

# Halting Parkinson's with cell therapy

Dr K M Taylor, CEO February 2017 www.lctglobal.com

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#### ASX:LCT | OTCQX: LVCLY | www.lctglobal.com | 5 LCTglobal





# The company

# Strong financial foundation



#### **Key statistics**

	ASX: LCT
Ticker code	OTCQX: LVCLY
Share price 14 February 2017	\$0.11
Share price range last 12 months	\$0.048-0.13
Shares on issue	570,606,391
Market capitalisation	\$63m
Cash position 31 December 2016	\$8.6m
Net operating cash burn 6 months to 31 December 2016	\$2.4m

# Share register at 13 February 2017Top 20<br/>Total number of shareholders56%<br/>2,632Geographic shareholding split<br/>Australia<br/>New Zealand<br/>Japan<br/>Other51%<br/>4%<br/>10%





# Parkinson's disease

# Parkinson's disease



Parkinson's disease (PD) is a progressive neurological condition characterised by a loss of brain cells that produce dopamine (a neurotransmitter that conveys messages between brain cells to ensure effective movement and planning of movement) as well as a range of other types of neurons.

# Parkinson's disease



People with PD experience reduced and slow movement (hypokinesia and bradykinesia), rigidity and tremors
7–10 million people living with PD worldwide
Incidence of PD increases with age, but 19% diagnosed aged 15–64 and withdraw from workforce

# Opportunity for first Parkinson's disease-modifying drug



- Symptomatic treatments available
  - but have a limited duration of efficacy
- No disease modifying treatment or cure currently available
- PD drug sales totalled \$US 2.4B in 2014. All symptomatic treatments
- Levodopa "gold standard" 50 years old





# NTCELL for Parkinson's disease

# Product: NTCELL treatment is implantation of encapsulated choroid plexus cells into the brain





#### **Choroid plexus:**

- Secretes cerebrospinal fluid (CSF)
- Provides neurotrophic factors
- Provides neuroprotective factors
- Removes toxin (drugs, metals, etc.)
- Clears waste products



# NTCELL is encapsulated choroid plexus cells

Designated pathogen-free herd of Auckland Islands pigs

- Surgical removal of the brain from anaesthetised and exsanguinated pathogen-free animals
- Enzyme digestion by collagenase and protease to make choroid plexus (CP) cell-free clusters
- CP cell-free clusters entrapped in calcium-alginate gel, coated in positively charged poly-L-ornithine and then layered with an outer coat of alginate



NTCELL alginate microcapsules containing porcine choroid plexus cells





Nutrients Secreted Proteins

The structure of the alginate microcapsules containing CP cells. The membrane excludes large globular proteins (>80,000 Da) and all cells, but nutrients, oxygen and carbon dioxide can diffuse freely and secreted proteins (<80,000 Da) can diffuse out.



# Advantages of NTCELL for Parkinson's

NTCELL is encapsulated porcine choroid plexus cells

- A "factory" approach for nerve growth: not single drug intervention
- **Supply:** Porcine advantage over human
- Brain: immuno-privileged
- Severe unmet medical need
- Cost to benefit: focus on benefit first disease modifying treatment
- **Plasticity:** NTCELL adapts to disease in vivo. PD first target due to acceptance of DBS procedure, identified site and endpoint
- Advantage over stem cells: No concern of tumorigenicity; A defined cell population rather than unknown mixed cell types; No current stem cell technology to generate choroid plexus cells





# **Clinical development**

# Phase I/IIa trial - NTCELL implantation procedure



#### Protocol

- 4 PD patients previously selected for Deep Brain Electrode implantation
- 40 NTCELL microcapsules (c. 40,000 CP cells) implanted into the putamen on the side contralateral to that of the greatest clinical deficit
- Primary endpoint safety



Sagittal MRI showing the cannula tract

Implanted NTCELL microcapsules are distributed through the putamen at the end of the tract Phase I/IIa trial completed No safety issues



### NTCELL "Improved every rating scale in first 4 patients" Dr Barry Snow, Principal Investigator

• Decrease in UPDRS is clinically and statistically significant



Total Unified Parkinson's Disease Rating Scale (UPDRS) with patients off medication

# Phase I/IIa completed trial NTCELL reversed progression of Parkinson's

- LCT
- NTCELL treatment has stopped the progression of Parkinson's disease as measured by globally accepted and validated neurological rating scales in all four patients
  - The 81 week post-implant data show there is a clinically and statistically significant improvement in the patients' neurological score from their pre-implant baseline in all four patients
- Improvement equivalent to approximately 3 to 5 years of PD remission
- Improvement maintained
- No safety issues

# Phase IIb study

#### **Group 1: Patients 1-6**

4 dosed and 2 placebo, randomly assigned 40 NTCELL microcapsules (± 5%) bilaterally [total of 80 microcapsules], or placebo [sham surgery]

#### Group 2: Patients 7-12

4 dosed and 2 placebo, randomly assigned 80 NTCELL microcapsules (± 5%) bilaterally [total of 160 microcapsules], or placebo [sham surgery]

