ARCA biopharma Announces FDA Approval of IND Application for AB201 as a Potential Treatment for COVID-19

- Initiation of Phase 2b clinical trial anticipated in Q4 2020
- Trial to enroll approximately 100 patients hospitalized with COVID-19
- Topline data anticipated Q2 2021

Westminster, CO, October 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 the U.S. Food and Drug Administration (FDA) has approved the Investigational New Drug (IND) application for AB201 (rNAPc2) as a potential treatment for patients hospitalized with COVID-19. ARCA anticipates initiating a Phase 2b/3 sequential clinical trial, ASPEN-COVID-19, of AB201 in approximately 100 patients hospitalized with COVID-19 in the fourth quarter of this year, with Phase 2b followed by a contiguous Phase 3 study that is dependent on Phase 2 results. The Company anticipates topline data from the trial in the second quarter of 2021.

The planned Phase 2b trial is anticipated to be a randomized comparison of two dose regimens of AB201 versus heparin prescribed per local standard of care. The clinical course of some patients with COVID-19 is complicated by a virus-triggered coagulopathy that includes thrombotic events and inflammatory processes, thought to be mediated in part by tissue factor production. AB201 is a potent tissue factor inhibitor anticoagulant with anti-inflammatory and antiviral properties. The primary endpoint of the trial will be change in D-dimer level from baseline to Day 8. 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. If Phase 2b indicates a favorable effect on D-dimer levels, following FDA review of the data and identification of the proposed Phase 3 AB201 dose, the Company anticipates that clinical investigative sites will begin enrolling in the planned Phase 3 clinical trial. The primary endpoint of Phase 3 will be clinical recovery as measured by the Adaptive COVID-19 Treatment Trial (ACTT-1) ordinal scale, with secondary endpoints that include D-dimer levels and the number of thrombotic events. Phase 3 will be event driven, with an estimated requirement of 450 patients. The Phase 2b and Phase 3 trials are described in a common protocol and use identical entry criteria and the same heparin regimen control.

Dr. Michael Bristow, ARCA's President and Chief Executive Officer, who is also an American Heart Association (AHA) funded COVID-19 investigator, commented, "The ASPEN-COVID-19 trial will use the coagulopathy biomarker D-dimer to identify an optimal dose from AB201 regimens that are both within the therapeutic range as determined from Phase 2 trials investigating cardiovascular thrombosis prophylaxis. If successful, we anticipate using this dose in a planned Phase 3 trial to evaluate potential improvement in clinical outcomes. We believe that the

combination of anticoagulant, anti-inflammatory and antiviral effects of AB201 may favorably impact clinical recovery of patients hospitalized with COVID-19."

The trial is being managed in collaboration with the Colorado Prevention Center (CPC), the University of Colorado's Academic Research Organization with extensive experience in managing vascular and anticoagulation clinical trials.

Marc Bonaca, MD, Executive Director of CPC, commented: "The ASPEN-COVID-19 trial will enable us to step beyond the question of intensity of anticoagulation and ask the question of whether specifically targeting tissue factor, a key step in the extrinsic pathway of anticoagulation and a key part of viral pathogenesis, improves outcomes in COVID-19. Dosing and safety are critical, and the Phase 2 trial will enable selection of a dose for safety, coagulopathy, and anti-viral parameters for use in a planned Phase 3 clinical trial. This selected dose will be deployed in the proposed Phase 3 pivotal outcomes study with the hope of translation to the clinical setting. We believe this therapy holds promise to improve outcomes in the current pandemic and given the positive findings in an Ebola animal model, has the potential for broader application in other severe viral infections characterized by coagulopathy."

About AB201

AB201 is a small recombinant protein being developed as a potential treatment for RNA virus-associated diseases, initially focusing on COVID-19. AB201 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 AB201 a combination of anti-coagulant, immuno-modulatory and anti-viral properties, and therefore the potential to be effective in addressing the impact of viral infections from multiple pathways. AB201 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 AB201 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 AB201 as a treatment for COVID-19 and other RNA 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 AB201 as a potential treatment for diseases caused by RNA viruses, initially focusing on COVID-19. ARCA is also developing Gencaro™ (bucindolol hydrochloride), an investigational, pharmacologically unique beta-blocker and mild vasodilator, as a potential pharmacogenetic treatment for atrial fibrillation in patients with heart failure. 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 AB201 and Gencaro, the expected features and characteristics of AB201 and Gencaro, including the potential for genetic variations to predict individual patient response to Gencaro, Gencaro's potential to treat atrial fibrillation, AB201's potential to treat COVID-19 or any other RNA virus associated disease, future treatment options for patients with COVID-19, 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 AB201 or 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, 2019, and subsequent filings. ARCA disclaims any intent or obligation to update these forward-looking statements.

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