

## BUSINESS WIRE

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Clinical studies indicate cardiac pharmacologic stress SPECT imaging agent detects heart disease as well as current agent and is better tolerated, with fewer, less intense side effects --

CHICAGO--King Pharmaceuticals, Inc. (NYSE: KG) today presented the positive results of its pivotal Phase III clinical trials evaluating CorVue™ (binodenoson for injection), a selective adenosine A2a receptor agonist that King is developing for cardiac pharmacologic stress imaging. The results showed that imaging using CorVue™ detects myocardial ischemia as well as imaging using adenosine, yet causes fewer and less severe side effects such as chest pain, shortness of breath, and flushing. In addition, there were no cases of atrioventricular (AV) block, a rare but potentially serious effect of approved agents.

In addition, CorVue™ was preferred over adenosine by 7 out of 10 patients studied. Moreover, it achieved the primary trial end points for efficacy and tolerability and is administered as a single bolus dose, making it a potentially easier-to-use alternative agent.

Cardiac pharmacologic stress SPECT imaging is a procedure used to diagnose the presence and severity of coronary artery disease. Many patients cannot perform the level of exercise typically required for disease diagnosis in a cardiac stress test, in which physicians often use perfusion imaging cardiac stress testing (SPECT) to view blood flow throughout the heart. For these patients – representing an estimated 3 million procedures annually – medications rather than exercise can be used to dilate the blood vessels so that physicians can accurately examine blood flow and detect the presence and severity of coronary artery disease.

“Currently available agents used to achieve the vasodilation necessary for cardiac imaging do not distinguish subtypes of adenosine receptors,” said lead trial investigator and Tufts Medical Center Acting Chief of Cardiology, James Udelson, M.D. “There is a need for a more targeted or specific agent such as CorVue™, which is designed to be more selective and, ideally, more comfortable for the patient. In addition to the clinical findings, the patient preference data further suggests it achieves that patient comfort.”

“We believe this clinical evidence demonstrates new levels of safety and comfort for patients, and provides physicians with an equally effective and easier-to-use agent to diagnose a disease that is a leading cause of death in the U.S.,” said Dr. Eric Carter, Chief Science Officer of King. The Company expects to file a New Drug Application with the U.S. Food and Drug Administration by early 2009 seeking approval to market CorVue™.

### **Key Findings**

The randomized, multicenter, double-blind crossover trials (VISION 302 and 305) compared CorVue™ to the vasodilator adenosine for efficacy and tolerability. Patients completed two rest-stress imaging procedures within seven days in random order, one with CorVue™ and one with adenosine. Images were read independently by blinded expert nuclear cardiologists who assigned perfusion scores to segments of the ventricle. The efficacy analyses were based on comparison of the extent and severity of ischemia, expressed as summed difference

scores (SDS). Efficacy was demonstrated if the mean paired difference between the CorVue™ and adenosine SDS scores did not exceed 1.5 SDS units, and no more than 10% of the patients had one normal and one severely ischemic image. The mean paired SDS difference of the CorVue™ and adenosine images was -0.09 in VISION 302 (N=374) and -0.68 in VISION 305 (N=391), and the 95% confidence intervals were well-within the pre-specified 1.5 SDS units; only 3% of the images were determined to be sufficiently discordant.

In the tolerability analysis, no subjects in the CorVue™ group suffered 2nd or 3rd degree atrioventricular block compared to 3% and 1% of the adenosine subjects who showed AV block ( $p=0.004$ ,  $p=0.041$ ). In study 302 (study 305 results were similar) flushing was reduced in the CorVue™ subjects by 36% ( $p<0.001$ ); chest pain was reduced by 38% ( $p<0.001$ ); and shortness of breath by 18% ( $p=0.007$ ). Compared to the adenosine group, CorVue™ patients rated intensities of these events as lower ( $p<0.001$ ). In addition, 71% of the patients preferred CorVue™ over adenosine while only 20% preferred adenosine ( $p=0.004$ ). Both agents produced comparable changes in blood pressure and heart rate.

### **Study Methodology**

A total of 419 (VISION 302) and 433 patients (VISION 305) at 40 and 39 U.S. sites, respectively, were randomized for pharmacologic stress tests and SPECT imaging for myocardial perfusion (MP). Prior to testing, the patients were stratified by their likely risk for coronary artery disease (CAD). Of those randomized, 374 (VISION 302) and 391 patients (VISION 305) with low, intermediate, and high likelihood for CAD and known CAD were 6%, 45%, 24%, and 26% (VISION 302); and 5%, 44%, 10%, and 41% (VISION 305). Patients completed two double-blinded MP procedures within seven days. In one procedure, patients received an IV bolus of CorVue™ (1.5 µg/kg) plus a six-minute placebo infusion. In the other procedure, patients received an IV bolus placebo plus a six-minute adenosine infusion. Blinded readers independently scored rest-stress images.

### **About CorVue™**

CorVue™, a selective adenosine A2a receptor agonist, is being developed as an alternative to exercise prior to cardiac perfusion imaging for the diagnosis of coronary artery disease. CorVue™ is designed to minimize side effects such as dyspnea, nausea, heart block, flushing and chest pain. For ease of administration, CorVue™ is being developed for dosing as a single IV injection with a fast onset while providing a sufficient duration of coronary blood vessel dilation for flexibility in diagnostic imaging. CorVue™ is an investigational drug that has not been approved by U.S. Food and Drug Administration.