Aim: CAVATAK, an oncolytic immunotherapy, is a bio-selected oncolytic strain of Coxackievirus A21. Following intratumoral injection, CAVATAK preferentially infects ICAM-1 expressing tumor cells, resulting in cell lysis and a systemic anti-tumor immune response. We here report on the key secondary endpoints in the Phase II CALM study.

Methods: The CALM study investigated the efficacy and safety of intratumoral CAVATAK in 57 patients with treated or untreated unresectable Stage IIIC-IVM1c melanoma. Patients received up to $3 \times 10^8$ TCID50 CAVATAK intratumorally on study days 1, 3, 5 and 8 and then every three weeks for a further 6 injections. Patients displaying immune-related progression-free survival (irPFS) or better at 6 months were eligible for 9 additional injections. Key eligibility criteria were ECOG 0-1, and at least 1 injectable cutaneous, subcutaneous, or nodal melanoma metastasis >1.0 cm. The primary endpoint was to achieve >9 of 54 evaluable patients with irPFS at 6 months. Secondary endpoints included median irPFS, 1-year survival, median time to response, irRECIST 1.1 best overall response (BORR) and safety.

Results: The primary endpoint of the study was achieved with 19 of 51 (37.3%) evaluable patients displaying irPFS at 6 months. Preliminary analysis of secondary endpoints showed: median irPFS of 4.2 months (95% CI 2.8, 8.3), 1-year survival 61.5% (16 of 26 pts), on-going BORR (irRECIST 1.1) 26.3% (15 of 57 pts) with responses seen in both injected and non-injected lesions, median time to response 2.8 months. To date 15 patients have received additional series of CAVATAK injections. The most common patient side effects observed were Grade 1 local injection site reactions, fatigue, chills and fever. There were no Grade 3 or 4 product-related AEs.

Conclusions: Intralesional CAVATAK is a promising novel oncolytic immunotherapeutic agent with limited toxicity and robust responses in both injected and non-injected lesions in patients with advanced melanoma. The effectiveness of CAVATAK warrants additional investigation as monotherapy and in combination with other targeted immunotherapies such as immune checkpoint blockade.