Preliminary results for the year to 31 December 2015

5 April 2016

Silence Therapeutics plc, AIM: SLN, a leader in the discovery, development and delivery of novel RNA therapeutics for the treatment of serious diseases, announces its preliminary results for the year ended 31 December 2015.

Highlights

- In the preliminary analysis of the Phase 2a trial in pancreatic cancer, Atu027 in combination with gemcitabine showed a good safety profile and early signs of efficacy
- US patent granted in December 2015, covering broad modifications of short interfering RNA (siRNA) molecules
- Encouraging proof of concept data obtained in animal models of pulmonary arterial hypertension (PAH) with our lung delivery system DACC targeting a validated gene
- Improved messenger RNA (mRNA) delivery to liver by 20 fold and translation to non-human primates (NHP) achieved
- Equity placing in April 2015 raised net proceeds of £38.9m
- Loss after tax for the period of £6.6m (2014: £11.1m)
- Net cash of £51.9m at 31 December 2015 (2014: £16.9m)

Post year end events

- Atu027 Phase 2a trial met its primary endpoint. The follow up data showed consistent Overall Survival (OS) with the Progression Free Survival (PFS) announced in the preliminary report in May 2015 (See separate release)
- Licensee Quark Pharmaceuticals initiated in Phase 3 and Phase 2 trials in Delayed Graft Function (DGF) and Acute Kidney Injury (AKI). First patient dosing confirms their financial commitment to two full trials
- Excellent results in GalNAc conjugated siRNA activity using an in house structure
- Promising therapeutic benefit obtained in a PAH animal model using DACC to target a novel gene
- The role of PKN3 (Atu027's target gene) in metastasis was validated by an independent publication presenting significant business development opportunities
- Legal opinions support our recently awarded US patent covering nucleotide modifications at the 2' position. AtuRNAi is now a significant value driver for the Company
- Arbitration proceedings instigated against licensee Quark Pharmaceuticals for a $3m milestone payment

- Continued discussions with US company to negotiate an AtuRNAi license for a single product
- Lars Karlsson and Stuart Collinson stepped down from the Board effective immediately. The Company will seek to make further non-executive appointments to the Board
- Current net cash of £50.0m

Chief Executive Officer **Ali Mortazavi** commented:

"2015 was a difficult year for the biotechnology sector globally but a significant one for Silence Therapeutics. Modulating gene expression on and off in vivo remains a serious technical challenge. However, for the first time in its history, the Company has the combination of world leading technologies and the balance sheet to create a world class biopharma company.
We believe we are making material improvements in new delivery systems as seen in the progress we have made in GalNAc siRNA conjugates. The ability to mediate RNAi in the liver subcutaneously as opposed to an invasive intravenous injection opens up entirely new indications which were not accessible to a liposomal system.

In addition to progress in delivery, our proprietary siRNA chemistry AtuRNAi has been strengthened with the granting of a new US patent. Although parts of our patent estate start to expire in 2023, the importance of our chemical modification technology is being realised as siRNA pipelines are maturing. We now expect to be able to capitalise on our intellectual property which was first filed in 2003.
With the commencement of the Quark trials, the approach from a potential licensee and the significant broadening of the AtuRNAi patent estate, we are of the belief that these opportunities alone could be very significant relative to the current size of the Company."

Chief Executive's Report

Overview
In a turbulent year for drug development globally, good progress has been made in new delivery systems. In addition, we have successfully completed our Atu027 Phase 2a pancreatic cancer trial, meeting its primary endpoint. Despite good technology advancements, senior hires and execution of the research plan could have been more efficient. We are committed to hiring highly motivated and capable leaders across the organisation and are aggressively addressing this issue in 2016.

