EDISON

Silence Therapeutics

Business update

Another major deal, this time with AstraZeneca

Pharma & biotech

Silence Therapeutics announced on 25 March 2020 that it has signed a collaboration agreement with AstraZeneca to develop novel drugs for cardiovascular, renal, metabolic and respiratory diseases. The deal includes an upfront of $60m, $20m in equity investment, and for each of the planned targets $400m in milestones, and high single- to low double-digit royalties. Additionally, the company announced that it would elevate SLN360 to the status of lead asset and expects to file an IND later in 2020 and to have interim results in mid-2021.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/17	0.0	(13.5)	(7.7)	0.0	N/A	N/A
12/18	0.0	(19.8)	(25.2)	0.0	N/A	N/A
12/19e	2.1	(17.8)	(20.4)	0.0	N/A	N/A
12/20e	21.9	(6.2)	(6.5)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

New programs to target hepatic/non-hepatic tissues

The AstraZeneca deal marks the third such agreement in the last 12 months (the others were with Mallinckrodt and Takeda). The current deal is a preclinical discovery collaboration (similar to the Takeda deal) in which Silence will develop five lead compounds (with the option to expand to 10) for a range of targets selected by AstraZeneca. In addition to liver-targeted therapies using the Silence platform, the companies will collaborate on delivery mechanisms for other tissues, including heart, kidney and lung, presumably based on AstraZeneca technology.

SLN360 elevated to lead program

In light of the improved cash position from the new deal, the company has made the strategic decision to elevate its program SLN360 for the treatment of cardiovascular disease to the status of lead asset and accelerate its clinical development. We currently expect it to initiate clinical studies before the end of 2020, pending further disruptions from COVID-19.

SLN124: Enrolment delays due to COVID-19

The company has opened several sites for the Phase Ib study of SLN124, but has not enrolled any patients yet, in part due to the disruption caused by COVID-19. The company has paused enrolment until it has a broader protocol in place to facilitate easier enrolment. The company now expects to provide interim results from the study in H121 (from H220).

Valuation: Increased to £462m or 559p per share

We have increased our valuation to £462m or 559p per basic share, from £345m or 440p per basic share. This is driven by the addition of the AstraZeneca deal metrics and its associated cash injections to our models (total £74m value uplift), an increase in the valuation of SLN360 to £167m from £112m and offset by the delay to SLN124 (£129m from £141m).

25 March 2020

Price	**408p**
Market cap	**£337m**
	US$1.24/£
Net cash (£m) at 31 December 2019	33.5
Shares in issue (estimated)	82.6m
Free float	41%
Code	SLN
Primary exchange	AIM
Secondary exchange	OTCMKTS

Share price performance

%	1m	3m	12m
Abs	(5.6)	1	795.3
Rel (local)	27.1	44.2	1088.6
52-week high/low	610.0p		41.0p

Business description

Silence Therapeutics (SLN) has a portfolio of siRNA drugs in early stage testing. SLN124 for iron overload is the most advanced and is entering the clinic in Q120. SLN360 is being developed for cardiovascular disease and is targeting an IND filed in H220. Silence recently signed a deal with Mallinckrodt for rights to the preclinical complement inhibitor SLN500, and a deal with Takeda to pursue an undisclosed target.

Next events

SLN360 IND filing	2020
SLN124 interim Phase Ib study results	H121
SLN360 Phase I interim results	Mid-2021

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Edison profile page

AstraZeneca deal: Over $4.0bn potential, to target extra-hepatic tissues

The AstraZeneca deal further validates the strength of the Silence siRNA platform in the marketplace of technologies. The investment from AstraZeneca marks the biggest deal to date for Silence in terms of upfront payments: $60m upfront (with $20m paid immediately and $40m by the first anniversary). Additionally, AstraZeneca will be making a $20m equity investment in the company ($4.07 per share based on new share information in the release). AstraZeneca has long had an interest in the company's technology, and previously had a different (but similarly structured) collaboration agreement with Silence, which was signed in 2007, and is a current Silence shareholder, stemming from shares associated with that deal.

