Press release

Synairgen plc

('Synairgen' or the 'Company')

Preliminary results for the year ended 31 December 2019

Southampton, UK – 26 May 2020: Synairgen plc (LSE: SNG), the respiratory drug discovery and development company, today announces its preliminary statement of audited results for the year ended 31 December 2019.

Highlights (including post period-end)

Operational

- Synairgen has paused the SG015 trial of SNG001 (inhaled interferon-beta 1a) in COPD patients due to the prevalence of COVID-19 in the community, with 109 out of 120 patients recruited. The Company has received approval from the Medicines and Healthcare products Regulatory Agency (MHRA) to conduct an unplanned interim analysis on the grounds that data from the 109 COPD patients with confirmed viral infection generates useful safety, biomarker and potentially efficacy data to support ongoing trials of SNG001 in COVID-19 patients. The results of this interim analysis are expected this Summer.

- In March 2020, Synairgen announced it had received expedited approvals from the MHRA and Health Research Authority (HRA) to conduct a trial of SNG001 in COVID-19 patients (SG016).

- The SG016 study has progressed well, with 98 patients out of the target of 100 now dosed in the hospital setting. Results from this part of the study are expected in July 2020.

- Synairgen is extending the SG016 study to patients in the home environment with confirmed COVID-19, to initiate dosing with SNG001 (or placebo) earlier in the course of the illness and before severe lower respiratory tract symptoms develop. Dosing in the home environment is expected to commence in May 2020, the details of which are included in a separate RNS announced today.

Financial

- In March 2020, Synairgen raised £14.0 million in a heavily oversubscribed equity issue to fund its COVID-19 related activities and strengthen its balance sheet.

- Research and development expenditure for the year amounted to £3.46 million (2018: £3.23 million) and the majority of this expenditure was focussed on running the IFN-beta Phase II clinical trial in COPD.

- The loss from operations for the year ended 31 December 2019 was £4.82 million (2018: loss £4.13 million).

- Cash and bank deposits of £2.45 million at 31 December 2019 (31 December 2018: £5.33 million).

Board changes

- Paul Clegg retired from the Board as a non-executive director after the Company's AGM in June 2019, with Iain Buchanan becoming the new Chairman of the Remuneration and Nomination Committee.

Richard Marsden, CEO of Synairgen, commented: *"Over the coming months we will have three major clinical trial read-outs for SNG001, our wholly-owned, inhaled IFN-beta asset: COPD patients with regular seasonal viruses; COVID-19 hospital-treated patients; and the early treatment of COVID-19 patients in the home setting. The Company is active on many fronts from designing and managing novel trials to developing the regulatory strategy and supply chain for potential demand in the future."*

This announcement contains inside information as contained in Article 7 of the Market Abuse Regulation 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 and COPD, 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

COVID-19

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.*

*Source: WHO website 20 May 2020 (https://www.who.int/health-topics/coronavirus#tab=tab_1)

Chairman's and Chief Executive Officer's Review

OPERATING REVIEW

Summary

In 2019 we recruited steadily into our SG015 Phase II trial of SNG001 in patients with Chronic Obstructive Pulmonary Disease (COPD). Due to the emergence of the SARS-CoV-2 virus, which causes COVID-19, recruitment into this trial was paused from March 2020. Post period-end, addressing whether SNG001 has potential utility as a therapeutic for COVID-19 has been a key priority for the business. Synairgen has commenced a placebo-controlled trial of SNG001 in hospitalised patients with COVID-19 and is aiming to commence dosing in home-based 'at risk' patients imminently. We are also investing in the supply chain to minimise the impact of long lead times in the event that there is demand for SNG001 to treat COVID-19 patients. Separately, Synairgen's partner in the LOXL2 programme, Pharmaxis, has continued its licensing discussions during the period, which in time could potentially yield financial benefit to Synairgen.

Progress with SNG001 programme

SNG001 is a formulation of IFN-beta 1a (IFN-beta) for inhalation via a nebuliser. Compared to injected formulations of IFN-beta, which have been used extensively as a treatment for patients with multiple sclerosis, SNG001 is pH neutral and is free of excipients which may be pharmacologically active in the airways such as mannitol and human serum albumin.

