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The Edison healthcare team

Robin Davison

Robin is the head of the biotech, med-tech and life science team at Edison Investment Research. He has over 15 years' experience covering the biotech, pharmaceuticals and healthcare sectors both as an investment analyst and as a journalist on specialist industry and financial publications. He was formerly biotech analyst for Durlacher Corporation, a contributor to Financier Worldwide, a co-founder and editor of Biopoly and editor of Scrip World Pharmaceutical News.

Lala Gregorek

Lala joined Edison's healthcare team in January 2010 from Canaccord Adams, where the focus of her coverage as a life sciences analyst was on UK and European biotech stocks. Before graduating with an M.Phil in bioscience enterprise from Cambridge University, she worked in risk management as a credit analyst covering European financial institutions and hedge funds at Dresdner Kleinwort and Lehman Brothers. Lala also holds a BA (Hons) in biological sciences from Oxford University.

Dr Mick Cooper

Mick joined Edison's healthcare team in January 2010, after working for three years at Blue Oar Securities as the pharmaceuticals & biotechnology equity analyst, where he covered a wide range of healthcare companies. He holds a doctorate from Cambridge University and completed an MBA at INSEAD business school in France after working as a parliamentary researcher. Mick is also a CFA charterholder.

Christian Glennie

Christian joined Edison's healthcare team in January 2012 and has 11 years' experience covering the global biotech/pharmaceutical sector as an analyst and a journalist. He came to Edison having held senior analyst and editorial roles at EvaluatePharma and EP Vantage. Christian also has prior experience as a marketing analyst at Zeneca Agrochemicals.

Franc Gregori

Franc is a pharmacist who started his career with Boots, Eli Lilly and Pfizer before moving into the City as an analyst. He has worked with Robert Fleming, BZW and BNP Paribas, where he was involved in a number of major transactions. He joined Edison's healthcare team from Charles Stanley, where he focused his coverage on small- and mid-cap life sciences stocks. Franc gained his pharmaceutical qualifications from the Welsh School of Pharmacy and King's College London.

Dr John Savin

John is an analyst working on biotech, pharma, medical device and diagnostics companies. As founder CEO of Physiomics plc, he devised the strategy, raised funds and took the company to AIM in 2004. At Greig Middleton, John was director in charge of the pharma and biotech analyst team and worked with corporate finance on fund-raising, IPOs and corporate restructuring. He has an industry background in sales and marketing with GE Healthcare and AstraZeneca and is a co-author on a number of scientific publications.

Emma Ulker

Emma has a strong background in broking, having worked for five years as an equity sales assistant at Société Générale on the European sales desk. After this she worked for Thomson Financial where she helped to ensure the integrity of financial data across all instruments. Emma is a qualified linguist with an MA in technical and specialised translation in Spanish and French. In addition, Emma recently earned the Investment Management Certificate, CFA level 4.

Dr Wang Chong

Wang is a physician with over 21 years of experience in the healthcare industry. He is also experienced in M&A transactions and has helped negotiate multi-million-pound out-licensing deals with Unilever and Schering-Plough. His previous roles include CFO of Phytopharm, life sciences analyst at Canaccord Capital (Europe), CEO of Osmetech, leader of UK healthcare initiatives at management consultants Arthur D. Little, and commercial roles at Glaxo Wellcome and SmithKline Beecham.

Chris Kallos

Chris has 14 years' experience as an equities research analyst in both Australian and US stocks. He has covered small-, medium- and large-cap stocks across a number of sectors with a focus on healthcare/biotech, mining, recruitment and telecommunications. Chris holds a BPharm (Sydney), an MBA from the Australian Graduate School of Management (UNSW), and a Masters in Applied Finance (Macquarie). He is a CFA charterholder and graduate of the Australian Institute of Company Directors.

Dr Michael Aitkenhead

Michael is a qualified physician with over 12 years' experience in the healthcare industry, including five years in clinical medicine and seven years in biopharmaceutical equity research. He was formerly a European pharmaceuticals analyst at the Royal Bank of Scotland (RBS) in London, and prior to this was a European biotechnology analyst with Piper Jaffray. Michael received his medical degree from the University of Otago, New Zealand, and subsequently completed an MBA at Judge Business School, University of Cambridge.

Dr Jason Zhang

Jason joined Edison's healthcare team in October 2012, after working as a biotech analyst at many investment banking firms, most recently Burrill & Company, and previously BMO Capital Markets, Prudential Equity Group and Stephens.

Pooya Hemami

Pooya is a licensed optometrist with over five years of experience in life sciences equity research. Prior to joining Edison, he covered the Canadian healthcare sector as a research analyst at Desjardins Capital Markets. He holds a doctor of optometry degree from the University of Montreal, and an MBA (finance concentration) from McGill University. He received his CFA charter in 2011.

Dr Philippa Gardner

Philippa joined Edison's healthcare team in January 2013, having previously worked as a biotechnology analyst on award-winning teams both at Jefferies and at Lehman Brothers. She has eight years' experience as a sell-side analyst covering European biotechnology, life science and mid-cap pharma stocks and has worked on a number of IPOs. Philippa holds a doctorate in biochemical engineering from UCL, with her research sponsored by GE Healthcare in Sweden.

Luke Poloniecki

Luke joined Edison's healthcare team in November 2012 from ING, where he was a vice president in its Number 1 Extel-ranked equity research team, covering Benelux Biotech and Emerging Market pharmaceutical names. He has seven years' experience as a pharma and biotech analyst, working in London and Paris at Société Générale and Bryan Garnier on sell-side coverage and ECM deals. Prior to investment banking, Luke acquired two years' experience in the pharmaceutical industry working for Schering-Plough on its cardiovascular, respiratory and allergy franchises. He holds a BSc (Hons) in human physiology from Newcastle University and the University of Rennes. He is a holder of the Association of the British Pharmaceutical Industry (ABPI) sales qualification.

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Immunotherapy takes centre stage

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A few years ago, cancer immunotherapy papers that made it into ASCO would be scheduled for presentation on the last half day of conference when most attendees were already heading out of town. Not so this year, when immunotherapies were featured in the prime Sunday and Monday sessions. Moreover, this year additional sessions were dedicated to this topic at ASCO, such has been its change of fortune. This reflects the progression the field has made in the last few years as well as the importance this type of therapy is set to play in cancer management. In this report we provide an overview of the immunotherapy field.

Attractive yet elusive

Classical cancer immunotherapy remains a highly attractive, yet elusive, strategy aimed at harnessing the body's immune system to seek out and destroy tumour cells. The field has a long history, but very few vaccines have yet made it to the market. A major breakthrough in the field came in recent years with the approval of Dendreon's Provenge, but the subsequent commercial issues with this product have left investors disappointed. The field in general has been littered with failed Phase III studies, including two in recent months. Thus investor expectations for cancer vaccines generally remain muted, although this could change quickly with a positive trial result. A number of Phase III trials of cancer vaccines are set to have readouts in the coming months.

Blocking the checkpoints

By contrast, investor interest in immune checkpoint blockers, the newest category entrant in the immunotherapy field, could hardly be higher. Products such as Yervoy, nivolumab and lambrolizumab are showing great promise because of their broad activity and long duration of response. The two companies at the forefront of the space, Bristol-Myers Squibb and Merck & Co, saw their market values rise by $12bn collectively in the run up to and during ASCO. BMS's nivolumab is now by a significant margin the most valuable oncology project in the pharmaceutical industry. Investor attention is thus likely to remain very focused on the clinical progress of these immune checkpoint blockers.

Edison intends to hold a seminar to explore investment opportunities in immunotherapy in October.

Dr Jason Zhang

Analysts

Robin Davison	+44 (0)20 3077 5737
Lala Gregorek	+44 (0)20 3077 5700
Dr Mick Cooper	+44 (0)20 3077 5734
Christian Glennie	+44 (0)20 3077 5727
Franc Gregori	+44 (0)20 3077 5728
Dr John Savin	+44 (0)20 3077 5735
Emma Ulker	+44 (0)20 3077 5738
Dr Wang Chong	+44 (0)20 3077 5728
Chris Kallos	+61 (0)2 9258 1160
Dr Michael Aitkenhead	+44 (0)20 3077 5736
Dr Jason Zhang	+1 646 653 7027
Pooya Hemami	+1 646 653 7026
Dr Philippa Gardner	+44 (0)20 3681 2521
Luke Poloniecki	+44 (0)20 3681 2527

healthcare@edisongroup.com

Prices as at 19 July 2013

Types of immunotherapy

All cancer immunotherapy approaches have a common goal of inducing a cytotoxic T lymphocyte (CTL) response against cancer cells. CTL are a type of T lymphocyte (white blood cell) that can recognise and destroy, via the help of other effector cells, a target cell that contains a specific antigen, such as a virus or tumour cell marker. However, tumour cells are able to evade the surveillance of the immune system through the induction of immune tolerance. They also develop resistance to killing by activated immune effector cells. Therefore, the first step in active immunotherapy is to make tumour cells "visible" to the immune system, normally by providing large quantities of tumour antigens. The second, also the more crucial step, is to stimulate and expand tumour-specific CTLs. An immunotherapy can only be effective after both of these steps are accomplished. Immunotherapy can be divided into vaccines, dendritic cell-based, antibody-based, cytokines, adoptive cellular transfer and immune checkpoint blockers.

Cancer vaccine: long history, few success

Early cancer immunotherapy approaches, which were tried more than a century ago, focused on activating the immune system through "vaccination" and non-specific stimulation. Mimicking the success of vaccines against infectious agents, early cancer vaccines were tumour lysates or irradiated tumour cells. A modern day example of this approach is Canvaxin, which was an irradiated, whole-cell melanoma vaccine. Despite promising Phase II data, the vaccine failed in a Phase III trial to show a survival benefit.[1] Defined vaccines, in the forms of peptides, proteins or fusion proteins, were also tested in numerous trials. Although many of these vaccines have shown signs of activity in small, but mostly uncontrolled Phase I or II trials, none has yet stood up against rigorous Phase III tests and demonstrated clinical benefits.[2]

Advances in molecular biology have helped to identify numerous tumour biomarkers, including a vast array of tumour oncogenes. In the last few decades, recombinant DNA technology also made gene expression and production of protein easy and cost effective. The new wave of cancer vaccine approaches takes advantage of various gene delivery technologies, and a number of different types of cancer vaccines, such as naked DNA vaccines and virus-vector delivered vaccines, have been tested in various types of cancer, either alone or in combination with other cancer treatment modalities. In order to boost immune responses, cancer vaccines have been given together with adjuvants or specific cytokines that non-specifically stimulate immune components (an example is Prostvac, developed by Bavarian Nordic A/S, administered with GM-CSF, a growth factor).

Unfortunately, the cancer vaccine field is littered with failed Phase III trials. Among the most recent are the START trial of L-BLP25/Stimuvax (Oncothyreon and Merck KGaA, anti-MUC-1) in non-small cell lung cancer (ASCO 2013 Abs 7500) and Kael-Gemvax's GV10001 in advanced pancreatic cancer. The START study did not meet its primary endpoint, but nevertheless a sufficiently strong response was detected in a subset of patients to justify continued development of the agent. Some further insights into the utility of MUC-1 as a target for cancer immunotherapy may also come in the outcome of Transgene's TIME Phase II/III trial of TG4010 in NSCLC, which is also due imminently.

One of the main reasons for the high rate of cancer vaccine study failure seems to be the fact that products have often been tested in the advanced stages of disease. Patients with advanced cancer are typically immune suppressed due either to disease itself or the side effects of chemotherapy. A patient with a suppressed immune system is unlikely to mount an effective immune response to tumour cells even if artificial antigens are abundant in the system. Realising this challenge,

1 Faries and Morton, BioDrugs, 2005: 19-247-260.

2 Kirkwood *et al*, CA Cancer J. Clin. 2012: 62:309-395.

companies have more recently sought to test products in earlier stage patients, including in adjuvant settings, but in this case, the survival benefits are harder to demonstrate conclusively because of subsequent therapies. Another problem is that the commonly employed evaluation criteria, such as RECIST, were developed to assess the effectiveness of chemotherapy and are poor at capturing later-onset immune system-driven tumour response.

Dendritic cell-based therapy

Dendritic cell (DC)-based therapy is an extension of the cancer vaccine approach. DCs are a type of antigen-presenting cells (APC) capable of processing antigen material and presenting it on the surface to other cells of the immune system. DC-based therapy involves isolating DCs from a patient, priming them with cancer antigen(s), and expanding tumour antigen-primed DCs *ex vivo*, before injecting them back into the patient. DC-based therapy therefore circumvents the limitation of traditional vaccination approach because it effectively presents cancer antigens to the immune system. The first clinically successful DC-based therapy is Dendreon's Provenge (sipuleucel-T), which contains a patient's own peripheral blood mononuclear cells, including DCs, mixed with a recombinant human protein, PAP-GM-CSF, consisting of prostatic acid phosphatase (PAP), an antigen expressed in prostate cancer tissue, linked to granulocyte-macrophage colony stimulating factor (GM-CSF), an immune cell activator. After many setbacks, Dendreon was able to show Provenge extended survival in a Phase III trial,[3] and ultimately gained approval for prostate cancer.

However, Provenge is still a first-generation DC approach, since it utilises partially mature DCs. Second-generation DC approaches employ mature DCs that stimulate stronger immune responses in animal models. The most advanced DC therapies in clinical testing are so-called "third-generation" DCs that are either treated with a cocktail of cytokines or genetically manipulated to elicit enhanced tumour-specific CTLs. One such example is called α-type-1 polarised dendritic cell-based vaccination, which is being tested in clinical trials against recurrent high-grade glioma.[4]

Cytokine therapy

Another immunotherapy approach that has seen limited success is the stimulation of the immune system by cytokines. Cytokines are peptides or proteins that modulate (activate or inhibit) various components of the immune system. Interferons (INFs) and interleukins (IL) are two such classes that can stimulate immune system cells such as macrophage, CTL and natural killer (NK) cells. Such non-specific stimulation of the immune system components can lead to anti-tumour activity, albeit with response rates in the single- to low double-digit range. Because stimulation of the immune system with cytokines is not specific, treatment with cytokines usually comes with significant side effects, because the activated immune system also attacks normal cells. In the US, INF-α 2a/b and IL-2 are approved for the adjuvant treatment of and treatment of metastatic melanoma, RCC and some haematological cancers (Exhibit 4). Lately, new cytokine-based therapy is aimed at improving the side effect profile through delivery of cytokines locally to avoid systematic exposure, or conjugated to antibodies to target tumour cells directly. Although clinical activity is seen in clinical trials, no such drugs are yet approved.

Antibody-based therapy

Many reviews have included antibody-based therapy, regardless of the target the antibody binds to, as a type of immunotherapy. Many commercially-successful antibodies, such as Rituxan (rituximab, Roche), Erbitux (cetuximab, BMS/Merck KGaA/Lilly) and Herceptin (trastuzumab, Roche), bind to cell surface proteins that are highly expressed on tumour cells. However, functions of the tumour cell surface proteins can be drastically different from one another, with the target of Erbitux, EGFR

3 Kantoff *et al*, N. Engl J. Med. 2010: 363:411-422.

4 Akiyama *et al* BMC cancer 2012, 12:623.

(epidermal growth factor receptor) and Herceptin, HER2, well characterised as tumour-driving oncogenes, whereas the target of Rituxan, CD20, plays no role in cancer development. An antibody targeting a tumour-driving oncogene most likely primarily exerts its anti-tumour activity by disrupting the signalling pathway of which that oncogene is a part. However, for an antibody such as Rituxan, it is proposed that its anti-tumour activity comes from processes called antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

ADCC is a process in which natural killer cells, T cells and macrophages are involved in recognising and killing antibody-labelled target cells. Similarly, CDC refers to binding of the antibody that recruits complement proteins, which punch holes in the cell membrane, flooding the cell and leading to cell lysis. Therefore, most antibody-based therapies are not strictly speaking immunotherapies because they do not rely on activation of CTLs as their primary means of mechanism of action. This is particularly the case in antibody conjugate therapies in which an antibody mainly serves as a delivery tool for the anti-cancer payload, including potent chemotherapy drugs, radioisotopes and toxins.

Immune checkpoint blockade

Because of the central role T-cells play in immune system function, they are highly regulated. After the binding of a T cell receptor (TCR) to an antigen on an antigen presenting cell (APC), the first event that leads to antigen specific T cell selection, a series binding between co-stimulatory ligands and receptors is necessary for T cell activation and expansion. Immunotherapies mentioned above in one way or another are trying to enhance this side of the T cell regulation. In order to avoid autoimmunity and to protect tissues from damage when the immune system is responding to pathogenic infection, T cells have multiple checkpoints that upon binding to various inhibitory ligands, dampen T cell activation and expansion. It is only in the last few decades that cancer immunologists have realised that tumour cells precisely co-opt these immune inhibitory pathways to avoid immune surveillances and develop immune resistance. It is found that some inhibitory ligands or receptors that regulate T cell effector function, ie killing of an antigen containing tumour cell, are overexpressed in tumour cells or non-tumour cells in the tumour microenvironment. This finding helps explain why most of the immunotherapy approaches up until this point have been ineffective, because in the tumour microenvironment where abundant inhibitory signals are present, providing vaccines and T cell stimulatory signals is not sufficient to activate enough tumour-specific CTLs. Therefore unlocking the inhibitory checkpoints of the immune system could be the most effective way of finally harnessing the power of the immune system to fight cancer.

CTLA-4 blockers

The first approved immune checkpoint blockade drug, Yervoy (ipilimumab, BMS), targets the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). CTLA-4 is exclusively expressed on T cells where it primarily counter-regulates the early stages of T cell activation. Neither CTLA-4 nor its ligands, CD80 and CD86, are differentially over-expressed in tumour cells, making it an unattractive cancer drug target at a first glance. Furthermore, mice in which CTLA-4 is silenced develop lethal systemic immune hyperactivation phenotype, suggesting the likelihood of significant side effects with any drug that targets this protein. This combination of findings originally made the strategy of blocking CTLA-4 appear questionable at best.

The anti-CTLA-4 antibody, tremelimumab, was discontinued by its original developer, Pfizer, for these reasons. Early Phase I trials only demonstrated a modest response (~10%) with profound autoimmune related toxicities (~30%) and a Phase III trial in advanced melanoma, in which tremelimumab was compared to dacarbazine, did not show a survival benefit. The product was, however, licensed to MedImmune, which resumed development and was later acquired by AstraZeneca.

Around the same time, Medarex, ipilimumab's original developer, was conducting its own Phase III trial in advanced melanoma. When BMS licensed ipilimumab from, and subsequently acquired, Medarex, it decided to modify the original trial's primary endpoint from progression free survival (PFS) to overall survival after initial findings suggested that it produced a delayed response, a hallmark of immunotherapy. Ultimately BMS showed in the Phase III trial in advanced melanoma after systematic treatment that ipilimumab extended survival (~4 months) in patients treated with the drug or in combination with a melanoma vaccine (gp100) as compared those treated with the vaccine alone, and gained approval in the US in 2010. Response rate was modest (5.7% in the Yervoy+gp100 arm and 10.9% in the Yervoy arm vs 1.5% in the gp100 arm), but duration of response was long with 11.5 months in Yervoy+gp100 arm and even longer in the Yervoy arm, confirming what was discovered in early clinical trials. Yervoy's roller-coaster path to market therefore officially opened the chapter of immune checkpoint-based therapy for cancer.

PD1/PD-L1 blockers

It is drugs that target another pair of inhibitory checkpoints, PD-1, or programmed cell death protein 1, and its ligands, PD-L1 and PD-L2, that have elevated the immune checkpoint blockade approach to its current high-profile status at meetings such as ASCO. PD-1 down-regulates T cells later in the process of T cell activation than CTLA-4 does, and its action is more profound in the tumour microenvironment than in normal tissues. Unlike CTLA-4 and its ligand, PD-L1 and L2 are highly expressed in close to 50% of tumour samples tested, suggesting tumours utilise this pathway to inhibit immune response. Based on this, it was hoped that blocking PD-1 and PD-L1 may have greater efficacy and a cleaner side effect profile than a CTLA-4 blocker. Indeed, anti-PD1 and anti-PD-L1 antibodies demonstrated a higher response rate than Yervoy in melanoma and also much broader activity in cancers including RCC and NSCLC, among others, and caused significantly fewer effects compared to Yervoy (Exhibit 1).

Clinically speaking, immune checkpoint blockers are distinctly different from chemotherapy and small molecule inhibitors of kinases at two fronts. Firstly, immune checkpoint blockers, most notably anti-PD1 and anti-PD-L1 antibodies, seem to have broad activities in a variety of cancer types. These drugs demonstrated not only significant activity in melanoma, traditionally the best model for immunotherapy, but also impressive responses in NSCLC, RCC and other cancer types. Secondly, immune checkpoint blockers tend to exhibit a unique response pattern in that tumour responses could take a longer time (a characteristic mainly of ipilimumab; six to eight weeks vs two to four weeks for chemo and kinases inhibitors) to achieve but last longer once achieved (responses of more than two years have been reported for several PD1 and PD-L1 blockers). In some cases, patients first experienced what appears to be tumour progression before they achieve late, but durable, responses. There are also reported durable responses (longer than six months) long after patients stopped treatment. This response pattern has been recognised as a hallmark of immunotherapy and supports the mechanism of action of these drugs, as the immune systems needs time to be "educated" before it exerts its anti-tumour response. At the same time, once a sophisticated immune system is turned on against cancer, its capacity for memory can keep the response alive even long after the cessation of treatment.

Many more checkpoints

In addition to CTLA-4 and PD1, there are several other immune checkpoints that are considered suitable therapy targets, including B7 family inhibitory ligands, lymphocyte activation gene 3 (LAG3), 2B4, B and T lymphocyte attenuator (BTLA), just to name a few (Exhibit 2). The success of anti-inhibitory checkpoints also renews interest in drugs that potentially stimulate positive checkpoints, such as CD40, CD137 (4-1BB) and OX-40. Activating antibodies targeting these positive checkpoints have already entered clinical testing in the last few years (Exhibit 4).

Exhibit 1: Summary of clinical data of selected immune checkpoint blockers

Drug/company/ trial type	Disease setting	Disease subtypes	Number of patients	ORR (RECIST)	Duration of response	Median PFS/24 wk PFS %	Median OS	Drug related Grade 3/4 toxicity	Autoimmune toxicity (grade 3/4)
Ipilimumab/BMS/ Phase III	Previously treated melanoma		676	11%	>11.5m		10.1m	23%	15%
MPDL3280A/ Roche (Genentech)/ Phase I/Ia	All patients refractory: RCC, melanoma, NSCLC, CRC, gastric		140	21%		45%		6%	2%
		In PD-L1 +	36	36%					
		In PD-L1 -	67	13%					
	Refractory NSCLC (median prior Rx: 4)		41	22%		48%			
		Non squamous	31	19%					
		Squamous	9	37%					
		In PD-L1 +		80%					
		In PD-L1 -		14%					
	Melanoma		38	29%		43%		14%	5%
		In PD-L1 +		27%					
		In PD-L1 -		20%					
	RCC		47	13%		53%			
	CRC			1/4					
	Gastric cancer			1/1					
Nivolumab/BMS/ Phase I/Ia	All patients refractory: NSCLC, melanoma, RCC, CRC and CRPC		306	21%				17%	6%
		In PD-L1 +	17	41%					
		In PD-L1 -	21	14%					
	NSCLC		129	17%	17m	2.3m	9.6m		
	Melanoma		107	31%	24m	3.7m	16.8m		
	RCC		34	29%	12.9m	7.3m	>22m		
	CRC		19	0%					
	CRPC		17	0%					
Nivolumab+ ipilimumab/(BMS /Phase I	Advanced melanoma	Concurrent	52	40% (CR 10%)			1-yr surv.: 82%	53%	
		Sequential: Ipi→Nivo	30	20% (CR 3%)				18%	
Lambrolizumab/ Merck/Phase I	Advanced Ipi- treated or untreated melanoma	Total	117	38%				12.6%	
		Ipi naïve	78	37%					
		Ipi treated	39	38%					
	refractory NSCLC			1/5					
BMS 936559/BMS/ Phase I	All patient refractory: melanoma, NSCLC, ovarian, CRC and RCC, pancreatic, breast		207(135 evalual)	12.5%				9%	5%
	Melanoma		52	17%		42%			
	refractory NSCLC		49	10%		31%		9%	
		Non squamous	36	11%		26%			
		Squamous	13	8%		43%			
	Ovarian cancer		17	6%		22%			
	RCC		17	12%		53%			

Source: Product label, ASCO 2013, N. Engl. J. of Med. 2012, 366:2455-2465 and company reports

Exhibit 2: Immune checkpoints on T cells and drugs in development

Ligand	Receptor	Effect on T cells	Drugs (company)
PD-L1 (B7H1) or PD-L2 (B7-DC)	PD-1	Inhibition	Nivolumab (BMS): anti-PD1; lambrolizumab (Merck & Co): anti-PD1; AMP-224 (GSK/ Amplimmune): PD-L2 IG fusion protein; MPDL3280A (Roche): anti-PD-L1; MDX-1105 (BMS): anti-PD-L1
CD80 or CD86	CTLA-4	Inhibition	Yervoy:anti-CTLA-4; tremelimumab: anti-CTLA-4
CD80 or CD86	CD28	Stimulation	None
B7H3, B7H4	?	Stimulation	MGA271 (MacroGenics):Anti-B7-H3
HVEM	BTLA	Inhibition	None
MHC class I or II	TCR	Activation	None
MHC class I or II	LAG3	Inhibition	IMG321 (Immutep S.A.): LAG3-Ig fusion protein; anti-LAG3 (BMS)
MHC class I or II	KIR	Inhibition	anti-KIR (Innate/BMS)
CD137L	CD137	Stimulation	anti-CD137 (BMS)
OX40L	OX40	Stimulation	None
CD70	CD27	Stimulation	None
GAL9	TIM3	Inhibition	None

Source: Pardoll, Nature Reviews Cancer 2012, 12: 252-264 and Edison Investment Research

Adoptive cell transfer (ACT) immunotherapy

ACT refers to treatment of cancer (mostly done in melanoma) with *ex vivo* expanded tumour-infiltrating lymphocytes (TILs) that were isolated from a patient's tumour biopsies. In practice, this approach is accompanied by depletion of endogenous lymphocytes before infusion to give the infused lymphocyte greater chances of engraftment. In addition, isolated TILs can be further stimulated with tumour specific antigens or cytokines during the process of *ex vivo* expansion, to achieve higher anti-tumour potency. A response rate as high as 50-70% was achieved in one clinical trial in melanoma, with complete response rate reaching 40%, which lasted from three to seven years.[5]

Despite these impressive clinical outcomes, autologous ACT is limited to a very small subset of patients, because of the requirement of tumour samples for TIL harvesting, the long period of time of *ex vivo* expansion, and the patient's ability to tolerate lymphocyte depletion regimens (typically high-dose chemotherapy). Genetic engineering techniques were used to insert T cell receptors (TCR, the molecule on T cell that recognises a specific antigen) into peripheral T lymphocytes to bypass the need of isolating and expanding TILs from tumour samples. Furthermore, genes that encode T cell co-stimulating factors or cytokines can be also added to peripheral T lymphocytes, resulting in highly activated antigen specific T lymphocytes. Such genetically modified T lymphocytes have been tested in clinical trials in melanoma and other solid tumours with early but encouraging activities.[6]

Autologous or genetically engineered ACT approaches could become a very robust immunotherapy approach if the practical hurdles generally associated with cell-based therapy, ie high manufacturing cost, stringent standard of quality control and logical challenges of delivery, are eliminated. Probably because of these challenges, we have not yet seen biotech companies taking up the approach.

Future directions

Immune checkpoint blockers to dominate the space

Clinically speaking, immune checkpoint blockers and ACT stand above all other types of immunotherapy, and are likely the main focus of clinical research in the next five to 10 years. We also expect the majority of resources to be spent on immune checkpoint blockers because they are clearly more commercially attractive to big pharma and biotech companies than ACT at this point. This is evident from the aggressive Phase II and III programmes that the three leaders of the field, BMS, Merck and Roche/Genentech, have planned for their drugs, respectively (Exhibit 3).

Commercially, we expect immune checkpoint blockers to meet or even surpass the most successful cancer antibody drugs such as Avastin (bevacizumab, Roche), the anti-angiogenesis antibody and antibodies targeting the EGFR/HER2 family, including Herceptin (trastuzumab, Roche), Erbitux (cetuximab, Roche) and Vectibix (panitumumab, Amgen). Assuming that Phase III results are positive in at least two to three indications, immune checkpoint blockers have several advantages over the aforementioned antibodies. Firstly, it appears that immune checkpoint blockers may have broader activity. Avastin is the most broadly active antibody so far, but its main use is in colorectal cancer and its activity in breast cancer and NSCLC is questionable. In contrast, all immune blockers showed higher responses in melanoma, NSCLC and RCC than Avastin did. Secondly, the unique response pattern and long duration of response of immune checkpoint blockers means that duration of use could be significantly longer than other anti-cancer antibodies (nivolumab has a

5 Rosenberg *et al*, Nat. Rev. Cancer 2008, 8:299-308

6 Yee *et al* Proc. Natl. Acad. Sci. USA 2002, 99:16168-16173 and Hunder *et al* N. Engl. J. Med. 2008, 358:2698-2703

median duration of response of 17 months vs five to six months for Avastin in NSCLC). Finally, based on the unique mechanism of action, immune checkpoint blockers could potentially be combined with many other types of cancer treatment and replace chemotherapy as the cornerstone of future cancer therapy. However, this remains to be proven in clinical trials that are already underway.

Exhibit 3: Selected Phase II/III trials of immune checkpoint blockers

Drug	Company	Treatment	Trial details
Ipilimumab	BMS	Ipilimumab vs high dose IFN-α2b	1,000-pt Phase III in high-risk stage III or stage IV melanoma after surgery. Result: 5/2018
		Ipilimumab/DTIC vs DTIC	500-pt Phase III in untreated melanoma. **Result: 8/2013**
		Ipilimumab vs placebo	950-pt Phase III in high risk stage III melanoma patients after surgery. **Result: 4/2015**
		etoposide/platinum ± ipilimumab	1,100-pt Phase III in Extensive-Disease Small Cell Lung Cancer. **Result: 3/2017**
		paclitaxel/carboplatin ± ipilimumab	1,100-pt Phase III in first-line NSCLC (stage IV). **Result: 12/2016**
		Ipilimumab vs placebo	600-pt Phase III in chemo-naïve CRPC. **Result: 11/2015**
		Ipilimumab vs placebo	800-pt Phase III in CRPC treated with Docetaxel. **Result: 2/2017**
Nivolumab	BMS	Nivolumab vs nivo/ipilimumab vs ipilimumab	915-pt Phase III (CheckMate-067) in previously untreated advanced melanoma. **Result: 10/2016**
		Nivolumab vs physician's choice of either DTIC or paclitaxel/carboplatin	390-pt Phase III (CheckMate 037) in anti-CTLA-4 treated melanoma patients. **Result: 5/2015**
		Nivolumab vs DTIC	410-pt Phase III (CheckMate 066) in previously untreated, unresectable or metastatic melanoma. **Result: 9/2015**
		Nivolumab vs docetaxel	264-pt Phase III in 2nd-line, squamous NSCLC. **Result: 8/2014**
		Nivolumab vs docetaxel	574-pt Phase III in 2nd-line, non-squamous NSCLC. **Result: 11/2014**
		Nivolumab vs everolimus	822-pt Phase III in pre-treated advanced or metastatic clear cell RCC. **Result: 2/2016**
Lambrolizumab	Merck	Lambrolizumab vs docetaxel	920-pt Phase II/III in 2nd-line NSCLC. **Result: 9/2015**
		Lambrolizumab (2 doses) vs ipilimumab	645-pt Phase III in advanced melanoma. **Result: 7/2016**
MPDL3280A	Roche	MPDL3280A vs docetaxel	180-pt Phase II trial in NSCLC after platinum-based first-line therapy. **Result: 3/2018**
		MPDL3280A single arm	100-pt Phase II in PD-L1 positive, untreated NSCLC. **Result: 5/2015**

Source: Clinicaltrials.gov, company reports and Edison Investment Research

Many combinations

The focus of clinical research has already started to move to test combinations of immune checkpoint blockers with almost all available cancer therapies. First, it is the combination of immune checkpoints blockers themselves, between anti-PD1 and anti-PD-L1 or between anti-PD1 and anti-CTLA-4. The rationale for the first is that PD1 has more than just one ligand, and the ligand PD-L1 can bind to more than one receptor in the body. It is therefore entirely possible that blocking both could yield even stronger T-cell activation. The rationale for the latter is that CTLA-4 and PD1 regulate T-cells at different time points of the T-cell activation process, and blocking both could result in a much deeper elimination of negative regulatory signals. The first result of this combination, nivolumab and ipilimumab, did indeed show much faster and deeper responses than ipilimumab could achieve alone in melanoma (Exhibit 2).

Second, it is the combination of immune checkpoint blockers with chemotherapy, most due to practical reasons similar to all new cancer therapies. Third, it has been proposed that immune checkpoint blockers be combined with targeted therapies, such as antibodies against oncogenes or small molecules targeting kinases. This approach is particularly attractive because of the difference of response patterns we discussed above. Targeted therapies are able to generate a fast response because they target cancer driving processes. However, they are also likely to succumb to resistance because tumour cells are genetically diverse and capable of developing escape mechanisms. Immune checkpoint blockers tend to produce a delayed but durable response and are less likely to encounter resistance. It is hoped, at least theoretically, that the combination of the two could produce a high and durable response, ultimately leading to longer survival.

One notable development in terms of combinations is perhaps lirilumab (BMS/Innate Pharma), which is being developed both in combination with nivolumab and, separately, with ipilimumab, in two parallel studies. Lirilumab is an antibody to the KIR (Killer-cell immunoglobulin-like receptor) on NK cells. Blocking these receptors facilitates activation of NK cells, which can destroy tumour cells.

A revival of vaccine and DC-based therapies?

Cancer vaccines have been a disappointment because of their low response rates and the lack of survival benefit shown in Phase III trials. With the success of immune checkpoint blockers, there is a renewed hope that they may finally be shown to be useful when they are combined with immune checkpoint blockers. However, the initial enthusiasm was damped with the combination result of ipilimumab+gp100 in the Phase III trial. The combination was not superior to ipilimumab alone. It is also entirely possible that the severe toxicity of ipilimumab did somehow hinder the benefit of this combination, because theoretically the combination of a cancer vaccine and an immune blocker should give rise to heightened tumour response. It remains to be seen whether a cancer vaccine added to anti-PD1 or anti-PD-L1 antibodies will do better than these antibodies alone.

The combination of DC-based therapy and immune checkpoint blockers also make sense similar to the reasoning of vaccine/immune checkpoint blockers. The challenge, however, will be to demonstrate additional benefit over immune checkpoint blockers in a clinical setting against the possible added toxicities. The logistic challenges of DC-based therapy in the market will also be an important consideration in the context of added benefit. To that end, we think investors should watch the progress of ACT in clinics closely because of the approach's impressive clinical efficacy shown so far. If logistical hurdles are no longer an issue for DC-based therapy, it will make ACT therapy more attractive than DC-based therapy based on stronger clinical efficacy.

Trials and companies to watch

BMS, Merck and Roche are clear leaders in the field of immune checkpoint blockers, with BMS having an approved drug (Yervoy) already, one anti-PD1 (nivolumab) in six Phase III trials and another PD-L1 (MDX-1105) and several other immune checkpoint blockers in early clinical and pre-clinical development (Exhibit 4). Merck's anti-PD1 antibody, lambrolizumab, is right behind nivolumab in development, with two ongoing Phase III trials, including one head-to-head against BMS's Yervoy in advanced melanoma. Roche's anti-PD-L1 antibody, MPDL3280A, is the most advanced anti-PD-L1, with impressive clinical results (both efficacy and safety) already achieved in a Phase I/Ia trial. Although MPDL3280A is about two years behind BMS's nivolumab, the drug's single-arm Phase II trial in PD-L1 positive NSCLC could lend the drug an accelerated approval if a robust response is achieved, similar to the fate of many targeted therapies that are approved with a high response rate in a biomarker enriched sub-population (ie crizotinib for ALK+ NSCLC patients). Beside these, there are a few biotech companies also focused on immune checkpoint blockers, such as Innate Pharma (anti-KIR, in collaboration with BMS), Amplimmune (PD-L2 Ig fusion protein, in collaboration with GSK) and Macrogenics (Anti-B7-H3 mAB, in collaboration with Servier). These drugs are still early in trials and are yet to render data. However, if signs of clinical activity are seen, they should open the door to more immune checkpoint blocker combinations.

There are over 40 cancer vaccines in various stages of clinical trials. As listed in Exhibit 4, the vaccines span a wide range of source of antigens and delivery technologies. Several imminent Phase III read-outs are expected, including Allovectin (Vical) in melanoma, and the first interim analysis for Hyperacute Pancreas (New Link Genetics) in pancreatic cancer (both estimated to be Q313). Given the past history of clinical trial failures, investor expectations for success of vaccine-based approaches are at this point muted, although this could change with a positive result.

By contrast, investor expectations for checkpoint inhibitors could hardly be higher. Two of the companies at the forefront of the space, BMS and Merck, saw their market capitalisations rise by $4bn and $8bn respectively, in the three weeks between the publication of abstracts and the conclusion of the ASCO conference in early June. Bristol-Myers Squibb's nivolumab has become by a significant margin the most valuable oncology project in the pharmaceutical industry, with an NPV of $11.5bn according to EvaluatePharma. In the near term, investor attention is therefore likely to remain very focussed on the progress of immune checkpoint blockers.

Exhibit 4: Immunotherapy in development

Category	Drug name	Company	Technology description	Status	Main indication
Vaccines					
Single antigen peptide	NeuVax (Nelipepimut-S or E75)	Galena Biopharma	Synthetic Her2/neu peptide vaccine	Phase III	Adjuvant treatment of Her2+ breast cancer
	Rindopepimut (CDX-110)	Celldex Therapeutics	Peptide vaccine containing EGFRv3-specific peptide sequence conjugated to KLH	Phase III	Newly diagnosed glioblastoma
	L-BLP25 (Stimuvax)	Merck KGaA and Oncothyreon	Liposome formulation containing core peptide of the MUC1 TAA	Phase III	Phase II in mPC, Failed Phase III in NSCLC
	GV1001	Kael-GemVax Co. Ltd.	Vaccine targeting human telomerase reverse transcriptase (hTERT)	Phase III	NSCLC. Phase III failed in pancreatic cancer.
	GSK1572932A	GSK	Cancer vaccine against MAGE-A3 antigen	Phase III	NSCLC
	AE37	Generex Biotechnology	Peptide vaccine containing fragment of HER2	Phase II	Her2- breast cancer
	ONT-10	Oncothyreon	Liposomal formulation of peptide containing two epitopes of MUC1A	Phase I	Solid tumour
Multi-epitope peptide	IMA901	immatics Biotechnologies	Vaccine containing 10 tumour-associated peptides (TUMAPs)	Phase III	mRCC
	PVX-410	OncoPep	Peptide vaccine covering four short peptide sequences of a MM surface antigen	Phase I	Smoldering multiple myeloma (SMM)
	ImMucin	Vaxil BioTherapeutics	21mer synthetic vaccine composed of the signal peptide domain of the MUC1	Phase I/II	Multiple myeloma
	IMA950	immatics Biotechnologies	Multi-peptide vaccine containing 11 tumour-associated peptides from glioblastomas	Phase I	Glioblastoma
Multi-epitope protein complex	HSPPC-96	Agenus	Heat shock protein-peptide complexes made from a person's own tumour tissue	Phase II	Glioblastoma
Single protein	Imprime PGG	Biothera	A soluble Beta-1,3/1,6 immunomodulatory glucan that targets neutrophils	Phase III	K-ras wild type colorectal cancer
Single antigen fusion protein	GSK2132231A	GSK	Fusion protein between MAGE-3 and lipidated protein D	Phase III	Adjuvant Melanoma
	ALT-801	Altor BioScience	A p53-specific scTCR/IL-2 fusion protein	Phase II	Metastatic melanoma
	CDX-1401	Celldex Therapeutics	Fully human mAB against dendritic cell receptor DEC-205 linked to NY-ESO-1	Phase I	Solid tumour
Single antigen, anti-idiotypic mouse mAB	Racotumomab	Recombio SL	Anti-idiotypic mouse mAB that mimics NGc gangliosides	Phase III	Advanced lung cancer
Multi-antigen mixture	POL-103A	Polynoma LLC	Vaccine comprising a combination of purified antigens shed from 3 melanoma cell lines	Phase III	Stage IIb, IIc, and III Melanoma
Multi-epitope, DNA based	VGX-3100	Inovio Pharmaceuticals	Electroporation based therapy with DNA vaccine containing epitopes of HPV16 and 18, E6 and E7	Phase II	Cervical cancer
	SCIB1	Scancell	Plasmid DNA expressing Tyrosinase-Related Protein 2 (TRP2) plus two helper T cell epitopes	Phase II	Melanoma
Single gene, DNA based	IL-1 plasmid	OncoSec Medical	Electroporation-mediated plasmid DNA of IL2	Phase II	Merkel cell cancer
	VXM01	Vaximm GmbH	VEGFR-2 DNA vaccine	Phase I	Pancreatic cancer
	GX-188E	Genexine, Inc.	DNA therapeutic vaccine GX-188E administered by electroporation	Phase I	Cervical intraepithelial neoplasia grade 3 (CIN3)
	Allovectin	Vical	DNA plasmid encoding MHC class I B7 (HLA-B7)	Phase III	Advanced melanoma
Multi-epitope, RNA based	RBL001/RBL002	BioNTech AG (Ribological GmbH)	Naked ribonucleic acid (RNA) based vaccine targeting two tumour-associated antigens	Phase I	Solid tumour
	CV9104	CureVac GmbH	Vaccine composed of 6 RNActive-based compounds, each encoding for an antigen that is overexpressed in prostate cancer	Phase II	mCRPC and NSCLC
Multi-gene, virus vector	Prostvac	Bavarian Nordic A/S	Recombinant poxviruses containing PSA, B7.1 (CD80), lymphocyte function-associated antigen (LFA)-3, and ICAM-1	Phase III	mCRPC
	TG4010	Transgene	A modified vaccinia of Ankara (MVA) vector containing MUC1 and IL-2	Phase III	Stage II/IIIB NSCLC
Single gene, virus vector	ProstAtak	Advantagene, Inc.	Adenoviral vector that expresses a herpes simplex virus thymidine kinase gene	Phase III	Localised prostate cancer
	TroVax	Oxford BioMedica	Adenoviral vector for tumour antigen 5T4	Phase II	Ovarian, mesothelioma
Single gene, listeria	CRS-207	Aduro BioTech (BioSante)	Attenuated form of Listeria monocytogenes expressing tumour-associated antigen mesothelin	Phase I	Malignant pleural mesothelioma
Multi-epitope, listeria	ADXS-HPV	Advaxis	Live attenuated Listeria monocytogenes expression HPV epitopes	Phase II	Cervical, head and neck cancers
Single gene, baker's yeast	GI-4000	GlobeImmune	Genetically modified yeast that expresses mutated RAS protein	Phase II	Pancreatic cancer
	GI-6301		Whole heat-killed yeast modified to express brachyury protein	Phase I	Solid tumour
	GI-6207		Whole heat-killed yeast modified to express CEA	Phase I	Thyroid cancer

Category	Drug name	Company	Technology description	Status	Main indication
Allogeneic tumour cells expressing single gene	Algenpantucel-L (HyperAcute pancreas)	NewLink Genetics	Irradiated pancreatic tumour cells modified to express alpha 1,3-galactosyltransferase	Phase III	Resectable or locally advanced unresectable pancreatic cancer
	Tergenpumatucel-L (HyperAcute Lung)		Irradiated NSCLC tumour cells to express alpha 1,3-galactosyltransferase (aGT)	Phase II/III	NSCLC
Allogeneic tumour cells expressing multiple gene	HS-110	Beat Biologics	Live cancer cells modified to secrete HSP gp96 and associated chaperoned antigens.	Phase II	NSCLC
	GVAX	Aduro BioTech (BioSante)	GM-CSF-transduced androgen-sensitive prostate cancer cell line (LNCaP) and a CRPC cell line (PC3)	Phase II	Phase II for pancreatic, MDS/AML and local PC (failed in Phase III for PC)
	MG-1601	Mologen	Tumour cells modified to express IL-7, GM-CSF, CD80 and CD154 with proprietary dSLIM immunomodulator.	Phase I/II	RCC
Allogeneic fibroblast cell lines expressing multiple cancer genes	Unknown	Immune Cell Therapy Inc.	Semi-allogeneic fibroblasts transfected with autologous tumour-derived DNA	Phase I	NSCLC
Autologous tumour cells express multiple genes	FANG	Gradalis	Adjuvant bi-shRNAfurin and GMCSF augmented autologous tumour cell vaccine	Phase II	Ovarian, melanoma and colorectal caner
Autologous modified tumour cells	OVAX	AVAX Technology	Autologous, DNP-modified ovarian cancer vaccine	Phase II	Ovarian cancer
Cytokines					
IFN-alpha	Intron-A	Merck	Recombinant IFN-a2b	Approved	Hairy cell leukaemia, adjuvant melanoma, follicular lymphoma
	Roferon-A	Roche	Recombinant IFN-a2a	Approved	Hairy cell leukaemia, chronic myelogenous leukaemia (CML)
IL-2	Proleukin	Prometheus	Recombinant IL-2	Approved	Metastatic RCC
Dendritic cells					
DC with defined antigen and protein	Provenge	Dendreon	Autologous PBMCs incubated in vitro with PA2024, a recombinant fusion protein composed of PAP and GM-CSF	Approved	Asymptomatic or minimally symptomatic mCRPC
DC with undefined antigens	DCVax-L	Northwest B`otherapeutics	Autologous dendritic cells pulsed with tumour lysate antigens	Phase III	Newly diagnosed GBM
DC with growth factor	DC-TC	California Stem Cell, Inc.	Autologous dendritic cell-tumour cell cultured with GM-CSF	Phase III	Metastatic melanoma
DC with growth factor and undefined antigens	AGS-003	Argos Therapeutics	Autologous monocytes incubated with cytokines and pulsed with patients' own amplified tumour RNA mixture	Phase III	Advanced RCC
DC with defined antigen fusion protein	CVac	PrimaBioMed	Autologous DCs pulsed with MUC-1-mannan fusion protein	Phase II/III	Ovarian cancer
DC with undefined peptide antigens	ICT-107	ImmunoCellular Therapeutics	Autologous DCs pulsed with peptides eluted from the surface of cultured autologous brain tumour cells	Phase II	Glioblastoma
DC with defined antigen	DN24-02	Dendreon	Autologous PBMCs incubated in vitro with Her2/Neu	Phase II	HER2+ urothelial carcinoma
DC with antigens and cytokines	a-type-1 polarised DC vaccine	Unknown	Autologous DCs activated with a cocktail of cytokines and growth factors	Phase I	Glioma
DC with cytokines	INTUVAX (COMBIG-DC)	Immunicum AB	Allogeneic, immortalised dendritic cells (DCs) stimulated with toll-like receptor IFN-Gamma	Phase I	mRCC
Immune checkpoint blockers					
Antagonist to inhibitory factor	Yervoy (ipilimumab)	BMS	Anti-CTLA-4 mAB	Approved	Metastatic melanoma
				Phase III	NSCLC, prostate, SCLC
	Tremelimumab	AstraZeneca	Anti-CTLA-4 mAB	Phase II	Malignant mesothelioma
	Nivolumab	BMS/Ono	Anti-PD1 mAB	Phase III	Melanoma, NSCLC, RCC
	Lambrolizumab	Merck	Anti-PD1 mAB	Phase III	2nd-L NSCLC, melanoma
	CT-011	CureTech/BMS	Anti-PD1 mAB	Phase I	Solid tumour
	MPDL3280A	Roche/Genentech	Anti-PD-L1 mAB	Phase II	2nd-line NSCLC
	BMS-936559	BMS	Anti-PD-L1 mAB	Phase I	Solid tumour
	MGA271	Macrogenics/Servier	Anti-B7-H3 mAB	Phase I	Solid tumour
	Lirilumab	Innate Pharma/BMS	Anti-KIR mAB	Phase II	AML and solid tumours
Competitor to inhibitory factor	IMP321	ImmuTune	Soluble LAG-3, plus 6 melanoma antigens	Phase II	Melanoma
	AMP-224	GSK/Amplimmune	PD-L2 Ig fusion protein	Phase I	Solid tumour
Inhibitor of inhibitory factor	Indoximod	NewLink Genetics	Small molecule inhibitor of Indoleamine 2,3 dioxygenase (IDO), an enzyme that down regulates the immune system	Phase II	Metastatic prostate cancer

Source: Clinicaltrials.gov, company reports and Edison Investment Research

Upcoming newsflow

Exhibit 5: Expected near-term newsflow catalysts for pharma/biotech

August		
Smith & Nephew	1 Aug	Q213 results
AstraZeneca	1 Aug	Q213 results
Biotie	2 Aug	Q213 results – updates on Selincro EU launch (Lundbeck) and outcome from pipeline portfolio review
Epigenomics	7 Aug	Q213 results
Paion	7 Aug	Q213 results
4SC	8 Aug	Q213 results
Evotec	8 Aug	Q213 results
Medigene	9 Aug	Q213 results
Algeta	11 Aug	Q213 results
ALK-Abello	14 Aug	Q213 results
Genmab	14 Aug	H113 interim results
Topotarget	14 Aug	Q213 results
Skyepharma	15 Aug	H113 results
TiGenix	20 Aug	Q213 results
Ablynx	21 Aug	H113 interim results
Clavis	28 Aug	H113 interim results
Lombard Medical	29 Aug	H113 interim results
Oxford BioMedica	29 Aug	H113 interim results
ThromboGenics	29 Aug	H113 interim results
Nanobiotix	30 Aug	H113 interim results
Athersys	Aug	Q213 results
Cleveland BioLabs	Aug	Q213 results
Lombard Medical	Aug	H113 results
Mast Therapeutics	Aug	Q213 results
NovaBay	Aug	Phase II data for NVC-422 (auricolsene) in urinary catheter blockage and encrustation
NovaBay	Aug	Q213 results
Pharming	Aug	Q213 results
Photocure	Aug	Q213 results
ProMetic Life Sciences	Aug	Q213 results
Skyepharma	Aug	H113 interim results
Sucampo	Aug	Q213 results
Sunesis	Aug	Q213 results
Addex	Aug	H113 interim results
Oncolytics	Aug	Q213 results
September		
Newron	10 Sep	H113 results
Abcam	10 Sep	FY13 prelim results
Futura Medical	12 Sep	H113 results
Transgene	12 Sep	Q213 results
Allergy Therapeutics	17 Sep	FY13 prelim results
Innate Pharma	19 Sep	H113 results
Skyepharma	20 Sep	Capital Markets Day and site visit, Muttenz, Switzerland
Animalcare	25 Sep	FY13 prelim results
Alliance Pharma	Sept	H113 results
Consort Medical	Sept	AGM & IMS
e-Therapeutics	Sept	AGM
Phylogica	Sept	FY13 prelim results
Sinclair IS Pharma	Sept	FY13 prelim results
Vectura	Sept	Respiratory presentations at ERS
Vectura	Sept	AGM & IMS
Deltex	Sept	Q213 results
Imperial Innovations	Sept	FY13 prelim results
Diaxonhit	Sept	H113 results
Epistem	Sept	FY13 prelim results
October		
Wilex	10 Oct	Q313 results
Actelion	17 Oct	Q313 results
Stallergenes	21 Oct	Q313 sales
Transgene	21 Oct	Q313 IMS
GSK	23 Oct	Q313 results
Bioinvent	24 Oct	Q313 results
Clavis	24 Oct	Q313 results
Shire	24 Oct	Q313 results
AstraZeneca	31 Oct	Q313 results

Source: Edison Investment Research

Exhibit 5: Expected near-term newsflow catalysts for pharma/biotech (continued)

Animalcare	Oct	FY13 results
Avacta	Oct	FY13 results
Bioinvent	Oct	Q313 results
BTG	Oct	Pre-close statement
Epistem	Oct	FY13 results
e-Therapeutics	Oct	H113 results
Hybrigenics	Oct	H113 prelim results
Imperial Innovations	Oct	FY12 results
Pharming	Oct	Q313 results
Photocure	Oct	Q313 results
Proteome Sciences	Oct	H212 results
Genfit	Oct	H113 results
Unspecified		
Alexza Pharmaceuticals	-	Initial EU launch of Adasuve
BTG	-	Potential EU approval of Lemtrada (alemtuzumab) in relapsing multiple sclerosis
Cleveland BioLabs	-	BARDA development contract for Entolimod in acute radiation syndrome
Topotarget	-	Belinostat - filing of NDA for PTCL
Verastem	-	Initiation of pivotal Phase II trial in mesothelioma
Conferences etc		
	31 Aug-4 Sept	European Society of Cardiology
	7-9 Sept	ASCO breast cancer symposium
	23-27 Sept	European Association for the Study of Diabetes
	27 Sept-1 Oct	ESMO/ECCO/ESTRO – European Multidisciplinary Cancer Congress
	2-5 Oct	ECTRIMS/ACTRIMS – European and Americas Committee for Treatment & Research in Multiple Sclerosis
	13-15 Oct	American Neurological Association
	25-30 Oct	ACR/ARHP – American College of Rheumatology

Source: Edison Investment Research

Company coverage

Company	Note	Date published
4SC	Review; Update	03/08/2012; 28/09/2012
Aastrom BioSciences	Update; Update	02/04/2013; 23/05/2013
Abcam	Outlook; Update	07/07/2011; 21/09/2011
Ablynx	Update; Update	10/10/2012; 12/03/2013
Addex Therapeutics	Update; Update	05/03/2013; 19/04/2013
Algeta	Update; Update	19/06/2012; 20/05/2013
Allergy Therapeutics	Update; Update	02/10/2012; 17/05/2013
AmpliPhi Biosciences	Outlook; QuickView	09/08/2011; 09/07/2013
Animalcare Group	Update; Update	05/12/2012; 03/04/2013
Ark Therapeutics	Outlook; Update	23/03/2012; 21/09/2012
ArQule	Outlook; Update	15/01/2013; 19/03/2013
Arrowhead Research	Update; Update	15/08/2012; 17/04/2013
Astex Pharmaceuticals	Update; Update	16/04/2013; 07/05/2013
Bellus Health	Update; Update	01/07/2013; 22/07/2013
BioAlliance Pharma	Outlook; Update	18/06/2013; 08/07/2013
BioInvent	Update; Update	04/02/2013; 14/03/2013
Bionomics	Update; Update	05/04/2013; 27/06/2013
Biotie Therapies Corp	Outlook; Update	04/01/2013; 07/06/2013
BTG	Update; Update	01/07/2013; 24/07/2013
Circadian Technologies	Outlook; Update	05/03/2013; 13/05/2013
Clavis Pharma	Update; Update	13/11/2012; 19/02/2013
Cleveland BioLabs	Outlook; Update	26/03/2013; 17/05/2013
Consort Medical	Outlook; Update	23/04/2013; 21/06/2013
Cytos Biotechnology	Update; Update	11/02/2013; 28/05/2013
CytRx Corporation	Update; Update	24/05/2013; 23/07/2013
Deltex Medical	Update; Update	15/04/2013; 15/07/2013
Diaxonhit	Update; Update	15/11/2012; 31/05/2013
e-Therapeutics	Update; Update	15/02/2013; 20/05/2013
EpiCept	Update; Update	16/10/2012; 22/11/2012
Epigenomics	Update; Update	02/01/2013; 14/06/2013
Epistem Holdings	Update	31/03/2011
Evolva	Update; Outlook	02/01/2013; 08/05/2013
Evotec	Update; Update	05/02/2013; 30/04/2013
GW Pharmaceuticals	Update; Update	15/04/2013; 07/05/2013
Hybrigenics	Update; Update	15/04/2013; 07/05/2013
ImmuPharma	Update; Outlook	26/10/2011; 05/07/2012
Imperial Innovations	Update; Update	02/01/2013; 24/07/2013
Innate Pharma	Update; Update	24/05/2013; 02/07/2013
LeMaitre Vascular	Outlook	25/06/2013
Lombard Medical Technologies	Outlook; Update	13/05/2013; 06/06/2013
Mast Therapeutics	Update; Outlook	11/03/2013; 03/07/2013
Medcom Tech	Update; Update	10/04/2013; 13/06/2013
Medigene	Update; Update	17/05/2013; 31/05/2013
Mologen AG	Update; Update	21/03/2013; 17/04/2013
MorphoSys	Update; Update	04/10/2012; 07/02/2013
Neovacs	Update; Update	21/01/2013; 17/05/2013
NovaBay Pharmaceuticals	Update; Update	19/12/2012; 13/05/2013
Omega Diagnostics	Update; Update	31/05/2013; 08/07/2013
Oncolytics Biotech	Update; Update	21/12/2012; 14/06/2013
OvaScience	Outlook; Update	07/01/2013; 04/04/2013
Oxford BioMedica	Outlook; Update	04/03/2013; 01/05/2013
Paion	Update; Update	02/04/2013; 11/07/2013
Phylogica	Update; Outlook	11/05/2012; 23/01/2013

Phytopharm	Update; Update	16/08/2012; 18/02/2013
Proteome Sciences	Update; Update	15/10/2012; 01/02/2013
SkyePharma	Update; Outlook	10/01/2013; 04/07/2013
Stratec Biomedical	Update; Update	19/06/2013; 18/07/2013
Sucampo Pharmaceuticals	Update; Update	05/03/2013; 01/05/2013
Sunesis Pharmaceuticals	Outlook; Update	21/03/2013; 03/04/2013
Sygnis Pharma	Quickview, Outlook	10/12/2012; 31/05/2013
Synta Pharmaceuticals	Update; Update	03/04/2013; 27/06/2013
TiGenix	Update; Update	22/03/2013; 26/04/2013
Topotarget	Update; Update	25/09/2012; 26/03/2013
Transgene	Outlook; Update	07/05/2013; 07/06/2013
Vectura	Update; Update	09/10/2012; 28/11/2012
Verastem	Update; Update	12/06/2013; 19/07/2013
Vernalis	Outlook; Update	01/05/2013; 16/07/2013
Wilex	Update; Update	14/03/2013; 14/06/2013

Investment Trusts

BB Biotech	Update; Investment Trust Review	31/07/2012; 07/03/2013
Biotech Growth Trust (The)	Investment Trust Review	26/07/2012; 26/04/2013
International Biotechnology Trust	Investment Trust Review	25/10/2012; 07/06/2013
Worldwide Healthcare Trust	Investment Trust Review	10/02/2012; 15/10/2012

To view the June edition of the Investment Trusts Quarterly, featuring biotechnology and healthcare trusts, see the investment companies and trusts sector profile on our website.

QuickViews

To view the following QuickViews see the healthcare sector profile page on our website.

AB Science	06/02/2012; 13/02/2013
Achillion	12/03/2012; 18/10/2012
Acorda Therapeutics	05/11/2012
Active Biotech	21/02/2012
Aegerion Pharmaceuticals	10/06/2013
Aixtron	26/10/2012
Alchemia	25/03/2013; 07/06/2013
Alexza Pharmaceuticals	23/05/2013
Algeta	20/05/2013
ALK-Abello	14/11/2012; 07/02/2013
Alkermes	05/11/2012; 05/02/2013
Alnylam Pharmaceuticals	10/02/2012
Amarin	21/11/2012; 13/12/2012
Ariad Pharmaceuticals	05/03/2012
Array BioPharma	08/02/2013; 30/07/2013
Anthera	24/02/2012
Athersys	26/06/2013; 16/07/2013
AVEO Pharmaceuticals	10/08/2012; 15/02/2013
Basilea	07/09/2012; 08/02/2013
Benitec Biopharma	15/10/2012
BioCryst Pharmaceuticals	20/02/2012; 25/07/2013
BioLineRx	20/02/2012; 12/12/2012
Biota Holdings	11/04/2012
Celldex Therapeutics	12/03/2012

Clinigen	02/04/2013; 26/07/2013
Clinuvel	05/01/2012
Core Laboratories	26/02/2013
Curis	31/01/2012
Cytori Therapeutics	10/10/2012
Dechra Pharmaceuticals	23/02/2012
Derma Sciences	13/02/2013
Endocyte	18/04/2012; 18/12/2012
EKF Diagnostics	23/03/2012
Exact Sciences	27/11/2012
Galapagos	05/03/2012
Genfit	07/03/2013; 24/07/2013
Genmab	12/03/2012; 09/01/2013
GI Dynamics	14/11/2012
Gilead Sciences	13/02/2013
Greiffenberger	31/08/2012
Halozyme Therapeutics	05/07/2013
Hutchison China Meditech	29/11/2012; 03/04/2013
Idenix	11/01/2012
Immunodiagnostic Systems Holdings	29/11/2011; 28/06/2012
Incyte Corporation	05/11/2012; 01/03/2013
Infinity Pharmaceuticals	06/01/2012; 30/01/2012
Insmed	05/07/2013
Ironwood Pharmaceuticals	22/10/2012
KaloBios Pharmaceuticals	23/07/2013
Karolinska Development	25/02/2013; 02/07/2013
Keryx Biopharmaceuticals	05/03/2012
LCA-Vision	31/01/2013
MagForce	03/02/2012
Medivir	09/01/2013
Merrimack Pharmaceuticals	17/04/2013
MethylGene	27/11/2012
MolMed	18/02/2013
Nektar Therapeutics	08/02/2013
NicOx	22/03/2012
Nordion	29/10/2012; 31/05/2013
NPS Pharmaceuticals	07/01/2013
Oncothyreon	05/06/2013
Onyx Pharmaceuticals	05/11/2012; 04/01/2013
Optos	21/05/2013
Orbite Aluminae	05/10/2012
Orexo	01/02/2012; 05/07/2013
Paladin Labs	02/11/2012
Patheon	14/11/2012
Pharmaxis	30/01/2012; 08/03/2013
Photocure	22/02/2012; 01/06/2012
Polymetals Mining	12/02/2013
Prima BioMed	17/10/2012; 02/07/2013
QRxPharma	28/03/2012; 06/03/2013
Resverlogix	29/04/2013; 14/06/2013
REVA Medical	21/06/2013
Sangamo BioSciences	03/02/2012; 18/02/2013
Sarepta Therapeutics	07/03/2012; 31/07/2012
Scancell	07/12/2012; 17/07/2013
Sirtex Medical	19/04/2013
Source Bioscience	27/03/2012; 22/07/2013
Stallergenes	25/02/2013; 12/03/2013

Sucampo Pharmaceuticals	11/05/2012; 13/07/2012
Synergy	14/11/2012
Tekmira Pharmaceuticals	16/11/2012; 15/04/2013
Threshold Pharmaceuticals	28/01/2013; 03/07/2013
ThromboGenics	25/10/2012; 14/01/2013
Tissue Regenix	11/10/2012
UCB	25/01/2013
United Drug	14/05/2012; 19/11/2012
Vertex Pharmaceuticals	06/11/2012; 26/04/2013
Viralytics	27/06/2013
ViroPharma	03/10/2012
Vivalis	15/01/2013
Vivus	23/02/2012
Zealand Pharma	22/11/2012; 18/02/2013
Zeltia	26/04/2012; 25/02/2013

Alternext stocks covered
Biosynex
CARMAT
Cellectis
Cerep
Diaxonhit
Genfit
GenOway
Hybrigenics
IntegraGen
MEDICREA International
Neovacs
Novacyt
Qiagen Marseille
Spineway
Theradiag
Vexim
Visiomed Group

Company profiles

Sector: Pharma & healthcare

Price:	€1.70
Market cap:	€87m
Forecast net cash (€m)	3.7
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

4SC is a Munich-based drug discovery and development company focused on the development of small-molecule compounds for treating cancer and autoimmune diseases. Its R&D pipeline has four NCEs in clinical trials.

Price performance

%	1m	3m	12m
Actual	(10.4)	6.0	15.2
Relative*	(11.9)	(5.1)	(6.5)

* % Relative to local index

Analyst

Michael Aitkenhead

4SC (VSC)

INVESTMENT SUMMARY

4SC's investment case now hinges on the successful development and commercialisation of resminostat for front-line hepatocellular carcinoma (HCC). There is a clear rationale for targeting front-line HCC and, as such, we are optimistic that 4SC will secure financing and/or a partner to conduct a pivotal Phase II/III study. Separately, the company's two active Phase I programmes (4SC-202, 4SC-205) have delivered promising interim data and render final results in H213.

INDUSTRY OUTLOOK

4SC's resminostat is emerging as a leader in solid tumour indications within the HDACi class. The company's recent decision to prioritise resminostat development in first-line HCC is supported by the clinical data, existing partnerships, and competitive developments.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.8	(17.1)	(17.3)	(43.1)	N/A	N/A
2012	4.4	(11.5)	(11.7)	(25.3)	N/A	N/A
2013e	2.9	(9.2)	(9.4)	(18.6)	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	US$0.40
Market cap:	US$17m
Forecast net debt (US$m)	49.1
Forecast gearing ratio (%)	95.0
Market	NASDAQ

Share price graph (US$)

Company description

Aastrom Biosciences uses autologous cell therapy, ixmyelocel-T, to process and inject the patient's own cells to treat orphan diseases. The current indication is dilated ischaemic cardiomyopathy (ixCELL-DCM).

Price performance

%	1m	3m	12m
Actual	(24.3)	(47.1)	(81.0)
Relative*	(27.1)	(51.3)	(84.5)

* % Relative to local index

Analyst

John Savin

Aastrom Biosciences (ASTM)

INVESTMENT SUMMARY

Aastrom's Q1 results show its consolidation onto affordable clinical studies and a determination to achieve a solid cash basis. The focus is on the Phase II ischaemic cardiomyopathy (IDC) orphan indication. The ixCELL-DCM study will cost about $7m and has recruited its first patients. If recruitment completes by early-2014, the data will be presented in Q215. New orphan indications are planned.

INDUSTRY OUTLOOK

Aastrom is reducing its headcount and cash burn by about 50% and plans to raise up to $25m in new equity. This will enable the ixCELL-DCM study to be completed by mid-2015 before further equity or a deal is needed. In Q1, Aastrom spent $6.8m cash offset by $2.4m from the "At the Market" equity facility. Cash use in Q2 might be $5m, including lay-off costs and final REVIVE payments. H2 in total will need about $8m. Cash at the end of Q1 was $9.2m.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	0.0	(28.4)	(29.0)	(75.1)	N/A	N/A
2012	0.0	(33.1)	(37.7)	(96.4)	N/A	N/A
2013e	0.0	(21.9)	(27.6)	(63.0)	N/A	N/A
2014e	0.0	(16.4)	(22.7)	(51.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	453.3p
Market cap:	£904m
Forecast net cash (£m)	37.9
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Abcam produces and sells antibodies and other protein tools for use in research via its website. Its main clients are universities, research institutes and pharmaceutical companies across the world.

Price performance

%	1m	3m	12m
Actual	12.1	6.2	8.1
Relative*	7.1	0.2	(8.7)

* % Relative to local index

Analyst

Mick Cooper

Abcam (ABC)

INVESTMENT SUMMARY

Abcam achieved c 25% revenue growth in FY13, or 11.8% on an underlying basis, adding back the pre-acquisition sales of its most recently acquired companies. The total catalogue size increased by 31.5%. As expected, US budget cuts are taking place and sequestration was passed into law. Uncertainty for Abcam's largest market is likely to continue. The de-rating of sterling, c 5% of sales, 20% of COGS and 65% of SG&A has led to forecast upgrades. However, sustained yen weakness since December (c 10% of revenue and minimal costs) led to a -1% impact on revenue. FY13 results will be reported on 10 September.

INDUSTRY OUTLOOK

More biological research is conducted into proteins, increasing the demand for protein research tools. However, the funding of academic research is coming under greater pressure as governments look to reduce their debts. Abcam is the market leader for research antibodies, but has a limited market position in the wider protein research tools market.

Y/E Jun	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	83.3	33.5	32.5	13.5	33.6	24.8
2012	97.8	40.4	39.3	16.2	28.0	25.8
2013e	122.1	48.1	46.8	17.9	25.3	18.0
2014e	136.4	53.8	52.4	20.6	22.0	17.1

Sector: Pharma & healthcare

Price:	CHF3.30
Market cap:	CHF30m
Forecast net debt (CHFm)	N/A
Forecast gearing ratio (%)	N/A
Market	Swiss Stock Exchange

Share price graph (CHF)

Company description

Addex Therapeutics is a Swiss biotech company with a proprietary allosteric modulator discovery platform and a pipeline in CNS, inflammatory and metabolic disorders. It has a partnership with J&J (Ortho-McNeil-Janssen).

Price performance

%	1m	3m	12m
Actual	(5.1)	(52.1)	(60.7)
Relative*	(7.5)	(54.0)	(68.7)

* % Relative to local index

Analyst

Michael Aitkenhead

Addex Therapeutics (ADXN)

INVESTMENT SUMMARY

Following the recent completion of restructuring and departure of its CEO, Addex's board has re-appointed former CFO, Tim Dyer, to take the company forward. The current plan is to minimise operating expenditure and secure further capital to advance Addex's pipeline and platform assets. The company's lead programme, ADX71149, is partnered with Janssen (J&J) and could render Phase II data in anxious depression in H213. Separately, Addex will target partnership discussions for its lead internal programme, dipraglurant, which has completed a Phase II study in Parkinson's disease levodopa-induced dyskinesia. Our forecasts are currently under review.

INDUSTRY OUTLOOK

Addex Therapeutics is a Swiss-based biopharmaceutical company focused on the clinical development of novel oral therapies for rare disease indications. The company's R&D pipeline is based on its proprietary allosteric modulator platform.

Y/E Dec	Revenue (CHFm)	EBITDA (CHFm)	PBT (CHFm)	EPS (CHFc)	P/E (x)	P/CF (x)
2011	3.7	(27.2)	(29.8)	(4.0)	N/A	N/A
2012	0.1	(24.7)	(26.7)	(3.4)	N/A	N/A
2013e	N/A	N/A	N/A	N/A	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	NOK235.30
Market cap:	NOK10300m
Forecast net debt (NOKm)	N/A
Forecast gearing ratio (%)	N/A
Market	OSE

Share price graph (NOK)

Company description

Algeta is a Norwegian biotech company with the leading position in alpha-emitting pharmaceuticals for oncology. Its lead product radium-223 has been approved in the US for the treatment of prostate cancer patients with bone metastases.

Price performance

%	1m	3m	12m
Actual	4.5	21.0	35.2
Relative*	0.4	17.2	21.9

* % Relative to local index

Analyst

Robin Davison

Algeta (ALGETA)

INVESTMENT SUMMARY

The US approval of Xofigo (radium-223) for metastatic prostate cancer in Q213 triggered a €50m milestone to Algeta from partner Bayer (following first sale). The accelerated approval, broad label and premium pricing could result in upgrades to 2013 consensus sales forecasts. Despite this, we anticipate a measured commercial launch initially targeting US sites involved in the early access programme (EAP). Algeta and partner Bayer will co-promote radium-223 in the US, with Algeta eligible for further milestones and tiered double-digit royalties in ex-US territories. While we see potential for Algeta's EV to rise further following a positive EU regulatory opinion (Q313), we also see potential downside risk to Algeta's current valuation if the US launch fails to meet expectations.

INDUSTRY OUTLOOK

Algeta is the world leader in alpha-pharmaceuticals. The company's current focus is the development and commercialisation, in collaboration with Bayer, of Xofigo for bone metastases arising from prostate cancer.

Y/E Dec	Revenue (NOKm)	EBITDA (NOKm)	PBT (NOKm)	EPS (öre)	P/E (x)	P/CF (x)
2011	250.4	23.7	19.9	49.75	473.0	N/A
2012	627.4	241.5	236.8	557.33	42.2	N/A
2013e	N/A	N/A	N/A	N/A	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	9.9p
Market cap:	£41m
Forecast net cash (£m)	0.7
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Allergy Therapeutics is a European-based speciality pharmaceutical company focused on the treatment and prevention of allergy.

Price performance

%	1m	3m	12m
Actual	0.0	(7.1)	29.5
Relative*	(4.4)	(12.3)	9.4

* % Relative to local index

Analyst

Wang Chong

Allergy Therapeutics (AGY)

INVESTMENT SUMMARY

Allergy Therapeutics' investment case hinges on its effort to secure a US partner for Pollinex Quattro (PQ). The company is six months into a licensing campaign, the outcome of which may become apparent later this year. The US allergy immunotherapy (AIT) market is potentially large, but undeveloped. PQ, an ultra-short-course subcutaneous injection, will potentially enter this market after two oral products, Grazax (Alk-Abello/Merck & Co) and Oralair (Stallergenes), both of which are in regulatory review. Allergy needs to secure a partner to commercialise PQ in the US. We have not included the US PQ opportunity in our valuation. Thus, a successful licensing deal would transform Allergy's prospects.

INDUSTRY OUTLOOK

Pollinex Quattro (c 50% of revenue) is an ultra short-course allergy vaccine, given as four shots over three weeks, which has comparable efficacy to existing vaccines (typically requiring 16-50 injections under specialist supervision pre-hayfever season).

Y/E Jun	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	41.6	2.0	(1.7)	(0.7)	N/A	N/A
2012	41.3	3.1	1.2	0.4	24.8	11.1
2013e	41.3	3.2	1.9	0.4	24.8	15.3
2014e	43.3	3.8	2.3	0.5	19.8	11.6

Sector: Pharma & healthcare

Price:	US$0.40
Market cap:	US$79m
Forecast net cash (US$m)	2.3
Forecast gearing ratio (%)	N/A
Market	OTC

Share price graph (US$)

Company description

AmpliPhi BioSciences is a US company developing bacteriophages, viruses that kill bacteria. A Phase I study for AmpliPhage-002 is planned for Q114, with a Phase II trial in wound infection in H214.

Price performance

%	1m	3m	12m
Actual	122.2	158.8	169.9
Relative*	113.9	137.9	119.6

* % Relative to local index

Analyst

Christian Glennie

AmpliPhi Biosciences (APHB)

INVESTMENT SUMMARY

A $7m private placement with RA Capital and Third Security, and a research collaboration with the US army, provide AmpliPhi with fresh impetus in its development of bacteriophages (naturally occurring viruses that kill bacteria). This follows the purchase of Special Phage Services (SPS) in 2012 and a strategic collaboration with Intrexon in April 2013. Phase I and II studies with the US army are planned for 2014, in skin infections due to Staphylococcus aureus; a Phase II study to treat Pseudomonas infections in cystic fibrosis (CF) will start in 2014. AmpliPhi plans to transfer its listing from the Pink Sheets to the OTC Bulletin Board.

INDUSTRY OUTLOOK

Resistance to conventional chemical antibiotics is a serious problem and pharma companies are increasingly seeking alternatives. AmpliPhi is the only company to have completed a controlled Phase I/II study with bacteriophages. TOBI (Novartis) and Cayston (Gilead) are approved drugs for Pseudomonas in CF (FY12 sales of $317m and $107m, respectively).

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.1	(3.7)	(4.0)	(8.40)	N/A	N/A
2012	3.8	(0.8)	(1.2)	(2.14)	N/A	N/A
2013e	0.5	(4.2)	(4.2)	(2.79)	N/A	N/A
2014e	0.8	(4.7)	(4.7)	(2.25)	N/A	N/A

Sector: Pharma & healthcare

Price:	141.0p
Market cap:	£29m
Forecast net cash (£m)	2.3
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Animalcare markets and sells licensed veterinary pharmaceuticals, animal identification products and animal welfare goods for the companion animal market across the UK. Its products are sold in Europe through distributors.

Price performance

%	1m	3m	12m
Actual	(0.4)	14.2	8.5
Relative*	(4.8)	7.8	(8.4)

* % Relative to local index

Analyst

Franc Gregori

Animalcare Group (ANCR)

INVESTMENT SUMMARY

Animalcare's trading update on 10 July shows revenues up 11%, with growth driven by a 22% increase in Licensed Veterinary Medicines. Companion Animal Identification and Animal Welfare revenues performed slightly better than expected. The sizeable growth is due to the new products introduced over the past 12 months and highlights the group's strategy. Animalcare has responded to an increasingly competitive market place by developing new medicines that are more differentiated than its previous products and it is these that should underpin the medium-term outlook. This strategic shift towards developing enhanced generics means the development process is costlier and more protracted, but the greater value added should help generate higher and more resilient earnings.

INDUSTRY OUTLOOK

The companion animal market remains surprisingly resilient, and although previously growing at c 5% in the UK, is forecast to remain essentially flat.

Y/E Jun	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	11.8	3.3	3.2	12.5	11.3	9.3
2012	10.9	2.5	2.5	10.5	13.4	11.4
2013e	11.9	2.8	2.8	11.1	12.7	13.9
2014e	12.3	3.0	2.9	11.2	12.6	11.0

Sector: Pharma & healthcare

Price:	US$2.80
Market cap:	US$87m
Forecast net cash (US$m)	23.9
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)

Company description

Arrowhead Research Corporation is a nanomedicine company with clinical programmes in several therapeutic areas, including cancer, obesity and HBV infection. It also has developed or acquired platform technologies for RNAi delivery and peptide targeting.

Price performance

%	1m	3m	12m
Actual	39.5	60.3	(24.6)
Relative*	34.3	47.4	(38.7)

* % Relative to local index

Analyst

Jason Zhang

Arrowhead Research Corporation (ARWR)

INVESTMENT SUMMARY

Arrowhead's $36m financing brings in much needed cash, as well as a group of biotech-specialist investors, which should move it up a league as it embarks on the clinical development of its hepatitis B treatment ARC-520. Pro forma cash of $36m should be sufficient to advance ARC-520, which is now central to the investment case, through to proof-of-concept (PoC) data, which we expect to be a major value inflection point. We have revised our rNPV to reflect the fund-raising and now indicate a value of $121.6m or $3.85 per basic share and $3.11 per diluted share (assuming full conversion of convertible notes plus warrants).

INDUSTRY OUTLOOK

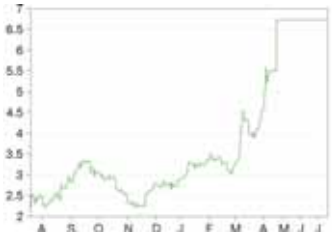
Gene silencing is a potentially exciting area for new product development, with targeted therapies offering better disease control and fewer side effects than current medications. Large and medium-sized pharmaceutical companies are likely to invest in this field via collaborations, of which Arrowhead would be a beneficiary.

Y/E Sep	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.3	(8.2)	(7.4)	(29.4)	N/A	N/A
2012	0.1	(18.1)	(20.9)	(179.4)	N/A	N/A
2013e	0.5	(18.3)	(20.2)	(90.0)	N/A	N/A
2014e	0.4	(25.1)	(27.0)	(83.4)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$6.73
Market cap:	US$607m
Forecast net cash (US$m)	102.1
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)



Company description

Astex Pharmaceuticals is a US-UK oncology-focused drug discovery. It has one approved drug, Dacogen, for myelodysplastic syndromes (MDS) and elderly acute myeloid leukaemia (AML).

Price performance

%	1m	3m	12m
Actual	N/A	N/A	N/A
Relative*	N/A	N/A	N/A

* % Relative to local index

Analyst

Robin Davison

Astex Pharmaceuticals (ASTX)

INVESTMENT SUMMARY

Astex has expanded its Phase II trial of SGI-110 to 200 patients, by adding a new cohort of relapsed/refractory (r/r) myelodysplastic syndromes (MDS) patients to the existing front-line acute myeloid leukemia (AML), MDS and r/r AML groups. Enrolment in the study is now over 50% complete and data from the r/r AML cohort should be presented at the American Society of Hematology (ASH) meeting in December 2013. Q113 Dacogen royalties were $22.1m and Astex has reaffirmed annual royalty guidance of $55m, despite the potential introduction of a US generic decitabine. We value Astex at $678m (including cash), equivalent to $7.25 per share (basic) or $6.73 per share (fully diluted).

INDUSTRY OUTLOOK

Astex offers a low-risk oncology play with multiple study read-outs from internal and partnered programmes. The investment case in the longer term is centred on Astex's ability to exploit its strong financial position to generate value from its R&D pipeline and from its fragment-based discovery technology.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	66.9	12.1	10.5	18.4	36.6	N/A
2012	83.2	12.0	12.7	27.6	24.4	23.6
2013e	55.0	(22.0)	(23.3)	(19.4)	N/A	N/A
2014e	21.0	(61.5)	(62.8)	(58.2)	N/A	N/A

Sector: Pharma & healthcare

Price:	C$0.33
Market cap:	C$1m
Forecast net cash (C$m)	13.9
Forecast gearing ratio (%)	N/A
Market	TSX

Share price graph (C$)

Company description

Bellus Health is a Canadian pharmaceutical company developing drugs for amyloid-related diseases. Its lead candidate, Kiacta, is in a pivotal Phase III trial for AA amyloidosis. BLU8499 is expected to start a Phase IIa study in AD in 2014.

Price performance

%	1m	3m	12m
Actual	(16.7)	53.9	(35.5)
Relative*	(20.3)	45.2	(45.5)

* % Relative to local index

Analyst

Pooya Hemami

Bellus Health (BLU)

INVESTMENT SUMMARY

Bellus Health's lead candidate, Kiacta, is in a pivotal Phase III trial for amyloid A (AA) amyloidosis, an orphan drug indication affecting up to 50,000 patients worldwide. We estimate the probability of success at 60%, given positive efficacy trends in a previous Phase II/III study and modifications in the pivotal study to increase its statistical power and target more responsive patients. Importantly, Bellus is fully funded until the Kiacta study results, expected in 2017. The firm is also advancing BLU8499 in Alzheimer's disease, which is expected to start a Phase IIa study in 2014. Bellus has made an offer to acquire Thallion Pharma, a developer of therapeutics for Shiga-toxin positive E.Coli infection, for C$6.3m in cash, subject to adjustments; no major shareholder is opposing this offer.

INDUSTRY OUTLOOK

The potential for premium pricing for Kiacta and a seven- to 10-year exclusivity period underscore the primary investment case, although with results in 2017, a long-term view is required.

Y/E Dec	Revenue (C$m)	EBITDA (C$m)	PBT (C$m)	EPS (c)	P/E (x)	P/CF (x)
2011	3.1	(0.6)	(1.7)	(19.0)	N/A	N/A
2012	2.3	(3.6)	(3.5)	(11.0)	N/A	N/A
2013e	1.5	(3.5)	(3.2)	(6.6)	N/A	N/A
2014e	1.4	(3.7)	(3.5)	(6.9)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$3.90
Market cap:	US$79m
Forecast net cash (€m)	10.1
Forecast gearing ratio (%)	N/A
Market	Euronext Paris

Share price graph (US$)

Company description

BioAlliance Pharma is a French drug development company focused on orphan cancer and supportive care treatments. It has two FDA-approved specialty products and three clinical-stage orphan oncology candidates.

Price performance

%	1m	3m	12m
Actual	(3.0)	(5.8)	0.8
Relative*	(5.2)	(12.6)	(16.6)

* % Relative to local index

Analyst

Luke Poloniecki

BioAlliance Pharma (BIO)

INVESTMENT SUMMARY

BioAlliance develops drugs for orphan oncology indications and to treat infections. Most of its products are widely used medicines in new formulations for use in novel indications. Its lead oncology product, Livatag, is in a Phase III for liver cancer and has passed the second Data Safety Monitoring Board (DSMB) assessment, so that the safety concerns following the Phase II trial are receding; preliminary efficacy data are due in H116. Its second oncology product, Validive for oral mucositis, is in Phase II with data due in H114. Also, it had its second US product approval with Sitavig (a treatment for cold sores) in April. The company has just raised €8.7m to accelerate development of Livatag and Validive and been awarded a €4.3m grant for Livatag. The additional funds should enable BioAlliance to operate to late-2014.

INDUSTRY OUTLOOK

BioAlliance targets niche markets with its products, which either address significant unmet medical needs or have a clear point of differentiation over current treatments. The former are the more valuable, but the latter still have considerable commercial potential.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	3.2	(15.3)	(14.6)	(0.83)	N/A	N/A
2012	4.0	(12.1)	(11.5)	(0.65)	N/A	N/A
2013e	3.8	(13.1)	(12.8)	(0.67)	N/A	N/A
2014e	6.3	(10.7)	(10.4)	(0.51)	N/A	N/A

Sector: Pharma & healthcare

Price: SEK2.30
Market cap: SEK195m
Forecast net cash (SEKm) 69.0
Forecast gearing ratio (%) N/A
Market NASDAQ OMX Mid Cap

Share price graph (SEK)

Company description

BioInvent is a human therapeutic antibody company based in southern Sweden. It has a lead product, BI-505 in Phase I for multiple myeloma.

Price performance

%	1m	3m	12m
Actual	2.7	(16.6)	23.5
Relative*	(1.3)	(22.3)	4.8

* % Relative to local index

Analyst

John Savin

BioInvent International (BINV)

INVESTMENT SUMMARY

BioInvent is raising SEK22m at SEK2.10/share to give enough working capital until the end of 2013. The new CEO, Mikael Oredsson, assumes his position on 19 August. The company has a cost base of SEK75m before revenues in 2013. There was SEK100m of cash on 31 December. The BI-505 Phase I dose-escalating and safety study indicated a dose of 10mg/kg. BI-505 is in a 10-patient Phase IIa in "smouldering" multiple myeloma. Two preclinical antibodies have entered development: ADC-1013, a co-development with Alligator to stimulate an anti-cancer immune response, and BI-1206, an in-house development against CD32b. This may be effective in non-Hodgkin's Lymphoma.

INDUSTRY OUTLOOK

BioInvent wants to partner BI-505. An example deal by GenMab gained $55m upfront and $88m in equity with milestones and a 10%+ royalty in a Phase I deal. The n-CoDeR licence with Mitsubishi Tanabe has been extended with further fee income. Another partner has paid a clinical milestone on an n-CoDeR antibody on Phase I entry.

Y/E Dec	Revenue (SEKm)	EBITDA (SEKm)	PBT (SEKm)	EPS (fd) (öre)	P/E (x)	P/CF (x)
2011	125.0	(66.0)	(67.0)	(1.00)	N/A	N/A
2012	43.0	(148.0)	(151.0)	(1.92)	N/A	N/A
2013e	45.0	(24.0)	(29.0)	(0.39)	N/A	N/A
2014e	47.0	(23.0)	(28.0)	(0.38)	N/A	N/A

Sector: Pharma & healthcare

Price: A$0.40
Market cap: A$148m
Forecast net cash (A$m) 12.5
Forecast gearing ratio (%) N/A
Market ASX, OTC

Share price graph (A$)

Company description

Bionomics is an Australian biotech company focused on developing small molecule products for cancer, anxiety, epilepsy and multiple sclerosis. Its lead programmes are a VDA and an anxiolytic compound.

Price performance

%	1m	3m	12m
Actual	2.9	(1.4)	20.7
Relative*	0.4	(2.1)	3.1

* % Relative to local index

Analyst

Robin Davison

Bionomics (BNO)

INVESTMENT SUMMARY

Bionomics has completed enrolment of the 135-patient randomised stage of its DisrupTOR-1 Phase II study of BNC105 in renal cell carcinoma. This puts data read-out on track for January 2014, which is likely to represent a major catalyst for the stock. Our risk-adjusted net present value of Bionomics' pipeline remains A$275m and adjusting for cash indicates an overall value of A$300m or A$0.72/share.

INDUSTRY OUTLOOK

Bionomics' lead compound is the small molecule vascular disrupting agent, BNC105, which is in separate Phase I/II trials for renal cell carcinoma and ovarian cancer. An anti-anxiety agent BNC210 (renamed IW-2143) is licensed to Ironwood Pharmaceuticals, which is currently conducting a Phase Ia/Ib study. A cancer stem cell targeting agent, BNC101, is in late preclincal development.

Y/E Jun	Revenue (A$m)	EBITDA (A$m)	PBT (A$m)	EPS (c)	P/E (x)	P/CF (x)
2011	3.7	(9.3)	(9.5)	(2.7)	N/A	N/A
2012	8.9	(3.3)	(2.5)	(0.7)	N/A	N/A
2013e	12.5	(4.5)	(4.5)	(1.2)	N/A	N/A
2014e	5.3	(11.6)	(11.6)	(3.1)	N/A	N/A

Sector: Pharma & healthcare

Price:	€0.34
Market cap:	€154m
Forecast net cash (€m)	5.1
Forecast gearing ratio (%)	N/A
Market	OMX

Share price graph (€)

Company description

Biotie Therapies is a Finnish/US biotech company focused on CNS disorders. Selincro (alcohol dependence) is marketed in Europe (partner: Lundbeck); tozadenant (Parkinson's) will start Phase III in H115 (partner: UCB).

Price performance

%	1m	3m	12m
Actual	0.0	(8.1)	(8.1)
Relative*	(1.8)	(14.2)	(23.4)

* % Relative to local index

Analyst

Christian Glennie

Biotie Therapies (BTH1V)

INVESTMENT SUMMARY

Biotie's review of its pipeline options and/or new licensing opportunities is expected to conclude in Q313. The company is planning to start Phase III studies of tozadenant (A2a antagonist) for Parkinson's disease in H115, with costs reimbursed by partner UCB (>$100m over six years). Partner Lundbeck is now commercialising alcohol dependence drug Selincro in the UK, Norway, Finland, Poland and the Baltic countries; further EU launches are expected in 2013 and 2014, with Biotie to receive milestones and royalties. A $1m option deal to acquire Neurelis, for its intranasal diazepam to treat acute epileptic seizures, was recently secured. Biotie holds c €45m in cash.

INDUSTRY OUTLOOK

The launch of Selincro in Europe heralds a new treatment concept for alcohol dependence (affecting 14m people in the EU), providing an alternative to complete abstinence, often not an attainable goal. The Phase IIb data for tozadenant are robust and competitive against current and pipeline Parkinson's agents.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	1.0	(28.3)	(20.8)	(3.58)	N/A	N/A
2012	4.8	(21.8)	(23.0)	(5.54)	N/A	N/A
2013e	34.1	3.6	3.4	0.76	44.7	44.0
2014e	24.8	(8.3)	(8.6)	(1.89)	N/A	N/A

Sector: Pharma & healthcare

Price:	390.6p
Market cap:	£1408m
Forecast net cash (£m)	27.9
Forecast gearing ratio (%)	N/A
Market	LSE

Share price graph (p)

Company description

BTG is a UK-based biopharmaceutical company with a direct commercial presence in US acute care medicine and interventional oncology. It has a number of internal and partnered R&D programmes.

Price performance

%	1m	3m	12m
Actual	6.0	13.4	(5.7)
Relative*	1.3	7.0	(20.4)

* % Relative to local index

Analyst

Michael Aitkenhead

BTG (BTG)

INVESTMENT SUMMARY

BTG's recent acquisitions of TheraSphere and EkoSonic represent an inflection point for its Interventional Medicine (IM) business. The addition of two profitable, growing and complementary platforms to its existing portfolio could take IM sales to c £450m within 10 years. We value BTG at £1.86bn, or 516p per share. With marketed assets worth 357p per share, this implies downside protection and material upside to the current price.

INDUSTRY OUTLOOK

BTG presents a defensive growth business whose valuation is underpinned by the DCF value of its marketed assets. The acquisitions of TheraSphere and EKOS have created a leading IM business with critical mass and significant growth potential.

Y/E Mar	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (fd) (p)	P/E (x)	P/CF (x)
2012	197.0	57.7	57.6	14.9	26.2	26.4
2013	233.7	75.1	70.4	18.9	20.7	21.0
2014e	284.3	66.5	64.4	15.9	24.6	39.1
2015e	351.5	90.6	88.0	18.6	21.0	26.4

Sector: Pharma & healthcare

Price:	A$0.30
Market cap:	A$12m
Forecast net cash (A$m)	8.4
Forecast gearing ratio (%)	N/A
Market	ASX

Share price graph (A$)

Company description

Circadian's focus is on its VEGF-C and VEGF-D portfolio, with a receptor blocking antibody (IMC-3C5) in Phase I trials with ImClone (Lilly), and a VEGF-C targeting antibody (VGX-100) due to enter glioblastoma trials in late 2011.

Price performance

%	1m	3m	12m
Actual	(13.8)	(3.8)	(41.9)
Relative*	(15.8)	(4.6)	(50.3)

* % Relative to local index

Analyst

John Savin

Circadian Technologies (CIR)

INVESTMENT SUMMARY

Circadian has three operating companies: Ceres Oncology, Opthea and Precision Diagnostics. The Ceres case is the potential of VGX-100 (completing Phase I) to reduce secondary lymphoedema, a side effect of major breast cancer surgery. This may start Phase II in Q413. The major market is the potential of VGX-100 in combination with Avastin in solid tumours. This requires a partnering deal, assumed in 2014. Opthea is developing VGX-300 (preclinical), which may be used in wet AMD. Precision is developing a speciality diagnostic business. The Imclone-partnered IMC-3C5 could produce Phase I data in H213. Cash on 31 December was A$12.1m.

INDUSTRY OUTLOOK

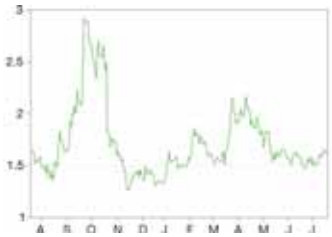
VGX-300 may have a market potential in wet Acute Macular Degeneration similar to that of Eylea and Lucentis: $2.6bn sales in 2012. VGX-300 needs funding or a deal to progress, but major pharma interest in a preclinical deal has been strong. The FDA has granted Humanitarian Use Device status for Precision's VEGF-D test to monitor lymphangioleiomyomatosis.

Y/E Jun	Revenue (A$m)	EBITDA (A$m)	PBT (A$m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	0.4	(11.5)	(10.1)	(20.9)	N/A	N/A
2012	0.5	(8.4)	(7.5)	(10.2)	N/A	N/A
2013e	0.6	(8.4)	(8.1)	(16.6)	N/A	N/A
2014e	0.7	(8.8)	(9.0)	(18.5)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$1.60
Market cap:	US$72m
Forecast net cash (US$m)	5.3
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)



Company description

Cleveland BioLabs is a clinical-stage US biotechnology company focused on biodefence and oncology. Entolimod (CBLB502) is being developed as both a radiation countermeasure (pivotal studies) and a cancer treatment (Phase I).

Price performance

%	1m	3m	12m
Actual	7.4	(14.0)	(3.0)
Relative*	3.4	(20.9)	(21.1)

* % Relative to local index

Analyst

Christian Glennie

Cleveland BioLabs (CBLI)

INVESTMENT SUMMARY

Recently published research supports the mechanistic rationale for CBL0137, Cleveland's curaxin candidate targeting FACT, a potential marker and target for aggressive cancers. Meanwhile, a US government (BARDA) development contract (c $50m) is awaited for Entolimod (CBLB502), a medical countermeasure to reduce death from total body irradiation. Pivotal animal efficacy and human safety studies have been completed, although further trials are required to gain approval for Entolimod under the FDA's Animal Efficacy Rule. Procurement contracts could also be secured by 2015. Entolimod (TLR5 agonist) is also in Phase I development as a targeted anti-cancer agent.

INDUSTRY OUTLOOK

Entolimod is the most advanced radiation countermeasure in development. To date, five biodefence products have gained approval under the FDA's animal efficacy rule (2002), and $2.6bn has been committed by the US government to develop/procure counter-terrorism agents through the $5.6bn Project BioShield Act (2004).

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	8.8	(25.6)	(25.1)	(0.73)	N/A	N/A
2012	3.6	(30.5)	(30.1)	(0.69)	N/A	N/A
2013e	13.7	(23.2)	(22.6)	(0.44)	N/A	N/A
2014e	14.0	(25.6)	(25.3)	(0.49)	N/A	N/A

Sector: Pharma & healthcare

Price:	779.0p
Market cap:	£228m
Forecast net cash (£m)	30.0
Forecast gearing ratio (%)	N/A
Market	LSE

Share price graph (p)

Company description

Consort Medical is an international medical devices company. It currently has only the Bespak division (inhalation and injection technologies) since King Systems (airway management products) was sold in Dec 2012.

Price performance

%	1m	3m	12m
Actual	(2.4)	(0.8)	11.9
Relative*	(6.7)	(6.3)	(5.5)

* % Relative to local index

Analyst

Franc Gregori

Consort Medical (CSRT)

INVESTMENT SUMMARY

Consort Medical's investment case hinges on Bespak's growth prospects, with the new product flow from the development pipeline set to underpin double-digit earnings growth over the medium term. The prospects appear very promising, although commercial sensitivity means that the visibility, both in terms of timings and revenue potential, is low. The new GSK respiratory products (based around the Ellipta inhaler device) are not the only drivers. Although having a much lower profile, Nicoventure's Oxette tobacco-free 'cigarette' device could be a valuable revenue generator. The earn-out from the King Systems divestment (completed in February) should see a $10.0m payment before 30 September 2013.

INDUSTRY OUTLOOK

Bespak is a leader in producing medical devices for the pharmaceutical industry, with proven expertise in high-volume, high-quality manufacture of regulated products. Bespak's core drug-delivery franchise is inhalation, although it has diversified into auto-injectors, nasal delivery and point-of-care diagnostics through the Atlas Genetics investment.

Y/E Apr	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (fd) (p)	P/E (x)	P/CF (x)
2012	93.5	25.5	16.8	54.4	14.3	9.1
2013	95.0	28.2	19.8	60.0	13.0	8.6
2014e	99.6	23.8	16.8	41.7	18.7	10.0
2015e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	CHF3.40
Market cap:	CHF76m
Forecast net debt (CHFm)	19.6
Forecast gearing ratio (%)	159.0
Market	Swiss Stock Exchange

Share price graph (CHF)

Company description

Cytos Biotechnology is a public biopharmaceutical company focused on developing targeted immunotherapies. Its lead candidate CYT003 is a biologic in Phase II clinical development as a potential new treatment for allergic asthma.

Price performance

%	1m	3m	12m
Actual	(10.1)	(16.5)	36.3
Relative*	(12.3)	(19.8)	8.7

* % Relative to local index

Analyst

Michael Aitkenhead

Cytos Biotechnology (CYTN)

INVESTMENT SUMMARY

Cytos Biotechnology's investment case hinges on how its main asset, CYT003, progresses through a Phase IIb study in moderate-to-severe allergic asthma. Headline results are expected in H114. The company navigated its way through a funding crunch and has sufficient cash to complete the trial. However, convertible loan notes and bonds are due for repayment in February 2015. A positive outcome should mean that some of the debt due in 2015 will be converted and the rest paid down from the exercise of warrants (assuming the share price rises as expected), and that Cytos will have sufficient time to partner CYT003. Cytos also has an immunotherapy partnered with Novartis (CAD106 in Phase II for Alzheimer's disease), with Pfizer (PF-753/752 in Phase I for allergic rhinitis) and A*STAR (an influenza vaccine in Phase I).

INDUSTRY OUTLOOK

The potential of immunotherapies is increasingly being recognised, especially in cancer and auto-immune indications.

Y/E Dec	Revenue (CHFm)	EBITDA (CHFm)	PBT (CHFm)	EPS (fd) (CHFc)	P/E (x)	P/CF (x)
2011	N/A	N/A	N/A	N/A	N/A	N/A
2012	1.1	(15.0)	(11.7)	(66.7)	N/A	N/A
2013e	1.2	(20.7)	(25.0)	(124.1)	N/A	N/A
2014e	1.2	(12.7)	(20.8)	(102.9)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$2.50
Market cap:	US$77m
Forecast net cash (US$m)	16.1
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)

Company description

CytRx is a US biopharmaceutical company focused on oncology. Lead programme, aldoxorubicin, is in a Phase II study for pancreatic cancer. Tamibarotene is in Phase II trial for NSCLC, while Bafetinib has completed a Phase II study in B-CLL.

Price performance

%	1m	3m	12m
Actual	20.0	(8.0)	(48.4)
Relative*	15.5	(15.5)	(58.0)

* % Relative to local index

Analyst

Michael Aitkenhead

CytRx (CYTR)

INVESTMENT SUMMARY

2013 could be transformative for CytRx as it delivers important clinical data and trial initiations for lead programme aldoxorubicin. The company is focused on exploiting the potential of this drug in advanced soft tissue sarcoma (STS) and primary brain cancer (GBM). Recent positive aldoxorubicin data increase our confidence in both the STS and GBM opportunities. We project peak aldoxorubicin sales of $1.1bn. Our rNPV is $139m, or $4.60 per share, which could rise to $170m following positive Phase IIb data in front-line STS.

INDUSTRY OUTLOOK

CytRx has a strong rationale for advancing aldoxorubicin, a tumour-targeted doxorubicin conjugate, into a pivotal Phase III study for the second-line treatment of STS. Intitation of Phase III development is supported by positive Phase I/II data in relapsed/refractory STS; doxorubicin's efficacy in STS; limited competition; high unmet medical need; and a clear regulatory pathway.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	0.3	(22.0)	(21.8)	(0.77)	N/A	N/A
2012	0.1	(19.0)	(18.9)	(0.47)	N/A	N/A
2013e	0.1	(22.2)	(22.2)	(0.53)	N/A	N/A
2014e	0.1	(23.8)	(23.9)	(0.57)	N/A	N/A

Sector: Pharma & healthcare

Price:	14.8p
Market cap:	£24m
Forecast net debt (£m)	0.4
Forecast gearing ratio (%)	14.0
Market	AIM

Share price graph (p)

Company description

Deltex is a UK medical device company that manufactures and sells the CardioQ-oesophageal Doppler monitor and disposable probes for haemodynamic monitoring to reduce recovery times after high-risk and major surgery.

Price performance

%	1m	3m	12m
Actual	(16.9)	(1.7)	(41.3)
Relative*	(20.6)	(7.2)	(50.4)

* % Relative to local index

Analyst

John Savin

Deltex Medical Group (DEMG)

INVESTMENT SUMMARY

The July interim trading update showed sales of £2.9m for the six months to 30 June 2013. 2012 interims of £3.2m were boosted by £0.4m of “barter” monitor sales, so in cash terms H113 sales are effectively level. The 2013 sales outlook is reliant on strong H2 surgical probe growth to the NHS plus EU growth. The 2013 forecast will be revised after interim results in September.

INDUSTRY OUTLOOK

Deltex gave a briefing on surgical fluid management in the NHS and on the Premier study in the US. In England, there are four surgical procedures covering 150,000 patients, where Enhanced Recovery with fluid management has very strong evidence. Doppler use is one aspect of the ER package, but has one of the slowest adoption rates. The NHS is initially targeting use in 75,000 procedures. In the US, Premier is currently analysing data from different member hospitals. The next, three-hospital study should start in Q114. As the US moves to fixed-fee payments, it is likely to become Deltex’s major market from 2015.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	6.3	(0.8)	(1.1)	(0.71)	N/A	N/A
2012	6.8	(0.7)	(1.2)	(0.72)	N/A	N/A
2013e	7.7	(1.0)	(1.3)	(0.80)	N/A	N/A
2014e	9.1	(0.1)	(0.3)	(0.21)	N/A	N/A

Sector: Pharma & healthcare

Price:	€0.70
Market cap:	€38m
Forecast net cash (€m)	1.0
Forecast gearing ratio (%)	N/A
Market	Alternext Paris

Share price graph (€)

Company description

Diaxonhit is a French fully integrated leader in in-vitro diagnostics from the discovery to commercialisation with products in infectious diseases, Alzheimer's disease and cancer. It is also developing therapeutic products for neurodegeneration.

Price performance

%	1m	3m	12m
Actual	(3.0)	(16.7)	(36.8)
Relative*	(5.2)	(22.7)	(47.7)

* % Relative to local index

Analyst

Wang Chong

Diaxonhit (ALEHT)

INVESTMENT SUMMARY

Diaxonhit is a new fully integrated IVD company formed in December 2012, when Exonhit acquired InGen BioSciences, the leading in vitro diagnostics (IVD) distributor in France. The investment case for the new company is the synergy provided by commercialising lead product, AclarusDx, a blood-based aid for the diagnosis of Alzheimer's disease (AD), and other proprietary products through its own salesforce. Diaxonhit also has an interest in the Phase II trial-stage neuropathic pain programme, EHT/AGN 0001, which is partnered with Allergan. Under the terms of a recent licence agreement, Diaxonhit will commercialise US molecular diagnostic company XDx's AlloMap heart transplant test.

INDUSTRY OUTLOOK

The molecular diagnostic market is worth c $1.5bn and growing at c 6% as diagnostic products enable patients to receive better treatments. Pharmaceutical companies are also forming more R&D partnerships with biotech companies with promising platform technologies, which increases the likelihood of Diaxonhit entering new R&D collaborations.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	5.0	(7.3)	(7.8)	(21.8)	N/A	N/A
2012	5.4	(6.1)	(6.4)	(17.1)	N/A	N/A
2013e	31.3	(9.0)	(9.2)	(15.9)	N/A	N/A
2014e	34.0	(9.1)	(9.4)	(16.0)	N/A	N/A

Sector: Pharma & healthcare

Price:	35.3p
Market cap:	£93m
Forecast net cash (£m)	41.2
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

e-Therapeutics is a drug discovery and development company with a proprietary network pharmacology discovery platform and a clinical pipeline (with potential to be out-licensed post-Phase II).

Price performance

%	1m	3m	12m
Actual	0.0	42.4	(3.4)
Relative*	(4.4)	34.4	(18.4)

* % Relative to local index

Analyst

Franc Gregori

e-Therapeutics (ETX)

INVESTMENT SUMMARY

e-Therapeutics is well placed, with funding in place (net cash of £48m) to support current spending plans through to 2017, by which time major value inflection points should be reached. ETS2101, for various solid tumours, is the major focus and is progressing through Phase I trials with encouraging early results. A proof-of-concept study for the antidepressant ETS6103 is due to produce results in H214. The first new drug candidate to emerge into development from the newly bolstered discovery platform is expected by end-2013.

INDUSTRY OUTLOOK

Network pharmacology could potentially revolutionise drug discovery and shorten the path to market by minimising technical risks (failure on safety or efficacy grounds) and drug development costs. e-Therapeutics is well positioned, with limited direct competition and growing industry interest in systems biology-based multi-target approaches to drug discovery.

Y/E Jan	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2012	0.0	(4.0)	(3.9)	(2.5)	N/A	N/A
2013	0.0	(5.2)	(5.0)	(3.0)	N/A	N/A
2014e	0.0	(8.8)	(8.3)	(2.9)	N/A	N/A
2015e	0.0	(8.9)	(8.5)	(2.7)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$0.10
Market cap:	US$9m
Forecast net debt (US$m)	N/A
Forecast gearing ratio (%)	N/A
Market	OMX, OTCQX US

Share price graph (US$)

Company description

EpiCept is a specialty pharmaceutical company focused on the development and commercialisation of pharmaceutical products for cancer treatment and pain management.

Price performance

%	1m	3m	12m
Actual	8.6	16.9	(45.7)
Relative*	4.5	7.5	(55.8)

* % Relative to local index

Analyst

Wang Chong

EpiCept (EPCT)

INVESTMENT SUMMARY

EpiCept's search for a strategic transaction has resulted in a planned reverse-merger with Immune Pharmaceuticals, a private Israel-based biopharma company focused on antibodies for inflammatory disease and cancer. The resulting company, to be called Immune Pharmaceuticals Inc, will have bertilimumab, which is ready to enter Phase II trials for ulcerative colitis (UC), as its lead product, together with three other clinical-stage programmes. EpiCept shareholders could end up with 22.5% of the new entity, which could offer its shareholders the best option to participate in economic value created by a potential future development/commercial partnership for AmiKet, its topical product for chemotherapy-induced peripheral neuropathy. A shareholder meeting to approve the terms of the deal is due on 6 August.

INDUSTRY OUTLOOK

Bertilimumab is one of relatively few biological therapies in development for UC. Aside from two approved biologicals for UC - Remicade and Humira - there are two candidates in registration and seven competing agents currently undergoing Phase II studies.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	1.0	(14.1)	(15.3)	(22.9)	N/A	N/A
2012	7.8	(0.6)	(1.8)	(3.0)	N/A	N/A
2013e	N/A	N/A	N/A	N/A	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	€1.60
Market cap:	€19m
Forecast net debt (€m)	5.0
Forecast gearing ratio (%)	154.0
Market	FRA

Share price graph (€)

Company description

Epigenomics is a German molecular diagnostics company focused on early detection of cancer. Its main product is Epi proColon, a blood-based DNA test for colorectal cancer that uses a sophisticated PCR assay to detect methylated copies of the septin9 gene.

Price performance

%	1m	3m	12m
Actual	(5.0)	(9.6)	2.1
Relative*	(6.5)	(19.1)	(17.2)

* % Relative to local index

Analyst

Wang Chong

Epigenomics (ECX)

INVESTMENT SUMMARY

Acceptance of its PMA application and notification of priority review status puts Epigenomics' bood-based Epi proColon on track for approval in Q413. The PMA was based on two large studies that showed sensitivity (across all CRC stages) of 68-72% at a specificity of 80-81%. However, the overall performance data may not be the key determinant of success in the market. The ability to identify early-stage CRC and the presumed patient preference for blood- vs stool-based tests may prove to be as important. Although Epigenomics has a cash runway until Q413, investors should expect the company to seek to raise further equity finance in 2013.

INDUSTRY OUTLOOK

Epi proColon offers patients a simple and convenient alternative to faecal occult blood testing and should increase compliance for colorectal screening by addressing individuals not currently participating in screening programmes. Epi proLung is an aid in the diagnosis of lung cancer from bronchial lavage using the SHOX2 biomarker.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	1.4	(7.9)	(8.3)	(96.9)	N/A	N/A
2012	1.0	(10.8)	(10.9)	(125.3)	N/A	N/A
2013e	2.0	(11.0)	(11.1)	(108.0)	N/A	N/A
2014e	13.1	(3.6)	(3.7)	(34.6)	N/A	N/A

Sector: Pharma & healthcare

Price:	580.0p
Market cap:	£56m
Forecast net debt (£m)	N/A
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Epistem has a profitable contract services business and an emerging clinical biomarker technology with Sanofi as a big client. Epistem is preparing to launch Genedrive, its novel molecular diagnostic device, initially in the TB market.

Price performance

%	1m	3m	12m
Actual	0.9	5.5	43.2
Relative*	(3.6)	(0.5)	21.0

* % Relative to local index

Analyst

Emma Ulker

Epistem Holdings (EHP)

INVESTMENT SUMMARY

Epistem reported H113 revenue of £3.1m - contract services and biomarker revenues remained stable at £1.3m. The planned commercial launch of GeneDrive has shifted into H114 (from H213) through Xcelris in India and the Indian sub-continent, and through Becton Dickinson for global ex-US sales. GeneDrive could provide a large potential market opportunity once Indian regulatory approval is finalised during 2013. The BD deal provides $1m cash with further milestone payments of up to $3m, plus escalating supply volumes to 2017. Epistem is looking for partnerships in the novel therapies division, targeting cash use for the GeneDrive launch. FY results will be announced in September.

INDUSTRY OUTLOOK

Epistem believes GeneDrive (a DNA-based diagnostic point-of-care system) will change the shape of the DNA diagnostics. The new global (ex-India) deal with BD on GeneDrive for TB adds strongly to this case. GeneDrive has now been CE marked, but published data are very limited. The TB market seems a good one as other tests are unreliable or expensive.

Y/E Jun	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	5.8	(0.4)	(0.6)	(6.6)	N/A	N/A
2012	5.6	(1.8)	(1.9)	(16.6)	N/A	N/A
2013e	N/A	N/A	N/A	N/A	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	CHF0.70
Market cap:	CHF166m
Forecast net cash (CHFm)	20.5
Forecast gearing ratio (%)	N/A
Market	Swiss Stock Exchange

Share price graph (CHF)

Company description

Evolva is an international biosynthesis company. It has developed a technology platform that it uses to create and produce high-value specialty chemicals for nutritional and consumer health products and medicines.

Price performance

%	1m	3m	12m
Actual	(2.8)	(10.4)	94.3
Relative*	(5.2)	(13.9)	55.0

* % Relative to local index

Analyst

Mick Cooper

Evolva (EVE)

INVESTMENT SUMMARY

Evolva has an innovative biosynthesis platform focused on developing new production methods for nutritional and consumer health products. Its key programme is for the sweetener stevia, which has recently been partnered with Cargill. As part of the agreement, Evolva has received a CHF4.5m equity investment from Cargill, could be paid up to $7.5m in milestones and has the right to a 45% participation in the final business. The products could be launched in 2015/16 and will initially be targeted at the $4bn beverage sweetener market. It also has a vanilla project (partnered with IFF, which could be launched in late-2013/early-2014), and ones for resveratrol (on market) and saffron. It has nutritional alliances with Ajinomoto and Roquette as well. Evolva raised CHF31.3m in equity in March, which could take it to profitability.

INDUSTRY OUTLOOK

The manufacturers of nutritional and consumer health products are always interested in cheaper production methods, especially if the product is natural and has health benefits. Evolva is primarily targeting this market.

Y/E Dec	Revenue (CHFm)	EBITDA (CHFm)	PBT (CHFm)	EPS (CHFc)	P/E (x)	P/CF (x)
2011	11.1	(22.4)	(25.5)	(13.4)	N/A	N/A
2012	7.0	(16.8)	(18.8)	(7.8)	N/A	N/A
2013e	11.0	(14.3)	(16.4)	(7.4)	N/A	N/A
2014e	12.7	(13.3)	(15.3)	(6.4)	N/A	N/A

Sector: Pharma & healthcare

Price:	€2.60
Market cap:	€304m
Forecast net cash (€m)	48.3
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

Evotec is a drug discovery business that provides outsourcing solutions to pharmaceutical companies, including Boehringer Ingelheim, Pfizer and Roche. It has operations in Germany, the UK and the US.

Price performance

%	1m	3m	12m
Actual	(7.5)	20.9	3.6
Relative*	(9.0)	8.3	(15.9)

* % Relative to local index

Analyst

Mick Cooper

Evotec (EVT)

INVESTMENT SUMMARY

Evotec's underlying sales grew by 5% in Q113 to €16.2m, although total revenues fell by 15% to €17.1m, as no milestone payments were received. However, Evotec is maintaining its FY13 financial guidance with sales of €90-100m, and it is expecting milestones this year to be weighted towards H213. A key focus of FY13 is to expand its academic collaborations, in particular its CureX initiatives. At least four more are expected to be formed this year. Their potential is shown by CureBeta with Harvard, which led to the major strategic alliance with Janssen to develop a product that could slow or even reverse disease progression in diabetics. Evotec remains focused on providing the best possible service to clients, and to this end is moving all its Indian operations to the UK, so they are closer to those of clients.

INDUSTRY OUTLOOK

Pharmaceutical companies are outsourcing drug discovery activities to improve their productivity and decrease the fixed costs associated with them. Evotec's growth depends on its ability to provide a high-quality integrated service.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	80.1	12.0	7.5	5.6	46.4	28.3
2012	87.3	9.1	1.3	0.4	650.0	25.0
2013e	97.2	14.6	6.8	5.0	52.0	25.2
2014e	107.9	18.7	10.7	8.2	31.7	15.7

Sector: Pharma & healthcare

Price:	48.0p
Market cap:	£85m
Forecast net cash (£m)	37.5
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

GW Pharmaceuticals is a UK speciality pharma company focused on developing cannabinoids as pharmaceuticals. Lead product Sativex is marketed in a number of European countries for multiple sclerosis-associated spasticity.

Price performance

%	1m	3m	12m
Actual	1.6	(15.4)	(34.3)
Relative*	(2.9)	(20.2)	(44.5)

* % Relative to local index

Analyst

Michael Aitkenhead

GW Pharmaceuticals (GWP)

INVESTMENT SUMMARY

GW Pharma is focused on fully exploiting the potential of its lead cannabinoid drug, Sativex, and its broad cannabinoid-based R&D pipeline. With pro forma cash of c £42m following its US IPO ($31.2m raised), GW is well capitalised to execute its commercial strategy (maximising the value of Sativex) and R&D plans (advancing its five cannabinoid therapies). The US listing also precedes key US clinical milestones for Sativex, including Phase III data in cancer pain (mid-2014) and the start of Phase III trials in MS spasticity (H114). Our base-case DCF valuation is £178m or 101p/share. The R&D portfolio and US opportunity for Sativex in MS offer pure upside.

INDUSTRY OUTLOOK

GW is the leader in the field of cannabinoid medicines, which have the potential to become novel therapies for a broad range of diseases. Cannabinoids are diverse chemical compounds that GW extracts from different cannabis plant varieties (chemotypes) it has bred. Sativex is GW's lead medicine; we estimate it will achieve 5-10% market share in its approved indications.

Y/E Sep	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	N/A	N/A	N/A	N/A	N/A	46.5
2012	33.1	2.8	2.2	2.6	18.5	N/A
2013e	23.7	(8.2)	(8.8)	(4.2)	N/A	N/A
2014e	23.0	(4.5)	(5.0)	(1.4)	N/A	N/A

Sector: Pharma & healthcare

Price:	€0.60
Market cap:	€12m
Forecast net cash (€m)	4.1
Forecast gearing ratio (%)	N/A
Market	Alternext Paris

Share price graph (€)

Company description

Hybrigenics is a French biotech company. It provides protein-protein and small molecule analysis services and is conducting Phase II studies on lead drug inecalcitol in chronic lymphocytic leukaemia and prostate cancer.

Price performance

%	1m	3m	12m
Actual	(6.1)	(25.3)	(31.9)
Relative*	(8.2)	(30.7)	(43.6)

* % Relative to local index

Analyst

Emma Ulker

Hybrigenics (ALHYG)

INVESTMENT SUMMARY

Hybrigenics' key value driver is its vitamin D3 analogue inecalcitol in development primarily for prostate cancer and chronic lymphocytic leukaemia (CLL). Interim results of the current PII CLL trial, targeting delaying start of chemotherapy in early stage patients, were promising. Notably, of the five patients who received inecalcitol for a minimum of six months, one saw a 50% drop in blood lymphocytes count (BLC) at six months falling 80% in month seven. Two patients showed a levelling-off of BLC growth rate with treatment. Meanwhile, Hybrigenics is progressing its strategy to expand its protein services division having acquired the yeast-two hybrid assets of key competitor, Swiss company Dualsystems.

INDUSTRY OUTLOOK

Inecalcitol is being developed in three major indications and faces competition from existing drugs and those in development. However, its good safety profile could give it an advantage. Hybrigenics is pushing into the innovative field of systems biology, applying its expertise for protein-gene analysis to better understand diseases and their therapies.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	6.6	(2.0)	(2.5)	(14.2)	N/A	N/A
2012	5.9	(2.3)	(2.4)	(13.2)	N/A	N/A
2013e	6.6	(2.4)	(2.6)	(10.3)	N/A	N/A
2014e	6.7	(2.0)	(2.1)	(6.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	285.0p
Market cap:	£284m
Forecast net cash (£m)	50.5
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Imperial Innovations is a technology transfer, incubation and venture investment company. It invests in ventures from Imperial College London, Cambridge and Oxford Universities and UCL. The majority of its investments are bio/med tech.

Price performance

%	1m	3m	12m
Actual	(10.2)	1.8	(0.5)
Relative*	(14.2)	(3.9)	(16.0)

* % Relative to local index

Analyst

Robin Davison

Imperial Innovations (IVO)

INVESTMENT SUMMARY

Imperial Innovations (IVO) invested £14m in 15 portfolio companies in H113 and locked in a £4.2m fair value gain. Its largest bio/med portfolio company, Circassia, started a pivotal Phase III trial of its lead allergy therapy, ToleroMune cat, which could reach the market by 2016. Trial initiation, data and potential regulatory filings (around end-2014) mark significant potential value inflection points for Circassia and for Imperial through its 20.3% holding. Portfolio company, Cell Medica, treated its first paediatric patient in a Phase I/II trial of Cytovir for treatment of adenovirus infections, while Autifony intiated a Phase I trial of hearing loss product, AUT00063. IVO's CEO Susan Searle recently stepped down and has been replaced by former CIO Russ Cummings.

INDUSTRY OUTLOOK

The investment case centres on the real value of the portfolio and the success of the strategy of investing in maturing companies. Portfolio companies are valued per International Private Equity and Venture Capital Valuation guidelines, and hence there is potential for significant value creation if exits are achieved at valuations in excess of these.

Y/E Jul	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	4.5	(4.4)	(2.8)	(4.5)	N/A	N/A
2012	4.3	(6.2)	(4.0)	(6.3)	N/A	N/A
2013e	3.6	(7.6)	(6.3)	(6.3)	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	€2.50
Market cap:	€96m
Forecast net cash (€m)	16.4
Forecast gearing ratio (%)	N/A
Market	NYSE Euronext

Share price graph (€)

Company description

Innate is a French biotech developing first-in-class immunotherapy drugs for cancer and inflammatory diseases by developing new monoclonal antibodies targeting receptors and pathways controlling the activation of innate immunity cells.

Price performance

%	1m	3m	12m
Actual	2.4	5.5	67.3
Relative*	0.1	(2.2)	38.5

* % Relative to local index

Analyst

Wang Chong

Innate Pharma (IPH)

INVESTMENT SUMMARY

Innate Pharma's investment case largely depends on clinical development milestones being achieved with lirilumab (IPH2102) in Phase II for cancer and IPH2201 in Phase I for inflammatory diseases, licensed to Bristol-Myers Squibb (BMS) and Novo Nordisk respectively. Data from a Phase I study with IPH2101 in acute myeloid leukaemia showed a significant overall survival benefit in patients receiving higher doses. Also, BMS started two large Phase I trials (n=150) in solid tumours (NSCLC, RCC, CRC, ovarian and melanoma) in combination with its anti-PD1 antibody and ipilimumab (Yervoy). Innate has two other products in preclinical studies, IPH33 and IPH41, and aims to out-license the former this year for the treatment of chronic respiratory inflammation. It had €32.6m at FY12, sufficient to run to mid-2015.

INDUSTRY OUTLOOK

Innate Pharma is a leader in the development of new monoclonal antibodies that target receptors and pathways controlling the activation of innate immunity cells.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	11.7	(6.7)	(7.0)	(18.5)	N/A	7.5
2012	14.3	(2.5)	(3.2)	(8.5)	N/A	N/A
2013e	12.4	(4.5)	(4.9)	(13.0)	N/A	N/A
2014e	11.5	(5.9)	(6.4)	(16.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$6.70
Market cap:	US$102m
Forecast net cash (US$m)	17.7
Forecast gearing ratio (%)	N/A
Market	

Share price graph (US$)

Company description

LeMaitre Vascular is a global provider of medical devices and implants for the treatment of peripheral vascular disease. The company develops, manufactures and markets vascular devices to addresses the needs of vascular surgeons.

Price performance

%	1m	3m	12m
Actual	1.5	10.4	9.0
Relative*	(2.3)	1.5	(11.4)

* % Relative to local index

Analyst

Jason Zhang

LeMaitre Vascular (LMAT)

INVESTMENT SUMMARY

By focusing on niche markets and offering high-quality and differentiated devices used by vascular surgeons, LeMaitre Vascular has been able to deliver sustained revenue growth outperformance. It has achieved sales growth averaging 8-10% a year, against a broader market that has grown at 1-2% a year over the past 15 years. With planned sales force increases, selected geographic expansion and acquisitions of complementary products, such as the recent acquisition of assets of Clinical Instruments International, the company should maintain this growth trajectory and deliver a low-risk but steady return of investment to investors.

INDUSTRY OUTLOOK

LeMaitre operates in markets with single-digit volume growth and increasing pricing constrains. However, the company is able to beat the secular trend by focusing on niche markets, increasing reach through sales rep growth and geography, and offering multiple complementary lines of products through acquisitions and R&D.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	57.7	8.3	6.9	13.40	50.0	32.8
2012	56.7	7.4	7.4	16.44	40.8	21.6
2013e	61.7	8.4	8.3	20.15	33.3	20.7
2014e	66.5	10.0	10.1	24.59	27.2	11.7

Sector: Pharma & healthcare

Price:	169.0p
Market cap:	£76m
Forecast net cash (£m)	21.5
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Lombard Medical Technologies is a manufacturer and supplier of cardiovascular implants. The lead product, Aorfix, a flexible endovascular stent graft for the treatment of AAA is commercialised in Europe and recently received FDA approval.

Price performance

%	1m	3m	12m
Actual	0.0	(18.9)	43.8
Relative*	(4.4)	(23.5)	21.5

* % Relative to local index

Analyst

Emma Ulker

Lombard Medical Technologies (LMT)

INVESTMENT SUMMARY

The US launch of Lombard Medical's endovascular stent Aorfix for abdominal aortic aneurysm (AAA) at a key industry conference this November is set to be a significant catalyst. The company has recruited and trained 15 sales reps and two managers for the region as planned. The lack of a competitor licensed to treat aneurysms with aortic necks over 60º, as well as strong clinical data are key commercial advantages - we forecast that revenue will more than triple by 2014. The H113 trading statement confirmed revenue of £2m, in line with our estimates, while the cash position of £34.3m, following £20.9m of equity financing, is sufficient to take Lombard through to profitability, forecast in 2016.

INDUSTRY OUTLOOK

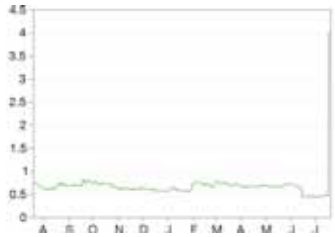
Lombard will compete with larger US corporations to achieve further penetration in the $1.3bn global AAA market on the basis of US FDA approval for Aorfix. The 0-90º label and clinical evidence provide a potential competitive edge for Aorfix in the endovascular aneurysm repair-receptive US market.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	4.0	(11.0)	(11.1)	(60.1)	N/A	N/A
2012	3.9	(8.3)	(8.9)	(42.2)	N/A	N/A
2013e	5.1	(14.6)	(14.6)	(40.2)	N/A	N/A
2014e	14.5	(7.4)	(7.6)	(15.7)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$4.00
Market cap:	US$41m
Forecast net cash (US$m)	39.0
Forecast gearing ratio (%)	N/A
Market	NYSE AMEX

Share price graph (US$)



Company description

Mast Therapeutics is a development-stage US pharmaceutical company focused on developing MST-188, undergoing a Phase III study for sickle cell disease.

Price performance

%	1m	3m	12m
Actual	0.0	0.0	0.0
Relative*	(1.6)	(10.5)	(18.9)

* % Relative to local index

Analyst

Christian Glennie

Mast Therapeutics (MSTX)

INVESTMENT SUMMARY

A recent $26m equity financing extends Mast's cash runway to 2015 when the pivotal Phase III study (EPIC) of MST-188, to treat severely painful 'crisis' episodes in patients with sickle cell disease (SCD), is expected to complete. Mast also plans to start a Phase II study in late-2013/early-2014 with MST-188 for acute limb ischaemia (ALI) (60 patients, 15-18 months). MST-188 has further potential in resuscitation following major trauma, acute decompensated heart failure, stroke and blood transfusions. Estimated end-Q213 cash of $53m is sufficient to complete the EPIC and ALI studies, and positive results could secure partners (especially ex-US) and/or fresh finance.

INDUSTRY OUTLOOK

MST-188 is the only NME in Phase III studies and could be the first approved therapy to reduce the duration of crisis episodes. Pfizer and Novartis have licensed rights to two mid-stage SCD candidates, indicating major pharma interest, and $230m has been invested in SCD-focused companies since October 2011.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.0	(13.4)	(13.3)	(47.06)	N/A	N/A
2012	0.0	(15.5)	(15.6)	(32.66)	N/A	N/A
2013e	0.0	(22.6)	(22.6)	(34.14)	N/A	N/A
2014e	0.0	(25.6)	(25.6)	(26.50)	N/A	N/A

Sector: Pharma & healthcare

Price:	€1.78
Market cap:	€18m
Forecast net debt (€m)	1.6
Forecast gearing ratio (%)	10.0
Market	MAB

Share price graph (€)

Company description

Medcom Tech distributes a wide range of innovative orthopaedic products across Spain, Portugal and Italy. Its portfolio includes knee and hip implants, plates and screws to repair bone and spine fractures, and advanced types of bone cement.

Price performance

%	1m	3m	12m
Actual	0.0	7.2	(20.9)
Relative*	2.0	6.9	(33.9)

* % Relative to local index

Analyst

Mick Cooper

Medcom Tech (MED)

INVESTMENT SUMMARY

Medcom Tech is maintaining strong revenue growth despite Spain's challenging trading conditions. Sales growth accelerated to 27.3% in H212 from 7.4% in H112, so that overall sales increased by 15.8% to €16.8m with PBT doubling to €0.5m in FY12. We forecast that this level of growth will continue with sales increasing at a CAGR of 15% over the next three years. This is possible as Medcom Tech has optimised its sales force and strengthened its balance sheet over the last year. In FY12, Medcom Tech's net debt went from €11.2m to €5.5m due to several initiatives, which have removed the working capital constraints. Its growth could still accelerate further as it is considering expanding into South-East Asia and it has established a new subsidiary, Medcom Flow.

INDUSTRY OUTLOOK

The Spanish orthopaedic market is estimated to be worth €400m. The market was growing at c 5% pa before the implementation of austerity measures, but is now estimated to be declining by c 5%. The ageing population, political pressure and technical innovations partially offset budget constraints.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	14.5	1.5	0.3	2.0	89.0	N/A
2012	16.8	2.3	0.5	4.0	44.5	5.4
2013e	19.5	4.0	2.5	17.3	10.3	3.0
2014e	22.3	5.3	4.0	28.3	6.3	5.3

Sector: Pharma & healthcare

Price:	€0.90
Market cap:	€36m
Forecast net cash (€m)	11.6
Forecast gearing ratio (%)	N/A
Market	Deutsche Börse

Share price graph (€)

Company description

Medigene is a German biotech company. Veregen (genital warts) is marketed through global partners, while RhuDex (autoimmune disorders) and EndoTAG-1 (breast cancer) are in development.

Price performance

%	1m	3m	12m
Actual	(7.6)	6.0	(26.5)
Relative*	(9.1)	(5.1)	(40.4)

* % Relative to local index

Analyst

Christian Glennie

Medigene (MDG)

INVESTMENT SUMMARY

Medigene has secured SynCore Biotechnology as a global partner for EndoTAG-1, a novel composition of paclitaxel, to fund a global Phase III study in triple negative breast cancer. The trial will start in H214 and an NDA is expected in 2018. Medigene is also developing RhuDex (CD80 inhibitor) for primary biliary cirrhosis (PBC) - a Phase II study will start in H114, dosing PBC patients for six months across four arms (3x dose and placebo), with results by end-2015. The genital warts ointment Veregen is sold in the US, Germany, Spain, Switzerland, Austria and Serbia through local partnerships (€12m in-market sales in FY12), by multiple global partners - further launches (particularly in Europe) and new partnerships are expected through 2013. Medigene's cash of c €19m (€17m at Q113 + €2.4m Syncore upfront) is sufficient to early-2015.

INDUSTRY OUTLOOK

RhuDex's development path in PBC, an orphan drug indication, offers a potentially lucrative market opportunity with limited pipeline competition.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	4.7	(16.6)	(15.5)	(0.26)	N/A	5.0
2012	6.3	(9.3)	(10.3)	(0.28)	N/A	N/A
2013e	7.5	(10.3)	(12.2)	(0.32)	N/A	N/A
2014e	10.0	(8.7)	(10.5)	(0.26)	N/A	N/A

Sector: Pharma & healthcare

Price:	€12.20
Market cap:	€189m
Forecast net cash (€m)	13.7
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

Mologen has two lead products. MGN1703 for metastatic colorectal cancer maintenance therapy and MGN1601, an allogeneic cancer cell vaccine for renal carcinoma. These use dSLIM, a stable DNA construct that stimulates the immune system.

Price performance

%	1m	3m	12m
Actual	(11.4)	(11.3)	33.2
Relative*	(12.8)	(20.6)	8.1

* % Relative to local index

Analyst

John Savin

Mologen (MGN)

INVESTMENT SUMMARY

Mologen develops anti-cancer immune maintenance therapies aimed at long-lasting responses. ASCO generated a lot of interest in cancer immune therapies and Mologen is well placed to use this to get an MGN1703 deal given the high-quality colorectal Phase II data. A lung cancer study is planned. Mologen aims to fund development of MGN1601, its cell-based vaccine for metastatic renal cancer. MGN1601 could be an orphan drug; Mologen intends to sell direct. FY12 results showed cash of €23.78m before any MGN1703 deal providing funding through 2014. Cash as of 30 March was €21.8m.

INDUSTRY OUTLOOK

MGN1703 is a stable, dumbbell-shaped DNA molecule (dSLIM) that activates innate immunity. New data showed that patients with a specific immune biomarker treated with MGN1703 had a PFS hazard ratio of 0.27 p=0.007. MGN1601 is an allogenic renal cancer cell vaccine. A new product, MGN1404, will enter Phase I to test three dose levels in metastatic melanoma. A chief medical officer has been appointed.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.1	(6.8)	(7.0)	(56.6)	N/A	N/A
2012	0.1	(6.9)	(7.2)	(51.6)	N/A	N/A
2013e	0.1	(10.0)	(10.2)	(66.5)	N/A	N/A
2014e	0.1	(13.6)	(13.7)	(88.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	€50.00
Market cap:	€1170m
Forecast net cash (€m)	161.6
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

MorphoSys is a German biotechnology company that uses its proprietary antibody platforms to produce human antibodies for therapeutic use across a range of indications for partners and to develop its own pipeline.

Price performance

%	1m	3m	12m
Actual	30.4	59.8	164.0
Relative*	28.3	43.0	114.1

* % Relative to local index

Analyst

Mick Cooper

MorphoSys (MOR)

INVESTMENT SUMMARY

MorphoSys has a broad portfolio of 19 antibodies in clinical studies, including three proprietary products with considerable potential. In June, its lead proprietary product, MOR103, was licensed to GSK in a €450m deal for development in rheumatoid arthritis and multiple sclerosis. A month later, it partnered MOR202 with Celgene in an $818m co-development agreement for multiple myeloma and other haematological cancers. A Phase II study with MOR208 in Non-Hodgkin's lymphoma is ongoing, after promising efficacy in Phase I in chronic lymphocytic leukaemia. MorphoSys will have a net cash position of c €300m following the two deals, so it is able to fulfill its commitments with MOR202's development and increase investment in its proprietary pipeline, including possibly in-licensing products.

INDUSTRY OUTLOOK

The pharmaceutical industry is out-licensing more drug discovery and developing more biological products, as it looks to increase R&D productivity and create better products that are more resistant to generic competition. Both trends should benefit MorphoSys.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	81.7	17.8	20.9	69.4	72.0	40.1
2012	51.9	8.8	7.1	27.9	179.2	553.7
2013e	71.1	3.4	4.4	17.5	285.7	121.0
2014e	52.2	(23.9)	(23.0)	(65.1)	N/A	N/A

Sector: Pharma & healthcare

Price:	€6.00
Market cap:	€65m
Forecast net cash (€m)	5.7
Forecast gearing ratio (%)	N/A
Market	Euronext Paris

Share price graph (€)

Company description

Nanobiotix is a French nanotechnology company developing radiotherapy enhancers for the treatment of cancer. Lead product NBTXR3 is currently in Phase I clinical development in Europe and is partnered with PharmaEngine in Asia-Pacific.

Price performance

%	1m	3m	12m
Actual	(6.3)	(2.8)	N/A
Relative*	(8.4)	(9.8)	N/A

* % Relative to local index

Analyst

Philippa Gardner

Nanobiotix (NANO)

INVESTMENT SUMMARY

Nanobiotix's nanotechnology products could enhance radiotherapy. The NanoXray technology consists of three products that can be incorporated into current treatment without any changes to medical practice. Lead product NBTXR3 is in a Phase I soft tissue sarcoma trial in Europe, and has approval for an EU Phase I head and neck trial. A €2.8m grant for liver cancer was recently awarded. It is partnered with PharmaEngine in Asia-Pacific and a US partnership is targeted for 2014. Follow-on products NBTX-IV and TOPO, with different modes of administration, are in preclinical and early research, respectively. Nanobiotix has sufficient cash to fund operations to mid-2014.

INDUSTRY OUTLOOK

Radiotherapy is a cornerstone cancer treatment used in around 50% of all cancer patients. NanoXray aims to improve the benefits of current radiotherapy without increasing the risks. The purely physical mechanism of action is supported by clinical data that have demonstrated encouraging efficacy with no serious adverse events.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	1.4	(5.0)	(5.2)	(0.7)	N/A	N/A
2012	1.0	(5.0)	(5.2)	(0.6)	N/A	N/A
2013e	1.5	(6.7)	(6.7)	(0.6)	N/A	N/A
2014e	2.0	(8.5)	(8.6)	(0.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	€1.90
Market cap:	€37m
Forecast net cash (€m)	3.0
Forecast gearing ratio (%)	N/A
Market	Alternext Paris

Share price graph (€)

Company description

Neovacs is a biotech company, focused on the development of targeted active immunotherapies for the treatment of severe chronic autoimmune and inflammatory diseases.

Price performance

%	1m	3m	12m
Actual	4.5	21.7	17.6
Relative*	2.2	12.9	(2.7)

* % Relative to local index

Analyst

Wang Chong

Neovacs (ALNEV)

INVESTMENT SUMMARY

Neovacs intends to initiate a Phase IIb trial with its lead product TNF-Kinoid in rheumatoid arthritis (RA). The strategy is designed to maintain momentum of the programme while it seeks a partner. The Kinoid approach has potentially significant commercial advantages versus existing anti-TNF products in this large, but highly competitive therapeutic area. The ability to partner this drug, which has also been in Phase II for Crohn's disease, is central to Neovacs's investment case. A partnership would be expected to transform its fortunes and allow further development of the IFN-Kinoid in lupus. We estimate that Neovacs has sufficient cash to complete the forthcoming Phase IIb RA trial.

INDUSTRY OUTLOOK

Neovacs's kinoids are immunotherapeutic products. Its lead product, TNF-kinoid, is being targeted at the anti-TNF market for the treatment of rheumatoid arthritis and Crohn's disease, which is worth over $20bn. For lupus, there are limited treatments available; the FDA has just approved the first new treatment for this indication in 50 years.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.4	(10.2)	(10.2)	(52.0)	N/A	N/A
2012	0.1	(8.2)	(8.3)	(45.6)	N/A	N/A
2013e	0.0	(9.1)	(9.1)	(39.8)	N/A	N/A
2014e	0.0	(9.2)	(9.2)	(39.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$1.30
Market cap:	US$49m
Forecast net cash (US$m)	6.1
Forecast gearing ratio (%)	N/A
Market	NYSE AMEX

Share price graph (US$)

Company description

NovaBay Pharmaceuticals is a US company developing a new class of topical anti-infective agents. NVC-422 is the lead candidate, undergoing three Phase IIb trials in impetigo, viral conjunctivitis and urinary catheter blockage and encrustation.

Price performance

%	1m	3m	12m
Actual	0.0	(12.0)	6.5
Relative*	(3.7)	(19.1)	(13.4)

* % Relative to local index

Analyst

Christian Glennie

NovaBay Pharmaceuticals (NBY)

INVESTMENT SUMMARY

NovaBay's auriclosene (NVC-422), a novel topical anti-infective, is being studied in three Phase II trials that read out in H213: a 450-patient trial in viral conjunctivitis (US/India/Brazil, data Q413), a 300-patient impetigo study (partner Galderma, data Q313), and a 20-patient Phase II study for urinary catheter blockage and encrustation (data Q313). Each study offers fresh financing/partnering opportunities. A Phase IIa study in bacterial conjunctivitis started in Q213. Global partners are being sought for NeutroPhase, a wound-cleansing agent with FDA 510(k) clearances – Pioneer Pharma is a strategic partner (5.6% shareholder) in China/South-East Asia. NovaBay's Q113 cash of $13m should extend to mid-2014.

INDUSTRY OUTLOOK

Resistance to conventional antibiotics is a serious problem and pharma companies are increasingly seeking alternative methods of combating bacterial (and viral) infections. NovaBay's Aganocide compounds hold the potential to overcome and avoid these resistance issues.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	11.0	(4.8)	(4.4)	(0.17)	N/A	N/A
2012	6.9	(8.8)	(8.5)	(0.29)	N/A	N/A
2013e	9.1	(11.2)	(10.9)	(0.29)	N/A	N/A
2014e	8.0	(13.6)	(13.4)	(0.35)	N/A	N/A

Sector: Pharma & healthcare

Price:	15.8p
Market cap:	£17m
Forecast net cash (£m)	2.4
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Omega is a UK-based company focused on developing and marketing in-vitro diagnostic products in infectious and autoimmune diseases and for food intolerance. Intolerance tests account for over 40% of revenues.

Price performance

%	1m	3m	12m
Actual	(10.6)	(3.8)	(3.8)
Relative*	(14.6)	(9.2)	(18.8)

* % Relative to local index

Analyst

John Savin

Omega Diagnostics (ODX)

INVESTMENT SUMMARY

Omega's sales rose 1.2% in FY13. FY14 sales of the existing products are expected to grow gently, with the level of profit growth depending on food intolerance performance in Brazil, India and China. The big upside should be the Visitect CD4 point-of-care (PoC) CD4 test in FY15. A £4m placing has provided the working capital to launch Visitect and complete allergy iSYS test development.

INDUSTRY OUTLOOK

The development of the allergy iSYS system has proved complex, but the "imprecision issues" have been resolved. An EU 40-test launch menu could be ready by March 2014. US approvals will take some years. The Visitect CD4 PoC test will undergo further evaluations once the final manufacturing protocol is determined and the manufacturing assembly line is ready. Significant sales may start in H214, but FY15 seems more realistic. Field trials are planned by the Clinton Healthcare Access Initiative (CHAI). Once available, sales to non-government organisations could rapidly reach £5m a year.

Y/E Mar	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2012	11.1	1.3	1.0	1.2	13.2	16.2
2013	11.3	1.1	0.8	1.3	12.2	13.4
2014e	12.0	1.3	1.0	1.2	13.2	17.0
2015e	15.7	3.3	3.1	2.7	5.9	8.9

Sector: Pharma & healthcare

Price: C$2.80
Market cap: C$239m
Forecast net cash (C$m) 13.8
Forecast gearing ratio (%) N/A
Market NASDAQ, TSX

Share price graph (C$)

Company description

Oncolytics Biotech is a Canadian company focused on developing Reolysin, a pharmaceutical formulation of the oncolytic reovirus, for the treatment of a wide variety of human cancers (Phase III trial in head and neck cancer).

Price performance

%	1m	3m	12m
Actual	12.4	(7.2)	(22.7)
Relative*	8.7	(11.8)	(29.0)

* % Relative to local index

Analyst

Wang Chong

Oncolytics Biotech (ONC)

INVESTMENT SUMMARY

Oncolytics has announced promising preliminary Phase II melanoma and lung cancer data. However, in view of the rapidly evolving treatment landscape in this poorly treated indication, the company has pragmatically decided to re-evaluate Reolysin in combination with the new and increasingly targeted immunotherapies before conducting the next melanoma clinical trial. By contrast, Oncolytics will be conducting further trials in squamous cell carcinoma of the lung (SCCLC) following the recent positive data. Oncolytics has two ongoing Phase II trials in non-small cell lung cancer (NSCLC) and SCCLC and lung adenocarcinoma.

INDUSTRY OUTLOOK

Oncolytics's rivals are the companies developing oncology products in the same therapeutic areas, but there are some interesting viral oncolytic companies, including Jennerex, Genelux and Viralytics, suggesting a new era in cancer treatment. Oncolytics is one of the two leaders in the area, with Amgen the other after its acquisition of BioVex for up to US$1bn.

Y/E Dec	Revenue (C$m)	EBITDA (C$m)	PBT (C$m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.0	(28.7)	(28.3)	(39.9)	N/A	N/A
2012	0.0	(36.6)	(36.3)	(47.3)	N/A	N/A
2013e	0.0	(39.9)	(39.7)	(46.8)	N/A	N/A
2014e	0.0	(36.6)	(36.3)	(42.2)	N/A	N/A

Sector: Pharma & healthcare

Price: US$13.10
Market cap: US$238m
Forecast net cash (US$m) 45.2
Forecast gearing ratio (%) N/A
Market NASDAQ

Share price graph (US$)

Company description

OvaScience is focused on developing and commercialising new treatments for infertility. Its products (AUGMENT, OvaTure) are based on the discovery of egg precursor cells in ovaries and designed to improve in vitro fertilisation.

Price performance

%	1m	3m	12m
Actual	(5.2)	32.0	N/A
Relative*	(8.7)	21.3	N/A

* % Relative to local index

Analyst

Michael Aitkenhead

OvaScience (OVSC)

INVESTMENT SUMMARY

OvaScience's near-term investment case effectively rests on the successful development and commercialisation of its lead product, AUGMENT, to improve the success rate of in vitro fertilisation (IVF). If study results are positive and AUGMENT retains its lower-risk regulatory status, we project peak US sales of $160m/year. The technology underpinning AUGMENT and OvaTure (preclinical) is based on the landmark scientific discovery of egg-producing stem cells (egg precursor cells, EggPC) in human ovaries.

INDUSTRY OUTLOOK

OvaScience's product candidates hold the potential to improve the current IVF process (AUGMENT) and provide a new treatment paradigm for infertility (OvaTure). In particular, we believe AUGMENT could substantially improve the success rate of IVF, where procedure numbers are growing due to delayed childbearing and rising infertility awareness.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	N/A	N/A	N/A	N/A	N/A	N/A
2012	0.0	(12.1)	(12.1)	(209.0)	N/A	N/A
2013e	0.0	(18.8)	(18.8)	(109.0)	N/A	N/A
2014e	1.0	(21.7)	(21.7)	(119.0)	N/A	N/A

Sector: Pharma & healthcare

Price:	1.4p
Market cap:	£20m
Forecast net cash (£m)	4.0
Forecast gearing ratio (%)	N/A
Market	LSE

Share price graph (p)

Company description

OXB is a UK biotech with a leading position in gene therapy, based on its LentiVector technology, and in cancer vaccines. It is focusing on ophthalmology, with four collaborative projects with Sanofi, and has two other clinical assets (ProSavin and TroVax).

Price performance

%	1m	3m	12m
Actual	(17.7)	(13.9)	(36.4)
Relative*	(21.3)	(18.7)	(46.3)

* % Relative to local index

Analyst

Franc Gregori

Oxford BioMedica (OXB)

INVESTMENT SUMMARY

Oxford BioMedica's future hinges on the value of the LentiVector gene delivery platform in clinical practice. This lentivirus technology has been shown to be effective and well tolerated at high vector doses, while the production agreement with Novartis helps validate the company's technical expertise. However, the key inflection point (expected in early-2014) is whether Sanofi decides to opt in for the further development of RetinoStat, a gene-based treatment for "wet" AMD (age-related macular degeneration). RetinoStat has a material commercial potential and the decision could be the defining moment for Oxford BioMedica.

INDUSTRY OUTLOOK

Gene therapy can correct dysfunctional cells and/or create endogenous therapeutic protein factories. The LentiVector platform is a flexible and efficient system that is particularly promising in ophthalmology indications, where a single administration could safely provide a sustained (or even permanent) effect.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	7.7	(10.1)	(10.3)	(0.9)	N/A	N/A
2012	7.8	(9.1)	(9.5)	(0.7)	N/A	N/A
2013e	4.7	(10.1)	(10.7)	(0.6)	N/A	N/A
2014e	1.9	(11.2)	(11.8)	(0.7)	N/A	N/A

Sector: Pharma & healthcare

Price:	€0.70
Market cap:	€17m
Forecast net cash (€m)	8.2
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

Paion is a biopharmaceutical company specialising in the development of anaesthesia products. It has four NCEs in its R&D portfolio, with the lead programme, remimazolam, partnered with Ono Pharmaceutical in Japan and Yichang in China.

Price performance

%	1m	3m	12m
Actual	3.6	2.0	(28.6)
Relative*	1.9	(8.7)	(42.0)

* % Relative to local index

Analyst

Emma Ulker

Paion (PA8)

INVESTMENT SUMMARY

Paion's option agreement with Hana Pharma is the third Asian deal for its lead programme, remimazolam, a short-acting anaesthetic. If the option is exercised, it would provide Paion with a modest upfront payment plus milestones and royalties. There are a number of potential value inflection points ahead for remimazolam, notably the read-out from the Japanese Phase II/III in general anaesthesia in Q114. A European Phase II trial is due to start in H213. Paion is funded into 2015.

INDUSTRY OUTLOOK

Remimazolam has important advantages over competing products, including fast onset and offset of action and the fact that a reversal agent exists if there is oversedation. Morphine-6-glucuronide has an interesting competitive profile, although Paion is funding only the maintenance of its patents at present.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	3.2	(6.2)	(6.9)	(25.9)	N/A	N/A
2012	26.8	19.2	18.6	64.2	1.1	1.1
2013e	1.5	(9.2)	(9.0)	(34.0)	N/A	N/A
2014e	1.0	(5.9)	(5.8)	(21.4)	N/A	N/A

Sector: Pharma & healthcare

Price:	A$0.00
Market cap:	A$8m
Forecast net cash (A$m)	2.0
Forecast gearing ratio (%)	N/A
Market	ASX

Share price graph (A$)

Company description

Phylogica is a drug discovery company with a proprietary technology platform based on naturally derived Phylomer peptides. Its business model centres on drug discovery collaborations with pharma partners, including Roche, MedImmune, Pfizer and Janssen.

Price performance

%	1m	3m	12m
Actual	(10.5)	(10.5)	(56.4)
Relative*	(12.6)	(11.2)	(62.8)

* % Relative to local index

Analyst

Chris Kallos

Phylogica (PYC)

INVESTMENT SUMMARY

Phylogica's strategy is to use its Phylomer peptide drug discovery platform to become a discovery partner for large pharma. The investment case rests on its ability to monetise its proprietary platform by achieving milestones under its four collaborations and securing further deals. Its collaboration with Janssen has just been extended by another six months and its proprietary technology for identifying cell-penetrating peptides could help it form new deals. It licensed its skin-repair Phylomer PYC35 for the cosmetic market and is collaborating with Bio-Link to commercialise anti-inflammatory Phylomers. Phylogica raised $1.6m in October and aims to become cash self-sustaining in 2013. It engaged a financial adviser in April to assess its strategic alternatives.

INDUSTRY OUTLOOK

Peptides have some advantages of small molecules (stability, formulation flexibility and COGS) and the binding specificity of antibodies, but their key benefit is the ability to address intractable intracellular targets. Phylomer libraries are a source of novel peptide drug leads that, due to their diversity, yield better quality and quantity hits vs random peptide libraries.

Y/E Jun	Revenue (A$m)	EBITDA (A$m)	PBT (A$m)	EPS (c)	P/E (x)	P/CF (x)
2011	2.4	(3.5)	(3.5)	(1.2)	N/A	0.0
2012	1.9	(3.9)	(3.9)	(0.9)	N/A	0.0
2013e	4.2	(1.8)	(1.9)	0.0	N/A	0.0
2014e	4.9	(1.3)	(1.3)	0.1	N/A	0.0

Sector: Pharma & healthcare

Price:	1.3p
Market cap:	£5m
Forecast net cash (£m)	3.4
Forecast gearing ratio (%)	N/A
Market	LSE

Share price graph (p)

Company description

Phytopharm is in negotiations for a reverse-merger with an undisclosed UK-based private company in the healthcare sector.

Price performance

%	1m	3m	12m
Actual	0.0	10.4	(78.6)
Relative*	(4.4)	4.2	(82.0)

* % Relative to local index

Analyst

Christian Glennie

Phytopharm (PYM)

INVESTMENT SUMMARY

On 21 May 2013, Phytopharm announced that it had signed heads of terms in connection with the possible acquisition of an undisclosed, revenue-generating, UK-based private company in the healthcare sector. The transaction will likely be classified as a "reverse takeover" and further announcements are expected in due course.

This proposed transaction follows Phytopharm's strategic review of its options, after the failure of Cogane to meet any primary or secondary end points in a Phase II study (Confident-PD) in 400 patients with early-stage Parkinson's disease in February 2013. Cogane had also showed encouraging preclinical data in amyotrophic lateral sclerosis (ALS) and a potentially pivotal Phase II/III study was being considered. The company held net cash of £5.5m as of 31 January 2013 and holds c £55m in accumulated tax losses.

INDUSTRY OUTLOOK

Y/E Sep	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	0.1	(8.4)	(8.0)	(2.2)	N/A	N/A
2012	0.0	(9.1)	(8.9)	(2.2)	N/A	N/A
2013e	0.0	(7.2)	(7.1)	(1.8)	N/A	N/A
2014e	0.0	(6.3)	(6.3)	(1.6)	N/A	N/A

Sector: Pharma & healthcare

Price:	41.8p
Market cap:	£80m
Forecast net debt (£m)	6.1
Forecast gearing ratio (%)	1180.0
Market	AIM

Share price graph (p)

Company description

Proteome Sciences is a protein biomarker contract research organisation. It has a broad patent portfolio covering isobaric mass-tagging in mass spectrometry and biomarkers for various neurological and oncology indications.

Price performance

%	1m	3m	12m
Actual	(28.9)	(36.7)	12.5
Relative*	(32.1)	(40.3)	(5.0)

* % Relative to local index

Analyst

Mick Cooper

Proteome Sciences (PRM)

INVESTMENT SUMMARY

Proteome Sciences has a broad IP portfolio covering mass spectrometry techniques and biomarkers, which is being commercialised. The company earns royalties and manufacturing payments from Thermo Fisher Scientific, which sells Proteome's TMT products. PS Biomarker Services carries out protein assays and biomarker discovery for pharmaceutical companies, including Eisai and J&J. Proteome Sciences out-licenses its proprietary biomarkers non-exclusively to diagnostic companies as well. Its sales in FY12 increased by 13% to £1.2m and its sales growth is expected to accelerate in FY13, in part because of the new $2.1m deal with Thermo Fisher Scientific for cancer pathway profiling assays. There is also the possibility of its preclinical CK1d inhibitors being partnered for Alzheimer's disease.

INDUSTRY OUTLOOK

Pharma companies are expanding their biomarker programmes due to pressure from regulators and to improve productivity. Protein biomarkers promise to be particularly useful as they provide a direct read-out of changes occurring in a person.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	1.0	(4.1)	(4.5)	(2.1)	N/A	N/A
2012	1.2	(4.8)	(5.2)	(2.2)	N/A	N/A
2013e	6.5	0.8	0.4	0.3	139.3	130.6
2014e	10.3	3.9	3.4	1.9	22.0	26.0

Sector: Pharma & healthcare

Price:	62.8p
Market cap:	£29m
Forecast net debt (£m)	77.5
Forecast gearing ratio (%)	161.0
Market	LSE

Share price graph (p)

Company description

Skyepharma is an expert oral and inhalation drug delivery company. It combines proven scientific expertise with validated proprietary drug delivery technologies to develop innovative oral and inhalation pharmaceutical products.

Price performance

%	1m	3m	12m
Actual	17.3	38.7	(37.3)
Relative*	12.1	30.9	(47.0)

* % Relative to local index

Analyst

Franc Gregori

Skyepharma (SKP)

INVESTMENT SUMMARY

flutiform's performance (particularly in Europe) will define Skyepharma's future. The encouraging sales uptake to date suggests our conservative expectations could be exceeded. Skyepharma's prospects have also been boosted by the first approval of GSK's COPD product Relvar/Breo Ellipta, which is expected to generate £6m pa royalties under a technology licence (a further £3m pa is likely once Anoro Ellipta is launched). Skyepharma still has a geared balance sheet, but the payments are now aligned to the expected cash inflows and equity holders benefit as debt is paid down. These early signs augur well for the refinancing of debt when the bond repayment is due in 2017.

INDUSTRY OUTLOOK

flutiform is an inhaled combination of fluticasone and formoterol for treating asthma. It has been launched in Germany, the UK, Italy and seven other European countries. It has been approved in a further 11 countries, with launch timing subject to pricing agreements. Kyorin, the Japanese partner, has submitted for approval there. flutiform is expected to contribute over half Skyepharma's royalty income by 2017, plus profit from supply of the product.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	55.2	14.7	1.9	5.4	11.6	1.2
2012	49.9	15.3	(14.2)	(27.8)	N/A	1.0
2013e	58.7	13.8	(2.9)	(8.1)	N/A	2.5
2014e	68.0	20.4	2.5	(0.6)	N/A	1.7

Sector: Pharma & healthcare

Price:	€26.30
Market cap:	€309m
Forecast net cash (€m)	14.1
Forecast gearing ratio (%)	N/A
Market	Deutsche Börse

Share price graph (€)

Company description

Stratec Biomedical designs and manufactures OEM diagnostic instruments. Design and assembly of systems from modules is in central Germany and Switzerland. There is a US subsidiary, a UK middleware company and a Berlin business.

Price performance

%	1m	3m	12m
Actual	(26.5)	(16.1)	(19.8)
Relative*	(27.7)	(24.9)	(35.0)

* % Relative to local index

Analyst

John Savin

Stratec Biomedical (SBS)

INVESTMENT SUMMARY

Stratec designs and manufactures sophisticated automated instruments and, crucially, software, for global companies like DiaSorin and Siemens. Stratec Biomedical has announced revised lower guidance following a client's decision to cancel a major contract. The client is conjectured to be Abbott, a company with which Stratec still has several projects. Compensation is being negotiated. Management guidance is that this will cut 2013 revenues to €127-138m, with EBIT of 14.0-15.58%. Interim revenues were €59m with EBIT of €8.35, 14%; revenues were down €3m and EBIT €1.2m due to water damage in Q2. H1 EBIT could have been 15.3%.

INDUSTRY OUTLOOK

A critical part of Stratec's valuation is growth in construction sales as this covers core costs and grows the profitable service parts business. Innovative products such as the digital Quanterix system (due for clinical launch by bioMérieux in H214) may avoid the tough mainstream market. A further contract might require higher-volume manufacturing from 2016/17.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	116.6	27.1	23.7	154.1	17.1	17.3
2012	122.4	22.2	19.4	137.1	19.2	40.3
2013e	131.8	25.2	22.3	152.1	17.3	14.3
2014e	150.9	28.0	25.1	170.5	15.4	18.4

Sector: Pharma & healthcare

Price:	US$6.60
Market cap:	US$277m
Forecast net cash (US$m)	1.6
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)

Company description

Sucampo Pharmaceuticals is a US-based company developing and commercialising medicines based on prostones. Amitiza (GI disorders), partnered with Takeda (US) and Abbott (Japan), and Rescula (ophthalmology) are key products.

Price performance

%	1m	3m	12m
Actual	(3.9)	(2.4)	48.3
Relative*	(7.5)	(10.3)	20.7

* % Relative to local index

Analyst

Christian Glennie

Sucampo Pharmaceuticals (SCMP)

INVESTMENT SUMMARY

The commercial launch of Amitiza's third indication, opioid-induced constipation (OIC), provides Sucampo with a $10m milestone from its US partner Takeda, and a significant new market opportunity to boost US product sales, given a lack of near-term competitors for OIC. Amitiza holds further potential from its commercial roll-out in Japan (launched by Abbvie in November 2012) and in Europe (directly in the UK and Switzerland; partnerships possible). Sucampo launched its second product, glaucoma drug Rescula (unoprostone), in the US in February 2013, with 40 reps and a targeted promotional campaign.

INDUSTRY OUTLOOK

Historical safety issues with using Rx drugs, for c 10m US patients with constipation disorders seeking alternatives to dietary/lifestyle changes and OTC therapies, give Amitiza's established track record (>7m prescriptions over seven years) a key differentiating factor. Ironwood/Forest's Linzess (linaclotide) launched in late-2012 is a key prescription drug competitor for constipation disorders.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	54.8	(17.7)	(19.9)	(41.4)	N/A	N/A
2012	81.5	8.3	6.2	11.6	56.9	39.4
2013e	100.5	9.7	7.7	13.0	50.8	24.7
2014e	135.5	32.5	30.5	58.8	11.2	7.9

Sector: Pharma & healthcare

Price:	US$5.50
Market cap:	US$284m
Forecast net cash (US$m)	8.1
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)

Company description

Sunesis Pharmaceuticals is US biotech company focused on the development of anticancer drugs. Its lead compound, vosaroxin, is in a Phase III study for relapsed/refractory AML.

Price performance

%	1m	3m	12m
Actual	5.6	6.2	86.4
Relative*	1.6	(2.4)	51.7

* % Relative to local index

Analyst

Robin Davison

Sunesis Pharmaceuticals (SNSS)

INVESTMENT SUMMARY

Sunesis's investment case depends entirely on the outcome – due in H114 – of the VALOR study of vosaroxin in relapsed/refractory acute myeloid leukaemia (AML). The study has enrolled 611 (91%) of its target 675 patients, with enrollment expected to complete by end-2013. Headline results are due in H114 after reaching 562 events and locking the final study database. A DSMB safety review is planned in June. Expectations for success in VALOR are high following last year's cohort expansion. Q113 gross cash of $61m (net cash of $37m) is sufficient to H214, well beyond the VALOR study readout. We value Sunesis at $438m.

INDUSTRY OUTLOOK

Vosaroxin is one of eight agents in Phase III studies for various AML settings, but is the lead compound in the relapsed/refractory setting. The recent failure of Clavis's Phase III study of elacytarabine removes a competitive threat to vosaroxin and confirms that cytarabine will remain the backbone of AML therapy. There is more competition in the front-line AML setting.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (c)	P/E (x)	P/CF (x)
2011	5.0	(25.8)	(26.1)	(56.2)	N/A	N/A
2012	3.8	(31.8)	(33.4)	(55.4)	N/A	N/A
2013e	8.0	(29.6)	(32.0)	(62.2)	N/A	N/A
2014e	8.0	(22.4)	(23.9)	(46.4)	N/A	N/A

Sector: Pharma & healthcare

Price:	€4.60
Market cap:	€43m
Forecast net debt (€m)	0.9
Forecast gearing ratio (%)	13.0
Market	FRA

Share price graph (€)

Company description

Sygnis is a Spanish/German company developing tools for molecular biologists. Its main focus is in the field of polymerases for the amplification and sequencing of DNA. Its lead product, QualiPhi, is partnered with Qiagen.

Price performance

%	1m	3m	12m
Actual	76.9	84.0	(12.9)
Relative*	74.1	64.8	(29.3)

* % Relative to local index

Analyst

Mick Cooper

Sygnis Pharma (LIOK)

INVESTMENT SUMMARY

Sygnis develops molecular biology chemistry products targeted at the fast-growing DNA analysis and sequencing markets. The core IP is a range of engineered DNA polymerase enzymes, a specialist area where it has leading scientific expertise. The lead product, QualiPhi, has superior activity to the currently marketed phi29 enzyme (global market size: $50m). It is licensed for amplification of DNA to Qiagen, the global leader in DNA preparation. The first QualiPhi kits could be launched from Q3. A second enzyme for amplifcation of DNA and RNA and sequencing of damaged DNA, PrimPol, may be partnered in 2013 and may offer more upside in a less-crowded market. A novel protein interaction analysis platform, DoubleSwitch, is also being licensed.

INDUSTRY OUTLOOK

The trend towards personalised medicine, technological improvements and scientific advances has resulted in the DNA sequencing market being worth over $1.5bn and growing at c 20%. Sygnis' products are being developed for this fast-growing market.

Y/E Mar	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	0.0	(0.8)	(0.8)	(11.0)	N/A	N/A
2012	0.2	(1.3)	(1.4)	(18.4)	N/A	N/A
2013e	1.4	(1.8)	(1.8)	(18.7)	N/A	N/A
2014e	2.4	(0.9)	(1.1)	(10.2)	N/A	N/A

Sector: Pharma & healthcare

Price:	€0.30
Market cap:	€29m
Forecast net debt (€m)	6.3
Forecast gearing ratio (%)	18.0
Market	Euronext Brussels

Share price graph (€)

Company description

TiGenix produces cell therapeutics. Its lead Phase III development candidate, Cx601, treats perianal fistulas in Crohn's disease. ChondroCelect is approved and sold direct in the EU for knee cartilage repair.

Price performance

%	1m	3m	12m
Actual	(56.1)	(67.4)	(43.1)
Relative*	(56.6)	(68.6)	(50.8)

* % Relative to local index

Analyst

John Savin

TiGenix NV (TIGB)

INVESTMENT SUMMARY

The CX611 data in Rheumatoid Arthritis (RA) released on 22 April show a clear numerical response but with no dose response. The responses at the more stringent ACR70 level were very impressive as these were patients highly refractory to all curent therapies. The standard DAS28 score shows some patients entered remission or moved to mild disease. Revenues for ChondroCelect sales in 2012 were €4.1m (€0.7m was carried from 2011) with €1.04m (up 55%) in Q113. A placement of 26m shares on 18 July raised €6.5m gross at €0.25/share.

INDUSTRY OUTLOOK

Spain is now paying the full reimbursement price for ChondroCelect. France has refused to pay for ChondroCelect. The Phase III for Cx601 in perianal fistula closure is due to complete by late-2014 with a 2015 filing. Cx601 could be highly lucrative from 2016 with direct EU sales from 2016 plus a US partner expected in 2013. In Cx611 (RA), the strategy needs to be developed, but a partner to co-develop the lucrative RA market is a strong option on these data.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	1.1	(14.9)	(14.4)	(21.0)	N/A	N/A
2012	4.1	(13.8)	(14.0)	(15.2)	N/A	N/A
2013e	5.0	(14.9)	(15.2)	(13.4)	N/A	N/A
2014e	7.1	(12.1)	(12.4)	(9.8)	N/A	N/A

Sector: Pharma & healthcare

Price:	DKK2.90
Market cap:	DKK409m
Forecast net cash (DKKm)	7.8
Forecast gearing ratio (%)	N/A
Market	OMX

Share price graph (DKK)

Company description

Topotarget is a Danish drug development company in the field of oncology. Its lead product is belinostat and it has out-licensed the North American and India rights to Spectrum Pharmaceuticals.

Price performance

%	1m	3m	12m
Actual	(5.9)	(2.4)	137.5
Relative*	(9.9)	(5.1)	109.0

* % Relative to local index

Analyst

Mick Cooper

Topotarget (TOPO)

INVESTMENT SUMMARY

Topotarget is only developing belinostat, partnered with Spectrum Pharmaceuticals. The pivotal Phase II trial, BELIEF for peripheral T-cell lymphoma (PTCL), met its primary end point with an overall response rate of 26%, similar to that seen with pralatrexate (Folotyn) and romidepsin (Istodax), approved in the same indication in recent years. Belinostat's safety profile appears to be superior to the latter two drugs, so it is increasingly likely that Topotarget will receive a c $10 milestone and 1m Spectrum shares in H213, with the drug launched in the US in 2014. These events should cause a significant re-rating of the shares. Topotarget has sufficient funds to operate into FY14 without the expected milestones after raising DKK26.5m in April.

INDUSTRY OUTLOOK

Topotarget's belinostat is a histone deacetylase inhibitor (HDACi). Two drugs have been approved and c 10 others are in clinical development. Belinostat has a favourable safety profile and could be the first HDACi approved for solid tumours in combination therapy.

Y/E Dec	Revenue (DKKm)	EBITDA (DKKm)	PBT (DKKm)	EPS (DKK)	P/E (x)	P/CF (x)
2011	65.6	(28.0)	(31.2)	(0.22)	N/A	N/A
2012	2.4	(77.6)	(80.2)	(0.60)	N/A	N/A
2013e	2.7	(50.7)	(52.7)	(0.37)	N/A	N/A
2014e	N/A	N/A	N/A	N/A	N/A	N/A

Sector: Pharma & healthcare

Price:	€10.00
Market cap:	€317m
Forecast net cash (€m)	5.5
Forecast gearing ratio (%)	N/A
Market	Euronext Paris

Share price graph (€)

Company description

Transgene is a French drug discovery and development company focused on the treatment of cancer and infectious diseases with immunotherapies. It has four products in Phase II development.

Price performance

%	1m	3m	12m
Actual	1.0	14.2	36.1
Relative*	(1.3)	5.9	12.6

* % Relative to local index

Analyst

Mick Cooper

Transgene (TNG)

INVESTMENT SUMMARY

Transgene has two immunotherapy products that could enter Phase III in FY14. TG4010 is in a Phase IIb/III trial in non-small cell lung cancer, which could lead to Novartis exercising the option to in-license the drug at the end of FY13, following data in Q313. Its second drug, an oncolytic virus Pexa-Vec, could enter Phase III in FY14 for hepatocellular carcinoma depending on data from a Phase IIb study in Q413. Its pipeline also includes TG4040 in Phase II for HCV and TG4001, which should start a Phase IIb study in HPV-related head and neck cancers in Q413. Transgene has recently formed a long-term production collaboration with Sanofi to enable it to become a fully integrated pharmaceutical company within four years. It has sufficient cash to operate to the end of FY14.

INDUSTRY OUTLOOK

There is currently considerable interest in immunotherapies - both therapeutic vaccines and oncolytic viruses, especially for the treatment of cancers - after the approval of Provenge and Yervoy. They are generally well tolerated and are showing promising levels of efficacy.

Y/E Dec	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	14.4	(42.1)	(42.9)	(137.1)	N/A	N/A
2012	13.1	(39.4)	(42.4)	(136.4)	N/A	N/A
2013e	13.3	(49.3)	(51.7)	(162.7)	N/A	N/A
2014e	12.6	(50.3)	(52.8)	(166.2)	N/A	N/A

Sector: Pharma & healthcare

Price:	US$15.60
Market cap:	US$389m
Forecast net cash (US$m)	125.3
Forecast gearing ratio (%)	N/A
Market	NASDAQ

Share price graph (US$)

Company description

Verastem is a biopharmaceutical company focused on discovering and developing novel drugs that selectively target cancer stem cells (CSCs). Its lead drug is VS-6063, a FAK inhibitor, currently in Phase II testing.

Price performance

%	1m	3m	12m
Actual	27.0	58.2	53.5
Relative*	22.3	45.4	24.9

* % Relative to local index

Analyst

Jason Zhang

Verastem (VSTM)

INVESTMENT SUMMARY

At its recent R&D update, Verastem highlighted research data that support its central cancer stem cell-targeting claims and disclosed a series of new clinical trial plans with data readouts over the next 12-18 months. In particular, new details on its lead programme, VS-6063 (defactinib), boost confidence that it will be able to capture clinical efficacy of the drug in mesothelioma and various other settings. We have revised our rNPV valuation to $425m or $15.3/diluted share to reflect new data, a new indication and the impact of a new financing.

INDUSTRY OUTLOOK

Verastem is a leader in the discovery and development of drugs that selectively target CSCs. It established a proprietary screening and assay platform and through it discovered CSC-specific targets and compounds. Its pipeline includes VS-6063 and VS-4718, two FAK inhibitors, and VS-5584, a PI3K/mTOR dual inhibitor.

Y/E Dec	Revenue (US$m)	EBITDA (US$m)	PBT (US$m)	EPS (fd) (c)	P/E (x)	P/CF (x)
2011	0.0	(13.7)	(13.7)	(10.57)	N/A	N/A
2012	0.0	(32.2)	(32.0)	(0.68)	N/A	N/A
2013e	0.0	(36.7)	(36.6)	(1.38)	N/A	N/A
2014e	0.0	(37.8)	(37.7)	(1.29)	N/A	N/A

Sector: Pharma & healthcare

Price:	19.5p
Market cap:	£86m
Forecast net cash (£m)	68.9
Forecast gearing ratio (%)	N/A
Market	AIM

Share price graph (p)

Company description

Vernalis is a UK speciality pharma company with a late-stage US cough/cold pipeline and an early to mid-stage R&D pipeline of CNS and cancer projects. Its latest fund-raising will enable it to build a US-based sales force for the former.

Price performance

%	1m	3m	12m
Actual	(10.3)	(13.3)	(15.2)
Relative*	(14.3)	(18.2)	(28.4)

* % Relative to local index

Analyst

Franc Gregori

Vernalis (VER)

INVESTMENT SUMMARY

Vernalis's outlook hinges on the development of a range of prescription-only cough cold formulations for the US market. An NDA filing for the first product, CCP-01, is likely in mid-2014, suggesting approval ahead of the 2015/16 winter cough and cold season. Vernalis's strategy to also realise value from the drug development and research units is bearing fruit, with progress on a number of fronts. Tight cost control, coupled with a healthy cash balance of £81.6m, means Vernalis is funded through to expected profitability. Half-yearly results are expected on 29 July.

INDUSTRY OUTLOOK

Vernalis is pursuing a strategy that aims to create value directly from its legacy R&D portfolio and research expertise, as well as through M&A/in-licensing that should enable it to achieve financial self-sustainability over the medium term.

Y/E Dec	Revenue (£m)	EBITDA (£m)	PBT (£m)	EPS (p)	P/E (x)	P/CF (x)
2011	12.2	(6.0)	(6.3)	(3.4)	N/A	N/A
2012	14.6	(2.6)	(4.7)	(0.8)	N/A	N/A
2013e	12.1	(8.1)	(8.4)	(1.6)	N/A	N/A
2014e	12.2	(10.2)	(10.6)	(2.1)	N/A	N/A

Sector: Pharma & healthcare

Price:	€1.30
Market cap:	€41m
Forecast net cash (€m)	2.8
Forecast gearing ratio (%)	N/A
Market	FRA

Share price graph (€)

Company description

Wilex develops therapeutic and diagnostic products for cancer. Lead development programmes are Redectane, Rencarex and Mesupron.

Price performance

%	1m	3m	12m
Actual	(1.9)	(1.4)	(65.2)
Relative*	(3.4)	(11.7)	(71.8)

* % Relative to local index

Analyst

John Savin

WILEX (WL6)

INVESTMENT SUMMARY

In FY13, Wilex will recognise €10.1m from the Rencarex deal with Prometheus as the ARISER trial did not meet its end point and the deal is being unwound. H113 cash was €12.9m; H1 cash flow was €10.7m so Wilex has cash into 2014 before deals or project funding. The value in 2013 lies in partnering Mesupron, which is essential to progress the project. Redectane for kidney cancer imaging should enter a second US Phase III once a partner is found. The Heidelberg Pharma subsidiary offers novel chemistry links between antibodies and therapeutic payloads and is expected to grow from the FY12 revenues of €1.9m.

INDUSTRY OUTLOOK

Analysis of the ARISER 864-patient Phase III Rencarex data has shown a disease-free survival advantage with a hazard ratio of 0.51 in patients who completed the protocol with a high score (over 2.6) of the CAIX. A further Phase III will be required and a global partner will be sought. Wilex has retained Burrill Securities to assist in project financing.

Y/E Nov	Revenue (€m)	EBITDA (€m)	PBT (€m)	EPS (c)	P/E (x)	P/CF (x)
2011	11.7	(12.8)	(13.6)	(65.8)	N/A	N/A
2012	16.1	(6.2)	(7.4)	(21.9)	N/A	N/A
2013e	13.6	(5.9)	(6.7)	(20.0)	N/A	N/A
2014e	5.0	(17.4)	(18.3)	(58.5)	N/A	N/A

Berlin +49 (0)30 2088 9525
Friedrichstrasse 95
10117 Berlin
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
United States

Sydney +61 (0)2 9258 1162
Level 33, Australia Square
264 George St, Sydney
NSW 2000, Australia

Wellington +64 (0)4 8948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand