Phase I Trial of Cobomarsen, a MiR-155 Inhibitor, in HTLV-1 Associated Adult T cell Lymphoma/Leukemia

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Cobomarsen Treatment Results in Durable Clinical Stabilization of Disease after Chemotherapy in Five Patients for up to 13 Months

Case Study: Acute ATLL Patient 101-008

- 49 year old male, diagnosed on 14DEC2016 with acute ATLL
- Relapsed after treatment with Zidovudine, Interferon alfa-2b, Lenalidomide and EPOCH chemotherapy
- Cobomarsen treatment was initiated on 06NOV2017. On cobomarsen monotherapy his tumor cells in peripheral blood have remain stable for over 13 months
- Cobomarsen treatment resulted in normalization of splenic uptake. Flow cytometry at the end of treatment showed 20% ATL cells in peripheral blood
- No deaths while on cobomarsen treatment. One subject (101-011) died from disease progression approximately 2 months after stopping cobomarsen treatment
- Two SAEs of febrile neutropenia and pyrexia (in the same subject 101-011) There have been no new opportunistic infections reported. Comorbid opportunistic infections are often seen as a result of immunosuppression caused by dysfunctional HTLV-1–infected T cells

Case Study: Lymphomatous ATLL Patient 101-010

- 47-year-old male, diagnosed on 21APR2017 with lymphomatous ATLL

Extensive and bulky lymphadenopathy on initial CT scan was reduced significantly by 6 cycles of CHOP chemotherapy regimen completed in June 2017
- Restaging PET scan showed resolution of adenopathy but with increased splenic uptake. Flow cytometry at the end of treatment showed 20% ATL cells in peripheral blood
- Cobomarsen treatment on 11DEC2017 has maintained stable lymph node size and peripheral blood tumor cell counts for 12 months. Recent CT scan remains normal
- No deaths while on cobomarsen treatment. Rhinovirus infection in November 2018 shows a normal immune response

Cobomarsen Decreases Activation and Proliferation Status of Circulating Tumor Cells in ATLL Subjects

- All ATLL subjects in current Phase 1 study have >20% Ki-67+ PMBCs at baseline, which correlates to less than 4 months predicted survival. Ki-67 expression correlates with poor survival in ATLL patients
- Cobomarsen treatment appears to decrease the proliferative index leading to prolonged survival
- The number of patients preselected is calculated so as to achieve 20% in the predicted population

CONCLUSIONS

- Cobomarsen is well tolerated with no evidence of immunosuppression. There are no reported opportunistic infections in these subjects, as normally seen in this patient population
- Acute and lymphomatous patients, who were enrolled after a partial response (remission) but remain with low tumor burden, have been candidates for any therapy known to benefit these patients
- Historical data demonstrates that tumor cells from acute ATLL patients have a higher proliferative index (Ki-67+) than cells from chronic ATLL patients, and this increased proliferative capacity correlates with decreased survival time

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