

iPierian Gains Stem Cell Research Leaders for Scientific Advisory Board

Cellular reprogramming and differentiation of disease-relevant induced pluripotent stem (iPS) cells represent the fastest and most promising means of transforming drug discovery and ushering in the new era of stem cell therapeutics, say leading experts from academia and the biotechnology and pharmaceutical industries who are joining forces to commercialize iPS-based technologies.

“This is the most exciting revolution in biology that I have ever witnessed,” says Dr. George Q. Daley, co-chair of the scientific advisory board of iPierian Inc.; director of the Stem Cell Transplantation Program at Children’s Hospital Boston, a Howard Hughes Medical Institute Investigator, immediate past president of the International Society for Stem Cell Research, and member of the Executive Committee of the Harvard Stem Cell Institute (HSCI). “iPS technologies that were created in the academic setting have enormous medical potential that should be applied in a more industrial context. We’re interested in moving beyond what we can accomplish as academics to accelerate the potential of iPS cells for drug discovery and to translate this very promising research into new therapies as quickly as possible.” iPierian is the first company to focus exclusively on developing disease models and human cell-based assays from iPS cells and to use iPS technology to generate its own therapeutic pipeline, Daley says. iPierian’s iPS cell lines, which are derived from patients with known diseases, represent a completely new way of approaching drug discovery and development.

Joining Dr. Daley on iPierian’s scientific advisory board are HSCI colleagues Dr. Lee Rubin, director of Translational Medicine and Principal Faculty Member at HSCI and Dr. Douglas A. Melton, HSCI co-director, Howard Hughes Medical Institute Investigator, chairperson of the Harvard University Department of Stem Cell and Regenerative Biology, a member of the National Academy of Sciences, and founding member of the International Society for Stem Cell Research.

The three scientists have been at the forefront of stem cell research since much of the last decade, following the first isolation of human embryonic stem cells by Dr. Jamie Thomson at the University of Wisconsin in 1998. More recently, these scientists have turned their attention to iPS cells, building upon the report of Dr. Shinya Yamanaka in 2006 of reprogramming of adult mouse cells into an embryonic state. iPS cells, which avoid ethical concerns over embryonic stem cells, offer significant technical advantages for exploring disease pathways and screening new drug candidates. Along with Drs. Thomson, Yamanaka, and importantly Kazuhiro Sakurada of Bayer Schering Pharma, AG , Dr. Daley’s group was one of the first to generate human iPS cells, and garnered headlines in August 2008 when he and his colleagues reported in the journal *Cell* the creation of the first large repository of 20 disease-specific human iPS cell lines from patients that carry the genetic components for 10 different diseases, including Parkinson’s Disease, diabetes, Huntington’s Disease, Down Syndrome, Lesch-Nyhan syndrome, Gaucher’s disease, and multiple forms of Muscular Dystrophy, immune deficiency, and bone marrow failure.

Dr. Daley says the goal of the team of scientific advisors to iPierian is to translate their academic achievements in stem cell research into more disease-relevant technologies for conducting drug discovery and ultimately developing new regenerative therapies for a broad range of diseases.

“It has been the goal of biomedical research for many years to make more faithful models of disease. Until now, the only patient cells we could grow in culture were transformed and didn’t

accurately model human disease,” Dr. Daley says. “What is exciting here is we can take a cell from virtually any patient with any disease and after reprogramming we can get it to grow in culture. Because these cells have the special properties of pluripotency, essentially any disease can be modeled in cellular terms. With the ability to study disease-relevant cells in the Petri dish, we can identify drugs that repair those cells or reverse disease behavior, and because we’ve started with human patients, we have a much greater confidence earlier in the course of drug development that a drug is going to work.”

John P. Walker, chief executive officer of iPierian, says the Harvard group possesses the perfect balance of expertise in the major therapeutic areas of neurodegenerative disorders, metabolic disease, cardiovascular disease and hematology/oncology.

Dr. Rubin, who has both academic and industry experience, saw the potential of stem cells to transform drug discovery early on. He has spent the past decade devoted to identifying therapeutics for disorders such as spinal muscular atrophy, amyotrophic lateral sclerosis, Huntington’s disease and multiple sclerosis using new kinds of stem cell-based screens. Earlier in his career, Dr. Rubin initiated the project at Athena Neurosciences (now Elan) that led to the discovery and development of Tysabri® for the treatment of multiple sclerosis. And while at Curis, Inc., he discovered a hedgehog pathway antagonist that is currently in multiple phase 2 studies being carried out by Genentech.

Dr. Rubin says the recent discoveries in cell programming and differentiation made by Yamanaka, the Harvard group and iPierian’s internal scientists have come together at a perfect time to launch a company that has a very high probability of revolutionizing drug discovery. He says the Harvard group had been exploring ways to translate the work they have done in the academic setting into more scientifically accurate models to discover drugs and faster ways to get new stem-cell therapies to patients. The expertise that the scientific advisory board will share regularly with iPierian should help ensure that the company becomes the world leader in the use of iPS cell-based technologies.

“Everyone knows that the current system of drug discovery is flawed and everyone has been struggling for years to change it. The technologies and expertise that are being joined under iPierian could be the fundamental game changer. The promise of this is really stupendous,” says Dr. Rubin. “As advisors to iPierian, our role will be to offer our experience to help the company make the best strategic decisions about the therapeutic areas we will work on and about the partners we choose to move forward with during this historic scientific revolution.”

iPierian is the melding of iZumi Bio with Pierian Inc., which was incorporated in 2008 by Drs. Daley, Rubin and Melton. “We were approached by iZumi and over time our ideas evolved together,” says Daley. “They have bricks and mortar and we have lots of common interests. It made sense to bring our skills together.”

The genesis for iZumi began in 2005 with Dr. Deepak Srivastava, co-chair of iPierian’s scientific advisory board, director of the Gladstone Institute of Cardiovascular Disease, professor of the departments of pediatrics and biochemistry and biophysics and Wilma and Adeline Pirag distinguished professor in pediatric developmental cardiology at the University of California, San Francisco. Dr. Srivastava attracted the interest of the investment firm Kleiner Perkins Caufield and Byers in launching a commercial stem cell venture, but they were waiting for a major development to move forward.

A year later Dr. Srivastava was attending the scientific conference where Dr. Yamanaka of Kyoto University announced that he had created iPS cells in mice. He seized the moment and convinced Yamanaka to start a laboratory at the Gladstone Institute, where Dr. Srivastava focuses on iPS cell research in cardiovascular disease, including common aortic valve calcifications that result in the need for valve replacement. Dr. Yamanaka had trained at Gladstone in the mid 1990's and was eager to establish a scientific effort at the institute, in addition to his laboratory in Kyoto, and currently is the L.K. Whittier Foundation Investigator in the Gladstone Institute of Cardiovascular Disease. "I've always thought that we would have the best chance at success if we could bring together the best minds in the field and create a single company to move the iPS technology forward," says Dr. Srivastava. "In all of science there are a couple of times, maybe once in a decade, when something major happens and this is that one."

Dr. Srivastava says iPierian could generate new small molecule drugs or biological drugs from the iPS technology platform within five years and introduce individualized regenerative therapy based on a patient's own iPS cells within 10 years. "There are a lot of discoveries to be done to make this happen and you need the best minds involved," Dr. Srivastava says.

In addition to the scientists from Harvard and the Gladstone Institute, Dr. Corey Goodman will serve as iPierian's chairman of the Board of Directors as well as a member of the Scientific Advisory Board. Dr. Goodman was a professor at Stanford University and the University of California, Berkeley for more than two decades, and is currently an adjunct professor at the University of California, San Francisco in the Departments of Anatomy and Biochemistry. While on the faculty at Berkeley, he was an investigator with the Howard Hughes Medical Institute, Evan Rauch Professor of Neuroscience, co-founder of the Wills Neuroscience Institute, and head of the division of Neurobiology. Dr. Goodman also is a member of the National Academy of Sciences and was chairman of the National Research Council's board on Life Sciences, which issued in 2002 the landmark national report "Stem Cells and the Future of Regenerative Medicine."

Dr. Goodman was appointed to the iZumi Board of directors in June after heading Pfizer Inc.'s Biotherapeutics and Bioinnovation Center and building the pharmaceutical industry's first stem cell and regenerative medicine group. In 2000, Goodman gave up his position as a Howard Hughes Medical Institute Investigator to launch the biotech company Renovis. Goodman says he has been scientific colleagues with Rubin since 1978 and with Melton since the early 1980s, and that Walker served as his chairman of the board at Renovis.

"I was delighted the way the groups came together to create iPierian. For me it really is a potential dream team," Goodman says. "We have the right people at the right time with the right technology. Together we have an enormous opportunity to change the entire landscape of drug discovery at an important juncture in history. I think this company will become the preeminent stem cell biotechnology company in the world. This is a dream opportunity."

-Written by Tim Friend of WeissComm Partners, Former USA Today Science Writer

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