GENETIC-AF PHASE 2B TRIAL RESULTS PUBLISHED IN THE JOURNAL OF AMERICAN COLLEGE OF CARDIOLOGY: HEART FAILURE

Westminster, CO, May 1, 2019 – ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases, today announced that the paper "GENETIC-AF: Bucindolol for the Maintenance of Sinus Rhythm in a Genotype-Defined Heart Failure Population" was published in *JACC: Heart Failure*, a journal of the American College of Cardiology.

The lead author on the paper is Jonathan P. Piccini, MD, MHS, FACC, Director, Duke Center for Atrial Fibrillation, Duke University Medical Center and Duke Clinical Research Institute and the senior author is Stuart J. Connolly, MD, Professor Emeritus, Division of Cardiology at McMaster University in Hamilton, Ontario.

"Atrial fibrillation (AF) is a common and serious medical problem associated with significant morbidity and mortality, especially in patients with heart failure (HF)," said Dr. Michael R. Bristow, President and Chief Executive Officer of ARCA and a co-author on the paper. "Development of AF is associated with increased risk of adverse cardiovascular outcomes, and when AF occurs in patients with HF these adverse effects are accentuated. AF and HF often co-exist and have common risk factors, as well as overlapping pathophysiologies."

Bucindolol is a beta-blocker whose unique pharmacologic properties provide greater benefit in HF patients who have the beta-one adrenergic receptor (ADRB1) Arg389Arg genotype. GENETIC-AF compared the effectiveness of bucindolol and metoprolol succinate for the maintenance of sinus rhythm in a genetically-defined HF population with AF. The trial enrolled 267 HF patients with a left ventricular ejection fraction (LVEF) < 0.50, symptomatic AF, and the ADRB1 Arg389Arg genotype. The primary endpoint of AF/atrial flutter (AFL) or all-cause mortality (ACM) was evaluated by electrocardiogram (ECG) during a 24-week period.

The hazard ratio (HR) for the primary endpoint was neutral (1.01 (95% CI: 0.71, 1.42)) but trends for bucindolol benefit were observed in several subpopulations. Precision therapeutic phenotyping revealed that a differential response to bucindolol was associated with: 1) the interval of time from the initial diagnosis of HF and AF to randomization, and: 2) the onset of AF relative to initial HF diagnosis. In a cohort whose first HF and AF diagnoses were less than 12 years prior to randomization, in which AF onset did not precede HF by more than 2 years (N=196), the HR was 0.54 (95% CI: 0.33, 0.87; p = 0.011). Moreover, in the HF with mid-range LVEF subpopulation, which comprised approximately 50% of randomized patients, the HR was 0.42 (0.21, 0.86); p = 0.017.

As expected based on its unique pharmacology, bucindolol reduced plasma venous norepinephrine

levels (by 124 pg/ml at 4 weeks, p <0.001) while metoprolol did not (p =0.30). Plasma NT-proBNP, a biomarker of both AF and HF, was reduced in the bucindolol group at 4 weeks (p= 0.003), 12 weeks (p = 0.002) and 24 weeks (p = 0.005) while in the metoprolol group a reduction was observed only at 24 weeks (p = 0.014).

"In this exploratory Phase 2 trial, pharmacogenetic-guided bucindolol therapy did not reduce the recurrence of AF/AFL/ACM compared to metoprolol in a broad population of HF patients at risk of AF," concluded Dr. Piccini, "however, the majority of patients in this trial demonstrated a more favorable response to genetically-targeted bucindolol compared to standard beta-blocker therapy. These data are very encouraging and merit further investigation in future Phase 3 trials."

"The precision therapeutic phenotyping methodology used in these analyses identified broad relationships that consistently manifested across the entire dataset." commented Christopher Dufton, PhD, Vice President of Clinical Development at ARCA and a co-author, "As such, we believe this approach increases the likelihood of reproducibility of these results in future Phase 3 trials."

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, GencaroTM (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator being developed for the potential treatment of atrial fibrillation in heart failure patients with mid-range ejection fraction. 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 heart failure and peripheral arterial disease (PAD). 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 atrial fibrillation (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; 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, 2018, and subsequent filings. ARCA disclaims any intent or obligation to update these forward-looking statements.

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