EDISON

Oxford BioMedica

Company outlook

Harnessing the CAR-T

Pharma & biotech

Over the past year, Oxford BioMedica's outlook has been transformed. The near term is now geared to the emerging specialist production capabilities, where the expertise in cell- and gene-based medicine is increasingly appreciated. Progress on the development pipeline, notably the RetinoStat programme and, further out, ProSavin/OXB102, would add to our valuation. The longer term should benefit from additional collaborations for the late-stage projects, license income from the patent estate and other pipeline products. Our valuation is £356.1m (13.9p a share), with OXB Solutions valued at £233.5m (9.2p a share) and the pipeline at £122.6m (4.7p a share).

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/13	5.4	(12.4)	(0.8)	0.0	N/A	N/A
12/14	13.6	(10.4)	(0.4)	0.0	N/A	N/A
12/15e	15.1	(10.6)	(0.3)	0.0	N/A	N/A
12/16e	24.0	(8.3)	(0.3)	0.0	N/A	N/A

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

Clinical programmes are progressing as expected

Oxford BioMedica's development portfolio is essentially a bet on the merits of gene therapy in general and the lenti-vector delivery platform in particular. The approach is promising; notably in ophthalmology indications where a single administration could safely provide a sustained (or even permanent) effect. RetinoStat and ProSavin/OXB102 are the most advanced clinical candidates with proof-of-concept trials likely to start in 2016. Other programmes, such as the 5T4-based projects for various cancers, are also approaching value-inflection points.

Manufacturing capabilities are considerable

The commercial manufacture of cell- and gene-based medicines is complex and challenging; plagued by low productivity and poor efficiency, coupled with a lack of batch consistency. Oxford BioMedica's expertise in production and process scale-up, quality control & assurance and regulatory affairs is particularly relevant as a raft of such products approaches the market. Novartis' use of the OXB Solutions expertise for its CTL019 programme is not just a source of revenues (up to $76m over three years), but a powerful external validation.

Valuation: Pipeline and production valued at £356.1m

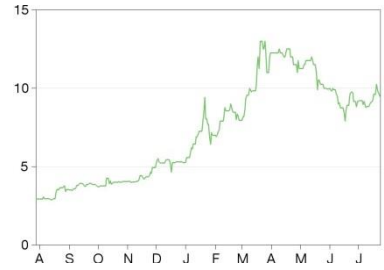
Our valuation of £356.1m (13.9p per share) is based on an rNPV model of the pipeline (£122.6m, 4.7p a share) coupled with a DCF value for the OXB Solutions business (£233.5m, 9.2p a share). We have conservatively not included the value of other less visible assets such as the intellectual property estate, which could provide material upside. Success in terms of clinical progression or timely delivery on the various aspects of the Novartis contract would increase our valuation.

27 July 2015

Price	**9.39p**
Market cap	**£241m**

Net cash (£m) at December 2014	£13.2m
Shares in issue	2,568m
Free float	98%
Code	OXB
Primary exchange	LSE

Share price performance



%	1m	3m	12m
Abs	(3.8)	(18.4)	235.4
Rel (local)	(0.3)	(13.3)	239
52-week high/low		13.0p	2.85p

Business description

Oxford BioMedica has a leading position in gene-based therapy. The lenti-vector technology is wide ranging and underpins much of the development pipeline, notably the ophthalmology projects. The manufacturing expertise, through OXB Solutions, is gaining valuable commercial traction.

Next events

AGM	June 2015
Interim Results	August 2015
Decision on RetinoStat clinical progress	By year-end 2015

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Edison profile page

Oxford BioMedica is a research client of Edison Investment Research Limited

Investment summary

Company description: well placed in an emerging field

Oxford BioMedica is a UK biopharmaceutical company specialising in the development of gene-based medicines, which listed on AIM in 1996 and moved to the full list in 2001. The company has built an R&D pipeline based largely on its proprietary viral delivery technologies. The core technology platform is the proprietary lenti-vector gene delivery system that uses lentiviral-derived vectors to accurately deliver genetic material into target cells. Internal development (and partnering) efforts were initially focused on ProSavin, addressing Parkinson's disease, and expanded into ocular indications, with two programmes partnered with Sanofi.

The investment case has altered materially over the past year, as the specialist expertise in manufacturing commercial quantities of gene- and cell-based pharmaceuticals is expected to generate sizeable revenues. A GMP manufacturing facility (established in 2011 and currently being expanded), known as OXB Solutions, has built a solid reputation for manufacturing commercial quantities of cell- and gene-based medicines. The extension of the Novartis production contract for its high-profile CTL019 CAR-T programme (first signed May 2013 and extended October 2014) has successfully validated the approach.

Equity of c £170m has been raised since inception, with additional receipts of c £88m from partners, principally Sanofi (including the now discontinued TroVax collaboration). Oxford BioMedica currently has c 200 employees.

Valuation: Our models suggest £356.1m (13.9p a share)

Oxford BioMedica's near-term investment case rests on the successful progression of the Novartis process development and manufacturing deal, with the longer-term outlook dependent on continuing development of the product pipeline. Our valuation of £356.1m (13.9p a share) is based on the DCF model of the projected OXB Solutions income streams (£235.5m, 9.2p a share) together with an rNPV model of the R&D pipeline (£122.6m, 4.7p a share). We employ conservative assumptions, excluding other less visible assets such as the intellectual property estate. Progress in the clinical trials and/or the securing of partners/funding for RetinoStat, ProSavin/OXB102 and TroVax represent potential upside.

