



## Arvinas Releases Updated Dose Escalation Data from Clinical Trial of PROTAC® Protein Degradar ARV-110 in Patients with Metastatic Castration-Resistant Prostate Cancer

May 29, 2020

*- Clear efficacy signal with two ongoing confirmed PSA responses, including one associated with a confirmed RECIST response -*

*- Data represent the first demonstration of PROTAC®-mediated degradation of a disease-causing protein in humans -*

NEW HAVEN, Conn., May 29, 2020 (GLOBE NEWSWIRE) -- Arvinas, Inc. (Nasdaq: ARVN), a clinical-stage biotechnology company creating a new class of drugs based on targeted protein degradation, today announced updated data from the dose escalation portion of the company's Phase 1/2 clinical trial of ARV-110 in men with metastatic castration-resistant prostate cancer (mCRPC), to be shared as an oral presentation at the 2020 American Society of Clinical Oncology (ASCO) Annual Meeting on May 29, 2020. ARV-110 is a potent, selective, orally available androgen receptor (AR) degrader, and the ASCO presentation highlights promising clinical activity, including both efficacy and AR degradation, in a heavily pretreated patient population.

"For ARV-110 to show signs of efficacy in these patients at this early stage of development is strong validation of our PROTAC® technology," said John Houston, Ph.D., President and Chief Executive Officer at Arvinas. "In addition, seeing AR degradation demonstrates that ARV-110 is acting on-mechanism to achieve this result, and we are excited to continue clinical development in the hope of bringing a new therapeutic option to patients with significant unmet need."

"The responses we see are the first powerful examples in patients of the potential benefits of protein degradation pharmacology compared to classic inhibition or antagonism, which failed in these patients while degradation showed clinical benefit," added Ron Peck, M.D., Chief Medical Officer at Arvinas. "This is a patient population where other therapies would be expected to have little to no benefit, and we are very pleased with the early clinical efficacy data and safety profile we are seeing and think it bodes well for both ARV-110 and the PROTAC® platform."

The dose escalation portion of Arvinas' Phase 1/2 clinical trial of ARV-110 is designed to assess safety, tolerability, and pharmacokinetics (PK) in men with mCRPC who have progressed on standard of care therapies, as well as to identify a recommended Phase 2 dose. To date, ARV-110 has shown a favorable safety profile, and PK have been generally dose proportional, reaching exposures associated with tumor inhibition in preclinical models at 140 mg. In the data released today, Arvinas also shared evidence of in-tumor AR reduction, the first demonstration of successful targeted protein degradation by a PROTAC® protein degrader in humans.

ARV-110 has demonstrated evidence of activity at doses and in AR mutational backgrounds in which responses would be expected based on preclinical data. As of the April 20, 2020 data cut-off, 20 patients were evaluable for prostate-specific antigen (PSA) response, including 12 patients treated at 140 mg or higher (these 12 patients exclude one patient who received two weeks of therapy prior to discontinuing due to a rosuvastatin-related dose limiting toxicity).

Of those 12 patients treated at 140 mg and above, circulating tumor DNA (ctDNA) analysis of five patients showed AR forms not degradable by ARV-110 in preclinical studies (i.e., L702H point mutations and AR-V7 splice variants). In the group of seven remaining patients who had forms of AR degradable by ARV-110 (other AR point mutations, AR amplification, and wildtype AR), two patients achieved confirmed PSA responses that remain ongoing with additional follow-up since the abstract was submitted.

One of these patients had a 74% decline from baseline in PSA and remained without progression after 30 weeks, as of the data cut-off. This patient did not have measurable disease at baseline for assessment by Response Evaluation Criteria in Solid Tumors (RECIST). The second patient had both a deep PSA response (97% decline from baseline) and a confirmed RECIST response (80% decrease from baseline in tumor mass) and remains without progression after 18 weeks. Both responses, which were in patients at the 140 mg dose, were achieved by ARV-110 despite prior enzalutamide, abiraterone, chemotherapy, and other therapies. Tumors from both patients have H875Y and T878A point mutations in AR, which are known to drive resistance to current standard of care treatments and have been degraded by ARV-110 in preclinical studies. In addition to these two patients, PSA reductions were observed in other patients but did not meet a 50% reduction in PSA threshold at data cutoff, and four patients remain on ARV-110 without radiographic progression for at least 20 weeks.

