EDISON

OvaScience

AUGMENT progressing

Preconception planning

Pharma & biotech

The US AUGMENT study was initiated in late-2012, which infers the first live birth could occur in late-2013/early-2014. However, we believe that interim updates on the trial are unlikely before final data in H214. OvaScience is increasing its commercial activities around AUGMENT and is progressing ex-US trial plans. The latter represents upside to our rNPV of $200m, which currently reflects the initial US opportunity for AUGMENT.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/12	0.0	(12.1)	(2.09)	0.00	N/A	N/A
12/13e	0.0	(18.8)	(1.09)	0.00	N/A	N/A
12/14e	1.0	(21.7)	(1.19)	0.00	N/A	N/A

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

US AUGMENT study ongoing…

Lead programme, AUGMENT, which adds a woman's egg precursor cell (EggPC) mitochondria to her eggs to increase the success of *in vitro* fertilisation (IVF), is in an ongoing US study with headline results expected in H214. Given that the AUGMENT study started in late-2012, the first live birth is likely to occur in late-13/early-14. However, interim efficacy/safety updates are unlikely (unless material) before final readout. Separately, a recent publication by OvaScience's scientific co-founders lends further support to using EggPC mitochondria to rejuvenate eggs.

…coupled with increasing commercial activities

OvaScience has also initiated commercial activities for AUGMENT, which includes presentations at key fertility conferences (increasing awareness of the procedure among physicians), new hires with significant commercial experience (the CSO was former R&D head for Shire) and creation of an International Product Advisory Board (IPAB). We project an H214 launch and peak US sales of $159m in the initial indication (women requiring donor eggs or aged >35 failing multiple IVF cycles).

Progressing ex-US AUGMENT plans

We expect an ex-US AUGMENT trial to start in H114. The IPAB members (primarily fertility experts from the UK, Spain and Germany) points to Europe (c 530k IVF cycles annually) as the most likely region. Moreover, UK government backing for three-person IVF (donor mitochondrial transfer) suggests the UK fertility regulator (HFEA) could be receptive to AUGMENT (autologous mitochondrial transfer). Pending further clarity, our financial model currently excludes ex-US sales of AUGMENT.

Valuation: rNPV of $200m reflects US opportunity

Edison's rNPV of $200m attributes $167m to AUGMENT in the US, adds cash of $45m and deducts general costs of $12m. Positive AUGMENT trial results would see our rNPV rise to $312m. The ex-US AUGMENT opportunity currently represents pure upside to our valuation, although it appears the market is already ascribing value to this. As the European market (annual IVF procedures) is c 4x larger than the US, this suggests significant upside potential to our rNPV.

12 August 2013

Price	**US$12.62**
Market cap	**US$230m**

Net cash ($m) at end-FY13e	$45.2m
Shares in issue	18.2m
Free float	51%
Code	OVSC
Primary exchange	NASDAQ

Share price performance

%	1m	3m	12m
Abs	(6.4)	11.8	N/A
Rel (local)	(8.5)	7.5	N/A
52-week high/low	US$15.6	US$7.5	

Business description

OvaScience is a US-based life sciences company focused on developing and commercialising new treatments for female infertility. Product candidates (AUGMENT, OvaTure) are based on the discovery of germline stem cells (egg precursor cells) in human ovaries. Both products are designed to improve the *in vitro* fertilisation (IVF) procedure, although OvaTure does not require hormone injections.

Next events

AUGMENT US study expansion	H213
AUGMENT ex-US study initiation	H114
OvaTure human preclinical POC data	H114
AUGMENT potential US/ex-US launches	H214

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Edison profile page

OvaScience datasheet

Exhibit 1: OvaScience's R&D pipeline

Programme	AUGMENT	OvaTure
Description	Procedure involves isolating mitochondria from a woman's own egg precursor cells (EggPC) and injecting them into her egg along with a sperm cell during IVF.	Creation of mature, fertilisable eggs *in vitro* using a woman's own egg precursor cells.
Therapeutic aim	Increase the success rate of IVF – adding EggPC mitochondria could improve egg quality and therefore increase the likelihood that a fertilised egg will develop into a viable embryo. This could reduce the number of IVF cycles and the number of embryos transferred to achieve a live birth.	Allow women to undergo IVF with high-quality non-donor eggs. This could (1) restore fertility in women with poor quality eggs (ie post-chemotherapy) and reduce the need for donor eggs, and (2) eliminate need for hormonal hyperstimulation required in IVF.
Stage	Clinical study	Preclinical development
Study details	AUGMENT study in up to 40 women aged 38-42 who have failed two to five cycles of IVF. Open-label study at two US IVF clinics with no formal control arm. Primary objective: safety; secondary objectives: embryo quality, fertilisation, pregnancy, live birth rates. Results for AUGMENT-treated patients will be compared to success rates (historical and concurrent, patient matched) for patients receiving standard IVF at the two clinics.	Broad outline of preclinical development plan: (1) Optimise the culture conditions used *in vitro* to transform EggPC into mature, fertilisable eggs – identify the optimal composition and sequence of proteins/factors necessary for creating new eggs. (2) Further preclinical mouse studies to confirm earlier research that EggPC can be matured into eggs, be fertilised and generate healthy offspring. (3) Preclinical human POC study using human EggPC – attempt to mature human EggPC *ex vivo* into fertilisable eggs using the optimised culture conditions.
Timeline	AUGMENT study initiated in late-2012, US study expansion in H213, headline results in H214, potential US and selected ex-US commercial launches from Q414. Ex-US study planned for H114.	Preclinical development started in 2012 and is expected to complete in H114.
Patent protection	Five patent families. Patents granted (and pending), which expire in May 2025. Additional patent applications that would, if granted, expire April-June 2032.	Five patent families. Patents granted (and pending) to May 2025. Additional patent applications, which would expire April-June 2032.
Potential regulatory pathway	361 HCT/P: a lower-risk human cell and tissue product (HCT/P) pathway.	New Biologics Licence Application (BLA) process.

Source: Edison Investment Research

Exhibit 2: Clinical studies of mitochondrial transfer

Procedure	Mitochondria source	Cell type	Number of mitochondria transferred	Number of cycles	Live births	Offspring delivered	Implied live-birth success rate	Clinical trial(s)
Cytoplasmic transfer	Donor	Egg	Unknown	30	12	16	40%	Cohen et al (1997,1998); Brenner et al (2000);Barritt et al (2000,2001)
Cytoplasmic transfer	Donor	Egg	Unknown	4	1	2	25%	Lazendorf (1999)
Cytoplasmic transfer	Donor	Egg	Unknown	9	4	5	44%	Huang et al (1999)
Mitochondrial transfer	Autologous	Granulosa (somatic cell)	3000 (average)	71	20	27	28%	Tzeng et al (2004)

Source: Edison Investment Research

Exhibit 3: AUGMENT criteria for regulation under 361 HCT/P

Criteria for 361 HCT/P	Does AUGMENT meet criteria?
HCT/P is minimally manipulated.	AUGMENT is prepared using simple cell-handling techniques to identify and isolate EggPCs, and centrifugation of EggPCs to separate out mitochondria. These steps do not alter the biological characteristics of the mitochondria.
HCT/P is intended for homologous use only.	AUGMENT supplements a woman's pre-existing egg mitochondria with fresh mitochondria from her own EggPCs.
Manufacture of the HCT/P does not involve the combination of cells or tissues with another article.	AUGMENT does not involve combining the HCT/P with any drugs, devices or synthetic materials. Mitochondria are diluted in standard ICSI buffer only.
HCT/P does not have a systemic effect and is not dependent on the metabolic activity of living cells for its primary function, or the HCT/P has a systemic effect or is dependent on the metabolic activity of living cells for its primary function and (a) is for autologous use, (b) is for allogeneic use in a first- or second-degree blood relative, or (c) is for reproductive use.	AUGMENT is intended for reproductive use and is autologous.

