EDISON

Oxford BioMedica

Corporate update

Validation achieved, growth expected

Pharma & biotech

Following the commercial launch in 2017 of partner Novartis's CAR-T Kymriah (in r/r paediatric ALL), Oxford BioMedica (OXB) has become one of a handful of regulatory approved gene and cell therapy manufacturers worldwide. This validation of its capabilities was most recently demonstrated in signing the £100m+ collaboration with Bioverativ to develop haemophilia gene therapies. We expect OXB to rapidly expand its manufacturing capacity to enable top-line growth. We have reassessed many of our valuation assumptions and now include the partnerships with Immune Design, Orchard and Bioverativ. Moreover, internal asset, OXB-102, will start a Phase II trial shortly. We value OXB at £513m (15.6p/share).

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/16	27.8	(20.0)	(0.59)	0.0	N/A	N/A
12/17	37.6	(11.5)	(0.28)	0.0	N/A	N/A
12/18e	54.6	(6.9)	(0.15)	0.0	N/A	N/A
12/19e	59.6	(9.1)	(0.22)	0.0	N/A	N/A

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

Top-line growth the focus as market expands

The global cell and gene therapy market is expanding rapidly as evidenced by the first approvals for both ex vivo (chimeric antigen receptor T-cells [CAR-Ts] Kymriah and Yescarta) and in vivo (Strimvelis for ADA-SCID and Luxturna for RPE65 inherited retinal disease) gene therapy products. As a leading supplier of lentiviral products for gene therapy, OXB is well placed to benefit and recently completed a net £19.3m capital raise to fund the construction of additional manufacturing capacity. We expect the new facilities to be commercially operational by end 2019.

Partnerships drive near-term value

As a supplier of LentiVector for Novartis's Kymriah, OXB's near-term revenues are driven by both the supply of lentiviruses and royalties on Kymriah's escalating sales. Kymriah is now approved in the US for DLBCL, a much larger indication then pALL, for which it is already approved in the US. EU approval for both is expected by year end. Partnered assets OTL-101 from Orchard Therapeutics and CMB305 from Immune Design are nearing key inflection points, with a BLA expected to be submitted in H218 and a Phase III clinical trial in synovial sarcoma starting shortly, respectively. We anticipate significant near-term revenue from the Bioverativ deal.

Valuation: £513m or 15.6p/share

Our increased valuation of OXB is £513m vs £284m. The major source of uplift reflects the inclusion of Bioverativ, Immune Design and Orchard Therapeutics in our valuation. We now model a second CAR-T in the Novartis collaboration and have updated our assumptions for all partnerships and internal assets to reflect changes in the gene and cell therapy sector. Our core drivers remain OXB's partnerships, which represent 8.9p of our total value, comprising development and bioprocessing revenue, milestones and royalties. Additionally, we have rolled forward our model, updated for net debt and now include a terminal value.

10 May 2018

Price	**14.10p**
Market cap	**£463m**

Net debt (£m) at end December 2017 (excluding March 2018 £20.5m gross capital raise)	22.5
Shares in issue	3,284.3m
Free float	83%
Code	OXB
Primary exchange	LSE
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	28.7	36.9	196.2
Rel (local)	20.9	26.9	183.6
52-week high/low		14.1p	4.8p

Business description

Oxford BioMedica's (OXB) LentiVector technology underpins the company's strategy. OXB generates significant revenue from partners that utilise its technology, notably Novartis, Bioverativ, Orchard Therapeutics and Immune Design. OXB is in partnering discussions about internally developed assets. OXB-102 will start a Phase II shortly.

Next events

OXB-102 Phase II trial start	Mid-2018
EU DLBCL/pALL Kymriah approval	H218
OTL-101 BLA submitted	H218

Analysts

Dr Daniel Wilkinson +44 (0)20 3077 5734

Dr Susie Jana +44 (0)20 3077 5700

healthcare@edisongroup.com

Edison profile page

Investment summary

Company description: Lentiviruses have arrived

Oxford BioMedica (OXB) is a UK biopharmaceutical company specialising in the development of gene and cell therapies. Its proprietary LentiVector gene delivery system uses lentiviral-derived vectors to place genetic material into target cells. As of 31 December 2017 OXB has 321 employees, which is expected to increase dramatically in the next 12-18 months as the company expands to meet increasing global demand for its technology. OXB currently has multiple partnerships, notably with Novartis, Bioverativ, Orchard Therapeutics, Immune Design, Sanofi and Green Cross LabCell. It has a range of internal assets in development, four of which are a priority to be either spun out or out-licensed, particularly OXB-102 in Parkinson's disease, in which OXB is planning to initiate a Phase II clinical trial to increase its value proposition before out-licensing. OXB recently raised net £19.3m, which will be used it its entirety for the creation of new manufacturing capacity. We expect these new facilities to be commercially operational by the end of 2019.

Valuation: £513m or 15.6p/share

We value OXB at £513m or 15.6p/share vs £284m (9.2p/share) previously. This is based on a risk-adjusted NPV of partnered products with Novartis (Kymriah and an undisclosed second CAR-T: 5.8p/share), Orchard Therapeutics (OTL-101 and OTL-201: 0.3p/share), Immune Design (CM305: 0.9p/share), Bioverativ (Factor VIII and Factor IX: 1.3p/share), Sanofi (SAR422459 and SAR421869: 0.6p/share) and internal assets OXB-102 (Parkinson's disease: 1.9p/share), OXB-201 (wet AMD: 0.9p/share), OXB-202 (corneal graft rejection: 0.8p/share) and OXB-302 (cancer: 0.1p/share). In all partnerships except with Sanofi, we value royalty, milestone and bioprocessing (manufacturing) revenues; with Sanofi we only value potential future royalties and milestones. We forecast that all internal assets are out-licensed post Phase II data. We value all partnerships out to 2040 and, due to an expanding and evolving long-term revenue stream, we now include a terminal value (10% discount rate, 1% growth) for OXB, which contributes 3.3p/share to our valuation.

Sensitivities: Operational risks as growth continues

While Oxford BioMedica's partnership model minimises many of the usual biotech and drug development risks, it is still susceptible to clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. The key short-term sensitivities for OXB relate to crystallising value from the early-stage pipeline, the reliance on Novartis for revenue and manufacturing capacity constraints. Additionally, OXB's current rapid growth in terms of both employees and facilities brings with it operational risks including, but not limited to increased costs, hiring shortfalls or failures, loss of company culture, company structure failures, cash flow limitations and implementation failures of the new manufacturing facilities.

Financials: Double-digit revenue growth continues

Gross income grew 28% to £39.4m in 2017, predominately as a result of bioprocessing revenues for both Novartis and Orchard Therapeutics. R&D costs decreased y-o-y (£21.6m vs £24.3m) but were offset by increased COGS (£18.4m vs £11.8m)) and admin costs (£7.3 vs £6.0m). The operating loss decreased to £5.7m vs £11.3m in the previous period. EPS loss decreased to 0.29p vs 0.60p. Gross cash as of 31 December 2017 was £14.3m (vs £15.3m as of 31 December 2016). Post period end in March 2018, OXB raised net £19.3m, which will enable the production of new manufacturing facilities. Debt increased to £36.8m (vs £34.4m), which consists wholly of the loan from Oaktree Capital Management. In June 2017, OXB redeemed its $50m Oberland Capital Healthcare loan facility by creating a new $55m debt facility with Oaktree.

A world-class provider of lentiviral vectors

The commercial launch of CAR-Ts, Kymriah and Yescarta, and in vivo gene products, Strimvelis and Luxturna, has boosted the gene and cell therapy sector, in turn driving significant investment. However, while many companies have adequate R&D facilities, OXB is one of a few globally that can manufacture lentiviral vectors on the commercial scale needed for use in these therapies. This manufacturing capability, coupled with both extensive IP and know-how, makes OXB an attractive partner for many in the field.

