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PHYLONIX GRANTED U.S. PATENT FOR HIGH THROUGHPUT DRUG SCREENING USING ZEBRAFISH

Cambridge, MA (March 30, 2004) – Phylonix today announced the recent award of Patent No. 6,656,449 “Methods of Screening Agents for Activity Using Teleosts” by the United States Patent and Trademark Office which includes claims for performing drug screening on zebrafish using microtiter plates. This high throughput format permits development of quantitative *in vivo* bioassays, which is not possible with other vertebrate animal models. Other key claims also include performing drug screening for toxicity, apoptosis, and angiogenesis using zebrafish.

“This is important recognition of our pioneering efforts to develop both visual and quantitative methods for drug screening, target identification, and target validation using zebrafish as a model organism,” said Patricia McGrath, President & CEO. Corresponding patent applications for this subject matter have been filed in major international markets, including Europe and Asia.

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. Microliters of drug are required for zebrafish compared with milliliters per mouse. Standard microtiter plate readers can be used for measurement, making this format particularly attractive for high throughput drug screening.

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Zebrafish Background

An important advantage of the zebrafish animal model is that the morphological and molecular bases of tissue and organ development are, in general, either identical or similar to other vertebrates, including man. The zebrafish completes embryogenesis in 120 hours and most of the internal organs, including the gut, liver, kidney, and heart develop rapidly in the first 48-72 hours. This rapid development allows organ toxicity and specific drug effects to be assayed in a comparatively short time frame. The sequence and presumed function of many genes that are important for development in vertebrates have been conserved in zebrafish. The cloning of zebrafish orthologues of important mammalian genes has been greatly facilitated by the creation of an EST database containing tens of thousands of clones for which sequences are available through GenBank.

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 has assembled embryo and chemical sample handling instrumentation to automate analysis. The Company has established a state of the art aquaculture facility that can produce thousands of embryos per week. Initially, the Company offers services for drug screening, 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 system.

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