Chimerix Announces Initiation of a Phase 2/3 Study of DSTAT in Acute Lung Injury for Patients with Severe COVID-19

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FDA Clearance to Proceed with Phase 2/3 Randomized, Double-Blind, Placebo Controlled Study

Mechanisms of Action May Address Overactive Inflammatory Response, Including Underlying Causes of Blood Coagulation Disorders Associated with COVID-19

Company to Host Conference Call Today at 8:30 a.m. ET

DURHAM, N.C., April 29, 2020 (GLOBE NEWSWIRE) -- Chimerix (NASDAQ:CMRX), a biopharmaceutical company focused on accelerating the development of medicines to treat cancer and other serious diseases, today announced the Company's initiation of a Phase 2/3 study of dociparstat sodium (DSTAT) in COVID-19 patients with acute lung injury (ALI).

DSTAT is a glycosaminoglycan derivative of heparin with robust anti-inflammatory properties, including the potential to address underlying causes of coagulation disorders with substantially reduced risk of bleeding complications compared to commercially available forms of heparin.[1]

"Given the severity of the COVID-19 pandemic, we have evaluated many potential targets to address the clinical manifestations associated with severe COVID-19,"said Joseph Lasky, M.D., Professor of Medicine, Pulmonary and Critical Care Section Chief, John W. Deming, M.D. Endowed Chair in Internal Medicine at Tulane University Medical School. "Based on the literature, we believe DSTAT has the potential to reduce the excessive inflammation, immune cell infiltration and hypercoagulation associated with poor outcomes in patients with severe COVID-19 infection."

"DSTAT is well-suited to unlock the anti-inflammatory properties of heparin as it may be dosed at much higher levels than any available form of heparin without triggering bleeding complications," said Mike Sherman, Chief Executive Officer of Chimerix. "We had planned to evaluate DSTAT in several indications of high unmet need, including ALI from different causes. The pandemic intensified our focus on ALI associated with COVID-19. Our team has worked closely with critical care physicians treating COVID-19 patients and with the U.S. Food and Drug Administration (FDA) to develop a Phase 2/3 protocol to determine if DSTAT can reduce the need for mechanical ventilation and improve the rate of survival in patients with severe COVID-19 infection."

Phase 2/3 Study Design

The study is a 1:1 randomized, double-blind, placebo-controlled, Phase 2/3 trial to determine the safety and efficacy of DSTAT in adults with severe COVID-19 who are at high risk of respiratory failure. Eligible subjects will be those with confirmed COVID-19 who require hospitalization and supplemental oxygen therapy. The primary endpoint of the study is the proportion of subjects who survive and do not require mechanical ventilation through day 28. Additional endpoints include time to improvement as assessed by the National Institute of Allergy and Infectious Disease ordinal scale, time to hospital discharge, time to resolution of fever, number of ventilator-free days, all-cause mortality, and changes in key biomarkers (e.g. interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), high mobility group box 1 (HMGB1), C-reactive protein and d-dimer).

The Phase 2 portion of the study will enroll 24 subjects to confirm the maximum safe dose and will then expand by an additional 50 patients (74 total) at the selected dose. A formal analysis of all endpoints, including supportive biomarkers will be performed at the conclusion of the phase 2 portion of the study. Contingent upon positive results, the Phase 3 portion of the study will enroll approximately 450 subjects.

Clinical Rationale for DSTAT in COVID-19 Patients with ALI

The clinical manifestations of COVID-19 range from mild, self-limited respiratory tract illness to severe alveolar damage and progressive respiratory failure, multiple organ failure, and death. Mortality in COVID-19 is associated with severe pulmonary disease and coagulation disorders such as disseminated intravascular coagulation (DIC).[2,3]

The mechanistic rationale supporting DSTAT's potential in ALI patients with COVID-19 is two-fold:

- *Potential to decrease inflammation/immune cell infiltration in COVID-19 patients with ALI:*
  - A primary anti-inflammatory effect of DSTAT is mediated by inhibition of HMGB1 activity. HMGB1 induces downstream proinflammatory cytokines, including but not limited to, IL-6, TNF-α, monocyte chemoattractant protein-1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α), all of which are elevated in COVID-19.[1,4-6]
  - Infiltration of monocytes and other immune cells into inflamed lung tissue is a key pathogenic driver of ALI.[7] DSTAT reduces lung infiltration by immune cells in ALI, likely by inhibition of MCP-1 and other ligands involved in migration of monocytes, neutrophils and other effector cells that promote hyperinflammation in the lungs.[1,8]
- *Potential to alleviate the underlying causes of coagulation disorders by inhibiting HMGB1 and platelet factor 4 (PF4)*

activities:

- Two recent studies have identified a high neutrophil/lymphocyte ratio and low platelet counts as clinically relevant indicators of disease severity and mortality in COVID-19.[9,10] Neutrophils are early responders to infection capable of extruding granular and nuclear contents to produce neutrophil extracellular traps (NETs). NETs may be beneficial (e.g., by trapping pathogens); however, excessive neutrophils and NET release can be pathogenic.[11] HMGB1 promotes NETs which may drive hypercoagulation by providing a substrate for platelet aggregation and upregulating tissue factor on endothelial cells.[12] Activated platelets in turn release PF4, which further exacerbates inflammation.[13] DSTAT's inhibition of inflammatory drivers of coagulation (e.g., PF4 and HMGB1) has the potential to prevent and treat coagulation disorders observed in COVID-19.[1,14,15]

In a recent Phase 2 Acute Myeloid Leukemia (AML) study DSTAT was well tolerated with adverse events similar across DSTAT and control groups. DSTAT is an investigational agent, not yet licensed or approved for use.

Conference Call and Webcast

Chimerix will host a conference call and live audio webcast today at 8:30 a.m. ET. To access the live conference call, please dial 877-354-4056 (domestic) or 678-809-1043 (international) at least five minutes prior to the start time and refer to conference ID 8263766.

A live audio webcast of the call will also be available on the Investors section of Chimerix's website, www.chimerix.com. An archived webcast will be available on the Chimerix website approximately two hours after the event.

About Chimerix

Chimerix is a development-stage biopharmaceutical company dedicated to accelerating the advancement of innovative medicines that make a meaningful impact in the lives of patients living with cancer and other serious diseases. Its two clinical-stage development programs are dociparstat sodium (DSTAT) and brincidofovir (BCV).

Dociparstat sodium is a potential first-in-class glycosaminoglycan compound derived from porcine heparin that has low anticoagulant activity In vitro and in vivo animal model data support DSTAT's potential to reduce the inflammation and cellular infiltration associated with acute lung injury and address coagulation disorders associated with COVID-19 pathology. Separately, DSTAT inhibits the activities of several key proteins implicated in the viability of AML blasts and leukemic stem cells in the bone marrow during chemotherapy (e.g., CXCL12, selectins, HMGB1, elastase). Randomized Phase 2 data suggest that DSTAT may also accelerate platelet recovery post-chemotherapy via inhibition of PF4, a negative regulator of platelet production that impairs platelet recovery following chemotherapy. BCV is an antiviral drug candidate in development as a medical countermeasure for smallpox. For further information, please visit the Chimerix website, www.chimerix.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include those relating to, among other things, the mechanism of action of DSTAT and its potential in ALI patients with COVID-19; Chimerix's ability to develop DSTAT, including the initiation of a Phase 2/3 clinical trial for DSTAT as a potential treatment for ALI associated with COVID-19; and Chimerix's ability to submit and/or obtain regulatory approvals for DSTAT. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks that DSTAT may not achieve the endpoints of the Phase 2/3 clinical trial; risks that DSTAT may not obtain regulatory approval from the FDA or such approval may be delayed or conditioned; risks that development activities related to DSTAT may not be completed on time or at all; Chimerix's reliance on a sole source third-party manufacturer for drug supply; risks that ongoing or future trials may not be successful or replicate previous trial results, or may not be predictive of real-world results or of results in subsequent trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for our drugs; risks that our drugs may be precluded from commercialization by the proprietary rights of third parties; and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forward-looking statements represent the Company's judgment as of the date of this release. The Company disclaims, however, any intent or obligation to update these forward-looking statements.

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note: DSTAT may be referred to as 2-O,3-O desulfated heparin, ODSH or CX-01 in these references.

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Source: Chimerix, Inc.