



Cost-Effective Diagnostic Screens for Early Detection and Treatment of Cancer

Snapshot

December 13, 2006

CytoCore, Inc. ("CytoCore" or "the Company") is a biomolecular diagnostics and medical device company engaged in the design, development, and commercialization of cost-effective systems for the early detection of **cancer**[†] and cancer-related diseases, and for the local delivery of drugs to sites affected by disease. CytoCore is developing the InPath™ System—a multi-component, comprehensive method to detect cervical precancer (**dysplasia**) and cancer **lesions** and to treat dysplasia in women worldwide. The InPath™ System is designed to be more accurate, rapid, cost-effective, and easier to use than traditional Papanicolaou ("Pap") or **human papillomavirus (HPV)** testing, and is capable of providing patients with **point-of-service (POS)** test results. The InPath™ System consists of a family of four novel, proprietary products designed to be used separately or as a unified solution: the e² Collector™ (a U.S. Food and Drug Administration [FDA]-approved cell collection device); the Cocktail-CVX™ and Cocktail-GCI (**assays** used to identify the presence of abnormal cells in the cervical **cytology** sample through **proteomics**, a fluorescent staining process); the Automated Imaging Proteomic System (AIPS) platform (a microscope workstation capable of high-throughput sample evaluation); and a Drug Delivery System ([DDS] to provide therapeutic treatment for cervical lesions at the point-of-care). CytoCore's assays employ the P2X₇ **biomarker**, which can detect cancerous uterine **epithelial cells**, as well as precancerous tissue and early **neoplastic** lesions. The P2X₇ biomarker has also recently shown to accurately detect bladder cancer, suggesting its potential for use in the early detection of cancer in other epithelial tissues. CytoCore is further developing an Endometrial Cancer Scan based on the P2X₇ marker, which has entered a **Fast Track** Phase I trial and has been shown in preliminary studies to represent more than 95% of uterine cancers.

Recent Financial Data

Ticker (Exchange)	CYCR.OB (OTC.BB)
Recent Price (12/13/2006)	\$0.34
52-Week Range	\$0.04 - \$0.43
Shares Outstanding	275.5 million
Market Capitalization	\$93.7 million
Avg. 3-month Volume	379,717
Insider Owners +5%	16%
Institutional Owners	0.06%
EPS (Qtr. ended 09/30/2006)	(\$0.00)
Employees	9*



*Four full-time employees and five part-time employees supplemented by additional consultants in the U.S.

Key Points

- CytoCore's technology utilizes automated, portable products that can be operated with nominal laboratory infrastructure and minimal training—a preferred option to combat cancer worldwide.
- The Company's e² Collector™ consists of a disposable, balloon-shaped device designed to gather cells in a single step from the 360° surface area of the cervix and lower third of the cervical canal. Utilizing a "touch" method for cell collection, the device is intended to improve the patient experience and the accuracy of the **Pap test** by replacing the current 'spatula and brush' scraping technique. The e² Collector™ is in preparation for production, with units expected for sale by the end of first quarter 2007.
- **Cervical cancer** is the second leading cause of female cancer mortality worldwide, with about 250,000 deaths each year and an annual cost for screening (Pap tests) of between \$5 billion to \$6 billion.
- CytoCore's Endometrial Cancer Scan could become the first of its kind, since there is no known screen for endometrial (uterine) cancer available.
- The Company has implemented a new management team, which has kept a strong focus on financially restructuring the Company. Dr. George Gorodeski, the Company's chief scientist, is the inventor of a majority of CytoCore's technology and has licensed his products to the Company.
- As of September 30, 2006, CytoCore had cash and cash equivalents of approximately \$873,000.

[†]**BOLD WORDS ARE REFERENCED IN GLOSSARY ON PAGES 60-65.**



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Executive Overview

CytoCore, Inc. (“CytoCore” or “the Company”) is a biomolecular diagnostics company engaged in the design, development, and commercialization of cost-effective screening systems for the early detection of cancer and cancer-related diseases, and for the local delivery of drugs to sites affected by disease. The Company is currently developing the InPath™ System—a comprehensive method to detect, diagnose, and treat cervical cancer in women throughout the world. The System is designed to be faster, easier, more cost-effective, and more accurate than the traditional Papanicolaou (“Pap”) or human papillomavirus (HPV) test, and is capable of providing point-of-service (POS) test results and a unique therapeutic treatment option. CytoCore is also developing an Endometrial Cancer Scan for the early detection of endometrial cancer in women. This screen could be the first of its kind, as there is no known screen for endometrial (uterine) cancer currently available for use. One component of the InPath™ System—the e² Collector™—is already U.S. Food and Drug Administration (FDA) approved and is currently being brought into production. Units could be ready for sale by the end of the first quarter 2007.

Current Standard of Care: The Papanicolaou (“Pap”) Tests

The Pap test, also known as the Pap smear, is the current standard of care used to screen for cervical cancer. The test detects precancerous lesions (which may develop into cancer if left untreated) and cancerous cells before they spread or become visible to the naked eye. The Pap test currently costs between \$70 to \$350 per test, depending on the laboratory and physician, and is administered to 55 to 60 million women each year in the U.S. Approximately 10% of these tests are considered abnormal. Globally, approximately 180 million Pap tests are performed each year, according to the International Consensus Conference on the Fight Against Cervical Cancer.

Despite the large number of Pap tests that are performed, there could be as many as 1.5 to 1.8 billion women around the world who still require annual Pap tests but are not receiving them. In the U.S. alone, roughly 60% to 80% of women with cervical cancer have not had a test in the past five years, and many have not had a test at all—particularly among woman who are elderly, African-American, or in a low-income bracket. In addition, the accuracy of the Pap test is perpetually disputed. The Brigham and Women’s Hospital, a teaching affiliate of Harvard Medical School, reports that approximately 20% of the time, abnormal cells in the cervix do not show up on a Pap test. It is further believed by some gynecologic physicians and researchers that the Pap test is typically between 50% to 70% accurate.

The InPath™ System and Endometrial Cancer Scan

The Company’s InPath™ System is based on a core of protein antibodies (biomarkers) that enable the rapid detection of abnormal or suspicious cells. It is composed of a family of four related products that can be used separately or as a unified healthcare solution. The components include: the e² Collector™; the Cocktail-CVX™ and Cocktail-GCI biochemical assays with the P2X₇ biomarker; the Automated Imaging Proteomic System (AIPS) platform; and the Drug Delivery System (DDS). There is also an Endometrial Cancer Scan, which is in addition to the Company’s InPath™ System. Together, these products represent an end-to-end system for the detection, diagnosis, and treatment of cervical cancer, as well as early detection of endometrial cancer.

CytoCore has developed automated, portable products designed to operate with little laboratory infrastructure and minimal operator training, making the InPath™ System a preferred option to assist in the task of combating cancer on a global basis. A brief description of each of the InPath™ System’s components is provided below (as well as the Company’s Endometrial Cancer Scan), with greater details provided on pages 26-40 of the Core Story section of this Executive Informational Overview[®] (EIO[®]).

- *e² Collector™*. CytoCore’s unique FDA-approved cell collection device, the e² Collector™, consists of a small, disposable, balloon-shaped device designed to gather cells in a single step from the 360-degree surface area of a woman’s cervix and lower third of the cervical canal. Utilizing a “touch” method for cell collection, the device is intended to improve the patient experience and the accuracy of the Pap test by replacing the current ‘spatula and brush’ scraping technique.