Source: Edison Investment Research

Update: Preconception planning

US AUGMENT study ongoing

Lead programme, AUGMENT, which adds a woman's egg precursor cell (EggPC) mitochondria to her eggs to increase the success of *in vitro* fertilisation (IVF), is in an ongoing US study with headline results expected H214. The AUGMENT study is enrolling female patients at two IVF clinics – we provided a detailed discussion of the open-label, non-randomised 40-patient trial in our initiation of coverage report. The AUGMENT study started in late-2012, which suggests that the first women are likely to have undergone the procedure in Q113. Based on a standard nine-month gestation, this infers that the first live birth could occur around late-2013/early-2014. However, the company has stated that interim efficacy/safety updates are unlikely (unless material) before final trial readout in 2014. Separately, a recent and detailed journal publication by OvaScience's scientific co-founders lends further support to using EggPC mitochondria to rejuvenate eggs.

Progressing ex-US AUGMENT plans

OvaScience has already announced its intention to start an ex-US AUGMENT trial in H114. Given the membership of the recently created IPAB members (primarily fertility experts from the UK, Spain and Germany), we see Europe (c 530k IVF cycles annually) as the most likely territory for initial ex-US development.

Interestingly, the UK government is pushing ahead with plans to allow three-person IVF (donor mitochondrial transfer) to treat inherited mitochondrial disorders. The procedure is designed to create a healthy embryo by replacing the defective (maternal) mitochondria with healthy (donated) mitochondria. The embryos are then used in standard IVF treatment. The result is a baby with genetic information from three people – the mother and father (nuclear DNA) and a donor (the mitochondrial DNA). UK government support for three-person IVF follows a consultation by the UK fertility regulator, the Human Fertilisation and Embryology Authority (HFEA) published in March 2013, which concluded that mitochondrial replacement is probably safe and that there is general public support. Draft regulations are expected to be ready by Q413 and debated in parliament in 2014.

With the UK government and HFEA backing donor mitochondrial transfer (albeit only for inherited mitochondrial disorders), it suggests the HFEA may also be receptive to autologous mitochondrial transfer (AUGMENT), which does not introduce third-party DNA into the embryo. The UK Human Fertilisation and Embryology Act (2008) currently prohibits IVF treatment using eggs in which the nuclear or mitochondrial DNA have been altered. While OvaScience interprets this legislation as not preventing the use of AUGMENT in the UK, the HFEA could take a different view and prevent IVF clinics from undertaking the procedure. However, in our view, further amendments of the Act to allow three-person IVF could reduce the clinical and commercial risks for AUGMENT in the UK market.

We also note that the US regulator (FDA) is convening a Cellular, Tissue and Gene Therapies Advisory Committee in Q413 (October 22-23) to discuss 'oocyte modification in assisted reproduction for the prevention of transmission of mitochondrial disease or treatment of infertility'. While the detailed background materials are not yet available, we assume this Adcom relates to the use of three-person IVF. In our view, the Adcom is relevant to OvaScience, as it may also provide an insight into the FDA's thinking on the use of autologous mitochondrial transfer in IVF.

Sensitivities

OvaScience is subject to the risks normally associated with biotech company development, including the possibility of unfavourable outcomes in clinical trials and the success of competitors. Because of its lack of diversification, there is particularly high sensitivity to the outcome of the AUGMENT study – negative data could represent a significant setback. Regulatory risk represents another key sensitivity. The FDA may decide to regulate AUGMENT as a new drug/biologic and require further clinical studies. This could substantially increase development costs and timelines, and may require additional capital.

Valuation

We value OvaScience at $200m, or $11.0 per share, based on a risk-adjusted NPV analysis. We forecast 10-year cash flows from AUGMENT in its initial indication (US women aged >35yrs failing multiple IVF cycles) and discount using a 12.5% WACC. We attribute $167m ($9.20/share) to AUGMENT, add cash of $45m ($2.50/share) and deduct general costs of $13m ($0.70/share), to arrive at our $11.0 fair value. Depending on the outcome of the AUGMENT study (ie unwinding our 60% risk adjustment for positive safety and efficacy data), our valuation could rise by c 55% to $312m, or $17.20 per share. We currently assign no value to AUGMENT in ex-US markets or to OvaTure, so these represent pure upside.

