Preliminary Results of the Stapled Peptide ALRN-6924, a Dual Inhibitor of MDMX and MDM2, in Two Phase IIa Dose Expansion Cohorts in Relapsed/Refractory TP53 Wild-Type Peripheral T-Cell Lymphoma

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Key Inclusion Criteria
- A histologically confirmed diagnosis of PTCL based on pathology review at the local institution, using the most recent edition of the WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues as guidance.
- Relapsed or refractory disease after at least one but not more than 7 prior systemic anticancer regimens.
- A histologically confirmed diagnosis of PTCL based on pathology review at the local institution, using the most recent edition of the WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues as guidance.
- WT TP53 status of T-cell lymphoma cells.

Background

Figure 1: The Cell-Permeating α-helical Peptide, ALRN-6924, is a First-in-Class Dual Inhibitor of MDMX and MDM2

A. The natural responder protein to disrupt its interactions with both its endogenous inhibitors, MDMX and MDM2. Stapled peptides mimic natural peptide sequences at the interface of protein-protein interactions, displaying a larger surface area of interaction with its target, and providing superior binding properties.

B. Targeting α-helical Peptide, ALRN-6924, is a First-in-Class Dual Inhibitor of MDMX and MDM2

C. Peptide interaction with α-helical Peptide, ALRN-6924.

Primary Objectives of the Two Expansion Cohorts

- Assessed overall response rate.
- Evaluated the safety and tolerability of ALRN-6924 given once weekly and three times per week.

Methods

- Patients with relapsed or refractory PTCL are receiving treatment with 3.1 mg/kg of ALRN-6924 IV over 1 hour on:
  - Cohort A (QW dosing) Days 1, 8, and 15 of a 28-day cycle.
  - Cohort B (TIW dosing) Days 1, 8, and 15 of a 28-day cycle.
- Response is evaluated by investigators according to IWG 2014. Additionally, an independent radiologist
- Preliminary activity observed in Cohort A (QW dosing) of this early phase clinical trial is similar to that reported with other available agents in relapsed/refractory PTCL patients.

Conclusions and Study Statistics

- ALRN-6924 as single agent has shown an acceptable safety profile on both QW and TIW dosing schedules,
- with better treatment compliance with QW schedule.
- Preliminary activity observed in Cohort A (QW dosing) of this early phase clinical trial is similar to that reported with other available agents in relapsed/refractory PTCL patients.
- Despite encouraging data from preclinical models, TIW dosing schedule islogically challenging. Reduced response rates observed with TIW dosing are likely due to poor treatment compliance resulting in shorter treatment duration.
- The potential for pseudoprogression was not initially recognized; hence raising the possibility that the response rate for QW may be higher had treatment with ALRN-6924 been continued.
- Enrollment expected to complete by year-end 2018; future development path for PTCL to be decided.

References

2. Meric-Bernstam F. et al., Phase I trial of a novel stapled peptide ALRN-6924 disrupting MDMX and MDM2-mediated

Figure 2: Treatment Duration

Figure 3: Example of Pseudoprogression in QW Patient