



**Living Cell Technologies Ltd**

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**COMPANY ANNOUNCEMENT**

**LCT to start clinical trial of Type 1 diabetes treatment**

*30 January 2007, Melbourne, Australia and Auckland, New Zealand:*

Living Cell Technologies Ltd (ASX:LCT) today announced its DiabeCell<sup>®</sup> Type 1 diabetes treatment has been approved for a Phase I/IIA clinical trial in Russia designed according to FDA guidelines and monitored by a Boston-based Contract Research Organisation.

DiabeCell<sup>®</sup> is a porcine pancreatic cell product for the treatment of insulin-dependent diabetes. The natural neo-natal pig islet cells are encased in capsules that allow insulin to be released but prevents the patient's immune system from attacking the cells. The islets are simply injected into the body and produce insulin as needed in response to the levels of glucose in the blood. This mimics the normal insulin release that occurs in healthy non-diabetic people and thus helps regulate blood glucose levels in those suffering from Type 1 diabetes.

The trial may enable an expedited route to commercialisation within the region. Initial response to treatment will be evident within six months. The trial will use cells from fully-screened and biocertified pigs, bred according to US FDA (Food and Drug Administration) guidelines.

"Along with international biopharmaceutical firms, LCT is taking advantage of the growing interest and availability of funds for biotechnology in Russia," said LCT CEO, Dr Paul Tan. "The pharmaceutical industry has noted Russia's centralised medical infrastructure and efficient recruitment of patients into clinical trials. The rapid regulatory process in Russia and the accepted use of animal cells in treating human disease may shorten the time to market."

"The approval of the DiabeCell<sup>®</sup> human clinical trial is a significant milestone for this new treatment option for type 1 diabetes," said Dr John Court<sup>1</sup>, expert on adolescent diabetes and scientific advisor to LCT. "This is the only human clinical trial of this kind approved anywhere in the world and recognises LCT's thorough pre-clinical testing of the product in animal models showing no adverse safety effects and a significant reduction in insulin requirements."

"DiabeCell<sup>®</sup> offers considerable advantages over other available treatments as there is no need for immuno-suppressive drugs and the supply of cells from LCT's natural biocertified pig herds are readily available, unlike human organ donors. Type 1 diabetes urgently needs a new treatment that is better than current regimens of insulin treatment," Dr Court said.

"As a Company at the forefront of the xeno-cell therapy industry – and clearly ahead of the competition, LCT's intention is to conduct more than one Phase I/IIA Clinical Trial," said Dr Tan.

"It is still LCT's plan to test a different dose and protocol for administering DiabeCell<sup>®</sup> in a separate New Zealand trial. The different study designs would expedite the selection of a safe and optimal clinical protocol of using DiabeCell<sup>®</sup> in the clinic," Dr Tan said.

In Russia, DiabeCell<sup>®</sup> would be trialled in six Type 1 (insulin-dependent) diabetics in two stages. It is anticipated that the trial would start in the second quarter of 2007, with potential patients already identified. There are currently nearly 500,000 people in Russia with Type 1 diabetes and this figure is rising rapidly. As a guide, rabbit islet cell transplants are available in Russia for up to AUD\$30,000 per course of treatment.

The 12-month phase I/IIA trial will be led by Professor Skaletsky of the ANO Institute of Biomedical Research in Moscow. Prof Skaletsky and the Institute have extensive experience in organ transplantation and xenotransplantation, having performed over 1,500 animal cell transplants in patients.

Boston-based GenyResearch Group will act as the project manager to ensure all elements of the trial adhere to international and FDA standards. They will oversee the protocols and be responsible for all data analysis and management, and provide a trial report that may be submitted along with data from international studies for regulatory approval in any jurisdiction.

GenyResearch has eight years of experience in providing clinical research services in Russia (including approximately 40 clinical trials in various therapeutic areas for international pharmaceutical firms such as Sanofi-Aventis and Hoffmann La Roche) and is fully licensed by the Ministry of Health of the Russian Federation.

Under the agreement, LCT will supply the cells and retain all IP and commercial rights to the product. The Russian partners will cover all costs of conducting the trial and the services of the US-based contract research organisation. Following a successful clinical trial, LCT and their Russian partners - the ANO Institute of Biomedical Research are to extend their agreement for commercialising DiabeCell® in Russia.

