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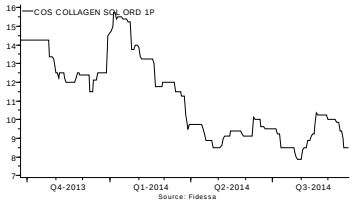
24 September 2014

Healthcare Equipment & Services



Source: Fidessa

Market data	
Price (p)	8.5
12m High (p)	14.0
12 Low (p)	8.0
Shares (m)	63.8
Mkt Cap (£m)	5.4
EV (£m)	3.9
EPIC	COS
Free Float* (%)	73%
Market	AIM

**As defined by AIM Rule 26*

Description

www.collagen solutions.com

Collagen Solutions develops and manufactures medical grade collagen components for use in regenerative medicine, medical devices and in-vitro diagnostics.

Company information

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Next event

Interims	Dec-14
Finals	Jul -15

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Collagen Solutions plc (COS.L) Initiation

The name gives it away….

A biomaterials company developing and manufacturing medical grade collagen components for use in regenerative medicine, medical devices and *in vitro* diagnostic products. Collagen Solutions supplies proprietary custom collagen formulations in addition to offering R&D and contract manufacturing services to a broad range of clients. The markets in which it operates are substantial; potentially as much as $16bn. Given its manufacturing know-how and recent access to next generation collagen processing IP, which is expected to lead to new development and manufacturing contracts, the opportunity for enhancing the value of this business is considered substantial.

Outlook positive: the company is at a very exciting point in its evolution; the benefits of 6 years development and relationship building pointing to increased revenues from external customers, whilst the development of a range of next generation collagen platforms, with enhanced functional and mechanical properties, is expected to drive increased revenues from customers, particularly within the regenerative medicine, *in vitro* diagnostics and medical device markets.

Valuation: there are very few quoted and appropriate comparator companies. Based on 2018 forecasts and assuming an EV/EBITDA multiple of 10x, the business could be worth around £30m implying a fully diluted value of c.38p per share. As visibility to contracts improves so too are forecasts likely to rise.

Risks: timing of development and manufacturing contracts, supply agreements, regulatory delays, collagen sources and potential competition from alternate biomaterials.

Investment summary: given the underlying growth of the biomaterials market, the embedded nature of its processes in its customers' products, expected new client wins as well as the commercial benefits that its exclusive access to novel collagen processing technology should bring, management's stated objective to create a business worth c.£100m by 2020 might not be considered an overly-ambitious goal.

Financial summary and valuation

Year end Mar (£,000s)	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Sales	24	1,040	2,525	4,360	7,000
Underlying EBITDA	(364)	(716)	68	1,155	2,780
Underlying EBIT	(381)	(802)	(23)	1,034	2,644
Reported EBIT	(480)	(852)	(73)	984	2,594
Underlying PTP	(381)	(796)	(21)	1,037	2,654
Statutory PTP	(480)	(846)	(71)	987	2,604
Underlying EPS (p)	(0.87)	(1.25)	(0.03)	1.64	2.66
Statutory EPS (p)	(1.10)	(1.33)	(0.11)	1.56	2.60
Net (debt)/cash	1,492	572	252	529	2,739
Shares issued	3,374	-	-	-	-
P/E (x)	-9.8	-6.8	-264.2	5.2	3.2
EV/sales (x)	214.0	4.9	2.0	1.2	0.7
EV/EBITDA (x)	-14.1	-7.2	75.3	4.5	1.8

Source: Hardman & Co Life Sciences Research

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Executive Summary

Company overview

Collagen Solutions is a biomaterials company developing and manufacturing medical grade collagen components for use in medical devices, regenerative medicine, and *in vitro* diagnostic products. It supplies value-added bio-functional collagen, provides R&D and contract manufacturing services to a broad range of clients, ranging from research organisations to multi-national corporates. The markets in which it operates are substantial; the end markets in which biomaterials such as collagen are utilised are valued as much as $16bn.

Collagen has been used to manufacture FDA and EU approved medical devices for more than 30 years in a variety of applications in wound care, oral surgery, cardiovascular systems, neurology, urology, orthopaedics and ophthalmology. Collagen Solutions sources its bovine collagen, which has BSE-free status, from a Geographical BSE Risk I country (GBR I). It has full sourcing and traceability upon receipt into its facilities, including European Directorate for the Quality of Medicines & HealthCare certification.

Formed by the acquisition of Collbio Ltd and Collagen Solutions LLC, via the reverse takeover of a cash shell, Healthcare Investment Opportunities plc, in January 2014, Collagen Solutions benefits from all the sunk development costs, manufacturing know-how and customer work undertaken over the past six years within these businesses. During this time the precursor companies developed its collagen product range and built its client base, working with the likes of Taxus Cardium to develop an FDA-approved topically formulated collagen gel for wound healing, called Excellagen. Not only does Excellagen provide a potential long term revenue stream but it clearly demonstrates also to the outside world the competencies that reside within the company.

The company's focus will be to build on its world class ISO-certified manufacturing facility capable of delivering high purity, bio-functional collagens that meet the evolving needs of its customers across a range of fields with a key focus on regenerative medicine, medical devices and *in vitro* diagnostics; markets that are exhibiting strong growth, particularly regenerative medicine where over 700 companies worldwide are developing novel medicines, many of which will require biomaterial scaffolds. Given its development and manufacturing expertise, it is not inconceivable that in the longer term the company could develop its own products although this has not been articulated by management.

Collagen Solutions – Growth opportunities

Clinical focus	Geographical thrust
Regenerative medicine	United States
Medical devices	Europe
In vitro diagnostics	Asia

Source: Collagen Solutions; Hardman & Co Life Sciences Research

Collagen Solutions already has an experienced sales & marketing team based in the US where the market already embraces the benefits of collagen-based products. It is not surprising that the US will be a key thrust for growth which will be supported by additional sales & marketing in Europe and Asia.

Business model reduces financial risk

The business model is focused on three business streams in the near term. Its manufacturing know-how, regulatory experience with customers and access to novel collagen processing capabilities should enable the company to consider developing its own proprietary products in the future. The business model supports a strategy for growth that provides the prospect of maximal revenue growth and new product opportunities whilst minimising financial risk.

Collagen Solutions – Growth opportunities		
Business stream	**Activity**	**Location**
Material supply	Bulk collagen supply	Glasgow
	Added value collagen supply	Glasgow/San Jose, USA
Development services	Development service for collagen formulations	San Jose, USA
	Development of medical devices	San Jose, USA/Glasgow
Contract manufacturing	Contract manufacturing of medical devices	Glasgow
	Contract manufacturing of regenerative medicine products	Glasgow
Manufacturing	Proprietary collagen products	Opportunity

Source: Collagen Solutions; Hardman & Co Life Sciences Research

Novel IP should generate significant growth opportunities

Novel collagen processing capabilities, exclusively licensed from UCL and for which a US patent has issued, enable the production of collagen with substantially enhanced physical strength, speed of production and concomitant seeding of the collagen scaffold with cells. This should allow surgeons to customise the collagen based products to an individual's needs and to perform the implants much more quickly, almost on an as needs basis. This is expected to lead to a new generation of tissue replacements similar to bio-laminated or 3D bio-printed collagen scaffolds, potentially an expanded client base seeking to develop novel bioactive tissue regeneration and repair products as well as the opportunity to create proprietary products.

Moving up the value chain

Its mix of revenues derived from a range of clients and services should provide protection to short term imbalances. The intention will be to move up the value chain, from supplying bulk and added value collagen formulations, to embedding its manufacturing knowledge and know-how into its customers' manufacturing process and regulatory compliance practices through to ultimately developing its proprietary range of products servicing the medical device market where the same collagens are perhaps valued in excess of $1,000/gram.

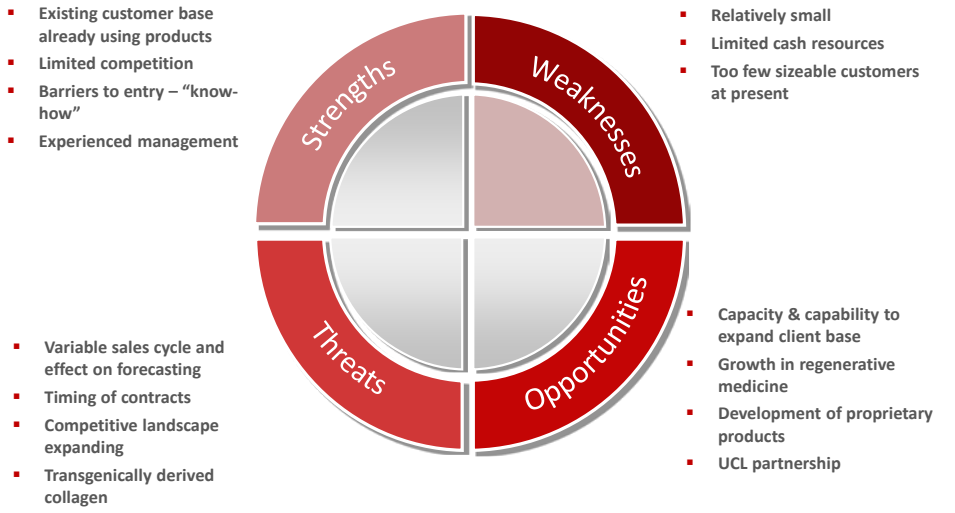
Collagen Solutions – Moving up the value chain

Source: Collagen Solutions & Hardman & Co Life Sciences Research

Financials

Revenues for the full year 2014/15 are expected to be £1.04m, although strongly skewed to the second half given that the technology transfer on a key product is not expected to be completed until October. These are expected to rise to £7m by 2018. Underlying EBITDA is expected to be around -£0.7m in the current financial year, about 2/3rd of which is expected to occur in the first half, be modestly positive in 2015/16 and rise to around £2.8m in 2018. As a consequence net cash is expected to fall from £1.49m at 31 March 2014, to £572,000 in 2015 to £252,000 in 2016 before rising thereafter. Although Collagen Solutions has limited cash head room in 2016 with forecast net cash of £252,000, given the contracts already in place as well as the flexibility that management has regarding R&D costs in the current year, we consider this risk to be manageable.

SWOT analysis



Source: Hardman & Co Life Sciences Research

Sensitivity/risks

Revenue forecasts are sensitive in the short term to existing customers retaining Collagen Solutions' services, variable sales cycle and signing with new customers. These in turn are dependent, albeit it to a lesser extent, on the success or failure of its customers' product clinical trials, changes to reimbursement for collagen-based therapies and the possibility that existing customers might use other collagen supplies or other biomaterials. We consider the latter to be less likely for existing products in which Collagen Solutions' bio-functional collagen is embedded into the manufacturing process and regulatory certification. To change would be costly and timely for the customer as they would need to go through a new regulatory approval process. With the spread of clients, exposure to different segments of the value chain we consider Collagen Solutions to have mitigated many of the near term revenue risks.

Valuation

There are few direct comparator companies to consider when looking at Collagen Solutions. However, Innocoll, which underwent an IPO on NASDAQ in July 2014, raising net $51.5m, provides a good example, in our opinion, of the potential value that can be achieved by moving from a company supplying collagen to one developing proprietary end products. The other comparator companies' current valuations in no way reflect the potential value that Collagen Solutions might generate in the next few years.

Comparator company valuations

Company	Ticker	Curr.	Share price	Shares (m)	Mkt Cap (m)	Mcap (£m)	EV (£m)	EV/Sales (x)
Holista Coltech	HCT.AX	AUD	0.05	141.3	7.1	3.9	3.2	1.1
Innocoll	INNL	USD	8.2	19.8	162.4	96.7	66.0	22.7
CollPlant	CLPT.TA	ILA	23.8	241.4	57.5	10.0	5.8	n/a
Collagen Solutions	**COS.L**	**GBP (p)**	**8.5**	**63.8**	**5.4**	**5.4**	**3.9**	**163.9**

Source: Hardman & Co Life Sciences Research

We have simplistically looked at the potential value of the company by taking 2018 forecasts and assuming an EV/EBITDA multiple of 8-15x. Using these assumptions the business could be worth around £22-42m implying a fully diluted value of c.31-56p per share.

Potential valuation based on 2018 multiples

EV/EBITDA (x)	EV £,000	Mcap £,000	Shares (m)	Price (p)
8	22,240	24,979	79.8	31
10	27,800	30,539	79.8	38
12	33,360	36,099	79.8	45
15	41,700	44,439	79.8	56

Source: Hardman & Co Life Sciences Research

Equally, there are few examples that we can cite with respect to published M&A activity within this space. Perhaps the most relevant was the acquisition of Kensey Nash in 2012 by DSM which paid $360m for a business with c.$90m of sales (inclusive of c.$30m of royalties).

Relevant identified M&A exits

Company	Technology	Acquirer	Year	Value $m	EV/Sales	EV/EBITDA
Kensey Nash	Collagen supply and products	DSM	2012	360	4x	10x
BioForm Medical Inc	Alginate dermal filler	Merz GmbH	2010	253	3.2x	-19x
Osteotech Inc	Demineralised bone matrix/collagen	Medtronic Inc	2010	123	1.3x	n/a
Radius Medical LLC	Collagen bone filler scaffold	NuVasive Inc	2007	18	6x	n/a

Source: Hardman & Co Life Sciences Research

Investment conclusion

We consider Collagen Solutions to offer investors a relatively de-risked investment proposition, given that it is currently loss making (although we forecast the company to be EBITDA-positive in the financial year ending March 2016). Its investment attractions lie in the fact that business model is based upon:

- a broad range of customers ranging from small research organisations through to large, blue chip multinationals
- collagen formulations with utility in multiple market segments; medical devices, regenerative medicine and *in vitro* diagnostics
- an ISO certified GMP manufacturing facility which can produce products that can be sold in all major geographic territories
- a range of value-added collagen processing technologies that are expected to create additional customer demand

Management has set an ambitious target of creating a business with a value of £100m by 2020, derived through organic growth and exploitation of its intellectual property (IP) as well as selective acquisitions. In our opinion, the leadership team has experience of generating substantial value in the life science industry. Given the underlying growth of the biomaterials market, expected new client contract wins, coupled with the added benefits that its exclusive access to UCL's novel processing technology is expected to bring, this is not considered an over-ambitious goal although investors should clearly be aware of the highlighted risks.

Biomedical Collagen

What is collagen?

Collagen derives its name from 'kolla', the Greek word meaning glue and suffix *-gen* denoting producing. Whilst known to the Romans its structure was not clearly defined until 1955 and it was not until the early 1970s that collagen was discovered to be a family of proteins, currently with at least 28 members having been identified.

Collagen is the principal structural protein present in all vertebrates and is used to support and connect bodily tissues and internal organs; found in blood vessels, dermis, ligaments, cartilage and tendon. Collagen is also found in in the body walls and cuticles of invertebrates (eg. Jellyfish). It is one of the most abundant proteins in the human body, comprising about 25% of the total protein mass, and is a major constituent of skin (50%+ of extracellular protein), bone, tendons (90%+), muscles and cartilage.

Collagen comprises a family of genetically distinct molecules that have a unique triple helix configuration of three polypeptide subunits known as α-chains in common. Three of these helixes then form a molecule of tropocollagen, the basic building block of collagen, by coiling around a central axis in a right-handed, triple-helical arrangement. Tropocollagen molecules associate in a staggered fashion to form collagen fibrils, which are stronger than steel wire of similar size. Collagen fibrils are strengthened and stabilized mainly by covalent cross-links, the extent of which depends on the specific function of the collagen molecule involved and the age of the animal. Older animals have more highly cross-linked and, therefore, more rigid collagen.

To date 28 types of collagen have been identified and described although collagen types XII-XXVIII are less well characterised. Type I collagen, however, is predominant (90%) in higher order animals, and is the collagen produced by Collagen Solutions and most other suppliers. Variations in the different collagen types are due to differences in the assembly of the polypeptide subunits, lengths of the helix, interruptions in the collagenous domains and terminations of the helical domains.

Collagen types

Type	Chain composition	Distribution
I	α1-2 (I)	Skin, tendon, bone, cornea, dentin, fibrocartilage, large vessels, intestine, uterus, dermis, tendon
II	α1 (II)	Hyaline cartilage, vitreous, nucleus pulposus, notochord
III	α1 (III)	Large vessels, uterine wall, dermis, intestine, heart valve, gingiva
IV	α1-6 (IV)	Basement membranes
V	α1-3 (V)	Cornea, placental membranes, bone, large vessels, hyaline cartilage, gingiva
VI	α1-3 (VI)	Descement's membrane, skin, nucleus pulposus, heart muscle
VII	α1(VII)	Skin, placenta, lung,, cartilage, cornea
VIII	α1-2 (VIII)	Descement's membrane
IX	α1-3 (IX)	Cartilage, vitreous body of eye
X	α1 (X)	Hypertrophic and mineralizing cartilage
XI	α1-3 (XI)	Cartilage, invertebral disc, vitreous humour
XII	α1 (XII)	Chicken embryo tendon, bovine periodontal ligament
XIII - XVIII	Unknown	Central skin, bone, intestinal mucosa

Source: Hardman & Co Life Sciences Research modified from ASTM International 2008, Designation: F 2212-08

Collagens predominantly reside outside the cell and provide the structure required to maintain tissue integrity. Collagens have also been shown to be involved in cell attachment and differentiation, as chemotactic agents, as antigens in the immunological response to particular diseases and as the defective component in certain pathological conditions. In culture, collagen substrates have been used for many cell types to promote adhesion, growth and/or differentiation.

Applications of collagen as a biomaterial

Biomedical collagen has been the industry's premier biomaterial of choice for decades due to its biocompatibility, biodegradability and low immunogenicity.

Collagen is used in the manufacture of biomaterials due to its ability to form strong fibres with high tensile strength. It is used in many forms, including gels, scaffolds and membranes, for a number of medical applications.

However, there are significant regulatory hurdles that have to be surmounted for certification of the final product to be granted, namely:

- tissue has to be sourced and qualified according to EN 22442 (animal tissues and their derivatives utilised in the manufacture of medical devices)
- collagen materials have to be manufactured according to ISO 13485 which regulates the documentation of processing procedures
- purity, biodegradability and biocompatibility have to be tested comprehensively (e.g. according to ISO 10993, ASTM F2212-11 (Standard Guide for Characterisation of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products)

Collagen has an important role in tissue repair. It has been used extensively in a wide range of medical fields, including wound healing, cartilage repair, bone grafts, haemostasis (halting bleeding), sutures, artificial heart valves and arteries, hernia repair and soft tissue augmentation. Its use in a wide range of implantable medical device products is summarised below:

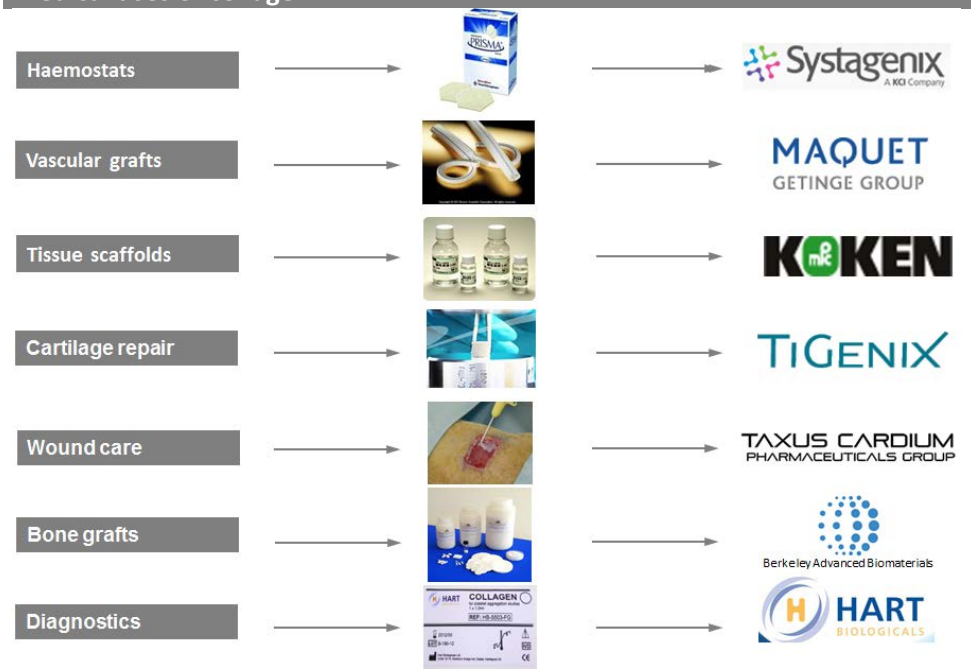
- Implantable biomedical devices; eg. vascular grafts
- Tissue engineering scaffolds; eg. Koken, Collagen Biomatrix
- Drug delivery applications to develop carriers for delivery of genes, growth factors, small molecules
- Haemostats, to enhance blood coagulation and platelet activation. Microfibrillar collagen is used as a topical agent in surgery settings to stop bleeding. It works by attracting platelets which start the blood clotting assuming the haemostatic pathway is functional.
- Topical wound dressings – eg Taxus Cardium's Excellagen, Organogenesis' Apligraf
- Tissue augmentation, for use in surgery
- Tissue sealants, artificial skin, implant coatings, corneal shields, prosthetic devices, incontinence treatments, bone graft substitutes, adhesion barriers

Advantages & disadvantages of collagen as a biomaterial

Advantages	Disadvantages
Available in abundance and relatively easy to purify	High cost of pure Type I collagen
Non-antigenic	Variability of isolated collagen
Biocompatible and non-toxic	Hydrophilicity thus leading to swelling and rapid release
High tensile strength and minimal expressibility	Variable enzymatic degradation rate vs hydrolytic degradation
Biodegradable and bioresorbable	Complex handling properties
Haemostatic – promotes blood coagulation and involved in the body's natural wound healing process	Potential risks/contamination, eg BSE and mineralisation
Multiple formulated formats	
Biodegradability regulated by cross linking	
Compatible with synthetic polymers	
Easy to modify functional groups to produce desired materials	
Ability to incorporate bioactive compounds into collagen matrix	

Source: Hardman & Co Life Sciences Research

Medical uses of collagen



Source: Company reports, Collagen Solutions & Hardman & Co Life Sciences Research

Sources of medical grade collagen

Animal-derived collagen

Historically, collagen has been extracted, isolated and purified from animal (bovine, porcine, chicken, fish) and human cadaver. Many suppliers have issues with respect to purity and immunogenicity, rendering the collagen unsuitable for bio-medical and research applications. There are two principal forms of purified collagen, namely:

- Insoluble collagen – involves the sequential extraction of non-collagenous material from the raw tissue material, resulting in an intact collagen matrix with their intrinsic intermolecular crosslinks and fibrils arranged in their native configuration. This so-called fibrillar collagen retains its natural physiological functions, namely the wound healing and haemostatic properties.
- Soluble collagen – extracted by dissolving source material (eg. skins, tendons etc) in a range of organic acids, pepsins (protease enzymes) and alkaline solutions. It can be purified either as an acid-solubilised collagen (telo-containing collagen) or as a pepsin-solubilised collagen (atelo-collagen). Treating with proteases/pepsin removes or cleaves the telopeptides from the collagen. Telopeptides are located at the ends of the collagen molecules. Whilst their presence confers functionality to the collagen they may also be associated with immunogenicity.

Comparison acid soluble and pepsin soluble collagen

Collagen	Telopeptide	Gel strength	Gel structure
Acid soluble collagen	Telopeptide intact	Slightly stronger than pepsin solubilised	Straight fibrils, mesh-like structure
Pepsin soluble collagen	Telopeptide removed	Slightly weaker than acid solubilised	Loosely twisted fibrils, smaller mesh work, sponge like

Source: Journal of Biological Chemistry, 2000, Vol. 275, no. 33 pp. 25870-25875

Human-derived collagen

Whilst it might be advantageous to supply human rather than bovine or porcine collagen for therapeutic purposes, the volumes required by the medical device industry are so large and the sources for purified human collagen are limited; sourced from human placenta or human cadaver (eg. Dermalogen for treating facial contour defects). The placenta contains several types of collagens, most notably types I, III, IV, and V. The process of separating and purifying one type from the others is imperfect and results in a predominant type with small amounts of the other types. Production of purified collagen from placentas further necessitates additional processing steps to ensure that the resulting collagen product is free from human viruses such as hepatitis and HIV. Most human placenta-derived collagens (mainly Type I and IV) are used for *in vitro* cell cultures. For example, MerckMillipore sell Type I collagen as a gel for cell attachment (£275/250µg) and Type IV as a reference molecule (£285/100µg).

Transgenically derived collagen

Researchers, corporates, consumers and regulators have been seeking alternatives to animal collagen for some time, given that these are associated with a very small, albeit real, incidence of adverse side effects due to adverse immunologic and inflammatory responses as well as the potential for contamination of bovine collagen with the agent that causes the fatal bovine spongiform encephalopathy (BSE) and its human variant, Creutzfeldt-Jacob disease (CJD). Transgenically derived collagen is such an approach.

Potential advantages of transgenically derived collagen

Advantage	Effect
Non-allergenic Non-immunogenic No pathogens	Safety Market access
Bio-functionality	Accelerates primary human cell proliferation
Hydrophilicity	Faster cell penetration and better controlled release of growth factors
Homogeneity Native	Strong reproducible structures

Source: CollPlant; Hardman & Co Life Sciences Research

The key alternative approaches to producing human collagen are summarised below:

1. Recombinant production in yeast and bacterial cells

The use of genetically engineered microorganisms is seen as a scalable technology for the production of recombinant human collagen (rhC). A number of groups, including FibroGen Inc and FujiFilm Diosynth, have looked at the use of yeast (*Pichia pastoris, Saccharomyces cerevisiae, Hansenula polymorpha*) and of bacteria (*Escherichia coli, Bacillus brevis*). FibroGen has developed recombinant human collagen type III (rhCIII) in a yeast expression system. Early clinical data from a Phase I trial in which 10 patients with corneal disease underwent resection followed by surgical implantation of synthetic corneas using rhCIII. All implants remained viable after 2 years, with 6 of the patients having improved vision, 2 unchanged and 2 decreased. BD Biosciences provide rhCI and rhCIII for biomedical applications in which purity is critical. Over the past decade Fujifilm Diosynth Technologies has developed a range of unique new collagen-based biomaterials produced by a yeast-based fermentation process in a consistent and reproducible manner. The main drawbacks, however, are still thought to be cost thereby limiting its uses.

2. Recombinant production in mammalian cell

Although mammalian cell lines have been proven to be effective in the induction of procollagen expression, one of the drawbacks has been the need for complex and stringent post-translational processing of collagen, a prerequisite of its viability and bio-functionality. This has set significant limitations on recombinant expression systems. In addition the yields are typically lower than seen in bacterial systems, thereby limiting its uses on the grounds of cost.

3. Recombinant production in plants.

Transgenic plant systems have potential advantages over other recombinant production systems in terms of lower cost, higher capacity, lower infective agents/toxins contamination risk, and inexpensive storage capability facilitating processing. The production of plant derived recombinant collagen I (rhCI) was reported in 2000 using tobacco and tobacco cell culture. rhCI has also been expressed in transgenic maize seed and barley. The plant extracted recombinant human collagen type I forms thermally stable helical structures, fibrillates, and demonstrates bioactivity resembling that of native collagen. CollPlant, an Israeli company, has generated a bio-engineered plant line (tobacco leaf) capable of expressing human genes that synthesise human protein chains and generate stable, triple helical procollagen which is extracted and processed into monomeric rhC1. CollPlant has five products in development for woundcare and orthopaedic applications and received CE Mark in December 2012 for VergenixWD, a wound care dressing/scaffold for cellular infiltration and capillary growth. CollPlant has indicated a price point of c.$1,000/gram for its plant-derived recombinant human collagen.

4. Production in milk of transgenic mammals

High yields of fully mature collagen have been secreted into the milk of transgenic mice bearing mammary gland-targeting genomic collagen- and P4H-encoding (an enzyme that stabilises collagen) inserts. However, the extensive development costs of such models limit significant progress of this expression system and, to date, we are not aware of anyone commercially working on this type of system.

Addressable collagen market

The addressable market size is not an easy one to ascertain. Data are scarce for the supply of collagen to the device, diagnostics and regenerative medicine market. Whilst the global biomaterials market at end user prices is worth >$50bn (Source: Markets and Markets) and estimated to be growing in excess of 10%, we estimate the current US market, for which data is more readily available, for collagen-based products to be in the order of $600-700m, implying a global market of c.$1.5bn. We have collated this from a number of sources.

The largest medical device market opportunity is bone grafts substitutes. Worth an estimated $3.3bn in the USA in 2013, the gold standard has either been autografts (bone from patient) or allografts (bone from other people). However, a number of publications, including a recent article in the Journal of Bone & Joint Surgery, 2012, v 94, provide clear evidence that collagen/hydroxyapatite scaffolds can perform as well as autogenous bone grafts, thus substantially increasing the addressable market for collagen-based products. Given that hydroxyapatite and collagen comprise c.65% and 25% by weight of healthy bone, this is perhaps not surprising.

Taking the bone graft market as well as the advanced wound healing market, suggests that the addressable market for collagen-based products in the USA is in fact around $7bn, implying a global market of c.$15bn at end market prices. If we include the estimated value of scaffolds into the regenerative medicine market and that of the in vitro diagnostic market, the addressable market potential rises to over $16bn.

Although the supply of collagen to these end markets may only be a small proportion of the overall value it is also clear that by moving up the value chain, from supply of raw materials, to development of higher added-value collagen formulations and customers' medical devices, to contract manufacturing services and ultimately to the development of proprietary products that the larger addressable market can indeed be targeted.

Collagen Solutions – Moving up the value chain

Source: Collagen Solutions & Hardman & Co Life Sciences Research

The following table provides a composite assessment of the potential addressable market for Collagen Solutions. We have looked at the Japanese Ministry's assessment of the regenerative medicine market. Assuming that the market is potentially worth £70bn by 2030, we have assumed that the scaffold component of this could perhaps be c.1-2%, implying an opportunity of £0.7-1.4bn ($1.2-2.4bn).

Addressable market

US$	US market	Potential market	
	2014E	US	Global
Collagen-based bone graft substitutes market[3]	100	3,300 [3,4]	
Wound dressing[1]	83	3,000 [4]	
Collagen-based haemostat[2]	16	763	
Cartilage repair market[3]	n/a	513	
Skin substitutes[3]	275	275	
Facial aesthetic dermal implants[1]	89	100	
Urinary incontinence[1]	48	50	
Collagen dressings[3]	40	50	
Corneal shields[1]	7	10	
	657	**8,061**	**15,000** [4]
Regenerative medicine market - scaffolds			1,200 [4]
In vitro diagnostics supply			200 [4]
			16,400

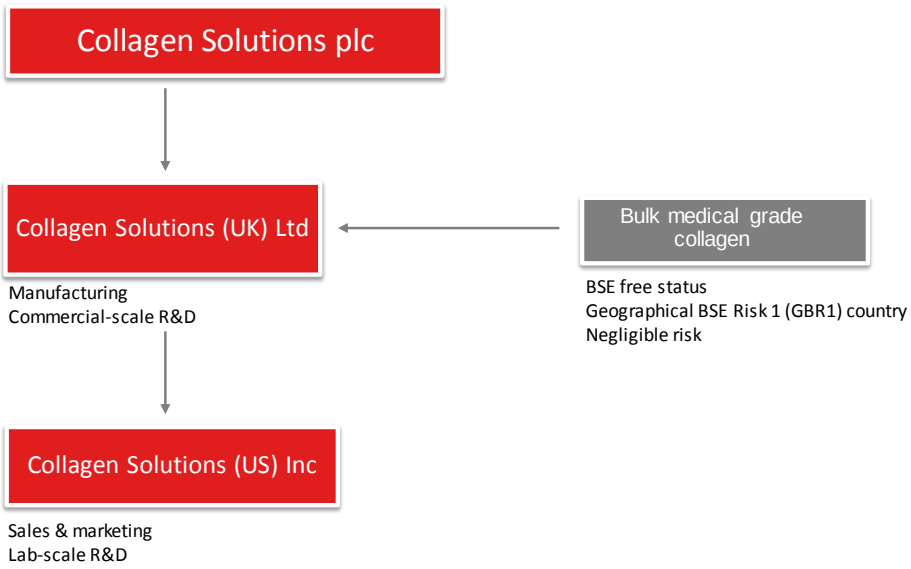
Source: BizAcumen[1], iDATA[2], Frost & Sullivan[3], Hardman & Co Life Sciences estimates[4]

Collagen Solutions

History

The business was established in 2008 as a subsidiary of Devro plc, with operations in Glasgow and San Jose, California, to exploit the biomedical application of collagen which was sourced from Devro's facilities in Australia. In 2011 these assets were sold to Angel Biotechnology Holdings plc which wanted to build on its contract manufacturing operations. However, Angel Biotechnology went into administration in 2013 and Collbio was established in order to acquire the collagen assets of Angel Biomedical in Glasgow.

Collagen Solutions plc



Source: Collagen Solutions & Hardman & Co Life Sciences Research

Collagen Solutions, as it currently stands, benefits from all the sunk development costs, manufacturing know-how and customer work undertaken over the past six years within previous businesses, developing its collagen product range, building its client base and working with the likes of Taxus Cardium to develop an FDA-approved topically formulated collagen gel for wound healing called Excellagen.

Overview

In January 2014 Collagen Solutions plc was formed by the acquisitions of Collbio Limited and Collagen Solutions LLC in the UK and USA, respectively, bringing together businesses with manufacturing, R&D and sales & marketing capabilities. The combined management teams had worked together previously as described above. The enlarged business is able to provide functional collagen biomaterials, the development of collagen formulations and products and the contract manufacture of collagen-based medical devices. It has immediate sales in both the USA and Europe, with facilities in both these locations, providing a strong foundation to build a global biomaterials business. Collagen Solutions already supports a broad range of medical device and life science customers manufacturing a wide range of products made from, or containing, collagen and other active ingredients.

Collagen Solutions is headquartered in Glasgow and comprises 6,500 sq ft of space mostly given over to manufacturing (Grade B/ISO 5 equivalent and C/ISO 7 equivalent clean room manufacturing) with additional laboratory and office space. It currently manufactures the FDA-approved product, Excellagen, for Taxus Cardium Inc, as well as other products for

unnamed customers, ranging in size from small research facilities to multi-national multi-billion dollar corporations. Collagen Solutions LLC, based in San Jose, California, was established in 2012, building on four years of sales and marketing history as Devro Medical, supplying GLP collagen intermediates devices to customers using pilot scale manufacturing, development and consultative services helping its customers to take their products from concept to clinical stage.

Collagen Solutions UK facilities

Glasgow HQ | Glasgow laboratory

Source: Collagen Solutions

The source material for its collagen processing has BSE-free status, is from a Geographical BSE Risk I country (GBR I) and has full sourcing and traceability upon receipt into its facilities, including European Directorate for the Quality of Medicines & HealthCare (EDQM) certification.

Collagen Solutions holds its own ISO 13485 certification (specifies requirements for a quality management system where an organisation needs to demonstrate its ability to provide medical devices and related services) and is in compliance with ISO 22442 (applies to medical devices other than *in vitro* diagnostic medical devices manufactured utilising materials of animal origin, which are non-viable or have been rendered non-viable) certification which is critical to both its customers as well as external regulatory bodies.

Manufacturing process

Production is carried out in accordance with current Good Manufacturing Practice (cGMP). The production process includes collagen extraction, purification as well as other transformational processes up to sterile medical devices. Processing of the collagen includes cross-linking, freeze drying and coating with end products including sponges, films and powders. Collagen composites are also produced in which additives are blended with collagen formats to produce customised products for different medical applications; for example, hydroxyapatite, synthetic polymers, hyaluronic acid and calcium phosphate.

Production vessels in Grade C clean room facility

Source: Collagen Solutions

Purified soluble collagen is manufactured under controlled conditions to ensure the triple helical structure is preserved during processing as this is integral for functionality. Collagen Solutions is capable of producing both acid-solubilised collagen (telo-collagen) and pepsin-solubilised collagen (atelo-collagen), although the latter is the predominant form.

Collagen can be manufactured to customer requirements in terms of aqueous solvent, pH and concentration. The purified soluble collagen solution is suitable for use in a variety of applications, including tissue engineering as a scaffold for cells, haemostats, wound healing dressings and prosthetic implant coatings. The company also provides reagents and protocols to ensure that the collagen will gel effectively and consistently in cell culture applications without the uncertainty of reagent make up. The soluble collagen process has been subjected to FDA-approved viral inactivation studies.

Technology access

Since the company's formation, it has entered two strategically important and relevant partnerships, namely:

5. UCL exclusive licence to next generation collagen products

This licence was exclusively granted to Collagen Solutions in June 2014. The production process (granted US patent 8,785,389) creates collagen materials with substantially enhanced physical strength as well as speed of production (hours as opposed to the weeks it currently takes). Collagen tissue contains two types of collagen: monomeric collagen which is acid soluble, forms short chains and represents up to 20% of the total collagen, and polymeric collagen which is insoluble, comprises aligned strands of collagen fibres which are covalently cross-linked and organised into large diameter fibrils. This process allows polymeric collagen to be purified and seeded with cells and other components of biomaterials which are mechanically stronger than monomeric collagen gel-based biomaterials and which can be engineered according to specific applications and requirements, unlike the preparation of whole tissues. Equally important is the fact that cells can be distributed interstitially within the biomaterial in any arrangement.

This is expected to lead additional clinical applications in the replacement of tissues such as skin, tendon, bone, cartilage, blood vessels and nerve conduits. From a clinical perspective it should allow surgeons to customise collagen-based products to individual needs of the patient and to perform the implants much quicker; almost on a need to basis.

From a manufacturing perspective the collagen sources for these materials are significantly more efficient than current collagen feed stocks, thus potentially benefiting margins. Not only will Collagen Solutions be able to extract monomeric collagen which is acid-solubilised but it will be able to extract polymeric collagens which make up c.80% of the collagen tissue.

From a commercial perspective, this platform technology should lead to the creation of:

- a new generation of collagen based tissue replacements
- expanded client base seeking to develop novel bioactive tissue regeneration and repair products
- proprietary medical device and regenerative medical opportunities

These collagens should be able to be used in a far wider patient population than is presently feasible with the potential to expedite both autologous and allogeneic cell therapies and accelerate the clinical application of novel tissues and scaffolds using bio-lamination or 3D bio-printing which are presently very difficult due to the lack of suitable support materials.

Collagen Solutions is currently undertaking additional development and formulation to achieve a product with the same functionality as that achieved in UCL's facilities and also with Collagen Solutions' bovine sourced raw material.

6. Jellagen – agency, distribution and development agreement

Jellagen is the first company to provide medical grade GMP and ISO certified Type I and II jellyfish collagen suitable for a range of medical device applications including implant coatings, haemostats and tissue engineering scaffolds and sourced from a natural and renewable marine source. Jellagen has shown that jellyfish collagen is able to induce similar responses in terms of cell adhesion, proliferation or migration, as mammalian collagens. The collagen is supplied by Collagen Solutions who also own 10.5% of the equity. Collagen Solutions is undertaking development work to get to a stage whereby the company can supply collagens under cGMP.

Business model

Collagen Solutions' activities can be broadly split into three business streams: material supply, development services and contract manufacturing. Its technical ability to create functional collagen should enable Collagen Solutions to partner with companies developing collagen-based products with the ultimate goal of manufacturing the product – embedding its technology and capabilities into a long term manufacturing and supply agreement. Given its development and manufacturing expertise as well as IP, it is not inconceivable that in the longer term the company could develop its own products, thereby capturing greater margin and generating incremental shareholder value, although this has not been articulated by management.

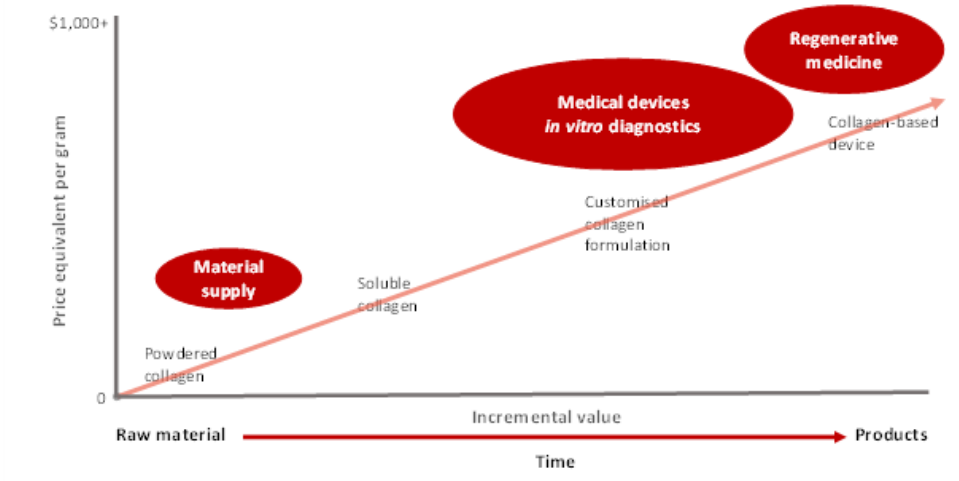
Business streams

Business stream	Activity	Location
Material supply	Bulk collagen supply Added value collagen supply	Glasgow Glasgow/San Jose, USA
Development services	Development service for collagen formulations Development of medical devices	San Jose, USA San Jose, USA/Glasgow
Contract manufacturing	Contract manufacturing of medical devices Contract manufacturing of regenerative medicine products	Glasgow Glasgow
Manufacturing	Proprietary collagen products	Opportunity

Source: Hardman & Co Life Sciences Research

The company's business model can be summarised in the following chart that looks at collagen pricing versus time and the incremental value to Collagen Solutions of its products and services.

Business model



Source: Hardman & Co Life Sciences Research

Currently the company supplies collagen in the form of bulk collagen; low value but nevertheless good margins, as well as customised collagen formulations with an inherently higher value on a per gram basis as well as contract manufacturing services. Current end markets are essentially in the medical device space. In the mid- term, the company will remain focused on developing improved added-value customised collagen formulations within the medical device as well as *in vitro* diagnostics markets. Longer term, the company will develop its own proprietary product range and equally importantly focus on the emerging regenerative medicine market which will require scaffolds designed to direct the organisation, growth and differentiation of cells to form functional tissue.

Material supply

Collagen Solutions provides a range of medical grade collagen products for early stage R&D projects with academic groups and corporations. Although orders are typically for low volume, in the gram to kilogram range, the economies of scale generated from other manufacturing activities ensures that the margins are still good. Collagen Solutions' current product list comprises approximately 30 lines; the key ones shown below:

Current product range

Name	Product	Concentration	Description	Application
CS001	Type I, Bovine Soluble Collagen	~3mg/ml and ~6mg/ml	Highly purified bovine corium pepsin solubilized collagen, atelo collagen, in 0.01 N HCl, pH2. Predominantly Type I collagen with approximately 5% Type III. Forms a gel when at pH 7. Sterile filtered.	3D scaffolds for culture or coating plastic ware for increased cell adhesion
CS004	Type I, Acid Swollen Gel	~10mg/ml	Bovine corium, limed, in the native state, telo collagen, predominantly Type I with about 5% Type III, pH3.	For further processing to fabricate custom formulations. Not suitable for gel formations.
CS006	Type I, Acid Swollen Gel	~4mg/ml or ~6mg/ml	Bovine corium, acid solubilized collagen, telocollagen, pH 2 in 0.01 N HCl. Predominantly Type I collagen with approximately 5% Type III. Forms a gel when at pH 7. Sterile filtered.	3D culture or coating plastic ware for increased cell adhesion
CS007	Titration Buffer		Titration buffer (0.2 phosphate, pH11.2). Premixed titration buffer to be used with CS001, CS006 and CS019 for forming 3D gels. Sterile filtered.	
CS010	Bovine Dermal Fibrous Powder		Bovine corium, limed, in the native state, telocollagen, predominantly Type I with about 5% Type III, pH 6.	For further processing to fabricate custom formulations. Not suitable for gel formations.
CS013	CS013, Type I, Fibrous Powder		Bovine corium in the native state, telocollagen, predominantly type I, with about 5% type III, pH6. I	For further processing to fabricate custom formulations. Not suitable for gel formations.
CS019	Type I, Bovine Soluble Collagen	~6mg/ml	Highly purified bovine corium pepsin solubilized collagen, atelo collagen, in 0.01 N HCl, pH2. Predominantly Type I collagen with approximately 5% Type III. Forms a gel when at pH 7. Sterile filtered.	3D scaffolds for culture or coating plastic ware for increased cell adhesion
CS022	Pulp		Bovine corium, limed, in the native state, telocollagen, predominantly Type I with about 5% Type III	
CS028	Type I, Acid Soluble Collagen	~6mg/ml	Bovine corium, acid solubilized collagen, telocollagen, pH 2 in 0.01 N HCl. Predominantly Type I collagen with approximately 5% Type III. Forms a gel when at pH 7. Sterile filtered.	3D culture or coating plastic ware for increased cell adhesion

Source: Collagen Solutions

Products sold include:

- Pepsin-solubilised collagen - suitable for use in various application such as tissue engineering as a scaffold for cells, haemostats, wound healing dressings and prosthetic implant coatings. In addition buffering solutions to create gels are also supplied. The process has been subjected to FDA and EU approval
- Acid-solubilised collagen, also referred to as native
- Powdered collagen – for example, when used in wound dressings
- Corium (dermis or inner layer of skin)
- Tendon

Development Services

Collagen Solutions provides a development service capability for collagen-based products with a view to building a long-term relationship with clients through early stage added value work. Its strategy is to collaborate with companies which are intent on developing new biomaterial-based medical devices, utilising Collagen Solutions' technical and regulatory expertise. Companies can customise their product needs, from product design to production of finished or semi-finished medical devices. Through external product development and/or technology transfer, the intention is to integrate its processes into customer's production needs from design to proof of concept studies through to commercialisation. In doing so, Collagen Solutions captures the long term value of being part of the value chain in a regulated market with an approved product in which manufacturing processes are difficult to change without seeking additional approvals.

Contract manufacturing

Collagen Solutions has the capacity and capability for the commercial production of devices, tissue scaffolds and other regenerative medicine products, supporting their clients as they progress products through regulatory approval and into commercialisation. Collagen Solutions (UK) Ltd, its contract manufacturing arm in Glasgow, is structured to provide the requisite documentation required by notified bodies and competent authorities. Contract manufacturing of formulations and devices is expected to become the growth driver of Collagen Solutions in the mid-term.

7. Taxus Cardium Inc

Probably the most significant public milestone achieved to date has been the integration of its collagen into Taxus Cardium's collagen manufacturing process for Excellagen. Excellagen is a novel syringe-based pharmaceutically-formulated 2.6% fibrillar Type I bovine collagen flowable gel for use in wound care management. It functions as a biological modulator, initiating the wound healing process by activating platelets which, in turn, trigger the release of growth factors which significantly accelerates the growth of granulation tissue and wound closure. It is topically applied through an easy-to-control, pre-filled, sterile, single-use syringe designed for once-weekly application. Collagen Solutions' Glasgow facility supported Excellagen's FDA-clearance (510k) which was granted in March 2013 with broad label claims in woundcare. Having initiated the program in 2011, not only does it provide a potential long term revenue stream for Collagen Solutions but it also clearly demonstrates to the outside world the competencies that reside within the company.

Taxus Cardium has a range of product extensions in mind that would utilise Collagen Solutions' collagen. Two areas of focus have been recently highlighted by Taxus Cardium, utilising Excellagen as a biologics delivery platform in the development of advanced regenerative therapeutics:

Gene therapy – in June 2014, the company presented a pre-specified interim analysis from its international ASPIRE Phase III registration study which uses Excellagen as a delivery platform for Generx, its angiogenic gene therapy product, for patients with myocardial ischemia due to coronary artery disease. Patients receiving Generx were found to have statistically significant improvements in myocardial blood flow

- **Stem cell therapy** – in May 2014, Excellagen flowable dermal matrix was selected as a delivery platform technology to be used with Orbsen Therapeutics' stem cell product, Cyndacel-M, for clinical evaluation in a Phase Ib safety study for the potential treatment of diabetic wounds to be funded by an EU Framework 7 grant in excess of €5m and carried out at Ireland's Regenerative Medicine Institute at the National University of Ireland Galway

Excellagen potential product line extensions	
Product name	Product area
ExcellagenMx	Antimicrobial
ExcellagenGx	Gene Therapy
ExcellaStem	Allogenic Stem Cell Therapy
ExcellagenDerm	Aesthetics
ExcellagenOrtho	Orthopaedics
ExcellagenAsc	Autologous Tissue Engineering
ExcellagenBio-printing	3-D therapeutic tissue
ExcellagenCCM	Conditioned cell media

Source: Taxus Cardium 2014 presentation

Taxus Cardium is unlikely to be able to fully commercialise these products on its own, given that it is a development company, and is likely, in our opinion, to seek marketing partners. For Excellagen, given that it has FDA approval and has been assigned a reimbursement Q-code from the CMS in the USA, finding a partner should not be that onerous although the timing of such, and the consequent impact on volume demand, is less easy to quantify.

8. Unidentified US medical device company

Collagen Solutions is undertaking a technology transfer of a collagen formulation for use in a bone graft to its Glasgow facilities from its San Jose laboratory. Having been developed in San Jose the process is now being scaled up to cGMP standards to enable expansion into EU markets. It is expected to be completed in October with supplies to the client commencing in late 2014. The bone graft is already approved and marketed by the unnamed, albeit large, blue-chip multinational medical device company.

9. Unidentified US medical device company

Collagen Solutions is the named manufacturer of a collagen scaffold for an autologous cell therapy product which has been granted an IND by the FDA. The product is about to commence clinical trials for which Collagen Solutions will provide the clinical trial material, which if successful should potentially secure a long term manufacturing supply agreement.

Additional discussions are taking place with a range of potential customers which are expected to drive growth for COS over the short to mid-term. Indeed, for the Collbio and Collagen Solutions LLC vendors to receive their deferred payments in 2017/18, management has to add at least three new contract manufacturing streams, two of which are described above, the agreement with Taxus Cardium having pre-dated the purchase agreements. Management remain confident that this objective will be met and bettered.

Product end markets

Collagen Solutions has identified three key end markets in which it will focus its development activities as well as proprietary R&D efforts.

Area of focus	
Category	Opportunity
Medical devices	Orthopaedic, dental, vascular, wound, haemostats
Regenerative medicine	Scaffolds, drug delivery, stem cells
In vitro diagnostics	3D living tissue, cell culture

Source: Hardman & Co Life Sciences Research

Medical devices

Collagen Solutions is targeting the medical device segment of the market in which collagen might be used to construct a device that is biodegradable or bioresorbable, both as a contract manufacturer to medical device companies as well as developing its proprietary range of products. It has the technical capabilities, regulatory experience and

manufacturing know how to move from just a supplier of purified, functional collagen at perhaps $500-1,000/gram to a medical device product that contains the same collagen, but which is priced at greater than $1,000/gram.

The properties that make collagen an attractive building block for medical devices can be attributed to the unique fibrillar structure of the molecule as well as defined functional regions that interact with the surrounding cells and other matrix components. As a medical product, collagen can be part of the natural tissue used in the device or it can be fabricated as a reconstituted product.

Medical devices

Surgical or medical application	Product types
Aesthetic surgery	Dermal fillers
Dental surgery	Bone substitutes and haemostatic sponges
General surgery	Haemostatic sponges
Orthopaedic surgery	Bone substitutes, matrixes for cartilage engineering
Vascular surgery	Coating solutions for vascular prostheses
Visceral surgery	Prosthetic coatings and anti-adhesion film
Haemodialysis	Compressive haemostatic sponges
Burns and dermal reconstruction	Bi-layered dermal regeneration matrixes

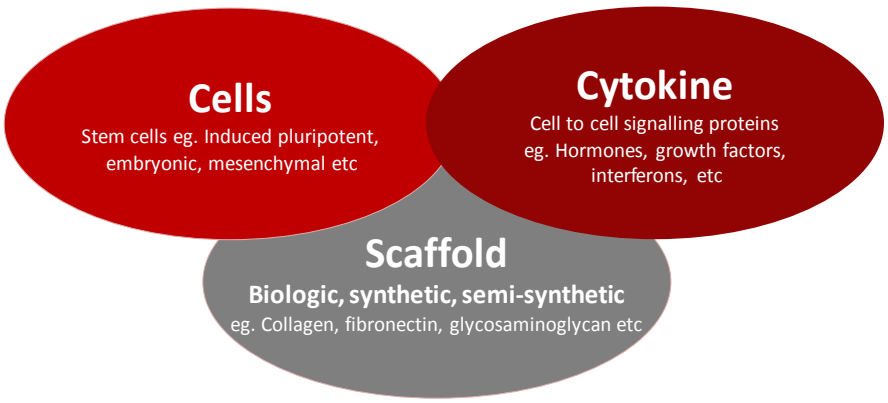
Source: Hardman & Co Life Sciences Research

Collagen has been used to manufacture medical devices for more than 30 years in a variety of applications in wound care, oral surgery, cardiovascular systems, neurology, urology, orthopaedics and ophthalmology. Examples of collagen products for tissue repair and regeneration include CR Bard's microfibrillar collagen haemostat, Avitene, Integra Lifescience's absorbable haemostatic collagen sponge, Collastat, STAAR Surgical's Collamer intraocular lens, Integra Lifesciences' NeuraGen resorbable peripheral nerve repair conduit, Cardiva Medical's vascular closure system (Vascade), DePuy's bone graft substitute, Healos, and Stryker/Orthovita's bone graft, Vitoss.

Regenerative medicine

The emerging field of regenerative medicine, worth an estimated £500m in 2012 and forecast by the Japanese Ministry of Economy, Trade and Industry to rise to c.Y12tn/£70bn in 2030 (source: February 2012), aims to repair, replace or regenerate organs and tissue that have been damaged by disease, injury or even the natural aging process.

Regenerative medicine – required components

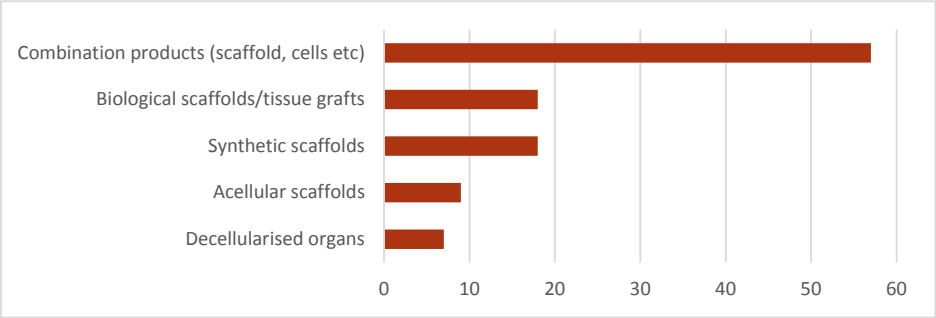


Source: Hardman & Co Life Sciences Research

Synthetic and bio-based materials (eg. collagen) are considered the cornerstones of the regenerative medicine field and are generally implanted in the body for reconstructive purposes. These are biologic, synthetic, semi-synthetic or hybrid matrices designed to direct the organisation, growth and differentiation of cells to form functional tissue.

Products are being developed for a wide variety of disorders and across numerous tissue types, for example, bone, cartilage, skeletal muscle, skin, blood vessels, nerve tissues, ocular tissues and whole organs. There are a number of regenerative medicine products already available and clinically successful with Alliance for Regenerative Medicine (ARM) estimating that in 2013 cell therapy products generated sales of $900m+ with 160,000 patients receiving treatments.

Tissue engineered products – by comparison

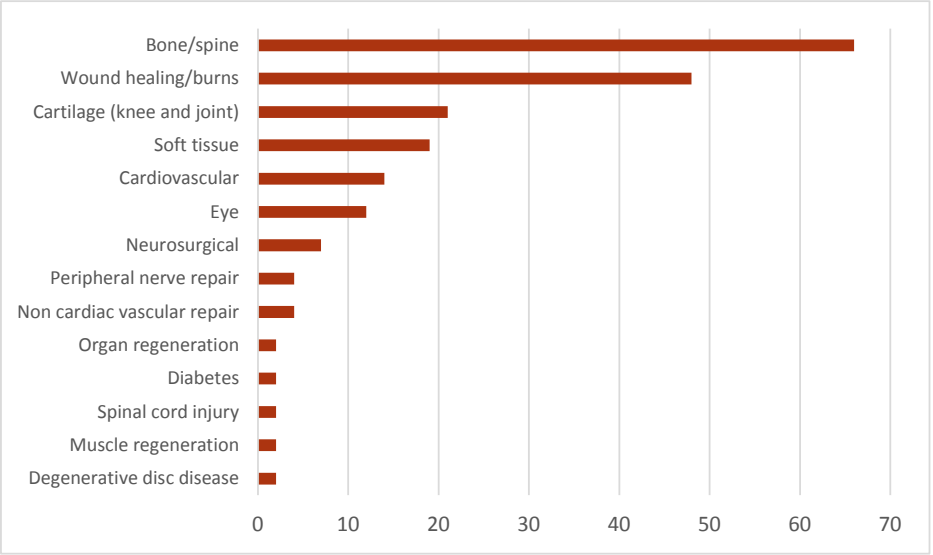


Source: Alliance for regenerative medicine (2012 Annual report)

Of these actively monitored companies the previous chart illustrates the importance of biological scaffolds and combination products in regenerative medicine, acting as a potential lead indicator to growth for those companies supplying scaffolds to the regenerative medicine companies.

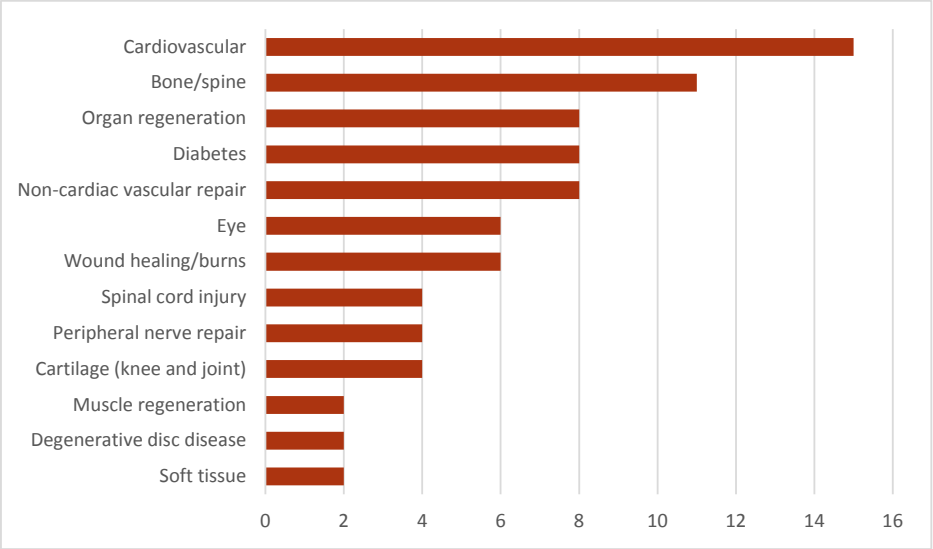
ARM also claim to be actively following 418 tissue engineering and biomaterials companies involved in developing regenerative medicine products with an estimated 700+ companies worldwide working in this field. These followed companies have 247 products that are at various stage of development from preclinical through marketed; up from 90 and 120 products, respectively in 2012 and illustrative of the explosion in regenerative medicine interest which bodes well for future growth in the added-value high end functional collagen market.

Tissue engineered products commercially available



Source: Alliance for regenerative medicine (2012 Annual report)

Tissue engineered products in development (pre-clinical and clinical)



Source: Alliance for regenerative medicine (2012 Annual report)

With the cornerstone matrix identified, companies can then seed these structures with:

- Cells – autologous cells, allogeneic cells, xenogeneic cells, stem cells and genetically engineered cells
- Biomolecules – angiogenic factors, growth factors and differentiation factors

Collagen Solutions believes that the combination of its internal know-how and its willingness to enter into arrangements such as the exclusive license to UCL's polymeric collagen technology should position the business as the "go to" technology provider for any company looking to create biomaterial-based tissue regeneration and repair products.

In vitro diagnostics

Collagen is the most widely used extracellular matrix protein for cell culture, facilitating cell attachment, growth, differentiation, migration, and tissue morphogenesis. Cell migration is a fundamental function of normal cellular processes, including cell proliferation, and migration. Cell behaviour *in vitro* is typically examined in a 2D environment. In the body; however, cells exist in a three-dimensional extracellular matrix environment rich in type I collagen. The goal of many has been to create 3D *in vitro* living tissues and organs with controlled tissue architecture and microvasculature by merging biomaterials science, nanotechnology and biology, the use of which could have innovative diagnostic and research applications for the testing of drug absorption and metabolism, toxicity and pathogenicity.

2D culture systems (monolayer), in which collagen is deposited as a monolayer, are inadequate for what is required by the research community. Although 3D systems are sold by the likes of Millipore one of the key drawbacks has been the ability to create mechanically suitable self-supporting structures. These 3D models will be useful for both *in vitro* diagnostics and drug screening applications, and ultimately reduce the amount of animal testing that has to be done before taking a drug candidate into clinical trials, thereby reducing cost, time and potentially improving early clinical success rates.

Many 3D models currently in use are still too far from the nature of human organs and like existing 2D cultures, traditional scaffolds (typically collagen hydrogels) do not organise as they would in normal tissues. Consequently, their metabolic properties are unsuitable for tissue engineering applications. Work is being undertaken to develop 3D engineered tissues that will mimic the complexity of native tissue structures by taking cell-laden collagen hydrogels with engineered microvasculature. The key challenge is to be able to seed cells directly within macroporous hydrogels to ensure uniformity.

Competition

There are considered to be five key medical grade suppliers, namely DSM/Kensey Nash, Integra LifeSciences and Collagen Matrix all of which serve the medical device, regenerative medicine and *in vitro* diagnostics markets, and Koken and Advanced Biomatrix which serve the research markets. In addition there are a number of other companies that we highlight below which supply collagen to end-users, some that develop their own products and some that do both.

Competitive landscape

Companys	Disadvantages
Integrated – collagen supplies and products	
Kensey Nash	Medical devices, regenerative medicine, *in vitro* diagnostics
Collagen Matrix	Medical devices, regenerative medicine, *in vitro* diagnostics
Encoll Corporation	Medical devices, cosmetics, research
Integra LifeSciences	Medical, devices, regenerative medicine, *in vitro* diagnostics
Innocoll GmbH	Medical devices, supply
Symatese	Medical devices, regenerative medicine
CollPlant	Medical devices, supply (plant based collagen)
Holista CollTech	Cosmetic applications, medical devices (ovine collagen)
Collagen supplies: Research reagents – cell culture, gels, coatings; aesthetics	
Koken	Research applications - cell culture, gels, coatings
Advanced Biomatrix	Research applications - cell culture, gels, coatings
TAP Biosystems	Research applications - cell culture, gels, coatings
NuCollagen	Medical devices, *in vitro* diagnostics, regenerative medicine

Source: Hardman & Co Life Sciences Research

DSM/Kensey Nash – DSM, which acquired Kensey Nash for $360m in May 2012, produces medical devices from various collagen formulations (fibre, fibril and soluble collagen forms with custom-tailored properties and architectures to include sheets, putties, injectables, gels, 3D shapes, coatings, fibres or powders as well as compounding many different active ingredients with collagen). Its products are used in cardiovascular, dental, orthopaedic, sports medicine and wound care markets.

Collagen Matrix – Collagen Matrix, headquartered in New Jersey, has two manufacturing facilities (Oakland, CA and Franklin Lakes, NJ), set up to manufacture proprietary products as well as offering contract manufacturing services. Its proprietary matrix engineering technology, based on insoluble collagen, is focused on three areas, Oral/Maxillofacial surgery, Neurosurgery and Orthopaedic/Spine surgery. Products include NeuroMatrix and Neuroflex Collagen Nerve Cuffs (treatment of severed peripheral nerves), NeuroMend Collagen Nerve Wrap (crushed, stretched, partially-severed or compressed peripheral nerves) and DuraMatrix Collagen Dura Substitute Membrane and DuraMatrix-Onlay Conformable Collagen (repair of dural mater), OssiPatch Collagen Bone Healing Protective Sheet for bone repair procedures, OssiMend Bone Graft Matrix, OssiMend Putty Bone Graft Matrix, OssiGuide Cancellous Granules, SynOss Synthetic Bone Graft Material, TenoMend Collagen Tendon Wrap, a family of dental wound dressings.

Integra LifeSciences Inc (IART) – Headquartered in New Jersey, Integra has a range of products used in orthopaedic extremity surgery, neurosurgery, spine surgery, and reconstructive and general surgery many of which utilise its biomaterials technological capabilities that include collagen, collagen ceramic composites (osteoconductive scaffolds) and demineralised bone matrix. In addition Integra provides custom applications of it UltraPure collagen for use as carrier technologies for drug / protein delivery, general haemostasis, wound healing, bone regeneration and soft tissue repair.

Koken – Headquartered in Tokyo, Koken is focused on research applications selling purified atelo-collagen and native collagen (acid-solubilised) in various forms, such as solutions, sponges, microspheres and permeable membranes to be used for coating of culture plates, 3D gel culture and general scaffolds for cell culturing.

Advanced Biomatrix – Headquartered in San Diego, Advanced Biomatrix is focused on life science research applications, marketing a range of collagens (beads, sponges, coated culture-ware) and reagents used in tissue culture, cell assay and cell proliferation.

Encoll Corporation – A Californian company developing, manufacturing and marketing Type-I collagen-based products, uses its patented technology for the preparation of high purity and charge modified collagen. The company's technologies and manufacturing system yields a series of products required for various medical fields such as general and plastic surgery (wound healing, burns, dermal ulcers/sores), orthopaedic surgery (bone regeneration, spinal fusion), oral, and neurological injuries (nerve regeneration), drug delivery, research, and cosmetic & dietary applications.

Innocoll GmbH (INNL) – A NASDAQ quoted specialty pharmaceutical company, headquartered in Ireland and with manufacturing facilities in Germany. It is developing a range of pharmaceutical products and medical devices using its proprietary collagen-based technologies. Purified from either bovine or equine Achilles tendons its collagen is processed to produce final finished products in the forms of sponges, films, powders, liquids and gels. It has three products in Phase III clinical trials; XaraColl for the treatment of post-operative pain; Cogenzia for the adjuvant treatment of diabetic foot infections and CollaGUARD as a barrier for the prevention of post-surgical adhesions. Approved products include: CollaGUARD (ex-US), Collatamp G, Septocoll, RegenePro, Collieva, CollaCare, Collexa, and Zorpreva, which are sold through strategic partnerships including Takeda, Biomet and Jazz Pharmaceuticals with reported revenues in 2013 of $4.9m.

NuCollagen LLC – Based in San Diego, CA and launched in December 2013, manufactures laboratory and medical grade cGMP bovine collagen, derived from an established U.S. closed herd, for the medical device, *in vitro* diagnostic and regenerative medicine markets. NuCollagen will partner with Bioserv Corporation and Stratum Medical for manufacturing and analytical services. Following a cGMP plant build-out, medical grade collagen is expected to be made available by the end of 2014.

Holista CollTech (HCT.AX) – Australian bio-industrial company specialising in the development and commercialisation of ovine (sheep) collagen products. The company currently markets Ovicoll for cosmetic applications and has reportedly products in development for research and medical applications.

Tap Biosystems – Part of Sartorius Stedim Biotech, based in the UK. It is a leading supplier of automated cell culture systems for the life science sector. Its RAFT technology allows multi-cellular 3D cell cultures to be made rapidly and consistently in standard plate formats which mimic the *in vivo* environment and enable researchers to better understand biological responses, including differentiation, proliferation and drug metabolism.

Symatese – Based in Lyon France, uses its collagen to develop implantable medical devices, cosmetic products and *in vitro* diagnostics with marketed products like Hemotese (haemostatic dressing), Collapat II (haemostatic sponge bone substitute) and Nevelia (silicone-collagen bio layer dermal matric).

CollPlant (CLPT.TA) – Based in Israel, is a medical device company focused on regenerative medicine by using it plant derived recombinant human collagen. The company has generated a range of biomaterials-based products applicable in multiple medical markets, including orthopaedics, wound management, cardiology and general surgery. It has one product with CE Mark, VergenixWD (wound dressing matrix) and five further products in development.

Financials and Investment

Financial history

Healthcare Investment Opportunities plc was established in April 2013, raising £3.6m net of expenses by issuing 40m shares at 10p per share, with the objective of acquiring and/or investing in businesses in the healthcare sector. Having reviewed 30 different proposals in *in vitro* diagnostics, biopharma, biomaterials, medical devices and software, Collagen Solutions plc was formed via the reverse takeover of Healthcare Investment Opportunities by Collbio Limited and the simultaneous acquisition of Collagen Solutions (US) and subsequent name change in January 2014.

A maximum acquisition price of £7.09m (£7.19m fair value) for the purchase of Collbio Limited and Collagen Solutions LLC was agreed, consisting of £1.4m in cash on completion, £3.06m (£3.38m fair value) in Healthcare Investment Opportunities shares and up to £2.63m (£2.41m fair value) in ordinary shares (£2m; £1.78m fair value) and cash dependent on performance criteria over three accounting periods ending 28 February 2017.

For these deferred payments to be made, three new contract manufacturing streams over the next three years have to be added. Given that we have already described two streams within the contract manufacturing section in which Collagen Solutions will contract manufacture a collagen bone graft for a multinational medical device company as well as the collagen scaffold for an autologous cell therapy product, which is currently entering clinical trials, it is considered likely and, indeed, management remain very confident, that this objective will be met and bettered.

Acquisition cost at fair value

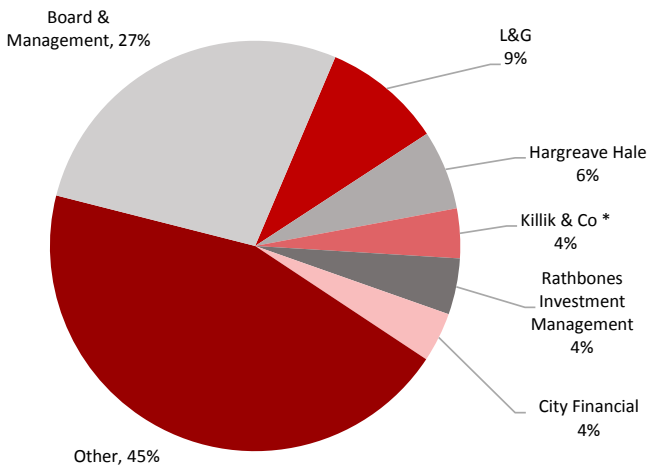
Collagen Solutions LLC	
Maximum consideration	**3,092,133**
Cash on completion	1,398,985
7,326,007 @14.5p shares on completion	1,062,271
Performance cash payment in 2 tranches based on agreed sales targets in 4 periods to 28 Feb 2017	630,877
Collbio Limited	
Maximum consideration	**4,102,122**
Cash on completion	-
16,000,000 @14.5p shares on completion	2,320,000
Performance payment in shares contingent on future sales up to 28 Feb 2017 and entering three new supply agreements	1,782,122
Total Maximum Consideration	**7,194,255**
Cash on completion	1,398,985
Shares on completions	3,382,271
Performance cash payment in 2 tranches based on agreed sales targets in 4 periods to 28 Feb 2017	630,877
Performance payment in shares contingent on future sales up to 28 Feb 2017 and entering three new supply agreements	1,782,122

Source: Collagen Solutions; Hardman & Co Life Sciences Research

Share capital

Healthcare Investment Opportunities raised £4m (£3.6m net of costs) in March 2013 through the issue of 40m Ordinary shares of 1p, taking the number of Ordinary shares in issue to 40.5m. In January 2014, as part of the acquisition of Collbio and Collagen Solutions a further 23,326,007 Ordinary shares were issued, taking issued share capital to 63.8m shares. An additional 16m Ordinary shares are expected to be issued to the vendors of Collbio and Collagen Solutions LLC, contingent on adding three new manufacturing contracts over the three accounting periods to 28 February 2017, in 2017 and achieving earn-out revenues.

Share capital – September 2014



** as per 10 September 2014 notification. Otherwise at 14 March 2014*
Source: Collagen Solutions

Financial discussion

Sales of £24,000 were recorded in the year ending 31 March 2014. This includes three months of sales from Collagen Solutions (UK), formerly Collbio, and Collagen Solutions (US) Inc. and a full year's PLC costs from the cash shell, Healthcare Investment Opportunities.

The reported sales are somewhat at odds with the sales generated by Collagen Solutions LLC prior to its acquisition which, for the 9 months ending 30 September 2013, were £384,655 with adjusted retained profits of £84,513. This can be explained by the fact that Taxus Cardium did not order collagen from Collagen Solutions in the period Jan-Mar 2014 as Taxus Cardium awaited reimbursement codes and completed an equity financing to ensure that the business remained viable. Equally, sales have been temporarily impacted by the technology transfer of a major client's production process from San Jose to Glasgow. This is expected to take until October to complete and validate, after which sales are expected to resume.

Revenues

Sales of £1.04m are expected for the year to March 2015; skewed to the second half of the financial year 2014/2015 as the technology transfer for a collagen formulation for use in a bone graft product, from San Jose to Glasgow, is unlikely to be completed until October 2014.

- Raw material supply sales are expected to be c.£0.65m in 2014/15 and are forecast to grow to around £1.6m in 2018.

- Sales from its development service activities are estimated to be £0.14m this year, rising to around £0.4m in 2018.

- Sales from contract manufacturing are expected to generate the majority of sales and are instrumental in driving the group sales over the next 4 years with £0.25m forecast in the current financial year. Visibility of sales derives from the fact that Collagen Solutions has three contract manufacturing customers; namely, Taxus Cardium, an undisclosed medical device company with a marketed bone graft and an undisclosed regenerative medicine company developing an autologous cell therapy product seeded onto Collagen Solutions' collagen scaffold.

Revenues are clearly sensitive in the near term to the ramp up of product sales by client companies which is not under Collagen Solutions' control. However, the longer term trajectory is expected to be strongly positive given the contracts currently visible and those that we understand the company to be in discussions over.

Costs

- Cost of Goods is expected to be in the range 25-30% of sales
- Administrative expenses are expected to be around £775,000 in the current year, rising to around £1.1m in 2018. Of this, the PLC costs are expected to be c.£0.5m in the current financial year
- Sales & Marketing expenses are expected to be c£300,000 in the current financial year, up from £72,000 in the last financial year which reflected 3 months inclusion of the acquisitions. It is the company's intention to add 1 or possibly 2 sales executives in the current year
- Research & Development is expected to amount to c.£400,000 in the current financial year, rising to c.£0.75m in 2018 as the company focuses on the development of next generation collagen biomaterials, through the exclusive UCL agreement, as well as in-house product development. Clearly this expense line is the most variable and can be flexed by management dependent on the sales trajectory

Cashflow

Underlying EBITDA is expected to be around -£0.7m in the current financial year, modestly positive in 2015/16 and rising to around £2.8m in 2018. As a consequence net cash is expected to fall from £1.49m at 31 March 2014, to £572,000 in 2015 to £252,000 in 2016 before rising thereafter.

Collagen Solutions has limited cash head room in 2016 ending the year in our forecasts with cash of £252,000. Assuming that the administrative, sales & marketing costs are largely fixed, that R&D is variable to a certain extent and that cost of sales are broadly fixed at around 25-30%, we estimate that there is a balance sheet risk if sales fall below £2m. Given the contracts that Collagen Solutions has in place, together with the stated goal of seeking additional IP and acquisitions, we consider this risk to be manageable.

Financials

Profit & Loss statement

Year end Mar (£,000s)	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Sales	**24**	**1,040**	**2,525**	**4,360**	**7,000**
Cost of goods	(12)	(281)	(682)	(1,155)	(1,820)
Gross Profit	**12**	**759**	**1,843**	**3,205**	**5,180**
Administrative expenses	(304)	(775)	(850)	(950)	(1,100)
Selling and marketing costs	(72)	(300)	(375)	(450)	(550)
R&D	-	(400)	(550)	(650)	(750)
Underlying EBITDA	**(364)**	**(716)**	**68**	**1,155**	**2,780**
Depreciation	(13)	(70)	(75)	(105)	(120)
Amortisation	(4)	(16)	(16)	(16)	(16)
Underlying EBIT	**(381)**	**(802)**	**(23)**	**1,034**	**2,644**
Share based costs	(25)	(50)	(50)	(50)	(50)
Exceptional items	(75)	-	-	-	-
Statutory Operating profit	**(480)**	**(852)**	**(73)**	**984**	**2,594**
Net financial income	-	6	2	4	10
Underlying Pre-tax profit	(381)	(796)	(21)	1,037	2,654
Exceptional items	-	-	-	-	-
Reported pre-tax	**(480)**	**(846)**	**(71)**	**987**	**2,604**
Reported taxation	**-**	**-**	**-**	**32**	**(531)**
Underlying net income	(381)	(796)	(21)	1,069	2,124
Statutory net income	**(480)**	**(846)**	**(71)**	**1,019**	**2,074**
Period-end shares in issue (m)	63.8	63.8	63.8	79.8	79.8
Weighted average shares (m)	43.7	63.8	63.8	65.2	79.8
Fully diluted shares (m)	47.7	67.9	67.9	69.2	83.9
Underlying Basic EPS (p)	**(0.87)**	**(1.25)**	**(0.03)**	**1.64**	**2.66**
Underlying fully-diluted EPS (p)	**(0.87)**	**(1.25)**	**(0.03)**	**1.55**	**2.53**
Statutory basic EPS (p)	(1.10)	(1.33)	(0.11)	1.56	2.60
Statutory fully-diluted EPS (p)	(1.10)	(1.33)	(0.11)	1.47	2.47
DPS (p)	-	-	-	-	-

Key metrics	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Growth					
Sales		4229%	143%	73%	61%
Operating profit		n/a	n/a	n/a	156%
EPS		n/a	n/a	n/a	62%
DPS		n/a	n/a	n/a	n/a
Operating ratios					
Cost of goods	50.3%	27.0%	27.0%	26.5%	26.0%
Gross margin	49.7%	73.0%	73.0%	73.5%	74.0%
Admin	1264.0%	74.5%	33.7%	21.8%	15.7%
Sales & Marketing	299.4%	28.8%	14.9%	10.3%	7.9%
EBITDA	-1513.6%	-68.8%	2.7%	26.5%	39.7%
Operating profit	-1584.2%	-77.1%	-0.9%	23.7%	37.8%
Reported tax rate	0.0%	0.0%	0.0%	-3.2%	20.4%

Source: Collagen Solutions; Hardman & Co Life Sciences forecasts

Balance sheet

At 31 March (£,000s)	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Shareholders funds	6,256	5,460	5,440	8,509	10,632
Cumulated goodwill	-	-	-	-	-
Total equity	6,256	5,460	5,440	8,509	10,632
Share capital	683	683	683	843	843
Reserves	5,573	4,777	4,756	7,666	9,789
less: Cash	1,492	572	252	529	2,739
less: Marketable securities	-	-	-	-	-
less: Non-core investments	(2,409)	(2,409)	(2,409)	-	-
Invested capital	**7,174**	**7,298**	**7,597**	**7,980**	**7,894**
Fixed assets	232	262	437	645	916
Intangible assets	6,894	6,878	6,862	6,846	6,830
Stocks	39	89	169	269	389
Trade debtors	-	100	220	350	500
Other debtors	167	167	167	199	167
Trade creditors	-	(40)	(100)	(170)	(250)
Tax liability	-	-	-	-	(499)
Other creditors	(160)	(160)	(160)	(160)	(160)
Debtors less creditors	7	67	127	219	(242)
Invested capital	**7,174**	**7,298**	**7,597**	**7,980**	**7,894**

Key metrics	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Net cash/(debt)	1,492	572	252	529	2,739
Net debt/equity (%)	24%	10%	5%	6%	26%
After-tax ROIC	-5.3%	-10.9%	-0.3%	13.4%	26.9%
Interest cover (x)	n/a	(134)	(10)	273	255
Dividend cover (x)	n/a	n/a	n/a	n/a	n/a
Cap-ex/depreciation (x)	0.0	1.4	3.3	3.0	3.3
Cap-ex/sales (%)	1.8%	9.6%	9.9%	7.2%	5.6%
Net asset value/share (p)	14.3	8.6	8.5	13.1	13.3
Stock days	593	84	69	69	66
Debtor days	-	18	23	24	22
Creditor days	-	26	37	43	42

Source: Collagen Solutions; Hardman & Co Life Sciences forecasts

Cashflow statement

Year end Mar (£,000s)	FY 14	FY 15E	FY 16E	FY 17E	FY 18E
Operating profit	**(381)**	**(802)**	**(23)**	**1,034**	**2,644**
Depreciation	13	70	75	105	120
Amortisation	4	16	16	16	16
Stocks	(13)	(50)	(80)	(100)	(120)
Working capital	(72)	(60)	(60)	(60)	(70)
Exceptionals/provisions	(75)	-	-	-	-
Other (Fx)	(1)	-	-	-	-
Net cash used in operations	**(525)**	**(826)**	**(72)**	**995**	**2,590**
Net interest	-	6	2	4	10
Tax	-	-	-	-	-
Operational cashflow	**(525)**	**(820)**	**(70)**	**998**	**2,600**
Capital Expenditure	(0)	(100)	(250)	(313)	(391)
Free cashflow	**(525)**	**(920)**	**(320)**	**686**	**2,210**
Dividends	-	-	-	-	-
Acquisitions	(1,357)	-	-	(409)	-
Other investments	-	-	-	-	-
Cashflow after investments	**(1,882)**	**(920)**	**(320)**	**277**	**2,210**
Share issues	3,374	-	-	-	-
Currency effect	-	-	-	-	-
Change in net debt	**1,492**	**(920)**	**(320)**	**277**	**2,210**
Opening net cash	-	1,492	572	252	529
Closing net cash	**1,492**	**572**	**252**	**529**	**2,739**
Hardman cashflow/share (p)	**-1.2**	**-1.3**	**-0.1**	**1.5**	**3.3**

Source: Collagen Solutions; Hardman & Co Life Sciences forecasts

Company Matters

Board of directors

Board of Directors				
Position		Nominations	Remuneration	Audit & Risk
Non-executive Chairman	David Evans	M	M	
Chief Executive Officer	Stewart White			
CFO & Company Secretary	Gill Black			
Non-executive director	Kevin Wilson	M	M	C
Non-executive director	Malcolm Gillies	C	C	M

C = Chair; M = Member
Source: Collagen Solutions

David Evans – Non-Executive Chairman

David Evans has a proven track record in acquiring, integrating and growing businesses in the diagnostic area and in value creation. As Chairman of BBI Holdings plc the company was taken from a value of £4m to £84m through acquisition and organic growth when sold into December 2007 to Inverness Medical Innovations Inc. He was chairman of DxS Limited, which was sold in September 2009 to Qiagen for £82m, having stepped down in June 2009. David was also chairman of Sirigen Group, an early stage medical technology company, which was sold in 2012 to Becton, Dickinson, a global medical technology company. David was also previously Chairman of Immunodiagnostics Systems Holdings plc. David is currently chairman of Epistem Holdings plc, EKF Diagnostic Holdings plc and Scancell Holdings plc. David is also chairman of Premaitha Health plc, Optibiotix Health plc, Omega Diagnostics Group plc and Venn Life Sciences Holdings plc. He is also a director and shareholder of Diagnostic Capital Limited.

Stewart White – Chief Executive Officer

Stewart was CEO of Collbio, prior to the reverse takeover of Healthcare Investment Opportunities and subsequent name change to Collagen Solutions. Stewart has international experience in operations, business and product development, and 'Good Manufacturing Practices' (GMP) compliant manufacturing of collagen medical devices, advanced biologics and Active Pharmaceutical Ingredients in both Small to Medium Enterprises as well as global pharmaceutical companies. He has recent and direct board experience at Angel Biotechnology Holdings plc, an AIM quoted company. He holds a First Class degree in Applied Microbiology, a PhD in Fermentation Technology and Bioprocessing and an MBA from the University of Strathclyde.

Gillian Black – Chief Financial Officer and Company Secretary

Gill joined the company in June 2014, bringing with her extensive financial Board-level experience, having been Financial Director and Company Secretary of A&E Russell Ltd, where she was instrumental in their expansion before taking them through the subsequent acquisition by Bunzl plc in 2008. After spending 2 years as Head of Finance at AKP Scotland Ltd, she became Head of Finance and Company Secretary of GVA James Barr Ltd, a privately owned property consultancy business which merged in 2013 with GVA Grimley. Previously, Gill was a Senior Manager at KPMG, Glasgow where she led a team advising many high growth businesses. She holds an MA in Accountancy and Economics from the University of Dundee and is a Chartered Accountant and ICAS member.

Kevin Wilson – Non-Executive Director

Kevin Wilson has been active in Investment Banking and Stockbroking for 25 years as a corporate finance adviser. He has a PhD in Finance and an MBA in Business and is a Visiting Fellow at Manchester Business School and Visiting Senior Lecturer in Finance and Accounting at the University of Lancaster Management School. He sits on the boards of EKF Diagnostic Holdings plc, Arcis, Altos Ltd and The Big Life Group of companies. He is a director and shareholder of Diagnostic Capital Ltd. He is an original investor in Collbio and is also a consultant to Zeus Capital.

Malcolm Gillies – Non-Executive Director

Malcolm is a director in several private companies mostly involved in the healthcare area including Aircraft Medical; Antoxis and Ohmedics. He has previously held positions as a non-executive director in public companies and was company secretary at Axis-Shield Plc. He has a background as a corporate finance lawyer, having been a senior partner with Shepherd and Wedderburn LLP.

Senior management

Senior management	
Position	
Chief Executive Officer	Dr Stewart White
Chief Financial Officer	Gill Black
Chief Scientific Officer	Jacqueline Burgin
Chief Commercial Officer	Diane Mitchell
Chief Operating Officer	To be announced

Source: Collagen Solutions

Diane Mitchell – Chief Business Officer

Diane is a co-founder of Collagen Solutions US. with 10 years sales and marketing experience in collagen and medical devices and experience managing a diverse customer base which includes blue-chip companies, academic collaborators and start-ups. During her career Diane has also established distribution networks for both biomaterials and electronics devices through multi-channel programs. Diane holds a Bachelors in Business and an MBA from the University of Phoenix and is responsible for marketing materials, trade shows, distribution and developing sales and marketing strategies for Collagen Solutions.

Jacqueline Burgin – Chief Scientific Officer

Jacqueline is a co-founder of Collagen Solutions US, acquired by Collbio Limited, having worked in the biomedical polymer field since 1987 with significant experience in product development to scale-up and manufacturing. She is co-inventor on 17 patents, most of which utilise collagen in medical devices. Other areas of research include polyethylene glycols, glyco-amino glycans and hyaluronic acid, obtained during a career with companies such as Allergan, Inamed and Collagen Corporation. Jacqueline holds a Bachelor of Science in Chemistry from the University of California.

TBA – Chief Operating Officer

It is envisaged that a chief operating officer is appointed in the coming financial year.

Scientific advisory board

Collagen Solutions' R&D activities are guided by Professor Robert Brown. It is the company's intention to build out the SAB, bringing on board persons with clinical and regulatory experience.

Scientific advisory board	
Officer	Experience
Professor Robert Brown	Director of Research at the Centre for Tissue Regeneration Science with the Institute of Orthopaedics and Musculo-skeletal Sciences at the Medical School at University College London (UCL)
Tom Hyland	General Manager of API Foils Europe. Experience in collagen chemistry, development, manufacturing and engineering requirements of collagen-based medical devices having worked with Johnson & Johnson, Microsoulis, Intercell, Alere and Invitrogen

Source: Collagen Solutions

Risks

Background
It goes without saying that investments in small early stage companies carry a significant risk and investors must be aware of this fact. In our opinion, the following risks are particularly relevant.

Revenue
The success of the business is reliant on generating sales of its collagen products, development services and contract manufacturing. These are highly sensitive in the short term to both existing customers retaining Collagen Solutions' services as well as the success or failure of its customers' clinical trials, changes to reimbursement for collagen-based therapies and the possibility that existing customers might use other collagen supplies or other biomaterials. We consider the latter to be less likely for existing products in which contract manufacture and source of collagen is embedded into the product's certification. To change would be costly and timely for the customer as they would need to go through a new approval process.

Regulatory
The mid to long term success of the company is largely dependent on customers' products gaining regulatory clearance. If these are not obtained future revenue streams could be impacted. To mitigate this Collagen Solutions intended to build multiple revenues streams, with multiple customers across three key areas in which biomaterials and collagen are expected to be highly relevant, namely medical devices, regenerative medicine and *in vitro* diagnostics.

Commercialisation
Collbio is contracted by Taxus Cardium to produce Excellagen. Should Taxus Cardium not be able to fully commercialise its lead product, either alone or through distribution/ marketing partners, or should it chose to stop the Collbio's manufacturing contract, the company could be impacted negatively.

Raw Material
Collagen Solutions uses collagen from bovine sources that have been used in regulated and approved medical devise for decades. Although raw materials are sourced from BSE-free areas with all the requisite quality systems and traceability demanded of them by the FDA and other regulators, any change to BSE status could impact supplies.

Manufacturing and suppliers
With only a single manufacturing site and despite having insurance to cover damage to facilities, any long term closure to its facility could impact business performance. The company has a sole supplier for its medical grade bulk collagen which might impact revenue generation should Collagen Solutions not be able to transition to alternate sources.

Glossary

Collagen	Family of extracellular, closely related proteins occurring as a major constituent of bone, cartilage, tendon, and skin giving it flexibility and strength
cGMP	Current Good Manufacturing Practice; followed by the pharmaceutical and biotech firms to ensure that the products produced meet specific requirements for identity, strength, quality, and purity. The FDA regulates these industries to ensure cGMPs are being followed
cGLP	Current Good Laboratory Practice. Regulations that apply to nonclinical laboratory studies supporting research or marketing applications for FDA-regulated products which outline basic requirements for study conduct, personnel, facilities, equipment, written protocols, operating procedures, study reports, and a system of quality assurance oversight for each study to help assure the safety of FDA-regulated products
Fibril	A minute fibre of collagen, composed of molecules aggregated in a linear array. In Type I collagen, the most common type, the tropocollagen molecules are associated in periodic, staggered arrays that give the appearance of cross-banding, forming unit fibrils. These unit fibrils are aggregated in bundles to form larger fibrils, with longitudinal striations, which may themselves be aggregated into fibres
Monomer	A molecule such as collagen that can combine with others to form a polymer
Polymer	Any of various chemical compounds of smaller, identical molecules (called monomers) linked together. Polymers have extremely higher molecular weights and make up, for example, collagen tissues in organisms
Procollagen	Precursor molecule of collagen, synthesised in the fibroblast, osteoblast, etc. and cleaved to form collagen extracellularly
Telopeptide	A peptide covalently bound in or on a protein, in this case collagen, protruding therefrom and subject to enzyme attack and/or modification and conferring immunogenic specificity
Tropocollagen	Basic structural unit of all forms of collagen; helical structure of three polypeptides wound around each other

Notes

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