EDISON

International Stem Cell

Development update

Dosing of first cohort complete

Pharma & biotech

International Stem Cell recently announced that the first cohort of four patients in its Phase I trial in Parkinson's disease (PD) had successfully undergone intracranial transplants of ISC-hpNSC. The study will ultimately enroll 12 patients at three dosing regimens (30m-70m cells) with a primary endpoint of safety, but will provide preliminary efficacy data measured at six and 12 months following the treatment.

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	7.6	(5.9)	(1.47)	0.0	N/A	N/A
12/18e	8.3	(8.2)	(1.96)	0.0	N/A	N/A

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

Parkinson's trial ongoing

Patients on the study will be treated in three cohorts with 30m, 50m and 70m stem cells, delivered via intracranial injection. The single-arm, open-label study is being conducted at the Royal Melbourne Hospital in Australia. Clinical assessments are scheduled at six and 12 months following surgery the data from this trial will be used in the design of a future Phase II trial expected to initiate in late 2017 or 2018.

Trial will provide first evaluation of efficacy

Besides safety, the trial will also provide physiological and functional assessments of the patients, which will give the first indication of the efficacy of the treatment in humans. Brain function will be directly assessed via PET scan to assess the degree of disease progression. Additionally, patients will be assessed via the six-point Unified Parkinson's Disease Rating Scale (UPDRS), a qualitative functional scale of a patient's mental state, muscle tone and ability to perform daily tasks. We expect to see some early efficacy data from the first cohort of patients in Q317.

Preparing to initiate trial in traumatic brain injury

The company is preparing to initiate a Phase II study of ISC-hpNSC in traumatic brain injury (TBI). According to the Centers for Disease Control, TBI accounts for 2.5m emergency room visits in the US annually and approximately 3.2-5.3 million people are living with a TBI-related disability.

Valuation: $28m or $6.97 per basic share

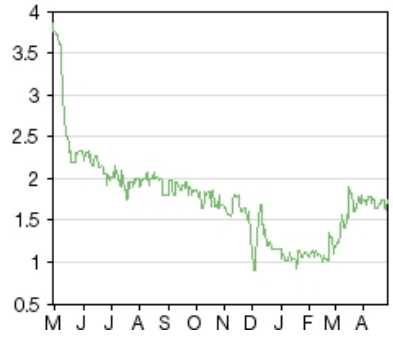
We have updated our valuation from $24m or $7.57 per basic share to $28m or $6.97 per basic share. The total valuation increased primarily due to rolling forward our NPV to 2017 but was mitigated by lower expected peak sales for the commercial business, and a lower cash balance. The per share value declined mainly due to a higher share count. There remain approximately 17.6m potentially dilutive shares from warrants, options and convertible preferred stock. We project that the company will need at least $70m (previously $73m) in additional financing before profitability in 2024, of which $7.5m will be required by the end of 2017.

27 April 2017

Price	**US$1.75**
Market cap	**US$7m**

Net cash ($m) at 31 December 2016	0.1
Shares in issue	3.95m
Free float	46.8%
Code	ISCO
Primary exchange	OTC
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(1.7)	60.6	(56.3)
Rel (local)	(3.5)	54.4	(61.7)
52-week high/low	US$3.9		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

Second cohort enrolment to commence	Q217
Initial efficacy data from first cohort	Q317
Initiation of Phase II in traumatic brain injury	Q317

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Edison profile page

ISC-hpNSC for Parkinson's disease

International Stem Cell Corporation has announced that the first cohort of four patients in its Phase I trial in Parkinson's disease (PD) have successfully undergone intracranial transplant of ISC-hpNSC. It had initiated the 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 the UPDRS over the course of 12 months.

The UPDRS is the most common standardized assessment used to monitor the progression and severity of PD in the clinical setting. It comprises six sections, including both patient and clinician evaluation of motor function, mood and the ability to perform daily tasks (Exhibit 1).

