EDISON

Mesoblast

Phase III study start

Positive data in discogenic low back pain

Pharma & biotech

Mesoblast has reported positive results from its 100-patient Phase II trial of mesenchymal precursor cells (MPCs) in patients with chronic moderate-to-severe discogenic low back pain. The data show strong indications of sustained efficacy across a broad range of clinical and radiographic parameters and support a planned move into Phase III studies. We maintain our recently increased valuation of A$3.0bn (A$9.06/diluted share), noting that the use of a higher probability (50%) to reflect a possible Phase III start of the two spinal programmes would increase the rNPV to A$3.2bn or A$10.04/share.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/12	27.8	(38.6)	(21.6)	0.0	N/A	N/A
06/13	24.2	(48.8)	(17.2)	0.0	N/A	N/A
06/14e	16.2	(76.9)	(24.1)	0.0	N/A	N/A
06/15e	16.2	(82.1)	(25.6)	0.0	N/A	N/A

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

Positive 12-month results in disc repair

Mesoblast has reported highly positive 12-month results from its 100-patient Phase II trial of MPCs in patients with chronic moderate-to-severe discogenic low back pain. The data show strong indications of sustained efficacy across a broad range of clinical and radiographic parameters after a single intra-disc injection and support the planned move into Phase III studies. Mesoblast intends to meet with regulatory authorities shortly to discuss the design of the registration trial.

Plan to start Phase III studies

The disc repair programme is one of two spinal programmes with MPC, both of which are proprietary (ie they fall outside the scope of the alliance with Teva). The second is the use of MPCs for lumbar spinal fusion. Both programmes may enter Phase III trials late this year, depending on the outcome of partnership discussions.

Teva moving ahead in CHF

Meanwhile, Mesoblast's partner Teva is set to recruit the first patients into its pivotal Phase III study of MPCs, coded as CEP-41750, in congestive heart failure (CHF), possibly as early as this week. CHF is the most important of the seven different indications being pursued with the MPC platform and, with US$4bn peak sales potential, it represents the largest component in our valuation.

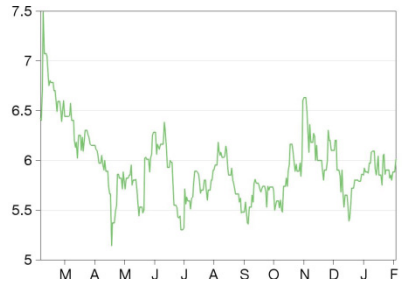
Valuation: rNPV of A$3.0bn (A$9.06/diluted share)

Edison maintains its recently updated valuation of A$3.0bn (A$9.34/share basic or A$9.06/share fully diluted). The potential start of Phase III trials in disc repair and spinal fusion would be allow for the use of a higher probability (50%) and increase the rNPV to A$3.2bn or A$10.04/share.

4 February 2014

Price	**A$6.0**
Market cap	**A$1,927m**
	US$0.92/A$
Net cash (A$m) as at 30 September 2013	292
Shares in issue	321.1m
Free float	60%
Code	MSB
Primary exchange	ASX
Secondary exchange	OTC Pink

Share price performance



%	1m	3m	12m
Abs	2.2	(9.4)	(3.8)
Rel (local)	5.2	(5.8)	(8.6)
52-week high/low	A$7.5		A$5.1

Business description

Mesoblast is developing adult stem cell therapies based on its proprietary MPC and culture-expanded MSC platforms. It has six late-stage clinical trials across four areas: immunologic/inflammatory (Phase III), spine disease (Phase II), cardiovascular (Phase III) and cancer (Phase III). The CV and BMT areas are partnered with Teva, and worldwide manufacturing of MPCs will be provided by Lonza.

