Pfizer Logo

Arvinas And Pfizer Announce Global Collaboration To Develop And Commercialize Protac® Protein Degrader Arv-471

Thursday, July 22, 2021 - 08:00am

– Collaboration combines Arvinas' investigational estrogen receptor-targeting breast cancer therapy with Pfizer's deep experience in breast oncology

therapeutics –

– ARV-471 is currently in Phase 2 development for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer –

– Arvinas to receive $650 million in an upfront payment, in addition to a potential $1.4 billion in milestone payments; profits and costs to be shared

50/50 worldwide –

– Pfizer to complete a $350 million equity investment in Arvinas –

– Investor call on ARV-471 collaboration to take place at 8:30AM ET today with Arvinas and Pfizer Oncology executives -

NEW HAVEN, Conn. and NEW YORK, July 22, 2021 (GLOBE NEWSWIRE) -- Arvinas, Inc. (Nasdaq: ARVN) and Pfizer Inc. (NYSE: PFE) today announced a global collaboration to develop and commercialize ARV-471, an investigational oral PROTAC® (PROteolysis TArgeting Chimera) estrogen receptor protein degrader. The estrogen receptor is a well-known disease driver in most breast cancers. ARV-471 is currently in a Phase 2 dose expansion clinical trial for the treatment of patients with estrogen receptor (ER) positive / human epidermal growth factor receptor 2 (HER2) negative (ER+/HER2-) locally advanced or metastatic breast cancer. Under the terms of the agreement, Pfizer will pay Arvinas $650 million upfront. Separately, Pfizer will make a $350 million equity investment in Arvinas. The companies will equally share worldwide development costs, commercialization expenses, and profits.

"This collaboration has the potential to be transformational, as it combines our leadership in targeted protein degradation with Pfizer's global capabilities and deep expertise in breast cancer. This should significantly enhance and accelerate the development and potential commercialization of ARV-471 while also advancing Arvinas' strategy of building a global, integrated biopharmaceutical company," said John Houston, Ph.D., Chief Executive Officer at Arvinas. "We share Pfizer's deep commitment to people with breast cancer and are thrilled to partner with them to develop this potentially best-in-class therapy. Despite advancements in oncology in

recent years, considerable unmet need persists in the treatment of HR+ breast cancer. Together with Pfizer, we will deploy our PROTAC technology in an effort to help people with this devastating disease."

"Building on Pfizer's established leadership position in breast cancer science and CDK 4/6 inhibition, we are excited to work with Arvinas to maximize ARV-471, the first PROTAC for breast cancer with encouraging early clinical data and a potential novel hormonal therapy backbone for HR+ breast cancer," said Jeff Settleman, Ph.D., Chief Scientific Officer for Oncology Research and Development at Pfizer. "This partnership complements Pfizer's robust research activities in breast cancer, including our multiple next-generation CDK inhibitors currently in early clinical development."

ER is the primary driver of hormone receptor (HR) positive breast cancer, which is the most common breast cancer subtype. Endocrine therapy is a backbone of ER+ breast cancer treatment and is used as monotherapy or as combination therapy as a standard of care across treatment settings. Arvinas and Pfizer are seeking to develop ARV-471 as the potential endocrine therapy of choice for patients and their physicians.

Interim data presented in December 2020 from the ongoing Phase 1 dose escalation clinical trial of ARV-471 in patients with locally advanced or metastatic ER+/HER2- breast cancer indicated its potential as a novel oral ER targeted therapy. This study has enrolled heavily pretreated patients, with all patients having received prior treatment with cyclin-dependent kinase (CDK) 4/6 inhibitors. Despite the advanced stage of disease and heavy pretreatment, these interim data, as of December 2020, demonstrated that ARV-471 can promote substantial ER degradation and exhibits an encouraging clinical efficacy and tolerability profile.

ARV-471 currently is being evaluated as a treatment for metastatic breast cancer in a Phase 1 dose escalation study, a Phase 1b combination study with Pfizer's IBRANCE ® (palbociclib), and a Phase 2 monotherapy dose expansion study (VERITAC). Arvinas and Pfizer expect to initiate two additional trials of ARV-471 in 2021, including a second Phase 1b combination trial with everolimus and a trial in the neoadjuvant setting. In 2022, Arvinas and Pfizer expect to initiate Phase 3 studies across lines of therapy in metastatic breast cancer, including combinations with IBRANCE, followed by pivotal studies in the early breast cancer setting. The two companies had previously announced in 2018 a separate research collaboration and license agreement for the discovery and development of drug candidates using Arvinas' PROTAC technology.

Terms of the Collaboration

The agreement is a worldwide co-development and co-commercialization collaboration. ARV-471 is wholly owned by Arvinas and under the financial terms of the agreement, Pfizer will pay Arvinas $650 million upfront. Separately, Pfizer will invest $350 million in Arvinas, receiving approximately 3.5 million newly issued shares of Arvinas common stock, priced at a 30% premium to the 30-day volume weighted average price on July 20, 2021. This represents an equity ownership stake by Pfizer of approximately 7%.

Arvinas is also eligible to receive up to $400 million in approval milestones and up to $1 billion in commercial milestones, in addition to sharing profits on ARV-471 worldwide.

Arvinas and Pfizer will jointly develop ARV-471 through a robust clinical program designed to position ARV-471 as an endocrine backbone therapy of choice across the breast cancer treatment paradigm, from the adjuvant setting through late-line metastatic disease.

