Press release

Synairgen plc

('Synairgen' or the 'Company')

Synairgen announces data from Home Cohort of SG016 Phase II trial of inhaled interferon beta in COVID-19 patients and encouraging combined data for whole SG016 trial

- *The vast majority of Home Cohort patients experienced mild disease - only two patients were hospitalised during the treatment period, both on placebo*
- *Home Cohort patients successfully self-administered SNG001*
- *The degree of breathlessness at start of treatment indicates which patients should be treated with SNG001 both in hospital and at home*
- *Analysis of the combined data from the Hospital and Home Cohorts showed that the more breathless patients are significantly more likely (>3 fold) to recover on inhaled interferon beta (SNG001) than placebo*
- *The study results reinforce confidence in ongoing Phase III study, with data readout on track for H2 2021*
- *Synairgen management and scientists to hold a 30 minute webcast with live Q&A at 9.00 BST today*

Southampton, UK – 30 April 2021: Synairgen plc (LSE: SNG), the respiratory company developing inhaled interferon beta (IFN-beta) for the treatment of severe viral lung infections, today announces results from the Home Cohort of its SG016 Phase II trial of SNG001 in SARS-CoV-2 infected patients and data from the combined analysis of the Hospital and Home Cohorts.

SNG001 is a formulation containing IFN-beta for nebulisation, allowing it to be delivered directly into patients' lungs. A number of studies have reported that the SARS-CoV-2 virus suppresses natural production of IFN-beta and prevents induction of anti-viral responses by infected cells. Furthermore, some people have deficiencies in antiviral IFN signalling that make them more vulnerable to spread of the virus from the nose into the lungs where it can cause severe breathing difficulties. These findings provide a rationale to deliver IFN-beta directly to the surface epithelial cells of the lungs, the primary site of virus infection in the lungs, to prevent severe lower respiratory tract illness caused by the SARS-CoV-2 virus.

The COVID-19 Phase II study (SG016)

Synairgen's placebo-controlled Phase II trial evaluated SNG001 for the prevention of severe lower respiratory tract (LRT) illness caused by SARS-CoV-2, determined by evaluating change in condition measured using the WHO Ordinal Scale for Clinical Improvement (OSCI) during the dosing period (the primary endpoint). The SG016 trial involved 221 patients in two cohorts:

- Hospital Cohort: 101 patients in the hospital setting, where patients on SNG001, compared to placebo were twice as likely to recover from severe LRT illness to the point where they had 'no limitation of activities' (level 1 on the OSCI) without rebound, and had reduced breathlessness.[1]
- Home Cohort: 120 'at risk' (aged over 65 or over 50 with a risk factor) patients in the home setting to investigate if SNG001 could prevent development of severe LRT illness.

Trial findings from Home Cohort

In total, only two patients were admitted to hospital during the treatment period, both from the placebo group. The hospitalisation rate (approximately 3% in the placebo group) in this 'at risk' COVID-19 patient population was lower than had been originally anticipated, but is in line with other recent large peer-reviewed therapeutic studies.[2] Consequently, the prevention of severe LRT illness could not be determined. The majority of patients exhibited only mild disease which we believe compromised the possibility of showing treatment effects in the Home Cohort. We therefore decided to analyse the subset of patients with most severe symptoms.

A *post hoc* analysis was conducted focusing on the 12% of patients who had significant breathlessness (marked or severe, as defined in Note a) at the time they began treatment. In these patients, the recovery to level 1 on the OSCI ('no limitation of activities') followed a similar pattern to that observed previously in the hospital population where SNG001 accelerated recovery. This led to an analysis of the impact of SNG001 across the Home and Hospital Cohorts in breathless patients.

A further finding from the Home Cohort was that patients can successfully initiate treatment "remotely", self-administering SNG001 at home without the need for a face-to-face meeting with a health care professional, reducing the burden on hospital facilities and minimising the risk of onward infection.

Overall analysis of SG016 trial, combining Hospital and Home Cohorts data

A combined analysis of the Hospital and Home Cohorts data was conducted to explore the impact of the different levels of breathlessness, which is one of the most prominent symptoms of COVID-19, on time to recovery.

- An assessment of placebo patients only indicated that those with marked or severe breathlessness at time of treatment initiation had slower recovery to no limitation of activities than those patients who were not as breathless.
- In the Hospital Cohort (reported in July 2020) patients were 2.19 times more likely to recover to level 1 on the Ordinal Scale compared to placebo, HR 2.19, p=0.043. The addition of the 12 markedly and severely breathless Home Cohort patients changes the Hazard Ratio to 2.49, p=0.009.
- Interestingly, not all hospitalised patients were markedly or severely breathless at time of treatment initiation. An analysis including only patients who were markedly or severely breathless at the time of treatment initiation, irrespective of whether they were in hospital or at home, showed that those treated with SNG001 (n=33) were 3.41 times more likely to recover than those on placebo (n=36) (HR 3.41 [95% confidence interval 1.47- 7.94], p=0.004).

Richard Marsden, CEO of Synairgen, said: *"I am delighted by the finding that SNG001 treatment led to a threefold likelihood of recovery to 'no limitation of activities' in the markedly/severely breathless population compared to those on placebo in the home and hospital setting, and that further analyses reinforce our previous findings. It increases our conviction in the approach we have taken to conduct an international Phase III trial in hospitalised patients requiring supplemental oxygen, which is scheduled to read out in the second half of this year.*

As Governments around the world, such as India, look to how future outbreaks and variants may be handled, our virus-agnostic therapeutic could help to save lives, release pressure on the world's healthcare systems, and thereby potentially mitigate the need for economically costly lockdowns."

