profit for the period	—	—	138	138
At 30 June 2005	217	8,903	138	9,258
Profit for the year	—	—	150	150
At 30 June 2006	<b>217</b>	<b>8,903</b>	<b>288</b>	<b>9,408</b>

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 20. Notes to the Cash Flow Statement

### (i) Reconciliation of operating loss to net cash outflow from operating activities

Group	2006 £000	Proforma 2005 £000
Operating loss	(1,673)	(908)
Depreciation & amortisation	48	34
UITF 17 charge	39	–
Increase in stocks	(13)	(55)
Decrease/(Increase) in debtors	136	(146)
(Decrease)/Increase in creditors	(67)	235
<b>Net cash outflow from operating activities</b>	<b>(1,530)</b>	<b>(840)</b>

### (ii) Reconciliation of net cash flow to movement in net funds

Group	2006 £000	Proforma 2005 £000
(Decrease)/Increase in cash in year	(45)	21
(Decrease)/Increase in short-term deposits	(1,141)	8,255
Cash used to repay capital element of finance leases and hire purchase contracts	1	–
<b>Change in net funds resulting from cash flows</b>	<b>(1,185)</b>	<b>8,276</b>
New finance leases and hire purchase contracts	(14)	–
<b>Movement in net funds</b>	<b>(1,199)</b>	<b>8,276</b>
Net funds at start of year	8,683	407
<b>Net funds at end of year</b>	<b>7,484</b>	<b>8,683</b>

### (iii) Analysis of net funds

Group	At 1 July 2005 £000	Cash Flow £000	Other non-cash movements £000	At 30 June 2006 £000
Cash at bank and in hand	78	(45)	–	33
Short-term deposits	8,605	(1,141)	–	7,464
Hire purchase contracts	–	1	(14)	(13)
	8,683	(1,185)	(14)	7,484

### (iv) Other non cash movements

During the year the Group entered into a hire purchase contract in respect of assets with a total capital value at the inception of the contract of £14,000 (2005: £nil).

## 21. Related party transactions and balances

During the year ended 30 June 2006, the Group incurred fees and expenses of £30,000 (2005: £45,000) with IP2IPO Limited for the provision of business consultancy services. IP2IPO Limited has an interest in the Company and Mr David Norwood is a director of IP2IPO Limited and a shareholder and director in its parent company, IP Group plc. Dr Bruce Campbell is a director of IP Group plc. At the balance sheet date the amount unpaid in respect of these charges was £4,000 (2005: £9,000).

# Notes to the Financial Statements

for the year ended 30 June 2006 (continued)

## 21. Related party transactions and balances (continued)

During the year ended 30 June 2006, the Group incurred costs, fees and expenses of £383,000 (2005: £423,000) with the University of Southampton in connection with premises, services and research and development activities. The University of Southampton is the controlling shareholder of Southampton Asset Management Limited which has an interest in the Company. At the balance sheet date the amount unpaid in respect of these charges was £138,000 (2005: £220,000).

During the year ended 30 June 2006, the Group incurred consultancy fees and expenses with Prof. Stephen Holgate, a director of the Company, amounting to £15,000 (2005: £16,000). At the balance sheet date the amount unpaid in respect of these charges was £4,000 (2005: £nil).

## 22. Synairgen plc (formerly called Synairgen Research plc) – Consolidated profit and loss account from the date of incorporation on 16 September 2004 to 30 June 2005

	£000
Turnover	178
Cost of sales	(114)
Gross profit	64
Administrative expenses	(838)
Operating loss	(774)
Bank interest receivable	295
Loss on ordinary activities before taxation	(479)
Tax on loss on ordinary activities	–
Loss on ordinary activities after taxation and retained loss for the period	(479)

The profit and loss account above is required by the Companies Act 1985 and covers the first statutory accounting reference period of Synairgen plc (formerly Synairgen Research plc) from its date of incorporation on 16 September 2004 to 30 June 2005.

Disclosure notes for this period, with the exception of directors' remuneration as disclosed below, are not presented as the directors do not believe they would provide meaningful information to the users of the accounts.

Directors' remuneration for this period was as follows:

£000	Notes	Salary/fee	Benefits	Bonus	Total (excl. pension)	Pension	Total (incl. pension)
<b>Executive directors</b>							
Richard Marsden		73	1	13	87	7	94
John Ward		54	–	9	63	4	67
<b>Non-executive directors</b>							
Simon Shaw		24	–	–	24	–	24
Prof. Stephen Holgate	(i)	3	–	–	3	–	3
David Norwood	(ii)	3	–	–	3	–	3
Susan Sundstrom	(iii)	3	–	–	3	–	3
		160	1	22	183	11	194

(i) In addition to this fee for his services as a director, Prof. Holgate received consultancy fees and expenses amounting to £13,000.

(ii) This amount was paid to IP2IPO Limited for the services of David Norwood.

(iii) This amount was paid to the University of Southampton for the services of Susan Sundstrom.

# Notice of Annual General Meeting

Notice is hereby given that the Annual General Meeting ('AGM') of Synairgen plc will be held at the offices of Stringer Saul LLP, 17 Hanover Square, London W1S 1HU on Wednesday, 15 November 2006 at 12 noon to transact the business detailed below.

## Ordinary Business

To consider and, if thought fit, to pass the following resolutions which will be proposed as ordinary resolutions:

1. To receive and adopt the audited accounts of the Company for the financial year ended 30 June 2006, together with the Directors' and the Auditors' reports in respect of such accounts.
2. To re-appoint as a director Bruce Campbell, who is retiring in accordance with Article 108 of the Company's Articles of Association and who, being eligible, offers himself for re-appointment.
3. To re-appoint as a director Richard Marsden, who is retiring by rotation in accordance with Article 102 of the Company's Articles of Association and who, being eligible, offers himself for re-appointment.
4. To re-appoint as a director Stephen Holgate, who is retiring by rotation in accordance with Article 102 of the Company's Articles of Association and who, being eligible, offers himself for re-appointment.
5. To re-appoint BDO Stoy Hayward LLP as the Company's Auditors to hold office from the conclusion of the meeting to the conclusion of the next meeting at which the accounts are laid before the Company and to authorise the directors to fix their remuneration.
6. To approve the Directors' Remuneration Report for the financial year ended 30 June 2006.

## Special Business

As special business to consider and, if thought fit, pass resolution 7, which will be proposed as an ordinary resolution of the Company, and resolution 8, which will be proposed as a special resolution of the Company.

7. That the directors be and they are hereby generally and unconditionally authorised pursuant to section 80 of the Companies Act 1985 (the 'Act') to allot relevant securities (within the meaning of section 80 of the Act) up to an aggregate nominal amount of £94,496. This authority shall expire on the conclusion of the 2007 Annual General Meeting (and all previous authorities under section 80 of the Companies Act 1985 shall cease to have effect) save that the Company may make an offer or agreement which would or might require relevant securities to be allotted after the expiry of this authority and the directors may allot relevant securities pursuant to that offer or agreement as if this authority had not expired; and this authority shall be in substitution for any other authority to allot relevant securities but without prejudice to the continuing authority of the directors to allot relevant securities in pursuance of an offer or agreement made before the expiry of the authority pursuant to which such offer or agreement was made.
8. That subject to the passing of the previous resolution the directors be and they are hereby empowered pursuant to section 95 of the Act to allot equity securities (within the meaning of section 94 of the Act) for cash pursuant to the authority conferred by the previous resolution and to sell or make offers or agreements to sell equity securities which immediately before the sale are held by the Company as treasury shares (as defined by section 162A of the Act) in each case as if section 89(1) of the Act did not apply to such allotment provided that this power shall be limited to:
  - (a) the allotment of equity securities, whether by way of rights issue, open offer or otherwise, to holders of Ordinary Shares and to holders of other securities in the Company that by their terms are entitled to participate in such rights issue, open offer or otherwise in such a manner that the number of equity securities allotted to them is in proportion (as nearly as may be) to their respective holdings of such securities or in accordance with the rights attached thereto and the directors may deal as they see fit with fractional entitlements, overseas shareholders and with the legal or practical problems or requirements of any regulatory body or stock exchange in any territory;
  - (b) the allotment of equity securities up to an aggregate nominal amount of £17,600 upon the exercise of options granted by the Company other than pursuant to an employee share scheme as defined in the Act; and
  - (c) (other than pursuant to sub-paragraphs (a) and (b) above) the allotment or sale of equity securities up to an aggregate nominal amount of £10,846 (representing 5% of the nominal value of the issued share capital of the Company at 10 October 2006);

and this power shall be in substitution for all such powers previously given but without prejudice to the continuing power of directors to allot equity securities pursuant to an offer or agreement made by the Company before the date this resolution is passed and unless previously renewed, varied or revoked by the Company in general meeting shall expire on the earlier of the conclusion of the Annual General Meeting of the Company to be held in 2007 save that the Company may, before such expiry, make an offer or agreement which would or might require equity securities to be allotted after such expiry and the directors may allot equity securities or sell equity securities which immediately before the sale are held by the Company as treasury shares (as defined by section 162A of the Act) in pursuance of such offer or agreement as if the authority conferred hereby had not expired.

By order of the Board

Registered Office:  
2 Venture Road  
Chilworth Science Park  
Southampton SO16 7NP

**John Ward**

Company Secretary  
10 October 2006



# Notice of Annual General Meeting (continued)

## Notes

1. A member entitled to attend and vote at the meeting convened by this notice is entitled to appoint one or more proxies to attend and, on a poll, to vote instead of him. A proxy need not be a member of the Company. A form of proxy is enclosed. To be effective, it must be deposited at the Company's registrars, Capita Registrars, The Registry, 34 Beckenham Road, Beckenham, Kent BR3 4BR, so as to be received not less than 48 hours before the time of the meeting. Return of the form of proxy does not preclude a member from attending and voting in person.
2. A statement or summary of transactions of directors (and their family interests) in the share capital of the Company and copies of their service contracts will be available for inspection at the Company's registered office during normal business hours (Saturdays and public holidays excepted) from the date of this notice until the conclusion of the AGM and will also be available for inspection at the place of the AGM for at least 15 minutes prior to and during the meeting.
3. The Company, pursuant to Regulation 41 of The Uncertificated Securities Regulations 2001 and Article 121 of the Company's Articles of Association, specifies that only those members on the register of the Company as at 6 pm on 13 November 2006 shall be entitled to vote at the Annual General Meeting in respect of the number of shares registered in their name at that time. Changes to entries on the register after 6 pm on 13 November 2006 shall be disregarded in determining the rights of any person to attend or vote at the meeting.

The explanatory notes below summarise the purpose of each resolution to be passed:

## Resolutions 1 to 6 comprise the ordinary business of the AGM.

### Resolution 1: Report and Accounts

For each financial year, the directors are required to lay the Directors' Report, the audited accounts and the Auditors' Report before the Company in general meeting. The Shareholders are requested to receive and adopt the Report and Accounts for the year ended 30 June 2006.

### Resolutions 2 to 4: Appointment of directors

Article 108 of the Company's Articles of Association requires that, at the AGM, each director appointed to the Board since the previous AGM shall retire from office. As a consequence, Bruce Campbell, who was appointed by the Board on 11 April 2006, shall retire and, being eligible, offers himself for re-appointment. Resolution 2 proposes his re-appointment.

Article 102 of the Company's Articles of Association requires that, at the AGM, one third of directors (excluding directors retiring in accordance with Article 108) shall retire. Accordingly, Richard Marsden and Stephen Holgate shall retire and, being eligible, offer themselves for re-appointment. Resolutions 3 and 4 propose their re-appointment.

Biographical details are given on page 13 of the Annual Report.

### Resolution 5: Appointment of auditors

At each general meeting at which the accounts are laid before shareholders, the Company is required to appoint auditors to serve until the next such meeting. Resolution 8 proposes the re-appointment of BDO Stoy Hayward LLP as the Company's auditors and that the directors be authorised to fix their remuneration.

### Resolution 6: Approval of the Directors' Remuneration Report

Resolution 6 proposes the approval of the Directors' Remuneration Report for the financial year ended 30 June 2006, as set out on pages 19 to 22 of the 2006 Annual Report. The Directors' Remuneration Report contains, amongst other things, a forward-looking statement of the Company's policy on directors' remuneration for subsequent financial years, details of the directors' service contracts and specific disclosures relating to each director's remuneration.

Resolution 6 will be proposed as an ordinary resolution.

## Resolutions 7 and 8 are the special business of the AGM.

### Resolution 7: Authority to Allot Shares

By a written resolution of the Company passed on 15 November 2005 at the 2005 AGM, shareholders authorised the directors under section 80 of the Companies Act 1985 to allot relevant securities without the prior consent of shareholders for a period from 15 November 2005 until the conclusion of the 2006 Annual General Meeting. Resolution 7 proposes to authorise the directors to allot relevant securities up to a maximum nominal amount of £94,496 (which equates to 9,449,600 shares), which represents the sum of:

- £72,308, being approximately 33.3% of the issued share capital of the Company as at 10 October 2006; and
- £22,188, being the nominal value of shares under option.

Other than pursuant to the exercise of share options and awards made under the Long-Term Incentive Plan, the directors have no present intention to issue any ordinary shares. This authority will expire on the conclusion of the 2007 Annual General Meeting.

Resolution 7 will be proposed as an ordinary resolution.

### Resolution 8: Disapplication of Pre-emption Rights

Also on 15 November 2005, a special written resolution was passed, under section 95 of the Companies Act 1985, empowering the directors to allot equity securities for cash without first being required to offer such shares to existing shareholders for a period from 15 November 2005 until the conclusion of the 2006 Annual General Meeting. It is proposed that this authority also be renewed. The authority relates to: pre-emptive issues; the allotment of up to 1,760,000 ordinary shares on the exercise of options already granted by the Company other than pursuant to an employee share scheme (as defined in the Companies Act 1985); and 1,084,600 shares, which represents approximately 5% of the issued ordinary share capital of the Company as at 10 October 2006. This authority will expire on the conclusion of the 2007 Annual General Meeting.

Resolution 8 will be proposed as a special resolution.

# Glossary

## Airways (or bronchial tubes)

The tubes that conduct air in and out of the lungs

## Allergen

A protein substance that may provoke an allergic response in a susceptible person. Common allergens include house-dust mite faeces, grass pollen and cat dander

## Antibody

A protein produced by cells of the immune system which specifically recognises a target molecule known as an antigen. A key component of the body's immune defence mechanism to foreign agents

## Antigen

A molecule that is capable of stimulating production of an antibody in the body, usually a foreign and potentially toxic molecule

## Assay

A laboratory test used to determine parameters such as the strength of a solution, the proportion of a compound in a mixture, the potency of a drug or the purity of a preparation

## Asthma

A disorder in which the airways become episodically narrowed, leading to wheeze, shortness of breath, cough and chest tightness. Also see Severe asthma

## $\beta_2$ -agonists

Also known as beta agonists – see Bronchodilators

## Barrier Function

Cells lining the airways create a physical barrier to the ingress of external agents (allergens, pollutants etc) by forming a tight seal which surrounds each cell and keeps close contacts between cells. These are called tight junctions. Failure of this 'barrier' results in access of toxic/harmful agents into the interior tissue of the lung

## Biobank

A collection of samples from clinically-characterised volunteers comprising blood, induced sputum, bronchial biopsies and epithelial cells. These samples are used to develop the complex *in vitro* human disease models

## Bronchodilators

Medicines which relax the muscles around the airways, helping the airways to open up, so making it easier to breathe. There are several types of bronchodilators, of which short acting beta-agonist drugs are the most commonly used

## Chronic

Persistent

## Chronic bronchitis

An inflammation of the airways accompanied by coughing and production of phlegm. The symptoms are present for at least three months in each of two consecutive years. See COPD

## Clinical Trial Authorisation

An authorisation from the MHRA to conduct a clinical trial

## COPD

Chronic obstructive pulmonary disease covers two conditions: chronic bronchitis and emphysema. COPD usually results from long-term exposure to irritants to the lungs, of which the most prevalent is tobacco smoking. Unlike asthma, where airflow obstruction varies, in COPD airflow obstruction is largely irreversible

## Drugable

Suitable for pharmaceutical development

## Emphysema

A destructive process involving the air spaces (alveoli) of the lungs, which leads to over-inflation of the lung and, when sufficiently advanced, causes breathlessness and lack of oxygenation of blood. See COPD

## Epithelium

In the lung, the epithelium is a thin layer of cells which lines the airway tubes in order to protect and regulate the tissue underneath

## Exacerbation

A rapid deterioration of a chronic disease that makes the symptoms worse

## Growth factor

A protein that signals for cells to grow and divide

## IFN $\beta$

Interferon beta is a natural protein found in the body which helps to regulate the immune system and fight off viruses. IFN $\beta$  is currently marketed by a number of companies as an intravenous (injectable) therapy for the treatment of multiple sclerosis

## IgE

Immunoglobulin E, a class of antibodies, which play a major role in allergic diseases

## Interferon lambda

Interferon lambda is another natural protein found in the body which helps to regulate the immune system and fight off viruses

## *In vitro*

Carried out in the laboratory, e.g. in a test tube or culture plate

## *In vitro* model (complex)

A research model which contains more than one cell type and allows the study of interactions between different cell types and 'test' agents relevant to the disease or a therapy

## Lower airway

The airway tubes in the lung running from the throat down, ending in the air spaces (alveoli) where gas exchange occurs

## MHRA

The Medicines and Healthcare products Regulatory Agency; a UK government body tasked with ensuring that medicines and medical devices work and are safe

## Morbidity

Incidence or prevalence of a disease

## Mucus

A gelatinous substance normally produced by the epithelium to protect and hydrate the airway surface from harmful agents

## Patent Cooperation Treaty

A system by which a patent application can be filed in many different countries at once. A single international application is filed initially at a receiving office. After a search and publication, the application may be converted to a series of national applications in different countries

## Phase I Clinical Trial

A study conducted in healthy subjects to determine the biological effects of a drug, especially safety and tolerability

## Phase IIa Clinical Trial

A study in a limited number of patients with the aim of making a preliminary determination of the efficacy of a drug to provide proof of concept and/or to study drug dose ranges

## Phase III Clinical Trial

A full scale clinical trial to determine drug efficacy and safety prior to seeking marketing approval

## Phlegm

See Sputum

## Protein

Large molecules constructed of smaller biological units known as 'amino acids'. Proteins are responsible for majority of the function and much of the structure of living things, including humans

# Glossary (continued)

## Proteomics

The systematic and comprehensive identification and characterisation of proteins expressed from cells, tissues or organisms in terms of quality, structural modification, location within cells, activity and function

## Pulmonary

Relating to, functioning like, or associated with the lungs

## Rhinovirus

Rhinoviruses are the most common viral infective agents in humans. The most well known disease caused by rhinoviruses is the common cold

## Safety study

See Phase I Clinical Trials

## Severe asthma

Severe asthma is defined by Asthma UK as the level of asthma which causes disturbed sleep on a weekly basis, or attacks of wheeze on a monthly basis, or one or more speech-limiting attacks in the last year

## Sputum

The thick mucus which is coughed up by a person. Sputum contains cells and soluble substances secreted into the airways (bronchi), some of which can mediate disease if present in amounts different to normal. Sputum is also commonly called phlegm

## Steroids

A group of chemicals that is produced naturally in the body by the adrenal gland. In asthma, steroids are given by inhalation or by mouth to reduce the inflammation of the airways

## Tissue engineering

The creation of living tissues for therapeutic purposes. In Synairgen's case, tissue is grown in complex *in vitro* models to recapitulate the airways

## Upper airway

The tubes in the nose and neck which conduct air into the lung

## Virus

A virus is a non-living small particle that infects cells in biological organisms. Viruses can reproduce only by invading and controlling other cells as they lack the cellular machinery for self reproduction

## Wheeze

A whistling sound made by a person who has airflow obstruction when breathing

# Corporate Directory

## Company number

5233429

## Directors

### Executive:

Richard Marsden, John Ward

### Non-executive:

Simon Shaw (Chairman), Dr Bruce Campbell, Prof. Stephen Holgate, Susan Sundstrom

## Secretary

John Ward

## Head office

Mailpoint 810, Level F, South Block,  
Southampton General Hospital, Tremona Road,  
Southampton SO16 6YD

Telephone and fax: +44 (0) 2380 512 800

## Registered office

2 Venture Road, Chilworth Science Park,  
Southampton SO16 7NP

## Website

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

## E-mail

[info@synairgen.com](mailto:info@synairgen.com)

## Advisers

### Independent auditors

BDO Stoy Hayward LLP  
Arcadia House, Maritime Walk,  
Ocean Village, Southampton SO14 3TL

### Bankers

HSBC Bank plc  
165 High Street, Southampton SO14 2NZ

### Financial public relations

Hogarth Partnership Limited  
No. 1 London Bridge, London SE1 9BG

### Nominated adviser and broker

Bridgewell Limited,  
Old Change House, 128 Queen Victoria Street,  
London EC4V 4BJ

### Patent agents

Marks & Clerk  
Nash Court, Oxford Business Park South,  
Oxford OX4 2RU

### Registrars

Capita Registrars  
The Registry, 34 Beckenham Road,  
Beckenham, Kent BR3 4TU

### Solicitors

Stringer Saul LLP  
17 Hanover Square, London W1S 1HU



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