GERON CORP
Form 10-K
March 16, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

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x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2006

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____.

Commission File Number: 0-20859

GERON CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**75-2287752**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

230 Constitution Drive, Menlo Park, CA 94025
(Address, including zip code, of principal executive offices)

Registrant□s telephone number, including area code: (650) 473-7700

Securities registered pursuant to Section 12(b) of the Act: Common Stock, $0.001 par value

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer" and "large accelerated filer" in Rule 12b-2 of the Exchange Act.

Large accelerated filer o Accelerated filer x Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No x

The aggregate market value of voting and non-voting common equity held by non-affiliates of the registrant was approximately $454,245,354 based upon the closing price of the common stock on June 30, 2006 on The Nasdaq Global Market. Shares of common stock held by each officer, director and holder of five percent or more of the outstanding Common Stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 2, 2007, there were 72,866,080 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Document	**Form 10-K Parts**
Portions of the Registrant's definitive proxy statement for the 2007 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days of the Registrant's fiscal year ended December 31, 2006	II, III

Forward-Looking Statements

This annual report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7, contains forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause the results of Geron Corporation ("Geron") to differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. The risks and uncertainties referred to above include, without limitation, risks inherent in the development and commercialization of Geron's potential products, dependence on collaborative partners, need for additional capital, need for regulatory approvals or clearances, the maintenance of Geron's intellectual property rights and other risks that are described herein and that are otherwise described from time to time in Geron's Securities and Exchange Commission reports including, but not limited to, the factors described in Item 1A, "Risk Factors", of this report. Geron assumes no obligation and does not intend to update these forward-looking statements.

EXPLANATORY NOTE

In this Form 10-K as of and for the year ended December 31, 2006 (the "2006 Form 10-K"), we are restating in Item 8 "Consolidated Financial Statements and Supplementary Data," our consolidated balance sheet as of December 31, 2005, the related consolidated statements of operations, stockholders' equity and cash flows for the years ended December 31, 2005 and 2004, and each quarter of 2005 and the first three quarters of 2006. This restatement is more fully described in Note 2, "Restatement of Consolidated Financial Statements." This 2006 Form 10-K also reflects the restatement of "Selected Consolidated Financial Data" in Item 6 for the fiscal years ended December 31, 2005, 2004 and 2003 and Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," as of and for the years ended December 31, 2005 and 2004. Previously filed annual reports on Form 10-K and quarterly reports on Form 10-Q affected by the restatements have not been amended and should not be relied on.

The restatement results from our review of recent guidance relating to Emerging Issues Task Force Issue 00-19, "Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock," (Issue 00-19). Recent guidance described the application of Issue 00-19, particularly the provisions related to settlement in unregistered shares and registered shares and timely filing and registration requirements under U.S. securities laws. In order for a warrant to be classified as permanent equity under Issue 00-19, the settlement of such warrant in shares must be within the company's control. We have issued certain warrants to purchase shares of our common stock in connection with equity financings pursuant to effective shelf registration statements, and the holders of such warrants have the right to exercise them for cash and to receive registered shares upon such exercise. In connection with the issuance of these warrants, we agreed to file timely any reports required under the Securities Exchange Act of 1934, as amended, to enable the delivery of registered shares upon exercise of these warrants. Issue 00-19 states that the ability to make timely filings and, therefore the delivery of registered shares, is not within the control of a company. As a result, Issue 00-19 presumes net-cash settlement, thus requiring these warrants to purchase shares of our common stock issued in connection with equity financings pursuant to effective shelf registration statements to be considered liabilities. We have reported 2006 and restated prior consolidated balance sheets to account for the value of these warrants to purchase shares of our common stock as a liability, and have restated prior consolidated statements of operations for the quarterly change in fair value of the warrants. This restatement had no impact on previously reported revenues, operating expenses, total assets or cash position.

The following table presents the cumulative adjustments for each affected component of warrant liabilities and stockholders' equity at the end of each restated fiscal year:

As of December 31,	Fair Value of Warrants to Purchase Common Stock	Decrease in Additional Paid-In Capital	Decrease in Accumulated Deficit	Decrease in Stockholders' Equity
		(In thousands)		
2005	$15,007	$ 16,877	$ 1,870	$ 15,007
2004 (unaudited)	18,524	20,555	2,031	18,524
2003 (unaudited)	7,044	8,228	1,184	7,044

PART I

ITEM 1. BUSINESS

Overview

Geron is developing first-in-class biopharmaceuticals for the treatment of cancer and chronic degenerative diseases, including spinal cord injury, heart failure, diabetes and HIV/AIDS. We are advancing telomerase targeted therapies, including an anticancer drug and a cancer vaccine, through multiple clinical trials. We are also the world leader in the development of human embryonic stem cell-based therapeutics, with our spinal cord injury treatment anticipated to be the first such product to enter clinical development.

We were incorporated in 1990 under the laws of Delaware. Our principal executive offices are located at 230 Constitution Drive, Menlo Park, California 94025. Our telephone number is (650) 473-7700.

We make available free of charge on or through our Internet website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after they are electronically filed with, or furnished to, the Securities and Exchange Commission. Our Internet website address is www.geron.com. Information on our website is not incorporated by reference and does not form a part of this report.

Major Technology Platforms

Telomeres and Telomerase: Role in Cellular Aging and Cancer

Cells are the building blocks for all tissues in the human body and cell division plays a critical role in the normal growth, maintenance and repair of human tissue. However, in the human body, most cell division is a limited process. Depending on the tissue type, cells generally divide only 60 to 100 times during the course of their normal lifespan.

We and our collaborators have shown that telomeres, located at the ends of chromosomes, are key genetic elements involved in the regulation of the cellular aging process. Our work has shown that each time a normal cell divides, telomeres shorten. Once telomeres reach a certain short length, cell division halts and the cell enters a state known as replicative senescence or aging. Thus, this shortening of the telomeres effectively serves as a molecular "clock" for cellular aging. We and others have shown that when the enzyme telomerase is introduced into normal cells, it can restore telomere length – reset the "clock" – thereby increasing the functional lifespan of the cells. Importantly, it does this without altering the cells' biology or causing them to become cancerous. Human telomerase, a complex enzyme, is composed of a ribonucleic acid (RNA) component, known as hTR, a protein component, known as hTERT, and other accessory proteins. In 1994, we cloned the gene for hTR, and in 1997, in collaboration with Dr. Thomas Cech, we cloned the gene for hTERT.

Our work and that of others has shown that telomerase is not present, or is present at very low levels, in most normal cells and tissues, but that during cancer progression, telomerase is abnormally reactivated in all major cancer types. We have shown that while telomerase does not cause cancer (which is caused by mutations in oncogenes and tumor suppressor genes), the continued presence of telomerase enables cancer cells to maintain telomere length, providing them with indefinite replicative capacity. We and others have shown in various tumor models that inhibiting telomerase activity results in telomere shortening and causes aging or death of the cancer cell.

Although telomerase is expressed in nearly all cancer cells, it is not expressed in most normal cells. That gives telomerase the potential of being both a universal as well as a highly specific cancer target. This specificity means that drugs and biologics that attack cancer cells by targeting telomerase may leave other cells unaffected, and thus should have fewer side effects than conventional chemotherapeutic agents that typically attack both cancer and non-cancer cells.

We are developing anti-cancer therapies based on telomerase inhibitors, telomerase therapeutic vaccines and, through our licensee, telomerase-based oncolytic (cancer-killing) viruses. Through our licensees, we also intend to continue to develop and commercialize products using telomerase as a marker for cancer diagnosis, prognosis, patient monitoring and screening.

We are also developing drugs that activate telomerase in certain cells to enhance cell repair/function in senescent tissues implicated in certain chronic diseases.

Human Embryonic Stem Cells: A Potential Source for the Manufacturing of Replacement Cells and Tissues

Stem cells generally are self-renewing primitive cells that can develop into functional, differentiated cells. Human embryonic stem cells (hESCs), which are derived from very early stage embryos called blastocysts, are unique because:

- they are pluripotent, which means they can develop into all cells and tissues in the body, and
- they self-renew indefinitely in the undifferentiated state.

