



PRESS RELEASE

Advanced Accelerator Applications Announces Two Phase II Studies Evaluating ^{99m}Tc -rhAnnexin V-128 Imaging in Cardiovascular and Cardio-Oncology Indications at University of Ottawa Heart Institute and Ottawa Hospital

Saint-Genis-Pouilly, France – September 6, 2016 – Advanced Accelerator Applications S.A. (NASDAQ:AAAP) (“AAA” or the “Company”), an international specialist in Molecular Nuclear Medicine (MNM), today announced the initiation of two Phase II clinical studies evaluating ^{99m}Tc -rhAnnexin V-128 (Annexin), a single-photon emission computed tomography (SPECT) diagnostic candidate for the assessment of apoptosis and necrosis, forms of cell death in cardiovascular and cardio-oncology indications at the University of Ottawa Heart Institute and The Ottawa Hospital.

Annexin V is a human protein that binds to phosphatidylserine (PS), which is expressed on the surface of physiologically stressed, depolarized, or apoptotic cells. Technetium-99m (^{99m}Tc) is a medical isotope widely used in diagnostic imaging. ^{99m}Tc -labeled annexin V has demonstrated the ability to image cellular stress, membrane depolarization, apoptosis and necrosis in a variety of inflammatory diseases including atherosclerosis, myocarditis, acute heart transplant rejection, rheumatoid arthritis, prosthetic joint infection and Crohn’s disease in both human and animal studies.

One proof of concept study will determine the feasibility of imaging apoptotic activity by using ^{99m}Tc -rhAnnexin V-128 in carotid atherosclerotic plaques of asymptomatic patients with significant carotid artery disease. The goal of this study is to demonstrate the potential utility of Annexin in staging plaque vulnerability, thereby enabling more precise stratification of patient risk, which may impact intervention decisions. Thirty-five evaluable, asymptomatic patients with diagnosed carotid atherosclerotic plaque will be enrolled in the trial, in addition to a control group of ten participants with normal carotid ultrasound imaging.

A second study will investigate ^{99m}Tc -rhAnnexin V-128 imaging of apoptosis in the evaluation of doxorubicin-induced cardiotoxicity in patients with early stage breast cancer. Thirty evaluable patients with early stage breast cancer will be enrolled in this trial.

Terrence D. Ruddy, MD, FRCPC, FACC, Director of Nuclear Cardiology at the University of Ottawa Heart Institute, and Professor of Medicine and Radiology at the University of Ottawa is the Principal Investigator for both studies. He commented, *“We completed a Phase I study of rhAnnexin V-128 in twelve normal volunteers, which demonstrated that this radiotracer was well-tolerated, with low radiodosimetry. In preclinical studies, we have demonstrated that imaging of apoptosis with ^{99m}Tc rhAnnexin V-128 can identify advanced atherosclerotic plaques and anticipate similar imaging of apoptosis in patients with carotid artery disease will also identify more advanced disease and facilitate patient management. In the second phase II study, we anticipate that imaging of apoptosis will be a sensitive imaging technique for identifying patients with early cardiotoxicity due to anthracycline chemotherapy for breast cancer and represent a new safety monitoring approach for this therapy. In both patient populations, we believe that apoptosis imaging will assist risk stratification and guide medical therapy.”*



Susan Dent, MD, FRCPC, Medical Oncologist at The Ottawa Hospital, Associate Professor of Medicine at the University of Ottawa, Director of the Ottawa Cardio-Oncology Program and a co-investigator on the cardiotoxicity study, stated, *“Anthracyclines continue to play an important role in the treatment of breast cancer. Anthracycline based therapy is associated with an increased risk of cardiotoxicity, in particular heart failure. Current cardiovascular imaging strategies (e.g. echocardiography) detect cardiotoxicity only once structural damage has occurred. The development and testing of diagnostic tools (such as imaging of apoptosis) that detect cardiotoxicity early, would facilitate the identification of cancer patients at high risk, leading to early medical management and completion of cancer therapy.”*

Stefano Buono, Chief Executive Officer of AAA said, *“Having diagnostic tools that can accurately detect apoptosis and necrosis in cardiovascular settings can facilitate early diagnosis of potentially life-threatening conditions, enable more precise risk stratification, and help physicians monitor the efficacy and safety of treatments in individual patients during the course of therapy. Our goal is to develop Annexin into a personalized disease management tool for multiple inflammatory diseases.”*

