Pharmacodynamic Biomarker Characterization of ALX148, a CD47 Blocker, in Combination with Established Anticancer Antibodies in Patients with Advanced Malignancy

Hong-I Wan1, Laura GM Chow2, Justin Gainor3, Nehal Lakhani4, Hyun Chung5, Kean-Wook Lee6, Jeeyun Lee6, Patrisia LoRussio4, Yang-Jue Bang7, Stephen Hod6, Rafael Santana-Davi8, Wells Mossersmith9, Philip Finnings10, Pierre Squifflet11, Feng Jin12, Tracy Kuo13, Sangeetha Bolli2, Jaime Pons14, Sophia Randolph15

1. The Johns Hopkins Medical Institutions, Baltimore, MD; 2. UCSF Benioff Children’s Hospital Oakland, Oakland, CA; 3. Dana Farber Cancer Institute and Harvard Medical School, Boston, MA; 4. Dana Farber Cancer Institute, Boston, MA; 5. University of Utah Cancer Center, Salt Lake City, UT, USA; 6. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; 7. University of Miami Sylvester Comprehensive Cancer Center, Miami, FL; 8. University of Florida College of Medicine, Jacksonville, FL; 9. Korea University Cancer Center, Seoul, Republic of Korea; 10. Korea University Anam Hospital, Seoul, Republic of Korea; 11. Samsung Medical Center, Seoul, Korea; 12. Tata Cancer Center, New Haven, CT, USA; 13. Yale National University Hospital, Incheon, Korea; 14. Vara Institute of Oncology, Bologna, Italy; 15. University of Colorado Cancer Center, Aurora, CO, USA.

Background

- CD47 signaling is a superficial transmembrane protein that supports immune evasion. In the context of the tumor microenvironment, CD47 plays a key role in engaging the high-avidity CD47 receptor (sLFA-1) on neutrophils and macrophages. ALX148 is a novel synthetic small molecule that targets a domain of CD47 distinct from sLFA-1.

Methods

**AT48501 Study Design**

- 1. Assessment of tumor infiltrating immune cells and molecular signatures in paired biopsies from patients with HNSCC that has progressed on prior systemic therapy.
- 2. Paired biopsies (C10) Day 188
- 3. Patients received ALX148, pembrolizumab, or ALX148 + trastuzumab.

**Clinical Results**

- ALX148 is associated with a reduction in patient mortality and a trend toward an improvement in clinical benefit compared with standard of care.

**Pharmacodynamic Results**

- ALX148 is a CD47 blocker that can block tumor infiltrating immune cell interactions.