The agreement is structured such that Silence will design and develop siRNA molecules directed against targets selected by AstraZeneca. The two companies plan to investigate five such targets over the first three years of the agreement, with the option to expand to five more targets at a future date. Silence will be financially responsible for early-stage discovery and for manufacturing sufficient material to support Phase I studies. For each such asset developed through the collaboration, AstraZeneca will have the option to acquire it for $10m option fee, $140m in development milestones and $250m in commercial milestones, along with high single-digit to low double-digit royalties. This corresponds to $4.0bn in combined milestones for all 10 potential programs combined, although we do not expect them all to progress to this indicative value of the relationship.

The new drugs will be developed to treat cardiovascular, renal, metabolic and respiratory diseases. The company intends to target diseases of hepatic origin (which is addressed using its well established GalNAc platform) as well as to target other tissues such as 'heart, kidney, and lung.' The precise technology or technologies to be employed to target these non-hepatic tissues has not been disclosed, although this has been an active area of research at AstraZeneca. For instance, the company published in 2018 on the targeting of pancreatic islets.[1] We therefore assume that this program to target other tissues will be largely driven by technology contributed by AstraZeneca.

SLN360

In light of the improved cash position following the AstraZeneca deal and delays in the SLN124 program (described below), the company has made the strategic decision to accelerate the SLN360 program targeting Lp(a) for the treatment of cardiovascular disease. This translates to an earlier initiation of clinical studies than originally planned. The company plans to submit an IND later in 2020 (previous guidance was H220), which we expect to translate into initiation of Phase I before year end. This assumes that the plan is not further derailed by COVID-19. The company guided towards interim results being available for the study by mid-2021. The elevation of this program to the lead position is an aggressive step by the company. The program has the potential to deliver a vast amount of value given the size of the cardiovascular disease market, but the development of these drugs requires significant clinical investment. We expect the company to partner the program to progress it through later stages of development, but in light of the many recent deals, have increased confidence in the company's ability to form such crucial partnerships.

[1] Ämmälä C, et al. (2018) Targeted delivery of antisense oligonucleotides to pancreatic β-cells. *Sci Adv* 4, eaat3386.

SLN124 delays due to COVID-19

In news unrelated to the announcement of the new deal, the company has reported that it is pausing enrolment in its Phase Ib study of SLN124. The company opened clinical sites in Q419 and began screening patients, but has not enrolled any yet. This is partially due to the disruption caused by COVID-19 and the impact on medical systems seen worldwide. The company has stated that it intends to suspend enrolment under this protocol and initiate enrolment again later this year under an amended protocol, although precise details on the amendments have not been announced. The net impact of these delays will be relatively small and likely measurable in months. We should note that although SLN360 has been elevated to lead program, and SLN124 has faced delays, the company has not deprioritized this program and it plans on a similar investment of resources compared to previously. On the new timeline, the new protocol is expected to start enrolling patients later in 2020 and interim results are expected in H121 (from previous guidance of H220). Additionally, in positive news, the company reported that SLN124 received a Rare Pediatric Disease designation from the FDA. This would entitle the company to a priority review voucher (PRV) if the drug is approved, which can be used to speed the approval process of a drug or sold by the company. The latest sale of a PRC we are aware of was for $111m from Sarepta to Vifor Pharma in February 2020.

Valuation

We have increased our valuation to £462m or 559p per basic share, from £345m or 440p per basic share. This is driven by multiple factors. First, we have added the AstraZeneca project to our model with a valuation of £40m. We currently only model the first drug from this program being developed. Similar to our other licensing agreements, in lieu of an announced target indication, we have used a proxy, which assumes $400m in peak sales, royalties in the range of 8–12% and $400m in clinical and commercial milestones. The majority of this AstraZeneca project value at this time is driven by the remaining (deferred) upfront payable ($40m), which we expect to transfer to the cash line once it is delivered. We assign a probability of success of 3% considering that the discovery process has not initiated yet. In addition to this line item in our valuation, we have also added the $20m immediate upfront cash and $20m from equity in our cash balance, bringing it to an estimated £67m (pro-forma net cash at year-end 2019). The total impact to our valuation from the AstraZeneca deal is £74m.

Additionally, we have upgraded our valuation of SLN360, based on it being the lead asset. We have increased the probability of success to 7.5% from 5% to reflect this change and the firm's commitment to bringing it to the clinic. We normally risk adjust preclinical programs to reflect that most never reach the clinic, and have partially lifted this adjustment to reflect the focus on the program. We have also accelerated the timeline slightly and expect it to launch in 2027 (compared to 2028 previously). These two factors have increased our valuation to £167m from £112m.

Offsetting these factors, we have lowered our valuation of SLN124 to £129m from £141m to reflect the new timeline and have pushed back our expected launch date to 2027 (from 2026). The other programs remain unchanged.

Exhibit 1: Valuation of Silence

Product	Indication	Clinical stage	Prob. of success	Launch year	Peak sales ($m)	Margin/ royalty rate	rNPV (£m)
SLN124	Beta-Thalassemia	Phase I ready	15%	2027	489.2	59%	62.7
	MDS	Phase I ready	15%	2027	683.7	60%	66.1
SLN360	Cardiovascular disease	Preclinical	7.5%	2027	5214.0	54%	167.1
SLN500	Complement disorder	Preclinical	5%	2027	*400	*11–19%	26.4
Takeda project	Undisclosed	Preclinical	3%	2028	*400	*11–19%	17.7
AZ project	Undisclosed	Preclinical	3%	2029	*400	*8–12%	39.9
QPI-1002	AKI & Kidney Transplant	Phase III	60%	2022	381.5	1.5–4.0%	9.7
Onpattro	hATTR Amyloidosis	Approved			361.6	0.33–1.0%	4.8
Total							394.5
Pro-forma net cash and deposits (at 31 December 2019 + AZ upfront est.) (£m)							67.4
Total firm value (£m)							**461.9**
Total basic shares (m) estimated following AstraZeneca $20m equity investment							82.6
Value per basic share (p)							**559**
Dilutive options (m)							4.7
Total diluted shares (m)							87.4
Value per diluted share (p)							532

Source: Silence Therapeutics reports, Edison Investment Research. Note: *Peak sales for SLN500 and Takeda are a placeholder, royalty rates described as 'low double digit to high teens' for SLN500.

Financials

We have added the AstraZeneca deal to our financials in a similar manner to the other recent deals, and record $40m of the $60m upfront payment as deferred revenue. The payment and investment from AstraZeneca has reduced our expected financing requirement to £80m (recorded as illustrative debt in 2024) from £105m previously. This was offset by a delay in profitability to 2027 and higher costs associated with SLN360 before profitability, on account of the accelerated timeline. We expect the company to meet these financing obligations at least in part through the partnering of SLN360 and potentially additional platform deals.

