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**NIH AWARDS PHYLONIX PHASE II SBIR TO DEVELOP  
ZEBRAFISH APOPTOSIS DRUG SCREENING ASSAYS**

**Cambridge, MA (June 2, 2004)** - Phylonix today announced that it had recently received a Phase II Small Business Innovation Grant (SBIR) from the National Cancer Institute to develop zebrafish apoptosis assays for drug screening. The amount of the award is \$993,463.

Apoptosis is the genetically programmed process of precise, predictable cell suicide. It occurs as a normal physiological process for removing unnecessary cells throughout the life of an organism. Inappropriate apoptosis has been shown to be the cause of many diseases. Development of agents that modulate apoptosis is a major focus of biopharmaceutical research. The ability to manipulate apoptosis could permit therapeutic intervention in: cancer, heart disease, stroke, AIDS, autoimmunity, and degenerative diseases.

“Apoptotic cells in live, transparent zebrafish can be visualized by acridine orange staining without complicated processing. At Phylonix, we are also developing a quantitative, vital dye assay for high throughput screening using an automated liquid handling workstation and a microplate reader”, Chuenlei Parng, Ph.D, the Principal Investigator for this research, said.

Conventional cell-based assays evaluate the potential effects of drugs in culture, but cannot assess the complex metabolism that affects actual drug efficacy or causes toxicity in animals and humans. Therefore, many drugs that appear effective in cell-based assays fail in subsequent, costly animal testing. To streamline the drug development time-line, prioritize drug candidates for animal testing, and reduce unnecessary costs for mammalian studies, we are developing a family of drug screening assays using the small vertebrate zebrafish. This convenient animal model will serve as an intermediate step between cell-based evaluation and animal testing for drug evaluation.

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## **Zebrafish Background**

Laboratory animals are critical for defining the mechanisms of drug activity and for testing therapeutic regimens, however, only a few useful models have been developed. Zebrafish has several important advantages for drug screening: they are small, inexpensive to maintain and easily bred in large numbers. Eggs are externally fertilized and a single mating produces 100-200 eggs. Single embryos can be maintained in fluid volumes as small as 100 microliters for the first six days of development and cultured in microtiter wells. Chemicals can then be added directly to the fish water, permeating the intact embryo. Standard microtiter plate readers can be used for quantitation, making this format particularly attractive for high throughput drug screening.

The Company is developing a family of zebrafish microplate assays with compelling advantages: 1) short assay time, 2) single dosing, 3) small amount of drug required for each test, 4) statistically significant numbers of animals can be assayed for each condition, 5) embryos maintenance during drug delivery is easy, and 6) low cost: the estimated cost of each zebrafish assay is <\$100.

Whole embryo testing has previously been performed on invertebrates, including fruitfly and nematode, however, these organisms are not closely related to humans and they lack many of the same organs and enzymes. Therefore, their use as comparative models for toxicity effects in humans is limited. All essential components of vertebrate form and organ development are mimicked in the transparent zebrafish and their molecular basis is either identical or similar, underscoring the potential for use in research on human diseases.

## **Company Background**

Phylonix Pharmaceuticals, Inc. is a Contract Research Organization focused on developing and marketing novel *in vivo* zebrafish based assays for therapeutic and industrial screening for cancers, central nervous system and cardiovascular diseases, apoptosis, and organ toxicity. The Company is assembling embryo and chemical sample handling instrumentation to automate analysis. The Company has established a state of the art aquaculture facility. Initially, the Company offers drug screening services, primarily to the pharmaceutical industry. Long term, the Company expects to contribute to the study and treatment of human diseases by genetic screening, gene cloning, and target identification using zebrafish as a model organism.

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