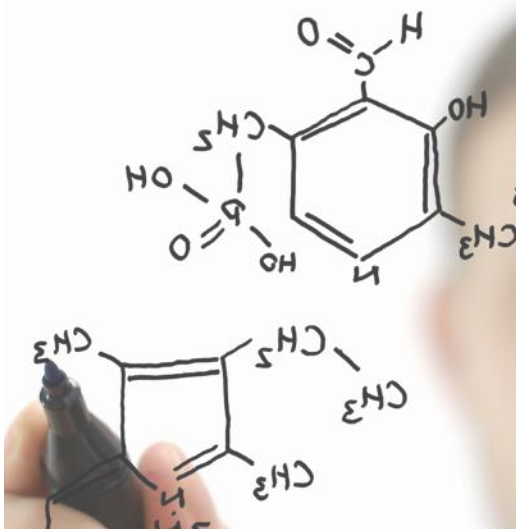
ORIL

ONCOLOGY RESEARCH INTERNATIONAL LIMITED

Annual General Meeting

November 26, 2015

Dr Philip Marshall, CEO

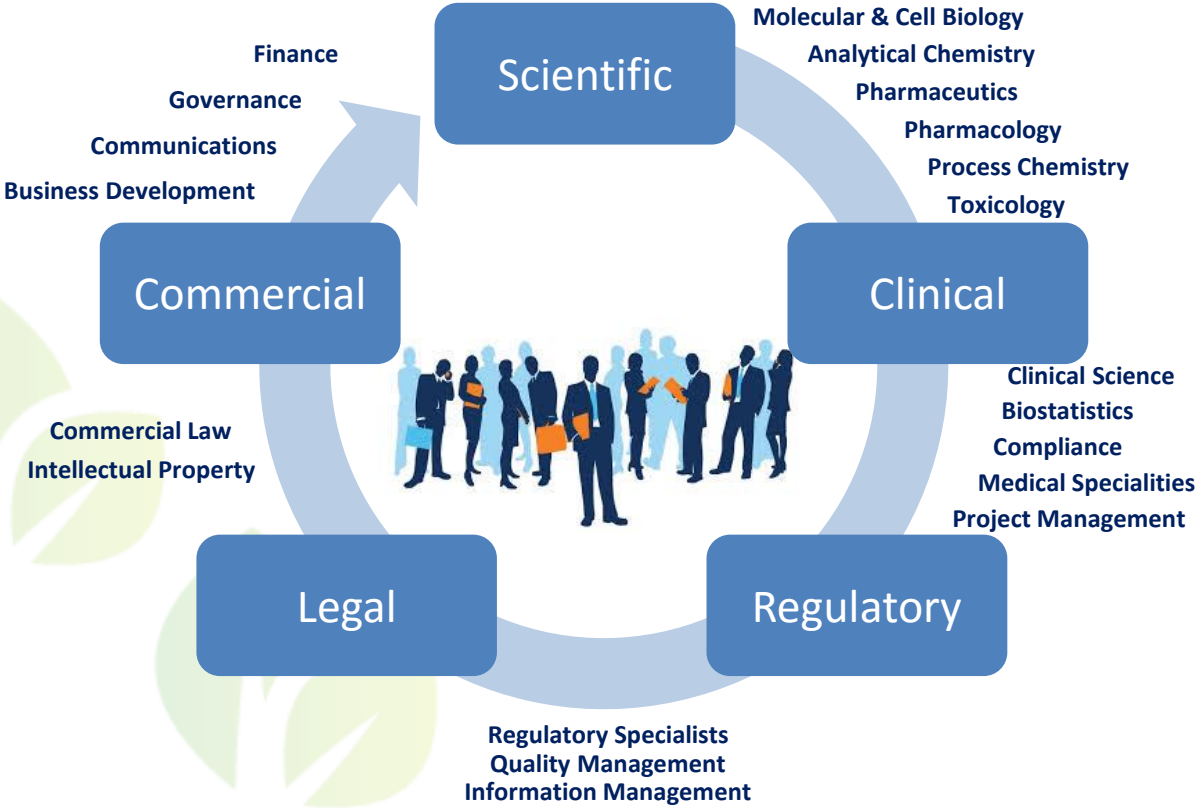


Contents

Summary of Results to end of 2015

November, 2014	November, 2015
Building the team	Strong, stable, experienced team
Demonstrated MoA	Further evidence for MoA (confidential)
Developed synthetic method for ORIL007	Patents for synthetic method for ORIL007 and related molecules
Focus on i.v. drug delivery system, introduction of other delivery systems	Parenteral, dermal and oral prototypes developed with ongoing *in vivo* testing.
Focus mainly on oncology applications for the ORIL platform technology	Diversifying by building product pipeline in addition to oncology using ORIL platform technology
Pre-clinical to be completed → IND-ready 2015 (i.v.)	Pre-clinical to be completed → IND-ready in 2016-17 (potentially for multiple routes of administration)
Planning for Phase I in early 2015	Planning for Phase I in 2017

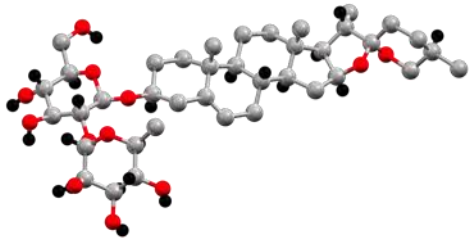
Building the Chain of Expertise: *Team strength through diversity*



Successes & Challenges

2015

Lead candidate API: ORIL007



- Novel method of synthesis developed for ORIL007 and analogues
  - ✓ Scaled for clinical supply under GMP
  - ✓ Drug Master File finalised
  - ✓ CMC complete for IND
  - ✓ Patents pending on synthesis and key polymorph – granted in Australia
- New water-soluble prodrugs under development for Composition of Matter patent applications

Oncology Product Development Summary

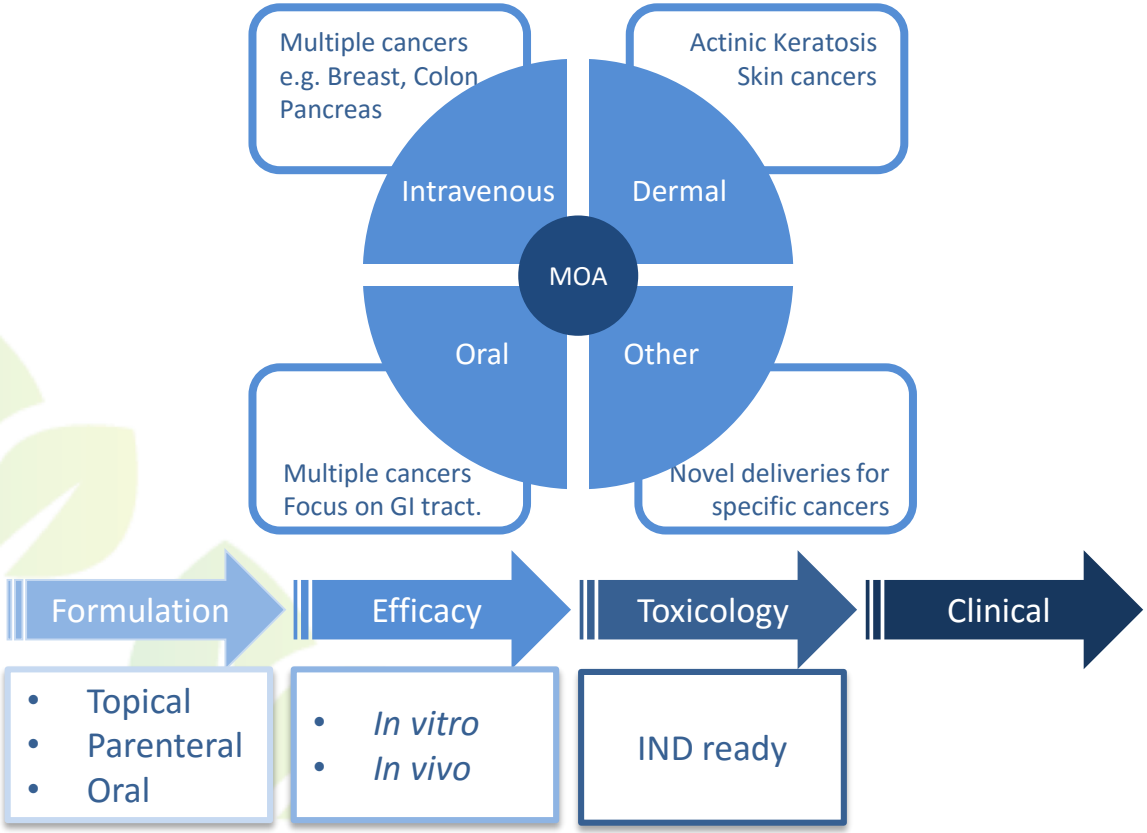
In vitro data

- Strong *in vitro* efficacy with over 40 NCI cancer cell lines showing consistent IC_{50} and high potency
- Novel mode of action demonstrated
  - interaction with cancer cell membrane switches on pathways that induce apoptosis (cell death)
  - First-in-class compounds

