BIOTECHNOLOGY PARTNERING OPPORTUNITIES

WITH

MASSACHUSETTS LIFE SCIENCE COMPANIES

March 2000

for the
Canadian Consulate General
3 Copley Place, Suite 400
Boston, Massachusetts 02116 USA

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This report was produced in partnership with *Trade Team Canada Bio-Industries.*

It is intended for use by Canadian businesses and institutions.

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FOREWORD

The Canadian Consulate General in Boston commissioned this survey of biotechnology/life science companies in Massachusetts in order to provide Canadian biotechnology companies and institutions with insight into the partnering interests of 100 Massachusetts Life Science firms.

For each company, you will find contact coordinates, a web url, if available, and the name and title of an appropriate contact for exploring partnering opportunities. This is followed by a brief profile of the company, a section on its product development activities and current partnerships, and a partnering assessment, indicating what types of partners the company might be seeking.

Because of the changing nature of this fast-paced industry, it is possible that some of the details you read in this survey today may have changed since it was written. We suggest you use the contact information provided to confirm details that are relevant to your partnering interests, as you explore research and business opportunities with the listed companies.

The Canadian Consulate General in Boston is ready to assist you in your efforts to connect with life science organizations in New England. The best way to contact us is by fax or e-mail. (See coordinates on title page.) We look forward to working with you.

A/F PROTEIN, INC

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Tel: (781) 899-7755
Fax: (781) 899-8482
Web: www.afprotein.com

Contact: Michael Erisman, VP Business Development (merisman@aol.com)

Profile

A/F Protein is a development-stage biotech company with offices in the US and Canada. It is seeking to develop the use of antifreeze proteins for the control of cold-induced damage in medical, food and cosmetic products. It is the world's only commercial producer of antifreeze proteins (AFPs) purified from natural sources for sale to the research development community. It is also developing fish with improved growth rates and other economically desirable traits through the use of gene constructs utilizing antifreeze protein gene promoters. The company is developing a broad array of products which incorporate AFPs or AFP-based transgenes. Products using AFPs include those designed to hypothermically preserve blood platelets and other cells, tissues and organs; to ablate tumor cells in conjunction with cryosurgery; to enhance the texture and quality of frozen foods; and to provide skin protection under adverse, cold conditions. AFP-based transgenes have been successfully used to increase the growth rate of fish and are being tested to protect fish and plants from freezing. The two primary technologies being developed by the company, AFPs for cold preservation and AFP-based transgenics, are proprietary commercial interests with numerous applications in medicine, agriculture, aquaculture, biotechnology and food processing. Proteins are sold to commercial companies and academic institutions worldwide for the purpose of product exploration and development, facilitating research.

Product/Partnership Status

A/F Protein has established a separate business unit, Aqua Bounty Farms, to develop and market AquAdvantage fish for commercial aquaculture. Aqua Bounty Farms maintains a hatchery on Prince Edward Island in Canada to develop improved strains of salmon, trout, Arctic char, and other fish species. To date, no other commercial company has been able to enhance the growth rates of fish for aquaculture to match the success of Aqua Bounty Farms. The company has recently licensed two world-wide commercial suppliers to develop AquAdvantage Salmon Brood stock, and has licensed rights to use the AquAdvantage technique to develop transgenic tilapia to a third firm in the US. In the short term, A/F Protein expects to conclude licensing negotiations with other aquaculture operations worldwide. They are interacting with a number of Canadian academics, notably at Toronto, Queen's and Calgary universities.

Partnering Assessment

The company is currently seeking partners to pursue the development of an AFP-based medium for hypothermic preservation of human platelets and AFP-based strategies for improved methods of cryosurgery. They describe themselves as highly opportunistic but are looking to license out their technologies. They are open to the approaches of multiple industries, including from the food and cosmetic sectors.

ACUSPHERE, INC

38 Sidney St.
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Tel: (617) 577-8800
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Contact: Sherri Oberg, CEO (oberg@acusphere.com)

Profile
Acusphere is a contrast imaging company focused on developing an ultrasound contrast agent. Ultrasound is a powerful and relatively inexpensive, and non-invasive technology. However, it is limited in its ability to evaluate and characterize blood flow and tissue perfusion. As a result, more expensive or invasive imaging technologies must be used. A recent Hambrecht & Quist report estimated that the market for an I.V.-administered ultrasound contrast agent is $1 billion. Other potential applications for Acusphere's technology include MRI and CT blood pool agents and various drug delivery systems.

Product/Partnership Status
To date, Acusphere do not have any partnership agreements in place.

Partnering Assessment
Acusphere are looking for partners in North America, Europe and Japan consistent with their product interests.

ADVANCED CELL TECHNOLOGY, INC

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Three Biotech
Worcester, MA 01605
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Fax: (508) 756-0937
Web: www.advancedcell.com

Contact: Dr. Robert Lanza, VP Medical and Scientific Development
(rlanza@advancedcell.com)

Profile

Advanced Cell Technology is a development-stage company engaged in the research and development of proprietary technologies enabling the genetic manipulation of cells to produce cloned transgenic animals for applications in cell transplant therapy, organ transplantation and pharmaceutical protein production. Since its formation in 1994, the company has concentrated its efforts on developing technologies to produce large transgenic animals (cows) as a source of pharmaceutical proteins and genetically-modified cells and organs that have important uses in the treatment of a wide range of human diseases for which there are currently few or no acceptable methods of treatment. The company's initial focus is on the development of a technology to produce cloned transgenic animals as donors of neural cells for transplant therapies in the treatment of neurodegenerative diseases, including Parkinson's disease, Huntington's disease and Alzheimer's disease. Diabetes and some types of heart diseases may also be treatable with related technologies. Their scientific objective in applying cloning to human medicine is to create human stem cells.

Product/Partnership Status

Under an agreement with *Genzyme Transgenics*, they are developing animals that will produce human serum albumin. This is currently derived from pooled human plasma and is used therapeutically to maintain blood volume. Approximately 440 metric tons of plasma-derived albumin are used annually and cows represent a cost-effective and safe alternative for producing large quantities of this protein. Among their collaborators in the recently announced work on reversing the aging process in cells is the *Terry Fox Laboratory and Cancer Research Centre* in Vancouver.

Partnering Assessment

ACT recently announced the successful reversal of the aging process in cells, a breakthrough that they view as a possible path to successful use of therapeutic cloning techniques to cure some of mankind's most intransigent age-related and degenerative diseases such as Parkinson's, Alzheimer's and diabetes, as well as heart, liver and kidney disease. They are interested in hearing from any entities interested in working with them in cell transplant therapy, organ transplantation and pharmaceutical protein production.

ADVANCED MAGNETICS, INC.

61 Mooney St.
Cambridge, MA 02138
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Fax: (617) 547-2445
Web: www.advancedmagnetics.com

Contact: Dr. Paula Jacobs, VP Development (jacobs@advancedmagnetics.com)

Profile

Advanced Magnetics is a biopharmaceutical company dedicated to the development and commercialization of pharmaceutical products for the diagnosis and treatment of cancer and other diseases, in particular contrast agents which play a significant role in improving the quality of diagnostic images by increasing the contrast between different internal structures or types of tissue in various disease states and medical conditions of interest. Their core imaging agent technology is based on the design and manufacture of extremely small, uniform, polysaccharide-coated superparamagnetic iron oxide particles. Feridex I.V., the company's contrast agent for use in Magnetic Resonance Imaging for the detection of liver lesions, is currently marketed in the US, Japan, western Europe, Argentina, Israel, China and South Korea. GastroMARK, for use in conjunction with MRI to distinguish the loops of the bowel from other abdominal structures, is marketed in the US and western Europe. A New Drug Application has been submitted to the FDA for the company's third product, Combidex, for use in MRI to diagnose lymph node and liver disease. R&D efforts include next-generation contrast agents and other related diagnostic products.

Product/Partnership Status

Licensing and Marketing Agreements:

- *Berlex Laboratories* for Feridex IV MRI cancer agent in the US
- *Eiken Chemical* for Feridex IV in Japan under trademark Feridex
- *Guerbet* for Feridex I.V. under trade name Endorem, GastroMARK under trade name Lumirem, Combidex under trade name Sinerem, Code 7228 in Western Europe and Brazil.
- *Mallinckrodt* for GastroMARK imaging for GI tumors in North America.

Distribution Partners:

- *Pharmagenesis* in China and Taiwan (Feridex)
- *TaeJoon Pharmaceutical* in South Korea (feride liver contrast agent)
- *Laboratorios Temis Lastalo* in Argentina
- *Discotrade* in Israel

Partnering Assessment

Approaches could be made from groups with interests in the contrast imaging area or academic groups whose activities mesh with Advanced Magnetics' R&D into next-generation contrast agents.

ALKERMES, INC.

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Contact: Duncan Higgons, VP Business Development
duncan_higgons@alkermes.com

Profile

Alkermes, Inc. is an emerging pharmaceutical company focused primarily on the development of sophisticated drug delivery systems that enable improved delivery of pharmaceutical and biopharmaceutical products. It is focusing its drug de[illegible] development efforts in two areas. The first is the development of techno[illegible] enable improved drug delivery to the brain by altering the chemical select[illegible]e blood-brain barrier. The company's lead product candidate in this area, RMP-7, is currently in Phase I/II human clinical trials. The second area of focus is the development of pharmaceutical products based on ProLease microencapsulation technology to enable injectable sustained release formulations to be made of biopharmaceutical products, such as proteins and peptides. Alkermes' diversified technology portfolio currently consists of four proprietary delivery systems: (1) ProLease and Medisorb injectable sustained-release systems; (2) RingCap and Dose Sipping oral delivery technologies; (3) AIR pulmonary delivery systems, and (4) Cereport blood-brain barrier permeabilizer. In addition, the company manufactures and supplies Medisorb Polymers, a wide range of standard and custom-developed pharmaceutical-grade, bioabsorbable PLG polymers.

Product/Partnership Status

The company is engaged in a number of research collaborations of drugs with biotechnology and pharmaceutical company partners.

- ProLease hGH Nutropin Depot with *Genentech*, NDA submitted mid-99.
- Medisorb Risperdal with *Janssen*, (J&J) in Phase III clinical trials.
- ProLease Erythropoetin with *Ortho Biotech*, first human trial complete.
- AIR pulmonary delivery with multiple collaborators in various stages including *Glaxo*.
- Oral Delivery technologies with multiple collaborators in various stages.
- Cereport with *ALZA*, in Phase II.
- Albulast being developed in-house, in Phase I.
- *Ares-Serono* for the development of Prolease formulation of an undisclosed growth hormone protein.
- *Glaxo Wellcome* for a broad license to Alkermes' pulmonary drug delivery technology for multiple product candidates
- *Eli Lilly* for development of an inhaled formulation of human growth hormone on Alkermes' pulmonary drug delivery system
- Licensed a patent for adeno-associated viral vector manufacturing to *Targeted Genetics*

- *MedImmune* for the development of an erythropoietin based on Alkermes' ProLease drug delivery technology as an inhalable monoclonal for RSV
- *Amylin Pharmaceuticals* for the development, manufacture and commercialization of an injectable long-acting formulation of AC2993, Amylin's second type 2 diabetes drug candidate.

Partnering Assessment

Alkermes are extremely focused on their own particular area of drug delivery. They are always interested in hearing from any pharmaceutical or biotechnology companies that feel that their product might be enhanced by utilizing a new drug delivery mechanism. To date these are pulmonary, sustained release and oral technologies at Alkermes. That does not forestall other delivery technologies. For instance, Alkermes has not yet come across any transdermal delivery vehicles (patches) that either work to their satisfaction or are available. They will only work with academic groups that are lending very specific assistance or input to particular Alkermes technologies. Therefore their focus is very much on the commercial front.

ALPHAGENE, INC.

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Web: www.alphagene.com

Contact: William Hough, VP Business Development (hough@globallaunch.com)

Profile
AlphaGene has developed AlphaGenomics, a group of interlocking gene and protein discovery technologies based on patented methodologies developed at Harvard Medical School. AlphaGene applies its proprietary technologies in functional genomics, gene expression and computational biology to discover genes and proteins that can be used as high value targets for drug discovery and development. Their scientists have developed a proprietary process to generate biological libraries highly enriched with full-length expressed genes. Using micro-array gene expression technology and large-scale automated gene sequencing capacity, the company rapidly and accurately determines the sequence of disease-related genes and delivers this information in a fully annotated, proprietary bioinformatics system.

Product/Partnership Status
Has recently entered into four strategic alliances.

- *Genetics Institute* is being provided with access to AlphaGene's full-length, novel human genes encoding secreted proteins for expression and inclusion in their DiscoverEase library where AlphaGene is the largest outside supplier of GI DiscoverEase clones.
- *NEN Life Science* products are being provided to develop and manufacture a line of gene expression biochips.
- *Pangea Systems* is isolating full-length genes that contain specific motifs by applying AlphaGene's high quality library array technology and bioinformatics expertise.
- An undisclosed firm is applying AlphaGene's new technology on library arraying to find Full Length Genes from partial clone sequences.

Partnering Assessment
The company expects to leverage the value of its technology platform by establishing collaborative arrangements with leading biotechnology and pharmaceutical companies to identify novel genes implicated in specific disease states. Strategic alliances that employ AlphaGene's innovative technologies should complement existing approaches and accelerate drug discovery via a new high-throughput paradigm for drug development. The company can profit from the formation of these strategic alliances and subsequently from the development of therapeutic compounds by its collaborative partners through upfront payments, milestone payments, and royalties on drug sales. They have an available inventory of 50,000 novel genes, most relating to the brain. There is an interest in research partnerships in the functional genomics field. They are currently offering a range of secretary proteins on a chip and are also offering contract research services.

They have a high opinion of the Canadian scene.

ALTAREX CORPORATION

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Contact: Robert Newman, VP Business Development (rnewman@altarex.com)

Profile
AltaRex is an emerging biotechnology company focused on research, development, and the commercialization of immunotherapeutics for the treatment of cancer. The company's products are based on its unique proprietary platform technology, Anti-idiotype Induction Therapy (or Anti-body based Immunotherapy) or AIT. AIT enhances the ability of the human immune system to produce a highly effective anti-tumor response. AltaRex currently has four AIT-based products in various stages of development that have the potential to effectively treat seven of the top ten most lethal cancers. The company is developing AIT products for ovarian, breast, colorectal and prostate cancers. AltaRex believes that its AIT technology could also be effective for lung, stomach and pancreatic cancers. The company has evidence to suggest that AIT enhances the ability of the human immune system to produce a highly effective anti-tumor response through multiple mechanisms. The most advanced product, OvaRex Mab is in two potentially pivotal Phase IIb trials for the treatment of ovarian cancer. The FDA has granted a Fast Track designation, making possible a 2002 commercialization.

Product/Partnership Status
The company started in Canada (Edmonton) and continues to maintain research and clinical labs there. Financial difficulties and lack of a partner has focussed the company on OvaRex. *Purdue Pharma L.P.* chose not exercise an option to license the product from AltaRex. They recently settled a past disagreement with *Biomira.*

Partnering Assessment
They are actively seeking commercial partners for the OvaRex product to complete clinical development and to market and distribute. In addition, they would be interested in hearing from anyone with early-stage antibodies applicable to their own early-stage products, AR-54, BrevaRex, ProstaRex and GivaRex. In the latter product area they would be willing to consider a research-oriented collaboration, with an initial focus on pancreatic cancer.

ANIKA THERAPEUTICS, INC.

236 West Cummings Park
Woburn, MA 01801
Tel: (781) 932-6616
Fax: (781) 935-4120
Web: www.anikatherapeutics.com

Contact: Ed Ross, VP Sales & Marketing

Profile
Anika Therapeutics specializes in the development, manufacture and commercialization of therapeutic pharmaceuticals and medical devices intending to repair, protect and heal bone, cartilage and soft tissues. These products are used in eye surgery and for the treatment of joint diseases, including osteoarthritis, a chronically painful disease that slowly degenerates the cartilage lining the body's movable joints. The company is also developing a patented new therapy to prevent surgical adhesions and another to inhibit the spread of tumor cells. Their product portfolio and research pipeline utilizes hyaluronic acid (HA), a naturally-occurring, non-toxic and non-inflammatory biopolymer found in tissues throughout the body. HA enhances joint function and coats, protects, cushions and lubricates soft tissues. Anika has developed proprietary manufacturing processes for the extraction of medical grade, high molecular weight HA rooster and hen combs. Anika has been developing and manufacturing HA and HA-based products since 1983.

Products/Partnership Status
The company is collaborating with *Orquest* in the development of a product called Ossigel, entailing a formulation of HA and a basic fibroblast growth factor to accelerate bond fracture healing. Some of the company's products are available in the US, while others are available in international markets. ORTHOVISC is a high molecular weight, highly purified, naturally derived form of HA designed to emulate the viscoelastic and cushioning properties natural HA found in the synovial fluid of healthy joints. It is marketed by *Zimmer*, a division of *Bristol-Myers Squibb*, in Canada and most of Europe, by *Grupo Ferrer International* in Spain and Portugal, *by Biomeks* in Turkey, and by *Rafa* in Israel. On the ophthalmic side they are working with *Bausch & Lomb*. Anika markets Hyvisc, an osteoarthritis product designed for horses that is co-marketed with a division of *Boehringer Ingelheim.*

Partnering Assessment
Recently, Anika suffered a setback when the FDA failed to approve Orthovisc for sale in the US. This was the second time that they had sought approval. In 1998, the FDA had said the product was not effective and had asked for additional studies. The product is approved for sale in Canada and Europe. This setback places their distribution agreement with Zimmer in some jeopardy since they can terminate their agreement if the drug is not approved by January 2001. It is not known whether further study and development of the product will occur. This should be borne in mind in any approach to them.

ANTIGEN EXPRESS, INC.

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Worcester, MA 01605-4306
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Fax: (508) 831-3521
Web: www.evertize.com/antigen/INDEX.HTM

Contact: Joseph Golfo, Chairman & CEO (jvgolfo@ix.netcom.com)

Profile
Antigen Express has discovered lead compounds that regulate the first step in the immune response. Its compounds enhance or inhibit presentation of antigenic peptides to T cells. Their compounds are derivatives of a segment of the Ii immunoregulatory protein which, during its cleavage and release from MHC Class II molecules, acts at an auxiliary regulatory site to control the insertion and locking in of antigenic peptides into the antigenic peptide binding through of the MHC class II molecules, for presentation to T cells. Clinically useful control of this first step in the immune response would allow antigen specific therapy of many diseases, perhaps associated with the genetic alleles of MHC class II linked to disease, without the many toxic side effects of current immunosuppressive therapies.

Product/Partnership Status
At this time, this small company is in active discussions with a number of companies with regard to collaborative development deals.

Partnering Assessment
Antigen would be interested in hearing from anyone in the cancer vaccine area or in areas relating to their lead compounds.

APOLLO BIOPHARMACEUTICS

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Fax: (617) 621-7156

Contact: Robert Leonard, VP Business Development (rleonard@apollobio.com)

Profile
Apollo is a virtual company that specializes in the development of hormonal-like pharmaceutical products for the prevention and treatment of neurodegeneration in chronic and acute diseases, including Alzheimer's, Parkinson's, stroke, cognitive impairment after surgeries, AIDS dementia and others in the CNS arena. They also have an interest in the oncology area with hormone dependent tumors. Apollo is also developing unique cytoprotective technology for coronary protection and other tissues in the body. All their compounds are polycyclic phenolic compounds (PPCs). They dominate all rights to estrogen and estrogen-related compounds for all neuroprotective and cytoprotective applications, both feminizing and non-feminizing.

Product/Partnership Status
Apollo has a major agreement with *American Home Products* for estrogens specifically as they relate to Alzheimer's disease. They have major academic collaborations with the Universities of *Florida, Kentucky* and *Washington* in St. Louis. Another major academic collaboration will be announced shortly.

Partnering Assessment
Apollo is actively seeking a merger with an appropriate company. MDS from Canada is one of their major investors. In addition, they would be interested in hearing from anyone in their fields of interest.

AQUILA BIOPHARMACEUTICALS, INC.

