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

- *Phase 3 atrial fibrillation trial planned in population with no effective or FDA approved therapies*
- *PRECISION-AF, planned Phase 3 clinical trial in patients with genotype that responds most favorably to Gencaro*

Westminster, CO, December 20, 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 an amendment to its Special Protocol Assessment (SPA) request to the U.S. Food and Drug Administration (FDA). The amendment addresses FDA feedback and guidance on the target population for ARCA's planned Phase 3 clinical trial. The SPA 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 atrial fibrillation (AF) in patients with heart failure (HF).

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 regulatory risk of bringing a drug to market.

ARCA's amended SPA incorporates guidance received from FDA during a December meeting regarding a Phase 3 clinical development program that could potentially provide sufficient evidence of the efficacy and safety of Gencaro in the treatment of atrial fibrillation in patients with heart failure.

"We greatly appreciate the FDA's commentary and guidance on the Gencaro clinical development program. We believe a successful SPA agreement with the FDA could help us solidify the development and regulatory pathway for Gencaro," said Michael R. Bristow, MD, PhD, Chief Executive Officer of ARCA biopharma. "Based on our analysis of Phase 2B data and our interactions with the FDA, we believe with our proposed Phase 3 clinical development plan we have the opportunity to potentially provide a new treatment for heart failure patients at risk for recurrent atrial fibrillation, who otherwise currently do not have good pharmacologic therapeutic

options."

The ARCA amended 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 HF patients with mid-range ejection fraction (HFmrEF), which is defined as HF with a left ventricular ejection fraction (LVEF) ≥ 40% and <50%. Eligible patients will have HFmrEF, a recent AF event and the genotype which responds most favorably to Gencaro. The primary endpoint of the submitted trial will be time to first event of atrial fibrillation/atrial flutter (AF/AFL) or ACM during the 26-week Follow-up Period. In the recently completed GENETIC-AF Phase 2 clinical trial, Gencaro showed a trend for benefit over Toprol-XL in reducing AF recurrence in a subgroup of patients with HFmrEF (hazard ratio = 0.42; 95% CI: 0.21, 0.86; p = 0.017). Subject to FDA approval of the amended 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, ARCA's ability to enter into a SPA agreement with the FDA or complete any Phase 3 clinical trial thereunder, 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.

Investor & Media Contact:
Derek Cole
720.940.2163
derek.cole@arcabio.com

###