

Harvard Bioscience, Inc. Acquires Union Biometrica, Inc., Whose Instruments Accelerate Drug Discovery

HOLLISTON and SOMERVILLE, Mass., May 31, 2001 /PRNewswire/ -- Harvard Bioscience, Inc. (Nasdaq: HBIO) today announced the acquisition of Union Biometrica, Inc. (UBI). UBI has breakthrough products that for the first time make the use of model organisms practical for high throughput applications in drug discovery. Today, nine out of ten drugs fail in clinical trials, overwhelmingly due to poor efficacy and ADMET (Absorption, Distribution, Metabolism, Elimination and Toxicity) properties. UBI has developed and markets a next generation technology in target validation and the efficacy and ADMET screening of drugs. The UBI system, named COPAS™ enables high relevance/high throughput screening much earlier in the drug discovery process, thus reducing late stage failures. Through the invention of large bore flow cytometry, COPAS™ enables the rapid analysis and sorting of all of the most popular model organisms -- *C. elegans* (worm), *D. melanogaster* (fly) and *D. rerio* (Zebra fish). These model organisms have similar disease genes to humans. The analysis of them in relation to humans, known as comparative genomics, is emerging as a powerful technique in drug discovery. By automating the handling of these model organisms COPAS™ provides a complete, integrated solution for both rapidly producing novel transgenic models of human disease and for the high throughput screening of compound libraries in these complete, living organisms. Before the invention of COPAS™, transgenic model organism production was a manual process and thus very slow. Before the invention of COPAS™, library screening on organisms was simply impractical as it could only be done one organism at a time under a microscope. The COPAS™ system can analyze about 1 million *C. elegans* in a normal, eight-hour day. The technology is protected by several patent applications. Customers for the COPAS™ system include GlaxoSmithKline, Novartis Pharmaceuticals, Janssen Pharmaceutica (a division of Johnson and Johnson), Exelixis and the Sanger Center. In addition, UBI has collaborative R&D agreements with major pharmaceutical companies for both instrument and model organism development. This is what some of the customers say about the system:

"This technology will enable us to perform high throughput genetic screens for genes in disease related pathways as well as compound screens for drugs affecting pathways."

H.H. Li, et. al., of Novartis

"It offers a clear advantage ... in a couple of years, we'll start to see more drugs coming out of this at a significant savings of time and cost."

John Geyson of Janssen Pharmaceutica (Johnson & Johnson)

The transaction was valued at approximately \$17.5 million.

"This is an excellent strategic fit to our focus on the target validation and ADMET bottlenecks in drug discovery" said Chane Graziano, CEO of Harvard Bioscience. "I believe this technology has the potential to change the landscape of drug discovery. We fully expect this acquisition to significantly increase our projected growth rate."

Joining HBIO as a result of the transaction are UBI co-founders Dr. Peter Hansen, Chairman and Chief Technology Officer and Dr. Petra Krauledat, President. Dr. Krauledat holds a Ph.D. in biochemistry from the University of the Ruhr in Bochum, Germany and has over 15 years experience guiding advanced systems technology programs from inception to product introduction for Behringwerke AG (Germany), PB Diagnostics (Germany/USA), and Johnson & Johnson (USA). Dr. Hansen is a graduate of Harvard College with a major in physics. He holds a Ph.D. in biophysics and biomedical engineering from Northeastern University and has worked in applied physics at Northeastern, MIT and Johnson & Johnson. A number of his 14 patents were cornerstones to the billion-dollar flow cytometry business licensed by every significant company in the field (Johnson & Johnson, Beckman-Coulter, Becton & Dickinson, and the Technicon division of Bayer). More than two thirds of his patents have been incorporated into successful products.

David Green, President of Harvard Bioscience commented, "We are very proud to have Petra and Peter join our company. They are truly exceptional people and will strengthen us enormously. We believe the UBI products and technology are of pivotal importance to drug discovery. UBI customers and collaborators include the top names in pharmaceutical and university research. Furthermore, the technology has so far been applied only to target validation and compound screening. Its potential for ADMET screening and real time gene expression haven't been tapped, and those markets are significant."

Petra Krauledat, founder and president of Union Biometrica commented further, "We are delighted with the merger. Ours is

truly a next generation technology, but it is here and available today. It has the potential to make an unprecedented contribution to the speed at which drugs can be brought to market. Harvard Bioscience fully appreciates our value and potential, with both the managerial and financial strength to assure UBI reaches its full potential."

Terms of the Acquisition and Guidance

Under terms of the agreement, Harvard Bioscience will issue approximately 659,282 unregistered shares of its stock, 263,202 options to purchase Harvard Bioscience common stock and pay \$7.5 million in cash for all UBI's outstanding shares and options. The transaction will be accounted for as a purchase transaction.

Jim Warren, Harvard Bioscience's CFO commented, "We anticipate that our 2001 revenues from UBI could be as much as \$5 million; 2002 revenues are expected to be in the range of \$15 million to \$20 million. We currently expect to expand sales, service and marketing as well as spending on new technology; therefore, on a cash basis, E.P.S. will experience dilution of approximately \$0.01 to \$0.03 for 2001. However for 2002, we expect a \$0.05 to \$0.10 contribution to E.P.S. We will give specific purchase accounting guidance during our second quarter conference call, currently expected to take place near the end of July."

Background of the Union Biometrica Inc. Technology

In December 1998 an ambitious, international, program to sequence the entire genome of a multicellular organism was completed successfully. Viewed by many as a "warm-up" for the human genome project, the results of sequencing the tiny earthworm *C.elegans* in fact acquired new importance when it was realized that up to 70% of human disease genes have similar genes in the worm and that Union Biometrica, Inc. had invented an automated system to study the function of the newly identified genes.

The COPAS™ system, invented and developed by Union Biometrica of Somerville MA, is capable of fluorescently analyzing and sorting multicellular organisms such as the nematode *C.elegans*, the fruit fly *D. melanogaster*, and the zebrafish *D.rerio*. These organisms are optically transparent, and thus can use fluorescent marker technology to detect and quantify the expression of mRNA and proteins. The COPAS™ system can analyze and sort thousands of organisms per minute on the basis of this fluorescence.

The COPAS™ system has two main applications: rapidly creating transgenic models of human disease and high throughput/high relevance screening of drug libraries against models of human diseases:

Rapidly creating transgenic models of human disease:

COPAS™ is an important tool for inserting new genes into multicellular organisms. These genes often function in ways that can be related to human gene function. The successful integration of these foreign genes is a rare event, and COPAS™ makes it possible to isolate and detect these rare events in parallel fashion and in time frames that are, in some cases, a thousand times faster than would be possible using manual microscopy approaches.

High throughput/high relevance screening:

COPAS™ bridges the gap between low relevance (to the human clinical experience), high throughput protein binding assays and high relevance, low throughput rat and mouse trials. Using COPAS™, scientists can now rapidly connect genes to gene function in living organisms complete with their complex biochemical pathways and signaling systems. If the genes are disease genes (either naturally occurring genes that are similar to the human disease genes or human genes that have been transgenically incorporated into the model organism) researchers can directly screen for new therapeutics. For this type of program, having new systems to avoid or reduce the use of laboratory mice is important. In efficacy testing, mode of action studies, and toxicity testing, model multicellular organisms and COPAS™ are providing alternatives to mice that are attractive to pharmaceutical laboratories and academic laboratories alike. COPAS™ enables the screening of drug libraries against living model organisms at little more than the cost of a protein binding assay.

The number of academic and commercial laboratories using model organisms has more than doubled in number in the 2 1/2 years following the sequencing of the nematode genome and the introduction of COPAS™. Now, most pharmaceutical and biotech companies have model organism programs. Model multicellular organisms cost almost nothing to maintain, they reproduce in days, and they can be examined repeatedly. Additionally, academic laboratories are identifying new small model organisms, such as those with immune systems that are similar to humans. These new models have surprised even veteran biologists by their new significance and potential in drug discovery.

COPAS™ systems operate by having organisms in liquid suspension enter an optically clear flow channel. The fluid mechanics of the flow channel solves a difficulty encountered in microscopy, which is that most organisms are constantly thrashing or

moving, making it impossible to visualize weak fluorescent detail. The COPAS™ system fluid design causes the organisms to be oriented and straightened for about one millisecond, which is long enough for the COPAS™ laser optics to acquire a complete set of data regarding the pattern of protein expression, and make software decision to sort (save) the organism for other work. Saving the organism means sorting single or multiple organisms into the individual wells of microtiter plates. COPAS™ systems are interfaced to plate handling robots for walk-away operation.

The sorting mechanism of COPAS™ maintains a very high level of viability. Multicellular organisms are more fragile and much larger than single cells. The conventional electrostatic sorters used in flow cytometry have proven to be lethal to these organisms and incapable of handling these organisms. The COPAS™ sorter uses an air activated switching principle that was invented by Union Biometrica and has proven itself to be gentle and efficient for the sorting of large, complex objects.

Harvard Bioscience is a global developer, manufacturer and marketer of innovative, enabling tools in drug discovery research at pharmaceutical and biotechnology companies, universities and government laboratories. HBIO sells approximately 10,000 products to thousands of researchers in over 60 countries through its 1,000 page catalog, and through its distributors, the most notable of which is AP Biotech. HBIO has sales and manufacturing operations in the United States, the United Kingdom, and Germany with sales facilities in France and Canada, and distributors around the world.

This press release contains certain statements that are "forward-looking statements" as that term is defined under the Private Securities Litigation Reform Act of 1995 and releases issued by the Securities and Exchange Commission. Such statements are subject to uncertainties and risks that could cause the actual results, performance or achievements of Harvard Bioscience to differ materially from anticipated future results, performance or achievements expressed or implied by such forward-looking statements. These uncertainties and risks include the risk that Harvard Bioscience will be unable to develop or acquire additional products to expand its product offerings, the risk that Harvard Bioscience will experience unforeseen problems affecting its ability to achieve revenue growth consistent with its goals or projections, uncertainties regarding the financial impact of the Union Biometrica acquisition on Harvard Bioscience's results of operations in future periods and particularly regarding whether its impact will be accretive to Harvard Bioscience's earnings, uncertainties regarding the technology, applications and customer acceptance of the Union Biometrica products, uncertainties regarding the impact of the events disclosed in this release on Harvard Bioscience's operations and its stock price, and other risks detailed in Harvard Bioscience's Securities and Exchange Commission filings.

Press releases and our product catalog can be found on our web site, <http://www.harvardbioscience.com>.

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