The ability of hESCs to divide indefinitely in the undifferentiated state without losing pluripotency is a unique characteristic that distinguishes them from all other stem cells discovered to date in humans. We have demonstrated that hESCs express telomerase continuously, a characteristic of immortal cells. Other stem cells such as blood or gut stem cells express telomerase at very low levels or only periodically; they therefore age, limiting their use in research or therapeutic applications. hESCs can be expanded in culture indefinitely and hence can be banked for scaled product manufacture.

We intend to use human embryonic stem cell technology to:

- enable the development of transplantation therapies by providing standard starting material for the manufacture of cells and tissues;
- facilitate pharmaceutical research and development practices by providing cells for disease models and screening, and for assigning function to newly discovered genes; and
- accelerate research in human developmental biology by identifying the genes that control human growth and development.

Commercial Opportunities for Our Major Technology Platforms

Oncology

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. The American Cancer Society estimated that approximately 1.4 million new cancer cases were diagnosed in 2006. Overall annual costs associated with cancer in 2005 were an estimated $209.9 billion in the United States alone. Because telomerase is detectable in more than 30 human cancer types and in the great majority of cancer samples studied, we believe that telomerase-based drugs could overcome the limitations of current cancer therapies and potentially be broadly applicable and highly specific drug treatments for cancer.

We, our collaborators and our licensees are developing a range of anti-cancer therapies, including anti-cancer therapies based on telomerase inhibitors, telomerase therapeutic vaccines and telomerase-based oncolytic (cancer-killing) viruses, and diagnostics based on telomerase detection. We believe telomerase is an ideal target for cancer therapeutics and diagnostics because it appears to be universal (expressed in all major types of cancers studied to date), specific (not expressed in most normal cells), and critical (required for long-term survival of cancer cells). We believe that we have the dominant patent position in the field of telomerase. Whether it is achieved by us or by our collaborators and licensees, we believe that progress in the development of any of these telomerase-based cancer therapeutics will further validate the importance of telomerase as a cancer target and therefore benefit all of our telomerase cancer programs.

Product	Product Description	Disease Treatment	Development Stage
GRN163L	Telomerase Inhibitor	Chronic Lymphocytic Leukemia (CLL)	Phase I/II trial
GRN163L	Telomerase Inhibitor	Solid Tumors	Phase I trial
GRNVAC1	Telomerase Cancer Vaccine	Acute Myelogenous Leukemia (AML)	Initiation of Phase I/II trial

Licensees	Product Description
Merck & Co.	Telomerase Cancer Vaccine
Roche Diagnostics	Telomerase Diagnostic
Cell Genesys, Inc.	Oncolytic Virus

Telomerase Inhibition (GRN163L). Telomerase activation is necessary for most cancer cells to replicate indefinitely and thereby enable tumor growth and metastasis. One of our strategies for the development of anti-cancer therapies is to inhibit telomerase activity in cancer cells. Inhibiting telomerase activity should result in telomere shortening and therefore cause aging and death of cancer cells. Recent data show that telomerase can protect tumor cells from genomic instability and other forms of cellular stress, suggesting that inhibiting telomerase can cause a more rapid suppression of tumor growth than predicted by telomere loss alone. Because telomerase is expressed at very low levels, if at all, in most normal cells, the telomerase inhibition therapies described below are not expected to be toxic to most normal cells.

We have designed and synthesized a special class of short-chain nucleic acid molecules, known as oligonucleotides, which target the template region, or active site, of telomerase. Our work has focused on two of these oligonucleotides, called GRN163 and GRN163L, and we have demonstrated that they have highly potent telomerase inhibitory activity at very low concentrations in biochemical assays, various cellular systems and animal studies.

Our compounds GRN163 and GRN163L are direct enzyme inhibitors, not antisense compounds. They are smaller (lower molecular weight) than typical antisense compounds or other oligonucleotide drug candidates, and we expect them to be administered either locally or systemically. *In vitro* and *in vivo* studies indicate that the compounds do not inhibit other critical nucleic acid-modifying enzymes and do not appear to be toxic to normal cells at concentrations expected to inhibit telomerase in tumor cells. Both compounds use a special thiophosphoramidate chemical backbone, for which we acquired key patents in March 2002 from Lynx Therapeutics.

We and our collaborators have tested GRN163 *in vitro* on 14 different cancer cells and demonstrated significant inhibition of telomerase activity in all of them. Research by our collaborators has shown that these compounds inhibit the growth of malignant human glioblastoma (brain cancer) cells, prostate cancer cells, lymphoma, multiple myeloma, hepatocellular carcinoma (liver cancer), melanoma, lung, breast, ovarian and cervical cancer cells in animals.

GRN163L is identical in structure to GRN163 except that it has a lipid molecule permanently attached to one end of the molecule, which increases potency and improves its pharmacokinetic and pharmacodynamic properties. The improved pharmacokinetic and pharmacodynamic characteristics of GRN163L suggest that it should be effective in inhibiting telomerase in tumor cells when administered intermittently (e.g., once per week). GRN163L is a potent inhibitor of telomerase and was selected as our lead compound to take forward into the clinic. Inhibition of telomerase activity by GRN163L in cancer cells results in telomere shortening, and leads to cell cycle arrest or apoptosis. GRN163L is a 13-mer oligonucleotide N3′-- P5′ thio-phosphoramidate (NPS oligonucleotide) that is covalently attached to a C16 (palmitoyl) lipid moiety. GRN163L binds directly with high affinity to the template region of the RNA component of human telomerase (hTR), which lies in the active or catalytic site of hTERT, the telomerase reverse transcriptase. GRN163L binding to hTR results in direct, competitive inhibition of telomerase enzymatic activity. The mechanism of action of the drug is not antisense mediated.

GRN163L has been characterized preclinically and shown to inhibit telomerase in human tumor cells of many cancer types, in both cell culture systems and animal models. These studies continue to demonstrate broad anti-tumor activity of GRN163L, alone and in combination with other anti-tumor agents including chemotherapy and radiotherapy, and support the potential utility of GRN163L in the treatment of patients with hematologic and solid tumor malignancies.

After completing a series of animal toxicology and preclinical efficacy studies of GRN163L in 2005, we prepared and submitted an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) to begin human clinical trials of GRN163L in patients with chronic lymphocytic leukemia (CLL). We received FDA concurrence to begin human studies and four clinical sites are currently designated as patient enrollment centers for the study. In 2006, under our existing GRN163L IND, we initiated a second Phase I study in patients with solid tumor cancers. At the end of 2006, we presented data at two international cancer meetings on the low-dose cohorts of these studies,

which showed safety and tolerability as well as the expected pharmacokinetic properties after multiple intravenous infusions of the drug. We also presented important new data showing that GRN163L is active against tumor stem cells taken from patients with multiple myeloma. We believe that this data is the first evidence of any drug that may be active against chemotherapy-resistant cancer stem cells, which are responsible for clinical relapse. Based on this finding, as well as data showing synergy between GRN163L and a drug widely used to treat multiple myeloma, we are planning to initiate an additional Phase I/II study in multiple myeloma in 2007. We are also planning to initiate a Phase I/II study in lung cancer in the coming year.

Telomerase Therapeutic Vaccine (GRNVAC1). The goal of therapeutic cancer vaccines is to "teach" the patient's own immune system to attack cancer cells while sparing other cells. This is done by repeatedly exposing the immune system to a substance (antigen) that is specific to cancer cells in a way that subsequently induces an immune response to any cells that express that antigen on their surface. We believe that the characteristics of telomerase make it an ideal antigen for cancer vaccines.

At Duke University Medical Center, a Phase I/II clinical trial in prostate cancer patients concluded in March 2005 and additional Phase I/II optimization trials for patients with hematologic, prostate and renal cancers concluded in 2006. The Duke Phase I/II clinical trials used an *ex vivo* process in which dendritic cells (the body's most powerful antigen-presenting cells) were isolated from the patient's blood, pulsed with RNA for the telomerase protein component, and then injected into the patient's skin, where they traveled to the lymph nodes and instructed cytotoxic T-cells to kill tumor cells that express telomerase. Data from these early human clinical trials confirmed and optimized the safety and efficacy of telomerase vaccine therapies.

