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Oxford BioMedica

New era for cell and gene therapies

OXB is a specialist advanced therapy viral-vector biopharmaceutical company. It offers vector manufacturing and development services, whilst retaining proprietary drug candidates. OXB will also receive royalties on commercial therapies developed with its LentiVector® platform. The first such therapy, also the first CAR-T therapy to ever be approved, was licensed by the FDA on 30th August 2017: tisagenlecleucel (Kymriah™) is manufactured by Novartis using lentivirus vector supplied by OXB. OXB will be the first UK company to manufacture viral vector for commercial production of a licensed gene-based medicine.

- **Strategy:** Oxford BioMedica has four strategic objectives: delivery of process development services that embed its technology in partners' commercial products; commercial manufacture of lentiviral vector; out-licensing of proprietary candidates; and investment in R&D and the LentiVector platform.

- **Advanced therapies:** In only a week, gene therapies and gene-modified cell therapies have entered the global limelight: the first approval of a CAR-T therapy; Gilead's $12bn acquisition of US CAR-T biotech Kite Pharma; and the UK government's announcement of focused investment in such therapies.

- **Kymriah approved:** The FDA has approved its first gene-based medicine, a Chimeric Antigen Receptor T cell (CAR-T) therapy that is manufactured by Novartis, for childhood leukemia. This is a historic decision that paves the way to the commercialisation of a multitude of gene-modified cell therapies for bigger markets.

- **Novartis deal:** In July, the existing deal was extended for a minimum period of three years for OXB to supply both clinical and commercial vector for Kymriah and other (undisclosed) CAR-T therapies. Key points are: $10m up-front; >$90m from a minimum off-take contract over 3 years; royalties on net sales.

- **Investment summary:** OXB is at an interesting juncture. Heavy investment in state-of-the-art GMP manufacturing facilities for production of gene therapy vector has enabled the deal with Novartis, placing the group on the cusp of significant bioprocessing service income and royalties in the near future. We have updated our DCF valuation from 7.5p/share to 10.3p/share on the back of Kymriah's approval. Forecasts suggest OXB will turn EBITDA positive in 2017.

Financial summary and valuation

Year end Dec (£m)	2014	2015	2016	2017E	2018E	2019E
Sales	13.62	15.91	27.78	38.80	47.00	54.00
EBITDA	-9.29	-11.73	-6.78	2.43	7.60	12.88
Underlying EBIT	-10.39	-13.35	-10.45	-2.01	3.16	8.45
Reported EBIT	-10.61	-14.08	-11.32	-2.97	2.10	7.28
Underlying PBT	-10.58	-16.25	-16.26	-6.69	-1.12	4.18
Statutory PBT	-10.80	-16.98	-20.31	-7.66	-2.18	3.01
Underlying EPS (p)	-0.42	-0.48	-0.45	-0.07	0.11	0.28
Statutory EPS (p)	-0.43	-0.51	-0.60	-0.10	0.08	0.25
Net (debt)/cash	13.20	-17.90	-19.05	-16.64	-14.09	-6.20
Shares issued	22.81	0.14	17.50	0.10	0.10	0.10
P/E (x)	-	-	-	-	76.38	30.70
EV/sales (x)	-	-	-	118.61	37.90	22.35

Source: Hardman & Co Life Sciences Research

Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data

EPIC/TKR	OXB
Price (p)	8.7
12m High (p)	11.5
12m Low (p)	3.0
Shares (m)	3,103.5
Mkt Cap (£m)	271.3
EV (£m)	287.9
Free Float	65%
Market	LSE

**As defined by AIM Rule 26*

Description

Oxford BioMedica is a UK-based biopharmaceutical company specializing in cell and gene therapies developed using lentiviral vectors, gene-delivery vehicles based on virus particles. In addition to vector development and manufacture, OXB has a pipeline of therapeutic candidates and undertakes innovative pre-clinical R&D in gene-medicine.

Company information

CEO	John Dawson
CFO	Stuart Paynter
Chairman	Lorenzo Tallarigo
	01865 783 000
	www.oxfordbiomedica.co.uk

Key shareholders

Directors	0.8%
Vulpes	18.8%
M&G	18.0%
Aviva	7.3%
Joy Group	4.9%

Diary

31 Mar	Hardman initiation
30 Aug-17	FDA decision: CTL019
Mar-18	2017 FY results

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New era for cell and gene therapy

First CAR-T approved: Kymriah™

First CAR-T therapy has been approved by the FDA...

On 30th August, the FDA approved the Biologics License Application (BLA) for tisagenlecleucel, a Chimeric Antigen Receptor T cell (CAR-T) therapy, for the paediatric leukemia B-ALL[1]. Although not a surprise – it had been recommended unanimously by the Oncologic Drugs Advisory Committee (ODAC) a month previously – this is a momentous decision that launches a new era of modern medicine, in which genetic engineering is harnessed to tackle cancer. The early approval, around one month ahead of the PDUFA date, is illustration of the industry's excitement as decades of research are formally realised.

...and OXB supplies the essential vector delivery system to Novartis

Kymriah re-programmes patients' immune systems...

Tisagenlecleucel, trade name Kymriah, was discovered at the University of Pennsylvania and developed in collaboration with Novartis. As a therapy that requires extraction of T cells from patients for genetic engineering in a laboratory, followed by their reintroduction to the patient, this is the first gene-modified cell therapy to be approved anywhere in the world. It is also the first time that the FDA has approved a therapy involving genetic engineering of patients' living cells.

...to kill cancer cells that cause B-cell acute lymphoblastic leukemia

OXB to supply vector

Deal with Novartis will deliver at least $90m to OXB...

For Oxford Biomedica, this is also a decision that moves it into a new phase – drawing income from a commercial therapy – and brings >£26m investment in facilities and three years of partnership with Novartis to fruition. In July, a deal was signed that extended OXB's term as the supplier of lentivirus vector for commercial and clinical manufacture of Kymriah and other CAR-T therapies. As described in detail in our July note '*Major deal to supply Novartis CAR-T programmes*', this includes a $10m upfront payment and a minimum offtake of at least $90m in bioprocessing fees over three years. Currently, OXB is the 'sole supplier'.

...plus (undisclosed) royalties on net sales

OXB will receive undisclosed royalties on net sales, presumed to be low single digit. Kymriah certainly has potential to reach blockbuster status given that label expansion to bigger indications is likely. However, a consensus on potential sales has not been reached, not least due to uncertainty on how the industry will respond to a new class of expensive drugs.

Kymriah™ gene-modified human cells

Source: Novartis media release

[1] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm

Advanced therapies market

The significance of the FDA's decision was recognised by the market, with OXB's share price hitting 11p (+22%) on the day of the announcement, on top of existing growth tracking the ODAC vote and closure of OXB's Novartis deal.

Gilead acquiring Kite Pharma...

...a US company developing CAR-T and other cell therapies...

...for $11.9bn

Days previously, CAR-T therapy entered the limelight with Gilead announcing that it would be acquiring Kite Pharma, a US biotech company specialising in CAR-T and other therapies, for $11.9bn (£9.1bn). Kite has no commercial-stage products; its late stage CD19 CAR-Ts are, however, a direct competitor to Novartis's CAR-T programmes. Its lead candidate, axicabtagene ciloleucel, is under priority review in the US (PDUFA: 29th Nov '17) and has Priority Medicines (PRIME) status in the EU, for Kymriah's second indication: refractory diffuse large B-Cell lymphoma (DLBCL). Kite was first to file a CAR-T marketing authorization application (MAA) in Europe, with Novartis around six months behind. The third-party manufacturer of retroviral vector for Kite's programmes does not appear to have been disclosed [2].

UK government focusing investment on advanced therapies

In the week's final endorsement of cell and gene therapy, the UK government revealed that at least £42m of the first £146m of the Industrial Strategy Challenge Fund would go to accelerating advances in UK manufacture and delivery of advanced therapies [3].

New commercialisation model

High efficacy and big unmet need...

...high COGS and high treatment price

There are, however, many unknowns. Novartis will be the first to navigate commercial CAR-T manufacturing, with initially 35 treatment centres supplied by two manufacturing sites. The COGS for a single (although highly efficacious) treatment is high, estimated at $200,000, and the price has been set at $475,000 [4]. Real-world outcomes will be closely scrutinised: one severe side effect, cytokine release syndrome (CRS), has plagued trials sponsored by both Juno and Cellectis.

Outcomes-based pricing – the solution?

Accordingly, the Kymriah approval was not only accompanied by FDA expansion of the Actemra (Roche) approval to include CAR-T associated CRS, by a specialised risk mitigation strategy, and by post-marketing observational study requirements, but also by details of a collaboration between Novartis and the Centers for Medicare & Medicaid Services (CMS) for a new outcomes-based pricing strategy. Payment of the $475,000 will only be due if there is a positive response to Kymriah within a month of treatment [5]. What 'response' entails has not been disclosed, although CRS in trials has occurred within days of administration [6].

OXB royalties

Royalty to OXB presumed to be around 4%

Following the approval, we have adjusted our model of OXB's royalty stream from Kymriah sales in two ways:

- **Price:** decreased by $125,000 per treatment (our estimate was $600,000)
- **Volume:** in part to reflect the commercial pricing initiative, peak sales have been increased by lifting market penetration by 5% in both the US and EU, for both the B-ALL and DLBCL indications

[2] Kite Pharma 10-Q SEC filing (2016)
[3] www.gov.uk/government/news/sir-john-bell-to-unveil-industry-led-proposals-to-build-uks-status-as-world-leader-in-life-sciences
[4] www.biopharmadive.com/news/the-next-challenge-for-car-t-large-scale-production/408395/
[5] www.novartis.com/news/media-releases/novartis-receives-first-ever-fda-approval-car-t-cell-therapy-kymriahtm-ctl019
[6] www.cellectis.com/en/press/cellectis-reports-clinical-hold-of-ucart123-studies/

Hardman estimates $82m peak royalty income per annum

This has not materially altered the magnitude of royalty forecasts, which remain around $82m per annum at peak. We have not altered any other assumptions (e.g. our royalty rate assumption remains 4%) and there are unknown factors that could have a significant effect on estimates:

Multiple unknown factors could materially alter royalty estimates

- **Market competition:** should other CAR-Ts be approved (e.g. for DLBCL, near term)
- **Market potential:** should there be expansion of Kymriah's label to other indications or to first- or second-line treatment
- **Price:** may be altered for additional indications or in certain jurisdictions
- **Market penetration:** in part depends on the reimbursement environment

OXB valuation update

We have, however, increased our sum-of-parts DCF valuation of OXB:

- **Kymriah approval:** the risk adjustment for the probability of not reaching the market has been removed
- **Royalty payment:** we have brought the early royalty payments forward into 2018, still allowing for peak sales in 2025 (Novartis expects to have all 35 treatment centres running by the end of the year [7])

OXB sum-of-the-parts valuation has increased +37% from 7.5p to 10.3p per share

This resulted in an estimated group enterprise value of £335m (cf. £244m previously) and a risk-adjusted valuation of 10.3p per share (cf. 7.5p previously). Further positive news flow from Novartis on Kymriah – approval in other jurisdictions or indications – would increase the valuation, suggesting that this share price level is likely to be reached relatively quickly. The book value of the GMP manufacturing and HQ fixed assets, £27.5m, is assumed to be inherent in the EV/sales multiple.

Summary valuation

Oxford BioMedica	Previous (£m)	New (£m)
Bioprocessing (EV/sales 4.0x)	188	188
Novartis royalty stream	46	137
Proprietary portfolio – risk adjusted	10	10
Group Enterprise Value	**244**	**335**
Net cash/(debt)	-19	-17
Market capitalisation	225	319
Shares in issue (m)	3,008	3,104
Valuation/share (p)	**7.5**	**10.3**

Source: Hardman & Co Life Sciences Research

[7] https://uk.reuters.com/article/us-novartis-fda/novartis-gene-therapy-approval-signals-new-cancer-treatment-era-idUKKCN1BA1ZY

Forecasts

Profit and Loss

- **Licensing income:** Up-front $10m/£7.7m from Novartis has been included in other income – spread over three years from 5th July 2017
- **Net interest:** Interest payable has been reduced by $0.55m/£0.4m in 2017 to reflect the six-month benefit from the new Oaktree loan facility. A further, similar, reduction has been included in fiscal 2018

Profit & Loss account

Year end Dec (£m)	2014	2015	2016	2017E	2018E	2019E
GBP:EUR	1.24	1.38	1.18	1.18	1.18	1.18
GBP:USD	1.65	1.53	1.35	1.35	1.35	1.35
Bioprocessing + PD*	7.80	14.44	23.98	35.06	42.42	48.56
Additional income	6.37	3.54	3.80	3.78	4.58	5.43
Group revenues	**13.62**	**15.91**	**27.78**	**38.80**	**47.00**	**54.00**
COGS	-4.42	-5.84	-11.84	-16.50	-19.30	-20.81
Gross profit	**9.20**	**10.07**	**15.94**	**22.30**	**27.70**	**33.19**
Gross margin (%)	67.6%	63.3%	57.4%	57.5%	58.9%	61.5%
SG&A	-3.74	-6.01	-5.09	-5.00	-5.26	-5.50
R&D	-16.99	-20.27	-24.30	-22.10	-23.35	-23.31
EBITDA	**-9.29**	**-11.73**	**-6.78**	**2.43**	**7.60**	**12.88**
Depreciation	-0.70	-1.26	-3.34	-4.10	-4.10	-4.10
Amortisation	-0.40	-0.36	-0.34	-0.34	-0.34	-0.34
Other income	1.13	2.86	3.00	2.78	4.07	4.07
Underlying EBIT	**-10.39**	**-13.35**	**-10.45**	**-2.01**	**3.16**	**8.45**
EBIT margin (%)	76.3%	83.9%	37.6%	-5.2%	6.7%	15.6%
Share based costs	-0.22	-0.73	-0.87	-0.97	-1.07	-1.17
Exceptional items	0.00	0.00	0.00	0.00	0.00	0.00
Stat. Operating profit	**-10.61**	**-14.08**	**-11.32**	**-2.97**	**2.10**	**7.28**
Net interest	-0.19	-2.90	-5.81	-4.68	-4.28	-4.27
Forex gain/loss	0.00	0.00	-3.18	0.00	0.00	0.00
Pre-tax profit	**-10.58**	**-16.25**	**-19.44**	**-6.69**	**-1.12**	**4.18**
Exceptional items	0.00	0.00	0.00	0.00	0.00	0.00
Reported pre-tax	-10.80	-16.98	-20.31	-7.66	-2.18	3.01
Tax payable/credit	2.14	3.96	3.67	4.42	4.67	4.66
Underlying net income	**-8.44**	**-12.29**	**-15.78**	**-2.27**	**3.55**	**8.84**
Statutory net income	-8.66	-13.02	-16.64	-3.24	2.49	7.67
Ordinary shares (m)						
Period-end	2,566	2,574	3,088	3,104	3,105	3,106
Weighted average	2,019	2,570	2,780	3,094	3,104	3,105
Fully diluted	2,108	2,670	2,909	3,351	3,361	3,363
U/lying Basic EPS (p)	**-0.42**	**-0.48**	**-0.57**	**-0.07**	**0.11**	**0.28**
Stat. Basic EPS (p)	-0.43	-0.51	-0.60	-0.10	0.08	0.25
U/l Fully-diluted EPS (p)	**-0.40**	**-0.46**	**-0.54**	**-0.07**	**0.11**	**0.26**
Stat. Fully-diluted EPS (p)	-0.41	-0.49	-0.57	-0.10	0.07	0.23
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

**PD: Process Development*

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Novartis up-front payment:** accrued and included in the P&L under other income, this drops through to cashflow, benefiting the period-end cash balance
- **Loan facilities:** There is no material change in the long-term debt, with little difference between the new $55m Oaktree facilities being used to repay the $50m loan from Oberland plus true-up payments
- **Ring-fenced cash:** Freeing up the $10m ring-fenced cash does not make any difference to the total cash held in the balance sheet at the period end
- **No changes to forecasts:** No changes have been made to our financial forecasts – only the valuation has changed to reflect the FDA approval. In our interim results update we included the £7.7m up-front from Novartis, which improved the net debt position at the end of fiscal 2017 from -£25.0m to -£16.9m, and also flowed through to subsequent years

Balance sheet

@31st December (£m)	2014	2015	2016	2017E	2018E	2019E
Shareholders' funds	23.04	10.89	12.62	9.48	12.06	19.84
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00	0.00
Total equity	23.04	10.89	12.62	9.48	12.06	19.84
Share capital	25.66	25.74	30.88	30.88	30.88	30.88
Reserves	-2.62	-14.85	-18.26	-21.40	-18.81	-11.04
Provisions/liabilities	3.46	4.42	3.94	0.00	0.00	0.00
Deferred tax	0.00	0.00	0.00	0.00	0.00	0.00
Long-term loans	1.00	27.26	34.39	37.12	39.85	42.58
Short-term debt	0.00	0.00	0.00	0.00	0.00	0.00
less: Cash	14.20	9.36	15.34	20.46	25.74	36.37
less: Deposits	0.00	0.00	0.00	0.00	0.00	0.00
Invested capital	**13.31**	**33.21**	**34.95**	**26.13**	**26.18**	**26.05**
Fixed assets	8.94	24.40	27.51	25.35	23.09	21.05
Intangible assets	2.11	1.74	1.33	1.00	0.66	0.33
Inventories	1.41	2.71	2.20	3.22	3.90	4.46
Trade debtors	*3.62*	*7.37*	*5.43*	*2.36*	*2.84*	*3.40*
Other debtors	*1.53*	*3.56*	*1.47*	*4.94*	*4.94*	*4.94*
Tax liability/credit	*-2.79*	*-3.59*	*-2.51*	*3.67*	*4.42*	*4.67*
Trade creditors	*2.00*	*2.72*	*3.00*	*-1.58*	*-1.58*	*-1.58*
Other creditors	*-3.52*	*-5.70*	*-3.49*	*-12.82*	*-12.09*	*-11.22*
Debtors less creditors	0.85	4.37	3.90	-3.43	-1.47	0.22
Invested capital	**13.31**	**33.21**	**34.95**	**26.13**	**26.18**	**26.05**
Net cash/(debt)	**13.20**	**-17.90**	**-19.05**	**-16.66**	**-14.11**	**-6.21**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Novartis up-front:** Received in July 2017 which, together with the R&D tax credits, suggests that OXB will be modestly cash generative in fiscal 2017
- **Depreciation:** The depreciation rate has risen following completion during 2016 of the new manufacturing facilities in Oxford
- **Working capital:** Given that much of OXB's work is on a fee-for service basis, there is no major working capital requirement for the group. However, preparation for the commercialisation of Kymriah has required increased short-term working capital in 1H'17, offset, more recently, by the freeing up of the $10m ring-fenced cash under the Oberland loan terms
- **Net interest:** The actual cash paid on loan interest is lower than the charge to the P&L account because there is no cash payment associated with the amortisation charge accruing
- **Cap-ex:** Completion of Windrush Court facilities is expected to see capital expenditure fall to maintenance levels, estimated at around £2m per annum

Cashflow

Year end Dec (£m)	2014	2015	2016	2017E	2018E	2019E
Underlying EBIT	-10.39	-13.35	-10.45	-2.01	3.16	8.45
Depreciation	0.70	1.26	3.34	4.10	4.10	4.10
Amortisation	0.40	0.36	0.34	0.34	0.34	0.34
Inventories	*-0.73*	*-1.30*	*0.50*	*-1.02*	*-0.68*	*-0.56*
Receivables	*-2.56*	*-5.78*	*4.03*	*-0.39*	*-0.47*	*-0.57*
Payables	*3.37*	*2.98*	*-3.28*	*0.00*	*0.00*	*0.00*
Change in working capital	0.08	-4.09	1.25	-1.41	-1.15	-1.13
Exceptionals/provisions	1.65	0.95	-0.75	5.65	-0.75	-0.75
Disposals	0.00	0.00	0.00	0.00	0.00	0.00
Other	0.13	0.00	-0.90	0.00	0.00	0.00
Company op cashflow	**-7.43**	**-14.87**	**-5.93**	**5.25**	**4.55**	**9.87**
Net interest	-0.19	-1.46	-3.21	-4.68	-4.68	-4.68
Tax paid/received	1.64	3.24	4.08	3.67	4.42	4.67
Operational cashflow	-5.98	-13.08	-5.06	4.24	4.29	9.86
Capital expenditure	-5.58	-16.72	-6.46	-1.94	-1.84	-2.06
Sale of fixed assets	0.00	0.00	0.00	0.00	0.00	0.00
Free cashflow	**-11.56**	**-29.80**	**-11.52**	**2.30**	**2.45**	**7.80**
Dividends	0.00	0.00	0.00	0.00	0.00	0.00
Acquisitions	0.00	0.00	0.00	0.00	0.00	0.00
Disposals	0.00	0.00	0.00	0.00	0.00	0.00
Other investments	0.00	0.00	0.00	0.00	0.00	0.00
Cashflow after invests.	**-11.56**	**-29.80**	**-11.52**	**2.30**	**2.45**	**7.80**
Share repurchases	-0.23	0.00	0.00	0.00	0.00	0.00
Share issues	22.81	0.14	17.50	0.10	0.10	0.10
Currency effect	0.00	-1.44	-7.13	0.00	0.00	0.00
Loans/cash acquired	0.00	0.00	0.00	0.00	0.00	0.00
Change in net debt	**11.03**	**-31.10**	**-1.15**	**2.40**	**2.55**	**7.90**
Hardman FCF/share (p)	-0.30	-0.51	-0.18	0.14	0.14	0.32
Opening net cash	2.17	13.20	-17.90	-19.05	-16.66	-14.11
Closing net cash	**13.20**	**-17.90**	**-19.05**	**-16.65**	**-14.11**	**-6.21**

Source: Hardman & Co Life Sciences Research

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