Arvinas Collaborators Present Data on BET PROTAC Degraders at 2016 ASH Annual Meeting

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NEW HAVEN, Conn., Dec. 6, 2016 /PRNewswire/ -- Arvinas LLC, a private biotechnology company creating a new class of drugs known as PROTACs which function via targeted protein degradation, today announced that preclinical data were presented by three Arvinas collaborators at the 2016 American Society of Hematology (ASH) Annual Meeting in San Diego, CA. The data presented demonstrate superior efficacy of PROTACs targeting the BET (bromodomain and extraterminal domain) protein family when compared to BET inhibitors in preclinical models of lymphoma and leukemia.

"The data further support our ongoing understanding of how the Arvinas BET PROTACs show pronounced efficacy improvements compared to BET inhibitors in *in vitro* and *in vivo* model systems. The advantages of BET degradation have now been demonstrated preclinically in a number of solid tumor and hematologic cancers including diffuse large B cell lymphoma, prostate cancer, ovarian cancer, mantle cell lymphoma and acute myeloid leukemia (AML)," said Manuel Litchman, M.D., President and CEO of Arvinas.

"These findings underscore the superior activity of BET PROTACs versus BET inhibitors against mantle cell lymphoma cells that are either sensitive or resistant to the drug ibrutinib, as well as against models of AML," said Kapil Bhalla, M.D., Professor of Leukemia at the University of Texas MD Anderson Cancer Center.

In a podium presentation titled "Novel BET PROTACs Exert Potent Single Agent and Synergistic Activity with Ibrutinib and Venetoclax Against Human Mantle Cell Lymphoma Cells" and presented by Dr. Bhalla, data show:

- Compared to BET inhibitors, in primary mantle cell lymphoma (MCL) cells and MCL cell lines, BET PROTACs provide greater down-regulation of the expression of genes important to tumor growth and survival, greater killing of cells resistant to ibrutinib and greater inhibition of the growth of ibrutinib-resistant MCL xenografts alone and in combination with rationally selected targeted agents.

Dr. Sujan Piya of the University of Texas MD Anderson Cancer Center presented data on Arvinas BET PROTAC ARV-825 in a podium presentation titled "BRD4 PROTAC ARV-825 Causes Sustained Degradation of BRD4 and Modulation of Chemokine Receptors, Cell Adhesion and Metabolic Targets in Leukemia Resulting in Profound Anti-Leukemic Effects."

- As a single agent, ARV-825 demonstrated substantial activity across multiple models of AML, including cell lines, primary AML blasts and a mouse model of human leukemia.
- In all tested cell lines and primary cells, the BET PROTAC was significantly more potent than a BET inhibitor.
- Importantly, in a co-culture model, ARV-825 was shown to modulate the tumor microenvironment and metabolism to overcome stroma-mediated drug resistance.

Dr. Warren Fiskus of the University of Texas MD Anderson Cancer Center delivered a podium presentation titled "Superior Lethal Activity of Novel BET PROTAC Versus BET Inhibitor Against Post-Myeloproliferative Neoplasm Secondary AML Cells (sAML)."

- Arvinas BET PROTACs were significantly more potent than a BET inhibitor in inducing apoptosis-driven cell death of patient-derived and cultured secondary AML (sAML) cells and caused greater depletion of several key sAML signaling and survival proteins.
- Co-treatment of BET PROTAC ARV-825 and JAK inhibitor ruxolitinib showed synergistic lethality against sAML cells.
- Notably, BET PROTACs both alone and in combination with either an HSP90 inhibitor or a BCL2/BcL-xL antagonist were highly active against JAK inhibitor-resistant sAML cells.
- Compared to a BET inhibitor, treatment with BET-PROTAC ARV-771 significantly reduced leukemia growth and improved survival of mice engrafted with sAML cell xenografts.

Abstracts are available on the Arvinas website under Publications at www.arvinas.com.

About Arvinas
Arvinas is a pharmaceutical company focused on developing new small molecules – known as PROTACs (PROteolysis TArgeting Chimeras) – aimed at degrading disease-causing cellular proteins. Based on groundbreaking research conducted at Yale University by Founder and Chief Scientific Advisor, Dr. Craig Crews, the company is translating innovative protein degradation approaches into novel drugs for the treatment of cancer and other diseases. The company's new PROTAC-based drug paradigm induces protein degradation, rather than protein inhibition, and offers the advantage of potentially targeting "undruggable" as well as "druggable" elements of the proteome. This greatly expands the ability to create drugs for many new, previously unapproachable targets. For more information, visit www.arvinas.com.

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