ARCA BIOPHARMA SUBMITS SPECIAL PROTOCOL ASSESSMENT REQUEST TO FDA FOR GENCARO PHASE 3 ATRIAL FIBRILLATION CLINICAL TRIAL

- *Gencaro potentially the first genetically-targeted treatment for heart failure patients at risk for atrial fibrillation*
- *PRECISION-AF, planned Phase 3 clinical trial in patients with genotype that responds most favorably to Gencaro*

Westminster, CO, September 18, 2018 – ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases, today announced that it has submitted a Special Protocol Assessment (SPA) request to the U.S. Food and Drug Administration (FDA). The request is part of the Company's ongoing interaction with the FDA focused on the planned Phase 3 clinical development program of Gencaro™ (bucindolol hydrochloride) as a genetically-targeted treatment for heart failure (HF) patients at risk for atrial fibrillation (AF).

The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing FDA to evaluate the proposed design and size of certain clinical trials that are intended to form the primary basis for determining a drug product's efficacy and safety. Upon specific request by a clinical trial sponsor, FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate for the indication studied. An SPA agreement can potentially reduce the risk of bringing a drug to market. The SPA submission is the next step in beginning a Phase 3 program for Gencaro after an End-of-Phase 2 Meeting with FDA in June 2018.

The protocol included with the SPA request incorporates guidance ARCA received from the FDA regarding a Phase 3 program that could provide sufficient evidence of the efficacy and safety of Gencaro in the treatment of atrial fibrillation.

"A successful SPA agreement with the FDA should help us solidify the development and regulatory pathway for Gencaro, including the details of our planned PRECISION-AF Phase 3 clinical trial," said Michael R. Bristow, MD, PhD, Chief Executive Officer of ARCA biopharma. "We greatly appreciate the FDA's commentary and guidance on the Gencaro development program. Gencaro is potentially the first genetically-targeted treatment for heart failure patients at risk for atrial fibrillation and we are excited to potentially move the program into Phase 3 development."

The ARCA SPA submission details a single adequate and well-controlled Phase 3 clinical trial

(PRECISION-AF) designed as a double-blind, active-controlled, multicenter, international, study comparing Gencaro with Toprol-XL (metoprolol succinate) for the prevention of recurrent AF or all-cause mortality (ACM) in HFrEF patients (HF with left ventricular ejection fraction (LVEF) < 50%). Eligible patients will have HFrEF, an AF event within the prior 180 days and the genotype which responds most favorably to Gencaro. The primary endpoint of the submitted trial will utilize AF Burden (AFB) methodology. AFB is defined as the amount of time per day a patient experienced AF, as measured by an implanted cardiac electronic device (CIED). In the recently completed GENETIC-AF Phase 2 clinical trial, Gencaro showed a trend for 25% benefit over Toprol-XL in reducing AF recurrence as measured by AFB in a subgroup of patients with continuous monitoring with a CIED. For U.S. patients in this substudy, a trend for 51% benefit was observed. The proposed trial will have an adaptive design with an interim analysis and use standard significance criteria ($p \leq 0.05$) for the primary endpoint. Subject to FDA approval of the SPA and securing additional financing, ARCA anticipates initiating PRECISION-AF in the second half of 2019.

About ARCA biopharma

ARCA biopharma is dedicated to developing genetically-targeted therapies for cardiovascular diseases through a precision medicine approach to drug development. ARCA's lead product candidate, Gencaro™ (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator being developed for the potential treatment of heart failure (HF) patients at risk for atrial fibrillation (AF). ARCA has identified common genetic variations that it believes predict individual patient response to Gencaro, giving it the potential to be the first genetically-targeted AF prevention treatment. The Gencaro development program has been granted Fast Track designation by FDA. ARCA is also developing AB171, a thiol-substituted isosorbide mononitrate, as a potential genetically-targeted treatment for peripheral arterial disease (PAD) and for heart failure (HF). For more information, please visit www.arcabio.com.

Safe Harbor Statement

This press release contains "forward-looking statements" for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, potential future development plans for Gencaro, the expected features and characteristics of Gencaro, including the potential for genetic variations to predict individual patient response to Gencaro, Gencaro's potential to treat AF, future treatment options for patients with AF, and the potential for Gencaro to be the first genetically-targeted AF prevention treatment. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, the risks and uncertainties associated with: ARCA's financial resources and whether they will be sufficient to meet its business objectives and operational requirements; ARCA may not be able to raise sufficient capital on acceptable terms, or at all, to continue development of Gencaro or to otherwise continue operations in the future; ARCA cannot guarantee that the FDA will issue an agreement on the SPA, and even if ARCA does obtain the FDA's agreement, a SPA would not guarantee approval of Gencaro or any other particular outcome from regulatory review; results of earlier clinical trials may not be confirmed in future trials; the protection and market exclusivity

provided by ARCA's intellectual property; risks related to the drug discovery and the regulatory approval process; and, the impact of competitive products and technological changes. These and other factors are identified and described in more detail in ARCA's filings with the Securities and Exchange Commission, including without limitation ARCA's annual report on Form 10-K for the year ended December 31, 2017, and subsequent filings. ARCA disclaims any intent or obligation to update these forward-looking statements.

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