BioPharma Dealmakers

A series of business profiles from leading biotech and pharmaceutical companies looking to develop relationships with prospective partners. Featuring Cancer Partnering and Contract Services.

January 2010

nature biotechnology

nature REVIEWS DRUG DISCOVERY

As originally published in the January 2010 edition of *Nature Biotechnology* and the February 2010 edition of *Nature Reviews Drug Discovery* as an advertising feature.

COMBINING OUR STRENGTHS SHARING OUR SUCCESSES

You've discovered something significant. Now discover us!

Please contact:

Barbara Yanni, JD, LLM
Vice President and Chief Licensing Officer
Merck & Co., Inc.
One Merck Drive
PO Box 100
Whitehouse Station, NJ 08889-0100 USA
Phone: 908-423-4350
Fax: 908-735-1201
www.merck.com/licensing

"Merck is passionate about our commitment to partnering. Our strengthened company provides even more opportunities for collaboration. Let's explore the possibilities of combining our strengths to deliver novel medical breakthroughs that save and improve lives."

– David Nicholson, PhD, Senior Vice President and Head Worldwide Licensing and Knowledge Management

MERCK & CO., INC.
Whitehouse Station, N.J., U.S.A.

Contents

PUBLISHING TEAM

Publishing Director
Peter Collins

Business Development Manager
Graham Combe
g.combe@nature.com

Business Profile Writers
Suzanne Elvidge
Crispin Littlehales
Barbara Nasto
Peter Vermij

Marketing
Samantha Savalio

Production
Tom Rose
Stephen Russell

Note: Companies that appear in this table of contents have paid for their advertisement features and have final approval of their content. If you would like to appear in the next BioPharma Dealmakers please contact:
Graham Combe,
Business Development Manager
g.combe@nature.com

Can We Win the Battle Against Cancer by Joining Forces?

Partnerships facilitate multifaceted strategies that include companion diagnostics and targeted treatments

Cancer is a genetic disease presenting thousands of variations on a theme, often evolving in ways that are singular to the individual host. The reason there is no Lone Ranger with a silver bullet is because we aren't dealing with a single enemy or even a gang. Cancer is more like a coliseum filled with very clever monsters that can morph at the drop of a hat. But, according to those interviewed for this article, it is the very intensity of the battle that keeps researchers and oncologists moving forward in an ever tightening circle.

"Cancer is an incredibly complicated disease," notes New Jersey-based Merck & Co.'s Dr. Mervyn Turner. "We need the best minds in the world to understand what drives a cell to proliferate; what drives it to migrate; and what makes it produce those life-threatening tumors." Turner is responsible for finding those minds in his role as Senior Vice President of Worldwide Licensing and External Research.

Merck's involvement in oncology has deepened considerably over the last few years with collaborations playing an increasingly large role. "Just as we are focusing on understanding networks inside cells we have to understand the network of science and scientists all across the world working on cancer. We have to find the best ways to collaborate across that network to allow us to solve this problem," explains Turner. "It is just not something that any one company is going to be able to do on its own."

Turner's attitude is echoed by just about everyone who is in the trenches of cancer R&D. Dr. Campbell Wilson who heads up oncology business development for AstraZeneca says that collaborations have been essential both in driving early discovery programs and in strengthening clinical development. The UK-based company recently signed a deal with Merck that exemplifies this very point.

A Merck scientist performs a cell transformation assay to evaluate the anti-proliferative activity of an investigational oncology compound.

Reconnoiter

Each with a promising investigational compound in hand—MK-2206 from Merck and AZD6244 (formerly ARRY-886 from Array Biopharma) from AstraZeneca—the two companies decided to move both entities forward as a novel combination anticancer regimen. "This is a very innovative deal," explains Turner. "Normally companies wouldn't talk at such an early stage, nor would they align their programs like this. It is a recognition of the kind of unique challenges and opportunities that oncology offers."

Another unusual aspect of the deal is that no money is to be exchanged. Under the terms, AstraZeneca and Merck will work side by side to evaluate co-administration of the compounds in a Phase I clinical trial for the treatment of solid tumors. All development costs are to be shared jointly.

Both drugs are designed to inhibit a protein known to be abnormally activated in human cancers. ASD6244 affects MEK (Mitogen-activated protein kinase 1), a signal that promotes cancer cell growth and survival. The compound has demonstrated proof of mechanism and clinical activity. It is currently in Phase II clinical trials in a range of tumor types. MK-2206 also has an effect on a signal affecting cell survival—AKT, which is a component of the phosphatidylinositol-3 kinase pathway. Phase I clinical data were presented at the 2009 ASCO annual meeting.

"Collaboration is of particular importance in oncology where, in the external world, there is more discovery research and more products in development than in any other therapeutic area," states Campbell. Indeed, according to a report released in 2009 by the Pharmaceutical Research and Manufacturers of America (PhRMA), 861 new cancer medicines and vaccines are being tested in human clinical trials or are awaiting approval by the US Food and Drug Administration (FDA).

Take Aim

At the heart of this and many other cancer collaborations is the desire to get the right treatment to the right patient as quickly as possible. This doesn't just involve telescoping time from discovery to distribution, it means creating therapies that are specifically targeted. In today's world, cancer drugs miss the mark more often than those for any other disease area working in only about one in four patients treated. A more focused approach whereby a molecular diagnostic can be used to link a patient to the most efficacious treatment for his or her cancer is expected to save money, heartache, and ultimately lives.

Netherlands-based Qiagen already markets an impressive armamentarium of companion diagnostics for cancer that includes CE marked assays for K-RAS and B-RAF for colon and other cancers as well as pyrosequencing-based methylation assays targeting the cancer biomarkers MGMT, P16, LINE1 and MLH1. The detection of particular

Surveillance

There is no better way to figure out if a cancer drug is really working than to test it in patients and there is no better way to improve that treatment than to feed information about the patient's response directly back to the manufacturer. That truth was what motivated Merck to establish a relationship with the H. Lee Moffitt Cancer Center & Research Institute (MCC) in Tampa, Florida three years ago. The multi-site project involves the analysis of tumor tissues and clinical data from thousands of patients.

The installation in 2008 of a high-level IT framework called the Biomarker Information Pipeline has facilitated progress. Upon enrolling in the MCC's Total Cancer Care program, patients sign a consent form and a random number is generated for each sample, thus de-identifying them. Data is automatically uploaded into a data warehouse without any human intervention. Standard operating procedures are in place to ensure that tissue samples are collected and processed consistently. At the end of each day the patient data are sent by MCC to Merck for analysis. The results are then transmitted back to the center. "It's all about translating what we learn on the molecular level into what we know about patients," says Merck's Dr. Mervyn Turner. "We get the opportunity to profile different types of tumors and to see if our ideas about pathway biology are reflected in real life."

Getting the right drug to the right patient is just part of the equation. With the windows of opportunity for treatment too few and far between, time is of the essence. In 2005, AstraZeneca forged a strategic alliance with the M.D. Anderson Cancer Center in Houston, Texas which included a master agreement for clinical and translational/preclinical research specifying terms for standard items. The idea was to ensure that research projects and clinical trials would not be held up by lengthy negotiations.

In August 2009 the two organizations reported that their efforts to collapse timetables—a project aptly dubbed, Zero Delay—had succeeded. Just two days after the FDA approved a first-in-human cancer trial, the patient number one was enrolled. According to the report's lead author, Dr. Robert C. Bast, Vice President for Translational Research at M.D. Anderson, the time between having a complete written protocol and enrollment is typically 135 days. With Zero Delay in place, that time was cut to 46 days with FDA clearance of the IND on day 44. What changed? Most of the tasks were done in parallel in stead of sequentially. What's more, administrative tasks such as budget and contract negotiations, site visits, preparation, training and mandatory reviews all were conducted prior to the FDA's final ruling.

"Zero Delay demonstrates what can be accomplished in an atmosphere of trust and coollaboration that we've cultivated through out strategic alliance with AstraZeneca," noted Bast in a recent press release. "The next challenge," he says, "will be to do this consistently in order to develop truly innovative therapies that will someday offer new benefits to cancer patients."

Merv Turner, Merck & Co., Inc

Kathleen Sereda Glaub, Plexxicon

Marie-Claude Marchand, Qiagen

mutation in oncogenes such as K-RAS or B-RAF helps to predict how patients suffering from metastatic colorectal cancer respond to certain EGFR inhibitors. Monoclonal antibody treatments often cost about $50,000 but work only in those individuals without mutations in the corresponding oncogenes.

"Qiagen is currently active in several collaborations for the development of novel biomarkers and companion diagnostics and has relationships with seven of the leading players in oncology," reveals Marie-Claud Marchand, Senior Global Marketing Director for Pharma at Qiagen. Marchand believes that the links between markers and pathways will be very important to support therapy combination in cancer disease management.

The sentiment is shared by Kathy Glaub, President of Berkeley, California-based Plexxikon. The company has developed a selective BRAF inhibitor for mutation-positive melanoma patients and other mutation-positive cancers, PLX4032. "When we first read about the oncogenic mutation in BRAF that drives about 50% to 60% of all melanomas and some 8% of all solid tumors we were intrigued, especially since this mutation only occurs in the tumor cells," Glaub recalls. "Given our platform to make particularly selective kinase inhibitors, we reasoned that a highly selective inhibitor should provide for a very wide therapeutic window." Researchers at Plexxikon have since discovered that while it is possible to modulate biomarkers with 50% inhibition of the target, over 90% inhibition of the target is necessary to see tumor shrinkage in patients. "Without a highly selective inhibitor, it may not be possible to witness such efficacy due to off target toxicities encountered before hitting the 90% inhibition hurdle," Glaub says.

Michael Yeomans, Bayer

Bjarte Reve, Oslo Cancer Cluster

In 2005, Plexxikon entered into a partnership with Roche Molecular Systems to create a companion diagnostic to identify best responders for PLX4032. A year later the company signed an agreement with Roche Pharma to develop and commercialize the drug. "Roche has initiated a Phase II pivotal trial in September 2009 and a Phase III controlled study in December on a highly accelerated timetable," notes Glaub. "We have also transitioned PLX4032 to a life cycle team that integrates Roche and Genentech individuals with the best experience and expertise to move the program to the next level."

Another way to pinpoint the target is through diagnostic imaging. German pharmaceutical giant Bayer Schering Pharma AG is developing a range of radioactive traces for binding to certain types of tumors. "We see a closer and closer link between the diagnostic, which can help you really focus in on tumor type, and the treatment," notes Dr. Michael Yeomans, Head of Global Business Development & Licensing for Bayer. "We are very interested in the personalized approach to cancer treatment," he continues. "There has been a great explosion of knowledge in the whole oncology field and the underlying causes and mechanisms of the disease. We are learning more each day about which drugs can help to treat specific tumor types."

Take No Prisoners

One of the most frustrating aspects of treating cancer is that patients often relapse. To prevent cancer from finding escape routes unknown to current therapies, Merrimack Pharmaceuticals, headquartered in Cambridge, Massachusetts, used its considerable expertise in network biology to find those hidden trails and block them. Using this technique, Merrimack Pharmaceuticals has developed MM-121, a fully human monoclonal antibody designed to block signaling of the ErbB3 receptor, a common mechanism of resistance to current therapies that cancer cells use to continue growing. MM-121 will be used in conjunction with other therapies to prevent rapid resistance to emerging therapies.

In October 2009, Merrimack signed its first partnership — a licensing agreement with Paris, France-based sanofi-aventis. "It is wonderful to find a partner who believes in what we are doing and has the confidence to let our approach lead MM-121 through Phase II proof of concept development," declares Ulrik Nielsen, Merrimack's Chief Scientific Officer and a co-founder. Under the terms of the agreement, sanofi-aventis is responsible for all development costs as well as Phase III clinical trials. Merrimack retains the right to co-promote the therapy in the US.

"We see network biology as a way to continue the science beyond the event of creating the drug,"

Reinforcements

Bayer Schering Pharma's mission is to provide new treatment options for diseases with high unmet medical need. In no area is this more apparent than in cancer where deaths are projected to rise to an estimated 12 million worldwide per annum by 2030. The big killers — lung (1.3 million deaths/annum), stomach (803,000), colorectal (639,000), liver (610,000) and breast (519,000) — cost healthcare systems everywhere billions of dollars and continue to defy the efforts of thousands of scientists and physicians.

In an attempt to accelerate the transition from basic research to promising treatment options, Bayer has started a program called "From targets to novel drugs". The program supports collaborative research projects in several areas with oncology heading the list. "We are taking the initiative to reach out to the academic community and small companies who have interesting or novel targets in oncology. We are asking them to share their ideas with us and providing some level of financial support," explains Bayer's Dr. Michael Yeomans. "We got quite a good response."

The Oslo Cancer Cluster is hoping to capture the imagination of would-be oncologists and research specialists before they ever enter the halls of advanced learning. The nonprofit has signed an agreement with the City Council of Oslo and the Norwegian Radium Hospital to build the world's first innovation park to integrate a high school. Due for completion in 2012, the Oslo Cancer Cluster Innovation Park will afford students the opportunity to receive guest lectures from researchers and do internships at the Norwegian Radium Hospital or at one of the 40 member companies within the Cluster.

According to Kaare Norum who is chairman of the board for the Oslo Cancer Cluster Innovation Park, "This endeavor will ensure and strengthen the recruitment to life science and research and at the same time improve the quality of the education within math, science, physics, and health."

Biological production at QIAGEN: The machine fills enzymes produced by QIAGEN for the subsequent packaging in kits ready for use.

Ulrik Nielsen, Merrimack

Dr. Frederick Hall, Epeius

explains Nielsen. "We can treat patients, look at their tumors and their responses to therapy on a molecular level. We then can integrate that information into creating the second and third generation therapies using network biology," he adds. "It is not our goal at Merrimack to stay at 'chronic' when it comes to cancer treatment. We all strive to cure cancer and we will continue to, but the reality for many of today's cancer patients is to treat cancer as a chronic disease. For some time, we'll have to continue to devise strategies to treat cancers that relapse on current medicines."

