Press Release – September 2, 2024

Anthos Therapeutics Unveils Additional Analysis from the Landmark AZALEA-TIMI 71 Study Demonstrating that the Factor XI Inhibitor Abelacimab was Associated with Remarkably Low Levels of Periprocedural Bleeding in Patients with Atrial Fibrillation

Only About 1% of Patients Randomized to Abelacimab Experienced a Major or Clinically Relevant Non-Major Procedural Bleed

Routine Interruption of Anticoagulation May Not be Necessary in Advance of All Invasive Procedures with Abelacimab

Late-Breaking Presentation at the European Society of Cardiology Congress Further Substantiates Impressive Safety Profile of Abelacimab, a Novel, Investigational, Once-Monthly Administered, Highly Selective, Fully Human Monoclonal Antibody Anticoagulant

CAMBRIDGE, Mass., September 2, 2024 – Anthos Therapeutics, Inc., a transformative, clinical-stage biopharmaceutical company developing innovative therapeutic options for the treatment of cardiovascular metabolic diseases, founded by Blackstone Life Sciences (BXLS), announced today, at a late-breaking session of the European Society for Cardiology (ESC) Congress, a new analysis from the landmark AZALEA-TIMI 71 study, demonstrated that approximately 1% of patients randomized to abelacimab, an investigational Factor XI inhibitor, experienced a major or clinically relevant non-major procedural bleed while undergoing invasive procedures.

An estimated 20% of patients treated with an anticoagulant undergo invasive procedures per year, with frequent interruption of therapy.[1,2] Thus, the perioperative management of therapies is a common scenario encountered among patients with atrial fibrillation treated with anticoagulants for stroke prevention.

"These results are encouraging and add to the growing body of evidence supporting the safety profile of abelacimab and suggest that long-acting factor XI inhibition is feasible in a contemporary atrial fibrillation patient population who commonly require invasive procedures," said Siddharth (Sid) Patel, MD, presenting Investigator from the TIMI Study Group and a Cardiologist at Brigham and Women's Hospital in Boston. "While traditionally the approach for DOACs (and warfarin) has been to interrupt anticoagulation for most elective procedures, these data suggest that such routine interruption may not be necessary with abelacimab for all elective procedures."

The most severe complication of atrial fibrillation is stroke[3], which can be prevented by taking an anticoagulant, or "blood thinner." Affecting 60 million people worldwide[4], the prevalence of AF is expected to increase by 60% by 2050 due to an aging population and rising cardiometabolic risk factors.[5] The Centers for Disease Control and Prevention (CDC) estimates that 12.1 million people in the United States will have atrial fibrillation by 2030.

"For patients who are taking current standard-of-care anticoagulants to mitigate their risk of stroke, it can be frightening to have to stop taking treatment – even temporarily – to undergo any procedure. Abelacimab has the potential to reduce this fear," said Mellanie True Hills, Founder and Chief Executive Officer at StopAfib.org, and the American Foundation for Women's Health. "The potential with abelacimab to no longer need to stop and restart treatment will minimize stress for the very large number of atrial fibrillation patients who undergo a broad range of procedures each year."

Abelacimab is a novel, highly selective, investigational, fully human monoclonal antibody that binds tightly to Factor XI to block its activation and prevent the generation of the activated form (Factor XIa).[6] This mimics natural Factor XI deficiency, which is associated with protection from thromboembolic disease.[7]

"Building on the overwhelmingly positive data released in late 2023, these new findings from the AZALEA-TIMI 71 study further reinforce the fundamental premise of the promise of Factor XI inhibition – preventing thrombotic events without effecting normal hemostasis," said Dan Bloomfield, MD, Chief Medical Officer of Anthos Therapeutics. "Even when the risk of bleeding is highest, during surgery or invasive procedures, patients treated with abelacimab have a very low rate of bleeding, despite near complete inhibition of Factor XI. The safety of abelacimab, a long-acting anticoagulant, in a patient population in whom invasive procedures are common, elevates its promise for patients, and if approved, as a potentially very attractive therapeutic option for those seeking a safer, more convenient anticoagulant."

AZALEA-TIMI 71 Peri-Procedural Data at the European Society of Cardiology Congress

- 1,287 patients followed for a median of 2.1 years
- 920 invasive procedures occurred *(34% in abelacimab arms vs. 36% for rivaroxaban)*
- Standard-of-care approach allowed for interruption of rivaroxaban 24-48 hours prior to procedures
- When analyzed at the patient level, 0.8% of patients randomized to abelacimab (7 events among 852 patients) versus 1.4% of patients randomized to rivaroxaban (6 events among 428 patients) experienced a procedure-related major/CRNM bleed (RR 0.58 [0.20-1.73])
- Assessed at the procedure level, 14 procedure-related major/CRNM bleeds occurred, 1.2% of all procedures in the abelacimab arms vs. 2.2% of all procedures in the rivaroxaban arm (RR 0.54 [95% CI, 0.19-1.58])

About the AZALEA-TIMI 71 Study

In September 2023, the AZALEA-TIMI 71 study was stopped early by the independent Data Monitoring Committee due to an overwhelming, greater-than-anticipated reduction in major and clinically relevant non-major bleeds in abelacimab and a benefit/risk profile also favoring abelacimab.

The AZALEA-TIMI 71 study enrolled 1,287 patients across 95 global study sites, including the U.S. and Canada, Europe and Asia. The independent data monitoring committee (IDMC) recommended that the study end early because of a substantially greater than anticipated reduction in major and clinically relevant non-major bleeding in the abelacimab arms compared to rivaroxaban and a benefit: risk ratio that favored abelacimab.

The study was an event-driven, randomized, active-controlled, blinded endpoint, parallel-group study with a primary endpoint that evaluated 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 was the composite of the rate of major or clinically relevant non-major bleeding events. The secondary endpoint was 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.

With a median follow-up of 21 months, spanning more than 2,000 patient-years, the AZALEA-TIMI 71 study is the largest and longest head-to-head study of a Factor XI inhibitor to provide definitive evidence of a highly significant reduction in bleeding as compared to a standard-of-care anticoagulant.

Summary of Results as Presented During the American Heart Association 2023 Scientific Sessions:[8]

- Primary endpoint met with a 67% reduction in major or clinically relevant non-major bleeding (CRNM) with abelacimab 150 mg compared with rivaroxaban 20 mg in patients with atrial fibrillation who are at moderate-to-high risk of stroke *(P<0.001, HR 0.33, 95% CI 0.19–0.55)*
- 74% reduction in major bleeding alone with abelacimab 150 mg vs rivaroxaban 20 mg *(P=0.002, HR 0.26, 95% CI 0.11-0.61)*
- 93% reduction in gastrointestinal (GI) bleeding with abelacimab 150 mg vs rivaroxaban 20 mg *(P=0.008, HR 0.07, 95% CI 0.01-0.50)*
- 51% reduction in net clinical outcome with abelacimab 150 mg vs rivaroxaban 20 mg *(P<0.001, HR 0.49, 95% CI 0.33-0.71)*
- Factor XI inhibition of ~99% with abelacimab 150 mg dosed once monthly

AZALEA-TIMI 71 Open-Label Extension (OLE)

As part of the AZALEA-TIMI 71 study protocol, an optional extension period was included to gather longer-term data. The study was stopped early by the independent data monitoring committee (IDMC) due to a notable imbalance of bleeding events favoring abelacimab over rivaroxaban, with the benefit-to-risk ratio clearly favoring abelacimab. Following this, an open-label extension commenced, and investigative sites had the option to participate or not. Patients who completed the end-of-treatment visit and met the eligibility criteria for the extension period had the choice to participate or not. Approximately

84% of eligible patients chose to transition to abelacimab, with 75% of patients in the rivaroxaban arm voluntarily transitioning from the once-daily oral anticoagulant to once-monthly abelacimab.

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 subcutaneous (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 Abelacimab

Abelacimab is a novel, highly selective, fully human monoclonal antibody that binds tightly to Factor XI to block its activation and prevent the generation of the activated form (Factor XIa).[6] This mimics natural Factor XI deficiency, which is associated with protection from thromboembolic disease.[7]

As a monoclonal antibody, abelacimab is not metabolized via the cytochrome P450 system or as a substrate for P-glycoprotein, meaning the risk of drug-drug interactions is very low.[9] There is no need to adjust the dose based on age or renal/hepatic status.[9]

Factor XI inhibition offers the promise of hemostasis-sparing anticoagulation for the prevention and treatment of arterial and venous thromboembolic events.[9] Abelacimab is the only Factor XI inhibitor being studied for both conditions.

In patients with atrial fibrillation, abelacimab is planned to be dosed subcutaneously (SC) monthly to maintain near-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 the AZALEA-TIMI 71 study, abelacimab 150 mg dosed subcutaneously once-monthly, inhibited Factor XI by 99%.[8] 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.[10] 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.[11]

Abelacimab received a Fast Track Designation from the FDA in July 2022 for the treatment of thrombosis associated with cancer. In September 2022, abelacimab was also granted a Fast Track Designation for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

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

About Anthos Therapeutics

Anthos Therapeutics was founded by Blackstone Life Sciences in 2019 and obtained from Novartis Pharma AG the exclusive global rights to develop, manufacture, and commercialize abelacimab. Anthos Therapeutics, Inc., a transformative, clinical-stage biopharmaceutical company developing innovative therapeutic options for the treatment of cardiovascular metabolic diseases. 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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