ASPEN-COVID-19 Data and Safety Monitoring Committee Recommends Continuing Phase 2b Clinical Trial to Completion Based on Interim Analysis of Efficacy and Safety Data

- ***Enrollment completion anticipated by year end 2021***
- ***Topline data anticipated in first quarter of 2022***

Westminster, CO, October 28, 2021 – ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company applying a precision medicine approach to developing genetically targeted therapies for cardiovascular diseases, today provided an update on the ASPEN-COVID-19 Phase 2b clinical trial evaluating rNAPc2 as a potential treatment for patients hospitalized with severe COVID-19. The Company announced that the Data and Safety Monitoring Committee (DSMC) has completed a pre-specified interim analysis and, based on the DSMC's review of approximately 75% of the projected final efficacy and safety data, recommended completion of the clinical trial with no modifications to the trial design. The rNAPc2 development program has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA). The Company now anticipates completion of target enrollment of 160 patients by year end 2021 and reporting of topline data in the first quarter of 2022.

Dr. Michael Bristow, ARCA's President and Chief Executive Officer, commented, "Clearing the final interim analysis with no recommended changes in the Phase 2b clinical trial design is an important step in a clinical trial and in the development of rNAPc2 for prevention of COVID-19-associated coagulopathy. We are focused on finishing the clinical trial, which we estimate will complete enrollment by year end. We look forward to sharing the top-line trial results in the first quarter of next year and reviewing the findings with the FDA."

About ASPEN-COVID-19

ASPEN-COVID-19 is a Phase 2b randomized, multi-center, international clinical trial evaluating two dose regimens of rNAPc2 versus heparin in approximately 160 hospitalized SARS-CoV-2 positive patients that also have an elevated D-dimer level. The primary endpoint of the trial is the change in D-dimer level from baseline to Day 8 relative to standard of care heparin. D-dimer is a biomarker commonly used for assessing coagulation activation, which is elevated in approximately 40% to 75% of hospitalized COVID-19 patients and is associated with adverse clinical outcomes. Heparin is an anti-coagulant commonly given to any patient hospitalized in the United States for COVID-19. Other objectives of Phase 2b are to assess safety, determine the optimal dose regimen of rNAPc2 for a potential Phase 3 clinical trial and evaluate multiple additional clinical endpoints as detailed in the ASPEN-COVID-19 listing on clinicaltrials.gov.

The U.S. Food and Drug Administration (FDA) has designated the investigation of rNAPc2 as a potential treatment for COVID-19 as a Fast Track development program. ARCA believes that

rNAPc2 is the only anticoagulant class new chemical entity in development for COVID-19.

About rNAPc2 (AB201)

rNAPc2 is a small recombinant protein being developed as a potential treatment for COVID-19 and potentially other viral diseases. rNAPc2 is a potent, selective inhibitor of tissue factor (TF), which has been identified as playing a central role in the inflammatory response to viral infections and in the process of viral dissemination. Its unique mechanism of action gives rNAPc2 a combination of anti-coagulant, anti-inflammatory and potential anti-viral properties, and therefore may be effective in addressing the impact of viral infections from multiple pathways. rNAPc2 has previously undergone Phase 1 and Phase 2 testing in more than 700 patients, including in clinical studies for prevention of venous and arterial thrombosis, where it showed efficacy in inhibiting the TF pathway and was well tolerated at therapeutic doses. Recent research suggests that the disease syndrome caused by coronavirus may have much in common with other severe infections in which the infection process causes inappropriate activation of the coagulation system and other aspects of the immune response, resulting in serious complications. Recent mechanistic discoveries, as well as prior data from studies in non-human primates (NHPs) given lethal doses of Ebola or Marburg filoviruses demonstrating morbidity and mortality reductions, decreases in inflammatory biomarkers and reduction in viral load, indicate that rNAPc2 may have important antiviral and anti-inflammatory activity in addition to its anticoagulant effects. The Company believes that collectively these observations provide a strong rationale for investigating rNAPc2 as a treatment for COVID-19 and other virus associated diseases.

About ARCA biopharma

ARCA biopharma is dedicated to developing genetically targeted therapies for cardiovascular diseases through a precision medicine approach to drug development. ARCA is developing rNAPc2 as a potential treatment for diseases caused by RNA viruses, initially focusing on COVID-19. The U.S. FDA has granted Fast Track designation to the rNAPc2 development program, currently in Phase 2 clinical testing. ARCA is also developing Gencaro™ (bucindolol hydrochloride), an investigational, pharmacologically unique beta-blocker and mild vasodilator, as a potential treatment for 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 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 potential future development plans for rNAPc2, the expected features and characteristics of rNAPc2, the anticipated development timeline for rNAPc2, rNAPc2's potential to treat COVID-19, or any other RNA virus associated disease, whether rNAPc2 is the only anticoagulant class new chemical entity in development for COVID-19 and the potential future treatment options and needs for patients with COVID-19. 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 rNAPc2 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, 2020, and subsequent filings. ARCA disclaims any intent or obligation to update these forward-looking statements.

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