Press release

Synairgen plc

('Synairgen' or the 'Company')

Preliminary results for the year ended 31 December 2020

- ***Significant progress continues towards a treatment for COVID-19***

Southampton, UK – 12 May 2021: Synairgen plc (LSE: SNG), the respiratory company developing inhaled interferon beta (IFN-beta) for the treatment of severe viral lung infections, today announces its preliminary statement of audited results for the year ended 31 December 2020.

Highlights (including post period-end)

Operational

- Positive results from Synairgen's Phase II trial (SG016) of inhaled interferon beta-1a (SNG001) in 101 hospitalised COVID-19 patients reported in July 2020
  - Further analyses announced in September 2020 and trial data published in The Lancet Respiratory Medicine in November 2020

- SG016 trial expanded to include a further 120 COVID-19 patients in the home environment
  - Analysis of combined data from Hospital and Home Cohorts in April 2021 showed that patients with significant breathlessness are three times more likely to recover to "no limitation of activities" on the OSCI scale when receiving SNG001 compared to placebo (p=0.004)

- SNG001 awarded Fast Track designation with IND cleared by the US FDA in December

- International Phase III trial (SG018) of SNG001 in hospitalised COVID-19 patients initiated in December 2020
  - First patient dosed in January 2021, initial trial results expected in H2 2021

- SNG001 included in US NIH government-funded ACTIV-2 Phase II/III trial in COVID-19 outpatients in January 2021 and commenced patient dosing in February 2021
  - Phase II evaluation will see the recruitment of up to 220 participants

- Investment in supply chain activities for SNG001 and the Aerogen aerosol delivery system have been made in preparation for launch

- Agreements signed with Akron Biotechnology for drug substance manufacture and Catalent Biologics for fill/finish

- Positive data from interim analysis of SNG001 trial in COPD patients supporting future progression of SNG001 for exacerbating COPD patients

- Patent applications made for use of inhaled interferon beta-1a to treat:
  - COVID-19 patients
  - Virus-induced exacerbations of COPD patients undergoing treatment with systemic corticosteroids

Financial

- In October 2020, Synairgen raised £87.1 million (before expenses) in an equity issue to fund SG018 Phase III trial, SNG001 manufacturing, regulatory activities, and to strengthen balance sheet

- In March 2020, Synairgen raised £14.0 million (before expenses) in an equity issue to fund initial COVID-19 clinical trial activity

- The loss from operations for the year ended 31 December 2020 was £17.7 million (2019: £4.8 million), with research and development expenditure amounting to £15.5 million (2019: £3.5 million)
    - £12.0 million year-on-year increase on research and development expenditure attributable to COVID-19 activities

- Cash balances of £75.0 million at 31 December 2020 (31 December 2019: £2.5 million)

Richard Marsden, CEO of Synairgen, said: *"Synairgen has made exceptional progress over 2020, with our broad-spectrum antiviral taking centre stage as a possible treatment for COVID-19, supported by a growing body of clinical evidence. Our inhaled interferon beta candidate, SNG001, has now demonstrated in a number of robust placebo-controlled clinical trials that it has the potential to prevent patient deterioration and accelerate recovery. Alongside vaccines, access to treatments that are both virus and strain agnostic is critical. Our efforts are focused on making such treatments available to the public as swiftly as possible by advancing our late-stage clinical trials, seeking marketing authorisations and ensuring the manufacturing and commercial capabilities can be rapidly up-scaled to meet potential demand."*

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 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 a Phase II trial, COVID-19 patients with marked/severe breathlessness demonstrated a threefold greater chance of recovery when treated with SNG001 versus placebo.

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 near to 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.

CHAIRMAN'S STATEMENT

Synairgen has made significant progress during 2020, from being one of the first movers in the UK to begin clinical trials to combat COVID-19, to ending the year with compelling clinical data and late-stage clinical trials underway both in the UK and internationally to investigate our inhaled interferon beta candidate (SNG001) in patients with COVID-19. The year has been unprecedented globally for all sectors, and the healthcare industry, and in particular biotechnology, has played a central role. Synairgen's expanded team and speed to action has enabled the Company to make significant strides in the fight against COVID-19. Synairgen has a potential role to play in the provision of a life-saving treatment against COVID-19 and other viruses, and in situations where the various vaccines may not prove effective or suitable.

In July 2020, we received landmark positive results in the Phase II study SG016 in hospitalised COVID-19 patients. This paved the way for our follow-on trial in the home setting and, ultimately, our larger multinational Phase III study SG018, which has been approved to commence by regulators in 12 countries. The importance of progress being made in trials of COVID-19 treatments cannot be understated. While vaccination efforts are crucial to defeating the pandemic, we also need therapeutics to save lives and to help those who become infected despite vaccination. Based on the compelling data published in November 2020 in the Lancet Respiratory Medicine journal supported by evidence from the recently announced home-based trial results, we believe Synairgen's inhaled interferon beta candidate could play a critical role in addressing the impact of COVID-19 and similar viruses by reducing the severity of the disease and accelerating patient recovery.

The inclusion of SNG001 in the US government-funded ACTIV-2 trial is a further indication of international interest in our inhaled interferon beta treatment. Unlike many other treatments, inhaled interferon beta, as a drug taken through a nebuliser, can be self-administered at home under virtual supervision, making it a key part of reducing strain on healthcare systems, both through preventing severe disease and through lowering the number of necessary hospital visits for patients suffering respiratory symptoms.

These successes reflect the scientific research supporting the role of interferons in orchestrating antiviral responses undertaken by our scientific founders, Prof Donna Davies, Prof Ratko Djukanovic, and Prof Sir Stephen Holgate, who continue to play an active role in Synairgen. 2021 is set to be an even more impactful year for Synairgen pending the clinical results from our late-stage trials evaluating SNG001. We are optimistic about the potential for inhaled interferon beta as a potentially effective treatment for COVID-19 and future viral outbreaks.

It has been a very challenging year for Synairgen's staff, combining the significant additional workload of our COVID-19 programmes and an escalation of our manufacturing and commercialisation strategies with the logistical limitations of lockdown and travel restrictions. On behalf of the Board, I wholeheartedly thank our staff and outsourced contractors for their hard work, perseverance and resilience.

Thanks to the support of our shareholders, Synairgen is in a robust financial position following two oversubscribed fundraises during the year. We continue to scale up operations and prepare for commercialisation of the product and look forward to reporting further progress in the coming months.

SIMON SHAW
CHAIRMAN

OPERATING REVIEW

Summary

2020 was an unprecedented year for Synairgen. We were able to respond rapidly to the COVID-19 crisis and continue on our mission to bring our inhaled interferon beta-1a drug product to patients for the treatment of COVID-19.

SNG001 has potential value in three settings:

1. The near term business objective is to gain registrations as soon as possible to treat patients with COVID-19:
(i) in the hospital setting, to prevent further deterioration and death, and to accelerate discharge from hospital and rate of recovery;
(ii) in non-hospitalised patients with significant breathlessness, to prevent hospitalisation and accelerate recovery; and
(iii) to reduce the number of patients who develop 'Long COVID'.

2. The medium term business objective is to work with governments to prepare for the next pandemic. The SARS-CoV-2 pandemic has demonstrated the value of being prepared. Providing SNG001 trials continue to produce positive data, SNG001, as a broad-spectrum antiviral, could be stockpiled for future pandemics. It can be stored in concentrated form in freezers for over six years, and in ready to use format for three years.

3. The long term business model envisages applying SNG001's broad-spectrum antiviral activity to treat patients hospitalised on account of a severe viral lung infection. Chest infections are the fifth largest cause of death globally[1] and approximately half of chest infections have a viral component.[2]

Progress in 2020

During the year Synairgen made significant clinical progress with its inhaled formulation of interferon beta, SNG001. Results from the SG016 Phase II trial of SNG001 in 101 hospitalised COVID-19 patients support its use as a valuable treatment option to prevent development of severe disease and to expedite patient recovery. Further safety, efficacy and other supporting data were provided from the interim analysis of Synairgen's SG015 Phase II COPD trial in September 2020. Expansion of the SG016 trial to include an additional 120 patients treated in the home environment was completed post period-end in January 2021, with analysis of the combined data from the Hospital and Home Cohorts announced in April 2021 showing that the more breathless patients are significantly more likely to recover to "no limitation of activities" on SNG001 than placebo.

Based on the positive outcome of these Phase II results, SNG001 is being trialled in COVID-19 patients around the world. Synairgen has initiated an international Phase III trial (SG018), which will involve a total of 610 hospitalised COVID-19 patients who require supplemental oxygen. Our inhaled interferon beta has also been included in the US government-funded ACTIV-2 Phase II/III trial in COVID-19 outpatients. Dosing began in both trials post period-end in Q1 2021.