OXB's ongoing value comes from a mixture of sources. To integrate its technology into partners' products is a significant undertaking and, as such, OXB receives process development revenue. Once a product has been developed, OXB will provide this through the commercial supply of vectors (bioprocessing revenue). The quantity needed can vary significantly depending on the indication, with both patient population and disease variables having an effect. For example, in haemophilia A and B, large patient populations exist in addition to the need for significant per-patient dosing (a significant amount of vector is required per patient due to having to genetically modify the liver, a large organ). As such, in these large indications, we forecast significant manufacturing revenues. In the long term we anticipate that OXB's royalty revenue will outstrip its manufacturing revenue, particularly in indications/partnerships where OXB's latest IP has been implemented.

OXB's partnered and internal programmes centre on its proprietary LentiVector technology platform, which is a flexible and efficient lentiviral gene delivery system that replaces/corrects a faulty gene or encodes for the expression of a therapeutic protein. This can be done either in the body (in vivo) or outside it (ex vivo).

- In the in vivo setting it can be used as a potential one-time treatment that addresses a patient's genetic failings. The approach is promising, particularly in ophthalmic and neurological indications. OXB's most advanced internal asset (OXB-102) is aiming to provide a 'one-and-done' treatment that encodes for key enzymes that will benefit Parkinson's patients.
- In the ex vivo setting, lentiviral vectors can be used to modify a patient's cells to express therapeutic proteins. One of the most well-known utilisations of this technology is in CAR-Ts like Kymriah (Novartis) that are approved to treat certain blood cancers. In the case of Kymriah, this involves the extraction of T-cells from a patient and modifying them to express cancer-hunting components by using OXB's LentiVector technology. In certain cancers, this approach has produced remarkable responses in patients who had no remaining treatment options.

The ability to utilise lentiviral vectors in an array of indications coupled with a growing manufacturing capacity makes OXB an ideal partner for many companies operating in the gene therapy space. Evidence of this comes from the multiple partners OXB currently has including Novartis, Bioverativ, Orchard Therapeutics, Immune Design, Sanofi and Green Cross Lab Cell.

We anticipate in the near term, OXB will capitalise on the validation its platform has received on the back of Kymriah's approval in the US in paediatric acute lymphoblastic leukaemia (pALL) and diffuse large B-cell lymphoma (DLBLC). We forecast that OXB will focus on growth and look to leverage its manufacturing capabilities, and we expect it to invest aggressively in the short term in both people and facilities to achieve this. In the long term, we forecast a growing multi-source royalty stream for OXB that will contribute alongside bioprocessing (manufacturing) revenue to its growing top line. An overview of OXB's internal and partnered pipeline can be seen In Exhibit 1.

Exhibit 1: OXB product pipeline

Product	Partner	Indication	Status	Notes
OXB proprietary programmes to be spun out or out-licensed				
OXB-102	N/A	Parkinson's disease (CNS)	Phase I/II	To be spun out or out-licensed. Will enter Phase I/II in H218.
OXB-202	N/A	Corneal graft rejection (ophthalmology)	Phase I/II	To be spun out or out-licensed
OXB-302	N/A	Cancer (multiple)	Preclinical	To be spun out or out-licensed
OXB-201	N/A	Wet AMD (ophthalmology)	Phase I/II	To be spun out or out-licensed
LentiVector platform				
Kymriah	Novartis	r/r ALL	US approved. Anticipated EU approval in H218	Process development and bioprocessing revenues in addition to royalties. Launched in US, Novartis recorded Q1 sales of $12m.
Kymriah	Novartis	r/r DLBCL	US approved. Anticipated EU approval in H218	Process development and bioprocessing revenues in addition to royalties
Undisclosed CAR-T	Novartis	Cancer (multiple)	Phase I/II	Process development and bioprocessing revenues in addition to royalties
CMB305	Immune Design	Advanced, relapsed, or metastatic sarcoma	Phase II	Process development and bioprocessing revenues in addition to royalties
OTL-101	Orchard Therapeutics	Adenosine deaminase deficiency (ADA) severe combined immunodeficiency	Phase II/III	Process development and bioprocessing revenues in addition to royalties
OTL-201	Orchard Therapeutics	Sanfilippo A syndrome	Preclinical	Process development and bioprocessing revenues in addition to royalties
Factor VIII	Bioverativ	Haemophilia A	Preclinical	Process development and bioprocessing revenues in addition to royalties
Factor IX	Bioverativ	Haemophilia B	Preclinical	Process development and bioprocessing revenues in addition to royalties
OXB partnered products				
SAR422459	Sanofi	Stargardt disease (ophthalmology)	Phase IIa	Undisclosed development milestones and royalties
SAR421869	Sanofi	Usher syndrome type 1B (ophthalmology)	Phase I/II	Undisclosed development milestones and royalties

Source: Edison Investment Research, Oxford BioMedica

Novartis partnership continues to drive OXB revenue

Kymriah, a CD19 targeting CAR-T, is now approved in the US in adult DLBCL and pALL. Unlike small molecules or antibodies, CAR-Ts are living cells that have to be removed from a patient, genetically engineered and reinfused. This dramatically increases the complexity of the manufacturing process.

CAR-Ts are individual treatments that are personalised to a patient (autologous) by the removal and isolation of their T-cells (leukapheresis), modification of these cells to express the relevant chimeric antigen receptors (CARs) by incubation with a viral vector (OXB's lentiviral vector, in the case of Kymriah), expansion of these cells and then reinfusion into the patient. Chimeric (foreign) antigen receptors in the most current generation of CAR-Ts are single-chain variable fragment antibodies (scFv), commonly murine (mouse) in nature. Combination of a cancer-recognising element with the cell-killing ability of T-cells makes for an effective therapeutic combination.

OXB's lentiviral technology is used to insert genetic material into a patient's isolated T-cells, which enables the cell to make and present cancer targeting receptors (CARs). It is the only supplier to Novartis and, as its technology and manufacturing process was involved in the regulatory application of Kymriah, we believe it is extremely unlikely that Novartis will switch supplier.

To date, revenue from the Novartis collaboration has come predominately from bioprocessing (the sale of vector batches) and development milestones. Now Kymriah is commercially approved, we expect this mix to alter as the royalty stream builds. We forecast that the royalty stream from Kymriah in both pALL and DLBCL will overtake bioprocessing royalty by 2021. We have readjusted some of our valuation assumptions based on market data received to date. In Q118, Novartis stated

Kymriah income of $12m, which was slightly above our initial expectations for Q1 revenue. We have therefore revised our US sales ramp estimates upwards. However, this has been offset by a delayed EU roll-out, which we initially forecast to start in Q118, but is now expected in H218.

With the recent approval in the US of DLBCL, a much larger indication then pALL, Novartis and OXB can realise a significantly larger revenue stream. Competitor Yescarta (Gilead), which was approved for DLBCL patients in October 2017, generated Q1 sales of $40m.

DLBCL approval to demonstrate commercial viability

Following approval of Kymriah in DLBCL, we now have prescribing information to compare with Gilead's Yescarta (Exhibit 2). Comparisons between separate clinical trials should be made with caution as they do not account for variables like differences in patient demographics, data reporting and treatment centres. However, bearing this in mind, comparisons do provide insight. Both products have yet to reach a median overall survival cut-off, which is remarkable given that the patients are relapsed or refractory to current treatments. Median follow-up currently remains less than a year for both treatments. 51% of patients were complete responders (those who have no detectable cancer) with Yescarta compared to 32% for Kymriah, while 18% of patients experienced a partial response with Kymriah compared to 21% with Yescarta. These differences could be associated with variances in the make-up of the different CAR-Ts, notably in the co-stimulatory domains (see Kymriah: Not a classical drug below). Yescarta uses a CD28 co-stimulatory domain, while Kymriah uses 4-1BB. One theory is that CD28 leads to quicker CAR-T cell proliferation than 4-1BB but the effect tends to be short lived, while 4-1BB has less immediate potency in generating cell expansion, but supports longer-term persistence better. Yescarta might therefore generate more patients who respond, but Kymriah patients who respond may achieve longer-lasting responses. We await longer-term data to provide clarity on these questions.