Hit the Beach

Located in Norway, where an estimated one out of three people will get cancer during their lifetime, the Oslo Cancer Cluster is unifying the private and public sectors to accelerate the development of new cancer treatments. The nonprofit organization is headed by Bjarte Reve whose background in healthcare and politics inspired him to take on the mantle of CEO. "Around 80% of all biotech companies in Norway focus on oncology—either in cancer diagnostics or cancer treatment," he explains. "Our group facilitates collaboration between cancer researchers, clinicians, VCs and biotech companies." The Oslo Cluster also sponsored its first international partnering meeting in the fall of 2009. There were 350 participants from 22 countries with 165 pharmaceutical and biotech companies attending. The effort moves from Scandinavia to France in 2010 and Reve expects an even bigger turnout.

One of the Oslo Cluster's local member companies, Algeta ASA, signed an agreement in September 2009 with Bayer Schering to develop and commercialize Algeta's alpha-emitting radiopharmaceutical, based on radium-223. The compound, called Alpharadin, is currently being evaluated in a global Phase III trial for the treatment of bone metastases in symptomatic hormone-refractory prostate cancer patients. Alpharadin delivers radiation directly to the tumor cells with low exposure to the surrounding tissue.

"It's a fascinating almost science fiction like treatment, but now it is in Phase III trials in some 70 hospitals around the world," says Reve. "This is the kind of deal we really like because it shows the potential of our companies. Algeta gets to keep 50% of the commercialization rights for the U.S. market and doesn't have to give up all the control to a large pharmaceutical company."

Reve is a firm believer that no single country is strong enough in science to win the battle against cancer single-handedly. "What we are trying to do in Europe is to network various cancer companies with clinics. We establish clusters around hospitals and find ways to combine science with academia and create a network to conduct Phase I and II clinical trials," explains Reve.

Escalate

A strategy that is often pursued with cancer patients today involves the use of combination therapies. "These products do not necessarily come form the same companies so there is a need for cooperation in clinical testing," explains Yeomans. In May 2009 Bayer, Onyx Pharmaceuticals, OSI Pharmaceuticals, and Roche initiated a Phase III trial examining Nexavar (Bayer/Onyx) in combination with Tarceva (OSI/Roche) as a potential new treatment option for patients with advanced hepatocellular carcinoma or primary liver cancer.

Another combination approach that's proving to be very potent is Waltham, Massachusetts-based ImmunoGen's T-DM1. This compound consists of Genentech's HER2-targeting antibody, trastuzumab

Campbell Wilson, AstraZeneca

Adelene Perkins, Infinity

(Herceptin), coupled with one of ImmunoGen's proprietary cell-killing agents that is attached to the antibody using a specially engineered linker. T-DM1 is in advanced clinical testing for the treatment of HER2-positive metastatic breast cancer and has shown encouraging activity in patients whose breast cancer progressed on Herceptin and other agents.

"Genentech brought to the collaboration not only the Herceptin antibody, but also extensive clinical experience in the development of HER2-targeting antibody-based therapeutics," notes Peter Williams, Vice President of business development for ImmunoGen. "In turn, we contributed not only our cell-killing agent and linker technology, but also assisted with aspects necessary for the timely advancement of a conjugate compound, such as the development of a commercial-scale manufacturing process."

Stealth Bomb

All who fight cancer are united in their desire to deal the final blow. But annihilating tumors without killing the humans who have them has proven to be an endlessly elusive goal. One company in San Marino, California called Epeius Biotechnologies believes it has a way to get at the heart of the disease using the precision technology of a stealth bomber in the form of a broad-spectrum, tumor-targeted, bio-compatible, systemically-injectable genetic medicine called Rexin-G.

"Physicians and others need to learn that genetic medicine is not the enemy, it is the future," proclaims Dr. Frederick Hall who co-founded Epeius and today serves as its CEO and Chief Scientific Officer. Rexin-G, which is commercially available in the Philippines and has received Fast Track Designation from the FDA, has been administered in escalating doses as a stand alone therapy to a number of patients with late stage disease and been shown effective in chemotherapy-resistant sarcomas, prostatic cancer, malignant melanoma, and pancreatic cancer.

Embodied within Rexin-G is a pathotropic or disease-seeking targeting mechanism based on the von Willebrand factor. This complex protein attaches to and guides the platelet to the site of vascular injuries to initiate the clotting process while laying down several powerful growth factors at the precise place of injury. Epeius was able to re-establish this wound-seeking capacity onto the envelope of another structurally durable, widely-circulating smaller medicinal unit.

Equally critical to the efficacy of Rexin-G is its therapeutic payload which destroys cancer cells with broad spectrum bioactivity. Creating this required an appreciation of the common final pathways of cellular growth control which are governed by the cyclin-dependent proline-directed protein kinases. "We put it all together like the Army Corps of engineers in a beautiful, elegant seek-and-destroy vehicle which does just what it was designed to do," says Hall.

Hoping for US regulatory approval shortly, Epeius is poised to explore its first partnership beyond the growing group of medical oncologists who are recommending Rexin-G as "best care" for patients. Hall emphasizes, "We are striving to gain the first approvals for Rexin-G with the realization that many patients with otherwise intractable cancers may benefit once tumor-targeted Rexin-G becomes available in the medical oncologist's arsenal."

Forward March

Beyond the 861 cancer therapies currently on the runway, hundreds, if not thousands more are on the way. Infinity Pharmaceuticals, located in Cambridge, Massachusetts, has developed a novel inhibitor of the Hedgehog signaling pathway called IPI-926. Derived from the natural product cyclopamine which binds to and inhibits a key regulator of this pathway, IPI-926 is being evaluated in a Phase I clinical trial in patients with advanced solid tumors. A year ago, Infinity created an alliance with Purdue Pharmaceutical Products L.P. and Mundipharma International Corporation to develop and commercialize the compound. The connection is paying off.

"Part of the courting process in business development is figuring out with whom you are best matched," explains Adelene Perkins, President and Chief Business Officer for Infiinity. "I spent a lot of my career putting partnerships like this in place. We always work hard to get it right, yet despite our best efforts, they often are tough to live out. I can say that with this partnership, living the relationship out is better than the way we structured it on paper," she adds. "The objective of the relationship—to develop a pipeline of robust oncology products—defines the way we need to operate."

The war against cancer wages on. What once looked like miracle drugs are now considered blunt instruments, but we are still no where near a cure for the most lethal forms of the disease. AstraZeneca's Wilson is optimistic. "The search for an agent that is efficacious against many tumor types in a wide range of patients will continue both in academia and in the pharmaceutical/biotech sector. Approaches that harness the host's own immune system offer the most promise," he says. "However, it is much more likely that progress will be made in small increments by developing narrower spectrum agents in conjunction with a diagnostic, thereby increasing the chances of efficacy in a given patient group and by the use of such agents in the right combination."

Written by
Crispin Littlehales,
Freelance writer in Covelo, California.

Epeius Biotechnologies, San Marino, CA, USA

www.epeiusbiotech.com

The Way to Seek and Destroy Cancer Safely

Epeius Biotechnologies was born out of inspiration, compassion, and invention. The company has created the first broad-spectrum, tumor-targeted, bio-compatible, systemically-injectable genetic medicine for cancer. Called Rexin-G, the anti-cancer agent is precise, selective, and extremely effective. Thus far, Rexin-G is commercially available in the Philippines. In Japan, where Rexin-G was administered to 35 patients, 75% experienced long term benefit. In the U.S. Rexin-G has received Orphan Drug designation for three clinical indications, as well as FDA Fast Track status. Recent studies have shown clinical remissions in chemotherapy-resistant sarcomas, prostatic cancer, malignant melanoma, and pancreatic cancer using Rexin-G as stand-alone therapy.

In addition to its strong IP portfolio, Epeius has developed a network of eminent medical oncologists who are currently recommending Rexin-G as "best care" for patients with refractory metastatic cancer. The company received approval from the Philippines in December 2007 for use against all solid tumors. To support the expanding clinical indications for Rexin-G, Epeius Biotechnologies recently completed the construction of a state-of-the-art GMP compliant facility for the large scale production of targeted genetic medicines.

CONTACT DETAILS:

Dr. Frederick L. Hall
CEO, CSO, and co-founder
475 Huntington Drive
San Marino CA 91108
Phone: + 1 (626) 441-6695
Fax: + 1 (626) 441-6692
Email: fhall@epeiusbiotech.com
www.epeiusbiotech.com

It is the hope of every oncologist to eradicate life-threatening tumors safely, without threatening the lives of their patients. At Epeius Biotechnologies, we have found a way to do just that. We use a sophisticated precision-targeted delivery system combined with stealth lipid envelope-cloaked nanoparticles that are virtually invisible to the patient's immune system and are neither inflammation-provoking nor immediately inactivated by the immune system. As a result, we have been able to successfully develop a cancer treatment named Rexin-G that allows for administration through repeated intravenous infusions—all without untoward side effects.

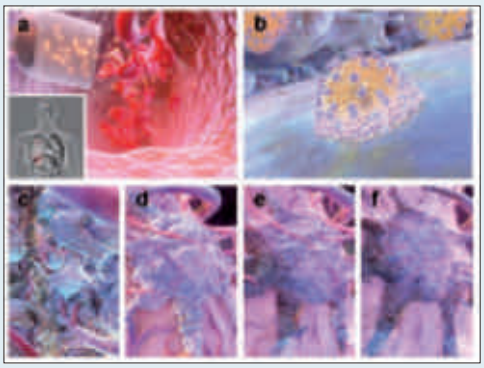
Precise, effective and safe—by design

Embodied within Rexin-G is a pathotropic or disease-seeking targeting mechanism based on the surveillant hematological protein, von Willebrand factor. This complex protein attaches to and guides the platelet to the site of vascular injuries to initiate the clotting process while laying down several powerful growth factors at the precise place of injury. Epeius was able to re-establish this wound-seeking capacity onto the envelope of another structurally durable, widely-circulating, and markedly smaller medicinal unit.

Equally critical to the efficacy of Rexin-G is its therapeutic payload which destroys cancer cells with broad spectrum bioactivity. Creating this property required an appreciation of the common final pathways of cellular growth control which are governed by the cyclin-dependent proline-directed protein kinases. When cyclin G1 is expressed, the cell cycle advances. Conversely, when cyclin G1 is blocked, proliferative cells, including cancerous ones, die. Indeed, the name, Rexin-G, reflects its engineering roots: Retroviral expression vector bearing an inhibitory construct of the gene-cyclin G.

End-stage patients in clinical remission

To us, no one matters more than the individual cancer patient. After years of indefatigable effort in clinical development, treating one very sick person at a time, we have finally achieved both progression-free survival and overall survival benefits in significant numbers. The results of our latest U.S. clinical trials confirm those of our pioneering studies conducted in the Philippines, where Rexin-G has recently been approved for the treatment of all solid cancers. Upon administering Rexin-G at optimal dosages to patients with Stage IV pancreatic cancer, more than 28% of these otherwise poor-prognosis patients are surviving beyond one year. Similar gains in survival benefits are seen in both osteosarcoma and soft tissue sarcoma. Three recent cases involving patients with late stage osteosarcoma, intractable prostate cancer, and pancreas cancer, further demonstrate that Rexin-G, used as a stand alone treatment, can beat back the disease into clinical remission.



Hundreds of millions of Rexin-G nanoparticles are injected into the patient intravenously (a) where they circulate in the bloodstream seeking out tumors and accumulating selectively (c) in metastatic lesions (inset). Armed with the human cyclin-G1 gene knockout construct as its molecular payload, the nanoparticles (enlarged in b) enter into a proliferative target cell where the therapeutic gene triggers the production of numerous copies of the cytocidal gene product, thereby disrupting cell cycle progression, inducing apoptosis in tumor cells and attendant vasculature, and causing tumor regression (d to f).

On a fast track

Historically, this represents a significant advancement in genetic medicine, as well as clinical oncology—providing the world's first tumor-targeted gene-based medicine to be fully validated in the clinic. After gaining regulatory approval in the Philippines, Rexin-G was granted Orphan Drug Status for pancreas cancer, osteosarcoma and soft tissue sarcoma, as well as Fast Track Designation for pancreas cancer by the U. S. Food and Drug Administration.

At this point, the scientific, biotechnological, and biopharmaceutical heavy lifting have all been accomplished, as has the landmark clinical validation. Currently, we are on the very cusp of regulatory approval for Rexin-G in the U.S. and are currently writing advanced protocols for Phase III pivotal trials. We are striving to gain the first approvals for Rexin-G with the realization that many patients with otherwise intractable cancers may benefit, once tumor-targeted Rexin-G becomes available in the medical oncologist's arsenal.

Meanwhile we are reaching out to biopharmaceutical partners and cancer centers that are in a position to play a constructive role in this inspired medical mission. It is no longer impossible to imagine that metastatic cancer can be overcome by innovations in medical delivery and that more lives can be saved—once the essential concepts of pathotropic targeting are fully appreciated and the surveillant properties of tumor-targeted nanoparticles are deployed in modern medical practice. The advent of pathotropic medicine in the treatment of metastatic cancer represents a quantum leap indeed.

Wellcome Trust

www.wellcome.ac.uk/techtransfer/biopharma

Seeding Drug Discovery: Funding and Partnering Opportunities

The Wellcome Trust's £91 million Seeding Drug Discovery initiative was launched in 2006 to develop drug-like small molecules that will be the springboard for further research and development by the biotechnology and pharmaceutical industry.

Two projects funded under the initiative, aimed at identifying inhibitors of BRAF and 11β-hydroxysteroid dehydrogenase (11β-HSD1), have now come to fruition and produced preclinical drug candidates with supportive data and profiles that make them attractive for development into effective new therapies.

The Wellcome Trust is now seeking commercial partners to take these candidates forward through clinical trials and towards market.