Atu027
The preliminary results of the Atu027-I-02 Phase 2a study did not identify any safety issues with the combination of Atu027 with gemcitabine in pancreatic cancer. In addition, patients exposed to a 33% higher dose of Atu027 (arm 2) presented a longer median duration of progression free survival (PFS): 5.33 months compared to 1.81 months for those on the lower Atu027 exposure regimen (arm 1). A post-hoc analysis of patients with metastatic pancreatic cancer showed a median PFS of 1.61 for arm 1 vs. 2.89 months for arm 2 (p=0.0247).
The current analysis, including the follow up data, showed that subjects in the higher dosed arm (arm 2) of the study had a median overall survival (OS) of 7.79 months compared to 5.62 months for the lower dose (arm 1, p=0.61), with 35% of patients being censored. For the metastatic group only, the median OS in the higher dosed group was 6.74 months vs. 3.29 (p=0.6) for the lower dose group, with 26% of patients being censored.

Separately, the importance of PKN3 in metastatic progression was validated during the period by a third party in a peer reviewed publication. Further Atu027 pre-clinical work to optimise effective PKN3 targeting is planned and we believe that this validation of our target could lead to business development opportunities.

Patent award

In December 2015, the Company was granted a new US patent (9,222,092). This addition to the Company's existing patent portfolio considerably strengthens its position with far broader claims that cover several nucleotide modifications at the 2' position and require shorter modified stretches than claimed in our previous patents. Further claims yet are being sought.

Since the granting of this patent and separately to the above licensing discussions, the Company has received advice from three separate law firms indicating that the issued claims potentially capture other development stage siRNA candidates.

We have invited and hereby invite any companies that are developing modified siRNA candidates that fall within the claims of our patents to enter into licensing negotiations with us.

GalNAc conjugation

During the period, Silence has increased investment in conjugation chemistry. In particular, substantial progress has been made in GalNAc conjugated siRNA for liver delivery. GalNAc conjugation allows receptor-mediated siRNA delivery to hepatocytes using less complex technology than liposomal nanoparticles, which has the important advantage of being administered subcutaneously rather than intravenously. This difference opens up new therapeutic areas.

We have obtained encouraging functional data using our own GalNAc structure: 80% knockdown was achieved in mRNA levels of a tool target with a 1mg/kg dose. Approximately 50% mRNA knockdown was observed 28 days after a single dose of 2mg/kg. We believe that the potency observed is competitive relative to our peers. In light of this development, those 'multiple shots at goal' projects better suited to GalNAc will be transitioned to this technology. Material achievements in GalNAc over a short period of time will result in the liver being a major focus for Silence going forward. Consequently, we are actively hiring experts in this space.

Liposomal siRNA delivery

Also in siRNA delivery, our liposomal systems targeting the vasculature continue to be optimised as we aim to maximise potency. Our lung targeted system (DACC) has shown promising proof of concept results in representative mouse models of pulmonary arterial hypertension, targeting both a validated and a novel gene. In both experiments, the therapeutic benefit was measured by a reduction in right ventricle systolic pressure (RVSP) as well as a reduction in pathologic pulmonary vessel remodelling.

mRNA therapeutics

The Company has improved its mRNA delivery capabilities, mainly for liver delivery, achieving a 20 fold increase in protein production from the delivered mRNA cargo in mice. In addition, our mRNA technology has successfully translated to higher species, showing activity in NHP. Progress in optimising our mRNA delivery capabilities will be key to enable both protein replacement and gene editing applications. Initial *in vivo* CRISPR/Cas9 studies have begun.

Construct engineering is being explored in parallel in order to optimise mRNA stability and improve the tolerability profile. We are actively investigating indications in this area.

Licensing

Silence is pleased to announce the progress of two of our licensee's clinical programmes into a pivotal Phase 3 for Delayed Graft Function and a Phase 2 for Acute Kidney Injury. First patients have now been dosed and we will be giving guidance as to the potential financial value of these trials to Silence.

As per the out-licensing deal terms and because of the Quark's arrangements with its partner Novartis, we believe that Silence is now due $3m, equating to a 15% milestone payment. After numerous unsuccessful attempts at resolving this issue with Quark, we have decided to instigate arbitration proceedings and will update the market accordingly. We remain confident of our case.

However, Quark has confirmed in writing that they will honour their financial obligations to Silence should both these trials come to a successful conclusion. Silence is entitled to 15% of all sub-licence revenues from Novartis. In 2010 Quark announced potential milestones of up to $650m from Novartis beyond the $30m already received. Silence's direct licence with Quark, in the absence of Novartis, sets out milestones of up to €2.5m on approval and launch, with royalties of 4%.