Exhibit 2: Comparison of prescribing information of Kymriah versus Yescarta in DLBCL

	Kymriah (DLBCL) – JULIET study	Yescarta (DLBCL)- ZUMA 1
Overall response rate (CR+ PR)	50% (n=34/68, 95% CI: 37.6% -62.4%)	72% (n=73/101, 95% CI: 62% -81%)
Complete remission rate (CR)	32% (n=22/68, 95% CI: 21.5% -44.8%)	51% (n=52/101, 95% CI: 41% -62%)
Partial remission rate (PR)	18% (n=12/68, 95% CI: 9.5% -28.8%)	21% (n=21/101, 95% CI: 13% -30%)
Median overall duration of response (DOR) (months)	NE (n=34, 95% CI: 5.1, NE). Range: 0.03-11.3 months. Median follow-up: 9.4 months (95% CI: 7.9, 10.8).	9.2 months (n=73, 95% CI: 5.4, NE). Range: 0.03-14.4 months. Median follow-up: 7.9 months.
Median DOR if best response is CR (months)	NE (n=22, 95% CI: 10.0, NE). Range: 1.5-11.3 months.	NE (n=73, 95% CI: 8.1, NE). Range: 0.4-14.4 months.
Median DOR if best response is PR (months)	3.4 months (n=12, 95% CI: 1.0, NE). Range: 0.03-11.3 months.	2.1 months (n=12, 95% CI: 1.3, 5.3). Range: 0.03-8.4 months.

Source: Kymriah and Yescarta prescribing information. Note: NE = not estimable at time of last data cut-off.

Kymriah: Not a classical drug

Kymriah is a living treatment, which is both incredibly complex to make and with completely different characteristics from classical drugs like antibodies or small molecules. Vectors are a key component in the creation of the currently commercially available CAR-Ts. In the case of Kymriah, the lentiviral vector encodes for the anti-CD19 chimeric antigen receptor, also called B-lymphocyte antigen, a type I transmembrane glycoprotein. CD19 (cluster of differentiation 19) is an ideal target for lymphomas and leukaemias due to its expression on B-cells and its absence in other cell lines. The natural role of CD19 is to enable immature B-cells to recognise new antigens (infections) and develop antibodies against them. As CD19 is expressed on the surface of both healthy and cancerous B-cells, targeting it causes the destruction of the whole cell lineage, resulting in B-cell aplasia (over time normal B-cell recovery is possible). This can make patients vulnerable to new infections until a T-cell response develops. However, this can be clinically solved by regular gamma globulin injections.

In first-generation CAR cells, CD3ζ was the only stimulatory component. While this proved effective in inducing cell death in a bound target, persistence and generation of a sustained T-cell response was elusive. In 1998, Krause et al (1998) showed that adding CD28 to scFvs gave better efficacy and persistence. Accordingly, second-generation CAR-T therapies use dual stimulation of the T-cell to obtain sustained and effective tumour cell killing. CD28 co-stimulation was the first CD protein to be used and is utilised in Kite Pharma's Axi-cel (Yescarta). Since then, 4-1BB co-stimulation, originally a type II transmembrane protein, has been developed. 4-1BB is used in Kymriah and one theory is that CD28 generates quicker CAR-T cell proliferation than 4-1BB but that the effect tends to be short lived, while 4-1BB has less immediate potency in generating cell expansion but better supports longer-term persistence. However, this currently remains a theory and long-term clinical data are needed to prove this theory.

Novartis valuation assumptions

For the Novartis partnership we have modelled the opportunities for Kymriah in pALL and DLBCL in addition to now valuing the second undisclosed CAR-T. For the purpose of our valuation we have assumed that the second undisclosed CAR-T is Novartis's most advanced second clinical candidate, MTV273, a BCMA targeting CAR-T for use in patients with multiple myeloma (MM). We forecast that OXB will sell vector batches to Novartis for $1.5m per batch, with peak gross margins of 30%.

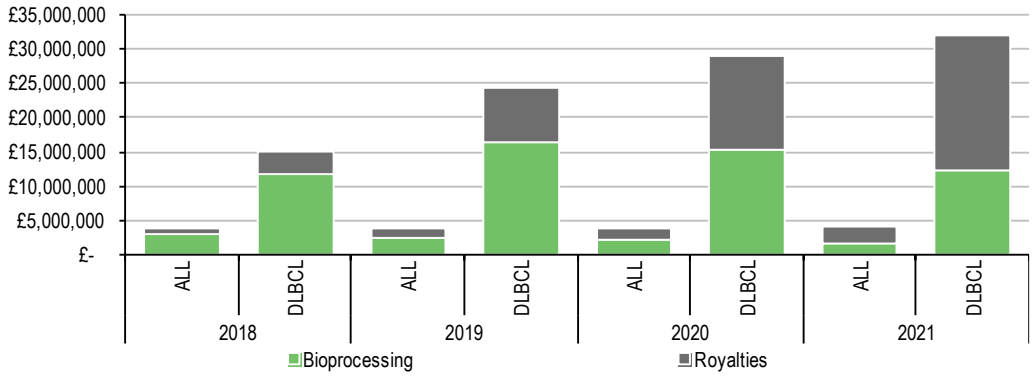
Our valuation assumptions are:

- Kymriah in pALL:
  - US and EU5 population.
  - 25% of population below 20 years of age.
  - 0.004% incidence of ALL, 15% of these fail first- and second-line therapies.
  - At peak we anticipate a maximum patient population of approximately 1,000 patients in both the EU and US.
  - Kymriah is first to market and for the foreseeable future the only CAR-T available in this indication. As such we anticipate a 50% peak market penetration.
  - We assume a price of $475,000 in the US, based on information from Novartis. In the EU, we assume a 20% discount.
  - We assume a peak royalty of 2%.
  - Kymriah is approved in the US, with an EU approval expected by year end.
- Kymriah in DLBCL:
  - US and EU5 population.
  - 0.02% incidence of non-Hodgkin's lymphoma, 48% have DLBCL, 35% of these fail first- and second-line therapies.
  - At peak we anticipate a maximum patient population of approximately 20,000 patients.
  - Kymriah is second to market and faces significant completion from Yescarta. As such we anticipate a 30% peak market penetration. This peak number will depend on the evolving dataset of the comparable long-term efficacy of both approved CAR-Ts. We also note Celgene's CAR-T JCAR017, which is expected to be launched in 2019/20.
  - We assume a price of $475,000 in the US, based on information from Novartis. In the EU, we assume a 20% discount.
  - We assume a peak royalty of 2%.
  - Kymriah is approved in the US, with an EU approval expected by year end.
- Second undisclosed CAR-T, which we assume is MTV273 in MM:

- US and EU5 population.
- 0.009% incidence of MM, 50% of these fail first- and second-line therapies.
- At peak we anticipate a maximum patient population of approximately 30,000 patients in both the EU and US.
- MTV273 faces significant completion in MM as multiple CAR-T and TCR products are in development, notably Bluebird's bb2121, which could be launched in 2019. We forecast a 25% peak market penetration.
- We assume a price of $475,000 in the US, based on information from Novartis. In the EU, we assume a 20% discount.
- We assume a peak royalty of 2%.
- We forecast that only a Phase II trial will be needed for approval and that there would be an accelerated approval process for MTV273. We forecast a launch in both EU and US in 2022.

We forecast that manufacturing revenue will decrease over time as OXB's vector manufacturing achieves higher yields. Our near-term revenue split in both pALL and DLBCL is shown in Exhibit 3.

