Potential of Arvinas' PROTAC® AR Degraders Reinforced by 11.1 months rPFS with Bavdegalutamide and Updated Positive Interim Data from Second Generation ARV-766 in mCRPC

October 22, 2023

Data presented at the European Society for Medical Oncology from the Phase 1/2 trial with bavdegalutamide showed 11.1 months radiographic progression free survival in mCRPC patients with tumors harboring AR 878/875 mutations

Interim data from the Phase 1/2 trial of Arvinas' second PROTAC AR degrader, ARV-766, showed robust efficacy in a broader mCRPC patient population with a tolerability profile well-suited to both early- and late-line settings

Company to prioritize the initiation of a Phase 3 trial with ARV-766 in mCRPC

Arvinas will host conference call to discuss results on Sunday, October 22 at 3:00 p.m. CEST / 9:00 a.m. ET

NEW HAVEN, Conn., Oct. 22, 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 the presentation of interim data from the Company's Phase 1/2 clinical trial for bavdegalutamide (ARV-110), a novel PROTAC® protein degrader targeting the androgen receptor (AR), in a poster session at the European Society for Medical Oncology Congress being held in Madrid from October 20 – 24, 2023. The Company will host a conference call to discuss these data and present new data from an updated analysis of its ongoing Phase 1/2 clinical trial with its second-generation PROTAC AR degrader, ARV-766, showing clinical activity extending across patients harboring tumors with AR LBD mutations and a tolerability profile that is superior to bavdegalutamide.

Extended follow-up of data from the Phase 1/2 clinical trial with bavdegalutamide showed radiographic progression free survival (rPFS) of 11.1 months in a subgroup of patients with metastatic castration-resistant prostate cancer (mCRPC) and tumors harboring AR T878X/H878Y mutations (AR 878/875; T878X=T878A or T878S) in the absence of co-occurring AR L702H mutations. AR L702H is a common AR ligand-binding domain (LBD) mutation that is not potently degraded by bavdegalutamide. In patients with tumors harboring any AR LBD mutation except L702H alone, bavdegalutamide showed an rPFS of 8.2 months.

"We are incredibly pleased with the results from bavdegalutamide's Phase 1/2 trial as they demonstrate the promise of our AR PROTAC degraders to help patients with prostate cancer," said John Houston, Ph.D., chairperson, chief executive officer, and president of Arvinas. "While bavdegalutamide's efficacy is very exciting, its breadth of activity could be limited to a small patient population in a late-line setting. Our second generation PROTAC AR degrader, ARV-766, has demonstrated a broader efficacy profile and even better tolerability compared to bavdegalutamide in clinical settings. Arvinas is committed to bringing forward the best PROTAC AR degrader for patients with prostate cancer. We believe ARV-766 has the potential to be a first- and best- in-class treatment for patients with castrate-sensitive and castrate-resistant prostate cancer, and we are prioritizing the initiation of a Phase 3 clinical trial in mCRPC with ARV-766."

Bavdegalutamide is a once-daily, oral, first-in-class PROTAC AR degrader that degrades wild type and all clinically relevant AR LBD mutations except AR L702H. ARV-766 was designed to improve upon the degradation profile of bavdegalutamide by also degrading AR L702H. The prevalence of all AR LBD mutations, especially AR L702H, has increased over time, and these mutations are present in approximately 25% of tumors after initial treatment with a novel hormonal agent (NHA) such as enzalutamide or abiraterone. This represents a potential addressable patient population for ARV-766 that is approximately three times that of bavdegalutamide in the post-NHA population due to its broader degradation profile.

New data from the ongoing Phase 1/2 clinical trial of ARV-766 continues to show robust efficacy in tumors with all LBD mutations (41% PSA_{50}) and in patients with tumors harboring AR L702H mutations (50% PSA_{50}). In addition to a tolerability profile that is superior to bavdegalutamide, early durability data for ARV-766 are encouraging and provide additional support for prioritizing ARV-766 over bavdegalutamide, with PFS data anticipated in 2024.

"I've been involved in trials with both bavdegalutamide and ARV-766. It's gratifying to see these innovative therapies developed in advanced prostate cancer where there remains a significant need for better treatments," said Daniel Petrylak, M.D., Professor of Medicine and Urology at Yale School of Medicine and investigator in the Phase 1/2 studies with bavdegalutamide and ARV-766. "In my experience, these novel therapies have the potential to be an important treatment choice for patients whose tumors harbor androgen receptor LBD mutations, which may be present in up to 25% of metastatic castration resistant prostate cancer. The increasing prevalence of the L702H mutation means that more patients could potentially benefit from the broader efficacy profile offered with ARV-766. The improvement in tolerability that ARV-766 has shown in clinical trials compared to bavdegalutamide is also a big advantage for patients with prostate cancer."

Highlights from the Phase 1/2 trial with bavdegalutamide (data cut-off date Aug. 11, 2023):
In a post-NHA (median prior therapies = 4) mCRPC population, bavdegalutamide at the recommend Phase 2 dose (420 mg, oral, once daily) demonstrated:

- Median rPFS of 11.1 months in patients harboring AR 878/875 mutations and without co-occurring AR L702H mutations (n=26), and median rPFS of 8.2 months in patients with tumors harboring any AR LBD mutation except L702H alone (n=45)
- PSA50 rates of 54% in patients with tumors harboring AR 878/875 mutations and without co-occurring AR L702H, and 36% in patients with tumors harboring any AR LBD mutation except L702H alone
- The presence of AR L702H mutations greatly diminished the efficacy of bavdegalutamide
    - In patients with any tumor harboring an AR L702H mutation, the PSA50 was 8%
- Bavdegalutamide had a manageable tolerability profile with no grade ≥ 4 treatment-related adverse events (TRAEs). The

most common TRAEs were grade 1 and 2 and included nausea (56%), fatigue (35%), vomiting (33%), decreased appetite (25%) and diarrhea (24%). The discontinuation rate due to TRAEs was 10%.

Interim data from the ongoing Phase 1/2 dose escalation and expansion trial of ARV-766 (data cut-off date Aug. 23, 2023)
Data from an updated analysis of the ongoing Phase 1/2 clinical trial demonstrate broad efficacy and excellent tolerability in mCRPC patients with tumors harboring AR LBD mutations, including AR L702H:

- PSA50 of 41% in patients with tumors harboring any AR LBD mutation, and a PSA50 of 50% in patients with any tumor harboring an AR L702H mutation
- ARV-766 was well-tolerated, with no grade ≥ 4 TRAEs. The most common TRAEs were grade 1 or 2 and included fatigue (29%), nausea (14%), vomiting (11%), and diarrhea (11%). The discontinuation rate due to TRAEs was 4%.

Based on ARV-766's superior tolerability profile and encouraging efficacy data to date, Arvinas believes ARV-766 will be a superior PROTAC AR degrader versus bavdegalutamide for both metastatic castration-sensitive prostate cancer (mCSPC) and mCRPC. Arvinas will prioritize the initiation of a Phase 3 clinical trial with ARV-766 in mCRPC instead of the previously planned Phase 3 clinical trial for bavdegalutamide. The Company will initiate discussions with regulatory authorities by 2Q 2024.

Bavdegalutamide Phase 1/2 Poster Presentation
Data from the Phase 1/2 trial is available during a poster session at the 2023 European Society for Medical Oncology (ESMO) Annual Congress in Madrid:

- Date: Sunday, October 22, 2023
- Presentation number: 1803P
- Time: 12:00 – 1:00 p.m. CEST / 6:00 – 7:00 a.m. EDT
- Speaker: Daniel Petrylak, M.D.

The Company will host a conference call and webcast call at 3:00 p.m. CEST / 9:00 a.m. EDT on October 22 to discuss these data as well as previously undisclosed data from the ongoing Phase 1/2 clinical trial with ARV-766. Participants are invited to listen by going to the Events and Presentation section under the Investor page on the Arvinas website at www.arvinas.com. A replay of the webcast will be archived on the Arvinas website following the presentation.

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 androgen receptor tumors in addition to tumors with AR mutations or amplification, both common potential 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: 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 locally advanced or metastatic 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 Arvinas' PROTAC® androgen receptor (AR) degraders, bavdegalutamide and ARV-766; the potential for bavdegalutamide and ARV-766 as treatment choices for patients whose tumors harbor AR ligand binding domain mutation; the potential breadth of activity of bavdegalutamide in a late-line setting; whether ARV-766 will be a first- and best-in class treatment for patients with early- and late-line prostate cancer; the addressable patient population for ARV-766, bavdegalutamide and ARV-766 as compared to bavdegalutamide; the timing of progression free survival data for ARV-766; whether ARV-766 will be a superior PROTAC® AR degrader versus bavdegalutamide for both metastatic castration-sensitive prostate cancer and metastatic castration-resistant prostate cancer; and the timing for Arvinas to initiate discussions with regulatory authorities. 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," "expect," "intend," "may," "plan," "predict," "target," "potential," "will," "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 ARV-766 and bavdegalutamide; 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; our ability to obtain marketing approval for and commercialize our androgen receptor program product candidates on our current timelines or at all; our ability to maintain, expand and protect our intellectual property portfolio; 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, 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