Syncona Limited

Quarterly Update

13 February 2019

Syncona Ltd, a leading healthcare company focused on founding, building and funding global leaders in life science, today issues its quarterly update covering the period from 1 October to 31 December 2018.

Highlights

Operational

- Continued strong performance across Syncona companies
- Blue Earth Diagnostics (Blue Earth) showed good sales momentum with US unit sales of Axumin for the treatment of prostate cancer of 7,575 in the period, a 16.5 per cent increase on the previous quarter; continued progress towards a label extension for Axumin in glioma, a form of brain cancer
- Three clinical-stage companies with Nightstar announcing plans to initiate a phase 2/3 expansion study in its second programme and Autolus and Freeline reporting encouraging early data
- In final stages of agreeing funding for two new companies, which fit with Syncona's model of building companies around exceptional science.

Financial

- Net assets of £1,302.1 million, 194.5p per share[1], a total return of (6.6) per cent over the three months, predominantly driven by the decline in Nightstar's share price; 23.9 per cent total return over the nine months from 31 March 2018
- Life science portfolio valued at £889.7 million, a return of (6.3) per cent over the three months; 58.2 per cent return over the nine months[2]
- Capital pool of £412.4 million (net cash of £130.3 million and funds investments of £282.1 million); £12.5 million of gross investment in life science over the three months; £120.7 million over the nine months

Martin Murphy, CEO, Syncona Investment Management Limited, said: "We are pleased with the strong progress across our companies over the period. Blue Earth is cash generative returning £10.8 million to Syncona during the period and continues to demonstrate strong sales momentum, whilst Nightstar, Autolus and Freeline are making excellent clinical progress.

We continue to have a high-level of conviction in our companies' fundamentals having built them in partnership with their world-class founders and are focused on working closely with them to achieve our ambition of delivering transformational treatments for patients and generating value for our shareholders over the long-term. As we look forward, we continue to see a strong pipeline of exciting opportunities where we can continue to build globally competitive companies around exceptional science."

Life science performance overview

Syncona's companies have delivered strong performance during the quarter and continue to make good progress against their business plans. Blue Earth demonstrated good sales momentum and was written up by £8.8 million, whilst Autolus has seen positive share price progression over the three months. The valuation increases at these companies were outweighed by a decline in Nightstar's share price, despite the company's positive clinical progress; Syncona's view on the strong prospects of the business remains unchanged. The life science portfolio delivered a negative 6.3 per cent return in the quarter.[2]

[1] Fully diluted

[2] Internal Rate of Return (IRR): method used for return calculations

Over the nine months to 31 December 2018, the life science portfolio has generated a return of 58.2[2] per cent with performance predominantly driven by positive valuation increases at Blue Earth and Autolus.

Strong progress across our companies

Blue Earth Diagnostics (PET imaging)

- Continued strong sales momentum for Axumin in prostate cancer
- Application to extend Axumin beyond prostate cancer screening to glioma

Over the three months, Blue Earth sold 7,575 doses of Axumin for the diagnosis of recurrent prostate cancer, up from 6,500 the previous quarter in the US. Following positive results from an investigational Phase 3 blinded image evaluation study, the U.S. Food and Drug Administration (FDA) has accepted a supplemental New Drug Application (sNDA) for the expanded use of Axumin in adults for glioma. Blue Earth is cash generative and Syncona received a £10.8 million return of capital in the quarter.

Nightstar (retinal gene therapy)

- Preliminary efficacy data from Phase 2/3 expansion study in X-linked retinitis pigmentosa (XLRP) expected in mid-2019
- Enrolment in Phase 3 trial in Choroideremia ongoing

Nightstar made good progress during the period, announcing that it plans to initiate a Phase 2/3 expansion study in XLRP. The company's Phase 2/3 expansion study in XLRP is designed to include a No-Sham Control Arm[3], which aligns with draft guidance from the FDA. Enrolment of patients in the company's pivotal programme in Choroideremia is ongoing and Nightstar is aiming to complete recruitment into the study in the first half of 2019.[4]

Autolus (CAR-T cell therapy)

- Significant period of clinical progress with encouraging data from AUTO3 programme
- Dosed first patient in AUTO4 and pre-clinical data read-outs for AUTO5

Autolus reported encouraging data in its AUTO3 programmes in paediatric Acute Lymphoblastic Leukaemia (pALL) and Diffuse Large B-cell lymphoma (DLBCL), with the preliminary data from both trials showing encouraging safety data and early clinical efficacy. Autolus also announced that it had dosed its first patient in the Phase 1/2 trial of AUTO4 in TRBC1-positive peripheral T cell lymphoma; alongside pre-clinical data from its sister program, AUTO5 targeting TRBC2-positive lymphoma.[4]

