

## **Patents and Proprietary Rights**

The Company believes that its patent portfolio gives it the dominant intellectual property position in the stem-cell field. StemCells vigorously seeks out intellectual property that it believes might be useful in connection with its products, and has an aggressive program of protecting its intellectual property. StemCells believes that its know-how also will provide a significant competitive advantage, and StemCells intends to continue to develop and protect its proprietary tools, methods, and know-how. StemCells also may acquire licenses to important externally developed technologies.

StemCells has exclusive or non-exclusive rights to a portfolio of patents and patent applications related to various stem and progenitor cells and methods of deriving and using them. These patents and patent applications relate to compositions of matter, methods of obtaining such cells, and methods for preparing, transplanting and utilizing such cells. Currently, the Company's U.S. patent portfolio in the stem cell therapy area includes thirty-nine issued U.S. patents. In addition, StemCells has foreign counterparts to many of the U.S. applications and patents, twenty-five of which have been issued. Approximately one hundred and five additional patent applications are pending worldwide.

In December 1998, the US Patent and Trademark Office granted Patent No. 5,851,832, covering the Company's methods for the human CNS cell cultures containing central nervous system stem cells, for compositions of human CNS cells expanded by these methods, and for use of these cultures in human transplantation. These human CNS stem and progenitor cells expanded in culture may be useful for repairing or replacing damaged central nervous system tissue, including the brain and the spinal cord. U.S. Patent No. 5,968,829, entitled "Human CNS Neural Stem Cells," which covers the Company's composition of matter for human CNS stem cells, was granted in 1999, and U.S. Patent No. 6,103,530, covering the media for culturing human CNS stem cells, was granted in 2000.

In 2002, the U.S. Patent Office issued a key strategic patent to the Company: U.S. Patent Number 6,468,794, entitled "Enriched central nervous system stem cell and progenitor cell populations, and methods for identifying, isolating and enriching for such populations." The patent issued on October 22, 2002 and covers the identification and purification of the human CNS stem cell. In 2001, StemCells was granted U.S. Patent No. 6,238,922 ("Use of collagenase in the preparation of neural stem cell cultures") which described methods to advance the *in vivo* culture and passage of human CNS stem cells that result in a 100-fold increase in CNS stem and progenitor cell production after 6 passages. The Company believes the methodologies of these two patents together augmented StemCells' leadership position in the stem cell field by providing a reproducible proprietary method for obtaining and expanding stem cells for therapeutic uses.

Another significant patent in the neural field, of which StemCells is the exclusive licensee, was issued in 2002. StemCells believes it may prove even more important: U.S. Patent Number 6,497,872, entitled "Neural transplantation using proliferated multipotent neural stem cells and their progeny," covers transplanting any neural stem cells or their differentiated progeny, whether the cells have been cultured in suspension or as adherent cells, for the treatment of any disease. The patent gives the Company the right to exclude others from practicing the claimed invention.

These patents, together with U.S. Patent Number 6,294,346 ("Use of multipotent neural stem cells and their progeny for the screening of drugs and other biological agents"), which issued September 25, 2001, have strengthened the Company's already extensive patent portfolio. That portfolio, StemCells believes, gives the Company the dominant intellectual property position in the field: It covers methods for identification, isolation, expansion, and transplantation of neural stem cells as well as drug discovery and testing.

The following table lists the Company's issued and allowed U.S. and foreign patents:

## U.S. PATENTS

U.S. Patent Number	Subject
<b>Owned by StemCells</b>	
5,968,829	Human CNS neural stem cells
6,103,530	Human CNS neural stem cells — culture media
6,238,922	Use of collagenase in the preparation of neural stem cell cultures
6,468,794	Enriched neural stem cell populations, and methods for identifying, isolating and enriching for neural stem cells
6,498,018	Human CNS neural stem cells
<b>Licensed from NeuroSpheres</b>	
5,750,376	<i>In vitro</i> genetic modification
5,851,832	<i>In vitro</i> proliferation
5,980,885	Methods for inducing <i>in vivo</i> proliferation of precursor cells
5,981,165	<i>In vitro</i> production of dopaminergic cells from mammalian central nervous system multipotent stem cell compositions
6,071,889	Methods for <i>in vivo</i> transfer of a nucleic acid sequence to proliferating neural cells)
6,093,531	Generation of hematopoietic cells from multipotent neural stem cells
6,165,783	Methods of inducing differentiation of multipotent neural stem cells
6,294,346	Methods for screening biological agents
6,368,854	Hypoxia-mediated neurogenesis
6,399,369	cDNA libraries derived from populations of non-primary neural cells
6,497,872	Neural transplantation using proliferated multipotent neural stem cells and their progeny
6,638,501	Use of multipotent neural stem cell progeny to augment non-neural tissues
<b>Licensed from University of California, San Diego</b>	
5,766,948	Method of production of neuroblasts
6,013,521	Method of production of neuroblasts
6,020,197	Method of production of neuroblasts
6,045,807	Method of production of neuroblasts
6,265,175	Method of production of neuroblasts
<b>Licensed from the California Institute of Technology</b>	
5,589,376	Mammalian neural crest stem cells
5,629,159	Immortalization and disimmortalization of cells
5,654,183	Genetically engineered mammalian neural crest stem cells
5,672,499	Methods for immortalizing multipotent neural crest stem cells
5,693,482	<i>In vitro</i> neural crest stem cell assay
5,824,489	Methods for isolating mammalian multipotent neural crest stem cells
5,849,553	Immortalizing and disimmortalizing multipotent neural crest stem cells
5,928,947	Mammalian multipotent neural crest stem cells
5,935,811	Neuron restrictive silencer factor proteins