Financials: Funding in place through to key inflection points

Oxford BioMedica reported net cash of £13.2m at the end of December 2014 and has a $50m loan facility from Oberland Capital. Non-dilutive sources of funding could include upfront payment(s) on the execution of partnering and/or technology-licensing deals. Success with the Novartis manufacturing tie-up (as well as possible new similar production collaborations) could result in operating break-even (assuming no increase in R&D spend) as soon as 2017.

Sensitivities: Delivery on Novartis contract is key driver

Despite the marked risk reduction brought about by the success of the OXB Solutions facilities, Oxford BioMedica's longer-term outlook remains largely a bet on the merits of gene therapy in general, and the lenti-vector delivery platform in particular. The near term will be largely determined by delivery on the Novartis manufacturing deal, which should lead to sizeable revenue streams. The newsflow for key development programmes, notably RetinoStat, OXB102 and 5T4, will also be important value drivers. Clearly much depends also on the nature and timing of future collaborations, which is in turn contingent on continued progress across the clinical portfolio.

Oxford BioMedica: Experts in gene and cell therapy

The investment case has altered materially over the past year. The progress in optimising the commercial production of cell therapies is expected to generate further contracts and underpin the company's cash requirements over the medium-term. Oxford BioMedica is a leading player in gene- and cell-based medicines; with several programmes in the clinic, a proven delivery system and a GMP production facility in place. The main programmes centre on its proprietary lentiviral vector technology platform, which is a flexible and efficient gene-delivery system that can be used to address genetic failings and so potentially transform the outcomes of many devastating diseases. The approach is promising; particularly in ophthalmic indications where delivery is relatively straightforward and a single administration could provide a sustained (or even permanent) effect.

Oxford BioMedica is well positioned to benefit from the growing interest in altering cells, both in vivo (gene therapy) and ex vivo (cell therapy) to treat currently intractable diseases. The appeal of successful therapies should not be underestimated, both from a clinical and commercial perspective. Where most current therapies merely address the symptoms of a disease, gene- and cell-based therapies offer the opportunity to address the underlying pathology of the condition, effecting repair or reversal of the disease.

The two most commonly used methods of altering the genetic material in cells employ either lentivirus or adeno-associated virus (AAV), with both offering different qualities. For many clinical applications the lentiviral vector offers a number of distinct advantages: efficacy in both dividing and non-dividing cells (so it can be used in cell therapy); a large cargo capacity for therapeutic genes (eg three genes in the new ProSavin construct); sustained expression (over five years so far with a single administration); and no toxicity or adverse immune reactions.

The lenti-vector platform is one of the best characterised and understood of the lentiviral vectors, with a wealth of development expertise, process engineering, regulatory know-how, and production scale-up knowledge (including the necessary quality control and analytical systems) accumulated over the past five years. Lenti-vector's versatility has underpinned the development pipeline (summarised in Exhibit 1), which ranges from ocular indications through Parkinson's disease to various oncology targets.

Exhibit 1: Summary of Oxford BioMedica's R&D pipeline

Project	Indication(s)	Development stage/notes
ProSavin and OXB102	Parkinson's disease	Phase I/II open-label trial completed. New construct (OXB-102) being developed, Phase I/II start due in 2016, partially funded by a £2.2m Innovate UK grant.
RetinoStat	Wet AMD	Phase I completed with primary end point met. Decision regarding future development pathway into Phase II (due to start 2016) by end-2015.
SAR422459	Stargardt's disease	Formerly StarGen. Phase I/IIa ongoing. Sanofi opted-in and taken over programme. Orphan drug status: EU/US.
SAR421869	Usher syndrome 1B	Formerly UshStat. Phase I/IIa ongoing. Sanofi opted-in and taken over programme. Orphan drug: EU/US.
EncorStat	Corneal graft rejection	Pre-clinical. Un-partnered. Phase I/IIa planned for 2016, partly funded by £1.8m Innovate UK grant.
Glaucoma-GT	Chronic glaucoma	Pre-clinical. Un-partnered. Collaboration with Mayo Clinic. Pre-clinical to complete in 2016.
MoNuDin	Motor Neurone Disease	Pre-clinical. Due to complete in 2016.
TroVax	Various cancers	Phase II: Investigator-sponsored trials on-going in mesothelioma, metastatic ovarian and colorectal cancers due to report during 2015/16.
CAR-T 5T4	Various cancers	Pre-clinical. Due to complete in 2016.

Source: Oxford Biomedica

Oxford BioMedica's expertise with the various aspects of developing and commercialising lentiviral products is being increasingly recognised. The progress within the OXB Solutions unit (including process development and manufacture) should not be underestimated, with the predicted efficiency and yield gains likely to translate into a further extension/expansion of the Novartis contract as well as attracting new partners. We expect the revenue streams to increase over the medium term, which are expected sufficient to underpin the development of the in-house pipeline to worthwhile value-inflection points.

Manufacturing – expertise and capability is being recognised

Cell- and gene-based therapies have been materially de-risked over the last few years, as the mounting body of clinical evidence supports the initial positive outcomes of the earlier studies, with valuations of numerous companies reflecting increasing investor optimism that such therapies will achieve commercial success. Less visibly, the regulatory risks have also diminished; with the European approval of UniQure's Glybera in November 2012 marking a pivotal point, as it effectively mapped a regulatory pathway. Although the FDA has yet to approve a human cell- or gene-therapy product, it has provided guidance for their development. For instance, the FDA has established the Office of Cellular, Tissue and Gene Therapies (OCTGT) to consolidate the review of such gene therapy and related products. It has also issued a raft of clinical guidelines, CMC (chemical, manufacturing and control) guidelines and other guidelines, all of which are intended to facilitate the development of gene-therapy products.

