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BIOMARKER TECHNOLOGY PLATFORMS FOR CANCER DIAGNOSES AND THERAPIES

(SAMPLE COPY, NOT FOR RESALE)

Trends, Industry Participants, Product Overviews and Market Drivers

TABLE OF CONTENTS

INDEX OF FIGURES

INDEX OF TABLES

1. Overview

1.1 Statement of Report

The purpose of this report is to describe the specific segment of the cancer diagnostics market that develops and uses new biomarker technology platforms. Such platforms include: IVDMIA technology, robotic and automated sample nucleotide extraction and real-time PCR machines, next-generation sequencers, comparative genomic hybridization (CGH) arrays, proteomics and SELDI-TOF-MS technology for cancer biomarker profiling and cancer diagnosis and treatment.

Biomarkers are useful in following the course of cancer and evaluating which therapeutic regimes are most effective for a particular type of cancer, as well as determining long-term susceptibility to cancer or recurrence. This study examines those clinical measurement devices and their reagents and supplies that are meant to be used in hospitals, clinics, and commercial laboratories to diagnose and monitor cancer. The examination also provides an in-depth discussion of the application of biomarkers in developing novel targeted cancer therapeutics, their predication response and efficacy, as well as their use in the diagnosis of cancer.

1.2 About This Report

The report describes new technology platforms developed for the analyses of constituents of blood, plasma, serum or tissue that are connected to the growth and progression of cancer. The emphasis is on those companies and products that are actively developing and marketing new clinical laboratory instrumentation, reagents and supplies for performing specific and well-targeted tumor marker tests, as opposed to the more routine and clinically-accepted tumor markers that are manufactured and marketed by large diagnostic companies (*e.g.*, DEA, Ca124, PSA, etc.). This study focuses on biotech companies that have novel new products and procedures in this sector. Research companies in the process of developing new ideas are not reviewed in any detail here.

The main objectives of this analysis are:

- Identifying viable technology drivers for cancer biomarkers and related companion diagnostics through a comprehensive examination of platform technologies, including: IVDMIA, probe-based nucleic acid assays, microarrays and sequencing, and mass spectroscopy.

- Obtaining a complete understanding of the new cancer biomarker diagnostic tests—*i.e.*, predictive, screening, prognostic, monitoring, pharmacogenomic and theranostic—from their basic principles to their applications.

- Discovering growing market opportunities by identifying high-growth applications in different cancer diagnostic areas, focusing on the biggest and expanding markets in oncology (*e.g.*, biomarkers for breast cancer and predictive biomarkers).

- Focusing on global industry development through an in-depth analysis of the major world markets for cancer diagnostics, including growth forecasts.

1.3 Scope of the Report

This analysis emphasizes companies that are actively developing and marketing new reagents and supplies for performing cancer biomarker diagnostics tests. It discusses the various market trends and opportunities using new biomarkers, while providing an in-depth analysis of market share, revenue forecasts, and market drivers and restraints. Specialty cancer diagnostics testing, such as pathology screening methods and special tissue stains to examine cancer cells *in situ* are mentioned here, since they are often part of the overall analytical focus of companies that market cancer technology platforms. However, no effort is made to quantify this older and broader market. The reader should consult other TriMark Publications reports at http://www.trimarkpublications.com for detailed discussions of important individual market segments related to cancer diagnostics and therapeutics markets, such as *Cancer Diagnostic Testing World Markets*, *Cancer Cell Therapy Markets* and *Cancer Therapeutics Markets.*

1.4 Objectives

The goal of this report is to review the market for new and novel cancer biomarker testing equipment and supplies using reagents and instruments for analysis of individual components in blood, serum or plasma, which depend on the breaking developments in the genomic and proteomic spaces. The study defines the dollar volume of sales, both worldwide and in the U.S., and analyzes the factors that influence the size and the growth of the market segments. Also examined are the subsections of each market segment, including: the specialty CLIA labs, hospital labs and commercial laboratories. Additionally, the numbers of institutions using this type of testing and the factors that influence purchases are discussed. The analysis examines:

- Opportunities and barriers for new cancer biomarkers.
- Use of IVDMIA biomarkers in CLIA clinical laboratories which specialize in applying biomarker-based technologies that address critical needs in the management of gynecologic cancers, and that aid in clinical decision making and advanced personalized treatment plans.
- Adaptive design using biomarkers.
- Pharmacodynamic biomarkers identified with broad-based phenotyping as companion diagnostics.
- Tools for improving measurement, safety and validation of biomarkers.
- Filling the gap between discovery and clinically validated biomarkers.
- Enabling technologies for oncology biomarker discovery.

This study answers the following questions:

- Which companies are utilizing cutting-edge technologies to develop, validate and implement cancer biomarkers for clinical use?
- What impediments still exist to incorporating promising research into clinical practice?
- Which cancer biomarkers show the most promise for approval?
- What are the economic challenges to approval?
- How can regulatory oversight drive approval and adoption of new technologies?
- Which alliances show the greatest synergy in bringing valid biomarkers to market?
- Which shared technologies are driving the most encouraging development?

1.5 Methodology

The author of this report holds a PhD in biochemistry from the University of Minnesota and has had post-doctoral experience at the University of Connecticut School of Medicine. He has taught at Quinnipiac University and the Tufts School of Medicine, and has been a senior scientist at Pfizer Pharmaceutical Laboratories in drug development. He also has many decades of experience in science writing and as a medical industry analyst. He has over 30 years of experience in laboratory testing and instrument and reagent development technology as a licensed clinical laboratory director, as well as extensive experience in senior level management positions in biotech and medical service companies. The editor of this report is a PhD in biochemistry from the University of Liverpool and an M.B.A. from Oxford Brookes University in the U.K. with over 35 year's experience in the medical industry, science writing and as a medical industry analyst.

Company-specific information is obtained mainly from industry trade publications, academic journals, news and research articles, press releases and corporate websites, as well as annual reports for publicly-held firms. Additional sources of information include non-governmental organizations (NGOs) such as the World Health Organization (WHO) and governmental entities such as the U.S. Department of Health and Human Services (HHS), the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). Where possible and practical, the most recent data available have been used.

Some of the statistical information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information or omission or for the results obtained by the use of such information. Key information from the business literature was used as a basis to conduct dialogue with

and obtain expert opinion from market professionals regarding commercial potential and market sizes. Senior managers from major company players were interviewed for part of the information in this report.

Primary Sources

TriMark collects information from hundreds of Database Tables and many comprehensive multi-client research projects, as well as Sector Snapshots that it publishes annually. TriMark extracts relevant data and analytics from its research as part of this data collection.

Secondary Sources

TriMark uses research publications, journals, magazines, newspapers, newsletters, industry reports, investment research reports, trade and industry association reports, government-affiliated trade releases and other published information as part of its secondary research materials. The information is then analyzed and translated by the Industry Research Group into a TriMark study. The Editorial Group reviews the complete package with product and market forecasts, critical industry trends, threats and opportunities, competitive strategies and market share determinations.

TriMark Publications Report Research and Data Acquisition Structure

The general sequence of research and analysis activity prior to the publication of every report includes the following items:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly available databases, proprietary databases, direct meetings and personal interviews with key personnel.

- Formulating a study outline with the assigned writer, including important items:

  - Market and product segment grouping and evaluating their relative significance.
  - Key competitors' evaluations including their relative positions in the business and other relevant facts to prioritize diligence levels and assist in designing a primary research strategy.
  - End-user research to evaluate analytical significance in market estimation.
  - Supply chain research and analysis to identify any factors affecting the market.
  - New technology platforms and cutting-edge applications.

- Identifying the key technology and market trends that drive or affect these markets. Assessing the regional significance for each product and market segment for proper emphasis of further regional/national primary and secondary research.

- Launching a combination of primary research activities including two levels of questionnaires, executive-direct focused, company-specific, and region-specific communications to qualified and experienced senior executives worldwide.

- Completing a confirmatory primary research assessment of the report's findings with the assistance of Expert Panel Partners from the industry being analyzed.

1.6 Executive Summary

Until superior therapeutic treatments are developed to prevent, treat and cure cancer, the best means of reducing mortality and morbidity in a disease this complex is early detection and diagnosis. In the major solid cancer types such as lung, breast, colon and prostate, long-term survival rates drop precipitously once metastasis has occurred. The case is clear for development of biomarkers for early detection and screening tests for diseases such as breast, colon, ovarian and lung cancer. In addition, diagnostic measurement of cancer disease progression is essential to successful disease management. For these reasons, development of new and effective biomarkers for cancer

detection and diagnosis is central to the cancer problem. The use of both nucleic acid and protein biomarker diagnostics has begun to answer these questions.

The cancer biomarker sector is divided into three parts:

- The current market opportunity in the cancer biomarkers space resides almost entirely in the sales of reagents, consumables and services to the clinical oncology community.

- There is also a burgeoning laboratory business emerging in cancer biomarkers, where samples are sent to a central CLIA certified lab for analysis.

- In addition, there are currently a handful of FDA-approved biomarkers for cancer therapeutic agents. There are a number of companies developing biomarkers for various therapeutic segments under the rubric of companion diagnostics.

As the pharmaceutical and diagnostic industries increase the availability of biomarkers, their importance and influence in all aspects of drug discovery and the development process will continue to grow. Co-development of molecular diagnostics and targeted therapeutics has already been proven to be a successful strategy in the development of novel anti-cancer drugs such as Gleevec®.

Although estimates for the value of the global cancer biomarkers market for all applications varies from $[redacted] to $[redacted] in [redacted], it is clear that the CAGR over the next four to five years will be between [redacted]% and [redacted]%. This rate of growth will ensure that the global biomarkers market value will be about $[redacted] by [redacted], and predicted to reach $[redacted] by [redacted]. The market could be sub-divided into the following segments based on technological applications. These are: Next-Generation Sequencing (NGS), Quantitative PCR, Immunohistochemistry, FISH/CISH, and Microarray.

Polymerase chain reaction (PCR)-based diagnostic assays claimed the largest share of the market in [redacted] and has been estimated to be valued at approximately $[redacted] in [redacted], and has grown with a CAGR of [redacted]% to reach a market value of $[redacted] in [redacted]. At the same predicted CAGR, the market would be predicted to be valued at approximately $[redacted] by [redacted]. It is mainly in this sector of the diagnostics market that cancer biomarkers are developed. The potential market for cancer biomarkers is enormous.

Unmet patient need is the major driver of innovation in both cancer diagnostics and therapeutics. There is significant need for high-sensitivity diagnostic methods to detect the presence of early-stage disease. Competitive pressures and reimbursement issues will increase the demand for better diagnostic testing information in order to satisfy the need for a diagnostic component to the clinical decision-making process.

The enormous developments in analytical instrumentation in the last [redacted] years fueled the $[redacted] worldwide biotechnology instrumentation market in [redacted], of which the U.S. biotechnology instrumentation market was estimated to be $[redacted]. Of course, the deoxyribonucleic acid (DNA) revolution has brought an entire new class of analytical instruments on board in the last [redacted] years. DNA structure and function has lead to new classes of cancer markers.

The cancer biomarkers space can be sub-divided into roughly three types, primarily based on their usage:

- *Routine Blood-based Traditional Markers such as CEA, PSA, CA-125, etc.*: These traditional tumor markers have been in clinical use for over [redacted] years (CEA was introduced by Dr. Phil Gold in [redacted]). These constitute a steadily growing market of $[redacted] worldwide.

- *New Tissue-Specific Cancer Biomarkers based on Proteomics and Molecular Diagnostics*: This is a new area that develops markers for early detection of cancer, assesses outcomes, and predicts recurrence. This is the segment with the largest potential market opportunity.

- *Companion Diagnostic Tests Developed in Conjunction with Therapeutic Agents*: The use of diagnostic tests to follow the progress of clinical trials, and later to assess efficacy for patient populations receiving anti-cancer therapeutics, is growing rapidly. The deployment of cancer biomarkers in preclinical Research & Development (R&D) as a tool to assess lead compound toxicity, as well as assess toxicity or efficacy (such as hERG toxicity screening) exists today. Products and services offered into this market are: toxicity screening in drug discovery and development using cancer biomarkers, reagents, media, cells, consumables and miscellaneous services.

Targeted therapies have revolutionized the way cancer is being treated (Personalized Medicine), opening up the possibility that many forms of the disease can be fought through long-term maintenance therapy. These therapies are helping to win individual battles against cancer, enabling us to think of it as a chronic illness, rather than a life-ending one. With the industry's innovation and ongoing scientific advances, growth in targeted therapies will continue to be very strong and the outcomes even more impressive, and this will drive the development of companion diagnostic tests. Cancer testing is one of the most important growth opportunities in the diagnostics segment for the next three to five years.

The efforts to diagnose cancer and other complex diseases have failed in large part because the disease is heterogeneous at the causative level (*i.e.*, most diseases can be traced to multiple potential etiologies) and at the human response level (*i.e.*, each individual afflicted with a given disease can respond to that ailment in a specific manner). Consequently, measuring a single protein biomarker when multiple protein biomarkers may be altered in a complex disease is unlikely to provide meaningful information about the disease state. The market for advanced cancer diagnostic testing will increase to over $[redacted] by [redacted]. This increase is attributable to multiple factors including increasing incidences of cancer in an aging population, new therapies and expanded testing panels. The patient market for breast cancer exceeds $[redacted] per year (although most of this is associated with mammography screening) and for cervical cancer testing exceeds $[redacted] per year.

By [redacted], [redacted] or so companies have developed proprietary molecular based cancer tests that were at or very near market. The market for these tests is getting very competitive, and some companies are finding out that even as a service, the test really has to respond to medical needs or the technological norms of routine laboratories. Case in point is Agendia's MammaPrint breast cancer test for cancer recurrence that has had limited success, and this in spite of having FDA clearance.

Other test services that have been launched include Bio Reference Laboratories' test for K-RAS mutation in the colon, Fujirebio Diagnostic's HE4 Ovarian Cancer Test, Rosetta Genomics' miRview meso for mesothelioma, Clarient's Prostate Gene Expression Profile, Neogenomics Laboratories' FISH probe service for melanoma, and Acupath Laboratories' test for bladder cancer genes.

In [redacted], CLIA-certified laboratories were operated by a diverse range of companies, including Affymetrix, CombiMatrix, deCode Genetics, Diagnocure, Ikonisys, Illumina, Predictive Biosciences, Sequenom, Siemens Diagnostics, and Xceed Molecular. These firms market their tests or technology platforms as commercial products and also offer testing services to other laboratories. Several companies established CLIA-certified laboratories for cancer testing, including Agendia, Beckman Coulter, bioMérieux, Sequenom and Celera Diagnostics.