After initial discussions in 2013, the Company has been again approached by a US company for a licence for a clinical product. As in the case of Quark, the licence is for the use of the critical chemical modifications of AtuRNAi to enable the safe transit of the siRNA into a target cell. We continue to exchange terms with this company. In light of the fact that these licensing negotiations have started late in the development of the US company's candidate and the absolute requirement of AtuRNAi to the therapeutic agent, we believe that we are in a strong position to secure robust financial terms. We will update the market accordingly.

Board changes and Technology Advisory Board

Lars Karlsson has stepped down as Head of Research and from the Board effective immediately. Silence is now seeking a new Head of Research, which is a challenging task in a highly specialised field such as RNA therapeutics. In the meantime, while we identify the ideal candidate, we are in the process of setting up a Technology Advisory Board. This board will consist of highly experienced executives from pharma and biotech with specific knowledge in RNA therapeutics. It is envisaged that this board will regularly convene with senior scientists from within the Company to assist in the implementation of the research plan that is currently being executed. Two members of this team have already been appointed.

Dr. Stuart Collinson has also resigned, effectively immediately, from the Board due to an unexpected increase in his commitments to Arcturus Therapeutics and other companies with which he is working. Both Dr. Collinson and the Board express their regret that he is unable to remain on the Silence Board.

The Company will seek to make a further non-executive appointment to the Board and continue to look to hire the highest calibre non-executives with specific expertise in different areas of the business.

Outlook

Silence Therapeutics remains one of the global leaders in RNA therapeutics. We have made significant strides in making the technology behind the platform more reproducible and robust.

A recruitment drive in the translational science team, focusing on liver indications, will transition the Company from technology to products. With the strength of our balance sheet to support the breadth of our platform we look forward to the future with great confidence.

FINANCIAL REVIEW

During 2015 Silence improved its cash position through the £38.9m net proceeds of its share placing in May 2015. The funds raised have allowed the Company to expand development of its platform technology, in particular with strong progress in delivery of messenger RNA.

Research and development expenditure
Research and development expenses during the year decreased to £7.1m (2014: £8.9m). The decrease reflects the slowing of the execution of our clinical and pre-clinical programmes.

Administrative expenses
Administrative expenses during the year decreased to £2.7m (2014: £3.3m). This reflects two non-cash reductions in costs. Firstly, a £0.4m fall in the charge for share-based payments. Secondly, in our US subsidiary, a £0.4m credit reflecting retirement of balances related to historic contracts.

Financial income
Bank interest included in finance income was higher at £0.2m (2014: £0.1m) mainly due to higher average cash balances during the year.

Taxation
During the year we received a research and development tax credit of £1.5m (2014: £0.9m) in the UK, in respect of R&D expenditure in 2014, whose cash value is reflected in the results for 2015. We have accrued £1.3m recognising a current tax asset in respect of 2015 R&D tax credits as we are now confident we are able to make this claim for the year.

Liquidity, cash, cash equivalents and money market investments
The Group's cash, cash equivalents and money market investments at year end totalled £51.9m. At the end of 2014, Silence had cash, cash equivalents and money market investments of £21.9m. A total of £39.2m net was raised during 2015 through the placing and exercise of options.

The net cash outflow from operating activities in 2015 was £8.3m (2014: £9.5m) against an operating loss of £9.8m (2014: £12.0m).

Other balance sheet items
Trade and other receivables at year end were £1.6m (2014: £0.4m) and trade and other payables were £1.1m at year end (2014: £2.0m). The decrease in payables reflects the drop in research spending at year end and the retirement of balances related to historic contracts.

Goodwill at year end was £6.7m (2014: £7.1m). The movement in goodwill during the year related to foreign exchange.

