



ASX and Media Release

CAVATAK™ Increases Anti-Cancer Immune Activity in the Tumour Micro-environment

**CALM Extension Study Results Presented at 2016 American Association for Cancer Research
Annual Meeting**

19 April 2016, Sydney, Australia: [Viralytics Limited](#) (ASX: VLA, OTC: VRACY) today reported the latest data from its CALM¹ extension clinical study, designed to assess changes in tumour tissue following the administration of [CAVATAK™](#) in patients with advanced melanoma. The results were reported in a poster presentation at the [American Association for Cancer Research \(AACR\) Annual Meeting 2016](#) in New Orleans, LA.

In the 13-patient CALM extension study, biopsies were taken from melanoma lesions following the intratumoral delivery of CAVATAK and then monitored for evidence of CAVATAK-induced changes in the tumour micro-environment. The results show that CAVATAK was able to influence the dynamics of the tumour micro-environment by inducing anti-cancer immune activity in the tumour tissue, as evidenced by the infiltration of immune cells (such as killer T-cells) and the up-regulation of key immune checkpoint molecules (such as PD-L1, CTLA-4, LAG-3, TIM-3 and IDO) on cancer cells.

“These changes in the tumour micro-environment were particularly evident within lesions displaying stable disease or response, and thus may provide some early predictive marker of a future tumour response.” noted Dr Robert Andtbacka M.D., C.M. of the Huntsman Cancer Institute, Utah, and Principal Investigator. “The up-regulation of immune checkpoint molecules LAG-3, TIM-3 and IDO, in addition to that of the more well known molecules PD-L1, CTLA-4 provides additional targets for new potential strategies of immune checkpoint blockade.”

Notably, such CAVATAK-induced changes signal the potential for complementary activity when combined with other immunotherapies such as checkpoint inhibitors – as indicated by positive initial results from the Phase 1b combination clinical trial assessing CAVATAK and the checkpoint inhibitor YERVOY®² in late-stage melanoma patients. In this study, known as the MITCI (Melanoma Intra-Tumoral CAVATAK and Ipilimumab) trial, preliminary overall response rates for the combination were higher than published response rates for either CAVATAK or YERVOY used alone.

As reported in the literature, elevated levels of the checkpoint molecule, PD-L1, have also been associated with improved response rates in cancer patients treated with anti-PD-1 monoclonal

¹ The CALM (CAVATAK in Late-Stage Melanoma) Phase 2 study

² Yervoy is a trademark of the Bristol-Myers Squibb Company



antibodies such as KEYTRUDA^{®3} (pembrolizumab). Viralytics' clinical evaluation of the activity of intratumoral injection of CAVATAK in combination with KEYTRUDA in patients with late-stage melanoma is also underway in the Phase 1b CAPRA (**CAVATAK** and **PembRolizumab** in **Advanced Melanoma**) study. In addition, a Phase 1b combination trial of CAVATAK and KEYTRUDA, known as the KEYNOTE-200 (STORM Part B) study, has recently been initiated in late-stage lung and bladder cancer patients.

According to Dr. Andtbacka, "Based on these results, CAVATAK may also have potential application in a rescue strategy to reconstitute the immune cells within the tumor micro-environment of cancers that currently respond poorly to immune checkpoint inhibitors."

As members of a new class of cancer treatments known as immunotherapies, CAVATAK, YERVOY and KEYTRUDA are designed to enhance the body's own defences in fighting cancer. CAVATAK is an investigational agent based on a proprietary bioselected common cold virus that has been shown to preferentially infect and attack cancer cells. YERVOY and KEYTRUDA are immune checkpoint inhibitors that work by taking the brakes off the body's natural immune response to cancer.

The abstract and poster presentation, entitled "*Intratumoral Coxsackievirus A21 increases immune-cell infiltrates and up-regulates immune-checkpoint molecules in the tumor micro-environment of advanced melanoma patients: Phase II CALM Extension study*", are available from 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. Intratumoral, 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 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 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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³ Keytruda[®] is a trademark of Merck & Company Inc



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