The first clinical trial at Duke University Medical Center was designed to enroll up to a total of 24 patients with metastatic prostate cancer, up to 12 of whom would receive three weekly vaccinations (low-dose group), and up to 12 of whom would receive six weekly vaccinations (high-dose group). Twenty-three patients were enrolled and treated, and results of this study for 20 patients (12 of the low-dose group and eight of the high-dose group) were published in the *Journal of Immunology* in March 2005. As reported by the investigator, none of the patients in either group had significant treatment-related adverse effects. All but one of the patients in the low-dose group showed a significant cellular immune response specific to telomerase. The eight patients in the high-dose group all showed very robust cellular immune responses to telomerase based on tests assessing the generation of telomerase-specific cytotoxic CD-8+ T-lymphocytes, as well as CD-4+ lymphocytes. The immune responses in the high-dose group were strong as well as specific: peak responses were 1-2% of circulating CD-8+ T-cells having anti-telomerase activity. Circulating cancer cells were also measured before and after vaccination. The data suggested that of ten subjects who had elevated levels of circulating prostate cancer cells before vaccination, nine of these ten had their levels reduced or cleared transiently after vaccination.

Serum PSA was measured before, during and multiple times after vaccination to calculate PSA doubling time as a surrogate marker for treatment response. No significant change in PSA doubling time after vaccination was reported in the low-dose group. A highly significant increase in PSA doubling time was reported in the high-dose group, suggestive of a clinical response to vaccination.

Several small additional Phase I/II trials for patients with prostate cancer, hematologic malignancies and renal cell carcinoma were performed at Duke in order to optimize the vaccination process. In the trials, a number of parameters were tested, including (i) the pre-vaccination administration of an approved compound to potentially augment vaccine potency; (ii) the use of a second approved compound applied to the vaccine injection site to potentially enable the use of dendritic cells produced by an alternative manufacturing process and; (iii) the use of boost vaccinations to potentially enhance the durability of the anti-telomerase immune response. Additionally, we have brought the vaccine manufacturing process in-house for further optimization and transferred it to a contract manufacturer. In 2006, we filed our own IND to initiate a Phase I/II clinical trial of the telomerase vaccine using

the prime/boost vaccination protocol in patients with acute myelogenous leukemia (AML). We received FDA concurrence for that IND in December 2006 and we are in the process of initiating multiple trial sites to begin enrolling patients into that study.

In 2004, we acquired rights from Argos Therapeutics, Inc. (formerly Merix) to commercialize the *ex vivo* dendritic cell processing technology used in the Duke clinical trials for telomerase and other defined tumor-specific antigens. We own the rights to the telomerase antigen and its use in therapeutic vaccines.

In 2006, we licensed rights from Immunomic Therapeutics Inc. to the LAMP antigen targeting sequence for use in cancer vaccines. The LAMP sequence causes an antigen to which it is attached to be taken up by the lysosomal subcellular compartment of the cell. This has been shown to increase presentation on MHC class II molecules, which in turn, can produce greater CD4+ T-cell responses against the antigen and a more potent and longer lasting overall immune response.

Also in 2006, we entered into a worldwide exclusive license and collaboration agreement with the University of Oxford to produce dendritic cells from hESCs. The scalable production of dendritic cells from hESCs could serve as an alternative to isolating dendritic cells from each patient, and possibly as a broadly useful vaccine delivery vehicle. In another form, dendritic cells may act to block an immune response against an antigen by teaching the immune system not to attack it a process known as tolerizing the individual to that antigen. Since the same pluripotent hESC line could be used to generate both tolerizing dendritic cells and therapeutic cells, co-administration of these two cell populations could potentially circumvent immune rejection without the need for immunosuppressive drugs.

In July 2005, we entered into a worldwide exclusive research, development and commercialization license agreement with Merck & Co., Inc. for cancer vaccines targeting telomerase by methods other than dendritic cell delivery. In addition, Merck acquired an exclusive option to negotiate a separate agreement for our dendritic cell-based telomerase vaccine.

Oncolytic Virus (OV1060 / CG5757). A third telomerase-based anti-cancer therapeutic strategy utilizes viruses that have been manipulated or engineered to have oncolytic, or cancer-killing, properties, enabling them to selectively target and destroy cancer cells that express telomerase. We cloned the promoter region of the telomerase gene and have shown that it can be used to regulate genes required for the virus to replicate within the cancer cell. Our data indicate that when tumor cells are infected with the virus, the telomerase promoter is active and the virus multiplies or replicates within the cancer cells and causes the rupture and death of the tumor cells. When these same engineered viruses infect normal somatic cells, the telomerase promoter is inactive and there is no killing effect and the virus dissipates. This selective lytic effect on cancer has been demonstrated *in vitro* in seven different tumor types: prostate, liver, lung, pancreatic, colorectal, breast and ovarian cancers. These *in vitro* results have been extended to animal models of liver and prostate cancer with similar effects against the animals tumors while sparing normal cells.

We initially granted a non-exclusive license to Genetic Therapy, Inc. (GTI), a subsidiary of Novartis AG, to use our telomerase promoter technology to develop an oncolytic virus product. Subsequently, GTIs oncolytic virus business including our license to GTI was acquired by Cell Genesys Inc., which also has its own oncolytic virus program and has continued the research and development of a potential oncolytic virus product.

Cancer Diagnostics (Telomerase Plus Test). Telomerase is a broadly applicable and highly specific marker for cancer because it has been detected in more than 30 human cancer types and in the great majority of cancer samples studied. We believe that the detection of telomerase may have significant clinical utility for cancer diagnosis, prognosis, monitoring and screening. Current cancer diagnostics apply only to a single or limited number of cancer types because they rely on molecules expressed only by particular cancer types. However, telomerase-based diagnostics could potentially address a broad range of cancers.

We have developed several proprietary assays for the detection of telomerase which are based on its activity or the presence of its RNA or protein components. The first-generation assay is the Telomeric Repeat Amplification Protocol (TRAP) assay which can be used to detect telomerase activity in human tissue or cells, including clinical samples. The second-generation assays detect the presence of hTR and hTERT in human tissues

and body fluids. We own issued patents for the detection of telomerase activity and the components of telomerase, including patents for the TRAP assay and diagnostic methods based on telomerase detection. To date, our licensees have commercialized 13 research-use-only kits that incorporate our technology.

Through Roche Diagnostics, we are participating in the development of fluids-based telomerase detection tests for clinical *in vitro* diagnostics. The tests are based on telomerase detection assays that have been commercialized for the research-use-only market. Roche is investigating the utility of an assay for telomerase for detecting bladder cancer, with potential utility in early detection screening and monitoring of patients for recurrence. Patients who have had bladder cancer now periodically undergo invasive cystoscopy to screen for recurrence.

Telomerase Activation

We are developing drug candidates to treat various degenerative diseases by the controlled activation of telomerase. Data published by us and others has indicated that cellular aging caused by shortening telomeres, which occurs in numerous tissues throughout the human body, causes or contributes to chronic degenerative diseases and conditions including anemia, HIV/AIDS, liver disease, macular degeneration (a chronic disease of the eyes often leading to vision loss), atherosclerosis (narrowing of arteries which reduces blood flow to internal organs) and impaired wound healing. Controlled activation of telomerase in normal cells can restore telomere length or slow the rate of loss, improve functional capacity, and increase the proliferative lifespan of cells.

Compound Product	Product Description	Disease Treatment	Development Stage
TAT2	Telomerase Activator	HIV/AIDS	Preclinical

HIV/AIDS (TAT2). Work by our collaborators has shown that telomere loss in cytotoxic T-lymphocytes, the blood cells responsible for killing HIV-infected cells, is accelerated in HIV/AIDS patients, and contributes to the loss of anti-HIV activity that occurs during disease progression. Our collaborators published data showing that telomerase activation using overexpression of hTERT, the catalytic component of telomerase, in T-lymphocytes both increased their lifespan and significantly enhanced their anti-HIV activity.

