27 March 2015 UK Results and Company Update

Imperial Innovations Group Plc

Uncovering the unquoted potential

Imperial Innovations has made significant progress in continuing not only to create new, exciting and innovative companies, but in nurturing existing companies towards important inflection points. The value creation being generated is highly impressive. Here we highlight progress in some of our seven rising stars and for the first time we write on some new companies which we believe could represent the next wave of rising stars emerging from the portfolio. We continue to believe that Imperial Innovations offers by far the best risk-reward ratio of all the companies in the IP University investment space and our peer group analysis strongly suggests an upward re-rating is long overdue. **BUY**.

- **World class companies** - Four companies in our review of several of the portfolio companies have significantly caught our attention: Cell Medica, PsiOxus, Autifony and Veryan Medical. Each of these businesses is positioned to enter a very exciting phase and data suggests that they could significantly outperform the rest of the portfolio in the near-term. Cell Medica and PsiOxus could have products emerging from their pipelines that could become blockbusters, a word often used in the sector, but the data that we have seen indicates a very real possibility of this being achieved. Autifony by contrast could resolve an age old problem in the hearing loss industry with multiple Phase II data points in the next 12 months.
- **Successful IPOs and potential future exits** - Innovations has had a number of successful IPOs from its portfolio whilst retaining meaningful equity positions in these companies, including Abzena, Circassia and Oxford Immunotec. These companies have been delivering multiple milestones but in some cases they have yet to reach significant value inflection points, which means that there is a significant level of upside in these investments.
- **Interim results** - Innovations has reported a pre-tax loss of £7.0m (H1 2014 profit £24.4m) driven by volatility in the quoted portfolio. Net assets decreased from £404.8m to £397.8m while the portfolio increased in value by £10m to £262.0m (from 1 August 2014). A total of £22.4m was invested in 13 portfolio companies.
- **Forecasts and valuation** - Since the period end the value of the quoted portfolio has recovered by £8.2m taking the Group back into a small profit. In addition we are confident on the outlook for the remainder of the year and therefore our full year forecasts remain unchanged. We note that similar quoted companies in the space (ie IP Group and Allied Minds) have achieved sizeable valuations at significant premiums to NAV. We believe that the quality of Imperial merits a significantly higher valuation and prudently applying a price/book sector multiple to the current share price suggests a target price of **743p** (from 506p).

Forecasts and Ratios

Y/E 31 July	Revenue (£m)	PBT (£m)	EPS (GBp)*	NAV (£m)	Net cash** (£m)
2014 A	3.64	27.42	26.7	404.8	176.5
2015 E	3.22	7.56	5.5	412.4	120.6
2016 E	3.28	9.23	6.8	421.7	76.8

Source: Cenkos Securities (Estimates) IVO (Actuals); *fully dilutive, ** No debt Includes STLI

BUY

Price at COB 26 Mar 2015	475p
52-week range	352-520p
Ticker:	IVO

Share Price Performance

Source: Factset

Performance	1m	3m	12m
Absolute (%)	4	-5	16

Stock Data

Market cap	£651.5m
Shares outstanding (m)	137.2

Key Indicators

Net debt/equity(%)	-39.9
EBIT margin (%)	-213.7

Activities

Imperial Innovations builds and invests in technology and healthcare companies.

Directors

Martin Knight	Chairman
Russ Cummings	CEO
Nigel Pitchford	CIO
Anjum Ahmed	CFO

Significant Shareholders

Invesco Asset Management Ltd.	42.0%
Lansdowne Partners (Uk) Llp	13.7%
Woodford Investments	13.4%
Mirabaud Asset Management Ltd.	0.9%
Tudor Investment Corp.	0.6%

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Interim results

Imperial Innovations has delivered a solid set of interim results for the period ended 31 January 2015, demonstrating significant progress within the portfolio.

Financial summary

- Revenue increased by 79% to £2.8m (H1 2014: £1.6m), principally driven by a strong license and royalty income stream.
- Pre-tax loss of £7.0m (H1 2014: £24.4m) resulting from a portfolio fair value loss of £7.4m (H1 2014: profit £33.2m), which was driven by volatility in the quoted portfolio.
- The £5.6m net gain in the unquoted portfolio was more than offset by the £13m decrease in the quoted portfolio, resulting in a £7.4m net fair value loss.
- Post period end there was a **recovery in the value of the quoted portfolio of £8.2m** (as at 25 March), principally driven by a bounce-back in the Circassia share price from 31 January.
- Net assets decreased from £404.8m to £397.8m.
- The portfolio increased in value by £10m (+4%) to £262m (from 1 August 2014).
- In the period Innovations invested £22.4m into 13 portfolio companies.
- Net cash at the end of the period sits at £152.8m (H1 2014: £48.1m), including short term liquidity investments, which combined with the EIB loan leaves £167.8m available for investment.

The table below illustrates the movement in the gross value of the portfolio in the period. The Group made £22.4m of new investments, disposing of £5.1m. The net revaluation loss of £7.2m (£7.4m net of revenue share) was largely as a result of the £13m quoted fair value loss. The unquoted portfolio contributed positively but unlike last year, there were no major trade sales or IPOs.

Table 1: Movement in portfolio value

	£m
Gross value of portfolio at 31 July 2014	257.1
Investments	22.4
Disposals	(5.1)
Revaluation gains (unquoted)	9.5
Revaluation losses (unquoted)	(3.8)
Revaluation losses (quoted)	(13.0)
Gross value of portfolio at 31st January 2015	**267.2**

Source: IVO, Cenkos Securities estimates

Operational highlights

Since the start of the period there have been a number of encouraging announcements from the holding companies of Innovations, including successful equity raises for Veryan and Cell Medica totalling £68m and of which Innovations committed £23.4m.

Funding

In the six months to 31 January 2015, the Group invested £22.4m in 13 portfolio companies (H1 2014: £17.8m in 17). This included a first tranche of £7.5m to Cell Medica as part of a £50m raise and a first tranche of £2.7m to Veryan as part of a £18m funding round.

Post-period end the Group has invested a further £9.6m into 5 companies, which takes the total amount committing to £32m (FY2014: £32.8m).

Cell Medica

Series B equity fundraise

In October Innovations led a major investment round in Cell Medica. Innovations invested £15m in this £50m series B round, increasing its stake to 27.0% and Woodford Investment Management and Invesco Perpetual invested alongside Innovations.

Cytovir™ manufacturing in Berlin (post-period end)

Cell Medica reached an important milestone in February when it began to manufacture cell therapy product, Cytovir™ out of its Germany facility at the Max-Delbrück-Centre of Molecular Medicine in Berlin-Buch and the first product has now been successfully delivered for use in the first patient in the clinical trial. The product is under development for the treatment of cytomegalovirus (CMV) infections following a hematopoieticstem cell (bone marrow) transplant, representing an area of high unmet clinical need.

Orphan Drug Designation granted for CMD-003 (post-period end)

Cell Medica recently announced that its lead cancer immunotherapy, CMD-003, has been awarded Orphan Drug Designation in the indication of Epstein - Barr virus (EBV) positive non-Hodgkin lymphomas. With Orphan Drug Designation CMD-003 will be entitled to a number of benefits through its development in the US, including seven year marketing exclusivity, accessibility to grants and tax credits on clinical trials.

First patient dosed in CITADEL trial (post-period end)

The company recently treated the first patient in the CITADEL Phase II trial, which is investigating the safety and efficacy of CMD-003 for the treatment of aggressive extranodal NK/T cell lymphoma (ENKTCL) in patients for whom conventional treatments have proved unsuccessful. The start of the Phase II clinical trial indicates strong progress by Cell Medica, which has been facilitated by the £50m equity funding last year.

PsiOxus

The company was granted Orphan Drug Designation for its oncolytic vaccine, enadenotucirev, by the European Medicines Agency (EMA) for the treatment of platinum-resistant epithelial ovarian cancer.

Veryan

Equity funding

Innovations led a second series B round in the period for another portfolio company, Veryan, with co-investors including Invesco Asset Management, Seroba Kernel and Seven Mile. Of the £18m total raised, Innovations invested a total of £8.4m, resulting in a post-investment equity holding of 48.2%. Prior to this round Innovations had invested a total of £11m. The equity financing will be used to commercialise its BioMimics 3D™ product (see below) in Europe and internationally as well as complete a registration study in the US to access a significant global market.

Agreement with Biosensors

Also in the period Veryan Medical entered into a distribution agreement with Biosensors International for Veryan's BioMimics 3D™, a helical stent which has CE mark approval. The agreement covers the EU, Asia Pacific and other markets.

Kesios Therapeutics

Innovations completed a seed investment of £1.85m in the oncology drug discovery company, Kesios Therapeutics. The company is developing novel therapeutics for the treatment of multiple myeloma and other blood-related cancers and has been created to commercialise research led by Professor Guido Franzoso.

Autifony

A phase IIa study for a first-in-class treatment for timmitus was initiated across 12 UK hospital sites.

Investment Thesis

Imperial Innovations has had a busy time in the interim period as it has put more capital to work across a greater number of companies, fulfilling its commitment to allocating greater levels of capital to businesses that offer significant returns in the future. By minimising the dilution when companies raise larger sums of capital, Imperial has been able in many cases not just to stand its corner but also increase its shareholding. When we step back and look at the progress that some of the underling companies in the portfolio have made, it is difficult to reflect this progress and the value creation being generated as most of the companies are private and below the radar screen for investors. However, our one-on-one meetings with a number of the companies which do not constitute a significant value in today's NAV, suggests multiple opportunities for the NAV to significantly move upwards as these companies hit major inflection points.

A quiet revolution

Some of the portfolio companies are undergoing a quiet revolution in our view. Veryan Medical for instance published two year efficacy data on its helical stent system that outperformed significantly the current standard of care. To us the implication of this high quality data is the potential for the Veryan technology to become standard of care in circulatory diseases (peripheral arterial disease) representing a market valued at US$1.6bn. Autifony by contrast is targeting the hearing loss and tinnitus market, a market that is very large indeed and where there are no pharmaceutical products that have worked. A highly innovative team spun out of GlaxoSmithKline is pursing novel small molecule drugs that could have a major impact in this space if successful and the company is looking to complete and readout two Phase II clinical trials in the next 12 months. Both of these companies have very modest valuations today. Nexeon, which has been quietly bulking up the team with highly experienced individuals from the battery industry, is moving closer to the point of its first revenues. Finally Plaxica is making progress towards commercially developing a low-cost technology to allow a commonly used intermediate by product material (lactic acid) to be produced from highly sustainable sources (paper and pulp manufacturing by products for example), rather than from the food chain.

As we look across the portfolio and see high calibre management teams and boards backing some the Imperial Innovations businesses, coupled to a blue chip list of investors, we can see the opportunity for significant future returns building into the overall portfolio. Investing into companies that start from an academic basis is a risky proposition, but Imperial Innovations' approach eloquently looks to mitigate this risk and the acceleration towards the next Circassias and Nexeons is well underway.

Within the portfolio we see the potential for several businesses to become larger in market cap and valuation terms than Imperial Innovations itself, which is why we view the importance of maintaining a healthy shareholding along the way to minimise dilution when the succession of winners reach the 'finish line'.

Valuation

When we look at similar quoted companies in the space we note that they have achieved sizeable valuations at significant premiums to their net asset values. IP Group's market cap (at 25 March 2015) is £1.1bn, which is 2.1x the book value at 31 December 2014 of £526m. This ratio increases to 2.5x if the intangibles are stripped out. Allied Minds now has a market cap of £1.5bn, a premium of 9x its book value at 30 June 2014 (last set of results).

By contrast Imperial Innovations has a market cap of 1.7x its current net asset value of £397.8m, demonstrating that it trades on a much lower premium than its peers. We believe that the level of quality within the Imperial portfolio, plus the upcoming company milestones, merit a valuation significantly higher than where it sits today and that surpasses multiple for the closest comparator which is IP group.

If we take the IP Group ex-intangibles premium of 2.5x and apply this to Imperial we reach a valuation of £1,012m, which translates to a **target price of 743p** based on the number of shares in issue. We believe that this is a more prudent method of calculating the price target than taking the average of the peer group as the Allied Minds book value is no longer recent and will therefore skew the calculation.

Competitive Landscape

The most similar London-listed companies to Innovations are IP Group and Allied Minds. IP Group (originally IP2IPO, and listed on AIM) has been listed on the main market for several years as a UK intellectual property investor and commercialisation business. US-based Allied Minds floated on London's main market last year raising £124.4m (July).

IP Group

IP Group has partnered with a number of UK Universities in order to help commercialise their ideas. The Group acts as an early stage venture capital business and has a portfolio of over 60 companies in the following five sectors:

- Energy & Renewables,
- Medical Equipment & Supplies,
- Pharma & Biotech,
- IT & Communications, and
- Chemicals & Material.

Last year two companies were spun out of IP Group and listed on AIM: Xeros and Medaphor.

Allied Minds

Allied Minds floated on London's main market last year. The company has a portfolio of 20 early-stage businesses of which half are in the life science sector and the other half in the physical science sector. Allied Minds has yet to exit any of its investments.

Comparison with Innovations

Net asset value

The table below compares the last quoted net asset value (book value) of each of the companies, illustrating that the NAVs of both Innovations and IP Group are considerably higher than that of Allied Minds, while the latter has a higher valuation. The NAVs are also shown with intangibles stripped out as this line is significant for IP Group.

Table 2: NAV comparisons

	IVO*	Allied Minds**	IP Group***
NAV	397.8	164.2	526.2
NAV ex intangibles	397.8	161.5	452.6
Market cap****	664.6	1,475	1,126

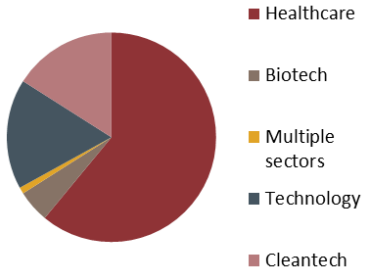
Source: Bloomberg, Cenkos, *NAV as at 31/01/2015, **NAV as at 30/06/2014, ***NAV as at 31/12/2014, **** as at 25/02/2015

At the last set of financial results for Allied Minds (interims, 30 June 2014) the net asset value of the company was $243m (c £164m). The share price has performed very well since the IPO and the market capitalisation of the company is now £1.4bn, demonstrating a significant premium.

Portfolio

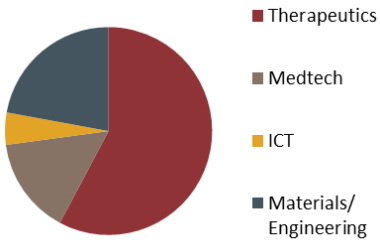
Innovations and IP Group both have diversified portfolios across a range of sectors with particular exposure to the healthcare sector. Charts 1 and 2 highlight the exposed sectors within the IP Group and Innovations portfolios respectively. The Allied Minds portfolio is composed of life sciences and physical sciences holdings, with 50% of the portfolio allocated to each of these sectors. As shown in the chart Innovations predominantly invests in healthcare companies (total of 73%), across the Medtech and Therapeutics sub-sectors. This compares to a 61% healthcare exposure for IP Group.

Chart 1: IP Group portfolio



Source: IP Group, Cenkos Securities

Chart 2: IVO portfolio



Source: IVO, Cenkos Securities

Portfolio companies

In total the Imperial Innovations portfolio comprises 98 companies within the healthcare, engineering/materials and ICT sectors. In the table below we have summarised the top 20 investments within the IVO portfolio, highlighting Innovations' holding and the net carrying value as at 31 January 2015 alongside the movement in the period.

Table 3: Portfolio companies at 31 January 2015

Company	Net carrying value as at 31 July 2014	Cash invested six months to 31 Jan 2015	Cash divested six months to 31 Jan 2015	Fair value movement six months to 31 Jan 2015	Net carrying value at 31 Jan 2015	Cumulative cash invested at 31 Jan 2015	% Issued share capital held at 31 Jan 2015
Circassia	78,359	-	-	-11,062	67,297	25,500	14.00%
Nexeon	34,086	-	-	-	34,086	22,373	40.10%
Veryan Holdings	18,109	2,743	-	41	20,893	13,711	48.20%
Cell Medica	7,979	7,500	-	3,668	19,147	12,310	27.00%
Abzena	17,998	-	-	-450	17,548	10,475	23.60%
PsiOxus Therapeutics	7,892	2,000	-	1,579	11,471	9,476	28.50%
Plaxica	9,446	-	-	-	9,446	8,997	45.70%
Oxford Immunotech	7,817	1,551	-	-1,301	8,067	7,584	4.60%
Econic	6,145	-	-	-	6,145	4,400	56.10%
Autifony	6,060	-	-	-	6,060	5,000	25.10%
MISSION Therapeutics	2,974	3,038	-	-	6,012	5,833	21.20%
Topivert	5,955	-	-	-	5,955	5,853	33.10%
Cortexica	5,428	-	-	-	5,428	5,553	30.00%
Abingdon	2,651	1,629	-	-	4,280	5,789	35.50%
EVO Electric	3,786	-	-	-	3,786	3,344	34.10%
CCS	3,672	-	-	-	3,672	1,200	8.80%
Crescendo	3,250	-	-	-	3,250	3,250	17.40%
Stanmore	6,268	-	-	-3,134	3,134	5,000	16.40%
Just Yoyo	2,857	-	-	-	2,857	1,967	36.20%
Nascient	2,750	-	-	-	2,750	2,750	78.80%
Other companies	18,512	3,983	-5,067	3,296	20,724	15,259	
Total	251,994	22,444	-5,067	-7,363	262,008	175,624	

Source: Imperial Innovations

In the remainder of the report we have performed a detailed analysis of seven companies within the unquoted portfolio which we believe hold significant long-term value for Imperial Innovations. A number of these companies have significant data-readouts in the coming year and we believe that several companies could secure licensing deals on the back of data, driving up the valuations.

Immunotherapy

Cell Medica

Cell Medica is a cellular immunotherapy company in the cell therapy space which is working on a number of approaches for the treatment of viral and cancer indications. Recently the company began the international CITADEL Phase II clinical trial, which is exploring the therapeutic benefit of a novel cancer immunotherapy product for the treatment of advanced NK/T cell lymphoma.

Oncology

MISSION Therapeutics

MISSION is a specialist biotech company which is utilising a greater understanding of cell biology to develop novel treatments for cancer. The company is specifically targeting ubiquitin pathways involved in the DNA damage response with the aim of inducing synthetic lethality, a powerful mechanism to selectively kill tumour cells.

PsiOxus

PsiOxus Therapeutics, an Oxford-based development stage biotech, is developing novel therapeutics for the treatment of cancer using a non-conventional approach. The company's approach is to produce novel cancer therapies with its tumour-targeted oncolytic vaccine, EnAd. PsiOxus is further enhancing this platform technology through genetic modification, enhancing the vaccine's potency as an anti-cancer therapy.

Medical Devices

Veryan Medical

Veryan is using an approach called biomimicry (the mimicking of life using imitation biological systems) to develop a range of solutions for the treatment of vascular disease. The company's product, BioMimics 3D™, has been shown to improve the performance of vascular stents through adoption of biomimicry. The technology has the potential to transform the treatment of patients with symptomatic peripheral arterial disease of the lower limbs.

Other Healthcare

Autifony Therapeutics

Autifony Therapeutics was formed in 2011 as a spin-off company from GSK and, using pioneering science, aims to develop new drugs to treat hearing disorders. The company is targeting specific ion channels which regulate neuronal activity within the auditory system in order to treat symptoms associated with hearing loss. The lead compound, AUT00063, has completed Phase I trials with Phase IIa that started in Q1 2015.

Engineering/ Materials

Nexeon

Nexeon is a technology company which has designed and patented a novel way of structuring silicon to allow the delivery of an extended life cycle and a significant increase in battery capacity. Using novel silicon materials it creates anodes with up to three times the energy capacity of carbon.

Plaxica

Plaxica is developing a transformational biopolymer technology which enables the production of low-cost lactic acid. Global demand for lactic acid is on the rise as the chemical is high-value and flexible and can be used as an intermediate for many applications. Plaxica's Versalac technology presents as a high performance, low cost chemical route to lactic acid production and is proven across a wide range of bio-feedstocks.

Nexeon

Nexeon is a battery materials company, which was spun out of Imperial College, London in 2006. The company is developing silicon anodes for the next generation of lithium-ion (Li-ion) rechargeable batteries. Silicon can absorb more lithium than carbon but in doing so it expands. Large particles of silicon therefore tend to fracture under the resultant stress. Nexeon is developing a novel and patented nano-structured silicon material with built-in porosity which expands less and is less prone to fracture resulting in improved cycle life.

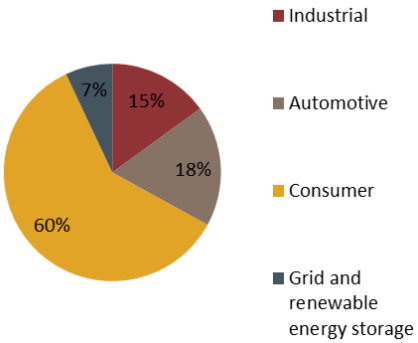
Nexeon's technology has the potential to revolutionise the battery industry, providing a number of advantages to a wide range of energy-hungry consumer goods (eg smart phones) plus the fast-growing areas of automotive batteries and renewable energy storage. The company has a solid IP base with almost 100 patents granted, and another 200 patent applications pending, to date.

Nexeon thus far has raised £55m in investment capital, of which £40m (series C) was raised to build a manufacturing facility. Of the total raised, £22.4m was invested by Imperial Innovations. The net carrying value of the investment sits at £34.1m.

Li-ion battery market

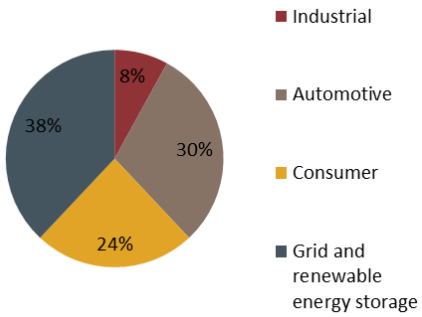
The lithium-ion battery market represents the highest growth component of the global battery market and, at the battery unit cell level, is expected to reach around US$15bn in 2015 and US$25bn in 2020 (Avicenne). Historically the majority of this market has been consumer batteries (ie laptops, phones etc) but other sub-sectors of this market are growing rapidly and automotive and energy storage systems are expected to account for 68% of the lithium ion battery market by 2020. Charts 3 and 4 illustrate the progression to a less consumables-focussed market, as forecast by Frost & Sullivan.

Chart 3: Global lithium ion battery market 2013



Source: Frost & Sullivan, Cenkos Securities

Chart 4: Global lithium ion battery market 2020

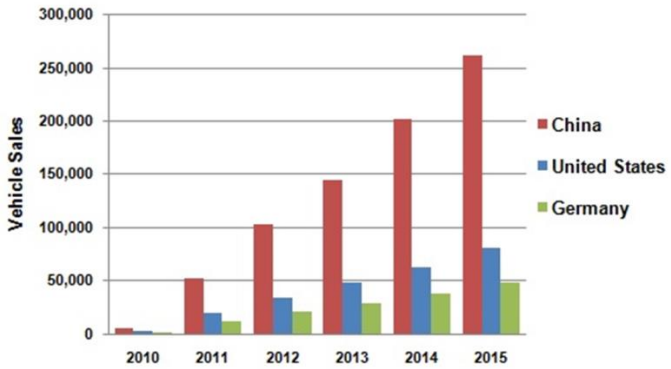


Source: Frost & Sullivan, Cenkos Securities

A key driver behind this is the general move towards electric vehicles (EVs), particularly in China where there have been strong government incentives for this type of vehicle. This follows on from the pollution problem in Chinese cities, particularly in Shanghai and Beijing where pollution has been linked to the large increase in respiratory disorders. Global sales of electric vehicles have been steadily rising in recent years (Chart 5) and it is expected that this trend will continue in coming years. The chart highlights the significance of China in driving the global increase in the sale of EVs, with sales here expected to surpass the 250,00 vehicles per annum mark this year.

The global surge in demand for electric vehicles presents a significant opportunity for Nexeon. As more electric vehicles are required, there is an increase in demand for lithium ion batteries and in turn the anode material which is Nexeon's product.

Chart 5: Battery electric vehicle sales



Source: Pike Research, Nexeon

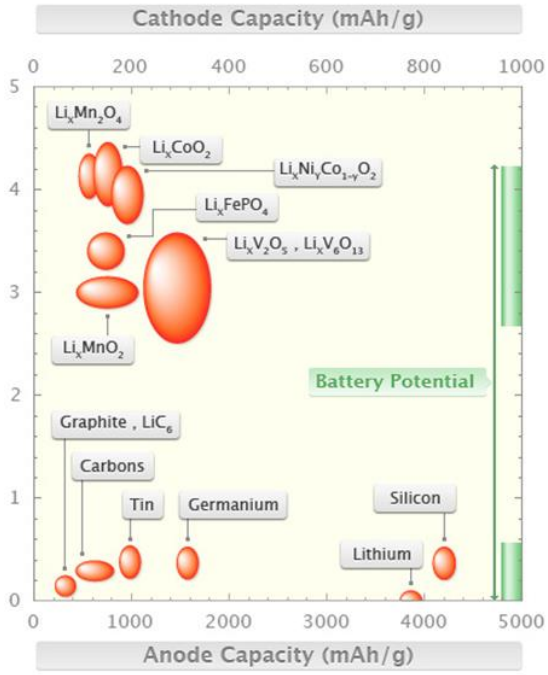
Another key driver behind the move away from consumer batteries is the trend towards grid and renewable energy storage, the sub-sector which is expected to increase the most to 2020, reaching an estimated level of $1.5bn (Avicenne Research). This trend is testament of the worldwide drive to source renewable forms of energy.

Nexeon's technology is evolving

Nexeon's technology originates from work carried out by Emeritus Professor Mino Green at the Department of Electrical and Electronic Engineering at Imperial College London. The company has a growing portfolio of patent families that relate to various structures, methods of production and associated components for the use of high capacity silicon material as an active agent in the negative electrode of a rechargeable lithium-ion battery.

It has become apparent that battery OEMs are initially seeking modest increases in cell energy by developing silicon-carbon hybrid electrodes which contain small amounts (less than 10%) of silicon. Nexeon's first generation material was not optimised to work in such a hybrid electrode and therefore the company is undertaking further work to provide materials that meet these alternative electrode designs.

Figure 1: Nexeon's silicon anode materials have high capacity for lithium



Source: Nexeon

Manufacturing capacity has strengthened

In April last year Nexeon completed the construction and commissioning of a brand new development and manufacturing facility at its Oxford site, which is able to handle a wide range of materials and reagents. The plant has a sizeable capacity and is able to produce **20 tonnes of product per year** with plans to increase this capacity going forward. The manufacturing facility was funded by a £40m series C funding round, which was led by Imperial Innovations and Invesco Perpetual.

Nexeon's state-of-the-art R&D facility is enabling them to optimise its materials and the production facility is now operational for customer sampling and for volume production according to customer demand.

Plaxica

Plaxica is a green chemicals technology business that is working on process technologies on a licensing basis, without seeking to own or operate its own manufacturing plants. The company's primary focus is on developing a transformational biopolymer technology which enables the production of low-cost lactic acid from a wide range of bio-based feedstocks.

Lactic acid is a platform chemical which can be used for the production of a variety of bio-chemical products including polylactic acid (PLA) and propylene glycol. These are high value chemicals with strong environmental credentials. PLA, offers the potential to displace traditional oil-based polymers such as PET (polyethylene terephthalate – also known as polyester) and nylon for example in packaging, consumer durables and textile manufacture. Propylene glycol is widely used in personal care and consumer products such as lipsticks and resins.

Plaxica has developed strong relationships with both upstream feedstock owners such as the pulp and paper industry and with leading players in the downstream lactic acid and derivatives market. The company's technology has been proven at demonstration scale at Plaxica's pilot plant facility based at Wilton in the north-east of England. Plaxica has appointed industrial partners to assist with industrial scale up – broadening this range of partners is a current focus.

Ultimately, we believe that the ability to manufacture lactic acid at low cost will allow Plaxica to compete with traditional petrochemical feedstocks. The company is well funded to 2016 having raised total funds of £19.3m and also benefits from non-dilutive grants (Innovate UK) raising a further £800k, with R&D tax credits expected of £0.5m per year.

Technologies

The technologies that Plaxica is developing are aimed at producing lactic acid, which represents a global market of 500,000 tonnes and growing. Lactic acid is a versatile platform chemical but its current high price restricts its use to food preservatives, speciality polymers and niche green solvents.

Traditionally lactic acid has been produced through the fermentation of food grade sugars, an expensive process that requires costly high-grade raw materials. This not only creates a strain on the food chain, but is also a slow and high cost production process. By contrast, Plaxica's technology is based on a chemical process which is tolerant of chemical impurities, and means that a wide range of feedstock can be used in production, including the waste from the forestry and agriculture industries. This results in production of a high-purity lactic acid with a very low variable cost base, which opens up the potential to use lactic acid in markets where it previously proved to be too costly.

Creating a sustainable source from non-food sources and at low cost creates a disruptive supply of lactic acid that is readily substitutable into existing proven markets. Importantly, Plaxica's low cost lactic acid allows penetration into markets which cannot be served competitively by current lactic acid.

End user markets

Plaxica's low cost lactic acid is a valuable and versatile platform chemical that can be used to produce the world's most successful biopolymer polylactic acid (PLA). It can also be converted into propylene glycol and acrylic acid using proven third party technologies.

Importantly, the raw material for the generation of a number of plastic materials does not come from food but from waste streams, which reduces the input raw material costs by a factor of 10 compared with fermentation. The use of non-food materials also addresses an important ethical concern.

Technology Platforms

Plaxica is developing two technologies:

- **Versalac** - the production of low cost racemic lactic acid from low cost sugars using a chemical process.
- **Optipure** - the separation of this racemic lactic acid into polymer grade L and D lactic acid isomers – opening up the possibility of PLA with improved material properties at low cost.

Both of the technologies can be manufactured in standard unit operations. The Optipure process has been validated at the company's facilities in Wilton, UK using an industrially relevant demonstration plant.

Figure 2 below shows a section of the plant in Wilton. Similar scale up work is underway for Versalac.

Versalac

Versalac is a process technology able to produce low cost lactic acid from a wide source of biologically sourced (natural) feed stocks including bio-based feedstocks (such as waste from the pulp and paper industry) and cellulosic based sugars.

Versalac is based on an innovative continuous chemical process, which leads to a closed loop system with low-cost and fast reaction times. All of the reagents are recovered. This leads to a step-change reduction in production costs. Chemical impurities in the feedstock also have a limited impact on the process, which is important when comparing this technology to others including fermentation.

To date Plaxica has taken a dozen real world samples from paper and pulp mills globally and successfully converted this highly impure low-cost material, into lactic acid. It has operated on a small scale so far, in 20 litre glassware (scaled up from round bottom flasks). Scale up to one tonne scale using third party equipment is underway in Q2/Q3 2015 – a successful start has been made.

Yield and process performance has been maintained through the scale up. Plaxica is working to develop partnerships between feedstock owners (eg in paper and pulp) and potential purchasers of lactic acid (eg PLA producers) and propylene glycol (eg biochemical companies). The company wants to bridge with key players in the paper and pulp industry (feedstock) and is now working with several industrial partners. It is also talking to players outside of the European Union, with a particular focus on China. Plaxica is also in advanced negotiations with a potential global licensing partner for its technology to help with scale up and chemical engineering.

Optipure

The lactic acid output from the Versalac process is referred to as racemic lactic acid. It contains a mixture of both the L-type isomer of lactic acid and the D-type isomer, which is its chemical 'mirror image'. By contrast, the lactic acid produced by fermentation only contains L-type isomers.

Optipure is a chemical process that separates racemic mixtures of lactic acid into its constituent components. This occurs through a robust and scalable chemical process at a low cost. This process is versatile and can also be configured to produce D lactic acid from L lactic acid.

This is significant because polymers based on L-type isomers tend to have inferior mechanical and thermal properties compared to traditional oil-based polymers such as PET (polyethylene terephthalate) and nylon. However, by controlling the mix of L- and D-type isomers used in the polymerisation process, it is possible to synthesise high performance PLA with enhanced properties that allow this biopolymer to compete more strongly with polyester and nylon, offering the potential for use in high value markets such as creating environmentally friendly textiles for the automotive industry.

Demonstration plant

Plaxica built its first plant for Optipure two years ago. It is now designed, commissioned and operated with a full digital control system, albeit a smaller version of the industrial scale that will be needed in the future.

Figure 2: Optipure manufacturing facility

Source: Plaxica

Scale up and demonstration of Versalac is underway, with space being rented from custom manufacturers in the local area.

Patents

Plaxica has a strong IP focus which is embedded in the culture.

- 1st technology (Optipure) patents starting to move to grant in EU, China and US. Freedom to operate studies are also completed successfully.
- 2nd technology (Vesalac) IP at early stage – confident that they will move to grant.
- No litigation or IP challenge.

Into the future

In 2016, Plaxica management are aiming to moving the business to revenue by executing licensing deals on its technologies, with initial focus on the Optipure technology. This should also include a licensing deal for Versalac once the manufacturing process has been successfully scaled up and at which point it will be ready to license.

We expect cash flow and revenues to flow next year as a result. The prospect of a trade sale should also not be discounted, with an exit to larger process technology licensing player which could be a broad spectrum chemical company.

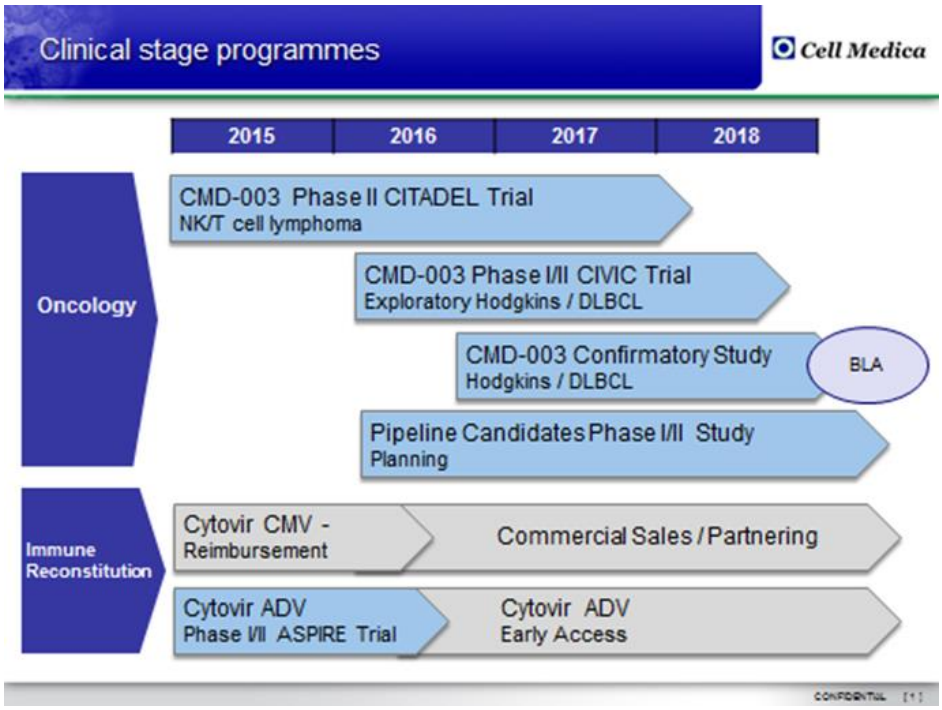
Cell Medica

One of the most promising companies in the portfolio is the cellular immunotherapy company, Cell Medica. The company is focussed on a number of approaches for the treatment of viral and cancer indications. The company maintains low manufacturing costs and is able to manufacture five doses of CMD-003 within one batch manufacturing run at a cost of US$20-25k. This could allow for competitive pricing in the T cell field and a low cost of goods, assuming pricing for the treatment in the US$100-150k range for multiple doses.

Pipeline

Figure 3 demonstrating the progress that has been made across the Cell Medica pipeline since we first wrote on the company in our initiation report in 2012 for Imperial Innovations.

Figure 3: Cell Medica pipeline



Source: Cell Medica

Alongside the excellent pipeline progression, the company recently completed a significant equity financing with a number of blue-chip institutional investors raising £50m equity to fund both the clinical development (including Phase II trials for CMD-003) and manufacturing expansion (to invest in closed system manufacturing, an important industry goal).

Phase II CITADEL trial

The first patient has now been treated in the Phase II clinical trial (CITADEL) evaluating CMD-003 in aggressive extranodal NK/T cell lymphoma (ENKTCL) patients who have failed asparaginase-based salvage treatments. Asparaginase-based treatments do generate a good response rate in the region of 50-70%; however, in clinical practice these response rates are not durable.

Primary aim

The primary aim of the CITADEL study is to evaluate whether CMD-003 is both safe and efficacious as a potential therapy in patients who have failed more conventional treatments in advanced extranodal NK/T Cell based lymphomas, and is being evaluated across 24 centres in five countries (US, Europe and Korea).

Given the sprint that a number of T cell companies are making to try to reach the market, and the expansion of their programmes into solid cancers moving away from just haematological cancers, it is important for Cell Medica to pursue a clinical route that can not only allow it to generate Phase II data rapidly but also potentially move along an expedited route to market to seek early conditional approval.

Primary endpoint

The primary endpoint of the CITADEL study (total of 35 patients), which is based on a cautious trial design, is to see an overall response rate of 30% across both stages of the trial and with 2 responses in the first 16 patients as a gating point for the first stage. We believe that the company should be targeting a higher overall response rate at a level of 50%, but a 30% success point would be clinically meaningful in this setting. If all progresses well, Cell Medica is targeting a BLA (filing for US approval) in 2018.

Significant market opportunity in EBV positive cancers

As we have highlighted previously there are a number of EBV-associated cancers including lymphoma and nasopharyngeal cancer where the market opportunity is likely to be at least US$1bn. In the immune reconstitution transplantation market (cytomegalovirus and adenovirus), the market opportunity in Europe is US$150m.

HPV

According to the World Health Organisation (WHO) the total number of cancers associated with pathogenic infections totals 18% globally. It is well known that in women, human papilloma virus (HPV) can lead over time to lesions being developed which can progress to cervical cancer. As a result, girls aged in their teens have been vaccinated with Cervarix (GSK) and Gardasil (Merck& Co) in order reduce this risk of developing cervical cancer later in life by harnessing the immune system to attack various HPV viral subtypes and create a memory effect against the infection. To date both the vaccination programme and levels of long-term immune memory in this population have been very promising.

EBV

Other viruses such as EBV, hepatitis B and C (liver cancer risk) and HIV (Kaposi's Sarcoma risk) have also been flagged as risk factors for cancer. In the case of EBV, 90% of all people worldwide are infected with EBV on a latent basis (ie be carrying the virus which is ‘hiding’ in the patient without presenting symptoms).

If we then extrapolate to the cancers associated with EBV infection, it is estimated that 15-20% of lymphomas (with potentially 100% in certain subtypes), 95% of nasopharyngeal carcinoma and 10% of gastric cancers are EBV-associated. This presents a major commercial opportunity for Cell Medica in this ‘niche’ setting. We believe that ultimately, Cell Medica has a desire to exploit all of these indications and certainly the former two in the short-to-medium term. This is why the CITADEL trial presents such an interesting opportunity as relapsed NK/T cell lymphoma is 100% associated with EBV infections, where there is no approved or clinically meaningful treatment in patients who have progressed to advanced disease and where the prognosis in terms of survival is very poor (less than 12 months in the relapsed setting).

Baylor provided strong proof-of-concept data for CMD-003

In previous studies in the US, Baylor College of Medicine (the original source for the technology behind CMD-003) evaluated the product in 300 patients who had EBV lymphomas and nasopharyngeal carcinoma. Since that time, a number of products and process enhancements have been made by Cell Medica to simplify the manufacturing process, reducing time to manufacture and costs. There has been a re-engineering of the product to allow its manufacturing in a closed system and hence reduce overall manufacturing costs both in terms of the product and infrastructure needed to make it. This is in our view a critical feature of our investment thesis for Cell Medica, which is very often overlooked. Competitor technologies from Novartis (CTL019), Juno Therapeutics and Kite Pharma are weighed down by very expensive and complex manufacturing processes, combining personalised T cells with a gene therapy.

In the clinical study conducted by Baylor called ALCI (LMP-specific T-cells for Patients with Relapsed EBV-positive Lymphoma) across a total of 21 evaluable patients there was a 50% complete response rate (2 partial responses and 8 progressive diseases). The duration of the clinical response has been highly impressive with a median in the range of 4 years (ranging from 9 months to 9+ years) with no significant side effects (unlike competing CART technologies!). This compares very favourably with median survival in this patient group which is typically less than 2 years for the more aggressive forms of lymphoma.

A parallel study in patients who were in remission found that of a total of 29 evaluable patients, a very high proportion (28) remained in remission with a median duration of remission of 3 years (ranging from 2 months to 8+ years). Whilst eight of the 29 patients have now died due to other issues such as infections, heart attacks and secondary cancers, the data once again is very impressive when compared to historical experience in this group.

The market continues to be buoyant for T cell stocks. The IPO of Cellectis raising $229m at a valuation of $1.5bn is strong evidence of the vivacious appetite for this space.

MISSION Therapeutics

MISSION Therapeutics was founded in 2011 to exploit the work of KuDos and AstraZeneca scientists who had been working on a number of enzymes called deubiquitylating enzymes or DUBs. These are based on cysteine proteases, which comprise of 100 enzymes and have been validated using an approach that involves siRNA (short interfering RNA molecules that help to elucidate function).

DUBs have historically been very difficult to validate and much like the kinome, which comprises 515 kinases of which the majority to date but not all have been mapped, represents an enormous challenge for the industry. The DUBs field could therefore be viewed as the next 'kinase'. To most investors kinases will be familiar territory.

MISSION is developing first-in-class inhibitors of DUBS which are a set of enzymes involved in DNA damage response (DDR), DNA repair and cell cycle and cell proliferation. To date, the company has successfully characterised and validated a large number of these enzymes and elucidated mechanism behind their involvement in synthetic lethality in cancer cells.

The DUB platform

The DUB platform has had extensive target validation completed, lead optimisation studies undertaken, and selectivity profiling to build a proprietary database. In the cancer setting, multiple pathways are being investigated and the company will target cancers of high unmet medical need where patients can be stratified according to their DUBs status and biomarker status. This will de-risk the clinical development by ensuring that patients who are potential responders are selected for the trial. The current pipeline is weighted towards a number of types of cancer including cancers where there are mutations, resistance and where there is a unmet medical need. An understanding of the biology behind this family of enzymes offers the opportunity of stratifying the patient population according their DUB status.

MN2 shows promise

So far MISSION has shown promising anti-cancer activity across a number of different cancers types based on DUB targeting. A compound called MN2, for example, which is targeting a ubiquitin carboxy-terminal hydrolase that is overexpressed on many cancers but minimally expressed on normal tissue has already shown proof-of-concept in preclinical studies in numerous cancer cell lines. Preclinical studies have shown efficacy in disease models of multiple myeloma and lung cancer. Importantly, excellent selectivity has been shown when compared to other DUB enzymes and a good safety and pharmacokinetic profile.

First programme into clinic in early 2017

Following a review of the preclinical data, there is an expectation of the first programme being eligible for IND and identifying the track at the end of 2015. This should allow the first drug to enter clinical trials in early 2017.

KuDOS case study

The KuDOS team identified PARP (poly-ADP-ribose polymerase) inhibitors and focussed heavily on the selectivity of these enzymes before going into the clinic in order to be confident of seeing activity. This area has been a real success.

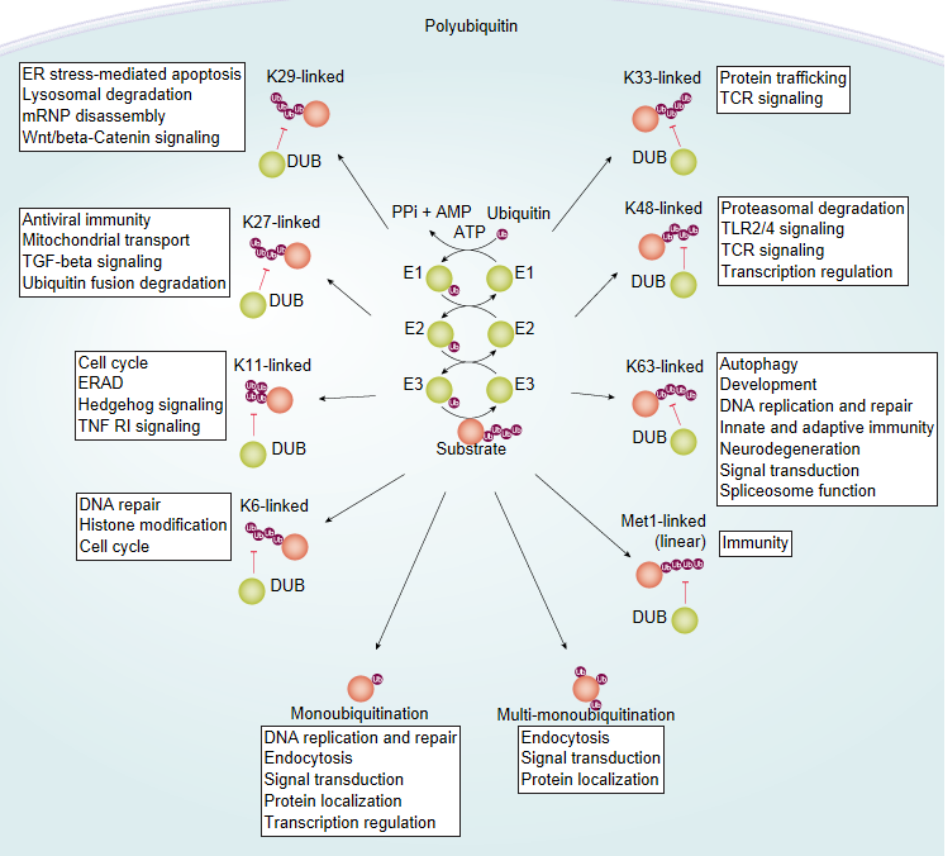
Patient stratification

The USP30 DUB found in mitochondria is a very interesting target, which we note may be involved in Parkinson's disease.

The DUB-Sphere™

MISSION therapeutics has identified a novel set of targets utilising its DUB Drug Discovery Platform: the Ubi-Sphere™.

Figure 4: DUBS



Source: R&D Systems Inc.

As can be seen from Figure 4, the range of interactions of the enzymes within the Ubiquitin cascade is significant and spans not only disease outcomes related to cancer but a host of other conditions including inflammation.

Avastin

Much like the analogies with VEGFR and Avastin, which has been one of the great success stories in the oncology space, even if the ultimate outcome in some cancers like breast and brain cancer has been disappointing, the value creation and ultimate revenue extraction from the cancer market for Roche (through the innovation at Genentech) has been spectacular.

Like Roche and the angiogenesis story behind Avastin, MISSION has strong patents (intellectual property or IP) on some of the targets (DUBs enzymes) and other patents further strengthen the chemistry.

Management team

Part of the team behind MISSION is the same team that was behind KuDOS Pharmaceuticals and certain members of the team previously worked within the pharmaceutical space at companies like AstraZeneca.

Professor Steve Jackson is the founder of the company and is an experienced scientist who has worked at the Sanger Institute. He was instrumental in performing the early work which allowed the company to gain key experience in the space.

The CEO, Dr. Anker Lundemose is a highly accomplished biotechnology CEO having worked in a number of larger pharmaceutical companies such as Novo Nordisk. Here he undertook major transactions and also oversaw the start-up and growth of a company which later saw the patents behind DPP-IV inhibitors sold to OSI Pharmaceuticals. At this business that he and his team built up they generated hundreds of millions of US$.

Autifony

Autifony Therapeutics is a UK biotechnology company that is focussed on hearing loss and tinnitus disorders, a set of conditions which could be seen as one of the holy grails in the pharmaceutical industry where no drug has ever been successful in clinical development or successfully been approved. The company's origins are from a quality base when it was one of the high profile CEDDs (Centres of Excellence for Drug Discovery) spun out of GSK (including its laboratories in Verona Italy). The company was backed by two leading GSK scientists Dr. Charles Large and Dr. Giuseppe Alvaro, previously Directors in GSK's Neuroscience CEDD and whose work revolved around the pathways that are the target of the company's focus.

Autifony is today based in the Imperial College Incubator in London with a subsidiary specialising in medicinal chemistry and biology laboratories still based in Verona, Italy. Autifony has a strong network of experts in the auditory space including experts at University College London's Ear Institute, Yale University, and Massachusetts Eye and Ear Infirmary, meaning that the science is world class.

In 2011, Autifony executed a successful series An equity fund raise of £16m, backed by SV Life Sciences (and International Biotechnology Trust), Pfizer Venture Investments, UCL Business and Imperial Innovations. Imperial Innovations committed £5m in this round. These high quality investors executed significant due diligence on the assets, bringing a strong endorsement to the biological and chemical (medicinal) approach being taken by the company.

Autifony is focussed on two areas of major unmet medical need.

There are two areas of focus:

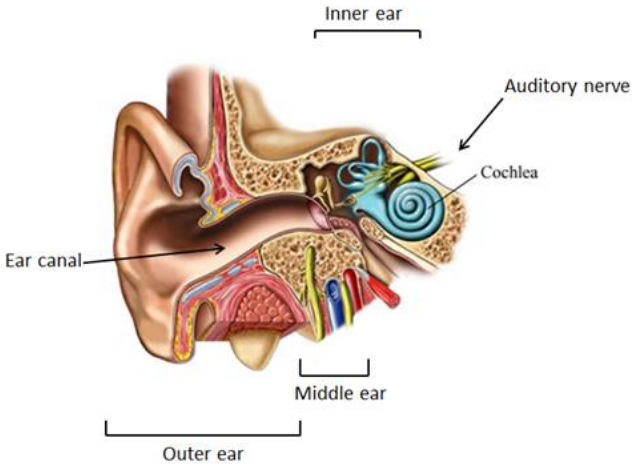
- Hearing disorders;
  - Age-related hearing disorders, and
  - Tinnitus,
- Schizophrenia.

The ear and hearing

Figure 5 below illustrates the internal and external anatomy of the human ear. Hearing occurs following sound waves being funnelled towards the ear drum from an external source. The ear canal then transmits the sound waves to the cochlea, which contains hair cells that convert sound waves into neural signals. The neural signals are then amplified, filtered and processed so that the sounds can be interpreted by the auditory circuits in the brain. Figure 6 illustrates how this process works.

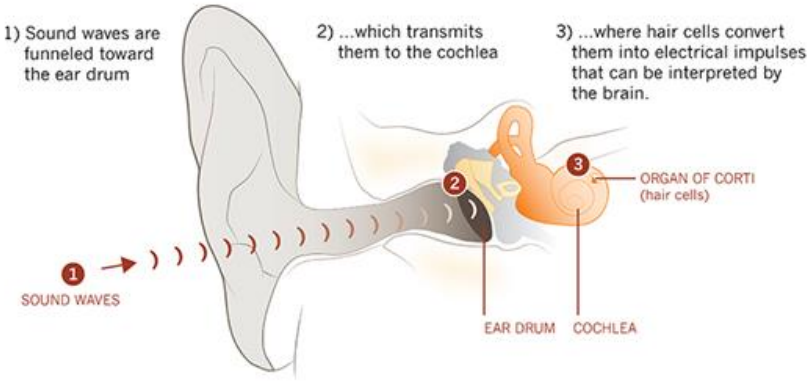
A total of 48m US citizens have some form of meaningful hearing loss in at least one ear, and 30 million have hearing loss in both ears, with 50% of over 75 year olds suffering significant hearing loss. Worldwide hearing loss affects 360m people with a third aged over 65 years (World Health Organisation). The reasons for hearing loss are numerous and likely multi-factorial and include acute causes such as damage caused by cancer chemotherapy or certain diseases (eg Meniere's disease).

Figure 5: Anatomy of the ear



Source: www.graphicwriters.medicalillustration.com

Figure 6: How hearing works



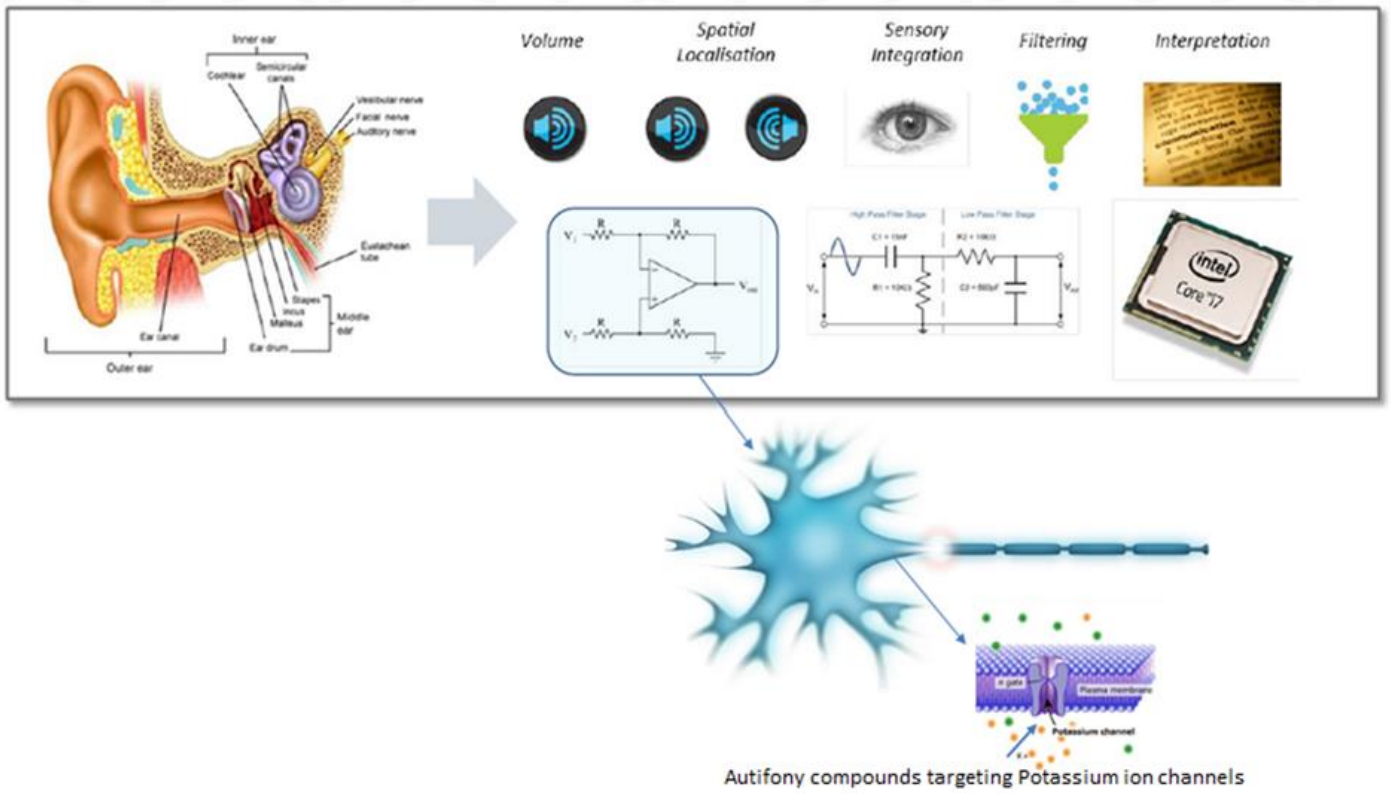
Source: Novartis

Autifony's target pathway: Kv3

Autifony has built a platform targeting Kv3 voltage gated potassium ion channels. These are a subfamily of potassium (K+) channels found all across the body. Kv3 potassium channels are activated by voltage changes that occur during a neuronal action potential and cause a rapid repolarisation of the neuron, thus allowing these neurons to fire accurately at high frequencies, making them ideal for transmitting fast auditory information, such as speech sounds. Kv3 channels are expressed at high levels in the auditory brainstem and at higher levels of the auditory pathway.

Figure 7 below highlights the Kv3 pathway, which is targeted by Autifony, and shows the Kv3 channels which are found in many points in the auditory system. One of the key features of the Kv3 potassium ion channel system is that in relation to neurons it can be used as a system that can fire rapidly and precisely.

Figure 7: Autifony's target pathway



Source: Autifony

The approach being pursued by Autifony is to 'fine tune or tune-up' the ion channels in the brain. It is not possible to replace dead cells or neurons that have degenerated, but it is possible to make the most of those that remain and to then look at options such as seeing if there are synergies with the use of hearing aids, which only help in amplifying all noise, rather than specifically helping to interpret speech against a background of noise – something with which many middle aged and elderly people struggle.

Disease targets

Autifony's approach to target Kv3 ion channels is predominantly focussed on hearing loss but there may also be some scope to treat psychiatric disorders such as schizophrenia.

Tinnitus

The market size for tinnitus is substantial with 10-15% of the population suffering from the condition at some point in their lifetime. Tinnitus is characterised by the perception of sound in the absence of any corresponding external sound, which results from the sufferer's own auditory pathways. Studies suggest that tinnitus arises from the central nervous system and therefore for treatments to be effective they should focus on the brain rather than the cochlea.

Age-related hearing loss

Age related hearing loss, or presbyacusis, is the most common form of adult auditory deficiency in the US. Hearing loss arises from both the loss of hair cell function and also the result of changes in auditory neurons. In preclinical models, hair loss in the ear has been found to begin in the base of the cochlea and then progressively migrating towards the apex of the ear.

Schizophrenia

The disease pathology seen in certain types of schizophrenia can be specifically related to the Kv3 mechanism where rapid firing of neurons occurs, leading to an issue with the synchronisation of neural networks and their break down. Autifony is looking to explore clinically the potential for its Kv3 targeted compounds on a range of different symptoms of schizophrenia, including positive, cognitive and negative symptoms, and certain other diseases of the central nervous system (CNS). Autifony is examining the therapeutic potential for its molecules in this space.

Clinical studies

Autifony's lead compound is currently in clinical trials for age-related hearing loss and tinnitus.

Phase I study

Autifony is taking a mechanistic approach to developing hearing solutions as therapeutics. As part of this approach it recently completed a Phase I clinical trial for its small molecule therapeutic AUT00063, in 60 healthy volunteers using a range of doses. The drug was found to be safe and well tolerated by both young and elderly (>65) volunteers, paving the way for Phase IIa proof of concept studies.

Phase IIa study

The company has opened a Phase IIa age-related hearing loss study in the US, and a Phase IIa clinical trial in tinnitus. This second trial is now recruiting and is partly funded by innovate UK.

In the UK tinnitus trial, a total of 150 patients are expected to be recruited into the study, called QUIET-1, evaluating an 800mg dose of AUT00063 over a 4 week period. The study will randomise 150 patients with stable noise and/or age-induced Tinnitus (with a TFI score of ≥24 and ≤68) and whose tinnitus has existed for not less than six months and not more than 18 months.

The aim of the QUIET-1 study is to show a clinically relevant improvement in the severity of the tinnitus following repeat dosing in the target patient group.

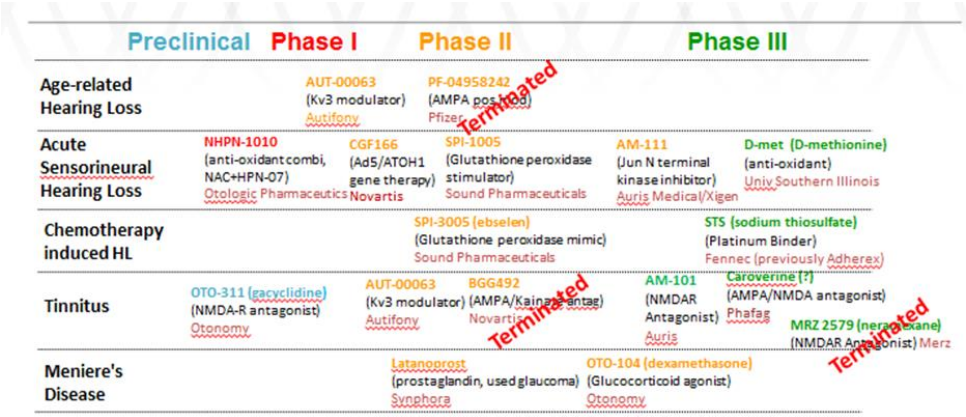
The US Age-related hearing loss study, called CLARITY-1, is seeking to enrol 100 subjects (both male and female) in an age group of 60 years or older who are experiencing hearing issues in relation to deciphering speech in an environment where there is noise. The dose of AUT00063 being evaluated is 600mg (once-a-day) over a 4 week period.

The primary objective of the CLARITY-1 study is to demonstrate a clinically relevant improvement in the signal-to-noise ratio in a speech-in-noise test after repeat dosing in patients with presbycusis.

Competitive landscape

The competitive landscape in the hearing loss space is highly limited and there have been a few failures in the hearing loss and tinnitus space. Figure 8 below summarises the products that are in various stages of preclinical or clinical development and demonstrates the variety of approaches being taken.

Figure 8: Competitive landscape in hearing loss



Source: Autifony

The takeaway from the competitive environment show in Figure 8 is that there are a limited number of competitors with limited competitive products and approaches in development in age-related hearing loss. Acute noise-induced hearing loss has more products in development, with intra-tympanic administration (an invasive procedure) the most frequent approach currently.

Other approaches in the regenerative medicine stage are still at an early stage, despite pragmatically being seen potentially as a logical route to take. The only more advanced product is a gene therapy that is being developed by Novartis which is in Phase I clinical trials (CGF166). The target for the gene therapy approach is the Atoh1 switch: which is involved in turning on hair cell growth. In preclinical studies, Atoh1 the switch is turned off at birth (in other species such as birds and amphibians, it remains on into adulthood). By switching this gene on, it is feasible that the cells supporting hair cells are instructed to divide and create new hair cells. The Novartis therapy will require fluid to be injected into the inner ear, a highly novel and potentially risky approach.

PsiOxus

PsiOxus develops novel therapeutics for serious diseases with a particular focus on cancer. The company's therapeutic areas are predominantly based on its oncolytic vaccine, enadenotucirev.

Enadenotucirev

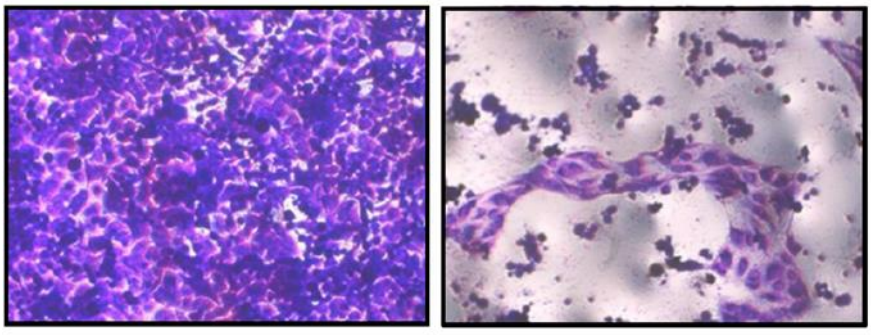
Enadenotucirev (EnAd) is being evaluated in a number of different cancers which include colorectal, ovarian, bladder, lung and renal cell carcinoma. The drug was developed from a library of chimeric adenoviruses which were allowed to replicate on human tumours in culture repeatedly until the most virulent or potent viruses able to kill tumour cells with a high degree of efficiency were further developed (a form of natural selection). These were then selected for a virus with a loss of activity in a variety of normal cell types to ensure that they would not be able to replicate in normal cell types. Once these viruses were further screened in the presence of human blood, EnAd was selected for the greatest level of potency and highest level of cancer cell selectivity in terms of its killing power.

Following an initial phase I study in colorectal cancer, the potential of EnAd is now being investigated in a range of different tumour indications in three different phase Ib studies.

Oncolytic technology

The activity of EnAd can be eloquently seen in Figure 9 below, which highlights the power of the virus and its replication in tumour cells in destroying them whilst leaving normal cells intact.

Figure 9: EnAd activity in tumour cells

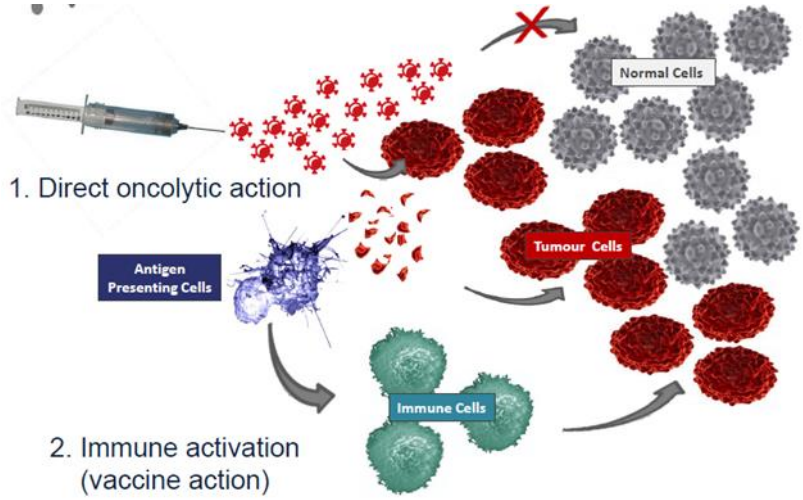


Endothelial cells co-cultured with tumour cells are spared despite extensive death of tumour cells infected with EnAd

Source: PsiOxus

As we explained in our initiation reoport for Imperial Innovations (2012) and as can be seen in Figure 9, direct injection into the patient results in death of the tumour cells, the tumour cell death (together with the inflammation produced by the virus) allows immune cells (antigen presenting cells) to process the biomarkers from the tumour and aid in mounting a further immune response against other tumour cells. Normal cells are left intact, where the virus is not able to replicate. One of the key features of the EnAd product is the fact that it is stable in human blood, a key differentiator when compared to other oncolytic viruses and this permits systemic administration. Figure 10 below highlights the eloquent mode of action for EnAd.

Figure 10: EnAd's oncolytic action



Source: PsiOxus

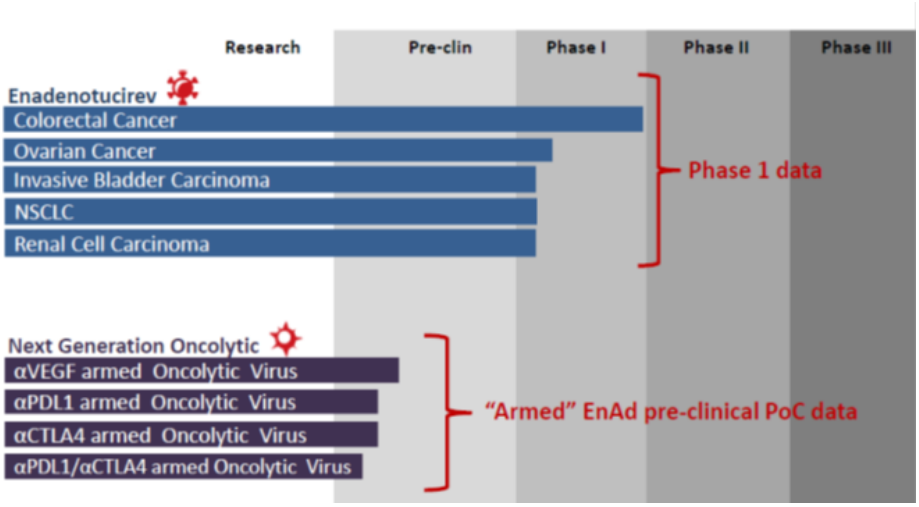
Next generation oncolytic viruses like EnAd offer a number of competitive advantages in the field of oncolytic cancer vaccines including:

- Being potentially highly selective against the tumour cells (the virus only replicates in cancer cells).
- The second feature of oncolytic viruses is their ability to induce tumour cell lysis. These viruses have a selective ability to offer lytic potential to replicate in tumour cells, with the progeny viral particles being able to infect neighbouring cells which results in a domino effect within the broader tumour itself.
- The induction of local or systemic tumour responses to attack the cancer following the virus replicating.

Clinical studies

The PsiOxus pipeline demonstrates the breadth of cancers that are being targeted with Enadenotucirev. The next generation oncolytic virus is a potentially very exciting product, that is in the early stages of development (preclinical), but which could be an important new product opportunity for the company. Figure 11 below highlights the pipeline progression made by the company.

Figure 11: PsiOxus therapeutic targets



Source: PsiOxus

PsiOxus recently completed a 10 patient Phase I study in primary resectable colon cancer in 10 cancer patients: 5 with EnAd injected directly into the tumour (although there is an issue surrounding getting uniform tumour distribution) and 5 patients where the EnAd virus was administered intravenously (3 doses). Following both treatment regimens, the tumour and lymph nodes were excised (biopsy) to understand where the virus was and whether it was getting broadly into the tumour. The virus was located by biomarker staining for a protein called Hexon which is found on the outside of virus capsid (90% makeup). Immune cells were also identified from the inflammatory infiltrates. The results were very interesting, and revealed a high level of replication in tumour cells, with tumour cells from intravenous injected patients showing a greater level of tumour infiltration and destruction. Of the five patients treated intravenously, 80% (n=4) had high numbers of immune cells infiltrating 'tumour islands'. At 21 days post injection, a patient with a skin tumour metastasis also had high levels of co-localisation of virus and immune cells (CD8+).

Given the breadth and depth of this technology, we are looking forward to Phase Ib data in colorectal, bladder, renal and non-small cell lung cancers. There is an ongoing Phase I/II in ovarian cancer patients in combination with paclitaxel.

Next generation technology: 'Arme' EnAd looks very exciting

The EnAd technology could be seen as a platform immune therapy technology that could deliver a wide variety of biologicals with the ability to operate as a gene cassette system to even incorporate three products that can be expressed by the virus in tumour cells at the same time. The 'Armed' EnAd has already been developed into multiple proof-of-concept species. By inserting a gene into the virus called NG135, the virus has already been forced in the tumour to produce Avastin at a level whereby both physically and chemically; it is identical to Avastin produced by Roche and without any compromise on the virus selectivity or potency.

PsiOxus has now gone on to make anti-PDL1 and anti-CTLA4 expressing viruses as well as viruses which have the capability of producing cytokines, enzymes, and even RNAi therapeutics. This could be a very exciting platform and we wait with interest to see further developments emanating from this next generation platform. We also believe that partnership deals could also be signed with large cap Pharmaceutical companies in this space over time.

Interesting checkpoint angle

TILs or tumour infiltrating T cells are not normally seen in colorectal cancer, and hence it is a cancer type that is not amenable to treatment with checkpoint inhibitors. It is believed that EnAd could in fact be sensitising the tumour to checkpoint inhibitors by generating TILs. This could allow combination with checkpoints (eg PD1) to be carried out, potentially opening up a very large market opportunity to the checkpoint inhibitors.

PsiOxus is looking at the possibility of the induction of tumour immunity by using EnAd as a treatment, thereby facilitating the combination with checkpoint inhibitors that may not work effectively with the cancers in question (eg colorectal cancer). In vitro work conducted with dendritic cells (DCs) from donor blood has already demonstrated that a combination with an anti-PDL1 antibody provides a synergistic effect (based on IL-2 production).

Following intravenous administration of EnAd, tumour infiltrating DC8+ cells in PDL1 negative tumours were shown to demonstrate increased PDL1 expression following EnAd dosing.

T Vec

In 2011, Amgen acquired a company called BioVex for US$500m in cash with a US$500m cash (milestone-based) earn-out. The product being developed by BioVex was an oncolytic herpes virus encoding granulocyte-macrophage colony stimulating factor (GM-CSF; a potent immune simulator), talimogene laherparepvec (T-Vec). This virus (unlike EnAd) is directly injected into the tumour.

At the time of the acquisition, T-Vec was in development for both melanoma and head and neck cancers. Subsequently, the melanoma indication was pursued as the head and neck cancer trial was stopped unexpectedly. Amgen continued with the melanoma indication in 439 patients randomised with unresectable stage IIIb, IIIc or IV melanoma (a highly immunogenic cancer). When the Phase III trial concluded it generated a promising durable response rate of 16%. The Phase III trial also met its primary endpoint but narrowly missed the secondary endpoint of overall survival prompting Amgen to file for approval by submitting a BLA, as the correlation between the two was strong. The PDUFA action date for the drug review by the FDA is on 27 October, with an advisory committee meeting on 29 April. The trial is being evaluated as a monotherapy in a field that is rapidly moving to checkpoints. That said T-Vec has shown some interesting data in combination trials with Yervoy (BMS) where in a combination study with Yervoy (Phase IIa) in a small number of patients, the trial showed an overall response rate of 55% with a complete response rate of 33%. If T-Vec is approved it would be an important milestone for the oncolytic virus field. The efficacy being seen further demonstrates the potential for EnAd to be combined positively with checkpoint inhibitors to generate high synergies and further open up cancer indications that might not be tractable alone by checkpoint inhibitors.

MT-102

In late 2013, the cachexia Phase II programme (MT-102) successfully met its primary endpoint of demonstrating a statistically significant difference (at the highest dose point 10mg twice a day) between treated and placebo patients in a cancer related cachexia clinical trial, showing that patients treated with MT102 had greater weight gain when compared to placebo over a 16 week period. MT-102 demonstrated a broad range of beneficial features including the ability to significantly halt weight loss, weakness and fatigue in late-stage cancer patients. A total of 87 patients with stage III or stage IV lung cancer or colorectal cancers were included in the study.

Given that MT-102 was not the core programme or technology in the company, PsiOxus is seeking to either out license the drug to a pharmaceutical partner or directly undertake the two Phase III clinical trials that would be required for approval. PsiOxus has already had scientific advice and regulatory meetings with FDA (US), EMA (EU) and NICE (UK).

Veryan Medical

Veryan Medical has made significant progress since our last update on Imperial Innovations when we had not yet seen the two year long-term data from the MIMICS study. The data from this study, which was a head-to-head comparison of Veryan's BioMimics 3D Nitinol stent with a helical curvature, was presented at the VIVA symposium in Las Vegas. Last year the two year data was much more positive than we had expected, in a number of ways, which we highlight in this report.

In January of this year Veryan completed a £18m series B fund raise, which was led by Innovations and well supported by Invesco. The investment is to fund the commercialisation of the BioMimics 3D stent in international markets.

MIMICS study

The study randomised patients into a trial comparing Veryan's BioMimics 3D stent against CR Bard's LIFESTENT® vascular stent, which is one of the leading vascular stents in the market in terms of its frequency of use and the gold standard in the market. On both measures: restenosis reduction and re-intervention reduction, the BioMimics 3D stent demonstrated a statistically significant effect over 2 years.

Significant improvement in patency

Over a two year period the BioMimics 3D stent demonstrated a significant improvement in patency ie how unblocked or open the blood vessel is and of course a direct measure of how much restenosis has occurred in the stented vessel. Veryan was able to show a correlation between swirling flow in stented vessel and patency. This, in our view, demonstrates conclusive evidence that this technological approach works.

Improvement in revascularisation

The other important fact which emerged from the two year data was the significant improvement in clinically driven revascularisation of the stented legs, which saw a threefold difference between Veryan BioMimics 3D stent and the Bard control. This is very important because of the three fold higher intervention required with the Bard stent. This makes for a strong economic argument (where the cost of the stent procedure is typically £3,000 to £7,000), which makes the Veryan BioMimics 3D stent the most cost effective therapy for vascularising the leg. Intervention in a failing stent also carries with it a significant morbidity risk, given the co-morbidity profile, for the patient as you cannot take an old stent out in a re-stenosed vessel, which means more costly and risky surgery and intervention.

We believe that this data is powerful enough to change clinical practice, especially with the short-comings of the existing technologies.

FDA focus

Besides the importance in terms of clinical benefit the regulatory bodies such as the FDA are increasingly focussed on patency as a measure of the performance of stents. This is important given the significant issues seen in the cardiovascular market, where several years ago a new generation of drug coated stents emerged. These demonstrated significant reductions in the risk of restenosis, only to show when the drug was eluted that levels of restenosis or blockage were increasing again.

Next stop: FDA trial

The next major clinical study for Veryan is the start of the FDA clinical IDE application study, where the IDE has already been filed. The study is expected to start recruiting in Germany in next few months (by summer) with US recruitment anticipated for later this year. So far the protocol has been agreed with the FDA and will likely comprise a registry study in c.280 patients measured against historical controls which is believed to be robust and statistically relevant. The object will be to compare stents with balloon angioplasty, where there is a two-thirds need for re-intervention after a year.

The design of the study will mean that it is conducted with an objective performance goal, with a study that is powered to show a minimum lower confidence interval of 66% patency at 12 months. The study will be conducted with a 12 month follow up and a recruitment time of between 12 and 18 months to fully recruit. On this basis, a PMA could be filed in late 2017, with an approval in 2018.

Strategy for company

The focus for the company is now to execute successfully in starting and completing the clinical study in US. From this perspective we view the risks as being low, given the strength of the data already seen in the European study. In parallel Veryan is beginning its commercialisation strategy for the product in Europe and as part of this it has signed a distribution deal with Biosensors.

Market opportunity

We believe that that there is an opportunity for Veryan to expand the market opportunity into other vascular applications, with the periphery being a low hanging fruit opportunity. The company strategy will be to continue to move up and down the leg into other parallel and related areas, which could double the market opportunity available to the company. In this respect the peripheral stent market globally is US$1.6bn. The company's current indication represents 65% of this and other applications are a valuable way to increase the target market.

Clinical evaluations

The product is now commercially rolling out, with a launch in February 2015. There are in parallel, quite a few clinical evaluations being undertaken with opinion leaders. The proposition here is to offer different valuation milestones in the development of interventional companies with a purist goal of outcome based medicines/devices under Obamacare. Veryan is playing into this thesis.

M&A in the stent market

In 2013, Abbott completed the acquisition of a private company called IDEV Technologies, which Abbot bought for US$310m. The company had developed a self-expanding nitinol stent system called SUPERA Veritas® which was already CE marked in Europe for the treatment of stensosis (blockages) in lower blood vessels as a result of a condition called peripheral artery disease. We believe that despite the dearth of new technologies in this space, Veryan could represent a future M&A opportunity in the stent space.

Financial Summary

Summary P&L

Table 4: Imperial Innovations summary P&L

Year end 31 July	2013A	2014A	H1 2015A	2015E	2016E
Revenue	3,290	3,636	2,840	3,220	3,284
Cost of sales	(788)	(1,005)	(986)	(1,002)	(818)
Gross profit	2,502	2,631	1,854	2,218	2,465
Gross profit margin (%)	76%	72%	65%	69%	75%
Change in fair value of investments	10,794	40,549	(7,363)	16,500	18,150
Administrative expenses	(10,608)	(15,870)	(2,007)	(11,270)	(11,495)
Operating (loss) / profit	2,688	27,310	(7,516)	7,448	9,120
Finance income	1,072	106	481	108	110
Profit before taxation	3,760	27,416	(7,035)	7,556	9,230
Taxation	-	-	-	-	-
Profit and total comprehensive income for the financial year	3,760	27,416	(7,035)	7,556	9,230
Basic earnings per Ordinary Share (pence)	4.6	26.8	(5.2)	5.5	6.8
Diluted earnings per Ordinary share (pence)	3.8	26.7	(5.2)	5.5	6.8

Source: IVO (Actuals), Cenkos (Estimates)

Summary cash flow

Table 5: Imperial Innovations summary cash flow

Year end 31 July	2013A	2014A	H1 2015A	2015E	2016E
Cash flows from operating activities					
Operating (loss) / profit	2,688	27,310	(7,516)	7,448	9,120
Reconciling adjustments	(13,051)	(35,594)	4,368	(16,400)	(18,040)
Working capital adjustments	2,898	1,761	(2,020)	(200)	(200)
Net cash used in operating activities	(7,465)	(6,523)	(5,168)	(9,152)	(9,120)
Cash flows from investing activities	3,956	(91,945)	17,631	(23,039)	(34,658)
Cash flows from financing activities	50,223	146,333	(1,173)	-	-
Net increase in cash and cash equivalents	46,714	47,865	11,290	(32,191)	(43,778)
Cash and cash equivalents at beginning of the year	11,883	58,597	106,462	117,752	85,561
STLI		70,000	35,000	35,000	35,000
Cash and cash equivalents at end of the year*	**58,597**	**176,462**	**152,752**	**120,561**	**76,783**

Source: IVO (Actuals), Cenkos (Estimates) * Includes short-term liquidity investments

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