Corporate Activity – Mergers and Acquisitions

In this section we bring you a summary of corporate transactions in the pharmaceutical and diagnostic industries. For your convenience, the transactions are listed in alphabetical order within each category. If you are seeking information about a specific company, the quickest method of locating it is to search this issue's company index (p60). Highlights reported in this issue include:

MGI Pharma has gone on a buying spree to build its cancer portfolio (p22). In addition to purchasing Zycos and Aesgen for $US50 million and $US32 million cash, respectively, MGI has also agreed to purchase exclusive worldwide rights to Dacogen™ (decitabine). The drug has been developed by SuperGen for the treatment of myelodysplastic syndromes. Phase III testing was completed in March and SuperGen plans to complete an NDA filing with the US FDA in Q4 of 2004. In October a Marketing Authorization Application (MAA) seeking approval of Dacogen was submitted to the European Agency for the Evaluation of Medicinal Products (EMEA) by SuperGen's European subsidiary EuroGen Pharmaceuticals.

The completion of Sanofi-Synthelabo's acquisition of Aventis has created Europe's largest pharmaceutical company (p26). A key issue facing Sanofi-Aventis remains the Plavix® (clopidogrel) patent case (a pre-trial hearing is scheduled for 8 December). On a positive note, Acomplia™ (rimonabant) for the treatment of obesity is one of the near-term bright spots in the combined company's pipeline. Recent interim data from the RIO-Europe study looks promising and has market analysts anticipating the full 2-year results. However, the analysts believe that data from RIO-Europe and RIO-North America will not be available until towards the end of Q1 2005, prior to filing in Q2.

In a similar vein, the world's biggest biotech Amgen has acquired Tularik and gained access to technology for treating cancer and inflammation via gene regulation (p24). The gene-regulation technology focuses on selectively blocking the cascade of chemical reactions in the body that can cause diseases, including inflammation, which has been increasingly linked to major illnesses such as heart disease and arthritis. Prior to the $US1.3 billion purchase, Amgen had a 21% stake in the biotech company.

Impending Mergers and Acquisitions

Agilent Technologies of Palo Alto, CA, has signed an agreement to acquire the privately held company **Silicon Genetics**, a leading provider of software solutions for life-science discovery based in Redwood City, CA. With the addition of Silicon Genetics' genomics data analysis and management tools to its portfolio, Agilent can become a market leader in life-science informatics. Silicon Genetics' key products include: GeneSpring, a genomic expression visualization and analysis platform; Varia, a line of genetic analysis software; GeNet, a scalable repository for expression data. *"We see informatics as a key to advancing integrated biological research, and our goal is to provide customers with functionality in new research areas to enhance their productivity, creativity and research success,"* said Fran DiNuzzo, vice president and general manager of Agilent's Integrated Biology Solutions business. Agilent's Life Sciences and Chemical Analysis business is a world-leading provider of instruments, supplies, software and services to the life-science and chemical analysis markets. In 2003, these markets generated revenues of $US1.2 billion for Agilent. The company has a website at http://www.agilent.com/ and Silicon Genetics has a website at http://www.silicongenetics.com/.

Boehringer Ingelheim is to acquire the micro-technology specialist **STEAG microParts** of Dortmund, Germany. STEAG microParts' core product is the innovative Respimat® Soft Mist™ Inhaler, which was co-developed with Boehringer Ingelheim. The company, under the name of Boehringer Ingelheim microParts, will be incorporated into the Boehringer Ingelheim Group as a legally independent company.

Canadian companies **Cytovax Biotechnologies** of Edmonton, AB, and **Millenium Biologix** of Kingston, ON, have entered into a definitive merger agreement; the transaction is expected to be completed by the end of November. Cytovax is a biotechnology company focused on developing peptide vaccines and monoclonal antibody therapeutics to either prevent the onset of the infection process in at-risk groups or treat those suffering from

bacterial infections including those resistant to antibiotics. Millenium is a biomedical company focused on the development and commercialization of next-generation orthobiologic and skeletal tissue regeneration products which promote the repair and natural healing of human bone and other tissues. The companies have websites at http://www.cytovax.com/ and http://www.millenium-biologix.com/.

DNAPrint genomics of Sarasota, FL, has agreed to acquire a 51.77 % stake in German pharmaceutical company **Biofrontera**. DNAPrint has agreed to invest €20 million (approximately $US25 million) over 2 years in Biofrontera Series B preferred shares (68% of B shares) representing a 51.77% equity interest. This strategic investment will form the basis of future joint ventures between the two companies, expanding DNAPrint's presence in Europe and giving Biofrontera a presence in North America. DNAPrint and Biofrontera have signed a joint venture framework agreement designed to integrate the companies' technologies in a mutually beneficial way. The acquisition will transform DNAPrint from a population genomics company into a genomics-based pharmaceutical company devoted to the development of theranostic products. 'Theranostics' blend genomics-based tests with drugs as products to target segments of the patient population for enhanced efficacy and reduced side effects. Management expects the use of genome-based testing to facilitate the drug development process and accelerate selected drugs through the clinical trial process. DNAPrint has a website at http://www.dnaprint.com/.

Enhance Biotech of New York, NY, has signed a definitive merger agreement with **Ardent Pharmaceuticals**. Based in Research Triangle Park, NC, Ardent is a privately held biotechnology company with number of preclinical and clinical candidates in the areas of moderate to severe pain, urinary incontinence, premature ejaculation, depression and cardioprotection. Enhance Biotech has a late-stage development portfolio of products focusing on sexual dysfunction and dermatology. Under the terms of the agreement, Enhance shareholders will retain 55% of the stock in the merged entity, which will continue under the name of Enhance Biotech. Ardent shareholders will acquire 45% of the stock. The company's operational headquarters will be located in North Carolina with corporate offices in New York and London. The merging companies have websites at http://www.ardentpharma.com/ and http://www.enhancelifesciences.com/.

Exelixis of South San Francisco, CA, has entered into a definitive agreement to acquire **X-Ceptor Therapeutics**, of San Diego, CA. Under the terms of the agreement, Exelixis will issue approximately 2.5 million shares of Exelixis common stock and pay approximately $US2.9 million in cash in exchange for all of the outstanding shares of capital stock of X-Ceptor on a fully diluted basis. X-Ceptor is developing small molecules that modulate nuclear hormone receptors (NHRs). NHRs represent a promising class of clinically and commercially validated gene targets that are implicated in a wide range of metabolic and cardiovascular disorders. The combination of Exelixis' small-molecule discovery engine and oncology pipeline with X-Ceptor's proprietary 'reverse endocrinology' platform and pipeline of NHR-targeted compounds advances Exelixis' strategy to diversify into new therapeutic areas and is expected to accelerate the development and commercialization of a diverse, highly differentiated pipeline of products to treat diseases including metabolic syndrome, lipid disorders, hypertension and congestive heart failure. The acquisition is expected to close in Q4 of 2004 subject to customary closing conditions. The companies have websites at http://www .exelixis.com/ and http:// www.x-ceptor.com/.

Hedley Technologies plans to acquire **Axxess Pharma**, a privately owned pharmaceutical and diagnostic company; both are Canadian companies. The acquisition is further progress in Hedley's efforts to build a specialty pharmaceutical and diagnostic company. Axxess is currently focused in the areas of dermatology, therapeutic nutrition and pain management both in prescription and over-the-counter (OTC) medicines. It has distribution networks within Canada and internationally, principally selling to hospitals and pharmacies. Hedley will continue to market the Axxess product line under the Axxess Pharma brand. The company has a website at http://www.hedleytech.com/.

Johnson & Johnson Consumer France has entered into an agreement to acquire **Biapharm**, a producer and marketer of skincare products centered on the leading brand Biafine®. The acquisition expands J&J's portfolio of pharmaceutical skin-care products. The Johnson & Johnson subsidiary is based in Issy-Les-Moulineaux, France; Biapharm is headquartered in Houdan, France.

Merck KGaA will acquire most of **NM Pharma**, the generics business of **Pfizer** in Scandinavia, for a purchase price of €53.8 million. After closing the transaction, Merck KGaA will integrate the product

portfolio into its own existing Merck Generics infrastructure in Scandinavia. As a result of this deal, Merck Generics consolidates its leading position and will be the number one player in the Nordic generics market. Because of the strong NM brand recognition, the new company will operate under the name of Merck NM. Headquartered in Stockholm, Sweden, NM Pharma achieved sales of €39.1 million in 2003. The company has a website at http://www.merck.de/.

MGI Pharma of Bloomington, MN, and **Aesgen** of Princeton, NJ, have signed a definitive merger agreement under which MGI Pharma will acquire all outstanding equity of the privately held company for $US32 million in cash. MGI Pharma may also be obligated to make performance milestone payments of $US33 million upon regulatory approval and $US25 million if sales exceed $US50 million in the second year following product launch. In addition, MGI Pharma will pay a 5% royalty on product sales, including sales of Saforis™, a product candidate in development for treatment of oral mucositis. Data from a phase III trial of Saforis, conducted in 326 breast cancer patients receiving anthracycline-based chemotherapy regimens, was the subject of an oral presentation at ASCO 2004. Data indicated that patients receiving Saforis experienced a 22% risk reduction of clinically significant (WHO ≥ to grade 2) oral mucositis compared with placebo. A second pivotal, phase III trial to support a New Drug Application (NDA) filing with the US FDA will be initiated in early 2005. It is estimated that more than 15% of patients receiving chemotherapy experience significant oral mucositis, and more than 90% of patients receiving combination chemotherapy and radiation therapy for head and neck cancer experience significant oral mucositis. There are no FDA-approved drugs for the prevention or treatment of oral mucositis. MGI Pharma and Aesgen expect the transaction to close during 2004. The companies have websites at http://www.mgipharma.com/ and http:// www.aesgen.net/.

MGI Pharma of Bloomington, MN, and privately held **Zycos** of Lexington, MA, have signed a definitive merger agreement under which MGI Pharma will acquire Zycos for $US50 million in cash. This transaction, which has been approved by the boards of directors of both companies, is subject to approval by the stockholders of Zycos. MGI Pharma and Zycos were expecting the transaction to close in September 2004. With this transaction, MGI Pharma takes a significant step toward building a leading oncology franchise. Zycos' iterative drug formulation process allows for the rapid development of immune response therapeutics and has generated two compounds that are currently in clinical development. The most advanced clinical candidate is ZYC 101a, which has completed phase II studies in patients with cervical dysplasia, a potentially precancerous condition. The second Zycos compound in clinical development is ZYC300, an encapsulated plasmid encoding a novel tumor antigen that has completed a phase I/IIa study in 17 patients with late-stage metastatic hematological and solid tumors. The companies have websites at http://www.mgipharma.com/ and http://www.zycos.com/.

Nanogen of San Diego, CA, and **Epoch Biosciences** of Bothell, WA, have signed a definitive agreement to merge Epoch into Nanogen in an all-stock transaction. Epoch has a variety of products that are complementary to Nanogen's and the merger will expand Nanogen's reach in the rapidly growing clinical lab and research markets. The companies serve many of the same customers and both market *in vitro* diagnostic products that provide physicians information to predict, diagnose and treat disease. Epoch has developed advanced technologies that it incorporates in its MGB Eclipse™ Probe System, which consists of reagents and software for improving all types of molecular analyses, including gene expression, SNP (single nucleotide polymorphism) and mutation detection, and identification of infectious organisms. Nanogen has begun incorporating Epoch's technology into its own assays. In July, Epoch launched 21 MGB Eclipse Detection Reagents, real-time analyte specific reagents (ASRs) for the molecular diagnosis of infectious and genetic diseases, and cancer. The real-time ASRs are complementary to the NanoChip® Molecular Biology Workstation, which accomplishes more complex analysis of multiple markers. Under terms of the merger, Nanogen has agreed to an offer price of $US2 per Epoch share, representing a 30% premium over the average closing price of Epoch's shares for the 20 trading days ending on 1 September 2004. The merger is expected to close by the end of 2004. The companies have websites at http://www.nanogen.com/ and http://www.epochbio.com/.

Pfizer is to purchase the remaining 90% ownership of **Meridica** of Cambridge, UK, a drug-delivery technology company for $US125 million and a contingent payment. Meridica specializes in the development of solutions for inhaled, nasal and parenteral routes of administration. In addition to its unique micro-dosing system for dispensing drug powders, it has developed a novel multi-unit dose dry-powder inhaler for the delivery of drugs to the lung for

the treatment of respiratory conditions. In October 2003, Pfizer purchased a 10% interest in the company and licensed the rights to Meridica's dry-powder inhaler. The transaction is subject to normal conditions and is expected to close in Q4 of 2004.

Serologicals of Atlanta, GA, and **Upstate Group**, a privately held company headquartered in Charlottesville, VA, have entered into a definitive merger agreement, pursuant to which Serologicals will acquire Upstate for total consideration of $US205 million in Serologicals Common Stock and cash. Serologicals will issue up to 5 million shares of its Common Stock to the stockholders of Upstate, with the balance of the consideration to be funded in cash. As a result of this transaction, Serologicals will acquire a leading provider of cell signaling research reagents to academic and pharmaceutical investigators, and an outsource supplier to the drug-discovery activities of the pharmaceutical and biotech industries. The deal also allows Serologicals to become a significant presence in the preclinical drug screening and target validation market, the fastest growing segment of the life sciences tools industry, with a unique focus on kinase screening and protein interaction driven by proprietary intellectual property. Serologicals expects the acquisition to be completed during Q4 of 2004. The company has a website at http://www.serologicals.com/.

