



ASX and Media Release

Viralytics' CAVATAK™ in Combination with KEYTRUDA® Provides Promising Results in Advanced Melanoma from the CAPRA 1b study

Other CAVATAK Trials Updated at Cancer Immunotherapy Conference

14 November 2016, Sydney, Australia: [Viralytics Limited](#) (ASX: VLA, OTC: VRACY) today reported updated positive clinical results from the ongoing Phase 1b CAPRA (CAVATAK and Pembrolizumab in Advanced Melanoma) clinical trial of the company's lead drug candidate, [CAVATAK™](#), in combination with KEYTRUDA®¹ at the [31st Annual Meeting of the Society for the Immunotherapy of Cancer \(SITC\)](#) in National Harbor, Maryland, USA.

Updates were also presented from four additional CAVATAK clinical trials in a range of combinations and cancer types, including late-stage melanoma, bladder cancer, and non-small cell lung cancer.

CAVATAK is a novel cancer immunotherapy based on a proprietary cold virus that has been shown to preferentially infect and attack cancer cells.

Patient Disease Control Rate of 100 Percent and Objective Response Rate of 70 Percent Shown in Phase 1b CAPRA Trial

The Phase 1b CAPRA trial is designed to evaluate the safety and tolerability of the established dose of intratumoral CAVATAK in combination with KEYTRUDA, an anti-PD-1 therapy, in 30 patients with advanced melanoma. Investigators are also assessing evidence of anti-cancer activity, including response rates and bio-markers of anti-tumour immunity.

According to the preliminary data from the first 10 patients evaluable for best overall tumour response assessment, a disease control rate² (DCR) of 100 percent (10/10 patients) was demonstrated, including seven patients (70 percent) with an objective tumour response and three patients (30 percent) with stable disease.

¹ KEYTRUDA® is a trademark of Merck and Co.

² Disease control rate includes patients that live with the cancer without it worsening. It includes patients that achieve a complete tumour response, partial tumour response or stable disease. A complete tumour response (immune related Response Criteria) is the disappearance of all tumour burden. A partial tumour response is a reduction in the total tumour burden by greater than 50%. Progressive disease is a 25% increase in tumour burden and all other cases are stable disease.

Currently, these response rates in a small number of patients exceed the published rates for either agent used alone (CAVATAK: 28 percent and KEYTRUDA: ~33 percent³) in patients with late-stage melanoma.

Responses were observed in injected lesions, non-injected non-visceral lesions, and in distant non-injected visceral lesions, including lung and liver metastases. The best overall response rate in six patients with advanced disease with liver, lung or other visceral metastases was 100 percent (6/6 patients).

Objective responses in 86 percent (6/7) and a disease control rate of 100 percent (7/7 lesions) were observed in individual non-injected visceral and non-visceral target lesions.

No grade 3 or higher CAVATAK or KEYTRUDA treatment-related adverse events⁴ have been observed, and no dose-limiting toxicities have been reported in patients receiving this combination treatment to date.

“Although the number of patients treated is small, I am impressed with these early results demonstrating very promising response rates, in patients with advanced metastatic disease,” said Dr Howard Kaufman, MD, FACS, Associate Director for Clinical Sciences at the Rutgers Cancer Institute of New Jersey in New Brunswick and Principal Investigator for the CAPRA trial. “The low incidence and grade of adverse events are also encouraging. The response rates and side event profile of this novel immunotherapy combination compare favourably with other combination clinical trials in melanoma.”

“We are very pleased with these initial results, which, along with the [MITCI](#)⁵ study, suggest that CAVATAK may be able to drive enhanced activity when used in combination with checkpoint inhibitors such as KEYTRUDA and YERVOY^{®6},” said Dr Malcolm McColl, Managing Director of Viralytics. “In both the CAPRA and MITCI studies, we are seeing increased activity in difficult-to-treat, late-stage patients with a low rate of adverse events, signalling the potential of CAVATAK in combination with the checkpoint inhibitors to improve the treatment of melanoma and other cancer types.”

The poster presentation, entitled “*Interim results of the CAPRA clinical trial: CAVATAK and pembrolizumab in advanced melanoma*” is available from the Viralytics website at <http://www.viralytics.com/our-pipeline/scientific-presentations/>.

³ Merck KEYTRUDA package insert: ipilimumab naïve patients treated with 10mg/kg pembrolizumab every 3 weeks.

⁴ Grade 3 adverse events are severe or medically significant but not immediately life-threatening; Grade 4 adverse events are life-threatening with urgent intervention indicated; Grade 5 is death related to an adverse event.

⁵ MITCI (Melanoma Intra-Tumoral CAVATAK and Ipilimumab) study.

⁶ YERVOY[®] is a trademark of the Bristol-Myers Squibb Company.

Disease Control Rate of 78 Percent Shown in Phase 1b MITCI Clinical Trial

Led by Dr Brendan Curti, MD, Director, Biotherapy Program, Earle A Chiles Research Institute at the Providence Cancer Center, Portland, Oregon, the Phase 1b MITCI (Melanoma Intra-Tumoral CAVATAK and Ipilimumab) clinical trial is evaluating the safety and anti-cancer activity of CAVATAK in combination with YERVOY (ipilimumab) in late-stage melanoma patients.

According to data from the first 18 patients evaluable for best overall tumour response assessment, a disease control rate (DCR) of 78 percent (14/18 patients) was demonstrated, including nine patients (50 percent) with a confirmed objective tumour response and five patients with stable disease. Of these 18 patients, 66 percent had been previously treated with at least one line of systemic therapy.

No dose-limiting toxicities, and no CAVATAK-related grade 3 or higher adverse events have been reported. There has been one YERVOY-related grade 3 fatigue adverse event.

The poster presentation, entitled “*A phase 1b study of intratumoral CAVATAK (coxsackievirus A21) and ipilimumab in patients with advanced melanoma*” is available from the Viralytics website.

Phase 1b KEYNOTE 200 (STORM) Clinical Trial Advances

Part B of the STORM (Systemic Treatment Of Resistant Metastatic disease) clinical trial, also known as the KEYNOTE 200 trial, is being conducted in collaboration with Merck (known as MSD outside the United States and Canada). The trial is evaluating intravenously delivered CAVATAK in combination with KEYTRUDA in patients with advanced non-small cell lung cancer (NSCLC) or metastatic bladder cancer in order to establish a recommended dosing regimen and to evaluate anti-cancer activity and patient tolerability.

Six patients in the first two cohorts have been enrolled in the KEYNOTE 200 trial. To date, the combination of CAVATAK and KEYTRUDA has been generally well tolerated. Only one grade 3 CAVATAK-related adverse event (awaiting confirmation) has been observed, with no dose limiting toxicities for the combination of CAVATAK and pembrolizumab being reached.

Part A of the STORM trial is complete. The trial was designed to establish a safety profile and determine an intravenous dosing schedule for successful tumour targeting for CAVATAK given as a single agent to patients with advanced solid tumours. In addition, clinical data from biopsies of tumour tissue from patients with melanoma, non-small cell lung cancer (NSCLC) and

metastatic bladder cancer confirmed successful systemic tumour targeting by detecting CAVATAK in these samples following three intravenous doses of the agent. There was also evidence of possible tumour-specific secondary viral replication, 48 to 72 hours following intravenous administration of CAVATAK. CAVATAK was well tolerated in this trial, with no dose-limiting toxicities.

The poster presentation, entitled “*A combination study of an intravenously delivered oncolytic virus, Coxsackievirus A21 in combination with pembrolizumab in advanced cancer patients: phase Ib KEYNOTE 200 (STORM study)*” is available from the Viralytics website.

Phase 1 / 2 CANON Clinical Trial Shows Successful Tumour Targeting

Results from the completed Phase 1/2 CANON (CAVATAK in NON-muscle invasive bladder cancer) clinical trial were reported in a podium presentation by Dr Nicola Annels BSc PhD, Senior Research Fellow, University of Surrey, England. The presentation was part of the *State-of-the-Art Immunotherapies: Challenges and Opportunities* session.

The CANON study investigated the tolerance of escalating doses of CAVATAK delivered intravesically (directly into the bladder through a catheter) in 16 first-line patients with non-muscle invasive bladder cancer (NMIBC) prior to routine surgical removal of the tumour tissue. The trial explored CAVATAK given either as a single agent or in combination with a sub-therapeutic dose of the chemotherapy, mitomycin C, also delivered intravesically.

Clinical activity of CAVATAK was demonstrated by evidence of viral replication and notable signs of tumour inflammation following either single or multiple administrations of CAVATAK in multiple patients. While the study was not designed to assess efficacy, a complete response was observed in one out of the three patients in the highest-dose cohort of the monotherapy.

Whether used alone or in combination with mitomycin C, CAVATAK facilitated notable changes within NMIBC tissue biopsies taken from treated patients by inducing increases in immune cell infiltrates and up-regulating immune checkpoint inhibitory genes such as PD-L1, compared to tissue samples taken from untreated patients.

In addition, the intravesicular administration of CAVATAK either as a single agent or in combination was generally well tolerated with no Grade 2 or higher product-related adverse events.

The presentation and accompanying slide presentation, entitled “*Phase I/II CANON study: oncolytic immunotherapy for the treatment of non-muscle invasive bladder (NMIBC) cancer using intravesical Coxsackievirus A21*”, are available from the Viralytics website.



Phase 2 CALM Extension Trial Demonstrates that CAVATAK Changes the Tumour Microenvironment

Results from the completed CALM (CAVATAK in Late-Stage Melanoma) extension trial were described in a poster presented by Lead Investigator Robert Andtbacka, MD, CM, of the Huntsman Cancer Institute at the University of Utah.

The CALM extension trial was conducted in a 13-patient cohort of the 70-patient Phase 2 CALM clinical trial, designed to investigate the efficacy and safety of intralesional CAVATAK in advanced melanoma. In the 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, including increased immune cell infiltrates and greater expression of PD-L1 and other immune checkpoint inhibitory molecules, in particular within lesions displaying stable disease or response.

The poster presentation and accompanying slide presentation, entitled *"Phase II CALM extension study: intratumoral CAVATAK™ increases immune-cell infiltrates and up-regulates immune-checkpoint molecules in the microenvironment of lesions from advanced melanoma patients"*, are available from the Viralytics website.

About Viralytics Ltd:

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 bladder and lung cancers. CAVATAK is a proprietary formulation of the common cold Coxsackievirus 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 potential 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.

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