



Arix Bioscience plc

Artios initiates Phase 2 study of Polθ Inhibitor ART4215 in Combination with PARP Inhibitor Talazoparib in BRCA Deficient Breast Cancer

LONDON, UK, 10 August 2022: Arix Bioscience plc (“Arix” or the “Company”) (LSE: ARIX), a global venture capital company focused on investing in breakthrough biotechnology companies, notes that its portfolio company, Artios Pharma, today announced it has initiated a Phase 2 study with ART4215, a small molecule inhibitor of polymerase theta (Polθ) in combination with talazoparib (TALZENNA®), an oral poly (ADP-ribose) polymerase (PARP) inhibitor in an expansion study for the treatment of BRCA deficient breast cancer.

ART4215 is the first selective, oral, small molecule inhibitor of the Polθ polymerase domain to enter the clinic. Polθ, a DNA polymerase, is a tumor-specific DDR target involved in microhomology mediated end joining (MMEJ) that is overexpressed in many tumors and found in low levels in healthy tissue. Extensive preclinical studies have demonstrated that ART4215 has broad potential clinical utility, as described in Artios’ recent Nature Communications publication, Zatreanu et al., 2021. The Polθ project was originally in-licensed from Cancer Research Technology (now Cancer Research Horizons) in 2016 as part of the initial formation of Artios.

The announcement can be accessed on Artios’ website at: <https://www.artios.com/> and the full text of the announcement from Artios is contained below.

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About Arix Bioscience plc

Arix Bioscience plc is a global venture capital company focused on investing in breakthrough biotechnology companies around cutting-edge advances in life sciences.

We collaborate with exceptional entrepreneurs and provide the capital, expertise, and global networks to help accelerate their ideas into important new treatments for patients. As a listed company, we are able to bring this exciting growth phase of our industry to a broader range of investors. www.arixbioscience.com

Artios Press Release

Artios initiates Phase 2 study of Polθ Inhibitor ART4215 in Combination with PARP Inhibitor Talazoparib in BRCA Deficient Breast Cancer

- ART4215 is a potentially first-in-class, highly selective, oral small molecule inhibitor targeting the Polθ polymerase domain
- Interim Phase 1 tolerability and pharmacokinetic data supports a well-tolerated safety profile
- Phase 1 safety and tolerability data for ART4215 in advanced solid tumors is expected in 1H 2023; Phase 2 data in BRCA deficient breast cancer is expected in 2024

CAMBRIDGE, UK and NEW YORK, USA, 10 August 2022: Artios Pharma Limited (Artios), a clinical stage biotech company pioneering the development of novel small molecule therapeutics that target the DNA damage response (“DDR”) process in order to treat patients with a broad range of cancers, announces it has initiated a Phase 2 study with ART4215, a small molecule inhibitor of polymerase theta (Polθ) in combination with talazoparib (TALZENNA®), an oral poly (ADP-ribose) polymerase (PARP) inhibitor in an expansion study for the treatment of BRCA deficient breast cancer.

ART4215 is the first selective, oral, small molecule inhibitor of the Polθ polymerase domain to enter the clinic. Polθ, a DNA polymerase, is a tumor-specific DDR target involved in microhomology mediated end joining (MMEJ) that is overexpressed in many tumors and found in low levels in healthy tissue. Extensive preclinical studies have demonstrated that ART4215 has broad potential clinical utility, as described in Artios’ recent Nature Communications publication, Zatreanu et al., 2021. The Polθ project was originally in-licensed from Cancer Research Technology (now Cancer Research Horizons) in 2016 as part of the initial formation of Artios.

Dr. Niall Martin, Chief Executive Officer at Artios, said: “Polθ is highly expressed in cancer cells, but has limited expression in healthy cells, making it an attractive cancer target. Initial Phase 1 data supports a favorable tolerability profile and the potential for broad treatment use, particularly in combination with agents like PARP inhibitors where combinations with other DNA damage response inhibitors have been limited by toxicity. We are highly encouraged that ART4215 may offer a new treatment option that can synergize to overcome both de novo and acquired PARP resistance. We look forward to reporting Phase 1 safety and tolerability data in the first half of 2023.”

Principal Investigator for the trial, Dr. Erika P. Hamilton, Director of the Breast Cancer and Gynecologic Cancer Research Program, Sarah Cannon Research Institute at Tennessee Oncology, said: “Patients with advanced solid tumors have achieved improved outcomes with the development of PARP inhibitors. However, there is still a need to address resistance mechanisms diminishing initial tumor responses and leading to disease progression. ART4215 has the potential to help overcome these limitations, and we are excited that the initiation of this Phase 2 trial represents an important step in the clinical evaluation of Polθ as a novel target.”

ART4215 is currently being evaluated in an ongoing, first-in-human, global, open-label Phase 1/2 study to assess the safety, tolerability, pharmacokinetics, and clinical activity of ART4215 as a monotherapy or in combination with talazoparib in patients with advanced or metastatic solid tumors. Initial safety data from the first Phase 1 dose cohorts have demonstrated ART4215 to be well tolerated. A recommended Phase 2 dose has been established for ART4215 in combination with talazoparib, and a randomized expansion cohort has been initiated to evaluate the combination in patients with BRCA deficient breast cancer.

The study will enroll up to 206 patients and will be conducted at multiple oncology centers across the USA and Europe. The trial is led by principal investigators Erika P. Hamilton, M.D., Director of the Breast Cancer and Gynecologic Cancer Research Program, Sarah Cannon Research Institute at Tennessee Oncology, and Timothy Yap, M.B.B.S., Ph.D., Associate Professor of Investigational Cancer Therapeutics and Medical Director of the Institute

for Applied Cancer Science at The University of Texas MD Anderson Cancer Center. Phase 1 safety and tolerability data is expected in the first half of 2023.

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About Artios

zArtios is a clinical-stage biotech company pioneering the development of novel small molecule therapeutics that target the DDR process to treat patients suffering from a broad range of cancers. Artios is led by an experienced scientific and leadership team with proven expertise in DDR drug discovery, including the discovery and early development of the poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitor Olaparib. It has a unique partnership with Cancer Research UK, and collaborations with leading DNA repair researchers worldwide, such as The Institute of Cancer Research, London, the Netherlands Cancer Institute and the Crick Institute, London. Artios is building a pipeline of next-generation DDR programs to target hard to treat cancers, including its ATR inhibitor, ART0380, and the Pol θ inhibitor, ART4215, as a monotherapy and with combination treatments. In December 2020, Artios entered into a collaboration agreement with Merck KGaA, Darmstadt, Germany to identify and develop precision oncology medicines targeting nucleases. Merck KGaA, Darmstadt, Germany has the right to opt into exclusive development and commercialization of compounds on up to eight targets and Artios is to receive up to US\$860 million in total milestones per target. In April 2021, Artios entered into a collaboration agreement with Novartis to identify DDR targets to use with Novartis' proprietary radioligand therapies, with Artios receiving a US\$20 million up-front payment in addition to near-term research funding to support the collaboration. Artios is eligible to receive up to \$1.3 billion in discovery, development, regulatory and sales-based milestones in addition to royalty payments. Artios has raised US\$320 million to date from investors and strategic partners, including the US\$153 million Series C financing announced in July 2021. Artios is based at the Babraham Research Campus in Cambridge, UK, with an office in New York City, USA.