Next events

Phase III plans in disc repair	H214
Update on Phase II trial of MPCs in AMI	2014

Analysts

Chris Kallos	+61 (0)2 9258 1160
Robin Davison	+44 (0)20 3077 5737

healthcare@edisongroup.com

Edison profile page

Mesoblast datasheet

Exhibit 1: Clinical-stage pipeline (summary)

Platform (product),	Indications	Dose (delivery)	Status	Next milestones
Cardiovascular				
MPCs/(CEP-41750) **Teva**	CHF	150m MPCs (transendocardial injection)	1,730-pt Phase III study	Q114: starts US enrolment, H214: start EU enrolment
MPCs, **Teva**	Acute myocardial infarction (AMI)	12.5m or 25m MPCs (intracoronary infusion)	225-pt Phase II study ongoing	2014: update on study 2015: headline data
Spinal disease				
MPCs (NeoFuse)	Lumbar spinal fusion	25m or 75m MPCs (implanted into intervertebral disc space)	24-pt Phase II completed	H214: potential Phase III trial
MPCs	Lumbar intervertebral disc repair	6m or 18m MPCs (intradiscal injection)	100-pt Phase II complete.	H214: potential Phase III start
Immunologic/Inflammatory				
MSCs (Prochymal, remestemcel-L)	Moderate-to-severe Crohn's disease (CD)	600m or 1,200m MSCs (intravenous infusion)	330-pt Phase III study ongoing	H214: complete Phase III recruitment
MPCs	Type 2 diabetes and diabetic nephropathy (DN)	Diabetes trial: 0.3m, 1m, or 2m MPC/kg (IV infusion); DN trial: 150m or 300m MPCs (IV injection)	60-pt Phase I/II study diabetes shows some evidence of efficacy. DN trial: 30-pt Phase II study ongoing	Q314: headline results from DN study
MPCs	Biologic refractory rheumatoid arthritis	Xm MPCs (IV injection)	48-pt Phase I/II study	H115: headline results
Oncology				
MSCs (Prochymal), **JCR Pharma**	Steroid-refractory acute graft versus host disease (aGvHD)	2m cells/kg twice weekly for four weeks (IV infusion)	Canadian/New Zealand conditional approval. Expanded Access Treatment in US. 190-pt Phase III aGvHD study and 240-pt Phase III steroid-refractory aGvHD study completed	Q114: Japanese filing by JCR H114: regulatory discussions (FDA, EMA) regarding potential filings
MPCs, **Teva**	Bone marrow transplantation (BMT)	One MPC expanded cord unit (IV infusion)	240-pt Phase III study ongoing	H217/H118: headline results

Source: Edison Investment Research

Exhibit 2: Mesoblast strategic partnerships

Partner/deal	Terms
Teva/Exclusive rights to selected CV, cancer and neurologic indications of MPCs	Teva has exclusive development and marketing rights, and is responsible for funding all late-stage development (Phase IIb, Phase III) and commercialisation. Mesoblast retains all manufacturing rights and has a negotiated a transfer price based on a percentage (Edison assumes 40%) of net in-market sales. Up to US$1.7bn in milestones are payable triggered by regulatory approvals for each product/indication in major territories (approval for CHF in US and EU triggers estimated payments of US$150m and US$100m, respectively). Teva holds a 17.6% equity stake in Mesoblast.
Lonza/Strategic alliance for supply MPC products	Long-term supply agreement with exclusive access to Lonza's Singapore manufacturing facility. Mesoblast has the option to require Lonza to construct a purpose-built manufacturing facility for exclusive use and in return would be obligated to purchase agreed quantities of marketed products. Mesoblast can also buy out this facility at a pre-agreed purchase price two years after it receives regulatory approval. The FDA has approved Lonza's manufacturing process to supply MPC products for US Phase III trials from both its Singapore and US facilities. Stockpiles of product to FDA specification are currently adequate for the next 12 months of Phase III trials.
JCR Pharmaceuticals/ Prochymal for aGvHD in Japan	JCR has exclusive Japanese rights to manufacture, develop and market Prochymal (known as JR-031) for steroid-refractory aGvHD. The annual number of hematopoietic stem cell transplants (HSCT) in Japan is c 3,500, of which a substantial proportion are likely to be autologous at risk of subsequent aGvHD. JCR will bear all costs of bringing Prochymal to market. Mesoblast is entitled to (undisclosed) milestones on regulatory filing and approval, milestones on achievement of pre-determined net sales levels, plus future royalties. JCR plans to file for Japanese approval under the existing regulatory pathway by March 2014.

