Testimony of John K. Fraser Ph.D.; Principal Scientist, Cytori Therapeutics

Good morning, my name is John Fraser, and I am Principal Scientist at Cytori Therapeutics Inc, a publically-traded stem cell company in San Diego, California. Cytori is at the forefront of brining adult stem cells to patients, as we are currently selling a stem cell-based product in Europe, are conducting three separate clinical trials, and have a technology, which has been used in over 200 patient procedures.

From my graduate studies in New Zealand, through to a postdoctoral and then faculty appointment at UCLA, and now at Cytori, my entire research career has been centered on adult stem cells.

The topic of today's meeting is consideration of stem cells as the future of medicine. Indeed, stem cells will be an important part of the clinical armamentarium going forward. But this is nothing new; hematopoietic stem cells have been used in medicine for at least 50 years. In pioneering work started in the late 1950's E. Donnall Thomas performed bone marrow transplant studies that ultimately led to the award of the Nobel Prize for Medicine in 1990 (1-3). Many consider 1961 as the birth date of the stem cell field as that was the year that James E Till and Ernest A McCulloch published research (4) that led to the description of the first stem cell (5), the hematopoietic stem cell; which is still widely considered to be the model for all adult stem cells (6).

Hematopoietic stem cells make bone marrow transplantation possible. This is because they have the ability to regenerate the entire blood system of the recipient for the rest of that person's life. Simply put, hematopoietic stem cells are the regenerative engine of the blood system.

In my opinion, this is a key point of distinction between adult stem cells and embryonic stem cells. Embryonic stem cells are capable of immense proliferation and essentially universal

plasticity. This is because they are, first and foremost, developmental cells; they are derived from a cell mass from which the entire organism develops.

By contrast, adult stem cells are, first and foremost, regenerative cells, responsible for maintaining and healing organs and tissues in the face of daily wear and tear, injury, and disease. They are, by their nature, repair cells; they activate in response to a need and shut off once healing is completed. One way to look at this is to view embryonic stem cells as responsible for generating all the tissues of an organism, while adult stem cells are responsible for maintaining and healing them.

The natural role of adult stem cells in repair and regeneration makes them ideally suited for clinical use. This has been proven in tens of thousands of bone marrow transplant patients in the last 40 years. This paradigm is now increasingly being repeated as other adult cell types associated with repair and regeneration are being applied in different diseases.

For example, Cytori has initiated several clinical studies using cells obtained from the patient's own fat tissue, which is recognized as one of the richest and most accessible sources for adult stem cells. The goal of these studies is to bring forth new treatments for the millions of patients suffering from heart disease as well as to help reconstruction breast defects in women who have undergone partial mastectomy. We also intend to start studies in intervertebral disc repair and potentially several other clinical applications, which look promising.

Other researchers have published case reports and clinical studies using fat tissue-derived stem cells in treating certain types of wound (7-9), in treating complications associated with bone marrow transplantation (10-14), and in bone defects (15). Published preclinical studies have indicated potential in treating renal damage associated with chemotherapy (16), preserving dopaminergic neurons in a Parkinson's disease model (17), treating liver damage (18), ischemic

(19) and hemorrhagic (20) stroke, and in tissues as disparate as the cornea (21), the lung (22,23), and the vocal fold (24).

Published clinical studies with other types of adult stem cell have shown improvement in cardiac function (25-27), in an inherited brittle bone disease (28-30), in liver disease (31-33), and peripheral vascular disease (34) to name but a few.

However, there are still many unanswered questions and clearly additional science is needed. In certain settings, the mechanisms through which adult stem cells provide benefit are not well understood. It is also not yet clear which adult stem cell sources provide greatest clinical efficacy in which diseases. These are important questions that companies such as Cytori have neither the resources nor oftentimes the incentive to address.

For example, certain potentially beneficial cell populations fall outside of patent protections limiting the incentive of companies to invest resources in proving a technology that may then be applied without their participation. Without federal support much of this promise could be left to wither on the vine.

Cytori believes that ultimately science and the marketplace will determine which technologies will succeed. We have looked at the field of regenerative medicine, performed our own basic science, pre-clinical and now clinical research and we are very optimistic regarding the ability of our approach to harness the natural role of adult stem and regenerative cells to provide clinically and cost-effective treatments for a range of human diseases in the near future. We urge your continuing support of adult stem cell research.

Thank you.

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