Exhibit 3: Comparison of ALL and DLBCL bioprocessing and royalty revenues



Source: Edison Investment Research

Bioverativ

In March 2018, OXB signed a partnership deal with Bioverativ to develop in vivo gene therapies for haemophilia A (Factor VIII deficiency) and haemophilia B (Factor IX deficiency). OXB was paid $5m on the closure of the deal and is entitled to up to $100m in revenue from product development, regulatory and sales milestones, in addition to undisclosed royalties. The collaboration gives Bioverativ a licence to OXB's LentiVector technology and manufacturing capabilities. However, like the original Novartis deal in 2014, the current deal does not cover a clinical supply agreement, and we assume that the majority of £100m in potential future revenue is weighted towards product development. We forecast that the majority of this revenue could be realised over the next five years. We note that Sanofi has acquired Bioverativ for $11.6bn. According to OXB management, the buyout will have no near-term impact on OXB's and Bioverativ's partnership.

Haemophilia A and B are indications with significant patient populations. Haemophilia A is approximately four times as common as B and is estimated to occur in approximately one in every 5,000 male births. Worldwide incidence is currently estimated to be approximately 400,000 cases. The gene therapies that OXB and Bioverativ are developing would encode for either Factor VIII (if addressing haemophilia A) or Factor IX (if addressing haemophilia B). Lentiviral vectors that carry the appropriate genes would be injected into a patient either systemically or directly into the liver. These vectors would then insert these genes into the appropriate cells in the liver, such that they

are able to produce Factor VIII or IX proteins. To address the liver will require huge quantities of vector, as such we anticipate that in order to meet both the large patient numbers and large individual doses, OXB will need to use both bioreactors and its TRiP system. Due to the complexities of delivering gene therapies on this scale, we forecast that OXB is likely to receive a higher royalty rate than it receives from products that need smaller vector quantities, eg Kymriah in pALL or DLBCL.

Currently, patients with haemophilia are treated directly with the missing clotting factors by regular injections. It is a multi-billion dollar market, with sales from key drugs of approximately $8.5bn in 2017 (source: EvaluatePharma).

AAV competition lights the way

Spark Therapeutics and BioMarin currently lead the field in haemophilia gene therapies and both are developing adeno-associated virus (AAV) product candidates. Of the two, the most impressive data so far are from BioMarin.

In December 2017, BioMarin initiated enrolment in a Phase III pivotal study testing its gene therapy, Valoctocogene Roxaparvovec (BMN 270) in haemophilia A patients. The trial is open label and will test two doses of the therapy with a primary endpoint of Factor VIII activity. Secondary endpoints include annualised Factor VIII replacement therapy use rate and annualised bleed rate.

Most recent data for BMN 270 come from a presentation at ASH 2017 of the Phase I/II study. Six patients with severe haemophilia A were dosed at the lowest level. All three patients with the longest follow-up (at week 48) had Factor VIII activity levels that were in or near the normal range. Median and mean values were 49% with the normal range often falling between 50% and 100%, while mild haemophilia is defined as between 5% and 40%. Median annualised bleed and Factor VIII use rates for these patients were zero after week 4.

At the higher dose level even more impressive data were observed. Seven patients were infused and eligible for assessment. Again, all had median annualised bleed and the Factor VIII use rates for these patients were zero after week 4. The median and mean Factor VIII values were more impressive, at 90% and 89% respectively.

While impressive, the data for the AAV vectors are early and questions over long-term efficacy and safety still need to be answered. Product candidates being developed by Bioverativ and OXB could gain significant market share if they are able to improve on the AAV products in development.

Bioverativ valuation assumptions

For the Bioverativ partnership we have modelled the opportunities in haemophilia A and B. We assume OXB receives $80m of the proposed $100m in milestone payments over the next five years as products in both indications are developed. We forecast that OXB sells vector batches to Bioverativ for $1.5m a batch, with peak gross margins of 30%. We assume an incidence of haemophilia A of 0.02% and 0.005% in haemophilia B. In haemophilia A and B, we note approximate maximum patient populations of 135,000 and 35,000 respectively in both the US and EU5. We estimate that both are priced at $350,000 in the US and 20% below this in Europe, with both prices at a discount to current gene therapy products. We assume that gene therapy prices for non-orphan diseases will need to be priced below the current standard to drive appropriate uptake. We also forecast that decreasing COGS and increasing yields will enable this. We believe both could launch in 2025 with accelerated approval after completing Phase II trials. Due to significant competition in the space, both in the form of gene therapies in development and existing treatments, we assume a 20% peak penetration rate. We assume a larger than usual royalty rate of 7%. We believe OXB will likely have to incorporate an array of next-generation technology like TRiP

to be able to reach the required manufacturing yields for these large indications, in turn driving increased royalties.

Orchard Therapeutics: Focus on orphan drug disease

Orchard therapeutics is a UK/US-based private biotechnology company focusing on the treatment of rare diseases with gene therapies. It is well financed, most recently raising $110m in a Series B financing round in December 2017. It has two products in development under its manufacturing agreement with OXB. OTL-101 for ADA severe combined immunodeficiency (SCID) and OTL-201 for Sanfilippo A syndrome are in Phase II and preclinical trials respectively. OXB noted in its FY17 results that Orchard continues to be a major contributor to its bioprocessing revenue.

In March 2018, Orchard Therapeutics announced that it had reached an agreement with GlaxoSmithKline (GSK) to transfer the entirety of the latter's gene therapy programme to it, including Strimvelis, the first approved gene therapy for ADA-SCID. Financial terms were undisclosed, but GSK took a 19.9% equity stake in Orchard and received a seat on the board. OXB's own partnership with GSK remains undisclosed; as such, this raises uncertainty around whether these programmes will continue. We do not currently value the previously partnered GSK assets that are now under Orchard's control and we await further information on which assets will be prioritised.

We note the recent first approval (October 2017) of an orphan gene therapy in the US in the form of Luxturna, which is an AAV-based gene therapy for RPE65 inherited retinal disease. It is priced at $425,000 per eye for a total cost of $850,000.

OTL-101: ADA-SCID orphan disease gene therapy

Orchard Therapeutics is developing a lentivirus-based vector (OTL-101) for ADA-SCID. It is currently in Phase II development. Severe combined immunodeficiency (SCID) due to adenosine deaminase deficiency (ADA-SCID) is a form of SCID where adenosine deaminase is deficient due to mutations in the ADA gene (autosomal recessive inheritance). ADA-SCID accounts for 10-15% of all cases of SCID. Its annual incidence is estimated to be between one in 200,000 and one in one million live births in the US.

Lack or lowering of the enzyme leads to a build-up of adenosine and its metabolites. These cause metabolic abnormalities that are directly toxic to lymphocytes. This rare disease is characterised by severe and recurrent opportunistic infections and can result in early death in infancy.

Approved treatments for ADA-SCID include Leadiant Biosciences' Adagen (pegademase bovine), a modified enzyme used as enzyme replacement therapy by injection (intramuscular). As an enzyme replacement therapy Adagen is highly efficacious but is not curative. Within four to eight weeks of starting the drug, metabolic corrections are achieved in almost all patients. The metabolic corrections are accompanied by improvement in lymphocyte counts and improved immune function within two to six months of starting the drug. Adagen is administered up to once a week.

In May 2016, Strimvelis, a gene therapy for ADA-SCID, was approved. Approval was based on data collected from 18 children, which demonstrated that Strimvelis administration improved patient survival. All 18 children were alive at the time of approval (median follow-up of approximately seven years). Strimvelis is an autologous product (cells taken from the patient and administered back into them after modification with a vector) and patients can only be treated at one site in Italy. It is priced at €594,000. Uptake to date has been slow, with only a handful of patients treated (less than five). We currently assume that Orchard Therapeutics will proceed with development of its own gene therapy for ADA-SCID, OTL-101. We believe the limitations of Strimvelis's cost and administration

will enable Orchard to discontinue it and replace it with OTL-101 once it is commercially approved. Orchard currently plans to submit a biologics licence application for OTL-101 by year end.

