

RegeneMed Announces Launch Of 3D Engineered Liver Tissue & Platform Technology for Drug Research & Discovery

Technology Addresses Number One Contributor to Drug Failure and The High Cost of Bringing New Drugs To Market

SAN DIEGO, CA February 19, 2007/PR Newswire – RegeneMed, Inc. announced today that it has begun sales of its 3D engineered liver tissue and customized platforms for use in throughput screening for ADME (absorption, distribution, metabolism, and excretion) and toxicity studies in the lead optimization phase of drug discovery. In addition, RegeneMed is providing contract testing service for pharmaceutical and biotechnology companies requesting support in connection with the utilization of the liver tissue for their ADME/Tox and drug discovery programs.

This announcement addresses a long-standing issue for pharmaceutical companies with regard to their discovery of unacceptable ADME/Tox properties in their drug candidates at late stages in the development process. Up to this point in time ADME/Tox studies have been performed on drug candidates in cell-based systems (*in vitro*) and in animals (*in vivo*) including the industry-standard hepatocytes to determine how the drugs are absorbed and distributed in the body (ADME) and if the drug or its metabolism breakdown products will cause toxicity. Once removed from their native, three dimensional, multicellular tissue environment, hepatocytes quickly lose viability and tissue-specific function including protein synthesis (for example, albumin, transferrin, and fibrinogen) and drug metabolizing capability (cytochrome P450 enzyme activity). RegeneMed's in vitro human liver co-cultures have validated cell growth, maintenance of cell viability, and expression of liver-specific proteins including extra cellular matrix proteins for extended periods of time (48 days for rat and 80 days for human). These times reflect the length of study of the in vitro cultures not the maximum possible time for maintenance of tissue function. This reproducible and scaleable characteristic enables researchers to test a candidate drug's chronic toxicity as well as acute.

The cost to bring a single new drug to market exceeds \$1 billion according to a 2006 Tufts University drug research and discovery economics report. Approximately one-fifth of this cost (\$200 million) is spent investigating the number one contributor to drug failure, poor liver metabolism and toxicity. Liver toxicity is responsible for two-thirds (66%) of drug failures in clinical trials, one-third of drug withdrawals from the market and over half of all warning labels on approved drugs.

According to **Dawn Applegate, Ph.D. RegeneMed co-founder and Chief Executive Officer**, “pharmaceutical companies presently spend over \$3 billion annually to test drug candidates for how they may be metabolized and if toxins will be produced when ingested by humans. To date, ADME/Tox testing systems, including animal and human cell-based systems are not fully predictive of the human function. As a result, discovery of unacceptable metabolism and toxicity characteristics occur late in the development process, during human clinical trials, well after these problems should have been discovered. Our full liver tissue assays enable pharmaceutical companies to discover problems with their drug candidates very early into the drug target identification and compound library stage, thereby saving them approximately one-half of the \$1 million per day in lost opportunity cost associated with their current drug failures.”

“Pharmaceutical company drug research and discovery economics reflect squeezed profit margins and significantly rising costs in concert with difficulties in discovering new treatments. The cost of bringing a new drug to market has soared dramatically. (Harvard Business School's Regina Herzlinger states that

"the era of the billion-dollar new drug signifying the cost, about \$1.2 billion +/- of a single successful drug reaching the market has arrived".) Drug discovery and development is an inherently risky business. Pharmaceutical companies want to "reduce the risk of failing late in the game" by having the means to either abandon unlikely candidates quickly or scaling rapidly with the promising drugs. It's a strategic culture called "*fast failing*". With us, they can accomplish this, thereby reconcentrating their research investment dollars on the high opportunity candidates. Our mantra is '*Fail Early, Fail Cheaply*'".

"Our announcement today marks the culmination of over sixteen years of tissue engineering research and the establishment of 35 United States patents. We are excited to offer this vital solution to our friends in drug development."

About RegeneMed 3D Engineered Liver Tissue

RegeneMed 3D co-cultures of primary human liver stromal and parenchymal cells function *in vitro* and *in vivo* as fully functioning human liver tissue on a long-term basis. The 3D culture system stabilizes the function of hepatocytes and other cells of the liver within a tissue. It is therefore a reliable indicator of liver function with accurate responses to candidate drug tests. 3D Liver Tissue Platforms are qualified as replacements for hepatocytes and animals as a lead resource for new drug discovery. They provide a resolution to an ongoing problem of hepatocytes as being not readily available, costly, and capable of survival for only a few days. (Hepatocytes also rapidly change, differentiate down their phenotype pathway into other cell types. They thus are continuously losing liver function while drug tests are being conducted.) 3D engineered liver tissue retains full liver-specific function, including all baseline liver characteristics, metabolism, and induction/inhibition capacity. The primary distinguishing characteristic of 3D engineered liver tissue is its measured, demonstrated constancy of full liver function for 80 days in culture, with the capacity for longer term viability when maintained. As a result, the tissue technology is scaleable and reproducible. It is incorporated into variable throughput systems that are used to evaluate candidate drug metabolism and hepatotoxicity. The technology is likewise specific and designed to provide normal, diseased and polymorphic liver tissue. RegeneMed's 3D co-culture platforms are available when and as needed compared to hepatocytes which limited to donor supply.

About RegeneMed

RegeneMed, Inc. is founded on technology, personnel and intellectual property spun out of Advanced Tissue Sciences, Inc. (ATS). Its purpose is to become the market leader in tissue-based solutions for drug discovery and development, and having additional applications as extra-corporeal and implantable medical devices. RegeneMed tissue technologies are protected by 35 U.S. and extensive WW patents.

RegeneMed is headquartered in San Diego, California.

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