**Press release**

# Synairgen plc

**('Synairgen' or the 'Company')**

## Preliminary statement of results for the year ended 31 December 2016

**Southampton, UK** – 17 May 2017: Synairgen (LSE: SNG), the respiratory drug discovery and development company, today announces its preliminary statement of audited results for the year ended 31 December 2016.

### Operational highlights

- Positive *in vitro* results in March 2016 from collaboration with Pharmaxis to develop the LOXL2 inhibitor as a novel treatment for idiopathic pulmonary fibrosis (IPF)

- AstraZeneca stopped the Phase IIa trial of AZD9412, as colds were not causing as many severe exacerbations as expected in the trial population potentially compromising the trial's ability to assess any effect of the drug on this endpoint

### Financial highlights

- Loss from operations for the year ended 31 December 2016 was £3.44 million (2015: £2.61 million)

- Research and development expenditure for the year was £2.42 million (2015: £1.36 million)

- Cash, cash equivalents and deposit balances of £4.77 million at 31 December 2016 (2015: £7.71 million). The Group remains debt free

### Post period-end highlights

- Further positive data in March 2017 from two preclinical models of Synairgen's LOXL2 inhibitor programme against IPF

- AZD9412 INEXAS clinical trial update, announcing AstraZeneca's decision to return the rights of inhaled interferon beta to Synairgen

**Commenting on the Annual Results, Simon Shaw, Chairman of Synairgen said:** *"We are pleased with the progress made with the LOXL2 programme and look forward to advancing it into the clinic later this year in collaboration with our partner, Pharmaxis.*

*"As a result of the forthcoming return of the interferon beta programme to Synairgen, the Company will conduct a thorough analysis of all data arising from the study and will provide an update on the programme and our plans for future development. In particular, and based on recently published and*

*unpublished work, we will examine the potential for inhaled interferon beta in COPD."*

- Ends -

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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 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. Leveraging its scientific and clinical facilities at Southampton General Hospital, the Company uses *in vitro* and *ex vivo* models to progress opportunities into clinical development. The BioBank of human samples is used in these models to increase confidence in the likelihood of successful drug development. Core to Synairgen's business strategy is the realisation of value via licensing transactions. In August 2015 the Company entered into a collaboration with Pharmaxis to develop an oral LOXL2 inhibitor to reduce fibrosis in patients with idiopathic pulmonary fibrosis (IPF). Synairgen is quoted on AIM (LSE: SNG). For more information about Synairgen, please see www.synairgen.com

## Chairman's and Chief Executive Officer's Review

## OPERATING REVIEW

### Summary

During 2016 we made excellent progress in collaboration with Pharmaxis to develop a LOXL2 inhibitor to treat or prevent fibrosis and are on schedule to progress a compound into the clinic in H2 2017. AstraZeneca progressed the INEXAS trial of AZD9412 (inhaled interferon beta or IFN-beta) through the midway point, but stopped the trial early due to a lower than expected number of exacerbation events across the trial population.

Post period-end, in April 2017, AstraZeneca decided to return the interferon beta programme to Synairgen. We are very encouraged to observe that in the INEXAS trial inhaled IFN-beta once again 'switched on' antiviral defences in the lung and improved lung function, confirming our earlier clinical trial findings. Furthermore, inhaled IFN-beta was well tolerated. All data are being returned to Synairgen from AstraZeneca for further scrutiny. Once an in-depth analysis of these data has been concluded, we will determine the future development plan for IFN-beta in respiratory indications and under Synairgen control. Based on encouraging and recently published and unpublished work (from emerging research at the University of Southampton) the opportunity for further clinical development for COPD patients will be actively investigated.

### LOXL2 inhibitor collaboration

In 2015 we signed a collaboration agreement with Pharmaxis to co-develop their orally bioavailable LOXL2 inhibitors for the treatment and/or prevention of fibrosis. Fibrosis or scarring is part of the normal wound-healing process. However, when excessive fibrosis occurs in an organ, the build-up of scar tissue can change its structure and stop it from functioning properly and cause disease. For example, in the fatal lung disease idiopathic pulmonary fibrosis (IPF) the accumulation of scar tissue affects the uptake of oxygen into the blood and stiffens the lungs, making it harder to breathe. Scar tissue is formed largely of collagen. LOXL2 is a member of a family of enzymes that stiffen scar tissue by forming cross-links between the collagen molecules. It is believed that treatment with a LOXL2 inhibitor will reduce the stiffness of fibrotic tissue and thus alter the course of disease. Supporting this approach, levels of LOXL2 have been found to be elevated in fibrotic disease and inhibition of LOXL2 has been shown to be protective in preclinical models of fibrosis in different organs.

In the collaboration, Synairgen is investigating the effects of the LOXL2 inhibitors for IPF, whilst in parallel, Pharmaxis is generating data to support the rationale for using these inhibitors in liver fibrosis (NASH), kidney fibrosis and heart fibrosis. Individually these diseases represent areas of high unmet medical need and consequently significant market opportunities. Together they represent a substantial opportunity for a novel approach, as reflected in the number and commercial value of recent licensing/acquisition transactions occurring in this area.

*In vitro* models, which use tissue from patients with IPF, have been developed in collaboration with University of Southampton scientists to test the LOXL2

inhibitors. During the year we have shown that we can reduce collagen cross-link formation in these models in a dose-dependent manner. Post period-end, as announced in March 2017, we have shown that this leads to a reduction in the stiffness of the tissue. We subsequently went on to show that the compounds reduced fibrosis and improved lung function in an *in vivo* model of lung fibrosis run by McMaster University, Canada. These data support the rationale and the development of these particular compounds for treatment of fibrotic disease. We are currently progressing these compounds towards the clinic and, subject to satisfactory completion of preclinical testing, a Phase I clinical trial is scheduled to start in H2 2017.

We are very pleased with the progress that has been made in this programme; this is an exciting area scientifically. We are encouraged by the significant level of interest in this programme from potential licensees, who will be following the Phase I trial developments closely.

**Inhaled interferon beta programme**

The majority of asthma exacerbations are caused by respiratory viruses (common cold viruses), and the rationale to use inhaled interferon beta in asthma patients came from an observation made at the University of Southampton that levels of IFN-beta were lower in cell cultures from asthmatic patients than non-asthmatics during viral infection experiments. Furthermore, by normalising the IFN-beta levels there was less cell death, lower inflammatory markers, and lower virus levels; IFN-beta was protective. We went on to show that the drug was well tolerated in a Phase I trial and that antiviral defences were 'switched on'. In our SG005 Phase II trial asthma patients were treated with inhaled IFN-beta at the start of a suspected cold infection, and again we demonstrated that the drug had 'switched on' antiviral defences in the lungs. We also showed that inhaled IFN-beta provided an overall improvement in morning peak expiratory flow (an important measure of lung function), and in a subgroup from the trial (the 'difficult to treat' patients), who represented about 40% of the trial population, inhaled IFN-beta prevented a worsening of asthma control. Furthermore, patients on inhaled IFN-beta used fewer puffs of their rescue medication, reaching statistical significance on some days.

The findings by AstraZeneca in its Phase II INEXAS study were unexpected and contrary to the literature reporting a link between viruses and exacerbations of asthma. We are however very encouraged to observe that the lungs' antiviral defences had been switched on – as demonstrated by significant changes in an accepted biomarker of the interferon pathway. Indeed this is the third trial where this activation has been shown. Furthermore on an objective measure we saw that treatment with inhaled IFN-beta resulted in an improved morning peak expiratory flow of 19.7L/min (p=0.01). The day-by-day changes in this parameter closely mirror the changes we observed in our Phase II study. Once again inhaled IFN-beta was well tolerated. All data from the INEXAS trial will be provided to Synairgen and we will study each parameter in detail to guide future development.

We are particularly interested in using inhaled IFN-beta in COPD. Two new publications[1,2] in 2017 have shown that cold viruses are highly likely to cause exacerbations in COPD, which contrasts with the findings in asthma from the INEXAS trial, where only around 10% of patients exacerbated during cold

infections. There is also a greater clinical need in COPD compared to asthma as exacerbations in COPD patients are linked to a rapid and permanent deterioration of disease and death. New technology has recently emerged which will enable us to confirm viral infection prior to commencing treatment, making trial management and interpretation easier. Thus the new data linking viruses to exacerbations, a better understanding of the underlying biology in COPD, the high clinical need, and new diagnostic technology presents us with an attractive opportunity to explore the drug's full potential.

## FINANCIAL REVIEW

### Statement of Comprehensive Income

The loss from operations for the year ended 31 December 2016 was £3.44 million (2015: loss £2.61 million). Research and development expenditure for the year amounted to £2.42 million (2015: £1.36 million), with the increase in expenditure being attributable to the increased expenditure on the LOXL2 programme. This programme commenced in August 2015 and during 2016, as discussed above, the major elements of expenditure have been on chemistry, manufacturing, pharmacology and preclinical studies.

Other administrative costs for the year amounted to £1.02 million (2015: £1.28 million), with the reduction over the prior year being attributable to lower staff costs (no executive bonuses) and lower legal costs (2015 included costs associated with the Pharmaxis transaction). The research and development tax credit amounted to £0.59 million (2015: £0.30 million), with the increase being attributable to the higher expenditure on the LOXL2 programme. The loss after tax for 2016 was £2.82 million (2015: loss of £2.26 million) and the basic loss per share amounted to 3.08p (2015: basic loss per share of 2.47p).

### Statement of Financial Position and cash flows

At 31 December 2016, net assets amounted to £4.69 million (2015: £7.35 million), including net funds of £4.77 million (2015: £7.71 million).

The principal elements of the £2.94 million decrease over the year ended 31 December 2016 (2015: £1.89 million decrease) in net funds were:

- Cash used in operations of £3.32 million (2015: £1.99 million); and
- Research and development tax credits received of £0.33 million (2015: £0.06 million).

## OUTLOOK

In summary we remain on track to advance a Pharmaxis compound into Phase I in H2 2017 and there is encouraging business development interest in similar anti-fibrotic assets. Building on the positive outcomes in the INEXAS trial, we will continue to analyse the full data set as it becomes available, alongside further published and unpublished work in COPD, to establish the best route forward for this programme.

References

1. Wilkinson TMA *et al*. A prospective, observational cohort study of the seasonal dynamics of airway pathogens in the aetiology of exacerbations in COPD. *Thorax 2017; 0: 1-9*

2. Johnston N *et a*l. Colds as predictors of the onset and severity of COPD exacerbations. *International Journal of COPD 2017:12 839–848*

## Consolidated Statement of Comprehensive Income
**for the year ended 31 December 2016**

| | Notes | **Year ended 31 December 2016 £000** | Year ended 31 December 2015 £000 |
|---|---|---|---|
| **Revenue** | | **-** | 25 |
| Research and development expenditure | | **(2,418)** | (1,355) |
| Other administrative expenses | | **(1,024)** | (1,279) |
| Total administrative expenses | | **(3,442)** | (2,634) |
| **Loss from operations** | | **(3,442)** | (2,609) |
| Finance income | | **38** | 50 |
| **Loss before tax** | | **(3,404)** | (2,559) |
| Tax | 2 | **587** | 304 |
| **Loss and total comprehensive loss for the period attributable to equity holders of the parent** | | **(2,817)** | (2,255) |
| **Loss per ordinary share** | 3 | | |
| Basic and diluted loss per share (pence) | | **(3.08p)** | (2.47p) |

## Consolidated Statement of Changes in Equity
**for the year ended 31 December 2016**

| | Share capital £000 | Share premium £000 | Merger reserve £000 | Retained deficit £000 | Total £000 |
|---|---|---|---|---|---|
| At 1 January 2015 | 913 | 25,771 | 483 | (17,731) | 9,436 |
| Recognition of share-based payments | - | - | - | 166 | 166 |
| Total comprehensive loss for the year | - | - | - | (2,255) | (2,255) |
| At 31 December 2015 | 913 | 25,771 | 483 | (19,820) | 7,347 |
| Issuance of ordinary shares | 1 | - | - | - | 1 |
| Recognition of share-based payments | - | - | - | 154 | 154 |
| Total comprehensive loss for the year | - | - | - | (2,817) | (2,817) |
| **At 31 December 2016** | **914** | **25,771** | **483** | **(22,483)** | **4,685** |

# Consolidated Statement of Financial Position
**as at 31 December 2016**

| | **31 December 2016 £000** | 31 December 2015 £000 |
|---|---|---|
| **Assets** | | |
| **Non-current assets** | | |
| Intangible assets | **62** | 81 |
| Property, plant and equipment | **13** | 17 |
| | **75** | 98 |
| **Current assets** | | |
| Inventories | **55** | 56 |
| Current tax receivable | **560** | 303 |
| Trade and other receivables | **90** | 112 |
| Other financial assets – bank deposits | **1,661** | 3,722 |
| Cash and cash equivalents | **3,104** | 3,992 |
| | **5,470** | 8,185 |
| **Total assets** | **5,545** | 8,283 |
| **Liabilities** | | |
| **Current liabilities** | | |
| Trade and other payables | **(860)** | (936) |
| **Total liabilities** | **(860)** | (936) |
| **Total net assets** | **4,685** | 7,347 |
| **Equity** | | |
| **Capital and reserves attributable to equity holders of the parent** | | |
| Share capital | **914** | 913 |
| Share premium | **25,771** | 25,771 |
| Merger reserve | **483** | 483 |
| Retained deficit | **(22,483)** | (19,820) |
| **Total equity** | **4,685** | 7,347 |

# Consolidated Statement of Cash Flows
**for the year ended 31 December 2016**

| | **Year ended 31 December 2016 £000** | Year ended 31 December 2015 £000 |
|---|---|---|
| **Cash flows from operating activities** | | |
| Loss before tax | **(3,404)** | (2,559) |
| Adjustments for: | | |
| Finance income | **(38)** | (50) |
| Depreciation | **9** | 10 |
| Amortisation | **19** | 21 |
| Share-based payment charge | **154** | 166 |
| **Cash flows from operations before changes in working capital** | **(3,260)** | (2,412) |
| Decrease in inventories | **1** | - |
| Decrease/(Increase) in trade and other receivables | **17** | (18) |
| (Decrease)/Increase in trade and other payables | **(76)** | 441 |
| **Cash used in operations** | **(3,318)** | (1,989) |
| Tax credit received | **330** | 56 |
| **Net cash used in operating activities** | **(2,988)** | (1,933) |
| | | |
| **Cash flows from investing activities** | | |
| Interest received | **43** | 58 |
| Purchase of property, plant and equipment | **(5)** | (10) |
| Decrease in other financial assets | **2,061** | 3,030 |
| **Net cash generated from investing activities** | **2,099** | 3,078 |
| | | |
| **Cash flows from financing activities** | | |
| Proceeds from issuance of ordinary shares | **1** | - |
| **Net cash generated from financing activities** | **1** | - |
| | | |
| **(Decrease)/Increase in cash and cash equivalents** | **(888)** | 1,145 |
| Cash and cash equivalents at beginning of the year | **3,992** | 2,847 |
| **Cash and cash equivalents at end of the year** | **3,104** | 3,992 |

## 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 2016 has been extracted from the Group's audited financial statements which were approved by the Board of directors on 16 May 2017 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 2015 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 2016 report and financial statements.

### 2. Tax

The tax credit of £587,000 (2015: £304,000) relates to research and development tax credits in respect of the year ended 31 December 2016 (£560,000) and an adjustment in respect of prior periods (£27,000).

### 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.