

ASX and Media Release

## **Viralytics to Commence Clinical Trial of CAVATAK™ Immunotherapy Combination**

**Trial to Assess CAVATAK in Combination with Leading Checkpoint Inhibitor**

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**04 December 2014, Sydney, Australia:** Viralytics Limited (ASX: VLA, OTC: VRACY) announced today that it has received final approval from the Institutional Review Board (IRB) of the Providence Cancer Centre in Portland, Oregon for a clinical trial to assess CAVATAK™ in combination with the blockbuster drug Yervoy®<sup>1</sup> (ipilimumab) in late-stage melanoma patients that will commence in early Q1 2015.

The company-sponsored Phase 1b open label study is designed to evaluate the safety and tolerability of the established dose of CAVATAK in combination with Yervoy in 26 patients with late-stage melanoma for whom Yervoy would be considered the standard of care. Investigators will also assess evidence of anti-cancer activity, including response rates and bio-markers of anti-tumour immunity.

The lead investigator for the trial is Dr Brendan Curti MD, Director, Biotherapy Program, Earle A Chiles Research Institute at the Providence Cancer Center, Portland, Oregon. Dr Curti is also an investigator in the ongoing Phase 2 CALM trial assessing CAVATAK as a monotherapy in late-stage melanoma patients.

CAVATAK is an investigational novel cancer immunotherapy based on a proprietary cold virus that has been shown to preferentially infect and attack cancer cells. In preclinical studies<sup>2</sup>, the combination of CAVATAK and the mouse homologue of ipilimumab produced superior efficacy outcomes in a mouse melanoma model, compared to the efficacy of either agent alone.

Yervoy (ipilimumab) belongs to a new class of cancer immunotherapy agents called immune checkpoint inhibitors. Launched by Bristol-Myers Squibb in 2011 for the treatment of late-stage melanoma, Yervoy achieved global sales of almost \$US1 billion in the first 9 months of 2014.

“While the checkpoint inhibitors represent a major advance in the treatment of melanoma, there remains considerable potential to both improve response rates and enhance the durability of response in patients,” said Dr Curti. “Based on the promising clinical performance of CAVATAK in the CALM study and the results from

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<sup>1</sup> Yervoy® is a trademark of the Bristol-Myers Squibb company

<sup>2</sup> <http://www.viralytics.com/wp-content/uploads/2014/09/140929-CVA21-and-PD-1-or-CTLA-4-blockade-combination-Poster-ESMO.jpg>

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the preclinical CAVATAK / ipilimumab studies, we are enthusiastic to explore this combination treatment in human trials.”

Dr Malcolm McColl, Managing Director of Viralytics said, “The results of our preclinical studies provide encouragement that the combination of Yervoy with CAVATAK may provide significant clinical benefits to patients. Checkpoint inhibitors are forecast to form the future backbone of cancer treatment; however there remains a need and considerable commercial opportunity to enhance their performance through the development of combination therapies.”

The conduct of a Phase 1b study is the first step and a prerequisite to commencing a randomized Phase 2 combination study. Subject to satisfactory results from the Phase 1b study the company will proceed into the randomized Phase 2 combination study.

**About the Trial:**

The study will use intratumoural CAVATAK in combination with Yervoy (ipilimumab) in patients with advanced melanoma for whom Yervoy would be considered standard of care.

Treatment with CAVATAK will be on days 1, 3, 5 and 8, and then both agents will be co-administered on days 22, 43, 64 and 85. Patients with clinical benefit can continue on CAVATAK every 3 weeks for up to one year.

Further information is contained in the following trial synopsis.

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## CAVATAK / YERVOY (ipilimumab) COMBINATION TRIAL SYNOPSIS

<b>Title of Study:</b>	Study of Intratumoral CAVATAK™ (Coxsackievirus A21) and Ipilimumab in Patients With Advanced Melanoma
<b>Objectives:</b>	<p><b>VLA013</b></p> <p><b>Primary Objectives:</b></p> <ul style="list-style-type: none"> <li>Evaluate the safety and tolerability of multiple intratumoral injections of CAVATAK when given in conjunction with ipilimumab as assessed by incidence of dose-limiting toxicities (DLT).</li> </ul> <p><b>Secondary Objective:</b></p> <ul style="list-style-type: none"> <li>Investigate the objective response rate to CAVATAK and ipilimumab in patients with advanced melanoma using irRC-WHO criteria.</li> </ul>
<b>Study Design:</b>	<p>This is a Phase Ib, single-site, open-label, study designed to evaluate CAVATAK in combination with Ipilimumab.</p> <p>Treatment with CAVATAK will be on days 1, 3, 5 and 8 and then both agents will be co-administered on days 22, 43, 64 and 85. Patients with clinical benefit can continue CAVATAK every 3 weeks for up to one year.</p> <p>CAVATAK will be administered by intratumoral injection up to a total dose of <math>3 \times 10^8</math> TCID50. Ipilimumab will be administered intravenously at the recommended dose of 3 mg/kg</p>
<b>Planned Sample Size:</b>	This study is expected to enrol 26 patients

### About Viralytics Ltd:

Viralytics is developing oncolytic immunotherapy treatments for a range of cancers. Viralytics' lead investigational product, CAVATAK™, is a proprietary formulation of the common cold Coxsackievirus Type A21 (CVA21). CVA21 binds to specific 'receptor' proteins highly expressed on multiple cancer types including, but not limited to: melanoma; prostate, lung, breast and bladder cancers; and multiple myeloma. CAVATAK™ acts to kill both local and metastatic cancer cells through cell lysis and the potential generation of an immune response against the cancer cells. Together this mechanism of action is known as oncolytic immunotherapy. CAVATAK's preferential targeting of cancer cells creates the potential for a more tolerable cancer treatment.

The company has extended enrolment to enable a deeper interrogation of the immunotherapeutic activity of CAVATAK, in a single arm Phase 2 clinical trial of intratumourally administered CAVATAK in the treatment of Late-stage Melanoma (the CALM study), at multiple prestigious cancer clinics in the US. The study is being conducted in patients with late stage (IIIC and IV) malignant melanoma.

In addition, Viralytics is progressing a Phase 1/2 trial of CAVATAK delivered systemically (intravenously). This trial, referred to as the STORM (Systemic Treatment Of Resistant Malignancies) study, is enrolling patients with melanoma, prostate, lung or metastatic bladder cancers. The second stage of the STORM trial will include combination treatments with existing chemotherapies in one of the above cancer types. The STORM trial is being conducted at three UK cancer centres.

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Viralytics has received approval from the MHRA for the CANON trial, a Phase 1 Trial to investigate the intravesicular use of CAVATAK for treatment of NON-muscle invasive bladder cancer conducted at the Surrey Cancer Research Institute. CAVATAK will be given in the frontline setting, with or without mitomycin C to patients who are scheduled to undergo surgery (transurethral resection, or TUR).

Based in Sydney Australia, the company is listed on the Australian Securities Exchange (ASX: VLA) while Viralytics' ADRs also trade under VRACY on the US OTCQX International market.

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