Source: Edison Investment Research

Exhibit 3: CEP-41750 Phase III trial design

Design	Multi-centre, randomised (1:1), double-blind, sham procedure-controlled Phase III trial in 1,730 subjects with CHF. Pts will receive a single dose of 150m MPCs administered by transendocardial injection (direct injection into left ventricle of the heart via NOGA catheter) or undergo a cardiac catheterisation involving a sham cardiac mapping and cell delivery procedure.
Endpoint	**Primary:** Time-to-event analysis of HF-MACE (includes cardiac death, resuscitated cardiac death, or non-fatal decompensated heart failure events). Study is powered to show a 25% relative reduction in primary endpoint (HF-MACE) for Revascor vs control – assumes c 20% event rate in controls and c 15% event rate on CEP-41750. **Secondary:** Various measures of heart function, changes in NYHA functional class and QoL questionnaires.
Interim analysis	Two planned interim efficacy and/or safety analyses: first analysis (not futility) after c 18 months will assess various efficacy and safety parameters to determine the risk/benefit ratio; second analysis (futility) on HF-MACE endpoint after c 30 months, at which time the majority (>60%) of pts will have been recruited and c 40% of expected HF-MACE events occurred.
Patient population	NYHA class II and III systolic heart failure (LVEF≤40%) of ischaemic or non-ischaemic origin.
Recruitment/timing	Initial recruitment in US, with European enrolment commencing in H214. Number of centres not known, but assumed to be large. A final readout of data is indicated for mid (July/August) 2018. US/EU approvals/launch could take place in H119.

Source: Edison Investment Research

Update: Positive results in disc repair

Mesoblast has announced positive 12-month results from its 100-patient Phase II trial of mesenchymal precursor cells (MPCs) in patients with chronic moderate-to-severe discogenic low back pain (ie lumbar degenerative disc disease or DDD). The data show strong indications of sustained efficacy across a broad range of clinical and radiographic parameters after a single intra-disc injection and support a planned move into Phase III studies. Mesoblast intends to meet with regulatory authorities shortly to discuss the design of the registration trial in this indication.

The Phase II trial enrolled 100 patients with moderate to severe low back pain, caused by early disc degeneration (less than 30% disc height loss, 83% below Pfirrmann Grade 5 by MRI). Enrolled subjects had chronic low back pain (>six months) due moderate DDD in the lumbar spine (from L1 to S1), which was unresponsive to three months of conservative therapy (including physiotherapy). Patients were randomised to one of four treatment groups, two control (saline and hyaluronic acid or HA) and two active (6m MPCs and 18m MPCs). Patients will be evaluated for safety and efficacy over a total of 36 months to evaluate long-term treatment effects.

Results from the 12 month evaluation are shown in Exhibit 4. The large majority of the outcome measures showed a statistically significant improvement vs controls with MPC-treated patients using less opioids for pain relief, achieving greater radiographically-determined disc stability and a lower requirement for additional surgical and non-surgical treatment interventions. From a clinical perspective, MPC was equally effective at the lower and higher dose.

Exhibit 4: Outcome data at 12 months

Outcome measure	Saline (n=20)	HA (n=20)	6m MPCs (n=30)	18m MPCs (n=30)
Improvement in chronic low back pain				
Reduction in mean pain score (VAS) vs baseline	27 points	27 points	37 points, p=0.11*	40 points, p=0.046*
Prop of pts achieving >50% reduction in pain score	31%	35%	69%, p=0.009	62%, p=0.038
Prop of pts achieving minimal residual back pain (VAS<20)	18% (pooled)		52%, p=0.01	42%, p=0.05
Mean daily opioid use, tablet/day	1.00	0.94	0.77	0.58, p=0.17 vs saline
Mean opioid use in pts achieving >50% reduction in pain score	1.3	1.2	0.7	0.6
Need for additional surgical/non-surgical intervention for persistent pain	25%	10%	6.9% (p<0.05)*	3.3% (p<0.05)*
Time to first additional treatment intervention	N/A	N/A	p=0.023 vs saline	p=0.010 vs saline
Improvement in function				
Reduction in mean disability score (Oswestry Disability Index, ODI)	28%	30%	35%	43%, p=0.09 vs saline
Prop of pts achieving min residual functional disability (ODI score <20)	18% (pooled)		36%, p =0.14	39%
Improvement in disc stability				
Reduction in radiographically-determined translational movement of the disc	3.5%	2.5%	2.0%	1.3%, p=0.021

Source: Mesoblast. Note: *Vs pooled controls.