In vivo data

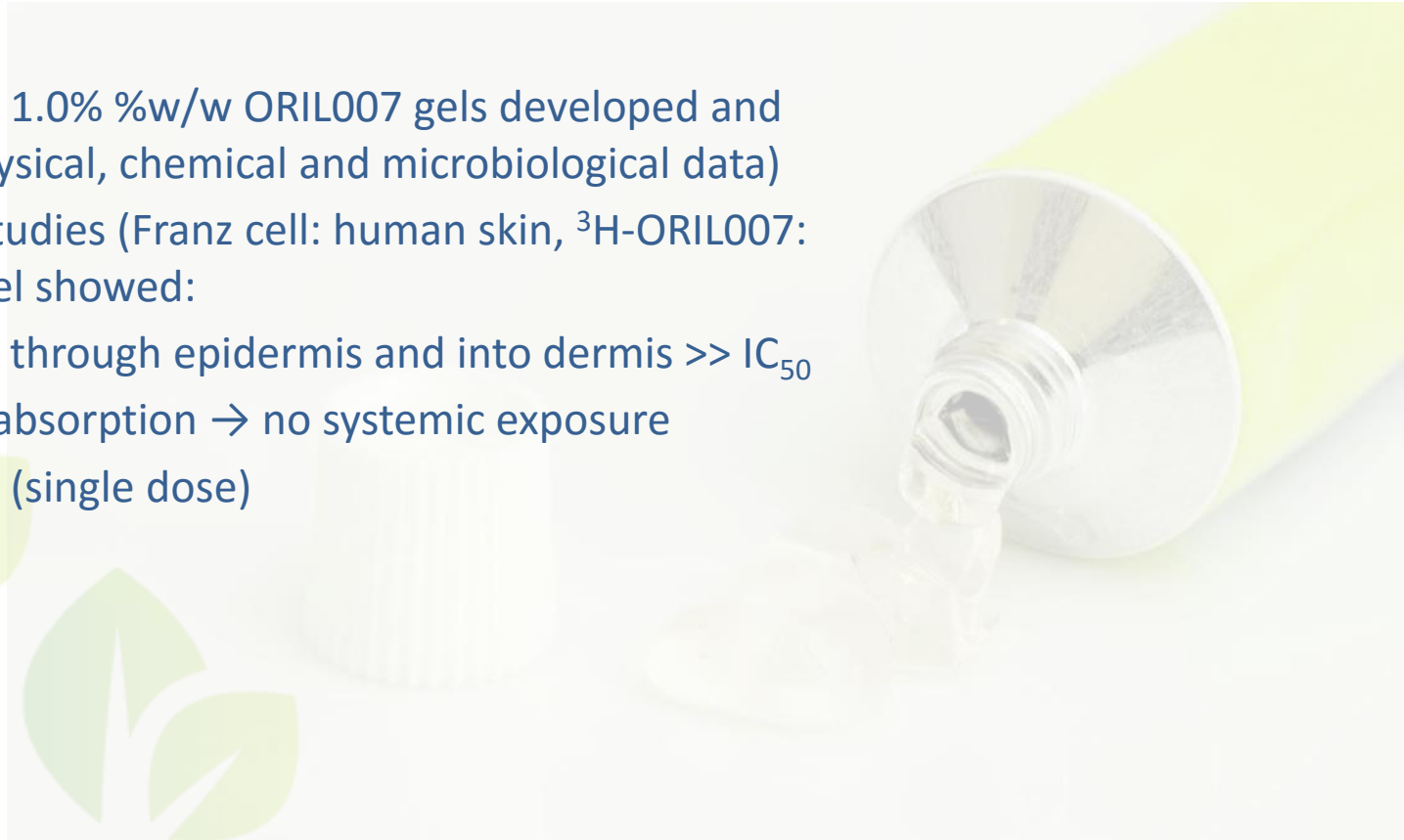
- Systemic indications using **parenteral** (i.v. and i.p.) formulations show mixed efficacy in mouse models: intratumoral, xenograft and blood-cancers
- i.v. remains a challenge
- Multiple formulation development ongoing
- Safety & toxicology profile building for IND
- PK/PD data