Freeline (gene therapy, systemic diseases)

- Encouraging results from first two patients treated for Haemophilia B
- Phase 1/2 trial ongoing with further data expected in 2019

Freeline reported initial positive data from the first two patients in its ongoing Phase 1/2 trial in Haemophilia B at the American Society of Haematology (ASH) Conference in December. Within four weeks of dosing, the FIX[5] activity in both participants, who were dosed in the low dose cohort, rose to greater than 30%, and at 15 weeks stabilised at 45% ±5%, which approaches the normal range of FIX activity in the general population's blood of between 50-150%. Post-period end, Freeline announced its third programme in Type 1 Gaucher Disease, an inherited metabolic disorder characterized by the build-up of glucocerebroside in lysosomes throughout the body and also presented pre-clinical data from its second programme, targeting Fabry's disease at the WORLD Symposium.

[3] The parallel Control group of patients in the trial will not receive the study drug nor surgical procedure
[4] Further detail on clinical data in Supplementary Information
[5] Level of Factor IX, an essential clotting protein

Achilles (neo-antigen cell therapy)

- Management team strengthened
- CTA approval to conduct Phase I/II study in first programme

In December, Achilles announced the appointment of Dr Edwin Moses as Chairman. Dr Moses was most recently CEO of Ablynx NV for 12 years, building it from a small R&D focused organisation to a commercial business with a broad biologics pipeline, through to its sale to Sanofi for $4.8 billion in 2018. Dr Iraj Ali became CEO of the business, following a period as Interim CEO.

Post-period end, Achilles announced that its Clinical Trial Application (CTA) to conduct a Phase I/II study with its lead product, a tumour-derived T cell therapy targeting clonal neoantigens, in development for the treatment of advanced Non-Small Cell Lung Cancer (NSCLC), has been approved by the UK regulatory authority, the Medicines and Healthcare products Regulatory Agency (MHRA). The study, an open-label, multi-centre Phase I/II trial evaluating the safety and clinical activity of clonal neoantigen T cells ("cNeT") in patients with advanced NSCLC, is expected to enrol the first patient in the second half of 2019.

The rest of Syncona's companies in the Life Science portfolio continued to make positive progress in the quarter.

Increase in cash-weighting in strategic capital pool

At 31 December 2018, our strategic capital pool was £412.4 million with £130.3 million held in cash and £282.1 million in fund investments. Over the nine months, the fund investments portfolio has produced a negative return of 1.4 per cent. Over the three months to 31 December, the fund investments generated a negative return of 8.7 per cent, with the significant increase in public market volatility in the final quarter of 2018 impacting performance.[6]

The cash weighting in our capital pool has increased to 31.6 per cent, with £113.3 million of redemptions made in the three months. Against this, two new fund investments were made in the quarter totalling £16.7 million. Since the period end, we have redeemed an additional £13.9 million of fund investments, further increasing our cash weighting and we expect to see this trend continue as we continue our strategy of transitioning the fund investments away from directionally biased funds.

Over the three months, we made a gross investment of £12.5 million from our capital pool into our life science companies (£120.7 million into life science over the nine months). We continue to expect investment for the financial year to be at the top end of guidance of £75 million to £150 million.

Company	30 Sep Value (£m)	Net invest-ment / return (£m)	Valuat-ion change (£m)	30 Dec 2018 value (£m)	% NAV	Valuat-ion basis	Fully diluted owner-ship stake (%)	Focus area
Established								
Blue Earth	231.6	(10.8)	8.8	229.6	17.6%	rDCF	89	Advanced diagnostics
Maturing								
Autolus	319.9	-	29.9	349.8	26.9%	Quoted	32	Cell therapy
Nightstar	207.0	-	(87.8)	119.2	9.2%	Quoted	38	Gene therapy
Freeline	93.5	-	-	93.5	7.2%	Cost	80	Gene therapy
Developing								

