Arvinas Announces Interim Data from the ARV-766 Phase 1/2 Dose Escalation and Expansion Trial Showing Promising Signals of Efficacy in Late-line mCRPC, Including in Patients with AR L702H Mutations

June 8, 2023

42% of patients with AR ligand binding domain (LBD) mutations achieved PSA_{50}; in patients with AR L702H mutations, 3 of 5 achieved PSA_{50}

ARV-766 was well-tolerated, and activity in a heavily pre-treated patient population supports its potential as a treatment in earlier line settings such as castration-sensitive prostate cancer (CSPC), with planned initiation of a pre-NHA trial in 2H 2023

NEW HAVEN, Conn., June 08, 2023 (GLOBE NEWSWIRE) -- Arvinas, Inc. (Nasdaq: ARVN), a clinical-stage biotechnology company creating a new class of drugs based on targeted protein degradation, today announced promising interim data from the Company's Phase 1/2 dose escalation and expansion trial of ARV-766 in men with metastatic castration-resistant prostate cancer (mCRPC). ARV-766 is an investigational orally bioavailable PROTAC® protein degrader designed to degrade all clinically relevant resistance-driving point mutations of the androgen receptor (AR), including L702H, a mutation associated with resistance to abiraterone and other AR-pathway novel hormonal agents (NHA). The company will provide an overview of these data during a fireside chat at the Jefferies Healthcare Conference today, June 8, 2023, at 11 a.m. ET, which will be available to view in the Investors and Media section of the Arvinas website.

Data from the Phase 1/2 dose escalation and expansion trial show that ARV-766 was well-tolerated and demonstrated promising activity in a heavily pre-treated, post-NHA, all-comers patient population:

- 42% of patients with AR ligand binding domain (LBD) mutations achieved PSA_{50}
  - In all patients with L702H mutations, 3 of 5 achieved PSA_{50}
    - In patients with co-occurring T878/H875/L702 mutations, 3 of 3 achieved PSA_{50}
- RECIST (Response Evaluation Criteria in Solid Tumors) partial responses were observed:
  - Of four RECIST-evaluable patients with AR LBD mutations, one achieved a confirmed partial response, and one achieved an unconfirmed partial response
- ARV-766 has been well tolerated and the majority of treatment-related adverse events (TRAEs) have been Grade 1 or 2, with no Grade ≥4 TRAEs and no dose limiting toxicities
- Low rates of discontinuation (1 of 47) and dose reductions (2 of 47)

"Tumor resistance mechanisms such as AR LBD mutations are increasing with earlier use of NHAs, leaving limited treatment options for men with prostate cancer in the post-NHA setting," said John Houston, Ph.D., president and chief executive officer at Arvinas. "It's very exciting to see ARV-766 show signs of efficacy in these late-line patients, including in patients with L702H mutations. Our AR franchise now includes data showing two active clinical compounds with good tolerability profiles and the potential to address high unmet need in castrate-resistant and castrate-sensitive prostate cancer."

"The patients in this trial received extensive prior therapy for mCRPC and had limited alternative treatment options," said Ron Peck, M.D., chief medical officer at Arvinas. "These data increase our confidence in our ability to bring innovative treatment options to a patient population with significant unmet need. We are excited by the progress in our AR franchise and the potential for bavdegalutamide and ARV-766 to address settings across the continuum of prostate cancer and potentially other AR-driven cancers."

About the Phase 1/2 dose escalation and expansion trial of ARV-766

The Phase 1/2 dose escalation and expansion trial of ARV-766 is a seamless trial that includes a Phase 1 dose escalation portion and a Phase 2 dose expansion portion (data cutoff: April 2023). The Phase 1 dose escalation of ARV-766 was designed to assess its safety, tolerability, and pharmacokinetics (PK) in men with mCRPC who have progressed on standard of care therapies, as well as to identify recommended Phase 2 doses for further dose optimization. The Phase 2 expansion cohort is designed to evaluate the antitumor activity of ARV-766 at the two recommended doses (100 mg and 300 mg) and determine the appropriate dose for future development.

In both the Phase 1 dose escalation and Phase 2 dose expansion, 100% of patients were previously treated with at least one or more novel hormonal agents. Patients had a median of 4 prior lines of therapy in the Phase 1 trial and 5 prior lines of therapy in the Phase 2 trial. Multiple prior therapies have been associated with a decreased responsiveness to AR-directed therapies and an increase in tumor heterogeneity.

