

Technology Platform for Regenerative Medicine

Snapshot

February 22, 2006

Advanced Cell Technology, Inc. ("Advanced Cell" or "the Company") is a biotechnology company applying human **embryonic stem (ES) cell**[†] technology to the emerging field of **regenerative medicine**. Regenerative medicine refers to "cell therapy", or treatments that are founded on the concept of producing new cells to replace malfunctioning or damaged cells as a vehicle to treat disease and injury. Advanced Cell's technologies are currently in the pre-clinical research stage, with the goal of commercializing their use in treating a wide array of **chronic** degenerative diseases, and in regenerative repair of **acute** injuries and conditions such as trauma, **infarction**, and burns. If approved, Advanced Cell's reprogramming technologies could produce cells that would maximize the potential for effective use as transplants for replacing diseased or destroyed cells in human patients. This technology is intended to avoid reliance on more limited approaches that involve the use of cell lines that may not be **histocompatible** with the patient, or therapies based upon the use of **adult stem cells**. Advanced Cell's research is focused within three core areas: (1) **Cellular Reprogramming**, which enables the transformation of a patient's own cells into ES cells, which can then be **differentiated** into specific cells for therapies for a variety of diseases, (2) a Reduced Complexity Library (RCL), enabling production of histocompatible stem cell lines for "off-the-shelf" deployment to treat acute disease in time-critical situations, which are not amenable to reprogramming technologies, and (3) Stem Cell Differentiation, which is designed to control the differentiation and re-differentiation of stem cells into specific cell types, such as **hematopoietic**, **myocardial**, skin, **retinal**, and **neuronal** cells for therapeutic applications. To date, the Company has announced its focus on three product programs to develop therapeutics for indications in the eye, skin, and blood. Advanced Cell is headquartered in Worcester, Massachusetts, where the Company houses a **Good Manufacturing Practices (GMP)**-capable facility to manufacture product for preclinical and clinical testing. The Company also has a facility in Alameda, California, which includes 10,000 square feet of GMP-capable production facilities.

Recent Financial Data

Ticker (Exchange)	ACTC.OB (OTC.BB)
Recent Price (02/22/06)	\$1.62
52-Week Range	\$1.58-7.00
Shares Outstanding	23.07 million
Market Cap.	\$37.4 million
Avg. 3-month volume	38,029
Beneficially-Owned Shares*	6.549 million (22.1%)
EPS (as of 09/30/05)	(\$0.10)
Employees	35



* As of 10/31/05, each person, or group of affiliated persons known to ACTC to be the beneficial owner of more than 5% of the outstanding shares of ACTC's Common Stock; each of ACTC's directors and named executive officers; and all of ACTC's directors and executive officers as a group.

Key Points

- Advanced Cell has recently published results in *Nature* magazine for derivation of ES cell lines in mice using a technique of single-cell biopsy. This technique does not interfere with the developmental potential of the embryos.
- Similar to the method used in **preimplantation genetic diagnosis (PGD)** to test for genetic defects, single-cell biopsy, as a method for deriving stem cell lines, removes one of the most debated ethical considerations in the area of ES cell research—creating stem cell lines without damaging the embryo.
- The Company's stem cell differentiation technology is focused within three areas: (1) **retinal pigment epithelium (RPE)** cells to treat **macular degeneration**; (2) **hemangioblast cells** to treat blood and cardiovascular disorders; and (3) dermal (skin) cells to treat burns and for wound repair.
- Drs. Michael West and Robert Lanza, key management figures within the Company, have been on the forefront of many of the breakthrough technologies discovered in the field of regenerative medicine, specifically cellular bio-engineering. Dr. Lanza has recently released a comprehensive new book on ES cell research and its real world applications, *Essentials of Stem Cell Biology* (Academic Press, November 2005, Hardcover).
- The Company is well-funded following a recently completed Convertible Debenture offering, and reported cash and cash equivalents of approximately \$16.5 million as of September 30, 2005.

[†]**BOLD WORDS ARE REFERENCED IN GLOSSARY ON PAGES 54-58.**

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Executive Overview

Advanced Cell Technology, Inc. (“Advanced Cell” or “the Company”) is a biotechnology company applying human embryonic stem (ES) cell technology to the field of regenerative medicine. Regenerative medicine refers to “cell therapy”, or treatments that are founded on the concept of producing new cells to replace malfunctioning or damaged cells as a vehicle to treat disease and injury. Advanced Cell is designing technologies as a portal for applying the area of **genomics** to the area of **cell biology**, with the intent on developing many potential innovative therapies. Currently, all of Advanced Cell’s technology is in the pre-clinical stage of research, with the goal of successfully developing and commercializing products for use in treating a wide array of chronic degenerative diseases and in regenerative repair of acute injuries and conditions such as trauma, infarction, and burns. To date, the Company has announced its focus on three product programs to develop therapeutics for indications in the eye, skin, and blood.

The ability to produce ES cells that are immunologically compatible with the patient is a key advantage of Advanced Cell’s technology platform. The Company believes that this platform could enable the transformation of a patient’s cells into an embryonic state where those cells can be differentiated into specific therapeutically-relevant cell types that are genetically identical to the patient. The Company also believes that its technology may enable the production of stem cell lines from sources external to the patient, which have a sufficiently high level of histocompatibility to be useful in making cell therapies readily accessible to a large segment of the patient population, without the need for exact genetic matching of tissues. Advanced Cell believes that its proprietary technology for solving immune rejection is fundamental for the advancement of the field of regenerative medicine.

Foundation for Technology

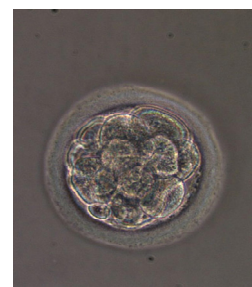
Regenerative medicine is an emerging field that was established in 1995-1996. The first isolation of the human ES cell occurred in 1998 at the University of Wisconsin. The term “regenerative medicine” refers to a field that approaches the repair or replacement of tissues and organs by incorporating the use of cells, genes, or other biological building blocks along with bioengineered materials and technologies. Advanced Cell is focused on utilizing advances in ES cell and nuclear transfer technology to replace malfunctioning or damaged cells as a way to treat disease and injury. Many serious and untreatable diseases arise from the loss or malfunction of specific types of cells in the body, including **Alzheimer’s disease**, **Parkinson’s disease**, macular degeneration, **Type 2 diabetes**, heart failure, **osteoarthritis**, and various **immune system** diseases. This is also true for medical conditions resulting from damage to cells due to acute injuries, such as trauma, infarction, and burns. The enthusiasm surrounding the field of regenerative medicine comes from the possibilities that arise from potential therapies to treat previously untreatable diseases.

Ethical concerns and debates raised when hearing the term “cloning” make it important to distinguish *therapeutic* cloning, the target of Advanced Cell’s technology versus *reproductive* cloning, which requires the transfer of an embryo into a surrogate mother, and then allows the embryo to develop fully into the species which had been cloned.

In 1998, Advanced Cell published a paper showing that therapeutic cloning with **somatic cell nuclear transfer (SCNT)** worked in the **bovine** model. Advanced Cell has also worked on the reproductive cloning of endangered species around the world, including a Gaur and a Banteng. One of the cloned Bantengs survived and has been integrated with the herd at the San Diego Zoo, introducing new genes into that population.

In 2003, Advanced Cell announced the cloning of a human embryo to the 16-cell **morula** stage (the stage from which stem cells have been obtained in animal studies), as shown in Figure 1. The Company was also successful in using **parthenogenesis** in primates (the process by which an unfertilized egg is

Figure 1
Advanced Cell Technology, Inc.
HUMAN CLONED MORULA



Source: Advanced Cell Technology, Inc.

encouraged to split into “**parthenotes**” or embryo-like products from which stem cells may be extracted) to coax eggs to divide into **blastocysts**, (the stage of embryonic development that is optimal for obtaining stem cells). Tissue from parthenogenesis would be easier to match with patients and less likely to be rejected because the parthenote would be **homozygous** in the histocompatibility antigen (HLA) genes, which significantly reduces the complexity of finding a match (i.e. matching “aa” instead of “ab”).

Industry’s Recent Turn of Events

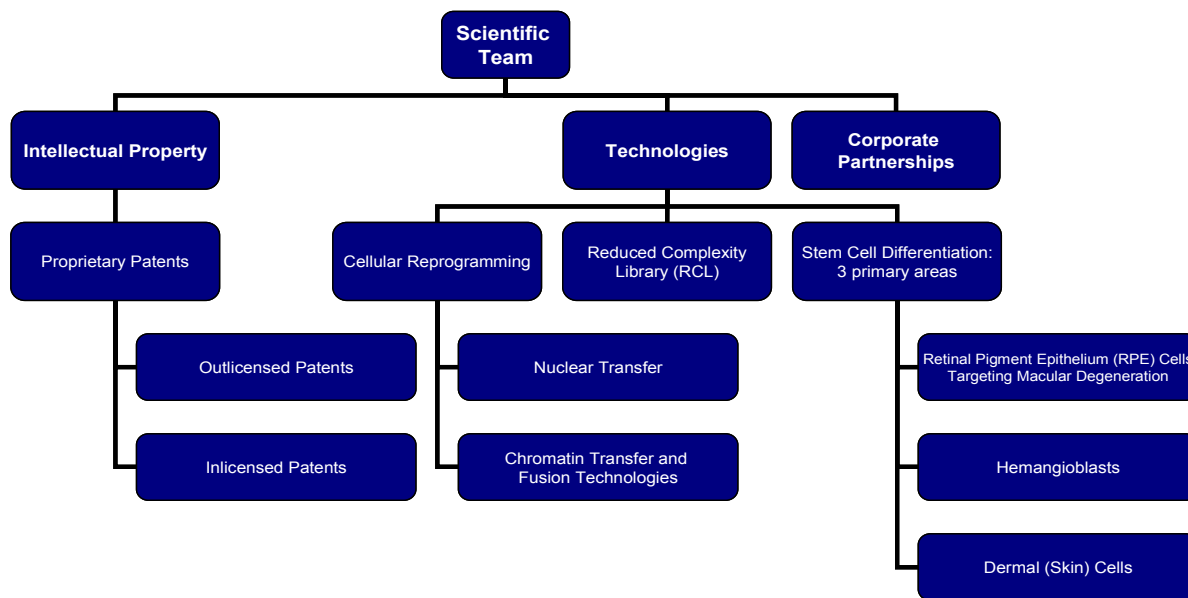
The stem cell arena, particularly human ES cell research, has been under scrutiny as of late due to the South Korean researcher Hwang Woo Suk’s recently revealed scandal—namely that the scientist faked 11 lines of ES cells he claimed to have created through cloning in May 2004. While this event has no bearing on the legitimacy of the science for other stem cell researchers in the U.S. and throughout the world, it may have a chilling effect on the receptivity of this technology. In addition, subsequent to the announcement of Suk’s alleged breakthrough, many companies’ sources of capital have dried up for human ES research. This presents a challenge in finding funding for the continuation of human ES research.

Currently, there are a limited number of Federal lines of human ES cells that qualify for government-subsidized research funding. California’s Proposition 71 (described on page 32), while paving the way for states to pass their own funding laws, is currently tied up by lawsuits challenging its constitutionality. Advanced Cell’s research is focused within the area human ES cell therapeutic cloning. The Company hopes to develop a line of customized human ES cells that can be the foundation of therapies for many diseases.

Corporate Structure

Advanced Cell’s corporate structure is divided into the following branches, as illustrated in Figure 2 and briefly outlined on page 5: Intellectual Property; Technologies; and Corporate Partnerships. Extensive details on each of these areas are provided within the Core Story section of this Executive Informational Overview® (EIO®).

Figure 2
Advanced Cell Technology, Inc.
CORPORATE STRUCTURE



Source: Advanced Cell Technology, Inc.

- *Intellectual Property.* Advanced Cell has filed numerous proprietary patents in the area of regenerative medicine, and has inlicensed and/or outlicensed further technologies as needed. The Company's current Intellectual Property position is detailed on pages 7-12.
- *Technologies.* This branch is divided into three core areas: (1) Cellular Reprogramming, (2) a Reduced Complexity Library (RCL), and (3) Stem Cell Differentiation. Each of these areas (described in greater detail on pages 21-30) provides the Company with a platform for which to produce novel technology with the intent of developing new treatments.
 - (1) *Cellular Reprogramming.* This technology involves developing therapies based on the use of genetically identical stem cells that have been cultivated into specific therapeutic lines derived for the exact needs of the patient. Cellular Reprogramming, also known as therapeutic cloning, takes the **deoxyribonucleic acid (DNA)** from the genetic host and implants it into an **ovum** to create ES cell lines that are genetically compatible to the recipient (or donor of that DNA). This ES cell line is then grown out and differentiated into the proper body cell line in order to heal the affected area.
 - (2) *A Reduced Complexity Library (RCL).* This technology could allow Advanced Cell to develop readily available cell therapy products for patients with acute medical needs (such as heart attack victims). The Company believes that this technology may result in a bank of a few hundred cell lines, which could be compatible with the majority of the population, without requiring the need for significant immunosuppressive drugs.
 - (3) *Stem Cell Differentiation.* This technology differentiates ES cells into various types of tissue or cell lines needed for therapeutic purposes. Advanced Cell is currently working on generating ES cell lines to target three specific therapeutic areas: (1) retinal pigment epithelium (RPE) cells, (2) hemangioblasts, and (3) dermal (skin) cells.
- *Corporate Partnerships.* The Company is focused on cultivating relationships with collaborative partners to launch various product lines intended to be developed as a result as its novel technology.

History, Headquarters, and Employees

Advanced Cell Technology, Inc. is a Delaware corporation that began operations in 1998 in Worcester, Massachusetts. The Worcester facility has Good Manufacturing Practices (GMP)-capable manufacturing facilities for the production of stem cell lines and differentiated cells for preclinical and clinical testing. The Company also has a facility in Alameda, California, which includes approximately 10,000 square feet of GMP-capable manufacturing capacity. Advanced Cell intends to produce product for preclinical and clinical testing from both of these facilities. Advanced Cell is also working toward establishing corporate partnerships with pharmaceutical and biotechnology companies. The Company employs 35 individuals, with the majority of these personnel focused on research and development activities. Figure 3 illustrates Advanced Cell's current laboratory space in Worcester.

Figure 3
 Advanced Cell Technology, Inc.
 LABORATORY SPACE



Source: Advanced Cell Technology, Inc.

Growth Strategy

Advanced Cell's corporate growth strategy includes cultivating relationships with partners in order to assist in developing and launching various product lines developed from its ES cell technology. Accordingly, the Company is focused on achieving the following goals, outlined below.

- *Driving human ES cells to the clinic.* To date, Advanced Cell has announced its focus on three product programs to develop therapeutics for indications in the eye, skin, and blood. The Company is currently deriving cell lines and conducting functional preclinical testing in animal models. Additionally, Advanced Cell is finalizing certification of its GMP-capable facilities in its Worcester and Alameda locations, believing that its significant manufacturing capacity, particularly in California, will be important to securing grant proceeds under California's Proposition 71. The Company plans to produce cell lines under GMP-capable conditions in both of its locations for additional preclinical testing and human clinical trials, as it sees itself further along in its eye program, in which it plans to use retinal pigment epithelium (RPE) cells to treat macular degeneration and other age-related diseases of the eye. In addition, Advanced Cell is focused on deriving dermal (skin) cells, which could be used to treat burns, wounds, and in surgery. Finally, the Company is focused on deriving hemangioblast cells (which include hemapoietic cells and myocardium cells), which could be used to treat blood and cardiovascular disorders.
- *Solving Immune Rejection.* The ability to produce ES cells that are immunologically compatible with the patient could become a key advantage of Advanced Cell's technology platform. The Company believes that this platform could enable the transformation of a patient's cells into an embryonic state where those cells can be differentiated into specific therapeutically-relevant cell types that are genetically identical to the patient. The Company also believes that its technology may enable the production of stem cell lines from sources external to the patient, which have a sufficiently high level of histocompatibility to be useful in making cell therapies readily accessible to a large segment of the patient population, without the need for exact genetic matching of tissues. Advanced Cell sees that its proprietary technology for solving immune rejection is fundamental for the advancement within the field of regenerative medicine.
- *Addressing the Ethical Debate.* Many scientists believe that the United States is falling behind in the field of regenerative medicine because of President George W. Bush's position on ES cell research. Advanced Cell believes it has proprietary technologies for alternative methods of deriving stem cells to address the far-right's ethical concerns. New technologies developed by Advanced Cell, and recently published in *Nature* magazine, have demonstrated in a mouse model that Advanced Cell can develop ES cell lines without damaging an embryo through the use of a technique similar to that used in preimplantation genetic diagnosis (PGD), which is used in testing for genetic defects. Thus, the Company's technology effectively addresses a key ethical concern around the source of embryonic stem cell lines (as described on page 30).
- *Forming partnerships with various institutions and corporations to leverage its Intellectual Property and proprietary technology, with the goal of bringing novel products into the development phase.*

Intellectual Property

Advanced Cell maintains a portfolio of patents and patent applications that have been developed and inlicensed to form the proprietary base for its research and development (R&D) efforts in the area of ES cell research. The Company's ownership or exclusive inlicensing includes over 30 issued patents and over 280 patent applications in the field of regenerative medicine and related technologies. Advanced Cell seeks patent protections for its inventions involving its core technologies and in ancillary technologies that support its core technologies, either alone or in collaboration with specific scientific partners. The Company plans to utilize its platform of intellectual property to address a host of diseases and conditions.

Proprietary Patents

Table 1 summarizes the Company's patents owned outright.

Table 1 Advanced Cell Technology, Inc. PROPRIETARY PATENTS				
Patent Number	Country	Title	Issue Date	Expiration Date
6,808,704	US	Method for Generating Immune-Compatible Cells and Tissues Using Nuclear Transfer Techniques	10/26/2004	2/18/2021
518191	New Zealand	Method of Differentiation of Morula or Inner Cell Mass Cells and Method of Making Lineage-Defective Embryonic Stem Cells	5/10/2004	10/13/2020
516236	New Zealand	Cytoplasmic Transfer to De-Differentiate Recipient Cells	4/7/2005	12/18/2021

Source: Advanced Cell Technology, Inc.

Advanced Cell believes that it holds significant intellectual property, including key patents and patent applications in the areas of somatic cell nuclear transfer (SCNT) technology and **chromatin transfer** technology. In addition, the Company believes it holds important proprietary positions that are likely to be important in both derivation of stem cell lines and differentiation of stem cell lines into specific cell types. This position provides Advanced Cell important potential protection from new competition and positions the Company to develop proprietary products and technologies in the industry of regenerative medicine.

Inlicensed Patents

The Company's intellectual property position is a key asset in forming relationships with collaborative partners. By maintaining a majority of the new intellectual property within this area, Advanced Cell believes it can derive a diverse platform of products based on the underlying technology while establishing long-term, valuable relationships with key partners in the industry. Tables 2, 3, and 4 (pages 8-9) describe each of these respective inlicensed intellectual property positions. In particular, Advanced Cell has inlicensed exclusive rights to various intellectual property from various institutions, as well as has acquired licenses from others.

To date, the Company has licenses for technology from the University of Massachusetts; Genzyme Transgenics Corporation; Wake Forest University; Infigen, Inc.; WiCell Research Institute, Inc.; Exeter Life Sciences, Inc.; and Lifeline Cell Technology. A summary of the license agreements with these companies is provided in pages 9-11. For a more comprehensive description of the terms of these licenses, please refer to the Company's SB-2 at (<http://www.sec.gov/Archives/edgar/data/140098/000104746905024796/a2163827zsb-2.htm>).

