# PhaseBio Doses First Patients in Canada as Part of the REVERSE-IT Global Phase 3 Trial of Bentracimab for Reversal of the Antiplatelet Effects of Ticagrelor

October 6, 2020

*Cardiovascular disease remains a leading cause of mortality in both Canada and globally; the lack of reversal agents for patients taking antiplatelet therapies who require urgent surgery or experience a major bleeding event remains a critical unmet need*

*Bentracimab (PB2452) has demonstrated immediate and sustained reversal of the antiplatelet effects of ticagrelor in both Phase 1 and Phase 2 clinical trials*

*Ongoing global Phase 3 trial of bentracimab has been named REVERSE-IT (Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial)*

MALVERN, Pa. & SAN DIEGO--(BUSINESS WIRE)--Oct. 6, 2020-- PhaseBio Pharmaceuticals, Inc. (Nasdaq: PHAS), a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies for cardiopulmonary diseases, today announced that it has expanded its pivotal Phase 3 REVERSE-IT trial for its lead product candidate bentracimab (formerly PB2452) into Canada, where the first patients outside of the United States have now been enrolled and dosed. Bentracimab is a novel, human monoclonal antibody fragment that in earlier trials has shown immediate and sustained reversal of the antiplatelet effects of Brilinta® (ticagrelor).

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20201006005383/en/

“Brilinta is the best-in-class antiplatelet drug for patients with acute coronary syndrome (ACS), recent stent placement, or a history of myocardial infarction. Like all antiplatelet therapies, it does create some challenges for patients with serious bleeding events or who need urgent surgery,” said John Lee, M.D., Ph.D., Chief Medical Officer of PhaseBio. “In these situations, doctors need an intervention that immediately and sustainably reverses the antiplatelet activity of ticagrelor; this is something that currently does not exist. Bentracimab has the potential to be an important solution as it provides immediate and sustained restoration of platelet function, with potential utility across a broad spectrum of bleeding events, urgent surgeries and invasive procedures.”

“With cardiovascular disease representing a leading cause of death in Canada, as in the rest of the world, we expect to continue to see widespread utilization of $P2Y_{12}$ inhibitors like ticagrelor to help prevent adverse cardiovascular events in vulnerable patients. While ticagrelor is highly efficacious it poses increased risk of serious bleeding, like other $P2Y_{12}$ inhibitors. The promise of a potential reversal agent addresses a significant unmet clinical need for a large number of patients at risk of severe bleeding or those who may suffer a serious bleeding episode while on ticagrelor,” said Subodh Verma, M.D., Ph.D., a cardiac surgeon and Professor at the University of Toronto, and a member of the REVERSE-IT steering committee and Canadian national lead investigator. “I am delighted that about 20 sites in Canada will participate in this important and potentially practice-changing clinical trial,” said Professor Verma.

“We have seen in prior trials that bentracimab provided immediate restoration of platelet function and believe that it can help ticagrelor patients receive the urgent care they need in cases of acute bleeding or in need of an urgent procedure,” said Dr. C. David Mazer, a Professor of Anesthesiology at the University of Toronto and Canadian investigator on REVERSE-IT. Dr. Mazer continued, “We are delighted to be the first Canadian REVERSE-IT site to participate in the development of this critical therapy for patients in need.”

Jonathan Mow, Chief Executive Officer of PhaseBio added: “With a generic version of Brilinta under regulatory review in Canada and a best-in-class efficacy profile relative to other $P2Y_{12}$ inhibitors, we anticipate significant growth in market share for ticagrelor in Canada and a growing need for a novel reversal agent like bentracimab. We view the expansion of REVERSE-IT enrollment into Canada as an important milestone for the global bentracimab program.”

Bentracimab has been studied in Phase 1 and Phase 2 clinical trials and has demonstrated the potential to bring life-saving therapeutic benefit through immediate and sustained reversal of the antiplatelet activity of ticagrelor, potentially mitigating concerns regarding bleeding risks associated with the use of antiplatelet drugs. Additionally, in a translational study, bentracimab achieved equivalent reversal of branded ticagrelor and multiple ticagrelor generics. AstraZeneca reported net sales of $845 million for Brilinta in the first half of 2020, which represents a 15% increase over the prior year’s global total and an increase of 34% in emerging markets.

The Phase 3 clinical study is called REVERSE-IT (Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial). REVERSE-IT is a multi-center, open-label, prospective single-arm trial designed to study reversal of the antiplatelet effects of ticagrelor with bentracimab in patients who present with uncontrolled major or life-threatening bleeding or who require urgent surgery or invasive procedure. Approximately 200 patients are being targeted to be enrolled from major health centers worldwide. Patients with reported use of ticagrelor within the prior 3 days who require urgent ticagrelor reversal will be eligible for enrollment.

More information about the REVERSE-IT Phase 3 trial is available at ClinicalTrials.gov, using the identifier NCT04286438.

**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 antiplatelet drugs. 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. Breakthrough Therapy Designation may be granted by the FDA when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapy. In September 2019, PhaseBio completed a Phase 2a trial in which bentracimab was investigated in 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 both arms of the trial, 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 the REVERSE-IT trial, a pivotal Phase 3 clinical trial of bentracimab, in March 2020 to support a Biologics License Application for bentracimab in both major bleeding and urgent surgery indications. There are currently no approved reversal agents for ticagrelor or any other antiplatelet drugs.

**About PhaseBio Pharmaceuticals**

PhaseBio Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies for cardiovascular and cardiopulmonary diseases. The company's pipeline includes: bentracimab, a novel reversal agent for the antiplatelet therapy ticagrelor; PB1046, a once-weekly vasoactive intestinal peptide receptor agonist for the treatment of pulmonary arterial hypertension and hospitalized COVID-19 patients at high risk for rapid clinical deterioration and acute respiratory distress syndrome; 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 PB1046, 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.

**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," "projects," 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, including REVERSE-IT, and our research, development and regulatory plans for our product candidates, including bentracimab (PB2452), 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 and marketed. 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 June 30, 2020. 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.*

View source version on businesswire.com: https://www.businesswire.com/news/home/20201006005383/en/

**Investor Contact:**
John Sharp
PhaseBio Pharmaceuticals, Inc.
Chief Financial Officer
(610) 981-6506
john.sharp@phasebio.com

**Media Contact:**
Will Zasadny
Canale Communications, Inc.
will.zasadny@canalecomm.com
(619) 961-8848

Source: PhaseBio Pharmaceuticals, Inc.