First Patient Enrolled in Phase 3 Trial Evaluating Abelacimab in High-Risk Patients with Atrial Fibrillation Deemed Unsuitable for Current Anticoagulants

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Anthos Therapeutics →
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FDA Fast-Track designation was granted to investigate abelacimab for the prevention of stroke and systemic embolism in patients with atrial fibrillation

LILAC-TIMI 76 trial is the third Phase 3 study with abelacimab initiated by Anthos Therapeutics

Abelacimab is a dual-acting, once-monthly, fully human monoclonal antibody targeting both Factor XI and Factor XIa with high affinity and selectivity

CAMBRIDGE, Mass., Jan. 03, 2023 (GLOBE NEWSWIRE) -- Anthos Therapeutics, a clinical-stage biotechnology company developing innovative therapies for cardiovascular and metabolic diseases, today announced that it has enrolled the first patient in LILAC-TIMI 76, a Phase 3 study to evaluate the efficacy and safety of abelacimab in high-risk patients with atrial fibrillation (AF) deemed unsuitable for current anticoagulants by their physician. The study is targeting to enroll approximately 1900 patients from more than 300 sites across North America, Europe, Latin America, and Asia.

“The use of currently available anticoagulants in patients with AF can significantly reduce the risk of stroke, however, the concern over bleeding risk can lead to underutilization of these agents in a significant proportion of patients who would otherwise benefit from therapy. Data from multiple registries show that approximately 40% of AF patients are not being optimally treated today[1],” said Dan Bloomfield, M.D., Chief Medical Officer at Anthos. “The gap in treatment is especially common in patients who are older adults, those with kidney or liver disease, those needing concomitant antiplatelet therapy, and patients with other factors associated with an increased risk of bleeding.”

Dr. Bloomfield added, “This is a unique patient population; they are among the most difficult to treat, and potentially stand to gain the most benefit from Factor XI inhibition. Dual-acting abelacimab may offer a safer treatment option that could shift the current treatment paradigm.”

“Enrolling the first patient in the LILAC-TIMI 76 study is an important clinical milestone as we continue to evaluate abelacimab as a potential new therapeutic option,” said Marc S. Sabatine, MD, MPH, Lewis Dexter, MD, Distinguished Chair in Cardiovascular Medicine at Brigham and Women’s Hospital, Professor of Medicine at Harvard Medical School, and Chair of the

Thrombolysis in Myocardial Infarction (TIMI) study group. “Our hope is that by inhibiting Factor XI, we can decouple hemostasis from thrombosis, thereby reducing bleeding, the major barrier to anticoagulation, and allowing more patients to benefit from such therapy.”

In addition to the LILAC-TIMI 76 study, Anthos has already initiated the AZALEA-TIMI 71 trial. It is an event driven phase 2b study evaluating the safety and tolerability of abelacimab compared head-to-head with rivaroxaban in 1287 patients with atrial fibrillation at moderate-to-high risk of stroke. It completed enrollment late last year.

Anthos is also enrolling patients in GARDENIA, a large international patient registry designed to evaluate treatment patterns and outcomes in segments of the atrial fibrillation population that have conditions associated with an increased risk of bleeding.

“The Afib patient community is watching these studies with great anticipation with the hope that the clinical trial results will lead to a safer treatment alternative for those patients who are not receiving optimal treatment today. This includes patients receiving a sub-therapeutic dose, skipping doses, or not receiving an anticoagulant at all due to an inherent fear of bleeding,” said Mellanie True Hills, patient advocate and founder and CEO of the American Foundation for Women's Health and StopAfib.org.

The Abelacimab Atrial Fibrillation Program

About the LILAC-TIMI 76 Phase 3 Trial

The LILAC-TIMI 76 trial 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 1900 patients from more than 300 sites in North America, Europe, Latin America, and Asia. Abelacimab received FDA Fast-Track designation for the prevention of stroke and systemic embolism in patients with atrial fibrillation in September 2022.

About the GARDENIA Atrial Fibrillation Patient Registry

The GARDENIA patient registry is a global, multicenter, prospective, non-interventional, observational study that will evaluate treatment patterns and outcomes in segments of the atrial fibrillation population that are often not treated with oral anticoagulants or not treated with oral anticoagulants at guideline recommended doses. The GARDENIA registry is recruiting patients across North America, Europe, and Asia.

About the AZALEA-TIMI 71 Phase 2 Trial

The AZALEA-TIMI 71 trial is an event-driven, randomized, active-controlled, blinded endpoint, parallel-group study to evaluate the effect of two blinded doses of abelacimab relative to open label rivaroxaban on the rate of major or clinically relevant non-major (CRNM) bleeding events in patients with atrial fibrillation (AF) who are at moderate-to-high risk of stroke. This event trial completed enrollment in December 2021, with 1287 patients across 95 global study sites including the U.S. and Canada, as well as parts of Europe, and Asia and is ongoing.

The Abelacimab Cancer Associated Thrombosis Program

The abelacimab phase 3 CAT program comprises two complementary studies targeting to enroll approximately 2700 patients across 220 sites in more than 20 countries -- the largest program of any anticoagulant performed in Cancer-Associated Thrombosis. Abelacimab received FDA Fast-Track

designation for the treatment of thrombosis associated with cancer in July 2022.

About the ASTER Phase 3 Trial

ASTER is an international multicenter, randomized, open-label, blinded endpoint evaluation, phase 3 study comparing the effect of abelacimab relative to apixaban on venous thromboembolism (VTE) recurrence and bleeding in patients with cancer associated VTE in whom direct oral anticoagulant (DOAC) treatment is recommended. Abelacimab 150 mg will be administered intravenously (IV) on Day 1 and subcutaneously (SC) monthly thereafter for up to 6 months; Apixaban 10 mg will be administered orally, twice daily (bid) for the first 7 days, followed by 5 mg bid up to 6 months.

About the MAGNOLIA Phase 3 Trial

MAGNOLIA is an international multicenter, randomized, open-label, blinded endpoint evaluation, phase 3 study in patients with gastrointestinal (GI) / genitourinary (GU) cancer in whom DOAC treatment is not recommended. The study will compare the effect of abelacimab relative to dalteparin on VTE recurrence and bleeding in patients with cancer associated VTE who are at a high bleeding risk with non-resectable, locally or regionally invasive GI / GU tumors. Abelacimab 150 mg will be administered intravenously (IV) on Day 1 and subcutaneously (SC) monthly thereafter for up to 6 months; dalteparin administered subcutaneously will be given daily, 200 IU/kg/day for the first month, and then 150 IU/kg/day up to 6 months.

About Abelacimab

Abelacimab is a novel, highly selective, fully human monoclonal antibody designed to induce effective hemostasis-sparing anticoagulation through Factor XI inhibition. Abelacimab targets the active domain of Factor XI, demonstrating dual inhibitory activity against both Factor XI and its activated

form, Factor XIa. 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.[ii] In a Phase 2 study whose results were 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.[iii] Factor XI inhibition offers the promise of hemostasis-sparing anticoagulation for the prevention and treatment of arterial and venous thromboembolic events.[iv]

Abelacimab, an investigational agent that has not been approved for any indication, received FDA Fast-Track Designations in July 2022 for the treatment of thrombosis associated with cancer, and for the prevention of stroke and systemic embolism in patients with atrial fibrillation in September 2022.

About Anthos Therapeutics

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 people living with cardiovascular and metabolic (CVM) diseases. Anthos Therapeutics aims to combine the agility of a biotech with the rigor of a large pharmaceutical company. Anthos Therapeutics was launched by Blackstone Life Sciences and Novartis in 2019 and has obtained the global rights to

develop, manufacture, and commercialize abelacimab (MAA868) under a license agreement with Novartis.

For more information, visit the company's website and follow on Twitter and LinkedIn.

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[i] Ko et al. *JAMA Network Open.* 2022;5(11):e2242964. doi:10.1001/jamanetworkopen.2022.42964

[ii] Yi BA et al. *J Thromb Haemost. Oct. 2021* (https://pubmed.ncbi.nlm.nih.gov/34714969/)

[iii] Verhamme P et al. New Engl J Med July 2021 (https://www.nejm.org/doi/full/10.1056/NEJMoa2105872)

[iv] Hsu et al. J Am Coll Cardiol. Aug. 2021 (https://www.sciencedirect.com/science/article/abs/pii/S0735109721053213?via%3Dihub)