Table 2
Advanced Cell Technology, Inc.
EXCLUSIVE LICENSE TO PATENTS FROM THE UNIVERSITY OF MASSACHUSETTS

Patent Number	Country	Title	Issue Date	Expiration Date
6,235,970	US	CICM Cells and Non-Human Mammalian Embryos Prepared by Nuclear Transfer of a Proliferating Differentiated Cell or its Nucleus	5/22/2001	9/22/2017
6,235,969	US	Cloning Pigs Using Donor Nuclei from Non-Quiescent Differentiated Cells	5/22/2001	7/3/2017
6,215,041	US	Cloning Using Donor Nuclei from a Non-Quiescent Somatic Cells	4/10/2001	1/8/2018
6,156,569	US	Prolonged Culturing of Avian Primordial Germ Cells (PGCs) Using Specific Growth Factors, Use Thereof to Produce Chimeric Avians	12/5/2000	8/4/2017
5,994,619	US	Production of Chimeric Bovine or Porcine Animals Using Cultured Inner Cell Mass Cells	11/30/1999	12/16/2016
5,945,577	US	Cloning Using Donor Nuclei from Proliferating Somatic Cells	8/31/1999	1/10/2017
5,905,042	US	Cultured Inner Cell Mass Cell Lines Derived from Bovine or Porcine Embryos	5/18/1999	4/1/2016
521426	New Zealand	Prion-Free Transgenic Ungulates	11/11/2004	3/26/2021
521026	New Zealand	Production of Mammals which Produce Progeny of a Single Sex	1/13/2005	2/26/2021
518365	New Zealand	Gynogenetic or Androgenetic Production of Pluripotent Cells and Cell Lines, and Use Thereof to Produce Differentiated Cells and Tissues	8/12/2004	10/27/2020
517609	New Zealand	Embryonic or Stem-Like Cell Lines Produced by Cross Species Nuclear Transplantation and Method for Enhancing Embryonic Development by Genetic Alteration of Donor Cells or by Tissue Culture Conditions	6/8/2004	9/14/2020
519346	New Zealand	Embryonic or Stem-Like Cell Lines Produced by Cross Species Nuclear Transplantation	6/8/2004	5/10/2020
759322	Australia	Embryonic or Stem-Like Cell Lines Produced by Cross Species Nuclear Transplantation	7/24/2003	3/2/2019
506808	New Zealand	Embryonic or Stem-Like Cell Lines Produced by Cross Species Nuclear Transplantation	3/29/2004	3/2/2019
502713	New Zealand	Production of Avian Embryonic Germ (EG) and Embryonic Stem (ES) Cell Lines by Prolonged Culturing of PGCs Use Thereof of Cloning and Chimeraization	1/5/2004	8/4/2018
502712	New Zealand	Avian Primordial Germ Cell (PGC) Cell Line and a Method for Long Term Culturing Thereof	5/12/2003	8/4/2018
742840	Australia	Cloning Pigs Using Donor Nuclei from Differentiated Cells	8/1/2002	7/1/2018
502124	New Zealand	Cloning Pigs Using Donor Nuclei from Differentiated Cells	5/12/2003	7/1/2018
742363	Australia	Cloning Using Donor Nuclei from Differentiated Fetal and Adult Cells	1/3/2002	1/5/2018
334016	New Zealand	Embryonic or Stem-Like Cell Lines Produced by Cross Species Nuclear Transplantation	12/7/2000	7/28/2017
717529	Australia	Cultured Inner Cell Mass Cell Lines Derived from Ungulate Embryos	7/13/2000	3/24/2017
126416	Israel	Cultured Inner Cell Mass Cell Lines Derived from Ungulate Embryos	9/21/2004	3/24/2017
332159	New Zealand	Cultured Inner Cell Mass Cell Lines Derived from Ungulate Embryos	6/8/2000	3/24/2017

Source: Advanced Cell Technology, Inc.

Table 3

Advanced Cell Technology, Inc.

EXCLUSIVE LICENSE TO PATENTS FROM GENZYME TRANSGENICS CORP.

Patent Number	Country	Title	Issue Date	Expiration Date
6,580,017	US	Methods of Reconstructed Goat Embryo Transfer	6/17/2003	4/23/2019
6,528,699	US	Transgenically Produced Non-Secreted Proteins	3/4/2003	3/22/2021
517930	New Zealand	Methods of Producing Cloned and Transgenic Mammals	5/10/2004	9/27/2020
88117	Singapore	Methods of Producing a Target Molecule in a Transgenic Animal and the Purification of the Target Molecule	3/31/2004	10/16/2020
518263	New Zealand	Methods of Producing a Target Molecule in a Transgenic Animal and the Purification of the Target Molecule	7/5/2004	10/16/2020

Source: Advanced Cell Technology, Inc.

Table 4

Advanced Cell Technology, Inc.

NON-EXCLUSIVE LICENSE FROM INFIGEN, INC.

Patent Number	Country	Title	Issue Date	Expiration Date
6,700,037	US	Method of Cloning Porcine Animals	3/2/2004	12/28/2020
6,680,199	US	In Vitro Activation of Mammalian Oocytes and Use in Cloning Procedures	1/20/2004	5/22/2020
6,603,059	US	Ungulates Produced by Sequential Nuclear Transfer	8/5/2003	10/16/2020
6,395,958	US	Method of Producing a Polypeptide in an Ungulate	5/28/2002	7/15/2019
6,258,998	US	Method of Cloning Porcine Animals	7/10/2001	11/24/2018
6,194,202	US	Parthenogenic Oocyte Activation	2/27/2001	3/4/2016
6,077,710	US	Parthenogenic Oocyte Activation	6/20/2000	10/12/2018
6,011,197	US	Method of Cloning Bovines Using Reprogrammed Non-Embryonic Bovine Cells	1/4/2000	1/28/2019
5,843,754	US	Parthenogenic Bovine Oocyte Activation	12/1/1998	12/1/2015
5,496,720	US	Parthenogenic Oocyte Activation	3/5/1996	3/5/2013
5,453,366	US	Method of Cloning Bovine Embryos	9/26/1995	9/26/2012
5,374,544	US	Mutated Skeletal Actin Promoter	12/20/1994	12/20/2011
4,994,384	US	Multiplying Bovine Embryos	2/19/1991	2/19/2018

Source: Advanced Cell Technology, Inc.

The University of Massachusetts (UMass) License

On February 1, 2002 and April 16, 1996, Advanced Cell entered into exclusive license agreements with the University of Massachusetts (UMass). Pursuant to these agreements, UMass exclusively licensed to Advanced Cell certain biological materials, patent rights, and related technology for commercialization in specified fields.

- 2002 License.** Under the 2002 license, UMass licensed to the Company certain patent rights relating to the cloning of non-human animals for use in connection with the development, manufacture, and sale of products and services in the field of non-human animals for agriculture, companion animals, research and diagnostic products, non-human and human therapeutics, and **nutraceuticals**, except production of **immunoglobulin** in the blood of *Bos taurus* and *Bos indicus*.
- 1996 License.** The 1996 license covers certain patent rights, biological materials, and know-how related to the cloning of non-human animals and cells for use in cell fields, except the production of immunoglobulin in the blood of *Bos taurus* and *Bos indicus*.

Genzyme Transgenics Corporation (GTC) License

On September 25, 1997, the Company entered into a development and commercialization agreement with GTC Biotherapeutics (GTC), formerly known as Genzyme Transgenics Corporation, pursuant to which each party exclusively licensed to the other certain patent rights and technology for use in defined fields and to which Advanced Cell agreed to provide certain related services. The agreement also requires each party to disclose to the other, on a periodic basis, a written report of developments relevant to the other party's field. In addition, under the agreement, the Company licensed to GTC certain patent rights and know-how useful to the cloning of animals for all purposes for the production of biopharmaceutical agents in milk, including, but not limited to, **proteins**, **peptides**, and **polypeptides** for pharmaceutical, nutraceutical, or other use.

Wake Forest University (WFU) License

On January 26, 2001, Advanced Cell entered into a materials and research data license agreement with Wake Forest University (WFU), pursuant to which WFU granted to Advanced Cell a worldwide, exclusive, royalty-free, perpetual and irrevocable right and license to use certain data, stem cells, and stem cell cultures created by Advanced Cell from biological materials provided by WFU to the Company for specified purposes only. The agreement allows the Company to utilize certain primate skin cells and ovary materials produced by WFU and transferred to it pursuant to an agreement relating to the transfer of biological materials. The Company has agreed to provide WFU samples of stem cells for WFU research, education, and teaching purposes—and it has a first option to obtain an exclusive license to any intellectual property rights claimed by WFU in connection with the use of such stem cells. The term of the license granted is perpetual and irrevocable absent a breach by Advanced Cell.

Infigen License

On August 1, 2003, Advanced Cell entered into a non-exclusive sublicense agreement with Infigen, Inc., pursuant to which each party non-exclusively licensed to the other certain patent rights and technology for use in defined fields. Under this agreement, Advanced Cell licensed certain patent rights to Infigen that are relevant to the “Infigen Field,” namely: (a) the research and discovery of genes or proteins or other molecules that play a role in the reprogramming of cells; (b) the development, making, using, selling, offering to sell, or importing of products that are composed of non-human cells or tissues or a formulation, including such cells or tissues for the purpose of **xenotransplantation** of such cells, tissues, or organs for therapy in humans; (c) the development, making, using, selling, or importing of proteins (excluding all immunoglobulin which is not sheep immunoglobulin) produced in the blood of cloned animals; and (d) the development, making, using, selling, or offering to sell genetically modified or non-genetically modified or non-genetically modified **ovine**, bovine, and **porcine** animals as models of human disease.

Infigen licenses to Advanced Cell certain patent rights that are relevant to the “ACT Cell Therapy Field,” namely: the development, making, using, selling, offering to sell, or importing of therapeutic products that are composed of (a) human cells for human cell therapy, or a formulation including such cells (with or without genetic modification), and the rendering of services that relate to the production of such products, or (b) non-human animal cells for veterinary cell therapy, or a formulation including such cells (with or without genetic modification), and the rendering of services that relate to the production of such products.

WiCell Research Institute (WiCell) License

In March 2002, Advanced Cell entered into an industry research license and material transfer agreement with WiCell Research Institute, Inc., (WiCell), pursuant to which WiCell granted to Advanced Cell a non-exclusive license, with no right to sublicense, to make, use, and sell or otherwise transfer certain primate ES cells and derivatives thereof for internal research purposes and to receive such primate ES cells or derivatives from third parties for internal research purposes.

Exeter Life Sciences (Exeter) License

On October 22, 2003, the Company entered into an exclusive license with Exeter Life Sciences, Inc., (Exeter) pursuant to which it exclusively licensed to Exeter certain technology and patent rights for use in the fields of agriculture, endangered species, companion animals, and equine animals. The license also granted Exeter a right of first negotiation to any improvement patents that are obtained by the Company that

relate to the licensed intellectual property or which are useful, necessary, or required to develop or manufacture certain animals, cells, or tissues within the defined fields of use. Under the agreement, Advanced Cell licenses rights to certain patent rights and technology useful for the fields of use of non-human animals for agriculture, endangered animals, and companion animals; excluding production of such animals for the primary purpose of producing human and non-human animal therapeutics and human healthcare products, including, without limitation, the production of biopharmaceutical agents in milk, such as proteins, peptides, and polypeptides for pharmaceutical, nutraceutical or other use, and excluding the production of immunoglobulin in the blood of *Bos taurus* and *Bos indicus*.

Lifeline Cell Technology (Lifeline) License

On May 14, 2004, Advanced Cell entered into three license agreements with Lifeline Cell Technology (Lifeline), formerly known as PacGen Cellco, LLC; the licenses were subsequently amended in August 2005. Pursuant to the license agreements, as amended, the Company licensed to Lifeline, on an exclusive or non-exclusive basis, as applicable, certain know-how and patent rights for, among other things, the research, development, manufacture, and sale of human cells for cell therapy in the treatment of human diabetes and liver diseases, and retinal diseases and retinal degenerative diseases.

- *Exclusive License Agreement Number 1*, as amended, covers patent rights and technology developed by the Company that are relevant to:
 - the research, development, manufacture, and sale of human and non-human animal cells for commercial research, and
 - the manufacture and selling of human cells for therapeutic and diagnostic use in the treatment of human diabetes and liver diseases, and retinal diseases and retinal degenerative diseases.
- *Exclusive License Agreement Number 2*, as amended, covers patent rights and technology developed by UMass relevant to:
 - the research, development, manufacture, and sale of human and non-human animal cells and defined animal cell lines for commercial research,
 - the manufacture and selling of human cells for therapeutic and diagnostic use in the treatment of human diabetes and liver diseases, and retinal diseases and retinal degenerative diseases, and
 - the use of defined animal cell lines in the process of manufacturing and selling human cells for therapeutic and diagnostic use in the treatment of human diabetes and liver diseases.
- *Exclusive License Agreement Number 3*, as amended, covers patent rights and technology developed by Infigen relevant to the research, development, manufacture, and sale of human cells for cell therapy in the treatment of therapeutic and diagnostic use in the treatment of human diabetes and liver diseases, and retinal diseases and retinal degenerative diseases.

WARF Patent

The Wisconsin Alumni Research Foundation (WARF) holds among its 40 stem cell patents a basic one that broadly covers the preparation of embryonic stem (ES) cells. Basic patents, often the foundation of whole new industries, are highly prized and frequently contested. This patent gives WARF the right to collect royalties until December 2018 on any products or therapies developed that utilize WARF technology.

Advanced Cell has a license from WARF for research use of WARF technologies, and has the ability to negotiate commercial licensing rights should they decide to produce products that utilize WARF technology. There is debate in the industry as to whether the WARF patents are valid, although Advanced Cell has not indicated any intention to dispute the validity of WARF's intellectual property, and has a positive relationship with WARF.

The Company has developed certain proprietary technology in the area of Direct Differentiation (described on pages 26-27) that it believes may allow for the production of products without relying on WARF's published intellectual property. This technology allows the scientist to take the ES cells and separate them into a dish, and then engineer a product directly, without having to grow a line of ES cells first to then direct them into the requested tissue. The decision to license WARF technology for commercialization of certain products, or whether to produce using techniques that do not infringe WARF technology, will be made based upon the relative economics of production.

Management, Board of Directors, and Ethics Advisory Committee

Management

Advanced Cell's management team, Board of Directors, and Ethics Advisory Committee contains individuals who are highly capable of driving the Company's ES cell technology from concept to commercialization and facilitating the creation of partnerships for commercialization. Table 5 summarizes Advanced Cell's key management, followed by detailed biographies. Biographies of individuals affiliated with Advanced Cell in the aforementioned roles are provided on pages 13-16.

Table 5
Advanced Cell Technology, Inc.
MANAGEMENT

Michael D. West, Ph.D.	Chairman, President, and Chief Scientific Officer
William M. Caldwell, IV	Chief Executive Officer
Robert P. Lanza, M.D.	Vice President of Medical and Scientific Development
James G. Stewart	Senior Vice President of Finance and Chief Financial Officer
Jonathan F. Atzen	Senior Vice President and General Counsel
Robert W. Peabody, CPA	Vice President of Grant Administration

Source: Advanced Cell Technology, Inc.

Michael D. West, Ph.D., Chairman, President, and Chief Scientific Officer

Dr. Michael West has academic and business experience in age-related degenerative diseases, **telomerase** molecular biology, and human ES cell research and development. Before joining Advanced Cell in 1998, Dr. West founded Geron Corporation (GERN-NASDAQ), and from 1990 to 1998, served as a director and senior executive officer of Geron, where he initiated and managed programs in telomerase diagnostics, telomerase inhibition, telomerase-mediated therapy, and human ES cell research. After leaving Geron, Dr. West co-founded and served as chairman of Origen Therapeutics, a company focused on the development of avian transgenic technologies. He is the inventor of patents assigned to the University of Texas Southwestern Medical Center at Dallas licensed to Geron Corporation relating to telomere biology. Dr. West was also the president, chief executive officer (CEO), and director of Advanced Cell Group prior to its dissolution. Dr. West received a B.S. degree from Rensselaer Polytechnic Institute in 1976, an M.S. degree in biology from Andrews University in 1982, and a Ph.D. from Baylor College of Medicine in 1989. Dr. West is also a director of Biotime, Inc. (BTIM.OB-OTC), a reporting company, a director of the Life Extension Foundation, and a director of the privately-held company BioMarker Pharmaceuticals, Inc.

William M. Caldwell, IV, Chief Executive Officer

Mr. William Caldwell has a 30-year management career working with emerging technologies and restructuring distressed corporate environments. During his career, he served in senior executive positions both in marketing and finance. He worked with Booz Allen and Hamilton, the Flying Tiger Line Inc., Von Vorst Industries, and Kidder Peabody. He started a firm specializing in strategy and financial planning, which was instrumental in restructuring over \$1.0 billion of debt for over twenty companies and partnerships. He was a pioneer in the satellite radio auctions as president of Digital Satellite Broadcasting Corporation, assisted in the financing, and became president and ultimately CEO in the restructuring of CAIS Internet. He has advised corporations, both public and private, in technology, telecommunications, retailing, real estate, hospitality, publishing, and transportation. He received his B.A. degree from the University of Southern California and was a Multinational Enterprise Fellow at the Wharton School of Finance. He serves as a director of Lee Pharmaceuticals (LPHM.PK) and King Koil Franchising Corp.

Robert P. Lanza, M.D., Vice President of Medical and Scientific Development

Dr. Robert Lanza has over 20 years of research and industrial experience in the areas of tissue engineering and transplantation medicine. Before joining Advanced Cell in 1998, from 1990 to 1998, Dr. Lanza was director of Transplantation Biology at BioHybrid Technologies, Inc., where he oversaw that company's xenotransplantation and bioartificial pancreas programs. He has edited or authored a dozen books, including *Essentials of Stem Cell Biology* (Academic Press, November 2005, Hardcover), *Principles of Tissue Engineering* (2d. ed. co-edited with R. Langer and J. Vacante), *Yearbook of Cell and Tissue Transplantation*, *One World The Health & Survival of the Human Species in the Twenty-First Century*, and *Xeno: The Promise of Transplanting Animal Organs into Humans* (co-authored with D.K.C. Cooper). Dr. Lanza received his B.A. and M.D. degrees from the University of Pennsylvania, where he was both a University Scholar and Benjamin Franklin Scholar.

James G. Stewart, Senior Vice President of Finance and Chief Financial Officer

Mr. James Stewart, prior to joining Advanced Cell, served as executive vice president of finance and administration for LRN, a technology company providing software solutions in corporate ethics and governance. Between April 2002 and July 2004, Mr. Stewart was the chief financial officer (CFO) of SS8 Networks, a company providing software solutions to telecommunications providers. Prior to his appointment at SS8 Networks, Mr. Stewart served as CFO for Graviton, a provider of wireless sensor and data applications, and from February 1999 to March 2001, he held the position of CFO for Ventro Corporation. At Ventro Corporation, Mr. Stewart was responsible for the raising of capital in the company's initial public offering (IPO) and subsequent debt offerings. Before his tenure at Ventro Corporation, Mr. Stewart served for over three years as CFO of CN Biosciences, Inc., a publicly-traded life sciences company. At CN Biosciences, he played an important role in the company's IPO and was responsible for the management of finance culminating in the sale of the business to Merck KGaA Darmstadt. Prior to joining CN Biosciences, he held key finance positions at two other companies after leaving Ernst & Young (formerly Arthur Young & Co.), where he served for 13 years, three years as an audit partner. Mr. Stewart holds a bachelor's degree in business administration from the University of Southern California.

Jonathan F. Atzen, Senior Vice President and General Counsel

Mr. Jonathan Atzen joined the Company in 2005. Prior to joining Advanced Cell, Mr. Atzen was an attorney at Heller Ehrman/Venture Law Group, LLP and worked as a corporate/securities attorney for other large international law firms including Brobeck, Phleger & Harrison, LLP, and Morrison & Foerster LLP. His corporate practice has focused on the representation of emerging growth and established technology companies in such areas as life sciences, semiconductors, wireless communications, software, and alternative energy technologies. Mr. Atzen has provided general corporate counsel to public companies with respect to securities offerings, including IPOs, secondary offerings, PIPEs, spin-offs, and reporting and compliance matters under the Securities and Exchange Act of 1934. Mr. Atzen also has experience in public and private company mergers and acquisitions. He received his B.A. degree in economics from the University of California at Santa Barbara and his J.D. from Loyola Law School.

Robert W. Peabody, CPA, Vice President of Grant Administration

Mr. Robert Peabody joined the Company on a full time basis in February 2005 as vice president, grant administration. Prior to this position, he was a regional controller of Ecolab, Inc. (ECL-NYSE), a Fortune 500 specialty chemical manufacturing and service company. Mr. Peabody has extensive experience in biotechnology investing and aiding in the start-ups of such companies as Geron Corporation, Origen Therapeutics, and ACT Group. Mr. Peabody also served as a member of the Board of Directors of ACT Group prior to its dissolution. Mr. Peabody received a Bachelors degree in business administration from the University of Michigan and is a Certified Public Accountant (CPA).

Board of Directors

Advanced Cell's Board of Directors oversees the conduct of and supervises Company management. Table 6 provides a summary of Board members, followed by detailed biographies.

Table 6	
Advanced Cell Technology, Inc.	
BOARD OF DIRECTORS	
Michael D. West, Ph.D.	Chairman of the Board
William M. Caldwell, IV	Member
Alan C. Shapiro, Ph.D.	Member
Erkki Ruoslahti, M.D., Ph.D.	Member
Alan G. Walton, Ph.D., D.Sc.	Member

Source: Advanced Cell Technology, Inc.

Michael D. West, Ph.D., Chairman of the Board

Biography on page 13.

William M. Caldwell, IV, Member

Biography on page 13.

Alan C. Shapiro, Ph.D., Member

Dr. Alan Shapiro has more than 30 years of experience in corporate and international financial management. Dr. Shapiro is currently the Ivadelle and Theodore Johnson professor of banking and finance at the University of Southern California, where he previously served as the chairman of the department of finance and business economics, Marshall School of Business. Prior to joining the University of Southern California, Dr. Shapiro taught as an assistant professor at the University of Pennsylvania, Wharton School of Business, and has been a visiting professor at Yale University, UCLA, the Stockholm School of Economics, University of British Columbia, and the U.S. Naval Academy. Dr. Shapiro has published over 50 articles in such academic and professional journals as the *Journal of Finance*, *Harvard Business Review*, and the *Journal of Business*, among many others. He frequently serves as an expert witness in cases involving valuation, economic damages, international finance, takeovers, and transfer financing. He received his B.A. in mathematics from Rice University, and a Ph.D. in economics from Carnegie Mellon University. Dr. Shapiro is a trustee of Pacific Corporate Group's Private Equity Fund and also serves as a director of Ramington Oil and Gas Corporation (REM-NYSE), a reporting company traded on the New York Stock Exchange (NYSE).

Erkki Ruoslahti, M.D., Ph.D., Member

Dr. Erkki Ruoslahti is a distinguished professor at the Burnham Institute for Medical Research and at University of California, Santa Barbara. He earned his M.D. and Ph.D. from the University of Helsinki in Finland. After postdoctoral training at the California Institute of Technology, he held various academic appointments in Finland and at City of Hope National Medical Center in Duarte, California. He joined the Burnham Institute in 1979 and served as its president from 1989-2002. Dr. Ruoslahti received the 2005 Japan Prize for his work in cell biology. Dr. Ruoslahti's other honors include the Gairdner Prize, and membership in the U.S. Academy of Sciences, Institute of Medicine, and American Academy of Arts and Sciences. He is a Knight of the Order of the White Rose in Finland. Dr. Ruoslahti's research has been the basis of several drugs currently on the market or in clinical trials. He has been founder and director of several biotechnology companies.

Alan G. Walton, Ph.D., D.Sc., Member

Dr. Alan Walton is a senior general partner of Oxford Bioscience Partners. Before joining Oxford in 1987, Dr. Walton was the president and CEO of University Genetics Co., a biotechnology company involved in technology transfer and seed investments in university-related projects. Prior to University Genetics, Dr. Walton taught at several institutions including Harvard Medical School, Indiana University, and Case Western Reserve, where he was professor of macromolecular science and director of the laboratory for biological macromolecules. Dr. Walton received his Ph.D. in chemistry, a D.Sc. in biological chemistry, and an honorary Doctor of Laws degree from Nottingham University in England. Dr. Walton holds patents in the fields of molecular biology and biotechnology, and serves on the boards of Alexandria Real Estate Equities (ARE-NYSE), Avalon Pharmaceuticals (AVRX-NASDAQ), and Acadia Pharmaceuticals (ACAD-NASDAQ). He is also on the board of Research!America, a philanthropic organization. Dr. Walton was a founder of Human Genome Sciences (HGS-NASDAQ) and GeneLogic and is the founding chairman of the Biotechnology Venture Investors Group.

Ethics Advisory Committee

Because the use of human ES cells gives rise to ethical, legal, and social issues, the Company has instituted an Ethics Advisory Board. Its Ethics Advisory Board is made up of highly qualified individuals with expertise in the field of human ES cells. These individuals are highlighted in Table 7.

Table 7	
Advanced Cell Technology, Inc.	
ETHICS ADVISORY COMMITTEE	
Ronald M. Green (Chairman)	Ethics Institute - Dartmouth College
Judith Bernstein, RNC, MSN, Ph.D.	School of Public Health, School of Medicine - Boston University
Kenneth W. Goodman, Ph.D.	University of Miami
Jeremy B.A. Green, Ph.D.	Harvard Medical School
Robert Kaufmann, M.D.	Southeastern Fertility Center, Medical University of South Carolina
Susan L. Moss, J.D., Ph.D.	San Diego State University
Carol A. Tauer, Ph.D.	Center for Bioethics, University of Minnesota

Source: Advanced Cell Technology, Inc.

Core Story

Advanced Cell is a biotechnology company applying human embryonic stem (ES) cell technology to the emerging field of regenerative medicine. The Company has developed a portfolio of patents and has patent applications pending that form the basis for its efforts in ES cell research. By conducting research at the cellular level, the Company is developing technology that could facilitate the successful development and commercialization of products for use in a wide variety of chronic diseases and in regenerative repair of acute conditions such as trauma, infarction, and burns.

Regenerative medicine is an emerging field that was established in 1995-1996. The first isolation of the human ES cell occurred in 1998 at the University of Wisconsin. The term “regenerative medicine” refers to a field that approaches the repair or replacement of tissues and organs by incorporating the use of cells, genes, or other biological building blocks along with bioengineered materials and technologies. Advanced Cell is focused on utilizing advances in ES cell and nuclear transfer technology to replace malfunctioning or damaged cells as a way to treat disease and injury. Many serious and untreatable diseases arise from the loss or malfunction of specific types of cell in the body, including Alzheimer’s disease, Parkinson’s disease, Type 2 diabetes, heart failure, osteoarthritis, and various immune system diseases. This is also true for medical conditions resulting from damage to cells due to acute injuries, such as trauma, infarction, and burns.

The enthusiasm surrounding the field of regenerative medicine comes from the possibilities that arise in potential therapies to treat previously untreatable diseases. Advanced Cell’s technology in development is the result of years of knowledge within the areas of genomics and cell biology, making it possible to genetically modify any type of human cell—something that has never been possible prior to innovations in regenerative medicine. Table 8 summarizes the potential U.S. patient populations that could be amenable to cell or organ transplantation, and thus the potential U.S. target markets for Advanced Cell’s regenerative medicine technology.

Table 8
Advanced Cell Technology, Inc.
POTENTIAL U.S. PATIENT POPULATIONS FOR CELL-BASED THERAPIES

Medical Condition	Number of Patients
Cardiovascular disease	70 million
Autoimmune disease	50 million
Diabetes	18 million
Osteoporosis	10 million
Cancer	10 million
Alzheimer’s disease	4.5 million
Parkinson’s disease	1 million
Burns (severe)	1.1 million
Spinal-cord injuries	0.25 million
Birth defects	0.15 million/year

Source: Advanced Cell Technology, Inc.

Advanced Cell was formed to focus exclusively on applications for human ES cells, and address issues of immune rejection in stem cell therapy. By addressing and attempting to develop a solution to the issue of immune rejection, the Company could pave the way for numerous technologies and therapies that were previously not possible. Advanced Cell has developed two technologies in particular that address the concerns surrounding the ethical debate of the derivation of human ES cells; specifically, single-cell biopsy and transdifferentiation (technologies which are described in the context of this ethical debate in greater detail on pages 30-32).

STEM CELL OVERVIEW

The cell is one of the most basic units of life. There are millions of different types of cells that are organisms unto themselves, such as microscopic amoeba and **bacteria cells**, as well as cells that only function when part of a larger organism, such as those that make up a human being. In the body, there are brain cells, skin cells, liver cells, stomach cells, etc. All of these cells have unique functions and features. For example, cardiac muscle cells come together to create the contracting heart tissues that squeeze the heart, which in turn sends red blood cells carrying oxygen throughout the arteries and veins that are made up of **endothelial** cells. The various systems that enable a human being to function are made up of their own distinctive cell types.

Stem cells differ from other types of cells within the body, where regardless of their source, they have three general properties:

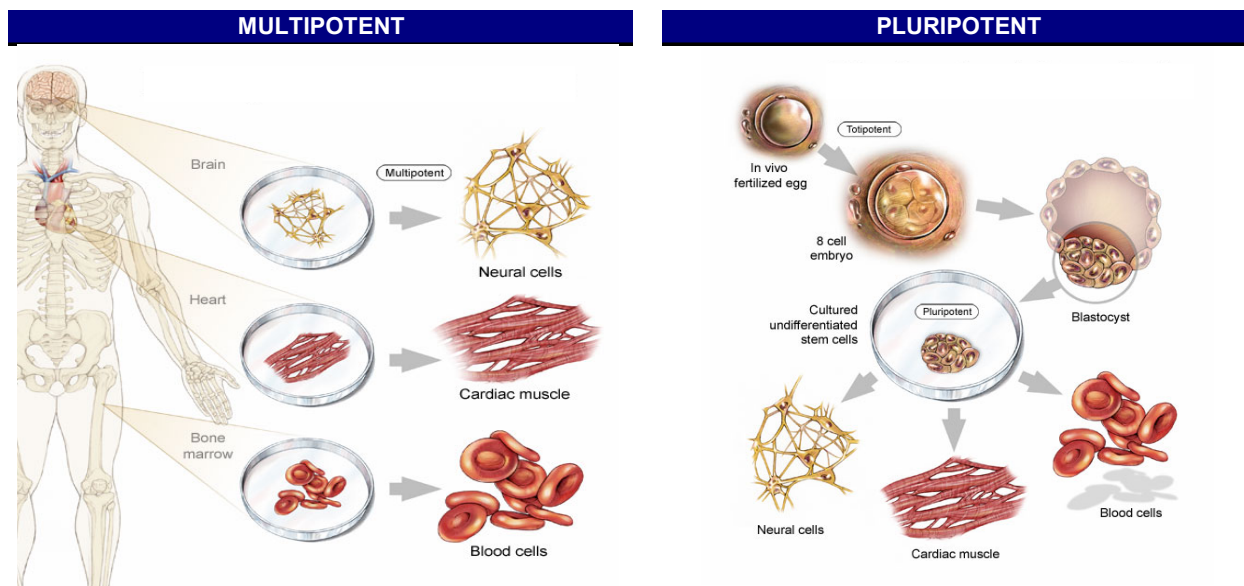
- (1) *They are capable of dividing and renewing themselves for long periods.* Unlike muscle cells, blood cells, or nerve cells, which do not normally replicate themselves, stem cells may replicate many times over. When cells replicate themselves it is called **proliferation**. A starting population of stem cells that proliferates for many months in the laboratory can yield millions of cells.
- (2) *They are unspecialized.* One of a stem cell's fundamental properties is a lack of tissue-specific structures that allow it to perform specialized functions. A stem cell cannot work with its neighbors to pump blood throughout the body (like a heart muscle cell); it cannot carry molecules of oxygen throughout the bloodstream (like a red blood cell); and it cannot fire electrochemical signals to other cells that allow the body to move or speak (like a nerve cell).
- (3) *They can give rise to specialized cells.* When unspecialized stem cells give rise to specialized cells, the process is called differentiation. Scientists are now beginning to understand the signals that trigger stem cell differentiation. The internal signals are controlled by a cell's genes, which are interspersed across long strands of DNA and carry coded instructions for all the structures and functions of a cell. The external signals for cell differentiation include chemicals secreted by other cells, physical contact with neighboring cells, and certain molecules in the microenvironment. As such, stem cells offer the possibility of renewable sources of replacement cells and new tissues to treat many kinds of diseases, conditions, and disabilities.

Sources of Stem Cells

There are three key sources of stem cells (1) certain adult tissues; (2) umbilical cord blood; and (3) the human embryo.

- (1) *Adult Stem Cells.* Stem cells obtained from a person after birth are called adult stem cells and are found within various tissues that make up the body. Adult stem cells are usually programmed to form a limited number of different cell types of their own tissue, and are referred to as “**multipotent**,” meaning they are only able to create several different types of cells within the same type of tissue. Examples of multipotent stem cells, by organ, are provided in Figure 4 (page 19).
- (2) *Umbilical Cord Blood Stem Cells.* Another source of stem cells is the umbilical cord blood of a newborn baby, containing “**pluripotent**” stem cells. These can develop into a wider variety of cell types in the human body. The umbilical cord is the tissue that ties a baby to the mother within the womb. After the baby is born, the blood can be collected from the umbilical cord and **cryopreserved**. Examples of pluripotent stem cells are provided in Figure 4 (page 19).
- (3) *Embryonic Stem (ES) Cells.* ES cells are considered “**totipotent**”—that is they have the total potential to develop into any human cell type. ES cells also have the ability to self-renew indefinitely in their undifferentiated state, which is a unique characteristic distinguishing them from other stem cells discovered in humans. Advanced Cell's research efforts are focused primarily within the area of ES cells.

Figure 4
EXAMPLES OF STEM CELLS



Source: Stem Cell Research Foundation.

Limitations of Existing Technology

One of the more significant obstacles facing regenerative medicine today is the potential rejection of ES cells in patients. Advanced Cell's research is focused on solving this problem by creating stem cell therapeutics which are histocompatible. By creating a technology that transforms a patient's cells into an embryonic state, where those cells can then be differentiated into specific therapeutically relevant cell types that are genetically identical to the patient, Advanced Cell believes it can successfully combat the difficulty of immunocompatibility in patients.

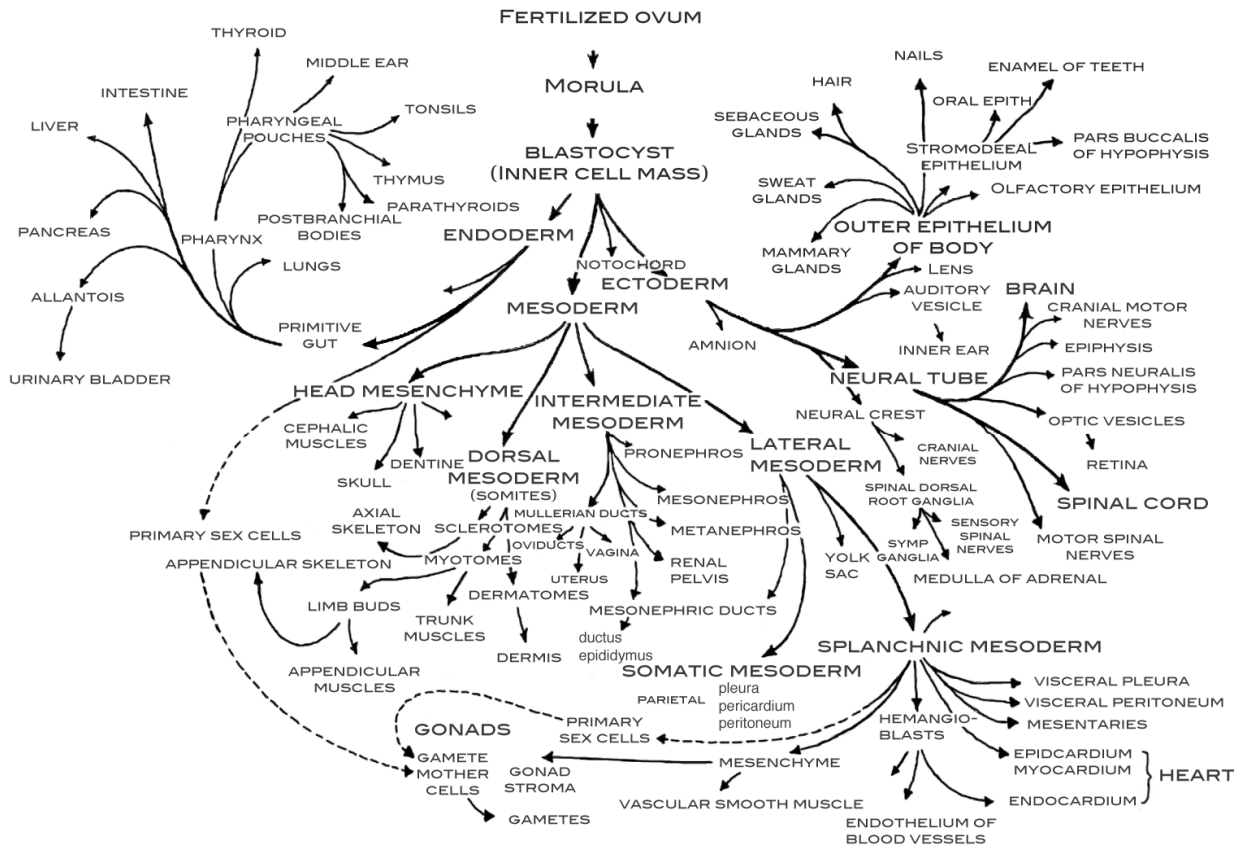
With the aging of the world's population and the limitations of current therapies, the potential markets for regenerative medicine, specifically stem cell therapy, could be significant. If any type of human cell can be derived from ES cells, there could be an unlimited product platform available for development. ES cells, therefore, could provide the ability to "self assemble" into complex tissue. Figure 5 (page 20) provides a sample of the different tissues which can be formed through the development of various stem cell lines. For example, the zygote develops through the stages to form the necessary tissues to support life (i.e. liver cells, heart cells, blood cells, etc.).

Telomeres

One of the key technologies that permits Advanced Cell to promote its therapeutic strategies is the re-lengthening of **telomeres** (enzymes that exist in cells that act as a "clock" for the aging of cells). Cells that are "telomere positive" are considered immortal. Human ES cells, if cultured in a laboratory, are so primitive that they have not yet made one of the first decisions that a cell makes—what type of cell to develop into.

Early embryo cells decide to either become a **germ cell** (such as a sperm and ovum) or a **body cell**. If the cell chooses to develop into a germ cell, it remains telomerase positive and has replicative immortality. However, if the cell decides to develop into a body cell, the telomerase enzyme disappears and upon development, the telomeres begin to shorten, and the aging of the cell begins (the cell stops dividing). ES cells were the first cells to be grown in a laboratory dish as a naturally immortal cell. Because ES cells have this property, they can potentially produce an immortal string of cells that can be expanded without limit, thus enabling genetic modification. After genetically engineering these cells in the proper therapeutic manner, they can be inserted into the body as young cells. For example, for a person with kidney disease, a cell line of histocompatible young kidney cells can be implanted into the patient's body, thereby giving the patient youthful kidney cells despite disease and biological age.

Figure 5
DIFFERENTIATION OF HUMAN TISSUES



Source: Advanced Cell Technology, Inc.

ADVANCED CELL'S TECHNOLOGY

Advanced Cell is developing ES cells that are immunologically compatible with human patients. By transforming a patient's cells into an embryonic state, the Company believes it may be able to differentiate the cells into specific therapeutically-relevant cell types that are genetically identical to the patient. This technology may also enable the production of stem cell lines from sources external to the patient with a sufficiently high level of histocompatibility, which could be useful in making cell therapies readily accessible to a large segment of the patient population, without the need for exact genetic matching of tissues. As such, Advanced Cell's technology is intended to address the difficulty in using cell lines that are not histocompatible with the recipient, or therapies based upon use of adult stem cells.

The Company's technology is *not* targeted towards traditional adult stem cell-based research. Adult stem cells are multipotent, where they are only able to create several different types of cells within the same type of tissue. This differs from totipotent stem cells, which have the full potential to develop into any human cell type (as described on pages 18-19). Additionally, adult stem cells are intrinsically mortal, whereby cellular aging is caused by shortening telomeres (the ends of chromosomes). This compares to Advanced Cell's ES cells, which are immortal, telomerase positive cells (as described on page 19). Through the process of nuclear transfer, Advanced Cell has been successful to date in regenerating the cell's lifespan through the reactivation of telomerase.

The Company's proprietary technology is focused on producing cell lines that are both histocompatible with the patient and pluripotent. These cells may therefore be able to maximize the potential for effective use as transplants to replace diseased or destroyed cells in human patients. If successfully developed, the Company's cellular reprogramming technologies may make it possible to produce cells that have specific therapeutic applications, are immunologically compatible with the patient, and have the proliferative capacity of young cells.

One of the objections to human ES cell research has been that the derivation of ES cells destroys the possibility of the embryo to further develop into a complete human being. ES cell lines are conventionally isolated from the inner cell mass of blastocysts and, in a few instances, from **cleavage stage** embryos.

Advanced Cell's technology includes derivation of stem cells from an alternative method, as illustrated in Figure 6, to establish ES cell lines. A technique of single-cell biopsy is similar to that used in pre-implantation genetic diagnosis (PGD) of genetic defects, which does not interfere with the developmental potential of embryos.

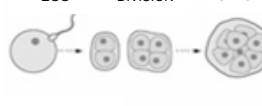
Figure 6
A NEW WAY TO CREATE EMBRYONIC STEM CELLS

In an effort to satisfy those who have moral or ethical objections, scientists have developed a new method to generate embryonic stem cells that does not destroy the embryo. One of the new methods is shown below.

CURRENT METHOD

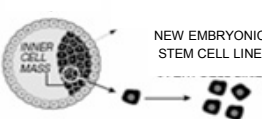
1. A fertilized egg undergoes cell division, becoming a mass of cells called a blastocyst after 5 days.

FERTILIZED EGG CELL DIVISION 8-CELL STAGE



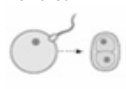
2. Stem cells are taken from the inner cell mass of the blastocyst, destroying the developing embryo.