Timothy Freeborn
Chief Financial Officer and Company Secretary

5 April 2016

CONSOLIDATED INCOME STATEMENT
year ended 31 December 2015

	Unaudited 2015 £000s	Audited 2014 £000s
Revenue	-	15
Research and development costs	(7,114)	(8,884)
Administrative expenses	(2,655)	(3,258)
Operating loss	(9,769)	(12,127)
Finance and other income	340	147
Loss for the year before taxation	(9,429)	(11,980)
Taxation	2,784	892
Loss for the year after taxation	(6,645)	(11,088)
Loss per ordinary equity share (basic and diluted)	(10.4p)	(22.0p)

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME
year ended 31 December 2015

	Unaudited 2015 £000s	Audited 2014 £000s
Loss for the year after taxation	(6,645)	(11,088)
Other comprehensive expense, net of tax:		
Exchange differences arising on consolidation of foreign operations	(616)	(701)
Total comprehensive expense for the year	(7,261)	(11,789)

CONSOLIDATED BALANCE SHEET
at 31 December 2015

	Unaudited 2015 £000s	Audited 2014 £000s
Non-current assets		
Property, plant and equipment	1,093	458
Goodwill	6,663	7,077
Other intangible assets	6	2
Other receivables	233	-
	7,995	7,537
Current assets		
Trade and other receivables	1,641	375
Investments held for sale	2	2
Other financial assets	-	5,000
Cash and cash equivalents	51,907	16,857
	53,550	22,234
Current liabilities		
Trade and other payables	(1,118)	(2,013)
Total assets less current liabilities	60,427	27,758
Net assets	60,427	27,758
Capital and reserves attributable to the Company's equity holders		
Share capital	3,490	2,605
Capital reserves	165,074	126,197
Translation reserve	1,298	1,914
Profit and loss account (deficit)	(109,435)	(102,958)
Total equity	60,427	27,758

CONSOLIDATED STATEMENT OF CHANGE IN EQUITY
year ended 31 December 2015

	Share capital £000s	Capital reserves £000s	Translation reserve £000s	Accumulated Losses £000s	Total equity £000s
At 1 January 2014	2,353	114,478	2,615	(91,870)	27,576
Recognition of share-based payments	—	1,127	—	—	1,127
Shares issued in year, net of expenses	252	10,592	—	—	10,844
Transactions with owners	252	11,719	—	—	11,791
Loss for year to 31 Dec 2014	—	—	—	(11,088)	(11,088)
Other comprehensive income					
Exchange differences arising on consolidation of foreign operations	—	—	(701)	—	(701)
Total comprehensive expense for the year	—	—	(701)	(11,088)	(11,789)
At 1 January 2015 (audited)	2,605	126,197	1,914	(102,958)	27,758
Recognition of share-based payments	—	777	—	—	777
Lapse of vested options in period	—	(168)	—	168	—
Shares issued in year, net of expenses	885	38,268	—	—	39,153
Transactions with owners	885	38,877	—	168	39,930
Loss for year to 31 Dec 2015	—	—	—	(6,645)	(6,645)
Other comprehensive income					
Exchange differences arising on consolidation of foreign operations	—	—	(616)	—	(616)
Total comprehensive expense for the year	—	—	(616)	(6,645)	(7,261)
At 31 December 2015 (unaudited)	3,490	165,074	1,298	(109,435)	60,427

CONSOLIDATED CASH FLOW STATEMENT
for the year ended 31 December 2015

	Unaudited 2015 £000s	Audited 2014 £000s
Cash flow from operating activities		
Loss before tax	(9,429)	(11,980)
Depreciation charges	180	90
Amortisation charges	2	242
Charge for the year in respect of share-based payments	777	1,127
Finance income	(175)	(139)
Corporation tax credits	1,513	892
Non-cash and other movements	—	260
	(7,132)	(9,508)
Increase in trade and other receivables	(228)	(15)
(Decrease)/Increase in trade and other payables	(895)	67
Net cash outflow from operating activities	(8,255)	(9,456)
Cash flow from investing activities		
Decrease in other financial assets	5,000	—
Interest received	175	137
Purchases of property, plant and equipment	(843)	(337)
Purchases of intangible assets	(7)	(1)
Net cash inflow / (outflow) from investing activities	4,325	(201)
Cash flow from financing activities		
Proceeds from issue of share capital, net of issue costs	39,153	10,844
Increase in cash and cash equivalents	35,223	1,187
Cash and cash equivalents at start of year	16,857	15,890
Net increase in the year	35,218	1,187
Effect of exchange rate fluctuations on cash held	(173)	(220)
Cash and cash equivalents at end of year	51,907	16,857