The relevance of interferons in virus defence
The Type I interferons, such as interferon alpha (IFN-alpha) and interferon beta (IFN-beta), are key mediators involved in responses to viral infection. Although these antiviral proteins bind to the same receptor, they differ in their antiviral and immunomodulatory effects. Cells produce interferons as an innate immune response to combat a viral infection. It is this innate immune response that provides a first line of defence against viruses until the adaptive immune system generates antibodies, which clear the virus infection and can provide long term immunity. IFN-alpha is produced in large quantities by specialised white blood cells called plasmacytoid dendritic cells and is approved for use in some systemic infections such as hepatitis. IFN-beta is made by many cell types, including epithelial cells and fibroblasts where it is produced as an immediate local response to viral infection and triggers an antiviral programme preparing the tissue to fight off the infection.

Various groups have shown that upon infection with a respiratory virus IFN-beta production is deficient in lung epithelial cells of patient groups such as those with asthma, COPD, cystic fibrosis, and also the elderly, who can become severely ill due to common respiratory viruses (e.g. influenza, RSV, rhinovirus) each winter.[1] The reasons for this are being explored, however treatment with exogenous IFN-beta *in vitro* has been shown to be protective irrespective of background co-morbidity risk factors and whether cells are treated with IFN-beta pre- or post-infection.

SNG001 programme in asthma and COPD
SNG001 has been progressed through three clinical trials in asthma. A Phase I safety and proof-of- delivery trial showed a dose-dependent upregulation of antiviral responses measured in lung (sputum) samples. In two Phase II trials, SNG001 accelerated a recovery in lung function from the losses caused by a range of common respiratory viruses. With the development of an immediate point-of-care testing system to validate viral infection in patients (bioMérieux BioFire FilmArray technology) in 2018, the SNG001 programme switched from asthma to COPD, a condition where the impact of viral infections can be very severe.

COPD patients are approximately five times more likely to become severely ill due to respiratory viruses than asthmatic patients,[2] and have always been recognised as a larger potential market for a broad spectrum antiviral product which could prevent exacerbations or accelerate recovery from exacerbation. However, half of infectious COPD exacerbations are caused by bacteria, with no virus present. This meant use of SNG001 in the context of COPD would be very challenging without a point-of-care test for viral infections. The bioMérieux BioFire FilmArray and other technologies which have subsequently become available, ensure the selection and treatment of solely those patients where the presence of a virus is confirmed.

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. 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. 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 virus. Hence in March 2020 the trial was paused, with 109 out of the targeted 120 patients recruited. We have received approval from the Medicines and Healthcare products Regulatory Agency (MHRA) to run an unplanned interim analysis on the grounds that data from 109 COPD patients with confirmed viral infection generates a useful safety, biomarker and potentially efficacy data to support ongoing trials of SNG001 in COVID-19 patients. We expect to have data from this interim analysis in the Summer 2020. In due course we will consider options as to how to progress SNG001 in COPD.

Rationale for using SNG001 in COVID-19 patients

The high-risk groups for severe COVID-19 illness are the elderly and those with chronic co-morbidities. These groups overlap with the observed innate immune deficiency in the elderly and in patients with COPD, many of whom will have other co-morbidities. Further to this compromised immunity, some viruses, including coronaviruses, have evolved to suppress IFN-beta production to enable them to evade the “first response” immune system. This therefore provides two reasons to warrant assessment of SNG001 in COVID-19 patients. In the laboratory, IFN-beta has been shown to protect cells from infection by SARS-CoV-2, the virus which causes COVID-19.[3]

Clinical trial (SG016) in COVID-19 patients

Patients initiated in hospital

In late March 2020, Synairgen dosed the first COVID-19 patients in a randomised placebo-controlled trial. This trial has received ‘National Priority’ status from the National Institute of Health Research, thereby enabling 9 top UK respiratory Translational Research Centre sites to participate. The trial has now recruited 98 COVID-19 patients who are hospitalised but breathing unaided; the trial does not include severe patients requiring ventilatory support. There has been a notable slowdown in recruitment during the last three weeks as the incidence of COVID-19 has reduced, but we would hope to reach our recruitment target of 100 shortly. A planned review of the data will inform onward clinical trial activity which will be agreed with regulatory agencies. Conducting high quality clinical trials in the current environment is very challenging. It is the efforts and support of the participating centres and key contributing partners, suppliers and the regulatory bodies which have enabled this trial to happen quickly. We anticipate producing initial trial data in July 2020.

Patients initiated at home

The SG016 protocol also allows the dosing of patients in the home environment; the objective being to initiate treatment earlier than the hospital study to prevent development of significant lower respiratory tract illness and subsequent hospitalisation. In order to minimise risks to patients and healthcare workers in this setting, all visits will be conducted by video link. Dosing is set to commence in May 2020.

Patients will interact with the trial team using Skype/Teams/Zoom or their preferred choice of video conferencing as soon as COVID-19 symptoms develop. Patients will be informed about the trial and provide online consent. Patients will self-swab under video supervision. Within a few hours of the swab having been taken, the virus test results will be known. If positive for SARS-CoV-2, the drug (placebo or SNG001), aerosol delivery device, and other trial equipment will be despatched to the patient. Each dose will be taken under video supervision. Endpoints will also be assessed during the video calls.

This is the first trial of its type to be conducted “remotely” in this way and if successful, may point towards a potential domiciliary care protocol for this and future viral outbreaks.

Supply chain in the event of success

In the event that the current trials prove successful, Synairgen has made good progress with suppliers to scale up production of SNG001 rapidly with the aim of being able to supply meaningful quantities by the end of this year.

LOXL2 inhibitor programme

Pharmaxis, the Company's Australian-based partner for the antifibrotic LOXL2 inhibitor programme, has updated the market (on 30 April 2020) stating that it is currently pursuing a number of different partnering options with international pharma companies to enable this drug to enter the clinic in phase 2 trials and will provide more information when the process concludes. Synairgen is entitled to receive circa 17% of Pharmaxis' licence receipts/royalties, net of allowable expenses.

Board changes

In April 2019, Paul Clegg announced his intention to retire from the Board as a non-executive director after the 2019 AGM in June. The Board thanks Paul for his significant contribution and advice to Synairgen over the last 10 years and for his Chairmanship of the Remuneration and Nomination Committee. Iain Buchanan became the new Chairman of the Remuneration and Nomination Committee.

FINANCIAL REVIEW

Statement of Comprehensive Income

The loss from operations for the year ended 31 December 2019 was £4.82 million (2018: loss £4.13 million). There were no revenues for the year (2018: £0.11 million). The 2018 revenue comprised fee for service work in relation to the LOXL2 programme, through our partnership with Pharmaxis Ltd.

Research and development expenditure for the year amounted to £3.46 million (2018: £3.23 million) and the majority of this expenditure was on running the IFN-beta Phase II clinical trial in COPD.

Other administrative costs for the year were £1.36 million (2018: £1.01 million), with the increase attributable to higher staff costs during the period. The tax credit for 2019 amounted to £0.91 million (2018: £0.80 million) and included £0.04 million in respect of prior periods. The loss after tax for 2019 was £3.89 million (2018: loss of £3.30 million) and the basic loss per share amounted to 3.55p (2018: basic loss per share of 3.47p).

Statement of Financial Position and cash flows

At 31 December 2019, net assets amounted to £2.25 million (2018: £6.03 million), including cash and bank deposits of £2.45 million (2018: £5.33 million).

The principal elements of the £2.88 million decrease over the year ended 31 December 2019 (2018: £1.51 million decrease) in cash and bank deposits were:

- Cash used in operations: £3.73 million (2018: £3.89 million);
- Research and development tax credits received: £0.84 million (2018: £0.07 million);
- Capital expenditure on property, plant and equipment: £0.01 million (2018: £0.39 million); and
- Share issue proceeds (net of costs): £nil (2018: £2.67 million).

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

- Net book value of property, plant and equipment reduced from £0.37 million to £0.30 million as we depreciated the bioMérieux multiplex PCR virus detection machines purchased in 2018 for use in the SG015 clinical trial;
- Following the adoption of IFRS 16 'Leases', we recognised right-of-use assets in 2019 and at 31 December 2019 the balance, net of depreciation charged, amounted to £0.26 million (2018: £nil). We also recognised the corresponding lease liabilities and at 31 December 2019 the non-current liability element amounted to £0.13 million (2018: £nil) and the current liability element £0.20 million (2018: £nil); and
- Trade and other payables increased from £0.78 million to £1.49 million, on account of higher accruals for clinical trial related activities and staff performance bonuses.

Post year-end fundraising

£14 million (before expenses) was raised in March 2020 by the issue of 40 million ordinary shares at a price of 35p per share to fund the following activities:

- COVID-19 clinical trial activity (£7 million);
- Manufacture of SNG001 drug product and other supply chain considerations (£4 million); and
- Strengthened balance sheet for potential partnering discussions, working capital and fees (£3 million).

OUTLOOK

During the calendar year 2019 we made good progress in the trial of our wholly-owned asset SNG001 in COPD. The emergence of SARS-CoV-2 has caused us to pause the COPD trial and to divert our expertise and investment to addressing the more pressing COVID-19 pandemic. Knowing that a broad spectrum antiviral agent delivered directly to the lungs may prevent the development of lower respiratory tract illness or accelerate the recovery of patients already hospitalised, we have raised additional funding of £14 million, which has enabled us to successfully initiate a trial of approximately 220 patients with COVID-19, some 100 of whom are in the hospital environment with severe respiratory symptoms, with a further 120 patients who will be dosed in the home environment upon early signs of COVID-19. Our staff and our key suppliers in both the UK and overseas have been able to continue working through lockdown. Data from the hospital trial will read out during the summer, and, if positive, the Company will work closely with regulators to determine an expeditious route to securing approval for SNG001, a treatment we believe could play an important role in addressing the current COVID-19 crisis and similar viruses in the future. In parallel, the Company is now working with manufacturers to scale up for potential demand for SNG001. The outlook for the business is positive and we look forward to updating the market on further progress in due course.

References

1. (i) Wark PA, *et al*. Asthmatic bronchial epithelial cells have a deficient innate immune response to infection with rhinovirus. *J Exp Med*. 2005;201(6):937-947 (ii) García-Valero J, *et al*. Deficient pulmonary IFN-β expression in COPD patients. PLoS One. 2019;14(6):e0217803 (iii) Chattoraj SS, *et al*. Pseudomonas aeruginosa suppresses interferon response to rhinovirus infection in cystic fibrosis but not in normal bronchial epithelial cells. *Infect Immun*. 2011;79(10):4131-4145. (iv) Prakash S, *et al*. Impaired secretion of interferons by dendritic cells from aged subjects to influenza : role of histone modifications. *Age (Dordr)*. 2013;35(5):1785-1797.
2. The risk that that a COPD patient will exacerbate due to a cold infection is approximately 50% (Johnston NW. *et al*. Colds as predictors at the onset and severity of COPD exacerbations *International Journal of COPD* 2017:12: 839-848) compared to asthma where it is less than 10% ((i) Aviragen Therapeutics presentation Directing Next Generation Direct-Acting Antivirals May 2017 (ii) Synairgen analysis of INEXAS trial results, dated 27 September 2017)
3. Mantlo E, *et al*. Antiviral activities of type I interferons to SARS-CoV-2 infection. *Antiviral Res.* 2020 Apr 29;179:104811

Consolidated Statement of Comprehensive Income
for the year ended 31 December 2019

	Notes	**Year ended 31 December 2019 £000**	Year ended 31 December 2018 £000
Revenue		**-**	105
Research and development expenditure		**(3,460)**	(3,232)
Other administrative expenses		**(1,357)**	(1,005)
Total administrative expenses		**(4,817)**	(4,237)
Loss from operations		**(4,817)**	(4,132)
Finance income		**30**	36
Finance expense		**(6)**	-
Loss before tax		**(4,793)**	(4,096)
Tax	2	**908**	795
Loss and total comprehensive loss for the period attributable to equity holders of the parent		**(3,885)**	(3,301)
Loss per ordinary share	3		
Basic and diluted loss per share (pence)		**(3.55)p**	(3.47)p

Consolidated Statement of Changes in Equity
for the year ended 31 December 2019

	Share capital £000	Share premium £000	Merger reserve £000	Retained deficit £000	Total £000
At 1 January 2018	914	25,771	483	(20,609)	6,559
Issue of ordinary shares	180	2,700	-	-	2,880
Transaction costs in respect of share issue	-	(209)	-	-	(209)
Recognition of share-based payments	-	-	-	98	98
Loss and total comprehensive loss for the year	-	-	-	(3,301)	(3,301)
At 31 December 2018	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**

Consolidated Statement of Financial Position
as at 31 December 2019

	31 December 2019 £000	31 December 2018 £000
Assets		
Non-current assets		
Intangible assets	**16**	29
Property, plant and equipment	**301**	374
Right-of-use assets	**255**	-
	572	403
Current assets		
Inventories	**41**	56
Current tax receivable	**865**	795
Trade and other receivables	**139**	216
Other financial assets – bank deposits	**-**	50
Cash and cash equivalents	**2,454**	5,284
	3,499	6,401
Total assets	**4,071**	6,804
Liabilities		
Non-current liabilities		
Lease liabilities	**(127)**	-
Current liabilities		
Trade and other payables	**(1,490)**	(777)
Lease liabilities	**(201)**	-
	(1,691)	(777)
Total liabilities	**(1,818)**	(777)
Total net assets	**2,253**	6,027
Equity		
Capital and reserves attributable to equity holders of the parent		
Share capital	**1,094**	1,094
Share premium	**28,262**	28,262
Merger reserve	**483**	483
Retained deficit	**(27,586)**	(23,812)
Total equity	**2,253**	6,027

Consolidated Statement of Cash Flows-
for the year ended 31 December 2019

	Year ended 31 December 2019 £000	Year ended 31 December 2018 £000
Cash flows from operating activities		
Loss before tax	**(4,793)**	(4,096)
Adjustments for:		
Finance income	**(30)**	(36)
Finance expense	**6**	-
Depreciation of property, plant and equipment	**83**	24
Depreciation of right-of-use assets	**67**	-
Amortisation of intangible fixed assets	**13**	16
Share-based payment charge	**111**	98
Cash flows from operations before changes in working capital	**(4,543)**	(3,994)
Decrease in inventories	**15**	-
Decrease in trade and other receivables	**81**	426
Increase/(Decrease) in trade and other payables	**713**	(326)
Cash used in operations	**(3,734)**	(3,894)
Tax credit received	**838**	71
Net cash used in operating activities	**(2,896)**	(3,823)
Cash flows from investing activities		
Interest received	**26**	27
Purchase of property, plant and equipment	**(10)**	(386)
Decrease/(Increase) in other financial assets	**50**	1,950
Net cash generated from investing activities	**66**	1,591
Cash flows from financing activities		
Proceeds from issuance of ordinary shares	**-**	2,880
Transaction costs in respect of share issue	**-**	(209)
Net cash generated from financing activities	**-**	2,671
(Decrease)/Increase in cash and cash equivalents	**(2,830)**	439
Cash and cash equivalents at beginning of the year	**5,284**	4,845
Cash and cash equivalents at end of the year	**2,454**	5,284

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 2019 has been extracted from the Group's audited financial statements which were approved by the Board of directors on 25 May 2020 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 2018 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') as adopted by the European Union, 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 2019 report and financial statements.

2. Tax

The tax credit of £908,000 (2018: £795,000) relates to research and development tax credits in respect of the year ended 31 December 2019 (£865,000) and an adjustment in respect of prior periods (£43,000).

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.