OTL-201: Sanfilippo A syndrome

Orchard Therapeutics is developing a lentivirus-based vector (OTL-201) for Sanfilippo A syndrome, which is currently in preclinical development. Sanfilippo A syndrome (also known as mucopolysaccharidosis III or MPS IIIA, a rare autosomal recessive lysosomal storage disease) is a metabolic disorder that arises from deficiency in the gene encoding for the enzyme N-sulphoglucosamine sulphohydrolase (SGSH). Lack of the enzyme leads to a build-up of complex sugars (heparan sulfate) in the brain and causes progressive brain damage from infancy. It primarily affects children as most do not reach adulthood. The disease is incurable and treatment focuses on palliative care of symptoms. Average life expectancy is currently 15-20 years. It is estimated to occur in approximately one in 70,000 births.

Efforts to develop enzyme replacement therapies by Shire, Alexion and BioMarin have all failed to date. One of the most advanced enzyme replacement therapies currently in development is Sobi's SOBI003, a recombinant human sulfamidase product candidate intended to be used as an enzyme replacement therapy. SOBI003 was granted orphan drug designation by the European Commission for MPS IIIA in October 2016 and by the FDA in June 2017. In January this year the FDA accepted its investigational new drug (IND) application, and it can now proceed with human clinical trials.

Gene therapies in development include Abeona Therapeutics' ABO-102, which is in Phase I/II trials, and Lysogene's LYS-SAF302, which has completed a Phase I/II study in four children that demonstrated moderate efficacy in addition to good tolerance. Lysogene is currently preparing a Phase II/III pivotal study for LYS-SAF302. Both these therapies are based on AAVs.

Orchard Therapeutics valuation assumptions

For the Orchard partnership we have modelled the opportunities for both OTL-101 and OTL-202. We forecast that OXB sells vector batches to Orchard for $1.5m a batch, with peak gross margins of 30%. With OTL-101, we assume an incidence of SCID of 0.0001%, of which 15% have ADA. We forecast a total market at peak of approximately 100 patients across the EU5 and US and assume a 50% peak penetration in both markets. We assume similar pricing to Strimvelis and have priced it at $700,000 in the US with a 20% discount in the EU5. We assume a peak royalty rate of 2%.

With OTL-201, we assume an incidence of Sanfilippo syndrome of 0.0014%, of which 50% are type A. We forecast a total market at peak of approximately 5,000 patients across the EU5 and US and a 50% peak penetration in both markets. We assume similar pricing to Strimvelis and have priced it at $700,000 in the US with a 20% discount in the EU5. We assume a peak royalty rate of 2%.

Immune Design: CMB305 for soft tissue sarcomas

Immune Design has two projects in development under its manufacturing agreement with OXB. It plans on initiating a pivotal Phase III trial of CMB305 in synovial sarcoma by mid-2018. Both projects are based on LV305, a product candidate based on Immune Design's ZVex platform, which uses OXB's LentiVector technology to carry the genetic information of a tumour antigen to a patient's dendritic cells (DCs). In theory, these dendritic cells will then initiate an immune response against the tumour antigens and, as a result, a patient's tumour. Immune Design's most advanced programme is CMB305, which is based on a combination of LV305 and an "immune boost" from its GLAAS (GLA adjuvant systems) platform. Glucopyranosyl Lipid A (GLA) binds to the TLR4 receptor on DCs that is believed to activate these cells.

Sarcomas are a rare form of cancer that arise from transformed cells of mesenchymal origin, usually meaning they arise in connective tissue of the bone, muscles, tendons, cartilage, nerves, fat and blood vessels. There are over 50 types of sarcoma (which can generally be grouped into soft tissue sarcoma or osteosarcoma). The incidence of soft tissue sarcoma is approximately five in 100,000 patients.

CMB305 is in multiple clinical trials, the most advanced of which is a fully enrolled Phase II with two types of soft tissue sarcoma (synovial sarcoma or myxoid/round cell liposarcoma). Patients receive CMB305 as a monotherapy or in combination with Roche's PD-L1 checkpoint inhibitor, Tecentriq.

Most recent data come from a Phase I monotherapy trial presented at ASCO 2017 where 25 soft tissue sarcoma patients with recurrent disease were treated with CMB305. They demonstrated a median overall survival (OS) rate of 23.7 months across all soft tissue sarcoma patients. Synovial sarcoma patients had yet to reach median OS at data readout. Immune Design noted that this compared favourably with approved second-line (and third/fourth-line) therapies, where median OS is typically between 12.4 and 13.5 months.

Immune Design valuation assumptions

For the Immune Design partnership we have modelled both the opportunities for CMB305. We forecast that OXB sells vector batches to Immune Design for $1.5m a batch, with peak gross margins of 30%. We assume CMB305 is advanced in soft tissue sarcomas and assume an incidence of 0.005%, 25% of which are refractory/relapsed to current treatments and 70% of these tumours present NY-ESO-1 antigen. We forecast a total peak population across the US and EU5 of approximately 7,000, with a peak penetration of 25%. We assume pricing of $350,000 and a 2% royalty rate.

Strength in manufacturing grows

OXB's know-how in lentiviral vector development and production, in addition to its ability to manufacture commercial quantities of viral vectors, is a unique advantage that few others have globally. At the forefront of this are its manufacturing facilities and techniques.

In 2017, OXB began transitioning much of its internal and partnered work to next-generation 200l bioreactors and away from its labour-intensive cell line manufacturing. Bioreactors bring multiple benefits including dramatically increased capacity, as well as reduced labour and cost of goods. All new partnerships now start development on bioreactors and all historic partnerships have or will shortly be transitioned over. OXB currently has three independent bioprocessing facilities totalling 1,200m^2, two of which are known to operate bioreactors. In addition to the bioprocessing facilities, OXB has 2,136m^2 of laboratory space at Windrush Court that was completed in 2016. This enabled OXB's R&D facilities to be majorly expanded and upgraded. It brought further capabilities to analytics, quality control and process development. The £26m capacity expansion, which also included the third clean room at Harrow House completed in 2016 and construction of the facilities, took approximately a year.

To be able to maintain its market edge, OXB has decided to invest in further capacity upgrades. In March 2018, it raised net £19.3m, which will be used in its entirety to construct new facilities that include four GMP suites, a fill-and-finish facility and a cold warehouse. The facility will be based in Oxford and consists of approximately 7,800m^2 of space, 4,200 m^2 of which will be initially used for the aforementioned facilities. The remaining space can be used for additional capacity expansion if and when required. In addition to bioreactors, OXB is developing a new system designated Transgene Repression in vector Production (TRiP). TRiP aims to further increase the yield and purity of the bioreactors. This new technology could provide further revenue streams for new

partners interested in using it for product candidates. In our view this technology is of particular importance in indications where large vector quantities are required, eg haemophilia A and B.

Lentiviral vectors: A technology entering its golden age

Lentiviruses like HIV can infect human cells; once inside the cytoplasm of a cell they use their own reverse transcriptase to make DNA from their single-stranded RNA genome. This DNA is then integrated into the genome of the host. Unlike some viral systems, lentiviruses have an ability to infect both mitotic (dividing) and post-mitotic (non-dividing) cells. Post-mitotic cells are unable to be infected by most retroviruses, which give lentiviruses a unique advantage. However, competing technologies exist such as AAVs, which are able to infect non-dividing cells. Post-mitotic cells include neuron and muscle cells that can be found in the brain, heart and skeletal muscle. These cells are key targets for neurological and cardiac diseases.

