



2-1250 Waverley Street  
Winnipeg, Manitoba, Canada R3T 6C6  
Phone: 204-487-7412  
Fax: 204-488-9823

## **Medicure Receives Response Letter from FDA on AGGRASTAT® sNDA for New Indication**

### ***FDA Does Not Approve Application in its Present Form***

WINNIPEG, CANADA – (July 7, 2016) Medicure Inc. ("**Medicure**" or the "**Company**") (TSXV:MPH, OTC:MCUJF), a specialty pharmaceutical company, announced that it has received a Complete Response Letter from the U.S. Food and Drug Administration (FDA) for its supplemental New Drug Application (sNDA) requesting an expanded indication for patients presenting with ST segment elevation myocardial infarction (STEMI).

The FDA issued a Complete Response Letter to communicate that its initial review of the application is complete; however, it cannot approve the application in its present form and requested additional information. The On-TIME 2 trial<sup>1</sup> provided the majority of supporting information for the sNDA submission. Medicure will work directly with the FDA to address these comments.

The efficacy and safety of the AGGRASTAT high-dose bolus (HDB) regimen has been evaluated in more than 30 clinical studies involving over 15,000 patients and is currently recommended in the ACCF/AHA/SCAI Guidelines<sup>2-4</sup>. The STEMI indication for AGGRASTAT HDB was approved in Europe based substantially on the same clinical data submitted in the Company's sNDA. As of now, none of the marketed Glycoprotein IIb/IIIa Inhibitors (GPI) are approved for STEMI in the United States.

"We are evaluating the FDA's response and will work closely with the Agency to address their comments," stated Dr. Albert Friesen, Chief Executive Officer and President of Medicure Inc. "In the meantime, AGGRASTAT continues to be the fastest growing GPI in the United States."

### **About On-TIME 2**

The On-TIME 2 trial was a multi-center, prospective, randomized, controlled clinical trial which was designed to assess the effect of AGGRASTAT using the HDB regimen (25 mcg/kg followed by a 0.15 mcg/kg/min maintenance infusion) in patients with STEMI planned for primary PCI. All patients received ASA, a 600 mg loading dose of clopidogrel, and unfractionated heparin. The study was completed in two phases: a pilot, open label phase (n=414) followed by a larger double-blind phase (n=984). A pooled analysis of data from both phases was pre-specified to evaluate the effect of the AGGRASTAT HDB regimen compared to control as measured by a primary endpoint defined as the 30-day MACE rate (death, recurrent MI and uTVR). In this pooled analysis, MACE at 30 days was significantly reduced by initiation of AGGRASTAT compared to control (5.8% vs. 8.6%; p=0.043). The clinical benefit seen in the primary PCI population at 30 days was sustained at one year, as results indicated a significantly lower total mortality (2.4% vs. 5.5%, p=0.007) and cardiac mortality rate (1.4% vs. 4.3%, p=0.003) associated with AGGRASTAT versus the control arm. In patients receiving a stent, the incidence of early (0–30

days) stent thrombosis was 2.1 vs. 5.2% ( $p = 0.006$ ) in the AGGRASTAT and control group, respectively, which was driven by a reduction in the incidence of acute (0–24 h) stent thrombosis between the two treatment groups (0.2% vs. 3.0%;  $p < 0.001$ ). The incidence of 30-day mortality was significantly reduced in patients receiving AGGRASTAT compared to control (1.0% vs. 3.1%;  $p = 0.02$ , respectively) among patients undergoing primary PCI and receiving a stent.

## **About Medicure Inc.**

Medicure is a specialty pharmaceutical company focused on the development and commercialization of therapeutics for the U.S. hospital market. The primary focus of the Company and its subsidiaries is the marketing and distribution of AGGRASTAT (tirofiban HCl) for non-ST elevation acute coronary syndrome in the United States, where it is sold through the Company's U.S. subsidiary, Medicure Pharma, Inc. For more information on Medicure please visit [www.medicure.com](http://www.medicure.com).

## **About AGGRASTAT**

### **Indications and Usage**

AGGRASTAT is indicated to reduce the rate of thrombotic cardiovascular events (combined endpoint of death, myocardial infarction, or refractory ischemia/repeat cardiac procedure) in patients with non-ST elevation acute coronary syndrome (NSTEMI-ACS).

