



**ONCOLOGY RESEARCH INTERNATIONAL LIMITED**  
**NEWSLETTER**  
**July 2016**

ORIL's major focus is the treatment of cancers with high unmet clinical need such as breast, lung, pancreatic, prostate, and bowel cancer, in multiple dosage forms. The company is also diversifying and building its product pipeline through utility of ORIL platform technology in:

- Anti-angiogenesis applications (in addition to cancer), e.g. inflammatory diseases of the gastrointestinal tract.
- Combination therapy with other agents for cancer
- Other applications e.g. Traditional Chinese Medicine (TCM), dietary supplements and veterinary
- Investigation of R&D and commercial opportunities e.g. new technology to complement ORIL

## **Key results and achievements in 2016**

### ***Oral Formulation***

Development of a novel oral solid dose formulation of ORIL compounds is well advanced. While the details remain confidential (as provisional patent applications are in preparation for submission later this year), the technology has potential application for other routes of administration. The product is being tested in the W&CH study detailed below.

### ***W&CH Collaboration***

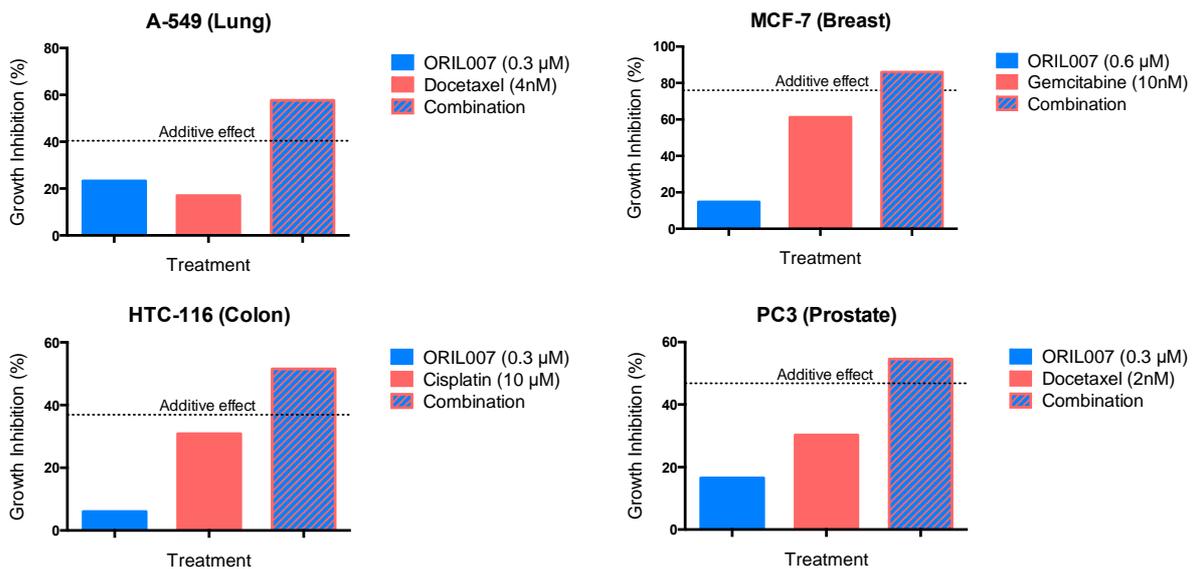
ORIL is delighted to announce that it has entered into a research collaboration with the Women & Children's Hospital (W&CH) and University of Adelaide, SA into the investigation of the application of a novel orally administered ORIL007 in colorectal cancer as both prevention and treatment. Colorectal cancer is still the second highest cause of death in Australia (after lung cancer). Professor Gordon Howarth and NHMRC Postdoctoral Fellow Dr Suzanne Mashtoub, (pictured), of the Department of Gastroenterology based at the W&CH in Adelaide, SA, are world recognised experts in the field. Dr Mashtoub recently won the prestigious University of Adelaide Faculty of Sciences, Science & Technology Award. Integral to the study ORIL has purchased a specialty instrument for monitoring disease progression for exclusive use by the W&CH in these and future studies.



Results to date of studies to establish dose indicate that the product is safe with no side effects, even when administered at the high dose of >150 mg/kg.

### Use of ORIL007 with other anticancer agents

The company is currently investigating the co-administration of ORIL compounds with other anti-cancer agents where earlier *in vivo* tests showed added or better than added efficacy – an application for which ORIL holds patents in the major jurisdictions. Additional advantages of combination therapy include potential reduction in side effects caused by the co-administered agent, (because less agent is required) and subsequent reduction in costs to the patient. Results to date show synergy with other agents as illustrated below.

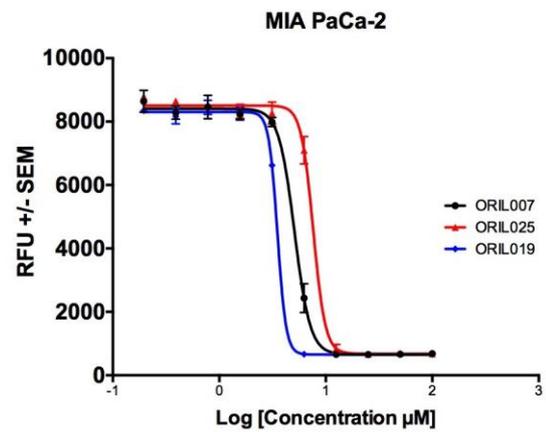
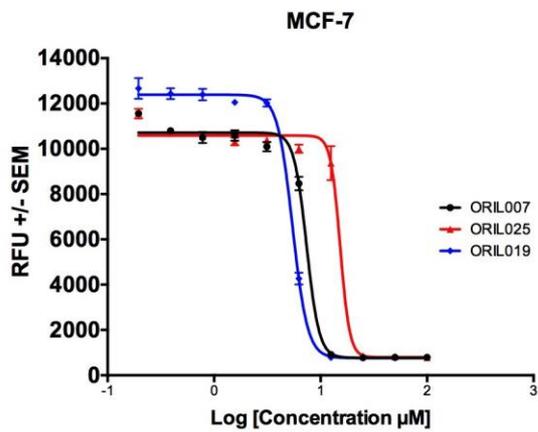
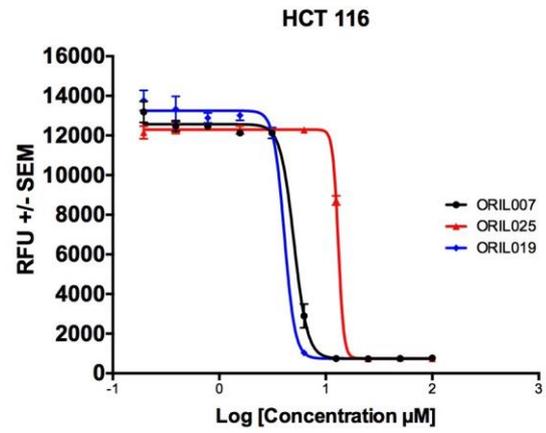
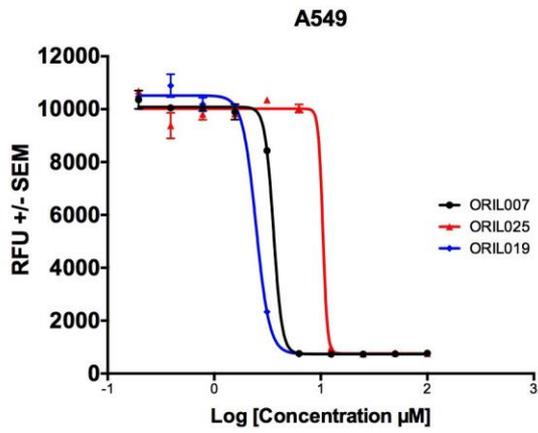


### Pro-Drugs of ORIL007

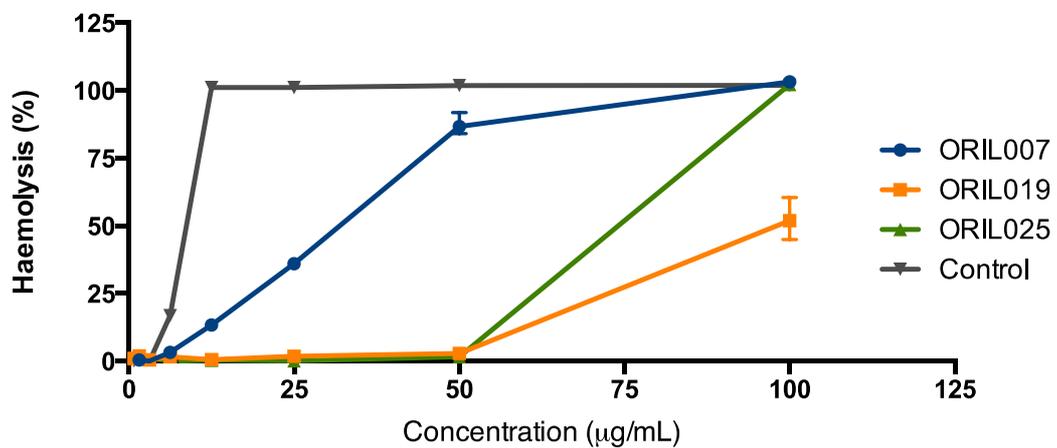
A **prodrug** is a medication or compound that, after administration, is metabolized (i.e., converted within the body) into a pharmacologically active drug. Instead of administering a drug directly, a prodrug might be used instead to improve how a medicine is absorbed, distributed, metabolized, and excreted (ADME). Prodrugs are often designed to improve oral bioavailability when a drug itself is poorly absorbed from the gastrointestinal tract. A prodrug may be used to improve how selectively the drug interacts with cells or processes that are not its intended target. This reduces adverse or unintended effects of a drug, especially important in treatments like chemotherapy, which can have severe unintended and undesirable side effects.

ORIL has designed and synthesized prodrugs of ORIL007 with improved properties. Initial results are promising in that ORIL019 has increased potency in 5 cancer types with reduced haemolytic activity (i.e. reduced lysis of human blood cells, a favourable indicator of safety) compared to the parent ORIL007. Not only does this present the potential opportunity for improvement as described above, it provides the company with high-value “Composition of Matter” patent protection.

A summary of the results to date is shown on the next page.



Cell Line	IC50 [ $\mu\text{M}$ ]		
	ORIL007	ORIL025	ORIL019
A549	3.60	10.47	2.46
HCT 116	5.02	13.11	4.08
MCF-7	7.38	15.28	5.45
MIA-PaCa-2	5.08	7.62	3.52
PC-3	5.85	10.96	4.32



## Intellectual Property

The patent application “Methods and Compositions for Promoting Activity of Anti-Cancer Therapies” has recently been granted in the USA, Japan, Canada and India. This is indeed **significant news** in important markets. Brazil is the only major market where the application is still under examination. A list of patent families and their status is provided in the Table below.

Title (Family)	Patent Application No.	Status
Methods and compositions for promoting activity of anti-cancer therapies	PCT/AU2007/001091	Granted in Australia, USA, Canada, China, Europe, Eurasia, Mexico, Taiwan, Japan, and India Under examination/pending in Brazil
Methods and compositions for inhibiting angiogenesis	PCT/AU2007/001092	Granted in Australia, China, Europe, Eurasia, Taiwan, Canada, Japan, Mexico Under examination/pending in Brazil, India, USA
Improved synthesis of a class of steroid saponins	PCT/AU2013/000416	National Phase Entry November 2014. Granted in Australia, Aust Patent 2013204005
Polymorph (ORIL007)	PCT/AU2013/000417	PCT filed in April 2013, National Phase Entry June 2015. Accepted in Australia
Pro-Drug		In draft for provisional filing
Novel Formulation		In draft for provisional filing

## USE OF PHYTOCHEMICALS AS NUTRACEUTICALS AND SUPPLEMENTS IN CANCER

We all know that bowel cancer is a world-wide health problem and the second-most dangerous type of cancer, affecting both men and women. As a result, there is a need to develop novel drug therapies for treatment and prevention of colon cancer and dietary supplements or nutraceuticals play an increasingly important role. Nutraceuticals are derived from various natural sources such as medicinal plants, marine organisms, vegetables and fruits and have shown the potential to reduce the risk of bowel cancer and slow its progression. These dietary substances target different molecular aspects of bowel cancer development.

ORIL compounds can be found in plants and herbs used in European and traditional Chinese medicine and have anti-inflammatory and anti-cancer properties making them suitable for use as dietary supplements as an aid in the management of bowel cancer.

ORIL considers the opportunity exists to bring a low-dose ORIL007 to market as a Traditional Chinese Medicine (TCM)/dietary supplement, as a single compound and/or in combination with other supplements. This plan is consistent with ORIL’s origins, mission and the recognition by the company of the need to out-license its technology, diversify its product pipeline and technology to become a sustainable business. It’s early days but preliminary discussions with suitable potential commercial partners have been initiated.