Lentiviral vectors and viral vectors in general are modified viruses that efficiently infect a target cell but are rendered replication deficient. Replication-deficient viral vectors are essential in preventing infection of a patient with a potentially deadly virus; as such, regulatory requirements covering lentiviral technology are strict, ensuring that generic CMOs and biotech companies entering the field have a high technical barrier to entry. Under FDA rules, for lentiviral vector products to be used in humans, there must be an absence of replication-competent lentivirus. Lentiviral vectors have evolved through multiple generations as they have been modified to become safer and more efficient. The generations are defined by which genes of the lentivirus are retained and how they are packaged. The most recent third-generation vectors removed all accessory genes that aided in virulence and pathogenicity while splitting the remaining genes, which are vital for expression of the transgene across three plasmids.

OXB's lentiviral technology

OXB's lentiviral vectors are based on the equine infectious anaemia virus (EIAV). While the exact modification will depend on the application, most recent developments will be proprietary in nature. However, we assume the current technology is based on a third-generation vector system where the accessory genes are removed and the genome is split among plasmids. Safety is paramount and, like all lentiviral vectors, EIAV-based vectors are made replication deficient. In addition, unlike HIV, EIAV is an equine-based virus and is not pathogenic in humans. OXB has developed the technology for 20 years and the lentiviral platform has been involved in multiple trials that demonstrate its efficacy and safety. For example, OXB-101 (ProSavin) demonstrated benefits in a small 15-patient study for treatment of Parkinson's disease (PD). All patients demonstrated an improvement in baseline after six and 12 months, which was sustained in some patients for four years.

Competing technologies

Competition in gene therapy is increasing and this is exemplified by the choice of virus in viral infection systems. Adenoviruses and AAVs present a major alternative to lentiviral systems. Both can infect non-dividing and dividing cells, but the expression of adenoviruses is transient in nature. Adenoviruses do not integrate into a genome, but the DNA molecule is still transcribed. However, it is not replicated during cell division, which results in limited long-term expression. The body also has an innate immune response to adenoviruses that limits the efficacy of the technology. Common adenovirus infections include tonsillitis, gastroenteritis and conjunctivitis.

While AAVs do not integrate into the host genome, they can potentially have a long-lasting effect similar to that of lentiviruses due to long-term expression that can be achieved by episomal monomeric and concatemeric circles. Uniquely, AAVs demonstrate distinct serotypes that are

specific to certain tissue types; however, lentiviral vectors can be altered to infect either a specific cell type or broader range of cells. While this can be a powerful advantage for AAVs over other viruses as it allows a degree of specific targeting, it can also be a disadvantage as low transduction efficiency can occur if the wrong serotypes are utilised.

OXB's internal pipeline update

OXB has prioritised four internal products that will either be spun out or out-licensed. These are OXB-102 (Parkinson's disease, Phase I/II), OXB-201 (wet AMD,Phase I/II), OXB-202 (corneal graft rejection, Phase I/II) and OXB-302 (cancer, preclinical). We understand that OXB is in active discussions with a number of third parties to out-license or spin out these products. Gene therapies that target neurological or ophthalmological indications remain highly attractive, often due to significant unmet need. In mid-2018, OXB plans to initiate a Phase I/II of OXB-102 in Parkinson's disease that will further increase its attractiveness to partners.

All eyes on OXB-102 as it moves into clinical development

OXB will move OXB-102 into Phase I/II clinical development in the coming months. OXB-102 is a gene-based therapy for PD, which uses the proprietary LentiVector system to deliver genes for three enzymes that help restore dopamine levels in the brain. PD is characterised by progressive loss of dopaminergic neurons in the basal ganglia in the brain, leading to a decline in dopamine levels. Since dopamine plays a critical role in movement and co-ordination, a reduction in its levels leads to the characteristic and progressive features of PD: tremor, slowness of movement and rigidity. This common neurological condition affected 2.25 million people in the US, Japan and the five main EU countries in 2012 (source: GlobalData 2015) and further growth will be driven by an increase in the ageing population. Importantly, many individuals are misdiagnosed or undiagnosed, so the actual prevalence is likely to be higher. The current mainstay of drug treatment is limited to oral therapies such as levodopa (L-dopa), dopamine agonists and monoamine oxidase-B inhibitors, drugs that aim to increase or substitute for dopamine. However, over time the benefits of drug treatment diminish (L-dopa provides symptomatic relief of around three to five years). Deep brain stimulation (DBS) is a surgical technique (FDA approved in 1997) reserved for very advanced PD patients who have unstable L-dopa response. The aim is to stabilise medication fluctuations and effectively control the erratic responses to levodopa or to control the dyskinesias (involuntary movements) that do not improve with adjustments in medication. DBS is not a cure, however, and does not address the progressive nature of PD. There is a significant unmet need for advanced PD patients who are no longer well controlled on L-dopa.

OXB-102 is a more potent (up to five times greater potency in preclinical models) form of original PD drug asset ProSavin/OXB-101, which is delivered locally to the brain striatum. ProSavin genes programme non-dopaminergic cells to produce dopamine and so help redress the balance of this essential neurotransmitter. The first patient in an open-label Phase I/II study using ProSavin was treated over five years ago and, since then, 15 advanced-stage PD patients have completed in four escalating-dose cohorts (1x, 2x, 2x with a new technique, and 5x). There were encouraging results, with positive safety and efficacy data, as measured by improvements in motor function. The four-year follow-up data show that the improvements in motor function relative to baseline seen at six and 12 months have been sustained in the majority of the 15 patients originally treated, on the backdrop of a good safety profile. These observations have led to the development of a more potent version of ProSavin, OXB-102 which, at fivefold the potency, translates in preclinical models to a 10x increase in dopamine production. The rationale is that the more potent construct could lead to longer-term sustained duration of action (five to 10 years) following a single dose and could also have utility at earlier, less advanced stages of PD.

We note that US-based gene therapy company Voyager Therapeutics also has a PD gene therapy in Phase I/II) trials (VY-AADC). Voyager's approach is different to OXB given 1) the use of AAV compared to lentiviral vector; 2) targeting of the enzyme that synthesises dopamine from its precursor L-dopa (AADC – aromatic L-amino acid decarboxylase); and 3) drug delivery into the putamen.

In addition, unlike OXB-102, which directly produces dopamine, VY-AADC has to be taken with oral levodopa that is then converted by the inserted enzymes into dopamine. Clinical efficacy results have been mixed; however, at the more optimal dosing of 900 µl per putamen, encouraging efficacy data have been published.

Internal pipeline valuation assumptions

For the internal pipeline, we value OXB-102 (PD, Phase I/II), OXB-201 (wet AMD, Phase I/II), OXB-202 (corneal graft rejection, Phase I/II) and OXB-302 (cancer, preclinical). We assume all will be out-licensed following Phase I/II data. We forecast that all are priced at $350,000 in the US, with a 20% discount in EU5. We forecast royalties of 15% for all assets and assume that partners will use OXB's manufacturing capabilities to provide vectors at $1.5m a batch, with peak gross margins of 30%. For OXB-102 in PD, we assume an incidence of 0.028% and peak penetration of 5%. For OXB-202, we forecast that 0.01% of the population will need a corneal graft, of which 15% will fail, and a peak penetration of 30%. For OXB-302, no specific cancer has currently been chosen for development, so we have assumed it is used in DLBCL with an incidence of non-Hodgkin's lymphoma of 0.02%, 48% of which have DLBCL, 35% fail first- and second-line treatments, and a peak penetration of 10%. For OXB-201 we assume 2% of the population have age-related macular degeneration (AMD), of which 10% have wet AMD, of which a further 10% can be treated, and a peak penetration of 2.5%.

Sensitivities: Operational risks as growth continues

While OXB's partnership model minimises many of the usual biotech and drug development risks, it is still susceptible to clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. The key short-term sensitivities for OXB relate to crystallising value from the early-stage pipeline, the reliance on Novartis for revenue and manufacturing capacity constraints. Additionally, OXB's current rapid growth in terms of both employees and facilities brings with it operational risks including, but not limited to increased costs, hiring shortfalls or failures, loss of company culture, company structure failures, cash flow limitations and implementation failures of the new manufacturing facilities.