### **Dosage and Administration**

Administer intravenously 25 mcg/kg within 5 minutes and then 0.15 mcg/kg/min for up to 18 hours. In patients with creatinine clearance  $\leq 60$  mL/min, give 25 mcg/kg within 5 minutes and then 0.075 mcg/kg/min.

### **Clinical Experience**

In clinical studies with the HDB regimen, Aggrastat was administered in combination with aspirin, clopidogrel and heparin or bivalirudin to over 8,000 patients for typically  $\leq 24$  hours.

### **Contraindications**

Known hypersensitivity to any component of Aggrastat History of thrombocytopenia with prior exposure to Aggrastat Active internal bleeding, or history of bleeding diathesis, major surgical procedure or severe physical trauma within previous month.

### **Warnings and Precautions**

Aggrastat can cause serious bleeding. If bleeding cannot be controlled discontinue Aggrastat. Thrombocytopenia: Discontinue Aggrastat and heparin.

### **Adverse Reactions**

Bleeding is the most commonly reported adverse reaction.

For more information on AGGRASTAT, please refer to Full Prescribing Information.

Neither the TSX Venture Exchange nor its Regulation Services Provider (as that term is defined in policies of the TSX Venture Exchange) accepts responsibility for the adequacy or accuracy of this release.

*Forward Looking Information: Statements contained in this press release that are not statements of historical fact, including, without limitation, statements containing the words "believes", "may", "plans", "will", "estimates", "continues", "anticipates", "intends", "expects" and similar expressions, may constitute "forward-looking information" within the meaning of applicable Canadian and U.S. federal securities laws*

*(such forward-looking information and forward-looking statements are hereinafter collectively referred to as "forward-looking statements"). Forward-looking statements, including the potential for approval of the STEMI sNDA, the timing of any such approval should it indeed be approved, and the expectation of continued growth in sales of AGGRASTAT, are based on the current assumptions, estimates, analysis and opinions of management of the Company made in light of its experience and its perception of trends, current conditions and expected developments, as well as other factors which the Company believes to be relevant and reasonable in the circumstances. Inherent in forward-looking statements are known and unknown risks, uncertainties and other factors beyond the Company's ability to predict or control that may cause the actual results, events or developments to be materially different from any future results, events or developments expressed or implied by such forward-looking statements, and as such, readers are cautioned not to place undue reliance on forward-looking statements. Such risk factors include, among others, the Company's future product revenues, stage of development, additional capital requirements, risks associated with the completion and timing of clinical trials and obtaining regulatory approval to market the Company's products, the ability to protect its intellectual property, dependence upon collaborative partners, changes in government regulation or regulatory approval processes, and rapid technological change in the industry. Such statements are based on a number of assumptions which may prove to be incorrect, including, but not limited to, assumptions about: general business and economic conditions; the impact of changes in Canadian-US dollar and other foreign exchange rates on the Company's revenues, costs and results; the timing of the receipt of regulatory and governmental approvals for the Company's research and development projects; the availability of financing for the Company's commercial operations and/or research and development projects, or the availability of financing on reasonable terms; results of current and future clinical trials; the uncertainties associated with the acceptance and demand for new products and market competition. The foregoing list of important factors and assumptions is not exhaustive. The Company undertakes no obligation to update publicly or otherwise revise any forward-looking statements or the foregoing list of factors, other than as may be required by applicable legislation. Additional discussion regarding the risks and uncertainties relating to the Company and its business can be found in the Company's other filings with the applicable Canadian securities regulatory authorities or the US Securities and Exchange Commission, and in the "Risk Factors" section of its Form 20F for the fiscal year ended December 31, 2015.*

**AGGRASTAT® (tirofiban HCl) is a registered trademark of Medicure International, Inc.**

1. ten Berg JM et al. Effect of early, pre-hospital initiation of high bolus dose tirofiban in patients with ST-segment elevation myocardial infarction on short- and long-term clinical outcome. J Am Coll Cardiol 2010;55:2446-2455
2. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61(4):485-510.
3. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58(24):e44-122.
4. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64(24):e139-228.

For further information: James Kinley, Chief Financial Officer, Tel. 888-435-2220, Fax 204-488-9823, E-mail: [info@medicure.com](mailto:info@medicure.com), [www.medicure.com](http://www.medicure.com)