



Dr K M Taylor

Presentation to AGM

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16 November 2016

<http://www.lctglobal.com>

# SAFE HARBOUR STATEMENT



This document contains certain forward-looking statements, relating to LCT's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other health authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any health authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialisation of the product candidates could be affected by, among other things, unexpected clinical trial results, including additional analysis of existing clinical data, and new clinical data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. LCT is providing this information as of the date of this presentation and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.



## Creating LCT shareholder value

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LCT's goal is to be a profitable company, earning revenue from the launch of NTCELL<sup>®</sup> as the first disease modifying treatment for Parkinson's disease.

A successful NTCELL implantation program in New Zealand alone will achieve this goal.

Currently LCT has the staff, product, technology, finance plan and necessary contacts to launch NTCELL in 2018.



## Need successful outcome of current trial

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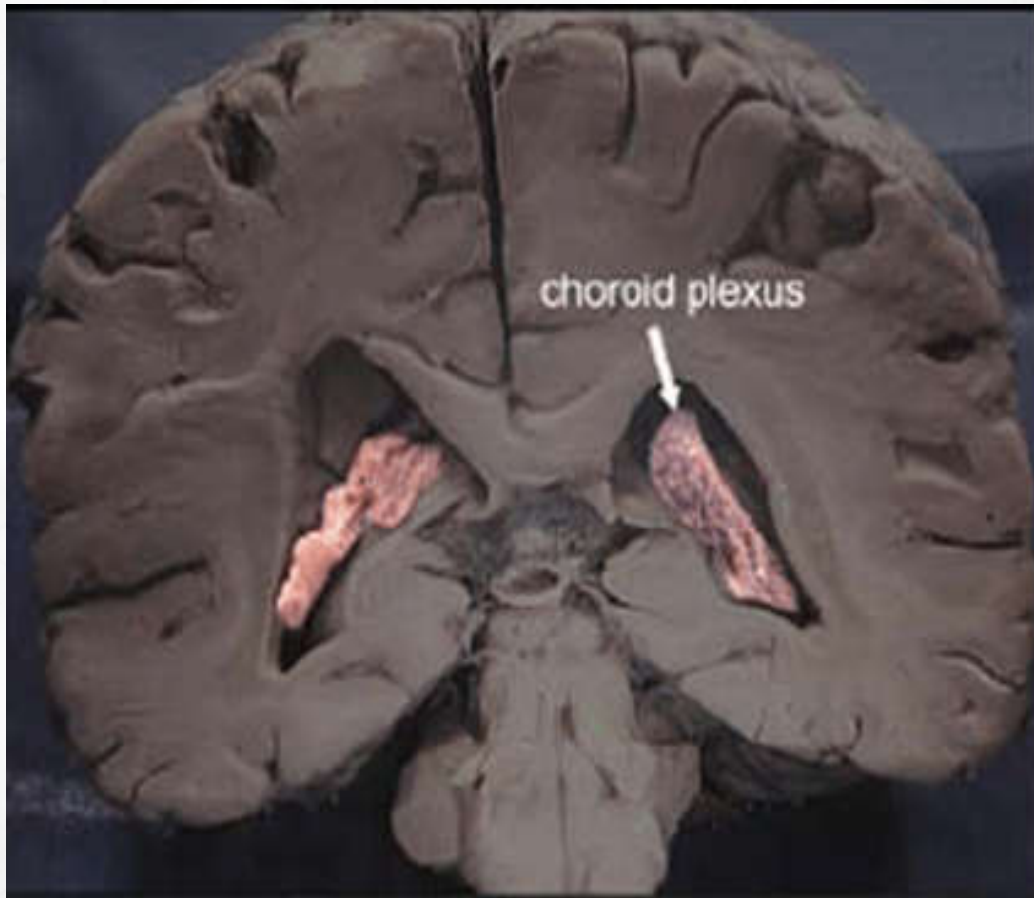


LCT is dependent only on completion and a successful outcome of its Phase IIb clinical trial of NTCELL in Parkinson's disease.