A potential drug-drug interaction between ARV-110 and rosuvastatin (ROS) was identified during the trial. Of the 22 patients enrolled, two had concurrent use of ROS. One patient receiving 280 mg ARV-110 experienced a Grade 4 dose-limiting toxicity (DLT) of elevated aspartate transaminase/alanine transaminase (AST/ALT) followed by acute renal failure. The second patient, receiving 70 mg ARV-110, experienced a Grade 3 AST/ALT elevation, which resolved after the removal of ROS, and the patient was retreated with ARV-110. Follow-up exploratory findings indicate that ROS concentrations were elevated in both patients who had liver function test (LFT) increases. Subsequent *in vitro* transport pump studies indicate that ARV-110 inhibits breast cancer resistant pump (BCRP) transporter, of which ROS is a substrate. Following the initial data that supported a potential interaction with ROS, concomitant use of ROS was precluded, and no other related Grade 3 or 4 adverse events have since been reported. Six other patients have received concomitant non-ROS statins without AST/ALT adverse events.

Dose escalation and enrollment continues, with the most recent cohort initiating dosing in May 2020 at 420 mg. The expansion portion of the Phase 1/2 trial is expected to begin once the recommended Phase 2 dose has been determined and will evaluate the anti-tumor activity of ARV-110 through assessment of PSA response, using the Prostate Cancer Working Group 3 Criteria, and overall RECIST response rate in patients with measurable disease. The expansion will further investigate a link between AR genomic profile and efficacy, which could inform an enrichment strategy. Arvinas plans to provide updated information on the ARV-110 Phase 1/2 study by the end of 2020.

**Arvinas Webcast Investor Meeting**

The company will host a conference call and webcast at 8:30 AM ET today to discuss these data. Participants are invited to listen by dialing (844) 467-7654 (domestic) or (602) 563-8497 (international) five minutes prior to the start of the call and providing the passcode access code 8069179. A listen-only webcast of the conference call can also be accessed through the "Investors + Media" tab on the Arvinas website, [www.arvinas.com](http://www.arvinas.com), and a replay will be available for six weeks following the call.

#### **About ARV-110**

ARV-110 is an orally bioavailable PROTAC<sup>®</sup> protein degrader designed to selectively target and degrade the androgen receptor (AR). ARV-110 is being developed as a potential treatment for men with metastatic castration-resistant prostate cancer.

ARV-110 has demonstrated activity in preclinical models of AR mutation or overexpression, both common mechanisms of resistance to currently available AR-targeted therapies.

#### **About Metastatic Castration-Resistant Prostate Cancer (mCRPC)**

In the United States, prostate cancer is both the second most prevalent cancer in men and the second leading cause of cancer death in men. The American Cancer Society predicts that one in nine men will be diagnosed with prostate cancer in his lifetime. Metastatic castration-resistant prostate cancer (mCRPC) is defined by disease progression despite androgen deprivation therapy and is often correlated with rising levels of prostate-specific antigen (PSA).

Current AR-targeted standard of care treatments for mCRPC are less effective in patients whose disease has increased levels of androgen production, AR gene or gene enhancer amplification, or AR point mutations. Up to 25 percent of patients do not respond to second-generation hormone therapies like abiraterone and enzalutamide, and the vast majority of responsive patients will ultimately become resistant, resulting in poor prognoses for men diagnosed with this devastating condition.

#### **About Arvinas**

Arvinas is a clinical-stage biopharmaceutical company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development, and commercialization of therapies that degrade disease-causing proteins. Arvinas uses its proprietary technology platform to engineer proteolysis targeting chimeras, or PROTAC<sup>®</sup> targeted protein degraders, that are designed to harness the body's own natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. The company has two clinical-stage programs: ARV-110 for the treatment of men with metastatic castrate-resistant prostate cancer; and ARV-471 for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer. For more information, visit [www.arvinas.com](http://www.arvinas.com).

#### **Forward-Looking Statements**

This press release contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the development and regulatory status of our product candidates, the conduct of and plans for our ongoing Phase 1/2 clinical trials for ARV-110 and ARV-471, the plans for presentation of data from our clinical trials for ARV-110 and ARV-471, the potential advantages and therapeutic potential of our product candidates and the sufficiency of cash resources. All statements, other than statements of historical facts, contained in this press release, including statements regarding our strategy, future operations, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make as a result of various risks and uncertainties, including but not limited to: whether we will be able to successfully conduct Phase 1/2 clinical trials for ARV-110 and ARV-471, complete our clinical trials for our product candidates, and receive results from our clinical trials on our expected timelines, or at all, whether our cash resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements, our expected timeline and other important factors discussed in the "Risk Factors" sections contained in our quarterly and annual reports on file with the Securities and Exchange Commission. The forward-looking statements contained in this press release reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this release.

#### **Media Contacts**

##### **Investors**

Will O'Connor, Stern Investor Relations  
[ir@arvinas.com](mailto:ir@arvinas.com)

##### **Media**

Kirsten Owens, Arvinas Communications  
[kirsten.owens@arvinas.com](mailto:kirsten.owens@arvinas.com)