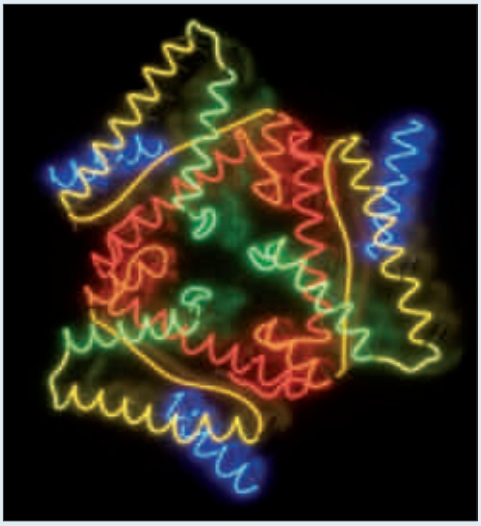
For more information see: ***www.wellcome.ac.uk/techtransfer/biopharma***

The Wellcome Trust's £91 million Seeding Drug Discovery initiative was launched in 2006, with the objective of developing drug-like small molecules that will be the springboard for further research and development by the biotechnology and pharmaceutical industry in areas of unmet medical need.

The initiative aims to facilitate interdisciplinary research groups within academic, biotechnology and pharmaceutical companies to engage in innovative, early-stage drug discovery projects that build on novel perspectives from the study of disease mechanisms or the activity of compounds. Programmes have been supported that are complementary to existing R&D programmes in industry and are driven to a target product profile for which pharmaceutical companies or other organisations see the technology as attractive because of a reduced level of early-stage risk.

Seeding Drug Discovery

- The initiative has considered 280 preliminary applications to date, of which half have focused on antimicrobial and oncology indications.
- It has already completed six rounds of funding, committing £67.9 million.
- It has established a broad portfolio, supporting 21 active research programmes across all main therapeutic areas, in the UK, Europe and the USA.
- Two-thirds of active programmes are within academic or research institutes, for which the Trust negotiates the exploitation of assets.
- Calls for proposals are made every six months, with the final deadline for proposals in May 2010.



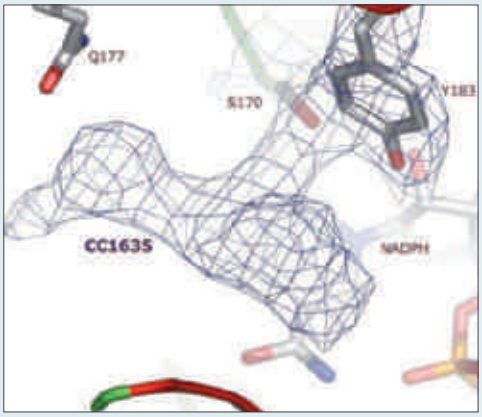
Seeding Drug Discovery is an initiative focused on the early development of small molecule therapeutics.

Two of the earliest projects funded under the initiative, aimed at identifying inhibitors of BRAF and 11β-hydroxysteroid dehydrogenase (11β-HSD1), have now come to fruition and produced preclinical drug candidates with supportive data and profiles that make them attractive for development into effective new therapies. We are now seeking commercial partners to take these candidates forward through clinical trials and towards market.

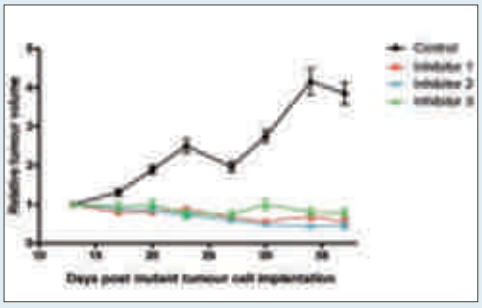
Strong patent portfolios exist for each programme with all key commercial territories pursued, for which the Wellcome Trust has the clear right to agree and negotiate with potential partners for all programmes that are undertaken within academic or research institutes.

We are flexible on the business model for partnering with our licensees, and would be pleased to consider either a straight licensing deal or those with a more collaborative structure.

For more information about Seeding Drug Discovery at the Wellcome Trust see:
www.wellcome.ac.uk/techtransfer/biopharma



Structure of 11β-HSD1 co-crystallised with an Edinburgh 11β-HSD1 inhibitor.



Oral therapeutic efficacy of selected candidate compounds in BRAF-driven melanoma xenograft model

wellcome trust

PARTNERING OPPORTUNITIES

11β-HSD1 inhibitors

We can offer opportunities for licences to a patent estate that include a worldwide exclusive licence on novel classes of clinical candidate 11β-HSD1 inhibitors and non-exclusive licenses to the therapeutic use of inhibitors of 11β-HSD1.

Chronically elevated glucocorticoid levels cause obesity, diabetes, heart disease, mood disorders and memory impairments. 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) catalyses intracellular regeneration of active glucocorticoids (cortisol and corticosterone) from inert 11-keto forms in liver, adipose tissue and brain, amplifying local action. Seminal observations that 11β-HSD1 activity is increased in key tissues in disease, and that reducing intracellular cortisol levels by inhibiting 11β-HSD1 activity is beneficial in preclinical and human studies, has validated this target in various diseases, including type 2 diabetes and obesity, age-related cognitive decline and myocardial infarction.

The identification and elucidation of the physiological and pathophysiological roles of 11β-hydroxysteroid dehydrogenases have been led by the team of Professors Jonathan Seckl and Brian Walker at the University of Edinburgh, and supported by the Wellcome Trust for over 15 years. The Trust has been responsible for maintaining and prosecuting to grant a patent estate on the therapeutic use of inhibitors of 11β-HSD1. To ensure that the field of use in the search for novel inhibitors is not restricted, we continue to provide freedom to operate with non-exclusive licences to those active in the field.

With Wellcome Trust support, the Edinburgh group established an in-house drug discovery capability in 2003, headed by Dr Scott Webster. It operates within a large University research group with world-leading tools and expertise in all relevant biology, and in collaboration with a major global medicinal chemistry company, to discover and optimise several series of 11β-HSD1 inhibitors. A recent £5 million Seeding Drug Discovery award enabled them to develop and patent a series of optimised preclinical candidates with favourable *in vivo* pharmacokinetic and pharmacodynamic characteristics and efficacy in preclinical models. Of these series, the group has selected a clinical candidate to advance into phase I clinical trials, and is now conducting formal enabling toxicological studies prior to regulatory submission. Bespoke pharmacodynamics and efficacy biomarkers developed in Edinburgh are available to support early clinical development.

We are seeking a commercial partner to license this orally bio-available candidate for further development and full efficacy clinical trials. The preferred licensing partner or partners may also access the expertise, knowledge and tools of this world-leading research group in Edinburgh in order to gain unique advantage in this very competitive field.

BRAF inhibitors

We are seeking a partner to license the worldwide rights to develop novel BRAF inhibitors developed by a team of researchers – funded jointly by Cancer Research UK (CR-UK) and the Trust – at the Institute of Cancer Research (ICR) in London.

The role of BRAF in cancer was first highlighted by scientists at the Wellcome Trust Sanger Institute in Cambridge and the ICR, who published a paper in *Nature* in 2002 showing that a mutation in the *BRAF* gene occurs in up to 70 per cent of malignant melanomas and around 7 per cent of all human cancers (including 30 per cent of thyroid cancers, 30 per cent of ovarian cancers and 15 per cent of colorectal cancers).

BRAF is a key part of the MAPK signalling pathway that stimulates cell proliferation, and has been shown to drive tumour growth.

The core BRAF inhibitor drug discovery research teams at the ICR are based in the laboratories of Professors Richard Marais, an author of the landmark 2002 Sanger Institute paper, and Caroline Springer at the CR-UK Centre for Cancer Therapeutics – a renowned onsite drug discovery unit that has developed many novel anticancer drugs.

The research teams identified four novel series of compounds from a high-throughput and structure-based design campaign, generating a panel of over 450 compounds that can inhibit BRAF. Three of these series were subjected to an extensive hit-to-lead and lead optimisation programme. As a result, the most potent compounds display excellent activity against BRAF. Investigation of the ADME properties of these compounds indicated they are cell-permeable, with good CYP450, hERG and microsomal stability profiles. These orally bio-available preclinical candidates have differing selectivity profiles, and inhibit tumour growth in BRAF-driven melanoma and colorectal carcinoma xenograft models.

All three candidates are at the same stage of development.

Our licensee can receive rights to all of the compounds developed in the programme and can choose to develop any or all of these three preclinical candidates, depending on their specific requirements and the target product profile they are seeking.

Our future partner will also, if they wish, have access to expertise at the ICR, which, in partnership with the Royal Marsden NHS Foundation Trust, forms the largest comprehensive cancer centre in Europe and one of the largest in the world; several drugs discovered or developed there have successfully entered the clinic and reached the market. The ICR and Marsden teams are well placed to provide support for this project going forward, as required. In particular, the teams are well placed to write the first clinical trial protocol and conduct the first trial.

The University of Edinburgh campus at Little France, where world-class research facilities are co-located with clinical research in a major teaching hospital and with commercialisation activities in the Edinburgh BioQuarter.

CONTACT DETAILS:

For information on BRAF inhibitors:
Dr Morag Foreman
Email: m.foreman@wellcome.ac.uk
Tel: +44 (0)20 7611 8753

For information on 11β-HSD1 inhibitors:
Dr Richard Davis
Email: r.davis@wellcome.ac.uk
Tel: +44 (0)20 7611 8287

Scil Proteins

www.scilproteins.com

Scil's scaffold skills

Scil Proteins is a privately held biotech company active in the area of protein therapeutics. The company's technological basis is the proprietary Affilin® protein therapeutics platform. From highly complex libraries, Affilin® therapeutics are screened and selected for binding disease-related targets with high affinity and selectivity. A specific strength of Scil Proteins is to combine elevated capabilities and cutting-edge techniques in drug discovery with strong expertise in the contract biomanufacturing field. This includes full process development and GMP production of recombinant proteins in microbial systems.

Over the past decade, antibody-based therapeutics have made a huge impact on how patients are treated. Indeed, some of the most important, clinically effective and best-selling cancer drugs are based on monoclonal antibodies. However, despite the well-documented advantages of high specificity, affinity, and acceptable safety profiles, antibodies are not without their limitations which has inspired the development of alternative approaches.

"Antibodies can trigger immune responses, have poor tissue penetration, normally require delivery by injection, are often very expensive to make, and have poor thermal stability," notes Henning Afflerbach, Chief Business Officer at Scil Proteins.

Moreover, intellectual property covering the area is very complex and reduces the freedom of developers to operate.

Consequently, a number of new approaches that embrace the advantages of antibody therapeutics while attempting to minimize the disadvantages are now emerging and are beginning to make a serious contribution to the development of new cancer treatments. These approaches are mostly based around antibody fragments or protein scaffolds and have been the focus of some high profile and high value acquisitions and licensing deals.

"What all these protein scaffolds have in common is that they are small, relatively easy and less expensive to manufacture, are very stable, can penetrate deep into tissue, and can have high affinity and specificity against certain disease-related targets," notes Afflerbach.

As a relatively late entry into the post-antibody space, Scil Proteins has developed its own drug discovery platform — Affilin® molecules. Affilin® is based on the human serum protein ubiquitin and will enable drug companies to develop highly effective treatments. While it has many of the attributes common to other post-antibody platforms, the Affilin® platform has some qualities that make it an attractive drug discovery option, such as reduced risk of immunogenicity, and greater preclinical predictability.

"Affilin® molecules are small proteins of about 78 amino acids and 8.4 kilodaltons in size, and because they are derived from a human serum protein, they are not immunogenic. In addition, ubiquitin possesses an immunosuppressive domain that has developed in nature, which reduces even further any immunogenic risk of our engineered Affilin® derivatives," he added.

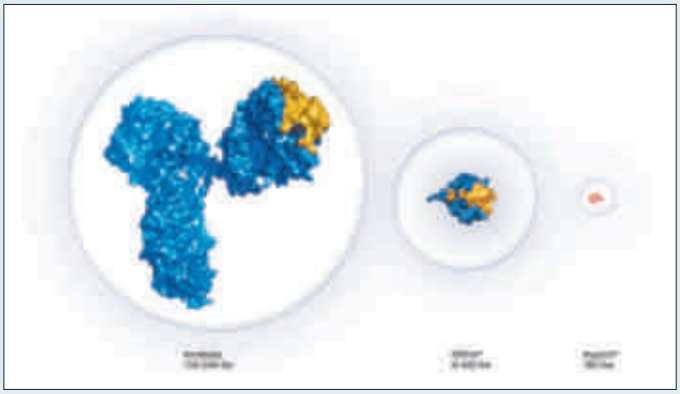
Immunogenicity is always an issue when using scaffolds and protein engineering in drug discovery.

Another important differentiator of Affilin®, according to Afflerbach, is that the ubiquitin molecule is highly conserved throughout the animal kingdom. "This means that the ubiquitin of the fruit fly, mouse, and monkey is identical to humans. Consequently, Affilin® molecules can be tested in all animal models without the need of surrogates," he added.

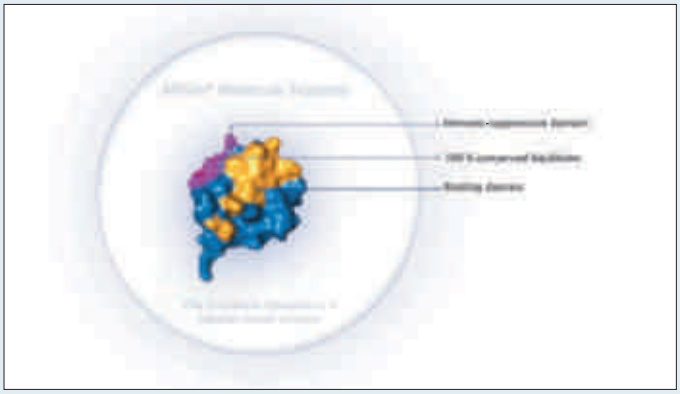
Scil Proteins has created libraries of Affilin® molecules by engineering the surface of the ubiquitin protein to create new binding sites that can be easily produced in bacteria. These changes do not alter the overall protein structure nor its stability. Using phage and ribosome display technologies that it has either acquired or in-licensed, Scil is able to select Affilin® molecules that bind to specific pre-defined targets.