[6] IRR: method used for return calculations

Gyroscope	11.0	4.0	-	15.0	1.2%	Cost	80	Gene therapy
Achilles	8.3	7.9	-	16.2	1.2%	Cost	69	Cell therapy
Orbit Biomedical	9.3	-	0.2	9.5	0.7%	Cost	80	Surgical devices
SwanBio	5.3	-	0.1	5.4	0.4%	Cost	72	Gene therapy
OMASS	3.5	-	-	3.5	0.3%	Cost	46	Therapeutics
Life science investments								
CRT Pioneer Fund	32.8	0.6	-	33.4	2.6%	Adjusted Third-party	N/A	
CEGX	6.5	-	-	6.5	0.5%	Adjusted PRI	9	
Adaptimmune	15.6	-	(8.9)	6.7	0.5%	Quoted	1	
Syncona Collaborations	1.4	-	-	1.4	0.1%	Cost	100	
TOTAL	**945.7**	**1.7**	**(57.7)**[7]	**889.7**	**68.4%**			

[ENDS]

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About Syncona:

Syncona is a leading FTSE250 healthcare company focused on founding, building and funding global leaders in life science. Our vision is to deliver transformational treatments to patients in truly innovative areas of healthcare while generating superior returns for shareholders.

We seek to partner with the best, brightest and most ambitious minds in science to build globally competitive businesses.

We take a long-term view, underpinned by a deep pool of capital, and are established leaders in gene and cell therapy. We focus on delivering dramatic efficacy for patients in areas of high unmet need.

Copies of this press release and other corporate information can be found on the company website at: www.synconaltd.com

Supplementary Information:

Blue Earth clinical data

The business announced results from an investigational Phase 3 blinded image evaluation (BIE) study (BED006) evaluating the diagnostic impact of Axumin, when combined with MRI, in the imaging of adults with glioma in November 2018. Results were positive with a Positive Predictive Value for Axumin in this setting of more than 90%. Importantly, the combination of Axumin and MRI identified additional malignant regions, which MRI alone was unable to identify.

Nightstar – Phase 2/3 expansion study

The Phase 2/3 expansion study is designed to evaluate the safety and efficacy of NSR-RPGR in patients with a diagnosis of XLRP due to RPGR mutations, as confirmed by genetic testing. The primary efficacy endpoint will evaluate changes in retinal sensitivity following treatment with NSR-RPGR. Secondary endpoints include both anatomical and functional endpoints of efficacy and safety similar to those evaluated in the dose escalation study as well as exploratory efficacy endpoints such as mobility maze

[7] Includes: update of rDCF model, change in quoted share prices and foreign currency exchange rates

assessments. Approximately 45 patients across six surgical centers in both the United States and the United Kingdom will be enrolled. The eligibility criteria for the expansion study will include patients with functional impairment as measured by microperimetry and the presence of viable photoreceptors as indicated by ellipsoid zone measurements on optical coherence tomography. Patients will be randomized on a masked basis into one of three study arms: approximately 15 patients receiving a high-dose of NSR-RPGR in one-eye (2.5x10^11 genome particles, or gp); approximately 15 patients receiving a low-dose of NSR-RPGR in one-eye (5x10^10 gp); and approximately 15 patients receiving no treatment (no-sham, parallel control arm). The two treatment groups correspond to doses used in cohorts 5 and 3 of the dose escalation study, respectively. A standardized eight-week steroid regimen will be included to maximize any potential treatment benefit.

AUTO3 clinical data

In the AUTO3 programme in paediatric ALL, Autolus reported data in 10 patients who received an AUTO3 infusion as a single dose or split dose. Safety data was encouraging with no grade two or higher Cytokine Release Syndrome (CRS) observed. In the higher dose group, four out of six patients have an ongoing molecular complete response (CR) and importantly, no loss of CD19 or CD22 was noted among relapsed patients, a key point of differentiation for the programme.

In the AUTO3 programme in DLBCL, seven patients were dosed in the trial with all patients receiving 50 million cells/kg at dose level one. Three patients received a consolidation with pembrolizumab, and 4 patients did not receive treatment with pembrolizumab. None of the treated patients developed CRS grade 3 or higher and one patient had neurotoxicity grade 3, considered possibly related to AUTO3. No dose limiting toxicities were observed and dose escalation continues. Six patients were evaluable for response, two achieved a CR and two a partial response (PR); two patients did not respond.

AUTO5 pre-clinical data

The company presented data from preclinical studies of AUTO5 targeting TRBC2 at the ASH conference. TRBC1 and TRBC2 are virtually identical in sequence, and antibody binders had to be designed to differentiate TRBC1 from TRBC2 extracellular domains by selectively recognizing a single inversion of two amino acids. Employing a structural biology approach and molecular modelling techniques, a binder was generated that could bind TRBC2 without binding to TRBC1, and when included in a CAR T approach, selectively eliminated TRBC2-positive cells.