The next major challenge is the manufacture of commercial product quantities, with consistent quality and of reproducible characteristics. However, producing sizeable batches of cell- and gene-based medicines is acknowledged as being one of the most complex processes in the industry and historically there has been a lack of manufacturing infrastructure to enable scalable production in a reliable and efficient manner. The challenges of industrialising the processes are many; producing material at a commercially viable scale is complex and few systems reliably and consistently provide adequate yield, scalability and potency. As a pioneer in gene therapy, Oxford BioMedica was one of the first to encounter these challenges and, as its clinical programmes progressed, management took the strategic decision to bring the manufacturing process in-house.

A GMP facility in Oxford was acquired in February 2011 for £1.9m and a further £1.6m was spent on upgrading the infrastructure, new laboratories and associated equipment. Following the MHRA approval of the site for the bulk manufacture of drug material in June 2012, the site became fully operational. The current facility (sited opposite the new corporate offices and laboratories) consists of 1,100m^2, including 390m^2 of clean rooms, with the potential to run three GMP suites in parallel. This is set to increase materially as a second facility nearby comes on stream within the next year. Once completed, the total clean room area will exceed 1,900m^2 across multiple independent suites that can be flexibly configured, together with a separate custom suite for fill/finish. This knowledge and expertise has been brought together under a business unit called OXB Solutions that offers process development and manufacturing services to third parties.

The importance, and inherent value, of this was shown when, in May 2013, Novartis signed a manufacturing agreement to produce clinical trial material for the CTL019 clinical development programme. CTL019 (also known as CART-019 and tisagenlecleucel-T) is a high-profile programme that addresses various forms of late-stage and refractive leukaemia and is showing promising Phase II results. It uses a lentiviral vector to genetically modify a patient's own T cells such that they express an antibody-like protein that targets the CD19 antigen on B cells. Such ex vivo techniques are typically difficult to scale up easily and Novartis's choice of production partner was an important early validation of both Oxford BioMedica's lenti-vector technology platform and its growing viral vector production expertise.

The first deal was specifically to manufacture several batches of clinical material and demonstrate OXB Solutions' capabilities. In October 2014, Novartis extended the deal, with an initial three-year manufacturing contract that could be worth a total of $90m. There was an upfront licence payment of $14m, of which $4.3m was an equity investment (70.81m shares at 3.8p). The manufacturing and process development elements could be worth up to $76m over the period and include a number of performance incentives to encourage optimisation of factors such as yield and efficiency, as well as supporting improvement in capacity and production systems. Although the licence to the lentiviral vector platform IP is non-exclusive, Oxford BioMedica has granted Novartis an exclusive licence for the development and commercialisation of all CART cell products arising from the

process development collaboration. Undisclosed royalties (assumed to be low single digit) will be payable on sales of CTL019 and other related cell products.

Assuming CTL019 progresses as planned (Novartis envisages filing CTL019 in 2016 for both US and EU approvals), this should lead to a longer-term supply agreement. The sales potential for CTL019 is hard to forecast since clearly much depends on the other possible indications it may be used in, but currently it is in the order of multi-billion dollars. Obviously the financial details for Oxford BioMedica are limited, but we estimate this could result in OXB Solution's income effectively underpinning the whole company's operating costs.

The incremental contribution from OXB Solutions could be significant, as additional manufacturing collaborations are brought in, which given the number of clinical CAR-T programmes underway and the scarcity of possible production partners that have the required expertise, we feel is likely

Patents – a number of players may have to licence

Oxford BioMedica has developed numerous patents that protect the technology platform and the individual product candidates; additionally it possesses substantial know-how and trade secrets relating to the development and commercialization of gene-therapy products. As one of the pioneers in the field, Oxford BioMedica has a broad patent estate, with a multi-layered portfolio covered by over 100 issued or pending patents in key jurisdictions. Some of these patents extend into 2023. Three companies have already signed licence agreements, for instance Glaxo SmithKline has taken an option for a non-exclusive licence for the lenti-vector technology patents for use in up to six undisclosed orphan diseases. Further licensing agreements are expected to be struck as these drug candidates progress along their clinical pathways.

Gene-therapy based programmes – seeing progress

Several of the in-house programmes use the lenti-vector platform to address orphan diseases in ophthalmology, where there is significant unmet medical need. Eye diseases are often genetic in nature and tend to affect a relatively small population (hence qualifying for Orphan Drug status), but are well-understood with highly predictive animal models and clearly defined clinical endpoints, hence they are attractive candidates for gene therapy technologies. Additionally, in many cases the genetic abnormality is known and is caused by mutations in a single gene (monogenic diseases), which means the gene sequence required is readily validated. The goal is to provide a sustained therapeutic benefit via continual expression of the protein(s) that modulate the pathogenesis of the relevant disease. There are a number of such ophthalmic programmes in clinical development, with most using the adeno-associated virus (AAV) vector.