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**About Living Cell Technologies:** [www.lctglobal.com](http://www.lctglobal.com)

*Living Cell Technologies Ltd (ASX: LCT) develops live cell therapy products to treat life threatening human diseases. The ASX listed, vertically integrated company focuses on developing treatments where healthy living cells are injected into patients to replace or repair damaged tissue, without requiring the use of toxic drugs to prevent rejection. The company's product portfolio focuses on treatments for people with insulin-dependent diabetes and neurological disorders. The company owns a specialised biocertified pig herd for a safe, reliable source of cells for treatment.*

**APPENDIX - Further Information:**

**Clinical Trial Protocol:**

- LCT's proposal for the human clinical trial of DiabeCell® in Russia will include six Type 1 (insulin-dependent) diabetics in two stages.
- There will be 6 adult patients treated with females over 35 years old and males over 25 years of age.
- The candidates must have had type 1 diabetes for at least 10 years with no other complications and provide full consent for follow-up monitoring.
- The patients will receive an initial transplant (a simple injection of encapsulated islets into the peritoneal cavity of the patient) followed by a second transplant six months later.
- The procedure is minimally invasive and will be administered into the abdomen through a laparoscope.

**Trial Name:** A Phase I/IIA, Open-Label Investigation of the Safety and Effectiveness of **DiabeCell**<sup>®</sup> (Immunoprotected alginate-encapsulated) Porcine Islets for Xenotransplantation in Patients with Type 1 Diabetes. Protocol LCT/DIA-07R

## **Primary Endpoints**

### Primary Safety Endpoints

- Occurrence of hypoglycaemic episodes in the post-transplant period in comparison with those occurring during the 8-week run-in period.
- Occurrence of perioperative reactions (e.g. wound infections, local tissue reactions to the alginate microcapsules at the time of transplantation).
- Occurrence of other adverse events or serious adverse events.
- Abnormal laboratory test results, physical examination findings, or ECG findings.
- Psychological impact (as assessed by the ADDQoL quality-of-life questionnaire).
- Clinical and laboratory evidence of xenogeneic infection in transplant recipients via regular monitoring at predefined time points (ongoing).
- Clinical and laboratory evidence of xenogeneic infection in partners/close contacts of the transplant recipients (ongoing).

### Primary Efficacy Endpoint

- Reduction in HbA<sub>1C</sub> levels over the 12-month post-transplant period compared with baseline (week -1).

## **Secondary Endpoints**

### Secondary efficacy endpoints include:

- Glucose lability assessed using 72-hour continuous glucose monitoring (CGMS<sup>®</sup>, Medtronic Minimed, Northridge, CA) at 3, 6 and 12 months post-transplant in comparison with baseline, reported as standard deviation of glucose values at these times (Paty et al. 2006).
- Reductions in hypoglycemia and nocturnal hypoglycemia, as assessed by a composite hypoglycaemic score (HYPO score) over the 12-month post-transplant period compared with baseline (Ryan et al. 2004). Patients will be asked to record the frequency, severity, and degree of unawareness of the hypoglycaemia on a scoring sheet.
- Reductions in the average daily insulin dose of >20% unaccompanied by objective evidence of deterioration of diabetes control at 6 and 12 months post-transplant compared with baseline, as measured by regular 7-point blood glucose profiles and monthly HbA<sub>1C</sub> levels, in the absence of evidence of major weight loss (>10%) or ketoacidosis.
- Changes in endogenous insulin secretion as determined by the plasma C-peptide response to intravenous glucagon stimulation at 3, 6 and 12 months post-transplant compared with baseline. Pre-transplant this test is expected to confirm a low human C-peptide level; after the xenotransplant, the test should detect porcine C-peptide/insulin.
- Quality-of-life changes, as assessed by the ADDQoL quality-of-life questionnaire (Appendix 2), at 6 and 12 months post-transplant compared with baseline.
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<sup>1</sup>Dr John Court MB,BS,FRACP – Dr Court has extensive experience in diabetes and adolescent medicine, as a consultant and clinician for The Royal Children’s Hospital Melbourne, the University of London, London’s Middlesex Hospital and in private practice.

## **Background Information:**

Scientific papers relating to DiabeCell<sup>®</sup> are available for download on the LCT website at [www.lctglobal.com/diabeCell](http://www.lctglobal.com/diabeCell).