6,001,654	Methods for differentiating neural stem cells to neurons or smooth muscle cells (TGFB)
6,033,906	Differentiating mammalian neural stem cells to glial cells using neuregulins
6,270,990	Neuron restrictive silencer factor proteins
6,555,337	Neurogenin
6,566,496	Neurogenin

**Licensed from the Scripps Research Institute**

6,242,666	An animal model for identifying a common stem/ progenitor to liver cells and pancreatic cells
6,541,251	Pancreatic progenitor I gene and its uses

**Licensed from Oregon Health Sciences University**

6,132,708	Liver regeneration using pancreas cells
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**FOREIGN PATENTS**

<b>Issued and Allowed Foreign Cases</b>	<b>Number of Countries Covered by Patent</b>	<b>Subject</b>
Australian patent # 758270	1	Cultures of human CNS neural stem cells
European patent # 594669 Australian patent # 700690 Mexican patent # 206298	3	Immortalization and disimmortalization of cells
Australian patent # 713577 New Zealand patent # 304570	2	Neuron restrictive silencer factor proteins
Australian patent # 678988 New Zealand patent # 256154	2	Mammalian neural crest stem cells
Granted in Australia	1	Use of collagenase in the preparation of neural stem cell cultures
European patent # 0594669, validated in 16 countries Australian patent # 665012 Canadian patent # 2113118	18	Novel growth factor-responsive progenitor cells which can be proliferated in vitro
European patent # 664832, validated in 16 countries Australian patent # 683023 Canadian patent # 2147162	18	Remyelination using mammalian central nervous system multipotent stem cell compositions
European patent # 0669973, validated in 16 countries Australian patent # 703729 Canadian patent # 2,148,138	18	Biological factors useful in differentiating mammalian central nervous system multipotent stem cell compositions
Australian patent # 687785 Canadian patent # 2,155,024 Notice of intent to grant received for Europe	3	Genetically engineered mammalian central nervous system multipotent stem cell compositions
Australian patent # 715246	1	In vitro induction of dopaminergic cells from mammalian central nervous system multipotent stem cell compositions
European patent # 0728194, validated in 12 countries Australian patent # 697894	12	In situ modification and manipulation of stem cells of the CNS
European patent # 0783693, validated in 17 countries	17	In vitro models of CNS functions and dysfunctions

The Company also relies upon trade-secret protection for confidential and proprietary information and takes active measures to control access to that information.

The Company's policy is to require employees, consultants and significant scientific collaborators and sponsored researchers to execute confidentiality agreements upon the commencement of an employment or consulting relationship with the Company. These agreements generally provide that all confidential information developed or made known to the individual by the Company during the course of the individual's relationship with the Company is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees and consultants, the agreements generally provide that all inventions conceived by the individual in the course of rendering services to the Company shall be the Company's exclusive property.

The Company has obtained rights from universities and research institutions to technologies, processes and compounds that the Company believes may be important to the development of its products. These agreements typically require the Company to pay license fees, meet certain diligence obligations and, upon commercial introduction of certain products, pay royalties. These include exclusive license agreements with NeuroSpheres, The Scripps Institute, the California Institute of Technology and the Oregon Health Sciences University, to certain patents and know-how regarding present and certain future developments in CNS, liver and pancreas stem cells. The Company's licenses may be canceled or converted to non-exclusive licenses if the Company fails to use the relevant technology or if the Company breaches its agreements. Loss of such licenses could expose the Company to the risks of third party patents and/or technology. There can be no assurance that any of these licenses will provide effective protection against the Company's competitors

A number of pharmaceutical, biotechnology and other companies, universities and research institutions have filed patent applications or have been issued patents relating to cell therapy, stem cells and other technologies potentially relevant to or required by the Company's expected products. The Company cannot predict which, if any, of such applications will issue as patents or the claims that might be allowed. The Company is aware that a number of companies have filed applications relating to stem cells. The Company is also aware of a number of patent applications and patents claiming use of genetically modified cells to treat disease, disorder or injury. The Company is aware of two patents issued to a competitor claiming certain methods for treating defective, diseased or damaged cells in the mammalian CNS by grafting genetically modified donor cells from the same mammalian species.