The lenti-vector platform, which is based on the recombinant equine infectious anaemia virus (EIAV), is particularly well suited for targeting diseases of the central nervous system and the eye, because it can integrate the desired gene into non-dividing cells, including neurons in the brain and retinal cells. In such cells, the resulting gene expression can in theory be maintained indefinitely, raising the potential for a single administration of a lenti-vector-based gene therapy to achieve a permanent benefit. Oxford BioMedica's gene-based programmes are detailed in Exhibit 2.

There are currently seven programmes undergoing various stages of development. ProSavin is the most advanced, with encouraging signs of continuing activity from the original Parkinson's patients that were treated. Bridging work to the new, more potent, construct (OXB102) is underway. Sanofi has licensed two specific projects (SAR422459 and SAR421869), which are in early clinical development (Phase I/IIa). RetinoStat was also part of the original Sanofi deal but was returned. Oxford BioMedica is looking at the data from the Phase I trial and will decide on the best pathway shortly. There are two additional ophthalmology assets in preclinical development: EncorStat, for corneal graft rejection, and Glaucoma-GT for chronic glaucoma. EncorStat will be progressed into Phase I/IIa trials using a combination of internal resources and a £1.8m grant from Innovate UK.

Glaucoma-GT is being developed in collaboration with Mayo Clinic. Management is also evaluating other therapy areas where lenti-based vectors have an advantage over AAV due to the greater payload capacity.

Exhibit 2: Oxford BioMedica R&D pipeline summary – lenti-vector based programmes

Programme	Indication	Vector: genes	Notes/partners
ProSavin/OXB 102	Parkinson's disease (Phase I/II)	Lenti-vector: genes for three enzymes required for dopamine synthesis injected into striatum	Open-label dose-escalation Phase I/II trial demonstrated safety and tolerability with long-term motor function improvement. Preclinical bridging studies with new ProSavin gene construct complete and entry into clinic expected 2016. 10-pt Phase IIa portion to evaluate new gene construct (largely funded by a £2.2m grant from Innovate UK). 50-/60-pt randomised placebo-controlled (sham surgery) Phase IIa/b placebo arm to be discussed with regulators.
RetinoStat	Wet (neovascular) AMD (Phase I)	Lenti-vector: endostatin and angiostatin genes	Initially a collaboration/option deal with Sanofi. 21-pt US open-label Phase I in wet AMD with dose escalation (three pts studied at three dose levels; dosing confirmatory cohort after two positive DSMB reviews) and dose confirmation (examination of highest safe/well-tolerated dose in 12 pts); results at ARVO 2015 demonstrated primary end-points of safety and tolerability met. Also showed substantial increase in protein expression, which was dose dependant. Over the 48 week period there was stabilisation of visual acuity and reduction in vascular leakage. Determining pathway for future development, with proof-of-concept Phase II study likely to start in 2016. Early funding partner: Foundation Fighting Blindness.
SAR422459 (previously known as StarGen)	Stargardt disease (Phase I/IIa)	Lenti-vector: ABCR gene	Licensed to Sanofi in Feb 14. 28-pt US/EU open-label Phase I/IIa dose-escalation (eight pts at first-dose level, with four each at next two-dose levels; dosing third cohort after positive DSMB review) and dose-confirmation (examination of highest safe/well-tolerated dose in up to 12 pts) trial ongoing, with a favourable safety profile to date. A single confirmatory Phase III study may be sufficient for approval. Assuming a smooth pathway (noting that the disease's rarity means suitable patients are hard to find), then could be launched in 2018. EU/US orphan drug status. Based on pricing of $20-30,000, we currently estimate peak sales for SAR422459 of $350m pa.
SAR421869 (formerly known as UshStat)	Usher syndrome 1B (Phase I/IIa)	Lenti-vector: MY07A gene	Licensed to Sanofi in Feb 14. 18-pt US open-label Phase I/IIa dose-escalation (three dose levels) trial ongoing, with a good safety profile to date. Depending on the strength of the results, a single confirmatory Phase III study likely sufficient for approval. EU/US orphan drug status. A similar pricing structure and treatment pathway to SAR422459 would suggest launch in 2018 and peak sales of around $45m pa.
EncorStat	Corneal graft rejection (preclinical)	Lenti-vector: endostatin and angiostatin genes	Regained rights from **Sanofi** in Feb 14. Plans to progress into Phase I/IIa (at Moorfields Eye Hospital) in 2016, partly funded by a £1.8m grant from Innovate UK.
Glaucoma-GT	Chronic glaucoma (preclinical)	Lenti-vector delivery of COX-2 and PGF-2 receptor genes	Collaboration with Mayo Clinic (established previous preclinical proof of concept). Encouraging prelim. results (effective/robust gene transfer to target ocular tissues) via trans-corneal admin. Dose optimisation activities are underway, with all preclinical phases to complete in 2016.
MoNuDin	Motor neurone disease (preclinical)	Lenti-vector delivery of VEGF gene	UK MNDA. Delivers a VEGF gene to the neuronal cells affected by motor neurone disease via direct administration into the cerebrospinal fluid. Preclinical efficacy demonstrated in gold standard in vivo amyotrophic lateral sclerosis model (SOD mouse). Product in optimisation for clinical trials. Further work to evaluate the efficacy of two VEGF forms is ongoing.

Source: Edison Investment Research.

ProSavin – new OXB102 construct shows promise

ProSavin/OXB102 is a gene-based therapy for Parkinson's disease (PD), which uses the lenti-vector system to deliver three genes to help restore dopamine levels. Dopamine is usually produced in dopaminergic neurons, but in PD these neurons are progressively destroyed, resulting in the characteristic loss of movement control. The ProSavin genes programme non-dopaminergic cells to produce dopamine and so help redress the imbalance. The first patient in an open-label Phase I/II study was treated over five years ago and since then, 15 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 three year follow up data show that the improvements in motor function seen at six and 12 months has been sustained in the majority of the 15 patients originally treated. The next step is a Phase I/II trial, now that the bridging work on a new ProSavin construct[1] (called OXB-102) is complete. The new construct uses the same three genes, but elicits a stronger dopamine-producing response. This optimisation of ProSavin should increase the potential clinical benefits for patients.

[1] The new construct differs from the existing construct only with respect to the assembly of the three dopamine-producing genes in the genome; it includes the same genes, promoter and viral envelope, and is manufactured via the same process. In the new construct, the genes are more closely linked, enabling a single copy to be between 5x and 10x more potent in its dopamine production capacity. A higher dosing effect could therefore be achieved with less drug vs the existing construct, reducing the cost of goods; coupled with longer IP protection, this should enhance ProSavin's commercial potential.

RetinoStat could be a sizeable commercial opportunity

RetinoStat represents one of Oxford BioMedica's largest commercial opportunities. It addresses the 'wet' form of AMD (age-related macular degeneration), a progressive condition that affects around 1.5m people in the US and over 2.3m in Europe. Wet AMD may account for only around 10% of AMD but is the single largest cause of blindness. It is caused by abnormal blood vessel growth in the retina, with the newly-formed vessels being weak and fragile and so prone to bleeding and protein leakage. This proliferation of abnormal blood vessels in the retina is stimulated by vascular endothelial growth factor (VEGF). Historically, treatment consisted mainly of laser photocoagulation, where a fine argon laser is used to seal the leaking vessels. More recently, treatment has been transformed by anti-VEGF (anti-angiogenic) agents that are injected directly into the vitreous humor of the eye, leading to regression of the abnormal blood vessels and improved vision.

Roche/Genentech's Lucentis (ranibizumab) is currently the market leader, with total sales of around $3.2bn in 2014 (although c 20% appears to be used in diabetic oedema). Ranibizumab is the Fab fragment of Roche/Genentech's Avastin (bevacizumab) that selectively binds to various isoforms of VEGF-A to prevent new blood vessel formation. In clinical trials, almost all (around 95%) of patients maintained their visual acuity, with between 31% and 37% experiencing a clinically significant improvement in vision (15 or more letters on a standard chart) at 12 months. Lucentis has been the subject of much clinical debate since Avastin is known to be similarly effective but, due to its use at much higher doses in cancer indications, is materially cheaper and so has led to sizeable 'off label' usage. Regeneron/Bayer's Eylea (aflibercept) is a fusion protein that also targets soluble VEGF, which has gained share due to largely its lower injection frequency (every 8 weeks vs 4 weeks) as well as the lower price (around 5% lower). Regeneron reported Eylea sales of $1.7bn in 2014.

RetinoStat uses the lenti-vector platform to deliver two genes that encode for the anti-angiogenic proteins endostatin and angiostatin directly to the retina. This produces modified cells at the injection sites that effectively manufacture the two proteins, which are released locally to prevent disruptive vascularisation of the retina. As with the other ocular lenti-vector projects, one procedure should produce long-lasting effects (which would compare favourably with the existing anti-VEGF agents which require multiple intravitreal injections). RetinoStat would target around 10-20% of the treated wet AMD patient groups, which with an estimated 200,000 new cases of wet AMD identified each year and $20-30,000 pricing, would suggest peak sales of between $400m and $1.2bn.

Management is evaluating the Phase I results and preparing for the start of a Phase II proof-of-concept study in 2016. The key question will be whether it is better to partner earlier, with lower payments but also a lower cash outlay, or to invest in the Phase II trial and partner afterwards, for hopefully better terms if the results are good. A decision is expected before end-2015.

Exhibit 3: Oxford BioMedica R&D pipeline summary – other programmes

Programme	Indication	Technology	Notes/partners
TroVax	Colorectal, ovarian, castration-resistant prostate (CRPC), mesothelioma (Phase II)	Modified Vaccinia Ankara (MVA) poxvirus: 5T4 tumour-associated antigen	Phase II in colorectal (inc adjuvant), ovarian, CRPC and mesothelioma. US 80-pt Phase II trial in CRPC (docetaxel ± TroVax) halted due to recruitment issues, given availability of new therapies and other clinical trials in this indication. Three investigator-sponsored Phase II trials underway: 26-pt SKOPOS trial in first-line mesothelioma + chemotherapy, 54-pt Phase II in metastatic CRC; and100-pt TRIOC trial in metastatic ovarian cancer. Top line results expected by end-2015 and in early-2016, which could trigger out-licensing opportunities. Data on 733-pt Phase III TRIST study published at ESMO/ECCO 2009: positive subset data informs future study design (use of haematological biomarkers to pre-select patients).
PF-06263507 (A1-mcMMAF)	Various cancers (Phase I)	Seattle Genetics ADC-linked anti-5T4 antibody	Exclusive global licence with Pfizer: upfront and milestones up to $24m, plus licence option fees and royalties. Amended (May 2011) to include non-exclusive rights for in vitro diagnostic use of 5T4 antibodies (including commercialisation option) with additional milestones up to $4m. Pfizer has synthesised an antibody-drug conjugate using Seattle Genetics ADC technology, which has shown promising preclinical results (eradication of tumour cells with heterogeneous 5T4 expression). Entered Phase I in August 2013, triggering a $1m milestone, with study ongoing. Low single-digit royalty payable to Cancer Research UK.
CAR-T 5T4	Various cancers (pre-clinical)	CAR-T T-cell activation with 5T4	In-house programme exploiting CAR-T expertise with 5T4 platform. Currently undergoing pre-clinical studies, with completion expected in 2016.

Source: Company and Edison Investment Research

Other research programmes have value

Oxford BioMedica also has a number of other interesting projects. Outside the lenti-vector platform, TroVax is a therapeutic vaccine targeting the 5T4 tumour antigen that is being evaluated for a number of solid cancer types. 5T4 is an onco-foetal tumour antigen that is expressed on the surface of the majority of solid tumours, with TroVax stimulating the immune system to destroy these cancerous cells. Results from 10 previous clinical trials in in over 500 colorectal, renal and prostate cancer patients have shown that TroVax demonstrates clear indications of efficacy and, importantly, can be with various other treatments (eg check point inhibitors). Interestingly, the earlier CAR-T 5T4 programme uses gene modified autologous T cells engineered with the lenti-vector to express an antibody against 5T4. Exhibit 3 details the non-lenti-vector research programmes.

TroVax – still making headway, albeit slowly

TroVax is a therapeutic vaccine that stimulates the immune system to target and destroy cancerous cells that express the 5T4 tumour antigen, which is common to many solid tumours. Targeted indications include castration-resistant prostate (CRPC), metastatic ovarian, colorectal (CRC) and mesothelioma. Oxford BioMedica's strategy is to work collaboratively with clinical networks to generate additional Phase II data, which – if successful – would then be used to secure a partner to fund a tailored larger-scale Phase III programme. Three investigator-led Phase II studies are underway. This approach uses minimal internal resources and existing drug supply (which had been built up in anticipation of previously-planned Phase III studies). Management has made clear that the initiation of any Phase III trials is contingent on securing an external funding partnership.

Sensitivities

Although Oxford BioMedica's success with its OXB Solutions manufacturing facilities have reduced its dependence on the success of its clinical pipeline, the longer term investment case remains essentially a bet on the merits of gene therapy in general, and the lenti-vector delivery platform in particular. The improved financial position, coupled with the greater visibility on the regulatory and clinical pathways required for a gene-based product approval, means Oxford BoMedica is materially de-risked when compared to a few years ago. Nonetheless, it is still exposed to the sensitivities normally associated with novel drug development by a smaller company.

These include the unpredictable outcomes of clinical trials (where the results are often binary in nature), the risks of development or regulatory delays (for instance, the FDA requiring additional clinical data), unexpected changes in clinical practice (an example being due to competitor breakthrough products being developed), altered re-imbursement environment (such as in countries with social healthcare systems), and limited funds (where a delay can result in the cash runway being insufficient to reach a value-creating point).

The company is investing around £20m in establishing a GMP facility (and the associated infrastructure) to manufacture cell- and gene-therapy products at commercial scale. The rationale is sound, with the potential to use spare capacity for third-party production offering the prospect of an additional revenue stream. However, were the in-house lenti-vector programmes delayed (or failed to progress), this would entail incurring operating costs (estimated at around £2m per annum) until the surplus capacity was utilised.

Valuation

From an investment perspective, not only are cell-based medicines in the spotlight (notably the CAR-T plays) but gene therapy appears to be returning into focus. A number of companies are enjoying solid valuations (eg AGCT and Bluebird) on the back of heightened expectations and in this context, Oxford BioMedica has arguably, been overlooked.

Oxford BioMedica's near-term outlook is geared to exploiting its growing expertise in the commercial manufacture of cell- and gene-based products and, further out, it will be continuing progress in developing its clinical assets that drives the valuation uplift. There are two core technology platforms: the lenti-vector gene delivery system, which uses lentiviral-derived vectors to accurately deliver genetic material into target cells and, to lesser degree, the 5T4 tumour antigen platform, which exploits the unique 5T4 protein that is highly expressed on the surface of many solid tumour cells to selectively target therapies. Both technologies are attractive and address markets with significant commercial potential and high unmet needs. Nonetheless, the risks do remain and building value in such innovative approaches takes time. However, we are approaching important inflection points with the potential of manufacturing capabilities coming to the fore.

Exhibit 4: Oxford BioMedica pipeline rNPV (including partnered products)

Product(s)	Status	Probability of success	Estimated launch year	Estimated maximum royalty	Estimated peak sales ($m)
ProSavin/OXB102	Phase I/II	23%	2022	20%	790
TroVax	Phase II	18%	2019	15%	350
RetinoStat	Phase I	24%	2019	15%	1,000
SAR422459 (StarGen)	Phase I/IIa	26%	2019	15%	400
SAR421869 (UshStat)	Phase I/IIa	28%	2019	15%	50
5T4 Tumour Antigen	Phase I	7%	2020	15%	650
EncorStat	Preclinical	7%	2021	15%	80
Glaucoma-GT	Preclinical	7%	2021	15%	150
MoNuDin	Preclinical	6%	2021	15%	150
CAR-T 5T4	Preclinical	5%	2022	15%	500

Source: Edison Investment Research

Our valuation consists of an rNPV model of the R&D pipeline, coupled with a simple DCF of the projected manufacturing revenues. The value of the pipeline is £122.6m, equivalent to 4.7p a share, and is based on conservative assumptions in terms of timings and adoption curves (see Exhibit 4). The success probabilities of each project are based on standard industry criteria for each stage of the clinical development process but are flexed to reflect the inherent risks of the individual programme, the indication targeted, and the trial design. Understandably, it follows that it is the later stage products that have a higher current value, with the step change occurring typically at Phase II when the proof of concept is usually established. We use a 12.5% discount rate, which is our standard rate for such early-stage companies, and net out the cash/debt position. Assuming even a relatively modest success within this element of the development pipeline could see a material uplift in our rNPV model.

Importantly, we have chosen not to include the value of other less visible, but arguably just as important, assets such as the intellectual property estate (which should lead to milestones and royalties under various technology IP licensing deals). The DCF model for the income streams associated with OXB Solutions simply forecasts the production revenues projected through to 2029. Initially these are based on the Novartis contract being extended (assuming CTL019 is approved) but a further two smaller deals are included later in the period, with a 28% operating margin (conservative for such specialist production) and 15% blended tax rate (due to the Patent Box and historic tax losses). Additionally, licence fees (of under 2%) on CTL019 product sales are included. These are summed and discounted at 10%, in line with other revenue generating units under Edison coverage. The result is a value of £233.5m, equivalent to 9.2p a share, which when added to the pipeline rNPV, gives a valuation of £356.1m (13.9p a share) for Oxford Biomedica.

Financials

Oxford BioMedica reported FY14 revenues were up from £5.4m to £13.6m. Licensing income grew from £1.0m to £5.1m, boosted by the £4.8m upfront payment from the extension of the Novartis manufacturing deal announced in October 2014. Manufacturing revenues jumped from £2.6m to £7.7m due mainly to process development activities for Novartis. R&D collaboration revenues fell from £1.7m to £0.8m and represents the residual recognition of the $26m received under the 2009 Sanofi agreement.

Gross profit increased by £5.0m from £4.2m to £9.2m, as around £3.1m of licence receipts and £2.1m from the Novartis manufacturing and process development activities were offset by the decline in Sanofi-related income. R&D costs increased from £13.8m to £17.0m, however £2.3m of this was one-off (the production of new batches of StarGen and UshStat clinical trial material and a viral vector for an unnamed pilot project). Administrative costs rose from £3.4m to £4.0m due to a combination of inflation and higher staffing levels as the business expands. The operating loss fell from £12.8m to £10.6m. Finance costs of £0.2m related mainly to the Vulpes £5.0m loan, with the tax credit rising from £1.7m to £2.1m. The loss after tax fell from £11.1m to £8.7m.

In cash terms, the cash used in operations fell from £13.0m to £7.4m, with non-cash items such as depreciation, amortisation, impairment and share options essentially flat at £1.5m (£1.4m 2013). This was also helped by the reversal in working capital from a £1.6m adverse movement in 2013 to a £1.7m benefit in 2014. Capex increased materially, from £0.8m to £5.6m, due mainly to the £3.2m acquisition of the Windrush Court laboratory and office complex (which is expected to become self-financing once the rental costs of Medawar Centre are removed) and £1.1m for manufacturing and laboratory equipment. The equity placing in June 2014 raised net proceeds of £20.1 million (£21.6m gross) and resulted in net cash of £13.2m (£2.2m at December 2013). The company plans to maintain the net cash burn at around £1m per month, a level sufficient to fund the essential R&D and sustain the manufacturing facility.

Looking ahead, our forecasts only include known revenue streams (with potential licensing, partnering or manufacturing deals representing upside). The Novartis contract is expected to start generating manufacturing and process development revenues in 2015 and 2016; however, the nature of the early payments (largely milestones linked to process development) means timings are uncertain. We expect these to be recognised when paid and not when the targets have been achieved, suggesting payments will be delayed by around a quarter. It is these payments that underpin our revenue expectations of £15.1m and £24.0m respectively. The expected increases in R&D expenditure to support pipeline development, coupled with the staff increases for the production site investment, mean we forecast these to translate to operating losses of £10.9m and £7.5m. Success with OXB Solutions means the immediate operating dynamics have been transformed, assuming progress as expected, we forecast operating break-even as soon as 2017.

To bridge that gap, in May 2015, Oxford BioMedica secured a $50m loan facility from Oberland Capital as non-dilutive funding to progress its manufacturing expansion. The loan has to be repaid by 1st May 2022, but may be prepaid at any time (an undisclosed fee is payable upon any repayment). Interest is payable quarterly at an annual rate of 9.5% plus the greater of 1% or 3-month Libor. A further 0.35% of net revenues is payable for eight years starting on 1 April 2017 for each $5m drawn down over $30m (this may be closed at any time but an undisclosed exit fee is payable). An initial $25m was drawn down immediately to fund the production expansion required for the Novartis contract, with the remainder available in tranches of a minimum of $5m prior to 31 December 2016. Any one of the last four tranches can be taken as an equity investment rather than a loan (the terms have not been disclosed). The then existing £5.3m AMSCI loan facility was terminated and the £3.0m drawn down at the time has been repaid.

Exhibit 5: Financial summary

£000s	2013	2014	2015e	2016e	2017e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	5,375	13,618	15,071	24,013	31,500
Cost of Sales	(1,140)	(4,416)	(7,490)	(12,889)	(12,600)
Gross Profit	4,235	9,202	7,581	11,124	18,900
R&D	(13,750)	(16,986)	(14,500)	(14,500)	(14,500)
General & admin	(3,422)	(3,957)	(4,056)	(4,178)	(4,303)
Other: revenue/(expenditure)	114	1,128	100	100	100
Operating Profit	(12,823)	(10,613)	(10,875)	(7,454)	197
Amortisation	(396)	(396)	(396)	(396)	(396)
Exceptionals	0	0	0	0	0
Share-based payments	0	0	0	0	0
EBITDA	(11,756)	(9,514)	(9,729)	(6,308)	1,343
Operating Profit (before GW and except)	(12,427)	(10,217)	(10,479)	(7,058)	593
Net Interest	60	(185)	(100)	(1,200)	(1,200)
Profit Before Tax (norm)	(12,367)	(10,402)	(10,579)	(8,258)	(607)
Profit Before Tax (reported)	(12,763)	(10,798)	(10,975)	(8,654)	(1,003)
Tax	1,667	2,137	1,824	1,824	1,824
Profit After Tax (norm)	(10,700)	(8,265)	(8,755)	(6,434)	1,217
Profit After Tax (reported)	(11,096)	(8,661)	(9,151)	(6,830)	821
Average Number of Shares Outstanding (m)	1,416.1	2,019.3	2,564.8	2,564.8	2,564.8
EPS - normalised (p)	(0.76)	(0.41)	(0.34)	(0.25)	0.05
EPS - reported (p)	(0.78)	(0.43)	(0.36)	(0.27)	0.03
Dividend per share (p)	0.00	0.00	0.00	0.00	0.00
Gross Margin (%)	78.8%	67.6%	50.3%	46.3%	60.0%
EBITDA Margin (%)	(218.7%)	(69.9%)	(64.6%)	(26.3%)	4.3%
Operating Margin (before GW and except) (%)	(231.2%)	(75.0%)	(69.5%)	(29.4%)	1.9%
BALANCE SHEET					
Fixed Assets	6,703	11,050	17,404	23,758	24,412
Intangible Assets	2,633	2,106	1,710	1,314	918
Tangible Assets	4,070	8,944	15,694	22,444	23,494
Investment in associates	0	0	0	0	0
Unquoted investments	0	0	0	0	0
Current Assets	6,941	22,755	4,339	4,831	4,674
Stocks	680	1,407	0	0	0
Debtors	2,592	5,153	2,200	2,400	2,400
Cash	2,169	14,195	139	431	274
Other	1,500	2,000	2,000	2,000	2,000
Current Liabilities	(4,214)	(9,231)	(4,597)	(18,597)	(18,597)
Short term borrowings	0	0	0	(14,000)	(14,000)
Creditors	(1,218)	(2,787)	(1,200)	(1,200)	(1,200)
Other creditors	(1,716)	(3,517)	(3,397)	(3,397)	(3,397)
Provisions	0	0	0	0	0
Deferred revenue	(1,280)	(2,927)	0	0	0
Long Term Liabilities	(532)	(1,535)	(535)	(535)	(535)
Long term borrowings	0	(1,000)	0	0	0
Deferred revenue	0	0	0	0	0
Other long term liabilities	(532)	(535)	(535)	(535)	(535)
Net Assets	8,898	23,039	16,611	9,457	9,954
CASH FLOW					
Operating Cash Flow	(13,005)	(7,431)	(6,956)	(6,508)	1,343
Net Interest	61	(185)	(100)	(1,200)	(1,200)
Tax	1,990	1,637	1,500	1,500	1,500
Capex	(839)	(5,577)	(7,500)	(7,500)	(1,800)
Acquisitions/disposals	0	0	0	0	0
Financing	0	22,808	0	0	0
Dividends	0	0	0	0	0
Other	(98)	(226)	0	0	0
Net Cash Flow	(11,891)	11,026	(13,056)	(13,708)	(157)
Opening net debt/(cash)	(14,061)	(2,169)	(13,195)	(139)	13,569
HP finance leases initiated	0	0	0	0	0
Other	(1)	0	0	0	0
Closing net debt/(cash)	(2,169)	(13,195)	(139)	13,569	13,726

Source: Oxford BioMedica and Edison Investment Research

Contact details	Revenue by geography
Windrush Court, Transport Way, Oxford OX4 6LT, 01865 783 000 www.oxfordbiomedica.co.uk	N/A

Management team

CEO: John Dawson	CFO: Tim Watts
Mr Dawson joined as non-executive director in August 2008; he was appointed CEO in October 2008 (acting CEO from August-October 2008). Previously he was at Cephalon (1996-2007), including as CFO and head of BD Europe.	Mr Watts joined as CFO in February 2012. He was previously CFO at Archimedes Pharma (2007–2011) and spent 22 years at ICI rising to be finance director of Zeneca Pharmaceuticals and then group financial controller of AstraZeneca in 2001.

Chairman: Nick Rodgers

Mr Rodgers has been chairman since May 2011 and a board member since March 2004. He is the current CEO of Ipso Ventures, previously having been head of Life Sciences and joint-head of corporate finance at Evolution Beeson Gregory until December 2003.

Principal shareholders	(%)
M&G Investment Managers	18.8
Vulpes Life Sciences	17.4
Joy Group	9.7
Aviva Investors	9.4
Hargreaves Lansdown AMs	3.9
TD Direct	3.5
Barclays Wealth Management	3.4
Tredie AP Fonden	3.3

Companies named in this report

AGCT, Bayer, Bluebird, Glaxo SmithKline, Novartis, Regeneron, Roche Sanofi

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