living cell technologies™

CEO Presentation to AGM

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AGENDA

- Cash Position 2020 Update
- LC-002 for Migraine
- LP-003 for Obesity
- NTCELL® for Parkinson's Disease
- DIABECELL®
- Next Steps

2019 AGM – LCT CASH POSITION

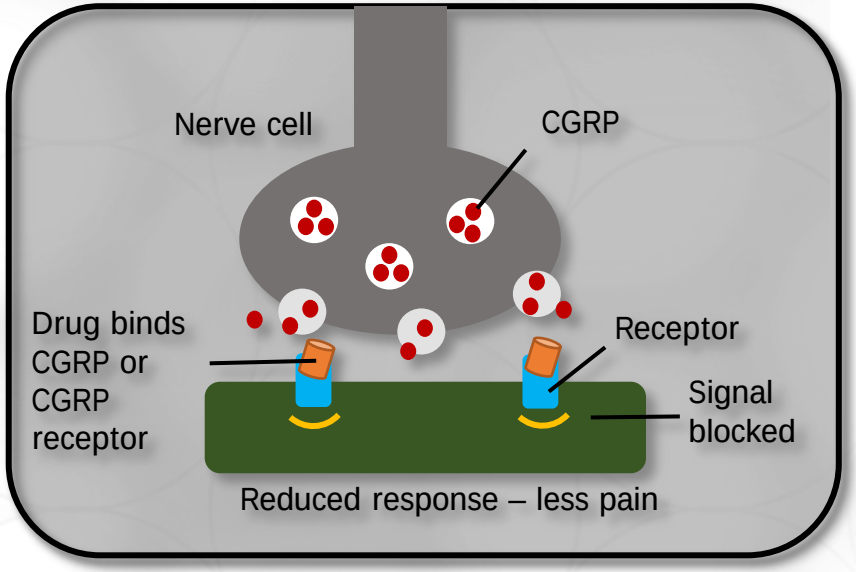
2020 Update

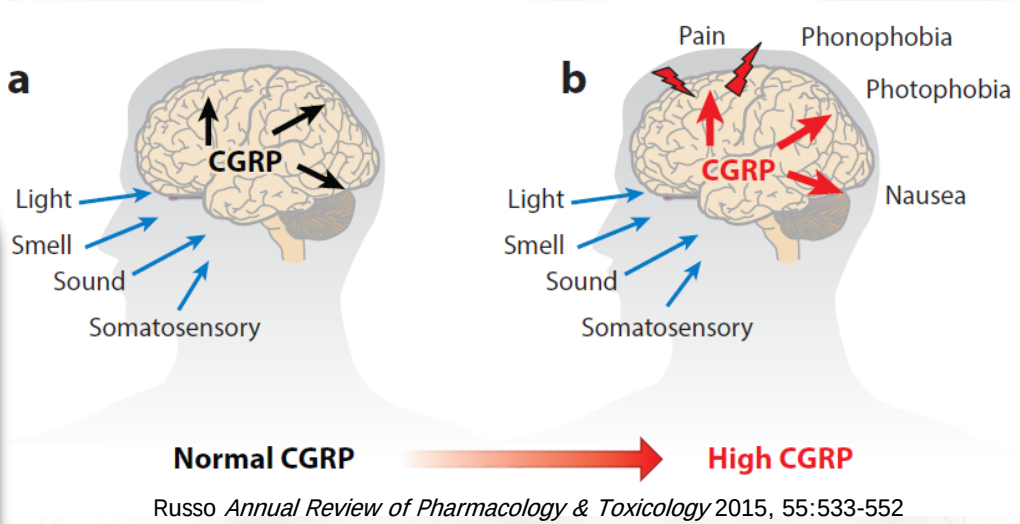
- Dec 2019 approx. NZD 4 million
  - Dec 2020 approx. NZD 2 million
- Callaghan Innovation Grant extended to Mar 2021
  - 20% Rebate on Research Spend
    - 2020: approx. NZD392k
  - Approx. NZD700k/yr (as a going concern)
    - 2020: Approx. NZD550k
- Cash Runway to approx. Mar 2021 (dependent on projects)
  - September 2021 without projects
- Complete obesity and migraine clinical proof of principle and out-license
  - Complete migraine pre-clinical and if positive data, Phase 1 clinical 2021
- NTCELL® – feasibility of larger clinical efficacy study
  - Partnership
    - ?