The Company is currently focused on progressing these trials to produce the data for accelerated regulatory approvals of SNG001 as a COVID-19 treatment. We are also working on the supply chain in preparation for launch.

COVID-19

COVID-19, caused by the SARS-CoV-2 virus, is a global pandemic and there has been, and continues to be, 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 obesity, heart and lung complications or diabetes are at greatest risk of developing severe or fatal disease.

The SARS-CoV-2 knowledge base is continually expanding with respect to transmissibility and pathogenicity of the virus and its variants, and the effectiveness of the interventions, which include social distancing, vaccines and therapeutics. The need for a therapeutic persists to cover the possibility that vaccine effectiveness wanes, or that vaccine rollout and uptake is sub-optimal.

Rationale for the use of inhaled interferon beta to treat COVID-19

Interferon beta ('IFN-beta') is a naturally-occurring protein, orchestrating the body's antiviral responses. 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. Furthermore, viruses, including coronaviruses such as SARS-CoV-2, have evolved mechanisms to 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. The Company is currently conducting further *in vitro* testing of SNG001 against two SARS-CoV-2 variants. Synairgen's SNG001 is a formulation containing the fully glycosylated form of IFN-beta (IFN-beta-1a) for direct delivery to the lungs via specific nebulisers. It is near to pH neutral, and is free of mannitol, arginine and human serum albumin, which may be pharmacologically active in the airways, making it suitable for inhaled delivery direct to the site of infection, where the aim is to halt progression of disease, reduce duration of stay in hospital and prevent further deterioration and death.

The inhaled route of delivery is necessary if levels of IFN-beta are to be attained in the lungs at the concentration needed to drive antiviral activity. We believe these concentrations could not be accomplished at the lining of the lungs via the injected route.

COVID-19 Phase II trial – SG016

Synairgen's Phase II clinical trial in COVID-19 patients, SG016, was a double-blind, placebo-controlled trial. The two cohort 221 patient trial comprised 101 patients randomised in the hospital setting (initial results reported 20 July with further analyses announced in September 2020), and a further 120 patients randomised in the home setting (trial recruitment completed, with initial data announced in April 2021).

SG016: Hospital Cohort

Synairgen's Phase II trial of SNG001 in hospitalised COVID-19 patients was conducted across nine NHS trusts in the UK and was adopted by the NIHR Respiratory Translational Research Collaboration, who gave it Urgent Public Health status.

The design of this trial, which began dosing patients in March 2020, was based on the recommendations contained within the World Health Organization (WHO) R&D Blueprint Novel Coronavirus COVID-19 Therapeutic Trial Synopsis issued in February 2020.

On 20 July 2020, the Company announced positive top-line results from the trial with further analyses announced in September 2020. The primary endpoint was the change in condition assessed using the WHO Ordinal Scale for Clinical Improvement (OSCI) during the dosing period.

In November these results were published in the peer-reviewed Lancet Respiratory Medicine journal. The full title of the publication is: *"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"*.

Key findings included:

- The odds of improvement across the entire OSCI scale were more than two-fold greater in the SNG001 group than the placebo group at the end of the treatment period in both the ITT (Intention-To-Treat) population (OR 2.32; p=0.033) and the PP (Per Protocol) population (OR 2.80; p=0.017).
- There was a trend towards reduced odds of progression to severe disease (requiring non-invasive ventilation, high-flow oxygen, intubation and mechanical ventilation) or

death in the ITT population (72% reduction; p=0.064) that became significant in the PP population (82% reduction; p=0.041).
- Patients who received SNG001 were more than twice as likely to recover (defined as "no limitation of activities" or "no clinical or virological evidence of infection") over the course of the treatment period compared to those receiving placebo in both the ITT population (HR 2.19; p=0.043) and the PP population (HR 2.29; p=0.033).
- Over the treatment period, patient-reported Breathlessness Cough and Sputum Scale (BCSS) and in particular breathlessness scores were markedly reduced in patients who received SNG001 compared to those receiving placebo (p=0.026 for BCSS and p=0.007 for breathlessness).
- Three subjects (6%) died after being randomised to placebo. There were no deaths among subjects treated with SNG001.

Other findings included:

- The median duration of COVID-19 symptoms at the point dosing commenced was 10 days. This goes against conventional wisdom with IFN-beta usage, where efficacy is expected based on early use. If treatment is administered to hospitalised patients after 10 days of illness, then this is late in terms of time (because the patient has been ill for 10 days) and late in terms of illness severity.
- Odds ratios for improvement, recovery and hospital discharge were in favour of SNG001 at day 28 suggesting that the treatment effect extends beyond the end of the dosing period. A treatment that accelerates full recovery may be especially relevant to patients with COVID-19 who experience wide-ranging long-term symptoms for at least a month and sometimes longer (known as Long COVID or Long-haul COVID).
- SNG001 was well tolerated.

SG016: Home Cohort

In April 2020, Synairgen received approvals to extend the SG016 trial into the home environment, with the objective of initiating dosing earlier in the infection cycle of COVID-19 to prevent severe lower respiratory tract symptoms. The trial recruited patients who were either aged over 65, or over 50 with a high-risk comorbidity. Patients must have had symptoms for less than eight days. The trial was fully recruited in January 2021.

The Home Cohort trial involved SNG001 (or placebo) being delivered to eligible participants by couriers observing appropriate social distancing measures. In order to minimise risks to patients and healthcare workers in this setting, all visits were conducted remotely by video link. If positive for SARS-CoV-2, the drug (placebo or SNG001), aerosol delivery device, and other trial equipment were despatched to the patient. Each dose was taken under video supervision. Safety and efficacy endpoints were also assessed during the video calls.

The study confirmed the feasibility of rapid roll-out of antiviral treatment in the context of a pandemic, where there is a need to limit the movement of people to minimise risks to patients, the public and healthcare providers.

The top-line results from the Home Cohort and combined data for the whole SG016 trial were announced in April 2021 and the key findings were:

- 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.
- Encouraging pattern of recovery and reduction in breathlessness in SNG001-treated patients compared to placebo in those with marked or severe breathlessness at the start of treatment.
- 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 only those patients on placebo 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. This is a strong indicator of those patients who should be selected for treatment with SNG001.

- 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 further improves 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; p=0.004). This further underlines the potential benefit of SNG001 for patients identified as breathless.

The data from the Home Cohort and the combined data analysis showing the potential importance of breathlessness as a stratification tool to identify patients most likely to benefit from SNG001 is invaluable. We now know better who not to treat and who to treat. Fortunately, when we designed the Phase III clinical trial, we selected patients most likely to be breathless and these data make us feel more confident of a positive outcome.

COVID-19 Phase III trial – SG018

Synairgen's global Phase III "SPRINTER" clinical trial in hospitalized COVID-19 patients, SG018, is a randomised, placebo-controlled study being conducted in 17 countries enrolling a total of 610 COVID-19 patients who require supplemental oxygen (ie they are by definition more likely to have marked or severe breathlessness). After reporting the results for the primary and secondary endpoints of the study, enrolled patients will continue to be assessed for Long COVID symptoms.

In October 2020 Synairgen appointed Parexel Biotech, a division of the leading global clinical research organisation, Parexel, to help conduct the Phase III trial. 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).

There are two primary endpoints: 'time to recovery to "no limitation of activities" up to Day 28'; and 'time to hospital discharge'. In addition, there are secondary endpoints relating to changes in OSCI score and symptoms, especially breathlessness, and Long COVID. There will also be a safety assessment.

First patient dosing commenced in the UK in January 2021, where the regulators were familiar with SNG001. The trial is now approved by regulators in 11 additional countries, with further approvals expected in five more countries in the coming weeks. Initial trial results are expected in H2 2021.

US NIH ACTIV-2 trial

In January 2021 Synairgen announced signature of a clinical trial agreement to include SNG001 in the ACTIV-2/A5401 Phase II/III trial in patients with COVID-19 not yet requiring hospitalisation. This is a government-funded trial sponsored by the US National Institute of Allergy and Infectious Diseases (NIAID), part of the US National Institutes of Health (NIH). NIH's ACTIV (**A**ccelerating **C**OVID-19 **T**herapeutic **I**nventions and **V**accines) is a public-private partnership to develop a coordinated research strategy to speed up the development of the most promising treatments and vaccine candidates for COVID-19. ACTIV-2 is a master protocol designed for evaluating multiple investigational agents compared to placebo in adults with mild-to-moderate COVID-19, not requiring hospitalisation.