These results were extended in a subsequent publication which showed that telomerase activation in bulk cultures of lymphocytes from HIV patients enhanced HIV-suppressing activity and improved the production of antiviral cytokines in response to HIV-specific stimulation. These results show that telomere shortening in HIV-specific lymphocytes plays a major role in the immune dysfunction seen in late stage HIV-1 disease and that telomerase activation, by enhancing the anti-HIV effects of CD8+ lymphocytes, is potentially a therapy for treating patients with HIV disease.

Our approach to the therapeutic use of telomerase activation in HIV/AIDS and other chronic diseases is based upon small molecule telomerase activators we have identified (TAT1 and TAT2). We have tested these telomerase activating drugs for enhancement of antiviral activity in lymphocytes from HIV patients. At several scientific meetings, we and our collaborators presented data showing that our two small molecule telomerase activators, TAT1 and TAT2 (formerly GRN139951 and GRN140665), activated telomerase *in vitro* in cytotoxic T-cells taken from HIV/AIDS donors. Moreover, the compounds increased the proliferative capacity, the secretion of gamma Interferon (a virus-fighting molecule) and the direct cytotoxic killing of HIV-infected CD4 T-cells when these treated cells were exposed to HIV peptides or HIV-infected cells.

In 2005, we formed a joint venture company, TA Therapeutics, Ltd. (TAT), with the Biotechnology Research Corporation (BRC) of Hong Kong, a company established by the Hong Kong University of Science and Technology. TAT conducts research and was established to commercially develop products that utilize telomerase activator drugs to restore the regenerative and functional capacity of cells in various organ systems that have been impacted by senescence, injury or chronic disease. TAT is owned 50% by Geron and 50% by BRC, our research partner in the development of telomerase activator drugs. TAT selected the TAT2 compound for clinical development in 2006. Scalable drug product manufacturing has been secured in China and IND-enabling studies are now in progress for the first indication: HIV/AIDS. Follow-on indications for development of TAT2 in other

diseases are being explored.

Human Embryonic Stem Cell Therapies

The two properties of hESCs, their immortality and pluripotency, enable the development of a potential new mode of commercialization for cell-based products and therapeutics, namely the development of "off-the-shelf" products available on demand. We have developed proprietary methods to grow, maintain, and scale the culture of undifferentiated hESCs that use feeder cell-free and serum-free media with chemically defined components. Moreover, we have developed scalable processes to differentiate these cells into therapeutically relevant cells. We have developed cryopreserved formulations of hESC-derived cells to enable our business model of delivering "on demand" cells for therapeutic use. We are now testing six different hESC-derived therapeutic cell types in animal models. In four of these cell types, we have demonstrated efficacy as evidenced by durable engraftment or functional improvements of the treated animals. From these studies, we are now advancing development of two hESC-based therapeutics to clinical testing. The most advanced hESC-derived product, GRNOPC1, which

contains oligodendroglial progenitor cells, is targeted for the treatment of spinal cord injury. Geron's second hESC product, GRNCM1, is a population of cardiomyocytes, the contractile cells of the heart, which is intended for the treatment of patients with myocardial disease. Geron also has made substantial progress in deriving pancreatic islet ß cells for diabetes, osteoblasts for osteoporosis, chondrocytes for osteoarthritis, hepatocytes for liver failure and ADME drug testing, and dendritic cells for two applications including, cancer immunotherapy and graft acceptance to prevent immune rejection of the other cell types used in therapeutic applications. We own or have licenses to intellectual property covering core inventions and enabling technology in this field.

Product	Product Description	Disease Treatment	Development Stage
GRNOPC1	hESC-Derived Oligodendrocytes	Subacute Spinal Cord Injury	IND-enabling studies
GRNCM1	hESC-Derived Cardiomyocytes	Heart Disease	Preclinical
GRNIC1	hESC-Derived Islets	Type 1 Diabetes	Research
Cell Types	Osteoblasts	Osteoporosis	Research
	Chondrocytes	Osteoarthritis	Research
	Hepatocytes	Liver Disease and ADME Toxicology Testing	Research
	Dendritic Cells	Immune Rejection and Cancer Immunotherapy	Research

Oligodendrocytes for Spinal Cord Injury (GRNOPC1). The major neural cells of the central nervous system typically do not regenerate after injury. If a nerve cell is damaged due to disease or injury, there is no treatment at present to restore lost function. Patients worldwide suffer from injury to the nervous system or disorders associated with its degeneration. In the case of spinal cord injuries, patients are often left partly or wholly paralyzed because nerve and supporting cells in the spinal cord have been damaged and cannot regenerate. Such patients are permanently disabled, often institutionalized and may require life support.

Embryonic stem cell-derived neural cells have been used by researchers to treat nervous system disorders in animal models. In the case of spinal cord injuries, neural cells derived from animal embryonic stem cells and injected into the spinal cord injury site produced significant recovery of the animal's ability to move and bear weight.

To apply those observations to humans, we have now derived oligodendroglial progenitor cells (GRNOPC1) from hESCs in culture and tested them in a rat model of spinal cord injury. In our collaboration with researchers at the University of California, Irvine, we have shown in animal models that GRNOPC1 can improve functional locomotor behavior after implantation in the injury sites 7 days after injury. Histological analysis also provided

evidence for the engraftment and function of these cells. These data were published in May 2005 in the *Journal of Neuroscience*. We have developed functional cryopreserved formulations of GRNOPC1 that can be readily implemented in clinical trials and have initiated cGMP production of GRNOPC1. We are currently completing IND-enabling studies for hESC-derived oligodendrocytes for application in spinal cord injury.

Cardiomyocytes for Heart Disease (GRNCM1). Heart muscle cells (cardiomyocytes) do not regenerate during adult life. When heart muscle is damaged by injury or decreased blood flow, functional contracting heart muscle is replaced with nonfunctional scar tissue. Congestive heart failure, a common consequence of heart muscle or valve damage, affects approximately 5.0 million people in the United States. This year, it is estimated that about 1.2 million people will have a heart attack, which is the primary cause of heart muscle damage.

We can potentially treat heart disease by using cardiomyocytes derived from hESCs. Researchers have demonstrated proof-of-concept of this approach in mice. Mouse embryonic stem cells have been used to derive mouse cardiomyocytes. When injected into the hearts of recipient adult mice, the cardiomyocytes repopulated the heart tissue and stably integrated into the muscle tissue of the adult mouse heart. In human medicine, it is therefore possible that hESC-derived cardiomyocytes could be developed for cellular transplantation therapy in humans suffering from congestive heart failure and the damage caused by heart attacks. We have derived human cardiomyocytes from hESCs (GRNCM1) using a process that can be scaled for clinical production. GRNCM1 has normal contractile function and responds appropriately to cardiac drugs. We have transplanted these cells into animal models of myocardial

infarction in which the cells engraft and improve the left ventricular function compared to those animals receiving injections without cells. In 2007, we will be testing GRNCM1 in large animal models of heart disease.

Islet Cells for Diabetes (GRNIC1). It is estimated that there are as many as one million Americans suffering from Type 1 Diabetes (Insulin Dependent Diabetes Mellitus). Normally, certain cells in the pancreas, called the islet ß cells, produce insulin which promotes the uptake of the sugar glucose by cells in the human body. Degeneration of pancreatic islet ß cells results in a lack of insulin in the bloodstream which results in diabetes. Although diabetics can be treated with daily injections of insulin, these injections enable only intermittent glucose control. As a result, patients with diabetes suffer chronic degeneration of many organs, including the eye, kidney, nerves and blood vessels. In some cases, patients with diabetes have been treated with islet ß cell transplantation derived from cadavers. However, poor availability of suitable sources for islet ß cell transplantation and the complications of the required co-administration of immunosuppressive drugs make this approach impractical as a treatment for the growing numbers of individuals suffering from diabetes.