Exhibit 4: rNPV valuation model and key assumptions

Product	Indication	rNPV ($m)	rNPV/share ($)	Probability of success	Launch	Peak sales ($m)	Key assumptions
AUGMENT	IVF	166.8	9.2	60%	2014	159	US market only: women >35yrs failing >2 IVF cycles; peak 25% share of 24k eligible women; price $15,000.
R&D expenses		(1.7)	(0.1)				Preclinical R&D expenses for OvaTure.
G&A expenses		(9.2)	(0.5)				General overhead costs not attributable to AUGMENT.
Capex		(0.8)	(0.1)				Laboratory supplies and equipment.
Net cash		45.2	2.5				Forecast net cash at year-end 2013.
Total		**200.3**	**11.0**				rNPV of $11/share based on 18.2m basic shares; rNPV based on fully diluted shares (20.8m) is $10/share.

Source: Edison Investment Research

Financials

Our financial model remains unchanged, pending details on the planned ex-US trial for AUGMENT. OvaScience ended 2012 with net cash of $31.4m. Factoring in the $35m ($33m net) financing in March 2013 and expected cash utilisation, we project net cash of $45.2m at year-end 2013. We estimate that the company's cash runway extends into late-2015/early-2016.

Exhibit 5: Financial summary

$'000s	2012	2013e	2014e
Year ending 31 Dec			
PROFIT & LOSS ($'000)			
Revenue	0	0	1,004
EBITDA	(12,054)	(18,846)	(21,740)
Operating profit (before GW and except)	(12,147)	(18,946)	(21,840)
Intangible amortisation	0	0	0
Exceptionals/special Items	0	0	0
Share-based payment	(1,382)	(1,000)	(1,000)
Operating profit	(13,529)	(19,946)	(22,840)
Net interest	19	192	171
Profit before tax (norm)	(12,128)	(18,754)	(21,669)
Tax	0	0	0
Profit after tax (norm.)	(12,128)	(18,754)	(21,669)
Average number of shares outstanding (m)	5.8	17.2	18.2
EPS - normalised (c)	(209)	(109)	(119)
Dividend per share (c)	0.0	0.0	0.0
EBITDA margin (%)	N/A	N/A	N/A
Operating margin (before GW and except) (%)	N/A	N/A	N/A
BALANCE SHEET			
Fixed assets	849	1,249	1,649
Intangible assets	0	0	0
Tangible assets	849	1,249	1,649
Investment in associates/other non-core assets	0	0	0
Trade investment & others	0	0	0
Associated with assets held for sale	0	0	0
Current assets	31,965	45,237	23,167
Stocks	0	0	0
Debtors	0	0	0
Cash	31,391	45,237	23,167
Other	574	0	0
Current liabilities	(2,086)	(2,086)	(2,086)
Creditors	(2,086)	(2,086)	(2,086)
Other creditors	0	0	0
Short-term borrowings	0	0	0
Provisions and other current liabilities	0	0	0
Associated with assets held for sale	0	0	0
Long-term liabilities	(7)	0	0
Long-term borrowings	0	0	0
Deferred taxation	0	0	0
Other long-term liabilities	(7)	0	0
Net assets	30,721	44,400	22,730
CASH FLOW			
Operating cash flow	(10,643)	(18,846)	(21,740)
Net interest	19	192	171
Tax	0	0	0
Capex	(849)	(500)	(500)
Purchase of intangibles	0	0	0
Acquisitions/disposals	0	0	0
Financing	39,031	33,000	0
Dividends	0	0	0
Other	(708)	0	0
Net cash flow	26,850	13,846	(22,069)
Opening net debt/(cash)	(4,541)	(31,391)	(45,237)
HP finance leases initiated	0	0	0
Other	0	0	0
Closing net debt/(cash)	(31,391)	(45,237)	(23,167)

Source: Edison investment Research, OvaScience accounts

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