



NEWS RELEASE

New Publication Provides Further Clarity of MultiStem's Mechanism of Action on Modulating the Inflammatory Response in Critical Care Indications

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CLEVELAND--(BUSINESS WIRE)-- Athersys, Inc. (NASDAQ: ATHX) announced today that data accumulated from several years of preclinical research was published in the peer-reviewed journal *Scientific Reports*. The publication describes the findings from extensive *in vitro* studies investigating the role Multipotent Adult Progenitor Cells (MAPC®), clinically known as MultiStem® (invivestem), have in modulating the inflammatory response. The report provides evidence of potential mechanisms by which MAPC cells promote regulatory T cell (Treg) differentiation and proliferation and influence their immune-suppressive phenotype. Tregs are important cells in the immune system, responsible for controlling inflammation and tissue repair after injury through several mechanisms. Dysregulated inflammatory responses are known to contribute to tissue and organ injury in multiple acute critical care indications, such as stroke, trauma, and acute respiratory distress syndrome (ARDS). Enhancement of endogenous, immunoregulatory mechanisms, including promoting Treg differentiation, proliferation, and phenotypic activity, is one way that MultiStem likely mitigates inflammatory organ injury and promotes recovery following tissue injury.

“Our work helps us understand how MAPC may induce Tregs *in vivo*, one of the potential mechanisms by which MAPC can help to reshape the hyperinflammatory response, thereby preventing exacerbated tissue damage,” commented Dr. Alice Valentin-Torres, Senior Scientist and Immunologist at Athersys, and primary author of the

article. "This study identifies factors secreted by MAPC and monocyte/macrophages as the primary mechanisms involved in MAPC induction of Tregs. We also observed that MAPC not only increase the number of Treg, but also enhance Treg suppressive function."

This study adds to the growing collection of scientific publications by Athersys and its collaborators relating to MAPC and the evidence elucidating how the cells modulate the inflammatory response initiated by acute injury, through down-regulation of inflammatory cytokines and immune cells that can exacerbate damage after an injury, such as a stroke. The described studies demonstrate that MAPC cells, via the secretion of soluble factors, not only increase the frequency of Tregs by promoting their differentiation and proliferation, but also promote Treg activation and suppressive functions. These data complement prior reports describing evidence of in vivo induction of Tregs in preclinical animal models and human volunteer participants in the Company's clinical development programs using MultiStem. The publication is available at <http://www.nature.com/articles/s41598-021-93025-x> and is listed on the Company's directory of **scientific publications**.

Athersys currently is undertaking three clinical studies evaluating MultiStem therapy, including a Phase 3 clinical study for the treatment of ischemic stroke, a Phase 2/3 clinical study for the treatment of ARDS, and a Phase 1/2 clinical study for the treatment of severe trauma. In addition, the Company's partner in Japan, HEALIOS K.K. (Healios), is nearing completion of its ischemic stroke study (TREASURE) and has recently completed enrollment in its ARDS (ONE-BRIDGE) study using MultiStem cell therapy. The data presented in this publication and other reports support the hypothesized mechanism of action for using MultiStem cell therapy in the ongoing clinical studies and provide support for other clinical indications in the future.

About MultiStem®

MultiStem® cell therapy (invimestrocel) is a patented regenerative medicine product candidate in clinical development that has shown the ability to promote tissue repair and healing in a variety of ways, such as through the production of therapeutic factors in response to signals of inflammation and tissue damage. MultiStem therapy's potential for multidimensional therapeutic impact may distinguish it from traditional biopharmaceutical therapies focused on a single mechanism of benefit. MultiStem represents a unique "off-the-shelf" stem cell product candidate that can be manufactured in a scalable manner, may be stored for years in frozen form, and is administered without tissue matching or the need for immune suppression. Based upon favorable outcome data, its novel mechanisms of action, and favorable and consistent tolerability data in clinical studies, we believe that MultiStem therapy may provide a meaningful benefit to patients, including those suffering from serious diseases and conditions with unmet medical need.

About Athersys

Athersys is a biotechnology company engaged in the discovery and development of therapeutic product candidates designed to extend and enhance the quality of human life. The Company is developing its MultiStem® cell therapy product, a patented, adult-derived "off-the-shelf" stem cell product, initially for disease indications in the neurological, inflammatory and immune, cardiovascular, and other critical care indications and has several ongoing clinical trials evaluating this potential regenerative medicine product. Athersys has forged strategic partnerships and a broad network of collaborations to further advance MultiStem cell therapy toward commercialization. More information is available at www.athersys.com. Follow Athersys on Twitter at www.twitter.com/athersys.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties. These forward-looking statements relate to, among other things, the expected timetable for development of our product candidates, our growth strategy, and our future financial performance, including our operations, economic performance, financial condition, prospects, and other future events. We have attempted to identify forward-looking statements by using such words as "anticipates," "believes," "can," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "should," "suggest," "will," or other similar expressions. These forward-looking statements are only predictions and are largely based on our current expectations. A number of known and unknown risks, uncertainties, and other factors could affect the accuracy of these statements. Some of the more significant known risks that we face are the risks and uncertainties inherent in the process of discovering, developing, and commercializing products that are safe and effective for use as therapeutics, including the uncertainty regarding market acceptance of our product candidates and our ability to generate revenues. The following risks and uncertainties may cause our actual results, levels of activity, performance, or achievements to differ materially from any future results, levels of activity, performance, or achievements expressed or implied by these forward-looking statements: our ability to raise capital to fund our operations, including but not limited to, the timing and nature of results from MultiStem clinical trials, including the MASTERS-2 Phase 3 clinical trial evaluating the administration of MultiStem for the treatment of ischemic stroke, and the Healios TREASURE and ONE-BRIDGE clinical trials in Japan evaluating the treatment in stroke and ARDS patients, respectively; the success of our MACOVIA clinical trial evaluating the administration of MultiStem for the treatment of COVID-19 induced ARDS, and the MATRICS-1 clinical trial being conducted with The University of Texas Health Science Center at Houston evaluating the treatment of patients with serious traumatic injuries; the impact of the COVID-19 pandemic on our ability to complete planned or ongoing clinical trials; the possibility that the COVID-19 pandemic could delay clinical site initiation, clinical trial enrollment, regulatory review and the potential receipt of regulatory approvals, payment of milestones under our license agreements and commercialization of one or more of our product candidates, if approved; the availability of product sufficient to meet commercial demand shortly following any approval, such as in the case of accelerated approval for the treatment of COVID-19 induced ARDS; the impact on our business, results of operations and financial condition from the ongoing and global COVID-

19 pandemic, or any other pandemic, epidemic or outbreak of infectious disease in the United States; the possibility of delays in, adverse results of, and excessive costs of the development process; our ability to successfully initiate and complete clinical trials of our product candidates; the impact of the COVID-19 pandemic on the production capabilities of our contract manufacturing partners and our MultiStem trial supply chain; the possibility of delays, work stoppages or interruptions in manufacturing by third parties or us, such as due to material supply constraints, contamination, operational restrictions due to COVID-19 or other public health emergencies, labor constraints, regulatory issues or other factors which could negatively impact our trials and the trials of our collaborators; uncertainty regarding market acceptance of our product candidates and our ability to generate revenues, including MultiStem cell therapy for neurological, inflammatory and immune, cardiovascular and other critical care indications; changes in external market factors; changes in our industry's overall performance; changes in our business strategy; our ability to protect and defend our intellectual property and related business operations, including the successful prosecution of our patent applications and enforcement of our patent rights, and operate our business in an environment of rapid technology and intellectual property development; our possible inability to realize commercially valuable discoveries in our collaborations with pharmaceutical and other biotechnology companies; our ability to meet milestones and earn royalties under our collaboration agreements, including the success of our collaboration with Healios; our collaborators' ability to continue to fulfill their obligations under the terms of our collaboration agreements and generate sales related to our technologies; the success of our efforts to enter into new strategic partnerships and advance our programs, including, without limitation, in North America, Europe and Japan; our possible inability to execute our strategy due to changes in our industry or the economy generally; changes in productivity and reliability of suppliers; the success of our competitors and the emergence of new competitors; and the risks mentioned elsewhere in our Annual Report on Form 10-K for the year ended December 31, 2020 under Item 1A, "Risk Factors" and our other filings with the SEC. You should not place undue reliance on forward-looking statements contained in this press release, and we undertake no obligation to publicly update forward-looking statements, whether as a result of new information, future events or otherwise.

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Ivor Macleod
Chief Financial Officer
Tel: (216) 431-9900
ir@athersys.com

Karen Hunady
Director of Corporate Communications & Investor Relations
Tel: (216) 431-9900
khunady@athersys.com

David Schull

Russo Partners, LLC

Tel: (212) 845-4271 or (858) 717-2310

David.schull@russopartnersllc.com

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