

Synairgen announces positive data from interim analysis of SNG001 trial in COPD patients

- ***SNG001 well tolerated in this older population with a significant co-morbidity (COPD)***
 - ***Strong interferon driven antiviral biomarker response***
- ***Data support future progression of SNG001 for exacerbating COPD patients***
 - ***Positive data supportive of SNG001 COVID-19 programme***

Southampton, UK – 8 September 2020: Synairgen plc (LSE: SNG), the respiratory drug discovery and development company, today announces positive data from the interim analysis of its exploratory Phase II clinical trial of inhaled SNG001 in Chronic Obstructive Pulmonary Disease (COPD) patients with a confirmed respiratory viral infection.

Key findings

- **Safety**

SNG001 was well tolerated during the treatment period in a study population that was elderly (mean age 66 years) and suffering from reduced respiratory function, as measured by forced expiratory volume in one second (FEV1) (59% of predicted value). The percentage of on-treatment adverse events was similar in the placebo and SNG001 treatment groups (48.1% versus 45.6%, respectively), with treatment-related adverse events being more frequent in the placebo group (25%) compared to the SNG001 group (15.8%). This safety data add to the safety database for SNG001, supporting Synairgen’s interactions with regulatory agencies in respect of COVID-19, where older age and poor lung function are risk factors.

- **Antiviral activity**

Over the treatment period, lung antiviral responses to viral infection were significantly enhanced in patients receiving SNG001 compared to those on placebo, as assessed by measuring increases in the gene expression of interferon beta-dependent antiviral biomarkers MX1 ($p < 0.001$) and OAS1 ($p < 0.001$) in lung (sputum) cells. Analysis of blood biomarkers is ongoing.

- **Clinical endpoints**

The impact of viral infection on COPD patients in the trial was most evident on peak expiratory flow rate (PEFR), a measure of lung function, and patient-reported symptoms assessed using the Breathlessness Cough and Sputum Score (BCSS), and was particularly apparent in exacerbating patients (i.e. patients already requiring treatment with oral corticosteroids and/or antibiotics at the time of randomisation, who represented one third of patients enrolled).

Exacerbating patients who received SNG001 had significantly better lung function during the treatment period (difference in change from baseline morning PEFR between patients receiving SNG001 and placebo over days 2-15 was 25.5L/min; $p = 0.041$). Although there was no significant difference in total BCSS in this group over the treatment period, there was a trend for the breathlessness component of the score, suggesting that patients may have recovered more rapidly if they received SNG001 rather than placebo.

Viral infections had less impact on non-exacerbating patients and there were no significant treatment effects.

- **Virology**

A range of common respiratory viruses including rhinovirus, influenza, adenovirus, respiratory syncytial virus (RSV), human metapneumovirus (HMPV), parainfluenza and coronavirus (the four strains that cause common cold symptoms, but not SARS-CoV-2, the virus that causes COVID-19) were identified in nasopharyngeal and/or sputum samples from the COPD patients in this trial. This is relevant because COVID-19 patients can be coinfecting with other respiratory viruses such as influenza. SNG001 has demonstrated antiviral activity against multiple viruses in cell-based assays. Further virology work is being conducted.

Next steps for COPD

COPD exacerbations are the second most common cause of unplanned hospital admission in England,¹ and occur most frequently in the winter virus season. The data from this trial, coupled with the data from the COVID-19 trial in hospitalised patients, provide a strong rationale for assessing SNG001 in COPD patients admitted to hospital with exacerbations from confirmed viral lung infections.

Next Steps for COVID-19

Synairgen is in discussions with a number of regulatory agencies worldwide to establish the regulatory route to the approval of SNG001 as a treatment for COVID-19. We are also working closely with the Company's manufacturing partners on scale-up activity and will provide a further update on these matters in due course.

Richard Marsden, CEO Synairgen, said: *“COPD exacerbations are the second most common cause of unplanned hospitalisation in England, behind cardiovascular disease. These interim data from our first trial of SNG001 in COPD show that SNG001 could be a valuable novel therapeutic for exacerbating COPD patients. Overall, SNG001 has now been shown to raise the body's natural viral defences when challenged by a wide variety of respiratory viruses, indicating that it could be an important treatment in the coming virus season, where there may be coinfection with influenza and other viruses alongside COVID-19.”*

“Our immediate priority is to progress SNG001 as a therapeutic for COVID-19 and, as such, our COPD programme will remain paused. We are, nevertheless, pleased to provide further evidence that supports SNG001 as a potential treatment for COVID-19 through the safety, biomarker, and efficacy data generated from patients in this interim review of the COPD trial.”

References

1. Department of Health. An Outcomes Strategy for Chronic Obstructive Pulmonary Disease (COPD) and Asthma in England. Published July 2011

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) No. 596/2014 ('MAR').

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Notes for Editors

About Synairgen

Synairgen is a respiratory drug discovery and development company founded by University of Southampton Professors Stephen Holgate, Donna Davies and Ratko Djukanovic. The business, focused primarily on lung viral defence in asthma, COPD, and COVID-19, uses its differentiating human biology BioBank platform and world-renowned international academic KOL network to discover and develop novel therapies for respiratory disease. Synairgen is quoted on AIM (LSE: SNG). For more information about Synairgen, please see www.synairgen.com

About COPD

COPD is a progressive lung disease, punctuated by periods of exacerbation characterised by acute worsening of symptoms which require treatment with oral corticosteroids and/or antibiotics, which have major implications for both the patient and the healthcare system. COPD exacerbations are the second most common cause of unplanned hospitalisation in England.

About SG015 - COPD Trial

In 2018 Synairgen commenced a two-part COPD trial (SG015) to assess initially, the safety and lung antiviral biomarker responses to SNG001 in the absence of viral infection. In the first part of the trial SNG001 was well tolerated in patients with moderate to severe COPD. A strong antiviral biomarker signal was also observed, which was comparable to the response previously observed in asthmatic patients. This paved the way for the second part of the trial, which was designed to dose 120 patients with confirmed, naturally-acquired respiratory virus infections.

The second part of the trial included biomarker outcome measures (expression of interferon-stimulated antiviral genes in cells from sputum and proteins in blood samples such as CXCL10) and a number of clinical outcome measures, including changes in the Breathlessness, Cough and Sputum Score (BCSS), and changes in peak expiratory flow rate (PEFR, a measure of lung function).

Patients were stratified at the time of randomisation into two groups according to whether they were already experiencing an exacerbation of their COPD symptoms requiring treatment with oral corticosteroids and/or antibiotics (exacerbating patients), or whether they just had a viral infection (non-exacerbating patients). Some 32% of patients were exacerbating patients. The aim of treatment was to accelerate recovery in exacerbating patients and prevent a deterioration in non-exacerbating patients.

Recruitment into the trial commenced in earnest in January 2019 and was progressing well until the emergence of SARS-CoV-2, which made it difficult to test for virus and dose patients without potentially exposing them and research staff to SARS-CoV-2. Hence in March 2020 the trial was paused, with 109 out of the targeted 120 patients recruited. MHRA approval was received to run an unplanned interim analysis on the grounds that data from 109 COPD patients with confirmed viral infection could generate useful safety, biomarker and potentially efficacy data to support ongoing trials

of SNG001 in COVID-19 patients. The results of this interim analysis are in the body of this press release.

About SG016 - COVID-19 Trial

Synairgen's clinical trial in COVID-19 patients (SG016) is a double-blind, placebo-controlled trial. The 220-patient trial comprised 100 patients treated in hospital and 120 patients to be treated in the home setting. The patients participating in the hospital setting, which completed recruitment in May 2020, were recruited across a number of NHS trusts and the trial was adopted by the NIHR Respiratory Translational Research Collaboration - comprised of leading centres in respiratory medicine in the UK whose internationally recognised experts are working together to accelerate development and discovery for COVID-19.

On the 20th July 2020 Synairgen announced positive topline data generated from the 101 hospitalized patients in the SG016 trial. The key findings were that the odds of developing severe disease were reduced by 79% in patients receiving SNG001 compared to placebo, that patients who received SNG001 were more than twice as likely to recover from COVID-19 as those on placebo, and that their breathlessness was markedly reduced. Further analysis of the full data set is being conducted, with a peer-reviewed publication expected in due course. A link to the announcement of the topline data can be found [here](#).

COVID-19

COVID-19, caused by the SARS-CoV-2 virus, is a global threat and there is an urgent need to assess new treatments to prevent and effectively treat the severe lower respiratory tract illness that can occur with this disease. Older people and those with co-morbidities such as heart and lung complications or diabetes are at greatest risk of developing severe or fatal disease.

Interferon beta (IFN-beta) applicability to COVID-19

Interferon beta is a naturally- occurring protein, which orchestrates the body's antiviral responses. There is evidence that deficiency in IFN-beta production by the lung could explain the enhanced susceptibility in 'at-risk' patient groups to developing severe lower respiratory tract (lung) disease during respiratory viral infections. Furthermore, viruses, including coronaviruses such as SARS-CoV-2 and MERS-CoV, have evolved mechanisms which suppress endogenous IFN-beta production, thereby helping the virus evade the innate immune system. The addition of exogenous IFN-beta before or during viral infection of lung cells either prevents or greatly diminishes cell damage and viral replication, respectively. Synairgen's SNG001 is a formulation of IFN-beta-1a for direct delivery to the lungs via nebulisation. It is pH neutral, and is free of mannitol, arginine and human serum albumin, making it suitable for inhaled delivery direct to the site of action.

Previously, two Phase II clinical trials in asthmatic patients showed that inhaled SNG001 treatment activated antiviral pathways in the lung, along with improving lung function in patients with a respiratory viral infection.