EDISON

International Stem Cell

Development update

Moving forward in Parkinson's and TBI

Pharma & biotech

International Stem Cell (ISCO) is an early-stage cell therapy company currently in clinical trials to treat Parkinson's disease (PD). In November, the company presented interim six-month results from the first cohort of four patients in its Phase I trial of ISC-hpNSC in PD. Positive signals were seen in a variety of measures, which include daily living, mobility, depression and compulsive disorders.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/16	7.2	(4.9)	(0.34)	0.0	N/A	N/A
12/17	7.5	(4.9)	(1.46)	0.0	N/A	N/A
12/18e	8.2	(7.3)	(1.13)	0.0	N/A	N/A
12/19e	8.8	(8.3)	(1.25)	0.0	N/A	N/A

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

Second cohort enrolled in PD trial

In March 2018, the company announced it had completed dosing of the second cohort of four patients in its Phase I trial of ISC-hpNSC in PD, who are being treated with the 50m cell dose. As a reminder, patients on the study are being treated in three cohorts with 30m, 50m and 70m stem cells, delivered via intracranial injection. Interim data from the first cohort, who were treated at the 30m cell dose, are encouraging. The company expects to start a Phase II PD trial later in 2018.

Phase II in TBI coming up in 2018

In September 2017, 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, which should commence in 2018. According to the Centers for Disease Control (CDC), 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.

Commercial operations help fund research

ISCO's commercial operations leverage its hpSC technology and generate revenues to partially offset R&D spending for therapeutic development. Lifeline Skin Care (LSC) develops and sells skincare products and Lifeline Cell Technology (LCT) produces human cell culture products for testing. Together they generate $7.5m in sales and $1.4m in operating profit though additional funding would be necessary to advance PD and TBI into Phase II trials.

Valuation: $34m or $5.45 per basic share

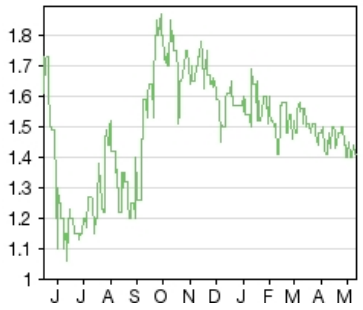
We have updated our valuation to $34m (previously $33m) or $5.45 (previously $5.52) per basic share. The difference is mainly due to rolling forward our NPV, which was mitigated by a lower cash balance and a higher share count. There remain approximately 12.7m potentially dilutive shares from warrants, options and convertible preferred stock. We project that the company will need at least $62.5m in additional financing before profitability in 2024, of which a total additional $7.5m will be required by the end of 2018.

14 May 2018

Price	**US$1.41**
Market cap	**US$9m**

Net cash ($m) at 31 December 2017	0.3
Shares in issue	6.2m
Free float	26.4%
Code	ISCO
Primary exchange	OTC
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(2.8)	0.0	(11.9)
Rel (local)	(5.8)	(4.0)	(22.6)

52-week high/low	US$1.9	US$1.1

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. Its lead candidate is a cell therapy treatment for Parkinson's disease.

Next events

Publication of interim results in scientific journal	2018
Initiation of Phase II in traumatic brain injury and PD	2018

Analysts

Maxim Jacobs	+1 646 653 7027
Nathaniel Calloway	+1 646 653 7036

healthcare@edisongroup.com

Edison profile page

Investment summary

ISCO is an early-stage biotechnology company developing therapeutic, biomedical and cosmeceutical applications for its proprietary form of pluripotent stem cells – human parthenogenetic stem cells (hpSCs). ISC California (the predecessor to ISCO) was created in 2006 and went public in December 2006 through a reverse merger, changing its name to International Stem Cell in January 2007.

With its hpSC technology, ISCO has created 15 stem cell lines to develop different cell types: liver cells, neural cells and three-dimensional eye structures. The company's technology platform does not require the use of fertilized eggs, embryos or foetal tissue to create stem cells, improving product cost and consistency while reducing the controversy associated with other types of stem cells. Its lead candidate is a set of neural cells currently undergoing Phase I clinical testing for PD. The company's portfolio includes preclinical candidates to address TBI, ischemic stroke, spinal cord injuries, metabolic liver disease, and retinal and corneal blindness.

ISCO's commercial operations leverage its hpSC technology and generate revenues to partially offset R&D spending for therapeutic development. LSC develops and sells skincare products and LCT produces human cell culture products for testing.

