Study Confirming Overwhelming Reduction in Bleeding of the Dual-Acting Factor XI/XIa Inhibitor Abelacimab as Compared to Rivaroxaban Selected as Late-Breaker Oral Presentation at the American Heart Association Scientific Sessions

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Anthos Therapeutics →
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Study Participants May Transition from the Rivaroxaban Arm to Abelacimab in an Extension Study

CAMBRIDGE, Mass., September 26, 2023 (BUSINESS WIRE) – Anthos Therapeutics, Inc., a clinical stage company developing innovative therapies for cardiovascular diseases, founded by Blackstone Life Sciences, announced today that primary data from the AZALEA-TIMI 71 study of patients with atrial fibrillation at moderate-to-high risk of stroke has been selected for a Late

Breaking session at the American Heart Association Scientific Sessions 2023, being held November 11-13 in Philadelphia.

This news comes just days after it was announced that the AZALEA-TIMI 71 study was stopped early by the independent Data Monitoring Committee (DMC) due to an overwhelming greater-than-anticipated reduction in major and clinically relevant non-major bleeds in abelacimab compared to rivaroxaban and a benefit/risk profile also favoring abelacimab.

“The substantial reduction in bleeding with the monthly administered, dual-acting Factor XI/XIa inhibitor abelacimab compared to a standard-of-care anticoagulant represents an enormous potential advance in the care of patients,” said Principal Investigator Christian T. Ruff, MD, MPH, Director, General Cardiology, Brigham and Women’s Hospital; Senior Investigator, TIMI Study Group; Associate Member, Broad Institute of MIT and Harvard; Associate Professor of Medicine, Harvard Medical School. "The ability of abelacimab to prevent thrombosis with an enhanced safety and tolerability profile will likely not only improve adherence, but also provide physicians with the confidence to extend anticoagulation to the most vulnerable patients who are frequently undertreated or not treated at all."

Late-Breaker Presentation Details

- **Oral Presentation:** *Abelacimab, a Novel Factor XI/XIa Inhibitor, vs Rivaroxaban in Patients with Atrial Fibrillation: Primary Results of the AZALEA-TIMI 71 Randomized Trial*
- **Session Title:** LBS.05 – Late Breaking Science: Shocking Decisions in AFib Care
- **Date:** Sunday, Nov. 12, 2023
- **Session Time:** 8:00am – 9:15am ET
- **Presentation Time:** 8:15am – 8:25am ET
- **Location:** Pennsylvania Convention Center; Philadelphia, Pennsylvania

Anthos Therapeutics and the TIMI Group have initiated an extension study to enable all patients from the rivaroxaban and abelacimab arms to transition to open label abelacimab. A Fast-Track Designation for abelacimab was previously granted by the U.S. Food and Drug Administration (FDA) for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

“This additional positive news further recognizes the confidence that Anthos Therapeutics placed early-on in the development program of abelacimab. The results of the AZALEA-TIMI 71 study firmly establishes that thrombosis can successfully be uncoupled from hemostasis,” said John Glasspool, CEO, Anthos Therapeutics. “We are now turning our full attention, along with our partners at the TIMI Study Group, to advancing our Phase 3 LILAC-TIMI 76

study in patients with atrial fibrillation deemed unsuitable for current anticoagulants, which is estimated to range from 40% to 60% of diagnosed patients."

About Abelacimab

Abelacimab is a novel, highly selective, fully human monoclonal antibody that locks Factor XI in the inactive state, resulting in dual inhibitory activity against both Factor XI and its activated form, Factor XIa. By uncoupling thrombosis from hemostasis, a dual-activity Factor XI inhibitor may provide a path forward for those patients who would benefit from the protection that anticoagulants can provide.

In patients with atrial fibrillation, abelacimab is planned to be dosed subcutaneously (SC) monthly to maintain nearly complete inhibition in a chronic setting. It is also planned to be administered via an initial intravenous (IV) infusion for acute indications requiring immediate onset of action and then followed by subsequent monthly SC administration.

In a PK / PD study, abelacimab administered IV provided profound suppression of Factor XI within one hour after the start of therapy and maintained near maximal inhibition for up to 30 days.[i] In a Phase 2 study published in the *New England Journal of Medicine* in 2021, a single intravenous dose of abelacimab after knee surgery reduced the rate of venous thromboembolism by 80%, measured 10 days after surgery, compared to enoxaparin.[ii] Factor XI inhibition offers the promise of hemostasis-sparing anticoagulation for the prevention and treatment of arterial and venous thromboembolic events.[iii]

Abelacimab is an investigational agent and is not approved for any indication in any country.

About the AZALEA-TIMI 71 Phase 2 Study

The AZALEA-TIMI 71 study is an event-driven, randomized, active-controlled, blinded endpoint, parallel-group study with a primary endpoint that evaluates the effect of two blinded doses of abelacimab relative to open-label rivaroxaban in patients with atrial fibrillation (AF) who are at moderate-to-high risk of stroke. The primary endpoint of the AZALEA-TIMI 71 study is the composite of the rate of major or clinically relevant non-major bleeding events. A secondary endpoint is major bleeding on its own. Patients were randomized 1:1:1 and administered subcutaneous (SC) abelacimab 150 mg once-monthly, abelacimab 90 mg once-monthly, or rivaroxaban 20 mg daily.

Data from AZALEA-TIMI 71 represent a median of 21 months of follow-up, spanning more than 2,000 patient years. The AZALEA-TIMI 71 study is now the largest and longest study of a Factor XI inhibitor head-to-head with a Factor X inhibitor and has demonstrated a highly significant reduction in bleeding in patients in the abelacimab arm.

This event-driven study completed enrollment in December 2021, with 1,287 patients across 95 global study sites including the U.S. and Canada, Europe and Asia.

About the LILAC-TIMI 76 Phase 3 Study

The LILAC-TIMI 76 study is an event-driven, randomized, placebo-controlled, double-blind, parallel-group study to evaluate the efficacy and safety of abelacimab relative to placebo on the rate of ischemic stroke or systemic embolism in patients with atrial fibrillation (AF) who have been deemed to be unsuitable for currently available anticoagulation therapy. Patients in the study will be randomized to receive abelacimab 150 mg SC or matching placebo once monthly. The study is targeting to enroll approximately 1,900 patients from more than 400 sites in North America, Europe, Latin America, the Middle East and Asia.

About Atrial Fibrillation

Atrial fibrillation, or AF, is the most common type of irregular heartbeat. The most severe complication of AF is stroke. The Centers for Disease Control and Prevention (CDC) estimates that 12.1 million people in the United States will have atrial fibrillation by 2030.[iv] Unfortunately, 40% to 60% of patients with atrial fibrillation are not prescribed anticoagulants today. This underuse of anticoagulants for stroke prevention has been cited as one of the greatest public health issues facing cardiovascular patients.[v] In a physician survey, the foremost barrier to patients taking oral anticoagulants was bleed related.[vi]

About Anthos Therapeutics

Anthos Therapeutics was founded by Blackstone Life Sciences in 2019 and obtained from Novartis Pharma the exclusive global rights to develop, manufacture, and commercialize abelacimab. Anthos Therapeutics is a clinical-stage biopharmaceutical company focused on the development and commercialization of genetically and pharmacologically validated innovative therapies to advance care for high-risk cardiovascular patients. For more information, visit the company's website and follow on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the initiation, and timing, of future clinical trials and its research and development. All statements, other than statements of historical facts, contained in this press release, including statements regarding the company's strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "become," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. In addition, the forward-looking statements included in this press release represent the company's views as of the date hereof and should not be relied upon as representing the company's views as of any date subsequent to the date hereof. The company anticipates that subsequent events and developments will cause the company's views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

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[i] Yi BA et al. J Thromb Haemost. Oct. 2021 (https://pubmed.ncbi.nlm.nih.gov/34714969/)
[ii] Verhamme P et al. New Engl J Med July 2021 (https://www.nejm.org/doi/full/10.1056/NEJMoa2105872)
[iii] Hsu et al. J Am Coll Cardiol. Aug. 2021 (https://www.sciencedirect.com/science/article/abs/pii/S0735109721053213?via%3Dihub)
[iv] Center for Disease Control and Prevention website; Atrial Fibrillation page (https://www.cdc.gov/heartdisease/atrial_fibrillation.htm)
[v] Pokorney et al, American Heart Journal, April 2019 (https://www.sciencedirect.com/science/article/abs/pii/S0002870318302989?via%3Dihub)
[vi] Yao C et al PEC Innov 2022;1:100062. (https://www.sciencedirect.com/science/article/pii/S2772628222000474)