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Tel: (508) 628-0100
Fax: (508) 766-2705
Web: www.aquilabio.com

Contact: Cheryl Murphy, Associate Director of Technology Development
(cmurphy@aquilabio.com)

Profile

Aquila Biopharmaceuticals is using its advanced capabilities in engineering, protein and peptide chemistry, and immunology to develop diagnostic and vaccine products for AIDS, cancer, gastroenteritis, respiratory disease, feline leukemia, and other human and animal infectious diseases. It creates and commercializes products that modulate the immune system to treat, control or prevent diseases, cancers, and autoimmune disorders. Their technology is based on proprietary Stimulon family of adjuvants which modulate the immune system, and their capability of producing disease-specific molecules recognized by the body's immune system, and the CDI antigen discovery and presentation system.. Aquila's most advanced products in development are Quilimmune-P for the prevention of human pneumococcal infections, Quilimmune-M for the treatment of malaria, Quilvax-M the control of bovine mastitis. The company focuses on human and animal health products for significant market opportunities. While most of Aquila's advanced products in development are designed to prevent disease, others are designed to treat or control established conditions.

Product/Partnership Status

The company's strategy is to develop products internally and in partnership with leading companies in the field. Thus far, these include *SmithKline Beecham, Pasteur Merieux Connaught, Wyeth-Lederle Vaccines and Pediatrics, Bristol-Myers Squibb (Progenics Pharmaceuticals), VaxGen*, and *Virbac S.A.*

Partnering Assessment

Aquila are always interested in working with other companies in the business of vaccine development. Recently, their lead product opportunity, the treatment for bovine mastitis, was shown not to have statistically different effects from a placebo control. In addition, the company has announced that they are having M&A discussions with a number of companies. Until such time as this situation is clarified, Aquila will continue to develop both its adjuvant programs and its CD1 programs.

ARIAD PHARMACEUTICALS, INC.

26 Landsdowne Street
Cambridge, MA 02139
Tel: (617) 494-0400
Fax: (617) 494-8144
Web: www.ariad.com

Contact: Jay Lamarche, CFO

Profile

Ariad Pharmaceuticals, Inc., founded in 1992, is a leader in the design and development of a new class of pharmaceuticals that target intracellular signaling pathways to alter the course of disease. The company discovers and develops small-molecule drugs based on intracellular signal transduction technology. It has established a functional genomics capability to identify genes that produce therapeutic proteins or small-molecule drug targets. Drug discovery programs under way include signal transduction inhibitors for osteoporosis and immune and inflammatory disease and small-molecule drugs that control gene expression to regulate the dose of therapeutic proteins delivered by gene therapy. Ariad's regulated gene expression technology, ARGENT, is initially being developed for the controlled delivery of therapeutic proteins such as human growth hormone (muscle wasting), erythropoietin (anemia) or alpha interferon (hepatitis C). The company is concentrating the majority of its resources on four drug discovery programs. The first three involve developing small molecules that inhibit signaling pathways in cells responsible for allergy/asthma, immune-related disorders and osteoporosis. The fourth program is developing a novel system for the pharmacologic regulation of gene therapy, employing small molecules to gain control of signaling pathways, providing a means to regulate the production of therapeutic proteins by engineered cells within the body.

Product/Partnership Status

Ariad has 12 product candidates in various stages of research and development, including one preparing to enter Phase II clinical trials, two in preclinical development and nine in earlier stage research. Earlier this year, Ariad completed the sale of its 50% interest in the *Hoechst-ARIAD Genomics Center* to *Aventis Pharmaceuticals*, having begun a collaboration with *Hoechst Marion Roussel* in 1997 to pursue functional genomics based upon state-of-the-art technologies in molecular and cellular genetics and bioinformatics to analyze human genes and identify those genes that encode novel therapeutic proteins or targets for small-molecule drug discovery. They had begun to collaborate in 1995 on the discovery and development of drugs to treat osteoporosis and related bone diseases. They have past agreements with *Mochida Pharmaceutical* (Fas license for gene therapy), *Genovo* (gene therapy JV), *Incyte Pharmaceuticals* (LifeSeq database) and *Mitotix* (now *GPC Biotech*) (purchase of FRAP).

Partnering Assessment

Ariad plans to develop some of their product candidates themselves. In addition, they intend to commercialize their enabling platform technologies by licensing them to pharmaceutical and biotechnology companies for their research and product development programs.

ARQULE

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Contact: John Sorvillo, VP Business Development (jsorvillo@arqule.com)

Profile
ArQule is a world leader in high-throughput parallel chemistry for drug discovery and other life sciences. It is developing businesses in the biopharmaceuticals, separations and materials areas based upon its proprietary chemistries. These enable the conversion of biological information such as peptide sequences, structural information, and info from assays, into small organic lead compounds. These compounds can be modified modularly to alter macro-level properties such as therapeutic index, solubility and bioavailability. ArQule's chemistries will be made available in a variety of formats, including customer-designed libraries which may be configured from an almost limitless array of chemical motifs and built to any size and diversity level.

Product/Partnership Status
The company participates in joint drug discovery programs with selected biotech and academic collaborators. Last year, they signed a comprehensive custom library and technology licensing agreement with *Pfizer* worth up to $117 million, a new approach to working with pharmaceutical companies. They are devoting designated technologies, scientists, and their AMAP system to generate compound libraries for *Pfizer*. Also last year, they entered into a three-year, $30 million collaboration with *Bayer* with teams of ArQule and *Bayer* scientists guiding the design of compounds.

Other pharmaceutical and agrochemical collaborations include:
American Home Products, Johnson and Johnson, Searle (Monsanto), Sankyo, Solvay.

Drug discovery collaborations include:
*Acadia (*neuropsychiatric and neurodegenerative disease), *Cubist* (infectious diseases), *Genome Therapeutics* (antibacterial, antifungal), *Genzyme* (cancer, infectious diseases, autoimmune and inflammatory diseases), *Immunex* (inflammatory disorders), *Sepracor* (antivirals).

Partnering Assessment
ArQule has had no concrete dealings with Canada thus far. Their interests lie in working with pharmaceutical companies regarding their compound libraries, while their interests with biotechnology and academic groups lie in the area of collaborative drug discovery with interesting leads.

ASCENT PEDIATRICS, INC.

187 Ballardvale Street, Suite B125
Wilmington, MA 01887
Tel: (978) 658-2500
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Web: www.ascentpediatrics.com

Contact: Michael Furlong, VP Business Development
(mfurlong@ascentpediatrics.com)

Profile
Ascent develops products that make a difference for children and those who care for them. They are currently working on the development of products in the areas of anti-infectives, bronchodilators, antipyretics, analgesics, children's vitamins and cough/cold medicines prescribed and recommended every day by pediatricians and pediatric nurses. Their strategy is to work with familiar, time-proven drugs, and make them better for kids by reducing dosing frequency, simplifying the method of administration, improving the side-effect profile, or improving taste by using novel technologies. Their belief is that pediatricians will be more willing to prescribe and recommend products that have specific efficacy and safety information available. Trials are conducted primarily with children.

Product/Partnership Status
Presently, Ascent sells products through an 87-strong sales force. They have not partnered for any of their internal products, but have co-promoted one product, Omnicef, with *Warner-Lambert.*

Partnering Assessment
Ascent are very interested in acquiring or in-licensing pediatric products and in out-licensing their existing products for marketing on a royalty our out-license basis. They anticipate an approval on a new product this year and then may actively seek marketing partners in the Canadian marketplace. They are happy to hear from any Canadian companies, with appropriate products, who are interested in marketing to the US market.

ATHENA DIAGNOSTICS

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Contact: Chris Palatucci, Manager Business Development
(cpalatucci@athenadiagnostics.com)

Profile

Athena Diagnostics is the leading provider of advanced diagnostic assays for neurological disorders, focusing in the three general areas of Alzheimer's disease, neurogenetic disorders, and peripheral neuropathies. They license advanced diagnostic assays for neurological disorders from the academic research environment and offer these tests on a commercial basis to physicians, as part of a comprehensive diagnostic reference laboratory service targeted to neurologists. The company is the diagnostic division of Athena Neurosciences, a wholly owned subsidiary of the Irish pharmaceutical concern, *Elan*.

Product/Partnership Status

Athena operates in a reference lab setting and therefore do not engage in partnership efforts.

Partnering Assessment

Athena is not interested in joint ventures or partnerships. They do interact with academic sources with regard to diagnostics for neurological disease only in a reference lab setting for tissue sample-based diagnostics, not imaging products or the like. They are not in the development field and are therefore only interested in well-published and validated product candidates. They do no basic R&D within the company, just acting as a technology transfer gate way.

AUTOIMMUNE, INC.

128 Spring Street
Lexington, MA 02173
Tel: (781) 860-0710
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Web: www.autoimmuneinc.com

Contact: Bob Bishop, CEO

Profile
AutoImmune is a biopharmaceutical company developing a new class of orally administered drugs to treat autoimmune and other cell-mediated inflammatory diseases. The company currently has products in clinical development for rheumatoid arthritis, Type 1 diabetes, uveitis, and the prevention of organ rejection following transplant. Each of these products is based on a common biological mechanism known as oral tolerance, which provides tissue specific immunosuppression to control disease without toxicity or significant side effects.

Product/Partnership Status
The company's product development activities include:

- multi-center studies in new-onset Type 1 diabetes
- a long-term prevention study in Type 1 diabetes
- a pilot trial in chronic organ transplant rejection
- sponsored research at the Brigham and Women's Hospital in Boston

The company has an exclusive agreement with *Teva Pharmaceutical Industries, Ltd* of Israel for two applications of AutoImmune's proprietary technology for oral immune modulation. The agreement covers the development by *Teva* of an oral formulation of COPAXONE, *Teva's* currently available injectable drug for multiple sclerosis. The exclusive agreement also covers an orally delivered product to treat myasthenia gravis developed by *Teva*.

Partnering Assessment
AutoImmune recently moved their headquarters to Pasadena in California. Having gone through various product disappointments, they are still hopeful of becoming a viable entity. Though they are not in the market for any partnering activities at the moment, they are outlicensing some of their technologies and are presently in discussions with an undisclosed Canadian company in this regard. They can still be contacted through the local numbers above, though they do not have a physical presence in Massachusetts any more.

AVANT IMMUNOTHERAPEUTICS

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Web: www.avantimmune.com

Contact: Una Ryan, President & CEO (uryan@avantimmune.com)
Thomas Fuerst, VP Business Development (tfuerst@avantimmune.com)

Profile
AVANT Immunotherapeutics, the result of a merger of T Cell Sciences and the Virus Research Institute, is engaged in the discovery, development and commercialization of products that harness the human immune response to prevent and treat disease. Their products include preventative vaccines and immunotherapies that target diseases caused by infectious organisms, and drugs and treatment vaccines that modify undesirable activity by the body's own proteins or cells.

Product/Partnership Status
The company has products in development to treat autoimmune diseases, cardiovascular diseases, cancer, inflammation, infectious diseases, and organ transplant rejection. These include: Complement Inhibitors B TP10 recently completed Phase I/II trials for reperfusion injury following lung transplantation and is partnered with *Novartis*. TP10 also being looked at for cardiac surgery and heart attacks in Phase I and is unpartnered outside Japan. In Japan, TP10 is partnered with *Yamanouchi*. TP20 for inhibiting neutrophils with stroke is in preclinical stage and is unpartnered.
Vaccines B CETP vaccine aimed at increasing HDL to combat atherosclerosis is in Phase I and unpartnered. A Rotovirus vaccine has completed Phase II partnered with *SmithKline Beecham*. Vaccines against Influenza (completed Phase II), Lyme Disease (preclinical) and RSV (Phase II) are all partnered with *Pasteur Merieux Connaught*. A vaccine for Cholera has completed Phase II partnered with Heska.
Delivery Systems B Therapore is a proprietary technology using an injectable bacterial protein system to deliver protein and peptide antigens into human cells to generate immune responses against those antigens. Immunotherapeutics for cancer (melanoma) and chronic viral infections such as HIV and Hepatitis are in preclinical stage and as yet unpartnered.

Partnering Assessment
Aggressively seeking partnerships now, particularly in cardiovascular, cancer and infectious disease areas. Considers itself weak on the manufacturing side. No interest in agrogenetics, medical devices or diagnostics. Might be interested in exploring new areas of research in immunology, cancer and infectious diseases. Little contact with Canada and unaware of relative strengths of IP and cutting edge technology there. Would benefit from more info on opportunities but stresses need for easy transport to and from Boston.

BASF BIORESEARCH CORP.

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Web: www.basf.com

Contact: Al Collinson, Director of Business Development (collinar@basf.com)

Profile
BASF Bioresearch Corporation is working to discover new drugs for treating immunological diseases and various forms of cancer. It also operates a facility for the manufacture of protein therapeutics and other biologicals for BASF Pharma and other companies on a contract basis. BASF Pharma operates four research centers worldwide, including Worcester. Departments within BBC's 370,000 square foot facility include Oncology, Immunology, Molecular Biology, Biochemistry, Chemistry, Process Development, and Animal Research. In immunology, BBS is working toward the discovery of novel anti-inflammatory compounds that block production of certain cytokines, key mediators of the immune system, and of novel immunosuppressive agents that block activation of immune cells. The first product candidate resulting from this research, a novel treatment for rheumatoid arthritis, recently entered clinical trials. Their research will one day add to the product portfolio of *Knoll Pharmaceutical Company*, a subsidiary of BASF Corporation.

Product/Partnership Status
On the technology side, BASF has partnered with *Bujard/Uni HD* (research into gene regulation), *Incyte* (licensing of genomics technology), *Genzyme Transgenics* (production of monoclonal antibodies in goats), *Lynx Therapeutics* (genomics research), and *MPI Munchen* (research into non-linear dynamics). They have distribution agreements with *Mitsui* (Japan for Clivarine for hemodialysis), *Genzyme* (US for Thyrogen as a specific cancer diagnostic), and *AstraZeneca* (Germany for Reductil to treat obesity). They have further research agreements with *Tularik* (an uncoupled protein antagonist for obesity) and *Cambridge Antibody Technology* (human Anti-TNF monoclonal antibodies in the immunology field). They have important development collaborations with *Alza* (Dilaudid OROS technology B registration/launch), *Eisai* (Sibutramin for obesity B early development in Japan), and *Genetics Institute/American Home Products* (Anti IL-12 B early development).

Partnering Assessment
Collinson is responsible for R&D licensing on a worldwide basis for BASF. They have multiple academic collaborations in many countries and are always interested in this. Particular research areas of interest are immunology, cardiovascular, and obesity. From a technology standpoint their principal interests lie in antibody technologies and mammalian fermentation technologies. Though he has personally had dealings with Canada in the past, he is unaware of any BASF interaction with Canadian industry at this time.

BIOGEN

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Web: www.biogen.com

Contact: Kees Been, VP Business Development (kees_been@biogen.com)

Profile
Biogen is a leading biotech firm with a strategic focus on the development of human therapeutics. Founded in 1978, the first group of products based on its research is being sold by licensees throughout the world. The next generation of Biogen-developed products will be targeted for use in the AIDS therapeutics, inflammation, and selected cancer markets. The company employs more than 1,000 people worldwide and has a regional office in Canada.

Product/Partnering Status
Biogen is currently conducting research in a number of therapeutic areas, including multiple sclerosis, inflammatory, respiratory and cardiovascular diseases, kidney disorders and cancer. Their products are being tested in more than 20 separate human clinical trials at more than 100 sites in the US, Canada and Europe.

Since 1997, Biogen and *Merck* have had a collaboration to develop oral and aerosolized small molecule VLA-4inhibitors for which *Merck* has begun a Phase I exploratory trial for a potential treatment for asthma. They are also working with *Merck* on an orally available molecule that Biogen will develop as a candidate for certain other indications. Also, since 1997, Biogen has had a collaboration with *CV Therapeutics* to develop and market CVT-124 as a treatment for CHF and its many symptoms by turning off a receptor involved with vasoconstriction and the reabsorption of fluids in the kidneys.

In the gene therapy area, Biogen is collaborating with *Genovo*, a gene-therapy company, and Dr. James Wilson of the University of Pennsylvania, on studies involving diseases of the liver and the lung. Biogen has exclusive worldwide rights to product candidates resulting from this research. Dr. Wilson is conducting a Phase I, proof-of-concept gene-therapy trial in cystic fibrosis.

In the genomics area, Biogen is collaborating with *CuraGen* on identifying disease-specific genes, and linking isolated genes into functional pathways that can present new therapeutic proteins or targets for drug discovery.

In the developmental biology area, Biogen is collaborating with *Ontogeny* on the study of hedgehog proteins for potential application in the treatment of CNS disorders and with *Creative BioMolecules* on the development of OP-1 for kidney diseases.

They have a number of drugs partnered with big pharma, *Schering Plough* (Alpha

Interferon for Hepatitis B and C, and certain cancers), *SmithKline Beecham* and *Merck* (Hepatitis B vaccines), *Abbott* (Hepatitis B diagnostics), *The Medicines Company* (Hirulog for angioplasty and acute myocardial infraction), and *Merck* (VLA-4 inhibitor for asthma).

Partnering Assessment

Biogen is particularly interested in late stage clinical opportunities and is always interested in partnerships, though these will be limited to therapeutic areas reflected by their current interests as outlined above. Breakthrough work in these areas will be of interest. The company has a sales and marketing office in Canada and considers that the country does have a sophisticated infrastructure with a high level of medical expertise.

BIOPURE CORPORATION

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Web: www.biopure.com

Contact: Paul Looney, President and COO (plooney@biopure.com)

Profile
Biopure is engaged in the identification, isolation, separation and purification of critical proteins, resulting in the industrial-scale production of ultra-pure products used in the pharmaceutical and healthcare markets. It is a leading developer of oxygen therapeutics. They are currently manufacturing a highly purified oxygen-carrying hemoglobin solution to be used as a temporary blood-substitute in humans and animals.

Product/Partnership Status
Currently the company has developed and manufactured two hemoglobin-based oxygen therapeutic solutions. Hemopure is currently in Phase III clinical trials for human use. Oxyglobin is the only hemoglobin-based oxygen therapeutic approved by the FDA and is a veterinary product commercially available since 1998 for the treatment of anemia in dogs, regardless of the cause. These products are 100% owned by the company, though previously they had enjoyed early and considerable funding support from *Upjohn*. This sponsorship dried up after it became *Pharmacia & Upjohn* with the subsequent rationalizations of resources. The Phase III trial is currently three-quarters enrolled and includes patients in Canada.

Partnership Assessment
Two longer-term opportunities for partnering will be on the product marketing side and possibly manufacturing.

BIOSTREAM, INC.

160 Second Street
Cambridge, MA 02142
Tel: (617) 492-5554
Fax: (617) 492-5664

Contact: Wendy Graham, Director of Development (wgraham@biostream.net)

Profile
Biostream is an early stage biopharmaceutical company focused on the development of novel agents for use in diagnostic imaging. Their goal is to impact the clinical management of major diseases by providing more specific and sensitive diagnostic agents. They are developing novel products that improve the diagnosis of cardiovascular disease and infection.

Product/Partnership Status
The lead product technology, MyoImage, was developed by Biostream's founding scientists at Massachusetts General Hospital (MGH) and is a unique diagnostic agent for use in non-invasive determination of myocardial viability. Its clinical validity has been established by *Nihon Medi-Physics* in Japan where it has been sold as a radio-pharmaceutical for over four years. Biostream has exclusive rights to this technology in the US. The Company is developing several other diagnostic imaging products in various stages of development. The portfolio also includes products for target infection, one Magnetic Resonance Angiography (MRA) imaging product and one X-Ray contrast agent. Two, Lumencin and BIO 10, are undergoing preclinical testing in anticipation of clinical studies that are expected to begin this year. The company has several development relationships with premier universities.

Partnership Assessment
Biostream wishes to contract with major pharmaceutical companies for manufacturing, marketing and distribution of each product.

BIOTRANSPLANT, INC.

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Charlestown, MA 02129
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Web: www.biotransplant.com

Contact: Elliot Lebowitz, CEO (elliot.lebowitz@biotransplant.com)

Profile
BioTransplant is engaged in the discovery and development of novel immunologic approaches to organ transplantation, cancer and autoimmune through its core proprietary ImmunoCognance-based technologies and systems. They are seeking to overcome current problems with graft rejection by developing, manufacturing and marketing products and services for patients requiring allograft and xenograft organ transplants. The systems to be sold to transplant surgeons will minimize systemic immunosuppression through the induction of specific immune tolerance.

