ADU-100 Combines with Checkpoint Inhibition to Elicit an Anti-Tumor CD8+ T Cell Response to Control Non-Injected Tumors

Kelsey Sivick Gautieri, Anthony L. Desbien, Gabrielle Reiner, Weiwen Deng, Leticia Corrales, Natalie H. Surh, Brian Francia,1 Laura Hix Glickman,2 David B. Kan, Justin L. Leong, Ken Mitchette, Lianxing Zheng, Charles Cho, Yan Feng, Jeffrey M. McKenna, Steven L. Bender, Chudi Nduabu, Meredith L. Leong, Andrea van Elsas,1 and Sarah M. McWhirter

1Aduro Biotech, Inc, Berkeley, CA, 2Currently in Research Therapeutics, Berkeley CA, 3Novartis Institute for BioMedical Research, Cambridge MA, 4Genomics Institute of the Novartis Research Foundation, San Diego, CA

Presented at the 2018 Society for Immunotherapy of Cancer, November 7-10, 2018, Washington, DC

**Background**

- T-cell infiltrated tumors in humans are correlated with an interferon (IFN)-α/-γ transcriptional signature in the tumor microenvironment.
- Approaches to stimulate priming of CD8+ T cells specific for any individual’s unique neo-antigen repertoire and/or initiate productive immune responses in “cold” tumors have potential as cancer immunotherapies.
- STING (stimulator of interferon genes) is a cytosolic Cyclic Dinucleotide (CDN) synthesize that can activate the innate immune system.

**Results**

- A cyclic dinucleotide containing two adenine units (ADU) in syngeneic flank tumor mouse models.
- ADU treatment optimized for CD8+ T cells and tumor-associated antigen.
- ADU injection induced high levels of IFN-γ in tumor-draining lymph nodes (TDLN).
- ADU treatment increased CD8+ T cell proliferation in TDLN, as well as in the injected TDLN.

**Conclusions**

- The magnitude of the tumor-specific CD8+ T cell response is dependent on the dose of ADU-100.
- Lower immunogenic dosing regimens result in local STING activation and durable adaptive immune responses.
- Higher ablative dosing regimens, while effective in clearing injected tumors, result in systemic drug distribution and compromised T cell immunity.
- In a dual flank setting, ablative dosing results in displacement of STING-dependent immune activation of the non-injected tumor and TDLN.
- Immunogenic doses of ADU-100 combine effectively with checkpoint inhibitors to elicit tumor-specific T cell responses, anti-tumor efficacy, and durable immunity.

**Acknowledgements**

- Phases I trials evaluating the safety and efficacy of nontoxic clinical candidate ADU-100 in combination with either ipilimumab or nivolumab are ongoing. (Clinicaltrials.gov: NCT03173639, NCT03173493; see poster P260).