

**TRIAL IN PROGRESS: A PHASE 1B/2 STUDY OF ALRIZOMADLIN (APG-115), ALONE OR COMBINED WITH 5-AZACITIDINE, IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (R/R AML)**

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**Background** Acute myeloid leukemia (AML) is the most common form of acute leukemia in adults, with an incidence that increases with age and a generally poor prognosis. This aggressive blood and bone-marrow malignancy is characterized by rapid and uncontrolled clonal proliferation of abnormal myeloid progenitor cells. Patients with R/R AML have very few approved treatment options, especially in the absence of a targetable mutation. Alrizomadlin is a novel, orally active, potent, small-molecule selective inhibitor that destabilizes the p53-MDM2 complex and activates p53-mediated apoptosis in tumor cells with wild-type TP53 and/or MDM2 amplification. In acute leukemia human wild-type TP53 AML cell lines and xenograft models, alrizomadlin potently inhibited tumor cell growth when administered alone or with concomitant chemotherapy.

**Methods** This US open-label study is evaluating the safety and tolerability of alrizomadlin, with or without 5-azacitidine, in adults with histologically confirmed R/R AML and adequate organ function. Eligible candidates will have AML with no known available therapies that are either indicated or expected to confer a durable response. In Part 1 of this trial, the safety and tolerability of alrizomadlin monotherapy are being assessed by evaluating the dose-limiting toxicity rate during the first 4 weeks of treatment, using a standard 3+3 design. The starting once-daily oral dose of alrizomadlin administered on Day 1 to 5 of every 28-day cycle is 100 mg, increasing to 150, 200, and 250 mg in each subsequent cohort. The severity of adverse events is being assessed using NCI CTCAE v5.0. Once the recommended phase 2 dose (RP2D) has been determined, 3 to 6 additional patients will be enrolled in the dose-expansion phase. In Part 2, alrizomadlin will be administered in combination with 5-azacitidine 75 mg/m<sup>2</sup>/day on Days 1–7 of a 28-day cycles. Alternatively, a 5-days-on, 2-days-off, 2-days-on schedule is allowed if consecutive day infusion is not available. A standard 3+3 design will also be implemented to determine the maximum tolerated dose/RP2D in the dose-escalation phase. Once the RP2D has been determined, there will be an expansion cohort of up to 15 patients. As of July 13, 2021, 2 patients have been enrolled in the alrizomadlin monotherapy dose-escalation phase. The overall estimated enrollment will be 69 study participants. Internal study identifier APG115AU101. ClinicalTrials.gov identifier: NCT04358393.

**Trial Registration** ClinicalTrials.gov identifier: NCT04358393

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