"We start with the exposure of an antigen to our library. We use the TAT phage display and ribosome display technologies, which are fast, robust and effective, to screen those Affilin® candidates that bind to the targets. It takes about ten weeks to go from original hit identification through protein characterization to determining the affinity of the Affilin® hits," added Afflerbach.

Scil accessed the ribosome display technology from Cambridge Antibody Technology, now part of AstraZeneca's MedImmune unit, in 2006 and acquired the TAT technology from the University of Berlin in September 2009.

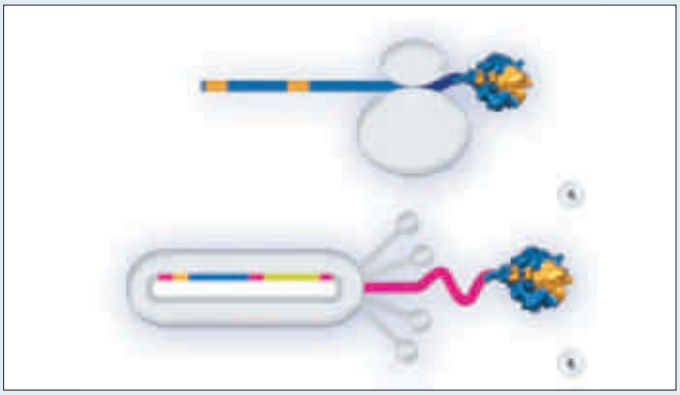


Comparison of Affilin® molecules with conventional small molecule drugs and antibodies

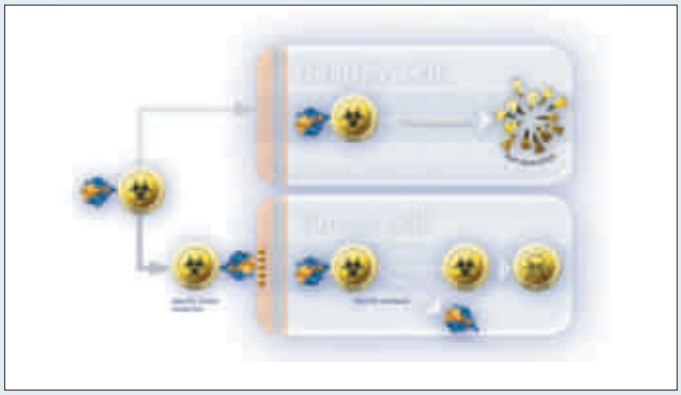


Competitive features of Affilin® molecules

scil proteins



Schematic representation of Affilin® display technologies, A) ribosome display and B) TAT phage display



Affilin® toxin fusions are enriched at tumor cells. In healthy cells the fusion is rapidly destroyed by the proteasome. In tumor cells the toxin is released through specific cleavage, leading to cell death

From the billions of different Affilin® molecules initially screened, Scil will subject 100 or so for detailed characterization. These selected molecules will already display dissociation constants in the low nanomolar range with high target specificity.

"We have so far generated two very complex libraries around a monomeric and dimeric format. The monomers are very small, very stable, and very effective, but sometimes we have to deal with issues relating to specificity which we can improve if we add another binding module to a monomer to create an Affilin® dimer. Ubiquitin is easily manipulated, so it is something that we can do to improve binding, half-life properties, or to support multiple targeting," he added.

So far, Scil has achieved picomolar affinities, completed pharmacokinetic and toxicity studies, and shown that it can create Affilin®-based molecules with high specificity against cancer cells.

Scil envisages Affilins being useful either on their own, as monomers or dimers, against cancer or inflammation targets —where they might block key receptors, cytokines or recruit other effector molecules — or as conjugates — where they essentially carry a therapeutic payload to a specific disease site.

The conjugates Scil is looking at involve pro-apoptotic cytokines, which bring cell death to the binding site, or radio-labeled molecules or cell toxins.

Indeed, Scil is going to take advantage of a unique property associated with ubiquitin biology with a toxin–Affilin® conjugate.

"The Affilin® part of the conjugate recognizes biomarkers that are specific to the cancer cell surface and binds to them. Once bound the whole complex gets internalized. Inside the cell the toxin is released from the Affilin® through proteolytic cleavage by a cancer cell-specific protease that is massively over expressed in cancer cells. On release, the toxin kills the cancer cell. This principle has been shown to work and has been published for ubiquitin toxin fusions," he added.

Interestingly, if some leakage of the Affilin®–toxin conjugate into healthy cells occurs, there is no cleavage of the complex, owing to the absence of the tumor-specific protease, but instead the ubiquitin scaffold mediates transfer to the proteasome complex, where the toxin gets degraded and inactivated.

"What we are currently doing is choosing targets that are clinically validated where we have seen convincing clinical data and there is an opportunity for us to go into different indications and create a best-in-class opportunity," he added. This does mean, however, that Scil is ignoring cancer targets, such as CD20 or VEGF, which are currently well-served by other approaches.

Affilin®-based molecules can also be used in diagnostics and analytics, and in chromatography applications. The specific coupling of Affilin® molecules to matrices or surfaces and their robust behavior underpins their potential use in protein chip technologies. Also, the fast clearance and straightforward coupling of labels to Affilin® makes them attractive as tools for *in vivo* diagnostic imaging.

To date, Scil Proteins has entered into agreements with academic partners to provide its technology for the development of Affilin®-based products. Scil is now looking to find partners for Affilin-based therapeutics that the company has already generated against clinically validated targets, or to partner with companies that have proprietary disease-related targets that they would like to generate Affilins against.

"Our Affilin® business model has three arms. We are looking to create technology partnerships where we identify Affilin® molecules that will bind to disease-related targets brought to us by the partner. We also envisage establishing product partnerships where we out-license late stage Affilin®-based therapeutic candidates that we have developed. We are also interested in establishing strategic partnerships which would sustain an influx of novel targets and revenues," added Afflerbach.

CONTACT DETAILS:

Affilin Technology
Dr. Henning Afflerbach
Chief Business Officer
E-mail: henning.afflerbach@scilproteins.com

Contract Manufacturing
Dr. Ole Fuetterer
Director Business Development
E-mail: ole.fuetterer@scilproteins.com

Menarini

www.menarini.com

Menarini outreach

CONTACT DETAILS:
Dr Andrew Slade
President Menarini Biotech
Via Tito Speri, 12
00040 Pomezia (Roma)
Tel: +39-06-91184491
Fax: +39-06-91601408
Cell: + 39-320-2193270
Email: aslade@menarini.it

Armed with a promising antibody-based vaccine against ovarian cancer, Menarini Group, a privately held fully integrated pharmaceutical company headquartered in Florence, Italy, is poised to enter the US market for the first time and has ambitions to become a major player in the biologicals field.

Recognizing the challenge of trying to grow a presence through organic growth alone, Menarini is now looking for partners from whom it can in-license and acquire promising development phase speciality medicines.

Over the past decade, Menarini has seen its revenues grow from €1.31 billion in 2000 to €2.63 billion in 2008. Andrew Slade, President of Menarini Biotech, now has ambitions to see a similar pattern of growth in the coming years using a double-edged strategy of developing home-grown and in-licensed products, especially in biologics.

"While we are not diminishing the importance of small molecules we are most interested in expanding our biologics pipeline because we think there is great medical need in this area. We have everything that is needed to get biologics into the marketplace: biology, analytical, regulatory and development/manufacturing experience and financial resources," said Slade.

Slade is looking at two potential sources of innovative products. One group is European companies that have assets that need developing clinically and are willing to give up US rights. Alternatively, he envisages potential deals involving US companies that have little experience or interest in commercializing their assets outside North America.

"We are not always looking for global rights, as we are willing to look at appropriate regional deals," added Slade.

One pillar of the growth strategy is abagovomab, an anti-idiotype antibody that mimics a tumor antigen that is highly expressed by ovarian cancer cells, which is currently in Phase II/III trials and is being studied for its ability to prevent the regrowth of tumors that occurs too often in such highly aggressive cancers.

"We believe it has the potential to prevent or delay tumor relapses, in those patients who responded to first-line chemotherapy, by activating an immune response to the cancer cells," added Slade.

Menarini in-licensed the antibody from CellControl AG, a small German biotech company, in 2006.

"It was clear that it would be very difficult for us to develop the vaccine and we would need a partner. We had a number of companies looking at the data we generated but we chose Menarini because they have strong development and regulatory capabilities and made a commitment to upgrade their manufacturing," explained Karl Krista, CellControl's founder and CEO.

Slade believes that being a medium-sized private pharma company, Menarini is able to make decisions quickly and its partners are unlikely to be victims of research strategy changes. "We take every investment made very seriously and have to develop all clinical assets as quickly as we can," he added.

Krista says he is delighted with how Menarini has developed abagovomab clinically. "Recruitment of such patients is not easy, certainly not for a small biotech, and any time it looked like they might be falling behind in their enrolment Menarini enlarged the number of hospitals and cranked up the advertising to principal investigators. They went all out to meet the deadlines," he added.

The Phase II/III MIMOSA trial involves 870 patients in 151 different treatment centers in nine countries. "We started recruiting patients in December 2006 and completed enrolment on time in December 2008. The first efficacy results are expected at the end of 2010," added Angela Capriati, Menarini's clinical director.

"We would like to replicate the abagovomab experience with other compounds and companies," noted Carlo Alberto Maggi, Menarini's R&D Director. However, Menarini is prepared to be as flexible as necessary to get a deal done. "If a US company has aspirations to establishing a fully integrated organization in its home market we would be quite happy with that so long as they leave us with Europe and other markets," he added.

Slade promises that Menarini will evaluate everything on a case-by-case basis. "We will look to align any opportunities with our existing activities in innovative businesses and emerging markets. We can now demonstrate to others that we have the competences to do what they need to do," he added.

Menarini employs 12,600 people, of which 740 are employed in research and development.

Maggi has a clear idea of what he is looking for. "We are seeking products which have at least completed Phase I but, depending on the indication, we are very flexible on this point. We are looking for niche, preferably orphan indications which have the potential for a fast track regulatory path,"he noted.

"We are very serious about acquiring other speciality products which we can use to leverage abagovomab in the market as well as having follow-on products to allow us to meet our goal of being a global company with a US presence. We are most interested in oncology, an area in which we have invested a lot of effort bringing the resources into the company necessary to clinically develop and manufacture biologics in an oncology setting," added Slade.

Bavarian Nordic A/S

www.bavarian-nordic.com

BAVARIAN NORDIC

PROSTVAC™: a therapeutic cancer vaccine showing great promise

Bavarian Nordic (Kvistgård, Denmark) is a leading European industrial biotechnology company that develops and produces novel vaccines for the treatment and prevention of life-threatening diseases with a large unmet medical need.
Best known for its multi-million dollar agreements to supply the U.S. Government with a national stockpile of third-generation smallpox vaccines, Bavarian Nordic is also moving ahead swiftly with novel cancer and infectious diseases vaccines.

Today, PROSTVAC™ is the company's most advanced therapeutic cancer vaccine candidate. Developed with the U.S. National Cancer Institute to become a subcutaneously injected vaccine against advanced prostate cancer, it has shown significant promise in Phase II studies and is expected to enter Phase III in 2010.

CONTACT DETAILS:
Jürgen Langhärig, Ph.D, MBA,
VP Business Development
Bavarian Nordic A/S
Hejreskovvej 10A
DK-3490 Kvistgård
Denmark
Tel: +45 33 28 83 18
Email: jla@bavarian-nordic.com

When Bavarian Nordic acquired the rights to a therapeutic prostate cancer vaccine in August 2008 as part of a collaboration agreement with the U.S. National Cancer Institute (NCI), the good news about the long-term follow up of its latest Phase II trial was still months away.

In October of that same year, however, the Danish company could announce[1] that PROSTVAC™ had increased median overall survival time by more than eight months compared with placebos among 125 men with advanced, metastatic prostate cancer.

"To see this extent of improvement in overall survival is very encouraging," Philip Kantoff, Professor of Medicine at Harvard Medical School and principal investigator of the study, said at the time.

U.S. Government contracts

The Danish company has won contracts of more than $600 million so far from the U.S. Government to develop and produce millions of doses of IMVAMUNE®, a human smallpox vaccine, for a national stockpile that will protect the U.S. population in case of a future biological attack.

While biodefense is an important segment of Bavarian Nordic's product portfolio, it certainly is not the only one. Using its specialized expertise, the company is moving ahead with a pipeline of novel therapeutic and prophylactic vaccine candidates against various cancers and infectious diseases.

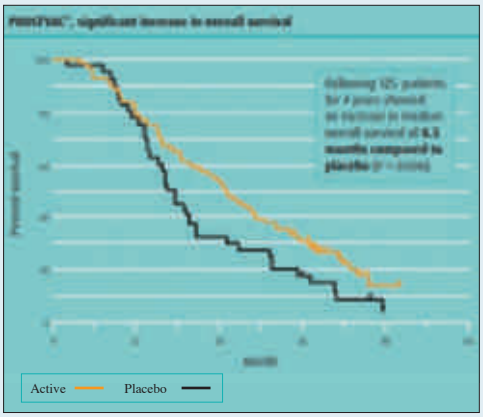
Seven shots and a "ready to use" vaccine

Prostate cancer is the second leading cancer-related cause of death in American men, with an estimated 27,000 fatal outcomes in the U.S this year. Today, patients with metastatic prostate cancer that is resistant to hormone therapy have just one approved treatment option: a chemotherapy with considerable side effects, extending median overall survival by little more than 2 months.

PROSTVAC™, made from genetically modified pox viruses, encompasses two separate vaccines delivered through a regimen of seven simple subcutaneous shots over the course of 6 months.

The first shot contains a vaccinia virus modified to encode prostate-specific antigen (PSA) and three T-cell-costimulatory molecules (TRICOM), which enhance the specific immune response against PSA-presenting cells. In subsequent months, the immune response is boosted with six follow-up shots containing a modified fowlpox virus that also encodes PSA and TRICOM. The whole regimen is designed to create a strong cytotoxic immune response against primary and metastatic prostatic tumors.

Both vaccine components are recombinant viral vectors, which makes PROSTVAC™ a potential off-the-shelf product that could easily be manufactured and marketed at industrial scales.



BAVARIAN NORDIC A/S

A pivotal Phase II trial has shown significant benefits of PROSTVAC™ compared with placebos among men with advanced prostate cancer.

Eight months survival benefit

Results of PROSTVAC™ trials have been highly promising. In all, PROSTVAC™ has undergone thirteen finalized Phase I and Phase II studies to date, with five more ongoing.

The most conclusive Phase II study to date was a double-blind, randomized, placebo-controlled (2:1) prospective Phase II study that enrolled 125 patients with advanced prostate cancer[2].

After four years of follow-up, patients who had received PROSTVAC™ turned out to live significantly longer than those in the placebo group (8.5 months median overall survival added). The advantage was highly significant (p=0.006). Importantly, PROSTVAC™ also had a favorable safety and tolerability profile, resulting in better quality of life compared with current approved therapy.

In clinical trials to date, PROSTVAC™ and related PSA-containing pox viral vaccines have been investigated in more than 500 patients over 10 years[3].

Phase III soon to begin

A soon-to-begin Phase III trial will now need to confirm these promising outcomes. If all goes well, PROSTVAC™ may significantly extend the lives of men with metastatic, castration-resistant prostate cancer, for whom very limited therapy options are now available. With time, it may also be shown that other patient groups, including those with cancers not yet resistant to hormone therapy, can be added to the list.

References:
1. *Bavarian Nordic announcement*, Oct 7, 2008
2. *J. Clin. Oncol.*, 27:15s, 2009 (suppl; abstr 5013)
3. *Expert Opinion on Investigational Drugs*, 18, Issue 7 (2009)

Plexxikon

www.plexxikon.com

Plexxikon

Plexxikon's PLX4032 - A New Personalized Medicine for Cancer Treatment

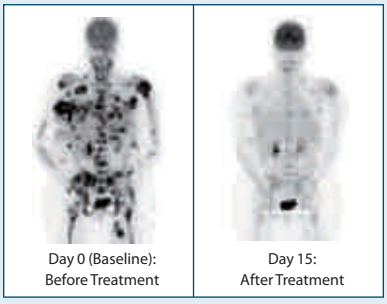
Plexxikon's PLX4032 – A New Personalized Medicine for Cancer Treatment — PLX4032 is a highly selective BRAF inhibitor that targets and destroys cancer cells harboring a specific cancer-causing mutation. Encouraging data from a Phase 1 extension study in mutation-positive metastatic melanoma patients showed that tumor shrinkage was observed in 70% of patients. Plexxikon, with partner Roche, has accelerated development for potential registration in melanoma and is conducting a Phase 2 pivotal trial with plans for a Phase 3 trial by the end of 2009.

CONTACT DETAILS:

Kathleen Sereda Glaub
President
Email: kglaub@plexxikon.com

PLX4032 is a novel, oral and highly selective BRAF inhibitor that targets and destroys cancer cells harboring a specific cancer-causing mutation called BRAF. This mutation is found in approximately 50% of malignant melanomas and approximately 8% of all solid tumors. Together, PLX4032, and its companion diagnostic to identify mutation-positive patients being developed in parallel, make this an ideal personalized medicine. Encouraging clinical data from a Phase 1 extension study in mutation-positive metastatic melanoma patients showed that tumor shrinkage was observed in 70% of the currently evaluable patients. Plexxikon, along with its partner Roche, has accelerated development plans for potential registration in melanoma with the initiation of a Phase 2 pivotal trial and plans to initiate a Phase 3 clinical trial by year end 2009.

With a co-promote option in the U.S. for PLX4032, and a pipeline of additional oncology drug candidates, Plexxikon is laying the groundwork for a commercial oncology franchise, while continuing its business model of leveraging its discovery and early development platform in multiple therapeutic areas and seeking co-development partners at the early development stage.



Day 0 (Baseline): Before Treatment | Day 15: After Treatment

BRAF Mutation-Positive Patient Treated on 320 Mg/BID

PLX3397—Plexxikon's Next Drug Candidate for Cancer Treatment

PLX3397 is a novel, oral investigational drug for treating multiple diseases, including metastatic cancer. PLX3397 is a highly selective kinase inhibitor that down-modulates certain immune system cells as well as certain tumor cells that promote tumor growth and metastases to the bone. PLX3397 is currently in Phase 1 clinical testing for metastatic disease, and may also have applicability in the treatment of autoimmune disorders such as rheumatoid arthritis.

Plexxikon's Oncology Pipeline and Platform

Among others, Plexxikon's oncology programs include as targets Raf, PI3K, Fms and Trk. Plexxikon is anticipating moving another compound into the clinic from its oncology pipeline in 2010.

Plexxikon's Scaffold-Based Drug Discovery™ platform and early development capabilities have been highly productive to date. The platform is particularly amenable to designing highly selective kinase inhibitors either targeting a single kinase, or selective dual inhibitors.

Pergamum AB

www.pergamum.com

PERGAMUM
A Karolinska Development Company

First-in-class opportunities in dermatology & wound healing

Pergamum focuses on the dermatology and wound healing markets. The company has four main projects — three of which are in clinical development. All offer first-in-class potential in markets with significant unmet medical needs. Pergamum is a Karolinska Development company.

Jørgen Thorball, Chairman

CONTACT DETAILS:

Jørgen Thorball, Chairman
Tel: +46 (0)8 52 48 91 00
jorgen.thorball@pergamum.com

Pergamum AB
Fogdevreten 2b, Solna
SE-171 77 Stockholm
Sweden

Pergamum is a new kind of biopharmaceutical company focusing on the dermatology and wound healing markets. Projects are based on highly innovative, proprietary technologies emanating from world-class research, and target therapeutic indications with unmet medical needs. During development, opportunities for partnerships, licensing and other commercial transactions are continuously evaluated.

Four first-in-class projects

Pergamum has four main projects in its pipeline, all of which offer first-in-class potential. Three projects are already in clinical phase development. Conditions covered include prevention of post-surgical adhesions, healing hard-to-heal-wounds, prevention of bacterial and fungal infections, atopic dermatitis, impetigo and infected wounds and burns.

Projects are developed within focused Operating Units. Pergamum supports these with strategic management, business development, drug development and operational assistance as required. This structure provides cost-efficiencies and synergistic advantages relating to both product development and commercial activities.

The recent appointment of Jørgen Thorball as Chairman and acting CEO has further strengthened Pergamum's capabilities. Dr. Thorball has a proven track record in the successful development and commercialization of new products within the pharmaceutical industry.

Pergamum is a Karolinska Development AB company, making it part of one of the largest life science portfolios in Europe.

Antimicrobial therapy — conquering microbial resistance

The Pergamum Operating Unit, DermaGen, is developing a new class of treatment targeting dermatological infections. The lead product is a novel antimicrobial peptide (AMP) that has a broad spectrum of activity and is both bactericidal and fungicidal. Being derived from an endogenous human protein there is minimal risk of microbial resistance — opening up unique opportunities for long-term and prophylactic use. A strong technology platform means that AMPs can be fine-tuned to target specific commercially interesting indications.

Promising clinical results — in a recent Phase I/IIa clinical trail, targeting atopic dermatitis, the candidate drug demonstrated a significant reduction of total microbes in eczemas compared to placebo. Although the trial was not designed to show clinical efficacy, a trend towards improved eczema status was also seen.

DermaGen

www.dermagen.se

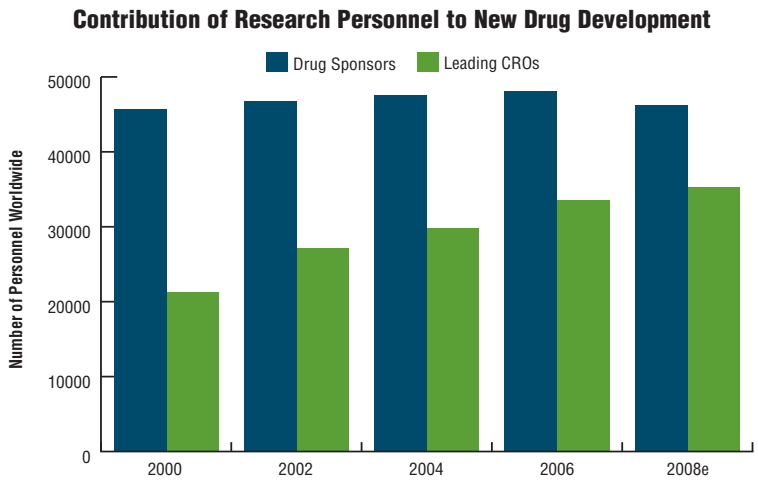
The Emergence of Integrated Partnerships in the Preclinical CRO Industry

Pharmaceutical outsourcing industry-focused research conducted by the Center for the Study of Drug Development at Tufts University (CSDD at Tufts) indicated that while the number of pharmaceutical and biotech companies with active clinical projects increased by 80% — from 1,167 in 2000 to about 2,100 in 2008, R&D headcounts have remained stable (see Figure 1). Concurrently, contract research organizations (CROs), a source of preclinical outsourcing services, increased their headcount by 65%, and pharmaceutical companies and CROs are under pressure to improve R&D efficiency, a situation that has been exacerbated by the economic downturn. According to Tufts University professor Ken Getz, who studies CRO dynamics, "Stronger, deeper partnerships between drug sponsors and CROs may be the key to reducing cycle time and lowering development costs."

The traditional role of a CRO is that of a service provider contracted by a sponsor to perform a specific task, such as drug optimization or toxicology screening. The attractiveness of using a particular CRO centers on a company's ability to perform the task more quickly and less expensively than the sponsor company can on its own. At one end of the preclinical CRO spectrum, simply being fast and efficient while adhering to the prevailing standards of quality is enough. However, that business model seems to be giving way to the dynamics of a rapidly evolving supply chain. According to Getz, "The historical, transactional approach to outsourcing, where sponsors manage the entire development process but engage CROs and other service providers to handle specific tasks, is giving way to more integrated partnerships. In this new approach, both parties interact more as equals, drawing on their respective experiences and knowledge, enabling them to leverage capabilities and create greater efficiency and flexibility to solve problems jointly."[1]

A deal inked about two years ago between Eli Lilly (Indianapolis, Indiana, USA) and Covance (Princeton, New Jersey, USA), the largest publicly traded CRO, clearly illustrates the shift in the balance of power that once routinely governed pharmaceutical outsourcing relationships. Covance, a company that offers both preclinical and early clinical services, purchased Eli Lilly's research facilities in Greenfield, Indiana, for US$50 million. In turn, Lilly scrapped its traditional R&D program and signed a ten-year, US$1.6 billion contract with Covance. Covance employed about 260 Lilly employees and took responsibility for Lilly's non-GLP toxicology, *in vivo* pharmacology, quality control laboratory and imaging services. The deal also included some level of commitment for clinical pharmacology, central laboratory, GLP toxicology studies and clinical Phase II–IV services. Lilly claimed the deal would help the company control the cost of drug development.

Demand for outsourced clinical services continues to grow



Source: Tufts Center for the Study of Drug Development

Figure 1. Globally, the number of companies with active clinical projects increased by 80%—from 1,167 in 2000 to about 2,100 in 2008 — while sponsors have kept their R&D headcount's stable. CROs made up the difference by increasing their headcount by 65%.

Integrated or entangled relationships are not unique to big players such as Covance. Smaller CROs are also adopting more flexible business models. On the far end of the more-than-a-provider spectrum sits Numerate, a California-based preclinical CRO founded a little over a year ago. Numerate is a technology–focused platform company based on a partnering business model. "Numerate was started assuming people wanted a partner." explains Guido Lanza, Numerate's CEO.

Not surprisingly, Numerate repeats the mantra of many preclinical service providers, claiming that it can deliver drug leads faster, cheaper and with more predictability regarding mode of action and toxicology. What is unique is the way the company goes about accomplishing this goal: it owns proprietary development algorithms, has a database of the known activity of 10 million compounds, and a supercomputer. The technology platform makes it possible to describe the specific profile of a desired drug and several weeks later create a handful of compounds the company can formulate and begin to test. Numerate's drug design technology and drug leads were acquired from Pharmix, a separate company that Lanza co-founded in 2000. Pharmix ran out of cash as a drug-development company. Acquiring the Pharmix drug-engineering system and its early-stage drug candidates now puts Numerate in a position to carry on Pharmix's work, but with a more sustainable business model.

Lanza explained that a distinct characteristic associated with Numerate's business model is that the company "will take on some of the risk in your preclinical program." Numerate actually guarantees the final product by tying their reimbursements to success in the laboratory, clinic and market. "We have not had a dissatisfied customer yet," says Lanza. In 2008, the company signed a partnership deal with Presidio Pharmaceuticals (San Francisco, California, USA) an infectious disease-focused drug-development company. The deal was aimed at developing improved versions of drugs against hepatitis C. It is hoped the partnerships like the one signed with Presidio will bring in additional cash to offset Numerate's burn rate, as the company pursues its own internally developed drug candidates.

According to the CSDD at Tufts report, sponsors and CROs expect their use of transaction-based outsourcing to diminish, but not disappear, over the next five years. The report argues that the partnering approach will be augmented increasingly by portfolio-based relationships. Ronald van der Geest, Chief Development Officer of Kinesis (Breda, the Netherlands), a privately owned company that supplies biometric support (i.e., pharmacokinetic, statistical analysis of data from preclinical and clinical studies), has a different perspective and says that there are powerful arguments in favor of a continued emphasis on "straight" service relationships.