Exhibit 1: Unified Parkinson's Disease Rating Scale

Section	Description	Assessments
1	Mental assessment	Intellectual impairment, thought disorder, depression and initiative
2	Patient scored evaluation of ability to perform daily activities	Hygiene, food preparation, dressing, avoiding falls, speech, tremor etc
3	Clinician scored motor assessment	Measures of function (tremor, rigidity, posture), functional assessments (ability to rise from a chair, gait, speech) and evaluation of specific muscle groups (fingers, face, legs)
4	Complications associated with therapy	Rate of dyskinesia, assessments of "off" periods, other complications of treatment (nausea, insomnia, etc)
5	The Modified Hoehn Yahr Staging	Global evaluation ranging from no visible signs of disease to wheelchair-bound state
6	Schwab & England Activities of Daily Living Scale	Degree of independence from care givers ranging from completely independent to inability to swallow or perform bowel movements

Source: National Parkinson Foundation

The study is being performed at the Royal Melbourne Hospital in Australia and has a targeted enrolment of 12 moderate to severe PD patients, with the second cohort expected to start enrolment in Q217 following a meeting of the Data Safety Monitoring Board at the beginning of May. We expect to see some early efficacy data from the first cohort of patients in Q317

PD affects 7-10 million people worldwide, with approximately 1.5 million in the US. The most widespread treatment for the disease is the combination of levodopa and carbidopa, which provides the brain with dopamine lost by the death of dopaminergic neurons. The majority of clinical development in the space has been focused on the reformulation of this and other treatment regimens and, to date, no disease-modifying therapies have been approved.

Moving into traumatic brain injury

The company recently announced plans to start a Phase II study of ISC-hpNSC for the treatment of traumatic brain injury (TBI) following preclinical results in rodents suggesting the therapy can improve cognitive performance and motor co-ordination in those with the condition. We expect the company to conduct the Phase II trial in Australia where it would only need Ethics Committee approval to start the trial. Also, 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 2.5m 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 expect the company to report on a dose-escalating animal study in the coming months and initiate the Phase II study in Q317.

Valuation

We have updated our valuation from $24m or $7.57 per basic share to $28m or $6.97 per basic share. The total valuation increased primarily due to rolling forward our NPV to 2017 but was mitigated by lower expected peak sales for the commercial business, and a lower cash balance. The per share value declined mainly due to a higher share count (much of it due to a 926,971 warrant exercise). There remain approximately 17.6m potentially dilutive shares from warrants, options and convertible preferred stock. We expect to review our valuation following the release of efficacy data in Parkinson's as well as additional detail regarding the traumatic brain injury program.

Exhibit 2: Risk-adjusted NPV valuation model

Product	Status	Launch	Peak sales ($m)	NPV ($m)	Probability	rNPV ($m)	NPV/share ($/share)
Cosmetic and Biomedical Business	Commercial	Current	18	24	90%	21	5.39
Parkinson's Disease (royalties at 12% of sales)	Phase I/IIa	2024	2,800	459	7.5%	34	8.72
G&A expense – after tax					100%	(28)	(7.17)
Net cash					100%	0.1	0.03
Valuation						**28**	**6.97**

Source: Edison Investment Research estimates

Financials

International Stem Cell reported 2016 revenues of $7.2m, down 5.1% compared to 2015. The biomedical business continues to grow with revenues of $4.3m, up 6.6% compared to last year, but the cosmetics business was down 18.7%. For the company as a whole, the operating loss was $4.9m for the year. We have adjusted our model to reflect weaker commercial sales than we had forecast as well as slightly lower SG&A expenses. The company reported only $110,000 in cash as of the end of Q4, though has subsequently raised $1.3m through a promissory note issued to the CEO. It has a 3.5% annual coupon that is payable on 1 September 2017.

Exhibit 3: Changes to estimates

$000s	Revenue			Operating profit			Profit after tax		
	Old	New	% change	Old	New	% change	Old	New	% change
2017e	8,311	7,593	(8.6%)	(5,130)	(5,290)	(3.1%)	(5,970)	(5,890)	1.3%
2018e	9,156	8,341	(8.9%)	(6,749)	(6,958)	(3.1%)	(8,189)	(8,158)	0.4%

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 $70m (previously $73m) in additional financing before profitability in 2024, of which $7.5m will be required by the end of 2017.

Exhibit 4: Financial summary

US$000	2013	2014	2015	2016	2017e	2018e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS						
Revenue	6,147	7,017	7,551	7,165	7,593	8,341
Cost of Sales	(1,643)	(1,921)	(2,056)	(1,944)	(2,050)	(2,169)
Gross Profit	4,504	5,096	5,495	5,221	5,543	6,172
Research and development	(3,560)	(5,386)	(2,707)	(2,856)	(4,000)	(6,000)
EBITDA	(8,010)	(9,138)	(5,036)	(5,182)	(5,621)	(7,289)
Operating Profit (before amort. and except.)	(7,546)	(8,680)	(4,564)	(4,851)	(5,290)	(6,958)
Intangible Amortization	0	0	0	0	0	0
Exceptionals	0	0	0	0	0	0
Other	(2,930)	(3,796)	1,929	3,772	0	0
Operating Profit	(10,476)	(12,476)	(2,635)	(1,079)	(5,290)	(6,958)
Net Interest	(3)	(2)	0	0	(600)	(1,200)
Profit Before Tax (norm)	(7,549)	(8,682)	(4,564)	(4,851)	(5,890)	(8,158)
Profit Before Tax (reported)	(10,479)	(12,478)	(2,635)	(1,079)	(5,890)	(8,158)
Tax	0	0	0	0	0	0
Profit After Tax (norm)	(10,479)	(12,478)	(2,635)	(1,079)	(5,890)	(8,158)
Profit After Tax (reported)	(10,479)	(12,478)	(2,635)	(1,079)	(5,890)	(8,158)
Average Number of Shares Outstanding (m)	0.8	1.3	2.0	3.2	4.0	4.2
EPS - normalised (US$)	(12.77)	(9.71)	(1.29)	(0.34)	(1.47)	(1.96)
EPS - normalised fully diluted (US$)	(12.77)	(9.71)	(1.29)	(0.34)	(1.47)	(1.96)
EPS - (reported) (US$)	(12.77)	(9.71)	(1.29)	(0.34)	(1.47)	(1.96)
Dividend per share (US$)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	73.3	72.6	72.8	72.9	73.0	74.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET						
Fixed Assets	3,113	3,563	4,147	4,553	5,087	5,636
Intangible Assets	2,250	2,795	3,223	3,484	4,032	4,579
Tangible Assets	830	714	864	1,011	997	999
Investments	33	54	60	58	58	58
Current Assets	4,626	3,616	2,991	2,492	4,797	4,670
Stocks	1,369	1,517	1,348	1,390	1,356	1,489
Debtors	306	453	539	574	542	595
Cash	2,243	1,111	532	110	2,482	2,168
Other	708	535	572	418	418	418
Current Liabilities	(7,021)	(6,858)	(5,544)	(3,601)	(3,858)	(3,966)
Creditors	(7,021)	(6,858)	(5,544)	(3,601)	(3,858)	(3,966)
Short term borrowings	0	0	0	0	0	0
Long Term Liabilities	0	0	0	0	(7,500)	(15,000)
Long term borrowings	0	0	0	0	(7,500)	(15,000)
Other long term liabilities	0	0	0	0	0	0
Net Assets	718	321	1,594	3,444	(1,474)	(8,660)
CASH FLOW						
Operating Cash Flow	(5,638)	(6,413)	(4,120)	(4,197)	(3,663)	(5,734)
Net Interest	(3)	(2)	0	0	(600)	(1,200)
Tax	0	0	0	0	0	0
Capex	(896)	(988)	(738)	(944)	(865)	(880)
Acquisitions/disposals	0	0	0	0	0	0
Financing	8,123	6,270	1,169	4,018	0	0
Dividends	0	0	0	0	0	0
Net Cash Flow	1,586	(1,133)	(3,689)	(1,123)	(5,128)	(7,814)
Opening net debt/(cash)	(654)	(2,243)	(1,111)	(532)	(110)	5,018
HP finance leases initiated	0	0	0	0	0	0
Other	0	1	3,110	701	0	0
Closing net debt/(cash)	(2,243)	(1,111)	(532)	(110)	5,018	12,832

Source: Edison Investment Research, International Stem Cell reports

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