Valuation

We value OXB at £513m or 15.6p/share vs £284m (9.2p/share) previously. This is based on a risk-adjusted NPV of partnered products with Novartis (Kymriah and undisclosed second CAR-T: 5.8p/share), Orchard Therapeutics (OTL-101 and OTL-201: 0.3p/share), Immune Design (CM305: 0.9p/share), Bioverativ (Factor VIII and Factor IX: 1.3p/share), Sanofi (SAR422459 and SAR421869: 0.6p/share) and internal assets OXB-102 (PD: 1.9p/share), OXB-201 (wet AMD: 0.9p/share), OXB-202 (corneal graft rejection: 0.8p/share) and OXB-302 (cancer: 0.1p/share).

In all partnerships except with Sanofi, we value the royalty, milestone and bioprocessing (manufacturing) revenues; with Sanofi we only value potential future royalties and milestones. We forecast that all internal assets are out-licensed post Phase II data. We value all partnerships out to

2040 and, due to an expanding and evolving long-term revenue stream, we now include a terminal value (10% discount rate, 1% growth) for OXB, which contributes 3.3p/share to our valuation.

We forecast that OXB will receive bioprocessing manufacturing revenue from partners throughout the collaborations and not just on commercial launch. We assume our standard 12.5% discount rate for assets, with a 10.0% discount rate for manufacturing revenues.

We note that pricing of gene therapies remains a key sensitivity and, as the market evolves and these dynamics change, we currently assume pricing of $700,000 for rare diseases and $350,000 for more common indications.

Exhibit 4: OXB valuation

	OXB products	Partnered products	Net cash	Terminal value	Total
Total value (£)	£117,693,596	£291,815,464	(£3,235,000)	£107,175,378	£513,449,439
Value per share (p)	3.58	8.89	(0.10)	3.26	15.64

Source: Edison Research Investment

A summary of our assumptions for each product can be seen in Exhibit 5.

Exhibit 5: Summary of Valuation assumptions and metrics

Product/partner/ indication/status	Peak royalties (£m)	Peak manufacturing revenue (£m)	NPV (£m)	rNPV (£m)	Per share (p)	Notes
Kyrmiah/Novartis/ r/r pALL/approved in US - registration in EU	£3	£2	£26	£26	0.80	EU (top 5) & US, 15% paediatric, 0.004% with ALL, 15% failed first- and second-line, 50% peak penetration, $475k US price, 20% discount EU, 2% peak royalty rate. Assume initial price to Novartis of $1.5m per vector batch. Initial COGS of 80%. 100% probability of success. Launch in EU in H218.
Kyrmiah/Novartis/ DLBCL/approved in US - registration in EU	£41	£25	£150	£150	4.55	EU (top 5) & US, 0.02% with NHL, 48% with DLBCL, 35% failed first- and second-line, 30% peak penetration, $475k US price, 20% discount EU, 2% peak royalty rate. Assume initial price to Novartis of $1.5m per vector batch. Initial COGS of 80%. 100% probability of success. Launch in EU in H218.
Second CAR-T/ Novartis/cancers/ Phase I/II	£23	£29	£76	£16	0.49	EU (top 5) & US, 0.009% with MM, 50% are r/r, 25% peak penetration, $475k US price, 20% discount EU, 2% peak royalty rate. Manufacturing initial price to Novartis of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 20% probability of success. Launch in 2022.
CMB305/Immune Design/sarcomas/ Phase II/III	£18	£17	£49	£29	0.89	EU (top 5) & US, 0.005% with soft tissue sarcomas, 25% relapsed/refractory, 70% NY-ESO-1 positive, 25% peak penetration, $350k US price, 20% discount EU, 2% peak royalty rate. Manufacturing initial price to Immune Design of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 60% probability of success. Launch in 2022.
OTL-101/Orchard/ ADA-SCID/Phase II/III	£0	£1	£6	£5	0.15	EU (top 5) & US, 0.0001% with ADA, 15% with SCID variant, 50% peak penetration, $700k US price, 20% discount EU, 2% peak royalty rate. Manufacturing initial price to Orchard of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 60% probability of success. Launch in 2019.
OTL-201/Orchard/ Sanfilippo A syndrome/ preclinical	£11	£9	£28	£6	0.17	EU (top 5) & US, 0.0014% with Sanfilippo, 50% with type A, 50% peak penetration, $700k US price, 20% discount EU, 2% peak royalty rate. Manufacturing initial price to Orchard of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 5% probability of success. Launch in 2025.
Factor VIII/ Bioverativ/ Haemophilia A/ preclinical	£432	£103	£633	£33	1.00	EU (top 5) & US, 0.02% with haemophilia A, 20% peak penetration, $350k US price, 20% discount EU, 7% peak royalty rate. Manufacturing initial price to Bioverativ of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 5% probability of success. Launch in 2025.
Factor IX/ Bioverativ/ Haemophilia B/ preclinical	£108	£26	£164	£9	0.28	EU (top 5) & US, 0.005% with haemophilia B, 20% peak penetration, $350k US price, 20% discount EU, 7% peak royalty rate. Manufacturing initial price to Bioverativ of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 5% probability of success. Launch in EU in 2025.
SAR422459/ Sanofi/Stargardt/ Phase II	£31	N/A	£43	£12	0.36	EU (top 5) & US, 0.01% with Stargardt disease, 20% peak penetration, $350k US price, 20% discount EU, 2% peak royalty rate. 25% probability of success. Launch in EU in 2025.
SAR421869 Sanofi/ Usher/Phase I/II	£25	N/A	£31	£7	0.20	EU (top 5) & US, 0.004% with Usher Syndrome 1B, 20% peak penetration, $700k US price, 20% discount EU, 2% peak royalty rate. 20% probability of success. Launch in EU in 2026.
OXB-102/NA/ PD/Phase I/II	£210	£23	£308	£61	1.87	EU (top 5) & US, 0.028% with PD, 65% treated, 5% peak penetration, $350k US price, 20% discount EU, 15% peak royalty rate. Assume asset is out-licensed post Phase II results, assume OXB retains contract to manufacture LentiVector for partner. Manufacturing initial price to partner of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 20% probability of success. Launch in 2024.
OXB-202/NA/ corneal graft/ Phase I	£104	£12	£128	£25	0.76	EU (top 5) & US, 0.01% need corneal graft, 15% grafts fail, 30% peak penetration, $350k US price, 20% discount EU, 15% peak royalty rate. Assume asset is out-licensed post Phase II results, assume OXB retains contract to manufacture LentiVector for partner. Manufacturing initial price to partner of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 20% probability of success. Launch in 2025.
OXB-302/NA/ cancer /preclinical	£55	£55	£70	£3	0.08	EU (top 5) & US, 0.02% with NHL, 48% with DLBCL, 35% failed first- and second-line, 10% peak penetration, $350k US price, 20% discount EU, 15% peak royalty rate. Assume asset is out-licensed post Phase II results, assume OXB retains contract to manufacture LentiVector for partner. Manufacturing initial price to partner of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 5% probability of success. Launch in 2025.
OXB-201/NA/wet AMD/Phase I/II	£116	£13	£145	£28	0.87	EU (top 5) & US, 2% with AMD, 10% with wet, 10% are treated, 2.5% peak penetration, $350k US price, 20% discount EU, 15% peak royalty rate. Assume asset is out-licensed post Phase II results, assume OXB retains contract to manufacture LentiVector for partner. Manufacturing initial price to partner of $1.5m per vector batch, initial COGS of 80%. Minimal R&D costs per year while in clinical development. 20% probability of success. Launch in 2025.

