Press release

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

Data update from clinical trial of inhaled interferon beta (SNG001) and clinical plan for COPD

- Significant positive findings in patients with a confirmed viral infection in the INEXAS trial

- COPD Phase II clinical trial designed

Southampton, UK – 27 September 2017: Synairgen (LSE: SNG), the respiratory drug discovery and development company, today provides a positive update on the development of its inhaled interferon beta programme (SNG001) and outlines its strategy to move into the substantial Chronic Obstructive Pulmonary Disease (COPD) market.

Synairgen has conducted a further analysis of clinical data from AstraZeneca's INEXAS trial in asthma, based on whether patients had a positive test for common respiratory viruses.

The aim of treatment with SNG001 is to boost the lungs' antiviral defences and prevent viruses causing exacerbations of respiratory disease.

Key new findings from the INEXAS trial (details in 'Detailed findings and background information" section below):

- 48% of patients in the trial had a positive test result for a respiratory virus
- Statistically significant changes in morning lung function and asthma control were observed in the virus-positive 'difficult to treat' patients who received inhaled IFN-beta; the same patient classification in which we had found the positive signal in our previous Phase II clinical trial (SG005)

Two Phase II trials (SG005 and INEXAS) suggest that SNG001 boosts antiviral responses in the lungs, has a beneficial effect on lung function and, in more difficult to treat patients, improves asthma control during cold infections. However, the unexpectedly low exacerbation rate (<10%) in the INEXAS trial population suggests that the economic viability of the drug in an asthma indication would be limited.

Viruses have often been isolated from samples collected from patients who have had an exacerbation of COPD and with COPD being the second most common cause of emergency admissions to hospital[1] it has always had the potential to be a substantial opportunity for a broad spectrum anti-viral. We have already shown in *in vitro* models that SNG001 protects the lung cells of COPD patients when infected with viruses that cause exacerbations such as flu and the common cold. However, up until now, our ability to identify those patients who may benefit from an inhaled anti-viral therapy made the design of a prospective study challenging. This is because exacerbations of COPD can be caused by other factors such as bacterial infections. Two key developments during 2017 have changed this landscape, opening up a route to the COPD market place for SNG001 and enhancing the prospects of achieving success in the clinical development phase:

First, studies in COPD patients published in 2017 suggest that, looking at all colds in the study period, the risk that a cold will cause an exacerbation of COPD is around 50%[2] and could be even higher in particular at risk patients[3], making COPD a very attractive market. The exacerbation rate in the INEXAS and Aviragen trials in asthma was below 10%.

Secondly, a novel point of care diagnostic tool has been developed which enables rapid confirmation of the existence of a respiratory viral infection when patients present themselves at the hospital or trial site. This enables us to treat only those patients who are infected with a virus, significantly reducing the number of subjects required to show the potential effect of SNG001. Clearly this has significant benefits in the future, allowing accurate prescribing of an anti-viral therapy quickly to those patients who could benefit from treatment.

Synairgen's strategy for its wholly-owned SNG001 programme is to progress into clinical development in COPD. The Company has therefore designed a short trial for the winter of 2017/18 to evaluate the potential of SNG001 in COPD, which is being submitted for regulatory approval. In parallel, we are considering optimal financing strategies to enable us to progress this exciting development over the medium term.

Richard Marsden, Chief Executive Officer of Synairgen, said: *"We have long been conscious that COPD is the key target market for a broad spectrum antiviral such as SNG001. Until recently, the difficulties of patient selection and the associated cost of the required trials made it prohibitively expensive to pursue. The fact that high viral exacerbation rates are now evident, combined with the launch of an effective diagnostic for viral infections, means that a COPD programme is now both highly attractive and economically viable.*

"Finally, our new analysis of the INEXAS trial data suggests a complementary result to our previous trial indicating that we can improve important clinical endpoints in the lungs, which increases our confidence as we move into the significant opportunity that is COPD."

***Prof. Tom Wilkinson, Chief Investigator for the forthcoming COPD trial, commented*:** *"The impact which COPD has on millions of patients' lives is one of the major unmet clinical problems of modern medicine. The problem of exacerbations of COPD - when patients become acutely unwell - is a particular issue and leads to many thousands of admissions to hospital every year, many more than other common respiratory diseases such as asthma.*

"A key cause of these exacerbations is viral infections such as the common cold and currently we have little or no effective treatments to limit the effects of these pathogens. Our own work in Southampton has established the exact nature of the infections which trigger exacerbations. This clinical trial of a new therapy is an important step forward in exploring better treatments for these important events."