Solexa of Cambridge, UK, and **Lynx Therapeutics** of Hayward, CA, have signed a definitive agreement to merge. The companies anticipate that the transaction will be completed in late 2004. The combination is expected to build a leading company in the area of future DNA sequencing technologies. Next-generation DNA sequencing is expected to be based on molecular arrays and the two companies have each been advancing toward this target for more than five years. By combining technologies, intellectual property and highly experienced staffs, the companies expect to accelerate development with the goal of releasing their first commercial instrument system in 2005. This system is expected to substantially advance the pursuit of whole genome resequencing and of gene expression measurement by sequencing. These capabilities will be marketed in the near term to various research institutions, a group that already spends more than $US1 billion annually on DNA sequencing and gene expression. In the longer term the technologies also have the potential to transform the world of genetic diagnostics, by making whole genome sequencing a universal medical baseline. Earlier in 2004, the two companies jointly acquired intellectual property rights for DNA amplification on single molecule arrays. These amplified arrays are referred to as cluster technology. The combined company will be unique in its ability to market both cluster systems and single molecule systems. The companies have websites at http://www.solexa.com/ and http://www.lynxgen.com/.

St. Jude Medical and **Endocardial Solutions**, both headquartered in St. Paul, MN, have signed a definitive agreement whereby St. Jude will acquire Endocardial Solutions for $US11.75 per share in cash consideration which represents an aggregate purchase price of approximately $US273 million. Endocardial Solutions has a strategic focus of increasing clinical adoption of its EnSite® System for the diagnosis and treatment of atrial fibrillation (AF) and other arrhythmias and will become part of St. Jude's AF Division. The agreement to acquire Endocardial Solutions follows St. Jude's earlier acquisition of Epicor Medical and its definitive agreement to acquire Irvine Biomedical. Completion of the acquisition of Endocardial Solutions will further broaden St. Jude's electrophysiology technology and programs consistent with the company's 'surround AF' strategy, offering physicians sophisticated devices and catheter systems to diagnose, suppress and cure atrial fibrillation. The acquisition is expected to close toward the end of 2004. St. Jude has a website at http:// www.sjm.com/.

Teva Pharmaceutical Industries of Israel has reached an agreement to acquire **Pfizer**'s Italian generic pharmaceutical marketing company **Dorom**. The all-cash transaction, which values Dorom at €69 million (around $US85 million at current exchange rates), is expected to close in December 2004, subject to conditions. Dorom is one of the two largest suppliers of generic pharmaceuticals to the Italian retail market. Dorom's sales for the 12 months ending 30 June 2004 were approximately €30 million ($US37 million). Teva has a website at http://www.tevapharm.com/.

Other Impending Transactions

Neurome plans to purchase `substantially all' the assets of **Digital Gene Technologies**, including the TOGA® technology, gene expression assays, existing datasets and know-how related to vaccine development programs. In conjunction with the asset purchase, Neurome will also acquire the entire patent estate. The acquisition will allow Neurome to successfully expand beyond its current core technologies in quantitative molecular neuropathology to include TOGA's highly sensitive gene expression based surveys designed to characterize the role of important target molecules

implicated in areas of important unmet medical need. TOGA – which stands for TOtal Gene expression Analysis – enables researchers to measure gene expression levels of both known and novel genes, and shortens the time required to identify and evaluate gene expression levels in various disease models. Both companies are based in La Jolla, CA; Neurome has a website at http://www.neurome.com/.

Peptech is in the very early stages of discussions with **Genera Biosystems**; both are Australian companies. Peptech's preliminary interest in Genera is consistent with Peptech's stated strategic objective of growth through strategic mergers and acquisitions that add shareholder value, as well as internally developed projects. While the Genera technology is in an area of general interest to Peptech, it has not yet been subjected to detailed scrutiny by Peptech's management. Peptech is focused on the research and development of peptides and proteins in the areas of human pharmaceuticals and animal health. The company is positioning itself to become a globally recognized leader in biopharmaceutical development. The companies have websites at http://www.peptech.com/ and http://www.generabiosystems.com/.

Schering's German subsidiary **Jenapharm** has agreed to sell its largely generic therapeutics business to **Dermapharm**, based in Bavaria, Germany, for an undisclosed price. The sale is part of Schering's restructuring program, which includes a sharpening of its portfolio, job cuts, and the closure of production sites as Germany's third largest pharma group aims to achieve an EBIT margin of 18% by 2006. The sale should be completed by Q4 of 2004. Jenapharm's therapeutics business generated net sales of €38 million in 2003. Financial details of the transaction were not disclosed. Schering has a website at http://www.schering.de/.

Completed Mergers and Acquisitions

The world's largest biotechnology company **Amgen** has acquired **Tularik** of South San Francisco, CA, in a stock-for-stock transaction worth $US1.3 billion. The deal combines Amgen's leadership in cellular and molecular biology and medicinal chemistry with Tularik's innovation in gene regulation. It also accelerates Amgen's planned expansion into the San Francisco Bay area, a major biotechnology hub. Amgen gains Tularik's five novel clinical programs in the areas of cancer (hepatocellular, gastric and esophageal), inflammatory diseases, type 2 diabetes and obesity. In the cancer area, Tularik is currently conducting a pivotal study of T67 for the treatment of hepatocellular carcinoma and phase II trials with T607 for the treatment of gastric and esophageal cancer. Tularik will operate as a wholly owned Amgen subsidiary. Amgen has a website at http://www.amgen.com/.

Canadian company **Angiotech Pharmaceuticals** has completed its acquisition of **NeuColl** for an all-cash transaction of $US12.9 million. NeuColl is a privately held orthobiologics company based in Los Gatos, CA. NeuColl will form one of the cornerstones for Angiotech's emerging orthopedic biomaterials franchise. Its initial product platform is a synthetic bone graft substitute comprised of collagen, a composite material of hydroxyapatite, and tricalcium phosphate. Angiotech has a website at http://www.angiotech.com/.

BioDelivery Sciences International (BDSI) of Newark, NJ, has acquired **Arius Pharmaceuticals** of Research Triangle Park, NC. Arius has now been reorganized with and into a newly formed, wholly owned subsidiary of BDSI. Arius is a specialty drug-delivery company whose portfolio of potential products will be focused on 'acute' treatment opportunities for surgical and oncology patients. BDSI is a biotechnology company that is developing patented and licensed delivery technologies for pharmaceuticals, vaccines, over-the-counter drugs, nutraceuticals and micronutrients. The company's technologies include the patented Bioral™ nanocochleate technology and the patented BEMA™ (buccal) drug-delivery technology being developed by its Arius subsidiary. In 2004, Arius acquired an exclusive worldwide license to the BEMA delivery technology developed by **Atrix Laboratories**. Arius is developing BEMA fentanyl for treating cancer pain that is expected to enter phase III trials by mid-2005. BDSI has a website at http://www.biodeliverysciences.com/.

Bio-Rad Laboratories of Hercules, CA, has completed the purchase of **MJ GeneWorks** and its subsidiaries, including MJ Research, for approximately $US32 million in cash and the assumption of certain liabilities of those companies. MJ Research, based in Waltham, MA, is a life-science company that specializes in instruments and consumables used in modern biological research, including thermal cycling instrumentation and reagents used to amplify DNA. MJ Research pioneered the use of Peltier-effect technology and has introduced a number of other innovations in the thermal-cycling field. Bio-Rad has a website at http://www.bio-rad.com/.

Cephalon of West Chester, PA, has completed its acquisition of all of the outstanding shares of **CIMA LABS**. As a result of the acquisition, CIMA is now a

wholly owned subsidiary of Cephalon. The company has a website at http://www.cephalon.com/.

Graffinity Pharmaceuticals of Heidelberg, Germany, and **MyoContract** of Liestal, Switzerland, have merged to form **Santhera Pharmaceuticals**. Santhera will focus on the discovery, development and commercialization of small-molecule drugs in the areas of neuromuscular and metabolic diseases. Santhera's drug pipeline comprises an advanced clinical program in a neuromuscular disease, which will enter pivotal trials by early 2005, and three advanced preclinical programs in diabetes, cachexia/anorexia, and Duchenne muscular dystrophy. Financial details of the all-share transaction were not disclosed. The new company will be headquartered in Liestal with research and development operations in both Liestal and Heidelberg. In conjunction with the merger, Santhera has raised an additional €7 million (approximately $US8.4 million), which will provide the new company with total funding of more than €20 million to last until late 2006. The new company has a website at http://www.santhera.com/.

The German-American biotech company **MediGene** has acquired the anticancer drug candidates and other technology assets from insolvent **Munich Biotech**. The acquisition of these assets strengthens MediGene's portfolio by adding a promising drug candidate and the EndoTAG™ platform technology to develop cutting-edge anticancer drugs. The drug candidate MBT-0206 has already gone through several clinical phase I trials in different cancer indications, on a total of more than 120 patients. Annual peak sales potential of the antiangiogenesis drug is estimated at more than €500 million. MediGene is a publicly quoted, German-American biotechnology company located in Martinsried, Germany and San Diego, CA, and is the first German biotech company with a marketed drug (Eligard® for the treatment of advanced prostate cancer). The company has a website at http://www.medigene.de/.

Canadian company **Micrologix Biotech** has completed the acquisition of **MitoKor** of San Diego, CA. The company created by the deal has a portfolio of clinical and preclinical development programs including five clinical-stage product candidates in hepatitis C, Alzheimer disease, catheter-related infections, acne, and human papillomavirus. Preclinical product opportunities include hepatitis B and C, arthritis, serious hospital acquired infections, Friedreich's ataxia, retinitis pigmentosa, glaucoma, stroke/ischemia reperfusion injury, and obesity. Micrologix' priorities for the next several months are to initiate the MBI-3253 phase IIa monotherapy trial for chronic hepatitis C infections, obtain a Special Protocol Assessment from the US FDA for the pivotal MBI-226 phase III catheter-related infection trial, advance MITO-4509 for Alzheimer disease into phase II, and partner MBI-594AN for the treatment of acne. Micrologix has a website at http://www.mbiotech.com/.

Neuro Discovery of Vancouver, BC, Canada, has closed the acquisition of **Allon Therapeutics** of San Diego, CA, for $US10.5 millon in equity, as well as converting $US8 million in special warrants held in escrow bringing the total deal to $US18.5 millon. The new company will trade as Allon Therapeutics. Allon is developing technology that has demonstrated potent neuroprotective capabilities in preclinical studies in a wide range of chronic and acute neurodegenerative diseases and conditions including Alzheimer disease, multiple sclerosis, stroke, and traumatic brain injury. Allon expects to file an investigational new drug (IND) application with the US FDA for its lead compound AL-108 in Q4 of this year and commence clinical trials early in 2005. The company has a website at http://www.allontherapeutics.com/.

OrthoLogic of Tempe, AZ, has completed the acquisition of **Chrysalis BioTechnology** of Galveston, TX. Under the terms of the definitive agreement, OrthoLogic paid $US2.5 million in cash and issued 3 462 124 shares of OrthoLogic common stock, valued at $US25 million, for substantially all of Chrysalis BioTechnology's assets and intellectual property. An additional $US7 million in OrthoLogic common stock will be paid to Chrysalis shareholders upon the occurrence of certain future events, including the acceptance for filing by the US FDA of a New Drug Application (NDA) for a Chrysalin-based product. OrthoLogic is a drug-development company focused on commercializing several potential therapeutics comprising the Chrysalin® synthetic peptide, also known as TP508. OrthoLogic owns an exclusive license for all worldwide medical indications for the peptide, and is actively pursuing five orthopedic indications for Chrysalin. These include fracture repair and spine fusion, which are in human clinical trials, and cartilage defect repair, which is in late-stage preclinical trials. In non-orthopedic areas, a human clinical trial for chronic diabetic ulcers has been completed. The company has a website at http://www.orthologic.com/.

PediaMed has acquired **Protein Therapeutics**, a company focused on the discovery and development of

new therapies for immunological diseases. The acquisition includes an investigational immunoglobulin drug that is entering phase II clinical trials for gastrointestinal dysfunction in autistic children. Headquartered in Florence, KY, PediaMed is a member of the Union Springs Portfolio of companies, which also includes Xanodyne Pharmaceuticals. PediaMed has a website at http://www.pediamedpharma.com/.

Sandoz (the generics business unit of **Novartis**) has completed the acquisition of **Sabex Holdings**, a leading Canadian generics pharmaceutical manufacturer in a $US565 million cash transaction that officially closed on 13 August 2004. Sabex was acquired from the US private equity firm RoundTable Healthcare Partners, which had held a majority stake in the company. The acquisition of Sabex establishes a new presence for Sandoz in Canada and provides an attractive global growth platform in the fast-growing injectable generics business. Sabex, which is based in Boucherville, Quebec, is a privately held generics manufacturer that offers a broad range of critical care and ophthalmic medicines as well as suppositories and other products covering more than 80 molecules.

Sanofi-Synthélabo has completed its acquistion of **Aventis** and has begun operating as **Sanofi-Aventis**. The new company is the world's third largest pharmaceutical company, ranking number one in Europe. The completion of Sanofi-Synthélabo's offer for Aventis occurred on 20 August 2004, with Sanofi-Synthélabo now controlling Aventis with 95.47% of the share capital. Sanofi-Synthélabo has a website at http://www.sanofi-synthelabo.com/.