#### Group 3: Patients 13-18

4 dosed and 2 placebo, randomly assigned 120 NTCELL microcapsules (± 5%) bilaterally [total of 240 microcapsules], or placebo [sham surgery]

- Study will be unblinded upon completion of 26-week follow-up period
- Placebo patients will receive optimal dose of NTCELL

# LCT

# Accelerating the programme

**3 October 2016**Completed implantation in group 1 patients**21 December 2016**Completed implantation of group 2 patients**February 2017**Approval to implant group 3 patients

- Maintain momentum at Auckland Hospital
- Saturday extra neurosurgical clinics targeting 2 patients each session
- 2 stereotaxic units commissioned
- Patients available due to success of Parkinson's NZ patient information meetings
- Five patients implanted in eight days



# Phase IIb study endpoints

- The trial endpoints will answer the 3 questions raised by the Ministry of Health to qualify for provisional (fast track) consent to market:
  - Define efficacy and any placebo contribution
  - Define optimal dose of NTCELL implantation
  - Define initial target Parkinson's disease patient subgroup

# Phase IIb planned study result



# Q4 2017

- NTCELL phase IIb trial result 26 weeks after implant of last patient in Group 3
- Placebo patients will be offered implant with most effective dose of NTCELL
- Follow up open study of all patients in both phase I/IIa and IIb NTCELL clinical studies





# The future is bright



# Progress of competitors to NTCELL

Stem Cells **ISCO/Cyto Therapeutics** initiated a 12 patient trial in Melbourne implanting neural stem cells from a pluripotent pathogenic cell line. Controversial differentiation and production QA and cost remain stem cell issues.

#### Vaccine

**AFFIRIS** has developed a vaccine (PD01A) to create antibodies to alpha syncline. Treatment to date is safe but "responders" antibodies do not last long.

#### Nilotinib

Anticancer drug that inhibits LRRK2 the most common gene defect in the 10% of PD cases that have a genetic link. Controversial, has side effects and placebo responses.

*Human ventral mesencephalic tissue transplants* **TRANSEURO** initiated study with ethical and logistical, QA issues.

*GDNF infusions* **Medgenesis** is undertaking a trial in UK with monthly brain infusions through 7 portals with ciliary derived nerve growth factor.

# Twenty-year patent protection



LCT patent

Treatment of CNS disease with encapsulated inducible choroid plexus cells

Published in USA and under PCT for rest of the world

United States Patent and Trademark Office Application Number 62/162,390 Treatment of CNS disease with encapsulated inducible choroid plexus cells Date 15/05/2015

## Go to market strategy



- LCT's goal is to launch NTCELL as the first disease modifying treatment for Parkinson's disease in 2018
- First country of launch is New Zealand which is the most efficient approach to increasing the number of NTCELL treated patients
- This will expand the NTCELL quality, safety, and efficacy data necessary to fully globalise the product and allow submissions to FDA, EMA and Asian authorities
- LCT may seek a global commercialisation partner to fully realise the market potential of NTCELL

**Regulatory strategy** 



# **Q4 2017** File NDA with NZ Medsafe (Ministry of Health) for provisional consent under Section 23 of Medicines Act to market NTCELL

Q1 2018 NTCELL market launch at Ascot Hospital, Auckland

## Partnering strategy



Partnership or out-license would be required to expand NTCELL implantation capacity to supply sites outside New Zealand

Manufacturing technology, regulatory expertise and marketing would have to be supplied by a partner

LCT's immediate strategic goal of a profitable company does not depend on successful partnering, therefore it can assess any partnering interest on its merits

# **Expansion of NTCELL indications**



# Alzheimer's disease is the most attractive target

- Largest neurodegenerative disease market
- Choroid plexus is located in lateral ventricle which would be injection site
- 4 Alzheimer's clinical research clinics in New Zealand, established by Centre for Brain Research (Prof Richard Faull)
- In vivo human cell studies only preclinical investigation required

# LCT personnel and advisors



Living Cell Technologies	Auckland Clinical Site	Scientific Advisors
Ken Taylor, PhD CEO	<b>Barry Snow, FRACP</b> Principal Investigator, Neurologist	<b>Anne B Young, MD</b> Professor of Neurology, Harvard Medical School, Boston, USA
Kathleen Durbin, PhD Head of Clinical and Regulatory	Mark Simpson, FRACP Investigator, Neurologist	<b>Roger Barker, MD</b> <i>Professor of Clinical</i>
Janice Lam, PhD Head of Operations	Ari Bok, FRACS Patrick Schweder, FRACS Neurosurgeons	Neurosciences ,Deputy Director, John van Geest Centre for Brain Research, University of Cambridge, UK
Sarah Carley, PhD Quality Assurance Manager	Data Safety Monitoring Board	<b>Richard Faull, MBChB, PhD</b> Professor of Anatomy, Director, Centre for Brain Research.
	Prof Tim Anderson FRACP Dr Rod Ellis-Pegler FRACP Dr Andrew Hughes FRACP	University of Auckland, NZ Jackie Lee, PhD

*Consultant, ex Research Director, Geron, USA*