

## London calling to the faraway biotech: Now a bubble is declared and IPOs hail down

Usually this time of year, the who's who of the Life Sciences' world have their eyes firmly on the US with the annual meeting of the American Society of Clinical Oncology (ASCO). Chicago becomes a battleground for over 30,000 doctors and scientists jostling with companies vying and hoping to get their clinical data in front of the right people.

In an extraordinary turn of events it would appear London has taken centre stage for the time being in the global biotech domain. Investors in the space do not bat an eyelid at European biotech companies looking for pastures new across the pond in search of their optimal valuation. However, the first for a long time to break ranks and go against the flow came in the form of a Californian biotech company, Verseon. The company chose London's AIM to IPO instead of New York's booming biotech market where they raised an impressive £65m to advance their proprietary computational drug discovery platform to design novel potential therapeutics for various diseases.

Initially, the UK market viewed this as an anomaly, only to see Boston-based healthcare technology company, PureTech, target London's main market for a potential \$160m IPO. PureTech boasts a strong team with the notable addition of ex Sanofi CEO Chris Viehbacher. Their business model will be focussed towards commercialising early-stage life science technology businesses – a model well known here in the UK with the presence of groups such as IP Group and Imperial Innovations.

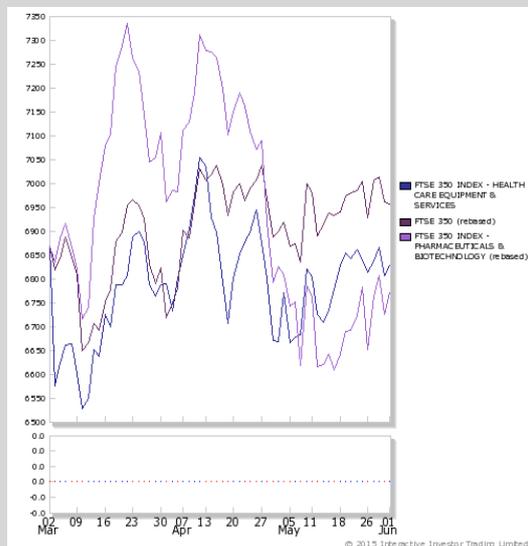
The rise in interest from foreign healthcare companies in London markets inevitably triggers the notorious scepticism that is currently rife with UK investors when it comes to overseas companies. "They are only trying to IPO here because they can't attract funds in their home country" is an all too familiar comment from UK investors. In the US Life Sciences context, such an argument is simplistic and does a disservice to the individual value proposition of the company in question. When we look at the biotech bubble in the US – it has largely been dominated by sector giants such as Gilead Sciences, Amgen, Biogen and Celgene to name but a few and have all experienced share price rises across the past year of up to 75% and their valuations are all well north of \$1bn. The bubble in the US has clearly been for the chosen view and created quite a graveyard for the many companies sub \$1bn in market value. Quite contrary to the myth that the US biotech bubble favours everyone.

The UK is experiencing quite a different reception to companies in the sector. As opposed to the US – the UK's strong sentiment towards biotech companies is all encompassing. From AIM's Motif Bio's successful IPO earlier this year raising £12.8m right up to the main market's Circassia raising £275m to finance its next two acquisitions and wildly tipped to be "the next Shire". However, unlike previous bubbles it hasn't all been started by sell side over-exuberance. The recent buy-side hysteria perhaps most notably led by Woodford Investment Management in April raising £800m for their investment trust focused towards long term early stage investing in the sector. In addition, Imperial Innovations recently led a £6m series A funding round for Auspherix, an early stage anti-infectives company from Australia that further supports the argument that the recent UK Institutional support for the sector is drawing international attention from all corners of the globe.

It is clear we can no longer compare the UK and US on a "like for like" basis in the small cap biotech sector due to the non-existence of one in the US. The danger now is creating a valuation void of similar stage companies within the UK itself. It remains one of the only sectors where investors pray their companies don't ever make any money as their valuation will be adjusted accordingly. Whilst the recent interest in the sector is very much welcoming, whether the surge in patient capital works in a historically impatient sector remains to be seen.

**Reviewed by Niall Pearson**

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FTSE ALL Share	CY 2014	CY 2015
PE	22.8	16.8
P/Book	1.9	2.0
EV/Sales	1.3	1.5
EV/EBITDA	8.5	9.3

FTSE 350 Pharma and Biotechnology	CY 2014	CY 2015
PE	26.6	18.0
P/Book	6.7	6.6
EV/Sales	3.9	4.1
EV/EBITDA	11.8	13.0

FTSE 350 Health Care Equipment and Services	CY 2014	CY 2015
PE	29.9	20.6
P/Book	3.7	3.4
EV/Sales	2.8	2.7
EV/EBITDA	13.0	12.6

**Source: Bloomberg**

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## **Economic Review**

The British economy has 'cranked up several gears', according to the Confederation of British Industry (CBI), after a hiatus in the first quarter. Experts have passed off the slowdown in the first quarter of 2015 as a minor bump in the road for growth within the economy. The Office for National Statistics (ONS) in April 2015 revealed the UK economy had turned in the slowest quarterly growth for two years at 0.3 percent, driven by a widening trade deficit according to economists, which strengthened fears that the economy could well be heading for a slowdown. However, research conducted by the CBI put forward that business activity stepped up markedly in the three months to May, particularly led by strong growth in the professional services sector. Moreover, The Organisation for Economic Co-operation and Development (OECD) said that in spite of weakness in UK GDP in Q1 2015, growth has carried on at a "healthy pace", boosted by reasonable rises in consumption, employment and in real wages.

Of the 811 companies surveyed by the CBI, 33 percent reported growth in output volumes in the three months to May rather than a decline, up from 19 percent in the three months to April. Moreover, optimism about future growth stayed buoyant, where 30 percent of companies are anticipating "above normal" or "more than adequate" growth over the next quarter, the strongest growth expectation expressed since August 2014. Business confidence has risen to an eight-month high post-election lifting fears of uncertainty. The Lloyds Bank Business Confidence Barometer suggested that 62 percent of firms were optimistic; it was the highest reading since September for the barometer, which tracks more than 300 firms' views of their own prospects and the wider economy.

Following the Conservative election victory, a period of stability is expected and consumers have benefit from a double boon of falling oil prices and increasing wages. With inflation set to stay relatively low, or non-existent, a poll by YouGov and the Centre for Economics and Business Research found that financial optimism in May 2015 reached the highest level recorded since May 2014 and the second highest since April 2007. The survey found that one in eight people's household budgets improved in the last month, indicating the highest

percentage since the question was first asked in February 2009. This was evident as retail sales showed a better-than-expected reading, increasing by 4.7 percent in April 2015 compared with April 2014 and by 1.2 percent from March 2015. This, according to the ONS, "was the 25th consecutive month of year-on-year growth, the longest period of sustained growth since May 2008.

Q1 2015 GDP grew by 0.3 percent and though this is only modest growth, it is an expansion nonetheless. Moreover, taking into account historical figures, the 0.3 percent growth in Q1 2015 is actually the ninth consecutive quarter for growth. However, challenges will still be faced by companies who are majority exporters to many overseas markets as a result of a strong pound and weak demand in many areas, especially Europe.

***Reviewed by Darshan Patel***

## **Sector specific trends**

In some respects however businesses engaged in lifesciences are less dependent on short and medium term swings in the economic cycle, and more and more exposed to inexorable socio-demographic changes and growing lifestyle burdens on human health. We touch on a few themes below.

### **Reimbursement**

Developers of new drugs and therapies, and their investors, need to remember that strong clinical results and gaining regulatory approval, is only one step along the way in converting candidates into commercial successes. The European payer landscape for example is highly fragmented and whilst there is a single EU regulator payment decisions can be made at many levels including regional. With healthcare budgets coming under increasing pressure pharma companies need to demonstrate value as well as efficacy, and what may be approved for prescription by NICE in the UK may fail to make the grade at IQWiG in Germany. The Bexsero meningitis C vaccine was licensed by the European Commission in January 2013 and yet will only be available on the NHS later this year.

Over in the US the situation is similarly complicated and evolving quickly. The perception has been for some time that pricing power in the US is very much in the hands of the drug companies. However back in 2014 oncologists took matters into their own hands at Memorial Sloan Kettering Cancer Center excluding Sanofi's Zaltrap for colorectal cancer due to its significantly higher price point against its peers which resulted in a 50% discount. The rise of generics means that Big Pharma cannot always sustain its price advantage.

Express Scripts, the largest pharmacy benefit management organisation in the United States, shelved 48 medicines from its national preferred formulary in January 2014. GlaxoSmithKline found this a particularly bitter pill with the loss of Advair. At the time the Chief Medical Officer noted that brand prices were up about 80 percent over the last five years, while prices for generic medicines had fallen about 50 percent, meaning that while generics may account for 80 percent of prescription drug use in the US, brands account for 70 percent of cost.

## **Rare Diseases**

Conversely pricing of drugs that treat rare diseases has held up very well, with little competition from generics which tend to target larger patient populations. Some drugs such as Viropharma's Cinryze (C1 esterase inhibitor) which treats hereditary angioedema (HAE) are being reimbursed for over \$417,000 a year. There are other advantages for companies pursuing the development of 'Orphan' drugs. Under the Orphan Drug Act the benefits provided to medications that have obtained Orphan Drug Designation include, seven-year marketing exclusivity after FDA approval of a designated drug, tax credits equal to 50% of clinical investigation expenses, waiver of PDUFA (Prescription Drug User Fee Act) filing fee which is over \$2m for an application requiring clinical data, assistance in development, and grant funding.

Companies targeting rare diseases have generated high investor returns with Shire being a case in point and the recent acquisition of Synageva by Alexion for US\$8.4bn, a 140% premium to Synageva's market capitalisation prior to the announcement. We believe Prometic Lifesciences and BELLUS Health are companies to watch with rapidly evolving development programmes targeting a number of rare diseases. However as more orphan drugs are licensed we will see an increasing percentage of health budgets being diverted to these treatments, and at some point resistance to high pricing may well emerge.

## **The ageing population**

The world is rapidly approaching a demographic tipping point with the number of people aged 65 and over set to overtake those under the age of 5 over the next 5 years. The major healthcare issues that affect our lives are moving away from infectious disease to non communicable diseases that more commonly affect adults and older people impose the greatest burden on global health. The rise of chronic non communicable diseases such as heart disease, cancer, and diabetes reflects changes in lifestyle and diet, as well as aging. Age specific conditions such as Alzheimer's disease which is yet to be met with an effective treatment regime offers challenges and opportunities for the biotech industry. It's not only drug development but also improved diagnostic testing such as Cambridge Cognition's computerised cognitive assessment products.

Cancer remains a major focus of medical research, and personalised medicine is one approach which may help patient outcomes. Understanding how cancer changes throughout a patient's journey is important and therefore powerful ongoing diagnostics such as Angle's Parsortix system will be key to delivering personalised treatment regimes. Drug discovery is a risky business and therefore a diversified programme and collaborative approach with partners as exemplified by Sareum helps to spread that risk whilst leaving scope for considerable upside.

There is still a focus on the treatment rather than prevention of disease, which in some ways would be a better way of addressing the financial and well-being burden of chronic diseases such as diabetes, which can lead to chronic kidney disease and the associated dialysis regime, which over a lifetime can cost over a million dollars per patient. New areas of science have the potential to reduce this burden not only through medical treatment but also by promoting well-being through novel food ingredients and supplements. Optibiotix Health for example is developing compounds to tackle obesity, high cholesterol and diabetes. Its microbiome modifying science (the collective genome of organisms that reside within the human body) is fast moving towards commercialisation, and the company has this month entered into an option agreement with a multinational consumer goods company in relation to its cholesterol reducing product.

## Top 5 risers and fallers

### As at 22 May 2015

Tiziana Life Sciences
Advanced Oncotherapy
Verona Pharma
Deltex Medical
Oxford Pharma
Port Erin
Plethora
Benchmark Holdings
Taihua
Electrical Geodesics

### 3 month Share price movement

152.14%
109.68%
107.14%
96.30%
90.57%
(26.60%)
(27.66%)
(30.62%)
(37.14%)
(42.24%)

Source: Fidessa



Source Fidessa

## Top 5 Risers

### **Tiziana Life Sciences (LON:TILS 147.5p/£136.2m 3mth +152.14%)**

In March the biotechnology company focused on targeted drugs to treat diseases in oncology and immunology, raised £2.55m at 75p and a further £6.1m in April through the issue of convertible loan notes at a conversion price of 70p per share. Interest shall accrue quarterly on the CLNs at a rate of four per cent. per annum. On 7 May CFO Phil Boyd stepped down although will continue to provide consulting services to the Company, together with other interim finance solutions during the search for a successor. In May Tiziana announced that it had exclusively licensed a novel anti-cancer stem cell agent, capable of targeting aggressive tumour forming cells originating from the breast, pancreas, colon and prostate, from Cardiff University scientists.

Under the terms of the agreement, Tiziana will fund £50,000 per year for a research project at the University focused on building the structure activity relationships (SARs) around OH14 and to improve the activity of this series of compounds. Additionally, Tiziana will pay to the University milestone payments up to c.£2 million and pay royalties on sales of any licensed products developed as a result of the project. If certain milestones are achieved Tiziana will also pay one per cent of its enterprise value to the University in the event of a trade sale of Tiziana to a third party.

### **Advanced Oncotherapy (LON:AVO 9.625p/£128.9m 3mth +109.68%)**

In March the developer of next-generation proton therapy systems for cancer treatment, secured a £2m loan with a related party. Later in the month it announced its first full commercial purchase order for one LIGHT proton therapy system to be installed in a hospital in China for approximately US\$40m also signing a 15 year distribution agreement in China and a select number of other countries in SE Asia. In May the company announced a £20m placing at 8p to continue the development of its LIGHT system, with the first unit expected to be installed in Harley Street, London, by the end of 2016 and first patient treatments expected in 2017.

### **Verona Pharma (LON:VRP 4.45p/£44.9 3mth +107.14%)**

In May the drug development company focused on first-in-class medicines to treat respiratory diseases reported results for the year ended 31 December 2014.

During the period, Verona Pharma completed a £14 million fundraising, the development of a novel nebulised formulation of RPL554 suitable for commercial deployment and initiated a phase 1/2

clinical trial using this new formulation. Interim data from healthy volunteers, published post period, demonstrated that this RPL554 formulation has excellent tolerability at the highest dose studied, which was a 16 times higher dose than the previously used bronchodilator dose and also suggests the drug could be dosed twice daily. The Company has also made valuable progress in broadening the potential indications for RPL554 to include cystic fibrosis.

**Deltex Medical (LON:DEMG 6.625p/£14.2m 3mth +96.30%)**

In March the global leader in oesophageal Doppler monitoring (ODM), announced its audited results for the year ended 31 December 2014. In a difficult year with the UK market affected by NHS cash constraints and the NHS failing to follow through its decision to implement ODM at pace, revenue decreased £0.7m to £6.5m and Deltex reported an operating loss of £2.99m (2013: operating loss of £2.1m) after US market development costs of £0.4m (2013: £0.6m). However Deltex made satisfactory progress in the USA and is on track to establish a platform for national roll-out towards the middle of 2016. The market leading businesses in France and Sweden continue to grow well and prior investment is creating opportunities to build additional strong businesses in Spain and Canada. Later in the month the company announced a new study validating the Pulse Pressure Waveform Analysis algorithm in its CardioQ-ODM+ monitoring system. The company has also appointed Chris Jones as a Non-Executive Director, a US citizen with over 25 years' experience in the medical technology industry in senior management positions for both large multi-national and smaller early stage companies.

**Oxford Pharmascience (LON:OXF 12p/£120.7m 3mth +90.57%)**

On 15 May the specialty pharmaceutical company that redevelops medicines to make them better, safer and easier to take, announced completion of the development of an immediate release, taste masked, chewable 400mg ibuprofen product that is now ready for clinical evaluation. OXPzero™ Ibuprofen (OXF001) delivers 400mg of reduced gastric irritation ibuprofen via the Company's patent protected OXPzero™ technology. The Company hopes to provide the market with a much differentiated product, offering both a GI safer alternative to current NSAIDs and varied finished product forms to improve compliance rates.

On 18 May OXF announced the initiation of dosing in its pilot clinical study of 250mg OXPzero™ Naproxen (OXF005). OXF005 uses Oxford Pharmascience's patented OXPzero™ technology in an immediate release oral formulation and aims to provide a significantly reduced gastrointestinal (GI) side effect profile compared to standard Naproxen tablets.

**Top 5 Fallers****Port Erin (LON: 8.625p/£2.0m 3mth -26.6%)**

On 30 March the company focussed on investing in the biotechnology and biopharmaceutical sectors, announced interim results for the six month period ending 31 December 2014. These are in the context of a post period tender offer at 14.18p per share. The period end NAV per share was 14.3p. The Company recorded a net loss of £143,388 for the half-year interim period. The company's significant investments are the Magna Biopharma Income Fund, Plethora Solutions (PEBI) and Summit Corporation (SUMM).

**Plethora Solutions (LON:PEBI 4.125p/£34.0m 3mth -27.6%)**

The speciality pharmaceutical company dedicated to the development and marketing of products for the treatment and management of urological disorders announced FY2014 results on 30<sup>th</sup> March. PLE reported revenues of £3.9m (2013: £nil), a loss before tax and pre-exceptional costs of £0.3m and a loss from continuing operations for the year (post exceptional costs) of £15.7m (2013: loss of £8.8m). In the release it was reported that tests on the first two GMP batches of the six dose canister of PSD502™ for the treatment of premature ejaculation identified variances outside the permitted specifications in the composition of the combined compound, which are the subject of an ongoing investigation.

The outlook stated that 'The next financial year is expected to be an exciting period to prepare for the initial commercial launch of PSD502™ in the EU and other territories. A decision was taken to instruct PSNW and Catalent to proceed in the manufacture of a 20 dose can in compliance with the existing EMA approval for preserving the sunset date of 14 November 2016. In the meantime, the Company will continue to work with its manufacturing partners to perfect the manufacturing process to develop a six dose canister, which will release a further €6 million milestone receipt from the Company's commercial partner Recordati on receipt of EMA approval.'

**Benchmark Holdings (LON:BMK 70p/£153.53m 3mth -30.6%)**

In April the international aquaculture breeding, animal health, technical publishing and sustainability science business updated for the half year ended 31 March 2015. Overall, the Company continues to make good progress with its strategy and it is successfully integrating the businesses it has acquired to form a new Breeding and Genetics division. It has however become clear that the competitive pressure in the market for its Salmosan product, a core part of the Animal Health division, has intensified. As a result, the company guided that it expects revenue and profits to be significantly below market expectations for the full year.

**Taihua (LON:TAIH 2.75p/£2.248m 3mth -37.1%)**

The producer of Active Pharmaceutical Ingredients and Traditional Chinese Medicines announced on 5 May that to date, the weather

conditions have not been optimal for the 2015 Forsythia harvest as there has been a substantial frost.

As previously announced, there are two key stages in the production of Forsythia, that of the flowering period, when it is important it is damp and there is no frost and the harvest period, when it is equally important there is no frost. To date there has been frost during the flowering season. At this stage, it is too early to tell what the actual impact on the Forsythia harvest will be but it is anticipated that as a consequence of the frost, the volume of the Forsythia harvest will be smaller than previous years.

### **Electrical Geodesics (LON:EGI 80p/£18.5m 3mth -42.2%)**

The neurodiagnostic medical technology company released FY December 2014 results on 24 March following a £2m placing at 65p earlier in the month. Revenues were up 14% to US\$13.2m but pre-tax losses widened by 13% to US\$3.4m. Over the coming months, EGI plans to release a series of new and improved diagnostic and imaging products for the research and clinical markets which it expects to drive further growth. With receipt of the IDE (Investigational Device Exemption) from the FDA, the company is preparing to commence a feasibility study for its GTEN product in mid-year, and remains excited by the opportunity which offers EGI access to the large and rapidly growing neuromodulation market, initially as a driver of research sales and later as an important clinical tool.

In April the company expanded its product line by agreeing to act as a distributor for EB Neuro in the US. Sold under the EGI name, the products will expand the Company's US product line to include long term monitoring and ambulatory EEG, and electromyography/evoked potential products, providing a broader portfolio of related neurology monitoring products for the clinical market.

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