The trial endpoints will answer the 3 questions raised by the NZ 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

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



### Choroid Plexus:

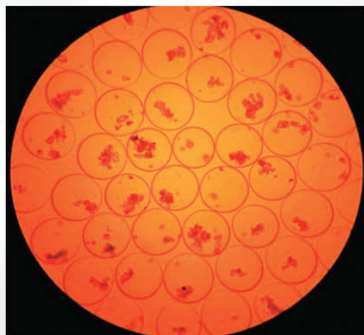
- Secretes cerebrospinal fluid (CSF)
- Provides neurotrophic factors
- Provides neuro-protective factors
- Removes toxin (drugs, metals, etc.)
- Clears waste products

# NTCELL is encapsulated choroid plexus cells



## ❖ Designated pathogen-free herd of Auckland Islands pigs

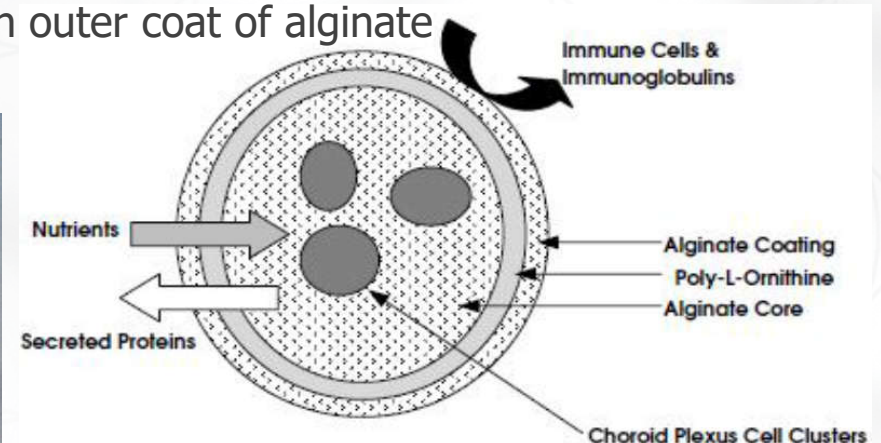
- Surgical removal of the brain from anaesthetised and exsanguinated pathogen free animals
- Enzyme digestion by collagenase and protease to make choroid plexus (CP) cell free clusters
- CP cell-free clusters entrapped in calcium-alginate gel, coated in positively charged poly-L-ornithine and then layered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



NTCELL alginate microcapsules containing porcine choroid plexus cells



Diameter: ~ 600μm



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.



# LCT has know-how and capabilities to deliver cell transplantation in the CNS



- Strong safety profile
- Proven quality raw materials (alginate & PLO)
- Not easily transferable skills
- GMP facility



# Twenty-year patent protection expected

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LCT patent

*Treatment of CNS disease with encapsulated inducible choroid plexus cells*

- Filed 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**

- Has received a favourable initial examination by the US examiner
- We are confident that we will get enough claims approved to get 20 year market exclusivity for NTCELL treatment of Parkinson's disease



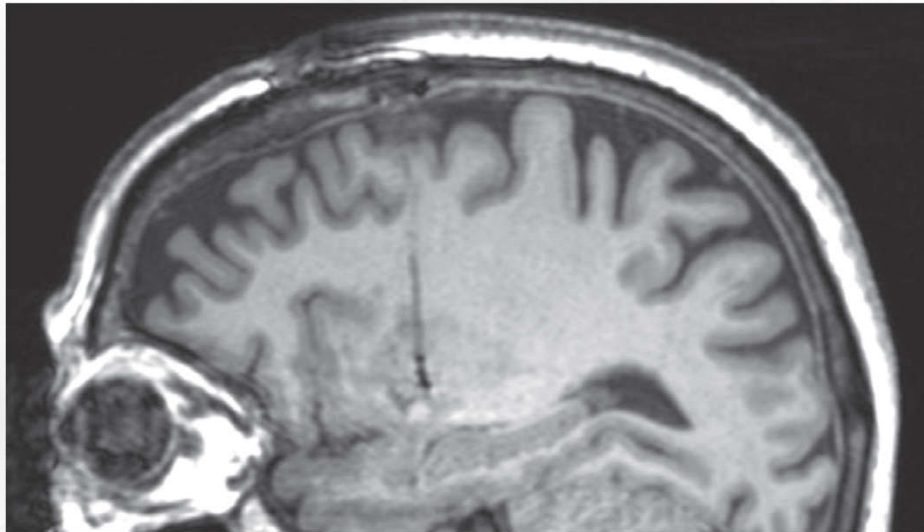
# Clinical development – first clinical study

