



For Immediate Release

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**NEW STUDY SHOWS PROMISE FOR HYDROGEN SULFIDE  
IN REDUCING HEART-ATTACK DAMAGE, IKARIA ANNOUNCES**

*-- Study led by Albert Einstein College of Medicine researchers published in major scientific journal--*

**Clinton, N.J., September 25, 2007** -- Producing a state of "hibernation on demand" in mice by administering an experimental drug from Ikaria (an injectable formulation of the biological gas hydrogen sulfide) showed promise in a study designed to reduce damage from heart attacks. The study was published in the online edition of the *Proceedings of the National Academy of Sciences*.

The preclinical study, conducted by researchers at New York's Albert Einstein College of Medicine and the University of Alabama, was funded in part by Ikaria and examined whether hydrogen sulfide could prevent "reperfusion injury" – caused when blood flow and oxygen supply to heart tissue plummet during a heart attack, then are abruptly restored when the heart attack is treated. This dramatic change in oxygen levels can be heavily damaging to the heart.

"Over the last few years, a number of reports have demonstrated the protective effects of hydrogen sulfide in various models of cardiovascular disease and inflammation," said Csaba Szabo, M.D., Ph.D., chief scientific officer of Ikaria and a study co-author. "This study can be considered a milestone not only because it defines the significant therapeutic potential of hydrogen sulfide during heart attacks, but also because it links these therapeutic effects to hydrogen sulfide-induced on-demand metabolic modulation, a new field of biological research championed by Ikaria."

The senior study author was David Lefer of Albert Einstein College of Medicine's department of pathology and the division of cardiology within Albert Einstein's department of medicine.

While hydrogen sulfide is more commonly known as a toxic gas when it occurs at high levels, it has demonstrated a biologically protective role when delivered in very low doses, Dr. Szabo said. Ikaria has submitted regulatory documents and is expected to start a Phase I trial later this year.

"The development of hydrogen sulfide as an ethical pharmaceutical may offer exciting new opportunities in the treatment of cardiovascular and inflammatory diseases," said David Shaw, chairman and CEO of Ikaria. "We are encouraged by the compelling results of this and other studies of our product as part of our overall efforts to improve outcomes for critically ill patients."

Ikaria's hydrogen sulfide clinical platform is based on its exclusive, worldwide license from the Fred Hutchinson Cancer Research Center (FHCRC). In April 2005, Mark Roth, Ph.D., a member of the research faculty of the FHCRC, demonstrated the ability of hydrogen sulfide to induce a state of reversible metabolic hibernation in mice, which was published in a landmark article in the prestigious journal *Science*.

Hibernation may be a latent ability in all mammals – a finding that may have important clinical benefits in humans. Temporary slowing of the metabolic rate, or inducing hibernation on demand, has the potential to lengthen the window of time that patients with trauma, stroke, cardiac arrest or surgery can be treated. This lengthened time window could help prevent injury and death from insufficient or inappropriate oxygen supply to organs and tissues. It also could increase the time that organs or tissues for transplant are viable outside the body during transportation over long distances. On-demand metabolic modulation of damaged tissue creates therapeutic benefit (a "protective pause") during which transportation or critical care procedures can be performed.

In addition to metabolic modulation, hydrogen sulfide offers therapeutic benefits as a cytoprotective and anti-inflammatory molecule: research previous to the present study has shown it to be effective in experimental models of inflammation, lethal hypoxia and a number of other diseases.

### **About Ikaria Holdings**

Ikaria Holdings is a fully integrated biotherapeutics company focused on the development and commercialization of innovative in-hospital pharmaceutical products and drug/device combinations that improve the lives of patients. The company's INOmax® product (inhaled nitric oxide) is an FDA-approved drug for the treatment of pulmonary hypertension in newborns, and is extensively used in critical settings in the United States, Canada, Europe, Latin America and Asia. Ikaria has a staff of over 300 people and is headquartered in Clinton, N.J., with research facilities in Seattle and Madison, Wis., and manufacturing in Port Allen, La.

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To view a related press release from the University of Alabama, visit [www.eurekaalert.org/pub\\_releases/2007-09/uoa-a-sha091807.php](http://www.eurekaalert.org/pub_releases/2007-09/uoa-a-sha091807.php).

To view the study abstract, visit [www.pnas.org/cgi/content/abstract/0705891104v1](http://www.pnas.org/cgi/content/abstract/0705891104v1).