Global Pharma (R) vs UK Pharma (B)

Source: Eikon Thomson Reuters

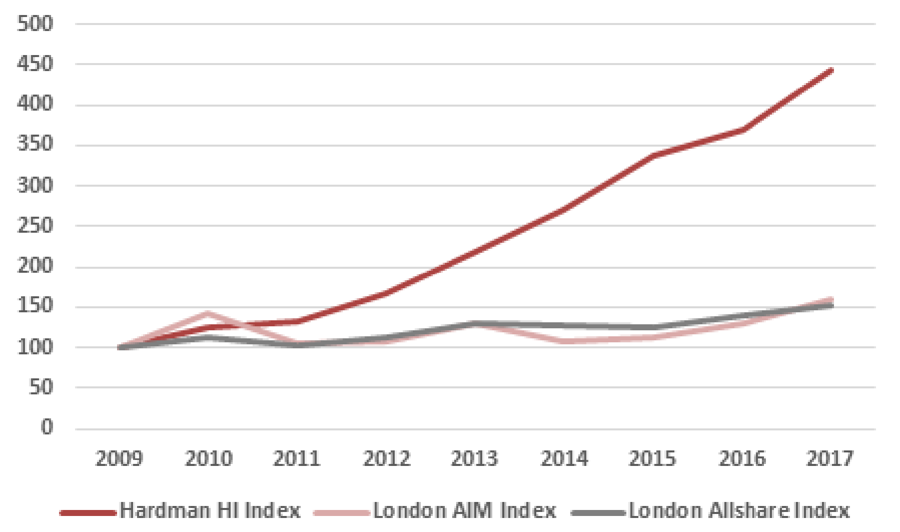
Hardman Healthcare Index

2017 – another year of outperformance

The Hardman Healthcare Index has been running since 2009. Its main function is to highlight the attractions of life sciences investments over the long term. 2017 was another successful year for the index, rising 20.3% to 437.3, and outperforming the London Allshare index, which grew 9.0% to 4,221.8. However, for the second year running, the index has trailed the performance of the AIM market, which rose 24.3% to 1049.6. Furthermore, several companies in our index increased their capital base – 21 of our 54 constituents raised new funds, three issued shares as part consideration for acquisitions, and two had share buybacks – all factors that influence the performance of the index. But even allowing for both capital increases and share buybacks, the index still increased by a creditable 11.5%.

- Since inauguration, the compound annual growth rate of the Hardman Healthcare Index has been +20.5%, compared with +5.4% for the Allshare Index and +6.1% for the AIM index, highlighting the attractiveness of the healthcare sector as a long-term investment, even though it is capital intensive.
- Of the 54 companies included in the Hardman index, 31 saw their share prices rise in 2017, whereas 23 fell, with no company simply marking time.
- The variance between the best and worst performing stocks was high at 301% – **Immupharma (IMM)** rising 227% and **Vernalis (VER)** falling 74% – the median share price change was +9%.
- Interestingly in relative terms, only 20 stocks outperformed the index over the last year, with the other 34 underperforming.
- **Tristel (TSTL)** has been one of the top five stocks in four out of the last five years on the back of strong financial performance indicators, rising eight-fold over the period.

Performance of Hardman Healthcare Index – rebased



Source: Hardman & Co Life Sciences Research

Analysts
Martin Hall 020 7194 7632
mh@hardmanandco.com
Dorothea Hill 020 7194 7626
dmh@hardmanandco.com
Gregoire Pave 020 7194 7628
gp@hardmanandco.com

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Share price performance

Listing	Company	Ticker	Share Price (p) 31 Dec 2016	Share Price(p) 31 Dec 2017	Market Cap (£m) 31 Dec 2017	Price Change (%)
AIM	Abcam	ABC	767.0	1,055.0	2,160.7	+38%
AIM	Advanced Medical Soln	AMS	221.8	318.0	676.2	+43%
AIM	Advanced Oncotherapy	AVO	75.5	57.5	46.5	-24%
AIM	Allergy Therapeutics	AGY	20.9	28.5	169.3	+37%
AIM	Alliance Pharma	APH	47.5	67.1	318.4	+41%
Full	Assura	AGR	57.0	63.9	1,518.2	+12%
AIM	Avacta	AVCT	72.0	64.0	44.1	-11%
Full	Bioquell	BQE	140.0	267.5	60.1	+91%
Full	BTG	BTG	590.0	762.5	2,946.4	+29%
Full	Cambian Group	CMBN	123.8	196.3	362.0	+59%
AIM	Caretech	CTH	316.0	430.0	325.4	+36%
Full	Cathay International	CTI	18.3	7.6	33.4	-58%
AIM	Circle Holdings	CIRC	19.0	30.0	75.2	+58%
AIM	Collagen Solutions	COS	6.3	2.8	8.9	-56%
Full	Consort Medical	CSRT	1,060.0	1,168.0	575.6	+10%
AIM	Deltex Medical Group	DEMG	3.9	2.1	6.6	-45%
AIM	Diurnal	DNL	106.5	146.5	77.0	+38%
AIM	Eco Animal	EAH	505.0	597.5	392.9	+18%
AIM	EKF Diagnostics	EKF	17.2	26.3	120.1	+53%
AIM	Emis	EMIS	964.5	1,011.0	642.6	+5%
AIM	e-Therapeutics	ETX	7.6	9.3	24.8	+21%
AIM	Futura Medical	FUM	56.3	29.8	35.9	-47%
AIM	Genedrive	GDR	60.0	33.5	6.3	-44%
Full	Genus	GNS	1,796.0	2,531.0	1,557.5	+41%
AIM	Immunodiagnostics	IDH	210.0	270.0	79.4	+29%
AIM	Immupharma	IMM	52.0	170.0	225.3	+227%
Full	IP Group	IPO	178.8	142.2	1,503.6	-20%
AIM	Ixico	IXI	31.5	36.5	9.9	+16%
AIM	Kromek Group	KMK	22.5	26.4	68.7	+17%
AIM	Lidco Group	LID	6.0	7.4	18.0	+23%
Full	MD Medical Group	MDMG	9.5	10.2	570.1	+8%
Full	MedicX Fund	MXF	89.8	84.0	357.9	-6%
AIM	Motif Bio	MTFB	24.7	41.0	108.0	+66%
AIM	Omega Diagnostics	ODX	18.3	17.0	21.6	-7%
AIM	OMG	OMG	49.0	58.3	71.7	+19%
Full	Oxford BioMedica	OXB	4.1	8.9	275.0	+117%
AIM	Premaitha Health	NIPT	8.4	5.1	16.5	-39%
Full	Primary Health Properties	PHP	111.3	117.0	724.8	+5%
AIM	Proteome Sciences	PRM	5.5	3.1	9.2	-43%
AIM	Realm Therapeutics	RLM	30.0	37.0	43.1	+23%
AIM	ReNeuron	RENE	2.6	1.9	59.5	-28%
AIM	Sareum	SAR	0.8	0.9	23.3	+13%
AIM	Scancell	SCLP	14.8	12.8	39.8	-14%
AIM	Sinclair Pharma	SPH	33.8	26.1	131.6	-23%
Full	Smith & Nephew	SN.	1,221.0	1,288.0	11,266.1	+5%
Full	Spire	SPI	337.7	253.6	1,017.1	-25%
AIM	Surgical Innovations	SUN	4.3	3.6	28.3	-15%
AIM	Tissue Regenix	TRX	20.5	9.3	108.3	-55%
AIM	Tristel	TSTL	156.0	250.0	106.1	+60%
Full	Vectura	VEC	137.1	117.7	798.0	-14%
AIM	Venture Life	VLG	51.5	43.0	15.8	-17%
AIM	Vernalis	VER	34.0	8.7	46.0	-74%
AIM	Verona Pharma	VRP	156.0	104.5	109.7	-33%

Review of 2017

The Hardman Healthcare Index was established in 2009. Its main function is to highlight the attractiveness of life sciences investments over the long term, and to try and identify those stocks that have disruptive technologies that consistently allow them to outperform the index and the markets. Many of the 54 constituents of the index are high risk, still being in the development stage, with micro-capitalisations and along way from sales and profitability. Despite this, some companies can still make extremely attractive returns for investors as evidenced by the top performing stock in 2017, Immupharma (IMM), which has seen its share price rise 227%.

Comparison of HI Index to London markets

@31st December	2009	2010	2011	2012	2013	2014	2015	2016	2017	CAGR
	Index	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	%
Hardman Healthcare index	98.4	25%	6%	26%	31%	24%	24%	20%	20%	20.5%
London AIM index	654.2	43%	-26%	2%	20%	-17%	5%	24%	24%	6.1%
London Allshare index	2,772.0	12%	-9%	9%	17%	-2%	-3%	9%	9%	5.4%

Source: The London Stock Exchange; Hardman & Co Life Sciences Research

Some failures

As we enter 2018, a change in constituents is required given that two underperforming companies are no longer listed: **Circle Holdings** was acquired during the year at 30p per share, a far cry from its IPO price of 152p in June 2011; and **Sphere Medical**, a perennial underperformer, was taken private by its major shareholders at 2.9p per share, having floated at 92.5p in November 2011. We will take this opportunity to add some more small-cap pharma/healthcare/MedTech companies that have interesting R&D pipelines to make up for the lost capitalisation of about £80m.

Comparison to the majors

In order to put the share price movement of our, generally small capitalisation, index constituent companies into perspective, the following table shows the performance of the four major UK healthcare companies over the same period. In 2017, Astrazeneca was the best performer by a considerable amount as he market is taking an optimistic view that its R&D pipeline will deliver. On the other hand, GlaxoSmithKline moved in the opposite direction, and also saw senior management changes. For historic reasons, 25% of the market capitalisation of Smith & Nephew is included in our index. Over the long-term, the performance of our index of small-cap companies has considerably outperformed the majors.

Performance of healthcare majors

Company	Ticker	Share Price (p) 31 Dec 2016	Share Price (p) 31 Dec 2017	Change 2017	CAGR 2009-2017
AstraZeneca	AZN	4438	5121	+15%	+6.5%
GlaxoSmithKline	GSK	1562	1323	-15%	0.0%
Shire	SHP	4684	2900	-17%	+13.9%
Smith & Nephew	SN.	1221	1288	+5%	+8.1%

Source: Hardman & Co Life Sciences Research

Movers and shakers

Given our large portfolio of constituent companies, we usually focus on both the top five and the bottom five, and try to offer a short explanation as to why the shares have performed in the way that they have.

Best and worst performers in 2017

Top five			**Bottom five**		
Rank	**Company**	**Δ**	**Rank**	**Company**	**Δ**
1	Immupharma	227%	49	Futura Medical	-47%
2	Oxford BioMedica*	117%	50	Tissue Regenix*	-55%
3	Bioquell	91%	51	Collagen Solutions*	-56%
4	Motif Bio	66%	52	Cathay International	-58%
5	Tristel	60%	53	Vernalis	-74%

** Client of Hardman & Co from whom we receive payment to provide research*
Source: Hardman & Co Life Sciences Research

The 'Top Five'

Immupharma (IMM) +227%

The top performing stock in our universe during 2017 was Immupharma (IMM), which is a late-stage drug development company that specialises in the field of autoimmune disease. Its leading asset, Lupuzor for the treatment of Lupus where there is only one other approved drug, is just about to complete a 200-patient double-blind Phase III trial over 52 weeks, that is being undertaken on three continents – America (11 sites, 70 patients), Europe (5 countries, 81 patients), and Mauritius (49 patients). In December, the company announced that the last patient completed dosing and headline data are expected to be announced during 1Q 2018. Over some years, the company has struggled with the funding of this key trial. Therefore, an over-subscribed Placing, at 52p per share, to raise gross new capital of £4.1m in March to support the cost of the trial through to its conclusion, coupled with regular trial progress reports has given the market considerable confidence, and significantly de-risked the drug. While there is still some risk regarding the trial outcome, positive data would pave the way to securing a commercialisation partner and a lucrative deal.

Oxford BioMedica (OXB) +117%*

Oxford BioMedica is a specialist advanced therapy viral-vector biopharmaceutical company that offers vector manufacturing and development services to other companies, while retaining its own proprietary drug candidates for out-licensing or partnering. Having made significant investments in state-of-the-art specialist manufacturing facilities, the company has an attractive offering. The first major client was Novartis, and 2017 was an important milestone, when Kymriah became the first-ever CAR-T therapy to be approved, for which OXB has a minimum three-year supply agreement, which will generate a total of $100m+ of income.

Having raised new capital in 2016, and with a re-financing of its long-term loan, the market's confidence suddenly grew that the current business would not need more capital in the near future. In addition, there have been many global deals announced between major pharma and specialist cell-based manufacturers, again highlighting OXB's position in the market and the opportunities within it. This positive news flow was reflected in the share price uplift during 2017.

Bioquell (BQE) +91%

Bioquell manufactures and sells specialist biological decontamination products to a range of life sciences, healthcare and defence industries. Following disposals and reorganisation, it has developed a more focused approach, with its main technology being based on hydrogen peroxide vapour, which is very effective at eradicating micro-organisms such as bacteria and viruses. Being broken down at the end of the process into water vapour and oxygen, it is a very 'green' alternative to traditional methods of decontamination. Having struggled for growth over a number of years, this focused approach has improved the company's growth prospects, such that the market was surprised by the level of growth, and cash generation, at the interim stage of fiscal 2017. The shares have also been supported by a share buyback programme, but with tightly held stock and low liquidity, this has had limited success, although it does provide natural market support.

Motif Bio (MTFB) +66%

Motif Bio was floated in April 2015 with the primary objective of raising the necessary funds to bring its new antibiotic, iclaprim, to the US market. Shortly after its IPO, the company reached an agreement with the FDA about exactly what was required in terms of clinical trial data and end-points for regulatory approval. Since then, the company has been undertaking two trials designed to satisfy the requirements of the FDA and during 2017, it reported regularly on progress, hitting targets, and publishing trial results that at least met the primary end-points. Concomitantly with trial progress being made, the company took the opportunity to raise additional capital, providing management with the resources needed to complete the second, REVIVE-2, phase III clinical trial. This was well supported by the market which has increased confidence in a project that has been significantly de-risked.

Tristel (TSTL) +60%

Tristel has been a consistent outperformer in four of the last five years. The company manufactures products to alleviate cross-contamination between patients in hospitals/clinics through cleaning of probes, surfaces etc, which are user-friendly and, unlike traditional cleaning products, not based on chlorine. Over the years, trading has consistently been better than market expectations – hence the positive movement in the share price. In addition, the company boasts some of the best financial performance indicators converting every 100p of operating profit into 105p of cash through improved working capital and benefits from capital investment. In 2016, its Return on Invested Capital was 22%, setting it alongside some of the best in the top 100 stocks in London. The stock was resurgent in 2017 following an announcement that the company had agreed a clear regulatory pathway for getting its products approved in the US, which would significantly boost long-term growth. At its recent AGM, management indicated that "*…the additional data requested by the United States EPA was submitted by the agreed deadline of 15 November 2017…*", keeping it on schedule with the project plan. Further strong financial performance and news from the US during 2018 are likely to see further progress in the shares.

The 'Bottom Five'

Vernalis (VER) -74%

For the second year running, Vernalis has found itself in the bottom five, and, in 2017, it was the worst performer among our company coverage. It is a commercial-stage pharmaceutical company that has adopted a buy-and-build strategy of older prescription pharmaceuticals for the US market, to support its own low-risk development programmes. It currently has two products approved in the US – for cough/cold and an amoxicillin antibiotic– and has a further four in development, all for cough/cold. In the UK, Vernalis has drug discovery and development activities with one out-licensed marketed drug, and a further eight drug candidates in development. There are four reasons behind the underperformance in 2017. First, since launch in the US, Tuzistra-XR utilisation has been significantly below expectations and there needs to be a large pick-up to see any meaningful sales traction. This has not been helped by increased negativity towards narcotic-based products in the US. Secondly, the FDA issued Complete Response Letters explaining why it did not approve CCP-07 (April) and CCP-08 (August). Vernalis' partner in the US, Tris, must provide clear evidence that it has addressed the manufacturing issues highlighted following a site inspection. Thirdly, the loss of patent on frovatriptan has markedly reduced the level of sales royalties on this migraine drug from Menarini. Fourthly, the company has struggled to replace the manufacturer of its amoxicillin formulation (Moxatag) with an alternative supplier following the financial liquidation of its original supplier, although new supplies enabled the company to relaunch the product in September 2017. Fortunately, the company still has a strong cash position (ca.£47m at end of December on our estimates), so there is no obvious need for a cash call in the short-term, but this is something that could become an issue as 2018 progresses.

Cathay International Holdings (CTI) -58%

Cathay International is an operator and investor in the growing healthcare sector in the People's Republic of China. 2017 was dominated by announcements about insurance claims and litigation at a subsidiary company of one of Cathay's key investments, Lansen Pharmaceutical Holdings, in which it owns 50.56%. While most of the judgements have been in Lansen subsidiary's favour, the overall impact has been a burden on the company, which has been reflected in the performance of the shares of its major shareholder, CTI.

Collagen Solutions (COS) -56%*

Collagen Solutions is a biomaterials company developing and manufacturing medical-grade collagen components for use in medical devices, research, and regenerative medicine. Management has embarked on an investment strategy through a series of initiatives to increase the growth opportunities and, in the process, COS has moved from a reliable quality medical-grade collagen supplier to one that also has high value-added proprietary products. In February 2017, the company announced a Placing and a venture debt agreement to provide a blend of financing for this strategy. On several product fronts, management has moved things forward during the year, particularly in the case of ChondroMimetic for the repair of small cartilage lesions, which will be the company's first proprietary product to be commercialised. Investment in marketing has resulted in eight new accounts so far in fiscal 2018, compared to nine for the whole of 2017, and a large number of live deals under negotiation. However, investment in products and commercial strategy will take time to benefit the company, and management dampened sales expectations again in December, which had a detrimental impact on the share price. Key will be the regulatory approval, commercial partnership, and launch of ChondroMimetic during 2018.

Tissue Regenix (TRX) -55%*

TRX has a broad portfolio of regenerative medicine products developed from decellularised human and porcine soft tissues for the wound care, orthopaedics, and cardiac markets. Since the launch of DermaPure, the focus has been on generating sales traction in the US wound-care market. In the early part of the year, the share price was under pressure because the market was wholly aware of the need for more capital for product commercialisation and working capital purposes. When this was eventually announced in July, it was much larger than expected, being accompanied by a significant acquisition in the US to expand the offering, accelerate its growth prospects, and shorten the time to reach profitability. However, the share price was further undermined by the unexpected resignation announcements of both the CEO (October) and the CFO (December). A new CEO with more commercial experience has been appointed and the company has indicated that trading remains in line with the Boards expectations, but the stock is only likely to recover only when there is much greater clarity regarding business performance, which is due to be announced with full-year results in March 2018.

Futura Medical (FUM) -47%

On the product front, newsflow from Futura Medical was generally positive throughout 2017, continuing the theme from 2016 when it was one of the best performers. Key to this was the satisfactory resolution of the shelf-life of CSD500, its erectogenic condom, close to the two-year industry standard, which has allowed the formal launch of the product in some territories by its international distributors. However, all of this was undone when Church & Dwight, its long-standing manufacturing, marketing and distribution partner in North America and certain countries in Europe decided to terminate the contract and return the rights to CSD500 to FUM because of a change in the strategic direction of the company. Although this highlighted the benefits of management's lower risk strategy to sign deals with several partners on a territory-by-territory basis for its products, this announcement in August completely undermined the share price, from which it has struggled to recover. The company has continued with its programme of product development and is seeking new distribution partners and any announcements along these lines could lead to a recovery in 2018.

Upcoming newsflow

- **Abzena (ABZA)*:** Partner, Gilead Sciences, is due to release interim Phase III data for GS-5745 (andecaliximab) for the treatment of gastric cancer in 1H 2018.
- **Amryt Pharma (AMYT):** Interim analysis of the AP101 Phase III trial in patients suffering from the orphan disease, epidermolysis bullosa, is expected in 1Q 2018. An independent data monitoring committee will conduct an initial efficacy analysis.
- **Avacta (AVCT)*:** Release of results on the feasibility studies for Affimer Drug Conjugates performed by its partner, Glythera, is due in 1Q 2018.
- **Collagen Solutions (COS)*:** Report on the findings from the 8-year follow-up trial in 15 patients originally implanted with ChondroMimetic in 2009/10. Due to be released in 1Q 2018, allowing re-submission of ChondroMimetic for CE Mark, and target launch in Europe in mid-2018.
- **Diurnal (DNL)*:** The European Commission is expected to give European Market Authorisation for Alkindi (cortisol replacement in infants and children up to 18 years of age) in February 2018.
- **Evgen (EVG)*:** Interim analysis of the Phase IIa STEM trial with SFX-01 in advanced breast cancer is expected in 1H 2018. Early results suggest it will meet its primary end-point of safety and tolerability.
- **Faron Pharmaceuticals (FARN):** Release of headline data from its European Phase III trial (INTEREST) with Traumakine in acute respiratory distress syndrome is due in 1H 2018.
- **Immupharma (IMM):** Headline data from its 200-patient Phase III trial with Lupuzor, for the treatment of Lupus, are expected to be announced during 1Q 2018.
- **Mereo BioPharma (MPH):** Results from a 268 patient Phase IIb trial with BGS-649 for use in hypogonadotrophic hypogonadism are due for release in 1Q 2018.
- **Motif Bio (MTBF):** Following completion of the two Phase III trials (REVIVE-1 and REVIVE-2) with iclaprim for acute bacterial skin infections, the company is expected to submit its NDA to the US FDA in 1Q 2018.
- **Premaitha (NIPT)*:** Form of Order Hearing is scheduled to be heard at the High Court at the end of January, which will determine the nature of any appeals and whether any interim penalties will be imposed.
- **Shield Therapeutics (STX):** Top-line data from its Phase III trial with Feraccru for chronic kidney disease are due to be release 1Q 2018.
- **ValiRx (VAL)*:** Positive preliminary data were release for both VAL201 (prostate cancer) and VAL 401 (lung cancer) in 4Q 2017. Full data read-out for trials with both products are expected in 1Q 2018.
- **Verona (VRP):** Top-line data from a Phase IIa study with RPL554 in adult cystic fibrosis patients are due for release in 1H 2018.

***Client of Hardman & Co Life Sciences**

Hardman Life Sciences clients

Hardman & Co Life Sciences Team

Dr Martin Hall

020 7194 7632

Dr Martin Hall has been a pharmaceutical and healthcare analyst in the City for 30 years and joined Hardman & Co in 2013.

He studied Pharmacy (B.Pharm.Hons) at The London School of Pharmacy, followed by a Ph.D at the Institute of Psychiatry, London investigating the underlying mechanisms of Parkinson's Disease and schizophrenia. After post-doctoral experience at the Collège de France, Paris, and at the Parke-Davis (Warner Lambert) Research Centre in Cambridge, entered the City as a pharmaceutical/healthcare analyst in 1987, working mostly at UBS and HSBC, taking the strategic view that the sector should be viewed on a global basis. From 2004 until 2012, Martin worked at Eden Financial where he undertook bespoke research before developing a corporate finance franchise. This work has continued at Hardman & Co since 2013.

Dr Dorothea Hill

020 7194 7626

Dr Dorothea Hill is relatively new to the City, joining the Life Sciences team at Hardman & Co in 2016.

Dorothea's expertise lies in next-generation sequencing, following her DPhil in molecular biology at the University of Oxford. Her academic research involved the use of genomics to understand the biology of bacterial pathogens in order to inform vaccine intervention. She was part of several public-private partnerships that involved biotech companies, patient charities, and Public Health England. Prior to her PhD, Dorothea worked for the Gates Foundation/Wellcome Trust-funded MenAfriCar Consortium, characterising the meningococcal epidemiology of countries of the African Meningitis Belt prior to MenAfriVac roll out. She is an author of nine peer-reviewed publications, and has a BA(Hons) in biological sciences from St Catherine's College, Oxford.

Dr Grégoire Pavé

020 7194 7628

Dr Grégoire Pavé is also relatively new to the City, joining the Life Sciences team at Hardman & Co in 2016.

Greg has considerable experience in the field of drug discovery and development. After successfully gaining his PhD in medicinal chemistry in 2003, he obtained a post-doctoral position at Imperial College London, working on natural product synthesis. He then joined Cancer Research Technology, the development and commercial arm of Cancer Research UK in 2005 where he was involved in multiple oncology projects. Greg has broad experience in drug discovery/development projects from target identification/validation all the way through to clinical trials. He also gained valuable experiences in evaluating life science projects and their commercial opportunities. He played a role of reviewer in peer-review journals from the American Chemical Society. He is author of 14 scientific papers and owner of 4 patents, and holds the IMC and PRINCE2 qualifications.

Notes

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Hardman & Co Research Limited (trading as Hardman & Co)
35 New Broad Street
London
EC2M 1NH

+44 (0) 20 7194 7622
Follow us on Twitter @HardmanandCo

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The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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Hardman & Co

35 New Broad Street
London
EC2M 1NH

Tel: +44(0)20 7194 7622

www.hardmanandco.com