AR LBD mutations were present in 28% (13 of 47) of patients' tumors in the Phase 1/2 trial as determined by plasma DNA analysis.

Efficacy

Across the Phase 1 and interim Phase 2 data, ARV-766 achieved a 42% PSA_{50} in patients with AR LBD mutations. Three of 5 patients with AR L702H mutations achieved PSA_{50}; the three responding AR L702H patients had co-occurring T878/H875 mutations.

Two of 4 RECIST-evaluable patients with tumors harboring AR LBD mutations had a best observed response of partial response (1 confirmed partial response, 1 unconfirmed partial response).

Safety

ARV-766 has been well tolerated to date and the majority of TRAEs in the Phase 1 dose escalation data and the Phase 2 interim dose expansion data were Grade 1/2. There have been no Grade ≥4 TRAEs. None of the 34 patients treated in the Phase 1 dose escalation portion experienced a dose limiting toxicity. The most frequent TRAEs (>10%) in Phase 1 have been fatigue, nausea, and diarrhea. At the time of data cutoff, no TRAE of >10% frequency was observed in Phase 2.

Forty-seven (47) patients across the Phase 1 and 2 trials were evaluable for safety. No patients discontinued treatment of ARV-766 due to TRAEs in Phase 1, and one patient discontinued treatment due to a TRAE in Phase 2. Two of 47 patients (both in Phase 1) were dose reduced due to TRAEs.

Based on pharmacokinetics, tolerability, and signals of activity in the Phase 1 dose escalation trial, 100 mg and 300 mg, once daily, were selected as the recommended Phase 2 expansion doses. The Phase 2 expansion (N = ~80) began enrolling in October 2022.

Anticipated 2023AR Franchise (bavdegalutamide/ARV-766) Milestones

- Submit and present updated data, including radiographic progression free survival, from the ongoing Phase 1/2 trial with bavdegalutamide at a medical congress (2H 2023).
- Initiate a global Phase 3 trial with bavdegalutamide in mCRPC (2H 2023).
- Complete enrollment in the Phase 1b combination study with bavdegalutamide plus abiraterone (2H 2023).
- Initiate a Phase 1b/2 trial with ARV-766 in combination with abiraterone in patients who have not previously received novel hormonal agents (2H 2023).

About bavdegalutamide (ARV-110) and ARV-766

Bavdegalutamide (ARV-110) and ARV-766 are investigational orally bioavailable PROTAC® protein degraders designed to selectively target and degrade the androgen receptor (AR). Bavdegalutamide and ARV-766 are being developed as potential treatments for men with prostate cancer. Preclinically, both investigational agents have demonstrated activity in models of wild type tumors in addition to tumors with AR mutation or amplification, both common mechanisms of resistance to currently available AR-targeted therapies.

About Arvinas

Arvinas is a clinical-stage biotechnology 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 PROTAC® Discovery Engine platform to engineer proteolysis targeting chimeras, or PROTAC® 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. In addition to its robust preclinical pipeline of PROTAC® protein degraders against validated and "undruggable" targets, the company has three investigational clinical-stage programs in development: bavdegalutamide and ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer; and vepdegestrant (ARV-471) for the treatment of patients with early and locally advanced or metastatic ER positive/human epidermal growth factor receptor 2 (HER2) negative (ER+/HER2-) breast cancer. For more information, visit www.arvinas.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the potential advantages and therapeutic benefits of bavdegalutamide (ARV-110) and ARV-766, the development and regulatory status of our product candidates, such as statements with respect to the potential of our lead product candidates bavdegalutamide and ARV-766, the initiation of and timing of the timing of clinical trials, including the timing to complete enrollment, as well as the presentation and/or publication of data from those trials and plans for registration for our product candidates, the potential utility of our technology, the potential commercialization of any of our product candidates, and the sufficiency of our cash resources. All statements, other than statements of historical facts, contained in this press release, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, 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 and complete development for bavdegalutamide and ARV-766, whether we initiate and complete clinical trials for our product candidates and receive results from our clinical trials on our expected timelines or at all; obtain marketing approval for and commercialize bavdegalutamide and ARV-766 and our other product candidates on our current timelines or at all; whether our cash and cash equivalent resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors discussed in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2022 and subsequent other 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.

Contacts
Investors:
Jeff Boyle
+1 (347) 247-5089
Jeff.Boyle@arvinas.com

Media:
Kirsten Owens
+1 (203) 584-0307
Kirsten.Owens@arvinas.com