Kinesis is strictly a service company. "Keep it simple, keep it clear — so that more people find it easy to work with you," says Geest as he describes why he feels resting on the service side of the part-

ner/service CRO continuum is optimal. "There is still plenty of business on a service basis. Kinesis is very healthy."

Drawing on his experience in pharmaceutical research, both with regulatory authorities and industry, Kees Groen founded Kinesis in 1997 and at the time served as its only employee. Ever since the headcount has been increasing, growing by 30% in 2008, while retaining profitability. The company currently has over 40 employees.

Geest believes that there are some pitfalls to the partner approach. He feels that 'shared interest' can lead to a loss of objectivity. He also explains that Kinesis' management is very careful to not have conflicts of interest "which is why we don't risk-share." Interestingly, Geest questions whether the industry is giving way to a reinvention of itself. "Some decisions are cyclic," he explains, "You see one trend appearing and then the opposite. Whether discovery is integrated or separated, the work does not change."

When asked whether the partnering model highlighted in his report could be a passing thing, Getz replied, "I couldn't disagree more with the notion that integrated partnerships between sponsors and CROs is a passing fad. Since the 1980s, sponsors and CROs have entered into transactional relationships that resulted in completed work. But they also generated out-of-scope costs, failed to deliver efficiencies due to redundant personnel assigned to micromanage the relationship, and established restrictive levels of oversight. Given the volume of global work that needs to be performed today combined with significantly limited capacity, sponsors must work smarter and more efficiently with large highly diverse CROs and niche service providers. Integrated partnerships represent an evolutionary step in establishing more effective and efficient collaborations. This trend toward higher levels of integration has already unfolded in other industries such as film, telecommunications and financial services."

"There is no question that demand for specialized, high quality niche service providers will always be there — but increasingly, these niche providers will find themselves hired and managed by major CROs who have entered into functional and alliance based partnerships with sponsors."

A view of the Shanghai Zhangjiang Hi-Tech Park from Zuchongzhi Road. The park is home to an abundance of CRO and leading pharmaceutical companies' R&D Centers. Photo by Baycrest.

Heading East

In an effort to increase productivity, large pharmaceutical companies have been looking East. This is not a new trend, but in the country that is now one of the largest outsourcing suppliers, China, the pace of change is rapid. A combination of Western demand, sustained government initiatives, and the nation's economic boom has created a highly dynamic atmosphere in China's CRO industry. China is now home to more than 250 CROs addressing every link along the pharmaceutical supply development chain. China is in a position to become a more integral part of the global pharmaceutical industry due, in part, to the activities of its CROs.

The CRO industry in China originated with chemistry services. China's contract manufacturing organizations (CMOs) began engaging in active pharmaceutical ingredient (API) production as early as the 1990s. Manufacturing may be the largest segment of the CRO market, but it is the other aspects, preclinical and clinical research, that are attracting new interest from abroad.

Major policy initiatives contribute to the momentum. China's 15-year science and technology roadmap names life sciences as an important industry for growth. The plan commits China to investing 2.5% of the country's gross domestic product (GDP, estimated at US$4,607 billion in 2009) in research and development. Reforms promote industrial development and small and medium size businesses, and provide tax breaks for high technology zones. Additionally, China's central and regional governments had been making heavy investments in life science start-ups clustered in R&D parks located in the country's major cities (Beijing, Shanghai, Suzhou, Tianjin, Taizhou and others). Large areas (i.e., 10–15 square miles or more) in R&D parks, such as in Zhangjiang Hi-Tech Park in Shanghai or China Medical City in Taizhou, have been set aside for life sciences, and these parks have provided a good deal of room for the growth of CROs and CMOs.

The Chinese government has also undertaken efforts to attract Chinese talent back from abroad by improving resource levels (financial and structural). Top government officials from the nation's science parks have also gone on the road pitching to talent pools working in places such as the biotech hubs of San Francisco and Boston.

An ability to provide a cost advantage to the industry has prompted the number of CROs in China to expand substantially over the last five to seven years. Originally, the new generation CROs were founded by sea turtles — the term used for overseas returnees. (The two words share a common pronunciation, 'hai gui', in Mandarin.) More recently, significant financial backing (local and foreign) has become available, therefore larger CROs are emerging with leadership that may or may not be Chinese.

For example, in 2008 HD Biosciences received financing not only from an Asian high-tech backer, Morningside Venture, but also from Lilly Asian Ventures and Pfizer Venture Investments. The financing marked one of the first examples (if not the first example) of more than one pharmaceutical company taking an equity position in a China-based CRO. The Morningside Group was founded in 1986 by the Chan family of Hong Kong and has

TOP TEN PHARMA BUILDING PRECLINICAL FACILITIES IN CHINA	
2004	• Roche opens an R&D in Shanghai representing the first R&D facility to be set up in China by a major pharmaceutical company • Astra Zeneca announces US$100 million for R&D investment over 3 years.
2005	• Pfizer inaugurates an R&D center in Shanghai and pledges to spend about US$25 million over the next five years. • Sanofi Aventis opens a drug discovery facility opens in Shanghai.
2006	• Novartis announces intentions to open Novartis (China) Biomedical Research Co., Ltd.,its first China R&D center to be located in Shanghai • Zhangjiang High-Tech Park. Total promised investment to be US$ 98 million.
2007	• Zhangjiang High-Tech Park announced as location for AZ Innovation Center China • GlaxoSmithKline opens an R&D centre in Shanghai to investigate neurodegenerative diseases and announced plans to channel US$100 million by the end of 2008 into China-based a neuroscience research center • Roche inaugurates Pharma Development Center China (PDCC) a drug development center designed to carry out all the stages of drug development.The primary budget for the center is 100 million U.S. dollars and it will target cancer and metabolic diseases.
2008	• Eli Lilly & Company inaugurates a Chinese R&D headquarters in the Shanghai • Zhangjiang Hi-tech Park and adopts an R&D management and venture capital investments model to seek,promote and manage the company's cooperation with Chinese companies and R&D institutes. • Foundation completed for a 38,000 sqmfacility to house 400 Novartis researchers at Shanghai Zhangjiang High-Tech Park. • Roche announces it will expand facilities at Shanghai's Zhangjiang Hi-Tech Park. In addition, Roche has established an office for Roche Pharma Partnering in Asia at the site. The goal of both initiatives is to discover innovative medicines in China • Announcing a new partnership with the Shanghai Institutes for Biological Sciences, the company will conduct work on drug discovery in the areas of cancer, diabetes and neurological disease (in China), and will put a new biometrics facility in Beijing.
2009	• AstraZeneca China breaks ground for its new site in Zhangjiang High-Tech Park. R&D to focus on common Asian diseases – liver cancer, stomach cancer and esophagus cancer, by exploring and accumulating knowledge on Chinese patients as well as their genetic and biological marks. The company will invest about US$150 million over the next five years to establish an R&D center in Beijing. • Bayer Schering Pharma/ Bayer Healthcare announces a strategic partnership with Tsinghua University, (Beijing) to establish a joint research center, the Bayer-Tsinghua (Institute of Biomedicine) Research Center of Innovative Drug Discovery. • Sanofi-Aventis announces plans to establish a joint laboratory of regenerative medicine with Xuanwu Hospital of Capital Medical University in Beijing, to research senile diseases, including CNS and metabolic diseases.

very actively invested over the last four years in early-stage biotechnology and life science companies in China. HD Biosciences specializes in conducting assay development and high-throughput screening services. The funds are to be used to support the expansion of its high-throughput screening program and build new capabilities in *in vivo* biology and DMPK bio-analytical services.

Large pharmaceutical companies are experimenting within China's dynamic CRO environment and employing a variety of drug-development strategies. Nine of the world's leading pharmaceutical companies have preclinical development facilities located in or around Shanghai (or are potential residents as some facilities are under construction). They include Roche, Novartis, Astra Zeneca, GlaxoSmithKline (GSK), Eli Lilly, Johnson and Johnson (J&J), Pfizer, Abbott and Sanofi Aventis. The R&D is either performed within dedicated facilities or a collection of CROs are managed to perform the task. Eli Lilly sits on the lean side of the scale, employing a staff of about ten people dedicated to outsourcing and overseeing diabetes and oncology drug discovery. The five-year budget is US$100 million. On the thicker side sit GSK and Novartis. GSK is building facilities for its neurodegenerative and neuroinflammatory drug-development programs in Puxi. According to Jingwu Zang, head of GSK's Research and Development Centre in Shanghai, the growing talent pool of scientists who trained overseas is one of the factors that attracted GSK to build a facility there. GSK plans to employ 1,000 people over the next 10 years. Novartis recently announced a continuing investment of US$1 billion into the R&D they are conducting in China.

Two other preclinical-CRO phenomena, both palpable in China, are the increases in complexity and consolidation within the industry. The industry in China is becoming more complex as more and more companies offer biological services. HD Biosciences' integration of biological services is just one example. Another flourishing company is Pharmalegacy, a firm dedicated to providing bone metabolism and other disease models. Darren Ji, Pharmalegacy's CEO, confirms that the company's growth in its first year of business was "formidable". In 2008, the veteran animal-model supplier, Charles River Laboratories International, Inc., seeing the writing on the wall, opened a 60,000 square foot preclinical facility in Shanghai. The maneuver was intended to position Charles River as the strategic partner to its multinational pharmaceutical clients located nearby.

Consolidation through M&A is also occurring to a significant degree. In China, Pharmaceutical Product Development (PPD) announced the acquisition of both Excel Pharmastudies and BioDuro, two prominent companies providing both clinical and preclinical services in China. These acquisitions made it feasible for PPD to offer a full line of services from preclinical to clinical trials. This places PPD in contention with other companies offering a more complete range of services.

In 2008, HD BioSciences, Sundia Meditech and NovaSecta entered into a strategic alliance to provide drug-discovery solutions. NovaSecta, a consulting and project management company, has an extensive client base of mid-sized pharmaceutical and biotech companies in Europe. The alliance is an organic progression for NovaSecta's evolution as an R&D services company for European pharmaceutical and biotech companies. This alliance brings together the high-quality scientific capabilities of HD BioSciences and Sundia with NovaSecta's extensive client base.

Reference

1. Moving Drug Development Outsourcing to a Higher Level: Tufts Center for Drug Development R&D Management Report • Page 4 Volume 4, Number 3 • June 2009

Bioyong

www.bioyong.com

A Catalyst In China's Emerging Biotechnology Industry

Bioyong, a biotechnology services company, is a manifestation of the Chinese government's desire to bridge the gap between academic research and industrial application. While advancing proprietary diagnostic and cloning technologies, Bioyong provides access to state-of-the-art genomics, proteomics and metabolomics services to the academic research community.

SPE-C nano-magnetic beads: Based on weak positive ion-exchange theory, from biological samples (serum, saliva, pleural fluid, plasma, urine, lymph, cerebrospinal fluid, tears, cell supernatant, cell lysis buffer, etc.), the beads can capture small molecules and low-abundance proteins and peptides, which can then be used directly for matrix-assisted laser desorption/ionization mass spectrometry (ABI, Bruker, Shimadzu, SAI, Waters, PE) analysis.

Advantages:

1. Capture many kinds of low-abundance proteins/peptides to ensure specificity of the system
2. Simple and quick operation
3. Superior reproducibility due to huge surface area of the nano-magnetic beads
4. Suitable for high throughput
5. Cost effective

China's biotechnology and pharmaceutical research sectors have made great strides in recent years and the growth of these prospective industries provides a clear example of areas where the country's economic boom is palpable. While the elements of the biotech industry and cluster growth (i.e., the provision of capital coupled with excellent research and available lab space to grow companies) are universal, every region provides its own local flavor. In addition to financial support provided directly by the Chinese government, close-knit collaboration and integration of research institutions and emerging biotechnology companies has augmented the number of opportunities for advancing research and growing new innovation-based businesses in China.

A look at Bioyong, a biotechnology services company set up with support from Peking University Investment Alliance (PKU PE), provides some insight into the workings of China's biotechnology industry. The PKU PE was created to bridge venture investment and the early development of academic projects with market potential.

Primarily based in the Beijing Zhongguancun High Tech Park, Bioyong is a young company that is fostering the advancement of biotechnology and pharmaceutical research and the growth of emerging biotechnology companies by providing state-of-the-art technical service platforms for biotechnology research. Entrenched with leading members of the biotechnology research community of China, Bioyong has been offering services that include genomics, proteomics, bioinformatics and, the relatively new technology on the block, metabolomics. Several of Bioyong's clients, including Peking University, Tsinghua University, China Agricultural University, Chinese PLA General Hospital, Peking Union Medical College Hospital, and Shanghai Rui Jin Hospital, are working to make the transition from research innovation to market application.

Behind some of Bioyong's extensive service offerings are a formidable handful of leading research scientists with international experience in applicable areas of expertise. The list includes Ning Li, a professor at China Agriculture University, Jun Yu, a professor and Associate Director of Beijing Institute of Genomics, Chinese Academy of Sciences (CAS), and Yaping Tian, Director of the Department of Clinical Biochemistry, Chinese PLA General Hospital. Because of their significant contributions to biology, these leading investigators have all gained recognition in the biology community. For example, Li became one of the youngest members of the Chinese Academy of Engineering owing to advances in animal cloning attributable to his research; Yu in 2002 received the Scientific American Research Leader of the Year award owing to his significant contribution to sequencing the rice genome. Li, Yu, and Tian were originally Bioyong's loyal customers but their relationship has evolved into collaborative partnerships for the sake of sharing both research facilities and proprietary technologies. According to Li: "There are still not enough biotechnology service companies in China. And, in the existing companies, the capability of the technical staff also needs to improve. Reliability is an attribute that is stressed throughout Bioyong." Li predicts that in the future there will be a huge market for biotechnology services in China.

Genomics and metabolomics

An extensive panel of genomics and biology services has been offered by Bioyong, including SNP screening, lentivirus/adenovirus packaging, RNAi vector construction, fluorescence real-time quantitative PCR and bioinformatics. And now they are expanding their genomics services to genome sequencing.

The genome sequencing services will be provided in collaboration with Yu. Yu is founder of the Beijing Institute of Genomics. The idea for a new institute was created in 1998 to conduct the research providing China's contribution to the International Human Genome Project (HGP). Yu applied his previous experience from University of Washington Genome Center where he worked on human chromosome 7 for the HGP. He brought a part of the HGP back to China (known as the "1% Project" which was completed in 2001, two years earlier than anticipated), with the encouragement by his mentor Maynard V. Olson, who is one of the major architects for the Project. The Institute has gone on to complete the sequencing of other major genome projects, such as the Superhybrid Rice Genome Project, the Silkworm Genome Project, and the Chicken Genome Diversity Project.

Another aspect of Bioyong's service offerings, metabolomics, has emerged as a key technology in pharmaceutical discovery and development. This system biology approach is evolving to be the small molecule counterpart of proteomics. Metabolomics provides an in vivo metabolic profile that can provide information on drug toxicity, disease processes and gene function at several stages in the discovery-and-development process. Qingwei Ma, the founder and CEO of Bioyong, added the technology to the service offerings in response to a growing interest in the research community.

Proteomics and serum polypeptide-spectrum technology

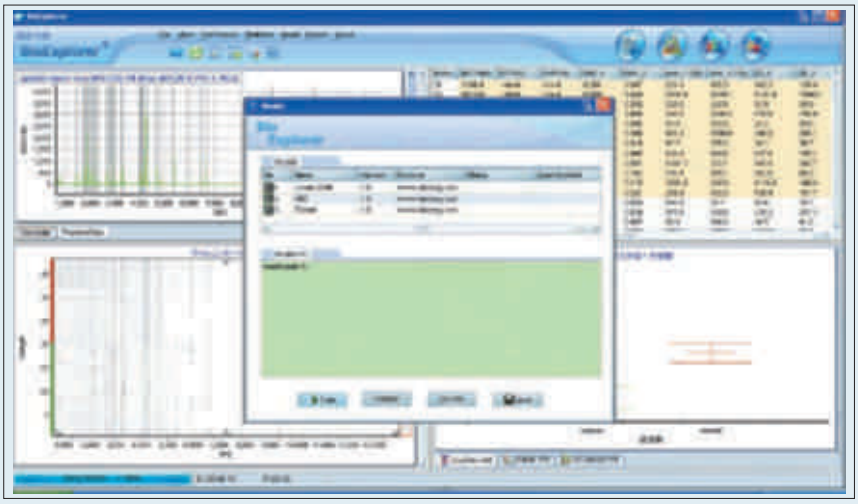
To enhance its proteomics services, Bioyong formed a partnership with the Beijing National Proteome Research Center. "This is a strong alliance and as a result of this cooperation, Bioyong can provide a progressive panel of proteomic solutions," says Ma, who developed the service because he identified a burgeoning need in the research community. Bioyong's proteomics services include the discovery of proteins and the identification of differ-

ences in protein profiles using liquid-protein chip fingerprint analysis, two-dimensional gel electrophoresis, and shotgun proteomics. Shotgun proteomics is named for its DNA sequencing counterpart. This method of identifying proteins uses a combination of high-performance liquid chromatography and mass spectrometry. The proteins in the mixture under investigation are digested and the resulting peptides separated using liquid chromatography. A mass spectrometer is then used to identify the peptides and create a proteomic profile. Bioyong also offers matrix-assisted laser desorption ionization – or MALDI – a mass spectrometry imaging technique that involves the visualization of the spatial distribution of proteins, peptides, drug candidate compounds, and their metabolites, biomarkers, or other chemicals within thin slices of sample.

Mass spectrometry is an integral part of Bioyong's unique service offerings and proprietary research. "Using mass spectrometry, we can obtain a high-resolution analysis of the healthy condition of the human body," explains Dr. Yaping Tian, the Director of the Department of Clinical Biochemistry, Chinese PLA General Hospital, and a client and collaborator of Bioyong. "Now diagnosis depends more and more on large-scale medical diagnostic equipment." Tian's research interests involve the identification of biomarkers for early diagnosis and prevention, and he is attempting to find them using mass spectrometry-based signatures aided by serum polypeptide-spectrum technology.

Serum polypeptide-spectrum technology can be used to find protein markers for early tumor diagnosis. By comparing the spectrum of proteins in patients at various stages of the disease and detecting and analyzing the corresponding changes in the protein profile, one can observe characteristics and chart the pathology. The information can be used in early diagnosis, drug efficacy monitoring, and eventually to find a new drug target, and to design a new drug based on the profile. To this end, Bioyong has detected and analyzed the polypeptide-spectrum in thousands of serum samples for its clients.

To sustain its growth, Bioyong has put a lot of effort into developing proprietary innovations in instrumentation, reagents and bioinformatics. Such innovations are often customized according to the needs of a client. "To grasp the initiative of the market, we perform R&D and innovate continuously in order to hold our own intellectual property. It's the only way to have sustainable development," said Ma. Bioyong applied for a total of 13 patents last year. For example, BioExplorer, a bioinformatics software system developed by Bioyong, facilitates their serum polypeptide-spectrum analysis services, and SPE-C nanomagnetic beads have superior performance for capturing small molecules, low-abundance proteins and peptides in biological samples.

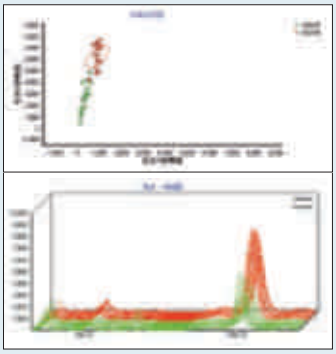


Main interface of the BioExplorer software: The interface consists of the mass spectrum (top left), the virtual gel map (bottom left), a sample table (top-right), a sample comparison chart displaying the mean values and standard variations of two selected protein peaks (bottom right), and the classification model selection window (forefront). BioExplorer is integrated with the Support Vector Machine (SVM), Fisher's Discriminant Analysis, and Radial Basis Function neural network algorithms. The software establishes an early warning model of high accuracy by selecting differential proteins through data mining algorithms after sample pretreatment.

Ning Li and pharming

The portmanteau, pharming (a combination of pharmaceutical and farming) refers to the use of genetic engineering to insert genes that code for useful pharmaceuticals into host animals or plants. Li, a long-time client and partner of Bioyong, took an interest in animal cloning in 1996, the year Dolly the sheep was born in the United Kingdom. Li brought the standard of somatic cell cloning technology in China to a new level when he returned after conducting research in several world-renowned animal biotechnology laboratories in Germany, Japan, and the United States. Li started by cloning a cow and then applied the technology to pigs. More recently, Li turned his attention to the issue of infant nutrition by breeding a cow genetically modified to produce milk with high levels of human lactoferrin. Lactoferrin is an important antimicrobial protein found in breast milk that can help to improve a baby's immunity. Cow's milk expressing human lactoferrin can serve as a replacement for human breast milk. Li expects that in the next 3 to 5 years the product will be able to enter the market. Li also has succeeded in genetically engineering cows to express two additional human milk proteins, lysozyme and lacoalbumin.

Transgenic animals (a subset of genetically modified organisms which have inserted DNA that originated in a different species) and the use of transgenic animals for the expression of pharmaceuticals are a major part of the Chinese "863" plan, a program funded and administered by the government of the People's Republic of China. The 863 plan, so named because it was incepted in the third month of 1986, is intended to stimulate the development of advanced technologies in a wide range of fields for the purpose of rendering China independent of financial obligations for foreign technologies. Li says: "The next step for our somatic cell cloning is to strengthen the industrial capabilities of genetically engineered animals. Bioyong will be one of our very important collaborators in this endeavor."



An example of the BioExplorer two-dimensional (top) and three-dimensional display (bottom) of the differential protein peaks. The color (red or green) represents two differential sample groups.

CONTACT DETAILS:
Bioyong
No.901, Unit 2,Tower C, Longrange Bldg.
HaiDian District, Beijing
P. R. China

Tel: 86-10-82609511 82608397 82608582
Fax: 86-10-82608397 ext.625
bioyong@163.com
www.bioyong.com

BioFocus

www.biofocus.com

BioFocus
A Galapagos Company

BioFocus: Cutting-edge drug discovery

BioFocus, headquartered near Cambridge in the UK, is a vibrant and cutting-edge contract research organization supplying drug discovery products and services from target to candidate. It employs 250 people and has research facilities in the UK, the US, the Netherlands and Switzerland, and sales offices in Tokyo and Singapore. BioFocus was founded in 1997 and acquired by Galapagos in 2005, and is now the biotechnology company's service division.

OFFERINGS

- Integrated drug discovery – gene to candidate drug discovery programs
- Target discovery – using human primary cells
- Assay development and screening – using tailored biochemical and cellular assays
- Fragment-based drug discovery
- Structural biology – using X-ray crystallography and NMR
- *In silico* drug discovery – accelerating discovery with computational technologies
- Medicinal chemistry – designing and synthesizing novel candidates
- ADME/PK laboratory – performing comprehensive analysis
- Compound libraries – synthetic and natural for high-throughput screening
- Compound management – acquiring, managing and distributing collections

CONTACT DETAILS:
BioFocus
Chesterford Research Park
Chesterford Park, Little Chesterford
Saffron Walden, Essex CB10 1XL, UK
www.biofocus.com
Tel: +44 (0)1799 533 500
Email: chris.newton@glpg.com

BioFocus provides large and small biopharma companies and non-profit organizations access to a comprehensive suite of discovery products and services. These cover all stages of the drug discovery process, from target identification to therapeutic candidate, as well as compound management services, and are available separately or as part of an integrated drug discovery solution.

Q: What can BioFocus offer that an in-house discovery group cannot?

We can support companies by providing cost-effective services, from a single technology to an entire, integrated, drug discovery program. We offer access to suites of technologies that our clients may use infrequently, obviating the need to invest in-house. For example, few companies want to create a structural-biology section to elucidate the structure of a single protein, or set up a natural-product division to develop an individual product candidate.

We have a very broad offering, and we have to be as good as, or better than, in-house research because our clients demand it, and we live in a competitive and fast-moving marketplace.

Q: What kinds of companies outsource drug discovery?

All kinds! Our customers fall into four categories, and we find that they all have different needs.

Big pharma companies have large in-house R&D departments but are looking for access to novel targets and flexibility in drug discovery and so will use us for the more specialist processes. These include natural-product discovery, structural biology, fragment-based screening and target discovery using our adenoviral platform.

Mid-size companies tend to have smaller in-house R&D departments, so will use us as a supplemental resource, employing our more generic capabilities, such as medicinal chemistry and biological screening.

Biotechnology companies are often virtual, and use us to gain access to our research scientists and their expertise. They are less likely to use us for target-finding as they usually know which protein they are focusing upon. Most often, they use our generic capabilities, including screening, hit-to-lead optimization and structural biology.

And finally, government and non-government organizations and charities are generally completely virtual and do not have any in-house research, and so will use our integrated drug discovery service, which covers the entire process from target screening to compound management.

Q: What makes BioFocus different to other drug discovery companies?

We are one of the most experienced companies in our field, and we have some great people, many of whom have come from big pharma but have also gained an edge from working in contract research, which is a vibrant and focused field.

To be successful in drug discovery needs strengths in the triangle of chemistry, biology and pharmacokinetics – what the molecule is, what the molecule does to the organism and what the organism does to the molecule. I believe that in our offerings and technologies we have one of the strongest examples of this triangle.

We also provide companies with access to the latest technologies through our close links with our partners, including Cresset BioMolecular, which has developed molecular field software; ZoBio, which has a highly sensitive NMR screening platform; Oncodesign, which specializes in oncology drug discovery; and Optibrium, our first spin-out company, with its StarDrop™ *in silico* optimization platform.

Q: Which is BioFocus' most exciting technology?

Our adenoviral target discovery technology was the founding technology for our group. It allows us to knock-down or knock-in single genes of interest, reducing or increasing levels of proteins produced. This gives us an idea of the effect of a drug directed to that particular target. BioFocus and its parent company, Galapagos, have signed a number of agreements for this technology, including with GlaxoSmithKline, Lilly, Johnson & Johnson, and Merck & Co.

Our fragment-based drug design technology is a relatively new offering and is very exciting. This allows us to identify the fragments that bind to a drug target, which can then be optimized into potential leads and can also include ZoBio's Target Immobilized NMR Screening (TINS) technology, which allows rapid screening at very high sensitivity.

Q: Which was BioFocus' most exciting collaboration?

We signed a significant drug discovery service contract with UCB in 2008, based around an undisclosed enzyme. This is an interesting medicinal-chemistry project working on an unusual target, and we have created an active series of lead compounds with good potential.

We have been working on an oncology target discovery program with Johnson & Johnson, using our adenoviral technology, since 2008. We have had to devise highly sensitive cellular assays for this project – this project has been scientifically very exciting.

Both of these projects will be completed during 2010.

Q: Where next for BioFocus?

We want to maintain BioFocus as a successful and sustainable business in a fast-moving environment, and offer our collaborators access to the most experienced people and the best technologies in the industry to support their drug discovery endeavors. In addition, we intend to exploit new relationships in the Asia–Pacific and developing nation markets.

Pharmidex

www.pharmidex.com

Fast-forwarding drug discovery

Pharmidex delivers world-leading CNS and ADMET solutions to support preclinical drug discovery and development in CNS and other disease areas.

Pharmidex offers:

- **CNS solutions** — assessment of brain penetrability and distribution of CNS therapeutics
- **ADMET solutions** — optimizing potential therapeutics using preclinical and human prediction data
- **Bioanalytical solutions** — determination of small and large molecules and biomarkers in tissues and biological fluids
- **Drug delivery** — formulation technology delivering drugs across the BBB
- **Free consultancy** — support in drug discovery and development
- **Collaboration** — partnering ongoing programs

CONTACT DETAILS:

UK Office:
72 New Bond Street
London, W1S 1RR
United Kingdom
Tel: +44 (0)870 240 5978
contact@pharmidex.com
www.pharmidex.com

USA Office:
11722-J Sorrento Valley Road
Suite J
San Diego, CA 92121
USA
Tel: +1-858-764-1816
usa@pharmidex.com
www.pharmidex.com

Pharmidex is unique in its focus on central nervous system (CNS) drug-discovery and development services, and has world-leading expertise and technologies in this field. Today the company has diversified to provide a wider range of platform technologies, including in vitro and in vivo absorption, distribution, metabolism and excretion (ADME), pharmacokinetics, bioanalysis, safety pharmacology, in vitro pharmacology, and efficacy and safety studies.