Product/Partnership Status
BioTransplant has two clinical stage products, MEDI-507 in Phase II and Allomune System just entering initial human testing. There are research stage products in XenoMune, which is in preclinical development, and other cancer, autoimmune and hematological applications. MEDI-507 for the treatment of graft-versus-host disease (GvHD), often a fatal outcome of bone marrow transplants, is being developed in collaboration with *MedImmune*. It is a humanized monoclonal antibody designed to treat and prevent organ and tissue transplant rejection and autoimmune disorders. Allomune, for human organ transplantation and blood cell cancers, is being evaluated specifically for kidney transplantation and refractory lymphoma. XenoMune is designed to increase the available supply of organs through use of porcine-to-human transplantation and the company is collaborating with *Novartis*. They have a number of academic collaborators, including at MGH. They have other collaborations and agreements with *Charles River Labs, Stem Cell Sciences* and *Massachusetts General Hospital.*

Partnering Assessment
The company reports that, in the first instance, any interested inquirers from Canada should first approach Dr. Calvin Stiller, a transplant surgeon now involved with the Canadian Medical Discovery Fund. Dr. Stiller acts on behalf of BioTransplant interests in Canada. He can be reached on (519) 858-1582 x235. Their strategy is to leverage the capabilities of partners, to create near-term value from milestone fees and R&D support, and long-term value from royalties and profit-sharing, while supporting internal development.

BOSTON BIOMEDICA, INC.

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West Bridgewater, MA 02379
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Web: www.bbii.com

Contact: William Prather, SVP Finance and Business Development

Profile
Boston Biomedica is a diagnostic manufacturer and technical support lab that supplies a growing diagnostic industry with fully characterized serum and plasma-based components, research products and technical services, with particular emphasis given to HIV-1 (AIDS), HTLV-1, HIV-2 and Viral Hepatitis. In addition, the company offers for research investigation 9 TRUE anti-HIV seroconversion panels that have been recognized worldwide as Agold standards@ for determination of anti-HIV-1 test kit sensitivity. They have nearly 200 off-the-shelf quality control products, sold to test kit manufacturers, regulators and labs in more than 30 countries worldwide. BBI also manufactures diagnostic test kit components and lab instrumentation, provides specialty lab testing and contract research services, and has significant R&D investments in pressure cycling technology (PCT) and drug discovery.

Product/Partnership Status
In 1998, BBI acquired *BioSeq*, a development stage biotech company, and with it the rights to develop and commercialize pressure cycling technology (PCT). A strong foundation of a good revenue stream and an extensive customer base in the diagnostic field has enabled them to pursue two cutting-edge research programs in PCT and HIV drug discovery. BBI has established close relationships with leading blood banks worldwide.

Partnering Assessment
BBI will already be selling into the Canadian market. They should be approached by groups that may be able to add to BBI's product line. Interested parties may also care to investigate BBI's new subsidiary operation, *Panacos Pharmaceuticals*, based in the DC area. Information can be gained from the BBI web site.

BOSTON PROBES, INC.

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Web: www.bostonprobes.com

Contact: Jack Johansen, President and CEO (jjohansen@bostonprobes.com)

Profile
Boston Probes (BPI) was founded to develop probe-based systems for the detection and analysis of infectious agents, genetic abnormalities and cancers. They have a license to use PNA (Peptide Nucleic Acid) technology in these applications as well as for the detection of microorganisms on water, food, beverage and pharmaceutical preparations and processes. Their intent is to develop their own assays and products as well as establish a limited number of strategic development, marketing and distribution relationships with existing diagnostic companies.

Product/Partnership Status
BPI is an affiliate of *DAKO A/S* , a worldwide leader in the manufacture and sale of antibodies to the molecular pathology market. They hold 80% of BPI's equity and were the first company develop and sell routine diagnostic tests that utilize the PNA technology, and BPI supplies DAKO with the probes sold in their products. BPI has established strategic partnerships with companies that wish to develop probe tests for their key markets. These companies include *Millipore* (filtration and analysis of microorganisms) and *AndCare*. (developer of portable instrumentation for point-of-care diagnostics). With *Millipore* they will develop and manufacture PNA probes, kits and systems to be used for the ID of environmental contaminants and toxic and disease-causing bacteria and microorganisms. With *AndCare* they will develop and manufacture PNA probe-based test strips for the detection of viruses and bacteria including Dengue virus, Neisseria gonorrhoeae, and Chlamydia trachomatis. Future applications could include testing for glucose and cholesterol levels and the detection of cancer and other genetic diseases, such as cystic fibrosis and sickle cell anemia.

Partnering Assessment
Boston Probes primary interest is in out-licensing to diagnostic or research materials companies that wish to utilize the PNA technology. Their primary targets will be in the following area:

- < Clinical and industrial microbiology
- < Human genetic analysis
- < Cytogenetics

They are involved in ongoing discussions with prospective partners in addition to those already in place. They will look to develop probes that work best with the PNA technology, often looking to academic groups that possess a little business savvy. The company already works with a couple of academic groups in Canada, at the Terry Fox

labs at UBC and with another group in Laval, both in the cytogenetics area with telomere biologists.

CAMBRIA BIOSCIENCES LLC

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Contact: Leo Liu, President and CSO (lliu@cambriabio.com)

Profile
Cambria was founded to apply genomic and model organism systems to discover of novel drugs and chemicals against medically and agriculturally important pathogens. Their approach targets molecules and cellular processes that are restricted to invertebrates, leading to screens and lead compounds that can address key plant and animal pests and parasites in a highly selective manner, enhancing the development of products with novel modes of action and highly desirable safety parameters. The founding team has extensive academic and industry experience in applied genomics, including bioinformatics, genetic model systems (yeast, nematode, and insect), target validation, and compound screening. Their goal is to build a unique integrated discovery platform leading to novel target-specific screening assays that will accelerate drug and pesticide discovery by Cambria and its agrochemical and pharmaceutical partners.

Product/Partnership Status
As a very young company of only eleven people to date, Cambria has yet to strike any corporate deals. They project that their first target-based screens for application against compound libraries and a novel rapid-acting and selective biopesticide candidate product are projected to be ready for testing by late 2000.

Partnering Assessment
Ultimately, Cambria will have an interest in partnering with large agrochemical and animal health companies. Any appropriate academic groups could also make approaches, although the field of endeavor is small enough for Liu to feel quite confident that he knows all the players in this area of interest. He is, for instance, aware of small academic start-ups out of the likes of McGill, Queen's and UBC, as well as Ag commodities businesses in western Canada.

CAMBRIDGE NEUROSCIENCE, INC

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Contact: David Gwynne, VP Biotech and Business Development
(david_gwynne@cambneuro.com)

Profile
CNI employs advanced drug discovery technologies, such as electrophysiology, molecular biology, neuropharmacology and genetics, to develop novel medications for the treatment of severe neurological and psychiatric disorders, including stroke, Alzheimer's and schizophrenia. Product candidates and programs include ion-channel blockers for the treatment and prevention of brain damage resulting from stroke or ischemia related to surgery, as well as for the treatment of certain forms of neuropathic pain, and growth factors for the treatment of MS and peripheral neuropathies.

Product/Partnership Status
A Phase III trial of CERESTAT (now known as Aptiganel) for stroke, was halted in 1997, though the company continues to pursue further development opportunities, spurred by input from an independent panel of stroke experts. A new Phase III trial for the subset of patients, who responded favorably at the first trial, is to be commenced. Other ion-channel blockers include CNS 5161 for neuropathic pain in Phase I (moving to Phase II later this year) and for neurological deficits from cardiac surgery in pre-IND, and NMDA, sodium, potassium and combination ion-channel blockers in preclinical development for cerebral ischemia, spinal cord injury, pain, migraine and epilepsy.

At the end of 1998 an agreement was made with *Bayer* to develop CNI's recombinant Glial Growth Factor 2 (GGF2) for the treatment of neurodegenerative diseases such as MS. In late 1996, CNI entered into a collaboration with *Allergan* to jointly develop NMDA ion-channel blockers, sodium ion-channel blockers and, in the area of ophthalmology, multiple ion-channel blockers, initially for the treatment of glaucoma. This agreement was extended for a year at the end of 1999.

Partnering Assessment
CNI are interested in partnering both Aptiganel and CNS 5161. In the case of the latter, they would prefer to partner this drug in tandem with other molecules as a distinct program, since they feel they have an outstanding drug discovery program in the pain arena. In addition, they have other NMDA and sodium ion channel blockers which they would be happy to discuss with potential partners.

CIRCE BIOMEDICAL, INC

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Lexington, MA 02173
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Web: www.circebio.com

Contact: Barry Solomon, President (solomon@circebio.com)

Profile
Circe is a privately-held biomedical systems company commercializing novel bioartificial organ systems based on its proprietary mammalian cell and biocompatible, semi-permeable membrane technologies. It is the result of a management buy-out last year from *W.R.Grace*. The lead product, the HepatAssist System, is an extracorporeal, bioartificial liver support system incorporating porcine hepatocytes (pig liver cells). The System has been designed to treat patients with liver failure by temporarily providing essential liver functions in order to allow sufficient time for the patient's own liver to regenerate to a life-sustaining state or to receive a suitable liver for transplantation. The company is currently enrolling patients in a pivotal Phase III to test the efficacy of the System for the treatment of acute liver failure arising from either fulminant hepatic failure or primary graft non-function.

Product/Partnership Status
To this point in time the company has no particular partnering relationships.

Partnering Assessment
The only previous contacts in Canada have been with hospitals in London, Ottawa and Montreal being considered for the clinical trials for the liver assist device, though none were apparently big enough. They have also worked closely with Professor Butterworth at McGill University. Circe would be interested in hearing from anyone involved in cell therapy or liver cell research.

COLEY PHARMACEUTICAL GROUP (CPG)

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Wellesley, MA 021481
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Web: www.cpgdna.com

Contact: Deanna Peterson, Executive Director Business Development
(dpeterson@cpgdna.com)

Profile
Until very recently known as CpG ImmunoPharmaceuticals, CPG is a company formed in 1997 to research, develop and commercialize innovative therapeutic and prophylactic products utilizing their breakthrough, broadly enabling immunotherapy that can either stimulate or redirect the body's immune responses. They have active research programs for the treatment or prevention of infectious disease as well as the treatment of cancer, allergy and genetic disorders. They are presently anticipating entering at least six Phase I/II clinical trials for indications in infectious disease and cancer, with a Hepatitis B trial already underway. CPG has European operations and labs in Hilden, Germany and Canadian operations based in Ottawa. Their CpG DNA technology promotes white blood cell proliferation and rapidly activates both cellular and humoral immune responses.

Product/Partnership Status
Coley have an existing collaborative relationship with *SmithKline Beecham* in the area of infectious disease vaccines.

Partnering Assessment
CPG is actively pursuing collaborative alliances with major pharmaceutical and biotech firms and are open to any approaches from entities involved in infectious diseases, allergy and cancer. They are conducting clinical trials in Canada and have had particular success with the University of Ottawa.

COMPUCYTE CORPORATION

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Web: www.compucyte.com

Contact: Tim Holzer, VP Biomedical Development (tholzer@compucyte.com)

Profile
CompuCyte develops and markets systems for the biochemical analysis of cells in virtually every type of cellular sample, based on their proprietary LSC (R) Laser Scanning Cytometer. Laser scanning cytometry allows multiple measurements of clinically important properties of cells in convenient formats never before possible, providing a new level of cellular information which has the potential to significantly advance medicine and biomedical research over the next decade. They also produce analyzers for near-patient point-of-care diagnostics.

Product/Partnership Status
At the end of last year, CompuCyte announced a Atheranostic@ collaboration with *Genetics Institute*, a unit of *Wyeth-Ayerst Labs*, the pharmaceutical division of *American Home Products*. Theranostic refers to a diagnostic test that aids in the selection of patients and has the ability to monitor the biological effects of a drug therapy rapidly, at the point of care. CompuCyte will develop cell-based assays for rapid monitoring of the effects of cell adhesion inhibitors currently in clinical development.

Partnering Assessment
Unless the approach is from an entity particularly germane to their existing interests, CompuCyte is not seeking partnerships with Canadian companies at this time. Should there be specific interest in their technology its is recommended that direct contact be made.

CONSENSUS PHARMACEUTICALS, INC

200 Boston Avenue
Medford, MA 02155
Tel: (781) 306-0808
Fax: (781) 306-1446
Web: www.consensus-pharm.com

Contact: Jack Talley, CEO (jtalley@consensus-pharm.com)

Profile
Consensus is a newly formed drug discovery company exploiting combinatorial chemistry screening technologies developed at Beth Israel Deaconess Medical Center in Boston. The technique was originally developed to obtain optimal peptides for binding to domains of signaling proteins. They synthesize libraries with very high degeneracy, sometimes consisting of more than 10 billion compounds, and then rapidly screen these libraries for compounds that bind to that protein. In contrast to many combinatorial screening approaches, their libraries are soluble and are screened based on their ability to bind to an immobilized target protein. This technique has been extended from peptide libraries to libraries of pseudo-peptides, peptoids and cyclic structures.

Product/Partnership Status
Consensus has a license from Beth Israel for certain patent rights to technology which identifies optimal ligands for protein-Tyr kinases, protein-Ser/Thr kinases, SH2 domains, PTB domains, SH3 domains, 14-3-3 proteins, proline isomerases, transcription factors, Lim domains and Adaptins.

Partnering Assessment
The core technology will be of particular interest to companies that have chosen to focus on families of proteins that are potential drug targets, with Consensus rapidly providing high affinity, soluble and specific ligands for each member of a family of related proteins. Their target is therefore a deal with pharmaceutical or large biotech firms capable of sponsoring research. On the research side, they have a historical and ongoing research interest in protein kinases, GPCRs (G-Protein Coupled Receptors), and single transmembrane receptors such as interleukins. Any work in these areas would be of interest.

CREATIVE BIOMOLECULES, INC

101 Huntington Avenue, Suite 2400
Boston, MA 02199
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Web: www.creativebio.com

Contact: Steven Basta, VP Finance and Corporate Development
(sbasta@creativebio.com)

Profile
Creative is a discovery and development company focused on proprietary protein-based therapeutics for human tissue regeneration. The company's therapeutics are based on proteins that act in initiating and regulating the cellular events involved in cell and tissue formation. These are based on bone morphogenetic proteins (BMPs). Their lead product is the OP-1 Implant and is designed to promote new bone growth to heal severe fractures. Additional products under development include therapies for kidney failure, stroke and other neurological disorders. Their research focus is also directed toward the discovery of new therapeutic applications of its morphogenic proteins and the understanding of signaling pathways to develop small molecules based on the biology of these proteins.

Product/Partnership Status
Recently it was announced that Creative, *Ontogeny* and *ReproGenesis* intend to merge their operations to form a single company engaged in the human tissue regeneration field to be called *Curis*. Creative is the only publicly traded company of the three and will become the largest shareholder in the new private entity. Historically they have had a longstanding arrangement with *Stryker Biotech* for orthopedic applications.

Partnering Assessment
Creative, which will continue to operate as per normal, remains interested in partnering with large companies from a development point of view. Like many such companies, they are always interested in hearing about any particular genes or proteins possessing novel properties and offering real product opportunities. They would be interested in out-licensing opportunities for some of their renal and neurology work. Assuming that the Creative Biomolecules shareholders approve the Curis merger sometime in June 2000, all Creative opportunities will revert to Curis.

CUBIST PHARMACEUTICALS, INC

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Web: www.cubist.com

Contact: Alan Watson, VP Business Development (awatson@cubist.com)

Profile
Cubist is focused on the discovery, development and commercialization of novel anti-infectives to treat infections caused by bacterial and fungal pathogens. Daptomycin, the company's lead product, is a unique agent with potent bacterial activity that addresses the critical need for new antibiotics to treat infections caused by resistant pathogens. They are also applying their expertise in microbiology, genomics and medicinal chemistry to identify additional novel compounds with a broad spectrum of activity against life-threatening infectious organisms such as methicillin resistant Staphylococcus (MRSA) and vancomycin resistant enterococci (VRE).

Product/Partnership Status
Bristol-Myers Squibb, *Merck* and *Novartis* all collaborate with Cubist to accelerate the discovery, development and commercialization of novel anti-infective products. The deals provide license fees, equity investments, R&D funding and scientific and product development milestone payments. With *Novartis*, Cubist has a target validation and assay development research collaboration. With *Merck*, they have transferred two unique chemical classes that will be carried forward with resources at Merck. These medicinal chemistry programs are designed to mature small molecule leads into full-scale anti-infective drug candidates.

To expand its access to novel small molecule libraries for screening and target discovery, Cubist has formed alliances with leading biotech companies such as *ArQule* (compounds for tRNA synthetase screens), *Genzyme* (screening of Genzyme's library), *Pharmacopeia* (screening of combinatorial libraries), *Neurogen* (anti-infectives) and *Helios Pharmaceuticals.*

Partnering Assessment
A high profile biotech company which should be approached by potential partners, academic and corporate, in the anti-infectives field.

CURIS, INC (See Creative BioMolecules, Ontogeny, Reprogenesis)

Web: www.curisinc.com

Profile

Curis is being formed by leveraging the combined strengths of Creative BioMolecules, Ontogeny and Reprogenesis to create a premier regenerative medicine company. It will combine a powerful functional genomics and developmental biology discovery engine with a strong pipeline of near-term commercial, late-stage clinical and earlier stage developmental opportunities. They have leading corporate partners, sustainable financial strength and near-term product revenue opportunities. Curis will develop cellular, protein or small molecule products to restore normal function.The combined entities will own or have rights to more than 150 issued patents and 225 pending patent applications world-wide.There will be some 155 staff.The following technologies will be used to identify, develop and/or commercialize novel products and there are plans to develop 1-2 INDs a year.

- < Model systems for functional genomics
- < Screening assays to identify antagonists and agonists of key biological pathways
- < Proprietary transgenic models of disease
- < Cell and tissue technology for correcting structural or functional disorders (Chondrogel for vesicourectal reflux, Vascugel for post-coronary artery bypass graft restenosis, pancreatic stem cells for type I diabetes, bladder augmentation)
- < Tissue engineering with biomaterials to create the right environment for the formation of tissue in a 3-dimensional space (guided tissue formation, natural biopolymers, semi-synthetic biopolymers, cell and drug delivery)
- < Proteins and peptides (OP-1 Implant for orthopedic reconstruction, sonic hedgehog for hair growth, OP-1 protein for stroke recovery, hedgehog derivatives that are neuroprotective for the treatment of neuropathies, peptide to restore and maintain normal beta islet function in type II diabetes)
- < Small molecules that can restore normal function by inhibiting or stimulating critical biological pathways (ONT-23 for the treatment of basal cell carcinoma and medulloblastoma, neurotrophic agonists, inhibitors of pathways involved in colon cancer)

Product/Partnership Status

Corporate collaborations include: *Stryker Corporation, Biogen, Becton Dickinson, Incyte Pharmaceuticals, Oxford Assymetry International, Genzyme Molecular Oncology, Perkin-Elmer's Tropix,* and *ComGenex.*
Academic collaborations include: *Harvard University, Harvard Medical School, University of Michigan, MIT, Stanford University, UCSF, NIH, Johns Hopkins University, University of Massachusetts* and numerous other leading American and European centers of academic excellence.

Partnering Assessment

Board approval is anticipated in June and business development should be clearer then.

CYTOLOGIX CORPORATION

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Web: www.cytologix.com

Contact: Richard Foemmel, CEO (rfoemmel@cytologix.com)

Profile
CytoLogix is focused on developing and commercializing technology for automating slide-based cellular diagnostics. Their first product automates the application of histochemical and immunohistochemical stains to tissue specimens destined for microscopic analysis. It employs a patented technology that creates a reaction chamber on a microscope slide and will allow for eventual use molecular (ISH) stains.

Product/Partnership Status
Cytologix has its own sales force in the US and works with OEMs on their products.

Partnering Assessment
Presently, they are not selling into Canada though they recently did uncover one potential customer, being handled by their Michigan salesperson. Cytologix is very open to hearing from prospective partners in the reagents, immunohistochemical, probes, and hybridization fields, as they look to expand their product offerings in the coming years.

CYTYC CORPORATION

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Web: www.cytyc.com

Contact: Mark Kirtland, Senior Director Marketing and Business Development
(mark.kirtland@cytyc.com)

Profile
Cytyc designs, develops, manufactures and markets a sample preparation system for medical diagnostic applications. Their ThinPrep System allows for the automated preparation of cervical cell specimens on microscope slides for use in cervical cancer screening, as well as for the automated preparation of other cell specimens on microscope slides for use in non-gynecological testing applications.

Product/Partnership Status
Cytyc has had a collaborative research agreement with *Digene* for diagnostics for cervical cancer and STDs. They have also co-promoted the ThinPrep pap smear test with *Mead Johnson*. They have established a small subsidiary in Canada last year to handle sales, service, training and distribution to clinical labs. Lack of reimbursement has been an issue for their product in Canada. A study is currently being undertaken in a hospital in Saskatchewan to compare the ThinPrep to the conventional Pap test, though Cytyc are not collaborators in the study per se.

Partnering Assessment
While they have had discussions with some Canadian firms related to licensing or investment in technologies, the number and level of these discussions has not been the same as in Europe or the USA. They also have academic collaborations in the US that in some cases involve funding. In general, Cytyc are interested in licensing and investment opportunities, as well as working with academic researchers, in any areas that would allow them to leverage their presence in the Ob/Gyn office or the clinical lab. Their main focus is on diagnostics, with a particular interest in developing additional diagnostic tests that can be performed out of the ThinPrep sample vial or on the slides themselves (tumor or infectious disease markers). For example, *Digene's* HPV test is FDA-approved to be performed on the clinical sample that remains after the ThinPrep slide is made. In terms of moving beyond diagnostics, Cytyc has an interest in medical devices and therapeutics fo. women's health problems (female cancers, STDs, osteoporosis). Their large Ob/Gyn sales force puts them in a position to be an excellent marketing partner for a company that is not in the position to build a specialty sales force.

DIACRIN, INC

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Web: www.diacrin.com

Contact: Michael Egan, SVP Corporate Development (emegan@diacrin.com)

Profile
Diacrin is developing transplantable cells for the treatment of human diseases which are characterized by cell dysfunction or cell death, and for which current therapies are either inadequate or nonexistent. To overcome the constraint of the lack of an adequate supply of human donor cells, Diacrin has pioneered the use of porcine cells for clinical transplantation since this is seen as a reliable source of a wide range of cell types suitable for transplantation into humans. They are also developing a proprietary immuno-modulation technology involving the selective treatment of isolated cell populations prior to transplantation. This induces a state of graft-specific immunological tolerance, which allows continued survival for the transplanted cells after transplantation. Products under development for the treatment of neurological disorders include NeuroCell-PD for Parkinson's and NeuroCell-HD for Huntington's, NeuroCell-FE for focal epilepsy, porcine neural cells for stroke and chronic intractable pain, and porcine spinal cord cells for spinal cord injury. Also under development are hepatocytes (porcine and human) for acute liver failure and cirrhosis, myoblasts for cardiac disease and retinal epithelial cells for macular degeneration.

Product/Partnership Status
Since 1996, Diacrin and *Genzyme* have had a joint venture to develop and commercialize NeuroCell-PD and NeuroCell-HD. The former product is in Phase II/III and has been fast-tracked by the FDA. The porcine neural cells for stroke are in Phase I at *Beth Israel* and *Brigham and Women's Hospitals*, as is NeuroCell-FE for focal epilepsy.

Partnering Assessment
Typically, Diacrin wait until they have completed Phase I trials and got their data before they actively seek partners. At this time, they are satisfactorily partnered. However, they are always interested in hearing of appropriate animal health work. For instance, they related a recent visit by a minister from PEI and noted the presence of a good veterinary school there. Therefore, institutions with relevant animal studies and research are encouraged to make contact.

DIATIDE, INC

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Web: www.diatide.com

Contact: Ron Kinder, COO (r_kinder@diatide.com)

Profile
Diatide is a specialty pharmaceutical company developing a novel line of disease-specific, diagnostic and therapeutic drugs with commercial and medical promise. They have applied their patented technologies in the areas of peptide engineering, molecular biology and radiolabeling chemistry produce a platform technology for its ASmart Drugs@ for the treatment and diagnosis of life-threatening conditions such as cancer and cardiovascular disease. Their smart-drug technology consists of small molecule peptides that bind with high affinity and specificity to targets on diseased tissue and to which a radioisotope can be attached for imaging or therapeutic purposes.

Product/Partnership Status
In 1995, Diatide entered into an agreement with *Nycomed* in a strategic alliance which called for R&D support and a marketing collaboration. This was *Nycomed's* entry into nuclear medicine. When it merged with *Amersham PLC*, a predominantly nuclear medicine company, in 1997, it exercised its rights to co-promote Techtides, the Diatide product, in the US and exclusive distribution and licensing rights in other parts of the world.

Partnering Assessment
Diatide expects to market and globally distribute the therapeutic products that it develops worldwide on a similar basis to the Amersham agreement. Its therapeutic products are not currently partnered. In 1998, *Nycomed Imaging AS* elected to discontinue its R&D payments for therapeutics and thus Diatide regains the rights to all non-optioned products. Thus, they are aggressively seeking other corporate partners to help fund and market the unpartnered products in their pipeline.

DYAX CORPORATION

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Contact: Pamela Hay, VP Corporate Development (phay@dyax.com)

Profile

Dyax invented and owns key patents in phage display or directed evolution technology. This technology is a combinatorial process used to engineer novel proteins and peptides ranging in size from 6 to 1500 amino acids long. These proteins/peptides bind to almost any biomolecular target, including enzymes, cell receptors, tumor cells, bacteria, viruses, small molecules, antibodies, growth factors, and nucleic acids. It uses this technology to develop highly specific affinity chromatography ligands for separations of complex mixtures of molecules such as racemates and biomolecules. It sells these ligands in coordination with its affinity chromatography columns and supplemental products, such as software systems for regulatory compliance. Dyax is also involved in the development of human therapeutics and diagnostic products using its patented phage display technology. Its engineered molecules as they have distinguishing features such as small size, high stability, and ultra high affinity and specificity for the target.

Product/Partnership Status

Dyax has a number of partnerships and collaborations to discover and/or develop therapeutic and imaging products derived from Phage Display. These include with *Genzyme* for the co-development of Dyax's lead compound which inhibits human kallikrien for hereditary angiodema and other indications, and with *DebioPharm SA* as a European development partner for Dyax's therapeutic lead compound inhibitor of human neural elastase, for cystic fibrosis and other pulmonary diseases. Dyax also has agreements with *Amersham Pharmacia Biotech* for innovative separations technology, and with *Pasteur-Merieux Connaught* for the development of systems to optimize the purification of a series of vaccines.

Partnering Assessment

Dyax is actively seeking additional collaborations with companies or medical researchers who have identified other targets associated with one or more diseases. They have three existing proprietary therapeutic lead compounds. These compounds are described as potent and selective inhibitors of enzymes implicated in inflammatory disorders, bleeding disorders, and cancer metastasis. They are also developing lead compounds for in vivo imaging using nuclear medicine, in which a targeting agent is linked to a radioactive compound to detect and localize a disease site. Currently, they have two lead imaging compounds being tested in animal models.

ELIGIX, INC

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Contact: Walter Ogier, CEO (wcogier@eligix.com)
Jim Fitzgerald, CFO (jfitzgerald@eligix.com)

Profile

Formerly Coulter Cellular Therapies, Eligix was established by Coulter Corporation and InterWest Partners in 1997. Its mission is to develop and commercialize enabling and novel cell therapies for the treatment of cancer and immune disorders. Their core technology includes a simple and powerful methodology to enable rapid, specific and highly efficient separation of blood and bone marrow cells useful for patient specific therapy. They initiated their first clinical trials of the therapy in 1997 and they are endowed with an extensive library of monoclonal antibodies that provides the potential for diverse applications of its technology including use in new forms of cellular immunotherapy directed towards cancer, immune disorders and genetic diseases. Its products are targeted for sale to oncologists, hematologists, and transplantation specialists in major hospitals worldwide.

Product/Partnership Status

Eligix's products are still very much in the research phase. Much of their technical and clinical collaborations have been with the major cancer centers (*Fred Hutchinson, Dana Farber, M.D. Anderson*), some with antibodies to license, the latter two for the clinical testing of their first two products. A feasibility clinical trial has been carried out for the removal of malignant cells from autologous stem cell transplants, and Phase III trials will provide pivotal testing by early to mid-summer of this year for the removal of cells responsible for graft versus host disease (GvHD) associated with allogeneic immune cell infusions. They are also developing High-Density Microparticle technology products based on patented technology for the selection, elimination, or activation of disease-specific immune cells to engineer a patient's immune response to disease..

Partnering Assessment

Eligix is targeting commercialization of its first products in the European market within the next year and a co-marketing partner is being sought there. They describe what they do as a mix of medical device and monoclonal antibody work. Eligix would be interested in any antibodies directed towards the autoimmune area. Their commercialization strategy includes establishing commercial marketing and distribution relationships for certain of its lead HDM products as well as its future immunotherapy products in various world markets.

ENDOGEN, INC

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Contact: Alan Kotik, VP Business Development (akotik@perbio.com)

Profile
Endogen develops, manufactures and supplies specialty research reagents and immuno-assay (ELISA) test kits to the growing biomedical research market. Their products are used by researchers who are investigating cytokines, adhesion molecules, and other components of the immunological system. They currently market over 360 specialty reagents and 54 immuno-assay kits worldwide and continue to enhance and expand its product lines. While their catalog business for research materials will remain, they are actively looking to build a new division geared towards drug discovery technologies.

Product/Partnership Status
In the past, Endogen acquired the diagnostic business of *T Cell Sciences* (subsequently became part of Avant Immunotherapeutics) and the immunoassay reagent assets of *Cytokine Sciences*, and licensed a mouse cytokine ELISA for research use from *Amersham Pharmacia Biotech* and T Cell receptors from *Becton Dickinson*. In 1997, they signed a development, distribution, and marketing agreement with *Third Wave Technologies* for mRNA quantitation kits. In May 1999, Endogen was acquired by the Swedish company, *Perstorp AB*, for $13.6 million.

Partnering Assessment
Endogen/Perstorp are very much interested in hearing of any in-licensing opportunities with regard to drug discovery technologies, for example high throughput screening and lead discovery optimization. These will typically come from industrial settings. Academic groups should continue to view the catalog business as a potential venue for new research materials, but Endogen feel it is unlikely they will come up with new drug discovery technologies.

EPIC THERAPEUTICS, INC

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Contact: Anthony Garramone, President (agarramone@epictherapeutics.com)

Profile
Epic is applying its proprietary drug delivery technology to the development of safe and practical protein and peptide therapeutics. Extensive in vivo data has demonstrated their sustained release ProMaxx microspheres can eliminate the need for frequent injections of protein or peptide based therapeutics. Sustained release formulations will add value to major protein and peptide pharmaceuticals such as alpha interferon, human growth hormone, beta interferon and anti-hemophilia Factor VIII. Their technology is also applicable to the delivery of small molecules and DNA.

Product/Partnership Status
Still in the R&D phase of their development, Epic is presently conducting clinical trials, all in the United States. They do not have any existing partnerships.

Partnering Assessment
One of Epic's funders is a Canadian VC. They are focused on drug delivery, with an emphasis on prostate cancer. They would welcome approaches from companies or academic groups involved in this area.

EPIX MEDICAL, INC

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Contact: Steve Knight, President (sknight@epixmed.com)
Randy Lauffer, CSO (rlauffer@epixmed.com)

Profile
EPIX is developing targeted contrast agents to improve the capability and expand the use of MRI as a tool for diagnosing human disease. Initial products under development include gadolinium-containing enhancement agents for MRI. The lead product, AngioMARK, is an injectable contrast agent designed for multiple vascular imaging indications, including coronary artery disease and peripheral vascular disease. It was originally developed at Massachusetts General Hospital and is presently in Phase II trials. They firmly believe that AngioMARK will significantly enhance the quality of images obtained by magnetic resonance angiography (MRA), possibly providing a clinically equivalent, non-invasive and cost-effective alternative for doctors to X-ray angiography, the current gold standard for diagnosing vascular disease. This product is the first developed from Epix's proprietary Receptor-Induced Magnetic Enhancement (RIME) platform technology.

Product/Partnership Status
EPIX currently has collaborative deals with *Daiichi Radioisotopes* and *Mallinckrodt*, both for MRI systems. They have collaborations with *Siemens, GE Medical Systems*, and *Phillips*. EPIX has recently received a $20 million equity investment from *Schering AG* in addition to a $10 million up-front fee and $20 million in milestone payments over the next few years, to be split with their partner *Mallinckrodt*. They are developing MS-325 as an agent to detect blockages in the cardiovascular system.

Partnering Assessment
EPIX do not appear to be actively seeking partnerships at this time in North America, but are doing so internationally. They have worked with a couple of Canadian principle investigators during their Phase III trials. Any molecule presentations should be directed to the CSO, while business development matters would be dealt with by the President.

EUKARION, INC

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Web: www.eukarion.com

Contact: Janet Smart, VP Corporate Development (j.smart@eukarion.com)

Profile
Eukarion is a development stage biotech company developing proprietary therapeutic products using two approaches to inactivate intracellular targets associated with diseases. The first targets ubiquitous, toxic reactive oxygen species using novel synthetic molecules, Synthetic Catalytic Scavengers (SCS). The second modifies proteins to enable their passage across cell membranes and their interaction with specific intracellular targets. Reactive oxygen species cause damage in various autoimmune, cardiovascular, neurological, and infectious diseases. The SCSs work in animal models of such diseases by catalytically eliminating the toxic oxygen reactive species, including oxygen radicals and hydrogen peroxide.

Product/Partnership Status
Eukarion had a collaborative research and license agreement with *Glaxo Wellcome* to develop products for the treatment of chronic diseases. They held onto their rights for acute neurological indications such as stroke, traumatic spinal and brain injury and carotid artery bypass surgery, and the agreement has since been terminated.

Partnering Assessment
Eukarion are carrying out contract research for a Toronto firm. They would be interested in discussion with any firms interested talking about SCSs for marketing and development. On the research side, their interest would be limited to any oxidative stress models of interest. They are actively seeking corporate partners to sponsor their research.

EXACT LABORATORIES, INC

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Web: www.exactlabs.com

Contact: Steve Lakin, Manager Business Development (slakin@exactlabs.com)

Profile
Exact is a newly formed company developing molecular diagnostic tests for the early detection of colorectal cancer. They intend to establish a clinical reference lab that will specialize in testing services to reduce mortality from colorectal cancer. Their approach is based on extracting DNA shed from abnormal colon cells and characterizing this DNA for mutations and genomic instability associated with colorectal cancer.

Product/Partnership Status
Exact are isolating DNA from stools to find abnormal DNA, i.e. heterogenous detection to lead to new gene markers, especially for the lung and pancreas.

Partnering Assessment
Exact are interested in partnering with companies who have chemotherapeutics in trials and would benefit from their monitoring abilities.

FOCAL, INC

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Web: www.focal.com

Contact: Ron Rudowsky, VP Sales and Marketing (rrudowsky@focal.com)

Profile
Focal develops, manufactures and commercializes synthetic, absorbable, liquid surgical sealants based on their proprietary polymer technology. Their family of products is being developed for use inside the body, with or without sutures and staples, to seal leaks resulting from lung, neuro, cardiovascular and gastrointestinal surgeries. They believe that their formulations, which are designed to have absorption times that parallel long-term and short-term synthetic absorbable polymer sutures, will be widely applicable in cardiovascular and gastrointestinal surgery, and other surgical applications.

Product/Partnership Status
FocalSeal-L is currently available in Europe and several other countries through the *Ethicon* unit of *J&J*. They recently announced that they had received marketing approval for Canada for the above product for lung surgery. *Genzyme's* Surgical Products Division will sell the product in Canada for Focal. Focal also has a collaboration with the *Montreal General Hospital Research Institute* to evaluate the effectiveness of their polymers in the local delivery of cancer drugs in a preclinical study. Investigators will deliver cancer drugs directly to the site of a tumor using Focal's polymers as the delivery vehicle. They have also had a collaboration with *Novartis Pharmaceuticals* and *Chiron* under which those companies funded development of a polymer-based local drug delivery system for anti-restenosis agents being developed by them.

Partnering Assessment
While Focal's interests in the North American market are very much being handled by *Genzyme Surgical Products*, they would be happy to entertain any interest in other potential applications of their technologies, not only its sealants, but also its polymers as drug delivery vehicles.

GELTEX PHARMACEUTICALS, INC

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Web: www.geltex.com

Contact: Tim Noyes, VP Business Development (tnoyes@geltex.com)

Profile

GelTex is engaged in the design, development and commercialization of a range of novel, non-absorbed pharmaceuticals that bind to and selectively eliminate target substances from the gastrointestinal tract. Their unique technology combines principles of molecular recognition and advanced polymer science to create drug that offer either significant improvements over available agents or treat diseases for which no effective therapy is available. Their products are orally administered, are not absorbed by the bloodstream and are eliminated from the body through normal digestive processes.

Product/Partnership Status

GelTex's lead product, Renagel, is approved in the US for the reduction of serum phosphorus in patients on hemodialysis, under review in Europe and in Phase II in Japan. They have a 50/50 joint venture with *Genzyme* to commercialize the product worldwide, except in Japan and the Pacific Rim, where it will be marketed by *Chugai/Kirin Pharmaceutical* (it is currently in Phase III trials there). A second product, Cholestagel for the treatment of hypercholesteremia, a condition characterized by undesirably high blood cholesterol levels, is under review. Late last year, GelTex signed an agreement with *Sankyo Pharma* on the licensing of Cholestagel. They are also working on an anti-obesity drug that acts to bind fat as well as polymer drugs for the treatment of non-systemic infections. Sublicensing agreements are in place with *Nippon Kayaku* whereby Geltex grants Nippon exclusive rights to develop and market a polyamine for cancer indications in Japan, and with *Schein Pharmaceutical* for exclusive rights to make and sell an injectable iron chelator in the US, EU, Canada, Cyprus, Australia and New Zealand.

Partnering Assessment

As a young company without its own sales force, Geltex's commercialization strategy has very much relied on developing partnerships. The stage of development at which they seek a partner varies according to the project, but typically they look for a partner with US and EU sales and marketing resources. No interaction has been had with the Canadian industry.

GENETICS INSTITUTE

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Contact: John Ripple, Director Business Development (jripple@genetics.com)

Profile
GI is a wholly owned subsidiary of *American Home Products* and is a leading biopharmaceutical company engaged in the discovery, development and commercialization of human pharmaceuticals through recombinant DNA and other technologies. They have a diversified portfolio of licensed and proprietary pharmaceutical products at various stages of development, including treatments for anemia, hemophilia, cancer bone damage, inflammatory conditions and infectious diseases. In addition to its Massachusetts R&D and production facilities, GI has offices in Paris and Tokyo.

Partnering Assessment
Much of the technology assessment for the Wyeth-Ayerst part of American Home Products is done via GI. The following are their technology interests.

- Therapeutic product candidates including small molecules, peptides and proteins that are agonists or antagonists of physiologic and/or pathogenic processes
- Molecules that are targets for therapeutic intervention
- Receptors and ligands involved in pathological processes
- Reagents and methods for performing manipulations in cells or whole animals, for example for targeted gene expression
- Reagents and methods for performing routine lab tasks, for example protein or gene sequencing
- Reagents, models and methods used in research, for example cell lines or knockout animals

Their technology acquisition interests are broken down as follows:

Women's Health
(Hormone replacement, oral contraception, osteoporosis, endometriosis, cancer)
- Progestins
- Tissue specific estrogen receptors
- Novel steroid hormone targets
- Differentiation of osteoblasts from stem cells
- Molecular biology of osteoblasts
- Differential display results indicating novel drug targets

Central Nervous System
(Alzheimer's, Anxiety, Depression, Schizophrenia, Sleep Disorders, Epilepsy, Nerve Repair, Migraine)

- Novel therapeutic approaches to Alzheimer's
- Ion channel genes and receptor assays (e.g., potassium, serotonin, glutamate)
- Genomics of Alzheimer's
- Biology of neuronal apoptosis
- Neural effects of estrogens
- Novel therapeutic approaches to schizophrenia and migraine
- Role of serotonin in cognition
- Differential display results indicating novel drug targets (especially anti-depressants and anti-psychotics)

Infectious Disease
(Antibacterials, antivirals B Herpes Viruses, Varicella-Zoster Virus, Cytomegalovirus, Hepatitis C B antifungals)

- Natural products/chemicals
- Novel non-resistant anti-bacterials
- Novel essential gene targets
- Cell division gene screens
- Hepatitis C drug screens

Oncology
(All cancers and particularly in-licensing prostate and colon, with no interest in cytotoxics, cytostatics, radiosensitizers, or adjuvant agents)

- Angiogenesis/metastasis
- Signal transduction
- Metalloproteases
- TNF metabolism inhibition
- Tumor apoptosis
- Tumor targeting with humanized monoclonal antibodies
- Novel molecular targets
- Assays for drug screens
- Mouse tumor models

Hemophilia/Clotting Disorders
(Hemophilia A and B, von Willibrand's Factor Deficiency)

- Gene therapy including nonviral gene delivery methods
- Suppression of inhibitor formation
- Alternative modes of administration
- Disease-specific models

Inflammation/Immunology
(Rheumatoid arthritis, transplantation, osteoarthritis, autoimmune diseases, allergy and

asthma, cancer)

- Immunosuppression/activation
- Cytokine discovery and blockage
- Cell trafficking/selection inhibitors
- Cytoplasmic phospholipase A2
- Hematopoesis
- Antibodies
- T-cell biology
- Costimulation and antigen presentation
- Bioassays
- Mouse autoimmune models
- Receptor-ligand interactions
- Knockout and transgenic mice
- Protein and DNA sequencing
- Antibody-based technologies
- Nonhuman SSTs

Tissue Repair

(Bone, cartilage, tendon and ligament repair, pancreas repair, neuron regeneration, muscle regeneration)

- Bone morphogenic proteins (BMPs)
- Growth differentiation factors (GDFs)
- Inhibitors of BMPs and GDFs (noggin, chordin)
- Pancreas biology
- Protein and peptide delivery
- Biomaterials and matrices for delivery
- Primary cell and organ culture
- Cloning
- Immunohistochemistry
- Xenopus misexpression
- Chick development assays
- Protein chemistry
- Transgenic gene expression
- Histology

Vaccines

(Herpes, Meningitis, Streptococcus, Respiratory, Encephalitis, Pneumonia, Influenza, Helicobacter)

- Vaccine adjuvants
- Polyvalent antigens
- Vaccine delivery

They have no diagnostic or device licensing interests, except in Women's Health to support the use of therapeutics.

Genomics/Chemistry

- Bioinformatics software and databases for drug discovery
- Computational chemistry
- cDNA gene expression assays
- Antibiotics that validate drug discovery targets
- X-ray crystallography determinations of drug targets

Research Tools

- Transgenic disease animal models
- Transgenic and knockout mice
- Developmental biology systems as functional assays for protein therapeutics (mouse, chick embryo culture, Xenopus)
- Toxicity pharmacogenetic drug screens
- Rapid development of humanized monoclonal antibodies
- Anti-sense
- Gene therapy therapeutics
- Protein and DNA sequencing
- Nonhuman SSTs
- Mouse autoimmune models
- Antibody-based technologies

GENETIX PHARMACEUTICALS, INC

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Web: www.genetixpharm.com

Contact: Ronald Dorazio, President (rdorazio@genetixpharm.com)

Profile
Genetix is a privately-held development stage biotech company developing gene therapy strategies for cancer and other chronic diseases. The core technology includes a proprietary retroviral packaging cell line that has been proven safe at the manufacturing level and in the clinic, as well as powerful gene expression enhancer elements. Current clinical research involves a Phase I/II trial of a chemotherapy-resistant bone marrow in cancer patients at Columbia University's Presbyterian Hospital in New York and at Toronto Hospital in Canada, where the multi-drug resistance gene is transduced ex vivo into hematopoietic stem cells. Those cells are then infused back into the patient with the hope of enabling transduced cells to withstand the toxicity of chemotherapy. Their research focus is on hematopoiesis and functional genomics.

Product/Partnership Status
Equity funders include *Johnson & Johnson Development Corporation* and *RPR/Gencell.* They have one announced deal with *Cordis*, a unit of *Johnson & Johnson,* and one other unannounced partnership, both in the cancer and AIDS areas..

Partnering Assessment
Genetix plans to develop its products to an appropriate stage, plus identify additional product opportunities for treating chronic diseases via long-term gene therapy. This may include in-licensing therapeutic genes for combination with their own vectors with the candidate products then being co-developed with a corporate partner for market approval. They are seeking corporate partners who have commercial rights to therapeutic genes for cancer, cardiovascular disease and other serious, chronic diseases, and for which long-term gene therapy is a logical product. In addition, companies with strong franchises in the treatment of such chronic diseases may be interested in co-developing novel gene therapy products, using Genetix's proprietary genes and vectors. They will provide non-exclusive licenses to companies wishing to use their retroviral vector, GenPak, and its ecotropic version, GP+E86, as research tools to transduce and integrate cDNAs into cell lines and mouse models for functional genomics assays.

GENOME THERAPEUTICS CORP.

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Web: www.genomecorp.com

Contact: Tony Del Campo, Director of Business Development
(anthony.delcampo@genomecorp.com)

Profile
Genome has been active in the genomics field for a decade. It is using and improving its strength in multiplex, high-throughput sequencing primarily to identify likely targets for drug design, focusing initially on M. tuberculosis and H. pylori, and other major bacterial pathogens. They are also working on human genes involved in disease, including cancer and CNS disorders such as manic depression and schizophrenia. They work with the pharmaceutical industry to improve the process of drug discovery. Their dual focus is in pathogen and human genomics.

Product/Partnership Status
Genome has signed four exclusive genomic alliances, three in pathogen genomics and one in human genomics. These are with *American Home Products* (osteoporosis), *bioMerieux* (infectious disease diagnostics), *Schering-Plough* (antifungals, asthma, and drug-resistant bacteria), and with *AstraZeneca* (Helicobacter pylori). They have signed PathoGenome Database subscriptions with *bioMerieux, Hoechst Marion Roussel, Scriptgen Pharmaceuticals, Schering-Plough, Bristol-Myers Squibb, Compugen* and *Bayer*. In their sequencing center they are working with *Hoechst Marion Roussel, Cubist Pharmaceuticals, Phylos, the Mouse Genome Sequencing Network, Biogen, Memorial Sloan Kettering Cancer Center, Cancer Research Center at Queen's University* in Belfast, Northern Ireland, and the *Human Genome Project*. Finally, Genome has collaborated with *ArQule* on the development of novel anti-infectives, *Versicor* on antibacterial compounds, *Byk Gulden* on the helicobacter pylori genome, *Cadus Pharmaceuticals* on G protein-coupled receptors (GPCRs), and with *Creighton University* on osteoporosis and high bone mass studies. They have licensed p53 tumor suppressor gene targets from *Princeton University*, yeast gene patents for infectious diseases from *Merck*, and a multiplex sequencing technique from *Harvard University*. They have a collaborative research agreement for the HDL-regulatory gene with *Massachusetts General Hospital* and *Tufts University*.

Partnering Assessment
Highly collaborative company and all partnership questions should refer to Business Development department. Interested in talking with companies/instititions possessing chemistry capabilities, any compounds with antiinfective traits, targets in cancer and/or the cardio field, and appropriate technologies.

GENZYME CORPORATION

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Contact: Richard Douglas, SVP Corporate Development (rdouglas@genzyme.com)

Profile

Genzyme is a highly diversified human healthcare company with product development, manufacturing and market capabilities in biotherapeutics, diagnostic products and services, and pharmaceuticals. They have four divisions, each with their own common stock. GENZYME GENERAL develops and markets health care products and services, including therapies for rare genetic diseases and other specialized therapeutics, genetic diagnostic services, and diagnostic products. GENZYME TISSUE REPAIR is a leading developer of biological products for the treatment of cartilage damage, severe burns, chronic skin ulcers, and neurodegenerative diseases. GENZYME MOLECULAR ONCOLOGY develops molecular approaches to cancer diagnosis and therapy through genomics, gene therapy, genetic diagnostics, and a small-molecule combinatorial chemistry drug discovery program. It was formed after the acquisition of *PharmaGenics*. GENZYME SURGICAL PRODUCTS is an established specialty surgical products business that develops and markets a comprehensive portfolio of instruments, devices, biomaterials and biotherapeutics primarily for the cardiovascular and general surgery markets. It plans to become a defining leader in the field of Abiosurgery@, the convergence of mechanical and biological approaches to surgical and other interventional procedures, with a focus on developing and commercializing gene therapy, cell therapy and other biosurgery products to treat cardiovascular disease.

Product/Partnership Status

Therapeutics

The first two therapeutics from Genzyme were Ceredase and Cerezyme, two replacement enzymes for people with Type 1 Gaucher's Disease, a chronic genetic disorder causing fatigue, anemia, and bone erosion leading to bone pain and frequent fractures. Two newer products are Renagel, developed by and commercialized with *GelTex Pharmaceuticals*, for reduction of serum phosphorus in patients with end-stage renal disease, and Thyrogen, to be sold by *Knoll Pharmaceutical*, for follow-up screening of patients who have been treated for thyroid cancer. Other products are in research.

Diagnostics

Clinical diagnostics is primarily focused on supplying product for use in the clinical chemistry, immunochemistry and infectious disease areas of the lab.

Gene Therapy

One of the largest gene therapy programs in the world, it was commenced in 1991 to develop treatments for cystic fibrosis. Since then its efforts have been expanded to target cardiovascular disease, cancer, and lysosomal storage disorders (Gaucher's and Fabry's disease). They have established more than a dozen gene therapy research collaborations

with academic groups to focus o these targets. In the lysosomal storage disorders area, Genzyme has a research agreement with the *University of Pittsburgh* and a development agreement with *Genovo*. In the cancer area, Genzyme Molecular Oncology is working with the *National Cancer Institute* (melanomas) and *Dana Farber Cancer Institute* (breast and ovarian cancer vaccines).

Genetics

Genzyme Genetics is providing a range of services, including prenatal biochemistry, prenatal, postnatal and cancer cytogenetics, and fluorescence in situ hybridization (FISH). It is the largest provider of genetic services in the US. In 1996 they formed a JV with *Symbiomed* for Aristogen for genetic diagnostics.

Molecular Oncology

Genzyme Molecular Oncology has entered into collaborations with academic and commercial leaders to develop cancer immunotherapies, angiogenesis inhibitors, and cancer pathway regulators. Commercial collaborators include *Schering-Plough* (lipid delivery system for p53), *Merck* (screening technology for MDM2 protein) *Isis/AstraZeneca* (non exclusive license to antisense compounds), *Hybridon/Searle* (antisense MDM2 inhibitors patent license), *Parke-Davis* (SAGE technology), *Bayer* (access to Genzyme's library and HTS screening), *Monsanto* (SAGE for agricultural work) and *Novartis* (SAGE for agricultural work). Academic collaborators include *National Cancer Institute, Dana Farber Cancer Institute, Ludwig Cancer Research Institute, Johns Hopkins University* and *The Children's Hospital Medical Center*. In the biotech arena, they have worked with *Ontogeny* (libraries using SAGE systems), *Xenometrix* (gene expression profiling), *Hexagen* (gene expression for diabetes), *Reprogen* (invitro diagnostics and a reproductive drug), and *Compugen* (SAGE database).

Pharmaceuticals

Genzyme offers a wide range of high-quality drug delivery materials and expertise, including synthetic lipids, hyaluronic acid, pharmaceutical peptides, peptide intermediates and segments, and amino acid derivatives.

Tissue Repair

As a result of acquiring *BioSurface Technology* in 1995, and combining it with several Genzyme programs, they have strong capabilities in three essential core technologies B autologous cell processing, therapeutic protein development, and biomaterials. They offer the product Carticel for orthopedic surgeons and the Epicel Service, autologous skin grafts for burn victims. Their development portfolio includes Vianain, an enzymatic debriding agent, under investigation for the treatment of ulcers and burns, and TGF-β_2, a recombinant protein under investigation for the treatment of chronic skin ulcers. They recently licensed an autologous chondrocyte graft technology from *Sentron Technology*. In 1997, they licensed BetaKine for tissue repair and MS, and TGF binding monoclonal antibodies from *Celtrix Pharmaceuticals*. Acquisitions have also included *Biomatrix*.

Genzyme has worked with numerous other companies on various projects, including *StressGen Biotechnologies* (JV for cancer treatment), *Cubist Pharmaceuticals* (screening of Genzyme's library), *ACADIA Pharmaceuticals* (cell-based screenings), *Diacrin* (porcine cells for Parkinson's and Huntington's diseases), *Novalon Pharmaceutical* (compound library and BioKey assays), *Biogen* (for Avonex in Japan), *Dyax* (DX-88 for angioedema), *Sequenom* (DNA MassArray beta system), *ImmGenics Pharmaceuticals* (SLAM technology for monoclonal antibodies), *PolyMASC Pharmaceuticals* (gene therapy with masking technology), *Introgene* (gene therapy for Gaucher's disease),

ArQule (mapping array for cancer and infectious diseases), *Repligen* (protein A and reagent business), *Pharming* (human alpha-glucosidase for Pompe's disease), *Focal* (marketing of surgical sealant in North America), *Aronex Pharmaceuticals* (lipid-based IV formulation of tretinoin), and *BioMarin Pharmaceuticals* (MPS-1 enzyme replacement).

Partnering Assessment

Clearly, Genzyme will have multiple interests from the partnering perspective in a number of bioscience areas. Initial approaches from interested parties should go to Corporate Development in the first instance. Genzyme has a presence in Canada.

GENZYME TRANSGENICS CORPORATION

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Contact: Mike Young, VP Business Development (myoung@transgenics.com)

Profile
GTC is a subsidiary of Genzyme and specializes in transgenic technology initiated at Integrated Genetics Labs in 1985. It became a publicly traded company in 1993. It touts itself as the world's leading transgenic company, having developed transgenic and proprietary purification technology simultaneously, and is a leader in the production of therapeutic proteins in the milk of transgenic animals. They have produced over 60 therapeutic proteins, including monoclonal antibodies, plasma proteins, and certain hard-to-express proteins in the milk of mice, rabbits, goats and cows.

Product/Partnership Status
GTC is currently involved in various collaborations with several companies for the development of biopharmaceuticals, and has formed numerous strategic alliances with technology-based companies for the purpose of increasing technical efficiency and future capabilities. They are currently developing or have developed transgenic versions of monoclonal antibodies and fusion proteins for biotech and pharmaceutical concerns such as *BASF Bioresearch Corporation, B Braun, Bristol-Myers Squibb, Centocor, Lilly, Interferon Sciences, Novopharm, , NeoRx, Neoprobe, COR Therapeutics, Elan Pharmaceuticals, Abgenix* and *Progenics.* They have formed collaborations for the transgenic production of human plasma recombinant antithrombin III (rhATIII) with *Genzyme* and recombinant human serum albumin with *Fresenius.* ATIII is a plasma protein that helps to regulate blood clotting. Complementary alliances include those with *Millennium Pharmaceuticals* (early development of monoclonals and other protein candidates), *Lonza* (downstream purification of antibodies and other transgenic proteins), *DSM Biologics* (downstream purification of transgenic therapeutic albumin, *Advanced Cell Technology* (production of cloned, transgenic animals), and *Invitrogen* (marketing agreement for protein expression kit).

Partnering Assessment
GTC is interested in working with commercial partners from the biotech and pharmaceutical industries to transgenically produce therapeutic proteins.

GPC BIOTECH

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Web: www.gpcbiotech.com

Contact: Tom Needham, VP Business Development (needham@gpcbiotech.com)

Profile
GPC Biotech is a German biotech company engaged in the discovery and development of products to diagnose and treat cancer, opportunistic fungal infections, certain cardiovascular conditions and other cell proliferation disorders. The US arm is a result of the acquisition of Mitotix by the German parent. Their development programs are based on proprietary and patentable knowledge of the molecular pathways that regulate the cycle of cell growth and division. They have advanced antifungal programs targeting the cell cycle and the signal transduction pathway required for cell wall integrity.

Product/Partnership Status
Based on its cell cycle expertise, Mitotix had formed several partnerships to identify therapeutic targets and develop drugs for the treatment of cancer and restenosis. In 1995, they initiated a collaboration with *Du Pont Pharmaceuticals* to discover and develop small molecule inhibitors of cdk/cyclins, including p16, p27 and cyclins D1 and E. In collaboration with *Cell Genesys*, they are pursuing gene therapy approaches in cancer and restenosis, based on using the Mitotix-discovered cell cycle regulatory genes, p16, p27 and a p27/p16 fusion gene, to cause tumor cell death and prevent the proliferation of vascular smooth muscle cells following angioplasty. Finally, they also have an R&D collaboration with *BASF Pharma* to identify and develop novel anti-cancer therapeutics that inhibit the cell cycle regulator cdc25 phosphotase. The p27 gene for cancer and the Cyclin E gene were licensed from the *Fred Hutchinson Cancer Institute* in Seattle, while the p16 tumor suppressor gene was licensed from *Cold Spring Harbor* in New York.

Partnering Assessment
GPC will be interested in potential partnerships and collaborations in the cancer and restenosis fields.

HEMAGEN DIAGNOSTICS, INC

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Web: www.hemagen.com

Contact: Jerry Ruyan, President and CEO (jruyan@hemagen.com)

Profile
Founded in 1985, Hemagen develops and produces clinical diagnostic tests focused primarily on infectious and autoimmune diseases. Included in its product portfolio are 40 different immunoassays, along with an array of clinical chemistry tests and controls, totaling more than 115 FDA-cleared products. Recently, they have produced unique kits to measure acute phase reactants and Chagas disease. They also have facilities in Maryland, San Diego, Buffalo, and in Brazil.

Product/Partnership Status
In addition to an OEM agreement with *Carter-Wallace*, Hemagen also recently signed a long-term agreement with *Roche Diagnostics*, the largest diagnostics concern in the world, to provide reagents and diagnostic kits. They have distribution agreements in place with *Donner*, *Olympus*, and *Phoenix Diagnostics*. In addition, they have also acquired other businesses such as *ZeptoMetrix* (cellular products business), *Cellular Products* (diagnostics company), and *Dade* (Analyst bench top clinical chemistry system). Hemagen licensed a HIV staging test from *Sheffield Pharmaceuticals*.

Partnering Assessment
Hemagen are currently working with a Canadian subsidiary of *PharmaGene* on the development of an AIDS product. There interest remains purely in the diagnostics side of the business only. They are interested in any opportunities in the infectious disease and clinical chemistry areas. Increasingly, they are also looking to expand into the veterinary market and are especially interested in enhancements to their ability to afford rapid testing in the veterinarian's office. This suggests any ways to upgrade simple assays for use in the office, though it should be stressed that they also seek to service the reference lab side of the business as well.

HYBRIDON, INC

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Contact: Maggie Flanagan, Senior Director of Business Development
(mflanagan@hybridon.com)

Profile
Hybridon is a leader in the discovery and development of novel genetic medicines based primarily on antisense technology. This involves the use of synthetic segments of nucleic acid, called oligonucleitides, constructed through rational drug design to modulate protein expression by interacting at the genetic level with target messenger RNA. They have established an integrated antisense technology platform based on proprietary medicinal chemistries, analytical chemistry and manufacturing technology that is applicable to a broad range of disease targets. They are concentrating on cancer, viral diseases and diseases of the eye. Their most advanced compound is in Phase II for patients with solid tumors who have failed other treatments. Another compound for the treatment of HIV infection has completed Phase I in which oral absorption of the antisense drug was demonstrated.

Product/Partnership Status
Hybridon's current partners had included, until recently, *Searle* for the discovery and development of antisense agents for the treatment of inflammatory disorders, with additional selected targets in cancer and cardiovascular diseases. *Perkin-Elmer* is a marketing partner for research scale-up of oligonucleitides, *Pharmacia & Upjohn* for marketing of a jointly developed antisense oligonucleitide synthesizer, and *Medtronic* for CNS drug delivery technology. In 1996, Hybridon span out *MethylGene*, a biotech company based in Montreal. It is focused on the development of antisense drugs to combat cancer by inhibiting DNA methyltransferase, a regulatory protein shown to be over-expressed in some tumors, such as cell lung cancer, colon cancer and breast cancer. Their second spinout was formed early last year in Quebec as *OriGenix Technologies*, focused on the development and marketing of drugs for the treatment of infectious diseases, with an initial focus on viral diseases, notably human papilloma virus and hepatitis B virus infections. Last year, Hybridon licensed antisense MDM2 inhibitors patent to *Genzyme*. In the past they have worked with multiple leading academic institutions such as *McGill, Mount Sinai Hospital New York, Harvard, University of Massachusetts, Maryland, Worcester Foundation, Institut Pasteur, Institut Gustave Roussy,* and *Massachusetts General Hospital.*

Partnering Assessment
Currently, VEGF for cancer angiogenesis, retinopathics and psoriasis is available for partnering in the preclinical stage, as is Hep C, a lead compound for Hepatitis and liver

problems. Both Hybridon's antisense drugs, GEM 231 for cancer and GEM 92 for HIV/AIDS are available for licensing to a pharmaceutical development partner. From the academic side, they would have interest in new targets and would consider collaborations where they would provide the initial antisense molecule, where this made sense.

IMMUNOGEN, INC

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Contact: Pauline Ryan, Senior Director of Business Development
(pryan@immunogen.com)

Profile
ImmunoGen develops products that deliver chemotherapy directly to cancer cells. Called Tumor-Activated Prodrugs (TAPs), their products are small-molecule based anti-cancer agents with high potency and reduced toxicity. They are produced by combining extremely potent chemicals with monoclonal antibodies that recognize and bind directly to tumor cells. Their product portfolio is focused on TAPs for colorectal cancer, small-cell lung cancer and other aggressive malignancies. In preclinical studies, all of their products have proven to be more potent and less toxic in animals than existing chemotherapeutics. In 1993, ImmunoGen founded Apoptosis Technology (ATI), a 97%-owned subsidiary. Its objectives are to identify defects in apoptosis pathways, develop screens based on these defects, and use the screens to develop anti-cancer drugs.

Product/Partnership Status
ImmunoGen has an agreement with *SmithKline Beecham* to develop their lead TAP for the treatment of colorectal and pancreatic cancer. ATI entered into a collaboration with *BioChem Pharma* for the development of novel cancer treatment s based on apoptosis, or cell death. On the licensing front they have worked with *Pharmacia* (C242 conjugate with maytansinoid drug), *Schering-Plough* (anti-gastrin 17 immunogen for horse ulcers via *Aphton*), *Genentech* (TAP technology with Herceptin) and *Oxford Molecular* (cross-license for designing humanized monoclonal antibodies). They have a development and marketing agreement with *British Biotech* (huN901-DM1 for small-cell lung cancer). On the academic side, ImmunoGen has a collaborative research agreement with the *State University of New York* for taxane-based tumor-activated prodrugs, and options on TAP technology from *Duke University* and *Johns Hopkins University.*

Partnering Assessment
ImmunoGen is seeking further opportunities to extend the markets for its TAP technology by pursuing relationships with companies that have antibodies specific to cancer targets outside of their current portfolio.

INTERNEURON PHARMACEUTICALS, INC

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Web: www.interneuron.com

Contact: Bobby Sandich, EVP R&D (sandichb@interneuron.com)

Profile

Interneuron and its majority-owned subsidiary Intercardia are engaged in the development and commercialization of a portfolio of products and product candidates for CNS, cardiovascular and other disorders, including multiple compounds in late-stage clinical development. Their lead products are citocoline for stroke (Phase III), bucindolol for congestive heart failure (Phase III), IP501 for liver disease (Phase III) and pagoclone for panic disorder (Phase II/III). Their strategy is to acquire products with defined pathways through the clinic and to the market, focusing on products with clinical data or market experience outside the US. Interneuron also formed two other companies called *Progenitor* in Ohio which has formed multiple collaborations with top institutes in the gene therapy field, and *Transcell Technologies*. Interneuron was notable for its Redux product, marketed in tandem with *American Home Products*.

Product/Partnership Status

Licensing, marketing and development agreements with corporate partners and research institutions are integral to Interneuron's corporate strategy. The following products were in-licensed by the Company. Citocoline for stroke (*Ferrer Pharma International*), pagoclone for panic disorder (*Rhone-Poulenc Rorer*), trospium for overactive bladder (*Madaus AG*), LidodexNS for acute migraine (*Algos Pharmaceutical*), PACAP for stroke, neurodegenerative diseases and diabetes (*Tulane University*), and exclusive licenses to a broad patent portfolio (*MIT*), including brain neurotransmitters, amyloid regulators for Alzheimer's and a melatonin hormone for insomnia. Citocoline has also been out-licensed to *Takeda Chemical Industries* and pagoclone to *Warner-Lambert*. Just recently, Interneuron licensed rights to develop an AIDS-preventing contraceptive gel from *HeavenlyDoor.com* (formerly *Procept*). These are exclusive rights to develop and market PRO 2000 Gel that is being evaluated for safety and efficacy in clinical trials by the *National Institute of Allergy and Infectious Diseases* in the US and South Africa.

Partnering Assessment

Interneuron continues to look for opportunities to in-license products that have at least generated some good animal data and Phase I clinical safety data. These do not need to come from a corporate source, but can equally emanate from an academic group. Having developed products further, they will continue to then pursue a strategy of partnering with larger companies for the marketing of the products. Lidodex and PACAP are both probably still too early to represent opportunities for Canadian companies. Trospium rights are only held by Interneuron for the US market.

KINETIX PHARMACEUTICALS, INC

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Contact: Nicholas Lydon, CEO (lydon@kinetixpharm.com)

Profile
Kinetix is a privately held biopharmaceutical company specializing in the discovery and development of small molecule drugs that regulate signal transduction by inhibiting specific protein kinases. Their strategy is to rapidly discover and optimize highly selective kinase inhibitors to meet important, unmet clinical needs in the area of Immunology, Asthma/Allergy, Inflammation, and Oncology/Angiogenesis. Their discovery targets have been validated by murine gene knockouts, transgenic animal models, human gene mutations and dominant negative cellular experiments. Targets selected by Kinetix are further characterized by being tissue restricted in their expression, functionally restricted to a limited set of receptors, and receptor associated rather than generic kinases used in multiple signaling pathways.

Product/Partnership Status
At this stage, Kinetix has not partnered with anyone.

Partnering Assessment
Kinetix are in active discussions with a number of companies regarding partnership deals and would welcome more, particularly from larger biotech companies. They have a small molecule focus and are looking especially for development partners. They have not tended to work with academic groups, though they do have a three year agreement with *Harvard University* and are working with an Italian group in the cancer area.

MATRITECH, INC

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Web: www.matritech.com

Contact: Stephen Chubb, CEO

Profile
Matritech is using proprietary nuclear matrix protein (NMR) technology to develop and commercialize innovative tests that enable physicians to reliably and inexpensively detect and monitor the presence of various forms of cancer (bladder, colorectal, prostate, cervical and breast). Their NMP22 test is the first quantitative, non-invasive test for bladder cancer patients. Tests using NMP technology are in various stages of development for the other cancers. They have a European office in Freiburg, Germany.

Product/Partnership Status
Matritech has distribution agreements with *Boehringer Ingelheim* (NMP-based cancer diagnostic test kits), *Konica* (NMP22 test for cancer in Japan), *Curtis Matheson Scientific* (diagnostic products), *Grupo Grifols* (bladder cancer diagnostic in Portugal and Spain), and *Toray-Fuji Bionics* (NMP4 cell death test kit in Japan). In the past, they have licensed and supplied a NMP-based test for cervical cancer to *Bayer*, worked with *Sangtec Medical* on a breast cancer diagnostic, licensed NuMA screening for cancer drugs from *Yale University*, and had a research agreement with the *NIH* for proteins as markers for cancer.

Partnering Assessment
The January announcement that the FDA had cleared the NMP22 Test Kit for expanded use as an aid in screening previously undiagnosed individuals who have symptoms of, or are at risk for, bladder cancer, has strengthened Matritech's negotiating position with regard to strategic alliances. They will continue to seek new corporate partners.

METABOLIX, INC

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Web: www.metabolix.com

Contact: Oliver Peoples, Chief Scientific Officer (info@metabolix.com)

Profile
Metabolix is a privately held biotech company looking to create a new sustainable industry based upon a class of environmentally friendly plastics, known as PHAs (polyhydroxyalkanoates). Their proprietary transgenic technologies allow PHA plastics to be produced by photosynthesis, either indirectly by fermentation, or directly in plant crops. After use, the plastics may be recycled, hydrolyzed or allowed to biodegrade. The PHA plastics have a wide range of properties with anticipated applications ranging from packaging, disposable diapers, lawn and leaf bags, fast food service ware, to paints and medical devices. The company's technology offers the promise of environmentally friendly plastics with price and performance levels that are competitive with oil-based plastics. This metabolic engineering was pioneered at MIT.

Product/Partnership Status
Metabolix has no partnerships at this time, since they are focused on the development of their product and will wish to develop them themselves.

Partnering Assessment
Metabolix does have a Canadian subsidiary in Calgary. If they were to partner with any companies, their primary interest would be with the major plant science companies. In terms of academic collaborations, they would wish to hear from plant science groups that may be able to offer unique insights in their particular area of expertise.

MICROBIOTIX, INC

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Contact: Wendy Rieder, VP Business Development and COO
(WRieder@Microbiotix.com)

Profile
Microbiotix is a drug discovery and development company with an emphasis on anti-infective agents that inhibit nucleic acid synthesis. Their current research focus is on the development of novel antibiotics to inhibit DNA polymerases in Gram+ and Gram- bacterial infections, especially those that are resistant to conventional antibiotics.

Product/Partnership Status
Microbiotix recently partnered their first major technology platform with *BioChem Pharma* in an R&D collaboration which also involved equity funding from BioChem.

Partnering Assessment
Microbiotix continues to seek partners to collaborate in the research and development of their anti-infectives technology, as well as any new opportunities for in-licensing promising early stage technology developed by others, corporate or academic. They have a particular interest in small molecule compounds that inhibit DNA replication in bacteria and viruses. Though they have no expansion plans outside Worcester at this time, a Canadian location would definitely be considered, and there is a definite interest in seeking venture funding from Canadian investors, a route they will be actively pursuing in the near future.

MILLENNIUM PHARMACEUTICALS, INC

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Contact: Peter Williams, Senior Director of Business Development
(pwilliams@mpi.com)
Ian Nisbet, Program Director for Therapeutics
(nisbet@mpi.com)

Profile

Millennium is a leading drug discovery and development company, incorporating large-scale genetics, genomics, high throughput screening and informatics in an integrated science and technology platform. This innovative drug discovery platform is applied across the entire healthcare sector, from gene identification through patient management, to accelerate and transform the discovery and development of proprietary therapeutic and diagnostic products and services. It is organized as a family of companies to create value in small molecules, biotherapeutics, and predictive medicine. These divisions include Millennium BioTherapeutics, Millennium Predictive Medicine, and Millennium Pharmaceuticals and the newly acquired LeukoSite. Their research programs are focused on major common diseases, including obesity, Type II diabetes, cardiovascular diseases, oncology, CNS disorders, respiratory disease, bacterial diseases and fungal diseases.

Product/Partnership Status

Millennium has entered into significant multi-year R&D partnerships with major pharmaceutical partners with more than $1 billion in potential partnership funding. These are with *Aventis* (small molecules for inflammation), *Hoffmann-La Roche* (obesity and Type II diabetes), *Pfizer* (fungal diseases as a result of the acquisition of *ChemGenics* in 1997), *Eli Lilly* (select cardiovascular diseases, such as atherosclerosis and congestive heart failure, and select areas of cancer), *AstraZeneca* (respiratory inflammatory diseases), *American Home Products* (CNS disorders, such as anxiety, depression and schizophrenia, and bacterial diseases), *Becton Dickinson* (select areas of cancer), *Bayer* (a goal of 225 important new drug targets as relevant for cardiovascular disease, osteoporosis, pain, cancer, liver fibrosis, hematology and viral infections). In addition Millennium has forged technology transfer collaborations with *Lilly* (atherosclerosis), *AstraZeneca* (inflammatory respiratory diseases), and *American Home Products* (CNS) each gaining certain genomics technologies, primarily high throughput sequencing, informatics and transcriptional profiling. *Monsanto* has a broad five-year collaborative agreement relating to the application of genomics technologies in Monsanto's life-science-based businesses, with Monsanto establishing a wholly-owned subsidiary called *Cereon Genomics LLC.* Millennium also has collaborations with *Caliper Technologies* (microfluidic systems for genomic targets), *Lexicon Genetics* (human gene trap and OmniBank databases, and custom knockout mice), *Biacore International* (SPR array chip), *Incyte Pharmaceuticals* (LifeSeq database access), and *Taisho Pharmaceutical* (letter of intent for LDP-977 in Asia and Europe).

Separately, Millennium BioTherapeutics, has a strategic alliance with *Lilly* in the field of therapeutic proteins, a development collaboration for monoclonal antibody production with *Genzyme Transgenics,* a collaboration with *Abgenix* for a XenoMouse for an inflammation antigen and one for an anti-inflammation antigen. They have a functional genomics collaboration with *Harvard University.*

Millennium Predictive Medicine has a strategic alliance with *Becton Dickinson* in the diagnostics field and one with *Bristol-Myers Squibb* in pharmacogenomics for oncology clinical markets.

The acquisition of LeukoSite brought many more deals into the fold. These included agreements with *Morphosys* (development and research of human therapeutic antibodies), *Boehringer Ingelheim* (a manufacturing agreement for the supply of CAMPATH), *Medarex* (development and licensing agreement of transgenic technology for humanization), *Schering AG* (Campath for CLL adult leukemia), *Parke-Davis* (small molecule inhibitors), and *Ilex Oncology* (joint development of a leukemia drug).

Partnering Assessment

Millennium will continue to look for a variety of relationships in disease-specific therapeutic areas, diagnomics and antibodies. They will also seek relationships which involve the transfer of high throughput processes for discovery and development of their life sciences products. Millennium is very acquisitive and its pharmaceutical deals have given it plenty of financial muscle. They will always be interested in any drug discovery technologies, novel gene targets and any associations between genes and disease. In the case of licensing opportunities or new technologies contact should be made with Peter Williams. In the case of therapeutics that have reached or passed the IND stage contact should be made with Ian Nisbet.

MOLECULAR GEODESICS, INC (Tenegra)

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Contact: Alison Skinner, CEO (askinner@molec-geodesics.com)

Profile
Molecular Geodesics is developing synthetic biomimetic materials that mimic the microstructural organization, mechanical responsiveness, and biochemical processing capabilities of living cells and tissues. Their approach is based on the recent discovery of fundamental geodesic building rules that guide biological organization at the molecular, cellular, and tissue levels. By combining these recent advances in molecular cell biology and bioengineering with new developments in polymer chemistry and computer-aided design and manufacturing, they will synthesize artificial Atissues@ and Aorgans@ that incorporate these design principles, material that may be used for biomedical, industrial, and military applications. They have just renamed the company as ATenegra@ in addition to moving their headquarters from downtown Boston.

Product/Partnership Status
Geodesics has a research collaboration with *Johnson & John· on* who are also an equity investor in the company.

Partnering Assessment
Describing themselves as a full-blown product development company, the company will continue to seek appropriate partnerships, though J&J are clearly very Ainvolved@ in the company and its principals are very much ex-J&J personnel. Their academic collaborations will tend to relate to clinical testing, either biomechanical or with animals. They are in the process of establishing a technical collaboration with a prominent Canadian institution and can foresee working with others on the clinical side.

NEOGENESIS DRUG DISCOVERY, INC

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Web: www.neogenesis.com

Contact: Satish Jindal, President (satjin@neogenesis.com)

Profile
NeoGenesis is a drug discovery company focused on applying advanced genomic techniques in conjunction with traditional techniques involving novel solution phase small molecule combinatorial libraries and highly sensitive screening methodologies to develop drugs against infectious diseases and therapeutics for human diseases associated with damaged or mutated genes.

Product/Partnership Status
They are currently in discussions for an alliance with a major Canadian biotechnology concern and are also putting together a term sheet for a potential partnership with another entity in Montreal. Previously, they have forged relationships with *Inspire Pharmaceuticals* (collaborative research into NeoMorph combichem libraries for the respiratory area) and with *Creative Biomolecules* (research into orally available small molecules).

Partnering Assessment
NeoGenesis is looking to forge creative strategic partnerships and, as can be seen from above, they are actively involved in and have an interest in alliances with Canadian pharmaceutical and biotechnology companies.

NITROMED, INC

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Contact: Joseph Grimm, CFO and VP Business Development
(jgrimm@nitromed.com)

Profile
NitroMed is seeking to become the leading supplier of nitric oxide based drugs designed to treat cardiovascular, gastrointestinal, pulmonary, and neurodegenerative diseases and male erectile dysfunction. Their technology is highly proprietary. Their medicines are capable of reducing the gastric toxicity of NSAIDs, increasing the efficacy of alpha blockers in the treatment of male erectile dysfunction, increasing the efficacy of tPA in the management of restenosis and acute myocardial infarction, reducing the rate of angioplasty associated restenosis and improving the efficacy of inhaled steroids and anticholinergics and other drugs in the treatment of asthma.

Product/Partnership Status
NitroMed has two existing corporate partnerhips, one with *J&J's Ortho-McNeil Pharmaceutical* subsidiary and the other with *J&J's Cordis Interventional Cardiology* Company. The Ortho-McNeil agreement is worldwide and uses their technology to reduce the GI-toxicity of existing NSAIDs. The Cordis agreement is also worldwide and is aimed principally at reducing the incidence of restenosis post angiopl[illegible]y covers certain stents. Additional in-house efforts are focused on male erectile d[illegible]ction (MED) and female sexual dysfunction (FSD).

Partnering Assessment
NitroMed will be interested to hear from any group involved in Nitric Oxide research or the MED FSD area.

NOVIRIO PHARMACEUTICALS, INC

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Contact: James Egan, VP Business Development (egan.james@novirio.com)

Profile
Novirio is a biopharmaceutical company focused on the discovery, development and commercialization of therapeutics for the treatment of life threatening viral diseases. Their principal targets are viral hepatitis and HIV/AIDS. Founded in 1998, the company is the culmination of years of private and academic research and development of antiviral therapies by its founders, leveraging its relationships and expertise in the scientific community. Their research network comprises over 100 scientists throughout the US and Europe.

Product/Partnership Status
Novirio has a collaborative research program with the *University of Cagliari* in Italy. Other agreements include those with the *University of Montpelier* and *Centre National de la Recherche Scientifique.* With the company at such a young stage of development, no corporate partnerships are, as yet, in place. They expect to produce clinical candidates within these areas beginning in 2000. Initial targets include:

HIV/AIDS
- < Nucleoside reverse transcriptase inhibitors (NRTI)
- < Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- < Integrase inhibitors

Hepatitis B
- < Specific inhibitors of viral DNA polymerase of HBV

Hepatitis C
- < Specific inhibitors of viral RNA-dependent RNA polymerase of HCV

Partnering Assessment
Novirio would be interested in hearing from any groups, industrial or academic, working in the area of antiviral research. They have one therapeutic in early clinical trials and two expected to enter trials later this year.

ONTOGENY, INC.

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Web: www.ontogeny.com

Contact: Raul Rodriguez, VP Business Development (raul@ontogeny.com)

Profile
Ontogeny is a privately held biotech company applying recent breakthroughs in the pioneering field of developmental biology (study of how cells, tissues and organs change as they interact during development) to human therapeutics. Ontogeny is the process whereby an organism changes its size, shape and organization from a fertilized egg to a mature individual. The same processes and molecules that are active during development are reactivated in adult regenerative processes. They are identifying ways to rejuvenate damaged systems by looking at the signaling processes of cells during development and restoring them in adults to trigger repair and regeneration. Their focus is on Ontonscreen (developmental biology-based screening system), neurodegenerative diseases (Parkinson's, Alzheimer's stroke), bone and cartilage disorders and repairs infertility, diabetes, and cancer.

Product/Partnership Status
Ontogeny has recently announced its intent to merge with two other local firms, *Creative BioMolecules* and *Reprogenesis*, the goal being to create a new regenerative medicine powerhouse to be called *Curis*. Their first alliance in 1996 was with *Biogen* and focused on the use of hedgehog proteins with a primary emphasis on CNS disorders. This was extended until 2001 and expanded to include certain areas of gene therapy. They are partnered with *Genetics Institute's* DiscoverEase program to give Ontogeny access to novel secreted proteins supplied by GI. In 1998, they partnered with *Genzyme Molecular Oncology* who will produce SAGE libraries enabling them to analyze differential gene expression. Early last year, they signed a partnership agreement with *Perkin-Elmer's Tropix* who will perform ultra-high-throughput screening of large combinatorial compound libraries for activity against Ontogeny's biological targets. The most recent corporate partnership is with *Becton Dickinson*, a collaboration focused on cell-based therapy for diabetes. They also entered a collaboration with *Oxford Assymmetry International* to optimize small molecule leads derived from its developmental pathway-based assays. Finally, Ontogeny has organized a consortium of leading academic dermatological oncology centers for the development of the company's leads in the areas of skin and hair growth. Participating are *Brigham & Women's Hospital* and the *University of California San Francisco.*

Partnering Assessment
Assuming that the Ontogeny shareholders approve the Curis merger sometime in June 2000, all Ontogeny opportunities will revert to Curis.

ORGANOGENESIS, INC

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Web: www.organogenesis.com

Contact: Greg Downing, VP Business Development
(downing@organogenesis.com)

Profile
Organogenesis designs, develops and manufactures medical therapeutics containing living cells and/or natural connective tissue components. Their products are designed to promote the establishment and growth of new tissues to restore, maintain or improve biological function. Apligraf is the first manufactured living organ skin to be approved for marketing by a major regulatory agency (Canada). In 1997, they received FDA marketing clearance for GRAFTPATCH for use in general surgical procedures involving reinforcement of soft tissue. Other programs include living tissue products for surgical reconstruction and repair, a liver assist device for liver-compromised patients, culturing islet cells for the treatment of diabetes, a small diameter graft for coronary artery bypass and peripheral vascular procedures, and products for female urinary incontinence.

Product/Partnership Status
Novartis Pharma has Apligraf skin and tissue global marketing rights. Last year, Organogenesis had an agreement with *Baxter* for liver assist devices, and, previously, they had had an agreement with *SciMed Life Systems* for the development and manufacturing of collagen-coated endovascular devices. They have a variety of research agreements with institutions including *Massachusetts General Hospital, Brigham & Women's Hospital, Harvard University,* and *Children's Hospital*, all in Boston.

Partnering Assessment
Organogenesis will have an interest in hearing from groups involved in the connective tissue field.

PENTOSE PHARMACEUTICALS, INC (V.I. Technologies)

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Web: www.pentose.com

Contact: Martin Williams, VP Business Development (mwilliams@pentose.com)

Profile
Pentose was founded to discover, develop and commercialize antiviral products for medical use based on nucleic acid chemistry. The first two product lines are Papirines, a family of antiviral pharmaceuticals including PEN203, and Inactines, a group of virus inactivating compounds including PEN103 and PEN113. These are proprietary technologies with near term commercial potential and which have global application for the treatment of specific viral infections and for inactivating viruses in blood products and biopharmaceuticals. They describe their approach to virology as a distinct departure from previous antiviral methods, being based on advanced understanding of the organic chemistry of nucleic acids.

Product/Partnership Status
Pentose merged last year with *VI Technologies (VITEX).* Previously, Pentose had forged a development and licensing agreement with *Cangene* for viral inactivation for manufacturing. Prior to the acquisition, they had had an agreement with V.I. Technologies for the viral inactivation of transfusion plasma.

Partnering Assessment
Pentose/V.I. Technologies is interested in forming partnerships with pharmaceutical companies to help with marketing its products and partially to offset the cost of drug development. Additionally, they are interested in continuing collaborations with noted scientific researchers in academia and government that will add breadth to their in-house scientific programs.

PERIODONTIX, INC

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Watertown, MA 02172
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Web: None

Contact: Robert Linke, CEO (rlinke@periodontix.com)

Profile
Periodontix is developing a broad range of products to treat all stages of periodontal disease, an infection of the gums and supporting structures of the teeth and a major cause of tooth loss in adults. There are no effective therapeutic products available to treat the disease. Current therapy involves mechanical and surgical treatment of infected sites and antibiotic therapy to halt progression. They are developing products to be used by dentists and periodontists, as well as by individuals for personal care to treat the disease and help maintain healthy gums and prevent infection or reinfection. The products are based on anti-microbial peptides derived from proteins found in saliva. These proteins, called Histatins, have evolved to help the body defend itself against periodontal disease. In addition, they are developing other anti-infective technologies that would be used by dental professionals as adjunctive therapy to treat severe cases of periodontal disease, including those leading to surgical cases.

Product/Partnership Status
Currently, Periodontix's pipeline consists of three proprietary antimicrobial therapeutic agents and one drug delivery system. The most advanced product is HistaWash, a histatin mouthrinse that just successfully completed a Phase IIB clinical trial.

Partnering Assessment
Approaches should be made to Periodontix by appropriate corporate and academic groups involved in the periodontal area.

PHYLOS, INC

128 Spring Street
Lexington, MA 021421
Tel: (781) 862-6400
Fax: (781) 402-8800
Web: www.phylos.com

Contact: Ashley Lawton, CEO (alawton@phylos.com)

Profile
Phylos is a privately held biotech company applying the principles of an in vitro selection and evolution to peptides and proteins. The technology was discovered at Massachusetts General Hospital and licensed exclusively to Phylos. Phylos plans to apply this technology to improvement of existing proteins and the development of alternatives to such proteins which fall outside the scope of existing patent protection. They are poised to exploit opportunities for directed protein evolution and the detection of protein-protein interactions across a broad spectrum of commercial applications, including those in the pharmaceutical, diagnostic, agricultural, chemical, and food processing industries.

Product/Partnership Status
In 1998, Phylos established a five-year collaboration with *Aventis*,, part of the *Hoechst* group, to develop one of its technologies, PROfusion. Last year, they signed an agreement for the development of anti-infective assays with *Cubist Pharmaceuticals*. They also have a deal with an, as yet, undisclosed company.

Partnering Assessment
Phylos have an interest in talking with anyone working with in vitro translation systems, protein folding, protein chip technology, and detection technologies. In addition, they are interested in any new genomics or proteomics technologies. They are also interested in high affinity peptides along the lines of their Cubist deal. Finally, they have available for use human libraries to look for proteins.

PHYTERA, INC

Four Biotech Park
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Web: www.phytera.com

Contact: Nancy Wetherbee, VP Business Development (nwetherbee@phytera.com)

Profile
Phytera is a global biotech company focused on the discovery, development and marketing of innovative drugs to treat major medical problems. Their proprietary approach is based on a platform of unique and novel culture technologies that access the untapped chemical diversity and pharmaceutical potential of both plants and marine microorganisms. They have developed a unique approach to the chemical extraction of natural species that enriches the resultant extracts in potentially novel chemicals. These technologies are coupled with robotic screening against novel targets for infectious diseases, state of the art natural products chemistry and combinatorial synthesis techniques. They operate a wholly owned subsidiary in the UK and in Denmark, and have additional R&D activities underway in Europe, the Far East and South America.

Product/Partnership Status
To date, Phytera has signed collaborative agreements with *Nycomed Amersham* (plant derived enzymes for research lab use or clinical diagnostics), *Tsumura* (inflammation and allergy), *Galileo Laboratories* (stroke and myocardial infarction), *NeuroSearch A/S* (asthma, depression, diabetes, memory and attention deficit disorders), *Chiron* (cancer and other areas), *Eli Lilly* (fungal disease/MDR knockouts), and *Unilever* (personal care products). In addition, last year, they signed a collaborative agreement with Costa Rica's *Instituto Nacional de Biodiversidad (INBio)* to source plant species from Costa Rica's biodiversity.

Partnering Assessment
Phytera is always looking out for prospective partners and has already identified several Canadian biotech companies with which they have initiated early stage discussions. They have found the caliber of science to be very strong, with an enthusiasm for partnering.

POINT THERAPEUTICS, INC

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Web: None

Contact: Rich Small, SVP and CFO (rsmall@lifespan.org)

Profile
Point's mission is to develop and commercialize, as therapeutic agents, a new class of molecules that modulate the immune system. This class of compounds is comprised of small molecules that have demonstrated significant biological effects in vitro and represent building blocks for a series of potential therapeutic compounds designed to modulate specific immune responses in the targeted diseases. They have a proprietary position on these molecules through a license agreement with Tufts University School of Medicine. They intend to align strategically with pharmaceutical companies. Its initial efforts will be focused on developing therapies for AIDS and cancer patients, with subsequent efforts being made in the treatment of infectious diseases.

Product/Partnership Status
Having originated from Tufts University, Point is in the early stages of developing their own compounds in the AIDS and cancer areas. To date, they have not partnered any of their compounds.

Partnering Assessment
Ultimately, Point Therapeutics will seek to partner their compounds with pharmaceutical companies or large biotech companies. They do not foresee any need to work with academic groups at this juncture.

POLYGENYX, INC

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Web: www.polygenyx.com

Contact: Christopher Simmons, President and CEO (csimmons@polygenyx.com)

Profile
PolyGenyx is focused on high-throughput SNP genotyping technology, developed at MIT Cancer Research Center, for use in drug discovery, pharmacogenomics, DNA-fingerprinting and marker-assisted selection for agricultural applications. They are in the process of establishing a high-throughput, multi-species genotyping factory to begin providing large population genotyping services to the pharmaceutical and agricultural industries by mid-2000. Longer term, they will market diagnostic/prognostic, DNA-fingerprinting and genotyping kits.

Product/Partnership Status
As a young company, though substantive discussions are underway with a number of potential partners in the genomics field, to date no alliance deals have been struck.

Partnering Assessment
PolyGenyx are talking to potential VC funders in Canada and, as a result, might set up some sort of Canadian operation in the future, presumably to meet certain funding requirements. From a partnering perspective, they would be interested in the bioinformatics field and also in access to large stable population bases, particularly family groups, for the acquisition of genomic data.

PROCEPT, INC (Heavenly Door.com, Inc)

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Web: www.procept.com

Contact: John Dee, Vice Chairman

Profile
In early 2000, Procept and Heavens Door Corporation, a funeral services company, merged their operations to afford the latter an opportunity to assume Procept's public listing and transform from a biopharmaceutical company into an internet provider of funeral products and services, to be called HeavenlyDoor.com (HVDC). The biotech assets of Procept are being transferred to its subsidiary, *Pacific Pharmaceuticals*, which will be renamed Procept. HVDC has stated that it intends to continue the clinical development of Procept's two lead compounds, both of which have substantial government support, until an appropriate acquirer or partner is found. PRO 2000 Gel is being developed as a vaginal, topical microbicide designed to provide protection against HIV infection, as well as herpes, chlamydial and gonorrhea infections. O_6-Benzylguanine (BG) is a chemosensitizer that is designed to overcome resistance to a significant class of commonly used chemotherapeutic agents known as O_6-alkylating agents. In preclinical animal studies, treatment with BG increased the anti-tumor activity of these agents in brain, colon, and prostate cancers, as well as melanoma. A Phase II development program has recently begun and will be conducted in accordance with a CRADA executed with the *National Cancer Institute*.

Product/Partnership Status
In the past, Procept had multiple agreements with the likes of *Abbott, Chiron, VacTex, Sandoz, Bristol-Myers Squibb* and *Upjohn*. They had also had had multiple academic collaborations with the likes of *Massachusetts General Hospital, Dana Farber Cancer Institute, UC San Francisco, the University of South Carolina,* and the *Joslin Diabetes Center*.

Partnering Assessment
It is clear that Heavenly Door is seeking to divest itself of its various biotechnology assets, as witnessed by the recent exclusive licensing of the PRO 2000 gel to *Interneuron Pharmaceuticals* who will enjoy worldwide development and commercialization rights. It will then completely focus its activities as an internet company. Canadian companies may therefore care to look over the remaining IP portfolio to see if there is a fit with their own IP arsenals.

REPLIGEN CORPORATION

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Web: www.repligen.com

Contact: Daniel Witt, VP Business Development (dwitt@repligen.com)

Profile

Repligen develops new drugs for autism, organ transplant and cancer, particularly for pediatric patients. Their products offer patients improved treatment options based on modulation of newly discovered disease mechanisms. Their major programs currently include developing the hormone secretin for use as an autism therapy, enabling bone marrow transplants between genetically unmatched donors using CTLA4-1g, and manufacturing and marketing Protein A to biopharmaceutical companies for use in the manufacture or production of therapeutic antibodies. Secretin has been reported to have benefits for some autistic children including increased awareness, improved social behavior and communication. They intend to manufacture a synthetic, human form of secretin, and pending regulatory approval, initiate a multi-dose Phase II clinical trial in autism patients this year.

Product/Partnership Status

Repligen recently secured an agreement to supply recombinant Protein A to *Amersham Pharmacia Biotech* for the next ten years. Protein A, Repligen's principal marketed product, is used for the safe and effective production of therapeutic antibodies. *AP Biotech* will incorporate Protein A into its products for sale to the pharmaceutical industry. They made a deal with the *Autism Research Institute* for secretin for use to treat autism. Before they concentrated their activities on autism, Repligen had sold off parts of their business to the likes of *Genetics Institute, Immunomedics, Apotex, Genzyme* and *Medco Research.* They had formerly had collaborations with *Pfizer, Pharmacia, Cambridge NeuroScience, Tularik, Glaxo, T Cell Sciences, Lilly* and *Calpyte Biomedical.*

Partnering Assessment

A private placement of $20 million in March of this year has given Repligen the resources to aggressively develop their clinical product candidates in large, underserved markets. Their strategy is to maintain rights to their lead products through Aproof of efficacy@ clinical trials. Repligen are involved in Canada through having a licensing deal and an alliance on certain compounds with *NeuroChem* in Montreal, and a relationship with the *Alberta Research Council* in Edmonton. Their primary interests, in addition to the autism field, will center on the pediatric health field, especially those opportunities that might fall into the orphan drug area.

REPROGENESIS

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Web:

Contact: Daniel Olmstead, President and CEO

Profile
Reprogenesis develops products for minimally invasive *in* vivo tissue augmentation and repair using their proprietary technology. It is the first company formed to solve problems of the genitourinary tract and breast using the principles of tissue engineering. Their core technology is licensed from MIT/Children's Hospital. The pipeline is represented by products that create structural tissue to augment or correct anatomical defects, restore physiological function, and repair or restore anatomical organs. The technology is initially being applied in the areas of urology, cardiovascular biology, and plastic and reconstructive surgery. Their first two products, treatments for vesicoureteral reflux and stress incontinence began clinical trials back in 1997. Recently it was announced that Reprogenesis will merge with *Creative BioMolecules* and *Ontogeny* to form one privately-held company to be called *Curis* (See entry for Curis).

Product/Partnership Status
American Medical Systems, a division of *Pfizer*, had exclusive rights to market and distribute these two products, but recently decided to exit the medical device business and thus terminated the agreement. They also have a collaborative research agreement devoted to breast tissue reconstruction at the *Cannon Research Center* in Charlotte, NC and at the *University of Michigan* in Ann Arbor. Recently, they in-licensed exclusive rights to a pioneering organ regeneration technology and a tissue engineering bladder substitute product from *Children's Hospital* in Boston, a Harvard Medical School affiliate, and *MIT*. This will, of course, become part of the Curis regenerative medicine pipeline. It is anticipated that Curis will seek approval to initiate a bladder reconstruction study in 2001.

Partnering Assessment
Assuming that the Reprogenesis shareholders approve the Curis merger sometime in June 2000, all Reprogenesis opportunities will revert to Curis.

SCRIPTGEN PHARMACEUTICALS, INC (Anadys Pharmaceuticals)

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Web: www.scriptgen.com

Contact: Michael Heslop, VP Commercial Development (mheslop@scriptgen.com)

Profile

Scriptgen (just renamed to Anadys) is a biopharmaceutical company dedicated to the development of a novel class of small molecule drugs that regulate gene expression, utilizing their proprietary high throughput technologies to enable and accelerate their discovery. The underlying philosophy of the company is that there are a variety of disease states that can be controlled at the level of gene expression, the process by which the genetic information in DNA is converted into proteins. Their lead therapeutic candidate is a novel anti-HIV compound that acts by inhibiting a viral protein/RNA interaction that is critical for the expression of viral structural proteins and essential for virus production. The compound binds to the REV Response Element and is the first example of a small molecule, non-peptide, non-nucleoside drug that inhibits a protein/RNA interaction and the first example of a small molecule HIV Rev inhibitor.

Product/Partnership Status

Scriptgen commercializes its technology platform through collaborations with pharmaceuticals and technology companies, and through their internal development program. In 1995 they entered into a collaboration with *Roche* to use their ATLAS technology to identify drug candidates for oncological applications. In 1997, they entered a collaboration with *Eli Lilly* to use ATLAS to screen Lilly compounds, with *Hoechst Marion Roussel* to discover and develop novel antifungal drugs using the GATE technology to identify fungal targets, with *Monsanto* to identify and validate novel fungal targets from plant and human pathogens, and with *BioChem Pharma* to identify drug candidates active against the Hepatitis B virus (HBV) and those which act as small molecule mimics of therapeutic proteins by activating dimerization of certain receptors. In 1998, *Lilly* extended its original agreement to encompass additional drug targets, and a licensing agreement was signed with *Genome Therapeutics* to provide access to Genome's microbial sequence database, PathoGenome. Last year, they entered a collaboration with *Du Pont* whereby Scriptgen transferred a lead series of antibacterial compounds and screened compounds from both companies' compound libraries. Additionally, they have collaborated with *Incyte Pharmaceuticals* (bacterial functional genomics), *ArQule* (RNA/protein interaction screening), and *BioFocus* (optimization of potential new antiviral agents).

Partnering Assessment

Highly collaborative company and initial approaches should be made to the Corporate Development department.

SEPRACOR, INC

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Web: www.sepracor.com

Contact: William Yelle, VP Business Development (byelle@sepracor.com)

Profile
Sepracor develops Improved Chemical Entities (ICE) that are enhanced forms of existing, widely sold pharmaceuticals. ICEs can be developed at less cost, time and risk than New Chemical Entities (NCEs), covering product opportunities with strong market potential. They have spun out several biotech companies, including publicly-traded BioSepra and HemaSure, and wholly-owned SepraChem and Versicor. Many drugs that Sepracor evaluates are chiral compounds, which exist as a mixture of two mirror-image forms called isomers.

Product/Partnership Status
They have an extensive portfolio of ICE candidates in preclinical or clinical development. Between them and their corporate partners, there are currently six ICE pharmaceuticals in Phase II clinical trials and three ICE candidates in Phase III. In 1993, Sepracor licensed its US patent relating to fexofenadine to *Hoechst Marion Roussel* which subsequently developed the drug and launched it later as ALLEGRA, a nonsedating anthistamine. In late 1997, they announced a licensing agreement with *Schering-Plough* granting the latter exclusive worldwide rights to DCL, an active metabolite of CLARITIN. In 1998, they agreed with *Janssen (J&J)* to jointly fund the development of their ICEs, a metabolite of HISMANAL for seasonal and perennial allergic rhinitis, and also signed a second licens-ing agreement regarding an isomer of PROPULSID for the symptomatic treatment of patients with nocturnal heartburn due to gastroesophageal reflux disease. Later that year, they announced a licensing agreement with *Eli Lilly* to allow Lilly to exclusively develop and globally commercialize a modified form of an active ingredient found in PROZAC. Last year, they announced a licensing agreement with *UCB Farchim SA*, an affiliate of *UCB* relating to an isomer of ZYRTEC for the treatment of allergies. This is Europe's leading antihistamine. Sepracor has had other collaborations with *Ross* (Xoponex bronchodilator for pediatrics), *Alza* (single-isomer transdermal drug), *SkyePharma* (aerosol formulations for asthma), *ArQule* (mapping array program for HIV and Hepatitis B), and *Tripos* (HIV protease inhibitors). Additionally, last year they licensed Zopiclone for the treatment of insomnia to *Rhone-Poulenc Rorer* in the US market.

Partnering Assessment
Sepracor is a very successful company that is working with numerous companies to Areinvent@ various products using their chiral technologies. Interested groups should approach the business development department in the first instance.

SEQUITUR, INC

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Web: www.sequiturinc.com

Contact: Tod Woolf, VP Technology Development (twoolf@sequiturinc.com)
Don Mossman, VP Sales and Marketing (dmossman@sequiturinc.com)

Profile
Sequitur is developing and marketing innovative sequence-based compounds for functional genomics research, diagnostic and therapeutic applications. They provide specialty research products and perform consulting and collaborative research. Their Antisense Functional Genomics Program offers some of the first commercially available 2nd generation antisense compounds. In addition to target validation studies, their program can assist in the development of a proprietary position on therapeutic antisense applications. Their compounds were developed through careful screening in a cell culture assay system.

Product/Partnership Status
Corporate clients pay a yearly licensing fee to obtain non-exclusive research use of their current and newly developed functional genomics technology. Research agreements are also available for Sequitur to experimentally determine optimal antisense sites within target genes. Clients include *Pharmacia & Upjohn, Chiron, Genome Therapeutics, Inex Pharmaceuticals, Mitotix, Monsanto-Searle, Genetics Institute, Incyte, Amgen, Wyeth-Ayerst,* and *Bristol-Myers Squibb.* Sequitur has also collaborated with a major synthetic DNA supplier to produce their first product and they are continuously testing new compounds developed externally and internally. Collaborative research projects have been carried out with *Inex Pharmaceuticals, Genome Therapeutics, Affymetrix* and others. They have had contact also with Merck-Frosst in Canada.

Partnering Assessment
Sequitur are of course always looking for clients for their functional genomics program which provides antisense functional genomics and target validation services.

SYNTONIX PHARMACEUTICALS

65 Cummings Park
Woburn, MA 01801
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Contact: Garen Bohlin, CEO (gbohlin@syntnx.com)

Profile
Syntonix Pharmaceuticals is an early stage company focused on the discovery, development and eventual commercialization of biopharmaceutical therapeutics and vaccines for human disease. Its proprietary technology centers around the delivery of proteins, peptides or small molecules across the mucosal barrier either orally or through inhalation.

Product/Partner Status
Company is totally focused on proof of concept for its technology. Once this is obtained, expects collaborations to be with big pharma and more mature US-based biotech organizations.

Partnering Assessment
CEO cites a business strategy that does not presently involve or consider Canada. There are no plans to consider partnering at this stage and no expressed interest in or knowledge of the Canadian industry. Any research germane to the delivery of proteins and peptides across the mucosal barrier might be worth bringing to their attention.

THE ALTHEXIS COMPANY, INC

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Web: www.althexis.com

Contact: Manuel Navia, CEO (mnavia@althexis.com)

Profile
Althexis is a privately held pharmaceutical company with world class expertise in structure-based drug design (SBDD), a process of drug selection, design and development that exploits atomic level structural information about disease targets. The founders are SBDD pioneers, having successfully established and applied SBDD programs in the discovery and development of novel, commercially successful drugs. Althexis is initially focusing its efforts on the discovery, development and commercialization of novel antibiotics.

Product/Partnership Status
Althexis is following a unique financing strategy, engaging in an early-stage major research collaboration to fund its initial development program. It entered into its initial collaboration with *PLIVA d.d.*, the largest pharmaceutical company in Central and Eastern Europe and creator of azithromycin, one of the world's most prescribed antibiotics. The agreement provides Althexis with a potential $14.5 million over three years in research funding and milestone payments to fund their work against mutually agreed upon antibiotic targets.

Partnering Assessment
Althexis intends to pursue other collaborations with strategic partners as it identifies targets and treatment areas that are directly applicable to Structure-Based Drug Design and embody risk reduction advantages similar to the initial antibiotic effort.

THE MEDICINES COMPANY

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Cambridge, MA 02142
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Web: www.themedicinescompany.com

Contact: Clive Meanwell, CEO

Profile
Founded in 1996 by a team of experienced pharmaceutical executives to acquire, develop and commercialize selected pharmaceutical products in late stages of development, Medicines seeks to unlock intrinsic product value by selectively acquiring a promising drug after early-development costs are incurred, and then executing a cost efficient development and commercialization strategy yielding the most competitively priced product. The company has now grown to more than 40 professionals worldwide with facilities in New Jersey, the UK, New Zealand and Switzerland in addition to its Massachusetts HQ.

Product/Partnership Status
In 1997, they acquired the exclusive worldwide rights to develop and market their first product, the anticoagulant Angiomax, formerly know as Hirulog, from *Biogen*. This has since completed Phase III trials and been submitted for an NDA with the FDA. In 1998, they acquired exclusive worldwide rights to IS-159 from *Immunotech*, a wholly owned subsidiary of *Beckman Coulter*, for the treatment of acute migraine headache. This is being developed as a fast-acting nasal treatment for migraine relief. Last year, they acquired the exclusive worldwide rights to CTV-05, a strain of human Lactobacillus currently under investigation for a broad range of applications in the areas of urogenital and reproductive health. The product, a patented biotherapeutic agent, will initially be studied in the treatment of bacterial vaginosis (BV), the most common gynecological infection in women of childbearing age.

To complement its core skill base, they have established strategic relationships with other companies in the areas of commercialization, clinical research and manufacturing. These include *Quintiles* as its partner for product development activities, and *Innovex*, a division of *Quintiles Transnational*, which is providing a wide array of integrated sales and marketing and customer education services.

Partnering Assessment
Medicines is seeking to acquire the rights to high quality pharmaceutical products in late stages of development. The company has developed an integrated capability to acquire products with attractive investment characteristics, using a flexible approach to licensing focused on solving each of its partner's needs.

THERION BIOLOGICS CORP

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Cambridge, MA 02142
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Web: www.therionbio.com

Contact: Richard Woodrich, SVP Business Development
(rwoodrich@therionbio.com)

Profile
Therion develops immunotherapies for the treatment of various cancers and preventive vaccines for AIDS. Advances in the understanding of tumor biology and immunology have fueled a renaissance in cancer immunotherapy, a treatment strategy that enhances the natural ability of the immune system to eliminate malignant cells. They are developing a new generation of therapeutic products that harness the power of the cellular immune system to treat major cancers including colorectal, lung, prostate, breast and ovarian, and melanoma. They are also capitalizing on the advanced understanding of the immune response to develop innovative, multi-genic vaccines for the successful prevention of AIDS. Further it has commercial rights to live, attenuated HIV vaccine technology developed at Harvard University. These multi-genic vaccines are designed to achieve the efficacy of live, attenuated AIDS vaccines with the safety of the company's recombinant pox virus products.

Product/Partnership Status
To date, their technology platform for rapid generation of products for clinical evaluation has yielded eleven products in Phase I and Phase II clinical trials. They have a major corporate alliance with *Aventis Pasteur* for the development of therapeutic colorectal and lung cancer and melanoma vaccines, and two significant collaborations with the *National Cancer Institute*. In addition, they are advancing a program to develop AIDS vaccines with the *National Institute of Allergy and Infectious Diseases (NIAID)*.

Partnering Assessment
Therion will continue to look for commercial collaborators and expect that they will be talking with major Canadian companies as they go forward. It is further anticipated that clinical trials will be conducted in Canada. There feelings towards Canada are also buoyed by their happiness with Sofinoff as one of their main investors. From the academic point of view they are always interested in hearing of any new technologies in the immunotherapy field and in cancer immunology.

TISSUE ENGINEERING, INC

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Contact: David Dove, CEO (ddove@tissueengineering.com)

Profile
TEI is a biotech research, development and manufacturing company focused on developing collagen scaffolds, tissue-specific complexes of chemical signals needed for cell and tissue differentiation, and cells, the three components that make up reconstituted replacement tissues. They have programs in the cardiovascular, orthopedic, skin and wound-healing, urological and dental areas, encompassing many prosthetic devices.

Product/Partnership Status
TEI has a collaboration with *Sofamor* Danek, recently acquired by *Medtronic*, on cardiovascular and neuro-orthopedic R&D initiatives. To date, this is the only partnership deal struck.

Partnering Assessment
Tissue Engineering is interested in exploring prospective corporate partnerships with companies in their remaining research areas, namely skin, orthopedics, cosmetics, urology and dental. While they are not particularly doing much in the way of any collaborative work with any academic groups, they would wish to be approached regarding any licensing opportunities, particularly relating to growth factors and possibly stem cells.

TRANSGENE, INC

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Profile
Transgene is a leading European-based biotech company converting genes into pharmaceutical products using novel vectors. Their proprietary technology platform includes synthetic, adenoviral, retroviral, and vaccinia vectors. By developing multiple vector systems, they can select the most appropriate vector family to combine with a specific gene for a particular clinical application. They are actively developing leading edge therapy products for cancer, cystic fibrosis, muscular dystrophy and AIDS. With product development, clinical, regulatory process development, formulation and manufacturing capabilities, they are capable of simultaneously developing and manufacturing products based upon its diverse families of gene delivery systems. They have successfully developed four gene therapy products into clinical development, all in Phase II.

Product/Partnership Status
A five-year agreement with *Schering-Plough*, completed in 1998, has Transgene licensing its adenoviral vectors for the delivery of the p53 tumor suppressor gene and up to five additional proprietary genes. Under the terms of a ten-year agreement with *Human Genome Sciences*, Transgene gains access to an extensive, high quality gene sequence and functional genomics database, strengthening its ability to access optimal genes and develop gene therapy products for desired markets.

Partnering Assessment
At this time, Transgene are not actively seeking any in-licensing opportunities or academic collaborations. There may be some out-licensing opportunities, but these will typically be with major pharmaceutical companies. At present they have no interactions with Canadian entities.

TRANSKARYOTIC THERAPIES, INC

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Contact: Christoph Adams, VP Business Development (cadams@earthlink.net)

Profile
TKT is a biopharmaceutical company focused on the production, replacement and delivery of proteins for a wide variety of human diseases. Based on three proprietary technology platforms, Gene-Activated proteins, Niche Protein products, and Gene Therapy, TKT is developing a broad and renewable pipeline aimed at the production of human proteins as well as the treatment of rare genetic diseases. Their pipeline is comprised of more than 15 R&D programs. Products currently being tested in human clinical trials include Gene-Activated erythropoietin (GA-EPO) for the treatment of anemia, alpha-galactosidase A (alpha-gal) for the treatment of Fabry disease, and Factor VIII for the treatment of hemophilia A.

Product/Partnership Status
GA-EPO is partnered with *Hoechst Marion Roussel (Aventis)* and the companies are conducting a Phase III trial for the treatment of anemia associated with renal disease in the US and UK. Alpha-gal is being put through a Phase II trial at the NIH for Fabry disease and TKT is also developing treatments for Hunter syndrome, Gaucher's disease, and other rare genetic disorders. They are collaborating with *Sumitomo Pharmaceuticals* on Fabry disease. Factor VIII is in a Phase I safety study at *Beth Israel Deaconess Medical Center* and they are working with *Genetics Institute*.

Partnering Assessment
TKT are very much focused on the commercial aspects of their business and therefore do not see much interaction with academic groups at this time. They are, of course, in the midst of an extremely high profile court dispute with Amgen over patent protection surrounding EPO. There is huge interest within the industry as to the result of the action since TKT will be not only well positioned to enter the EPO market (the largest biotech drug in the world in terms of revenues) but others too by dint of their novel manufacturing method in producing certain products. As such, their primary interests right now would be in gaining access to products possessing clinical data in niche product areas, preferably with potential orphan status, and in the cancer field.

TRANXENOGEN

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Contact: Steven Parkinson, President and CEO (ParkinTXG@aol.com)

Profile
TranXenoGen is a development stage biotechnology company with three generic biological products in development. TranXenoGen is applying its proprietary second-generation technology platforms in sperm-mediated transgenesis, in vitro-in vivo animal cloning and other technologies to create transgenic chickens expressing these proteins in the albumin of their eggs. They are also offering their transgenic and cloning technology for the efficient manufacture of novel products and to create genetically modified animals as donors of organs and cells for xenotransplantation to human recipients.

Product/Partner Status
The company expects to commence production of its first product later in 2000. The other two products are in development and the company expects to begin manufacture of both next year. It recently announced that it had signed a letter of intent with *U.S. Transgenics* of Washington DC to form an equally owned joint venture to develop recombinant Human Serum Albumin (HSA) and a collaboration to produce other proteins in the albumin fraction of transgenic chicken technology. Commercial production is anticipated in 2003.

Partnering Assessment
Would have an interest in collaborations for manufacturing proteins and research collaborations with both novel proteins and any technologies to complement their existing technologies, in particular antibodies. CEO has travelled in Canada before with a former company (Genzyme Transgenics) and is therefore aware of some of the creative funding vehicles in Canada which would hold some interest, particularly as it relates to manufacturing and R&D. Would be interested in acquiring transgenic, cloning and purification technologies, and in acquiring products.

VARIAGENICS

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Contact: Bruce Maloff, EVP Commercial Operations (bmaloff@variagenics.com)

Profile
Variagenics is developing novel pharmaceutical products targeted to the normal genetic variance of human populations. Through its proprietary Variagenic Targeting technologies, they will develop a new class of anti-cancer therapies that are selectively toxic to proliferating cells. They will also apply their core competency in the rapid analysis of genetic variance using proprietary Variance Imaging mismatchrecognition methods to the pharmacogenetic development and commercialization of conventional pharmaceutical products that are preferentially efficacious in selected populations. In 1997, they acquired Avitech Diagnostics which provided a broad portfolio of technologies for variance discovery.

Product/Partnership Status
Variagenics has established alliances with the two leading CROs worldwide. In December 1998, they established a marketing alliance with *Quintiles* whereby they will become a preferred provider of pharmacogenomics to Quintiles' clients engaged in clinical trials. In August 1999, they entered into a collaborative agreement with *Covance* that will provide funding for the development of novel pharmacogenomic testing technologies which allow for the rapid detection of genetic variation in clinical patient samples. Variagenics also has marketing rights to apoE, a genetic marker associated with Alzheimer's and other neurological disorders, through its relationship with *Nova Molecular*.

Partnering Assessment
In addition to the evolving relationship with *Nova Molecular* in Canada, Variagenics also enjoys a significant relationship with *McGill University* in Montreal from whom they have licensed a gene and to whom they have provided considerable research support. In addition, they have other regular contact with scientists across Canada. Variagenics' partnering interests will revolve around applying pharmacogenetics by bringing together CROs, diagnostic companies, and instrument and reagent companies to participate in platforms geared to genotyping. Additionally, they will always be interested in any science regarding polymorphisms.

VERTEX PHARMACEUTICALS, INC

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Contact: James Feeney, Senior Director Business Development
(jfeeney@vpharm.com)

Profile
Vertex is developing human therapeutics through the integrated application of structure-based rational drug design. They are using the latest advances in chemistry, biology and physics to design unique molecules based on the structural features of proteins involved in the control of disease processes. Their goal is to become a fully-integrated pharmaceutical firm by exploiting the advantages of rational drug design in the discovery and development of novel drugs. They have nine product candidates in clinical development to treat viral diseases, inflammation, cancer, autoimmune diseases and neurological disorders. Five of these products are in Phase II.

Product/Partnership Status
Their first approved product is Agenerase, an HIV protease inhibitor that Vertex co-promotes with *Glaxo Wellcome*. They are collaborating with *Aventis* on the development and commercialization of HMR 3480/VX-740, as well as other compounds, for the treatment of inflammatory disease. They have an agreement with *Eli Lilly* to collaborate on research, development and commercialization of novel, orally active protease inhibitors for the treatment of chronic infection caused by the hepatitis C virus. Vertex is collaborating with *Kissei Pharmaceutical* on the development and marketing of amprenevir for the treatment of HIV and AIDS in Japan and the Far East, and on Vertex's p38 MAP kinase program for the development and commercialization of novel, orally active drugs for the treatment of inflammatory and neurological diseases. With *Schering AG* Vertex are collaborating on the research, development and commercialization of novel, orally active neurophilin compounds to promote recovery of nerve function for the treatment of a number of neurological diseases. Vertex and *Taisho Pharmaceutical* are collaborating on the discovery, development and commercialization of caspase inhibitors for treatment of diseases associated with activation of apoptosis. They are collaborating with *BioChem Pharma* on the development and marketing of Incel (VX-710) for the treatment of cancer multidrug resistance in Canada.

Most recently, Vertex signed a potentially massive deal with *Novartis*. This alliance has been formed to discover, develop, and commercialize small molecule drugs directed at targets in the kinase protein family. Subject to milestones and other conditions, pre-commercial payments to Vertex could total $800 million, based on the successful discovery and full development of eight compounds. The alliance will combine Vertex's integrated parallel drug discovery approach in target families with the Novartis portfolio management system, with its emphasis on optimizing the early development phase of new compounds and promotion of selected compounds to rapid clinical development. In

April, Vertex entered into an agreement with *Harvard Medical School's Institute of Proteomics* to accelerate small molecule drug discovery using genomic and proteomic information from the Institute. The company has also licensed ICE patents from *Sanofi*, accessed *Incyte Pharmaceuticals'* LifeSeq Gold database, and conducted collaborative research with *Oxford Assymetry* in combinatorial chemistry.

Partnering Assessment

Vertex is a large and successful company with multiple partnering opportunities which should be broached with the Business Development team.

VIACELL, INC

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Contact: Sharon Pick, VP Business Development (spick@tbreed.com)

Profile

In April of this year, Viacord of Boston and t. Breeders of Worcester closed a merger agreement to form a new cellular medicine company called ViaCell. This new entity will leverage its high quality cord blood banking service infrastructure and patented stem cell expansion technology to build a premier cellular pharmaceutical company providing products and services geared towards the treatment of diseases using stem cells. T. Breeders was a development stage company pioneering a proprietary technology designed to selectively expand (breed) a clonogenic pool of relatively undifferentiated cells. Their novel approach allows them to breed extremely rare cells to clinically meaningful numbers. This technological breakthrough will have a profound impact on multilateral markets such as cell replacement therapy, gene therapy, production of blood and blood products, cancer research, clinical diagnostic, and biopharmacology.

Product/Partnership Status

ViaCell plans to file an application later this year with the FDA to begin human trials in a patient population yet to be determined. If the technology works, future applications might involve using stem cells in gene therapy to distribute therapeutic genes through the body or giving healthy stem cells to patients suffering from genetic diseases. They might also develop a library of stem cells. Currently, the company has no corporate partnerships in place, but is developing a strategy for such developments. They do have undisclosed relationships with academic groups, including one in Canada.

Partnering Assessment

The research arm of ViaCell will continue to operate out of Worcester. The company aims to become a product and technology company in the future and will always be interested in hearing from those groups involved in stem cell biology and transplantation whereby ViaCell would be afforded the opportunity to leverage its own technology to lead to more rapid development of their stem cell technologies.

ZYCOS, INC

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Profile
ZYCOS (formerly known as Pangaea Pharmaceuticals) develops novel therapies that modulate immune responses at their inception. Their technology platform comprises of a rapid antigen discovery system, a DNA non-viral expression vector and a microsphere DNA drug delivery system, and represents a breakthrough in the activation of cytotoxic cells. For the first time, the core technology provides an effective and direct method for the treatment of chronic viral infections and cancer as well as a single product that mat work on all autoimmune diseases. Thi- technology overcomes the obstacles encountered by others in the modulations of the immune system.

Product/Partnership Status
Zycos has ongoing collaborative relationships with *Pasteur Merieux Connaught* for the discovery of cancer antigens, *Visible Genetics, Cytyc,* and *Moldyn.* They have collaborative relationships with a number of academic partners including *Harvard Medical School, Brigham & Women's Hospital, MIT, University of North Carolina at Chapel Hill, UCSF* for a Phase I/II anal dysplasia study and *King's College in London.*

Partnering Assessment
Always interested in hearing from corporate and academic groups with technologies and opportunities germane to Zycos' core efforts.