Valuation: $34m or $5.45 per basic share

We value ISCO based on a risk-adjusted net present value (rNPV) methodology, using a 10% discount rate and 90% probability for the skincare/biomedical businesses and a 12.5% discount rate and 7.5% probability for the PD candidate, due to its early development stage. Our model does not ascribe any value to the rest of ISCO's therapeutic pipeline but we shall revisit that once additional candidates enter the clinic. Our rNPV value is $34m, or $5.45 per share on an undiluted basis.

Financials: Dilution risk dominates

The company had $0.3m in cash on the balance sheet at 31 December 2017. This was supplemented in March 2018 through a promissory note that provided $0.35m in funds in cash from the co-chairman and CEO of the company. Operating cash burn is approximately $0.18m per month and is likely to increase as clinical trials progress. Minority investors should note that under the current capital structure, there are c 12.7m potential common shares from convertible preferred stock (including anti-dilution provisions, which could increase potential dilution), options and warrants that are outstanding, on top of the 6.2m common shares outstanding, which potentially creates sizeable dilution. Also, as the funds have come primarily from management, they 83% of outstanding shares as of 31 December 2017. We project financing needs as illustrative long-term debt of $62.5m by 2024, with an estimated $7.5m required by the end of 2018.

Sensitivities: An early-stage, cell therapy asset

As with any early-stage biotechnology company, ISCO faces numerous risks and uncertainties, especially preclinical risk. The investment case rests largely on the successful execution of the PD cell therapy clinical trials and the company's ability to attract a licensing/development partner to continue clinical development and, if approved, commercialization. The company's therapy for PD is in Phase I human trials and, due to its early-stage nature, has not been shown definitively to be efficacious although there are encouraging signs of efficacy from the interim six-month data from the first cohort of patients. Another risk stems from the capital structure, which, as mentioned, potentially creates sizeable dilution risk for minority investors.

A lasting treatment for PD?

ISCO is an early-stage biotechnology company developing therapeutic, biomedical and skincare applications for its proprietary form of pluripotent stem cells – hpSCs. With its hpSC technology, ISCO has created 15 stem cell lines, each of which is a different HLA type. From this, it creates different cell types such as liver cells, neural cells and three-dimensional eye structures. Its lead candidate is a set of neural cells currently undergoing Phase I clinical testing for PD.

ISCO's technology platform is based on hpSCs which are differentiated using chemical means. There are several techniques for turning an oocyte into a parthenote. One example uses a chemical catalyst such as $SrCl_2$, ethanol, Ca^{2+} ionophore, or ionomycin. This is followed by another chemical, for instance 6-DMAP (a broad protein synthesis inhibitor) or cytochalasin B or D (inhibitors of actin filaments polymerization), which blocks second polar body (PB2) extrusion. Thus, the resulting parthenote is a "pseudodiploid" heterozygous embryo containing the two sister chromatids of each maternal chromosome present in the MII oocyte.

Basic parthenogenetic cells are expanded, characterized and cryopreserved into a master cell bank under Current Good Manufacturing Practices (cGMP) conditions. These cells are then chemically directed to differentiate into a pure population of neural stem cells (ISC-hpNSC) under feeder-free conditions. The differentiated cells are grown in an incubated environment, characterized for the presence of neural markers and the lack of pluripotent markers, and then tested for microbial and viral contaminants before being used.

The Parkinson's market

According to the Parkinson's Foundation, there are nearly one million Americans with PD, with 60,000 diagnosed a year. PD is a progressive, irreversible neurodegenerative disorder. It arises from a lack of dopamine in the brain, owing to the death/damage of dopamine-generating cells in the substantia nigra located deep in the mid-brain just above where the spinal cord connects to the brain. The cause of cell death is currently unknown.

PD patients are evaluated using the Unified Parkinson Disease Rating Scale (UPDRS), which consists of three parts: mentation, behavior, mood; activities of daily living; and motor symptoms. Of a total possible score of 199 points (0 = no disability, 199 = worst/total disability), motor symptoms can account for just over half (108 points at worst) of the patient rating.

There are a number of different classes of therapeutic molecules available for PD (see Exhibit 1); however, these therapies only address the symptoms and do not slow or halt progress of the disease. The main families of drugs useful for treating motor symptoms are levodopa (L-DOPA), dopamine agonists and MAO-B inhibitors and are dominated by generics.

L-DOPA is one of the most commonly used treatments for PD symptoms with generics constituting almost all prescriptions. When patients begin to take L-DOPA, motor improvements of 25% (off-patient baseline so -7 points on an initial baseline of 28) have been cited. However, long-term studies suggest that after four or five years patients see modest improvement (6 points on the UPDRS scale) on L-DOPA compared to baseline. Also, after five to 10 years of treatment, between 50-70% of PD patients develop levodopa-induced dyskinesia, which is characterized by involuntary random and jerky movements similar to those motor symptoms for which the L-DOPA was originally prescribed. Current management includes adjusting L-DOPA dosing and/or adding a dopamine receptor D2 agonist to the regimen to spare L-DOPA.

Exhibit 1: Select currently marketed drug therapies for PD

Company name (originator)	Product names	Description	Comments/regulatory designation
AbbVie	Duodopa, Duopa, levodopa/carbidopa	Levodopa-carbidopa intestinal gel	US – orphan drug (treat PD)
Boehringer Ingelheim	Mirapex, Mirapex ER, Mirapexin, Sifrol, pramipexole (pexola)	Dopamine agonist	In one of the two early PD studies (n=335) the mean improvement from baseline on the UPDRS Part III total score was 5.0 in the MIRAPEX arm vs -0.8
Vernalis (Stada Arzneimittel in Japan)	Apokyn	Combines melevodopa, a methyl ester prodrug of levodopa, with carbidopa	Three blinded clinical studies (n=29, 17, 62) showed statistically significant benefit of Apokyn vs placebo on UPDRS motor scores (improvement of 20-24pt off baseline averaging 40)
Bristol Myers	Sinemet CR	Controlled release Levodopa-carbidopa	First approved controlled release CD LD formulation
GlaxoSmithKline	Adartel, Requip, ropinirole (Adartrel)	Dopamine D2 and dopamine D3 receptor agonist	Requip trial on early PD patients without L-DOPA (n=63) showed 30% improvement in UPDRS motor score on responders vs placebo. Similar results vs placebo from two other studies
Acadia	Nuplazid	Atypical antipsychotic	Indicated for the treatment of hallucinations and delusions associated with PD psychosis
Impax Laboratories	Rytary, carbidopa/levodopa (IPX066, GSK587124, Patrome)	Extended-release capsule formulation of carbidopa, an inhibitor of aromatic amino acid decarboxylation, and levodopa, an aromatic amino acid	In a 381 patient study, Rytary showed a 33-40% improvement from baseline in UPDRS Part II plus Part III scores at week 30
UCB	Neupro, rotigotine transdermal system	Dopamine agonist patch	Mean change in UPDRS (parts II + III) from baseline ranged from 13-23% across various studies
Novartis	Stalevo, Comtan, entacapone	Catechol-O-methyltransferase (COMT) inhibitor that inhibits breakdown of levodopa	Study data show improvement in "on" time (no symptoms) vs placebo (p=0.001). Approximately 15% improvement in UPDRS motor score (p<0.05)
Orion Corp	Eldepryl, selegiline	Selective monoamine oxidase B (MAO-B) inhibitor	Patients treated had a 13% reduction from baseline in daily "off" time, compared with a 5% reduction for patients treated with placebo
Roche	Tasmar (tolcapone)	COMT inhibitor that inhibits breakdown of levodopa	Adjuct therapy only
Teva Pharmaceutical Industries	Agilect, Azilect, rasagiline (mesylate)	Irreversible MAO-B	Study showed 15% improvement in UPDRS motor score at 1mg dosage as monotherapy
Valeant Pharmaceuticals	Zelapar, selegiline	MAO-B inhibitor	

Source: BioCentury, EvaluatePharma, Edison Investment Research

Much of the advanced small molecule pipeline for PD focuses on enhancements to existing therapies such as ways to provide more consistent delivery of L-DOPA (see Exhibit 2). However, the clinical challenge may be that the mechanisms of L-DOPA in the brain are more complicated than originally believed. For example, L-DOPA is released on an intermittent or as needed basis in the brain, not at a consistent level. In addition, the oral dosage of L-DOPA needed to achieve therapeutic benefits is considerably higher than would be needed under more direct delivery methods, which may contribute to long-term L-DOPA resistance.

Exhibit 2: Levodopa treatment axis programs

Company	Name	Molecule(s)	Status	Notes
BIAL	Ongentys	Opicapone	Filed	'Third generation' COMT inhibitor
LobSor Pharmaceuticals	LECIGon	Carbidopa; entacapone; levodopa	Phase III	Gel formulation deliver directly to duodenum via a pump
Acorda Therapeutics	CVT-301	Levodopa	Phase III	Inhalable levodopa
Depomed	DM-1992	Carbidopa; levodopa	Phase II	Gastroretentive immediate release/extended release co-formulation. Development suspended
SynAgile	DopaFuse	Carbidopa; levodopa	Phase II	Drug delivered via a continuous oral pump
IMPAX Laboratories	IPX203	Carbidopa; levodopa	Phase II	Follow on for Rytary. Fast onset followed by extended release
NeuroDerm	ND0612H	Carbidopa; levodopa	Phase II	Liquid formulation delivered via a dermal pump
XenoPort	XP21279	Levodopa prodrug	Phase II	Sustained release levodopa prodrug designed to improve absorption. Development halted pending a partnership
Aposense	ATT-LD	Levodopa prodrug	Preclinical	Long-acting levodopa prodrug
Cerecor	CERC-406	-	Preclinical	COMT inhibitor that passes the blood brain barrier

Source: EvaluatePharma, company documents

When medications are not enough to control symptoms, surgical techniques such as deep brain stimulation (DBS) can relieve the associated movement disorders; however, patients undergoing DBS frequently develop side effects such as short-term memory loss. Another invasive therapy is

Duopa (AbbVie, Duodopa ex-US), which is a gel formulation of carbidopa and levodopa that is delivered directly to the duodenum via an implanted pump. This device continuously infuses the drugs and is effective at reducing off states (63% reduction, twice the effect of immediate release pills) and dyskinesia (86% more on time without dyskinesia compared to immediate release pills), but requires major surgery. We therefore expect it to be limited to only the most poorly controlled patients. The product was approved in the US in early 2015, but has been approved in Europe since 2004. In 2017 the product sold $355m, with 83% of sales in Europe.

There are several cell therapy and gene therapy treatments looking to address the cause of PD. Cell therapies introduce new neural cells to supplement or replace cells damaged or destroyed by the disease. One of the most advanced is Living Cell Technologies' NeutrophinCell (NTCELL), an implantable choroid plexus cell product that contains specialized brain cells, which produce and secrete neurotrophins and cerebrospinal fluid (CSF). In a Phase IIa clinical study, NTCELL was injected in four patients under guidance by neuroimaging into the affected area of the brain. NTCELL decreased UPDRS by an average of 16 points after 58 weeks, representing a three- to four-year reversal of neurological deterioration. Data from the 18-patient Phase IIb trial is currently expected in May 2018.

Furthest along in gene therapy research is Voyager Therapeutics' VY-AADC, an adeno-associated virus (AAV) serotype 2 vector encoding dopa decarboxylase (DDC; AADC) that is delivered to the posterior putamen using image-guided, convection-enhanced delivery. In March 2018, the company reported Phase Ib results from 15 patients across three cohorts. In cohort 2, which will likely be the dose for Voyager's pivotal program, patients had a mean increase of 5.1 hours a day of on-time without any dyskinesia and experienced 65% less off-time. The company expects to initiate its pivotal trial in mid-2018.

Exhibit 3: Selected clinical-stage cell and gene therapy candidates in PD

Company	Product (company)	Stage of development	Therapeutic modality	Description
Living Cell Technologies	NTCELL	Phase IIb	Cell therapy	Choroid plexus cell product that secretes neurotrophins and CSF
International Stem Cell	ISC-hpNSC	Phase I	Cell therapy: stem cell	Neuronal cells derived from hpSC
Voyager Therapeutics	VY-AADC	Phase II/III	Gene therapy: viral vector: adeno-associated virus (AAV)	AAV serotype 2 encoding the DDC; AADC gene injected into the putamen
Oxford Biomedica	OXB-102	Phase I/II	Gene therapy: viral vector: lentivirus	LentiVector carrying three genes encoding enzymes for dopamine synthesis

Source: Biocentury, Edison Investment Research

ISCO's PD program

ISCO 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 an hpSC that are delivered intracerebrally to the striatum and substantia nigra via a one-time injection over a four- to five-hour period. The trial is an open-label, single-center (at Royal Melbourne Hospital in Australia), uncontrolled clinical trial that is evaluating three different dose regimens of 30m, 50m and 70m cells. A total of 12 participants with moderate to severe PD are to be enrolled. Patients are monitored to evaluate the safety and biologic activity of ISC-hpNSC for a year. A PET scan is performed at baseline, as part of the screening assessment, and at six and 12 months after surgical intervention. Clinical responses compared to baseline will be evaluated using various neurological assessments such as UPDRS, Hoehn and Yahr and other rating scales. The company expects to begin a Phase II PD trial later in 2018.

In November 2017, at the Society for Neuroscience annual meeting in Washington DC the company announced interim results from the first cohort of four patients, 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 4), 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. The decrease in 'off time', which is defined as the periods during the day when the PD medication is not working well in controlling symptoms, and the increase in 'on-time without dyskinesia', defined as the periods during the day when the PD medication is working optimally without a key side effect are particularly encouraging as these have the most direct impact on a patient's quality of life. 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.

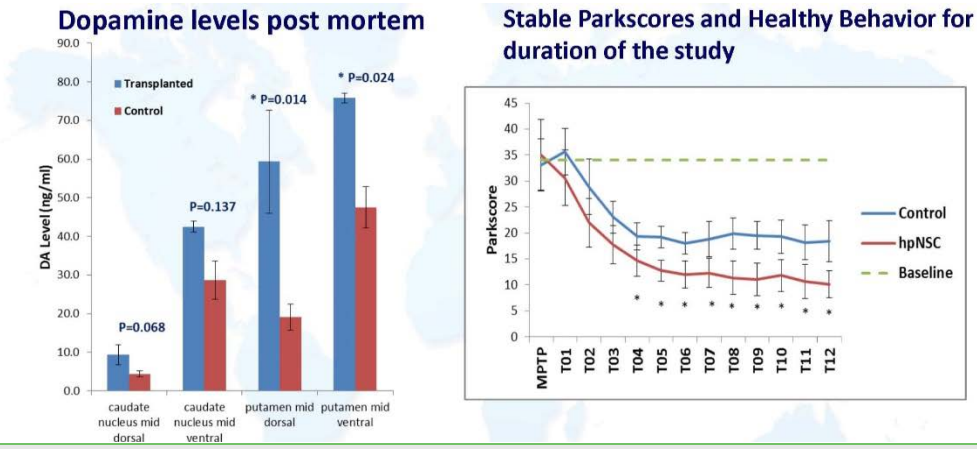
Exhibit 4: Interim data of ISC-hpNSC in PD

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 PD	A brief self-completed questionnaire with 15 questions related to impulse control disorders in PD	Decreased 53%
PD 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 six items	Improved 33%
PDQ-39 - Activities of Daily Living dimension	Six items in the PDQ-39	Improved 22%
PDQ-39 - Mobility dimension	10 items in the PDQ-39	Improved 15%
PDQ-39 - Bodily Discomfort dimension	Three items in the PDQ-39	Improved 12%
PDQ-39 – Cognitive Impairment dimension	Four items in the PDQ-39	Improved 14%
PDQ-39 - Stigma, Social Support, Communications dimensions	Stigma consists of four items, social support three items and communications 3 items	Not disclosed
UPDRS during off period	The UPDRS is a six-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 end point at 12 months	Not disclosed
Proportion of patients with improvement defined as any reduction in the UPDRS motor score	This is a secondary end point at 12 months	Not disclosed

Source: International Stem Cell

The company presented results of its PD preclinical studies in October 2015 at Neuroscience 2015 in Chicago. The preclinical studies on 18 non-human primates showed that at 12 months, the transplanted cells had integrated into the dopamine fibres and dopamine levels post-mortem were significantly higher in the transplanted group versus the control group.

Exhibit 5: ISCO preclinical data



Source: International Stem Cell presentation

We do not anticipate sales from ISCO's PD therapy until 2024, and expect the company to identify a licensing partner after Phase II data is released. Our model includes a 50/50 share of R&D costs

for the PD product between ISCO and its licensee, milestone payments of $10m in 2021, $15m in 2022 and $30m on US FDA approval (currently modelled in 2024) and a 12% royalty on sales to ISCO. We assume a treatment price of $20,000 (excluding surgical costs) in the US and $15,000 outside the US and we forecast peak sales in 2032 of $2.8bn resulting in royalties to ISCO of $334m.

Traumatic brain injury Phase II coming soon

ISCO recently announced it has completed the preclinical studies of ISC-hpNSC in TBI and plans to start a Phase II study of ISC-hpNSC by the end of 2018. A TBI can be any injury that disrupts the normal function of the brain and is usually the result of a fall, being hit by an object, or a car accident.

Exhibit 6: Estimated average annual number of TBI-related hospital visits and deaths, 2002-2010

Mechanism of injury	Emergency room visits	Hospitalizations	Deaths
Falls	658,668	66,291	10,944
Struck by or against an object	304,797	6,808	372
Motor vehicle traffic	232,240	53,391	14,795
Assault/Homicide	179,408	15,032	5,665
Self-inflicted/Suicide	N/A	N/A	14,713
Other	122,667	25,478	4,990
Unknown	97,018	113,172	-

Source: CDC Report to Congress, Traumatic Brain Injury in the United States

According to the CDC, in 2010 TBI accounted for approximately 2.5m emergency room visits, hospitalizations and deaths in the US and approximately 3.2-5.3 million people are living with a TBI-related disability with no effective long-term treatments outside of rehabilitation. Increased awareness, especially of sports-related concussions, has resulted in a greater level of emergency room visits as more patients seek care.

Exhibit 7: Age-adjusted rates of TBI-related hospital visits and deaths, 2001-10

Source: CDC Report to Congress, Traumatic Brain Injury in the United States

Once Phase II data in TBI 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. The company may also become eligible for priority review and accelerated approval.

TBI could be as meaningful to the company as PD, for which we forecast $2.8bn in peak sales. We do not yet include TBI in our valuation (either in terms of revenues or R&D expense) as we await more clarity on the start of the company's Phase II trial.

Cosmeceutical and biomedical business lines

Lifeline Skin Care (LSC) develops, manufactures and markets a line of luxury skincare products sold in the US and internationally through a branded website, professional channels (including dermatologists, plastic surgeons, medical, day and resort spas) and a network of distributors including Amazon. Products sold include cleansers, exfoliators and a range of specialized moisturizers and serums based on proprietary human non-embryonic stem cell extract and small molecule technologies. The global skincare market, while large, is very competitive and challenging which resulted in LSC sales falling 20.8% in 2017 compared to 2016. However, Q4 sales were up 33.3% sequentially and down only 4.1% compared to 2016. We are projecting a CAGR of 3.4% from 2017-2022 for the skincare business.

Lifeline Cell Technology (LCT) develops, manufactures and commercializes over 130 human cell culture products, including frozen human 'primary' cells and the reagents (called media) needed to grow, maintain and differentiate the cells. Cell types include endothelial, epithelial, fibroblasts, melanocytes, stem and smooth muscle among others.

Exhibit 8: LCT product categories

Airway cell systems	Mouse cells
Bladder cell systems	Prostate cell systems
Corneal epithelial cell systems	Renal cell systems
Cryopreservation solutions	Reproductive cell systems
Custom products and services	Skeletal muscle cell systems
Endothelial cell systems	Skin cell systems
Fibroblast systems	Smooth muscle cell systems
Hematopoietic systems	Stain kits
Keratinocyte systems	Human stem cell systems
Lung cell systems	Subculture reagents
Mammary cell systems	Supplements
Melanocyte systems	

Source: Company website

Unlike the skincare business, LCT has been growing briskly, up 20.5% in 2017 compared to the prior year. This growth rate has improved operating margins, which grew from 29.0% to 35.1% in 2017. We are projecting a CAGR of 9.1% from 2017-2022.

Exhibit 9: Commercial business segment reported financials

$000s	2016	2017
Revenues		
Skin care	2,849	2,256
Biomedical	4,316	5,200
Total	7,165	7,456
Operating expenses		
Skin care	2,797	2,634
Biomedical	3,065	3,373
Total	5,862	6,007
Operating income (loss)		
Skin care	52	(378)
Biomedical	1251	1827
Total	1,303	1,449

Source: International Stem Cell 2017 10-K

Sensitivities

As with any early-stage biotechnology company, ISCO faces numerous risks and uncertainties, especially preclinical risk. The investment case rests largely on the successful execution of the PD cell therapy clinical trials and the company's ability to attract a licensing/development partner to continue clinical development and, if approved, commercialization. The company's therapy for PD is in Phase I human trials and, due to its early-stage nature, has not been shown definitively to be efficacious although there are encouraging signs of efficacy from the interim six-month data from the first cohort of patients.

Another risk stems from the capital structure, which, as mentioned, potentially creates sizeable dilution risk for minority investors. To date, ISCO has relied primarily on funds from management in the form of a combination of convertible preferred shares, warrants and options to fund its growth so that on a fully diluted basis management controls 83% of outstanding shares as of 31 December 2017. While management has not converted or sold its sizeable holdings (and says it does not intend to), investors need to consider the possibility of significant dilution risk at some point in the future. There remain approximately 12.7m potentially dilutive shares from 4.0m warrants, 2.3m options and 6.4m convertible preferred shares on top of the 6.2m common shares outstanding. Also, investors should note that the convertible preferred shares are subject to anti-dilution provisions under certain circumstances, creating further dilution potential.

Valuation

We value ISCO based on an rNPV methodology, using a 10% discount rate and 90% probability for the skincare/biomedical businesses and a 12.5% discount rate and 7.5% probability for the PD candidate, due to its early development stage. Our model does not ascribe any value to the rest of ISCO's therapeutic pipeline but we shall revisit that once additional candidates enter the clinic. We have updated our valuation to $34m (previously $33m) or $5.45 (previously $5.52) per basic share. The difference is mainly due to rolling forward our NPV, which was mitigated by a lower cash balance and a higher share count.

Exhibit 10: International Stem Cell valuation

Product	Status	Launch	Peak sales ($m)	NPV ($m)	Probability	rNPV ($m)	NPV/share ($)
Cosmetic and biomedical business	Commercial	Current	18	23	90%	21	3.36
PD (royalties at 12% of sales)	Phase I	2024	2,800	521	7.5%	39	6.31
G&A expense - after tax					100%	(26)	(4.28)
Net cash				0.3	100%	0.3	0.05
Valuation				544		34	5.45

Source: Edison Investment Research

Financials

ISCO reported 2017 revenues of $7.5m, up 4.1% compared to 2016. In Q417, revenues were $1.8m, up 9.0% compared to Q416. The biomedical business had revenues of $5.2m for the year, up 20.5% compared to 2016. The cosmetics business, however, was down 20.8% in 2017. For the company as a whole, the operating loss was $4.9m for 2017, up 1.9% compared to the prior year as the profitability of the biomedical business improved to a greater extent than the profitability of the cosmetic business deteriorated, while spending on therapeutics increased somewhat. We have made slight adjustments to our model, increasing our 2018 revenue estimate for the commercial business by $0.15m, as it was stronger than expected in Q4, and adjusted our 2018 SG&A expense

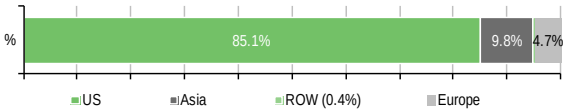
estimates higher by $0.05m due to a higher run rate. We have also introduced our 2019 estimates, which include growth in commercial business revenues to $8.8m.

The company had $0.3m in cash on the balance sheet at 31 December 2017. This was supplemented in March 2018 through a promissory note that provided $0.35m in funds in cash from the co-chairman and CEO of the company. Operating cash burn is approximately $0.18m per month and is likely to increase as clinical trials progress. We project that the company will need at least $62.5m in additional financing before profitability in 2024, of which a total additional $7.5m will be required by the end of 2018 and a further $10m by the end of 2019.