About the University of Ottawa Heart Institute

The University of Ottawa Heart Institute (UOHI) is Canada's largest and foremost heart health centre dedicated to understanding, treating and preventing heart disease. UOHI delivers high tech care with a personal touch, shapes the way cardiovascular medicine is practiced and revolutionizes cardiac treatment and understanding. It builds knowledge through research and translates discoveries into advanced care. UOHI serves the local, national and international community, and is pioneering a new era in heart health. For more information, please visit: www.ottawaheart.ca.

About The Ottawa Hospital

The Ottawa Hospital is one of Canada's largest learning and research hospitals with over 1,100 beds, approximately 12,000 staff and an annual budget of over \$1.2 billion. Our focus on research and learning helps us develop new and innovative ways to treat patients and improve care. As a multi-campus hospital, affiliated with the University of Ottawa, we deliver specialized care to the Eastern Ontario region, but our techniques and research discoveries are adopted around the world. We engage the community at all levels to support our vision for better patient care. For more information, please visit: www.ottawahospital.on.ca.

About Advanced Accelerator Applications

Advanced Accelerator Applications (AAA) is an innovative radiopharmaceutical company that develops, produces and commercializes Molecular Nuclear Medicine (MNM) products. AAA's lead therapeutic product candidate, Lutathera, is a novel MNM compound that AAA is currently developing for the treatment of Neuro Endocrine Tumors, a significant unmet medical need. Founded in 2002, AAA has its headquarters in Saint-Genis-Pouilly, France. AAA currently has 22 production and R&D facilities able to manufacture both diagnostics and therapeutic MNM products, and has over 450 employees in 13 countries (France, Italy, UK, Germany, Switzerland, Spain, Poland, Portugal, The Netherlands, Belgium, Israel, U.S. and Canada). AAA



reported sales of €88.6 million in 2015 (+26.8% vs. 2014) and sales of €54.6 million for 1H 2016 (+26.9% vs. 1H15). AAA is listed on the Nasdaq Global Select Market under the ticker "AAAP". For more information, please visit: www.adacap.com.

Cautionary Statement Regarding Forward-Looking Statements

This press release may contain forward-looking statements. All statements, other than statements of historical facts, contained in this press release, including statements regarding the Company's strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements reflect the Company's current expectation regarding future events. These forward-looking statements involve risks and uncertainties that may cause actual results, events or developments to be materially different from any future results, events or developments expressed or implied by such forward-looking statements. Such factors include, but are not limited to, changing market conditions, the successful and timely completion of clinical studies, the timing of our submission of applications for regulatory approvals, EMA, FDA and other regulatory approvals for our product candidates, the occurrence of side effects or serious adverse events caused by or associated with our products and product candidates; our ability to procure adequate quantities of necessary supplies and raw materials for Lutathera and other chemical compounds acceptable for use in our manufacturing processes from our suppliers; our ability to organize timely and safe delivery of our products or product candidates by third parties; any problems with the manufacture, quality or performance of our products or product candidates; the rate and degree of market acceptance and the clinical utility of Lutathera and our other products or product candidates; our estimates regarding the market opportunity for Lutathera, our other product candidates and our existing products; our anticipation that we will generate higher sales as we diversify our products; our ability to implement our growth strategy including expansion in the U.S.; our ability to sustain and create additional sales, marketing and distribution capabilities; our intellectual property and licensing position; legislation or regulation in countries where we sell our products that affect product pricing, taxation, reimbursement, access or distribution channels; and general economic, political, demographic and business conditions in Europe, the U.S. and elsewhere. Except as required by applicable securities laws, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.



Contacts:

AAA Corporate Communications

Rachel Levine

Director of Communications

rachel.levine@adacap.com

Tel: + 1-212-235-2395

AAA Investor Relations

Jordan Silverstein

Director of Investor Relations

jordan.silverstein@adacap.com

Tel: + 1-212-235-2394

Media inquiries:

Axess Public Relations (Italy)

Dario Francolino

dario.francolino@axesspr.com

Tel: +39 3488818029