Development Strategy – *multiple dosage forms*

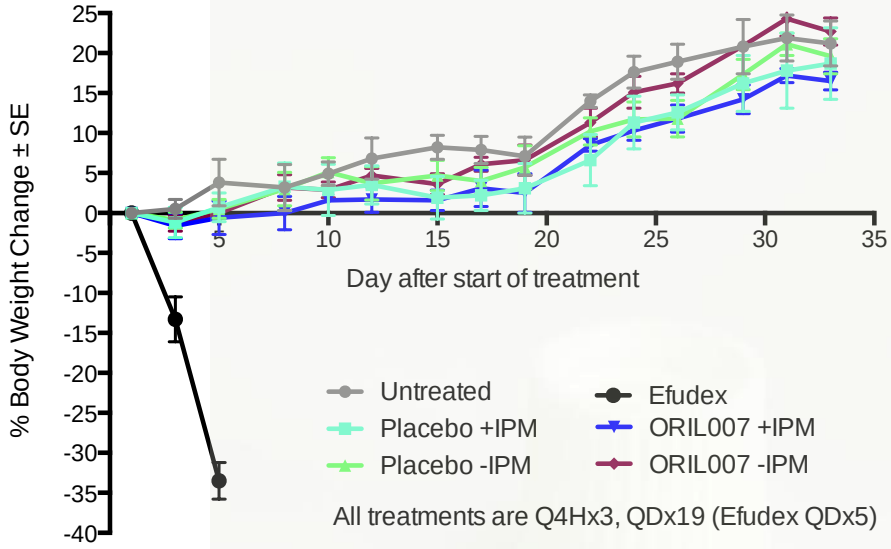


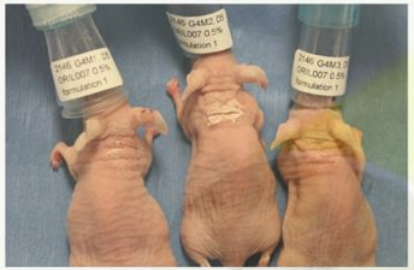
Dermal Product: Results to date

- ✓ 0.01, 0.05, 0.5 and 1.0% %w/w ORIL007 gels developed and stable (support physical, chemical and microbiological data)
- ✓ Skin penetration studies (Franz cell: human skin, ^{3}H-ORIL007: pig skin) of 0.5% gel showed:
  - ✓ skin penetration through epidermis and into dermis >> IC_{50}
  - ✓ no transdermal absorption → no systemic exposure
  - ✓ confirmed by PK (single dose)

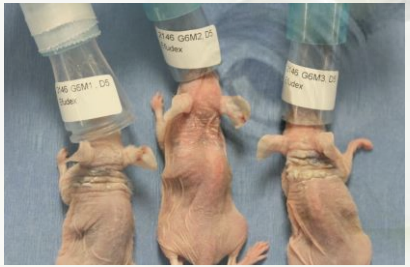


Dermal Product: Results to date





ORIL007 (0.5%) + IPM, Day 5



Efudex (0.5%), Day 5

Repeat dose application in intradermal (A431) or subcutaneous (B16) models three times daily for 21 days: 👍 no adverse effects, 👎 no tumour reduction

Dermal Product: Investigation Plan

- Formulation development as 1.0 %w/w gel
  - ✓ Stability data
  - ✓ Released from gel ➔"available" as free agent
  - ✓ Easily scaled-up

- Collaboration with University of Queensland School of Medicine (Dermatology Research Centre), based at the Translational Research Institute, Brisbane, Qld to investigate:
  - effect of ORIL007 gel in (clinically relevant) UVB induced Actinic Keratosis and Melanoma transgenic mouse models
  - prevention and treatment of melanoma and non-melanoma skin conditions.

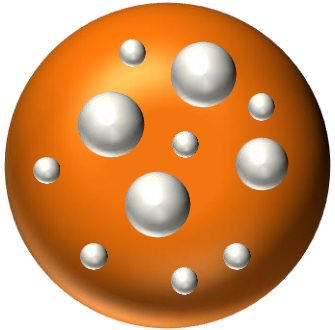
- Phase I protocol & IB development (in draft)

Next steps:

➔Pre-clinical efficacy ➔Pre-clinical Toxicology (IND) ➔Scale-up ➔ Phase I/IB

Drug Delivery Systems – Oral solid dose

- Significantly enhanced water-solubility using dispersion technique of API in polymer matrix ➔prototypes for evaluation
- Low bioavailability ➔ low systemic toxicity
- Regional GI effect – *cf.* other natural products (e.g. curcumin)
- Study effect in IBD and chemically induced *in vivo* colorectal cancer models with Dept Gastroenterology, Women & Children's Hospital, Adelaide, SA
- Patent application (draft) for oral and other dosage forms



Dispersion of API in solid matrix

Next steps:

➔Pre-clinical efficacy ➔Pre-clinical Toxicology (IND) ➔Scale-up ➔ Phase I/IB

Clinical Programme

IND
- CMC data completed for the API (ORIL007) for IND (US-FDA, TGA-CTX)
- INDs ready in 2017

Phase I
- Phase I study in multiple cancer types → drug safety and tolerability, indicative clinical efficacy

Phase IB
- Efficacy studies in multiple indications, susceptible to MoA and high unmet clinical need: eg, pancreatic, lung, “triple -ve” breast, liver, colorectal, skin cancers
- Provides further safety data and potential for out-licence

Phase II
- Pivotal study based on Phase IB and discussion with FDA
- Potential for out-licence

Orphan
- **Orphan drug status** based on pivotal Phase II

Oncology Market Opportunities

- ✓ FDA approves “First in Class” products at higher rates than fast follower or “me-too” products
  - ORIL has First-in-class compounds with unique mode of action
  - Multiple products for specific indications
- ✓ Opportunities exist in niche markets such as difficult-to-treat, other rarer forms of cancer and those with increasing numbers of cases or unmet clinical need e.g.
  - GI cancers constitute 10.6% of deaths, 2nd in Aust after lung cancer
  - Breast cancer (particularly triple-negative)
  - Skin cancers (MSC and NMSC) with numbers of cases increasing
- ✓ Low COG compared to many treatments → **affordability** for patients, health care providers, government, etc.

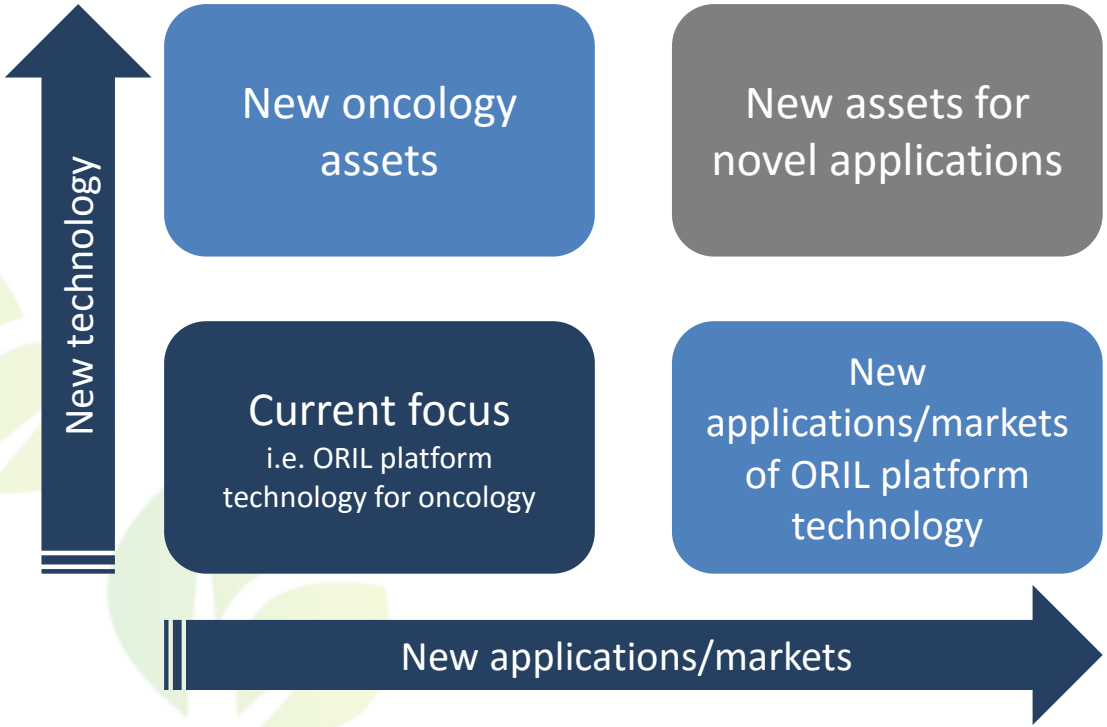
ORIL Patent Family Status

Title (Family)	Patent Application No	Status
Methods and compositions for **promoting activity of anti-cancer therapies**	PCT/AU2007/001091	Granted in Canada, China, Europe, Australia, Eurasia, Mexico, Taiwan and Japan Under examination or pending in USA, India and Brazil
Methods and compositions for **inhibiting angiogenesis**	PCT/AU2007/001092	Granted in China, Australia, Canada, Mexico, Europe & Eurasia (including Russia), Taiwan and Japan Under examination or pending in USA, India, Brazil
Improved **synthesis** of a class of steroid saponins	PCT/2013/000416	Granted in Australia National Phase Entry Nov 2014 Favourable international search report
Polymorph (ORIL007)	PCT/2013/000417	Granted in Australia National Phase Entry Nov 2014 Favourable international search report
Novel formulations		In draft for provisional filing
Pro-Drug synthesis for Composition of Matter		In draft for provisional filing

Business Development Strategy

Moving forward by building the pipeline and diversification for revenue stream(s)

