CLINICAL DATA EVALUATING GENCARO FOR THE TREATMENT OF ATRIAL FIBRILLATION IN HEART FAILURE PATIENTS FEATURED IN THREE PRESENTATIONS AT THE 2020 HEART RHYTHM SCIENTIFIC SESSIONS

New data provide additional evidence of efficacy for Gencaro compared to active control in a pharmacogenetically-defined HF population at risk for AF recurrence

- ***26% reduction in total time spent in AF ($p < 0.001$)***
- ***30% decrease in AF interventions and cardiovascular adverse events ($p = 0.008$)***
- ***55% lower incidence of dose limiting bradycardia ($p < 0.001$)***

Westminster, CO, May 7, 2020 – ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company applying a precision medicine approach to developing genetically targeted therapies for cardiovascular diseases, today announced that clinical data evaluating Gencaro™ (bucindolol hydrochloride) as a potential treatment for atrial fibrillation (AF) in patients with heart failure (HF) was presented at the 2020 Heart Rhythm Scientific Sessions, the annual scientific conference of the Heart Rhythm Society (HRS). While the in-person meeting was cancelled due to the continued global escalation of COVID-19, HRS has provided author presentations virtually through its online learning platform Heart Rhythm 365 and all abstracts will be published in a supplement to the May edition of the Heart Rhythm Journal.

The data come from a Phase 2 clinical trial, GENETIC-AF, that enrolled 267 HF patients with a current or recent history of paroxysmal or persistent AF and the ADRB1 Arg389Arg genotype. Patients were randomized to bucindolol or the active comparator, metoprolol succinate, and were followed for approximately 24 weeks.

"Pharmacogenomic Guided Beta-Blocker Therapy with Bucindolol Reduces Atrial Fibrillation Burden Compared to Metoprolol Succinate: The GENETIC-AF Trial," authored by Jonathon P. Piccini et al, presented data from the device substudy of the GENETIC-AF trial. A total of 69 HF patients underwent continuous heart rhythm monitoring via implanted cardiac devices to evaluate the total time spent in AF during 24 weeks of follow-up, also known as cumulative AF burden. The paper's authors concluded that:

- Bucindolol decreased cumulative AF burden by 26% ($p < 0.001$) compared to active control.
- Treatment effect estimates for cumulative AF burden were consistent with time to first AF event analyses.
- Cumulative AF burden evaluates more information than time to first event methods, providing greater power to detect clinically meaningful differences between groups with limited sample size.

"Impact of Pharmacogenetic-guided Bucindolol versus Metoprolol Succinate on the Overall Burden of Clinical Events in Patients with AF and Heart Failure: The GENETIC-AF Trial," authored by Jeff S. Healey et al, presented data on the frequency of AF rhythm interventions (i.e., electrical cardioversions, ablations, and Class 3 antiarrhythmic drug use) and cardiovascular (CV) adverse events in the GENETIC-AF trial. The paper's authors found that:

- Bucindolol decreased a composite endpoint of AF interventions and CV adverse events by 30% ($p = 0.008$) compared to active control.
- Bucindolol decreased AF interventions by 33% ($p = 0.009$) compared to active control.
- Significant and numerically greater results were observed (46% and 51%, respectively) in a subgroup previously identified by precision therapeutic phenotyping (PTP cohort).
- Similar significant results were observed (55% and 58%, respectively) for a subgroup of the PTP cohort with baseline LVEF values of 40% to 55%.

"Bucindolol is Associated with a Lower Incidence of Dose Limiting Bradycardia in Heart Failure Patients with Atrial Fibrillation: The GENETIC-AF Trial," authored by William T. Abraham et al, reviewed drug dosing and safety data for the GENETIC-AF trial. The paper's authors found that:

- Bucindolol was associated with a 55% ($p < 0.001$) lower incidence of bradycardia compared to active control.
- Bradycardia was associated with a 4-fold increase in study drug dose reductions.
- Differences in study drug dosing were primarily observed in patients with heart rates less than 60 beats per minute, which was much more common in the metoprolol group ($p < 0.0001$).
- Fewer bradycardia adverse events in the bucindolol vs. metoprolol groups (5 vs. 20 events, $p = 0.003$).
- Bradycardia may limit dosing of conventional beta-blockers in HF patients with AF, which would be expected to compromise effectiveness for reducing HF clinical events.

The individual presentations can be found on the Scientific Publications page of the ARCA website and at HRS' Heart Rhythm 365.

Michael Bristow, MD, PhD and CEO of ARCA commented: "Evaluated by the most sensitive and comprehensive measure of atrial fibrillation, continuous heart rhythm monitoring by an implanted device, these data indicate a clear efficacy signal for bucindolol compared to metoprolol succinate. Even more striking is the beneficial effect of bucindolol on downstream AF-related events occurring after an initial AF episode, with fewer clinical interventions to manage heart rhythm seen in the bucindolol group. Finally, the lower incidence of dose-limiting bradycardia with bucindolol provides a clue as to why conventional beta-blockers have not demonstrated efficacy for reducing heart failure events in patients with atrial fibrillation, while bucindolol has."

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. 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 U.S. FDA has granted the Gencaro development program Fast Track designation and a Special Protocol Assessment (SPA) agreement for a single Phase 3 clinical trial. ARCA is also developing AB171, a thiol-substituted isosorbide mononitrate, as a potential genetically targeted treatment for heart failure and peripheral arterial disease. For more information, please visit www.arcabio.com or follow the Company on LinkedIn.

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 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, the significance of the new additional data from GENETIC-AF contained in these presentations and whether these data may be confirmed in future clinical trials, 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's ability to raise sufficient capital on acceptable terms, or at all, to continue development of Gencaro or to otherwise continue operations in the future; that 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, 2019, 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

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