Press release

Synairgen plc
('Synairgen' or the 'Company')

Positive results in viral pneumonia study for Synairgen's IFN-beta

Southampton, UK – 25 November 2011: Synairgen plc (LSE: SNG), the respiratory drug discovery and development company with a particular focus on viral defence of the lungs, is pleased to announce positive data from its pre-clinical study evaluating the effectiveness of aerosolised interferon beta ('IFN-beta') against viral pneumonia.

Pneumonia is a major cause of morbidity and mortality and is most frequently caused by respiratory viruses; both highly pathogenic viruses such as influenza or SARS-like viruses and, in vulnerable populations, many other common respiratory viruses. Viral pneumonia results when infections spread to the lower respiratory tract and compromise lung function by damaging the cells that make up the air sacs (alveoli) and by causing leakage of fluid (oedema) and blood cells (haemorrhage) into the lungs.

The effect of aerosolised IFN-beta was evaluated in a model of viral pneumonia caused by pandemic H1N1 ('swine flu'). Similar models have successfully predicted the clinical potential of antiviral therapies and vaccines. This study compared the potential use of aerosolised IFN-beta against placebo as either a pre-infection protective measure or as a post-infection treatment measure:

- Pre-infection ("protective") IFN-beta

The effect of IFN-beta was assessed to test "post exposure prophylaxis" usage, whereby inhaled IFN-beta would be used after the individual had been exposed to virus but before the infection had spread to the lung. Inhaled IFN-beta would be used in this way as a protective drug to boost lung antiviral defence in people who have been, or might be, exposed to a life-threatening virus such as SARS (a natural threat) or potentially an aerosolised highly pathogenic virus (bioterrorist threat). This is an increasing area of concern for some governments.

- Post-infection ("treatment") IFN-beta

Aerosolised IFN-beta was administered after the infection to simulate the treatment of patients who are hospitalised with persistent severe viral lung infection, for which there is currently no broad spectrum antiviral therapy available. Synairgen's inhaled IFN-beta would be used to lessen the severity of illness and accelerate the patient's recovery and discharge from hospital by boosting the immune antiviral response.

<u>Study Results</u>

- Both Pre- and Post-infection administration significantly reduced viral load measured using molecular methods ($p<0.001$ and $p<0.05$ when compared to placebo, respectively).

- Pre-infection administration also significantly ($p<0.05$) reduced measures of pneumonia (alveolitis, alveolar haemorrhage, and oedema). Histopathology scores in the alveolar region were reduced by an average of approximately 55% when IFN-beta was compared to placebo. In the more challenging

setting of Post-infection administration, there was also a clear trend for a reduction in the same measures of pneumonia (with average histopathology scores being approximately 40% lower than placebo).

Conclusions

Aerosolised IFN-beta in this study reduced virus-induced pneumonia. This finding, along with other supporting *in vitro* data, suggests that inhaled IFN-beta may have potential in two areas:

- Broad spectrum post exposure prophylactic treatment for emerging viral threats e.g. severe influenza, SARS-like virus or bioterrorism threats
- Treatment of patients hospitalised with a severe viral lung illness to reduce morbidity and mortality

Prof. Stephen Holgate, Non-executive Director and Founder of Synairgen, observed, "*Every year thousands of people are hospitalised due to lung complications of influenza-like illness. If these findings translate into the clinical setting, inhaled interferon beta could become an important treatment with broad antiviral activity in this area of high unmet medical need."*

Richard Marsden, CEO of Synairgen, commented, "*We are very encouraged by these data which support the further development of IFN-beta as a novel therapeutic approach to the threats posed by respiratory viruses such as influenza, new emerging viruses and aerosolised bioterrorism threats. This development complements our current program targeting viral infections in asthma sufferers, which is drawing near to the end of its Phase II proof of concept study."*

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Notes for Editors

About Synairgen
Synairgen is a respiratory drug discovery and development company founded by Professors Stephen Holgate, Donna Davies and Ratko Djukanovic, with a particular focus on viral defence of the lungs in asthma, COPD and influenza. Synairgen is listed on AIM (LSE: SNG).

For more information about Synairgen please see www.synairgen.com.

Synairgen's interferon beta ('IFN-beta') programme
Synairgen is developing inhaled IFN-beta as a therapy in the following indications:

- virus-induced asthma and COPD exacerbations;
- "post exposure prophylaxis" for emerging viral threats; and
- patients hospitalised with severe viral lung illness

Using *in vitro* human models, it was discovered that epithelial cells (cells which line the airways) from both subjects with asthma[1] and COPD have significantly weaker antiviral responses to the common cold virus than healthy control subjects. The addition of low levels of IFN-beta into the models restored antiviral responses (simulating aerosolised IFN-beta therapy). This suggests that local delivery of IFN-beta to the lungs could limit the spread of virus to lungs in subjects with respiratory disease and the consequent worsening of their symptoms.

Synairgen has entered into a supply and licence agreement for a patent-protected formulation of IFN-beta from the Rentschler Group in Germany.

SG004
SG004, a placebo-controlled Phase I study in controlled asthmatics taking inhaled corticosteroids, used the Company's exclusively in-licensed Rentschler formulation of inhaled IFN-beta and was designed to establish its safety at three different dose regimens over a 14 day period. In addition, biomarker activity (see below) was measured as an indicator of antiviral activity. The trial was completed in September 2009 and showed that inhaled IFN-beta was well tolerated, causing no adverse effect on standard measures of lung function and inflammation.

SG004 Biomarkers
Neopterin is a well-recognised biomarker of IFN-beta activity. Having developed and validated a test for measuring neopterin in airway secretions, analysis of the SG004 samples showed statistically significant and dose dependant increases in neopterin levels, indicating that biologically active drug had been successfully delivered to the lung. Furthermore, there were increases of between 4-fold and 64-fold in the gene expression of three antiviral proteins (MxA, 2-5-OAS and IP-10) in the lung cells of the asthmatic volunteers 24 hours after inhaling IFN-beta, indicating that inhaled IFN-beta stimulated a broad antiviral response in the lung.

Activity of IFN-beta against 2009 H1N1 ('swine flu') and seasonal influenza
Laboratory experiments were undertaken in November 2009 for Synairgen by the Health Protection Agency's Centre for Emergency Preparedness and Response (Porton Down, Salisbury) which confirmed the antiviral potency of IFN-beta against

2009 H1N1. In the experiments lung cells were grown in cell culture and then exposed to the 2009 H1N1 (Strain: Influenza A/California/04/2009(H1N1)), resulting in around 70% of cells becoming infected. In the presence of IFN-beta, the proportion of cells infected with the virus was reduced by at least 94% over 3 experiments.

Synairgen has undertaken similar *in vitro* experiments which also confirm the antiviral potency of IFN-beta against seasonal influenza and H5N1 'Bird' flu.

SG005

SG005 is a placebo-controlled Phase II study of inhaled interferon beta ('IFN-beta') for the treatment of exacerbations of asthma caused by respiratory viruses including influenza. Following on from the discovery that IFN-beta significantly reduced the ability of influenza to infect lung cells, SG005 was broadened to allow the inclusion of subjects who contract influenza as well as common cold viruses. The study, which aims to randomise between 140 and 160 subjects, started in 2010 and results are expected in Q1 2012.

Patents granted

The patents for inhaled IFN-beta to treat rhinovirus infections in asthma and COPD were granted in the USA in 2009, Europe in 2010 and Japan in 2011. The patents form part of a patent portfolio owned by the University of Southampton, which is exclusively licensed to Synairgen.

Asthma statistics

- In 2009, approximately 25 million Americans had asthma[2]
- The economic cost to the USA of asthma is projected to be $20.7 billion for 2010[3]
- In 2006, asthma accounted for 1.7 million emergency department visits in the USA[2]
- The cost of emergency department visits and in-patient care in relation to asthma in the USA for 2010 is projected to be $5.5 billion[3]
- The average duration of a hospitalisation for an asthma exacerbation in the USA is 2.7 days at a cost of $9,078[4]
- 50% of the total cost of the asthma is apportioned to 10% of the asthmatic population with the severest disease[5]

COPD statistics

- COPD includes chronic bronchitis and emphysema
- COPD is forecast to be the third leading cause of death worldwide (after heart attack and stroke) by 2030[6]
- In 2009, 13 million adults in the USA were estimated to have COPD[7]. However, as many as 24 million adults have some evidence of impaired lung function, implying an under-diagnosis of this disease[8]
- The economic cost to the USA of COPD is projected to be $49.9 billion for 2010[3]
- Hospital care for COPD in the USA is projected to cost $13.2 billion for 2010[3] and in 2006 there were 672,000 hospitalizations for COPD in the USA[7]

Rhinovirus (common cold virus) and exacerbations (worsening of symptoms) of asthma

- Adults get an average of two to four colds per year, mostly between September and May. Young children suffer from an average of six to eight colds per year[9]
- Rhinovirus infections are the major cause of asthma exacerbations, accounting for 50% to 80% of all such attacks in both children and adults[10]

Influenza statistics

In the USA there are in excess of 200,000 hospitalisations[11] each year associated with influenza and the total economic cost of influenza is estimated to be in excess of $80 billion per year[12]. During the period 1976 to 2007, there were an average of 23,000 deaths per year in the USA associated with seasonal influenza[13]. Influenza accounts for approximately 50% of the viruses identified as causing severe viral lung infections; other viruses such as RSV, parainfluenza virus, rhinovirus, coronavirus and others account for the rest. Synairgen believes it has an advantage because its IFN-beta has shown activity against all of these viruses, whereas virus specific therapies such as Tamiflu and Relenza are active against specific viruses (in this case only influenza).

Pneumonia statistics[14]

- Every 20 seconds, somewhere in the world, a child dies from pneumonia
- Pneumonia is an infection of the lungs that is usually caused by bacteria or viruses. The most common viral causes are influenza, parainfluenza and respiratory syncytial viruses.
- In 2007, 1.2 million people in the US were hospitalised with pneumonia and more than 52,000 people died from the disease

Government grant activity to support antiviral research and development[15]

In recent years, US government agencies have awarded contracts with a total value in excess of $500 million to assist companies with the development of non-vaccine antiviral therapies. Companies who are developing such products with support from US government agencies include BioCryst Pharmaceuticals Inc., Biota Holdings Limited, and Tekmira Pharmaceuticals Corporation.

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