## 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

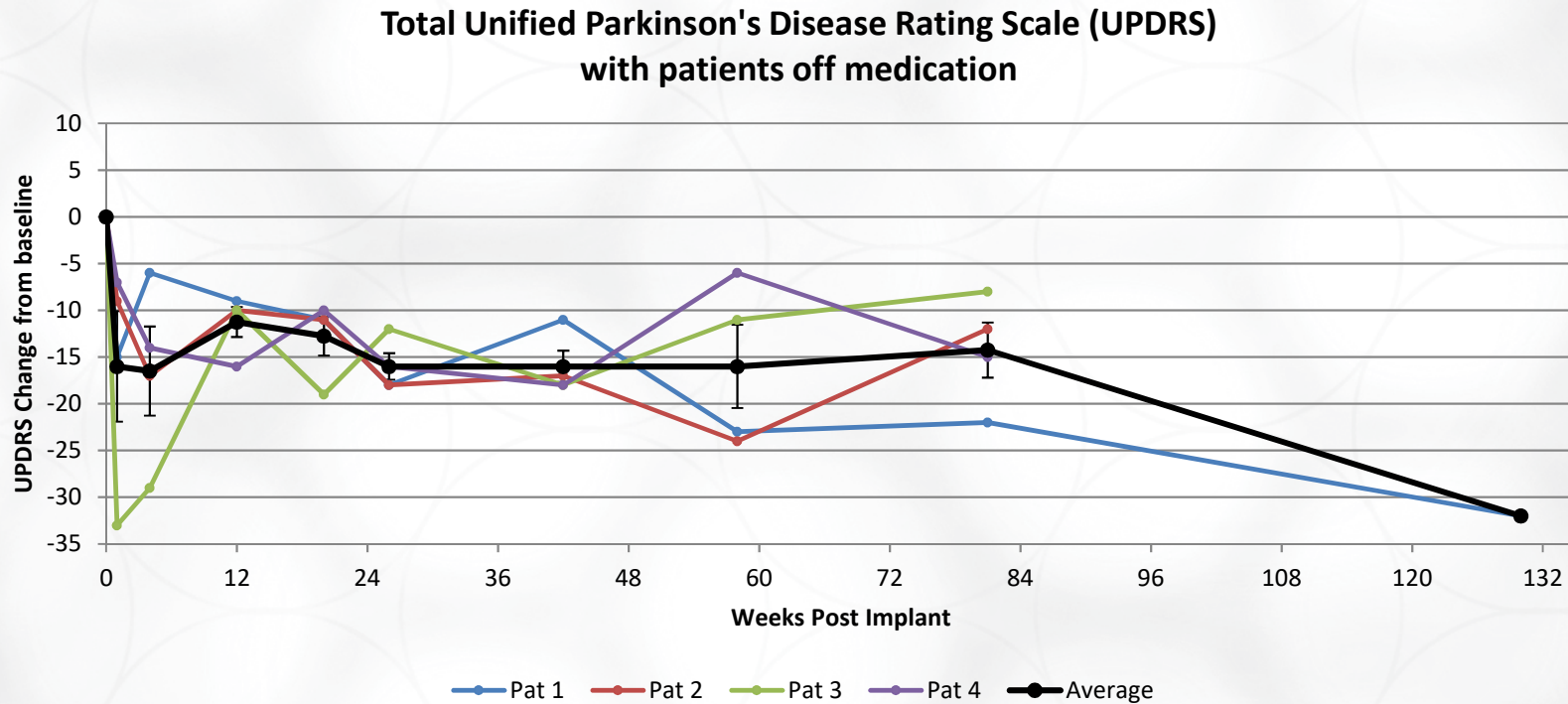
# Phase I/IIa trial completed - no safety issues

## NTCELL "Improved every rating scale in first 4 patients"

Dr Barry Snow, Principal Investigator



- ❖ Decrease in UPDRS is clinically and statistically significant



# Phase I/IIa completed trial

## NTCELL reversed progression of Parkinson's

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- In all four patients
  - NTCELL treatment has stopped the progression of Parkinson's disease as measured by globally accepted and validated neurological rating scales
  - 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
- Improvement equivalent to approximately 3 to 5 years of PD remission
- Improvement maintained
- No safety issues



# Milestones achieved since AGM 2015

## All focus on pivotal phase IIb clinical trial



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- 12 November 2015**    **Phase IIb Parkinson's study authorised**  
Minister of Health authorised application to conduct a Phase IIb study of NTCELL in Parkinson's.
- 2 December 2015**    **Supply and manufacture of NTCELL secured**  
Contracts to secure the supply and manufacture of NTCELL completed, including purchase of plant, designated pathogen-free pigs and inventory. Facilities will provide sufficient capacity to manufacture NTCELL for the Phase IIb clinical trial and treat patients under provisional consent.
- 3 February 2016**    **Ethics Committee approved Phase IIb clinical trial of NTCELL for Parkinson's**
- 17 February 2016**    **54,607,546 shares privately placed to NZ residents raising \$2,764,621;** share purchase plan announced enabling existing shareholders to buy up to \$15,000 worth of new shares.
- 24 March 2016**    **Auckland Hospital Research Review Committee approved Phase IIb clinical trial of NTCELL for Parkinson's.** Patient recruitment commences.
- 4 April 2016**    **9,532,034 shares issued under the share purchase plan, raising \$0.5m**
- 21 April 2016**    **8,349,010 shares privately placed to NZ residents raising \$431,034,** bringing total funds raised in round to \$3.7m.
- 23 June 2016**    **NTCELL demonstrates continued reversal of Parkinson's in Phase I/IIa trial patients**  
Principal Investigator Dr Barry Snow presented data on safety and clinical effects of NTCELL in Parkinson's at the 20<sup>th</sup> International Congress of Parkinson's Disease and Movement Disorders in Berlin. At 81 weeks after implant, patients showed a statistically and clinically significant improvement in neurological scores from pre-implant baseline. Improvement equivalent to approximately 3 year reversal of neurological deterioration.

## Phase IIb study

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

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

### **Group 2: Patients 7-12**

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

### **Group 3: Patients 13-18**

4 dosed and 2 placebo, randomly assigned  
120 NTCELL microcapsules ( $\pm 5\%$ ) 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

# Phase IIb study recruitment accelerates

## Six patients implanted in one week

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**3 October 2016**

Completed implantation in group 1 patients

**21 December 2016**

Target completion date for implantation of group 2 patients

**February 2017**

Target completion date for implantation of group 3 patients

- Maintain momentum at Auckland City Hospital
- Saturday extra neurosurgical clinics targeting 2 patients each session
- 2 stereotaxic units commissioned
- Patients available due to success of Parkinson's New Zealand patient information meetings



# Phase IIb study result

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## August – September 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

## Regulatory strategy

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**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

## NTCELL – market expansion

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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



## Strategy

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- 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

# First Parkinson's disease-modifying drug – significant market opportunity

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- ❖ 7–10 million people living with Parkinson's disease (PD) worldwide
- ❖ Incidence of PD increases with age
- ❖ But 19% diagnosed aged 15–64 and withdraw from workforce
- ❖ 64,000 Australians affected by PD. Will double in 20 years
- ❖ No disease modifying treatment or cure currently available
- ❖ Symptomatic treatments available but have a limited duration of efficacy
- ❖ PD drug sales totalled \$US 2.4B in 2014. All symptomatic treatments
- ❖ Levodopa “gold standard” – 50 years old

# Parkinson's disease

## Progress of competitors to NTCELL

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### *Stem Cells*

**ISCO/Cyto Therapeutics** initiated a 12 patient trial in Melbourne implanting neural stem cells from a pluripotent pathenogenic 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 synuclein. 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.



NTCELL clinical trial supported by patient organisation – Parkinson's is their disease. Video on [www.lctglobal.com](http://www.lctglobal.com).



**UPDATES FROM DR BARRY SNOW ON**  
**the most recent and advanced**  
**treatments for Parkinson's disease.**



If you missed out last time or if you would just like to come along again Parkinson's NZ invite you to come and listen to Dr Barry Snow on

**Monday 14 November from 7pm at the QBE Stadium Function Centre** Level 1 North Lounge, Stadium Dr, Albany, Auckland 0752

Dr Snow will update you on the current clinical research using NTCELL, including the results from the latest study. You are welcome to bring family members along with you, light refreshments will be provided.

Free car parking is available in Carpark A, entry is through Gate A off Stadium Drive.

Contact Bev Rakich on 09 278 6918 if you have any questions about this event.

# NTCELL pricing – Pharmacoeconomics

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## Cost of Parkinson's disease

(Ref. Johnson et al. Pharmaco Economics 31.799 – 806,2013)

### Direct costs (USD) per year

Newly diagnosed	\$ 9,175
Significant mobility limitation, need assistance	\$ 31,800
Nursing care or institution	\$ 43,506

## NTCELL

- Phase IIa study – 3-5 year reversal of UPDRS, mobility and quality of life score
- Predicts delay or prevention of disease progression
- Benefit would be 3x-5x yearly direct cost of patient care required for mobility limitation and nursing care plus quality of life

## Financing

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- See annual report 2016
- Awarded Callaghan Innovation grant
  - 20% rebate on eligible Research and Development expenditure
- Considering fundraising opportunities



# LCT Personnel and Advisors



## Living Cell Technologies

**Ken Taylor, PhD**  
*CEO*

**Kathleen Durbin, PhD**  
*Head of Clinical and Regulatory*

**Janice Lam, PhD**  
*Head of Operations*

**Sarah Carley, PhD**  
*Quality Assurance Manager*

## Auckland Clinical Site

**Barry Snow, FRACP**  
*Principal Investigator, Neurologist*

**Mark Simpson, FRACP**  
*Investigator, Neurologist*

**Ari Bok, FRACS**  
**Patrick Schweder, FRACS**  
*Neurosurgeons*

### Data Safety Monitoring Board

*Prof Tim Anderson FRACP*  
*Dr Rod Ellis-Pegler FRACP*  
*Dr Andrew Hughes FRACP*

## Scientific Advisors

**Anne B Young, MD**  
*Professor of Neurology, Harvard Medical School, Boston, USA*

**Roger Barker, MD**  
*Professor of Clinical Neurosciences, Deputy Director, John van Geest Centre for Brain Research, University of Cambridge, UK*

**Richard Faull, MBChB, PhD**  
*Professor of Anatomy, Director, Centre for Brain Research, University of Auckland, NZ*

**Jackie Lee, PhD**  
*Consultant, ex Research Director, Geron, USA*

# Advantages of NTCELL for Parkinson's



- ❖ NTCELL is encapsulated porcine choroid plexus cells
- ❖ Rationale:
  - **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

## Business plan

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With successful Phase IIb trial completion and outcome, LCT can be a profitable company focusing on NTCELL implantation in New Zealand

LCT currently has control of all necessary inputs to achieve this goal