A Message from the Managing Director

We are pleased to report ongoing excellent progress in the clinical development of our lead product CAVATAK™ across multiple cancer indications. A recent highlight was our well received presence at the leading European oncology conference, the European Society for Medical Oncology (ESMO) 2014 Congress, in late September. At that conference, we provided an update on our US phase 2 CALM study and the impressive response rates, progression-free survival percentage and overall survival rates. These results, together with the excellent tolerability in this patient population with difficult-to-treat disease were met with great interest by an audience including leading oncologists, pharma company representatives and institutional investors. It was gratifying to receive a best poster award as recognition of the high quality of our program and the excellent results achieved to date.

The ESMO conference also provided a prestigious venue to present further results from our important preclinical work on the combination of CAVATAK with immune checkpoint inhibitors, a new class of cancer immunotherapies with blockbuster potential. Our results provide great encouragement for this combination approach, and we are working hard to advance this promising combination into the clinic.

We also presented a poster that generated strong interest in our results at the recent Society for Immunotherapy of Cancer (SITC) conference in the USA. The largest such conference, SITC showcases the latest developments in cancer immunotherapy treatments, which are forecast to become the single biggest class of drugs with the global market estimated at $35 Billion by 2023. Understandably, pharma companies are actively searching for new products with activity demonstrated in the clinic.

Our clinical program has met additional recent milestones with the commencement of the CALM extension study, which is designed to help us better understand the role of CAVATAK in triggering an immune response against cancer cells, as well as the UK regulatory authority approval to commence the Phase 1 UK study to assess CAVATAK in non-muscle invasive bladder cancer (NMIBC), a common cancer type with an urgent need for better therapies. This Phase 1 trial is supported by a body of strong preclinical results.

Our Phase 1/2 STORM study of CAVATAK in various cancer types also continues to progress, with recruitment in the third cohort of patients underway. We look forward to providing an update of this important study in the first quarter of 2015. We also have plans to initiate combination studies with CAVATAK in late-stage melanoma patients in the near term.

It continues to be a very busy time at Viralytics, and we are delighted to welcome Peter Turvey, who joined our board of directors in September, bringing a wealth of corporate and licensing experience from many successful years at CSL.

The support of our investors and the efforts of our hardworking team is greatly appreciated as we continue to advance CAVATAK as an important new cancer immunotherapy. We look forward to providing further updates through the remainder of 2014 and into early 2015.

With kind regards,

Dr. Malcolm McColl
Managing Director and Chief Executive Officer
STORM Study Update

Our Phase 1/2 STORM trial assessing the intravenous activity of CAVATAK in patients with late-stage melanoma, lung, metastatic bladder and prostate cancer is well underway. CAVATAK has been well tolerated in the first two cohorts of patients, and a third cohort of patients is now being treated at the highest dose level. We look forward to announcing preliminary results on the first stage of the study in early 2015.

CALM Trial Results Highlighted at ESMO

In September, we announced strongly positive results from our US Phase 2 CALM trial of CAVATAK in late-stage melanoma at the European Society of Medical Oncology (ESMO) 2014 Congress in Madrid. To date, 22 of the 57 (38.6%) patients had achieved the irPFS endpoint, significantly exceeding the initial target of 18.5%, or 10 of 54 evaluable patients reporting irPFS at six months after the first dose of CAVATAK.

Investigators also reported an overall response rate in 16 of 57 (28%) patients. Furthermore, CAVATAK continues to demonstrate activity in both injected tumours and non-injected tumours, including local and distant lymph nodes, lungs and other distant sites, suggesting an anti-tumour immune response.

An impressive interim one-year survival rate of 73% (33 of 45) patients was achieved in this challenging population with advanced, difficult-to-treat disease.

According to Dr Robert Andtbacka, Lead Study Investigator from the Huntsman Cancer Institute, Utah, “CAVATAK’s activity and tolerability in these late-stage melanoma patients is impressive. Given this growing body of clinical and pre-clinical data, CAVATAK appears to be an excellent candidate for use, either as a single agent in earlier disease, or in combination with other new therapies, including anti-PD-1 and other checkpoint inhibitors. I look forward to contributing to the further clinical development of this promising immunotherapy agent.”

Bladder Cancer Trial Begins

We are excited to announce that we have received final approval from the UK Medicines and Healthcare Products Regulatory Agency (MHRA) to undertake a Phase 1 clinical trial of CAVATAK in patients with non-muscle invasive bladder cancer (NMIBC), also known as superficial bladder cancer.

The Phase 1 trial, called the CANON (CAVATAK in NON-muscle invasive bladder cancer) study, is designed to evaluate the safety and tolerability of CAVATAK administered alone, as well as in combination with the standard chemotherapy, mitomycin C, in patients with NMIBC. In preclinical studies, the combination of CAVATAK and mitomycin C synergistically enhanced the cancer-killing activity in bladder cancer cell lines. As part of this trial, biopsies of the tumour tissue will be taken to assess the response to CAVATAK administration.

This trial will be undertaken by Professor Hardev Pandha, Director of the Surrey Cancer Research Institute at the University of Surrey. The trial has been designed so that, CAVATAK will be given in the frontline setting, or ahead of other therapies, to patients who are scheduled to undergo surgery to treat their disease.

"Based on the significantly increased oncolytic activity of the CAVATAK/chemotherapy combination observed in bladder cancer cell cultures, we are excited to further explore this treatment in human trials", said Professor Pandha. “There is an urgent need for improved therapies for bladder cancer, and this combination appears promising.”

Bladder Cancer Facts

The most common malignancy of the urinary tract, bladder cancer is one of the most costly cancers to treat. An unmet need exists for new treatment options associated with fewer complications, better patient compliance and decreased healthcare costs.

Bladder cancer:

• Is the sixth most common cancer type in the US, with over 74,000 new cases each year
• Affects three times as many men as women
• Occurs mostly in people over the age of 55
• Has a tendency to recur, or return, after treatment
• Accounts for more than 15,000 U.S. deaths per year
• Is initially treated with surgery (transurethral resection, or TUR) to remove the tumour
• Is then often treated with the live bacterial preparation Bacille Calmette Guerin (BCG) directly into the bladder to help keep the cancer from coming back

REF: http://www.cancer.gov/cancertopics/types/commoncancers
Focusing on CAVATAK in Combination with New Therapies

Combination treatment has become a key theme in our deliberations on the clinical programme for CAVATAK. This focus is based on extensive consultation within the Viralytics’ clinical team and the broader clinical community, as well as feedback from various representatives of the pharmaceutical industry. Our discussions have been underpinned by preclinical studies announced at major global oncology conferences showing that CAVATAK combined with several promising checkpoint inhibitor agents (anti-PD-1 and anti-CTLA4 monoclonal antibodies) is well tolerated and able to provide significantly greater anti-tumour activity than checkpoint inhibitors alone.

The new-generation anti-PD-1 monoclonal antibodies represent a major advance in the treatment of melanoma and other cancers and have the potential to become the backbone of cancer immunotherapy in the future. Nonetheless, the clinical advice indicates that, as good as these anti PD-1 agents are, many patients still do not respond or retain stable disease at best. The opportunities for combination treatments include reducing the number of non-responders, translating stable disease into a complete response, and increasing the durability of complete response in the patient population.

We are exploring several opportunities for clinical trials of CAVATAK in combination with these new agents and anticipate further announcements in the coming months.

Our Investigators Speak

For our recent annual report we asked key members of our clinical team for their thoughts on CAVATAK and its progress through the clinic. Below is a selection of their comments. These and other quotes can be found on page 6 of our 2014 Annual Report.

**Professor Kevin Harrington**

Professor of Biological Cancer Therapies, Royal Marsden Hospital, UK.

**Investigator Viralytics**

Phase 1/2 ‘STORM’ Trial,

Member of the Viralytics Scientific Advisory Board.

“Having seen impressive single-agent response rates after intratumoural administration in patients with melanoma, I am very pleased to be involved in the STORM study in which CAVATAK is administered by intravenous injection. The next phase of studies in which the agent will be combined with established systemic drugs is likely to be very exciting.”

**Dr Howard L. Kaufman MD**

Associate Director for Clinical Sciences, Professor and Chief, Division of Surgical Oncology, Rutgers Cancer Institute of New Jersey USA.

**Investigator Viralytics**

Phase 2 ‘CALM’ Trial

“The preliminary data from the CAVATAK™ melanoma clinical trial is very encouraging with a favorable response rate and an acceptable safety profile. Based on these results, further studies combining CAVATAK with approved T cell checkpoint inhibitors should be a high priority for maximizing the potential of these agents for patients with melanoma.”
New Board Member Peter Turvey

In September, we welcomed Peter Turvey to our Board of Directors. Peter brings outstanding commercial licensing expertise to Viralytics, having spent the last 30 years in various roles in the biotechnology industry, including Group General Counsel, Company Secretary and Executive Vice-President Licensing of the specialty biopharmaceutical company CSL Limited. Mr. Turvey was heavily involved in CSL’s acquisitions and divestments over those years and directly responsible for the protection and licensing of its intellectual property. In addition to his new role at Viralytics, Peter is a Non-Executive Director of the ASX-listed companies, Starpharma Holdings Limited and Admedus Limited; a Non-Executive Director of Victorian State Government-owned Agriculture Victoria Services Pty. Ltd. and a Principal of Foursight Associates Pty. Ltd.

Outside of his busy corporate life, Peter enjoys nothing better than the pleasures that come with travel, good food and wine in the company of family and friends.

Viralytics in the News

Our company continues to garner attention in both the industry and general media. On 24th October, the journal Bioshares featured Viralytics in an article entitled, “Viralytics and the Next Wave of Cancer Immunotherapies”. The full story can be found in the ‘Analyst Reports’ section of our website:

http://www.viralytics.com/investor-centre/analysts-reports/analyst-reports-2014/

On 2nd September, our program was featured, along with several other technologies, in a Channel 7 News Report “Brain Drain,” highlighting some of the challenges involved in developing novel technologies in Australia. In addition, on 30th September James Dunn of Dunn Media identified Viralytics as one of four biotechs to watch during his appearance on Switzer on Sky Business News.

Links to both videos can be found at the ‘In the Media’ section of our website: