Data: ATSP-7041 as first-in-class p53 pathway re-activator for solid, hematologic cancers

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Aileron Therapeutics, Inc., a clinical stage biopharmaceutical company that is developing first-in-class therapeutics based on its proprietary Stapled Peptide drug platform, announced today the publication of preclinical data on ATSP-7041, a potent and selective stapled peptide re-activator of the wild type p53 tumor suppressor protein. P53, known as "the guardian of the genome" because it repairs damaged DNA or triggers cell death in pre-cancerous cells, is one of the most important known tumor suppressors, as it is shown to be inactivated in virtually all human cancers. As 50% of all cancers circumvent P53's protective mechanisms by the over-expression of the inhibitory proteins MDM2 and MDMX, Aileron's stapled peptide is novel in that it can selectively bind to and inhibit both proteins equally and, thereby, restore the P53 function.

The research, published in *Proceedings of the National Academy of Sciences* (*PNAS*), provides the first detailed publication by Aileron of one of its cell penetrating peptides that is a precursor molecule to one that the company is developing for the treatment of both liquid and solid tumors. The paper, entitled "Stapled ??Helical Peptide Drug Development: A Potent Dual Inhibitor of MDM2 and MDMX for p53-Dependent Cancer Therapy," expands on data reported by the company in poster presentations at the 2012 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics and the 2013 International MDM2 workshop in Cambridge, England.

"As evidenced by the multitude of research and clinical efforts, the full activation of p53 has been the goal of cancer researchers for decades given its [ubiquitous] role in all human cancers" said Joseph A. Yanchik III, president and chief executive officer of Aileron Therapeutics. "Our stapled peptide drug will be the first full-activator of wild type p53 of its kind to our knowledge to enter clinical trials. Our unique approach to restore p53 activity through direct inhibition of both MDM2 and MDMX has the potential to deliver greater efficacy and safety than existing small molecule approaches, which are primarily limited to inhibition of just MDM2. We look forward to advancing the p53 program into clinical trials next year that will represent our second stapled peptide drug to enter human clinical trials."

Key findings from the paper showed that ATSP 7041:

- suppressed tumor growth in animal models of multiple human xenograft models, including breast cancer and bone cancer
- is an equipotent dual inhibitor of MDM2 and MDMX that restores p53 specific activity
- is a peptide that efficiently penetrated cell membranes and exhibited a more durable on mechanism effect on p53 signaling than small-molecule MDM2-selective inhibitors
- exhibited favorable drug-like and pharmacokinetic properties that can support convenient clinical dosing regimens [including the potential for once-weekly dosing]

Provided by Aileron Therapeutics, Inc.