



**GENETIC-AF PHASE 2B CLINICAL TRIAL RESULTS PRESENTED IN LATE  
BREAKING PRESENTATION AT EUROPEAN SOCIETY OF CARDIOLOGY HEART  
FAILURE 2018 WORLD CONGRESS**

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**End-of-Phase 2 Meeting with the U.S. FDA Scheduled for the Last Week of June to Review  
Gencaro Phase 2 Data and Future Development Plan**

*Westminster, CO, May 29, 2018* – [ARCA biopharma, Inc.](http://arcabio.com) (Nasdaq: ABIO), a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases, today announced that data from the [GENETIC-AF](#) clinical trial was presented in a “Late Breaking Clinical Trials” oral presentation at the European Society of Cardiology [Heart Failure 2018 World Congress](#) on Sunday May 27, 2018. [William T. Abraham](#), M.D., Professor of Medicine, Physiology and Cell Biology and Director, [Division of Cardiovascular Medicine](#) at the Ohio State University presented the data. The presentation is available at <http://arcabio.com/investors/investor-presentations/>.

In the overall study population of heart failure patients who were at high risk for recurrent atrial fibrillation (AF), pharmacogenetic guided Gencaro™ did not reduce AF/AFL/ACM recurrence compared to the active comparator TOPROL-XL. However, in U.S. patients (48% of the entire cohort), a trend for potential benefit in favor of Gencaro (approximately 30% risk reduction over TOPROL-XL), was observed for the primary endpoint of all-cause mortality (ACM) or time to recurrence of AF or atrial flutter (AFL). A trend for potential benefit in favor of Gencaro was also observed in a subset of patients from the U.S., Canada and Europe who underwent continuous heart rhythm monitoring with Medtronic implanted devices (approximately 25% risk reduction over TOPROL-XL). Safety data indicated that Gencaro was well-tolerated in the AF-HFrEF population investigated with a safety profile similar to TOPROL-XL.

“With additional analysis of the trial data, and taking into consideration recent studies in animal models of AF, it is likely that AF-HFrEF phenotypic differences are responsible for the heterogeneity in treatment response observed. These Phase 2B data support and provide guidance for potential additional development of Gencaro as a treatment for atrial fibrillation in patients with heart failure, an indication for which there are currently no FDA approved therapeutics,” commented Dr. Abraham.

GENETIC-AF was a Phase 2B, double-blind, superiority clinical trial evaluating Gencaro (bucindolol hydrochloride) as a genetically-targeted treatment for AF in patients with HF and reduced left ventricular ejection fraction (HFrEF). The trial enrolled 267 patients from the United States, Canada and Europe.

The primary analysis was conducted to evaluate the evidence of safety and efficacy of Gencaro

versus an active comparator with demonstrated effectiveness and safety in this patient population TOPROL-XL. The primary endpoint of the trial was time to recurrent AF, atrial flutter (AFL) or all-cause mortality (ACM). The trial was not powered to conventional significance for this endpoint and utilized Bayesian statistical modeling of predictive probability of success (PPoS) of the primary endpoint to estimate outcome if the trial had enrolled 620 patients with 330 primary events.

Gencaro was generally safe and well-tolerated, with 84% of patients attaining their target dose compared to 72% of patients receiving TOPROL-XL. The most frequently reported adverse events were similar in both groups and consistent with the known safety profile of the beta-blocker class of drugs. Adverse events assessed as related to study drug by the investigator occurred in 23.8% of patients in the Gencaro group and in 30.1% of patients in the TOPROL-XL group. Of note, adverse events of bradycardia were less frequently reported in the Gencaro group (3.7%) compared to patients receiving TOPROL-XL (12.0%). During the 24-week efficacy follow-up period there were three deaths (ACM) in the TOPROL-XL group and none in the Gencaro group. Three patients died in the long-term treatment extension period after receiving Gencaro for more than a year.

In the overall study population, pharmacogenetic guided Gencaro did not reduce AF/AFL/ACM recurrence compared to the active comparator TOPROL-XL (143 total events, hazard ratio of 1.01 (95% confidence interval: 0.71, 1.42), which was associated with a PPoS of 14%. In the U.S. patient cohort of 127 patients (approximately 50% of all patients and events), a trend for potential superior benefit in favor of Gencaro over TOPROL-XL was observed (73 events, hazard ratio 0.70, [95% confidence interval: 0.41, 1.19]), with a PPoS of 61%, which was greater than the prespecified criteria set by the company to proceed to Phase 3 development.

The Company believes the difference in treatment response between the overall and U.S. patient cohorts was primarily due to the inclusion of a higher number of patients with long-standing AF who had asymptomatic/mild heart failure in two countries exhibiting hazard ratios >1.0 for the primary endpoint. In a subgroup analysis that excluded these patients (77% of the overall study population), a trend for potential benefit in favor of Gencaro was observed (17% risk reduction over TOPROL-XL). The Company believes this type of population, in which AF is being driven by underlying HF pathophysiology, would be the focus of any future clinical trials of Gencaro.

An End-of-Phase 2 meeting is scheduled with the U.S. Food and Drug Administration (FDA) for the last week of June to review the GENETIC-AF data and potential future Gencaro development plans. Within 30 days following the meeting, the FDA will provide written minutes of the meeting to confirm the discussions. ARCA plans to provide an update on Gencaro potential future development plans subsequent to receiving the FDA meeting minutes.

## **About GENETIC-AF**

A **Genotype-Directed Comparative Effectiveness Trial of Bucindolol and TOPROL-XL for Prevention of Symptomatic Atrial Fibrillation/Atrial Flutter in Patients with Heart Failure**

GENETIC-AF was a Phase 2B multi-center, randomized, double-blind, clinical superiority trial

comparing the safety and efficacy of Gencaro™ against an active comparator, the beta-blocker TOPROL-XL (metoprolol succinate) for the treatment and prevention of recurrent atrial fibrillation or flutter (AF/AFL) in heart failure patients with reduced left ventricular ejection fraction (HFrEF). Eligible patients had HFrEF, a history of paroxysmal AF (episodes lasting 7 days or less) or persistent AF (episodes lasting more than 7 days and less than 1 year) in the past 6 months, and the beta-1 389 arginine homozygous genotype that we believe responds most favorably to Gencaro™. A subset of patients in the trial also underwent continuous heart rhythm monitoring to assess AF burden, which is defined as the amount of time per day that a patient experiences AF. Topline results of GENETIC-AF were reported on February 26, 2018.

## **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 patients with atrial fibrillation (AF) and chronic heart failure with reduced left ventricular ejection fraction (HFrEF) which recently completed a Phase 2B clinical trial. 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. ARCA has a collaboration with Medtronic, Inc. for support of the GENETIC-AF trial. The Gencaro development program has been granted Fast Track designation by FDA. ARCA also plans to develop 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](http://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, statements regarding the ability of ARCA's financial resources to support its operations through the end of 2018, potential future development plans for Gencaro, the expected features and characteristics of Gencaro or AB171, including the potential for genetic variations to predict individual patient response to Gencaro, Gencaro's potential to treat AF, AB171's potential to treat HF, 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, 2017, and subsequent filings. ARCA disclaims any intent or obligation to update these forward-looking statements.*

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