LC-002 FOR MIGRAINE

CGRP STRONGLY LINKED TO MIGRAINE

- **C**alcitonin **G**ene-**R**elated **P**eptide (CGRP) – 37 amino acid neuropeptide
- Found in sensory nerves
- Modulates pain
- Levels are higher in migraine sufferers
- CGRP triggers migraine





Russo *Annual Review of Pharmacology & Toxicology* 2015, 55:533-552

Antagonists needed to treat migraine

MIGRAINE

ADVANCED TREATMENTS BLOCKING CGRP ARE BEING LAUNCHED

Antibodies that block CGRP activity:

https://migrainepal.com/cgrp-antibodies-migraine/

vyepti™
(eptinezumab-jjmr)
100 mg/mL injection

Monthly or quarterly injections, subcutaneous or intravenous depending on the drugs

Small molecule antagonists that block CGRP activity:

Allergan

Atogepant (in clinical trials)

biohaven pharmaceuticals

Vazegepant (in clinical trials)

Nurtec™ ODT
(rimegepant)
orally disintegrating tablets 75 mg

UBRELVY™
(ubrogepant) tablets 50mg 100mg

PUBLICATIONS AND PATENTS

- Yang S-H, Harris PWR, Williams GM, Brimble MA. *Lipidation of Cysteine or Cysteine-Containing Peptides Using the Thiol-Ene Reaction (CLipPA)*. Eur. J. Org. Chem.2016, 2608–2616

- Williams ET, Harris PWR, Jamaluddin MA, Loomes KM, Hay DL, Brimble MA. *Solid-Phase Thiol–Ene Lipidation of Peptides for the Synthesis of a Potent CGRP Receptor Antagonist*. Angew Chem Int Ed. 2018,57: 11640–11643

- Lu BL, Loomes KM, Hay DL, Harris PWR, Brimble MA. *Synthesis of isotopically labelled αCGRP8-37 and its lipidated analogue*. J. Labelled Comp Radiopharm. 2020, 63: 325-332

- Harris PWR, Loomes KM, Hay DL, Jamaluddin A, Walker CS, Williams ET, Brimble MA. 06 November 2018. *Peptide Conjugate CGRP Receptor Antagonists and Methods of Preparation and Uses Thereof*. WO2019/087161 A1
  - National Phase Filing

- Brimble MA, Dunbar PR, Williams GW, Verdon D. *Amino Acid and Peptide Conjugates and Uses Thereof*. PCT International Patent WO2016/103192 30 Jun 2016. (Application Number PCT/IB2015/059901, filed 22 Dec 2015) United States Patent Application 15/535,956, 2018, Published 04 Jan 2018

POINT OF DIFFERENCE

"to perform better than a triptan, a new acute treatment should have a faster onset, a longer duration of action, improved response and relapse rates, and a lower incidence of drug-induced side effects."[1]

[1]Andrea Negro, Paolo Marelletti. *Gepants for the treatment of migraine*. Expert Opin Investig Drugs. 2019 Jun;28(6):555-567.

- Extended activity at CGRP receptor sites
- Also blocks CGRP activation of Amylin1 receptor site
- Lipidation extends half life and protects peptide from proteolytic degradation
- No side effects – Derivative of natural peptide

VALUE PROPOSITION:

LOW ENTRY COST FOR OPPORTUNITY TO LEAD THE MIGRAINE ADVANCED TREATMENT MARKET

- LCT Neurology Advisory Board conclusions:
  - Future lies in combination therapies
  - Need for acute parenteral treatments for severe events
  - That aborts the progression of the migraine attack “process”
  - Followed by “maintenance /preventative” treatment with small molecule gepants, CGRP antibody or botox

Commercial Opportunity

Provider of initial acute treatment will have greatest influence on choice of maintenance/preventative treatment ie. disease management.

COVID-19 REVISED MILESTONES

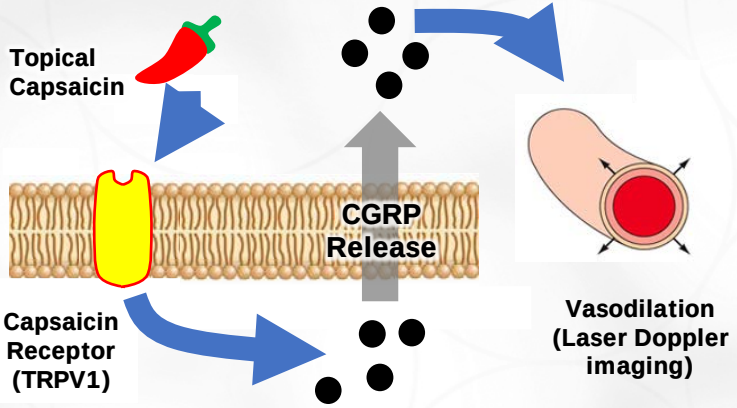
Comparison of $CGRP_{8-37}$ (LC-001) with LC-002	
1) Rodent study to determine *in vivo* pharmacokinetic parameters of LC-002 in comparison with $CGRP_{8-37}$.	
a. Surgery and subcutaneous dosing in 6 animals in each group, plus 3 for a vehicle control group; male rats only	3 months
b. Measurement of the peptide in blood samples from a. and data analysis	5 months
2) *In vivo* dose-ranging/duration blood flow study in rodents using laser doppler imaging, using LC-002 in comparison with $CGRP_{8-37}$ and vehicle.	
a. Dosing of 6 animals per group; males only, 3 doses per group, and data analysis	Commencing after completion of 1a. Surgeries, with completion in 3 months

LC-002 WORK FLOW

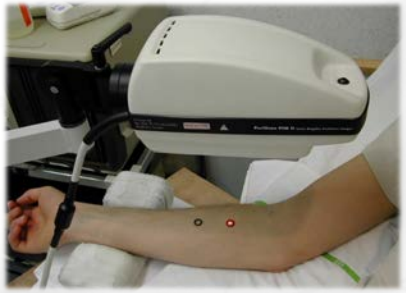
Work flow:

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



PRE-CLINICAL DATA

(Work in progress)

- Developed a HPLC/MS analytical technique that measures nanomolar concentrations in plasma
- Initial data indicates LC-002 blood levels can be measured and LC-002 can block capsaicin induced vasodilation
- Onset/duration studies in progress

FUNDING POSSIBILITIES

Non Dilutive – Callaghan and Tax Rebates

Debt Equity

Investment

OUT-LICENSE INTEREST

MIGRAINE

- Investor and Company Feedback
  - All agreed valid target
  - All wanted clinical data
  - Expand pipeline – increase efficacy and combo
  - But – no face-to-face meetings
  - No new project decisions during lockdown

LP-003 FOR OBESITY

ALL DIETS FAIL DUE TO HUNGER:
LP-003 INJECTIONS BLOCKS CNS HUNGER CENTRE

- Market need
  - 1.9 billion overweight
  - Morbid obesity treatment
- Pramlintide (Symlin®)
  

  FDA approved for diabetes in conjunction with insulin
- Known safety profile; mimics natural actions of amylin
- Obesity patients treated with Pramlintide lose weight
- Mechanism is reduced food intake
- Short duration of effect – requires three times daily injections

LONG ACTING PRAMLINTIDE
PRODUCT OPPORTUNITY IN OBESITY

- Longer-acting Pramlintide analogue
  - Patented
  - Once Daily subcutaneous injection
  - Opportunity for combination therapy
    e.g. with GLP-1 receptor agonists
  - Lipidation as a strategy

Lipidated (palmitate) GLP-1 agonist

  - Extended Plasma Half-life:
    - Albumin Binding
    - Protection for Protease Degradation

LP-003 – ANTI-OBESITY: PRECLINICAL PROGRESS TOWARDS HUMAN CLINICAL TRIALS

Prioritisation of lead peptide candidates	**Progress comment**
Synthesis of next generation leads designed to improve receptor selectivity and/or potency/solubility	Completed
In vitro pharmacology at amylin and related receptors of all synthesised peptides to determine potency	Completed
Single dose comparison *in vivo* rodent body weight study, comparing three lipidated pramlintides vs. pramlintide	Completed
Dose-ranging *in vivo* body weight rodent study LP-003	Completed
Dose-frequency *in vivo* rodent study to determine treatment duration vs. pramlintide	paused
Development of peptide drug measurement assay	initiated
Rodent study to determine *in vivo* pharmacokinetic parameters of one or more lipidated peptides compared to pramlintide	initiated
Biomarker *in vivo* rodent study with lead lipidated pramlintide (s). Study will determine blood biomarkers (e.g. leptin) that may be useful in clinical studies.	not started
Physicochemical properties study i.e. solubility, aggregation properties of lead lipidated peptides	initiated

LP-003 – ANTI-OBESITY: PRECLINICAL PROGRESS TOWARDS HUMAN CLINICAL TRIALS

- Mouse studies
  - High fat feeding so mice are obese
  - Once daily subcutaneous dosing of LP-003
  - Monitor food intake and body weight
  - LP-003 dose-dependently reduces food intake and body-weight gain

PUBLICATIONS AND PATENTS

- Brimble MA, Harris P.W.R, Yule L, Hay D.L, Tups A, PCT Application Filed 08 May 2020, *Peptide Conjugate Amylin Agonists and Uses Thereof*. US Patent Application 34772US01
- Yang S-H, Harris PWR, Williams GM, Brimble MA. *Lipidation of Cysteine or Cysteine-Containing Peptides Using the Thiol-Ene Reaction (CLipPA)*. Eur. J. Org. Chem.2016, 2608–2616
- Brimble MA, Dunbar PR, Williams GW, Verdon D. *Amino Acid and Peptide Conjugates and Uses Thereof*. PCT International Patent WO2016/103192 30 Jun 2016. (Application Number PCT/IB2015/059901, filed 22 Dec 2015) United States Patent Application 15/535,956, 2018, Published 04 Jan 2018

DRAFT CLINICAL TRIAL DESIGN

- Design
  - Randomised, double-blind, placebo-controlled cross-over
  - Overnight fast
  - Single subcutaneous injection and standardised pre-load meal
  - *Ad libitum* buffet meal offered one hour later
  - Total calorie intake and meal duration measured
- Single Ascending Doses
  - 6 x LP-003 and 2 x Placebo per cohort

PROGRAMME PRIORITY

- Migraine target priority – closer to clinic, pharma company interest
- Obesity milestones delayed but achievable
  - Pharmacokinetic study needed
  - Complete pre-clinical then if positive data → phase 1 clinical
- Obesity Advisory Board

NTCELL® FOR PARKINSON'S DISEASE

NTCELL FOR PARKINSON'S DISEASE

- Large numbers needed to overcome individual data variability
  - 30 treated vs 30 placebo
- Not possible in New Zealand
- Needs very large investment
- Need approvable GMP manufacturing facility
- At least 3-year follow-up
- 5-year project

FUNDING POSSIBILITIES

Non Dilutive Grant

Regional Out-license

Merger & Acquisition

DIABECELL®

DIABECELL® PROGRESS

DIATRANZ OTSUKA LIMITED (DOL)

- DOL continued commitment to DIABECELL development program in USA
- Funding more than NZD 10million per year
- Monkey safety and efficacy studies
- Pre IND meeting FDA Feb 2021
- LCT has 5% royalty on eventual product sales

NEXT STEPS

NEXT STEPS

- LC-002 for Migraine
  - Complete pre-clinical in Q2 2021
  - Positive pre-clinical data → Phase 1 Clinical in 2021
  - With positive clinical data target out-license in 2022
- LP-003 for Obesity
  - Complete Pre-clinical in 2021
- NTCELL for Parkinson's disease
  - Out-license

THANK YOU