Professor Tom Wilkinson, Professor of Respiratory Medicine at the University of Southampton, commented: *"The SG016 COVID-19 trial of inhaled interferon beta*

has been very successful. Although the vast majority of non-hospitalised patients had very mild symptoms, the effects of SNG001 on the small group of markedly and severely breathless patients indicated who might be benefitting most from SNG001. Assessment of breathlessness as a predictor of protracted recovery in the combined Home and Hospital Cohorts showed us that non-breathless patients have no need for the innate immune response boost that interferon beta provides, whereas the patients who were breathless derive strong benefit from SNG001. This tells us that we should target SNG001 at COVID-19 patients with marked or severe breathlessness where it has a potentially significant benefit."

Professor Nick Francis, Professor of Primary Care Research at the University of Southampton, commented: *"With the knowledge gained from this trial, identifying patients likely to benefit from SNG001 in primary care will be a relatively simple task, starting with an assessment of breathlessness. In parallel with the Phase III trial in the hospital setting, there is now an urgent need to assess SNG001 in the non-hospital setting, focussing entirely on breathless COVID-19 patients. I look forward to discussing with primary care platform study teams around the world whether SNG001 can be included in their existing studies.*

As a GP, I recognise the potential importance of these findings, especially for countries that are still struggling with this disease at the moment, and for reducing the burden for patients and the healthcare system in any future waves that may be coming our way."

Synairgen plans to submit the findings for peer review at an upcoming medical conference or publication.

Members of the management team and scientists at Synairgen will hold a webcast for analysts, followed by a live Q&A, at 9:00 BST today. Please find a link to this webcast here.

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

References

1. *The Lancet Respiratory Medicine*: *"Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial". Monk, P D PhD, et al., 12 November 2020, accessible here*.
2. *'https://investor.regeneron.com/news-releases/news-release-details/phase-3-trial-shows-regen-covtm-casirivimab-imdevimab-antibody'.*

Notes

a. Breathlessness scoring system from the Breathlessness, Cough and Sputum Scale (BCSS)

How much difficulty did you have breathing today?
0 = None – unaware of any difficulty
1 = Mild – noticeable when performing strenuous activity (e.g. running)
2 = Moderate – noticeable even when performing light activity (e.g. bedmaking or carrying groceries)
3 = Marked – noticeable when washing or dressing
4 = Severe – almost constant, present even when resting

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Notes for Editors

About Synairgen

Synairgen is a clinical-stage respiratory drug discovery and development company founded by University of Southampton Professors Sir Stephen Holgate, Donna Davies and Ratko Djukanovic.

Synairgen is currently focused on developing its product candidate, SNG001 (inhaled interferon beta) for the treatment of COVID-19. SNG001 is potentially the first host-targeted broad-spectrum antiviral treatment delivered directly into the lungs. The Company is evaluating nebulised SNG001 in its Phase III clinical programme, which has been deemed an Urgent Public Health study by the UK's National Institute for Health Research (NIHR). SNG001 has also been granted Fast Track status from the US Food and Drug Administration (FDA). In Phase II trials, COVID-19 patients with marked/severe breathlessness demonstrated a threefold chance of recovery when treated with SNG001 versus placebo. For more detailed information, please see the notes below.

Synairgen is quoted on AIM (LSE: SNG). For more information about Synairgen, please see www.synairgen.com

COVID-19

COVID-19, caused by the SARS-CoV-2 virus, is an ongoing global pandemic and there is widespread recognition of the urgent need for antiviral therapies, alongside vaccination programs, both for this and future pandemics. Such therapies could be used to prevent and effectively treat the severe lower respiratory tract illness that can occur with these types of diseases.

SNG001 (inhaled Interferon beta) applicability to COVID-19

Interferon beta ('IFN-beta') is a naturally-occurring protein, which orchestrates the body's antiviral responses. It is used widely in the treatment of multiple sclerosis and is a safe and well tolerated drug. There is growing 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.

Viruses, including coronaviruses such as SARS-CoV-2, have evolved mechanisms which suppress endogenous IFN-beta production, helping the virus to evade the innate immune system. The addition of exogenous IFN-beta before or during viral infection of lung cells *in vitro* either prevents or greatly reduces viral replication, potentially reducing the severity of infection and accelerating recovery.

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. Phase I and II trial data have shown that SNG001 activates lung antiviral defences as measured in sputum cells, and that SNG001 has been well tolerated in approximately 280 asthma/COPD/COVID-19 patients to-date. SNG001 has the potential to address the urgent need for antiviral therapies for COVID-19 and for future pandemic respiratory infections, alongside vaccination programmes.

In July 2020, Synairgen announced the results of its Phase II double-blind, placebo-controlled study of 101 randomised COVID-19 hospitalised patients, which showed that SNG001 given for 14 days was associated with greater odds of improvement versus placebo on the WHO Ordinal Scale for Clinical Improvement (OSCI) and more rapid recovery to the point where patients were no longer limited in their activity, with a greater proportion of patients recovering during the 28-day study period.

The results were published in The Lancet Respiratory Medicine: "Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial". Monk, P D PhD, et al., 12 November 2020, accessible here.

The Company's global Phase III trial (SG018) evaluating SNG001 for the treatment of hospitalised COVID-19 patients is ongoing. The trial is deemed an Urgent Public Health study by the UK's National Institute for Health Research (NIHR). In the US, SNG001 has been granted Fast Track status from the US Food and Drug Administration (FDA). The Company is seeking further equivalent prioritisations and support from governments in participating countries.

About Southampton Clinical Trials Unit

The Southampton Clinical Trials Unit (CTU) is a National Institute for Health Research (NIHR) supported CTU with expertise in the design, conduct and analysis of interventional clinical trials. The CTU is based within the University of Southampton with offices at the University Hospital Southampton NHS Foundation Trust Southampton General Hospital site. (www.southampton.ac.uk/ctu/index.page)