Arvinas Presents New Preclinical Data on Oral Androgen Receptor PROTAC® ARV-110 at ASCO 2018 Genitourinary Cancers Symposium

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Data show complete degradation of androgen receptor in models of enzalutamide-resistant prostate cancer

NEW HAVEN, Conn., Feb. 9, 2018 /PRNewswire/ -- Arvinas LLC, a private biotechnology company creating a new class of drugs based on protein degradation, today announced the presentation of new preclinical data on ARV-110, its oral androgen receptor (AR) PROTAC degrader, during a poster session at the American Society of Clinical Oncology 2018 Genitourinary Cancers Symposium (ASCO GU) in San Francisco.

"More than half of patients whose disease progresses on enzalutamide or abiraterone, exhibit genetic aberrations in the AR gene in their tumors, confirming that the androgen receptor remains a principal driver of metastatic prostate cancer," noted John Houston, Ph.D., President and Chief Executive Officer of Arvinas. "Our preclinical data on oral AR PROTAC ARV-110 suggests that eliminating the receptor will be beneficial to patients, particularly those that would recur on standard of care."

The poster titled, "An oral androgen receptor PROTAC degrader for prostate cancer" (abstract 381), highlights the *in vitro*and *in vivo* pharmacodynamics and efficacy of ARV-110 in preclinical prostate cancer models. The studies show that degradation of the androgen receptor with ARV-110 leads to inhibition of AR target gene expression and the proliferation of prostate cancer cell lines. In both classical *in vivo* prostate cancer xenografts and enzalutamide-resistant prostate cancer models, ARV-110 is well tolerated and demonstrates robust efficacy at low oral doses, accompanied by AR degradation and inhibition of AR signaling.

Regulating AR signaling has long shown benefit in controlling the progression of prostate cancer but efficacy is limited using current standard of care AR inhibitors. Arvinas' approach to addressing prostate cancer focuses on degrading the AR, resulting in more profound anti-cancer effects and differential biology, versus inhibition. Inhibition is a competitive process so increased androgen production, and increased expression of the AR and specific mutations of the receptor are well-studied mechanisms of resistance to AR inhibition. PROTAC-mediated degradation is an iterative, event-driven process, and therefore less susceptible to increases in endogenous ligand, target expression, or mutations in the target.

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

About PROTAC Platform
The PROTAC Platform offers potential improvements over traditional small molecule inhibitors by using the cell's natural and selective ubiquitin proteasome system to degrade disease-causing proteins. By removing target proteins directly rather than simply inhibiting them, PROTACs can provide multiple advantages over small molecule inhibitors which can require high systemic exposure to achieve sufficient inhibition, often resulting in toxic side effects and eventual drug resistance. With multiple protein targets, Arvinas' PROTAC platform has demonstrated that a transient binding event at a range of binding sites and affinities can translate into very potent degradation of the target protein.

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 via proteolysis. Based on innovative research conducted at Yale University by Dr. Craig Crews, Founder and Chief Scientific Advisor, the company is translating natural protein degradation approaches into novel drugs for the treatment of cancer and other diseases. The proprietary PROTAC-based drug paradigm induces protein degradation, rather than protein inhibition, using the ubiquitin proteasome system 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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