



ASX and Media Release

## **Updated clinical trial data on CAVATAK™ tumour targeting and immune-activation presented at the American Society Clinical Oncology (ASCO) Annual Meeting**

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**6 June 2016, Sydney, Australia:** [Viralytics Limited](#) (ASX: VLA, OTC: VRACY) today announced that it has presented posters updating the results of the ongoing Phase 1 STORM/KEYNOTE 200 and the completed Phase 2 CALM clinical trials of Viralytics' lead drug candidate, [CAVATAK™](#), at the [American Society of Clinical Oncology \(ASCO\) Annual Meeting 2016](#) in Chicago, IL, USA.

CAVATAK is an investigational novel cancer immunotherapy based on a proprietary bio-selected common cold virus that can preferentially infect and attack tumour cells.

### **STORM (KEYNOTE 200) Clinical Trial**

An overview of the ongoing two-part [Phase 1 STORM](#) (Systemic Treatment of Resistant Metastatic disease) clinical trial was provided in a poster presentation lead by Chief Investigator Professor Hardev Pandha, MD, PhD, Director of the Surrey Cancer Research Institute at the University of Surrey in the UK.

Part A of the STORM trial, now near completion, is designed to establish a safety profile and determine an effective intravenous dosing schedule for successful tumour targeting for CAVATAK given as a single agent to patients with advanced solid tumours. Updated clinical data from biopsies of tumour tissue from patients with melanoma, non-small cell lung (NSCLC) and metastatic bladder cancer confirmed successful systemic tumour targeting by detecting CAVATAK in these samples following three intravenous doses of CAVATAK. Infection of the tumour by CAVATAK can potentially strengthen anti-cancer activity by increasing levels of immune-cell infiltration, enhancing a potential systemic antitumour immune response and increasing the levels of target immune-checkpoint molecules for potential checkpoint inhibitor combination strategies.

The recently initiated Part B of the STORM study (KEYNOTE 200) being undertaken in collaboration with Merck & Co is designed to assess the safety and efficacy of intravenously delivered CAVATAK in combination with KEYTRUDA<sup>1</sup> (pembrolizumab) in patients with advanced non-small cell lung (NSCLC) or metastatic bladder cancer. KEYTRUDA, a checkpoint inhibitor, is a human programmed death receptor-1 (PD-1) blocking antibody that has yielded significant tumour responses in patients with solid tumours.

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<sup>1</sup> KEYTRUDA is a trademark of Merck & Company Inc.



Preclinical studies in an immune-competent mouse model of NSCLC confirmed that the combination of intravenous delivered CAVATAK and the murine form of anti-PD-1 monoclonal antibody resulted in a greater survival benefit compared to use of either agent alone.

"Based on the results in Part A of the STORM study, which demonstrated tumour targeting by CAVATAK, and the positive outcomes from the preclinical combination studies, there is considerable encouragement for potential synergy from the combination of intravenous CAVATAK with checkpoint inhibitors such as KEYTRUDA," stated Professor Pandha. "Part B of the STORM study has recently been initiated at two sites, and we look forward to assessing the combination of these two novel immunotherapies."

#### Poster Presentation

- *Phase I STORM study (KEYNOTE 200): Intravenous delivery of a novel oncolytic immunotherapy agent, Coxsackievirus A21 in combination with pembrolizumab in advanced cancer patients. (Abstract # TPS3108)*

The poster and abstract are available on the Viralytics website at:

<http://www.viralytics.com/our-pipeline/scientific-presentations/>

#### **CALM Clinical Trial and CALM Extension Study**

Additional results from the 70-patient Phase 2 CALM (CAVATAK in Late-Stage Melanoma) clinical trial, including an extension cohort, were reported in a poster presentation by Lead Investigator Robert Andtbacka, MD, CM, of the Huntsman Cancer Institute at the University of Utah.

The CALM trial investigated the efficacy and safety of intralesional CAVATAK in 57 patients with advanced melanoma, resulting in a confirmed overall response rate<sup>2</sup> (ORR) of 28.1 percent and a durable response rate<sup>3</sup> (DRR) of 21.1 percent. Additionally, tumour responses were observed in injected lesions; non-injected, non-visceral lesions, and in distant non-injected visceral lesions.

CAVATAK demonstrated anti-cancer activity in pre-treated patients, with a similar ORR observed in patients administered with prior immunotherapy<sup>4</sup> of 29 percent

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<sup>2</sup> Overall response rate includes either complete or partial responses that may occur at any time after initiation of treatment. A complete tumour response (irRECIST 1.1) is the disappearance of all tumour burden. A partial tumour response (irRECIST 1.1) is a reduction in the total tumour burden by greater than 30%

<sup>3</sup> Durable response is a response lasting continuously for  $\geq 6$  months as assessed by irRECIST 1.1 criteria

<sup>4</sup> Immunotherapy including agents such as ipilimumab (YERVOY, trademark of Bristol-Myers Squibb Company), pembrolizumab (KEYTRUDA, trademark of Merck & Company Inc) or talimogene laherparepvec (IMLYGIC, trademark of BioVex, Inc., a subsidiary of Amgen Inc.)



(9/31), compared to patients administered other treatments (i.e. non-immunotherapy) of 27 percent (7/26).

The level of the tumour volume at the initiation of CAVATAK therapy was shown to affect the response rate. The median baseline tumour burden<sup>5</sup> (BTB) in the CALM study was 3.9 cm. A less-than-or equal to median BTB vs greater-than-median BTB was associated with a superior ORR (39.3 percent vs 17.2 percent), superior DRR (35.7 percent vs 6.9 percent), and a statistically significant greater rate of overall survival ( $p = 0.003$ ).

In the 13-patient CALM extension study, biopsies were taken from melanoma lesions prior to and after the administration of CAVATAK. Results from the tumour tissue analysis demonstrate that CAVATAK was able to facilitate notable changes within the tumour microenvironment by:

- Inducing increases in immune cell infiltrates (CD3+ and CD8+ T cells) and increased expression of PD-L1, in particular within lesions displaying stable disease or response. Reconstitution of immune cell infiltrates was observed in a number of CAVATAK-treated lesions from patients failing prior treatment with checkpoint inhibitors<sup>6</sup>.
- Significantly up-regulating a number of immune checkpoint inhibitory molecules in injected melanoma lesions, including CTLA-4, PD-L1, LAG-3, TIM-3 and IDO.

Increases in the number of immune cell infiltrates and up-regulation of the checkpoint molecules in tumour tissue may be predictive of future tumour response, particularly when used in combination with checkpoint inhibitors, an important new class of anti-cancer agents that work by taking the brakes off the immune response to cancer and have application across a broad range of cancer types.

According to Dr Andtbacka, "CAVATAK has demonstrated the potential to increase the immunological heat within the tumour micro-environment, thereby generating a systemic anti-tumour immune response and driving widespread non-injected lesion responses. The changes induced by CAVATAK set the scene for potential enhanced activity when combined with checkpoint inhibitors, as demonstrated in the early promising response data from the Phase 1b MITCI<sup>7</sup> study. I look forward to further exploring the activity of CAVATAK in the combination setting."

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<sup>5</sup> The baseline tumour burden is the sum of the measurable length (the longest diameter in the plane of measurement) of the tumour lesions.

<sup>6</sup> Checkpoint inhibitors include the anti-PD1 antibodies such as nivolumab (OPDIVO, trademark of Bristol Myers Squibb Company) and pembrolizumab (KEYTRUDA, trademark of Merck & Company Inc) and the anti-CTLA4 antibodies such as ipilimumab (YERVOY, trademark of Bristol Myers Squibb Company). Analysts forecast these three agents may achieve total annual revenues of more than US\$20Bn by 2020.

<sup>7</sup> MITCI (Melanoma Intra-Tumoural CAVATAK and Ipilimumab)



#### Poster Presentation

- *Dynamics of tumour response in advanced melanoma patients treated with Cocksackievirus A21 (Abstract # 9553)*
- Presenter: Dr Robert Andtbacka MD, CM, Associate Professor at the University of Utah-based Huntsman Cancer Institute and Lead Study Investigator for the CALM trial.

The poster and abstract are available on the Viralytics website at:

<http://www.viralytics.com/our-pipeline/scientific-presentations/>

#### **About VIRALYTICS and CAVATAK™**

Viralytics is developing oncolytic immunotherapy treatments for a range of cancers. The company's lead investigational product, CAVATAK™, is currently being studied in Phase 1 and 2 clinical trials for the treatment of melanoma, as well as prostate, bladder and lung cancers. Intratumoural, intravenous and intravesicular delivery routes are under investigation. Two combination studies with checkpoint inhibitors are underway in advanced melanoma patients, as well as a combination study of CAVATAK and KEYTRUDA in late-stage lung and bladder cancer patients.

Further details on our clinical and pre-clinical data can be found at:

<http://www.viralytics.com/our-pipeline/clinical-trials/>

CAVATAK is a proprietary bioselected formulation of the common cold Cocksackievirus Type A21 (CVA21) that preferentially binds to specific 'receptor' proteins highly expressed on multiple cancer types. CAVATAK acts to kill both local and metastatic cancer cells through cell lysis and the generation of an immune response against the cancer cells – a two-pronged mechanism of action known as oncolytic immunotherapy.

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. For more information, please visit [www.viralytics.com](http://www.viralytics.com).

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