EDISON

International Stem Cell

Clinical update

Interim Parkinson's data

Pharma & biotech

International Stem Cell recently announced interim six-month results from the first cohort of four patients in its Phase I trial of ISC-hpNSC in Parkinson's disease (PD). Positive signals were seen in a variety of measures, which include daily living, mobility, depression and compulsive disorders. The trial is continuing and the second cohort is almost enrolled, with the third patient of four recently undergoing surgical implantation. The study will enroll 12 patients at three dosing regimens (30-70m cells).

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/15	7.6	(4.6)	(1.29)	0.0	N/A	N/A
12/16	7.2	(4.9)	(0.34)	0.0	N/A	N/A
12/17e	7.3	(4.3)	(0.72)	0.0	N/A	N/A
12/18e	8.0	(7.3)	(1.17)	0.0	N/A	N/A

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

Trial in Parkinson's disease progressing

Patients on the study are being treated in three cohorts with 30m, 50m and 70m stem cells, delivered via intracranial injection. Clinical assessments are scheduled at six and 12 months following surgery, with six-month results recently announced. While early and from a small, single-arm trial, the interim data is encouraging. The seventh patient recently underwent surgical implantation.

Preparing for a Phase II in traumatic brain injury

In September, the company announced that it had completed preclinical studies of ISC-hpNSC in traumatic brain injury (TBI) and was preparing to commence a Phase II trial. According to the Centers for Disease Control, TBI accounts for 2.5 million emergency room visits in the US annually and approximately 3.2-5.3 million people are living with a TBI-related disability.

3D bioprinting of liver cells developed

The company recently announced that it has developed a 3D bioprinter that utilizes proprietary liver progenitor cells that differentiate into different types of liver cells. Once implanted, these could potentially provide a treatment for damaged livers. According to the United Network for Organ Sharing, there are currently over 14,000 on the liver transplant list, but only around 7,800 transplants are performed annually.

Valuation: $33m or $5.52 per basic share

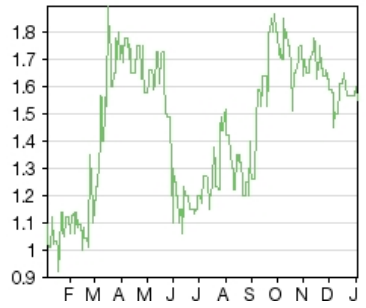
We have updated our valuation to $33m (previously $27m) or $5.52 (previously $6.62) per basic share. The difference is mainly due to lowered expenses, to help conserve cash, rolling forward our NPV and a higher net cash level, mitigated mainly by a higher share count due to the conversion of $2.7m in debt into shares. There remain approximately 14.1m potentially dilutive shares from warrants, options and convertible preferred stock. We project that the company will need at least $62.5m (previously $70m) in additional financing before profitability in 2024, of which a total additional $9m will be required by the end of 2018.

03 January 2018

Price	**US$1.55**
Market cap	**US$9m**

Net debt ($m) at 30 September 2017	2.2
Shares in issue	6.0m
Free float	31.1%
Code	ISCO
Primary exchange	OTC
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(2.5)	(9.9)	50.5
Rel (local)	(4.5)	(15.5)	25.0
52-week high/low	US$1.9		US$0.9

Business description

International Stem Cell is an early-stage biotechnology company developing therapeutic, biomedical and cosmeceutical applications for its proprietary stem form of pluripotent stem cells – human parthenogenetic stem cells (hpSCs). Its lead candidate is a cell therapy treatment for Parkinson's disease.

Next events

Efficacy data from second cohort	2018
Publication of interim results in scientific journal	2018
Initiation of Phase II in traumatic brain injury	2018

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Edison profile page

Some positive early signs in Parkinson's trial

International Stem Cell initiated its Phase I trial of ISC-hpNSC for the treatment of PD in July 2016. ISC-hpNSC are the company's proprietary neural stem cells (NSC) derived from a human parthenogenetic stem cell line (hpSC). The trial is a dose escalation study designed to evaluate the safety of the intracranial injection of 30m, 50m and 70m cells. The trial is also evaluating the treatment for efficacy by monitoring changes in brain function via PET scan, as well as functional assessment via various measures over the course of 12 months. In November, at the Society for Neuroscience annual meeting in Washington, DC, the company announced interim results from the first cohort of patients, those who received an intracranial injection of 30m cells.

Importantly, there were no serious adverse events reported related to the cells themselves and no evidence of tumors, cysts, enhanced inflammation or infection. Also, there are some early signs of efficacy across a variety of measures (see Exhibit 1), though of course certain caveats apply as this is a single-arm, open-label study, these data are only interim (the key datapoint is 12 months) and no p-values were provided. Additional data on the first cohort may become available upon publication of the interim results in a scientific journal which the company expects to happen sometime in 2018. We await that event as well as data from additional cohorts before updating our valuation for the PD program.

Exhibit 1: Interim data of ISC-hpNSC in PD

Measure	Description	Result at six-month time point
% OFF-Time	% of day when levodopa medication is not performing optimally and PD symptoms return	Decreased 24%
% ON-Time without dyskinesia	% of day that medication is working optimally without dyskinesia	Increased 19%
Beck Depression Inventory	21-question multiple-choice self-report inventory	Improved 35%
Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease	A brief self-completed questionnaire with 15 questions related to impulse control disorders in PD	Decreased 53%
Parkinson's Disease Quality of Life Score (PDQ-39) - Emotional Wellbeing dimension	The PDQ-39 is a 39-item tool to assess the quality of life in PD patients and is self-completed. The Emotional Wellbeing section consists of 6 items	Improved 33%
PDQ-39 - Activities of Daily Living dimension	6 items in the PDQ-39	Improved 22%
PDQ-39 - Mobility dimension	10 items in the PDQ-39	Improved 15%
PDQ-39 - Bodily Discomfort dimension	3 items in the PDQ-39	Improved 12%
PDQ-39 – Cognitive Impairment dimension	4 items in the PDQ-39	Improved 14%
PDQ-39 - Stigma, Social Support, Communications dimensions	Stigma consists of 4 items, Social Support 3 items and Communications 3 items	Not disclosed
UPDRS during OFF period	The UPDRS is a 6 part rating scale and is the most commonly used scale in the clinical study of PD. It is a qualitative functional scale of a patient's mental state, muscle tone and ability to perform daily tasks used to follow the course of the disease over time.	No improvement
Change in UPDRS score from baseline	This is a secondary endpoint at 12 months	Not disclosed
Proportion of patients with improvement defined as any reduction in the UPDRS motor score	This is a secondary endpoint at 12 months	Not disclosed

Source: International Stem Cell

Traumatic brain injury Phase II coming soon

International Stem Cell recently announced that it has completed the preclinical studies of ISC-hpNSC in TBI and plans to start a Phase II study of ISC-hpNSC. Once Phase II data are in hand, we would expect the company to apply to the FDA for the new Regenerative Medicine Advanced Therapy (RMAT) designation, which came into existence as part of the 21st Century Cures Act. Sponsors of regenerative medicine products, like ISC-hpNSC, may obtain the designation if the drug is intended to treat a serious or life-threatening condition and there is some preliminary clinical evidence of the ability to address unmet medical needs for that condition. RMAT designation allows for increased interactions with the FDA, similar to the interactions available to those with breakthrough designation, and the company may also become eligible for priority review and accelerated approval.

According to the Centers for Disease Control, TBI accounts for 2.5 million emergency room visits in the US annually and approximately 3.2-5.3 million people are living with a TBI-related disability with no effective long-term treatments outside of rehabilitation. Given the size, TBI could be as meaningful to the company as PD, for which we currently forecast $2.8bn in peak sales. We do not yet include TBI in our valuation as we await more clarity on the start of the company's Phase II trial.

Valuation

We have updated our valuation to $33m (previously $27m) or $5.52 (previously $6.62) per basic share. The difference is mainly due to lowered expenses, to help conserve cash, rolling forward our NPV and a higher net cash level, mitigated mainly by a higher share count due to the conversion of $2.7m in debt into shares. There remain approximately 14.1m potentially dilutive shares from warrants, options and convertible preferred stock.

Exhibit 2: Risk-adjusted NPV valuation model

Product	Status	Launch	Peak sales ($m)	NPV ($m)	Probability (%)	rNPV ($m)	NPV/share ($)
Cosmetic and biomedical business	Commercial	Current	18	22	90%	20	3.31
Parkinson's disease (royalties at 12% of sales)	Phase I/IIa	2024	2,800	505	7.5%	38	6.30
G&A expense – after tax					100%	(26)	(4.25)
Net cash				1.0	100%	1.0	0.17
Valuation				**528**		**33**	**5.52**

Source: Edison Investment Research estimates

Financials

International Stem Cell reported Q317 revenues of $1.8m, down 4.9% compared to Q316. Through the first nine months of the year, the company reported $5.6m in sales, up 2.5% compared to the same period last year. The biomedical business had revenues of $1.3m in Q317, up 2.7% compared to last year, and is up 21.0% year to date. The cosmetics business, however, was down 20.3% in Q317 and is down 26.4% year to date. For the company as a whole, the operating loss was $1.0m for the quarter, down 22.7% compared to the same quarter last year and down 17.9% for the year, as the profitability of the biomedical business improved to a greater extent than the profitability of the cosmetic business deteriorated. Also, the company was able to reduce its legal and filing fees and investor relations expenses. We have adjusted our model to reflect a weaker commercial business than we had forecast as well as lower R&D and SG&A expenses. The company reported $510,000 in cash and has had an operating cash burn of $183,000 per month this year.

In December, the company announced a note conversion and stock purchase agreement with their CEO. In exchange for the cancellation of a $2.7m note and a cash payment of $500,000 to the company, the CEO was issued 1.86m shares at a conversion and purchase price of $1.75 per share.

Exhibit 3: Changes to estimates

	Revenue ($000s)			Operating profit ($000s)			Profit after tax ($000s)		
	Old	New	% change	Old	New	% change	Old	New	% change
2017e	7,601	7,316	(3.7%)	(4,286)	(4,281)	0.0%	(4,886)	(4,321)	11.6%
2018e	8,343	8,044	(3.6%)	(6,957)	(6,715)	3.5%	(8,157)	(7,315)	10.3%

Source: Edison Investment Research. Note: Operating profit and profit after tax exclude amortization of acquired intangibles, exceptional items and share-based payments.

We project that the company will need at least $62.5m (previously $70m) in additional financing before profitability in 2024, of which an additional $7.5m will be required by the end of 2018.

Exhibit 4: Financial summary

US$000	2015	2016	2017e	2018e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS				
Revenue	7,551	7,165	7,316	8,044
Cost of Sales	(2,056)	(1,944)	(1,975)	(2,092)
Gross Profit	5,495	5,221	5,341	5,953
Research and development	(2,707)	(2,856)	(2,800)	(6,000)
EBITDA	(5,036)	(5,182)	(4,612)	(7,046)
Operating Profit (before amort. and except.)	(4,564)	(4,851)	(4,281)	(6,715)
Intangible Amortisation	0	0	0	0
Exceptionals	0	0	0	0
Other	1,929	3,772	(40)	0
Operating Profit	(2,635)	(1,079)	(4,321)	(6,715)
Net Interest	0	0	0	(600)
Profit Before Tax (norm)	(4,564)	(4,851)	(4,281)	(7,315)
Profit Before Tax (reported)	(2,635)	(1,079)	(4,321)	(7,315)
Tax	0	0	0	0
Profit After Tax (norm)	(2,635)	(1,079)	(4,321)	(7,315)
Profit After Tax (reported)	(2,635)	(1,079)	(4,321)	(7,315)
Average Number of Shares Outstanding (m)	2.0	3.2	6.0	6.3
EPS - normalised ($)	(1.29)	(0.34)	(0.72)	(1.17)
EPS - normalised fully diluted ($)	(1.29)	(0.34)	(0.72)	(1.17)
EPS - (reported) (US$)	(1.29)	(0.34)	(0.72)	(1.17)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	72.8	72.9	73.0	74.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	4,147	4,553	5,165	5,708
Intangible Assets	3,223	3,484	4,032	4,579
Tangible Assets	864	1,011	1,060	1,055
Investments	60	58	74	74
Current Assets	2,991	2,492	4,050	5,147
Stocks	1,348	1,390	1,306	1,436
Debtors	539	574	522	574
Cash	532	110	1,803	2,719
Other	572	418	418	418
Current Liabilities	(5,544)	(3,601)	(3,818)	(3,923)
Creditors	(5,544)	(3,601)	(3,818)	(3,923)
Short term borrowings	0	0	0	0
Long Term Liabilities	0	0	0	(7,500)
Long term borrowings	0	0	0	(7,500)
Other long term liabilities	0	0	0	0
Net Assets	1,594	3,444	5,397	(568)
CASH FLOW				
Operating Cash Flow	(4,120)	(4,197)	(666)	(5,111)
Net Interest	0	0	0	(600)
Tax	0	0	0	0
Capex	(738)	(944)	(841)	(874)
Acquisitions/disposals	0	0	0	0
Financing	1,169	4,018	3,200	0
Dividends	0	0	0	0
Net Cash Flow	(3,689)	(1,123)	1,693	(6,585)
Opening net debt/(cash)	(1,111)	(532)	(110)	(1,803)
HP finance leases initiated	0	0	0	0
Other	3,110	701	0	0
Closing net debt/(cash)	(532)	(110)	(1,803)	4,781

Source: International Stem Cell accounts, Edison Investment Research

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