Diversification strategy - building the pipeline

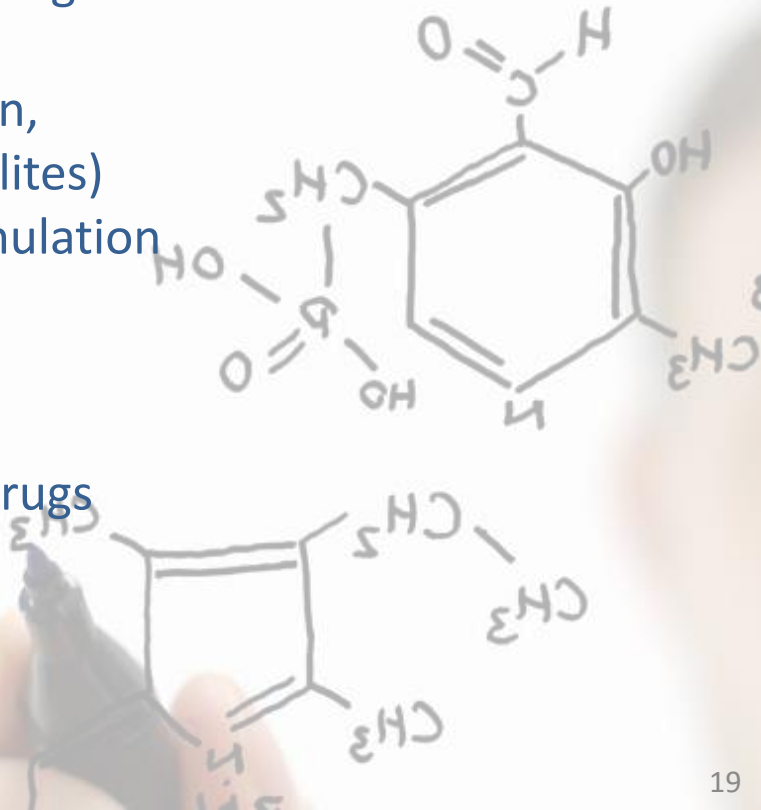


Building the Pipeline

- **Oncology is current and major focus**
  - Oncology: multiple dosage forms for specific cancer indications
  - Pro-drug (NCE)
- **New oncology assets**
  - New technology through JV, collaboration, etc., e.g. small molecule at advanced pre-clinical stage
- **Other applications of patented platform technology ➔revenue**
  - Combination therapy, (patent)
  - Anti-angiogenesis (e.g. IBD, cardiovascular, diabetic retinopathy)
  - TCM as “pharma grade”
  - Veterinary
  - Other (*commercial in confidence*)
- **New assets for novel applications**
  - Low priority

Pro-Drug (ORIL007) Synthesis

- Potential benefits of Pro-drug
  - New Chemical Entity (NCE) ➔ Create strong IP (composition of matter patent)
  - *In vivo* release ➔ ORIL007 ✚ safe, known, naturally occurring by-products (metabolites)
  - Increase water solubility for ease of formulation
  - Improve ADME and efficacy
  - Improve bioavailability from GI tract
  - Improve selectivity & reduce side effects
- Based on precedence from many marketed drugs
- Underway with collaborative CRO



Building the Pipeline *Examples: applications of platform technology*

Application	Dosage Form(s)	Indication & Rationale	Approx. Market Size
Combination Therapy	i.v. Oral	Oncology Improve efficacy Reduce side effects Reduce cost to patient	Total global market size USD 100 billion, USD 147 billion by 2018.
Anti-angiogenesis	Oral Oral i.v., oral	Inflammatory Bowel Disease (IBD) Cardiovascular Disease Diabetic retinopathy	4% annual growth. USD 10 billion by 2017. USD 187 billion in 2016 USD 10 billion by 2022.
Traditional Chinese Medicine (TCM)	Oral	Various Oncology Gut health and well being	20% annual growth over the past 5 years. USD 40 billion in 2015.
Veterinary	i.v. Oral	Oncology for companion and high value animals	Mostly an untapped market. High growth. US market $500 million annually

Budget & Finance

Budget and Finance Summary to June 30th 2017

	AU$MM
Budget to June 30th, 2017	**8.48**
Less Cash at bank as at 31 October, 2015	0.92
Less Estimated R&D offset 2015	0.75
Less Estimated R&D offset 2016	1.25
Sub Total	**2.92**
Total capital to be raised	**5.56**

Budget: October 1st, 2015 to June 30th 2017

Item	Budget AU$MM
Preclinical **Oncology: Multiple product/indications** (dermal, oral, parenteral), for **IND-ready** Formulation prototypes Pro-drug development Safety & toxicology Pharmacokinetics Pharmacodynamics, Efficacy **Pipeline activities** New applications New opportunities	**4.65**
IP portfolio: maintenance of portfolio & new patent applications	**0.28**
R&D management, expert advisors and support activities	**1.74**
Operations, administration, governance, overheads etc.	**1.46**
General contingency	**0.35**
TOTAL	**8.48**