# CEO Presentation to AGM

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# 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.

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LCT is providing this information as of the date of this presentation and, subject to law, 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.

# LCT Current Status – Time and Money

1. Annual Report 2018-2019 outlines strategy
2. Includes audited finance report
3. LCT going concern - No tags
4. NZD 4million (Dec 2019) cash - Runway to Mar 2021
5. Complete obesity and migraine projects to out-license exit
6. NTCELL® – feasibility of 3 year clinical efficacy study

# Complete Obesity and Migraine Projects

Both projects target an exit within 2 years
Exit - Clinical efficacy – out-license to big pharma
Huge markets of big pharma interest
Globally competitive science and scientists
Long patent life
Attractive in-license condition
Clinical efficacy biomarker – short duration of clinical studies

**LP-003**

- Targets Obesity

**LC-002**

- Targets Migraine

# LP-003 for Obesity

# All diets fail due to hunger
# LP-003 injection blocks CNS hunger centre

## Market Need

- 1.9 billion overweight
- Morbid obesity treatment – must lose 100kg before bariatric surgery

## LP-003 is Long-acting Pramlintide

- Pramlintide (Symlin®) - FDA approved for Diabetes in conjunction with insulin
- Known safety profile
- **Obese patients treated with Pramlintide lose weight**
- Short duration of effect – requires three times daily injections

## Product Opportunity in Obesity

- Long-acting Pramlintide Analogue
  - Patented
  - Once daily injection
  - Extended plasma half-life
    - Albumin binding
    - Protection from protease degradation
  - Subcutaneous administration

# LP-003 Anti-obesity Mechanism of Action

- **Amylin** infusions reduce eating and increase energy expenditure
- **Amylin** is the satiation signal that is a physiological regulator of meal size
- **Pramlintide** is an amylin receptor stimulant
- **Pramlintide** in humans causes weight loss
- But it is very short acting as plasma half-life is 13min

- LP-003 is long acting pramlintide analogue
- LP-003 targets once a day injection
- This can be validated in clinical study where blood level and food intake can be measured after a single injection of LP-003

# Project – Lipidated Pramlintide: BACKGROUND

Key indications:

- Obesity
- Pre-bariatric surgery weight loss
- Type 1 diabetes

Advantages:

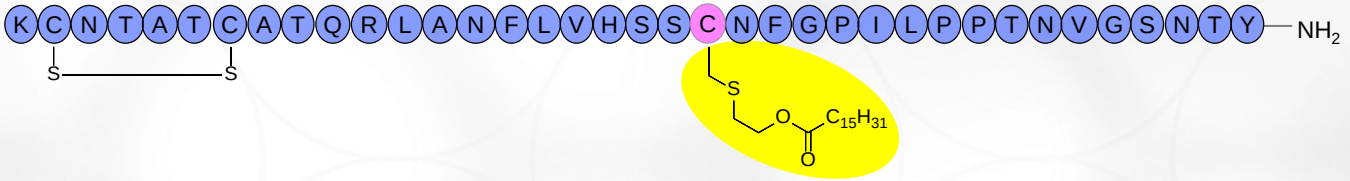
- Tri-amylin receptor agonism
- Once-daily dosing
- No liver toxicity concerns

Work flow:

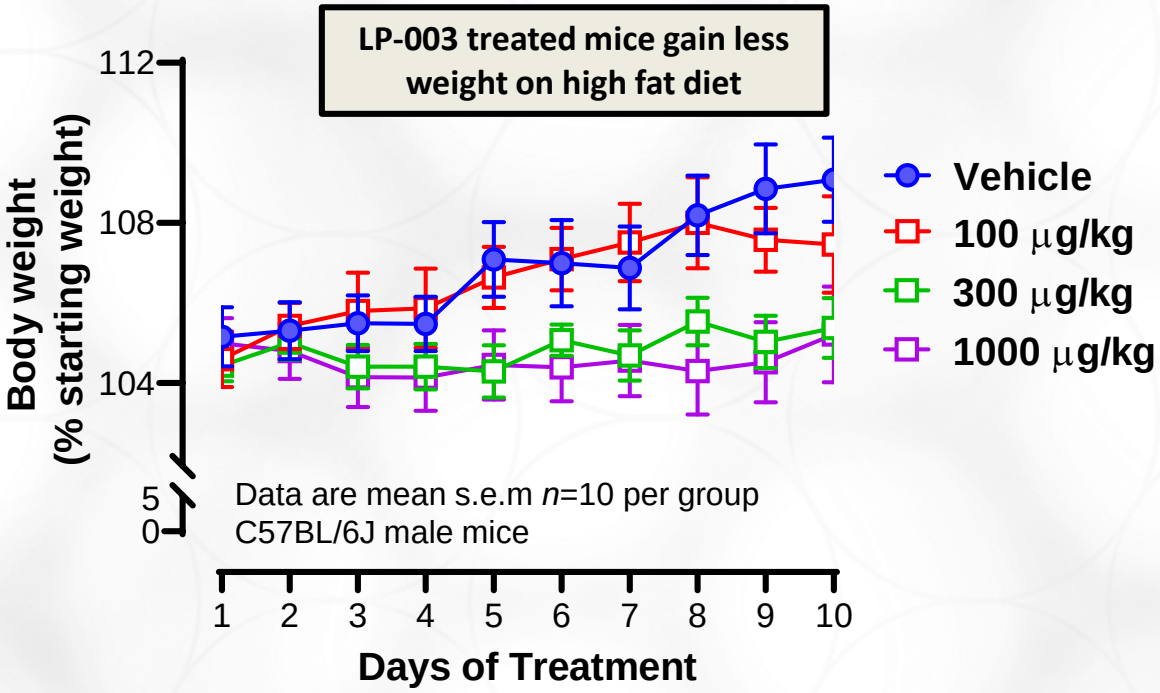
**Chemical synthesis** ⟷ ***In vitro*** **receptor screen** → ***In vivo*** **efficacy model**

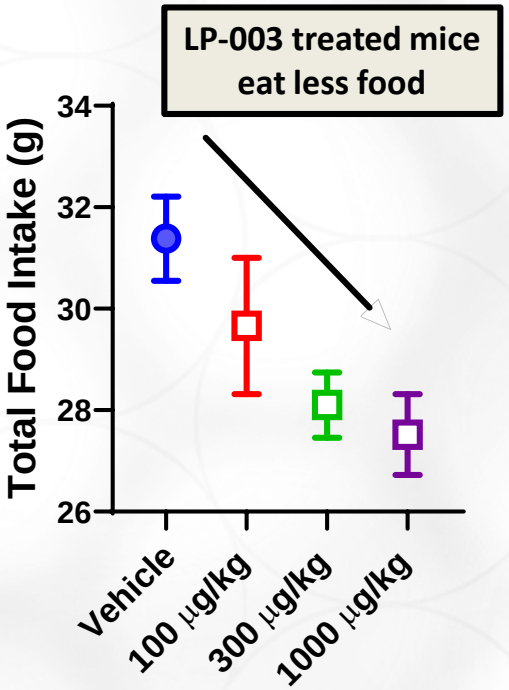
- Mice fed high fat diet
- Once-daily dosing
- Measure body weight and food intake
- Food intake measurements readily translatable to humans

**Current lead: LP-003**



# LP-003 - Pre-clinical efficacy



# Anti-obesity - Project Status

- Lead compounds designed by Distinguished Professor Margaret Brimble and Professor Debbie Hay
- Global patent protection
- Current Progress
  - Lead compound synthesized — Dist. Prof. Margaret Brimble
  - Synthesis/Manufacturing — GMP Facility Available
  - *In vitro* activity confirmed — Prof. Debbie Hay
  - *In vivo* activity in progress — Assoc. Prof Alex Tups (UoO)
  - LP-003 inhibits food consumption and inhibits weight gain
  - Analytical method confirmed — HPLC/Mass spec. (Brimble)
- Attractive in-license

UoO = University of Otago

# LP-003 - Anti-Obesity Next Steps

**1. Completion of Pre-clinical Characterisation of Lead Compound**

- *In vitro* profiling and characterisation
- Biomarker bioassay
- Pharmacokinetics
- Toxicology
- *In vivo* studies – Prof Alex Tups (University of Otago)
  - Food intake
  - Body weight changes
  - Energy Expenditure

**2. Clinical Proof of Principle**

- Phase I clinical trial
  - Single ascending dose and blood levels.
  - Food intake
  - Safety
- Clinical trial site – Auckland Clinical Studies Trust (ACST)

**3. Out-license Opportunities**

- Interested global parties
- Deal Structure – upfront cash, milestone payments, royalties

# Obesity - Costs, Timeline and License

- Costs
  - Complete pre-clinical, GMP manufacturing: $NZD1,346,000
    - Milestone payment schedule
  - Phase 1: Approx. $NZD360,000
    - 3 groups of 8 participants (6 active + 2 placebo)
- Timeline
  - Nov 2019 – Mar 2021

- License Terms
  - LCT exclusive license from University of Auckland (UoA)
  - 92% of revenue to LCT after cost recovery by LCT and UoA

# LC-002 for Migraine

# LC-002 – Mechanism of Action vs Migraine

## Calcitonin Gene Related Peptide (CGRP)

- Neuropeptide hormone found throughout the central and peripheral nervous system
- Elevated levels in migraine sufferers
- Infusion induces migraine

## CGRP Receptors

- Located within pain signaling pathways, intracranial arteries and mast cells
- Activation causes migraine attacks

## LC-002 targets migraine treatment by blocking CGRP receptors:

- Blocking neurogenic inflammation
  - Blocks actions of CGRP released onto outer covering of brain (meninges)
- Decreases artery dilation
  - Inhibits by blocking CGRP receptors located on smooth muscle cells within vessel wall
- Inhibiting pain transmission
  - Suppresses CGRP-induced enhancement of trigeminal nerve pain signals

# Migraine – Market Opportunity

## CGRP blockade prevents migraine

- CGRP small molecules
  - First generation gepants – demonstrated efficacy
    - Olcegepant (Boehringer Ingelheim) – discontinued, formulation issues
    - Telcagepant (Merck) – discontinued, liver toxicity
  - Next generation gepants in development – no liver toxicity issues
    - Rimegepant (Biohaven) – NDA submitted Q2 2019
    - Ubrogepant (Allergan) – NDA submitted Q1 2019
    - Atogepant (Allergan) – Phase III clinical trials
- Monoclonal CGRP Antibodies
  - Three currently FDA approved, fourth submitted to FDA for approval
    - Erenumab (Novartis/Amgen) – FDA approved
    - Fremanezumab (Teva Pharmaceuticals) – FDA approved
    - Galcanezumab (Eli-Lilly) – FDA approved
    - Epitinezumab (Alder Pharmaceuticals) – FDA submission Q2 2019

## Opportunity in migraine

- Long-acting CGRP Peptide Antagonist
  - Extended half-life/activity
  - Longer acting than small molecules, but shorter acting than antibodies
  - Potential multiple receptor activity
  - Once daily dosing
  - Subcutaneous Administration

# Project – Lipidated CGRP Antagonists: BACKGROUND

Key indications:

- Migraine
  - Includes menstrual migraine
- Trigeminal neuralgia

Advantages:

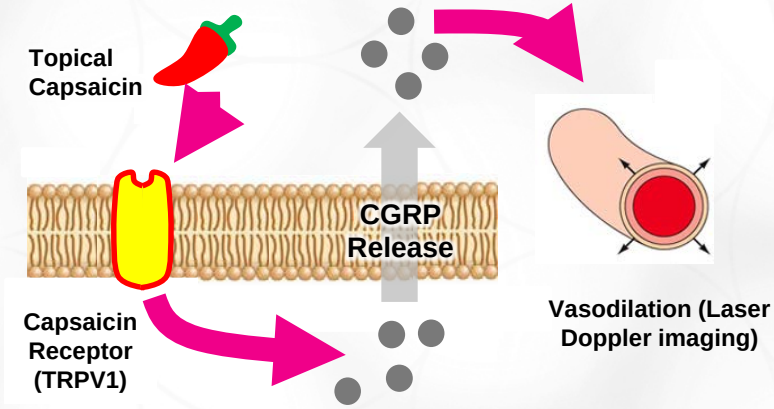
- Dual CGRP receptor antagonism
- Flexible dosing compared to antibody
- Fewer liver toxicity concerns relative to small molecules

Work flow:

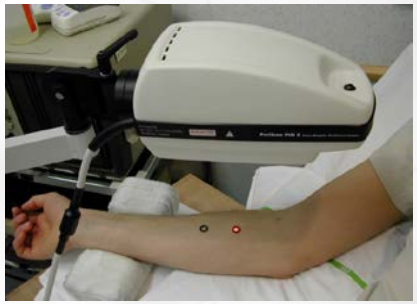
**Chemical synthesis** ⟷ ***In vitro* receptor screen** → ***In vivo* target engagement**

- Mouse target engagement model
- Capsaicin-Induced Dermal Vasodilation (CIDV)
- Gold standard model for CGRP blockade
- Translatable to humans

**CGRP antagonist reduces CIDV by blocking CGRP receptor binding on blood vessels**

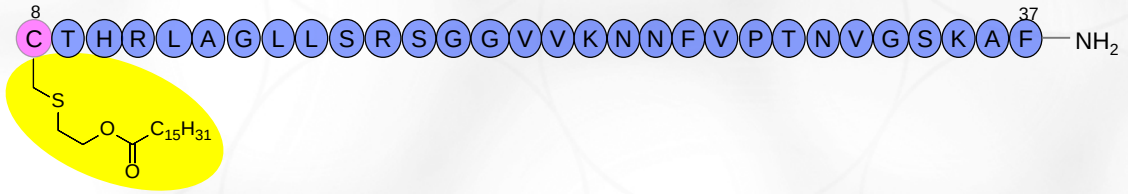


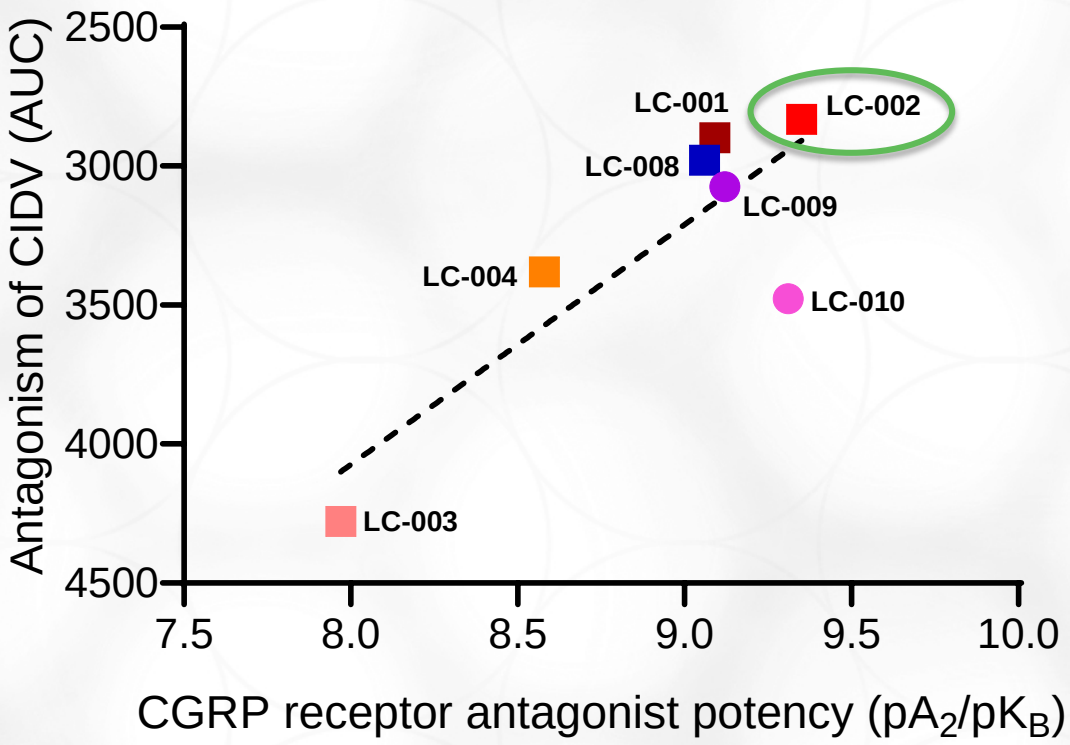

Vasodilation (Laser Doppler imaging)



# LC-002 has high receptor potency and effectively reduces blood flow

**Current lead: LC-002**



# Migraine – Project Current Status

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  - Synthesis/Manufacturing — GMP Facility Available
  - *In vitro* activity confirmed — Prof. Debbie Hay
  - *In vivo* activity in progress — Prof. Debbie Hay
  - LC-002 inhibits capsaicin-induced vasodilation
  - Analytical method confirmed — HPLC/Mass spec. (Brimble)
- Attractive in-license

# Migraine – Next Steps

**1. Completion of Pre-clinical Characterisation of LC-002**

- *In vitro* profiling and characterisation
- Biomarker bioassay
- Rodent Pharmacokinetics
- Toxicology
- Laser Doppler Rodent Model – Target engagement
- Light Aversion Rodent Model – Behavioural model

**2. Clinical Proof of Principle**

- Phase I clinical trial
  - Single ascending dose
  - Safety
  - pK
  - Laser doppler measurement
- Clinical trial site – Auckland Clinical Studies Trust (ACST)

**3. Out-license Opportunities**

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# Migraine – Costs, Timeline and License

- Costs
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# NTCELL for Parkinson's Disease

# NTCELL Parkinson's Disease

1. Market approval requires compelling efficacy data
2. No current disease modifying treatments to define "compelling"
3. Symptomatic treatments ie. L-Dopa define clinical significance as 6 point improvement
4. NTCELL efficacy is greater than 6 points vs baseline at 6, 12, 18 months
5. To progress market approval for NTCELL another clinical study to provide compelling efficacy data vs placebo is required

# NTCELL Parkinson's Disease

- Large numbers needed to overcome individual data variability  30 treated vs 30 placebo
- Not possible in NZ
- Need to raise greater than 10million
- Need approvable GMP manufacturing facility
- At least 3 year follow-up
- 5 year project

# LCT Cash

- Dec 2019 Approx. NZD 4 million
- Callaghan Innovation Grant extended to Mar 2021
  - 20% Rebate on Research Spend
  - Approx. NZD700k/yr (as a going concern)
- Cash Runway to approx. Mar, 2021 (dependent on projects)
- Complete obesity and migraine clinical proof of principle and out-license
- NTCELL® – feasibility of 3 year clinical efficacy study
  - Partnership

# Thank You