The Phase II/III study is an adaptive, randomized, blinded, placebo-controlled trial which commenced patient dosing in February 2021. The Phase II evaluation of inhaled interferon beta will see the recruitment of up to a maximum of 220 participants across US sites in home-based settings. A positive result enables progression into the Phase III stage of the study.

As in the case with the Home Cohort of Synairgen's Phase II study, the inclusion in another home-based trial reflects the ease of use that inhaled treatments offer, making it possible for patients to self-administer treatment at home with professional supervision, reducing the risk of virus transmission during hospital visits and reducing pressure on healthcare systems. At-home treatments also have the potential to be taken earlier in the course of the illness, preventing the

progression of the virus in the lower respiratory tract and the concomitant risk of hospitalisation, which could be of very significant benefit if hospitals are overstretched.

Manufacturing and Delivery of SNG001

In preparation for gaining approval for inhaled interferon beta, the Company announced deals in October with Akron Biotechnology and Catalent Biologics.

Akron Biotechnology is manufacturing inhaled interferon beta drug substance to meet clinical and commercial demand.

Catalent Biologics is a leading global provider of advanced development and manufacturing solutions for drugs and biologics, and is supporting the inhaled interferon beta fill/finish at its Brussels, Belgium facility, where it is conducting manufacturing scale-up of the drug candidate into pre-filled syringes. The Company is also evaluating blow fill seal technology as an alternative to glass syringes.

Synairgen is collaborating with Aerogen, a leader in high-performance aerosol drug delivery in the acute care setting. Aerogen is providing the Aerogen Solo/Ultra aerosol delivery system, which is already widely used in hospitals in the EU and US, for delivery of SNG001 directly into the lungs of patients.

Managed Access Program

In September 2020 Synairgen put in place a Managed Access Program facility with Clinigen to enable physicians in the UK and EU to access SNG001 for hospitalised patients.

Chronic Obstructive Pulmonary Disease (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. Worldwide, COPD affects approximately 384 million people[3] and is the third leading cause of death according to the World Health Organisation.[4] COPD exacerbations are the second most common cause of unplanned hospitalisation in England.[5]

COPD trial – SG015

In 2018, Synairgen commenced a two-part COPD trial (SG015) to assess the safety and lung antiviral biomarker and efficacy 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. We also observed a strong antiviral biomarker signal, which was comparable to the response previously observed in asthma. This paved the way to proceed into the second part of the trial, which was designed to dose 120 patients with confirmed, naturally-occurring, respiratory virus infections and in addition to look at lung function. Recruitment into the trial commenced in earnest in January 2019 and was progressing well until the emergence of COVID-19.

<u>Impact of COVID-19 on SG015 programme</u>

COVID-19 made it difficult to dose COPD patients in trial units without potentially exposing vulnerable patients and research staff to SARS-CoV-2. Hence in March 2020 the trial was paused (now stopped), with 109 out of the targeted 120 patients recruited. MHRA approval was then received to run an interim analysis on the grounds that the data from COPD patients with confirmed viral infection could generate useful safety, biomarker and efficacy data to support ongoing trials of SNG001 in COVID-19 patients.

<u>Results of interim analysis of SG015 trial in COPD patients</u>

On 8 September 2020, Synairgen announced a positive interim analysis of SNG001 in COPD patients, supporting progression of SNG001 in COVID-19. Key findings included:

- 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%).
- 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.
- 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, in exacerbating patients 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.

The trial data is supportive of not only the near term COVID-19 development activity, but also the longer term aim to use SNG001 to treat patients admitted to hospital with severe viral lung infections. COPD patients represent one of the largest groups of patients in this setting.

LOXL2

Pharmaxis, the Company's Australian-based partner for the antifibrotic LOXL2 inhibitor programme, updated the market post period-end on 30 April 2021[6] to state it is currently pursuing a number of different options to enable PXS-5382 to enter the clinic in Phase II trials in a chronic kidney disease. Pharmaxis also states that it continues to have discussions with potential partners and independent investigators in relation to study protocol design and funding options including grants. In the event of a qualifying licensing agreement or other commercialisation of the product, Synairgen is entitled to receive circa 17% of Pharmaxis' licence receipts/royalties, net of allowable expenses and we have no ongoing financial obligations to the programme.

Intellectual Property

Patent filings

Adding to the Company's IP portfolio, patent applications were filed following (i) the results from the study for the use of inhaled IFN-beta in COVID-19 patients and (ii) the interim analysis of the data from the trial that used inhaled IFN-beta to treat virus-induced exacerbations in COPD patients undergoing treatment with systemic corticosteroids. Further updates regarding pending patents will be provided in due course.

Addition to the management team

Richard Hennings joined Synairgen as Chief Commercial Officer in March 2021. Between 1999 and 2017 he held Commercial leadership roles at Gilead Sciences, Novartis and AstraZeneca. During his eight-year Gilead tenure, Richard led the expansion of respiratory and anti-viral portfolios in the EU and US markets, launching inhaled Cayston® for Cystic Fibrosis and HIV treatment Stribild®. During his subsequent AstraZeneca assignment, Richard led Antibiotic Zavicefta® EU/ LATAM launch readiness and divestment of the antibiotics business unit to Pfizer. Between 2017 and 2020 Richard was VP & Commercial Head of Verona Pharma.

FINANCIAL REVIEW

Statement of Comprehensive Income

The loss from operations for the year ended 31 December 2020 was £17.74 million (2019: £4.82 million) with research and development expenditure amounting to £15.50 million (2019: £3.46 million) and other administrative expenses £2.25 million (2019: £1.36 million).

During 2019 our research and development activities were solely focussed on the Phase II trial in COPD patients. During 2020 we continued to work on the COPD trial until it was halted on account of COVID-19. However, the majority of the £12.0 million year-on-year increase in research and development expenditure is attributable to our COVID-19 clinical trials and manufacturing scale-up activities.

Clinical trial expenditure was initially focussed on the SG016 hospital and home Phase II trial activities. This was followed by preparatory activities for the international SG018 Phase III trial in hospitalised patients and finally for participation in the ACTIV-2 study, where we have provided study product for the trial. The clinical trial preparatory and execution activities necessitated a very significant scale up of our clinical trial infrastructure and this resulted in a much greater use of outsourced experts.

Significant investment was made into manufacturing scale-up. Two batches of active and placebo pre-filled syringes were manufactured to meet clinical trial requirements. Process Performance Qualification (PPQ) preparation activities (in advance of commercialisation) were commenced at both a new drug substance manufacturer and at a new drug product manufacturer, with the latter involving both pre-filled syringes and blow-fill-seal ampoules. The Company's advisory base in both regulatory and CMC activities was also significantly expanded.

Other administrative expenses increased from £1.36 million to £2.25 million. The increase was attributable to higher personnel costs, as we scaled up to handle greater volumes of transactions, higher investor relations activity costs, and the costs of hedging an element of our future foreign exchange exposures on manufacturing costs denominated in US dollars and Euros.

Despite the significant increases in cash on hand after the two fundraisings during the year, finance income reduced on account of the reduction in interest rates during the period. Finance expense relates to interest expense on lease liabilities and the increase reflects the first full year of interest expense, due to the lease signed in mid-2019 being the first to be accounted under IFRS 16.

The research and development tax credit increased from £0.91 million to £3.82 million on account of the increased qualifying expenditure. The credit equates to 25% of our 2020 research and development expenditure (2019: 26%).

The loss after tax for 2020 was £13.92 million (2019: £3.89 million) and the basic loss per share was 9.46p (2019: basic loss per share of 3.55p).

Fundraisings

During 2020, two fundraisings were conducted to fund our ongoing COVID-19 clinical and manufacturing activities.

The first of these, conducted in March 2020, raised £14 million (before expenses) by the issue of 40 million ordinary shares at a price of 35p per share to fund: COVID-19 clinical trial activity; manufacturing of SNG001 drug product and other supply chain considerations; and strengthen the balance sheet.

The second fundraising took place in October 2020 and raised £87.07 million (before expenses) by the issue of 49.75 million ordinary shares at a price of 175p per share. 45.71 million shares were issued pursuant to an institutional placing and 4.04 million shares on account of a fully subscribed Open Offer. The proceeds were raised to fund: the Phase III trial in COVID-19 patients; SNG001 manufacturing and device scale-up activities; the generation of further data to support SNG001 clinical development, manufacturing processes and regulatory activities; strengthening the balance sheet; and the net settlement of option costs.

Statement of Changes in Equity

In addition to the net proceeds from the share issues, the recognition of share-based payments and the loss after taxation, a charge of £1.29 million was taken to reserves in respect of net settled options for the year ended 31 December 2020 (2019: £nil). At the time of the second fundraising, two of the executive directors exercised options over some 1,176,334 ordinary shares. The Company net settled by paying the income tax and NICs on the option holders' behalf and issuing 534,172 new ordinary shares. The cost of the income tax and NICs paid by the Company amounted to £1.29 million and, in accordance with IFRS 2, was charged directly to reserves as it equated to the fair value of the number of shares withheld by the Company.

Statement of Financial Position and Cash Flows

At 31 December 2020, net assets amounted to £85.14 million (2019: £2.25 million), including cash balances of £74.98 million (2019: £2.45 million).

The principal elements of the £72.53 million increase during the year ended 31 December 2020 (2019: £2.88 million decrease) in cash balances were:

- Cash used in operations: £24.73 million (2019: £3.73 million);
- Research and development tax credits received: £0.91 million (2019: £0.84 million);
- Share issue proceeds (net of costs): £97.89 million (2019: £nil);
- Net settlement of options £1.29 million (2019: £nil); and
- Lease payments: £0.21 million (2019: £nil).

The other significant changes in the statement of financial position were:

- Current tax receivable increased from £0.87 million to £3.77 million on account of the higher research and development tax credit;
- Manufacturing and clinical trial prepayments were the principal reasons for the increase in Trade and other receivables from £0.14 million to £9.37 million; and
- Trade and other payables increased from £1.49 million to £3.28 million, reflecting the increased level of activity.

OUTLOOK

Trial readouts are due over the coming months which we anticipate will add to the growing body of evidence supporting the use of inhaled interferon beta as a potential treatment for patients with COVID-19. These include data from our international SG018 Phase III trial and the US ACTIV-2 Phase II trial in COVID-19 outpatients, with initial data for SG018 expected in H2 2021. Beyond these trials Synairgen is in regular dialogue with government bodies and companies regarding the progress of inhaled interferon beta and its application as an effective treatment in both hospitalized and home-based patients.

In the second half of 2021 Synairgen will continue its commercialisation and manufacturing plans in order to scale up manufacturing and supply capacity, with the aim of making the drug readily available internationally and to meet potential commercial demand in the event of a regulatory approval.

References

1. *Lancet Infect Dis*. 2017 Nov;17(11):1133 1161. doi : 10.1016/S1473 3099(17)30396 1. Epub 2017 Aug 23
2. *Clin Microbiol Infect.* 2018 Nov; 24(11):1158-1163. Doi: 10.1016/j.cmi.2018.02.004. Epub 2018 Feb 12
3. Adeloye D *et al.* Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. *J Glob Health.* 2015 Dec; 5(2): 020415.
4. *https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death*
5. Department of Health. An Outcomes Strategy for Chronic Obstructive Pulmonary Disease (COPD) and Asthma in England. Published July 2011
6. https://www.pharmaxis.com.au/investor-centre/news/view/shareholder-update-march-2021

Consolidated Statement of Comprehensive Income
for the year ended 31 December 2020

	Notes	**Year ended 31 December 2020 £000**	Year ended 31 December 2019 £000
Research and development expenditure		**(15,495)**	(3,460)
Other administrative expenses		**(2,246)**	(1,357)
Total administrative expenses and Loss from operations		**(17,741)**	(4,817)
Finance income		**19**	30
Finance expense		**(10)**	(6)
Loss before tax		**(17,732)**	(4,793)
Tax	2	**3,816**	908
Loss and total comprehensive loss for the period attributable to equity holders of the parent		**(13,916)**	(3,885)
Loss per ordinary share	3		
Basic and diluted loss per share (pence)		**(9.46)p**	(3.55)p

Consolidated Statement of Changes in Equity
for the year ended 31 December 2020

	Share capital £000	Share premium £000	Merger reserve £000	Retained deficit £000	Total £000
At 1 January 2019	1,094	28,262	483	(23,812)	6,027
Recognition of share-based payments	-	-	-	111	111
Loss and total comprehensive loss for the year	-	-	-	(3,885)	(3,885)
At 31 December 2019	1,094	28,262	483	(27,586)	2,253
Issue of ordinary shares	905	100,170	-	-	101,075
Transaction costs in respect of share issues	-	(3,187)	-	-	(3,187)
Recognition of share-based payments	-	-	-	207	207
Net settlement of share options	-	-	-	(1,291)	(1,291)
Loss and total comprehensive loss for the year	-	-	-	(13,916)	(13,916)
At 31 December 2020	**1,999**	**125,245**	**483**	**(42,586)**	**85,141**

Consolidated Statement of Financial Position
as at 31 December 2020

	31 December 2020 **£000**	31 December 2019 **£000**
Assets		
Non-current assets		
Intangible assets	**44**	16
Property, plant and equipment	**250**	301
Right-of-use assets	**94**	255
	388	572
Current assets		
Inventories	**41**	41
Current tax receivable	**3,771**	865
Trade and other receivables	**9,372**	139
Cash and cash equivalents	**74,976**	2,454
	88,160	3,499
Total assets	**88,548**	4,071
Liabilities		
Non-current liabilities		
Lease liabilities	**-**	(127)
Current liabilities		
Trade and other payables	**(3,279)**	(1,490)
Lease liabilities	**(128)**	(201)
	(3,407)	(1,691)
Total liabilities	**(3,407)**	(1,818)
Total net assets	**85,141**	2,253
Equity		
Capital and reserves attributable to equity holders of the parent		
Share capital	**1,999**	1,094
Share premium	**125,245**	28,262
Merger reserve	**483**	483
Retained deficit	**(42,586)**	(27,586)
Total equity	**85,141**	2,253

Consolidated Statement of Cash Flows
for the year ended 31 December 2020

	Year ended 31 December 2020 £000	Year ended 31 December 2019 £000
Cash flows from operating activities		
Loss before tax	**(17,732)**	(4,793)
Adjustments for:		
Finance income	**(19)**	(30)
Finance expense	**10**	6
Depreciation of property, plant and equipment	**90**	83
Depreciation of right-of-use assets	**161**	67
Amortisation of intangible fixed assets	**9**	13
Share-based payment charge	**207**	111
Cash flows from operations before changes in working capital	**(17,274)**	(4,543)
Decrease in inventories	**-**	15
(Increase)/Decrease in trade and other receivables	**(9,244)**	81
Increase in trade and other payables	**1,789**	713
Cash used in operations	**(24,729)**	(3,734)
Tax credit received	**910**	838
Net cash used in operating activities	**(23,819)**	(2,896)
Cash flows from investing activities		
Interest received	**31**	26
Purchase of intangible assets	**(37)**	-
Purchase of property, plant and equipment	**(39)**	(10)
Decrease in other financial assets	**-**	50
Net cash (used in)/generated from investing activities	**(45)**	66
Cash flows from financing activities		
Proceeds from issue of ordinary shares	**101,075**	-
Transaction costs in respect of share issues	**(3,187)**	-
Net settlement of share options	**(1,291)**	-
Principal paid on lease liabilities	**(196)**	-
Interest paid on lease liabilities	**(15)**	-
Net cash generated from financing activities	**96,386**	-
Increase/(Decrease) in cash and cash equivalents	**72,522**	(2,830)
Cash and cash equivalents at beginning of the year	**2,454**	5,284
Cash and cash equivalents at end of the year	**74,976**	2,454

Notes

1. Basis of preparation

The financial information of the Group set out above does not constitute "statutory accounts" for the purposes of Section 435 of the Companies Act 2006. The financial information for the year ended 31 December 2020 has been extracted from the Group's audited financial statements which were approved by the Board of directors on 11 May 2021 and will be delivered to the Registrar of Companies for England and Wales in due course. The financial information for the year ended 31 December 2019 has been extracted from the Group's audited financial statements for that period which have been delivered to the Registrar of Companies for England and Wales. The reports of the auditors on both these financial statements were unqualified, did not include any references to any matters to which the auditors drew attention by way of emphasis without qualifying their report and did not contain a statement under Section 498(2) or Section 498(3) of the Companies Act 2006. Whilst the financial information included in this preliminary announcement has been prepared in accordance with the recognition and measurement criteria of International Financial Reporting Standards ('IFRSs'), this announcement does not itself contain sufficient information to comply with those IFRSs. This financial information has been prepared in accordance with the accounting policies set out in the December 2020 report and financial statements.

2. Tax

The tax credit of £3,816,000 (2019: £908,000) relates to research and development tax credits in respect of the year ended 31 December 2020 (£3,771,000) and an adjustment in respect of prior periods (£45,000).

3. Loss per ordinary share

Basic loss per share is calculated by dividing the loss attributable to ordinary equity holders of the parent company by the weighted average number of ordinary shares in issue during the year.

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 loss per share. This is because the exercise of share options would have the effect of reducing the loss per ordinary share and is therefore antidilutive under the terms of IAS 33.