Geron gets green light for human trial of ES cell–derived product

After an eight-month delay, on 23 January, the US Food and Drug Administration (FDA) approved the first human trials of embryonic stem (hES) cells, a surprise decision that came on the eve of President Barack Obama's expected policy change concerning hES cell research.

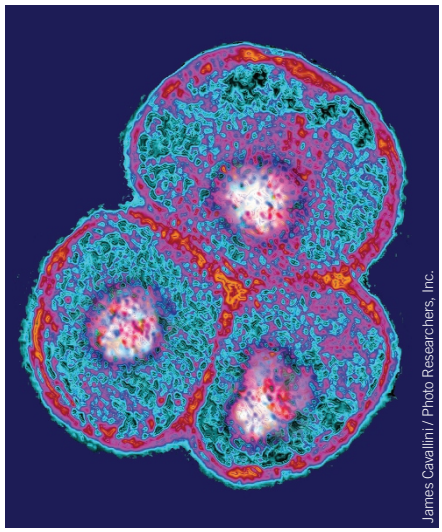
This summer, Geron Corporation of Menlo Park, California, will begin treating ten patients who have suffered a complete thoracic-level spinal cord injury in a phase 1 multicenter trial. The pioneering therapy is Geron's 'GRNOPC1 product', which contains hES cell–derived oligodendrocyte progenitor cells that have demonstrated remyelinating and nerve growth–stimulating properties.

For a company that held its ground during the Bush administration's assault on hES cell research, the FDA's clearance is part triumph, part vindication for sticking with the Sisyphean task of preparing a gargantuan 22,000-plus page Investigational New Drug (IND) application for their product. "There was plenty of crying going on here when we received notification that the FDA had cleared our IND," says Thomas Okarma, Geron's president and CEO.

Although they may not have shed tears of joy, many players in the budding regenerative medicine sector sounded a note of relief, and even optimism. "I've been talking to my colleagues in this field, and the overall feeling is that this is an important milestone because it means that FDA will approve clinical trials using human embryonic stem cells, and that, in fact, there is [regulatory] support for developing therapies based on embryonic stem cells," says Michael West, CEO of BioTime and Embryome Sciences, both in Emeryville, California, who cofounded Geron in 1990.

Other CEOs of stem cell firms are also upbeat: "Clearly, this opens the door not only for Geron, but other companies that develop strong IND packages for stem cell–based therapeutics. And given the compelling evidence that there's a reasonable chance for clinical success, this is a very positive development for the regenerative medicine field," says Richard Garr, president and CEO of Rockville, Maryland–based Neuralstem, which in December filed an IND to use human neural stem cells for treating amyotrophic lateral sclerosis. On the same day, StemCells, Inc. received approval to begin clinical trials of a purified human neural stem cell to treat Pelizaeus-Merzbacher disease—a fatal brain disorder that affects children.

But West, who spurred Geron's support for the research of human stem cell pioneers James Thomson and John Gearhart before leaving the company in 1998 and then ran Worcester, Massachusetts–based stem cell company Advanced Cell Technology (ACT) until 2007, says there's also a sense of unease with Geron's planned trial. "While we all want [the clinical trials] to work, there's a concern among many of us that some of these patients will develop ectopic growths, and that would be a disaster."



Embryonic stem cells. Companies are rapidly gearing up to follow in Geron's footsteps, as the firm receives the first approval to carry out embryonic stem cell work in humans.

Ectopic growths, also known as teratomas, are encapsulated, usually benign tumors that may grow from residual hES cells. They can occur naturally, but the fear, based on some animal studies, is that some proportion of the cells derived from hES cells injected into the body could stray from their intended developmental pathway. Last month, a group of Israeli researchers reported that a boy with ataxia telangiectasia who had received several fetal neural stem cell transplants developed teratomas in his brain and spinal cord four years after treatment (*PLoS Med.* **6**, e1000029). "Concerns about tumorigenicity are bang on," says Melissa Carpenter, a San Diego–based independent consultant on stem cell therapeutics. "Yes, Geron and others have done extensive testing in rodents that show that teratomas don't form from their preparations, but a rat's lifespan is short. What we really don't know is how these cells will behave in a human that might live 10–50 years after receiving treatment."

Although acknowledging that teratoma formation might be a concern, Geron's Okarma

IN brief

Alnylam dealt blow

The European Patent Office (EPO) has revoked a patent covering RNA interference (RNAi) technology from Alnylam Pharmaceuticals. The '945 patent (EP 1214945), which belongs to the Kreutzer-Limmer patent family, protects the use of small interfering RNAs 15–49 nucleotides long. Alnylam's claim was disputed by London-based Silence Therapeutics, Abbott Park, Illinois–based Abbott and San Francisco–based Sirna, owned by Merck. The ruling—made in part because the patent was deemed too broad—is not final and will be appealed. "In an area like this, companies don't expect to get their patents through unobjected to," says patent lawyer Simon Cohen, of Taylor Wessing, a European law firm. "They start off with broad claims and they realize they have to narrow down their scope." Cambridge, Massachusetts–based Alnylam had another of its Kreutzer-Limmer patents revoked by the EPO last December. A spokesman for Silence Therapeutics says the whole Kreutzer–Limmer patent series may eventually fall, creating space for other companies who want to work with RNAi. This is "very much the start of litigation and opposition, rather than the last phase of it," Cohen stresses. In the US, Alnylam received recent FDA approval for phase 1 trials of an RNAi-based treatment for liver cancer. *Asher Mullard*

C-Path sets diagnostics standard

A newly launched diagnostics evaluation service for companies could help standardize tests and ease their transition to market. The United States Diagnostic Standards (USDS), a nonprofit organization set up by the Critical Path Institute (C-Path), will provide independent test evaluations, effectively functioning as a voluntary "Underwriters Labs" for diagnostics companies, says Jeffrey Cossman, chief scientific officer at C-Path, of Rockville, Maryland. Analytic evaluations performed by the new entity will take place at carefully selected neutral sites. Under USDS policy, the clinical samples (e.g., blood, tumor tissue) used as standards in the evaluation of diagnostic assays must be approved by an independent, outside panel of experts. In some instances, well-established clinical samples may serve as standards so that assays from different suppliers can be compared. Although the group has no regulatory authority, diagnostic test manufacturers can use evaluation results to support an application for FDA approval. Alternatively, as one of its many services, the USDS will certify a Laboratory Developed Test (LDT) and ensure its performance. As Cossman explains, "The information [USDS provides] would be useful for [insurance] payers, clinical pathology laboratories, providers, as well as for regulators such as FDA, [and] might help with reimbursement decisions, as well as approval or assurance that an LDT (not evaluated by FDA) performs as labeled." *Jim Roberts*