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Detailed findings and background information

About the INEXAS trial:

In the INEXAS trial 121 patients were randomised to receive the broad spectrum 'antiviral' protein inhaled IFN-beta or placebo when suspected of suffering a respiratory virus. The primary endpoint was to assess whether inhaled IFN-beta could reduce the number of exacerbations caused by cold infections. The trial was stopped early because too few exacerbations were occurring to enable a determination of the efficacy of IFN-beta on this endpoint; furthermore enough patients had been entered into the trial to assess secondary endpoints. Less than 10% of patients had a severe exacerbation of asthma in the INEXAS trial (very similar to the rate (7%) in a trial conducted by Aviragen, which also reported in 2017). This low rate makes inhaled IFN-beta challenging to develop in asthma as the exacerbation endpoint is important for healthcare providers; essentially the virus-driven exacerbation of asthma does not occur frequently enough to make the drug health economically viable.

AstraZeneca returned the asset and the INEXAS data to Synairgen in April 2017 quoting "strategic reasons"; at that time the data from the trial showed elevation in a marker of antiviral activity (serum IP-10/CXCL-10) and a faster recovery on the lung function parameter Peak Expiratory Flow Rate (PEFR). Changes in other endpoints were not clinically relevant, providing little opportunity for the drug to have an effect.

At the end of July, Synairgen received data confirming which of the 121 patients had a positive respiratory virus test. 48% of patients had a confirmed respiratory virus. Exploratory analysis of the data from these patients and patients who are also in the British Thoracic Society (BTS) Step 4/5 'more difficult to treat' category of asthma showed that the drug had a positive effect on lung function as measured by morning Peak Expiratory Flow (difference of 38.59 L/min/day days 1-7 p=0.0208, n=18 in active group, 19 in placebo group) and also on asthma control over the first week of treatment (Asthma Control Questionnaire or ACQ) difference of -0.492, p=0.0320 n=16 in active group, 21 in placebo group). This data is similar to the findings from our own trial (SG005) of inhaled IFN-beta[4]: PEF change of 31.42 L/min/day days 2-14 p=0.029 (n=22 in active group, 25 in placebo group) and ACQ -0.63 p=0.004 (n=27 in active group, 31 in placebo group) who also came from the BTS Step 4/5 category of asthma (n=24 in active group, 30 in placebo group).

COPD

Chronic Obstructive Pulmonary Disease (COPD) is a lung condition characterised by airflow limitation that is not fully reversible. This airflow limitation is normally progressive and is associated with an abnormal inflammatory response of the lung to pathogenic stimulus. The majority of COPD is associated with long-term cigarette smoking. Symptoms of COPD include cough, excessive sputum production and shortness of breath.

Exacerbations of COPD are defined as the worsening of COPD symptoms beyond normal day-to-day variations and are associated with irreversible loss of lung function and, therefore, accelerated disease progression. Exacerbations severely impact on the patient's quality of life (patients typically take a number of weeks to recover) and are a major healthcare burden. Exacerbations are currently treated with oral corticosteroids and antibiotics. Systemic administration of corticosteroids is associated with unwanted side effects and there is a drive to reduce antibiotic usage.

Respiratory viral infections, such as the common cold and flu, are a major driver of exacerbations in patients with lung disease when infections spread from the upper respiratory tract to the lungs to worsen pre-existing lung inflammation. Furthermore, particularly in COPD, there is growing evidence that virus infections increase susceptibility to follow on bacterial infections. Therefore, there is strong rationale to develop anti-viral treatments to prevent or treat exacerbations of COPD.

COPD statistics

- COPD is the 3rd leading cause of death worldwide (after heart attack and stroke)[5]
- US national medical costs attributable to COPD and its consequences were estimated at $32 billion in 2010 and are forecast to increase to $49 billion in 2020[6]
- More than 15 million Americans have COPD[7]
- In 2010 there were 715,000 hospitalisations for COPD in the USA[8]
- The average cost of a hospitalisation in 2010 for a COPD patient was $7,400[9]

Planned COPD trial:

The trial plan involves dosing a small cohort of stable un-infected COPD patients with SNG001 or placebo to confirm safety in the new indication and show upregulation of anti-viral biomarkers. In the second part of the trial, up to 80 patients will receive either SNG001 or placebo. The objectives of this study are to ensure that antiviral pathways are elevated in COPD patients with a confirmed respiratory virus, and to assess other clinically important endpoints to guide the design of a Phase IIb trial (in which the effect on acute exacerbations will be assessed).

Point-of-care diagnostic:

Although exacerbations of asthma are less predictable than expected, when they do occur they are highly likely to be caused by viruses, as rhinovirus infections account for 50% to 80% of asthma exacerbations in both children and adults[9]. In COPD, other triggers can cause exacerbations, and it is less clear as to whether cold symptoms can be easily identified over and above COPD symptoms. Recently, a point of care test has been launched that has made entry into COPD much easier; it is now possible to confirm the presence of a virus in about 1 hour. This means that COPD patients presenting with cold like symptoms or COPD symptoms will only be entered into the trial if they test positive for a respiratory virus making trials more efficient, and paving a route to market.

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