Strakan and **ProSkelia** have completed their merger, with the newly merged company called **ProStrakan.** The new company has a broad portfolio of clinical and preclinical R&D projects, including a pure antagonist of the estrogen receptor, osteoclast adhesion receptor antagonists, an oral testosterone and oestradiol glucoside, a new generation SERM for osteoporosis, a topical antiandrogen for alopecia and acne, and a novel antiemetic patch. The company is headquartered in Scotland with the principal R&D operation being based at the former ProSkelia's site at Romainville, near Paris. ProStrakan also announced the completion of the acquisition of the Spanish company **Devon Farmaceutica**.

Treasure Mountain Holdings of Salt Lake City, UT, has completed its merger with privately held **Vyteris** of Fair Lawn, NJ. Under the terms of the merger agreement, Vyteris became a wholly owned subsidiary of Treasure Mountain. Vyteris has developed and produced a prefilled, active transdermal drug-delivery system that delivers drugs through the skin comfortably, without needles. In May 2004, Vyteris received approval from the US FDA to launch its first product, the LidoSite™ Topical System. LidoSite is a topical delivery system indicated for use on normal intact skin to provide local anesthesia for needle stick procedures such as injections and intravenous therapies as well as superficial dermatological procedures. Vyteris has a website at http://www.vyteris.com/.

Other Completed Transactions

Accelrys has completed its merger with **SciTegic**, a leading provider of workflow software solutions for the research science market. The transaction is valued at about $US21.5 million. SciTegic is now a wholly owned subsidiary of Accelrys. Both companies are based on San Diego, CA. Accelrys has a website at http://www.accelrys.com/.

Aerovance has been spun out of **Bayer** to create an independent company focused on developing and commercializing biologic products for respiratory diseases. Aerovance has raised $US32 million through a Series B financing led by Apax Partners. In exchange for a minority equity stake in Aerovance, Bayer Pharmaceuticals has spun out the rights to two lead products to Aerovance: an IL4/13 receptor antagonist (AER-001) for severe asthma entering phase II studies and Bikunin (AER-002), a recombinant therapeutic protein for cystic fibrosis and chronic obstructive pulmonary disease (COPD) on track for the filing of an investigational new drug (IND) application. Bayer also spun out additional research-stage and preclinical programs in respiratory disease to Aerovance. The new company will be based in Berkeley, CA, and has a website at http://www.aerovance.com/.

Canadian company **Altachem Pharma** has sold the business assets and its interest in leasehold improvements associated with the manufacture of the medical diagnostic breath kit to **Isodiagnostika** for the sum of $Can500 000. Altachem received a $Can300 000 cash payment and the remaining $Can200 000 will be paid based on breath kit production until 30 November 2007, when the balance outstanding if any, will be paid. Based in Edmonton, Alberta, Altachem is developing a multi-tiered, integrated approach for the treatment of HIV/AIDS and cancer using novel therapeutic products and adjunct therapies. The lead products of Altachem are Bionex and its four proprietary drugs: ACP-HIP, HB Injectable (ACPSL-017), HB Topical and ACP 2127.

ACP-HIP is currently in phase I clinical trials. Also based in Edmonton, Isodiagnostika develops and commercializes diagnostic test kits utilizing stable isotopes. Isodiagnostika developed the Helikit™ , a ^{13}C urea breath test for the detection of *Helicobacter pylori* and the Diatest™ , a stable isotope breath test for the detection of insulin resistance. The companies have websites at http://www.altachempharma.com/ and http://www.isodiagnostika.com/.

Bayer and **Schering-Plough** have formed an alliance under which Schering-Plough will take over US marketing of Bayer's primary-care medicines. The partnership was expected to become effective on 1 October. The deal could give Bayer a bigger presence in the world's largest drug market, while offering Schering-Plough badly needed new products to sell and a potentially key marketing partner for some of its drugs in Europe and Japan. Under the alliance, Schering-Plough will take over US marketing of Cipro® [ciprofloxacin] and Avelox® [moxifloxacin], both broad-spectrum antibiotics for respiratory and skin infections, plus the antihypertensive Adalat® [nifedipine] and some small established primary-care drugs. The company will also handle US promotion of Bayer's impotence treatment Levitra® [vardenafil]. Outside the US, Bayer will begin promoting some Schering-Plough cancer drugs in Europe; these could include Temodar® [temozolomide] for brain cancer and Caelyx® [liposomal doxorubicin] for brain and ovarian cancer and Kaposi's sarcoma. The companies have websites at http://www.bayer.com/ and http://www.sch-plough.com/.

Boston Biomedica of West Bridgewater, MA, has completed the sale of substantially all of the assets and selected liabilities of its BBI Diagnostics and BBI Biotech divisions to **SeraCare Life Sciences** of Oceanside, CA. The purchase price was $US30 million in cash, plus the assumption of certain liabilities. At a special meeting, stockholders approved an amendment to the company's restated articles of organization to change the company's name to **Pressure BioSciences** (PBI). PBI is a publicly traded, early-stage company focused on the development of a novel technology called Pressure Cycling Technology (PCT). PCT uses cycles of hydrostatic pressure between ambient and ultra-high levels (35 000 psi and greater) to control biomolecular interactions. PBI currently holds 13 US and foreign patents covering multiple applications of PCT in the life-sciences field, including in such areas as genomic and proteomic sample preparation, pathogen inactivation, control of enzymes, immunodiagnostics, and protein purification. The companies have websites at http://www.bbii.com/ and http://www.seracare.com/.

Computer Sciences Corporation (CSC) has acquired **Porton International's** interest in **DynPort Vaccine Company** (DVC), a biopharmaceutical company focused on the development of biodefense biologics products. Formerly a joint venture between CSC and Porton, DVC has been the prime systems contractor for the US Department of Defense Joint Vaccine Acquisition Program since 1997. Products in development at DVC include vaccines for botulinum neurotoxin, tularemia, Venezuelan equine encephalitis, anthrax and plague, and a therapeutic blood product, vaccinia immune globulin, to treat complications of smallpox vaccination. CSC has a website at http://www.csc.com/.

Galapagos Genomics of Mechelen, Belgium, has created a new business unit for its viral-based discovery and validation service. This unit will operate under the name **Galádeno** from the Galapagos facility in Leiden,The Netherlands. The drug-discovery business will be conducted from the Mechelen facility and continueto trade under the name Galapagos. Galádeno will offer both individual adenoviral-based siRNA and full-length gene reagents for drug-target discovery and validation. Furthermore, the company will provide access to its human drugable genome collections FLeXSelect™ (cDNA) and SilenceSelect™ (siRNA), for customers wishing to perform functional screens. In addition, Galádeno will continue to offer its unique human primary cell-based functional screening platform to partners who wish to apply genome-wide siRNA and cDNA screening to novel target discovery and drug mechanism of action studies. The company andits new service unit have websites at http://www.galapagos genomics.com/ and http://www.galadeno.com/.

Netherlands-based **QIAGEN** has completed the acquisition of the key assets of **Molecular Staging** (MSI) of New Haven, CT. Under the terms of the acquisition agreement, QIAGEN has acquired the major assets of MSI (which include over 160 applied or issued patents) for $US28.5 million in cash plus potential earn-outs of up to $US6.75 million. MSI, a privately held company, has developed a range of proprietary products and services based on its Multiple Displacement Amplification (MDA) technology. The key application of MDA is whole genome amplification (WGA). WGA is distinct from PCR since it allows nonspecific amplification of the complete genome to create more DNA for analyses, whereas PCR amplifies only specific, mostly very short stretches of DNA matching a predefined target sequence and is designed to detect specific sequences. The two technologies, WGA and PCR, are therefore often synergistic as samples can be pretreated

with WGA to create sufficient sample amount for many subsequent analyses using PCR and other downstream applications. QIAGEN intends to launch a series of kits integrating MSI's WGA technology to address specific customer needs in early 2005. QIAGEN also acquired MSI's technology portfolio related to rolling circle amplification (RCA), which includes the exclusive rights to use this technology for protein applications. QIAGEN expects that products arising from this technology can target applications for both nucleic acids and proteins. The company has a website at http://www.qiagen.com/.

Quintiles Transnational of Research Triangle Park, NC, has completed the previously announced sale of assets relating to its specialty dermatology products company **Bioglan Pharmaceuticals**. **Bradley Pharmaceuticals** of Fairfield, NJ, through its wholly owned subsidiary **BDY Acquisition**, paid $US188.3 million in cash, including approximately $US5.4 million of direct costs for transferred inventory. Quintiles intends to use proceeds from the transaction to potentially pay down debt, to fund business growth initiatives and for other appropriate purposes. President and CEO of Bradley Pharmaceuticals, Daniel Glassman, said that *"the addition of its* [Bioglan's] *products and sales force will add significantly to Bradley's existing dermatology presence"*. The companies have websites at http://www.quintiles.com/ and http://www.bradpharm.com/.

Shire Pharmaceuticals of Basingstoke, England, and **ID Biomedical** of Vancouver, BC, Canada, have closed the sale of Shire's vaccines business to ID Biomedical. The consideration was $US120 million, of which $US60 million is to be received in cash in two equal installments – one at closing and the other on the first anniversary of closing of the transaction. The remaining $US60 million was paid through the issuance of 4 931 864 subscription receipts to acquire common shares of ID Biomedical. If ID Biomedical completes one or more cash offerings within 22 months after closing, Shire may elect to exchange all or part of its subscription receipts for up to $US60 million cash. As part of the transaction, Shire provides ID Biomedical with a loan facility of up to $US100 million, which can be drawn down over the next 4 years. This facility can be used by ID Biomedical to fund development of injectable flu and pipeline products within the vaccines business acquired from Shire. The companies have websites at http://www.shire.com/ and http://www.idbiomedical.com/.

Name Changes

BioMedicines of Emeryville, CA, has changed its name to **Intarcia Therapeutics**. The privately held pharmaceutical company is developing therapies for the treatment of cancer, immunological, and infectious diseases. The company specializes in redirecting the development of drugs to new indications that meet significant unmet medical needs. Intarcia has agreements with ALZA, Boehringer Ingelheim, Chiron, Pfizer and Schering. The company has a website at http://www.intarcia.com/.

Chiral Quest of Princeton, NJ, has changed its name to **VioQuest Pharmaceuticals** and has created a new wholly owned subsidiary **VioQuest Drug Development**, which will concentrate on acquiring, developing and commercializing human therapeutics. The company also plans to assign substantially all of its operating and technology assets relating to its proprietary chemical catalysis platform to a second wholly owned subsidiary which will be re-named Chiral Quest. This second subsidiary will focus on providing chiral products, technology and services to the pharmaceutical and fine chemical industries. It will develop chemical catalysts and other products used in the synthesis of desired isomers of chiral molecules. VioQuest has a website at http://www.chiralquest.com/.

EPIX Medical of Cambridge, MA, has changed its corporate name to **EPIX Pharmaceuticals** to better reflect its focus on developing pharmaceutical products. EPIX develops pharmaceuticals for imaging that are designed to transform the diagnosis, treatment and monitoring of disease. The company uses its proprietary Target Visualization Technology™ to create imaging pharmaceuticals targeted at the molecular level, enabling physicians to use MRI to obtain detailed information about specific disease processes. The company's lead product, MS-325, is the first imaging pharmaceutical specifically designed for Magnetic Resonance Angiography. A New Drug Application (NDA) for MS-325 was accepted for filing by the US FDA in February 2004. Germany-based Schering is the worldwide sales, marketing and development partner for MS-325, and has submitted MS-325 for marketing approval in the EU. The companies are also collaborating on the development of a second product, EP-2104R, for imaging blood clots using MRI. EPIX has a website at http://www.epixpharma.com/.

Large Scale Biology Corporation of Vacaville, CA, has renamed its wholly owned subsidiary **Eclipse Diagnostics**, which will now be called **Predictive Diagnostics**. The name change was undertaken to more accurately reflect the company's

ongoing focus in the new field of predictive diagnostic medicine. Predictive Diagnostics has developed its proprietary BAMF™ Technology for *in silico* biomarker discovery for use in early diagnosis of life-threatening diseases such as ovarian cancer. The subsidiary has a website at http://www.predictivediagnostics.com/.

Medeus Pharma of Oxford, UK, has changed its name to **Zeneus Pharma**. The company has also relocated its headquarters to The Oxford Science Park. The company has a website at http://www.zeneuspharma.co.uk/.

Micrologix Biotech has changed its name to **Migenix**. Migenix is headquartered in Vancouver, BC, Canada, with US operations in San Diego, CA, and is focused on advancing its pipeline of product candidates in the areas of infectious and degenerative diseases. The company has a website at http://migenix.com/.

Paradigm Genetics is now called **Icoria.** It is a biotechnology company applying its proprietary systems biology platform to the discovery and development of safer, more effective drugs and agrochemicals. Icoria is located in Research Triangle Park, NC, and has a website at http://www.icoria.com/.

Pharmadigm is now called **Inflabloc Pharmaceuticals**. It is a privately held, development-stage biotechnology company based in Salt Lake City, UT. Inflabloc's therapeutic targets stem from the anti-inflammatory properties of dehydroepiandrosterone (DHEA) The company has a website at http://www.pharmadigm.com/.

SCOLR has changed its name to **SCOLR Pharma**. It is a specialty pharmaceutical company engaged in the development and licensing of its Controlled Delivery Technology® (CDT). The CDT platform consists of three patented oral drug-delivery technologies for prescription, over-the-counter and nutritional compounds. The company has a website at http://www.scolr.com/. ■

Summary of Recent Deal Activity
Drug Discovery Technologies

Companies	Type of Deal	Details
4SC, Mutabilis	R&D agreement	4SC and Mutabilis have signed a research partnership agreement. This partnership aims to identify new molecules as a basis for drug discovery against an undisclosed target provided by Mutabilis. 4SC will use its proprietary virtual high-throughput screening technology 4Scan to screen a database of 4.6 million small organic molecules in order to identify new active compounds that bind to the specific target. Mutabilis will then receive a selection of best ranked molecules for biological testing and further evaluation. In return, 4SC receives undisclosed research funding and will be eligible for milestone payments.
Abbott Laboratories, Compound Therapeutics	Licensing agreement	Compound Therapeutics has granted Abbott Laboratories nonexclusive rights to use the company's PROfusion technology and certain antibody libraries. PROfusion is an *in vitro* display technology for the selection and rapid optimization of high-affinity antibodies and other binding proteins. Under the terms of the agreement, Abbott receives the right to use the licensed technology and libraries for purposes of drug-discovery research directed to the generation of highly potent leads for development and commercialization of human antibody products. Compound Therapeutics will receive an upfront payment, milestone payments contingent upon meeting specified clinical and commercial objectives, and potential royalty payments related to therapeutic antibody products that may result from the license agreement with Abbott. Compound Therapeutics will provide training and support in the use of PROfusion technology, as well as reagents and human antibody libraries useful to practice the PROfusion technology.
Affymetrix	R&D agreement	Affymetrix and the Broad Institute of Massachussets Institute of Technology and Harvard are collaborating on three landmark research projects. Scientists at the Broad Institute will use the company's new GeneChip High-Throughput (HT) system to perform pioneering research projects in RNA expression analysis, SNP genotyping and DNA resequencing. The scale, depth and precision of these studies is unprecedented and will enable scientists to perform research that just a year ago was virtually impossible. The Broad Institute plans to use the GeneChip HT system to undertake large-scale genomic and genetics projects, including genome-wide SNP association studies to understand the genetics of complex disease, genome-wide RNA expression analyses to discover the molecular signatures of disease and drug response, and large-scale DNA resequencing for genetic studies of cancer.
Alba Therapeutics	Licensing agreement	Alba Therapeutics has acquired exclusive rights to the intellectual property portfolio surrounding the zonulin pathway for all applications, excluding human clinical diagnostics. Zonulin was discovered and first described by Dr Alessio Fasano and his group at the Mucosal Biology Research Center (MBRC) at the University of Maryland, Baltimore. It is an endogenous signaling pathway, which allows for the transient, reversible, physiologic opening and closing of tight junctions, at will. As part of the license, Alba will expand the exclusionary zone around the IP estate, initiate drug development of the first two leads, and sponsor continued discovery research at the MBRC.
Alnylam Pharmaceuticals, Hybridon	Licensing agreement	Alnylam Pharmaceuticals and Hybridon have entered into an agreement providing Alnylam with an exclusive license to Hybridon's rights to target vascular endothelial growth factor (VEGF) for ocular indications with RNA interference molecules (RNAi). Hybridon received an upfront payment and is eligible for future milestone payments and royalties.

Companies	Type of Deal	Details
Anadys Pharmaceuticals, Aphoenix	R&D agreement	Anadys Pharmaceuticals and Aphoenix have entered into a 3-year drug-discovery collaboration. Under the terms of the agreement, Anadys will utilize its drug-discovery capabilities to discover and advance lead compounds against Aphoenix targets in multiple therapeutic indications. Financial terms of the agreement include upfront and future research funding plus additional milestone payments to Anadys. Anadys will also share in potential downstream value through milestone and royalty payments. Aphoenix is a Tokyo-based chemical genomics company with a proprietary technology called reverse targeting, spanning from small molecules to protein targets. The company exploits drugs or other biologically active compounds with unknown mechanisms of action as probes for discovering valuable and druggable targets using proprietary bead-based affinity chromatographic techniques.
Antigen Express	R&D agreement	Generex Biotechnology's wholly owned subsidiary Antigen Express has entered into a Collaborative Research and Development Agreement (CRADA) with the Uniformed Services University of the Health Sciences (USU) and the Henry M Jackson Foundation for the Advancement of Military Medicine (Foundation) to advance HER-2/neu vaccine efforts for breast cancer. HER-2/neu vaccine efforts under the CRADA will incorporate the Antigen Express proprietary Ii-Key technology to stimulate cancer patients' immune cells to attack HER-2/neu expressing tumor cells.
Aphton, XOMA	R&D agreement	Aphton and XOMA have signed a worldwide collaboration agreement for the treatment of gastrointestinal and other gastrin-sensitive cancers using antigastrin monoclonal antibodies. Under the terms of the agreement, Aphton and XOMA will share all development expenses and all commercialization profits and losses for all product candidates. One of the strategies to be utilized in the collaboration will be the application of XOMA's Human Engineering technology to monoclonal antibodies developed by Aphton.
Array BioPharma, QLT Inc.	R&D agreement	Array BioPharma and QLT Inc. have initiated a drug-discovery collaboration to create a series of small-molecule therapeutics aimed at important cancer targets identified by QLT. The company will provide research funding to Array based on the number of Array scientists working on the research phase of the agreement. Array will be entitled to receive success payments based on reaching certain development milestones and royalties based upon the sales of products resulting from the collaboration.
Artemis Pharmaceuticals, Acceleron Pharma	R&D agreement	Artemis Pharmaceuticals and Acceleron Pharma have signed a cooperation agreement in mouse genetics. As part of this cooperation, Artemis will apply its ArteMice technology platforms to generate a specifically genetically engineered mouse model system for Acceleron. ArteMice CONDITIONAL gene targeting and ArteMice SPEED technologies allow the rapid and efficient generation of complex genetically modified mouse lines. These are used as model systems in drug-discovery research and functional target validation to identify genes that play a central role in disease processes and disease therapy. Acceleron will use the mouse model to develop drugs for the treatment of musculoskeletal and metabolic disorders.
Artemis Pharmaceuticals, Regeneron Pharmaceuticals	Licensing agreement	Artemis Pharmaceuticals has granted Regeneron Pharmaceutical a nonexclusive sublicense to use, for internal research purposes, its patented gene switch technology based on ligand regulated DNA recombination. The technology allows very specific and tightly regulated temporal control of gene expression in adult mice. Inducible gene inactivation represents an optimal method for studying the biological function of selected genes, including those related to human diseases, in specific tissues and organs of the animals. Therefore it provides a powerful basis for drug target validation and the development of new therapeutic products.
Auvation, ExpressOn Biosystems	R&D agreement	Two privately held Scottish biotechnology companies have forged a collaborative, risk-sharing alliance aimed at validating a range of potential new molecular targets within tumor cells, and selecting the most promising as the focus of new anticancer drug development programs. Auvation is developing next-generation anticancer

Companies	Type of Deal	Details
		medicines and diagnostic tests that target its portfolio of proprietary tumor marker proteins. Auvation will provide up to 20 target genes from its cancer marker portfolio, and ExpressOn will use its ACCESSarray technology to determine regions on the corresponding RNA molecules that are optimally accessible to silencing reagents. ExpressOn will then use this information to design silencing reagents that Auvation can use to determine how cancer cells cope when deprived of these tumor targets.
Aventis, atugen	R&D agreement	atugen has signed a collaboration agreement with Aventis to identify siRNA compounds with the potential for therapeutic development. It is planned to combine atugen's proprietary siRNA (short-interfering RNA) technology and expertise in gene silencing with Aventis' pharmacology expertise to inhibit pharmacologically relevant targets. atugen will use its stabilized siRNA compounds and delivery vehicles, which work through a promising, novel mode of action.
Bayer, Seattle Genetics	Licensing agreement	Bayer has licensed Seattle Genetics' proprietary antibody-drug conjugate (ADC) technology. The license provides Bayer with rights to utilize Seattle Genetics' ADC technology to link cell-killing drugs to antibodies against a specific tumor target selected by Bayer. Bayer has paid Seattle Genetics a $US2 million fee and, under the terms of the multi-year license agreement, has agreed to make progress-dependent milestone payments and pay royalties on net sales of resulting ADC products. Bayer is responsible for research, product development, manufacturing and commercialization of all products under the collaboration. Seattle Genetics will receive material supply and annual maintenance fees as well as research support payments for any assistance provided to Bayer in developing ADC products.
Benitec	R&D agreement	Benitec and City of Hope, Los Angeles, CA, have commenced a sponsored research agreement relating to the development of an HIV/AIDS drug using Benitec's proprietary DNA-directed RNAi (ddRNAi) technology. Benitec anticipates that this ddRNAi therapeutic, which attacks multiple targets of the HIV virus simultaneously, will enter the clinic in 2005, and will be the subject of a further agreement with City of Hope. The research will be based on the work of Dr John Rossi from the Beckman Research Institute at City of Hope, in researching HIV and the potential of nucleic acid based technologies (including RNAi) as a possible new treatment. Dr Rossi commented that *"with ddRNAi, we have identified a new therapeutic approach which we hope will extend the lives of those patients in advanced stages of HIV/AIDS when current drugs fail. The experimental treatment we are planning will give patients their own blood stem cells that have been genetically modified using ddRNAi to generate HIV resistance. If this engraftment of HIV resistant stem cells is successful, the new blood cells would be a barrier to continued HIV replication."*
Biogen Idec, Sunesis Pharmaceuticals	R&D agreement	Sunesis Pharmaceuticals and Biogen Idec have entered into a collaboration to discover and develop small-molecule cancer therapeutics targeting kinases, a family of cell-signaling enzymes that play a major role in the progression of cancer. The companies will apply Tethering, Sunesis' proprietary fragment-based drug-discovery technology, in an effort to generate small-molecule leads that inhibit oncology kinase targets. Under the terms of the agreement, Sunesis will receive upfront a $US7 million technology access fee and $US14 million equity investment, research funding to support Sunesis scientific personnel over an initial 4-year research term, precommercialization milestone payments, and royalty payments based on product sales. Sunesis retains an option to participate in the co-development and co-promotion of several products that may emerge from this collaboration. A team of Biogen Idec and Sunesis scientists will work together on the identification, optimization, and development of kinase drugs. Joint efforts will initially focus on six targets.

Companies	Type of Deal	Details
Bioheart	R&D agreement	Bioheart and the University of Florida's Powell Gene Therapy Center are collaborating on the development of a second-generation stem cell-recruiting myoblast technology with the addition of controlled release of angiogenic growth factors for improving blood supply. This technology is targeted at recovering scarred heart tissue damaged from a heart attack.
Bio-Rad Laboratories, Strand Genomics	R&D agreement	Strand Genomics, a Bangalore-based life-sciences informatics company, has entered into an collaborative agreement with Bio-Rad Laboratories to integrate its predictive human pharmacokinetic models in Bio-Rad's KnowItAll platform for *in silico* ADME/Tox assessment. Strand's ADME-Predict models generate predictions for human pharmacokinetic parameters used in drug discovery, such as bioavailability, volume of distribution, plasma half-life, and protein binding when a user enters a chemical structure of a potential drug candidate into the system.
Boehringer Ingelheim, Evotec OAI, Evotec Neurosciences	R&D agreement	Evotec OAI and Evotec Neurosciences have entered a 3-year research collaboration with Boehringer Ingelheim (BI). The companies aim to jointly identify and develop small-molecule therapeutics acting on selected G-protein coupled receptors (GPCRs). They will collaborate with BI on selected GPCR targets with an initial focus on CNS diseases. BI will have global responsibility for all clinical development activities, manufacture and commercialisation of the compounds identified in the collaboration. Under the terms of the collaboration, all three companies will jointly identify and develop preclinical development candidates. In return for Evotec OAI's and Evotec Neurosciences' contributions to the research programme, BI will make research payments, additional discovery and development payments, and royalties.
Boehringer Ingelheim, MorphoSys	R&D agreement	MorphoSys and Boehringer Ingelheim entered into a new program for the development of a therapeutic antibody against an undisclosed target molecule involved in cardiovascular diseases. MorphoSys will generate this antibody using its proprietary HuCAL GOLD technology. Boehringer Ingelheim will carry out the preclinical and clinical development, as well as subsequent marketing of all resulting products. MorphoSys will participate in the successful progress of the project, receiving milestone payments and royalties.
Boehringer Ingelheim, Spotfire	Licensing agreement	Spotfire has entered into a new global licensing agreement with Boehringer Ingelheim to deploy Spotfire DecisionSite analytic software worldwide for pharmaceutical product research and development. A Spotfire customer since 1997, the agreement allows Boehringer Ingelheim to extend use of DecisionSite across the research organization from target discovery through preclinical research in Germany, Austria, Italy, Canada and the US. The company is currently using DecisionSite in genomics, lead discovery and medicinal chemistry.
Cell Signaling Technology, Cisbio, Upstate	R&D agreement	Cisbio international has formed new business collaborations with Cell Signaling Technology (CST) and Upstate. These latest partnerships will allow Cisbio to extend its HTRF technology into one of the largest fields within drug discovery – kinase screening. Through these collaborations, Cisbio intends to demonstrate that its HTRF assay development technology has potential as a reference solution for kinase screening. Under this agreement with Cisbio, Cell Signaling Technology will supply a select group of native antibodies and substrates that Cisbio will label and market for use in conjunction with HTRF. The agreement with Upstate entails the use of its assay for PI-3 kinase along with Cisbio's HTRF, which will demonstrate a high level of HTRF compatibility, resulting in quality assays.
Centocor, Chromos Molecular Systems	R&D agreement	Chromos Molecular Systems has entered into a collaborative agreement with Centocor to develop cell lines using the Artificial Chromosome Expression (ACE) system for potential use in the clinical and commercial manufacture of two undisclosed therapeutic proteins. Under the Centocor-funded collaboration, Chromos will engineer cell lines specific for the expression of two of Centocor's therapeutic proteins using the

Companies	Type of Deal	Details
		ACE system. Centocor has the option to use the cell lines for scale up and manufacture of the proteins, following the research phase of the agreement. The ACE System is a chromosome-based gene delivery and expression platform that enables the rapid engineering of high-quality cell lines for production of proteins. Unique features of the ACE System is that it allows 'auditioning' the expression capabilities of several cell lines in a short time.
Centocor, MorphoSys	Licensing agreement	Centocor has exercised an option to retain a commercial license for HuCAL antibodies directed against an undisclosed Centocor target molecule involved in inflammatory diseases. In exchange, MorphoSys received a license payment from Centocor. The cooperation between MorphoSys and Centocor was initiated in December 2000.
Chiron, InterMune	Licensing agreement	Chiron has granted Intermune a nonexclusive license to its hepatitis C virus (HCV) technology. The licensing agreement allows InterMune to discover, develop and commercialize small-molecule therapeutic agents against certain hepatitis C targets that are covered by patents owned by Chiron.
Cisbio international, BMG LABTECH, Tecan, Molecular Devices	Licensing agreement	Cisbio international has formed strategic partnerships with BMG LABTECH, Tecan, and Molecular Devices. Each of the three companies will deploy Cisbio's homogenous time-resolved fluorescence (HTRF) technology within the context of their proprietary measurement instrumentation systems involved in drug discovery and additional life-science research applications. Under the terms of these agreements, each company will license Cisbio's HTRF technology for use in their high-performance time-resolved fluorescence microplate readers that are used in HTRF-based assays. HTRF is a leading technology within this drug discovery field and has a diversified application capability that includes kinases, GPCR screening and immunoassays.
CombiMatrix	R&D agreement	CombiMatrix has entered into an agreement with Intel Corporation to collaborate on the feasibility of various projects utilizing CombiMatrix' core technology. CombiMatrix is developing a platform technology to rapidly produce customizable active biochips, which are semiconductor-based tools for use in identifying and determining the roles of genes, gene mutations and proteins. The technology has a wide range of applications including DNA synthesis/diagnostics, siRNA synthesis, drug discovery, and immunochemical detection. CombiMatrix provides DNA arrays to researchers under the CustomArray brand. CombiMatrix's Express Track drug-discovery program is a systems biology approach, using its technology, to target common viral diseases with siRNA compounds.
CombinatoRx	R&D agreement	CombinatoRx and the Spinal Muscular Atrophy Foundation have initiated an R&D agreement aimed at identifying combination drugs for the treatment of spinal muscular atrophy (SMA). The sponsored research will use the company's combination high-throughput screening (cHTS) platform in an effort to discover innovative drug combinations that upregulate SMN protein levels. The cHTS platform can detect synergistic drug combinations acting on multiple targets in a disease network. Under the terms of the agreement, CombinatoRx will receive 2 years of research and development funding, the ownership of all intellectual property, and commercial rights to all discovered products. In addition, CombinatoRx will also receive milestone payments as programs advance to IND and is also eligible for increased funding to support clinical development of promising new therapeutics for SMA. SMA is a genetic, motor neuron disease characterized by the wasting of skeletal muscles. Caused by progressive degeneration of nerve cells in the spinal cord, the disease leads to increasing muscular weakness and atrophy.

Companies	Type of Deal	Details
CombinatoRx	R&D agreement	CombinatoRx,and the nonprofit foundation Accelerate Brain Cancer Cure (ABC2) have initiated a research collaboration aimed at identifying multi-target drugs for the treatment of brain cancer. The sponsored research will leverage the CombinatoRx proprietary combination high-throughput screening platform in an effort to discover drug combinations that hit multiple targets relevant to glioblastoma multiforme, a deadly form of brain cancer. Under the terms of the agreement, CombinatoRx will receive research funding from ABC2, and the intellectual property and commercial rights to all products discovered in the collaboration. Duke University, which has a pre-existing relationship with ABC2, will provide certain research materials and conduct the preclinical assessment of synergistic drug combinations emerging from the collaboration.
CompuCyte	R&D agreement	CompuCyte and the National University of Singapore (NUS) have entered into a collaborative program to study the apotosis-inducing activity of small compounds for their application in treating cancer and other disease conditions. Under the agreement, NUS will provide CompuCyte with compounds, and CompuCyte will develop assays and perform high-content cell-based analysis of their effect on cells, using the company's iCyte and iCys imaging cytometers.
Corgentech, Cyclacel Group	R&D agreement	Corgentech and Cyclacel Group have entered into an exclusive license to utilize Cyclacel's Penetratin Endonuclear Delivery System with Corgentech's transcription factor decoy (TF Decoy) technology platform. The Penetratin system is a proprietary peptide with carrier properties for delivery into cells. Corgentech's TF Decoy technology is a new class of therapeutics that blocks the activity of multiple genes linked to a disease. Cyclacel will receive an up-front payment, milestone payments, and royalties if licensed products are commercialized. Corgentech will have responsibility for the development and commercialization of TF Decoys combined with a Penetratin peptide.
Crucell	Licensing agreement	Crucell and the International AIDS Vaccine Initiative have signed an exclusive license agreement to develop an AIDS vaccine based on Crucell's AdVac technology. Crucell expects to receive development funding and substantial upfront, annual and milestone payments, as well as royalties on future HIV vaccine sales.The AdVac vectors, adenovirus serotypes 11 and 35, have shown promising results as vectors for AIDS vaccines in a series of studies by Crucell in collaboration with Harvard Medical School. AdVac technology is also being applied by Crucell in the production of a malaria vaccine in collaboration with GlaxoSmithKline, Walter Reed Army Institute of Research and the US National Institute of Allergy and Infectious Diseases of the NIH, as well as a TB vaccine in collaboration with the Aeras Global TB Vaccine Foundation.
Diversa	R&D agreement	The US National Institute of Allergy and Infectious Diseases (NIAID) has awarded Diversa a grant for the discovery and development of antibodies to diagnose and treat severe acute respiratory syndrome (SARS). Diversa will apply its OmniMab antibody program to screen more than 1 billion fully human antibodies against targets associated with the SARS-coronavirus. In collaboration with Diversa, the US Army Medical Research Institute of Infectious Diseases (USAMRIID) will then test antibody candidates selected and optimized by Diversa for their ability to neutralize live SARS-coronavirus.
Evotec OAI, Hydra Biosciences	R&D agreement	Hydra Biosciences has signed an agreement with Evotec OAI to advance the discovery of ion channel modulators. Under the terms of the agreement, Evotec OAI will provide Hydra with a range of biology and screening services to identify novel active compounds against a proprietary ion channel target being developed by Hydra. Using its proprietary high-throughput screening technology, Evotec OAI will produce reagents, develop assays and screen compounds as well as characterize hits generated by the program.

Technology Deals

Companies	Type of Deal	Details
Evotec OAI, Seikagaku	R&D agreement	Evotec OAI and Seikagaku have entered into a collaboration to identify small-molecule therapeutics for inflammatory diseases. Evotec OAI will apply its skills in assay development and ultra-high-throughput screening to rapidly identify biologically active compounds from its corporate library that interact with selected disease targets of Seikagaku. Active compounds identified in screening will be further characterized and prioritized by Evotec OAI for progression into subsequent lead optimization programs.
Evotec Technologies, QIAGEN	Marketing agreement	Evotec Technologies and QIAGEN have signed an agreement to promote the benefits of combining QIAGEN's proprietary TOM-amidites chemistry based RNAi products with Evotec's Opera platform. By combining the results from both platforms, systems biologists can obtain high-quality functional gene analysis and thereby decipher the role of genes identified by the human genome project with unknown functions. The two companies will develop a series of scientific application notes that describe challenging applications that can be more easily accomplished using the combination of Evotec and QIAGEN products. The first application note, 'Ultra high-throughput gene silencing for rapid, economical functional genomics studies' will be published in the near future.
eXegenics, NLC Pharma	Licensing agreement	eXegenics has licensed the company's QCT drug-discovery technology to NLC Pharma. The company will receive up to $US20 million from royalties, licenses or the sale of QCT technology to third parties that are generated by NLC Pharma. QCT is a rational drug-design technology that is based on quantum chemistry, proprietary computational software and molecular modeling. The quantum mechanism-based drug creation technique combines quantum mechanics and physical organic chemistry to project estimates of essential biochemical reactions that occur at an atomic rather than molecular level. Looking at core mechanisms in this way could produce a wide range of drug leads.
ExonHit Therapeutics, Mitsubishi Pharma	Licensing agreement	ExonHit Therapeutics and Mitsubishi Pharma have entered into a site license agreement for the use of Safe-Hit, a microarray-based system developed by ExonHit that allows evaluation and ranking of compounds for toxicity. Safe-Hit allows companies to invest their time and resources into compounds with a lower chance of failure in development due to safety issues. This agreement follows a 1-year evalution of Safe-Hit by Mitsubishi. The content on the Safe-Hit microarray was derived by applying ExonHit's DATAS (Differential Analysis of Transcripts with Alternative Splicing) profiling technology to a proprietary model of cellular stress. DATAS allowed the identification of the stress-specific nucleic acid signatures in the model system, and thus allowed the creation of a library of splicing events specific to toxicity that are generally distinct from changes induced by the intended pharmacological activity of drugs. Safe-Hit can be used with both human and rodent cells, making it particularly useful for the various needs of pharmaceutical R&D.
Genencor International, Ablynx	R&D agreement	Ablynx has entered into an oncology drug-discovery collaboration with Genencor International. Through this agreement, Ablynx will use its unique and patent protected nanobody platform to discover and develop new drug candidates against tumor targets specified by Genencor. Under the terms of the partnership, Ablynx will receive research funding and license fees in addition to milestone payments, and royalties upon commercialization. Ablynx will be responsible for discovering Nanobodies that meet a predefined profile. Genencor will assume responsibility for the preclinical and clinical development of lead Nanobodies, as well as the commercialization of any resulting drug products. Through this collaboration, Genencor will develop Ablynx's Nanobodies in several drug formats including 'Antibody Directed Enzyme Prodrug Therapy'.

Companies	Type of Deal	Details
Genentech, Celera Genomics Group	R&D agreement	Celera Genomics Group has initiated a collaboration with Genentech to discover and develop targeted therapies for cancer. Genentech may develop various products against therapeutic targets licensed from Celera, including antibodies, antibody fragments, proteins or small molecule drugs. Under the terms of the multi-year agreement, Celera Genomics will nominate a number of cell-surface antigens discovered and validated through its proprietary proteomic platform as potential therapeutic targets. Any of these antigens may be designated by Genentech for further validation and research to identify therapeutics for subsequent development solely by Genentech. Genentech will make progress-dependent milestone payments to Celera Genomics, based on achievement of preclinical, clinical and commercial milestones, and shall pay royalties on net sales of any resulting therapeutic products. Celera Diagnostics retains certain diagnostic rights associated with the designated targets.
Genentech, Lexicon Genetics	R&D agreement	Lexicon Genetics has completed the second performance milestone in its drug discovery alliance with Genentech. The companies entered into a drug-discovery alliance in December 2002 to discover therapeutic proteins and antibody targets. Under this alliance, Lexicon is discovering the functions of potential therapeutic proteins and antibody targets identified through Genentech's internal drug discovery research. The milestone payment is related to Lexicon's production of gene knockouts in mouse embryonic stem cell lines for all of the proteins selected for inclusion in the alliance. Lexicon completed the generation of knockout mice and identified the physiological functions of many of the proteins in the alliance. Lexicon is in the process of discovering the therapeutic potential for the remaining proteins. The amount of the milestone payment was not disclosed.
Genzyme, Mirus Bio	Licensing agreement	Mirus Bio has entered into an agreement with Genzyme covering research applications of Mirus' proprietary hydrodynamic gene-delivery technology. Under this agreement, Genzyme will have the nonexclusive right to use a range of Mirus' technologies in its research programs, including its Pathway IV protocol, a novel method to efficiently deliver genes to muscle via the bloodstream.
Genzyme, Valentis	Licensing agreement	Valentis has expanded its existing license agreement with Genzyme that grants the company increased use of Valentis' GeneSwitch gene-regulation technology. In return, the agreement provides Valentis certain rights to Genzyme's static mixer intellectual property for use in plasmid DNA manufacturing.
Global Genomics, Rheoscience	R&D agreement	Global Genomics has entered into an agreement with Rheoscience for the use of its tangerine gene expression profiling to study targets in metabolic diseases. Global Genomics' tangerine technology is based on PCR, capillary electrophoresis, proprietary databases and algorithms that generate gene-expression profiles.
Illumina	R&D agreement	Illumina has signed a commercial agreement to conduct an extensive, two-phase genotyping study for the North American Rheumatoid Arthritis Consortium to identify genes associated with this complex and debilitating disease. *"Enabling the life science community to expand understanding of the genetic cause of disease is a core application of our BeadArray technology platform"*, commented Jay Flatley, Illumina President and CEO.
ImClone Systems, Neurome	R&D agreement	Neurome has entered into a research agreement with ImClone Systems, in which Neurome will apply its proprietary technologies and expertise in quantitative neuropathology to assist ImClone in the discovery stage investigation of preclinical candidate molecules. Specific financial terms were not disclosed.
International Therapeutics, Rosetta Inpharmatics	Licensing agreement	International Therapeutics has granted Rosetta Inpharmatics a worldwide nonexclusive license to its proprietary ProxiQuant technology for research and development applications. ProxiQuant is an enzymatic application enabling

Companies	Type of Deal	Details
		stoichiometric generation of surrogate DNA targets from primary RNAi molecules in biological samples. ProxiQuant has been used to quantify RNAi dose with a sensitivity of one zeptomole (10^{-21} mole). ProxiQuant is an accurate nonradioactive method to measure RNAi in biological samples.
Intra-Cellular Therapies, Shamrock Structures	Service agreement	Shamrock Structures has signed an agreement with Intra-Cellular Therapies to provide integrated structural proteomics services. Under the agreement, Shamrock Structures will perform structure-activity relationship (SAR) co-crystallization, synchrotron data collection, and structure determination of an Intra-Cellular Therapies protein target to which inhibitors are bound. The agreement terms include an upfront fee and performance-based milestone payments.
Invitrogen, Exelixis	R&D agreement	Invitrogen is to provide validated high-throughput screening (HTS) assays for drug discovery in single live cells that Exelixis will use for lead discovery and optimization. Under the agreement Invitrogen's Drug Discovery Solutions group (formerly PanVera) will provide Exelixis with GeneBLAzer and Voltage Sensor Probe technologies for compound screening. The GeneBLAzer cell-based ß-lactamase (BLA) system combines traditional molecular and cellular biology with a Fluorescence Resonance Energy Transfer (FRET)-based detection method to conduct high-throughput screening experiments. This method enables drug-discovery scientists to more accurately measure subtle functional cellular responses related to specific drug targets, in living cells and in highly miniaturized formats (1–2 μL volumes).
Juvaris BioTherapeutics	R&D agreement	Juvaris BioTherapeutics is collaborating with Dr David Claxton at Penn State University on the development of immunostimulant and therapeutic vaccine approaches for the treatment of acute myelogenous leukemia (AML). Juvaris' potent immunostimulation technology will be tested in rodent tumor models established by Dr Claxton to evaluate the impact on leukemia using either an antigen-specific immunotherapeutic AML vaccine (JuvaVax) or a non-antigen immunostimulant (JuvImmune) to augment immune responsiveness.
Lundbeck, Norak	R&D agreement	Lundbeck has exercised its option to screen another of its G protein-coupled receptor (GPCR) targets of interest using Norak's Transfluor technology. The option was part of the screening collaboration agreement signed in December 2002. Under the terms of the agreement Norak will develop a Transfluor cell line expressing the GPCR target of interest to Lundbeck and then screen this cell line at Norak on its high-throughput imaging systems against a compound library of Lundbeck's choice.
Medarex, diaDexus	R&D agreement	Medarex and diaDexus have expanded their existing collaboration for the research and development of fully human antibody therapeutics against cancer targets provided by diaDexus. Under the terms of this expansion, diaDexus and Medarex expect to develop antibodies against three cancer targets outside of the lung cancer field, which is the focus of the original 2003 collaboration between the two companies. Both companies expect to share the cost of development and commercialization as well as potential profits resulting from any products developed through this collaboration. Separately, diaDexus also granted Medarex an exclusive right to develop and commercialize therapeutic antibodies to a novel target for use in ovarian cancer for which diaDexus expects to receive an upfront payment and potential milestone payments and royalties on future sales of products developed and commercialized by Medarex. Medarex plans to use its UltiMAb Human Antibody Development System to generate antibodies to the targets provided by diaDexus.
Merck & Co., BioImage	Licensing agreement	BioImage has signed a licensing agreement with Merck & Co. granting Merck the freedom to use BioImage's Redistribution technology in its drug-discovery research. The Redistribution patent portfolio covers a broad range of methods aimed at studying intracellular signalling events. The technology enables high-throughput

Companies	Type of Deal	Details
		screening on a number of drug-discovery, live cell screening applications, such as protein translocations, receptor internalizations, protein trafficking, and secretions. BioImage is presently out-licensing the portfolio to a number of leading companies within the life-science industry.
Merck & Co., TransTech Pharma	R&D agreement	TransTech Pharma and Merck & Co. have entered into a research collaboration using TransTech's proprietary TTP Translational Technology to discover and develop small molecules for a therapeutic target of interest to Merck. Under the terms of the agreement, Merck has the exclusive right to develop and commercialize all compounds directed at the target covered by the collaboration. TransTech could receive payments of just over $US26 million for the discovery, development and marketing approval of a small molecule for the top priority indication. The agreement also provides for milestone payments for the discovery and development of additional small molecules and lower priority indications. TransTech would receive an upfront payment, research support and payments upon the achievement of specified research, clinical and commercialization milestones. In addition, TransTech would receive royalties on future product sales.
MorphoSys, Crucell	Licensing agreement	MorphoSys has entered a nonexclusive license agreement with Crucell. Under the terms of the agreement, MorphoSys received rights to Crucell's PER.C6 fully human cell line technology for use in its own and partnered antibody research programs conducted at MorphoSys. Furthermore, MorphoSys and its partners have an option to obtain a license for the clinical and commercial production of antibodies isolated from the MorphoSys HuCAL library.
MorphoSys, GeneFrontier	Marketing agreement	MorphoSys has formed a strategic marketing cooperation with the Tokyo-based company GeneFrontier in order to access the Japanese life-science market. The objective of the cooperation is to drive new business opportunities by establishing MorphoSys' HuCAL technology as the premium brand for both research and therapeutic antibody generation in Japan. As part of an ongoing premarketing agreement between the two companies, several research projects conducted with Japanese partners have been successfully completed. Under the multi-year collaboration, both parties will invest in customer development and marketing in Japan as part of a wider MorphoSys effort to expand geographically into new markets.
Morphotek	R&D agreement	Morphotek has signed a cooperative research and development agreement (CRADA) with the US Army Medical Research Institute of Infectious Diseases (USAMRIID) for the development of biochemicals and antibodies for detection and therapy against pathogenic agents causing infectious diseases of public health and biodefense importance. Under the CRADA, Morphotek will apply its proprietary MORPHODOMA technology to develop fully human antibodies that can specifically target high-priority pathogenic agents as well as employ its DIRECT-LINE technology to develop evolved human epithelial cells that are naturally resistant to biological pathogens for discovery and product development. USAMRIID will provide its expertise in characterizing and evaluating lead antibodies and antimicrobial compounds for specificity and therapeutic efficacy.
Nautilus Biotech, Creabilis Therapeutics		Nautilus Biotech and Creabilis Therapeutics have signed a collaboration agreement for the identification and development of an improved variant of CT 500, a non-antibody protein selected by Creabilis, with antagonist activity against HMGB1. The new anti-HMGB1 variant protein, object of the agreement, is expected to have potential applications in various acute and chronic clinical indications such as autoimmune diseases, infective diseases, sepsis, tumours, cardiovascular and also neurological and amyloid pathologies. Nautilus' proprietary technology for protein evolution, based on systematic mutagenesis and already successfully applied to a number of well known therapeutic proteins, will be used to improve the pharmacodynamic profile of CT500.

Technology Deals

Companies	Type of Deal	Details
NeoGenesis Pharmaceuticals, Achaogen	R&D agreement	NeoGenesis Pharmaceuticals has signed a research and discovery collaboration agreement with Achaogen, an emerging biotechnology company based in South San Francisco, CA. Under the terms of this agreement, NeoGenesis will use its drug-discovery technologies, including its proprietary ALIS (Automated Ligand Identification System) platform, NeoMorph compound libraries, and lead optimization technologies to discover drug candidates against selected targets. The company anticipates drug candidates from its collaborative efforts to enter into human clinical trials in 2005 and 2006.
Nucleonics, Novosom	R&D and licensing agreement	Nucleonics and Novosom are collaborating to evaluate Novosom's SMARTICLES formulation technology for the delivery of Nucleonics' expressed interfering RNA (eiRNA) lead candidates for hepatitis B and C. In addition, Nucleonics has taken an option to exclusively license and commercialize Novosom's delivery technology for Nucleonics' eiRNA therapeutics for these indications. Novosom's liposomal formulations, termed SMARTICLES, are charge-reversible particles that enable the targeted delivery of oligonucleotides, plasmids and other materials directly into living cells. SMARTICLES are stable in blood and distribute in the same manner as conventional liposomes. In contrast to conventional liposomes, however, SMARTICLES become positively charged when they cross cell membranes, leading to effective delivery of their cargo within cells. The liver and spleen, along with sites of inflammation and tumors are primary targets for the SMARTICLES.
Nuvelo, Kirin Brewery	R&D agreement	Nuvelo has extended and expanded its research and development collaboration with the pharmaceutical division of Kirin Brewery Co. The amended agreement extends the term of the current collaboration to 31 December 2005 and expands the scope of the collaboration to include additional secreted protein genes from Nuvelo's full-length gene portfolio. The collaboration is expected to foster further development of therapeutic candidates using Kirin's proprietary site-directed transgenic mouse technology to identify and develop secreted proteins and associated antibodies with therapeutic utility.
OncoTherapy Science, BioWa	R&D agreement	OncoTherapy Science (OTS) has signed a memorandum with Kyowa Hakko Kogyo's US subsidiary BioWa to forge a new business partnership in antibody drug development. Under the expected alliance, the companies will develop an advanced antibody drug designed for the treatment of cancer, based on antibodies produced by OTS and POTELLIGENT, BioWa's proprietary technology for the enhancement of antibody-dependent cellular cytotoxicity.
Organon, BioImage	R&D agreement	BioImage has signed a research agreement with Organon. The agreement outlines the use of BioImage's Redistribution assays for pathway profiling of selected lead compounds produced by Organon's discovery projects. BioImage's Redistribution technology enables high-throughput, high-content screening on many targets of current interest in drug discovery, including a range of intracellular signaling molecules and cell surface receptors. Under the new research agreement, a series of Redistribution assays will be used to perform pathway profiling to accelerate development efforts for selected Organon discovery projects.
OriGene Technologies, Xantos Biomedicine		Xantos Biomedicine has acquired access to OriGene Technologies' TrueClone collection of non-redundant full-length human cDNA clones. Xantos uses its proprietary high-throughput cellular screening technology XantoScreen and the full-length human clone collection to identify and functionally validate targets. The 22 000 human full-length cDNAs in OriGene's TrueClone Collection are largely derived from cDNA libraries avoiding the artifacts associated with other clone collections isolated by PCR methods. Each cDNA clone matches an annotated mRNA reference sequence from established public domains and is housed in non-proprietary expression vectors suitable for transfection and direct *in vivo* or *in vitro* expression.

Companies	Type of Deal	Details
PerkinElmer, BioImage	R&D agreement	PerkinElmer is to collaborate with BioImage to develop cell-based assays on the PerkinElmer EnVision HTS multilabel plate reader platform. The collaboration combines the BioImage assay technology with the PerkinElmer EnVision detection platform to develop a series of cell-based screening methods. BioImage has developed a suite of assay technologies for measuring protein-protein interactions in living cells using PerkinElmer's EnVision platform. The platform provides extremely sensitive fluorometric detection at high speeds, making it the ideal detection platform for the BioImage assays. This powerful combination enables customers to perform robust cell based identification of inhibitors of protein/protein interactions at throughput levels previously not available.
Pfizer, Medarex	R&D agreement	Medarex has entered into a global collaborative agreement with Pfizer for the discovery and development of up to 50 antibody products over 10 years. Pursuant to the agreements, Pfizer will make an initial cash payment to Medarex of $US80 million and will purchase $US30 million of Medarex's common stock. Medarex expects to use its UltiMAb human antibody technology to create product candidates to disease-associated targets identified by Pfizer. Pfizer will be responsible for the worldwide development and commercialization of any products generated. Medarex has the potential to receive research funding, license fees and milestone payments, if certain milestones are met, exceeding $US400 million if all 50 products obtain regulatory approval, as well as royalties on any commercial sales of the products.
Roche, Ambit Biosciences	R&D agreement	Roche and Ambit Biosciences have initiated a multi-year collaboration, alongside a new equity financing round for Ambit, led by Roche. Under the collaboration, Roche will use Ambit's proprietary kinase screening platform to profile and select small-molecule kinase inhibitors. Ambit will receive milestone payments and royalties on drugs developed through the collaboration. Additionally, Roche led a Series C round of financing that raised over $US21 million in the initial close.
Roche, Glycart Biotechnology	R&D agreement	Roche and Glycart Biotechnology have formed an agreement to discover next-generation therapeutic antibodies using GlycoMAb technology. Roche will have the option to develop and market worldwide all antibodies generated by Glycart from an undisclosed product candidate. Glycart will receive an up-front fee, research funding, milestone payments and royalties on product sales. According to Glycart, during an initial technology evaluation it has rapidly generated GlycoMAb versions of Roche's antibodies with dramatically enhanced potency, and as a result, Roche has decided to license GlycoMAb. GlycoMAb is a fully developed technology platform that efficiently increases the specific biological activity of therapeutic monoclonal antibodies for target cell ablation. It is based on an active modulation of antibody glycosylation during production leading to antibody products with increased antibody-dependent cellular cytotoxicity.
Roche, Norak	R&D agreement	Roche has exercised its second-year option to screen more of its G protein-coupled receptor (GPCR) targets of interest using Norak's Transfluor technology. The option was part of the agreement signed in September 2002 between Norak and Roche. Under the terms of the agreement Norak will provide its Transfluor cell lines expressing GPCR targets of interest to Roche for use in a primary screen of its compound libraries.
Roche, Structural GenomiX	R&D agreement	Roche and Structural GenomiX (SGX) have formed an alliance to discover new antiviral therapeutics. Using its proprietary FAST technology, SGX will be responsible for discovering small-molecule inhibitors for Roche to develop and commercialize worldwide. SGX will receive an upfront payment, research funding and milestone payments as product candidates advance through development, and royalties on product sales. FAST is a proprietary fragment-based approach to identify novel drug candidates that capitalizes on SGX's core expertise in high-throughput protein crystallography, state of the art computational chemistry and automated parallel synthesis.

Technology Deals

Companies	Type of Deal	Details
Sangamo BioSciences, LifeScan		Sangamo BioSciences is collaborating with LifeScan and will provide its proprietary zinc finger DNA-binding proteins (ZFPs) for use in a program to develop therapeutic cell lines as a potential treatment for diabetes. By engineering ZFPs that recognize a specific DNA sequence, Sangamo has created ZFP transcription factors (ZFP TFs) that can control gene expression and, consequently, cell function. Sangamo is also developing sequence-specific ZFP-Nucleases (ZFNs) for therapeutic gene modification as a treatment and possible cure for a variety of monogenic diseases such as sickle cell anemia and for infectious diseases such as HIV.
Schering, Valentis	Licensing agreement	Valentis has received a $US1 million license fee in the company's collaboration with Schering in Germany. This fee was paid as a result of Schering's decision to use certain of Valentis' technologies in an additional product development program. In 2002, the two companies signed a multiproduct license and option agreement to develop and commercialize products that incorporate Valentis' proprietary PINC polymer-based gene-delivery system and the GeneSwitch gene-regulation technologies.
Serono, ZymoGenetics	R&D and licensing agreement	ZymoGenetics and Serono are collaborating to develop and commercialize novel protein and antibody therapeutics based on discoveries made by ZymoGenetics. As part of this alliance Serono gains access to a large portfolio of ZymoGenetics' genes and proteins for in-house evaluation and screening, and rights to license such proteins over the next 5 years. Over this period Serono will also have rights to license up to 12 products arising from ZymoGenetics' internal core research projects. ZymoGenetics will have an option to co-develop and co-commercialize in the US any products selected by Serono. Three license agreements for Fibroblast Growth Factor 18 (FGF-18), Interleukin 22 Receptor (IL-22R) and Interleukin 31 (IL-31) are part of this alliance. Serono gains worldwide exclusive rights for FGF-18 and IL-22R, which may be useful for repairing cartilage damaged by osteoarthritis or physical injury, and psoriasis, respectively. ZymoGenetics will retain co-development and co-commercialization rights in the US for IL-31, which may have a role in asthma, psoriasis and inflammatory bowel disease.
Sigma-Aldrich, Caliper Life Sciences	R&D and marketing agreement	Sigma-Aldrich and Caliper Life Sciences are collaborating to develop and co-market a series of automated turnkey solutions for a variety of applications in genomics, proteomics, and drug discovery. The two companies are developing a series of pre-optimized automation protocols using Caliper's Sciclone ALH 3000 Liquid Handling Workstation with a variety of Sigma-Aldrich's biochemicals and reagent kits. The first kits to have been automated include Sigma's Extract-N-Amp Blood and Tissue kits (systems for the rapid extraction and subsequent amplification of genomic DNA from blood and animal tissues), as well as HIS-Select Integrated Lysis and Purification (iLAP) plates (a platform for purifying recombinant proteins).
Vaxin, Crucell	Licensing agreement	Vaxin has entered into a nonexclusive license agreement with Crucell that allows Vaxin to use Crucell's PER.C6 cell line for the development, manufacture and commercialization of its recombinant adenoviral vaccines against certain respiratory viruses. Under the terms of the agreement, Crucell will receive an upfront payment, annual maintenance fees and royalties on future sales.
Viventia Biotech, Acceptys	Licensing agreement	Viventia Biotech and Acceptys have entered into an option agreement related to a specific collection of Viventia's completely human anticancer antibodies. Under the agreement, Acceptys obtains the exclusive right to evaluate the antibody collection, together with the right to license and develop those antibody candidates selected by Acceptys, as either human antibody anticancer therapeutics or diagnostic tools. Viventia will receive an initial upfront payment, acquisition fees, clinical milestone payments and royalties on any commercial sales of antibodies that Acceptys licenses and develops.

Companies	Type of Deal	Details
		Acceptys is developing human antibody therapies in cancer and infectious diseases using its Immunoprospecting platform. Through its proprietary technology, Acceptys can capture thousands of antibodies from strategically targeted patient populations and then isolate the most effective antibodies from that pool using its proprietary Immunoscreening technology. Those select antibodies are then administered to patients in their natural, human form as therapeutic products.
Wyeth, Dharmacon	Supply agreement	Dharmacon has entered into an agreement to supply custom siRNA reagents to the genomics research operations at Wyeth Pharmaceuticals. Dharmacon will supply SMARTpool reagents and individual SMARTselection designed duplexes covering 800 gene targets. The custom siRNA reagents will be used by Wyeth to support and accelerate the company's genomic-based drug-development research. The agreement expands and extends the relationship between Dharmacon and Wyeth based on the success of a previous supply agreement. Wyeth was an early adopter of Dharmacon's SMARTselection and SMARTpool technologies dating back to December 2002.

Diagnostic Technologies

Companies	Type of Deal	Details
Abbott Laboratories, Calypte Biomedical	Licensing agreement	Calypte Biomedical has signed a sublicense agreement with Abbott Laboratories for certain worldwide rights to patents relating to the design, manufacture and sale of lateral-flow rapid diagnostic tests. Under the terms of the agreement, Calypte was granted certain worldwide rights to use a family of patents known as the Guire/Swanson patents. The technology underlying these patents is fundamental to all lateral-flow rapid diagnostic tests. *"The technology covered by these patents is critical to the design of lateral-flow rapid tests"*, said Dr Richard George, CEO of Calypte. *"We believe it is one of the essential licenses that will provide us the freedom to manufacture and sell our emerging HIV rapid diagnostic tests in the US and around the world."*
Aspect Medical Systems	Licensing agreement	Aspect Medical Systems has obtained an exclusive license for Cordance technology, an EEG-based brain assessment tool for diagnosis and management of neurological diseases developed at the Neuropsychiatric Institute and David Geffen School of Medicine at UCLA. The company plans to combine its proprietary BIS technology with Cordance in an effort to develop new products that aid healthcare providers in diagnosing and treating psychiatric and neurodegenerative diseases, such as Alzheimer disease and depression. These products may also enable pharmaceutical and device developers to quantify the effects of CNS therapies early in the development cycle. The licensing agreement follows two years of research collaboration between Aspect's neuroscience division and UCLA.
Aventis, Cell Signaling Technology	R&D agreement	Cell Signaling Technology (CST) has entered an agreement with Aventis to perform a pilot study employing CST's PhosphoScan technology to identify phosphorylation sites and prospective biomarkers of protein tyrosine kinase (PTK) targets. CST's PhosphoScan phospho-proteomics technology is a patent-pending methodology combining immunoaffinity purification and mass spectroscopy to determine cellular PTK phosphorylation profiles (TKSignatures). Biomarkers that are discovered with PhosphoScan may enable target validation and profiling assays to monitor kinase targeted therapeutic pharmacodynamics and efficacy.
Beckman Coulter, NPE Systems	R&D and licensing agreement	Beckman Coulter has entered into an exclusive licensing and development agreement with NPE Systems for NPE's novel flow-based cellular analysis systems. Beckman Coulter plans to integrate NPE's Quanta family of products into its Cell Lab suite of cellular analysis solutions. As cell-based assays, as opposed to biochemical assays, become the solution of choice for investigative biology the requirement for simpler and automated systems becomes ever more pressing. These systems will prove useful from early-stage biomarker discovery to clinical trials, with a particular focus being in the growing secondary screening and ADME/toxicology segment. *"Our agreement with NPE provides an immediate entry into the distributed testing segment of the flow cytometry market and allows us a development path for our expansion into this underserved portion of the cellular analysis marketplace,"* said Elias Caro, president of Beckman Coulter's Biomedical Research Division.
Bionomics, Athena Diagnostics	Licensing agreement	Bionomics has granted a licence to Athena Diagnostics to market Bionomics' childhood epilepsy diagnostic to neurologists in North America and Japan. Athena plans to make the gene-based Severe Myoclonic Epilepsy of Infancy (SMEI) test available later this year to over 5000 neurologists for whom it currently performs diagnostic tests. Under the terms of the licence agreement, Athena will pay Bionomics upfront fees on signing, milestone payments linked to sales targets and royalty payments on net sales. Bionomics considered Athena's reach into the neurology market to be important in realizing the value of its SMEI intellectual property. Under the agreement, potentially substantial cash flows to Bionomics will be in the form of milestone payments and royalties on sales achieved by Athena.

Companies	Type of Deal	Details
Bruker Daltonics, ProteoGenix	R&D agreement	ProteoGenix has selected Bruker Daltonics as a strategic partner for the development of high-throughput protein biomarker discovery and mass spectrometry-based multianalyte assay platforms. Under their collaboration, the companies will collaborate to implement the ProteoGenix protein biomarker discovery methods on the Bruker Daltonics autoflex II TOF/TOF instrument. The teams plan to increase the speed, efficiency and throughput of the protein biomarker discovery methods by employing Bruker Daltonics magnetic bead-based ClinProt platform for automatic processing of serum samples, as well as samples of other body fluids. Other aspects of the collaborative effort will be the use of ClinProTools comprehensive analysis, visualization and statistical model building software for biomarker discovery, and ProteinScape software to manage the data processing and archiving from the protein biomarker discovery workflow.
Celera Diagnostics, GenData Research	Supply agreement	GenData Research has entered into an agreement to provide Celera Diagnostics with DNA samples and associated clinical information in support of discovery research studies that Celera Diagnostics is conducting on behalf of Celera Genomics for the identification of genetic markers associated with an autoimmune disease. GenData will provide Celera Diagnostics with DNA samples from affected individuals, corresponding clinical data, and well-matched controls from its comprehensive biomedical research repository that integrates biological samples with decades of medical and genetic information from population-based studies and from studies on multigenerational families. Celera Diagnostics plans to analyze these samples with the goal of identifying genetic markers of the disease.
Corgenix Medical	R&D and manufacturing agreement	Corgenix Medical has developed an APA ELISA test kit for diagnosing fibromyalgia. The product was developed under a development and manufacturing agreement with Autoimmune Technologies. The new product employs Autoimmune's patented technology, and is expected to enter clinical trials in the US by Q4 of 2004. The test kit detects anti-polymer antibodies (APA) and serves as the first serum-based assay specific for fibromyalgia, a common pain and fatigue disorder. Corgenix and Autoimmune are collaborating on distribution of the product, and expect to launch the patented APA ELISA test kit in Europe by Q4 this year. "*Current data suggests that APA-positive fibromyalgia patients comprise the majority of fibromyalgia patients*," said Dr Luis Lopez, CEO of Corgenix. "*This test is intended for use as an aid in the diagnosis of patients presenting with the symptoms and signs of fibromyalgia syndrome, as an aid in differentiating fibromyalgia patients from patients with other autoimmune diseases, and as an aid in determining which fibromyalgia patients have an immune response that is associated with their symptoms.*"
Cytyc	R&D and licensing agreement	The University of Massachusetts Medical School (UMMS) and Cytyc have signed licensing and sponsored research agreements related to cancer detection technology developed at UMMS that may predict the onset and severity of certain cancers before a tumor actually forms. The agreement gives Cytyc a worldwide exclusive license to use the technology for developing products in the areas of cancer diagnostics and prognostics. Cytyc will also sponsor research to further explore the science as it applies to breast and cervical cancers.
Diagnostic Products Corporation, Compugen	R&D agreement	Diagnostic Products Corporation (DPC) and Compugen are collaborating on the development and commercialization of diagnostic products, with an anticipated focus in the cancer and cardiovascular fields. Terms of this agreement allow DPC to develop and commercialize immunoassay and nucleic-acid based diagnostic products based on Compugen-discovered biomarkers, including certain biomarker candidates already discovered by Compugen, as well as additional candidates arising out of the collaboration. Compugen is entitled to receive development milestone payments and royalties on the sales of the diagnostic

Companies	Type of Deal	Details
		products. In some cases, the discovered proteins may also have therapeutic applications, in which case Compugen will have the right to pursue further development in this field, and DPC will be entitled to milestone payments and royalties from any successful therapeutic applications.
Eiken Chemical	R&D agreement	Eiken Chemical is working with the Kobe Institute of Health to develop a reagent to detect tubercle bacillus using Eiken's proprietary loop-mediated isothermal amplification (LAMP) method. The partners aim to provide an innovative reagent kit that enables a simple, rapid, accurate and inexpensive detection, paving the way for a decline in the number of tuberculous infections.
Evident Technologies	R&D agreement	Evident Technologies has entered into a Cooperative Research and Development Agreement (CRADA) with the US National Institute of Standards and Technology (NIST) to explore the use of quantum dot composite fluorescent standards for biotech instrumentation. Fluorescence-based measurements are becoming the standard for genomic research, clinical diagnostics, high-throughput screening, forensic determination and drug discovery. However, absolute fluorescent measurements are difficult since there are few fluorescent standards available today. *"A fluorescence standard is necessary, especially for clinical applications, where quantification is required. It is nearly impossible to quantify the fluorescence from an assay today, but our collaboration with NIST should greatly advance the state of the art,"* said Clint Ballinger, CEO of Evident Technologies. Under the CRADA, Evident Technologies will provide quantum dot composites and NIST will be providing itsexpertise in fluorescent measurement to characterize these materials. This initial work will help determine how this technology can be used to produce stable fluorescent standards.
GenData Research, Battelle	R&D agreement	GenData Research and Battelle have entered into collaboration for the discovery, development, and commercialization of biomarkers for diagnostic and therapeutic applications in chronic obstructive pulmonary disease (COPD). The immediate result of this collaboration will yield the best-characterized COPD population by combining Battelle's state-of-the-art technology with extensive longitudinal clinical treatment data provided by GenData. In the future, this same population will be used to elucidate the mechanisms of this disease and its progression and to identify the underlying genetic factors associated with COPD. Both GenData and Battelle see this collaboration as the initiation of a long-term relationship.
Iconix Pharmaceuticals	R&D agreement	Iconix Pharmaceuticals has entered into an agreement with Dr Roderick Jensen, Acting Director of the Biotechnology Center and Laboratory for Functional Genomics at the Brigham and Women's Hospital/Harvard Medical School, to study and validate gene expression patterns in patients with neurological diseases. Jensen's laboratory has devised a high-throughput validation strategy that uses multiple gene expression platforms to assay important tissue samples in disease and drug studies. The goal of the study is to validate gene expression changes in human peripheral blood for diagnostics, prognostics and drug response. The project will test the high throughput validation strategy with samples from patients with Parkinson disease.
Illumina	R&D agreement	Illumina has signed a commercial agreement to conduct an extensive, two-phase genotyping study for the North American Rheumatoid Arthritis Consortium to identify genes associated with this complex and debilitating disease. Phase 1 of the RA study will involve genetic mapping of over 3125 samples using Illumina's standard Linkage IV single nucleotide polymorphism (SNP) panel, which includes over 5800 SNP markers distributed evenly across the genome. The second phase will involve development of a custom panel of SNP loci for dense mapping of specific candidate gene regions identified in the first phase.

Companies	Type of Deal	Details
Illumina	Services agreement	Illumina has signed an agreement to conduct a large-scale mouse genotyping study for The Wellcome Trust Centre for Human Genetics at Oxford University. The deal will see Illumina generate >25 million mouse genotypes for Wellcome Trust researchers, who will use SNP (single nucleotide polymorphism) variants to search for quantitative trait loci (QTL). Since specific genes and gene order are highly conserved between mouse and human species, QTL information should, in turn, promote accelerated identification of disease genes and genetic function in humans. The study follows a successful pilot completed in 2003 and is expected to result in Illumina marketing a standard mouse panel(s) for generating genotypes with predictive value for behavioral disorders. The Wellcome Trust will publish genotyping results and make this information freely available to other researchers and to the public. The genotyping project, one of the largest of its type ever conducted, will examine over 15 000 SNP loci in 2700 animals from a unique multigenerational mouse collection derived from inbred strains.
Illumina, Galileo Genomics	R&D agreement	Illumina and Galileo Genomics have signed a collaborative agreement with a value exceeding $US1.5 million. Under the terms of the deal, Galileo has purchased two Illumina BeadStation 500GX genotyping systems for use in fine mapping candidate regions in a minimum of five gene-discovery programs. The resulting information will be used to produce GeneMaps, comprised of multiple interacting genes unequivocally associated with disease, which will be used for the development of innovative therapeutics, diagnostics and pharmacogenomics services. Illumina is also licensing the diagnostic rights to Galileo's osteoarthritis gene-discovery program. The agreement is extendable to additional fine mapping projects that Galileo is conducting in a total of 27 diseases. The first study is in Crohn's disease and will analyze single nucleotide polymorphism (SNP) markers within candidate regions associated with Crohn's disease that were recently identified by Galileo from genome-wide scans of 1500 samples from the Quebec Founder Population.
Immunicon, Quest Diagnostics	Purchase agreement	Immunicon has entered into an agreement with Quest Diagnostics for the purchase of the Immunicon CellTracks AutoPrep System and the Immunicon CellSpotter Analyzer to enable Quest Diagnostics to run the CellSearch Circulating Tumor Cell Kit, a cancer diagnostic test that identifies and counts circulating tumor cells (CTCs) in blood samples from patients being treated for metastatic breast cancer. The CellSearch Circulating Tumor Cell Kit is manufactured and sold by Veridex and incorporates Immunicon proprietary reagents and other technology. Veridex has exclusive worldwide rights to commercialize products incorporating Immunicon technology in the cancer field.
IVAX Diagnostics, Dia.Pro Diagnostic BioProbes, DiaSorin	Licensing and distribution agreements	IVAX Diagnostics has signed a license agreement with Dia.Pro Diagnostic BioProbes of Milan, Italy, that allows IVAX Diagnostics access to Dia.Pro's technology for manufacturing certain hepatitis products. IVAX Diagnostics has also signed a distribution agreement with DiaSorin of Stillwater, MN, that allows it to distribute DiaSorin's line of hepatitis products in the US. Company CEO and president Giorgio D'Urso commented that the two agreements allow IVAX *". . . to enter the worldwide hepatitis testing market place. The addition of hepatitis testing complements the other assays that we currently provide in the autoimmune and infectious disease testing sectors."*
Kereos, Dow Chemical	Licensing agreement	Kereos and Dow Chemical have entered into a licensing agreement to allow both companies access to patent portfolios for the development and commercialization of targeted imaging agents. The agreement is intended to facilitate further development and marketing of targeted imaging agents for more accurate diagnosis of cancer and cardiovascular disease. Under terms of the new licensing agreement, Kereos gains

Companies	Type of Deal	Details
		commercial rights to the chelating molecules and to certain chelate technology previously developed by Dow. The agreement also allows Dow to use the molecules created under the collaboration in other applications.
Merck & Co., Genaissance	Licensing agreement	Merck & Co. and Genaissance have signed a licensing agreement that will see Genaissance use its haplotyping technology to discover genetic markers identifying patients that respond to an antidepressant that it has licensed from Merck. Genaissance is planning to commence enrolment for a phase II clinical trial in the first half of 2005; this trial will include pharmacogenomic characterization of patients. The agent, vilazodone, is a selective serotonin inhibitor and a partial 5HT1A agonist.
Metabolon	R&D agreement	Metabolon is collaborating with Massachusetts General Hospital on a new biomarker study funded by the US National Institute of Neurological Disorders and Stroke (NINDS). Metabolon and Massachusetts General Hospital researchers will work together on 'Metabolic Signatures in ALS', a study to identify unique metabolic signatures for ALS that will lead to a more rapid and accurate diagnostic test using biomarkers found in cerebrospinal fluid and blood. Metabolon will test samples obtained from patients using its metabolomics platform that searches for signatures of ALS by measuring the spectrum of biochemical changes and mapping these changes to metabolic pathways. In pilot studies, Metabolon has established metabolic profiles from the blood of ALS patients for comparison with profiles from control groups. Metabolon will be able to extend its findings by expanding the study to a larger sample set and analyzing the profiles in cerebrospinal fluid.
PerkinElmer, Predictive Diagnostics	R&D agreement	PerkinElmer and Predictive Diagnostics (PDI) have entered into a collaborative partnership for advanced biomarker discovery technology to accelerate drug development and diagnostic testing. Under the terms of the agreement, PerkinElmer will provide access to PDI's proprietary Biomarker Amplification Filter (BAMF) technology customized for PerkinElmer's prOTOF 2000 MALDI O-TOF mass spectrometer to create the 'industry standard' platform for biomarker discovery and analysis. BAMF technology is a comprehensive suite of *in silico* machine learning technologies and advanced informatics tools that use a simple blood test for the discovery of biomarker fingerprints to diagnose diseases utilizing high-resolution mass spectrometry data. PDI has developed its BAMF technology for use in serum-based tests for early diagnosis of cancer and other life-threatening diseases.
PerkinElmer, Vivascience	R&D agreement	PerkinElmer and Vivascience have entered into a collaborative agreement in biomarker screening and discovery. Under the terms of the agreement, Vivascience's patented membrane adsorber (MA) chromatography technology will be combined with PerkinElmer's proprietary elution chemistries to create fractionation kits for proteomics-based biomarker analysis. This reagent platform will be incorporated into PerkinElmer's integrated biomarker screening solution that includes automated sample preparation with the MultiPROBE II liquid handling workstation and world-class biomarker detection with the prOTOF 2000 MALDI O-TOF mass spectrometer. In contrast to traditional resins and beads, Vivascience's unique MA technology, features a rigid format that makes it highly reproducible and robust. The technology also has significant ease-of-use advantages when incorporated into the PerkinElmer biomarker screening solution.
Power3 Medical Products	R&D agreement	Power3 Medical Products has entered into a research agreement with Baylor College of Medicine for the purpose of discovering biomarkers in serum and plasma that are of particular utility in the diagnosis and drug targeting for metabolic syndrome and associated disorders including diabetes, cardiovascular disease, hypertension, and stroke. According to Dr Ira Goldknopf Chief Scientific Officer at Power3 Medical, *"by utilizing our very sensitive and reproducible proteomic methods with definitive patient samples, we have initially discovered a series of proteins whose concentrations may lead to diagnosis and drug targeting for metabolic syndrome and other associated*

Companies	Type of Deal	Details
		disorders. The initial results are quite promising as we continue to work with additional patient samples." Dr Christie Ballantyne, Professor of Medicine at Baylor explained that "*what we are seeking are more definitive blood tests about what is happening at the protein level that can help us design and monitor more effective treatments*."
Power3 Medical Products	R&D agreement	Power3 Medical Products has signed a research agreement with Mercy Women's Center focusing on the identification of protein biomarkers for the early indication of breast cancer in blood serum. Under this agreement, Mercy Women's Center will provide Power3 Medical up to 600 blood serum samples from normal subjects and subjects with various stages of breast cancer. According to Dr Alan Hollingsworth, Research Director of Mercy Women's Center, "*such a test would revolutionize screening and diagnosis of breast cancer, yet very little attention has been given to this goal in the past due to the reliance on mammography*." With the 'miss rate' of mammography established, and while ultrasound and MRI are not accepted by insurance carriers as screening tools, there is a strong need for a 'prescreening' blood test.
Roche Diagnostics, Dade Behring, Chiron, Ortho Clinical Diagnostics	Licensing agreement	Roche Diagnostics and Dade Behring have been granted a nonexclusive license under patent rights of Chiron/Ortho Clinical Diagnostics relating to the development, manufacturing and marketing of immunoassays for the detection of HIV type 1 (HIV-1). Within the same agreement Chiron/Ortho Clinical Diagnostics were granted a nonexclusive license under patent rights of Roche Diagnostics and Dade Behring relating to the development, manufacturing and marketing of immunoassays for the detection of HIV-1 group O. At present, two major types of HIV have been identified, defined as HIV-1 and HIV-2. For HIV-1 the current classification recognizes three groups which are group M (main group), group O (for outlier) and group N (for non-M, non-O). HIV-1 group M is antigenically different from HIV-1 group O and HIV-2. A composition of different virus proteins allows the reliable and sensitive recognition of all HIV variants in blood samples.
Sequenom	R&D agreement	Sequenom has an agreement with the Institute of Medical Genetics and the Microarray Facility at the University of Tuebingen in Germany for Sequenom's MassARRAY Quantitative Gene Expression (QGE) application. The institute is one of the largest users of expression profiling arrays in Europe and will use the application on the MassARRAY Compact system to validate pre-existing microarray data and to explore gene expression levels in various neurodegenerative diseases and cancers. Researchers at the institute hope to use the research to develop diagnostic approaches for conditions such as Parkinson disease, Huntington disease and for different cancers.
Sequenom	R&D agreement	Sequenom has extended a research collaboration with the Chinese University of Hong Kong (CUHK) for further development of prenatal diagnostic applications on the MassARRAY platform. The goal of the collaboration is to accelerate the introduction of noninvasive prenatal tests from the laboratory into the clinical diagnostic market through the immediate implementation of large-scale studies and benchmark analysis against existing invasive methods for prenatal testing. Earlier this year, Sequenom and CUHK jointly announced that MassARRAY technology had enabled the detection of genetic mutations in circulating fetal nucleic acids in maternal plasma. This approach has the potential to eliminate risks associated with current prenatal testing procedures such as amniocentesis and chorionic villus sampling. Previous noninvasive fetal DNA analysis techniques had been unreliable on a large scale due to their dependence on sample concentration and lack of sensitivity and specificity.
Sequenom, Translational Genomics Research Institute	R&D agreement	Sequenom has a research agreement with the Translational Genomics Research Institute (TGen) where it will provide TGen access to its candidate gene portfolio of targets associated with an individual's predisposition for skin cancer. TGen will

Companies	Type of Deal	Details
		further validate these candidate genes against its expression databases with regard to their potential use as diagnostic markers for skin cancer risk and the clinical prognosis of skin cancer patients. As appropriate, products developed from this study will be jointly owned and commercialized.
Third Wave Technologies, 3M Bioanalytical Technologies	Supply agreement	Third Wave Technologies and 3M have signed a supply agreement that will provide Third Wave customers with the option of coupling its Invader technology, a novel DNA and RNA analysis chemistry, with 3M's microfluidic technology. This new platform option will enable clinical laboratories to forgo the numerous liquid-handling steps, improving lab efficiency and shortening the time to test results. 3M Bioanalytical Technologies will supply Third Wave with the microfluidic technology.