# Cytori Announces Top-Line 24- and 48-Week Results from the STAR Trial of Habeo™ Cell Therapy in Patients with Scleroderma

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- Statistical significance not achieved in primary or secondary efficacy endpoints
- Clinically meaningful efficacy trends observed in primary and secondary endpoints in pre-specified diffuse cutaneous scleroderma subgroup
- No significant safety related issues
- Conference call scheduled for 8:30am EDT

SAN DIEGO, July 24, 2017 (GLOBE NEWSWIRE) -- Cytori Therapeutics, Inc. (NASDAQ:CYTX) today announced top-line, preliminary data from its pivotal STAR trial of HabeoTM Cell Therapy in patients with scleroderma. While the primary endpoint, Cochin Hand Function Score (CHFS), did not reach statistical significance at 24 or 48 weeks, the trial data reported clinically meaningful improvements in the primary and secondary endpoints of both hand function and scleroderma-associated functional disability, for Habeo treated patients compared to placebo, in a subgroup of patients with diffuse cutaneous scleroderma.

The U.S. multi-center STAR trial enrolled and evaluated 88 patients with scleroderma, including 51 patients within the diffuse cutaneous subset and 37 with limited cutaneous scleroderma. In the combined study population, the primary endpoint, specifically mean improvement in the Cochin Hand Function Score, did not show statistical difference between treated patients and those receiving placebo at 24 weeks and 48 weeks as determined by both analysis of covariance and mixed model repeated measure analysis.

The Raynaud's Condition Score, a secondary endpoint, improved in both the treatment and placebo group but was not statistically different between the Habeo treated and placebo groups.

However, in the pre-specified subgroup analysis of patients with diffuse cutaneous scleroderma, a more severe form of the disease, improvements in the Cochin Hand Function Score and the Health Assessment Questionnaire-Disability Index (HAQ-DI), a measure of functional disability and an important secondary endpoint, met or exceeded the published criteria for minimally important clinical differences in these measures (6.5 points for Cochin1, 0.22 points for HAQ-DI2).

| Endpoint | Timepoint | Habeo † / ‡ | Placebo † / ‡ | p value † / ‡ |
|---|---|---|---|---|
| **All Subjects** | | **n=48** | **n=40** | |
| CHFS - mean improvement | 24 weeks | 11.5 / 11.8 | 10.2 / 9.8 | 0.442 / 0.3943 |
| | 48 weeks | 11 / 11.3 | 8.9 / 8.51 | 0.2989 / 0.2650 |
| HAQ-DI - mean improvement | 48 weeks | 0.22 / NA | 0.11 / NA | 0.105 / NA |
| **Diffuse Cutaneous Subgroup** | | **n=32** | **n=19** | |
| CHFS - mean improvement | 24 weeks | 12.8 / 13.3 | 8.0 / 7.2 | 0.111 / 0.078 |
| | 48 weeks | 12.0 / 12.4 | 6.6 / 5.9 | 0.069 / 0.058 |
| HAQ-DI - mean improvement | 48 weeks | 0.20 / NA | 0.00 / NA | 0.044 / NA |

† Analysis of co variance using ANCOVA mean changes from baseline.

‡ Mixed model repeated measure analysis, MMRM mean changes from baseline.

NA Data not available.

"The safety and efficacy results from this trial in the diffuse subset of patients with scleroderma are impressive and represent important new information for the field," said Dinesh Khanna, MD, Frederick G.L. Huetwell Professor of Medicine and Director of the University of Michigan Scleroderma Program. "The STAR trial suggests that Habeo may provide clinically meaningful improvements in the hand function and functional disability to patients with diffuse form of the disease who have no other treatment options. The diffuse subset has a more severe disease burden with significant hand dysfunction and internal organ involvement as well as the highest mortality rate among all rheumatic diseases. It is important for these patients that this innovative technology moves forward in the clinical and regulatory process."

"We are disappointed that the study missed the primary and secondary endpoints. However, we are very encouraged by the trends toward improved hand function and scleroderma-related health status in patients with diffuse cutaneous scleroderma," said Marc H. Hedrick, MD, President and Chief Executive Officer of Cytori Therapeutics, Inc. "We thank the STAR investigators and patients for participating in this trial, which has yielded new insights into scleroderma and shows yet again that discrete patient populations may respond differently to investigational therapies – an important consideration for individuals currently lacking treatment options for rare diseases. After we review the complete data set, we will work collaboratively with our team, trial investigators, patient advocates and the regulatory bodies in our key markets, to chart the next steps for this therapy."

In general, the adverse events were rated as mild to moderate in the majority of cases and there were no significant safety issues identified for Habeo or the procedure itself (including liposuction and finger injection in the placebo group) during the trial.

“We are pleased with both the efficacy trends as well as the safety profile of Habeo,” said Dr. Mark Marino, MD, Senior Vice President and Chief Medical Officer of Cytori Therapeutics, Inc. “Following the evaluation of the full STAR data set, Cytori, in conjunction with the investigators, intends to submit the full data set, as a late-breaking abstract, to the American College of Rheumatology meeting in November 3-8, 2017. Simultaneously, we anticipate seeking a post-trial meeting with FDA as soon as possible to define next steps. We further plan to continue to support the investigator-initiated SCLERADEC-II trial in France, which is over 50 percent enrolled.”

**Management Conference Call Webcast**

Cytori will host a management conference call at 8:30 a.m. Eastern Time today to further discuss the preliminary top-line results from the STAR trial. The webcast will be available live and by replay two hours after the call and may be accessed under "Webcasts" in the Investor Relations section of Cytori's website. If you are unable to access the webcast, you may dial in to the call at +1.877.402.3914, Conference ID: 60408495.

**About STAR**

The STAR trial was a prospective, double-blind, randomized, multicenter, parallel-group Phase III pivotal study assessing the safety and efficacy of a single, subcutaneous administration of Habeo Cell Therapy (40 million cells per subject) into the fingers of patients with hand dysfunction due to scleroderma. The subjects were randomized 1:1 to receive either Habeo Cell Therapy or placebo. Investigators conducted final assessments at 48 weeks.

The primary study endpoint was improvement in the Cochin Hand Function Score, a self-reported measure of hand function, which was assessed at 24 and 48 weeks. The Cochin score is based on 18 questions relating to hand function; each question is graded on a 0–5 scale, with a total score of 90 points reflecting maximal disability.

The Health Assessment Questionnaire-Disability Index (HAQ-DI), a measure of functional disability and a secondary endpoint in the STAR trial, consists of questions pertaining to activities of daily living graded on a 0–3 scale (with 3 representing “unable to perform”); the HAQ-DI also includes several visual analog scales (VAS) for different body systems.

The Raynaud’s Phenomenon Condition Score, a secondary endpoint in the STAR trial, is a patient reported outcome measure asking the patients how much difficulty they had with their Raynaud’s symptoms over the past 24 hours graded on a scale of 0 – 10 with 0 being no difficulty and 10 being extreme difficulty.

Details of the STAR trial, including inclusion and exclusion criteria, can be found at clinicaltrials.gov.

**About Scleroderma**

Scleroderma is a rare and chronic connective tissue disease generally classified as an autoimmune rheumatic disorder. The word “scleroderma” is derived from two Greek words: “sclera,” which means hard, and “derma,” meaning skin, as hardening of the skin is one of the most visible manifestations of the disease. An estimated 300,000 Americans have scleroderma, about one-third of whom have the systemic form of the disease, known as systemic sclerosis (SSc). SSc is further sub-classified as diffuse cutaneous and limited cutaneous SSc. Patients with diffuse cutaneous SSc have more severe disease with significant hand dysfunction and internal organ involvement. Diffuse scleroderma accounts for between one-third and one-half of all cases of systemic sclerosis.3,4

SSc contributes to hand impairment through inflammatory arthritis or inflammation of the joints, joint contractures, Raynaud’s Phenomenon (RP, skin discoloration resulting from narrowing of the blood vessels in response to cold, emotional upset, or stress), digital ulcers, puffy hands and skin fibrosis over the fingers and hands, and calcinosis (calcium deposits in the soft tissues of the hand). These manifestations, which often coexist, can contribute to difficulty with occupational activities and activities of daily living, which can impair quality of life. Whereas current treatment recommendations focus on management of internal organ involvement, there is little treatment available for hand impairment.

**About SCLERADEC-II**

SCLERADEC-II is an investigator initiated, multicenter, double blind, placebo controlled trial of a single administration of Habeo Cell Therapy. The trial contemplates enrollment of up to 40 patients randomized in a 1:1 fashion to receive either active treatment or placebo control. The primary endpoint is the Cochin Hand Function Score at 3 months following treatment. Key secondary endpoints include Raynaud’s Condition Score, HAQ-DI, pain, the modified Rodnan Skin Score, capillaroscopy and functional hand assessment. Patients receiving placebo will be eligible for cross-over to the active arm after 6 months with their respective cryopreserved cells.

**About Habeo Cell Therapy**

Cytori is developing cell therapies that harness the unique attributes of adipose-derived regenerative cells (ADRCs), which are living

cells that are present in an adult human's own adipose tissue.

Habeo Cell Therapy is a suspension of ADRCs that are manufactured from a single lipoaspirate (material removed via liposuction, a procedure in which fat is removed from under the skin by suction). The process concentrates ADRCs intended for autologous re-implantation subcutaneously into the digits. The resultant cell suspension contains critical cells naturally occurring in the patient's own tissue. Preparation of autologous ADRCs for subcutaneous delivery involves no cell culture and can be prepared and re-implanted into the same patient within four hours.

**About Cytori Therapeutics**

Cytori is a therapeutics company developing regenerative and oncologic therapies from its proprietary cell therapy and nanoparticle platforms for a variety of medical conditions. Data from preclinical studies and clinical trials suggest that Cytori Cell Therapy™ acts principally by improving blood flow, modulating the immune system, and facilitating wound repair. As a result, Cytori Cell Therapy™ may provide benefits across multiple disease states and can be made available to the physician and patient at the point-of-care through Cytori's proprietary technologies and products. Cytori Nanomedicine™ is developing liposome encapsulated therapies for regenerative medicine and oncologic indications. For more information, visit www.cytori.com.

**Cautionary Statement Regarding Forward-Looking Statements**

This press release includes forward-looking statements regarding events, trends and business prospects, which may affect Cytori's future operating results and financial position. Such statements, include, but are not limited to, statements regarding, Cytori's plans to evaluate the STAR data in consultation with various internal and external resources, experts and the FDA; Cytori's conduct of its STAR trial, and possible future clinical trials of Habeo Cell Therapy; Cytori's intention to continue its support of the investigator-initiated SCLERADEC II trial; the ability to fully characterize the efficacy and safety profile of Habeo Cell Therapy through further study and the potential to yield additional insights into its clinical utility; and the ability of Cytori Cell Therapy™ to provide benefits across multiple disease states and be made available to the physician and patient at the point-of-care through Cytori's proprietary technologies and products. These statements are subject to risks and uncertainties that could cause Cytori's actual results and financial position to differ materially. Some of these risks and uncertainties include: risks in the conduct of Cytori's STAR trial and future clinical trials (including risks in the collection and results of clinical data); risks associated with the conduct of investigator-initiated trials using our cellular therapeutics, including the French, investigator-initiated SCLERADEC II trial; risks associated with potential benefits of Cytori's products (including any potential benefits of Habeo Cell Therapy identified in the STAR trial); risks associated with development of Cytori's clinical pipeline, including the possibility that Cytori may determine that there may not be a viable continued development path for Habeo Cell Therapy; final clinical outcomes (including the risk that top-line data may not accurately reflect the complete results of a particular study or trial); regulatory risks and uncertainties, including the risk that FDA and other regulatory authorities may not approve Habeo Cell Therapy, or that any marketing approvals, if granted, may have significant limitations on their use; risks related to reimbursement (including failure to achieve desired pricing for Habeo Cell Therapy); risks related to dependence on third party performance; the risk that Habeo Cell Therapy may never be successfully commercialized, or receive anticipated levels of commercial acceptance; Cytori's ability to raise additional funding that it may need to continue to pursue its commercial and business development plans; and other risks and uncertainties described under the "Risk Factors" section in Cytori's Securities and Exchange Commission filings on Form 10-K and Form 10-Q. Cytori assumes no responsibility to update or revise any forward-looking statements contained in this press release to reflect events, trends or circumstances after the date of this communication.

1 Nguyen C, Bérezné A, Mestre-Stanislas, et al. Changes over time and responsiveness of the Cochin Hand Function Scale and Mouth Handicap in Systemic Sclerosis Scale in patients with systemic sclerosis: a prospective observational Study. *American Journal of Physical Medicine & Rehabilitation*. 2016;95(12):e189-e197.

2 Pope J. Measures of systemic sclerosis (scleroderma): Health Assessment Questionnaire (HAQ) and Scleroderma HAQ (SHAQ), Physician- and Patient-Rated Global Assessments, Symptom Burden Index (SBI), University of California, Los Angeles Scleroderma Clinical Trials Consortium Gastrointestinal Scale (UCLA SCTC GIT) 2.0, Baseline Dyspnea Index (BDI) and Transition Dyspnea Index (TDI) (Mahler's Index), Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR), and Raynaud's Condition Score (RCS). *Arthritis Care & Research*. ol. 2011;63(S11):S98 –S111. doi 10.1002/acr.20598.

3 http://www.scleroderma.org/site/PageNavigator/patients_whatis.html#.WWZdOYjyvGh

4 Arthritis Rheumatism Vol 48, (8), August 2003, pp 2246–2255 DOI 10.1002/art.11073

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