Source: Edison Investment Research

Financials

OXB reported FY17 gross income of £39.4m, an increase of 28% from £30.8m in FY16. Growth was driven by bioprocessing and commercial development, which saw income grow from £24.0m in FY16 to £32.6m as a result of increased development activities for Novartis and Orchard Therapeutics. Income from licences, incentives and grants stayed flat at £6.8m. We forecast 2018 and 2019 gross income of £54.6m and £59.6m, respectively. Near-term revenue forecasts are driven in core by increasing bioprocessing income from Bioverativ, Orchard Therapeutics and Novartis. Additionally, forecast near-term milestones across partnerships and the forecast Kymriah royalty contribute significantly to our near-term revenue growth.

As to be expected with increased bioprocessing activity, COGS increased year-on-year to £18.4m in FY17 from £11.8m previously. We forecast COGS to increase in FY18 and FY19 in line with anticipated improvements in margin over the coming years as OXB moves projects across to bioreactors and further refines its processes. We forecast FY18 and FY19 COGS of £24.1m and £26.8m, respectively. R&D and bioprocessing costs decreased to £21.6m in FY17 (£24.3m in FY16) as OXB focused on technical improvements and early-stage/preclinical work. We anticipate a small increase in R&D costs over FY18 and FY19 as OXB continues to invest in its technical capabilities and initiates a Phase I/II trial for OXB-102 in PD. We forecast FY18 and FY19 R&D of £23.3m and £24.2m, respectively. Administrative costs increased to £7.3m in FY17 from £6.0m in FY16. We expect this trend to continue as OXB aims to rapidly grow its workforce from 321 employees as at 31 December to approximately 500 by the end of 2019. We forecast FY18 and FY19 administrative costs of £9.8m and £13.3m, respectively.

Operating loss decreased in FY17 to £5.7m (£11.3m in FY16), driven by the aforementioned increased gross income and decreased operating expenses. We forecast an operating loss of £2.6m in FY18 and £4.6m in FY19.

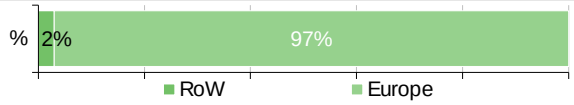
Finance costs decreased to £6.1m in FY17 from £9.0m in FY16. Interest payable increased to £9.4m from £4.9m year-on-year. However, this was offset by a revaluation of liabilities in foreign currencies, which resulted in a positive benefit of £3.3m in FY17 compared with a negative £4.1m in FY16. Debt increased to £36.8m (vs £34.4m) in 2017, which consisted wholly of the loan from Oaktree Capital Management. In June 2017, OXB redeemed its $50m Oberland Capital Healthcare loan facility by creating a new $55m debt facility with Oaktree. The loan is to be paid back by 29 June 2020 and has a 9% interest rate plus US$ Libor (minimum 1%). Subject to achieving certain conditions, the interest rate could drop by 0.25% in both the second and third years.

Gross cash as of 31 December 2017 was £14.3m (vs £15.3m as of 31 December 2016). Post the period end in March 2018, OXB raised net £19.3m, which will enable the production of new manufacturing facilities. As a result, we now forecast significant increases in capex in FY17 and FY18 to £14m and £17.5m, respectively.

Exhibit 6: Financial summary

£'000s	2016	2017	2018e	2019e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	27,776	37,590	54,640	59,621
Cost of Sales	(11,835)	(18,442)	(24,092)	(26,764)
Gross Profit	15,941	19,148	30,547	32,858
R&D	(24,299)	(21,611)	(23,335)	(24,232)
Administrative expenses	(5,957)	(7,276)	(9,823)	(13,261)
Other operating income	3,002	4,071	0	0
EBITDA	(7,638)	(1,293)	2,544	2,129
Depreciation	(3,340)	(4,113)	(5,135)	(6,748)
Operating profit (before amort. and except).	(10,978)	(5,406)	(2,591)	(4,619)
Amortisation	(335)	(262)	(20)	(16)
Exceptionals	0	0	0	1
Operating profit	(11,313)	(5,668)	(2,610)	(4,635)
Net Interest	(8,994)	(6,093)	(4,353)	(4,510)
Other	0	0	0	1
Profit Before Tax (norm)	(19,972)	(11,499)	(6,944)	(9,129)
Profit Before Tax (reported)	(20,307)	(11,761)	(6,963)	(9,145)
Tax	3,666	2,744	2,000	2,000
Profit After Tax (norm)	(16,306)	(8,755)	(4,944)	(7,129)
Profit After Tax (reported)	(16,641)	(9,017)	(4,963)	(7,145)
Average Number of Shares Outstanding (m)	2,778	3,096	3,284	3,284
EPS - normalised (p)	(0.59)	(0.28)	(0.15)	(0.22)
EPS - reported (p)	(0.60)	(0.29)	(0.15)	(0.22)
Dividend per share (p)	0.00	0.00	0.00	0.00
Gross Margin (%)	57.4%	50.9%	55.9%	55.1%
EBITDA Margin (%)	(27.5%)	(3.4%)	4.7%	3.6%
Operating Margin (before GW and except) (%)	(39.5%)	(14.4%)	(4.7%)	(7.7%)
BALANCE SHEET				
Fixed Assets	29,501	28,421	37,266	48,003
Intangible Assets	657	2,954	2,954	2,954
Intangible Assets	1,330	97	77	62
Tangible Assets	27,514	25,370	34,235	44,987
Current Assets	27,441	36,981	45,001	29,582
Stocks	2,202	3,332	3,300	3,666
Debtors	6,904	17,088	17,964	19,602
Cash	15,335	14,329	22,249	4,826
Other	3,000	2,232	1,488	1,488
Current Liabilities	(9,316)	(21,762)	(22,973)	(24,071)
Creditors	(6,003)	(8,690)	(9,901)	(10,999)
Provisions	0	0	0	0
Deferred income	(3,313)	(13,072)	(13,072)	(13,072)
Long Term Liabilities	(35,011)	(37,494)	(38,811)	(40,176)
Long term borrowings	(34,389)	(36,864)	(38,181)	(39,546)
Other long term liabilities	(622)	(630)	(630)	(630)
Net Assets	12,615	6,146	20,483	13,339
CASH FLOW				
Operating Cash Flow	(5,979)	(1,551)	2,911	1,223
Net Interest	(3,258)	(10,800)	(3,074)	(3,183)
Tax	4,131	4,530	2,744	2,000
Capex	(6,458)	(1,969)	(14,000)	(17,500)
Acquisitions/disposals	0	0	0	0
Financing	17,497	385	19,300	0
Dividends	0	0	0	0
Other	47	8,399	38	38
Net Cash Flow	5,980	(1,006)	7,920	(17,422)
Opening net debt/(cash)	17,900	19,054	22,535	15,932
HP finance leases initiated	0	0	0	0
Other	(7,134)	(2,475)	(1,318)	(1,365)
Closing net debt/(cash)	19,054	22,535	15,933	34,720

Source: Company accounts, Edison Investment Research

Contact details	Revenue by geography
Windrush Court Transport Way Oxford OX4 6LT United Kingdom +44 (0) 1865 783 000 www.oxfordbiomedica.co.uk/	

Management team

CEO: John Dawson	CFO: Stuart Paynter
John joined as non-executive director in August 2008 and was appointed CEO in October 2008 (acting CEO from August to October 2008). He previously worked at Cephalon (2008-14), including as CFO and head of BD Europe.	Stuart joined as CFO in August 2017. He previously held multiple roles at Shire Pharmaceuticals including senior director of finance business partnering and global head of internal audit. Prior to joining OXB, he was head of finance business partnering at De La Rue.

Principal shareholders	(%)
Prudential	34.0
Vulpes Investment Management	17.7
Aviva	5.54
Hargreaves Lansdown	4.94

Companies named in this report

Bioverativ, Gilead (GILD), Novartis (NVS), Sanofi (SNY).

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
295 Madison Avenue, 18th Floor
10017, New York
US

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia