Cambridge Science Park
Founded by Trinity College
in 1970

Spring 2004

catalyst

CAMBRIDGE SCIENCE PARK NEWSLETTER

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New arrivals

Business Web Software

Business Web Software provides products that allow business users to share and receive information from customers without any technical complexity. AchieveForms enables organisations to publish intelligent, web-based forms quickly that integrate with back-end systems using XML, ODBC, HTTP or SOAP. AchieveInformation makes information available both as searchable FAQs and as service information, enabling end users to find answers quickly to questions without having to pick up the phone.
www.businesswebsoftware.com

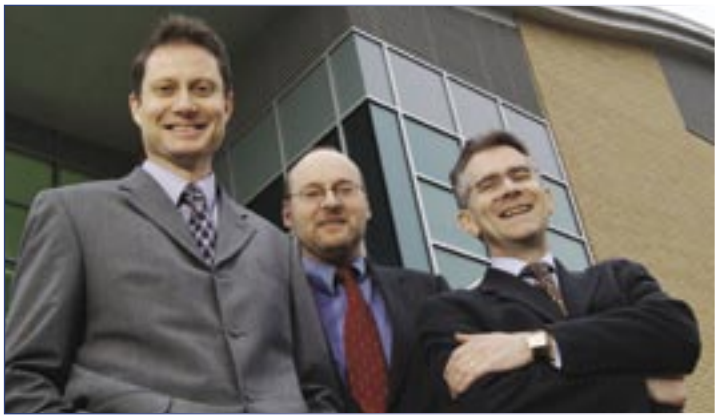
Cambridge Photonics Limited

Cambridge Photonics Limited (CPL) was founded in 2001 to develop and market reconfigurable add drop multiplexers for the telecommunications industry. CPL's products will offer substantial increases in performance and reliability at the same time as large reductions in operating costs. Working in collaboration with Cambridge University's Engineering Department, CPL's technology is based on liquid-crystal-on-silicon spatial light modulators.

Genzyme Corporation

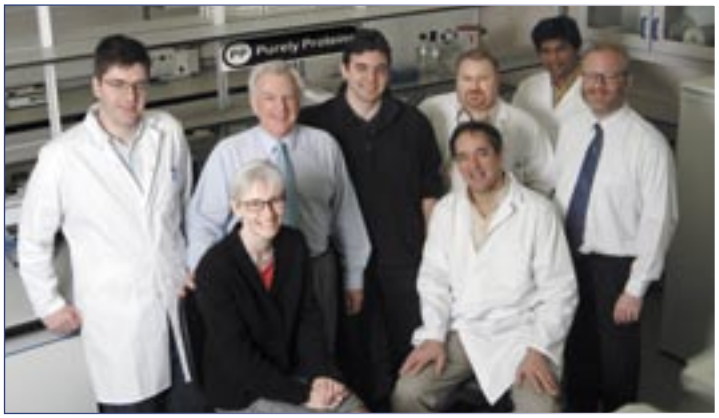
Genzyme Corporation, founded in 1981, is one of the world's most successful biotechnology companies.
Genzyme will be opening a new research facility at 310 Cambridge Science Park in April 2004. The New Discovery Science Centre will focus initially on antibody technology and its applications in oncology, renal disease and immune-mediated diseases.
www.genzyme.co.uk

Front cover image: Astex Technology building, 436 Cambridge Science Park



NCE Discovery

NCE Discovery is a spinout company from the Wolfson Institute for Biomedical Research, University College London. NCE was formed to meet the growing need for flexible synthetic chemistry consultancy and services in the biotechnology sector. Services include consultation on library selection and purchase, the design of novel molecules, preliminary structure activity work and first-patent filings.
www.ncediscovery.com



Purely Proteins

Purely Proteins expresses, purifies and supplies human proteins at any scale to accelerate drug discovery research. It provides a broad range of related protein-based solutions including informatics, therapeutically relevant purified proteins and client-driven purification, chemical-screening and drug-profiling programmes.
www.purelyproteins.com

TKT

Transkaryotic Therapies (TKT) is a leading biopharmaceutical company that specialises in developing products for treating rare diseases, especially lysosomal storage disorders. Currently Replagal™ is marketed for the treatment of Fabry's disease and Idursulfase is at the pivotal stage of its development for the treatment of Hunter's syndrome. TKT's headquarters and manufacturing facility is in Cambridge, Massachusetts while the UK office is responsible for European regulatory affairs and global drug safety.
www.tktx.com

Plastic revolution

Disruptive technology from Plastic Logic

Not many companies can realistically claim to be on the verge of transforming the industry they are working in. Plastic Logic, however, might just be one of them – Catalyst went to their Cambridge Science Park headquarters to find out why.

34 Cambridge Science Park is an unassuming enough place at first glance, but it's certainly been attracting some high-profile attention since Plastic Logic moved in back in July 2002.

Co-founder Professor Sir Richard Friend recently received his knighthood from the Queen in June 2003, and was also the subject of an in-depth article by the internationally renowned magazine *Newsweek* earlier this year. The company itself, meanwhile, was listed as one of 40 Technology Pioneers by the World Economic Forum for 2004 in a global list of companies most likely to become the "next big thing".

Evidently there is much ado about something at Plastic Logic – and that something is plastic electronics. The company is the commercial spinout from the pioneering work carried out by Sir Richard and co-founder Professor Henning Sirringhaus at the Cavendish Laboratory at Cambridge University into the use of ink-jet printing of polymers (plastics) to form transistors, the component at the heart of digital circuitry. At first glance, it may not seem a particularly glamorous or trail-blazing field, but the potential of such technology in the twenty-first century is every bit as revolutionary as the introduction of silicon-based circuitry in the second-half of the last century.

"Perhaps the best way of summing it up is to say that it's about combining the power of electronics with the pervasiveness of printing," says Cranch Lamble, Marketing Executive at Plastic Logic. "This is potentially a disruptive technology which will put electronics into new places, and perhaps ultimately make electronics cheaper as well."

Imagine, for example, reading this article on a high-quality electronic screen cheap enough to be distributed like paper and flexible enough to be rolled up and put in your pocket. Intrigued? Flexible, low-cost electronic displays and signage – known as e-paper – are one major area in which Plastic Logic has been working with commercial partners in the US to develop a whole new range of applications.

"E-paper has got all sorts of advantages compared to other electronic screens," explains Lamble. "It's got a look that's very much closer to paper and because of its high contrast you can read it much more comfortably – in direct sunlight without trouble, for example. We provide a component which enables much higher levels of information to be shown on these displays whilst retaining the fundamental advantages of e-paper such as its flexibility.

"Initially we're focused on several applications in this area. One company we work with is targeting signage applications, creating updateable signs for use by major retailers such as supermarkets. Other leaders in the e-paper field are looking at electronic book applications. The devices can potentially be used for a wide range of other tasks, such as reading emails that you would normally print out or downloading content via your mobile phone."

Flexible electronic displays are not, however,

Left: selection of the materials used in Plastic Logic devices
Below: semiconductor being prepared in solution
Far left: multi-nozzle inkjet printer of the type used by Plastic Logic

the only area in which Plastic Logic is developing the use of its technologies. The ability to print electronic circuits at a low cost and on a wide variety of surfaces points to its ultimate use in electronic barcodes and intelligent packaging for consumer goods, allowing retailers to monitor stock more closely than ever and to improve security.

Indeed, if you let your imagination wander, the implications of the widespread introduction of such technology are staggering: food packaging that knows what's inside it, newspaper adverts that respond to your personal tastes and interests, or tickets that bring you real-time travel information and updates, to list just a few possibilities.

The launch of the world's first mini-fabrication facility for plastic electronics alongside their office space at Cambridge Science Park will assist Plastic Logic in developing the prototypes that could soon be seen in mass production around the world – another milestone in what's been an auspicious start for a young company founded in November 2000.

Of course, there's still much work to be done on this emerging technology before it accomplishes the kind of disruptive step-change which many predict it will achieve. Plastic electronics does not have the performance capabilities of silicon-based circuits, but it has other characteristics and capabilities which mean that it will enable circuitry to be put into new and interesting places.

Furthermore, the printing techniques used to create plastic electronics are potentially much less capital-intensive than those for conventional semiconductor manufacture, meaning that when the technology matures, the model for this industry may be one of widely dispersed mini-fabrication sites that offer rapid design cycles, low economic build quantities and faster operational turnaround – in short, the breeding ground for a hugely diverse market of potential applications.

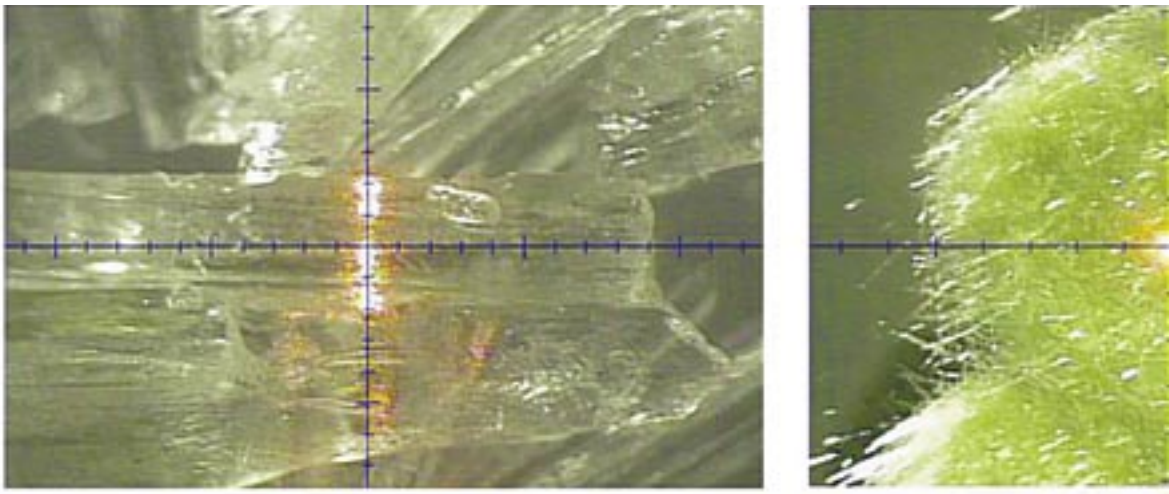
It's this vision, as well as the very real applications currently in development, that keeps the Plastic Logic team both inspired and open-minded as to the potential of what they are working on.

"Ultimately we want to get the technology to the point at which we can enable our customers to have total freedom to develop their own visions – to give them a toolbox of capabilities, that's what really excites me," says Lamble.

"Probably the most ingenious application for the technology is yet to be conceived. But when you enable people to understand its potential and think about using it in the way they want for their own specific needs – that's when it will really have a major disruptive impact."

www.plasticlogic.com

4-Methyl-2-nitroacetanilide



White and yellow polymorphs first reported by Gattermann in 1885

- White – tabular and monoclinic
- Yellow – filamentary and triclinic

Reported stability: White > Yellow

Part of the process

Finding the right form with Pharmorphix

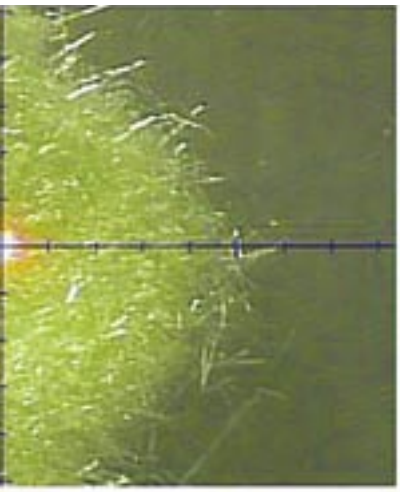
It can mean the difference between successful commercialisation and costly delays – yet polymorph screening and salt selection is still an often undervalued aspect of the drug discovery process. Catalyst met Dan Cowell and Alan Chorlton of Pharmorphix to find out about a start-up setting new standards in this multidisciplinary field.

One of only four serious contract research or outsource companies working exclusively in this specialism in the world, it's perhaps not surprising that Pharmorphix already lists major pharmaceutical and biotech organisations across Europe and the US as clients, despite the fact that the new company is still less than 12 months old.

Nevertheless, the solid-form selection and related services the company provides are still commonly misconceived by parts of the industry as "bolt-on" extras, a process to be endured simply as a means of getting a drug onto the market. Alan Chorlton, Chief Scientific Officer at Pharmorphix, explains.

"The pressures in the biotech field are greater than ever these days," he says. "That means that many companies, particularly the smaller ones, don't want to think about polymorph screening or salt selection until the very last moment. Their endpoint is to get their drug into phase one trials and start producing positive results.

"Companies need to understand that finding the best solid form for a drug is very much on the critical path. Regulatory authorities are very tough in this area now, and treating it as an afterthought can mean serious and costly problems later on."



Above: Microscopic images of two polymorphs for the compound 4-Methyl-2-nitroacetanilide. The white polymorph on the left clearly has a very different structure and properties to the yellow polymorph on the right, and is the more stable of the two forms.

The selection of a suitable polymorph – one of the crystal lattices which are created as molecules in a drug compound crystallise – is crucial to the way in which a drug functions in solid form. Different polymorphic forms of the same drug can have widely varying properties, such as solubility, bioavailability, stability, hygroscopicity, melting point, compressibility and flow properties, which in turn can affect the efficacy, safety and suitability of a drug for mass production.

The abundance of possible polymorphs for a particular compound presents further challenges to the aspiring drug developer. Dr Walter McCrone, the American pioneer in chemical microscopy who famously discredited the authenticity of the Turin Shroud, once said that "the number of polymorphs found for a chemical substance is proportional to the time and effort spent researching it". With each different polymorphic form requiring its own patent protection, it becomes ever more evident that, as one industry insider has put it, "knowledge of the solid state properties and identifying all the crystalline forms of such compounds for successful crystallisation scale-up and development are key issues for any pharmaceutical group".

Using a combination of automated technology and traditional analytical techniques, Pharmorphix responds to this challenge with a multidisciplinary approach encompassing crystallography, thermal techniques, process chemistry, physico-chemical property determination and spectroscopic techniques. Nevertheless, as Technical Director Dan Cowell is keen to point out, the provision of accurate data is only the starting point in a complex and variable process.

"What we really want to do is to provide relevant guidance and analysis to help a company with its drug all the way through the lifecycle of a product," he says. "That means giving the right services at the right time, whether that's determining physico-chemical properties when the drug is in its initial stages, advising on early salt selection and polymorphic forms, or helping with patent protection at a later date. Our clients are looking to get their drugs to market – and we can help them do that more effectively."

It was as providers of synthetic chemistry services to the pharmaceutical industry at Cambridge Discovery Chemistry (CDC) that many of the current Pharmorphix team were first brought together. In the late 1990s, Dan, Alan and others were part of a team working in collaboration with their client Pfizer to develop a more comprehensive and rational approach to polymorph screening.

When CDC was acquired by Massachusetts-based drug-discovery company Millennium, the group became internal service providers and a centre for excellence for all solid-form issues within the new company. But although the team had already formed initial plans to set up independently, the decision by Millennium to close down their UK operation in July 2003 increased the time pressure to achieve this.

"At the time, the closure came as a shock," says Dan, "but we were in a good position to move on. We were a fairly autonomous group and we'd built up our technology internally – we'd also been told by Millennium that they were still keen to engage our services independently."

Formally founded in July 2003, Pharmorphix didn't actually move onto Cambridge Science Park until October of the same year. "We had an ongoing service agreement with Millennium," says Alan, "so we needed to get the new operation up and running as soon as possible. We looked at a number of facilities, but it was the flexible approach offered by Trinity College which swung it for us. Since we've been here, that decision has seemed very well founded."

Having commenced work promptly, the team is already developing ambitious plans for a company as yet privately funded by its founding employees. "The next couple of years will see growth, definitely," says Dan. "We expect to double in size within the next 18 months, and to double again within three years to fill this facility. At the moment, however, we're focused on delivering high quality research."

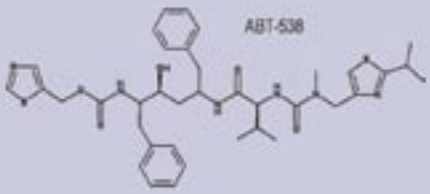
Building on the strengths of a team that has already been together for years, it seems like there will be exciting times ahead for a new company already forging a firm reputation as a leader in its field. "We all really believe in what we're doing as a group, and there's a great dynamic between us," says Dan. "Every one of us was keen to take the next step, so you could say it was the right move at exactly the right time."

www.pharmorphix.com

Paying the price: when things go wrong

Not identifying fully the properties of different polymorphic forms can prove a costly omission in the drug-discovery process. Perhaps the most high-profile recent example of this occurred in 1998 when supplies of the capsule form of AIDs drug Norvir® were severly limited due to the unexpected appearance of a new polymorph during manufacturing.

The molecular structure of Norvir®

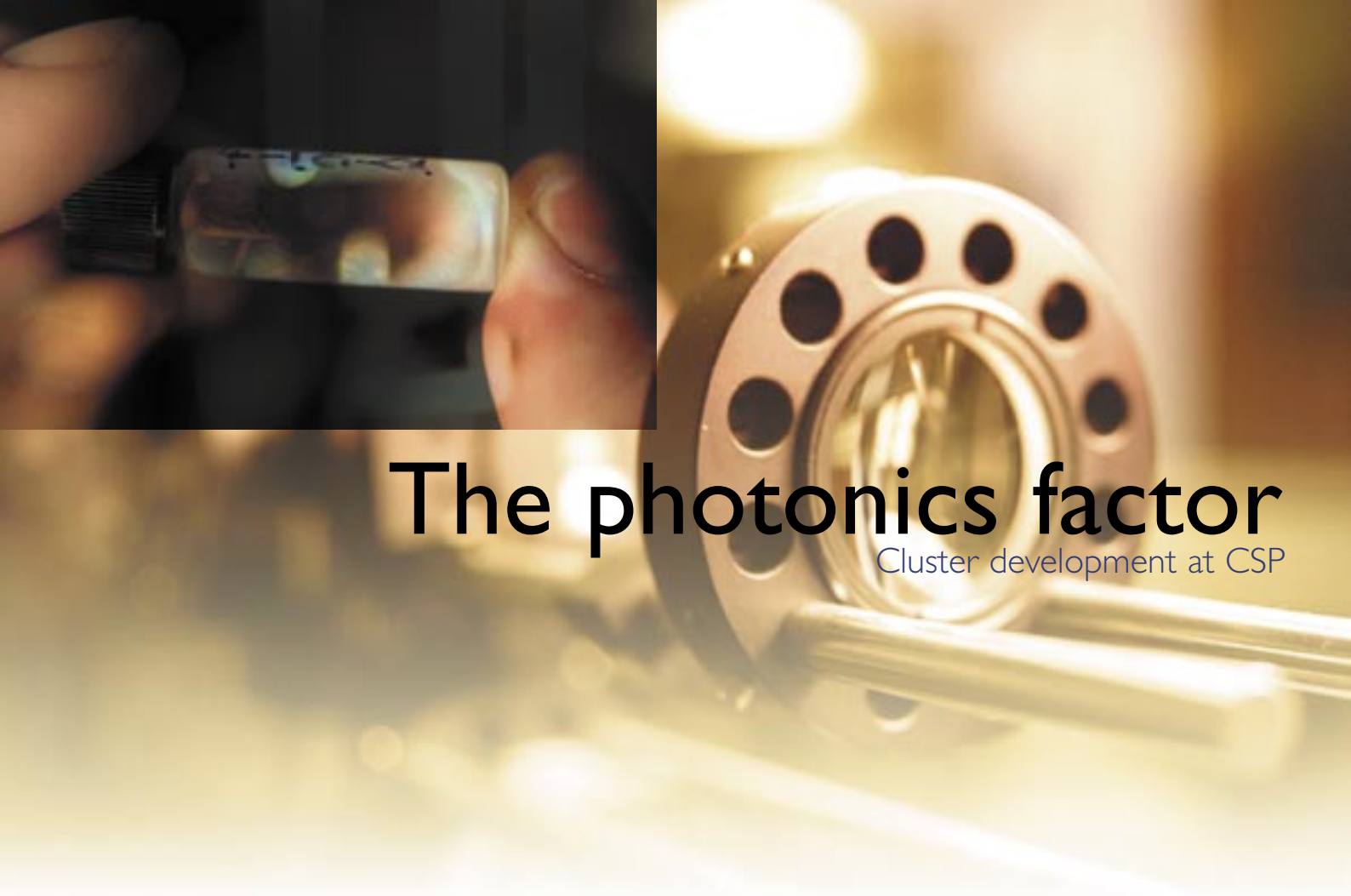


Different properties of two polymorphic forms of Norvir®

Solubility effects example: Norvir®

- **95/5 Ethanol / Water at 5°C**
  - **» Form I: 188 mg / ml**
  - **» Form II: 41 mg / ml**
- **Solubility in Ethyl Acetate at 70°C**
  - **» Form I: 1250 mg / ml**
  - **» Form II: 825 mg / ml**

REF: Org. Process Res. Dev. **2000**, 4, 413-417



The photonics factor

Cluster development at CSP

One year on from the opening of the Centre of Molecular Materials for Photonics and Electronics (CMMPE) on Cambridge Science Park, Catalyst talked to its Director, Professor Harry Coles, about its progress to date and the reasons behind the development of a unique cluster of photonics activity.

"It's been a productive year – tiring but productive!" smiles Professor Coles as he looks back on a hectic 12 months since Lord Sainsbury opened CMMPE as a part of Cambridge University's Department of Engineering in February last year.

Already involving 50 specialists in its field, CMMPE is a focal point for academic research into photonics-based devices, with a focus on practical applications and commercial collaborations.

"I think it's unique in Europe," says Professor Coles, "because we have a much broader remit than anywhere else. We do chemistry, physics, engineering systems; we cover the whole process from conception of an idea, through gestation, to birth and out into product.

"We're academics but we have one very big foot in industry. We still do blue-sky research, but whereas it used to be maybe ten years out to product, we're now fitting it more into the corporate research lab model. Companies are expecting work to be done on a fairly fast turnaround – it can be very exciting."

Clearly, Professor Coles is enthused by the on-site possibilities for collaborations which have already developed since the Centre opened last year. "Since we've started here, we've begun two new collaborations with Pi Photonics and we've also had interaction with Cambridge Photonics Limited – it's all part of the same loop of networks," he says.

"It's also helped by the innovative work that a company like Plastic Logic is doing just a few hundred metres from here – we've had discussions with them about ways of exploiting a different aspect of photonics in display devices."

Add to these the existing collaborations that CMMPE has developed with Merck NBSC, Dow Corning and its interactions through the COMIT Faraday Partnership with global giants such as Hewlett Packard and Sharp, and it becomes clear that there is a critical mass building in terms of activity in photonics-based research.

"What's interesting about the current situation is that we're finding a lot of companies who want to use photonics in different areas," explains Professor Coles. "For example, we're talking with a biotech company about using wave-guide type applications in their particular biological sphere, so it really is photonics with a difference."

Looking at the cluster of photonics development that has emerged in the Cambridge region and on Cambridge Science Park in particular, Professor Coles is clear that this is not simply the result of the city's academic reputation. "That's played a big part," he says, "but it's also due to the willingness within the University to build an infrastructure for exploitation routes and commercialisation."

With the recent approval of funding for a new building in West Madingley to house CMMPE's sister body – the Centre of Advanced Photonics and Electronics – it seems that Cambridge is a highly productive place to be for anyone involved in this fast-moving field.

"The brakes are coming off in the photonics industry," concludes Professor Coles. "The investment will keep growing, as will the number of new companies and spin-offs. There are inventions that have been waiting for an upturn in the economy. It's just a matter of time before they start taking off, and we'll certainly be there playing our part."

Business class

Taking a trip with Cambridge Business Travel

For more than ten years Cambridge Business Travel (CBT) has been providing Science Park clients with a high-quality service in a rapidly changing industry sector. Founding partners Stuart Scott and William Burnett talked to Catalyst about the journey so far.

Surrounded by companies in fields such as biotech, IT, photonics and telecoms, Cambridge Business Travel (CBT) is one of only a handful of companies on Cambridge Science Park on the periphery of the hi-tech sector (it acts as a beta site for one of the four global travel computer systems). Nevertheless, it shares more than a few common experiences with many of its fellow start-ups that have also established themselves here.

"We started off ten years ago with three staff as part of a drive to build the service infrastructure here," says Stuart Scott, co-founder of CBT. "I think it helped that we were a new and independent start-up company. The history of this site is about small companies that come and grow."

Seven years of steady growth and the addition of eight members of staff saw CBT's turnover peak at £7.5 million in 2000, but a major blow to customer confidence in the travel industry was only just around the corner.

However, with business now back to within 15% of its original volume prior to 9/11, CBT seems to have weathered the worst of the storm which has also seen crises such as SARS and Asian flu having a significant impact on this volatile sector, as well as additional pressures on financial margins.

"When we started, airlines used to pay us 9% commission on tickets we sold, but those days have long gone," says Scott. "Now, most only pay between 1% and 4% commission, but we've actually absorbed a lot of the original cuts ourselves. Our objective is not to be greedy and to beat the competition on service. We know that our competitors charge for all transactions including refunds – we don't do anything like that."

The dramatic growth of the Internet and the arrival of the low-cost, short-haul airlines have created further challenges for the industry, but William Burnett, co-founder of CBT, is in no doubt as to the value of the service CBT provides its clients.

"We get most of our new business through referrals and we don't advertise," he says, "so I think that says something. If a PA books a return flight to Paris for the CEO via the Internet, that's fine if it's cost-effective, but we can offer the alternatives at the same time and double-check the date!

"For more complex arrangements like multi-trip tickets or additional services, that's where our expertise really comes to the fore – it takes our people a long time to learn all the ramifications of the travel industry.

"Ultimately, we provide our clients with a valuable service because we have knowledge and expertise in this area. It's an outsourced service, and very often it's a false economy to bring it back in house when a company's skills and resources are better used elsewhere."

www.cambridgebusinesstravel.co.uk

Below: the team at Cambridge Business Travel

Lorantis

Regulating immunity

Right: the new Lorantis building at 410 Cambridgde Science Park

Lorantis is a company raising the stakes in immunology with some potentially revolutionary approaches to selectively treating immune diseases – Catalyst talked to Chief Financial Officer Andrew Muncey to find out more.

Having raised the largest private equity funding round for biotech in the UK in 2003 – some £25 million led by Apax Partners – it's clear that Lorantis is a drug-discovery operation making quite an impression on discerning investors. Certainly it was a moment to savour for the man responsible for how those funds would be spent, CFO Andrew Muncey.

"Obviously we were very pleased because the financing will enable Lorantis to develop its products over the next few years," he says. "I also think it's very encouraging for the whole sector because it shows that pre-clinical companies can raise the significant amounts of money needed to take their products into the clinic.

"During our fundraising, potential investors in this sector seemed to be looking for companies with products at a later stage of development – products already in the clinic, and preferably in phase two – and yet we were a company which was still at the pre-clinical stage. Our challenge was to communicate the fact that our work is unique, groundbreaking and has enormous commercial potential.

"Part of my job was getting investors to understand that even though the risks may be higher at an earlier stage of development, the potential rewards are enormous. So it's a vote of confidence in what we're doing as a company, but also a good sign for other companies who are at a similar stage in the development process."

Such confidence is based on the company's unique work on the Notch signalling pathway and its role in the peripheral immune system – work that has diverse applications from treating autoimmune diseases such as rheumatoid arthritis or multiple sclerosis to encouraging successful organ acceptance in transplant patients.

Lorantis's three founding scientists Maggie Dallman, Jonathan Lamb and Gerry Hoyne were first brought together as a collaborative team at Imperial College in London looking at a cell surface receptor known as Notch, and in particular its role in the developmental fates and function of cells.

This Notch receptor is present on the surface of T-cells, the cell type that is central

to coordinating our immune responses to antigens – the toxic or foreign substances that our bodies encounter as a normal part of everyday life. It was found that the degree of Notch signalling in the T-cell controls the balance between the suppression and activation of an immune response, a breakthrough with major implications, as Muncey explains.

"By delivering Notch signalling in the presence of the antigen we're interested in, we're able to create populations of those antigen-specific T-cells with the mode of action that we want. But one of the beauties of this new approach is its specificity – you're not generating any other T-cells, only those with the specific immune response you're looking for.

"Another key point about using the Notch signalling pathway is that we're not only able to activate an immune response when the natural response is too low – as in cancer, for example – but we're also able to suppress a T-cell response that is inappropriate, as in allergies or autoimmune diseases."

This breakthrough has provided the foundation upon which Lorantis has been able to develop its dual platform of Antigen-Specific biological therapeutics (ASPECT™): ASPECT-Suppression and ASPECT-Activation. Currently in the later pre-clinical stage of the development process, Muncey is enthusiastic about the opportunities that this technology will present over the coming years.

"Most biotech companies are lucky if they have two or three potential products to work with. For us, the great thing about what we're doing with Notch is the broad range of applications it has. There are over 50 autoimmune diseases, and so that means potentially over 50 different products – and that's just looking at one particular area of immunology. And because we have the platform to generate multiple products, we can also be very flexible in when and how we license them out."

It's been an interesting journey from when the company was first founded by the three collaborating scientists back in July 1998. Existing at first solely as a virtual entity, initial seed funding from venture capital group Abingworth was used to fund further scientific research before the company secured its first premises and employees in early 2000. With £3 million secured in first-round funding in June 2000 and £16.2 million in a second round in April 2001, Lorantis moved to Cambridge Science Park in September 2001.

"On our previous site at Babraham we basically ran out of room," explains Muncey. "Some space came up in the Xenova building here on the Cambridge Science Park which was ideal for us, because it had previously been used by Cantab who were an immunology company – the facilities were almost perfect for our specific needs."

Nevertheless, this was a short-term move because Trinity College had agreed to build Lorantis a new building on the Park which they moved into in July 2003. Home now to 48 Lorantis employees, Muncey is upbeat about what the future holds.

"I'm still as motivated by the same thing that enticed me to join the company in the first place," he says, "the fact that we've got a technology here which is so fundamental and with such amazing potential.

"We're looking to build a very large, sustainable business, but also to do that with products that will have a meaningful impact on people's health and reduce the impact of debilitating diseases like multiple sclerosis. The whole pharmaceutical sector is moving to a stage now where there's a real opportunity to tackle the underlying causes of disease, rather than just relieve the symptoms – and I think Lorantis can be a part of that."

www.lorantis.com

Pushing back the pain barrier

A new approach to pain relief with Ionix Pharmaceuticals

Right: the main entrance and reception area at Ionix's new facilities at 418 Cambridge Science Park

Pain relief is big business – a pharmaceutical market worth some $38 billion annually and yet still largely based on the same types of drugs used over 40 years ago. Ionix Pharmaceuticals is a company looking to change all that – Catalyst spoke to Director of Business Development Nigel Low to find out how.

Secure in its brand new laboratory facility on Cambridge Science Park and with a second round of venture capital financing worth £10 million completed during the last 12 months, Ionix Pharmaceuticals certainly seems comfortable with its growing status as Europe's leading biotech specialist in the development of novel analgesic drugs for the treatment of acute and chronic pain.

It has developed a portfolio of product candidates that will address pain associated with a wide variety of conditions, including surgical procedures, trauma and chronic debilitating conditions such as arthritis and diabetes. Such a broad range of potential new therapies for pain has, however, only recently become an attractive area of activity for drug discovery after decades languishing as a largely static area of medical research – an unfortunate state of affairs for such a ubiquitous condition.

"Everyone who's in pain knows they're in pain," says Low, "and everyone is seeking to avoid that. It's something we all experience – in fact it's a 'fifth vital sign' that medical staff should check for in patients, alongside pulse, blood pressure, core temperature and respiration.

"But until recently there was relatively little understanding about how the whole process of pain occurred. Up until now, in the main, the leading therapies have been opioids and non-steroidal anti-inflammatories. The former date from the century before last and have major side effects, while non-steroidal anti-inflammatories, which started off with the development of aspirin, have little impact on severe pain. Of late, however, we've begun to unravel the biology and pharmacology of pain, so we can follow a targeted rather than a random approach to try to treat it."

In particular, as the name of the company suggests, Ionix is focused on modulating ion channels in the peripheral nervous system as a way to combat pain. "Pain is essentially the result of a flow of electrical activity," explains Low, "and this flow is controlled by ion channels.

"We look at ion channels in the peripheral nervous system and how they are involved in pain signals – their initiation, transmission along the sensory nerve, or the jump-off point from the sensory nerve into the central nervous system. You might put it simply by saying it's about specifically shutting off the signal before it reaches the brain. And because we're working in the periphery, we're looking to produce therapies which are able to modulate pain without any of the central nervous system side-effects – like dizziness, addiction and sedation – that you get with drugs like opioids."

It was the advances in such areas made by Professor John Wood at University College London (UCL) that formed the starting point of several of Ionix's current programmes, and encouraged venture capitalists Apax Partners to invest in a new start-up company focused on this area, formally launched in July 2001.

Chief Executive Officer Andy Sandham, a key driver in the creation of several successful drug discovery companies in both Europe and the US, brought together a core management team which included Ann Hayes of GlaxoWellcome and Phil Birch of Nycomed Amersham as founding members to draw up plans for the development of Ionix's portfolio of drug candidates and formalise intellectual property agreements with Professor Wood and UCL.

Nearly three years later, the company now has more than 50 employees (more than half of whom hold PhDs) as well as its new custom-built facilities which it moved into in summer 2003.

"We have a mixed platform approach to drug discovery," says Low, "so what we wanted was to have laboratories that enabled us to have molecular biology, high-throughput screening, the scale of medicinal chemistry we want, plus all of our management in one place – a fully equipped drug discovery company under one roof. The only way to get all this was to design it and build it."

However, with most of its novel targets still at least five or six years away from hitting the market, Ionix has been careful to ensure investors can benefit from a mixed portfolio of products combining both shorter- and longer-term potential.

"I think the investment environment we've seen over the last few years has shaped how we've developed our product range," says Low. "You're very aware that you must balance risk in the things you take on, and I think we've done that well. Our first programme has a decidedly lower risk profile than the others, which are addressing proprietary drug targets and offer real opportunities to make a major impact on the market."

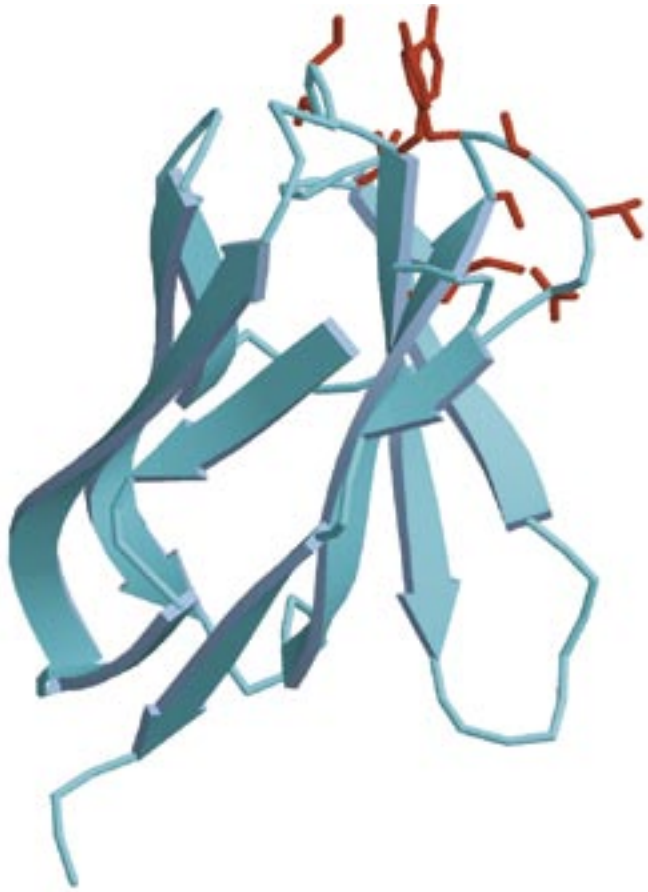
It's an approach that bodes well for the longer-term future of this innovative and ambitious company. "I think Ionix is unique among biotech companies in being totally focused on the area of pain relief and having all the capabilities in house to discover new drugs," adds Low.

"Generally speaking, comparable operations are those within the large pharmaceutical companies. There are a number of other pain companies, but most of them focus on reformulating drugs or simply on late-stage development rather than drug discovery. Our focus on innovative, totally new drugs is distinctive and gives us an exceptional opportunity to deliver the next wave of pain therapies to patients."

www.ionixpharma.com

Domantis

Masters of the domain



Left: the molecular structure of a domain antibody
Right: Domantis's facilities at Cambridge Science Park

With a unique approach based on the use of domain antibodies – the smallest fragment of human antibodies – Domantis is a company working to create a new generation of drugs with a broad therapeutic potential. Catalyst met Chief Scientific Officer Dr Ian Tomlinson to find out more.

Not long after announcing the completion of a US$33 million (£17.5 million) Series B financing round in February this year, Ian Tomlinson has good reason to feel pleased with the progress of the company he helped to found back in December 2000.

"It's one of the biggest private fundraisings in Europe for biotech in the last year, and it gives us a window where we can really focus on our work and make some significant progress," he says. Evidently the company has made a positive impact on investors impressed by the potential to generate a new class of drug using domain antibodies, as Tomlinson goes on to explain.

"If you look at drugs currently in development or on the market, there are essentially two types: small-molecule drugs, which have a molecular weight of about 1,000, and antibody-based drugs, which have a molecular weight of about 150,000. Obviously that's a big size difference.

"There are advantages and disadvantages to both types. Small molecules are great because you can make them cheaply and, because they are small, you can take them as a pill. But they tend to have side-effects and are sometimes not particularly potent.

"On the other hand, antibodies are very large, so you can really only inject them, which is not ideal. They're also very expensive to make. However, on the positive side, they are extremely specific drugs, so when you put them in the human body, they only do the one thing that they are designed to do – quite different to small molecules, which tend to be more cross-reactive.

"What we're trying to do is to make a drug which gives the best of both worlds. Domain antibodies have a molecular weight of about 11,000, so they're much smaller than regular antibodies. It means we can make them more cost-effectively and also they can be

taken in pill form or inhaled into the lung. But like antibodies, they're very specific for the targeted disease, so they have a very strong therapeutic potential in conditions which include respiratory disease, inflammation, cancer and cardiac disorders."

The smallest functional binding units of antibodies, domain antibodies provide a number of significant advantages over larger antibodies and proteins due to their shape and size. As well as the diverse formulation and delivery options they provide (e.g. oral and pulmonary administration), they also support multiple product formats, such as dual-targeting molecules that can hit two separate therapeutic targets in a single product. In addition, the ability to produce them in bacteria and yeast means they are very cost-effective to manufacture on a large scale.

After a period spent as a Fellow at Trinity College, it was while working at the Medical Research Council (MRC) laboratories on the Addenbrooke's site with co-founder Greg Winter that Tomlinson and his group were able to advance the technology related to domain antibodies to the point where commercialisation seemed a viable option. With $1 million of start-up funding, Domantis hired its first employee in early 2001 before completing a $20 million financing round in April the same year. Interestingly, though not coincidentally, Domantis also opened offices in Cambridges on both sides of the Atlantic, as Tomlinson explains.

"I think sometimes European biotech companies can get involved in the US too late, and we didn't want to let this happen to us. It's the biggest market for any drug we'll ever develop, and most of the deals we're ever going to do will be in the US, so it makes sense for us to have a strong commercial focus there."

Initially spread across two sites in the city, the company has recently brought all its UK operations under one roof at 315 Cambridge Science Park. It's a timely and important move for the company, according to Tomlinson. "It's a challenge to find good facilities, particularly for the kind of science we're doing," he says. "Consolidating our operations here is really a big deal to us."

With its first drug due to enter the clinical phase in early 2006, Domantis is still at the mid stage in its journey towards getting domain antibodies out of the lab and onto pharmacy shelves. Nevertheless, with exclusive rights in this therapeutic field gained through agreements with the MRC, Tomlinson is confident that the company is in a strong position to move forward.

"What we've established over the last two years is a broad pipeline of different drugs. We've got 12 ongoing programmes both on our own and with partners, so we're not going to be a one-hit wonder. In five or six years' time we'd like to see one of our drugs coming to market, and maybe a number of drugs following very closely behind – that's what it's all about."

There's a clear commercial edge to a man who previously spent 11 years as an academic. Nevertheless, Tomlinson plays down the differences in approach from his days as a Cambridge University don.

"I think a lot of the principles you establish as an academic are the same as those you would use in a commercial setting – you want to do good science, you need to be organised, and you need to be able to present what you're doing to others in an effective way.

"Part of our job here is to sell our technology to potential investors and partners, so you need to have a good feeling for what the big picture is and to be able to get that over to other people," he adds. If the evidence of recent funding rounds is anything to go by, the message from Domantis is coming through loud and clear.

www.domantis.com

Location, location, location

A longer-term perspective on life at the Park

Above: Richard Dickinson, Laboratory and Facilities Manager, Astex Technology

It's been more than 20 years since Richard Dickinson, Laboratory and Facilities Manager at Astex Technology, took his first job as a junior lab technician on Cambridge Science Park. Several companies and a number of promotions later, Catalyst talked to him about some of the changes he's noticed – and new buildings he's been involved with – along the way.

There aren't many people whose careers on the Cambridge Science Park stretch back to the distant days of its first-phase development – but Richard Dickinson is one of them. For the best part of two decades, he's been a part of the collective success story that's seen Cambridge Science Park become one of Europe's premier hi-tech locations, and it's most definitely not been a view from the sidelines.

Fresh-faced from one of the city's local schools, Richard took his first post at Cambridge Science Park aged 16 for a company called Goodfellow Metals back in 1983. It was not the most promising of career starts.

"In those days, being a junior lab technician included washing the company cars and cleaning the toilets – it really was starting at the bottom. So in the end, I didn't last very long at Goodfellow Metals," admits Richard.

After a spell on the government's Youth Training Scheme, Richard began a career as a trainee research scientist for early biotech companies Coralab and Cambridge Research Biochemicals.

Later, he landed a job with Immunology Ltd, which moved onto the Park in 1990. Changing its name to Cantab Pharmaceuticals in 1994, this was also the point at which Richard veered course to develop his current area of expertise as a laboratory and facilities manager, finally arriving at Astex Technology in June 2001.

It was Richard who masterminded Astex's move from Units 250–254 and Unit 128 Cambridge Science Park into their new facility at Unit 436, and so he knows better than most some of the pitfalls associated with this critical procedure.

"Companies often overlook how long the full process of relocation can actually take. The path from first thinking about a possible move to actually starting operations in a new building is rarely straightforward," says Richard.

Importantly, he sees consultation with staff as an essential part of any successful move. "If it's simply a process that's seen as coming from management downwards, you won't get buy-in and you could miss some important factors," he adds.

Having seen the growth of the Park from an early stage and been a part of the development of several new sites on it, Richard also has a unique perspective from which to comment on the role Trinity College has played in creating this hub of hi-tech infrastructure.

"Trinity has become very experienced in providing facilities for the hi-tech sector over the years. They've also learnt that biotech in particular starts small and usually wants to expand – providing capacity for this from the beginning is a big advantage."

As for his own future, Richard is in no hurry to move any time soon. "I enjoy it, especially building buildings," he says. "There's a lot of pressure and stress moving people in, but I seem to thrive on that. Maybe they'll start knocking down some of the earlier buildings so that we can start the whole process again!"

www.astex-technology.com

PARKLIFE

International visits to Cambridge Science Park

Delegations from Botswana, China, Germany, Malaysia and South Korea have all made recent visits to Cambridge Science Park to build international links and learn more about the success of this centre for hi-tech enterprise.

A visit from delegates of the Malaysian Government's Multimedia Super Corridor took place on 13th January 2004, while on 3rd February a delegation from Andong City in South Korea visited CSP to learn more about the Park and in particular the development of its biotech industry.

Building on existing ties between Cambridge and Munich, the Cambridge Network welcomed a Bavarian delegation to Cambridge Science Park on 5th February as part of a three-day visit with the objective of strengthening links between the two regions' financial, entrepreneurial and academic communities.

Twelve senior Chinese science park managers visited CSP on 16th February during a two-week training programme resulting from a China–UK science park link formally endorsed and supported by both governments. On 24th February, members of a task force for the establishment of a second university in Botswana came to the Park in a visit organised by the British Council.

Above: two members of the Botswanan delegation, including delegation leader Mr Lucky Tebalebo Moahi (left)

Student entrepreneurs looking for hi-tech impact

Cambridge University's Centre for Entrepreneurial Learning (CfEL) is looking for hi-tech companies to participate in the third year of its Enterprising Students Programme, providing short-term placements for individual students to work on a specified project as defined by business needs.

Placement lengths are flexible depending on the nature of the project and the commitments of the student, but generally last 4–12 weeks. Students receive training and support from CfEL and are to be paid a minimum of £250 per week by the host companies.

The programme works through the submission of project details to CfEL by companies on a strictly confidential basis. These are then matched with potential candidates, and the company then chooses whom to interview and employ. To find out more about getting a talented and motivated student to make a difference in your business, please contact CfEL.

Tel: 01223 766900
Web: www.entrepreneurs.jims.cam.ac.uk
Email: entrepreneurs@jims.cam.ac.uk

Above: Enterprising Students – catching up with their mentors at a networking event

TeraView secures £6 million second-round funding

TeraView Ltd, the Cambridge Science Park company dedicated to the commercialisation of the new field of Terahertz radiation imaging and diagnostic technology, completed a second round of funding led by Amadeus Capital Partners on 9th January 2004.

TeraView, a spinout of Toshiba Research Europe Laboratories, has developed a unique technology to emit and detect Terahertz light, which lies between microwave and infrared and represents the last unexplored region of the radio wave and light spectrum.

Amadeus Director Herman Hauser commented: "TeraView's technologies lead the world in the generation and detection of Terahertz light and, with first mover advantage, the company looks set to build a significant business."

CSP runner in multi-marathon challenge

Dr Karen Thomas, Head of Business Development at Amedis Pharmaceuticals, is celebrating turning 40 by completing four "ultra marathons" in 2004 – 193 miles in total.

With races in South Africa, Holland and Britain, Karen is raising money for the charity COCO – Comrades of Children Overseas – which works with underprivileged children around the world. Last year she raised £1,100 in sponsorship for the same charity by completing the Comrades Challenge ultra marathon in South Africa (56 miles), an event in which she will again be competing in 2004.

Left: Dr Karen Thomas, having just completed the 56-mile Comrades Challenge in 10h 26 min in June 2003

Anyone interested in sponsoring Karen or finding out more about her progress can visit **www.justgiving.com/KarenThomas** or email her directly at **Karen.thomas73@ntlworld.com** .

Facilities Managers' Forum gets started

A new forum for facilities managers at Cambridge Science Park has been set up to share experiences, facilitate networking and discuss common issues. With ten companies already involved including Lorantis, Ionix and Astex Technology, the forum provides the opportunity for facilities managers to meet once a month over lunch to listen to a guest speaker and discuss issues such as utilities, local services, regulations and other topics of interest.

The next meeting takes place on Wednesday 19th May at 12pm. To find out more or to confirm venue and attendance, please contact Andrew Taylor, Facility Manager for Lorantis, on 01223 702500 or by email at: **facility.forum@ntlworld.com** .

Astex merges with German oncology company

Astex Technology, the fragment-based drug discovery company, merged with Berlin-based oncology specialist MetaGen Pharmaceuticals in October 2003. With funds resulting from the merger and further investment by Astex's existing investors, the company improved its cash position by £23 million (US$39 million) as a result of the transaction

Peter Fellner, Chairman of Astex, said: "This merger and the linked financing enables Astex to further develop its powerful and highly competitive drug discovery technologies and it will strengthen our valuable partnership with Schering AG."

Launch of networking group for Science Park women

The Association for Women in Science and Engineering (AWISE) is holding a series of networking lunches for Science Park women. The first meeting was held in February in the Q.ton forum. Further meetings are planned for Monday 19th April and Tuesday 8th June 2004 at the Royal Society of Chemistry building on Cambridge Science Park from 12.30pm to 1.30pm.

The first meeting included a promotion for the MentorSet scheme, which aims to provide female scientists with local mentors. The scheme has been running for over a year and many successful partnerships have been formed. There is currently a shortage of mentors in the Cambridge area – more information on becoming a mentee or a mentor can be found on the MentorSet website at **www.mentorset.org.uk** .

Further information about AWISE, including membership and details of other events in Cambridge, can be found on the AWISE Cambridge branch website at **http://cambridge.awise.org**

PARKLIFE connections

The Science Park HR Group, a support network for HR managers/representatives, provides a forum for sharing of common issues/problems, discussion of best practice, updates on legislation, and the opportunity to offer support to each other in what can often be a solitary role. We meet every other month over lunch.
Contact: Wendy Hepburn
Email: whepburn@xaar.co.uk

A Facilities Managers' Forum is an opportunity for representatives from CSP companies to meet once a month over lunch to share experiences, facilitate networking and discuss issues of common interest in this field.
Contact: Andrew Taylor
Tel: 01223 702500
Email: facility.forum@ntlworld.com

Biology in Business (BiB) is a Park- and University-wide organisation focusing on career development and the exploitation of novel technologies applicable to the life sciences. BiB organises formal and informal events, including the region's only careers fair for life scientists (CoiLS).
Contact: Charles Bailey
Email: cbailey@cantab.net

The 4Bio Network is an informal network focused on commercial management issues for Cambridge Science Park companies involved in the biotechnology, pharmaceuticals and life-science sectors. Meetings take place every two months, usually on the first Wednesday of the relevant month at 5pm at the Q.ton forum (May 2004 is an exception).
Contact: Charles Bailey, Nigel Low, Karen Thomas
Email:
nlow@ionixpharma.com
charles.bailey@mundipharma.co.uk
karen.thomas@amedis-pharma.com

The European Chapter of the Lab Robotics Interest Group is a forum for the exchange of ideas on robotics and programmable automation in the field of high-throughput screening, assay development, proteomics, genomics and general lab automation. Regular meetings bring together scientists, engineers, users and vendors of equipment and instruments.
Website: www.lab-robotics.org

The Eastern Region Biotechnology Initiative (ERBI) offers members substantial discounts on supplies through its Purchasing Consortium. Membership also gives access to ERBI's special interest groups that include human resources, finance and business development.
Contact: Jeanette Walker
Email: jeanettewalker@erbi.co.uk.

Enterprise Link, a Business Link service for Cambridgeshire, is a membership network providing advice and support for early-stage, entrepreneurial/aspirational businesses. It holds a variety of networking events and seminars at the St John's Innovation Centre in Cambridge, and also sends out regular bulletins to members with information, advice and opportunities. It can also arrange access to sector specialists.
www.enterprise-link.co.uk

The Entrepreneurs' Club helps like-minded people and companies share ideas, network and discover opportunities through regular meetings at Cambridge Science Park, as well as providing guest speakers and discussions on topics chosen by members. The Cambridge Club is part of a wider network established by Kleinwort Benson Private Bank.
Contact: Derek Wright
Tel: 020 7475 5476
Email: derek.wright@kbpb.co.uk
Web: www.the-entrepreneurs-club.com

The Cambridge Science Park is managed by Bidwells on behalf of Trinity College.

Catalyst is a forum for companies on the Cambridge Science Park. The next issue will be published in Autumn 2004. If you have any comments or suggestions for stories to be included in the next issue, please get in touch with the editor, Dr Sarah Tasker.

www.cambridgesciencepark.co.uk

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Viewpoint

A Global Perspective from the Science Park

CSR is a leading developer and supplier of single chip wireless solutions designed to support data and voice communications between a wide range of consumer products. CSR's reputation has been built in Bluetooth, the rapidly growing personal area networking standard that uses short range radio links at a frequency of 2.4GHz.

CSR's Integrated Circuits (ICs or chips) are incorporated in over 500 customer designs representing over 60% of all Bluetooth qualified end products and modules. These designs cover a broad spectrum of end products, many of which may be found in shops in the high street, including mobile phones and headsets, PCs and PC peripherals, PDAs and in-car communications systems from companies including NEC, Nokia, Panasonic, Sharp, Motorola, Apple, Dell and IBM.

The Fabless Model

With its BlueCore1TM chip, CSR led the wireless communications industry in introducing the first single chip implementation of the Bluetooth standard. From its first commercial shipments in May 2000, CSR has shipped more than 25 million Bluetooth ICs.

As a fabless semiconductor company, CSR does not manufacture its chips but contracts their fabrication to silicon foundries in Taiwan, France and the USA. The fabless model is very appropriate for companies in Cambridge as it plays to the region's strengths which include a large pool of talented engineers together with the spirit of innovation needed to produce a continuous flow of innovative ideas, technologies and materials. From the 1960s, the Cambridge-based technology consulting companies including Cambridge Consultants, TTP and Generics generated a continuous flow of talent and ideas which has led to the creation of companies such as CSR.

Growing CSR

CSR decided at an early stage to build a global company. We recruited a good collection of venture capitalists and decided that we would raise the significant amount of capital necessary to grow a successful fabless semiconductor company. Our experience has been that there is no shortage of development capital available to companies with the right proposition.

CSR has grown rapidly as it was only in April 1999 that the nine founders of CSR spun out of Cambridge Consultants. By the end of 2000, a hundred staff were housed in four buildings plus a collection of portacabins on the Science Park. We moved to Unit 400 in September 2001 and by the end of 2003 had grown to 150 staff with another 50 around the world.

CSR is a products company and there was no turnover in the first year whilst we were developing BlueCore1TM. By 2003, however, turnover had grown to US$67 million. CSR became profitable in the second half of 2003 and floated on the London Stock Exchange in February this year.

Going Global

Cambridge is a good place to operate a business as the environment is attractive and communications are good - with London and Stansted airport not too far away. The founders are often asked why they chose Cambridge – the answer, of course, is that we were already here !

Some 75% of CSR's staff are based in Cambridge and we have been able to grow organically by recruiting from both the UK and elsewhere – staff from eleven nations currently work at CSR in Cambridge. However, there are some skills lacking in the region. For example, as Cambridge is not home to companies that manufacture silicon chips, this has necessitated the recruitment of experienced staff with manufacturing skills from Scotland, Wales and the USA where silicon fabrication is a well established activity.

CSR is connected electronically to its customers and suppliers and it is not a problem for us that there is no silicon manufacturing in the Eastern region. Many of our chips are manufactured in AsiaPacific and most of our customers make their products there too.

Cambridge has proved to be a good place to found CSR. The challenge for the company in its next period of growth is to continue to innovate and execute whilst supporting our customers wherever they are. A sound foundation in Cambridge will provide the strengths required for CSR to perform effectively in the global community.

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