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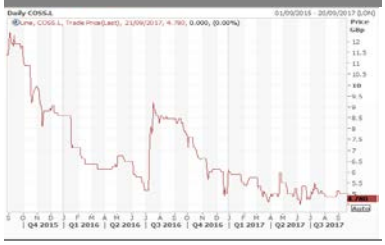
Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	COS
Price (p)	5.0
12m High (p)	8.5
12m Low (p)	4.2
Shares (m)	324.5
Mkt Cap (£m)	16.2
EV (£m)	9.2
Free Float*	66%
Market	AIM

**As defined by AIM Rule 26*

Description

COS develops, manufactures and supplies medical grade collagen biomaterials, tissues and devices. Its products are used in research, *in vitro* diagnostics, medical devices and regenerative medicine. The company provides R&D and contract services to a global and diverse customer base.

Company information	
CEO	Jamal Rushdy
CFO	Gill Black
Chairman	David Evans
	+44 141 648 9100
	www.collagensolutions.co.uk

Key shareholders	
Directors + management	20.7%
Seneca	13.2%
Calculus Capital	9.5%
Livingbridge	4.6%
Helium Rising Stars	4.0%
Rathbones IM	4.0%

Diary	
Dec-17	Interims
4Q-17	CM CE Mark filing
Jul-18	Finals

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Collagen Solutions

Engineering towards CE Mark

Collagen Solutions is a biomaterials company developing and manufacturing medical grade collagen components for use in medical devices, research, and regenerative medicine. A number of investment initiatives have been introduced recently to accelerate the rate of growth, including global commercial infrastructure and development of a pipeline of finished medical devices, the first of which will be ChondroMimetic for repair of small cartilage lesions. In June 2017, COS embarked upon an 8-year (average) follow-up study of patients originally implanted with the device in 2009-10. The last patient has now been reassessed.

- **Strategy:** Management has embarked on an investment strategy through a series of initiatives to increase the growth opportunities. This strategy is moving COS from a reliable quality collagen supplier to one that also has proprietary products that will move it into profitability, and cash generative, at a faster pace.

- **ChondroMimetic:** Best described as a clever bi-layered and easy to use sponge that allows the regeneration of cartilage and bone. The product has good provenance having received CE Mark in 2008 and implanted into ca.200 patients. However, for reasons prior to COS's ownership the CE Mark lapsed.

- **Patient re-evaluation:** As part of the process of re-applying for CE Mark, COS has undertaken an extension study to reassess 15/17 patients from the original trial in 2009-10. This will provide unprecedented 8-year follow-up data about the quality of the cartilage repair and support CE Mark and marketing material.

- **Next steps:** The last patient has now been rescanned. All the data has to be compiled, audited and analysed for completion of a Clinical Study Report. This will form part of the package for submission to the regulators for CE Mark around the end of 2017. It will also assist in commercial partner negotiations.

- **Investment summary:** ChondroMimetic fulfils COS's stated strategy to move further up the value chain. The 8-year data will significantly differentiate it from competing therapies, and with the last patient now assessed the enrolment phase has been de-risked. In order to maximise returns, COS will need to sign a strong commercial partner in readiness for launch around the middle of 2018, and capable of undertaking the trials needed to launch the product in the US.

Financial summary and valuation

Year end March (£000)	2015	2016	2017	2018E	2019E	2020E
Sales	973	3,130	3,946	5,200	7,230	9,785
Underlying EBITDA	-663	-374	-1,209	-1,170	30	1,603
Underlying EBIT	-793	-721	-1,658	-1,880	-701	853
Underlying PBT	-920	-983	-1,790	-2,141	-1,030	665
Statutory PBT	-1,102	-866	-1,614	-2,241	-1,130	565
Underlying EPS (p)	-0.98	-0.64	-1.04	-0.72	-0.38	0.11
Statutory EPS (p)	-1.17	-0.57	-0.95	-0.75	-0.41	0.08
Net cash/(debt)	3,282	2,384	7,072	3,471	438	-508
Capital increase	5,422	207	6,462	1,000	0	0
P/E (x)	-5.1	-7.8	-4.8	-7.0	-13.2	44.1
EV/sales (x)	9.4	2.9	2.3	1.8	1.3	0.9
EV/EBITDA (x)	-	-	-	-	-	5.7

Source: Hardman & Co Life Sciences Research

ChondroMimetic

Moving closer to market

ChondroMimetic will be Collagen Solutions' first proprietary product to reach the market, supporting management's strategy to move up the value chain. This product has very good provenance having received CE Mark in 2008, which was followed by a clinical study for osteochondral defects of the knee undertaken by a key opinion leader in 2009-10. At this point, the then-owners of ChondroMimetic changed focus and the regulatory approval was allowed to lapse. As part of the process for re-establishing CE Mark, COS has commissioned an 8-year follow-up study by the original surgeon to reassess the long-term improvements produced by ChondoMimetic. The final patient, out of a total of 15, has now been scanned, which keeps COS on schedule to resubmit the product for CE Mark around the end of 2017.

Background

Orthomimetics (OM) was the first spin-out from the Cambridge-MIT Institute (CMI). It incorporated in March 2005 to commercialise a family of surgical implants for the repair of cartilage, ligaments and tendons that had been developed during a four-year programme supported by ca.£4.0m of CMI funding.

OM successfully completed two large-animal (goat) trials with its lead product, ChondroMimetic, for the repair of articular cartilage, and obtained CE Mark in 2008. Following this, the company commissioned a small confirmatory trial in humans undertaken by a key opinion leader in surgical cartilage repair, which was to be used to support commercial marketing.

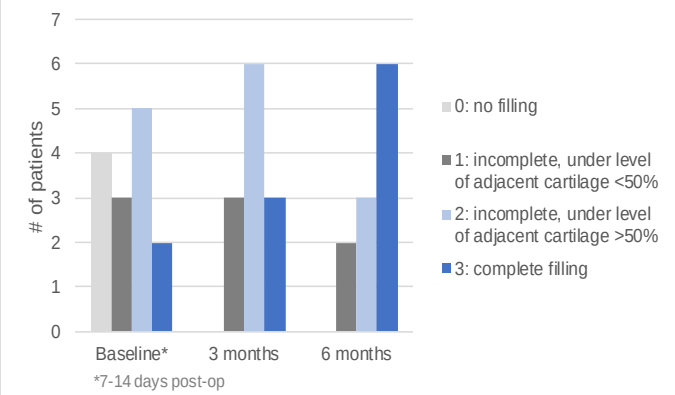
At this point, Orthomimetics was acquired by TiGenix BV, for £14.8m/$26.9m. However, a management change and restructuring resulted in the loss of interest in ChondroMimetic. In 2012, the assets of ChondroMimetic and associated IP were re-acquired by the founders of OM, which were purchased subsequently by COS in September 2015 for £200k + a single digit royalty, with the aim of re-applying for CE Mark and re-launching the product.

Original open label study

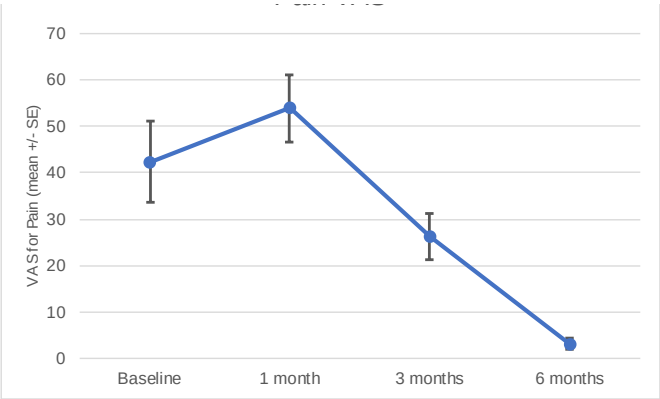
- Single centre (Sándor Károlyi Hospital, Budapest) study to confirm the safety and early outcomes with Chondro-Mimetic for osteochondral repairs of the knee
- Clinical trial in 17 humans with cartilage defects under $2cm^2$ conducted during 2009-2010 by Dr Laszlo Hangody, a world renowned orthopaedic surgeon
- Assessment of repairs six months following implantation using both MRI scan and biopsy
- Clinical outcomes were supported by a patient survey where 94% gave an overwhelming acclamation, rating the results "very good or excellent"

One month post-surgery, the increase of the Visual Analogue Scale scores – a psychometric response scale – and the decrease of the Cincinnati scores – measure of disability – show an increase in pain and disability for the patients. But this is due to the normal inflammation and swelling expected after surgery. The same scores noticeably change for the better after 3 and 6 month post-surgery, with clear recovery and a diminished knee pain level for all the patients.

Results from original Chondromimetic trial



MOCART (MRI)



Pain Visual Analogue Scale (VAS)

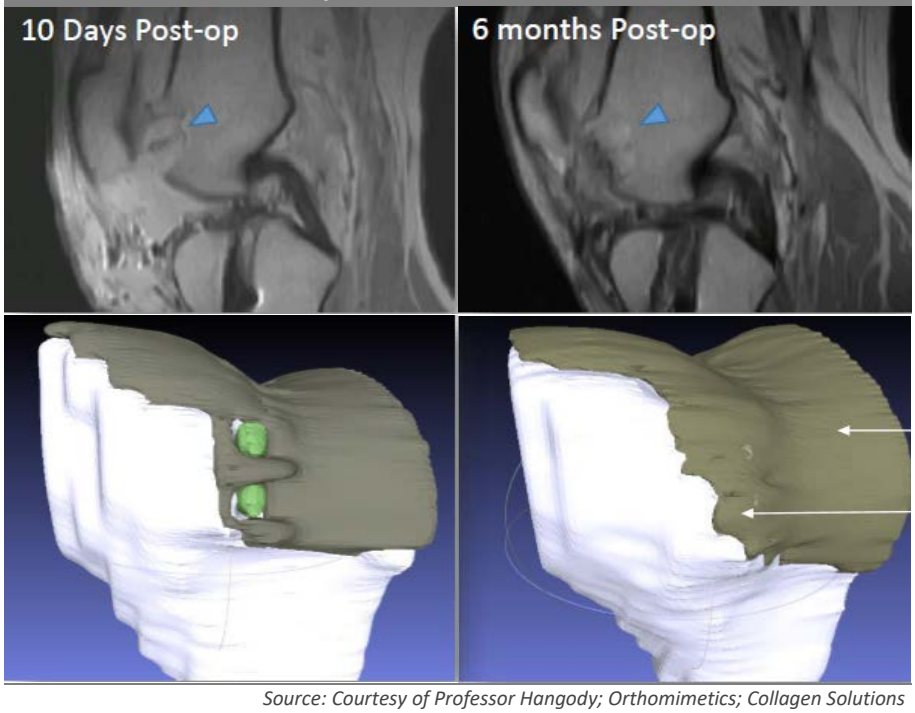
Source: Collagen Solutions; Orthomimetics

ChondroMimetic was very well tolerated and gave a lower level of post-surgery complications compared to other methods. MRI illustrated that the performance of the cartilage defect, lateral integration, and subchondral bone condition all improved. Biopsy indicated good integration of transplant material into host tissue and proved that the cartilage repair was mostly hyaline in nature. Finally, patients reported a clinically relevant decrease in pain.

Retrospective advanced MRI analysis

Since acquisition of the license to ChondroMimetic, COS has commissioned an advanced MRI analysis to assess the sustainability, completeness and quality of the repaired bone and cartilage defects. To prove that the technique would be suitable for such an assessment, it was first applied to the MRI scans originally taken by Professor Hangody back in 2010 and retrospectively analysed. Once this had been proven, the aim of COS was to try to contact, recall and reassess as many of the 17 patients as possible that took part in the original study.

ChondroMimetic – Post-operative MRI scans



Source: Courtesy of Professor Hangody; Orthomimetics; Collagen Solutions

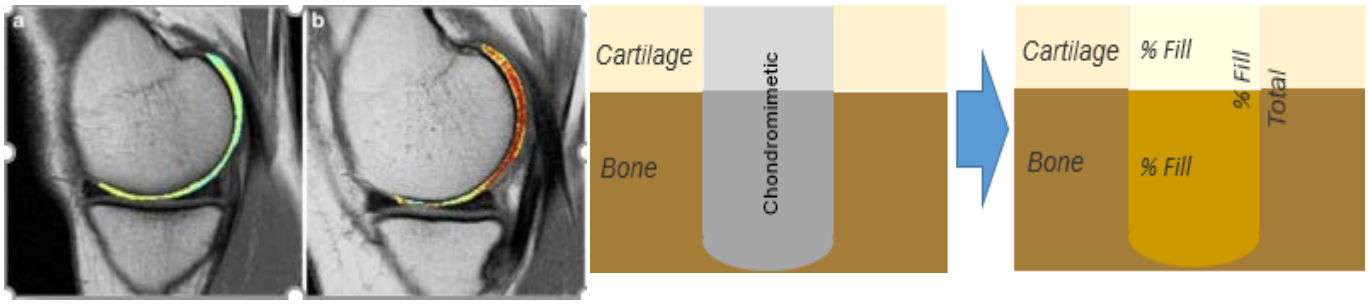
The degree of defect repair and filling was assessed for 14 subjects by MRI using the magnetic resonance observation of cartilage repair tissue (MOCART). The example photographs above illustrate outcomes in a single patient (study subject 02, female, 39 years of age) receiving two implants, at 10-days and six-months post-surgery. Although difficult to visualise by the untrained eye, after 10 days, boundaries between the implants and the bone are clearly defined and there is no cartilage repair. However, six months after surgery, there is little differentiation between the implant and the bone and the scaffold has been filled with new 'bone'. But, more importantly the cartilage scaffold has been filled by cartilaginous repair.

Advanced MRI analysis

In order to assess accurately and quantify the cartilage and bone repair, COS is liaising with a specialist industry consultant (Dr Matthew Shive) and Qmetrics Technologies, which provides a specialised imaging service. Using these experts, COS is aiming to convert the MRI scans taken from patients six months after the original surgery and produce a 3-dimentional MRI image, from which the level of cartilage and bone repair can be quantified. The technique will then be applied to the new scan of patients from the extension study.

Use of advanced MRI analysis

T2 Mapping	3D Quantitative MRI
► Technique to evaluate knee cartilage	► Technique to quantify the percentage fill of both cartilage and bone
► Assesses the 3D structure of cartilage	► Used to provide quantitative and statistical analysis of completeness of bone and cartilage defect filling
► Used in research studies to detect cartilage disease	
► Used in research to detect treatment-related changes to cartilage	



Normal | Degenerative | Time of surgery | Outcomes

Source: Collagen Solutions; Orthomimetics; Hardman & Co Life Sciences Research

Extension study – 8-year follow-up

- MRI scan – enabling 3D fill assessment and T2 analysis
- Modified Cincinnati Rating System
- Knee injury and osteoarthritis outcome score (KOOS)

Key to the resubmission of ChondroMimetic for renewal of the CE Mark is an open label extension of the original study to reassess the cartilage defect repairs in the 17 patients involved in the trial in 2009-10. Amazingly, 15 of these patients were contactable and indicated their willingness to take part in this extension study, which will generate data on average 8 years after the implant surgery, representing unparalleled depth of clinical knowledge on this subject.

On 30th June 2017, the first of these patients returned to have the cartilage repair re-assessed. Although it started a few months later than originally planned, this was the direct result of a greater number of patients being contactable and willing to return for reassessment than had been expected. It also means that the data will be far more robust. Collagen Solutions has now announced that the final (15th) patient has been re-scanned. All the data that have been collected will now undergo the advanced MRI analysis mentioned above, so that COS will end up with 6 month and ca.8 year paired data for each of the 15 patients.

Full analysis of these data should be complete by the end of the year, which will be fundamental in the re-submission for CE Mark. It is also expected to provide very strong information for use in commercialisation material.

Next steps

- Compilation and auditing of all the data
- Analysis of the data by Qmetrics Technologies using advanced MRI analysis (ongoing since first patient re-scanned), including T2 Mapping and 3D MRI
- Preparation and completion of the clinical study report
- Complete internal manufacturing validation
- In conjunction with the Notified Body, submit package to the regulatory authorities for re-establishment of CE Mark
- Continue to discuss/negotiate with potential commercial partners
- Launch in Europe mid-2018

Commercial opportunity

Details of the commercial opportunity for ChondroMimetic were described in our report: '*Engineering cartilage repairs*' dated 13th March 2017: http://www.hardmanandco.com/docs/default-source/company-docs/collagen-solutions-plc-documents/cos-chondromimetic---13-march-2017.pdf

Terminology & Definitions

Modified Cincinnati Rating Score – A comprehensive rating system to assess the knee condition for activity and function after ACL reconstruction (and other surgical procedures). Measures a variety of symptoms, sports and daily activity functions, patient satisfaction, and objective physical findings
http://www.orthopaedicscore.com/scorepages/cincinnati.html

VAS – Visual Analogue Scale unidimensional measure of pain intensity, which has been widely used in diverse adult populations, including those with rheumatic diseases

MOCART – Evaluation of repaired cartilage after autologous chondrocyte implantation using the Magnetic Resonance Observation of Cartilage Repair Tissue scoring system

KOOS – Knee injury and Osteoarthritis Outcome Score evaluates short-term and long-term symptoms and function in subjects with knee injury and osteoarthritis
http://www.orthopaedicscore.com/scorepages/knee_injury_osteopaedic_outcome_score.html

Financial summary

- No changes have been made to our forecasts in this document
- Full financial analysis of Collagen Solutions is available in our report dated 25th July 2017 '*Transitioning to accelerated sustainable growth*':

  http://www.hardmanandco.com/docs/default-source/company-docs/collagen-solutions-plc-documents/cos---2017-results---25-july-2017.pdf

Forecast summary

Year end March (£m)	2015	2016	2017	2018E	2019E	2020E
Profit & Loss:						
Sales	973	3,130	3,946	5,200	7,230	9,785
COGS	-214	-811	-984	-1,302	-1,771	-2,393
SG&A	-1,325	-2,440	-3,722	-4,265	-4,591	-4,893
R&D	-160	-367	-594	-954	-1,013	-1,072
EBITDA	**-663**	**-374**	**-1,209**	**-1,170**	**30**	**1,603**
EBIT	**-793**	**-721**	**-1,658**	**-1,880**	**-701**	**853**
EBIT margin (%)	-	-	-	-36.2%	-9.7%	8.7%
Net interest	-128	-262	-132	-260	-330	-188
Pre-tax profit	**-920**	**-983**	**-1,790**	**-2,141**	**-1,030**	**665**
Tax	-21	-114	-142	-185	-231	-288
Net income	-942	-1,097	-1,932	-2,325	-1,261	377
Weighted av. shares (m)	96.4	171.2	185.8	325.0	332.5	332.5
Underlying EPS (p)	**-0.98**	**-0.64**	**-1.04**	**-0.72**	**-0.38**	**0.11**
Fully diluted EPS (p)	-0.98	-0.64	-1.04	-0.72	-0.38	0.11
Balance sheet:						
Share capital	1,755	1,759	3,288	3,368	3,448	3,528
Reserves	11,099	12,137	16,998	15,493	14,052	14,249
Provisions	285	253	222	166	125	94
Debt	109	109	1,906	3,786	2,566	841
less: Cash	3,391	2,493	8,978	7,258	3,004	333
Invested capital	**14,176**	**14,203**	**15,786**	**16,706**	**17,127**	**18,320**
Net cash/debt	3,282	2,384	7,072	3,471	438	-508
Cashflow:						
Operating profit	-793	-721	-1,658	-1,880	-701	853
Change in working capital	-105	469	-76	-114	-8	7
Tax & interest	-28	-191	-102	-402	-514	-418
Operational cashflow	**-1,180**	**-338**	**-1,360**	**-2,106**	**-1,624**	**-736**
Capital expenditure	-159	-464	-137	-294	-200	-210
Free cashflow	**-1,326**	**-801**	**-1,497**	**-2,400**	**-1,824**	**-946**
Acquisitions	-2,192	-207	-342	-1,200	-1,209	0
Share issues	5,422	207	6,462	0	0	0
Change in net debt	**1,790**	**-898**	**4,687**	**-3,600**	**-3,033**	**-946**
Hardman FCF/sh. (p)	-1.22	-0.20	-0.73	-0.65	-0.49	-0.22

Source: Hardman & Co Life Sciences Research

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