Discogenic back pain is the result of a complex process initiated by degeneration and loss of proteoglycan and water content of the nucleus pulpous, and increased stress on and fissure formation of the annulus fibrosis. Treatment varies from conservative options (analgesia, anti-inflammatory agents, epidural steroid injection) to surgical intervention (spine fusion, discectomy or artificial disc replacement).

While the majority of patients are treated non-surgically, more severe cases may require surgery. Chronic lower back pain can result from a wide variety of conditions including DDD. Major risk factors are age, genetics and mechanical injury/stresses to the disc. This leads to structural disruption and cell-mediated changes in disc composition. Some 30m people in the US suffer from lower back pain, of which c 15% (c 4.5m) fail to respond to conservative therapy. A proportion (c 500,000) has severe DDD that warrants surgery, which leaves c 4m with limited options. We estimate that 25% (c 1m) have moderate DDD that could be targeted with MPC injections. Exhibit 5 outlines our key model assumptions for MPCs in DDD.

Exhibit 5: Edison forecast assumptions for MPC in intervertebral disc repair

	US	Europe	Total	Notes
Addressable market – 2013	1m	1.5m	2.5m	
Launch year (FY)	2018	2018		
Peak year (FY)	2023	2023		Peak sales at year six post launch.
Peak market share, n (%)	20%	20%		Limited non-surgical treatment options for moderate lumbar DDD.
Pricing (US$)	5,000	3,750		Medtronic's InFuse (BMP-2) typically costs c US$5,000 in the US.
Peak in-market sales (US$m)	1,210	621	1,831	
Peak revenues to Mesoblast (US$m)	363	186	549	Assumes product is partnered before/during Phase III development. Forecast transfer price equivalent to 30% of net sales price.

Source: Edison Investment Research

Spinal fusion programme

The disc repair programme is one of two spinal programmes with MPC, both of which are proprietary (ie they fall outside the scope of the alliance with Teva). The second is the use of MPCs for lumbar spinal fusion. Both programmes may enter Phase III trials later this year.

Lumbar spinal fusion surgery is undertaken in patients who have severe lower back and/or neurological deficits that have not responded to conservative treatment. It is considered in conditions such as severe DDD, spinal disc herniation and spondylolisthesis (slipped disc). The procedure is to fuse two or more lumbar vertebrae, eliminating motion between them and decreasing pain from the joint. This is achieved by surgical placement of bone – an autograft (from the hip) or allograft (donor bone or demineralised bone matrix [DBM]) – or a bone-replacement (bone morphogenic protein) between the vertebrae. This stimulates the body's natural bone growth processes.

The standard against which all bone grafts are measured is autograft. However, because a procedure is required to harvest bone (from the hip) potential drawbacks include: poor candidate for harvesting, a longer surgical procedure, harvest-site infection, increased recovery time and long-term pain. An alternative to bone grafting is NuVasive's Osteocel Plus, an allograft cellular matrix that contains living bone cells (mesenchymal stem cells, osteoprogenitor cells) and a DBM scaffold. Osteocel is not FDA regulated (it came to market via the HCT/P pathway) and did not undergo extensive clinical trials.

Results of a Phase II FDA study of MPCs in lumbar fusion that were reported last year showed comparable efficacy and safety outcomes to autograft without the requirement for a bone-harvesting procedure (and its associated risks). The open-label study recruited 24 patients undergoing 1- or 2-level (ie two or three vertebrae) lumbar interbody fusion via posterior procedures. Enrolled subjects had lumbar DDD, clinical symptoms of neurogenic pain, and failed six months of conservative therapy. Patients were randomised to receive 25m MPC (n=8), 75m MPC (n=8) or autograft (n=8), with the latter taken from the patient's hip (iliac crest). Results from 23 patients were available at 12 months and are shown in Exhibit 6.

