



ARCA BIOPHARMA ANNOUNCES FDA AGREEMENT FOR A SINGLE PHASE 3 CLINICAL TRIAL TO SUPPORT APPROVAL FOR THE FIRST GENETICALLY-TARGETED CARDIOVASCULAR DRUG

- *FDA Special Protocol Assessment agreement granted for PRECISION-AF clinical trial evaluating Gencaro as a potential treatment for atrial fibrillation in a heart failure population that has no FDA approved drug therapies*
- *58% treatment benefit seen versus active comparator in Phase 2B for planned Phase 3 target population*
- *Gencaro development program has FDA Fast Track designation*
- *U.S. and European cardiovascular patents and regulations may provide commercial exclusivity for Gencaro for 10 years post approval*

Westminster, CO, February 20, 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 it has reached agreement with the U.S. Food and Drug Administration (FDA) regarding a [Special Protocol Assessment \(SPA\)](#) on the design of a pivotal Phase 3 clinical trial, PRECISION-AF, to assess the safety and efficacy of Gencaro™ (bucindolol hydrochloride) as a genetically-targeted treatment for atrial fibrillation (AF) in patients with a specific type of heart failure (HF). The target population for the planned Phase 3 clinical trial, partially identified by precision therapeutic phenotyping, currently has no FDA approved drug therapies. This SPA provides agreement that the Phase 3 protocol design, clinical endpoints, trial population and statistical analyses adequately address objectives that, if met, would support a regulatory submission seeking approval of Gencaro for the prevention of AF recurrence in a genotype-defined HF population.

If PRECISION-AF is successful and Gencaro gains regulatory approval, it has the potential to be unique in several aspects, including:

- The first genetically-targeted cardiovascular therapy;
- The only drug therapy indicated in HF patients with mid-range ejection fraction (HFmrEF); and,
- The only drug therapy for AF approved against an active comparator.

The SPA process is designed to facilitate review and approval of drugs by allowing FDA to evaluate the proposed design and size of specific clinical trials that are intended to form the primary demonstration of a drug product's efficacy and safety. 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.

"Consistent with our mission to develop precision therapies on a pharmacogenetic platform, this SPA agreement with the FDA provides a clearly defined regulatory pathway for the Phase 3 development of Gencaro in a genotype-specific heart failure population that currently has no FDA approved drug therapy," said Michael R. Bristow, MD, PhD, Chief Executive Officer of ARCA biopharma. "If the previous foundational therapeutic observations in the GENETIC-AF and BEST trials are confirmed in PRECISION-AF, we believe Gencaro could potentially provide a new standard of treatment for AF prevention for the estimated 2.5 million HFmrEF patients in the major markets in U.S., Europe and Japan."

In accordance with the Company's SPA agreement with FDA, PRECISION-AF is designed as a single, adequate and well-controlled Phase 3 clinical trial that may be sufficient to support an New Drug Application (NDA) submission for an AF indication if the objectives of the trial are achieved consistent with the requirements of the SPA. The trial is designed as a double-blind, active-controlled, multicenter, international study comparing Gencaro with Toprol-XL (metoprolol succinate) for the prevention of AF recurrence or all-cause mortality (ACM) in HFmrEF patients. HFmrEF is defined as HF with a left ventricular ejection fraction (LVEF) $\geq 40\%$ and $< 50\%$, which constituted approximately half of the enrolled population in the Phase 2 GENETIC-AF trial. PRECISION-AF is designed to enroll approximately 400 patients who have: HFmrEF, a recent AF event, and the genotype which responds most favorably to Gencaro. The primary endpoint of the 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 trial, Gencaro showed a 58% treatment benefit compared to Toprol-XL in reducing AF recurrence in the HFmrEF population targeted for Phase 3 (hazard ratio = 0.42; 95% CI: 0.21, 0.86; p = 0.017). With 400 patients (200 per arm) the trial will have 90% power at a p-value of 0.01 to detect a 45% treatment benefit for Gencaro compared to Toprol-XL. Subject to securing additional financing, ARCA anticipates initiating PRECISION-AF in the fourth quarter of 2019.

About Special Protocol Assessment (SPA)

An SPA is an agreement with the FDA that the proposed trial protocol design, clinical endpoints and statistical analyses are acceptable to support regulatory approval. For further information regarding the SPA process, please visit the FDA website, www.fda.gov. A SPA agreement is not a guarantee of approval, and there are no assurances that the design of, or data collected from, the planned Gencaro clinical trial (PRECISION-AF) will be adequate to obtain the requisite regulatory approvals for the marketing of Gencaro.

About Atrial Fibrillation (AF)

AF, the most common sustained cardiac arrhythmia, is a serious disorder in which the normally regular and coordinated contraction pattern of the heart's two small upper chambers, or the atria, becomes irregular, rapid and uncoordinated. AF can cause distressing symptoms that significantly impact quality of life and can also bring potentially serious medical consequences, including increasing the risk of stroke and serious cardiovascular complications. AF is considered an epidemic cardiovascular disease and a major public health burden. In 2015, there were approximately 5.2 million patients who had been diagnosed with AF in the United States. It is

estimated that AF costs the U.S. economy about \$6.0 billion annually.

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 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, ARCA's ability to complete any Phase 3 clinical trial, the likelihood for PRECISION-AF results to satisfy the requirements of the SPA, ARCA's ability to raise sufficient capital to fund the PRECISION-AF trial and its other operations, 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 and/or HFmrEF, future treatment options for patients with AF and/or HFmrEF, 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; an FDA SPA agreement does 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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