NOTES
year ended 31 December 2015

1.0 Basis of preparation

Silence Therapeutics plc ("the Company") and its subsidiaries (together "the Group") are primarily involved in the research and development of novel pharmaceutical products. Silence Therapeutics plc, a Public Limited Company incorporated and domiciled in England, is the Group's ultimate parent Company. The address of Silence Therapeutic plc's registered office is 27-28 Eastcastle Street, London W1W 8DH and the principal place of business is 72 Hammersmith Road, London W14 8TH.

The unaudited financial information set out in this statement does not constitute the Company's statutory accounts for the years ended 31 December 2014 or 31 December 2015, as defined in section 434 of the Companies Act 2006. The auditors have not yet reported on the 2015 accounts.

Statutory accounts for 2014 have been delivered to the Registrar of Companies and those for 2015 will be delivered in due course. The Company's auditors PwC, have reported on the 2014 accounts; their report was unqualified, did not draw attention to any matters by way of emphasis without qualifying their report and did not contain statements under s498 (2) or (3) Companies Act 2006. Whilst the financial information included in this announcement has been computed in accordance with International Financial Reporting Standards as adopted by the EU ("IFRS") this announcement does not itself contain sufficient information to comply with IFRS.

The principal accounting policies used in preparing this preliminary results announcement are those that the Company will apply in its statutory accounts for the year ended 31 December 2015 and are unchanged from those disclosed in the Company's Annual Report and Accounts for the year ended 31 December 2014.

Full financial statements for the year ended 31 December 2015 will be posted to shareholders in April 2016.

2.0 Going concern

The financial statements have been prepared on a going concern basis that assumes that the Group will continue in operational existence for the foreseeable future. The Directors consider that the continued adoption of the going concern basis is appropriate and the financial statements do not reflect any adjustments that would be required if they were to be prepared on any other basis.

As at 31 December 2015 had cash balances of £51.9m (including a Euro cash balance of €14.5m). The Directors have reviewed the working capital requirements of the Group for the next twelve months and are confident that these can be met.

The Directors, having prepared cash flow forecasts, believe that existing cash resources will provide sufficient funds for the Group to continue its research and development programmes and to remain in operation for at least twelve months from the date of approval of these financial statements.

3.0 Loss per share

The calculation of the loss per share is based on the loss for the financial year after taxation of £6.6m (2014: loss £11.1m) and on the weighted average of 64,023,900 (2014: 50,424,784) ordinary shares in issue during the year.

The options outstanding at 31 December 2015 and 31 December 2014 are considered to be non-dilutive as the Group is loss making.

4.0 **Related party transactions**

The group had transactions during the year and balances at the year end with the following organisations which are considered to be related parties:

	2015	2014
	Group	Group
	£000s	£000s
Pharmalogos Limited		
Expenses charge for services	**20**	120
Balance owed at 31 December 2015	**—**	—

Pharmalogos Limited, a company controlled by Dr Stella Khan, wife of Dr Michael Khan, supplies research services to Silence Therapeutics plc at an agreed price of £120,000 per annum. Notice was given to cease Pharmalogos services in September 2014, with effect from February 2015.

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Notes to Editors:

About Silence Therapeutics plc

Our technology harnesses the body's natural mechanisms to create therapeutic effects within its own cells. This technology can selectively silence or replace any gene in the genome, modulating gene expression up as well as down in a variety of organs and cell types, *in vivo*. We have developed proprietary modifications to improve the robustness of RNA sequences, together with advanced liposomal chemistries to enhance the delivery of therapeutics.

AtuRNAi

AtuRNAi® is a proprietary chemical modification pattern used to increase the stability of siRNA molecules to reduce degradation and increase potency. AtuRNAi modification enhances the delivery of intact functional siRNA molecules to target cells *in vivo*.