Exhibit 6: Phase II results in lumbar spinal fusion

Spinal fusion success	Comparable rates of fusion for all three groups, although 25m (7 pts, 86%) was slightly better than autograft (6 pts, 75%) and 75m (five pts, 63%).
Pain relief	MPCs (both doses) and autograft offered similar improvements in back pain relief at 12 and 24 months.
Blood loss	Significantly lower (30-43%) reduction in blood loss versus autograft, although we view the absolute reduction (120-170ml) as unlikely to be clinically meaningful. The higher blood loss for autograft likely relates to the surgical harvesting of iliac crest bone.
Safety	No reoperations/revisions in any groups, similar AE rate across all groups, no treatment-related SAEs, no heterotopic (abnormal) bone formation, and no immune responses.

Source: Edison Investment Research

An estimated 1.7m spinal fusion procedures were performed globally in 2011, of which 1m (c 60%) were lumbar. The US represents the largest market with c 380k lumbar fusions undertaken in 2012. We estimate that posterior approaches account for c 60% (228k) of procedures. In Europe, we estimate that c 350k lumbar fusions are undertaken annually, resulting in c 175k posterior

approaches. As a cross reference for Europe, recent UK data (2010/11) indicate that c 35k surgical procedures are undertaken annually in the UK for back pain or radicular pain, the majority of which are lumbar fusions/decompressions.

Exhibit 7: Edison forecast assumptions for MPCs in lumbar spinal fusion

	US	Europe	Total	Notes
Addressable market – 2013	230k	170k	400k	US: estimated 380k lumbar spinal fusions, of which 60% (230k) posterior approaches. EU: estimated 350k lumbar fusions, with 60% (175k) posterior.
Launch year (FY)	2019	2019		Assumes Phase III start in 2014, data 2017, submission 2018, approval/launch H119.
Peak year (FY)	2024	2024		Peak sales at year six post launch.
Peak market share, n (%)	40%	40%		Unmet need for alternative spinal fusion products that are safer (than Medtronic's InFuse), more convenient (than autografts) and better regulated (than Osteocel).
Pricing (US$)	5,000	3,750		MPC dose is 25m or 75m on carrier graft. Medtronic's InFuse (BMP-2) typically costs c US$5,000 in the US.
Peak in-market sales by partner (US$m)	590	293	883	Peak sales of InFuse were c US$900m. Global market for bone graft substitutes US$1.6bn in 2012 (70% from spinal fusions)
Peak revenues to MSB (US$m)	177	88	265	Assumes NeoFuse is partnered before/during Phase III trial. Forecast transfer price equivalent to 30% of net sales price.

Source: Edison Investment Research

Sensitivities

Mesoblast remains subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable outcomes in clinical trials and regulatory reviews, success of competitors, and commercial decisions by partners or potential partners. The key stock-specific sensitivity is the future of the Teva alliance – this partnership underwrites the development of MPCs in three major therapeutic areas (CHF, AMI and BMT).

Valuation

Edison maintains its recently updated valuation of A$3.0bn (A$9.34/share basic or A$9.06/share fully diluted). The potential start of Phase III trials in disc repair and spinal fusion would allow for the use of a higher probability (50%) and increase the rNPV to A$3.2bn or A$10.04/share.

Financials

Mesoblast has filed an Appendix 3c, which shows that cash was A$250m as of 30 December. We have adjusted our financial model to reflect a higher manufacturing and commercialisation spend, now A$35m, than was previously modelled (A$23m), in the light of the A$17.5m spent in H1. Forecast R&D spend is unchanged at A$47.4m for FY14 (A$21.5m was spent in H1) and A$47.9m in FY15. On this basis, operating cash outflow would be c A$94-95m/year over the next three years. In the absence of additional financing and/or partnerships, our model now suggests the cash runway extends into FY17.

Revenues principally comprise staged recognition of the US$130m Teva upfront (A$16.2m/year). We have not modelled any revenue from partnering of spinal indications, but assume that potential future partners would fund all or part of Phase III trials or G&A.

Exhibit 8: Financial summary

A$'000s	2011	2012	2013	2014e	2015e
30-June	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	116,221	27,808	24,185	16,176	16,176
Cost of Sales	0	0	0	0	0
Gross Profit	116,221	27,808	24,185	16,176	16,176
R&D Expenses	(11,948)	(36,937)	(43,108)	(47,419)	(47,893)
SG&A Expenses	(11,792)	(28,051)	(30,734)	(32,271)	(32,593)
EBITDA	90,238	(48,764)	(58,668)	(86,520)	(87,626)
Operating Profit (before amort and except)	90,103	(49,078)	(59,338)	(87,223)	(88,365)
Intangible Amortisation	(44)	(65)	(102)	(107)	(112)
Exceptionals	0	0	0	0	0
Share-based payments	(2,465)	(10,052)	(11,163)	(11,163)	(11,163)
Operating Profit	87,595	(59,195)	(70,603)	(98,493)	(99,640)
Net Interest	4,648	10,472	10,526	10,277	6,256
Profit Before Tax (norm)	94,751	(38,606)	(48,812)	(76,946)	(82,109)
Profit Before Tax (FRS 3)	92,243	(48,723)	(60,077)	(88,216)	(93,384)
Tax	(1,634)	(22,422)	(1,585)	0	0
Profit After Tax (norm)	93,117	(61,028)	(50,397)	(76,946)	(82,109)
Profit After Tax (FRS 3)	90,609	(71,145)	(61,662)	(88,216)	(93,384)
Average Number of Shares Outstanding (m)	216.8	282.9	292.8	318.8	321.2
EPS - normalised (c)	42.95	(21.58)	(17.21)	(24.13)	(25.56)
EPS - normalised and fully diluted (c)	40.88	(20.78)	(16.60)	(23.34)	(24.73)
EPS - (IFRS) (c)	41.79	(25.15)	(21.06)	(27.67)	(29.07)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0
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	497,755	503,877	551,868	552,389	552,874
Intangible Assets	475,326	497,219	547,834	547,834	547,834
Tangible Assets	609	1,998	2,757	3,278	3,763
Investments	21,820	4,660	1,277	1,277	1,277
Current Assets	265,495	216,579	331,844	215,077	130,787
Stocks	0	0	0	0	0
Debtors	2,101	10,669	12,063	12,063	12,063
Cash	263,228	205,591	315,309	198,542	114,252
Other	166	319	4,472	4,472	4,472
Current Liabilities	(30,794)	(44,495)	(50,588)	(37,484)	(37,484)
Creditors	(30,794)	(40,179)	(37,484)	(37,484)	(37,484)
Deferred revenue	0	(4,316)	(13,104)	0	0
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(216,610)	(197,113)	(202,858)	(186,479)	(170,303)
Long term borrowings	(81,334)	(56,361)	(56,617)	(40,441)	(24,265)
Other long term liabilities	(135,276)	(140,752)	(146,241)	(146,038)	(146,038)
Net Assets	515,846	478,848	630,266	543,503	475,874
CASH FLOW					
Operating Cash Flow	108,229	(65,204)	(67,716)	(93,520)	(93,626)
Net Interest	2,790	9,308	10,338	10,277	6,256
Tax	0	(7,038)	3,297	3,000	4,304
Capex	(462)	(1,983)	(1,224)	(1,224)	(1,224)
Acquisitions/disposals	0	0	0	(35,300)	0
Financing	126,093	4,883	169,349	0	0
Dividends	0	0	0	0	0
Other	2,386	(3,015)	(3,818)	0	0
Net Cash Flow	239,036	(63,049)	110,226	(116,767)	(84,290)
Opening net debt/(cash)	(32,049)	(263,228)	(205,591)	(315,309)	(198,542)
HP finance leases initiated	0	0	0	0	0
Other	(7,857)	5,412	(508)	0	0
Closing net debt/(cash)	(263,228)	(205,591)	(315,309)	(198,542)	(114,252)

Source: Mesoblast accounts, Edison Investment Research. Note: Revenue is adjusted to exclude interest income, per IFRS.

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
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand