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POSTER ABSTRACTS

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Safety and Efficacy Results from CLI120-001 a Phase 1 Study in RR-AML and HR-MDS: Update from Higher Dose Levels

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Background: RVU120, a first-in-class CDK8/19 kinase inhibitor, showed antileukemic activity mediated by inhibition of STAT5 phosphorylation in AML cell lines and patient-derived cells.Clinical activity in a population of patients with relapsed/refractory AML and HR-MDS with poor prognostic factors was shown in a currently ongoing phase 1 dose escalation study (NCT04021368) consistent with the preclinical evidence of both cytotoxic and erythroid and myeloid differentiation effects in cell and mouse models.
Aims: The primary objective of the study is to determine the safety profile and the recommended phase 2 dose (RP2D) of RVU120 as a single agent in R/R AML and HR-MDS. Secondary objectives include the characterization of PK, antitumor activity, and exploratory pharmacodynamic (PD) effects.
Methods: CLI120-001 is an open-label, multi-center, dose escalation study. RVU120 is administered orally every other day, for a total of 7 doses, in a 3-week treatment cycle until disease progression or unacceptable toxicity. Adverse events are graded according to NCI-CTCAE v.5.0. DLTs are assessed at the completion of Cycle 1. Disease evaluation is performed according to Dohner 2017 and Cheson 2006 response criteria for AML and MDS respectively. Pharmacodynamic assessments (PD) include a flow cytometry assay to assess target engagement by evaluating changes in phosphorylated STAT5.
Results: As of 26 Jul 2023, 31 patients received RVU120 at doses between 10 and 175 mg, median age 71 years, median of 3 prior lines of therapy. ECOG PS was 2 in 8 pts, 1 in 20 pts, and 0 in 3pts. No severe drug reactions, no DLT have been reported, with manageable nausea and vomiting being the most frequent treatment-emergent adverse events. Twelve out of the 24 evaluable patients showed clinically relevant benefit. Four patients achieved a reduction of blasts to <5% in the BM: One patient with NPM1 and FLT3 mutated AML, achieved a CR, 3 patients with HR-MDS had a marrow CR, one of those had G3 BM fibrosis and is currently in C3 of treatment. 3 additional patients treated across different dose levels experienced a sustained BM blast reduction: 2 patients with TP53+ AML with 37% and 74% BM blast reduction, 1 patient with AML-MRC and monosomy 7 with 28% blast reduction; 1 patient with AML-MRC failing 4 lines of therapy received allogeneic BM transplantation after 6 cycles of RVU120 treatment. 5 patients achieved hematology improvement including: 1 patient with HR-MDS failing 2 lines of therapy, 1 patient with AML secondary to MF, became RBC transfusion independent (TI) and is still ongoing after >18 months with nearly normal Hgb and Plts values. 2 patients with AML-MRC, with baseline RBC and

Plt transfusion dependance (TD), became TI and reached normal Plts values. 1 patient with AML-MRC with RBC and Plt TD and severe neutropenia showed RBC and Plt TI and ANC recovery and is currently in C7 of treatment. A correlation between pSTAT5 inhibition and RVU120 exposure was observed.

Conclusion: In the ongoing phase 1 trial, RVU120 shows clinical activity in both AML and HR-MDS, inducing RBC transfusion independence and blast reduction with a tolerable safety profile. Clearance of BM blasts including a formal CR were observed in patients treated at different dose levels. Relevant target inhibition is achieved from 110 mg onwards with expected higher pSTAT 5 inhibition with further dose escalation.

Disclosures Patkowska: *KCR US:* Consultancy; *Amgen:* Honoraria; *Novartis:* Honoraria, Other: support for attending/traveling to meetings; *Servier:* Honoraria, Other: support for attending/traveling to meetings; *Angelini:* Honoraria, Other: support for attending/traveling to meetings; *Astellas Pharma:* Honoraria, Other: support for attending/traveling to meetings; *Bristol Myers Squibb:* Other: support for attending/traveling to meetings; *Jazz Pharma:* Other: support for attending/traveling to meetings; *Pfizer:* Other: support for attending/traveling to meetings. **Jakacka:** *Ryvu Therapeutics, Regeneron and Celgene:* Research Funding. **Burris:** *Roche/Genentech, Bristol-Myers Squibb, Incyte, AstraZeneca, MedImmune, Macrogenics, Novartis, Boehringer Ingelheim, Lilly, Seattle Genetics, Merck, Agios, Jounce Therapeutics, Moderna Therapeutics, CytomX Therapeutics, GlaxoSmithKline, Verastem, Tesaro, B:* Research Funding. **Angelosanto:** *Ryvu Therapeutics:* Current Employment. **Rzymski:** *Ryvu Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Littlewood:** *Ryvu Therapeutics:* Consultancy, Current Employment, Current equity holder in publicly-traded company. **Kuś:** *Ryvu Therapeutics:* Current Employment. **Sroka-Porada:** *Ryvu Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Dudziak:** *Ryvu Therapeutics:* Consultancy. **Nogai:** *Ryvu Therapeutics:* Current Employment, Current equity holder in publicly-traded company; *Bayer Consumer Care:* Current equity holder in publicly-traded company, Ended employment in the past 24 months. **Glasmacher:** *Brystol Meyers Squibb:* Divested equity in a private or publicly-traded company in the past 24 months, Honoraria; *Ryvu Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Bradley:** *Gilead:* Membership on an entity's Board of Directors or advisory committees; *Geron Corporation:* Consultancy; *NOVARTIS:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau. **Borthakur:** *Catamaran Bio, Abbvie, PPD Development, Protagonist Therapeutics, Janssen:* Consultancy; *Astex Pharmaceuticals, Ryvu, PTC Therapeutics:* Research Funding; *Pacylex, Novartis, Cytomx, Bio Ascend::* Membership on an entity's Board of Directors or advisory committees. **Mouhayar:** *Ryvu Therapeutics:* Honoraria. **Kościółek- Zgódka:** *ABBVIE:* Honoraria. **Szymańska:** *Regeneron:* Research Funding; *Roche:* Research Funding; *Jansen:* Research Funding; *BeiGene:* Research Funding. **Zaucha:** *Abbvie:* Honoraria; *Pfizer:* Honoraria; *Amgen:* Honoraria; *Takeda:* Honoraria; *Roche:* Honoraria; *Novartis:* Honoraria; *Gilead:* Honoraria; *AstraZeneca:* Honoraria; *Medical University of Gdańsk:* Current Employment; *BMS:* Honoraria, Research Funding; *Pierre Fabre:* Honoraria; *MSD:* Research Funding.

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