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# ASLAN's DHODH inhibitor shows efficacy in AML patients

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**New positive data from the ongoing phase 2a study of ASLAN003 for the treatment of acute myeloid leukaemia (AML) was presented at the 60th American Society of Hematology (ASH) Annual Meeting in San Diego, US.**



**Singapore -** ASLAN Pharmaceuticals, a clinical-stage biopharmaceutical company targeting cancers that are both highly prevalent in Asia and orphan indications in the United States and Europe, announced the presentation of new positive data from the ongoing phase 2a study of ASLAN003 for the treatment of acute myeloid leukaemia (AML) at the 60th American Society of Hematology (ASH) Annual Meeting in San Diego, US.

ASLAN003 is an orally active, potent inhibitor of dihydroorotate dehydrogenase (DHODH) that has the potential to be first-in-class in AML. As of 16 November 2018, 14 patients with AML ineligible for standard treatment (including relapsed, refractory and treatment naïve) had been enrolled in the multicentre dose optimisation study to evaluate ASLAN003 monotherapy administered as a 28-day cycle. Eight patients had received at least one post-treatment assessment at the cut-off date and were evaluable for efficacy. Of the 8 evaluable patients, 4 patients showed clinical signs of efficacy: 2 patients (1 in the 100mg once daily [QD] cohort and 1 in the 200mg QD cohort) exhibited evidence of myeloid differentiation and 1 patient in the 100mg QD cohort developed suspected differentiation syndrome. Overall, 4 patients had stable disease for more than 3 months.

ASLAN003 has been well tolerated in patients treated to date. The most commonly occurring related adverse events were leukocytosis, nausea and rash, with grade 3 / 4 leukocytosis in 1 patient. The study contains 4 cohorts for the optimum dose determination (100 mg, 200 mg QD, and 100 mg, 200 mg BID with planned enrolment of 6 patients for each cohort), and an additional expansion cohort with the selected optimum dose (20 patients).

Dr Carl Firth, CEO of ASLAN Pharmaceuticals, commented: “This study is the first time that a DHODH inhibitor has been tested in this subset of AML patients and we are encouraged to observe signs of clinical activity and safety, even at the lowest dose, in patients who have limited treatment options and poor clinical outcomes. We continue to dose cohorts and hope to see further promising signs of efficacy as we optimise the dose.”

AML is a rapidly progressing blood cancer that is characterised by the uncontrolled proliferation of immature blast cells in the bone marrow. The five-year cancer survival rate for AML patients is 26.9%. The majority of AML patients relapse or present with refractory disease and have overall poor prognosis.

The primary outcome of the phase 2a study is to determine the optimum monotherapy dose of ASLAN003 and provide a preliminary estimate of efficacy evaluated by overall complete remission rate (OCRR). A phase 1 trial showed that ASLAN003

demonstrated dose proportional pharmacokinetics and was safe and well tolerated in healthy volunteers compared to the side effect profiles of existing AML induction and maintenance chemotherapies. ASLAN003 has demonstrated potent inhibition of DHODH (up to two orders of magnitude stronger than first generation DHODH inhibitors), lack of toxicities associated with first generation inhibitors and other novel AML therapies, and the potential to induce differentiation in blast cells and applicability in a broad range of AML patients. The US Food and Drug Administration has granted ASLAN003 Orphan Drug Designation as a treatment for AML.

ASLAN will also present new data from a preclinical study evaluating the effects of ASLAN003 on cell growth, differentiation, apoptosis, and gene expression changes in AML cell lines and primary bone marrow cells from patients with AML.