PhaseBio Announces Interim Results from Pivotal REVERSE-IT Phase 3 Trial of Bentracimab for the Reversal of Antiplatelet Effects of Ticagrelor in Patients Requiring Urgent Surgery or Experiencing Uncontrolled Major or Life-Threatening Bleeding

November 15, 2021

Global Phase 3 trial of bentracimab achieved primary reversal endpoint with immediate and sustained reversal of the antiplatelet effects of ticagrelor in both surgical and bleeding populations

Co-primary endpoint of clinical hemostasis achieved in greater than 90% of patients

Bentracimab appeared well tolerated with no drug-related serious adverse events

Results presented today in Late-Breaking Science Session at the American Heart Association's 2021 Scientific Sessions and accepted for publication in NEJM Evidence, a new digital journal from the NEJM (New England Journal of Medicine) Group

Investor webcast scheduled for today at 12:30 p.m. ET

MALVERN, Pa. & SAN DIEGO--(BUSINESS WIRE)--Nov. 15, 2021-- PhaseBio Pharmaceuticals, Inc. (Nasdaq: PHAS), a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies for cardiopulmonary diseases, in conjunction with its financing and co-development partner for the European Union and China, SFJ Pharmaceuticals, today announced interim results from REVERSE-IT (**R**apid and Sustain**E**d Re**VERS**al of Ticagr**E**lor – **I**ntervention **T**rial). REVERSE-IT is PhaseBio's ongoing pivotal Phase 3 trial designed to study the reversal of the antiplatelet effects of ticagrelor with lead product candidate bentracimab in patients who present with urgent surgery or an invasive procedure or experiencing uncontrolled major or life-threatening bleeding.

The prespecified interim analysis of 150 enrolled patients (142 of whom enrolled requiring urgent surgery or an invasive procedure and eight of whom enrolled with uncontrolled major or life-threatening bleeding) demonstrated that bentracimab achieved the primary endpoint of the trial by immediately and sustainably reversing the antiplatelet effects of ticagrelor. As measured by the point-of-care VerifyNow® PRUTest® platelet function assay (VerifyNow), a 135% reduction in platelet inhibition ($P<0.001$) was observed within five to ten minutes after initiation of bentracimab infusion and sustained through all timepoints over 24 hours. More than 90% of eligible patients achieved the co-primary endpoint of the trial, defined as good or excellent hemostasis within 24 hours of initiation of bentracimab therapy ($P<0.001$). Thrombotic events were reported in 5.3% of patients, with none resulting in death or considered by investigators to be related to bentracimab. Bentracimab was generally well tolerated, with only five non-serious adverse events, reported in three patients, considered by investigators to be related to bentracimab. The most common adverse events were related to pain associated with surgical procedures.

The results were presented today by Deepak L. Bhatt, M.D., M.P.H., Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital and professor at Harvard Medical School, during a Late-Breaking Science Session at the 2021 American Heart Association Scientific Sessions and have been accepted for publication in *NEJM Evidence*, a new digital journal from the NEJM (New England Journal of Medicine) Group.

"With no approved reversal agents for oral $P2Y_{12}$ inhibitors, patients who are prescribed these medications to reduce the risk of cardiac events are at increased risk for spontaneous major bleeding events, and physicians are faced with a complex dilemma of balancing bleeding risk and thrombotic risk, should these patients require urgent surgery," said Dr. Deepak L. Bhatt. "The emerging safety and efficacy profile of bentracimab is quite compelling based on these prespecified interim data from the REVERSE-IT trial presented today, and if approved, bentracimab has the potential to become an important tool in the management of patients who could benefit from ticagrelor therapy."

Cardiovascular disease remains a leading cause of mortality globally. Orally-administered $P2Y_{12}$ inhibitors, including ticagrelor, continue to be the mainstay of pharmacotherapy in patients diagnosed with acute coronary syndrome, coronary artery disease and other common cardiovascular diseases because of their demonstrated efficacy in preventing thrombotic events such as myocardial infarction and ischemic stroke. However, hospital admissions of patients on $P2Y_{12}$ inhibitors who require surgery or experience major bleeding events while persistent on their medication remain a significant driver of global healthcare resource utilization. Within the orally-administered $P2Y_{12}$ inhibitor class, ticagrelor is unique in that it is the only member of the class that can be reversed, creating a potential safety advantage for patients taking ticagrelor should bentracimab be approved.

"The data presented today from the Phase 3 REVERSE-IT trial of bentracimab are a continuation of the favorable results we've seen in the Phase 1, Phase 2a and Phase 2b trials that have been completed to date," said John Lee, M.D., Ph.D., Chief Medical Officer of PhaseBio. "These interim data continue to support the potential of bentracimab to help address a clear unmet need for patients on ticagrelor worldwide who lack an effective reversal agent. Having the ability to immediately restore platelet function, and ultimately achieve hemostasis in patients taking ticagrelor who require urgent surgery or an invasive procedure or experience uncontrolled major or life-threatening bleeding, would be significant for cardiologists, surgeons and, most importantly, patients. Propelled by these pivotal data, we remain on track to submit our planned Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) in mid-2022, as we move one step closer to potentially commercializing bentracimab in the future."

REVERSE-IT Interim Results Detail

Ticagrelor Reversal Endpoint

The primary ticagrelor reversal endpoint in the REVERSE-IT trial, the minimum percent inhibition of $P2Y_{12}$ reactivity units (PRU) within four hours of bentracimab initiation, was assessed using VerifyNow by measuring the difference in PRU inhibition before the initiation of bentracimab infusion and up to four hours after initiation of bentracimab infusion. Per the prespecified analysis plan, patients with pre-treatment PRU in the normal range (> 180) were excluded from reversal assessments, with

adjudication resulting in the inclusion of 129 patients in the reversal efficacy analysis. A 135% reduction in inhibition was observed with bentracimab, indicating achievement of the primary reversal endpoint (P<0.001). PRU measured at multiple timepoints rose from a mean of 65 PRU before bentracimab administration to 230 PRU within five to ten minutes after initiation of bentracimab infusion and remained between 230 and 300 PRU through 24 hours after initiation of infusion (P<0.001 across all timepoints). All prespecified subgroups, including the bleeding subgroup, exhibited similar, statistically significant reductions in PRU inhibition.

Clinical Hemostasis Endpoint

The co-primary endpoint for the trial is achievement of effective hemostasis in the overall study population as adjudicated by an independent Clinical Endpoints Committee (CEC). The hemostasis endpoint was defined using prespecified efficacy criteria adapted from the Global Use Strategies for Opening Occluded Coronary Arteries (GUSTO) bleeding scale and a clinical trial of andexanet alpha for surgical and bleeding patients, respectively. The CEC adjudicated hemostasis in a total of 122 patients determined to have met eligibility criteria and found that 98.4% (P<0.001) achieved effective hemostasis within 24 hours of initiation of bentracimab infusion.

Safety Results and Immunogenicity

Safety results were assessed in all 150 patients who were treated with bentracimab and followed for 35 days after enrollment in the trial. Treatment emergent adverse events (TEAEs) were reported in 91% of enrolled patients; the most common TEAE was pain associated with surgical procedures. Cardiac and metabolic disorders, such as atrial fibrillation, sinus tachycardia, and electrolyte abnormalities, were also common. Four patients died of events considered by investigators to be unrelated to treatment with bentracimab: two patients from septic shock and two patients from cardiogenic shock. Five adverse events, reported in three patients, were considered by investigators to be potentially related to treatment with bentracimab, and none were considered to be serious adverse events (SAEs). The adverse events considered related to treatment with bentracimab included infusion site bruising (0.7%), infusion site warmth (0.7%), bundle branch block (1.4%) and catheter-related jugular thrombosis (0.7%). Bentracimab immunogenicity was also measured in the trial by testing patients for anti-drug antibodies (ADA) before and after the initiation of bentracimab infusion. Results of the immunogenicity testing found that 22.6% of patients had pre-existing ADA, 24.3% of patients developed ADA after bentracimab infusion, and 53.0% of patients had no ADA. The presence of ADA had no apparent effect on ticagrelor reversal as measured by VerifyNow or on achievement of effective hemostasis.

Thrombotic Events and Assessment of Potential Prothrombotic Rebound

Eight of the 150 bentracimab-treated patients (5.3%) reported SAEs determined to be thrombotic events, although none resulted in death, and none were considered by investigators to be related to treatment with bentracimab. An assessment of whether bentracimab induced potentially prothrombotic changes in platelet activity was also conducted. Biomarkers of platelet activation, including circulating P-selectin and mean platelet volume, were measured prior to bentracimab initiation and at multiple timepoints following the infusion of bentracimab. Neither biomarker changed after the infusion of bentracimab compared with pre-dose levels, indicating that bentracimab did not show signs of a prothrombotic rebound effect. Taken together, the platelet biomarker analyses, and the relatively low number of thrombotic events seen in this trial, suggest that the risk of a post-reversal prothrombotic rebound effect on platelets is low. Completion of the trial will provide additional insight into this important question.

REVERSE-IT Clinical Program

The REVERSE-IT trial is expected to enroll approximately 200 major bleeding or urgent surgery patients at sites in the United States, Canada, the European Union and China. Based on prior guidance from the FDA, to balance the two patient populations, the REVERSE-IT trial does not allow enrollment of more than approximately two-thirds of either the uncontrolled major or life-threatening bleeding population or urgent surgery or invasive procedure population. Because the total number of patients enrolled in the prespecified interim analysis included 142 patients who required urgent surgery or an invasive procedure, PhaseBio has determined that the surgery cohort of the trial has been fully enrolled. With the successful completion of enrollment in this surgery cohort, REVERSE-IT trial sites have shifted focus to enrolling patients with uncontrolled major or life-threatening bleeding events. PhaseBio is seeking to accelerate enrollment of patients with uncontrolled major or life-threatening bleeding, including by working to increase the number of enrolling clinical trial sites as it believes that a broader site footprint will increase the probability of enrolling these patients. The FDA also previously indicated that an interim analysis of the first approximately 100 patients enrolled in the REVERSE-IT trial would be sufficient to support the submission of a BLA for accelerated approval of bentracimab. The FDA recommended that the 100 patients comprising the interim analysis include approximately 50 patients from each of the major or life-threatening bleeding population and urgent surgery or invasive procedure population, although the FDA noted that whether there are an adequate number of patients from either cohort would be a review issue and considered in the context of other data submitted with the BLA. PhaseBio is commencing preparation of the BLA and is targeting a BLA submission to the FDA in mid-2022.

Bentracimab has been studied in Phase 1 and Phase 2 clinical trials and demonstrated immediate and sustained reversal of the antiplatelet activity of ticagrelor. If these data are reproduced in the final results from the Phase 3 study, bentracimab may have the potential to bring life-saving therapeutic benefit to patients by potentially mitigating concerns regarding bleeding risks associated with the use of ticagrelor. Additionally, in a translational study, bentracimab achieved equivalent reversal of branded ticagrelor and multiple ticagrelor generics.

Investor Event Webcast Information

Members of the PhaseBio senior management team will review these new interim results during a conference call and live video webcast today at 12:30 p.m. ET (9:30 a.m. PT) following the late-breaking science session. The PhaseBio management team will be joined by the following key opinion leaders:

- Deepak L. Bhatt, M.D., MPH, Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School
- Charles Pollack, M.D., MA, FACEP, Clinician-Scientist, Department of Emergency Medicine, University of Mississippi Medical Center in Jackson
- Ph. Gabriel Steg, M.D., FESC, FACC, Interventional Cardiologist and Chief of Cardiology of Hôpital Bichat in Paris, France and Professor of Cardiology at University of Paris

To access the live and subsequently archived webcast, go to the Investor Relations section of PhaseBio's website at https://investors.phasebio.com. Interested parties may RSVP to join the virtual event through the following registration link: https://onlinexperiences.com/Launch/QReg/ShowUUID=19CB5A76-2767-43C6-A132-B025301158EB. The webcast can also be accessed by phone by calling 833-942-2359 from the United States and Canada or 470-414-9401 internationally and using the conference ID/passcode 5616009.

About Bentracimab (PB2452)

Bentracimab is a novel, recombinant, human monoclonal antibody antigen-binding fragment designed to reverse the antiplatelet activity of ticagrelor in major bleeding and urgent surgery situations. In a Phase 1 clinical trial, bentracimab demonstrated the potential to bring life-saving therapeutic benefit through immediate and sustained reversal of ticagrelor's antiplatelet activity, mitigating concerns regarding bleeding risks associated with the use of this antiplatelet drug. Data from the Phase 1 clinical trial of bentracimab in healthy volunteers was published in the New England Journal of Medicine in March 2019. In April 2019, bentracimab received Breakthrough Therapy Designation from the FDA. In September 2019, PhaseBio completed a Phase 2a trial in which bentracimab was investigated in healthy, older and elderly subjects on dual antiplatelet therapy of ticagrelor and low-dose aspirin. Additionally, the Phase 2a trial investigated a bentracimab regimen for the reversal of supratherapeutic doses of ticagrelor in healthy younger subjects. In November 2021, PhaseBio completed a Phase 2b trial in which bentracimab was investigated in healthy, older and elderly subjects on dual antiplatelet therapy of ticagrelor and low-dose aspirin. In all active treatment arms in both the Phase 2a and Phase 2b trials,

bentracimab achieved immediate and sustained reversal of the antiplatelet effects of ticagrelor and was generally well-tolerated, with only minor adverse events reported. These results are consistent with the results observed in healthy younger subjects treated with ticagrelor in the previously published Phase 1 trial. PhaseBio initiated REVERSE-IT, a pivotal Phase 3 clinical trial of bentracimab, in March 2020 to support a potential Biologics License Application for bentracimab in both major bleeding and urgent surgery indications.

About PhaseBio

PhaseBio Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies for cardiovascular and cardiopulmonary diseases. PhaseBio's pipeline includes: bentracimab (PB2452), a novel reversal agent for the antiplatelet therapy ticagrelor; pemziviptadil (PB1046), a once-weekly vasoactive intestinal peptide (VIP) receptor agonist for the treatment of pulmonary arterial hypertension; and PB6440, an oral agent for the treatment of resistant hypertension. PhaseBio's proprietary elastin-like polypeptide technology platform enables the development of therapies with potential for less-frequent dosing and improved pharmacokinetics, including pemziviptadil, and drives both internal and partnership drug-development opportunities.

PhaseBio is located in Malvern, PA, and San Diego, CA. For more information, please visit www.phasebio.com, and follow us on Twitter @PhaseBio and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "potential," "projects," "target," "will," "would" and "future" or similar expressions are intended to identify forward-looking statements.

Forward-looking statements include statements concerning or implying the conduct or timing of our clinical trials and our research, development and regulatory plans for our product candidates, the timing of availability or disclosure of data from those clinical trials and the timing of planned regulatory submissions, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed, marketed and commercialized. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements.

Risks regarding our business are described in detail in our Securities and Exchange Commission filings, including in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021. These forward-looking statements speak only as of the date hereof, and PhaseBio Pharmaceuticals, Inc. disclaims any obligation to update these statements except as may be required by law.

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