Exhibit 11: Financial summary

US$000	2015	2016	2017	2018e	2019e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS					
Revenue	7,551	7,165	7,456	8,193	8,846
Cost of Sales	(2,056)	(1,944)	(2,122)	(2,130)	(2,300)
Gross Profit	5,495	5,221	5,334	6,063	6,546
Research and development	(2,707)	(2,856)	(2,658)	(6,000)	(6,500)
EBITDA	(4,092)	(4,520)	(4,616)	(6,333)	(6,616)
Operating Profit (before amort. and except.)	(4,564)	(4,851)	(4,942)	(6,659)	(6,942)
Intangible Amortisation	0	0	0	0	0
Exceptionals	0	0	0	0	0
Other	1,929	3,772	(1,127)	0	0
Operating Profit	(2,635)	(1,079)	(6,069)	(6,659)	(6,942)
Net Interest	0	0	0	(600)	(1,400)
Profit Before Tax (norm)	(4,564)	(4,851)	(4,942)	(7,259)	(8,342)
Profit Before Tax (reported)	(2,635)	(1,079)	(6,069)	(7,259)	(8,342)
Tax	0	0	0	0	0
Profit After Tax (norm)	(2,635)	(1,079)	(6,069)	(7,259)	(8,342)
Profit After Tax (reported)	(2,635)	(1,079)	(6,069)	(7,259)	(8,342)
Average Number of Shares Outstanding (m)	2.0	3.2	4.2	6.4	6.7
EPS - normalised ($)	(1.29)	(0.34)	(1.46)	(1.13)	(1.25)
EPS - normalised fully diluted ($)	(1.29)	(0.34)	(1.46)	(1.13)	(1.25)
EPS - (reported) (US$)	(1.29)	(0.34)	(1.46)	(1.13)	(1.25)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	72.8	72.9	71.5	74.0	74.0
EBITDA Margin (%)	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
BALANCE SHEET					
Fixed Assets	4,147	4,553	4,009	4,599	5,202
Intangible Assets	3,223	3,484	2,922	3,511	4,100
Tangible Assets	864	1,011	1,013	1,014	1,028
Investments	60	58	74	74	74
Current Assets	2,991	2,492	2,855	4,245	6,779
Stocks	1,348	1,390	1,307	1,463	1,579
Debtors	539	574	465	585	631
Cash	532	110	304	1,419	3,790
Other	572	418	779	779	779
Current Liabilities	(5,544)	(3,601)	(4,800)	(5,155)	(5,249)
Creditors	(5,544)	(3,601)	(4,800)	(5,155)	(5,249)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	0	0	0	(7,500)	(17,500)
Long term borrowings	0	0	0	(7,500)	(17,500)
Other long term liabilities	0	0	0	0	0
Net Assets	1,594	3,444	2,064	(3,811)	(10,768)
CASH FLOW					
Operating Cash Flow	(4,120)	(4,197)	(2,142)	(4,869)	(5,300)
Net Interest	0	0	0	(600)	(1,400)
Tax	0	0	0	0	0
Capex	(738)	(944)	(864)	(916)	(929)
Acquisitions/disposals	0	0	0	0	0
Financing	1,169	4,018	3,200	0	0
Dividends	0	0	0	0	0
Net Cash Flow	(3,689)	(1,123)	194	(6,385)	(7,629)
Opening net debt/(cash)	(1,111)	(532)	(110)	(304)	6,081
HP finance leases initiated	0	0	0	0	0
Other	3,110	701	0	0	0
Closing net debt/(cash)	(532)	(110)	(304)	6,081	13,710

Source: Edison Investment Research, company reports

Contact details	Revenue by geography
5950 Priestly Drive, Carlsbad, CA 92008 US +1 760 940 6383 www.internationalstemcell.com	

Management team

Co-chairman and chief executive officer: Andrey Semechkin, PhD

Dr Semechkin has over 20 years of experience creating and managing businesses ranging from startups to multi-billion dollar market cap companies, across different industries and scientific sectors. He is a specialist in system analysis, strategic planning and corporate management. Dr Semechkin is a member of the Russian Academy of Sciences.

Executive VP and chief scientific officer: Russell Kern, PhD

Dr Kern was trained in medical genetics, embryology and stem cell biology. He was part of the team, along with scientists from the NYU Medical School, which elucidated the physiological changes that occur in the brains of PD patients. Dr Kern is a well-known speaker on stem cell biology, including the use of stem cells for neurology and skin regeneration. He has more than 40 publications in the field of PD and stem cell biology.

Acting chief financial officer: Jennifer Stephens, CPA

Ms Stephens has served in the director of finance position since February 2017. She has served an extensive number of companies in various management level accounting positions. Preceding her years as an accounting and finance consultant, Ms. Stephens worked with Ernst & Young LLP in a senior supervisory role in the San Diego audit practice where she worked with clients ranging in size from start-up companies to billion dollar SEC registrants. Ms. Stephens received a BA in Business Economics and Accounting from the University of California, Santa Barbara and is a licensed CPA.

President of Lifeline Cell Technology: Francisco Bustamante

Mr Bustamante has over 18 years of experience in operations of biotechnology companies, including senior management positions in the areas of manufacturing, procurement, planning, warehousing, distribution and project management. He has an excellent understanding of the manufacture and logistics of cell culture products, biological instruments, molecular biology kits and diagnostics His industry experience includes Clonetics, BioWhittaker (Cambrex), Digene and Meso Scale Diagnostics. Mr Bustamante received his BS degree in biology from the University of San Diego and his MBA degree from Frostburg State University. He has been with Lifeline Cell Technology since 2007.

Principal shareholders (fully diluted)	(%)
Dr. Andrey Semechkin and Russell Kern	83

Companies named in this report

Abbvie (ABBV), Vernalis (VER:LN), Bristol-Myers (BMY), GlaxoSmithKline (GSK), Acadia (ACAD), Impax (IPXL), UCB (UCB:BB), Novartis (NVS), Roche (ROG:VX), Teva (TEVA), Valeant (VRX), Voyager (VYGR), Living Cell Technologies (LCT:AU), Oxford Biomedica (OXB:LN)

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

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

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

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