VENCLYXTO Clinical Trial Program

Study 1: Previously treated patients with CLL harboring 17p deletion
The safety and efficacy of VENCLYXTO was evaluated in a Phase 2, single arm, open-label, multi-center study in 107 patients (main cohort) with previously treated CLL with 17p deletion, with an additional 51 patients in a safety expansion cohort. Patients followed a 4- to 5-week dose-titration schedule starting at 20 mg and increasing to 50 mg, 100 mg, 200 mg and finally 400 mg once-daily. Patients continued to receive VENCLYXTO 400 mg once daily until disease progression or unacceptable toxicity was observed. The median time on treatment at the time of evaluation was 12 months (range: 0 to 22 months) for the main cohort. The median time on treatment for the combined cohort (main cohort plus safety expansion cohort, N=158) was 25 months (range: 0.5 to 50 months). The main cohort was assessed by an independent review committee, while the combined cohort was assessed by the investigators. Results showed:**Error! Bookmark not defined.**

- The primary efficacy endpoint, overall response rate (ORR), was 79 percent (95% Confidence Interval [CI]: 70.5, 86.6) in the main cohort and 77 percent (95% CI: 69.9, 83.5) in the combined cohort.
- Median duration of response (DOR) was not reached in the main cohort and was 27.5 months (95% CI: 26.5, NR) for the combined cohort.
- Median progression-free survival (PFS) was not reached in the main cohort and was 27.2 months (95% CI: 21.9, NR) for the combined cohort.
- Complete remission (CR) plus complete remission with incomplete marrow recovery (CRi) was achieved in 7 percent of patients in the main cohort and 18 percent of patients in the combined cohort.
- Partial remission (PR) was reached in 69 percent of patients in the main cohort and 53 percent of patients in the combined cohort.
- Nodular partial remission (nPR) was reached in 3 percent of patients in the main cohort and 6 percent of patients in the combined cohort.
- Minimal residual disease (MRD) was evaluated in 93 of 158 patients who achieved CR, CRi or nPR with VENCLYXTO. MRD negativity in peripheral blood was achieved in 27 percent (41/158) of patients, including 15 patients who were MRD negative in the bone marrow. MRD negativity is an exploratory endpoint.

Study 2: Patients with CLL who have failed a B-cell receptor inhibitor
The safety and efficacy of VENCLYXTO was evaluated in a Phase 2 open-label, multi-center, non-randomized study in patients with CLL who had been previously treated with and failed ibrutinib (median number of prior oncology treatments was 4 [range: 1 to 12]) or idelalisib (median number of prior oncology treatments was 3 [range: 1 to 11]) therapy. Patients received VENCLYXTO via a recommended dose-titration schedule. Patients continued to receive VENCLYXTO 400 mg once daily until disease progression or unacceptable toxicity was observed. At the time of data cut-off, 64 patients were enrolled and treated with VENCLYXTO. Of these, 43 patients had received prior ibrutinib therapy (Arm A) and 21 had received prior idelalisib therapy (Arm B). Of the patients, 91 percent (39/42) in Arm A and 67 percent (14/21) in Arm B had relapsed on or were refractory to ibrutinib and idelalisib, respectively. Chromosomal aberrations were 11q deletion (30%, 19/62), 17p deletion (36%, 23/61), TP53 mutation (26%, 16/61) and unmutated IgVH (86%, 36/42). At the time of

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evaluation, median duration of treatment with VENCLYXTO was 11.7 months (range: 0.1 to 17.9 months). Results showed:

- The primary efficacy endpoint, ORR, was 67 percent (95% CI: 51.5, 80.9) in Arm A, 57 percent (95% CI: 34, 78.2) in Arm B and 64 percent (95% CI: 51.1, 75.7) in the total study population based on investigator assessment. The efficacy data were further evaluated by an IRC demonstrating a combined ORR of 67 percent (Arm A: 70 percent, Arm B: 62 percent).
- The ORR for patients with 17p deletion/TP53 mutation was 71 percent (15/21) (95% CI: 47.8, 88.7) in Arm A and 50 percent (1/2) (95% CI: 1.3, 98.7) in Arm B.
- For patients without 17p deletion/TP53 mutation, the ORR was 68 percent (15/22) (95% CI: 45.1, 86.1) in Arm A and 63 percent (12/19) (95% CI: 38.4, 83.7) in Arm B.
- Median PFS and DOR were not reached with median follow-up of approximately 12 months for Arm A and 9 months for Arm B.
- CR plus CRi was achieved in 7 percent of patients in Arm A, 14 percent of patients in Arm B and 9 percent of patients in the total patient population, per investigator assessment.
- PR was reached in 56 percent of patients in Arm A, 43 percent of patients in Arm B and 52 percent of patients in the total patient population, per investigator assessment.
- nPR was reached in 5 percent of patients in Arm A, zero percent in Arm B and 3 percent in the total patient population, per investigator assessment.

The safety of VENCLYXTO is based on pooled data of 296 patients treated in two Phase 2 studies and one Phase 1 study. In all, the studies enrolled patients with previously treated CLL, including 188 patients with 17p deletion and 92 patients who had failed a B-cell receptor inhibitor. The most commonly occurring adverse reactions (≥20 percent) of any grade in patients receiving VENCLYXTO were neutropenia/neutrophil count decreased, diarrhoea, nausea, anemia, upper respiratory tract infection, fatigue, hyperphosphatemia, vomiting and constipation. The most frequently reported serious adverse reactions (≥2 percent) were pneumonia, febrile neutropenia and tumour lysis syndrome (TLS). Discontinuations due to adverse reactions occurred in 9.1 percent of patients. Dosage adjustments due to adverse reactions occurred in 11.8 percent of patients.