Gary Manchee, Global Head of Business Development at Pharmidex, and previously director of drug metabolism and pharmacokinetics (DMPK) at GlaxoSmithKline, says: "The broadening of our offer is a natural development for Pharmidex and provides clients with a strong scientific rationale for compound progression into drug development, ultimately saving time and money prior to, and during, clinical evaluation."

Pharmidex offers drug-discovery and development solutions in three key areas: CNS drug-discovery and delivery solutions; ADMET, PK and bioanalytical solutions; and collaboration and consultancy.

CNS drug-discovery and delivery solutions

Pharmidex is the only company in the world that offers direct assessment of brain penetrability and concentration of free compounds in the extracellular fluid.

"We started Pharmidex to address the main obstacles that blocked the successful development of CNS medicines," says Dr Mohammad Alavijeh, co-founder and Managing Director. "These were the absence of robust predictive models, the inability to get most compounds across the blood–brain barrier (BBB) and the inability to accurately assess their action when they did cross into the cerebral spinal fluid."

Pharmidex aims to offer a total 'blood–brain barrier package' — prediction, assessment and delivery. The company's unique technology platforms include direct assessment of levels of therapeutic agent in the blood and brain (NeuroPK®), measurement of neurochemical markers of therapeutic activity in the brain (NeuroPD™), and measurement of CNS side-effect profiles (NeuroTox™). These have their origins in the work conducted by Alavijeh's research into the dampened efficacy of anti-epileptic drugs at the National Hospital for Neurology and Neurosurgery (Institute of Neurology, Queen's Square, London, UK). This research led to the development of a highly innovative technique for neuropharmacokinetic measurements to elucidate drug distribution in different brain regions.

With a highly qualified team and state-of-the-art assessment technologies in place, 2010 will be the year that Pharmidex intends to focus on developing a range of delivery options. The most advanced of these, under a collaborative agreement with Genzyme Pharmaceuticals, is Cerense℠. According to Dr Peter Hoffmann, Vice President of New Technology at Genzyme Pharmaceuticals, Cerense℠ oligoglycerolipids can deliver compounds up to 250,000 daltons, including proteins, across the BBB.

To strengthen its predictive offering Pharmidex, in collaboration with major players in the field, is working on the development of highly robust BBB screening models using exclusive novel cell lines and validated by NeuroPK® and NeuroPD™ studies.

ADMET, PK and bioanalytical solutions

Pharmidex provides technologies to understand the link between drug level and drug effect in preclinical animal models (PKPD) while balancing ADMET/PK properties, which aids in the selection of the most appropriate drugs for clinical evaluation.

Pharmidex uses an extensive range of in vitro and in vivo ADMET technologies together with human extrapolation science to rapidly select those molecules that are more optimised for development purposes and possessing a greater probability of clinical success.

Together with a wealth of knowledge and experience in CNS, cardiovascular, respiratory and inflammatory discovery programs, Pharmidex can aid more rapid progression and improvement in the probability of success of potential new medicines.

Collaboration and consultancy

The knowledge and experience of the staff at Pharmidex, combined with its cost-effective platform technologies and high-quality data, can help to move drug-development programs quickly and cost-effectively through preclinical development. This can be through collaborations, under a shared risk–shared reward model or on a consultancy basis.

Arrow Therapeutics, founded by Ken Powell, was Pharmidex's first client in 2003, and the company, now part of AstraZeneca, is still one of Pharmidex's clients. Ken Powell was so impressed by the quality of the Pharmidex offering that he has joined the board as Chair. "Pharmidex has consistently provided high-quality data and very rapid turnaround times to clients, and continues to grow through offering efficient, cost-effective support and consistent delivery," says Powell.

"Pharmidex will succeed as a broad-based preclinical services provider, with unique CNS expertise, because of our unequalled ability to combine scientific capabilities with extensive drug-discovery expertise. Clients get real value for money in terms of quality, cost and study design," concludes Dr Chishty (Pharmidex Head of Science).

PharmaLegacy

www.pharmalegacy.com

PharmaLegacy: Championing the Growth of Preclinical Services in China

PharmaLegacy is a new company postured to play a progressive role in China's fast-growing pharmaceutical contract resource industry.

PharmaLegacy uses videostreaming technology in order to enable clients to observe procedures in real time from anywhere in the world.

CONTACT DETAILS:

PharmaLegacy Laboratories
Building 7, 388 Jialilue Road
Zhangjiang High-Tech Park
Shanghai 201203
China
Tel: +(86) 21-6100 2280
Tel: +1 513 276 4645 (24 hour service)
info@pharmalegacy.com
www.pharmalegacy.com

One year after opening its doors, PharmaLegacy, the leading preclinical service company with a Shanghai address, boasts an international client base and a 60 percent proposal acceptance rate. Their 20 clients include large pharmaceutical companies as well as small and medium enterprises.

The rapid financial growth observed in PharmaLegacy's first-year of business may be explained, at least in part, by PharmaLegacy's alignment with two major trends expanding the outsourcing industry. The ubiquitous need for companies to control the cost of drug development and improve efficiency has prompted continued growth of the outsourcing industry as a whole. CEO Darren Ji explains, "PharmaLegacy provides a unique value proposition to clients. Pharmacology studies in animals demand a high level of expertise and specialized knowledge to deliver reliable and consistent results. Our company is able to provide these services while reducing the cost of early stage development and shortening turnaround times. These advantages combined with adherence to a world-class quality standard make PharmaLegacy an attractive service provider."

Ji realized he could take months off a project's turnaround time by streamlining the proposal process and implementing the proposal upon acceptance. PharmaLegacy maintains a staff count that is at least 20-30 percent larger than what is needed to service current clients. "This is done with no extra cost to the customer," he emphasizes. Potential clients can expect an initial response within 24 hours of making an enquiry. Additional cost savings come with being very clear about what is spent. Using an elaborate financial control system, all laboratory costs are tracked and calculated down to the single digit and the information is retrievable on any given day. "Our project cost management system enables us to provide to our clients the highest value for their project dollars." Ji explains.

Another major trend in the outsourcing industry, described by Ken Getz of the Tufts Center for the Study of Drug Development, characterizes service providers to the pharmaceutical and biotech industry as more often becoming valued strategic partners. When discussing PharmaLegacy, Ji illustrates this trend. "Outsourcing needs for drug development have become more sophisticated. Sponsors look for more than just a pair of hands to do the work. They need the service providers to participate in the work design, data interpretation and trouble shooting. Essentially the suppliers become intellectual contributors in the research process. This is where specialty expertise like ours comes into play."

PharmaLegacy's expertise is focused in the areas of bone metabolism, orthopedic research and tissue engineering, immune diseases, inflammation, and oncology. The company provides efficacy studies, histopathology, molecular pharmacology and pharmacokinetic and pharmacodynamic assays, as well as preliminary toxicology screening. Though a young company, the leadership has effectively developed a robust research platform that integrates a great deal of experience with methods for validating the pharmacological effects of drug candidates and testing orthopedic devices for efficacy and biocompatibility. About 15% of company employees were either thought leaders or worked for many years in the US and European pharmaceutical industry in their respective fields. PharmaLegacy specializes in providing the research and development to support investigatory new drug or device evaluation applications to national regulatory agencies throughout the world.

Though located in the Zhangjiang High-Technology Park in Shanghai, China, Ji says technology shortens the distance between the facility and foreign clients. Seventy cameras are installed in the facility's animal and surgery rooms. This makes it possible for clients to observe procedures in real-time through the use of video-streaming. Enabling clients to observe or even supervise during procedures "adds an extra layer of assurance for the client and can help when trying to understand the result," according to Ji.

PharmaLegacy continually strives to integrate rapid service and cost savings into a system that assures a rigorously high standard of quality. All operations are based on Good Laboratory Practice (GLP) standards and Standard Operating Procedures (SOP). Representatives from eight of the top 20 pharmaceutical and biotech companies have inspected and accredited the facilities. Six of them have started working with PharmaLegacy. As these potential clients came to inspect, opinions on optimizing operations were sought. One multinational corporation representative paid PharmaLegacy's management the ultimate compliment saying, "Many people can set up a nice facility like this, but you guys seem to know how to run it."

Recently, PharmaLegacy received an accreditation from the International Association for Assessment and Accreditation for Laboratory Animal Care (AAALAC). The established animal pharmacology models provided by PharmaLegacy include rodents, dogs, mini-pigs, sheep/goats and non-human primates. An AAALAC accreditation means the institution is serious about setting, achieving, and maintaining high standards for animal care and use in science.

Within one year, PharmaLegacy has become a very attractive service provider that stands postured to continue growing. The company is actively recruiting technical talent from overseas. Those who are both passionate about providing outsourcing services and willing to take part in charting a course for the company's future are encouraged to apply.

InvivoSciences LLC

www.invivosciences.com

InvivoSciences LLC
Discovery with a Human Touch™

InvivoSciences Brings a New Dimension to Drug Discovery

InvivoSciences (IVS) have combined three-dimensional (3D) human-cell cultures with high-throughput screening to provide a powerful system for addressing questions about toxicity, therapeutic benefit and even genetic variation. The technology developed by the founders can best be described as high-throughput physiology. By quantifying the body's response to biologic therapies, this company takes some of the guesswork out of drug development.

CONTACT DETAILS:

Ayla Annac, CEO, Co-Founder
InvivoSciences LLC
10437 Innovation Drive, Suite 172
Wauwatosa, WI 53226, USA

Tel: 1 800 930 9838
Email: aannac@invivosciences.com

InvivoSciences LLC (IVS) provides a three-dimensional (3D), tissue-based, high-throughput, high-content physiological-profiling system for the pharmaceutical and biotech industries. "Our products consist of living tissue constructs and we can quantify their physiological responses to pharmaceuticals, environmental stresses, and biological agents such as virus", explains Dr. Wakatsuki, co-founder and CSO of IVS. The company's globally patented proprietary device Palpator™ assesses tissue mechanics as well as optical readouts of physiological parameters, and combining this device with a 3D tissue model derived from human cells results in a highly sensitive platform for predicting toxicity, therapeutic benefit, and the pharmacogenomic effects of drug candidates.

The platform is adaptable to various tissue types, including connective, skin, and heart muscle tissues. Custom assays designed by IVS's scientists provide a closer approximation to *in vivo* conditions compared with the industry-standard two-dimensional cultures. "In two-dimensional cell culture systems the mechanical microenvironment of cells departs critically from the normal condition," describes Dr. Elson, co-founder and Alumni Endowed Professor at Washington University. IVS developed a 3D cell culture system to address this limitation. "We were pleasantly surprised by the recent finding that the tissue mechanics are significantly altered in three-dimensional culture by viral infections, including human cytomegalovirus," Wakatsuki continued.

IVS's cosmetic corporate partner has applied the technology to predict the efficacy of investigative agents to improve elasticity of the skin and potential toxicity.

The system can also be applied to drug and disease target discovery. The National Institutes of Health recently funded a collaboration between IVS and the Medical College of Wisconsin to identify and develop drug candidates to reverse or at least slow the expansion of fibrotic scar tissues caused by cardiac infraction. Screening for candidates will be assayed using the Palpator system and a 3D tissue model that mimics spontaneously contractile cardiac heart muscle.

3D models can be fabricated using human cells or pluripotent stem cells; therefore, the model can also be applied to measuring the influence of DNA polymorphisms on the efficacy of a drug candidate. Drug discovery and treatment can be personalized during the preclinical phase. Animal model-based drug discovery is incapable of addressing this critical need. IVS's intellectual property extends to drug discovery. Currently IVS is optimizing and validating their human tissue model-based technologies for quickly screening and identifying drugs that are effective at delivering to individuals cancer chemotherapy with minimal cardiac toxicity.

WHERE THE GLOBAL BIOTECH INDUSTRY COMES TO PARTNER

4th ANNUAL INTERNATIONAL PARTNERING CONFERENCE

BIO-EUROPE SPRING® 2010

Online Partnering starts January 25!

MARCH 8–10, 2010
BARCELONA, SPAIN

CENTRE CONVENCIONES INTERNACIONAL BARCELONA (CCIB)

BIO-Europe Spring® is the springtime counterpart to EBD Group's flagship conference, BIO-Europe, and continues the tradition of providing life science companies with high caliber partnering opportunities. The event enables delegates to identify, meet and network with companies across the life science value chain from large biotech and pharma companies to financiers and innovative start-ups. In addition to productive partnering, the conference offers high level workshops, panels, company presentations and a lively exhibition.

For further information, please view our conference website at **www.ebdgroup.com/bes**

Producer

EBD GROUP

Supported by

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

biocat

TVG

Your Global Life Science Network™

> "At TVG conferences I have been introduced to partners, closed deals, and celebrated the fruits of successful partnerships over the last 10 years. These are the single most productive partnering conferences in the industry."
>
> Paul Grayson | President & CEO, Fate Therapeutics

We are your network in a global life science world

TVG's Global BioPartnering Platform includes leading industry events in the US, Canada, Europe, China, Latin America, and India. This new network allows life science companies to access global innovation, raise new sources of capital, and tap into skilled workforces around the world.

Vancouver, BC, Canada
January 24-26, 2010

Napa, CA, USA
May 25-27, 2010

Bangalore, India
June 2-4, 2010

Rio de Janeiro, Brazil
September 2010

London, UK
October 10-12, 2010

Shanghai, China
October 31 - November 2, 2010

www.techvision.com/network