BLASTOCYST EMBRYO DESTROYED

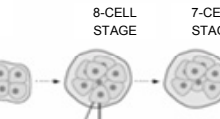


A NEW METHOD

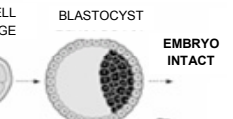
1. After the third division, at the 8-cell stage, a single cell called a blastomere is removed.



2. The blastomere is cultured with an established embryonic stem cell line and then separated to form new lines.



3. Because the blastocyst is left intact, the developing embryo can still be implanted in the uterus.

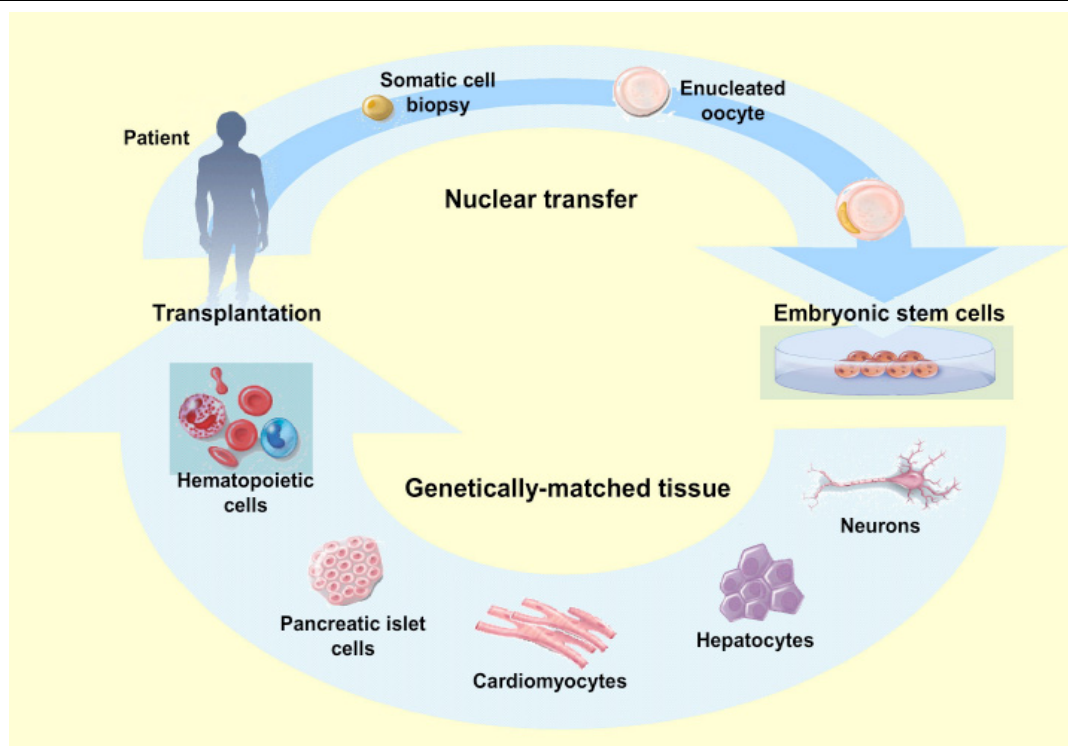


Source: New York Times, October 16, 2005 (Nature).

Cellular Reprogramming

One of the key aspects to Advanced Cell's cellular reprogramming technology is the production of certain types of young cells that are histocompatible with the patient. The purpose of the cellular reprogramming technologies is to prepare effective and customized therapies through the reprogramming of the patient's own cells. These technologies can be used to generate patient-specific pluripotent cells and tissues for transplantation. With its technology, Advanced Cell is attempting to develop a new avenue for the introduction of targeted genetic modifications in cells and for the regeneration of a cell's lifespan, thereby making youthful cells available for aging patients. Figure 7 depicts the process of this cellular nuclear reprogramming therapy.

Figure 7
Advanced Cell Technology, Inc.
PROCESS OF CELLULAR REPROGRAMMING THERAPY



Source: Advanced Cell Technology, Inc.

Nuclear Transfer

Somatic cell nuclear transfer (SCNT) refers to the process whereby the DNA from a body cell is transferred to an egg cell from which the nuclear DNA has been removed. This reprogramming by the egg cell transforms the cell from the type of cell it was previously, into an embryonic cell with the power to become any cell type in the body. The DNA has already been removed from the egg cell, leaving the cell with no genetic blueprint. The next step of this process is to take the DNA from another cell (for example, a skin cell) and transfer it into the egg cell and electrofuse the cell back together. The egg cell then takes the DNA and reprograms it back to the beginning of human life, or an embryonic cell, which can then be persuaded to develop into any needed type of cell line (lungs, heart, kidney, etc.). Figure 8 provides an illustration of the SCNT process.

Figure 8
SOMATIC CELL NUCLEAR TRANSFER PROCESS



Source: Advanced Cell Technology, Inc.

Chromatin Transfer and Fusion Technologies

In addition to SCNT, some of the other technologies that support cellular reprogramming are chromatin transfer and **fusion technologies**. Chromatin transfer is a procedure whereby the DNA and attached proteins, or chromatin, of the **somatic cell** is reprogrammed prior to transfer into an egg cell. Chromatin transfer has the potential to improve the efficiencies and reduce the cost of nuclear transfer. One advantage to Advanced Cell's proprietary SCNT and chromatin transfer technologies is that the cells become "rejuvenated" by returning the cell to a youthful state. These healthy replacement cells, which are genetically identical to the patient's own cells, could then be used for cell transplantation.

Advanced Cell further utilizes fusion technology, which involves the fusion of the cytoplasm of one cell into another. In the same manner that the cytoplasm of an egg cell is capable of transforming any cell back into an embryonic state, the fusion of the cytoplasm of other cell types, including differentiated cell types (such as blood cells), is capable of reprogramming another cell type, such as a skin cell. These technologies have the potential to transform a cell from a patient into another medically-useful cell type that is also identical to the patient.

Advanced Cell has the potential to fuse the cytoplasm of undifferentiated cells, such as ES cells, with somatic cells to transport the somatic cell DNA back to pluripotency. The Company's fusion technology can further be developed into as broad and powerful a technique as SCNT, producing histocompatible, youthful stem cells that are multi- and potentially even pluripotent. If successfully developed, this technology may also provide a pathway that does not utilize human egg cells, thus reducing the cost of the procedure and potentially increasing the number of patients that could benefit from its implementation.

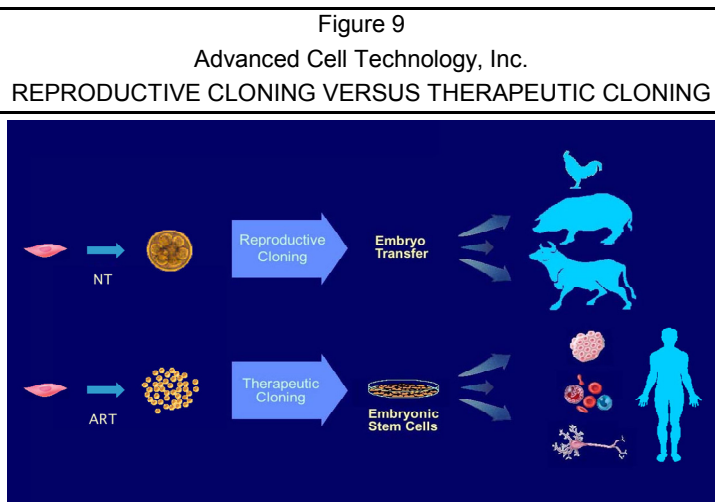
Emerging ES cell-based technologies offer the potential for a variety of new therapies, noting that utilization of these therapies requires a resolution of the histocompatibility problem. The ability to generate totipotent stem cells that carry the nuclear genome of the patient using nuclear transfer techniques could have the ability to overcome this challenge in transplantation medicine. Since the cells are totipotent, virtually every cell and tissue type could be produced carrying the same DNA as the patient; and since the starting somatic cell can be modified by gene targeting, the resulting cells could be modified as well. These genetically-modified cells could then be implanted into the recipient, providing youthful and healthy cells to the affected area.

Reproductive versus Therapeutic Cloning

Since the cloning of Dolly the sheep in July 1996, scientists have successfully utilized nuclear transfer amongst different species. This technology has created a number of ethical questions, as the cloning of animals, often referred to as reproductive cloning, has introduced appropriate concerns regarding cloning of humans. In addition, there are a number of scientific and ethical concerns, as described on pages 30-36, Addressing the Ethical Debate.

Due to these concerns, it is important to clarify the distinction between *therapeutic cloning*, an area being targeted by Advanced Cell, and *reproductive cloning*. While Advanced Cell has significant intellectual property that is useful in reproductive cloning of animals, and has early experience from pioneering work with endangered species and other animals, the Company has no focus on animals and believes that any work on reproductive cloning of humans is unethical.

Therapeutic cloning is important to the potential of regenerative medicine. The technique takes the DNA from the genetic host and implants it into an ovum to



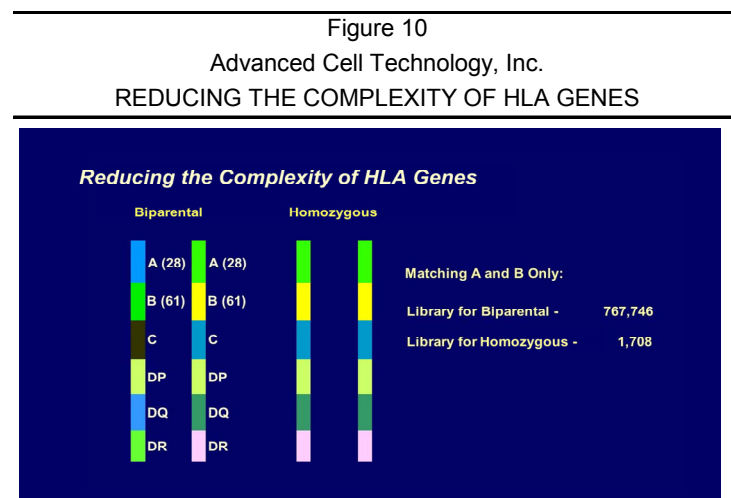
Source: Advanced Cell Technology, Inc.

create ES cell lines which are genetically compatible to the recipient (or donor of that DNA). This ES cell line is then grown out and differentiated into the proper body cell line in order to heal the affected area of the recipient. A comparison between the two types of cloning is provided in Figure 9 (page 23).

To accomplish human therapeutic cloning, it is necessary to isolate and culture ES cells from the preimplantation stage embryos. Until implantation is underway, no “decisions” have been made by the cell and most ethicists would agree that there has been no “human development”. Therefore before this stage, twinning and recombination are possible, and developmental individuality or ‘singleness’ has not been established.

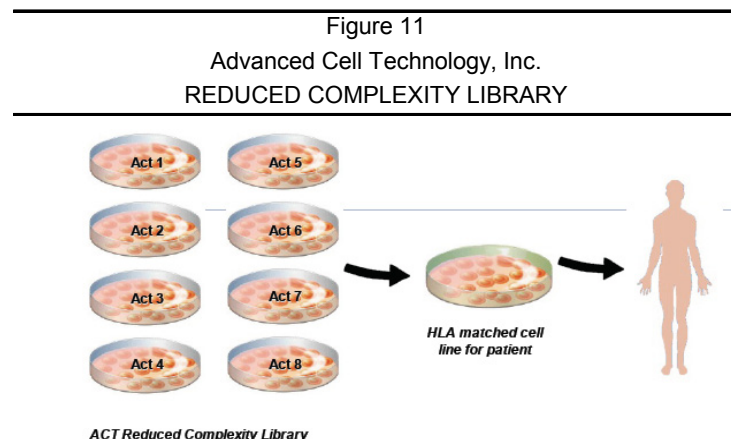
Reduced Complexity Library (RCL)

Advanced Cell has proprietary technology that may be applied to generate readily available therapeutic products for patients with acute medical needs that require immediate treatment and therefore may not allow for the patient-specific reprogramming of cells. The Company’s technology has been developed to target a wide array of readily available stem cell therapies for rapid deployment across a broad patient population without the need for patient-specific reprogramming of cells.



Source: Advanced Cell Technology, Inc.

Current organ and tissue transplantation technology requires a high degree of compatibility between the donated organ or tissue and the recipient. Genes for histocompatibility antigen (HLA) play a critical role in achieving donor/recipient compatibility and resulting transplant success. Advanced Cell is developing reduced complexity technology with the goal of assembling a bank of stem cell lines that are homozygous and **hemizygous** to the HLA genes. Figure 10 illustrates the difficulties encountered in finding matches for organ or cellular therapies in the current population, and the proposed solution of reducing the complexity developed by Advanced Cell.



Source: Advanced Cell Technology, Inc.

Advanced Cell’s technology is intended to develop a ‘bank’ of a few hundred cell lines (at most), which could provide a close enough match that, when combined with immunosuppressive drugs, could provide stem cell therapies for certain common applications in most patients. Figure 11 illustrates the concept for a library in which to bank the stem cells.

One example of a potential application could be the introduction of stem cell therapy for a time-sensitive case of heart attack to repair damaged heart tissue. Timely, cost-effective introduction of cell therapies are critical to the technology’s commercial application. Without reduced

complexity technology, producing a readily-available, off-the-shelf supply may require many hundreds of thousands of cell lines.

Advanced Cell believes that reduced complexity applications resulting from its research could offer an important tool in the field of regenerative medicine, yielding readily available cell lines for researchers produced at a level of quality and quantity appropriate for clinical applications. The Company's ability to genetically modify cells, while assuring quality control of the cell lines, could give it a decided advantage over its competition in providing readily-available, closely-matched cell lines at a lower cost.

Parthenogenesis

Several unique technologies could be used to create a bank of stem cells with reduced complexity in the HLA genes. One of these is called parthenogenesis. Parthenogenesis is similar to SCNT (described on page 22), however there is no somatic cell being transferred. In contrast, Advanced Cell uses its proprietary technology to take one egg cell and stimulate it to begin cell division as though it has been fertilized. This results in a parthenote or a blastocyst with a duplicate set of the egg's chromosomes from which Advanced Cell can harvest ES cells. This duplication gives a parthenote a full complement of genes. The Company believes that parthenogenesis and certain of its other technologies could be used to generate a master cell bank of clean homozygous stem cell lines, which could provide matches for a majority of the U.S. patient population.

LifeMap™

Advanced Cell has developed a proprietary program called LifeMap™, which is used to mark and later identify the cell lineages derived from ES cells. With ES cell technology, this process is critical since having the markers enables researchers to pull out the appropriate cells and purify them to be used in therapy. Advanced Cell has filed one of the first patents on this technology. Figure 12 illustrates a mouse embryo with the ES cells marked with the LifeMap™ technology (the darkened portion of the mouse shows the marked cells). These cells are easily visible due to the markers, enabling scientists to isolate and purify these cells for therapeutic purposes.

Figure 12
 Advanced Cell Technology, Inc.
 MOUSE EMBRYO WITH
 LIFEMAP™ ES CELLS



Mef2C

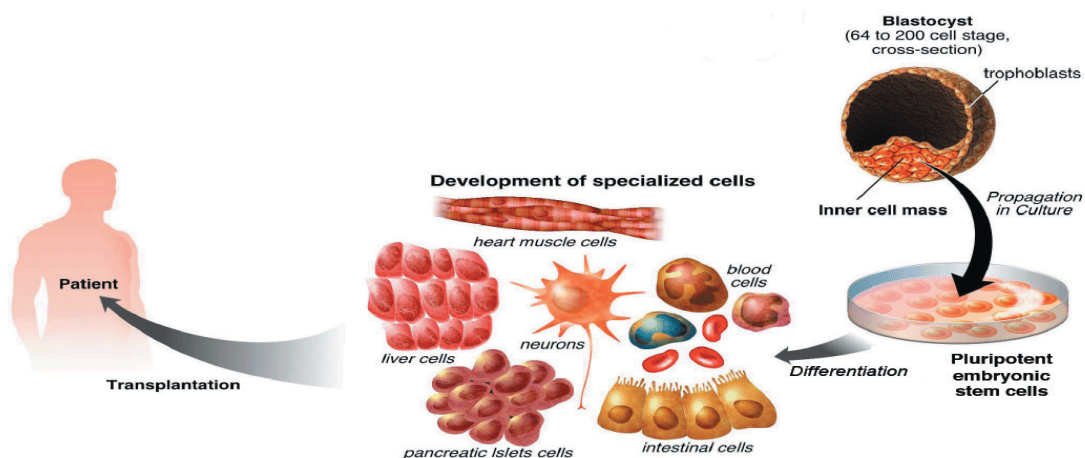
Source: Advanced Cell Technology, Inc.

Stem Cell Differentiation

Regenerative medicine requires that stem cells be differentiated, or re-differentiated, into specific body cell types and then physically transplanted into a patient. Differentiation into tissues, such as cardiac muscle, blood, and other tissues, occurs in ES cells being cultured in a dish. The successful application of stem cell technology requires control over the specific types of cells into which stem cells differentiate.

Advanced Cell is currently researching control of differentiation and the culture and growth of stem and differentiated cells utilizing both animal and human stem cell lines. Although progress has been slow to date, some scientists have achieved success in developing stem cells into specific lineages. Figure 13 (page 26) illustrates the process of cell differentiation into specified cells in order to be used effectively to combat certain maladies.

Figure 13
Advanced Cell Technology, Inc.
DRIVING HUMAN ES CELL THERAPIES TO THE CLINIC



Source: Advanced Cell Technology, Inc.

WARF Patent

The Wisconsin Alumni Research Foundation (WARF) holds among its 40 stem cell patents a basic one that broadly covers the preparation of ES cells. Basic patents, often the foundation of whole new industries, are highly prized and frequently contested. This patent gives WARF the right to collect royalties until December 2018 on any products or therapies developed that utilize WARF technology.

Advanced Cell has a license from WARF for research use of WARF technologies, and has the ability to negotiate commercial licensing rights should they decide to produce products that utilize WARF technology. There is debate in the industry as to whether the WARF patents are valid, although Advanced Cell has not indicated any intention to dispute the validity of WARF's intellectual property, and has a positive relationship with WARF.

The Company has developed certain proprietary technology in the area of Direct Differentiation (described below) that it believes allows for the production of products without relying on WARF's published intellectual property. This technology allows the scientist to take the ES cells and separate them into a dish, and then engineer a product directly, without having to grow a line of ES cells first to then direct them into the requested tissue. The decision to license WARF technology for commercialization of certain products, or whether to produce using techniques that do not infringe WARF technology, will be made based upon the relative economics of production.

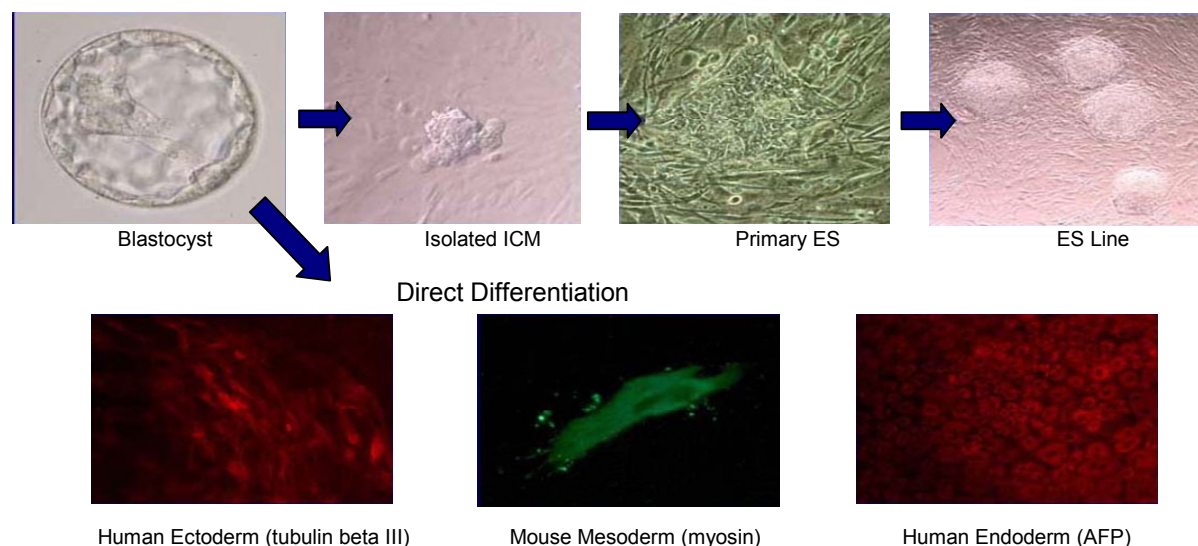
Direct Differentiation

Direct Differentiation of stem cells occurs several ways. One way is to specifically alter the growth conditions of the ES cells, such as adding growth factors to the medium or changing the chemical composition on the surface of which the ES cells are growing. For example, the plastic culture dish in which the ES cells are housed may be treated with a variety of substances that allow adhesion to the dish or conversely, prevent adhesion and force the cells to float in the culture medium.

Adherent substances prevent the cells from interacting and differentiating; conversely, nonadherent substances allow the cells to amass and interact with each other. Cell-to-cell interactions are necessary for normal embryonic development; therefore, allowing some of these "natural" *in vivo* interactions to occur in the culture dish is a fundamental strategy for inducing ES differentiation. Adding particular growth factors to the culture medium initiates the activation or inactivation of specific genes in ES cells. The activation of these genes is what causes the cells to differentiate in a particular direction.

Another way to achieve Direct Differentiation of ES cells is to introduce foreign genes into the cells. When adding an active gene to the ES cell, one triggers the cell to differentiate down a particular pathway. Although this approach allows scientists to precisely control ES cell differentiation, there are several complexities that make this method of Direct Differentiation cumbersome at this time. Lastly, similar to cloning technology, injecting the nucleus of an already differentiated cell into an **oocyte** could reprogram that ES cell. The theory behind this method is that the resultant pluripotent cell would be immunologically compatible because it would be genetically identical to the donor cell. Figure 14 illustrates Advanced Cell's patented "Direct Differentiation" technology.

Figure 14
Advanced Cell Technology, Inc.
ES CELL LINES VS. DIRECT DIFFERENTIATION



Source: Advanced Cell Technology, Inc.

All of the aforementioned techniques are in the development stage; nevertheless, within the past several years, it has become possible to generate specific, differentiated, functional cell types by manipulating the growth conditions of mouse ES cells *in vitro*. It is not possible to explain how the Direct Differentiation occurs, as no one knows how or when gene expression is changed, what signal-transduction systems are triggered, or what cell-to-cell interactions are necessary to stimulate specific differentiation.

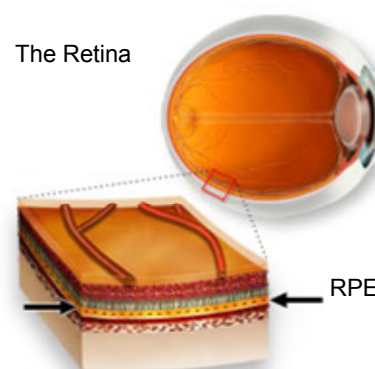
Targeted Therapeutic Indications

Advanced Cell is focused on generating stable cell lines, including retinal pigment epithelium (RPE), hemangioblast cells, and skin (dermal) cells. Each of these areas is described in more detail in the accompanying section.

Retinal Pigment Epithelium (RPE)

Retinal pigment epithelium (RPE) is a **neuroectodermal** derivative essential for the survival of photoreceptors in the eye. This densely pigmented epithelia **monolayer** is located between the **choroids** and natural retina (as shown in Figure 15) and serves as part of the barrier between the bloodstream and the retina. The degeneration of RPE with age is believed to play a critical role in the pathogenesis of **age-related macular degeneration (AMD)**, a common eye disease that causes deterioration of the **macula** (the central area of the retina, or the paper-thin tissue at the back of the eye where

Figure 15
RETINAL PIGMENT EPITHELIUM



Source: Florida Eye Center.

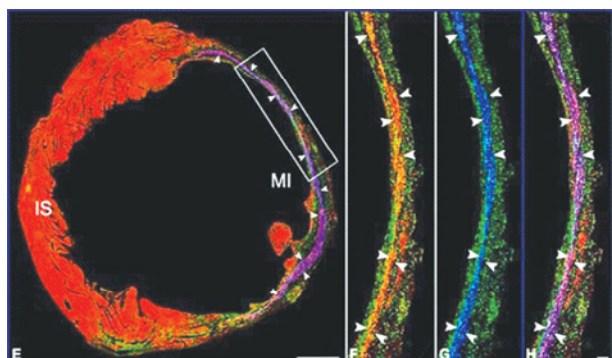
light-sensitive cells send visual signals to the brain). Sharp, clear, “straight ahead” vision is processed by the macula. Damage to the macula results in the development of blind spots and blurred or distorted vision. When the macula becomes damaged, many daily activities such as driving and reading become increasingly difficult. Although a variety of approaches have been proposed to treat AMD, none have proven successful in treating this disease.

AMD is estimated to affect over 10 million U.S. citizens and is the leading cause of irreversible severe central vision loss in Caucasians 50 years and older in the U.S. and most of the developed world. The incidence and progression of AMD increases significantly with age. Approximately 10% of patients ages 66 to 74 years have AMD; the prevalence increases to approximately 30% of patients age 75 to 85.

RPE cells were first successfully developed into several stable lines of ES cells by Advanced Cell scientists. After purifying and establishing banks of these cells, Advanced Cell is now conducting pre-clinical research in the restoration of vision loss in small animal models to determine if these cells may be used to treat macular degeneration. Stem cell derived RPE cells could be an important source of tissue for **subretinal** transplantation in the future.

Hemangioblast Cells

Figure 16
Advanced Cell Technology, Inc.
HEMANGIOBLAST CELLS



Source: Advanced Cell Technology, Inc.

Hemangioblast cells are unique in that they address the needs of both cardiac applications and hematopoietic, or blood applications. Advanced Cell is currently developing the utilization of hemangioblast cells for engraftment to repair the age-related endothelial dysfunction associated with numerous age-related diseases, including cardiovascular disease, stroke, and cancer.

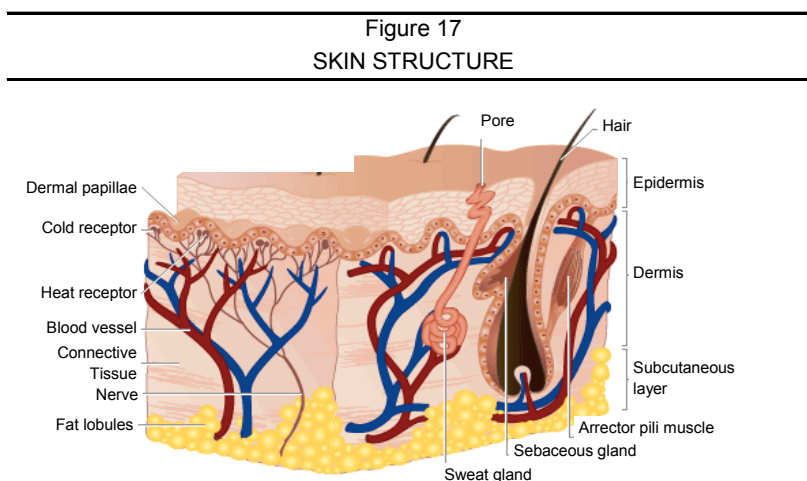
Figure 16 illustrates the infarcted wall heart attack muscle in a mouse, where genetically-engineered hemangioblast cells were inserted into this ruptured wall resulting in a dramatic band of regenerating muscle all throughout the heart zone. In this figure, different fluorescent (shading) represent regenerated tissue.

Advanced Cell has published important results using hemangioblasts cells to address immune system issues in a bovine model. The hemangioblasts were transplanted into the original adult animals and persisted and multiplied in the blood and lymph supply of those cows, demonstrating a significant competitive advantage over adult stem cells for targeted therapies. Advanced Cell is currently continuing research within this area, working toward differentiating different types of hematopoietic cells. In particular, there are a variety of potential applications for hemangioblasts, with researchers at Advanced Cell pursuing opportunities to use hemangioblasts to combat cardiac diseases, blood diseases, and even cancer.

In particular, scientists have recently been developing ways in which to genetically engineer hemangioblasts as a “Trojan horse” to combat cancer. Ordinary cancers block antigens to tumors, therefore the tumors metastasize. Companies such as Imclone Systems Inc. (IMCL-NASDAQ) have been researching ways to block the growth factors of tumors. Advanced Cell is researching a separate yet complementary approach to this treatment, employing the genetic engineering of hemangioblasts to possess a radiation inducible promoter driving a clotting factor. Therefore, when these cells become part of the tumor bed, a beam of x-rays on the tumor activates the clotting factor and stops the tumor, thereby stopping the metastases.

Dermal (Skin) Cells

In addition to RPE and hemagioblast cells (described on pages 27-28), Advanced Cell is researching technology to use ES cells to assist in healing skin damage, specifically burns and wounds. The skin is the largest organ in the human body, consisting of three layers that together provide protection, temperature regulation, and sensory functions for the body. An illustration of the skin's structure is provided in Figure 17.



Early embryonic skin, or skin in the first trimester of development, is in the process of forming. As the process progresses, the skin regenerates. If the embryo suffers a full thickness incision in the first trimester, the skin repairs all layers of itself not only without scarring, but also with the hair follicles, sweat glands, etc.

Source: msn.com.

Wounds

A wound is an injury, especially one in which the skin or another external surface is broken, torn, pierced, or cut. Remarkable advancements have been made in understanding the processes of wound healing. The cell types and the order in which they appear in the wound have been established and many growth factors and their functions have been clarified. However, even with the advances in understanding the science of wound healing, many more steps have yet to be discovered. Advanced Cell is currently researching technology to consistently isolate, purify, and develop skin cells with patterns of gene expression that are analogous to early embryonic skin. Early embryonic skin is capable of regenerating after wounding without scar formation, and these types of cells may provide a means of improving wound repair in surgery, burns, and chronic skin ulcers.

Burns

Advanced Cell is currently researching a process using human ES cells for burn treatment. Embryonic skin has a unique property. In the first trimester of human development, skin cells can regenerate completely. After the first trimester, and in adult skin, they do not regenerate. Skin heals but does so with scarring. Using embryonic skin cells, regeneration of the skin without scarring may be possible.

Severe burns often require extensive and painful treatment and therapy in order to heal. Furthermore, a burn victim often acquires significant scars in the damaged areas. By developing embryonic skin cells that are histocompatible with the patient, Advanced Cell's technology could help burn victims heal faster and with less scarring than they could with methods available today.

Solving Immune Rejection

One of the key focuses for Advanced Cell is to address the issue of immune system rejection of cell-based therapies. While human ES cells could hold significant potential, Advanced Cell believes that successful commercialization of stem cell technologies is likely to require the ability to produce cells that are immunologically compatible with the patient, have the proliferative capacity of young cells, and have specific therapeutic application. If ES cells prove to be immunologically compatible with the patient, Advanced Cell's cellular reprogramming technologies may be able to produce cells that maximize the potential for effective use as transplants in replacing diseased or destroyed cells in human patients. Successful development of Advanced Cell's technologies could provide cell-based therapies targeted at a broad range of diseases, including those cited in Table 9 (page 30).

Table 9

Advanced Cell Technology, Inc.

POTENTIAL THERAPEUTIC USES OF HUMAN ES CELLS

- Hematopoietic cells for blood diseases and cancer
- Myocardial and endothelial vascular tissue for cardiovascular disease
- Skin cells for dermatological conditions
- Retinal pigment epithelium (RPE) cells as a treatment for macular degeneration and retinal pigmentosis
- Neuronal cells for spinal cord injury, Parkinson's disease, and other neuro-degenerative diseases
- Pancreatic islet β cells for diabetes
- Liver cells for hepatitis and cirrhosis
- Cartilage cells for arthritis
- Lung cells for a variety of pulmonary diseases

Source: Advanced Cell Technology, Inc.

ADDRESSING THE ETHICAL DEBATE

Advanced Cell has developed proprietary technologies that address concerns most frequently cited in the ethical debate surrounding the derivation of human ES cells. The Company recently published in *Nature* magazine the results of work done in a mouse model, where stem cells were derived from an embryo utilizing single-cell biopsy, without damaging the development potential of the embryo. This technique is similar to a genetic biopsy, whereby a single cell from the blastocyst is removed for genetic testing. Parents utilizing *in vitro* fertilization (IVF) technology currently have the option to use this technique to determine any genetic defects the embryo might have before making the decision to implant that embryo. Scientists have found that the incidence of genetic defects is essentially the same in the embryos that have had the biopsy as those which have not.

Stem cell research has received a great deal of attention in the past several years. In particular, the ethical debate over ES cell research has spurred passionate responses both for and against the technology's utilization. The debate breaks down to the age-old question: "When does life begin?" Despite differing opinions on this issue, certain Federal and State legislation has been passed in support of ES cell research.

Federal Funding for IVF-ES Research

In August 2001, the President George W. Bush set guidelines for Federal funding of research on ES cells from human embryos created by *in vitro* fertilization, referred to as IVF. The initiative, approved by President Bush, granted Federal funds to be used on 60 "Presidential" ES cell lines, developed from embryos which had already perished. Further funding was granted toward researching umbilical cord, placental, adult, and animal stem cells. President Bush also established a Presidential Council, chaired by Dr. Leon Kass, a leading biomedical ethicist from the University of Chicago, to monitor stem cell research, and recommend various guidelines and regulations considering all the medical and ethical variables which must be considered in this research.

Characteristics of IVF-ES Cells

IVF-ES cells are not genetically matched to the recipient patient and are therefore **allogeneic**. Therapies using allogeneic cell lines can result in immune system incompatibility, where the host immune system attacks and rejects the transplanted cells or the transplanted cells attack the host. These incompatibilities may be partially suppressed with powerful immunosuppressive drugs, but the side effects can be severe and result in life-threatening complications. As a result, significant inefficiencies occur in the application of cell therapies. Furthermore, Advanced Cell believes that the Federally approved stem cell lines may be inferior in quality due to the exposure to mouse cells used to keep them alive. Exposure by these lines to the live animal cells presents a risk of contamination with viruses and pathogens that could be transmitted to the patient and the overall population. Therefore, these cell lines may be unfit for human transplantation.

Federal Legislation

H.R. 810

While President Bush placed a ban on Federal funding for any new ES cell lines in September 2001, there is a bipartisan House of Representatives Bill (H.R. 810) working its way through Congress. The President's decision, in summary, was to allow Federal funds to be used for research on the 60 genetically diverse, already existing stem cell lines.

H.R. 810, or the Stem Cell Research Enhancement Act of 2005, amends the Public Health Service Act to require the Secretary of Health and Human Services to conduct and support research that utilizes human ES cells, regardless of the date on which the stem cells were derived from a human embryo. This Act limits such research to stem cells that meet the following ethical requirements:

- (1) The stem cells were derived from human embryos donated from *in vitro* fertilization clinics for the purpose of fertility treatment and were in excess of the needs of the individuals seeking such treatment;
- (2) The embryos would never be implanted in a woman and would otherwise be discarded; and
- (3) Such individuals donate the embryos with written informed consent and receive no financial or other inducements.

H.R. 3144

Another bill being proposed to gain funding for stem cell research is H.R. 3144. This bill, if passed, would fund four different approaches cited by the President's Council on Bioethics:

- (1) The harvesting of stem cells from frozen embryos, which are considered dead, therefore unable to be implanted into the womb;
- (2) Taking one cell from a blastomere (an embryo at the 8 or 16 cell stage), and allowing the rest of the cells to develop into a viable fetus. This procedure, called preimplantation genetic diagnosis (PGD), is already conducted to test for genetic defects with IVF;
- (3) Genetically or biochemically changing cells to create an embryo-like tissue that has no chance of developing into a fetus but is capable of producing ES cells; and
- (4) Reprogramming somatic cells, or bringing them back to the embryonic stage of development so they have pluripotency.

Public support for stem cell research is gaining momentum, with strong bipartisan support. Developments along the legislative lines are likely to continue to evolve and influence the state of ES cell research in the U.S.

State Legislation

The development of new technologies has caused states to evolve their positions on embryonic and fetal research. State laws may restrict the use of ES cells from some of the four primary sources: (1) existing stem cell lines, (2) aborted or miscarried embryos, (3) unused *in vitro* fertilized embryos, and (4) cloned embryos, or specifically as they permit certain activities. The distinctions of permissibility of research vary greatly among the states.

States such as California, Connecticut, Massachusetts, and New Jersey encourage ES cell research, including on cloned embryos. South Dakota, on the other hand, strictly forbids research on embryos regardless of the source. Other states that specifically permit ES cell research have instituted guidelines, including consent requirements and review processes for projects.

California and Proposition 71

The passage of Proposition 71 in California was a “watershed” event for the field of ES cell research in the U.S. This initiative established a new state medical research institute and authorized the issuance of \$3 billion in State general obligation bonds to provide funding for stem cell research and research facilities in California. Due to this support, and importantly in the advancement of its technology, Advanced Cell has opened a facility in California to further its research efforts and apply for any funding that may become available. Additionally, as part of its Growth Strategy (described on page 6), the Company is seeking collaborations with academic and other institutions also eligible for funding under this Proposition for research in the use of ES cells for various diseases and conditions.

Funding of Stem Cell Research

State Funding

Following the passage of Proposition 71, a number of other states, including Florida, Massachusetts, Connecticut, New Jersey, New York, and Illinois, have followed suit and passed or are in the process of proposing initiatives to provide additional funding for research in this area. Table 10 outlines the type of research funded, by state, and each state’s specific funding toward the different issues listed.

Table 10 STATE FUNDING OF STEM CELL RESEARCH		
Jurisdiction	Funding	Type of Research Funded
California	\$3 billion	California Institute of Regenerative Medicine
New Jersey	\$150 million	New Stem Cell Research Center
New Jersey	Proposed \$230 million	Stem Cell Research Funding
Connecticut	\$100 million	Adult and Embryonic Stem Cell Research
Illinois	\$10 million	New Stem Cell Research Institute
Massachusetts	Proposed \$100 million	Stem Cell Research Funding
North Carolina	Proposed \$10 million	Stem Cell Research Funding
Texas	Proposed \$41.1 million	Stem Cell Research Facility
New York	Proposed \$100 million	New York State Institute for Stem Cell Research
Maryland	Proposed \$23 million (died in Senate)	Stem Cell Research Fund
Pennsylvania	Proposed \$500 million	Stem Cell Research Council

Source: www.reason.com - Ronald Bailey - *Do We Really Need The Feds?*

International Funding

Table 11 outlines the international funding efforts within the area of stem cell research.

Table 11 INTERNATIONAL FUNDING OF STEM CELL RESEARCH		
Country	Funding	Type of Research Funded
United Kingdom	\$175 million	Stem Cell Research
Australia	\$43.55 million	Australia Stem Cell Centre
South Korea	\$11 million	Cloning and Human ES Cells

Source: www.reason.com - Ronald Bailey - *Do We Really Need The Feds?*

Private Funding

Table 12 (page 33) outlines the significant contributors to the private funding of stem cell research and the amounts being contributed by each.

Table 12
PRIVATE FUNDING OF STEM CELL RESEARCH

Foundation	Funding	Type of Research Funded
Starr Foundation	\$50 million	Human ES cell research in New York medical institutions
Private Funding	\$100 million	Harvard University Stem Cell Institute
University of California, Los Angeles	\$20 million	Institute for Stem Cell Biology and Medicine
Stanford University	\$120 million	Institute for Cancer/Stem Cell Biology and Medicine
Andy Grove (former Intel [INTC-NASDAQ] CEO)	\$5 million	University of California, San Francisco - Developmental and Stem Cell Biology Program
Private Donor	\$58.5 million	Johns Hopkins University - Institute for Cell Engineering
University of Minnesota	\$15 million	Stem Cell Institute
Private Donor	\$25 million	University of Texas Health Center - Houston

Source: www.reason.com - Ronald Bailey - Do We Really Need The Feds?

U.S. and European Legislation for Funding of Stem Cell Research

With the restrictions set up by President Bush for Federal funding of ES cell research, various institutions and private companies have turned to their state legislatures for funding. Table 13 (pages 33-35) outlines different state legislative initiatives and decisions regarding stem cell research. Table 14 (page 36) depicts the most current regulations in European member states regarding human ES cell research. These are the positions of these states as of July 2003.

Table 13
STATE LEGISLATIVE INITIATIVES ON STEM CELL RESEARCH (ARIZONA-ILLINOIS)

State/Jurisdiction	Restricts research on aborted fetus/embryo	Consent provisions to conduct research on fetus/embryo	Restricts research on fetus or embryo resulting from sources other than abortion	Restrictions of purchase/sale human tissue for research
Arizona	Yes, prohibits research on aborted living/non-living embryo or fetus	No	Yes, prohibits the use of public monies for cloning for research	No
Arkansas	Yes, prohibits research on aborted live fetus	Yes, consent to conduct research on aborted fetus born dead	Yes, prohibits research on cloned embryos	Yes, prohibits sale of fetus/fetal tissue
California Health & Safety	Yes, prohibits research on aborted live fetus	Yes, consent to donate IVF embryo to research	No	Yes, prohibits sale for the purpose of reproductive cloning or for stem cell research
Connecticut	No	Yes, consent to donate IVF embryo to research	No	Yes, prohibits payment for embryos, embryonic stem cells unfertilized eggs or sperm donated following IVF treatment
Florida	Yes, prohibits on aborted live fetus	No	No	No
Illinois	Yes, prohibits on aborted living/non-living fetus	Yes, written consent to perform research on cells or tissues from a dead fetus other than from an abortion	Yes, prohibits research on fetus/fertilized embryo; prohibits funding under E.O. 6 (2005) of research on fetuses from induced abortions and the creation of embryos through the combination of gametes solely for the purpose of research	Yes, prohibits sale of fetus/fetal tissue; also prohibits award of funds for stem cell research under E.O. 6 (2005) to a person who purchases or sells embryonic or fetal cadaveric tissue for research

Source: NCSL, Westlaw (<http://www.ncsl.org/programs/health/genetics/embfet.htm>).

Table 13 (continued)

STATE LEGISLATIVE INITIATIVES ON STEM CELL RESEARCH (INDIANA-NEW MEXICO)

State/Jurisdiction	Restricts research on aborted fetus/embryo	Consent provisions to conduct research on fetus/embryo	Restricts research on fetus or embryo resulting from sources other than abortion	Restrictions of purchase/sale human tissue for research
Indiana	Yes, prohibits research on aborted living/non-living embryo or fetus	Yes, consent required for fetal stem cell research	Yes, prohibits research on cloned embryos	Yes, prohibits sale of human ovum, zygote, embryo, or fetus
Iowa	No	No	Yes, prohibits research on cloned embryos	Yes, prohibits transfer or receipt of oocyte, embryo, or fetus for somatic cell nuclear transfer
Kentucky	No	No	No	Yes, prohibits sale of fetus/fetal tissue
Louisiana	No	No	Yes, prohibits research on fetus/embryo in utero, <i>in vitro</i> fertilized embryo	No
Maine	No	No	Yes, prohibits research on fetus/embryo born or extracted alive, only applies to <i>in vitro</i> fertilized embryos post-implantation	Yes, prohibits sale of fetus/fetal tissue
Massachusetts	Yes, prohibits research on embryo/live fetus	Yes, written consent to perform research on a dead fetus and informed consent to donate egg, sperm, or unused preimplantation embryos created for IVF	Yes, prohibits research on live embryo or fetus; also prohibits creation on fertilized embryo solely for research	Yes, prohibits sale of neonate, embryo or fetus for illegal purposes; prohibits sale of embryos, gametes or cadaveric tissue for research
Michigan	Yes, live embryo/fetus	Yes, written consent of mother to donate dead embryo, fetus, or neonate to research	Yes, prohibits research on a live embryo or fetus, cloned embryo	No
Minnesota	No	No	Yes, prohibits research on a live embryo up to 265 post fertilization or fetus	Yes, permits the sale/purchase of cell culture lines from nonliving human conceptus
Missouri	Yes, prohibits research on a fetus alive pre-abortion	No	No	Yes, prohibits receipt of valuable consideration for aborted fetal organs or tissue
Montana	Yes, prohibits research on a live fetus	No	No	No
Nebraska	Prohibits research on aborted live fetus or the use of state funds for research on fetal tissue obtained from an abortion	No	Yes, limits the use of state funds for embryonic stem cell research; restrictions only apply to state healthcare cash funds provided by tobacco settlement dollars	Yes, prohibits sale, distribution or donation of viable aborted child
New Hampshire	No	No	Yes, prohibits the maintenance of a unfrozen fertilized pre-embryo past 14 days	Yes
New Jersey	No	Yes	No	No
New Mexico	No	No	Yes, prohibits research on a fetus/embryo born or extracted alive, only applies to <i>in vitro</i> fertilized embryos post-implantation	Yes, prohibits abortion for the purpose of selling the fetus to researchers

Source: NCSL, Westlaw (<http://www.ncsl.org/programs/health/genetics/embfct.htm>).

Table 13 (continued)

STATE LEGISLATIVE INITIATIVES ON STEM CELL RESEARCH (NORTH DAKOTA-WYOMING)

State/Jurisdiction	Restricts research on aborted fetus/embryo	Consent provisions to conduct research on fetus/embryo	Restricts research on fetus or embryo resulting from sources other than abortion	Restrictions of purchase/sale human tissue for research
North Dakota	Yes, prohibits research on a living/non-living embryo or fetus	Yes, requires consent to conduct research on a nonliving fetus or embryo other than from an abortion	Yes, prohibits research on a fetus born or extracted alive; cloned embryos	Yes, prohibits the sale of a fetus to be used for illegal purposes
Ohio	Yes, prohibits research on a living/non-living embryo or fetus	No	No	Yes, prohibits sale of fetus or fetal remains from an abortion
Oklahoma	Yes, prohibits research on a fetus/embryo	No	No	Yes, prohibits sale of fetus or fetal remains
Pennsylvania	Yes, prohibits research on a live embryo or fetus	Consideration may not be given to mothers consenting to research; in cases involving abortion, consent must be provided after decision to abort	No	Yes, consideration may not be given to mothers consenting to research or other transferring tissue except for expenses involved in actual retrieval, storage, etc.
Rhode Island	No	Yes	Yes, prohibits research on a fetus/embryo born or extracted alive, only applies to <i>in vitro</i> fertilized embryos post-implantation	Yes, prohibits sale of neonate, embryo, or fetus for illegal purposes
South Dakota	Yes, prohibits research on a living/non-living embryo or fetus	No	Yes, prohibits research on embryo outside of a woman's body; research on cells or tissues derived from an embryo outside a woman's body	Yes, prohibits sale of embryo
Tennessee	No	Yes, consent required to conduct research on aborted fetus	No	Yes, prohibits sale of aborted fetus
Texas Penal	No	No	No	Prohibits sale of fetus/fetal tissue
Utah	No	No	Yes, prohibits research on a live fetus, fertilized embryo post-implantation	Yes, prohibits sale of fetus/fetal tissue; also prohibits sale of live unborn children, which is not defined, but are referred to in abortion statute
Virginia	No	No	May prohibit research on a cloned embryo or fetus	Yes, prohibits shipping or receiving of the product of human cloning for commerce
Wyoming	No	No	No	Yes, prohibits sale, distribution or donation of live or viable aborted child, defined to include embryos, for experimentation

Source: NCSL, Westlaw (<http://www.ncsl.org/programs/health/genetics/embfet.htm>).

Table 14

REGULATIONS IN EUROPEAN MEMBER STATES REGARDING HUMAN EMBRYONIC STEM CELL

EU Member States	Policy
Italy, Luxembourg, Portugal	No specific legislation regarding human embryo research
Belgium, United Kingdom	Allowing for the creation of human embryos for stem cell procurement by law
Austria, Spain, France, Ireland	Prohibition of the procurement of embryonic stem cells from human embryos
Germany	Prohibition of the procurement of embryonic stem cells from human embryos but allowing by law for the importation of human embryonic stem cell lines
Belgium, Denmark, Finland, Greece, Netherlands, Sweden, United Kingdom	Allowing for the procurement of human embryonic stem cells from supernumerary embryos by law
Austria, Denmark, Germany, Spain, Finland, France, Greece, Ireland, Netherlands, Portugal	Prohibition of the creation of human embryos for research purposes and for the procurement of stem cells by law or by ratification of the Convention of the Council of Europe on Human Rights and Biomedicine signed in Oviedo on April, 4 1997

Source: International Society for Stem Cell Research - (<http://www.isscr.org/scientists/legislative.htm>).

Competition

Although companies involved in stem cell research are generally highly specialized, focusing on different aspects within this area, there are several companies within this sector which can be considered competitors to Advanced Cell. Typically, these companies are defined by the type of stem cell research they conduct (1) embryonic; (2) umbilical cord; or (3) adult stem cells. Figure 18 outlines some of the companies to which to Advanced Cell believes it could be considered competitive to within this space, accompanied by company descriptions.

Figure 18
COMPETITION WITHIN THE STEM CELL ARENA



Source: Advanced Cell Technology, Inc.

Embryonic Research

Geron Corp.

Based in Menlo Park, California, Geron Corp. was formed in 1992 by Dr. Michael West (biography on page 13), Advanced Cell's chairman, chief scientific officer, and president, as a biopharmaceutical company developing and commercializing three groups of products: (1) therapeutic products for oncology that target telomerase; (2) pharmaceuticals that activate telomerase in tissues impacted by aging, injury, or degenerative disease; and (3) cell-based therapies derived from its human ES cell platform for applications in multiple chronic diseases. Within this last group, Geron is currently working on a form of stem cell differentiation, attempting to "tell" ES cells which type of cell to become. The company also has created its own lines of stem cells that are free of all animal-cell contaminants. Geron selectively enters into, and intends to continue to enter into, collaborative research agreements with leading academic and research institutions. Geron holds the exclusive rights to the WARF patent (described on pages 11 and 26), along with exclusive rights to technology (via the WARF technology) for developing **beta cells**, neurons, and heart muscle cells.

Umbilical Cord Research

ViaCell Inc.

ViaCell Inc. (VIAC-NASDAQ) is a biotechnology company dedicated to enabling the widespread application of human cells as medicine. The company is developing a pipeline of proprietary product candidates intended to address cancer, cardiac disease, and diabetes by developing cord blood and adult-derived stem cell product candidates in therapeutically useful quantities. In addition to its therapeutic focus, ViaCell commercializes ViaCord®, a product for the preservation of umbilical cord blood within its Reproductive Health Business Unit. The company is looking to leverage its commercial infrastructure and product development capabilities by developing ViaCyte™, an investigational product intended to broaden reproductive choices for women through the cryopreservation of human unfertilized eggs. ViaCell was founded in 1994 and has research and development centers and commercial operations in the U.S., and a research center in Singapore.

Amgen, Inc.

In partnership with ViaCell, Amgen Inc. (AMGN-NASDAQ) is harvesting and cultivating umbilical stem cells for transplantation in other patients.

Celgene Corporation

Celgene Corporation, based in Summit, New Jersey, is an integrated global pharmaceutical company, primarily engaged in the discovery, development, and commercialization of therapies to treat cancer and immunological diseases through regulation of genomic and **proteomic** targets. On December 31, 2002, Celgene acquired Anthrogenesis Corporation, a privately-held New Jersey-based biotherapeutics company and cord blood banking business, which has also pioneered the recovery of stem cells from human placental tissue following the completion of a full-term, successful pregnancy. Anthrogenesis now operates as Celgene Cellular Therapeutics (CCT), a wholly-owned subsidiary. CCT has developed proprietary technology for collecting, processing, and storing placental stem cells with potentially broad therapeutic applications in cancer, as well as autoimmune, cardiovascular, neurological, and degenerative diseases. Stem cell-based therapies offer the potential to provide disease-modifying outcomes for serious diseases, which today lack adequate therapy. CCT is currently researching stem cells derived from the human placenta and umbilical cord (both non-controversial sources of stem cells). In December 2004, Celgene filed an **Investigational New Drug Application (IND)** with the FDA for its initial stem cell trial in **sickle cell anemia**. In sickle cell anemia, CCT's research has shown that its IMiDs can interact with stem cells and modulate them in such a way that they differentiate into **erythrocytes**, or red blood cells. CCT has also discovered a method of expanding the stem cell population in cord blood, to help generate the increased number of stem cells that may be necessary for treating patients with cancer and other indications in the future.

Adult Stem Cell Research

StemCells, Inc.

StemCells, Inc. (STEM-NASDAQ), based in Palo Alto, California, is focused on the discovery and development of stem cell therapeutics to treat damage to or degeneration of major organ systems, such as the central nervous system, liver, and pancreas. StemCells uses a proprietary process to isolate, purify and expand rare candidate stem cells found in adult human tissue. To date, the company has discovered the human neural stem cell as well as a population of rare candidate stem cells found in human liver and pancreas. StemCells has over 40 issued U.S. patents, plus foreign equivalents to some 14 U.S. patents and applications, for a total of over 170 individual patents worldwide.

Aastrom Biosciences

Aastrom Biosciences Inc. (ASTM-NASDAQ), based in Ann Arbor, Michigan, is developing patient-specific products for the repair or regeneration of human tissues, utilizing the company's proprietary adult stem cell technology. Aastrom's strategic position in the tissue regeneration sector is enabled by its proprietary Tissue Repair Cells (TRCs), a mix of bone marrow-derived adult stem and **progenitor cells**, and the Aastrom Replicell® System, an industry-unique automated cell production platform used to produce cells for clinical use. TRCs are the core component of the products Aastrom is developing for severe bone fractures, **ischemic vascular disease**, jaw reconstruction, and spine fusion, with Phase I/II level clinical trials active in the U.S. and EU for some of these indications.

Potential Milestones

- Advanced Cell's growth strategy is based on cultivating corporate partnerships in order to assist in developing and launching various product lines derived from its ES cell technology, with the Company making investments in moving from a pure research company into a research and development company.
- The Company is certifying GMP-capable facilities in Worcester, Massachusetts and Alameda, California, for production of stem cell lines and differentiated cells to be used in preclinical and clinical testing.
- Advanced Cell plans to derive human ES cells and derive differentiated cell types under GMP.
- The Company is working toward systematically differentiating ES cells for therapeutic use, and then scaling production of these cells to be used in its Reduced Complexity Library (RCL).
- Advanced Cell intends to present and launch its preclinical and clinical plan for the development and differentiation of human ES cells.
- The Company plans to recruit senior clinical executives to oversee the clinical trials that are to be conducted "in-house".
- Advanced Cell has stated its plans to achieve a stock listing on the AMEX or NASDAQ.

Key Points to Consider

- Advanced Cell has developed a method of embryonic stem (ES) cell research in mice using a technique of single-cell biopsy, which does not interfere with the developmental potential of the embryos. This method, similar to that used in preimplantation genetic diagnosis (PGD) to test for genetic defects, removes one of the largest ethical objections to ES cell research—the fact that embryos are deprived of any further potential to develop into a complete human being.
- One of the more significant obstacles facing regenerative medicine today is the potential rejection of ES cells in patients. Advanced Cell's research is focused on solving this problem by creating stem cell therapeutics which are histocompatible. By creating a technology that transforms a patient's cells into an embryonic state, where those cells can then be differentiated into specific therapeutically relevant cell types that are genetically identical to the patient, Advanced Cell believes it can successfully combat the difficulty of immunocompatibility in patients.
- Advanced Cell is currently developing three technologies in ES cell research:
 - (1) Cellular Reprogramming—enabling a transformation of a patient's own cells into ES cells, which can then be differentiated into therapies for a variety of diseases,
 - (2) Reduced Complexity Library (RCL)—enabling the production of stem cell therapies for “off-the-shelf” deployment to treat acute disease in time critical situations not amenable to reprogramming technologies; and
 - (3) Stem Cell Differentiation—which is the development of technologies designed to control the differentiation and re-differentiation of stem cells into specific cell types, such as hematopoietic, myocardial, skin, retinal, and neuronal cells, for therapeutic applications.
- Drs. Michael West and Robert Lanza (biographies on pages 13 and 14) are key figures in the field of ES cell research. Both Dr. West and Dr. Lanza have been on the forefront of many of the breakthrough technologies discovered in the field of regenerative medicine, specifically Cellular Bio-Engineering. In January 2006, the Company announced that Dr. Lanza has released a comprehensive new book on ES cell research and its real world applications, *Essentials of Stem Cell Biology* (Academic Press, November 2005, Hardcover).
- The Company's growth strategy is focused on cultivating relationships with collaborative partners to launch various product lines intended to be developed as a result as Advanced Cell's new technology.
- Advanced Cell is well funded as a result of its recently completed Convertible Debenture offering, and is targeting conversion of existing Notes to equity and closing of the second tranche of the funding contemplated in its transaction.
- Due to recent legislation in California, specifically the passage of Proposition 71 allowing for \$3 billion to be granted to fund stem cell research, Advanced Cell opened a facility in Alameda, California to take advantage of this funding and expand its research and development capabilities.
- Since President Bush's edict on ES cell research was issued, allowing for Federal funding of research only on certain existing stem cell lines, different states have taken the initiative to pass their own ES cell research guidelines, as described on pages 31-32 and 33-35. As more states and entities allow and fund ES cell research, advancements and collaborations in this area that were previously improbable are now much more likely. Advanced Cell expects to benefit from the competition of ideas in the marketplace, finding collaborative partners with which to move forward with its technology.
- Advanced Cell is supported by a broad intellectual property portfolio. The Company currently owns or has exclusive licenses to over 30 patents and has over 280 patent applications pending worldwide in the field of regenerative medicine and stem cell therapy.

Historical Financial Results

Tables 15, 16, and 17 provide a summary of key historical financial statements, including its Statement of Operations, Balance Sheet, and Statement of Cash Flows.

Table 15
Advanced Cell Technology, Inc.
CONSOLIDATED STATEMENT OF OPERATIONS (Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
Revenue:				
License fees and royalties	\$ 83,127	\$ 250,972	\$ 311,880	\$ 690,705
Cost of revenue	41,189	14,868	145,131	185,166
Gross profit	41,938	236,104	166,749	505,539
Operating expenses:				
Research and development	734,065	152,725	1,667,684	689,628
Grant reimbursements	(171,980)	(89,438)	(597,198)	(229,609)
General and administrative	2,330,767	497,954	5,572,267	1,583,605
Total operating expenses	2,892,852	561,241	6,642,753	2,043,624
Loss from operations	(2,850,914)	(325,137)	(6,476,004)	(1,538,085)
Other income (expense):				
Interest income	6,083	—	32,042	—
Gain on settlement of debt	966,301	—	1,052,814	—
Interest expense and late fees	(432,077)	(26,397)	(500,806)	(62,627)
Interest expense - stockholder	—	(30,000)	(60,000)	(90,000)
Total other income (expense)	540,307	(56,397)	524,050	(152,627)
Net loss	\$ (2,310,607)	\$ (381,534)	\$ (5,951,954)	\$ (1,690,712)
Net loss per share, basic and diluted	\$ (0.10)	\$ (0.05)	\$ (0.26)	\$ (0.20)
Weighted average shares outstanding, basic and diluted	23,191,111	8,325,883	23,209,742	8,325,883

Source: Advanced Cell Technology, Inc.

Table 16
Advanced Cell Technology, Inc.
CONSOLIDATED BALANCE SHEET (Unaudited)

	September 30, 2005	December 31, 2004
	(Unaudited)	
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 16,483,058	\$ —
Cash held in escrow for stock subscriptions	—	3,676,000
Accounts receivable, net of allowance for doubtful accounts of \$636,399 and \$128,684	71,848	104,150
Prepaid expenses	147,914	31,300
Deferred royalty fees, current portion	131,013	119,763
Total current assets	16,833,833	3,931,213
Property and equipment, net	343,060	98,455
Due from stockholder	—	394,015
Deferred royalty fees, less current portion	628,752	718,573
Deposits	82,954	17,954
Debt issuance costs	2,484,351	12,000
Total assets	\$ 20,372,950	\$ 5,172,210
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable and accrued expenses	\$ 2,489,457	\$ 3,867,282
Deferred revenue, current portion	332,508	332,508
Interest payable - stockholder	—	296,877
Advances payable - other	130,000	130,000
Convertible debentures current portion, net of discounts of \$6,436,787	988,629	—
Warrant liability under convertible notes payable	5,892,665	—
Beneficial conversion liability under convertible notes payable current portion	3,101,671	—
Note payable - stockholder	—	1,000,000
Notes payable - other, net of discounts of \$21,818	748,816	967,014
Total current liabilities	13,683,746	6,593,681
Convertible debentures less current portion and net of discounts of \$12,873,575	1,977,259	—
Beneficial conversion liability under convertible notes payable less current portion	6,203,343	—
Deferred revenue, net of current portion	1,745,670	1,995,049
Preferred units subscribed	—	4,175,999
Total liabilities	23,610,018	12,764,729
Stockholders' deficit:		
Common stock, \$0.001 par value; 100,000,000 shares authorized, 23,068,059 and 8,325,883 shares issued and outstanding, respectively	23,068	8,326
Additional paid-in capital	16,473,202	6,158,954
Deferred compensation	(21,585)	—
Accumulated deficit	(19,711,753)	(13,759,799)
Total stockholders' deficit	(3,237,068)	(7,592,519)
Total liabilities and stockholders' deficit	\$ 20,372,950	\$ 5,172,210

Source: Advanced Cell Technology, Inc.

Table 17
Advanced Cell Technology, Inc.
CONSOLIDATED STATEMENT OF CASH FLOWS (Unaudited)

	Nine Months Ended September 30,	
	2005	2004
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	\$ (5,951,954)	\$ (1,690,712)
Adjustments to reconcile net loss to net cash provided by operating activities:		
Depreciation and amortization	73,221	106,093
Bad debt	32,715	—
Amortization of deferred charges	89,821	149,541
Amortization of debt discount	413,952	—
Amortization of deferred revenue	(249,379)	(317,858)
Gain on settlement of accounts payable	(1,052,814)	—
Shares issued for services	15,000	—
Amortization of deferred compensation	316,117	—
Changes in operating assets and liabilities:		
(Increase) decrease in:		
Accounts receivable	(413)	323,547
Prepaid expenses	(116,614)	23,641
Other current assets	—	5,000
Deferred charges	(11,250)	(108,000)
Deposits	(65,000)	—
Increase (decrease) in:		
Accounts payable and accrued expenses	568,013	1,094,702
Interest payable	101,394	104,210
Deferred revenue	—	250,000
Advances to Stockholder	(327,235)	(141,861)
Net cash used in operating activities	(6,164,426)	(201,697)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Proceeds from sale of equipment	—	(6,377)
Cash acquired in acquisition	10,000	0
Purchases of property and equipment	(317,826)	—
Net cash used in investing activities	(307,826)	(6,377)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from preferred unit subscriptions, net of cost	3,735,201	—
Proceeds from convertible debentures	16,223,713	—
Offering costs	(95,671)	—
Payments on notes and leases	(250,000)	(23,752)
Settlement payment	(332,524)	—
Cash overdraft	(1,409)	—
Proceeds from issuance of notes and loans	—	230,000
Net cash provided by financing activities	19,279,310	206,248
Net increase (decrease) in cash	12,807,058	(1,826)
Cash and cash equivalents, beginning of period	\$ 3,676,000	\$ 3,782
Cash and cash equivalents, end of period	\$ 16,483,058	\$ 1,956
Cash paid for:		
Interest	\$ —	\$ 1,247
Income taxes		

Source: Advanced Cell Technology, Inc.

Risks

Some information in this report relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in Advanced Cell's reports on Forms 10-QSB, 10-KSB, 8-K, and other forms filed with the Securities and Exchange Commission (SEC) from time to time. The content of this report with respect to Advanced Cell has been compiled primarily from information available to the public and released by Advanced Cell through news releases and SEC filings. Advanced Cell is solely responsible for the accuracy of that information. Information about other companies has been prepared from publicly available documents and has not been independently verified by Advanced Cell. For more complete information about Advanced Cell, refer to the Company's website at www.advancedcell.com.

Investors should carefully consider the risks and the information about Advanced Cell's business described below. Investors should not interpret the order in which these considerations are presented as an indication of their relative importance. The risks and uncertainties described below are not the only risks that Advanced Cell faces. Additional risks and uncertainties not presently known to Advanced Cell or that Advanced Cell currently believes to be immaterial may also adversely affect its business. If any of the following risks and uncertainties develop into actual events, the business, financial condition, and results of operations could be materially and adversely affected, and the trading price of its stock could decline.

The Company has a limited operating history on which potential investors may evaluate its operations and prospects for profitable operations.

Advanced Cell has a limited operating history on which a potential investor may base an evaluation of it and its prospects. If the Company is unable to begin and sustain profitable operations, investors may lose their entire investment in it. Advanced Cell is in the pre-clinical stage, and its prospects must be considered speculative in light of the risks, expenses, and difficulties frequently encountered by companies in their early stages of development, particularly in light of the uncertainties relating to the new, competitive, and rapidly evolving markets in which Advanced Cell anticipates it will operate. To attempt to address these risks, the Company must, among other things, further develop its technologies, products and services; successfully implement its research, development, marketing, and commercialization strategies; respond to competitive developments; and attract, retain, and motivate qualified personnel. Substantial risk is involved in investing in the Company because, as a development stage company, it has fewer resources than an established company; the Company's management may be more likely to make mistakes at such an early stage; and Advanced Cell may be more vulnerable operationally and financially to any mistakes that may be made, as well as to external factors beyond its control.

These difficulties are compounded by its heavy dependence on emerging and sometimes unproven technologies. In addition, some of Advanced Cell's potential revenue sources involve ethically sensitive and controversial issues, which could become the subject of legislation or regulations that could materially restrict its operations and, therefore, harm its financial condition, operating results, and prospects for bringing its investors a return on their investment.

The Company has a history of operating losses, and cannot provide assurance that it will achieve future revenues or operating profits.

Advanced Cell has generated modest revenues to date from its operations. Historically, the Company has had net operating losses each year since its inception. The Company has limited current potential sources of revenue from license fees and product development revenues, and cannot assure investors that it will be able to develop such revenue sources or that its operations will become profitable, even if Advanced Cell is able to commercialize its technologies or any products or services developed from those technologies. If the Company continues to suffer losses, as it has in the past, investors may not receive any return on their investment and may lose their entire investment.

Although the Company has revenues from license fees and royalties, it has no commercially marketable products and no immediate ability to generate revenue from commercial products, nor any assurance of being able to develop its technologies for commercial applications. As a result, Advanced Cell may never be able to operate profitably.

The Company is just beginning to identify products available for pre-clinical trials and may not receive significant revenues from commercial sales of its products for the next several years, if at all, although it does generate revenues from licensing activities. Advanced Cell has marketed only a limited amount of services based on its technologies and has little experience in doing so. The Company's technologies and any potential products or services that it may develop will require significant additional effort and investment prior to material commercialization and, in the case of any biomedical products, pre-clinical and clinical testing and regulatory approvals.

Advanced Cell cannot assure investors that it will be able to develop any such technologies or any products or services, or that such technologies, products, or services will prove to be safe and efficacious in clinical trials, meet applicable regulatory standards, be capable of being produced in commercial quantities at acceptable costs, or be successfully marketed. For that reason, the Company may not be able to generate revenues from commercial production or operate profitably.

Advanced Cell has sold the agricultural portion of its business in order to finance operations. The agricultural applications of its technology generally have a more rapid realization of revenues due to more limited regulatory requirements and testing. The Company's ability to generate revenue from any agricultural applications of its technology is limited to existing license royalties, if any.

The Company will require substantial additional funds to continue operating, which may not be available on acceptable terms, if at all.

Advanced Cell believes its cash from all sources, including cash, cash equivalents, and anticipated revenue stream from licensing fees and sponsored research contracts is sufficient for it to continue operations through March 31, 2007. However, without substantial additional financing during this period, the Company will need to significantly limit its capital and operational spending and will therefore be limited in its ability to advance its scientific efforts or further its efforts to operate profitably.

In addition, Advanced Cell's cash requirements may vary materially from those now planned because of results of research and development, potential relationships with strategic partners, changes in the focus and direction of its research and development programs, competition, litigation required to protect its technology, technological advances, the cost of pre-clinical and clinical testing, the regulatory process of the United States Food and Drug Administration (FDA) and foreign regulators, whether any of its products become approved or the market acceptance of any such products and other factors. The Company's current cash reserves are not sufficient to fund its operations through the commercialization of its first products or services.

Advanced Cell's competition includes both public and private organizations and collaborations among academic institutions and large pharmaceutical companies, most of which have significantly greater experience and financial resources than it does.

The biotechnology and pharmaceutical industries are characterized by intense competition. Advanced Cell competes against numerous companies, both domestic and foreign, many of which have substantially greater experience and financial and other resources than it has. Several such enterprises have initiated cell therapy research programs and/or efforts to treat the same diseases targeted by the Company. Companies such as Geron Corporation, Genzyme Corporation, StemCells, Inc., Aastrom Biosciences, Inc. and Viacell, Inc., as well as others, many of which have substantially greater resources and experience in its fields than it does, are well situated to compete with Advanced Cell effectively. Additionally, any of the world's largest pharmaceutical companies represents a significant actual or potential competitor with vastly greater resources. These companies hold licenses to genetic selection technologies and other technologies that are competitive with its technologies. These and other competitive enterprises have devoted, and will continue to devote substantial resources to the development of technologies and products in competition with Advanced Cell.

Private and public academic and research institutions also compete with Advanced Cell in the research and development of human therapeutic or agricultural products. In the past several years, the pharmaceutical industry has selectively entered into collaborations with both public and private organizations to explore the possibilities that stem cell therapies may present for substantive breakthroughs in the fight against disease.

In addition, many of the Company's competitors have significantly greater experience than it has in the development, pre-clinical testing, and human clinical trials of biotechnology and pharmaceutical products, in obtaining FDA and other regulatory approvals of such products, and in manufacturing and marketing such products. Accordingly, its competitors may succeed in obtaining FDA approval for products more rapidly or effectively than Advanced Cell can.

The Company's competitors may also be the first to discover and obtain a valid patent to a particular stem cell, which may effectively block all others from doing so. It will be important for the Company or its collaborators to be the first to discover any stem cell that it is seeking to discover. Failure to be the first could prevent the Company from commercializing all of its research and development affected by that discovery. Additionally, if Advanced Cell commences commercial sales of any products, it will also be competing with respect to manufacturing efficiency and sales and marketing capabilities, areas in which it has no experience.

The U.S. is encountering significant competition from many foreign countries that are providing an environment more attractive for stem cell research. The governments of numerous foreign countries are investing in stem cell research, providing facilities, personnel, and legal environments intended to attract biotechnology companies, and encourage stem cell research and development of stem cell-related technologies. These efforts by foreign countries may make it more difficult to effectively compete in this industry and may generate competitors with substantially greater resources than the Company's.

Advanced Cell relies on nuclear transfer and embryonic stem (ES) cell technologies that it may not be able to successfully develop, which may prevent it from generating revenues, operating profitably, or providing investors any return on their investment.

The Company has concentrated its research on its nuclear transfer and ES cell technologies, and its ability to operate profitably will depend on being able to successfully develop these technologies for human applications. These are emerging technologies with, as yet, limited human applications. The Company cannot guarantee that it will be able to successfully develop its nuclear transfer and ES cell technologies or that such development will result in products or services with any significant commercial utility. Advanced Cell anticipates that the commercial sale of such products or services, and royalty/licensing fees related to its technology, would be its primary sources of revenues. If it is unable to develop its technologies, investors will likely lose their entire investment in the Company.

The outcome of pre-clinical, clinical, and product testing of the Company's products is uncertain, and if it is unable to satisfactorily complete such testing, or if such testing yields unsatisfactory results, Advanced Cell may be unable to commercially produce its proposed products. Before obtaining regulatory approvals for the commercial sale of any potential human products, the Company's products will be subjected to extensive pre-clinical and clinical testing to demonstrate their safety and efficacy in humans. Advanced Cell cannot assure investors that the clinical trials of its products, or those of its licensees or collaborators, will demonstrate the safety and efficacy of such products at all, or to the extent necessary to obtain appropriate regulatory approvals, or that the testing of such products will be completed in a timely manner, if at all, or without significant increases in costs, program delays or both, all of which could harm its ability to generate revenues.

In addition, the Company's prospective products may not prove to be more effective for treating disease or injury than current therapies. Accordingly, Advanced Cell may have to delay or abandon efforts to research, develop, or obtain regulatory approval to market its prospective products. Many companies involved in biotechnology research and development have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to adequately demonstrate the safety and efficacy of a therapeutic product under development could delay or prevent regulatory approval of the product, and could harm the Company's ability to generate revenues, operate profitably, or produce any return on an investment in Advanced Cell.

While the marketing of cloned or transgenic animals does not currently require regulatory approval, such approval may be required in the future. The Company cannot assure investors that it would obtain such approvals or that its licensees' products would be accepted in the marketplace. This lack of approval could reduce or preclude any royalty revenues it might receive from its licensees in that field.

Advanced Cell may not be able to commercially develop its technologies and proposed product lines, which, in turn, would significantly harm its ability to earn revenues and result in a loss of investment.

Advanced Cell's ability to commercially develop its technologies will be dictated in large part by forces outside its control and which cannot be predicted, including, but not limited to, general economic conditions, the success of its research and pre-clinical and field testing, the availability of collaborative partners to finance its work in pursuing applications of nuclear transfer technology, and technological or other developments in the biomedical field which, due to efficiencies, technological breakthroughs or greater acceptance in the biomedical industry, may render one or more areas of commercialization more attractive, obsolete, or competitively unattractive.

It is possible that one or more areas of commercialization will not be pursued at all if a collaborative partner or entity willing to fund research and development cannot be located. The Company's decisions regarding the ultimate products and/or services it pursues could have a significant adverse affect on its ability to earn revenue if it misinterprets trends, underestimates development costs, and/or pursues wrong products or services. Any of these factors either alone or in concert could materially harm Advanced Cell's ability to earn revenues and could result in a loss of any investment in the Company.

If Advanced Cell is unable to keep up with rapid technological changes in its field or compete effectively, it will be unable to operate profitably.

The Company is engaged in activities in the biotechnology field, which is characterized by extensive research efforts and rapid technological progress. If it fails to anticipate or respond adequately to technological developments, its ability to operate profitably could suffer. Advanced Cell cannot assure investors that research and discoveries by other biotechnology, agricultural, pharmaceutical, or other companies will not render its technologies or potential products or services uneconomical, or result in products superior to those it develops or that any technologies, products, or services it develops will be preferred to any existing or newly-developed technologies, products, or services.

The Company may not be able to protect its proprietary technology, which could harm its ability to operate profitably.

The biotechnology and pharmaceutical industries place considerable importance on obtaining patent and trade secret protection for new technologies, products, and processes. Advanced Cell's success will depend, to a substantial degree, on its ability to obtain and enforce patent protection for its products, preserve any trade secrets, and operate without infringing the proprietary rights of others.

Advanced Cell is aware of certain patents that have been granted to others and certain patent applications that have been filed by others with respect to nuclear transfer technologies. The fields in which the Company operates has been characterized by significant efforts by competitors to establish dominant or blocking patent rights to gain a competitive advantage, and by considerable differences of opinion as to the value and legal legitimacy of competitors' purported patent rights and the technologies they actually utilize in their businesses.

Advanced Cell's business is highly dependent upon maintaining licenses with respect to key technology.

Several of the key patents the Company utilizes are licensed to it by third parties. These licenses are subject to termination under certain circumstances (including, for example, the Company's failure to make minimum royalty payments or to timely achieve development and commercialization benchmarks). The loss of any of such licenses, or the conversion of such licenses to non-exclusive licenses, could harm its operations and/or enhance the prospects of its competitors.

Certain of these licenses also contain restrictions, such as limitations on Advanced Cell's ability to grant sublicenses that could materially interfere with its ability to generate revenue through the licensing or sale to third parties of important and valuable technologies that it has, for strategic reasons, elected not to pursue directly. The possibility exists that in the future the Company will require further licenses to complete and/or commercialize its proposed products. Advanced Cell cannot assure investors that it will be able to acquire any such licenses on a commercially viable basis.

The Company may not be able to adequately protect against piracy of intellectual property in foreign jurisdictions.

Considerable research in the areas of stem cells, cell therapeutics, and regenerative medicine is being performed in countries outside of the U.S., and a number of Advanced Cell's competitors are located in those countries. The laws protecting intellectual property in some of those countries may not provide protection for its trade secrets and intellectual property adequate to prevent its competitors from misappropriating its trade secrets or intellectual property. If the Company's trade secrets or intellectual property are misappropriated in those countries, it may be without adequate remedies to address the issue.

Patent litigation presents an ongoing threat to Advanced Cell's business with respect to both outcomes and costs.

Advanced Cell has previously been involved in patent interference litigation with Infigen, Inc., and is currently involved in two patent disputes with Geron Corporation, and it is possible that further litigation over patent matters with one or more competitors could arise. The Company could incur substantial litigation or interference costs in defending itself against suits brought against it or in suits in which the Company may assert its patents against others. If the outcome of any such litigation, including its current disputes with Geron Corporation, is unfavorable, the Company's business would likely be materially adversely affected. To determine the priority of inventions, Advanced Cell may also have to participate in interference proceedings declared by the United States Patent and Trademark Office (USPTO), which could result in substantial cost to it. Without additional capital, the Company may not have the resources to adequately defend or pursue this litigation.

The issuance of shares upon conversion of the convertible debentures and exercise of outstanding warrants will cause immediate and substantial dilution to Advanced Cell's existing stockholders.

The issuance of shares upon conversion of the convertible debentures and exercise of warrants will result in substantial dilution to the interests of other stockholders since the selling security holders may ultimately convert and sell the full amount issuable on conversion. Although no single selling security holder may convert its convertible debentures and/or exercise its warrants if such conversion or exercise would cause it to own more than 4.99% of its outstanding common stock, this restriction does not prevent each selling security holder from converting and/or exercising some of its holdings and then converting the rest of its holdings. In this way, each selling security holder could sell more than this limit while never holding more than this limit. There is no upper limit on the number of shares that may be issued which will have the effect of further diluting the proportionate equity interest and voting power of holders of the Company's common stock, including investors in this offering.

Companies such as Advanced Cell which are engaged in research using nuclear transfer and ES cells are currently subject to strict government regulations, and its operations could be harmed by any legislative or administrative efforts impacting the use of nuclear transfer technology or human embryonic material.

Advanced Cell's business is focused on human cell therapy, which includes the production of human differentiated cells from stem cells and involves the use of nuclear transfer technology, human oocytes, and embryonic material. Nuclear transfer technology, commonly known as therapeutic cloning, and research utilizing ES cells are controversial subjects, and are currently subject to intense scrutiny, both in the U.S., the United Nations, and throughout the world, particularly in the area of nuclear transfer of human cells and the use of human embryonic material.

The Company cannot assure investors that its operations will not be harmed by any legislative or administrative efforts by politicians or groups opposed to the development of nuclear transfer technology generally, or the use of nuclear transfer for therapeutic cloning of human cells specifically. Further, it cannot assure investors that legislative or administrative restrictions directly or indirectly delaying, limiting, or preventing the use of nuclear transfer technology or human embryonic material or the sale, manufacture, or use of products or services derived from nuclear transfer technology or human embryonic material will not be adopted in the future.

The government maintains certain rights in technology that Advanced Cell develops using government grant money and the Company may lose the revenues from such technology if it does not commercialize and utilize the technology pursuant to established government guidelines.

Certain of the Company's and its licensors' research has been or is being funded in part by government grants. In connection with certain grants, the U.S. government retains rights in the technology developed with the grant. These rights could restrict its ability to fully capitalize upon the value of this research.

Advanced Cell depends on its collaborators to help it develop and test its proposed products, and its ability to develop and commercialize products may be impaired or delayed if collaborations are unsuccessful.

Advanced Cell's strategy for the development, clinical testing, and commercialization of its proposed products requires that it enters into collaborations with corporate partners, licensors, licensees, and others. The Company is dependent upon the subsequent success of these other parties in performing their respective responsibilities and the continued cooperation of Advanced Cell's partners. The Company's collaborators may not cooperate with it or perform their obligations under its agreements with them. Advanced Cell cannot control the amount and timing of its collaborators' resources that will be devoted to its research and development activities related to its collaborative agreements with them. The Company's collaborators may choose to pursue existing or alternative technologies in preference to those being developed in collaboration with it.

The development and commercialization of potential products will be delayed if collaborators fail to conduct these activities in a timely manner or at all. In addition, Advanced Cell's collaborators could terminate their agreements with it and the Company may not receive any development or milestone payments. If it does not achieve milestones set forth in the agreements, or if its collaborators breach or terminate their collaborative agreements with the Company, Advanced Cell's business may be materially harmed.

The Company's reliance on the activities of its non-employee consultants, research institutions, and scientific contractors, whose activities are not wholly within its control, may lead to delays in development of the Company's proposed products.

The Company relies extensively upon and has relationships with scientific consultants at academic and other institutions, some of whom conduct research at its request, and other consultants with expertise in clinical development strategy or other matters. These consultants are not the Company's employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to it. Advanced Cell has limited control over the activities of these consultants and, except as otherwise required by its collaboration and consulting agreements to the extent they exist, can expect only limited amounts of their time to be dedicated to its activities.

In addition, the Company has formed research collaborations with academic and other research institutions throughout the world. These research facilities may have commitments to other commercial and non-commercial entities. Advanced Cell has limited control over the operations of these laboratories and can expect only limited amounts of time to be dedicated to its research goals.

The Company also relies on other companies for certain process development or other technical scientific work. Advanced Cell has contracts with these companies that specify the work to be done and results to be achieved, but it does not have direct control over their personnel or operations. If any of these third parties are unable or refuse to contribute to projects on which it needs their help, Advanced Cell's ability to generate advances in its technologies and develop its products could be significantly harmed.

Advanced Cell's products are likely to be costly to manufacture and they may not be profitable if the Company is unable to control the costs to manufacture them.

Advanced Cell's products are likely to be significantly more costly to manufacture than most other drugs currently on the market today. The Company's present manufacturing processes produce modest quantities of product intended for use in its ongoing research activities, and it has not developed processes, procedures, and capability to produce commercial volumes of product. The Company hopes to substantially reduce manufacturing costs through process improvements, development of new science, increases in manufacturing scale, and outsourcing to experienced manufacturers.

If Advanced Cell is not able to make these or other improvements, and depending on the pricing of the product, its profit margins may be significantly less than that of most drugs on the market today. In addition, the Company may not be able to charge a high enough price for any cell therapy product it develops, even if it is safe and effective, to make a profit. If the Company is unable to realize significant profits from its potential product candidates, its business would be materially harmed.

Advanced Cell depends on key personnel for its continued operations and future success, and a loss of certain key personnel could significantly hinder its ability to move forward with its business plan.

Because of the specialized nature of its business, the Company is highly dependent on its ability to identify, hire, train, and retain highly qualified scientific and technical personnel for the research and development activities it conducts or sponsors. The loss of one or more certain key executive officers, or scientific officers, would be significantly detrimental to it. In addition, recruiting and retaining qualified scientific personnel to perform research and development work is critical to Advanced Cell's success.

The Company's anticipated growth and expansion into areas and activities requiring additional expertise, such as clinical testing, regulatory compliance, manufacturing, and marketing, will require the addition of new management personnel and the development of additional expertise by existing management personnel. There is intense competition for qualified personnel in the areas of its present and planned activities, and there can be no assurance that it will be able to continue to attract and retain the qualified personnel necessary for the development of its business. The failure to attract and retain such personnel or to develop such expertise would adversely affect its business.

Advanced Cell's credibility as a business operating in the field of human ES cells is largely dependent upon the support of its Ethics Advisory Board.

Because the use of human ES cells gives rise to ethical, legal, and social issues, the Company has instituted an Ethics Advisory Board. Its Ethics Advisory Board is made up of highly qualified individuals with expertise in the field of human ES cells. The Company cannot assure investors that these members will continue to serve on the Company's Ethics Advisory Board, and the loss of any such member may affect the credibility and effectiveness of the Board. As a result, Advanced Cell's business may be materially harmed in the event of any such loss.

The Company presently has members of management and other key employees located in various locations throughout the country, which adds complexities to the operation of the business.

Presently, Advanced Cell has members of management and other key employees located in both California and Massachusetts, which adds complexities to the operation of its business. The Company intends to maintain its research facilities in Massachusetts and establish corporate offices and an additional research facility in California. It will likely incur significant costs associated with maintaining multiple locations.

The Company's securities are quoted on the OTC Bulletin Board, which may limit the liquidity and price of its securities more than if its securities were quoted or listed on the NASDAQ Stock Market or a national exchange.

Advanced Cell's securities are currently quoted on the OTC Bulletin Board, an NASD-sponsored and operated inter-dealer automated quotation system for equity securities not included in the NASDAQ Stock

Market. Quotation of the Company's securities on the OTC Bulletin Board may limit the liquidity and price of its securities more than if its securities were quoted or listed on the NASDAQ Stock Market or a national exchange. Some investors may perceive the Company's securities to be less attractive because they are traded in the over-the-counter market.

In addition, as an OTC Bulletin Board-listed company, Advanced Cell does not attract the extensive analyst coverage that accompanies companies listed on NASDAQ or any other regional or national exchange. Furthermore, institutional and other investors may have investment guidelines that restrict or prohibit investing in securities traded in the over-the-counter market. These factors may have an adverse impact on the trading and price of its securities.

The Company's common stock is subject to "penny stock" regulations and restrictions on initial and secondary broker-dealer sales.

The Securities and Exchange Commission (SEC) has adopted regulations which generally define "penny stock" to be any listed, trading equity security that has a market price less than \$5.00 per share or an exercise price of less than \$5.00 per share, subject to certain exemptions. Penny stocks are subject to certain additional oversight and regulatory requirements. Brokers and dealers affecting transactions in its common stock in many circumstances must obtain the written consent of a customer prior to purchasing its common stock, must obtain information from the customer, and must provide disclosures to the customer. These requirements may restrict the ability of broker-dealers to sell its common stock and may affect an investor's ability to sell shares of the Company's common stock in the secondary market.

Recent Events

02/09/2006—Announced that it has opened a new 15,000 square foot state-of-the-art facility in Alameda, California that encompasses a 10,000 square foot Good Manufacturing Practice (GMP)-capable laboratory. The Company is opening its new facility in California in order to participate in the Proposition 71 initiative.

01/17/2006—Announced that Dr. Lanza, vice president, medical and scientific development for Advanced Cell Technology, has released a comprehensive new book on ES cell research and its real world applications, *Essentials of Stem Cell Biology* (Academic Press, November 2005, Hardcover). The material has been reworked in an accessible format suitable for both students and general readers interested in following the latest advances in stem cells, and includes numerous full color presentations. The new format is designed to promote better understanding of the scientific and ethics issues posed by adult and ES cell research and the associated real-life applications.

11/23/2005—Announced in collaboration with other scientists that the lack of Federal funding in the U.S. for ES cell research is hampering this country's efforts, especially while competing with other countries around the world.

11/21/2005—Announced the appointment of Dr. Erkki Ruoslahti and Dr. Alan G. Walton to its Board of Directors. Dr. Ruoslahti is a professor at the Burnham Institute for Medical Research and at the University of California, Santa Barbara. He has been a founder and director of several biotechnology companies. Dr. Walton is a senior general partner of Oxford Bioscience Partners. Prior to joining Oxford, Dr. Walton was president and CEO of University Genetics Co., a public biotechnology company involved in technology transfer and seed investments in university-related projects.

10/16/2005—Announced the generation of ES cell lines using an alternative approach that does not interfere with the developmental potential of embryos. This method was shown by deriving stem cells in mice using a technique of single-cell biopsy similar to that used in preimplantation genetic diagnosis (PGD) to test for genetic defects.

07/12/2005—Announced that Dr. Robert Lanza testified before a Senate subcommittee addressing alternative methods for obtaining ES cells and creating pluripotent stem cell lines—that of single-cell biopsy of embryos and the dedifferentiation of somatic cells back to pluripotency. His testimony was in strong support of the Stem Cell Research Enhancement Act of 2005.

06/29/2005—Reported the long-term transplantation of clone-derived stem cells in the animal model of aging. The somatic cell nuclear transfer (SCNT) gave old animals youthful immune cells. The cells generated by SCNT offer the potential for treatment of a wide range of degenerative diseases.

06/22/2005—Announced a name change from A.C.T. Holdings, Inc. to Advanced Cell Technology, Inc. The company's trading symbol also changed to ACTC-OTC.BB.

06/17/2005—Announced the expansion of their senior scientific team with the addition of senior scientists that will add to the existing California team. These senior scientists are, David Larocca, Ph.D., James T. Murai, Ph.D., and Geoffrey Sargent, Ph.D.

05/26/2005—Announced the appointment of seven new members to the Massachusetts-based scientific research team. Joining Advanced Cell are Shi-Jiang Lu, Ph.D., MPH; Sandy Becker, M.A.; Qiang Feng, M.Sc.; Katherine Holton, M.S.; Rebeca E. Ramos-Kelsey, M.A.; Gary DiPerna, M.A.; and Yordanka Ivanova, M.S. Each of these individuals brings years of experience and knowledge in contemporary biomedical science to the team.

05/19/2005—Announced the entrance into two separate agreements to expand its portfolio of intellectual property in regard to SCNT and cellular reprogramming. In the first agreement, Advanced Cell acquired an option to exclusively license cloning patents from TranXenoGen, Inc. of Shrewsbury, Massachusetts.

Separately, Advanced Cell announced that it acquired the patents to a second generation cloning technology known as “cell fusion” and additional patents related to their gene trap technology.

05/04/2005—Announced that Dr. Michael West will deliver the keynote presentation “Human Embryonic Stem Cells and Nuclear Transfer” at the *Stem Cells in Regenerative Medicine* conference, sponsored by the University of California, Berkeley. Dr. West will be speaking of Advanced Cell’s gene trap technology for isolating and tracking particular differentiated cell types.

04/20/2005—Announced that Jonathan F. Atzen has been named general counsel for Advanced Cell. Mr. Atzen comes to Advanced Cell with an extensive background in life sciences and corporate law.

04/11/2005—Announced that Dr. Michael West will deliver a keynote address at the GTCbio Stem Cell Research and Therapeutics Conference. Dr. West will describe Advanced Cell’s efforts to address the challenges of translating the opportunity of human ES cell and nuclear transfer technology into new therapeutic products.

04/04/2005—Announced James Stewart will come on as chief financial officer (CFO) of the Company. Mr. Stewart brings over 15 years experience in managing financial accounting and reporting, tax issues, financial systems, forecasting, and litigation assistance for clients.

03/22/2005—Announced that Dr. Robert Lanza, vice president of medical and scientific development, was awarded the 2005 Rave Award for Medicine by *Wired Magazine*; recognizing Dr. Lanza for his commitment to finding cures through stem cell research and the Company’s recent work in coaxing stem cells to develop into retinal cells, thereby leading to a cure for some forms of blindness.

03/08/2005—Announced the first derivation of human ES cells in completely feeder-layer-free and serum-free conditions. This research describes a system for producing ES cells which markedly reduces the risk of contamination with pathogens that could be transmitted to patients and the population at large.

02/24/2005—Announced the decision of the Board of Patent Appeals and Interference between itself and Geron Corporation over methods of producing cultured inner cell mass cells, often referred to as ES cells. The Board granted Advanced Cell’s motion to remove from the interference its patent claim relating to the human species, affirming in its decision that “this claim is not properly before us.”

02/01/2005—Announced that A.C.T. Holdings, Inc. and Advanced Cell Technology, Inc. have closed their previously announced reverse merger transaction. The closing of the triangular reverse merger was the final step in bringing the combined company to the public market.

01/24/2005—Announced that Advanced Cell appointed Mr. William Caldwell, IV as chief executive officer (CEO) and appointed Dr. Michael West as chairman, president, and chief scientific officer. Mr. Caldwell brings over 30 years of experience in managing corporate organizations. Dr. West is regarded as one of the leaders and founders of the field of regenerative medicine and stem cell research.

01/07/2005—Announced its intent to appeal the decision of the Board of Patent Appeals and Interference, between itself and Geron Corporation to the U.S. District Court. Advanced Cell disputes Geron Corporation’s claim that Advanced Cell’s patent at issue in the interference has been invalidated.

Glossary of Lesser-Known Terms

Acute—Having a short and relatively severe course.

Adult Stem Cell—An undifferentiated cell found in a differentiated tissue that can renew itself and (with certain limitations) differentiate to yield all the specialized cell types of the tissue from which it originated.

Age-related macular degeneration (AMD)—A common macular degeneration beginning with drusen (small bright structures seen in the retina and in the optic disc) of the macula and pigment disruption and sometimes leading to severe loss of central vision.

Allogeneic—Any body tissue from another person, not one's own body or genetic makeup.

Alzheimer's disease—A disease marked by the loss of cognitive ability, generally over a period of 10 to 15 years, and associated with the development of abnormal tissues and protein deposits in the cerebral cortex.

Apoptosis—Programmed cell death; this physiological process is necessary for the elimination of superfluous, diseased, or damaged cells, and the formation of new cells. Also known as programmed cell death.

Bacteria cells—Very small, single-celled life-forms that can reproduce quickly.

Beta cells—A type of cell in the pancreas. Within the pancreas, the beta cells are located in areas called the islets of Langerhans where they constitute the predominant type of cell. The beta cells make and release insulin, a hormone that controls the level of glucose (sugar) in the blood. Degeneration of the beta cells is the main cause of Type 1 (insulin-dependent) diabetes mellitus.

Blastocyst—The preimplantation embryo of mammals consisting of a sphere of cells with an outer cell layer that forms the placenta and a cluster of cells on the interior called the inner cell mass that forms the embryo.

Body cell—Any cell of a plant or an animal other than a germ cell. Also referred to as a somatic cell.

Bovine—Relating to, affecting, resembling, or derived from a cow or bull.

Cell biology—An academic discipline which studies cells. This includes their physiological properties, such as their structure and the organelles they contain, their environment and interactions, their life cycle, division and function (physiology), and eventual death.

Cellular reprogramming—Also known as therapeutic cloning, takes the deoxyribonucleic acid (DNA) from the genetic host and implants it into an ovum to create ES cell lines that are genetically compatible to the recipient (or donor of that DNA). This ES cell line is then grown out and differentiated into the proper body cell line in order to heal the affected area.

Choroids—The layer of the eye behind the retina that contains major blood vessels.

Chromatin transfer—In cloning, the transfer of the chromatids (DNA strands) from the nucleus of a somatic (body) cell into the nucleus of an egg that has had its own genetic material removed. The new individual will develop from that cell and be genetically identical to the donor of the chromatids.

Chronic—Persisting over a long period of time.

Cleavage stage—The embryo in its earliest stage, lasting from the first mitotic division of the fertilized ovum into two blastomeres to the formation of the morula, a compact mass of blastomeres.

Cryopreservation—Ultra-low temperature storage of cells, tissues, embryos, or seeds. This storage is usually carried out using temperatures below 100° C.

Deoxyribonucleic Acid (DNA)—The genetic material of all living organisms (except for RNA-carrying viruses, such as HIV). DNA is a double-stranded, helical, molecular chain found within each cell. DNA contains the information necessary for cells to produce proteins, which enable cells to reproduce and carry out their functions.

Differentiation—The process by which cells or tissues undergo a change toward a more specialized form or function, especially during embryonic development.

Embryonic stem (ES) cell—A totipotent cell cultured from an early-stage embryo.

Endothelial—Relating to the endothelial cells, the main type of cells found in the inside lining of blood vessels, lymph vessels, and the heart.

Erythrocytes—A cell in the blood of vertebrates that transports oxygen and carbon dioxide to and from the body's tissue. In mammals, the red blood cell is disk-shaped and biconcave, contains hemoglobin, and lacks a nucleus.

Fusion technologies—Involves the fusion of the cytoplasm of one cell into another. In the same manner that the cytoplasm of an egg cell is capable of transforming any cell back to an embryonic state, the fusion of the cytoplasm of other cell types, including differentiated cell types (such as blood cells), is capable of reprogramming another cell type (such as a skin cell).

Genomics—The study of genes and their function.

Germ cell—The reproductive cells of the body, that is, ova (eggs) or sperm.

Good Manufacturing Practice (GMP)—The quality system regulation overseen by the Food and Drug Administration (FDA), which includes requirements related to the methods used in, and the facilities and controls used for designing, manufacturing, packaging, labeling, storing, installing, and servicing of medical devices intended for human use.

Hemangioblast—A bipotential cell that gives rise to hematopoietic and endothelial cells.

Hematopoietic—The formation of blood or blood cells within the body.

Hemizygous—Having only a single copy of a gene.

Histocompatibility—Compatibility between two organs or tissues so that a graft (of an organ or of cells) is not rejected. This compatibility depends on the genetic similarities between donor and recipient.

Homozygous—The state of having two identical alleles of a particular gene.

Immune system—A complex system that is responsible for distinguishing humans (host) from everything foreign to humans, and for protection against infections and foreign substances. The immune system works to seek and kill invaders.

Immunoglobulin—A specific protein substance that is produced by plasma cells to aid in fighting infection.

Infarction—Tissue death due to lack of oxygen-rich blood.

Investigational New Drug (IND)—Status given an experimental drug after the FDA approves an application for testing it in people.

Ischemic vascular disease—The second most common cause of dementia in the Western world. Hypertension and diabetes are the leading causes of small-artery disease, subcortical brain ischemia, and stepwise or slowing progressive decline in cognitive function. The pattern of cognitive impairment in SIVD, as compared with Alzheimer's disease, is characterized by greater impairment of executive function but better preservation of recognition memory.

Macula—A small spot. A macula on the skin is a small flat spot while the macula in the eye is a small spot where vision is keenest in the retina.

Macular Degeneration—See age-related macular degeneration (ARMD)

Monolayer—A complete layer only one cell thick.

Morula—An early stage of embryonic development (roughly 16-64 cells) at which the embryo is a solid spherical mass of cells, resulting from the early cleavage divisions of the zygote.

Multipotent—Multipotent stem cells can give rise to several other cell types, but those types are limited in number. An example of multipotent cells is hematopoietic cells—blood stem cells that can develop into several types of blood cells but cannot develop into brain cells.

Myocardial—Refers to the heart's muscle mass.

Neuroectodermal—Pertaining to or relating to the neuroectoderm (the portion of the ectoderm of the early embryo which gives rise to the central and peripheral nervous systems, including some glial cells.

Neuronal—Pertaining to a neuron or neurons (conducting cells of the nervous system).

Neuropathy—An abnormal and usually degenerative state of the nervous system or nerve.

Nutraceuticals—A food or naturally occurring food supplement that has a beneficial effect on health.

Oncogene—A gene that is capable of causing the transformation of normal cells into cancer cells.

Oocyte—Unfertilized egg cell.

Osteoarthritis—Also known as degenerative arthritis, osteoarthritis is caused by the inflammation, breakdown, and eventual loss of cartilage in the joints.

Ovine—Relating to, affecting, resembling, or derived from a sheep.

Ovum—A mature egg cell released during ovulation from an ovary.

Parkinson's disease—A chronic progressive nervous disease chiefly of later in life that is linked to decreased dopamine production in the substantia nigra and is marked by tremor and weakness of resting muscles and by a shuffling gait.

Parthenogenesis—Human conception without fertilization by a man.

Parthenote—Cell resulting from parthenogenesis.

Peptides—Any of various natural or synthetic compounds containing two or more amino acids linked by the carboxyl group of one amino acid to the amino group of another.

Pluripotent—The ability to develop into all three embryonic tissue layers which in turn form all the cells of every body organ. Used to describe stem cells that can form any and all cells and tissues in the body.

Polypeptides—Compounds consisting of two or more amino acids.

Porcine—Relating to, affecting, resembling, or derived from a pig.

Preimplantation genetic diagnosis (PGD)—A technique used during *in-vitro* fertilization (IVF) to test embryos for genetic disorders prior to their transfer to the uterus. PGD makes it possible for individuals with serious inherited disorders to decrease the risk of having a child who is affected by the disorder.

Progenitor cell—In development, a parent cell that gives rise to a distinct cell lineage by a series of cell divisions.

Proliferation—The reproduction or multiplication of similar forms, especially of cells and morbid cysts.

Protein—A large molecule composed of one or more chains of amino acids in a specific order. The order is determined by the base sequence of nucleotides in the gene that codes for the protein. Proteins are required for the structure, function, and regulation of the body's cells, tissues, and organs. Each protein has unique functions.

Proteomics—The study of the proteome, the complete set of proteins produced by a species, using the technologies of large-scale protein separation and identification. The term proteomics was coined in 1994 by Marc Wilkins who defined it as “the study of proteins, how they're modified, when and where they're expressed, how they're involved in metabolic pathways, and how they interact with one another.”

Regenerative medicine—An emerging field that approaches the repair or replacement of tissues and organs by incorporating the use of cells, genes, or other biological building blocks along with bioengineered materials and technologies.

Retina—The retina is the nerve layer that lines the back of the eye, senses light, and creates impulses that travel through the optic nerve to the brain. There is a small area, called the macula, in the retina that contains special light-sensitive cells. The macula allows people to see fine details clearly.

Retinal pigment epithelium (RPE)—Pigmented cell layer that lies between the retinal visual cells and the choroid, which is the eye's major vascular system.

Sickle cell anemia—A chronic, usually fatal anemia marked by sickle-shaped red blood cells, occurring almost exclusively in Blacks from Africa or of African descent, and characterized by episodic pain in the joints, fever, leg ulcers, and jaundice. The disease occurs in individuals who are homozygous for a mutant hemoglobin gene.

Somatic cell nuclear transfer (SCNT)—The transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

Somatic cells—Any cell in the body other than an egg or sperm.

Subretinal—Between the retinal pigment epithelium and the choroid.

Telomerase—An enzyme composed of a catalytic protein component and an RNA template which synthesizes DNA at the ends of chromosomes and confers replicative immortality to cells.

Telomere—The end of a chromosome. Telomeres contain repeated DNA sequences and are associated with the replication and stability of the chromosome.

Totipotent—Cells that have the ability to develop into any of the many different cell types which make up multicellular organisms. Embryos are composed of large numbers of totipotent cells which decline in number as development proceeds and cell specialization begins to occur.

Type 2 diabetes—Also referred to as adult-onset diabetes. A common form of diabetes mellitus that develops especially in adults and most often in obese individuals and that is characterized by hyperglycemia resulting from impaired insulin utilization coupled with the body's inability to compensate with increased insulin production.

Xenotransplantation—Transplanting a foreign tissue into another species. For example, pig organs have been used in transplantation studies to replace certain diseased human organs.

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Crystal Research

a s s o c i a t e s

Jeffrey J. Kraws and Karen B. Goldfarb

Phone: (609) 306-2274

Fax: (609) 395-9339

Email: eio@crystalra.com

Web: www.crystalra.com

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