



Innovation, Access, Commercialisation,

LCT is listed on the Australian (ASX: LCT) and US (OTCQX: LVCLY) stock exchanges. The company is incorporated in Australia, with its operations based in New Zealand.

## Dr Ken Taylor (CEO) & Dr Janice Lam (COO)

20 March 2019

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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.

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# LCT Pipeline



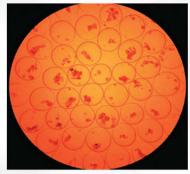
- 1. NTCELL® in Parkinson's disease
  - Partnership opportunity
- 2. Long-acting Pramlintide Analogue for Obesity
  - Phase I clinical data -> Out-licence
- Long-acting Calcitonin Gene Related Peptide (CGRP) Antagonist for Migraine
  - Phase I clinical data -> Out-licence

## NTCELL is Encapsulated Choroid Plexus Cells



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

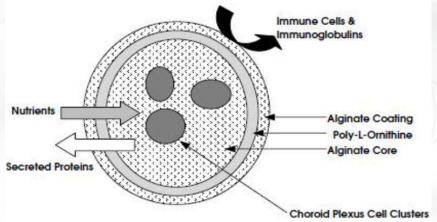
- Surgical removal of the brain from anaesthetised and exsanguinated pathogen free animals
- Enzyme digestion by collagenase and protease to make CP cell free clusters
- CP cell-free clusters entrapped in calcium-alginate gel, coated in positively charged poly-L-ornithine and then layered with an outer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



NTCELL alginate microcapsules containing porcine choroid plexus cells



Diameter: ~ 600µm

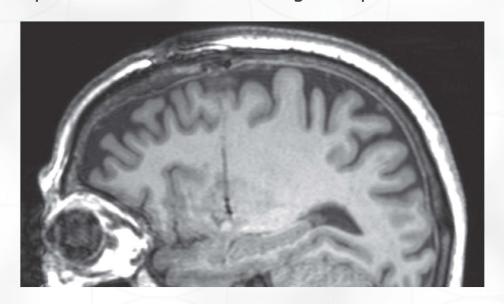


The structure of the alginate microcapsules containing CP cells. The membrane excludes large globular proteins (>80,000 Da) and all cells, but nutrients, oxygen and carbon dioxide can diffuse freely and secreted proteins (<80,000 Da) can diffuse out.

## **NTCELL** Delivery



- Stereotaxic guided delivery to the putamen
- Targeting catheter (same as that used for DBS surgery) with delivery catheter containing NTCELL capsules
- Controlled delivery using Microdrive system
- Sagittal MRI showing the cannula tract
- NTCELL microcapsules are distributed through the putamen at the end of the tract







- PD treatment remains symptomatic
- DBS advanced treatment
- No disease modifying treatments available
- PD progression measured clinically using UPDRS
- Trials focus on UPDRS improvements
  - Estimated minimal effect -2.5 points,
  - Moderate effect -5.2 points and
  - Large effect -10.8 points
- Motor (movement) effects
  - UPDRS Part III (Motor subscale)
  - Usual efficacy trial endpoint







### The rationale for NTCELL treatment

- Encapsulated porcine choroid plexus cells offer a "factory" approach for nerve growth: only one treatment
- Personalized therapy: NTCELL adapts to disease in vivo
- Reliable supply: Porcine advantage over human
- > Immuno-privileged target: Xenotransplant safe and not rejected

## Advantage over stem cells

- NTCELLs are natural, not reprogrammed by DNA, RNA manipulation...
- No concern of tumorigenicity
- Defined cell population, QA specs rather than unknown mixed cell types
- No current stem cell technology able to generate choroid plexus cells
- Manufacturing cost acceptable