Exhibit 2: Financial summary

£000s	2017	2018	2019e	2020e
31-December	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Revenue	16.0	0.0	2,147.1	21,928.8
Cost of Sales	0.0	0.0	0.0	0.0
Gross Profit	16.0	0.0	2,147.1	21,928.8
R&D	(7,943.0)	(9,743.0)	(12,259.8)	(20,192.9)
SG&A	(6,464.0)	(10,828.0)	(8,377.2)	(8,628.5)
EBITDA	(13,958.0)	(20,172.0)	(18,070.9)	(6,513.6)
Normalised operating profit	(13,753.0)	(19,890.0)	(17,788.4)	(6,170.1)
Depreciation & amortisation	(433.0)	(399.0)	(419.0)	(379.0)
Exceptionals	0.0	0.0	0.0	0.0
Share-based payments	(638.0)	(681.0)	(701.4)	(722.5)
Reported operating profit	(14,391.0)	(20,571.0)	(18,489.9)	(6,892.6)
Net Interest	206.0	45.0	0.0	0.0
Joint ventures & associates (post tax)	0.0	0.0	0.0	0.0
Exceptionals	10,410.0	0.0	0.0	0.0
Profit Before Tax (norm)	(13,547.0)	(19,845.0)	(17,788.4)	(6,170.1)
Profit Before Tax (reported)	(3,775.0)	(20,526.0)	(18,489.9)	(6,892.6)
Reported tax	2,157.0	2,115.0	3,661.3	4,383.4
Profit After Tax (norm)	(5,806.4)	(17,800.2)	(15,955.5)	(5,534.3)
Profit After Tax (reported)	(1,618.0)	(18,411.0)	(14,828.5)	(2,509.1)
Minority interests	0.0	0.0	0.0	0.0
Discontinued operations	(1,306.0)	0.0	0.0	0.0
Foreign exchange adjustment	404.0	94.0	0.0	0.0
Net income (normalised)	(5,402.4)	(17,706.2)	(15,955.5)	(5,534.3)
Net income (reported)	(2,520.0)	(18,317.0)	(14,828.5)	(2,509.1)
Basic average number of shares outstanding (m)	70	70	78	85
EPS - basic normalised (p)	(7.72)	(25.18)	(20.37)	(6.50)
EPS - diluted normalised (p)	(7.72)	(25.18)	(20.37)	(6.50)
EPS - basic reported (p)	(2.31)	(26.18)	(18.93)	(2.95)
Dividend (p)	0.00	0.00	0.00	0.00
BALANCE SHEET				
Fixed Assets	9,460.0	9,387.0	9,157.5	8,968.0
Intangible Assets	8,057.0	8,191.0	8,151.0	8,151.0
Tangible Assets	1,170.0	921.0	731.5	542.0
Investments & other	233.0	275.0	275.0	275.0
Current Assets	45,547.0	29,498.0	36,548.4	83,770.2
Stocks	0.0	0.0	0.0	0.0
Debtors	733.0	0.0	0.0	0.0
Cash, cash equivalents, and deposits	42,745.0	26,494.0	33,544.4	80,766.2
Other	2,069.0	3,004.0	3,004.0	3,004.0
Current Liabilities	(2,657.0)	(3,830.0)	(5,049.8)	(5,468.0)
Creditors	(2,657.0)	(3,830.0)	(5,049.8)	(5,468.0)
Tax and social security	0.0	0.0	0.0	0.0
Short term borrowings	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0
Long Term Liabilities	0.0	0.0	(16,129.0)	(47,580.6)
Long term borrowings	0.0	0.0	0.0	0.0
Other long term liabilities	0.0	0.0	(16,129.0)	(47,580.6)
Net Assets	52,350.0	35,055.0	24,527.1	39,689.6
Minority interests	0.0	0.0	0.0	0.0
Shareholders' equity	52,350.0	35,055.0	24,527.1	39,689.6
CASH FLOW				
Op Cash Flow before WC and tax	(13,320.0)	(19,491.0)	(17,369.4)	(5,791.1)
Working capital	1,711.0	913.0	1,219.8	418.2
Exceptional & other	3.0	6.0	16,129.0	31,451.6
Tax	2,007.0	1,812.0	3,661.3	4,383.4
Net operating cash flow	(9,599.0)	(16,760.0)	3,640.8	30,462.2
Capex	(173.0)	(188.0)	(189.5)	(189.5)
Acquisitions/disposals	0.0	0.0	0.0	0.0
Net interest	(15.0)	39.0	0.0	0.0
Equity financing	48.0	341.0	3,799.2	16,949.2
Dividends	0.0	0.0	0.0	0.0
Other	13,202.0	319.0	(200.0)	0.0
Net Cash Flow	3,463.0	(16,249.0)	7,050.4	47,221.8
Opening net debt/(cash)	(39,012.0)	(42,745.0)	(26,494.0)	(33,544.4)
FX	270.0	(2.0)	0.0	0.0
Other non-cash movements	0.0	0.0	0.0	0.0
Closing net debt/(cash)	(42,745.0)	(26,494.0)	(33,544.4)	(80,766.2)

Source: Silence Therapeutics reports, Edison Investment Research

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