ARCA biopharma Provides Update on ASPEN-COVID-19 Phase 2b Clinical Trial Evaluating rNAPc2 as a Potential Treatment for COVID-19

- ***rNAPc2 development focused on unmet need for treatments in hospitalized COVID-19 patients***
- ***Trial expanded to South America, with regulatory approvals for Argentina and Brazil***
- ***Target trial enrollment increased to 160 patients***
- ***Topline trial data anticipated in the fourth quarter of 2021***

Westminster, CO, July 13, 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 ASPEN-COVID-19, the Phase 2b clinical trial evaluating rNAPc2 as a potential treatment for patients hospitalized with COVID-19.

ARCA has received approval from regulatory authorities in Argentina and Brazil to enroll patients in ASPEN-COVID-19. The trial is currently enrolling patients at seven investigative sites in the United States. The Company anticipates enrolling the first South American patients in July 2021.

Trial target enrollment is being increased from 100 to 160 patients in order to maximize the sample size for determining if there are differences in the two rNAPc2 dose regimens being investigated, to minimize variance in the standard of care heparin control arm, in recognition of the study now being conducted in different geographic regions and to account for evolving changes in the clinical course of COVID-19. To date, 77 patients have been enrolled in the trial. The Company also updated its guidance and now anticipates topline data from this international Phase 2b clinical trial in the fourth quarter of 2021.

"With the pandemic continuing to impact patients around the world and the emergence of multiple variants, there remains a critical need for safe, efficacious treatments for hospitalized COVID-19 patients," said Dr. Michael Bristow, ARCA's President and Chief Executive Officer, who is also an American Heart Association (AHA) funded COVID-19 investigator. "Many pathogenic viruses, including SARS-CoV-2, increase host cell expression of tissue factor, the primary initiator of the extrinsic coagulation pathway that also signals a parallel inflammatory response. rNAPc2 is a high affinity inhibitor of tissue factor, and with its combination of anticoagulant, anti-inflammatory and potential antiviral effects, we believe rNAPc2 may favorably impact clinical recovery of patients hospitalized with COVID-19, and thus has the potential to be a uniquely beneficial therapy for these patients, and possibly for other virus associated diseases. Argentina and Brazil are experiencing a higher COVID-19 case rate than the U.S. and, with their excellent investigators and track record in clinical trials, are logical countries in which to expand the Phase

2 trial and, ultimately, a potential Phase 3 trial."

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. Other objectives of Phase 2b are to assess safety and determine the optimal dose regimen of rNAPc2 for Phase 3. D-dimer is a biomarker commonly used for assessing coagulation activation, which is elevated in approximately 50% of hospitalized COVID-19 patients and is directly associated with adverse clinical outcomes.

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 RNA virus-associated diseases, initially focusing on COVID-19. 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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