We have derived insulin-producing cells (i.e. similar to pancreatic islet ß cells) from hESCs and are working to improve the yield of islet cells and characterize their secretion of insulin in response to glucose. We are transplanting the islets to animal models of diabetes and early results show prolonged survival of cells in the engrafted animals and the detection of human insulin in their blood.

Osteoblasts for Osteoporosis and Non-Union Bone Fractures. Osteoporosis, or loss of bone density, is a common condition associated with aging and hormonal changes in post-menopausal women. In addition to skeletal deformities, back pain and loss of height, the disease causes over 1.5 million fractures per year in the United States alone. These fractures often occur after minimal trauma and if severe, as in hip fracture, carry mortality rates as high as 24% for patients age 50 and over. Nearly one in five hip fracture patients ends up in a nursing home. Total health care costs for osteoporosis and its complications are estimated at $18 billion per year in the United States.

The primary cause of the disease is metabolic bone loss (mediated by osteoclasts - cells which resorb bone) that is incompletely compensated by new bone formation (mediated by osteoblasts - cells which form new bone). Osteoblast activity declines over the human lifespan and fails to keep pace with the increasing activity of osteoclasts, resulting in progressive loss of bone density leading to fracture, pain and deformity.

We have made osteoblasts from hESCs and are now conducting preclinical tests in animals. If these preclinical tests are successful, we may test the cells in patients with non-union fractures (fractures of the long bones of the leg or arm that do not heal) or in patients with severe refractory osteoporosis.

Chondrocytes for Osteoarthritis. Osteoarthritis, or Degenerative Joint Disease, is an extremely common condition characterized by degradation of cartilage in joints, often accompanied by bone remodeling and bone overgrowth at the affected joints. The disease affects an estimated 21 million adults in the United States, mostly after age 45. The disease has many causes, but the end result is a structural degradation of joint cartilage and a failure of chondrocytes (cartilage-forming cells) to repair the degraded cartilage collagen matrix. We have derived chondrocytes from hESCs and, if *in vitro* and animal testing results are positive, we may test these cells in patients with osteoarthritis by injecting them directly into the affected joints.

Dendritic Cells for Cancer Immunotherapy and to Enable Therapeutic Graft Acceptance. The hematopoietic system (the circulating cells of blood) is one of the tissues of the human body that can replenish itself throughout life. One of the cell types produced by the hematopoietic system is the dendritic cell. Dendritic cells, depending on their type can either induce or downmodulate immune responses. Therefore, dendritic cells derived from hESCs can be used for two purposes: (i) to upregulate immune responses to particular antigens such as telomerase, for cancer immunotherapy applications; and (ii) to prevent rejection of hESC-derived therapeutic grafts.

We are now developing procedures to differentiate hESCs to dendritic cells which will subsequently be used in both *in vitro* and animal models to assess their immunotherapeutic and immunomodulatory activity.

Products for Research and Development

Immortalized Cells for Research. Scientists study specific cells from targeted tissues in order to understand their biological function. For these studies, cells are usually isolated from tissue and maintained in culture. The progressive changes in biological activity, morphology and proliferation as a result of normal cell aging in tissue culture potentially limit the utility of these cells in serial experiments and long-term research. Because of these limitations, most research laboratories utilize transformed cell lines for their studies. Cells can be transformed by using viruses which ultimately cause the cells to grow indefinitely in culture. However, such immortalized cell lines have abnormal characteristics compared to non-transformed cells. For this reason, they are not good models of normal tissue in the human body.

Telomerase-immortalized cells may be ideal for use in biological research because these cells proliferate indefinitely and function in culture in the same manner as the normal, mortal cells from which they were derived. Moreover, telomerase-immortalized cells can function in the body to form normal tissue and their capacity to differentiate into mature tissue is maintained. The ability of these cells to maintain normal physical and biological characteristics while retaining proliferative capacity allows them to be a constant source of cells for repeat and long-term studies of the function of cells both in culture and in the body. Telomerase-immortalized cells can be used to study any of the normal biological pathways in cells and can be used to screen for factors which influence the appropriate function of those cells. Moreover, cells taken from diseased tissues which are then telomerase-immortalized in culture can be used to explore the mechanism of the disease process and to develop interventions to prevent or treat that disease.

We are making telomerase-immortalized cell lines commercially available to the research market and to companies for basic research and for use in drug discovery and biologics production applications. We have granted royalty-bearing licenses to the American Type Culture Collection and Cambrex BioSciences under which these organizations will produce and sell telomerase-immortalized cells for both academic research and commercial drug discovery.

hESC-Derived Hepatocytes for Drug Screening and Toxicology. Three of the major hurdles of pharmaceutical drug development are: (i) identifying compounds with activity in diseased tissue; (ii) understanding the metabolism and biodistribution of the compound; and (iii) determining the potential toxic side effects of the compound. Undesirable activity of a compound being evaluated as a drug candidate in any one of these areas can impact the development and commercialization of the drug. The earlier in development that a compound is found to have undesirable characteristics, the faster these characteristics can be potentially corrected. This potentially translates into reduced costs and time in drug development, and less harmful patient exposure in clinical trials.

Many prospective new drugs fail in clinical trials because of toxicity to the liver or because of poor uptake, distribution or elimination of the active compound in the human body. Much of the efficacy and safety of a drug will depend on how that drug is metabolized into an active or inactive form, and on the toxic metabolites that might be generated in the process. Hepatocytes, the major cells of the liver, metabolize most compounds and thereby can be used to predict many pharmacological characteristics of a drug.

There are no completely effective systems available today to accurately predict the metabolism or toxicity of a compound in human livers. Rat and mouse metabolism models only approximate human metabolism. The development of several drugs has been terminated late in human clinical trials because rodent systems utilized early in the development process failed to predict that the drug would be toxic to humans. Human hepatocyte cell lines available today do not have the same attributes as their normal counterparts in the body and must be transformed in order to maintain their proliferative capacity in culture. Access to fresh primary human liver tissue for use in toxicity studies is very limited and substantial variability can be observed depending on the individual donor, the time and process of collection and the culture conditions for the experiments.

We are developing methods to derive standardized functional hepatocytes (liver cells) from hESCs to address the significant unmet need for a reliable predictor of the metabolism, biodistribution and toxicity of drug development candidates. If we are successful, these cells would provide a consistent source of normal human liver cells that can reliably predict how a new drug will affect the livers of the people who take it. We believe that an unlimited supply of human hepatocytes, which retain normal drug-metabolizing enzyme activity, would address one of the largest bottlenecks in new drug research and accelerate the drug development process. In addition, the availability of hepatocytes from numerous

individuals would allow a more thorough understanding of the effects of a drug candidate on a specific individual, promoting development of the field of pharmacogenomics - the study of how a compound□s activity varies with an individual□s genetic make-up. Our scientists have succeeded in demonstrating that hepatocyte-like cells derived from hESCs express normal markers of hepatocyte function, including Phase 1 and Phase 2 drug-metabolizing enzymes. We have been awarded a U.S. patent covering human hepatocytes derived from hESCs and a second U.S. patent covering the use of hESC-derived hepatocytes for drug screening.

Nuclear Transfer: Agriculture/Xenotransplantation/Biologics

Nuclear transfer is a method for producing animals whose nuclear genetic material is derived solely from a donor cell from an individual animal (□clones□). In this process, the nucleus containing the chromosomal DNA is removed from the animal egg cell and subsequently replaced with a nucleus from a donor somatic (non-reproductive) cell. Fusion between the resulting egg cell and the donor somatic nucleus results in a new cell which gains a complete set of chromosomes derived entirely from the donor nucleus. Mitochondrial DNA, providing some of the genes for energy production, resides outside the nucleus and is provided by the egg. After a brief culture period that enables the reconstituted egg cell to initiate embryonic development, the early embryo is implanted into the uterus of a female animal, where it can fully develop and result in the live birth of a cloned offspring animal. The offspring is essentially a genetic clone of (genetically identical to) the animal from which the donor nucleus was obtained.

In early 1997, Dr. Ian Wilmut and his colleagues at the Roslin Institute were the first to demonstrate, with the birth of Dolly the sheep, that the nucleus of an adult cell can be transferred to an enucleated egg to create cloned offspring. The birth of Dolly was significant because it demonstrated the ability of egg cell cytoplasm, the portion of the egg outside of the nucleus, to reprogram an adult somatic nucleus. Reprogramming enables the adult somatic cell nucleus to express all the genes required for the full embryonic development of the animal. In addition to sheep, the technique has been used to clone mice, rats, goats, cattle, rabbits, cats and pigs from donor cells and enucleated eggs from each respective animal species. In 1999, we acquired Roslin Bio-Med Ltd., a commercial subsidiary of the Roslin Institute, and an exclusive license to the use of nuclear transfer technology for multiple applications in animal and human biology.

Agriculture. Our nuclear transfer technology can be used for applications in agriculture that could improve livestock by producing unlimited numbers of genetically identical animals with superior commercial qualities. Such applications can be extended to major agricultural sectors, such as beef, dairy, pork and poultry, to provide large numbers of animals with superior characteristics of disease resistance, longevity, growth rate or product

quality. In 2006, the FDA announced its intention to allow milk and meat from cloned animals into the U.S. food supply. The proposed new regulations are now open for public comment.

Transgenic Animals. Our nuclear transfer technology can be applied to clone animals that have been genetically engineered to produce proteins for human therapeutic or industrial use. For example, herds which carry the genes to make human antibodies could be cloned, thereby allowing for the large-scale production of therapeutic antibodies or vaccines.

Xenotransplantation. Our nuclear transfer technology can be used for applications in xenotransplantation to create animals whose cells, tissues or organs could be used in human organ transplantation settings. This approach could be used either as a bridge to human organ transplantation or as a long-term therapy.

In previous years, we granted a number of licenses to our nuclear transfer technology to companies who are utilizing it for applications in agriculture and production of biologicals. In 2005, following successes in three patent interference proceedings, we formed a joint venture company, Start Licensing, Inc. (Start), with Exeter Life Sciences Inc. Start is exclusively focused on managing and licensing intellectual property rights for animal cloning, including our nuclear transfer technology and rights conveyed to Start by Exeter Life Sciences. We received an upfront license payment when Start was created and own 49.9% of Start. We will be entitled to a proportionate share of any revenues distributed by Start. We have retained all rights for use of the technology in human cells.

Patents and Proprietary Technology

A broad intellectual property portfolio of issued patents and pending patent applications supports our product development and out-licensing activities. We currently own or have licensed over 145 issued or allowed United States patents, 240 granted or accepted foreign patents and 450 patent applications that are pending around the world.

Our policy is to seek appropriate patent protection for inventions in our principal technology platforms telomerase, human embryonic stem cells and nuclear transfer as well as ancillary technologies that support these platforms or otherwise provide a competitive advantage to us. We achieve this by filing patent applications for discoveries made by our scientists, as well as those that we make in conjunction with our scientific collaborators and strategic partners. Typically, although not always, we file patent applications in the United States and internationally through the Patent Cooperation Treaty. In addition, where appropriate, we try to obtain licenses from other organizations to patent filings that may be useful in advancing our scientific and product development programs.

Our telomerase platform is the mainstay of our oncology program and it serves as the basis for other product opportunities. Our patent portfolio includes over 100 issued or allowed United States patents, 160 granted or accepted foreign patents and over 180 patent applications pending worldwide relating to our telomerase product opportunities. The foundational patents include those covering the cloned genes that encode the RNA component (hTR) and the catalytic protein component (hTERT) of human telomerase. Related issued and pending patents cover cells that are immortalized by expression of recombinant hTERT, cancer diagnostics based on detecting the expression of telomerase in cancer cells, the use of hTERT as a cancer vaccine, the use of the hTERT promoter to power cancer-killing genes and viruses, and telomerase inhibitors for use as cancer therapeutics. We own issued patents that cover the sequences of GRN163 and GRN163L, as well as patents covering the chemistry that is used to build these oligonucleotides. We have a license to the dendritic cell-loading technology used in our telomerase cancer vaccine. Recently filed patent applications covering the telomerase-activating compounds TAT1 and TAT2 that we discovered in collaboration with our colleagues at the Hong Kong University of Science and Technology have been exclusively licensed to our joint venture company, TAT, for therapeutic applications.

Our human embryonic stem cell platform is protected by patents rights that we either own or have licensed. The patents that we have licensed include foundational hESC patents that arose from work that we funded at the University of Wisconsin-Madison. We have also filed patent applications to protect technologies developed by our scientists in our ongoing efforts to develop products based on hESCs. By way of example, these patent applications cover technologies that we believe will facilitate the commercial-scale production of hESCs, such as

methods for growing the cells without the need for cell feeder layers. Patent applications that we own or have licensed also cover cell types that can be made from hESCs, including hepatocytes (liver cells), cardiomyocytes (heart muscle cells), neural cells (nerve cells, including dopaminergic neurons and oligodendrocytes), chondrocytes (cartilage cells), pancreatic islet ß cells, osteoblasts (bone cells), hematopoietic cells (blood-forming cells) and dendritic cells. Currently our portfolio includes over 210 patent applications pending around the world covering various aspects of our stem cell technology. Examples of granted stem cell patents that we own include, U.S. Patent Nos. 6,458,589 and 6,506,574 relating to hESC-derived hepatocytes; 6,800,480 relating to the feeder-free growth of hESCs; and 6,833,269 covering methods of producing neural cells from hESCs.

Our third technology platform, nuclear transfer, is protected in part by the patent rights that we purchased in 1999 with the acquisition of Roslin Bio-Med, which we now operate as Geron Bio-Med. Six United States patents have now issued, and 40 foreign patents have been granted or accepted. In addition, we have more than 50 pending patent applications worldwide relating to nuclear transfer, arising both from the acquired patent rights and subsequent research that we funded at the Roslin Institute. As discussed above, these patent rights are now a major asset of Start Licensing, Inc., the joint venture company that we created in 2005 for the purpose of managing and licensing intellectual property rights for animal cloning.

We endeavor to monitor worldwide patent filings by third parties that are relevant to our business. Based on this monitoring, we may determine that an action is appropriate to protect our business interests. Such actions may include the filing of oppositions against the grant of a patent in overseas jurisdictions, and the filing of a request for the declaration of an interference with a U.S. patent application or issued patent. Similarly, third parties may take similar actions against our patents. By way of example, in 2005 we were involved in interference proceedings that we had initiated at the U.S. Patent and Trademark Office involving patents and patent applications for nuclear transfer technology; judgments in those

actions were entered in our favor. We are currently also involved in patent opposition proceedings before the European Patent Office, the Australian Patent Office and the New Zealand Patent Office, both as the party holding the opposed patent, and in opposition to patents granted or proposed to be granted to another entity.

Government Regulation

Regulation by governmental authorities in the United States and other countries is a significant factor in the development, manufacture and marketing of our proposed products and in our ongoing research and product development activities. The nature and extent to which such regulation applies to us will vary depending on the nature of any products which may be developed by us. We anticipate that many, if not all, of our proposed products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and other approval procedures of the FDA and similar regulatory authorities in European and other countries. Various governmental statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and recordkeeping related to such products and their marketing. The process of obtaining these approvals and the subsequent compliance with appropriate statutes and regulations require the expenditure of substantial time and money, and there can be no guarantee that approvals will be granted.

FDA Approval Process

Prior to commencement of clinical studies involving humans, preclinical testing of new pharmaceutical products is generally conducted on animals in the laboratory to evaluate the potential efficacy and safety of the product candidate. The results of these studies are submitted to the FDA as a part of an IND application, which must become effective before clinical testing in humans can begin. Typically, human clinical evaluation involves a time-consuming and costly three-phase process. In Phase I, clinical trials are conducted with a small number of people to assess safety and to evaluate the pattern of drug distribution and metabolism within the body. In Phase II, clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety. (In some cases, an initial trial is conducted in diseased patients to assess both preliminary efficacy and preliminary safety and patterns of drug metabolism and distribution, in which case it is referred to as a Phase I/II trial.) In Phase III, large-scale, multi-center, comparative trials are conducted with patients afflicted with a target disease in order to provide enough data to demonstrate the efficacy and safety required by the FDA. The FDA closely monitors the progress

of each of the three phases of clinical testing and may, at its discretion, re-evaluate, alter, suspend, or terminate the testing based upon the data which have been accumulated to that point and its assessment of the risk/benefit ratio to the patient. Monitoring of all aspects of the study to minimize risks is a continuing process. All adverse events must be reported to the FDA.

The results of the preclinical and clinical testing on non-biologic drugs and certain diagnostic drugs are submitted to the FDA in the form of a New Drug Application (NDA) for approval prior to commencement of commercial sales. In the case of vaccines or gene and cell therapies, the results of clinical trials are submitted as a Biologics License Application (BLA). In responding to a NDA or BLA, the FDA may grant marketing approval, request additional information or refuse to approve if the FDA determines that the application does not satisfy its regulatory approval criteria. There can be no assurance that approvals will be granted on a timely basis, if at all, for any of our proposed products.

European and Other Regulatory Approval

Whether or not FDA approval has been obtained, approval of a product by comparable regulatory authorities in Europe and other countries will likely be necessary prior to commencement of marketing the product in such countries. The regulatory authorities in each country may impose their own requirements and may refuse to grant an approval, or may require additional data before granting it, even though the relevant product has been approved by the FDA or another authority. As with the FDA, the regulatory authorities in the European Union (EU) and other developed countries have lengthy approval processes for pharmaceutical products. The process for gaining approval in particular countries varies, but generally follows a similar sequence to that described for FDA approval. In Europe, the European Committee for Proprietary Medicinal Products provides a mechanism for EU-member states to exchange information on all aspects of product licensing. The EU has established a European agency for the evaluation of medical

products, with both a centralized community procedure and a decentralized procedure, the latter being based on the principle of licensing within one member country followed by mutual recognition by the other member countries.

Other Regulations

We are also subject to various United States federal, state, local and international laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research work. We cannot accurately predict the extent of government regulation which might result from future legislation or administrative action.

Scientific Consultants

We have consulting agreements with a number of leading academic scientists and clinicians. These individuals serve as key consultants or as members of clinical focus group panels with respect to our product development programs and strategies. They are distinguished scientists and clinicians with expertise in numerous scientific fields, including embryonic stem cells, nuclear transfer and telomere and telomerase biology, as well as developmental biology, cellular biology and molecular biology.

We use consultants to provide us with expert advice and consultation on our scientific programs and strategies, as well as on the ethical aspects of our work. They also serve as important contacts for us throughout the broader scientific community.

We retain each consultant according to the terms of a consulting agreement. Under such agreements, we pay them a consulting fee and reimburse them for out-of-pocket expenses incurred in performing their services for us. In addition, some consultants hold options to purchase our common stock, subject to the vesting requirements contained in the consulting agreements. Our consultants are employed by institutions other than ours, and therefore may have commitments to, or consulting or advisory agreements with, other entities or academic institutions that may limit their availability to us.

Executive Officers of the Company

The following table sets forth certain information with respect to our executive officers:

Name	Age	Position
Thomas B. Okarma, Ph.D., M.D.	61	President, Chief Executive Officer and Director
Alan B. Colowick, M.P.H., M.D.	44	President, Oncology
David L. Greenwood	55	Executive Vice President, Chief Financial Officer, Treasurer and Secretary
David J. Earp, Ph.D., J.D.	42	Senior Vice President, Business Development and Chief Patent Counsel
Calvin B. Harley, Ph.D.	54	Chief Scientific Officer
Melissa A. Kelly Behrs	43	Senior Vice President, Therapeutic Development, Oncology
Jane S. Lebkowski, Ph.D.	51	Senior Vice President, Regenerative Medicine

Thomas B. Okarma, Ph.D., M.D., has served as our President, Chief Executive Officer and a member of our board of directors since July 1999. He is also a director of Geron Bio-Med Limited, a United Kingdom company and our wholly-owned subsidiary, TA Therapeutics, Ltd., a Hong Kong company and a joint venture between us and Biotechnology Research Corporation of Hong Kong. From May 1998 until July 1999, Dr. Okarma was the Vice President of Research and Development. From December 1997 until May 1998, Dr. Okarma was Vice President of Cell Therapies. Dr. Okarma currently serves on the Board of BIO and was Chairman of the Board of Overseers of Dartmouth Medical School from 2000 to 2006. From 1985 until joining us, Dr. Okarma, the scientific founder of Applied Immune Sciences, Inc., served initially as Vice President of Research and Development of Applied Immune Sciences and then as chairman, chief executive officer and a director of Applied Immune Sciences, until 1995 when it was acquired by Rhone-Poulenc Rorer. Dr. Okarma was a Senior Vice President at Rhone-Poulenc Rorer from the time of the acquisition of Applied Immune Sciences until December 1996. From 1980 to 1992, Dr. Okarma was a member of the faculty of the Department of Medicine at Stanford University School of Medicine. Dr. Okarma holds a A.B. from Dartmouth College, a M.D. and Ph.D. from Stanford University and an executive M.B.A. from Stanford Graduate School of Business.

Alan B. Colowick, M.P.H., M.D., has served as our President, Oncology since October 2006. From January 2005 until joining us, Dr. Colowick was the Chief Medical Officer of Threshold Pharmaceuticals Inc., where he was responsible for all aspects of non-clinical and clinical development and manufacturing. From 1999 to 2005, Dr. Colowick held various management positions with Amgen, Inc., most recently serving as Vice President of European Medical Affairs, where he was responsible for all products in multiple therapeutic areas, including hematology/oncology, nephrology and internal medicine. From 1996 to 1999, Dr. Colowick was a clinical and research fellow in hematology-oncology at Harvard University and the Brigham and Women□s Hospital/Dana Farber Cancer Institute. Dr. Colowick holds a B.S. in molecular biology from the University of Colorado, a M.D. from Stanford University and a M.P.H from Harvard University.

David L. Greenwood has served as our Chief Financial Officer, Treasurer and Secretary since August 1995 and our Executive Vice President since January 2004. He is also a director of Geron Bio-Med Limited, our joint ventures TA Therapeutics, Ltd. and Start Licensing, Inc., and Clone International, an Australian company. From August 1999 until January 2004, Mr. Greenwood also served as our Senior Vice President of Corporate Development. From April 1997 until August 1999, Mr. Greenwood served as our Vice President of Corporate Development. He also serves on the Board of Regents for Pacific Lutheran University. From 1979 until joining us, Mr. Greenwood held various positions with J.P. Morgan & Co. Incorporated, an international banking firm. Mr. Greenwood holds a B.A. from Pacific Lutheran University and a M.B.A. from Harvard Business School.

David J. Earp, J.D., Ph.D., has served as our Senior Vice President of Business Development and Chief Patent Counsel since May 2004. He is also a director of TA Therapeutics, Ltd. and Start Licensing, Inc. From October 1999 until May 2004, Dr. Earp served as our Vice President of Intellectual Property. From 1992 until joining us in June 1999, Dr. Earp was with the intellectual property law firm of Klarquist Sparkman Campbell Leigh and Whinston, LLP where his practice focused on biotechnology patent law. Dr. Earp holds a B.Sc. in microbiology from the University of Leeds, England, a Ph.D. from the biochemistry department of The University

of Cambridge, England, and conducted postdoctoral research at the University of California at Berkeley/U.S.D.A. Plant Gene Expression Center. He received his J.D. from the Northwestern School of Law of Lewis and Clark College in Portland, Oregon.

Calvin B. Harley, Ph.D., has served as our Chief Scientific Officer since July 1996. From May 1994 until July 1996, Dr. Harley served as our Vice President of Research. From April 1993 until May 1994, Dr. Harley served as our Director, Cell Biology. From 1989 until joining us, Dr. Harley was an Associate Professor of Biochemistry at McMaster University, and from 1982 to 1989, was an Assistant Professor of Biochemistry at McMaster University. Dr. Harley was also an executive of the Canadian Association on Gerontology, Division of Biological Sciences from 1987 to 1991. Dr. Harley holds a B.S. from the University of Waterloo and a Ph.D. from McMaster University, and conducted postdoctoral work at the University of Sussex and the University of California at San Francisco.

Melissa A. Kelly Behrs has served as our Senior Vice President, Therapeutic Development, Oncology since January 2007. Ms. Behrs served as our Vice President of Oncology since January 2003. From April 2002 until January 2003, Ms. Behrs served as our Vice President of Corporate Development. From April 2001 until April 2002, Ms. Behrs served as our General Manager of Research and Development Technologies. Ms. Behrs joined us in November 1998 as Director of Corporate Development. From 1990 to 1998, Ms. Behrs worked at Genetics Institute, Inc., serving initially as Assistant Treasurer and then as Associate Director of Preclinical Operations where she was responsible for all business development, regulatory, and project management activities for the Preclinical Development function. Ms. Behrs received a B.S. from Boston College and an M.B.A. from Babson College.

Jane S. Lebkowski, Ph.D., has served as our Senior Vice President of Regenerative Medicine since January 2004. From August 1999 until January 2004, Dr. Lebkowski served as our Vice President of Regenerative Medicine. From April 1998 until August 1999, Dr. Lebkowski served as our Senior Director, Cell and Gene Therapies. From 1986 until joining us in 1995, Dr. Lebkowski served as Vice President, Research and Development at Applied Immune Sciences. In 1995, Applied Immune Sciences was acquired by Rhone-Poulenc Rorer, at which time Dr. Lebkowski was appointed Vice President, Discovery & Product Development. Dr. Lebkowski received a B.S. in chemistry and biology from Syracuse University and received her Ph.D. from Princeton University.

Employees

As of December 31, 2006, we had 103 full-time employees of whom 29 hold Ph.D. degrees and 23 hold other advanced degrees. Of our total workforce, 85 employees were engaged in, or directly support, our research and development activities and 18 employees were engaged in business development, finance and administration. We also retain outside consultants. None of our employees are covered by a collective bargaining agreement, nor have we experienced work stoppages. We consider relations with our employees to be good.

ITEM 1A. RISK FACTORS

Our business is subject to various risks, including those described below. You should carefully consider these risk factors, together with all of the other information included in this annual report on Form 10-K. Any of these risks could materially adversely affect our business, operating results and financial condition.

Our business is at an early stage of development.

Our business is at an early stage of development, in that we do not yet have product candidates in late-stage clinical trials or on the market. One of our product candidates, a telomerase therapeutic cancer vaccine, has been studied in clinical trials conducted by an academic institution. We have begun clinical testing of our lead anti-cancer drug, GRN163L, in patients with chronic lymphocytic leukemia and solid tumor malignancies. We have no other product candidates in clinical testing. Our ability to develop product candidates that progress to and through clinical trials is subject to our ability to, among other things:

- succeed in our research and development efforts;
- select therapeutic compounds or cell therapies for development;
- obtain required regulatory approvals;
- manufacture product candidates; and
- collaborate successfully with clinical trial sites, academic institutions, physician investigators, clinical research organizations and other third parties.

Potential lead drug compounds or other product candidates and technologies will require significant preclinical and clinical testing prior to regulatory approval in the United States and other countries. Our product candidates may prove to have undesirable and unintended side effects or other characteristics adversely affecting their safety, efficacy or cost-effectiveness that could prevent or limit their commercial use. In addition, our product candidates may not prove to be more effective for treating disease or injury than current therapies. Accordingly, we may have to delay or abandon efforts to research, develop or obtain regulatory approval to market our product candidates. In addition, we will need to determine whether any of our potential products can be manufactured in commercial quantities at an acceptable cost. Our research and development efforts may not result in a product that can be approved by regulators or marketed successfully. Because of the significant scientific, regulatory and commercial milestones that must be reached for any of our development programs to be successful, any program may be abandoned, even after we have expended significant resources on the program, such as our investments in telomerase technology and human embryonic stem cells, which could cause a sharp drop in our stock price.

The science and technology of telomere biology and telomerase, human embryonic stem cells and nuclear transfer are relatively new. There is no precedent for the successful commercialization of therapeutic product candidates based on our technologies. These development programs are therefore particularly risky. In addition, we, our licensees or our collaborators must undertake significant research and development activities to develop product candidates based on our technologies, which will require additional funding and may take years to accomplish, if ever.

We have a history of losses and anticipate future losses, and continued losses could impair our ability to sustain operations.

We have incurred operating losses every year since our operations began in 1990. As of December 31, 2006, our accumulated deficit was approximately $399.1 million. Losses have resulted principally from costs incurred in connection with our research and development activities and from general and administrative costs associated with our operations. We expect to incur additional operating losses and, as our development efforts and clinical testing activities continue, our operating losses may increase in size.

Substantially all of our revenues to date have been research support payments under collaboration agreements and revenues from our licensing arrangements. We may be unsuccessful in entering into any new corporate collaboration or license agreement that results in revenues. We do not expect that the revenues generated from these arrangements will be sufficient alone to continue or expand our research or development activities and otherwise sustain our operations.

While we receive royalty revenue from licenses of diagnostic product candidates, telomerase-immortalized cell lines and other licensing activities, we do not currently expect to receive sufficient royalty revenues from these licenses to sustain our operations. Our ability to continue or expand our research and development activities and otherwise sustain our operations is dependent on our ability, alone or with others, to, among other things, manufacture and market therapeutic products.

We also expect to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. This will result in decreases in our working capital, total assets and stockholders equity, which may not be offset by future financings. We will need to generate significant revenues to achieve profitability. We may not be able to generate these revenues, and we may never achieve profitability. Our failure

to achieve profitability could negatively impact the market price of our common stock. Even if we do become profitable, we cannot assure you that we would be able to sustain or increase profitability on a quarterly or annual basis.

We will need additional capital to conduct our operations and develop our products, and our ability to obtain the necessary funding is uncertain.

We will require substantial capital resources in order to conduct our operations and develop our product candidates, and we cannot assure you that our existing capital resources, interest income and equipment financing arrangements will be sufficient to fund our current and planned operations. The timing and degree of any future capital requirements will depend on many factors, including:

- the accuracy of the assumptions underlying our estimates for our capital needs in 2007 and beyond;
- the magnitude and scope of our research and development programs;
- the progress we make in our research and development programs and in preclinical development and clinical trials;
- our ability to establish, enforce and maintain strategic arrangements for research, development, clinical testing, manufacturing and marketing;
- the number and type of product candidates that we pursue;
- the time and costs involved in obtaining regulatory approvals; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims.

We do not have any committed sources of capital. Additional financing through strategic collaborations, public or private equity financings, capital lease transactions or other financing sources may not be available on acceptable terms, or at all. The receptivity of the public and private equity markets to proposed financings is substantially affected by the general economic, market and political climate and by other factors which are unpredictable and over which we have no control. Additional equity financings, if we obtain them, could result in significant dilution to stockholders. Further, in the event that additional funds are obtained through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies, product candidates or proposed products that

we would otherwise seek to develop and commercialize ourselves. If sufficient capital is not available, we may be required to delay, reduce the scope of or eliminate one or more of our programs, any of which could have a material adverse effect on our business.

We do not have experience as a company conducting large-scale clinical trials, or in other areas required for the successful commercialization and marketing of our product candidates.

We will need to receive regulatory approval for any product candidates before they may be marketed and distributed. Such approval will require, among other things, completing carefully controlled and well-designed clinical trials demonstrating the safety and efficacy of each product candidate. This process is lengthy, expensive and uncertain. We have no experience as a company in conducting large-scale, late stage clinical trials, and our experience with early-stage clinical trials with small numbers of patients is limited. Such trials would require either additional financial and management resources, or reliance on third-party clinical investigators, clinical research organizations (CROs) or consultants. Relying on third-party clinical investigators or CROs may force us to encounter delays that are outside of our control.

We also do not currently have marketing and distribution capabilities for our product candidates. Developing an internal sales and distribution capability would be an expensive and time-consuming