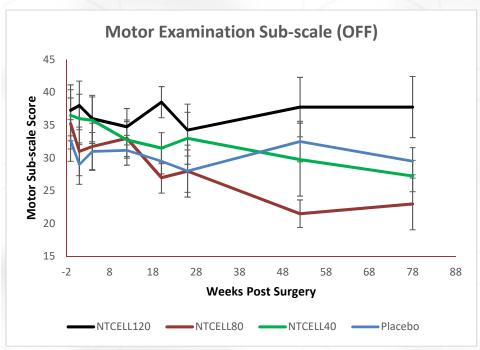


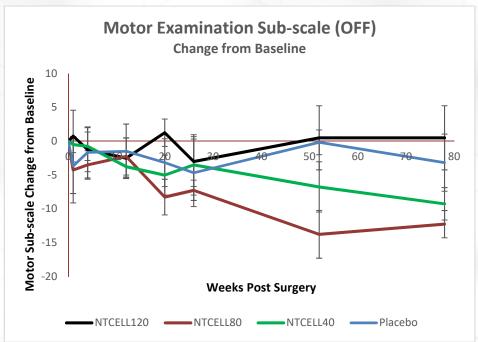


## LCT/PD-015 UPDRS Motor Sub-scale OFF (78 Weeks)

7 point benefit in 80 capsule group vs placebo (p = 0.1)

12 point benefit in 80 capsule group vs baseline (p = 0.01)

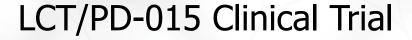




Placebo n = 6; NTCELL n = 4 / group

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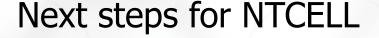






- The trial endpoints address the 3 questions raised by the Ministry of Health to qualify for conditional (fast track) consent to market:
  - Define efficacy and any placebo contribution
    - Clinical and statistical significant effect at 12 and 18 months in both UPDRS total and motor sub-scale measurements.
  - Define optimal dose of NTCELL implantation
    - 80 capsules bilaterally as 2 implants spaced to putamen.
  - Define initial target Parkinson's disease patient subgroup
    - Patients failing symptomatic treatment, candidates for DBS
- Safety
  - No safety issues up to 80 capsules bilateral

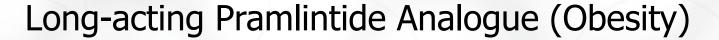




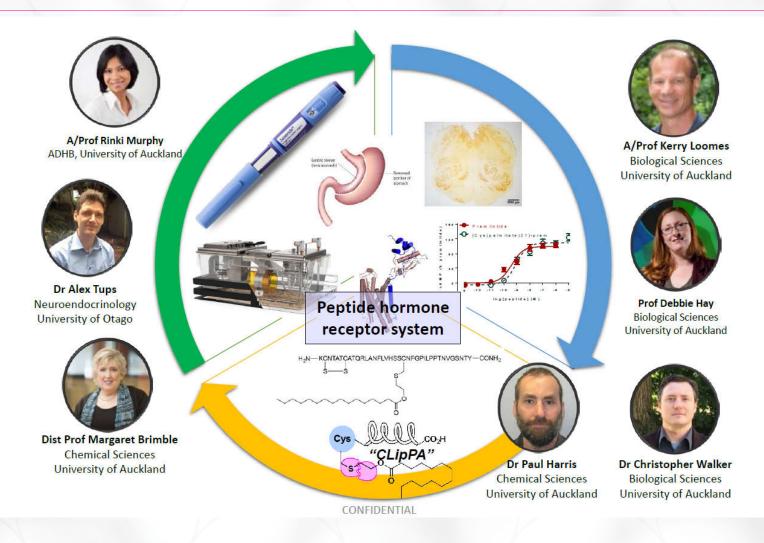


- May 2019 Confirm regulatory strategy (Medsafe, NZ).
- Global filings of patents
  - PCT application No. PCT/US2016/032543 entitled "Treatment of CNS disease with encapsulated inducible choroid plexus cells" and US application No. 15/154,709 was published 15 December 2016
  - PCT Application No. PCT/US2018/58797 entitled "Pericyte" protective agents for neurological disorders including neurodegenerative diseases, central nervous systems diseases and others"
  - Encapsulation patents











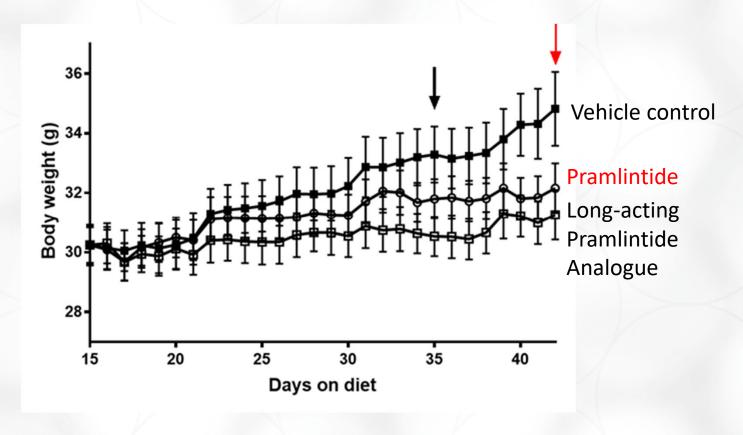


- Targets obesity
- Pramlintide (Symlin) is marketed for diabetes treatment
- Patients lose weight
- Target once daily treatment for obesity
- Phase I clinical study in 2020
- Seek out-licence partner



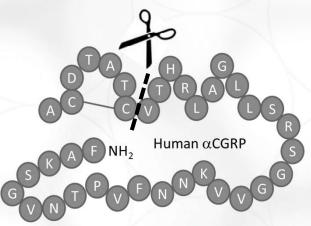
# Long-acting Pramlintide Analogue

Result: Long-acting Pramlintide Analogue more active than Pramlintide in reducing body weight



# Long-acting CGRP Peptide Antagonist (Migraine)







**Ms Elyse Williams Chemical Sciences** University of Auckland



Mr Aqfan Jamaluddin **Biological Sciences** University of Auckland









A/Prof Kerry Loomes **Biological Sciences** University of Auckland



**Prof Debbie Hay Biological Sciences** University of Auckland



**Dr Christopher Walker Biological Sciences** University of Auckland



**Dist Prof Margaret Brimble Chemical Sciences** University of Auckland



**Dr Paul Harris** Chemical Sciences University of Auckland



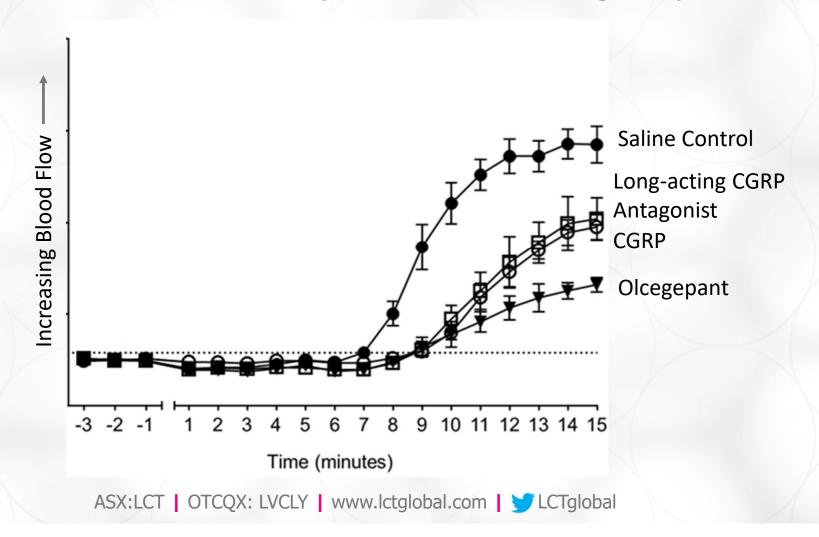


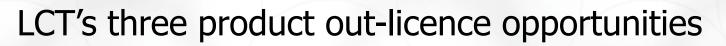
- Targets migraine
- Olcegepant is a CGRP antagonist with known clinical activity but has toxicity issues
- Target a safe CGRP antagonist that is administered once daily
- Phase I clinical study in 2020
- Seek out-licence partner

# Long-acting CGRP Antagonist



Result: Reduces Vasodilation (is a biomarker for migraine)







	Jun 2019	Dec 2019 (Nov AGM)	Jun 2020	Dec 2020 (Nov AGM)	Jun 2021	Dec 2021 (Nov AGM)
NTCELL for Parkinson's Disease	Strategic Decision					
Long-acting Pramlintide Analogue	Pre-clinica	l Developm	ent	hase I ical Trial	Out-li	cence
Long-acting CGRP Peptide Antagonist	Pre-clinica	l Developm	ient >	Phase I nical Trial	Out-li	cence

### **Investment and Licensing Opportunity**



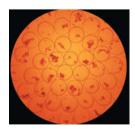
### Parkinson's disease – Xenotransplant NTCELL® Obesity – Long-acting Pramlintide Analogue Migraine – Long-acting CGRP Antagonist

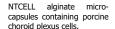
## Parkinson's disease – Xenotransplant NTCELL

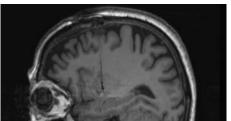
NTCELL comprises encapsulated porcine neonatal choroid plexus cells that, when implanted into the putamen, act as a neurochemical factory secreting multiple neuroactive agents. Clinical improvement has been observed in Parkinson's patients at 18 months post implantation.

### **NTCELL Technology**

Porcine choroid plexus cells produce a range of neurotrophic and growth factors (e.g. VEGF, IGFs and BDNF). The secretion of VEGF has been shown to a neuroprotective effect upon dopaminergic neurons in an experimental model of Parkinson's disease. cells also release agents that are antioxidants and chaperone proteins responsible for removing plaque-generating proteins and neurofibrillary tangles. LCT has developed choroid plexus cells from a breed of domesticated designated pathogen free pigs. These cells are encapsulated in alginate microcapsules which permit the inward passage of nutrients and the outward passage of neural proteins and compounds normally secreted by choroid plexus cells, but shield them from the recipient's immune system. Implantation utilizes existing technologies employed in Deep Brain Stimulation (DBS).







Sagittal MRI showing the cannula tract. Implanted NTCELL microcapsules can be seen distributed through the putamen at the end of the tract.

#### Obesity – Long-acting Pramlintide

LCT has completed a pre-clinical pilot study demonstrating that a long-acting pramlintide analogue has anti-obesity activity. We will complete pre-clinical development in 2019 enabling a Phase 1 clinical study in 2020. The study goal is to demonstrate that this compound can be given as a once daily injection to treat morbid obesity.

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### Migraine - Long-acting CGRP Antagonist

Calcitonin gene related peptide (CGRP) is known to be a key neurochemical in causing migraine. Recently CGRP antibodies and receptor blockers have shown clinical activity. LCT has completed a pre-clinical pilot study demonstrating that long-acting CGRP peptide antagonists has activity in a pre-clinical model. We will complete pre-clinical development in 2019 enabling a Phase 1 clinical study in 2020. The study goal is to demonstrate that this compound can be given as a once daily injection to treat migraine.

### **Project Timelines**



### **Investment Out-licence Opportunity**

Living Cell Technologies is an Australasian biotechnology company improving the wellbeing of people with serious diseases worldwide by discovering, developing and commercialising regenerative treatments which include naturally occurring cells to restore function.

LCT's operations are based in Auckland, New Zealand. It has a close liaison with University of Auckland. LCT's expertise is in translational neuroscience. It can take an innovative compound through pre-clinical development to clinical proof of principle. LCT would then consider global out-licence or investment to complete product commercialisation.

#### **Key People**

Ken Taylor – Chief Executive Officer Janice Lam – Chief Operating Officer Daya Uka – Chief Financial Officer Michelle Lockhart - Regulatory

### **Key Advisors**

Barry Snow – Principal investigator (Parkinson's disease)
Richard Faull – Scientific Advisory Board
Roger Barker – Medical Advisory Board
Margaret Brimble – Principal investigator (Obesity & Migraine)
Debbie Hay – Principal investigator (Obesity & Migraine)

#### **Further Information**

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