Closing of the equity investment agreement is contingent on completion of review under antitrust laws, including the Hart-Scott-Rodino (HSR) Antitrust

Improvements Act of 1976 in the U.S., and other customary closing conditions.

Goldman Sachs & Co. LLC is acting as the exclusive financial advisor to Arvinas.

Investor Conference Call Details

A conference call and webcast will be held at 8:30 AM ET today with Arvinas and Pfizer Oncology executives to discuss the collaboration. 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 6569429.

Supporting materials for the conference call and webcast will be available here or on the Company's website at www.arvinas.com under Events + Presentations. A replay of the webcast will be archived on the Arvinas website following the presentation.

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 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 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.

Arvinas Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties, including statements regarding the closing of the collaboration with Pfizer, the receipt of upfront, milestone and other payments under the Pfizer collaboration, the investment by Pfizer in Arvinas common stock in connection with the collaboration, the future development and potential marketing approval and commercialization of ARV-471, the potential benefits of the collaboration and the potential advantages and therapeutic benefits of ARV-471 and our other product candidates. 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: the satisfaction or waiver of the conditions to the closing of the Pfizer collaboration and equity investment, each party's performance of its obligations under the collaboration, whether we and Pfizer will be able to successfully conduct and complete clinical development, obtain marketing approval for and commercialize ARV-471 on our current timelines or at all 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.

About IBRANCE® (palbociclib) 125 mg tablets and capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,1 which are key regulators of the cell cycle that trigger cellular progression.2,3 In the U.S., IBRANCE is indicated for the treatment of adult patients with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or with fulvestrant in patients with disease progression following endocrine therapy.

The full U.S. Prescribing Information for the IBRANCE tablets and the IBRANCE capsules can be found here and here.

IMPORTANT IBRANCE® (palbociclib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. One death due to neutropenic sepsis was observed in PALOMA-3. Inform patients to promptly report any fever.

Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 15 of first 2 cycles and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) and/or pneumonitis** can occur in patients treated with CDK4/6 inhibitors, including IBRANCE when taken in combination with endocrine therapy. Across clinical trials (PALOMA-1, PALOMA-2, PALOMA-3), 1.0% of IBRANCE-treated patients had ILD/pneumonitis of any grade, 0.1% had Grade 3 or 4, and no fatal cases were reported. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g. hypoxia, cough, dyspnea). In patients who have new or worsening respiratory symptoms and are suspected to have developed pneumonitis, interrupt IBRANCE immediately and evaluate the patient. Permanently discontinue IBRANCE in patients with severe ILD or pneumonitis.

Based on the mechanism of action, IBRANCE can cause **fetal harm**. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may **impair fertility in males** and has the potential to cause genotoxicity. Advise male patients to consider sperm preservation before taking IBRANCE. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women **not to breastfeed** during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

The **most common adverse reactions (?10%)** of any grade reported in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (80% vs 6%), infections (60% vs 42%), leukopenia (39% vs 2%), fatigue (37% vs 28%), nausea (35% vs 26%), alopecia (33% vs 16%), stomatitis (30% vs 14%), diarrhea (26% vs 19%), anemia (24% vs 9%), rash (18% vs 12%), asthenia (17% vs 12%), thrombocytopenia (16% vs 1%), vomiting (16% vs 17%), decreased appetite (15% vs 9%), dry skin (12% vs 6%), pyrexia (12% vs 9%), and

dysgeusia (10% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (66% vs 2%), leukopenia (25% vs 0%), infections (7% vs 3%), and anemia (5% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were decreased WBC (97% vs 25%), decreased neutrophils (95% vs 20%), anemia (78% vs 42%), decreased platelets (63% vs 14%), increased aspartate aminotransferase (52% vs 34%), and increased alanine aminotransferase (43% vs 30%).

The **most common adverse reactions (?10%)** of any grade reported in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (83% vs 4%), leukopenia (53% vs 5%), infections (47% vs 31%), fatigue (41% vs 29%), nausea (34% vs 28%), anemia (30% vs 13%), stomatitis (28% vs 13%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (66% vs 1%) and leukopenia (31% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Avoid concurrent use of **strong CYP3A inhibitors**. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided. Avoid concomitant use of **strong CYP3A inducers**. The dose of **sensitive CYP3A substrates** with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

For patients with **severe hepatic impairment** (Child-Pugh class C), the recommended dose of IBRANCE is 75 mg. The pharmacokinetics of IBRANCE **have not been studied** in patients **requiring hemodialysis.**

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local

communities to support and expand access to reliable, affordable health care around the world. For more than 170 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Forward-Looking Statements

The information contained in this release is as of July 22, 2021. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about ARV-471 and a global collaboration between Pfizer and Arvinas to develop and commercialize ARV-471, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from the clinical studies; whether and when any applications may be filed for ARV-471 for any potential indications in any jurisdictions; whether and when regulatory authorities may approve any potential applications that may be filed for ARV-471 in any jurisdictions, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether ARV-471 will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of ARV-471; risks related to the satisfaction or waiver of the conditions to closing the transaction in the anticipated timeframe or at all; whether the collaboration between Pfizer and Arvinas will be successful; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

1 IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2019.

2 Weinberg, RA. pRb and Control of the Cell Cycle Clock. In: Weinberg RA, ed. The Biology of Cancer. 2nd ed. New York, NY: Garland Science; 2014:275-329.

3 Sotillo E, Grana X. Escape from Cellular Quiescence. In: Enders GH, ed. Cell Cycle Deregulation in Cancer. New York, NY: Humana Press; 2010:3-22.

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