- **Cocktail-CVX™ and Cocktail-GCI biochemical assays and P2X₇ biomarker.** CytoCore's proteomic-based biochemical assays are used to identify abnormal cells in the cytology sample. The newly discovered P2X₇ biomarker may improve the accuracy of the Pap test from the current range of 50% to 70% to a range of 85% to 90%. The P2X₇ is used in the assays to identify cells that show signs of slowed **apoptosis** (cell death). Decreased apoptosis is a trait of cancerous cells.
- **Automated Imaging Proteomic System (AIPS) platform.** The AIPS platform is a fully automated microscope workstation for high-throughput analysis of cytological and **histological** specimen slides.
- **Drug Delivery System (DDS).** The DDS supplies a therapeutic, non-surgical treatment option for the early stages of cervical cancer. It operates in a manner similar to the e² Collector™, while delivering and seating a polymer patch directly onto the surface of the cervix. The patch provides a timed release of a therapeutic agent to the cervix for three to seven days.

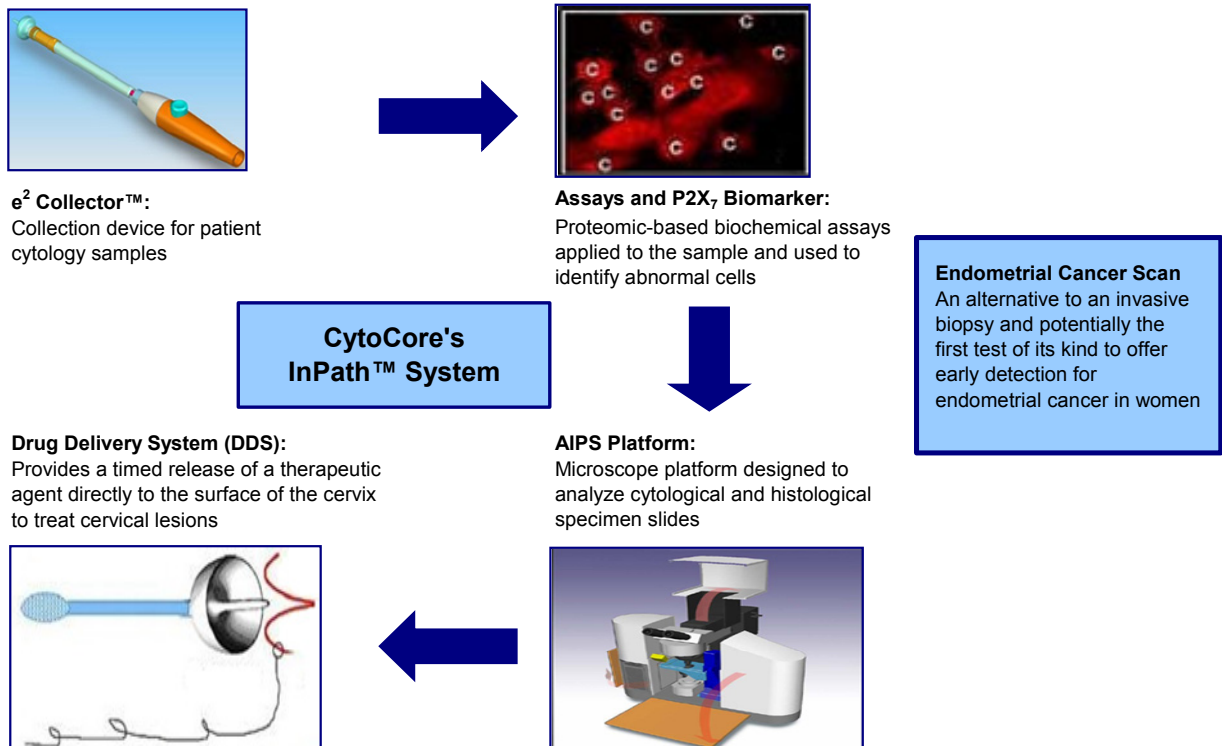
Endometrial Cancer Scan. The Endometrial Cancer Scan, which is in addition to the InPath™ System, could become the first early detection method for endometrial cancer in women. It uses a saline solution flush to gather cells from the **uterus** and identifies the dispersed cancerous cells with the P2X₇ biomarker and the AIPS platform, returning test results through a process that is almost identical to CytoCore's improved cervical cancer screen. This Endometrial Cancer Scan, which consists of three products (listed below), could provide an alternative to currently used biopsy procedures:

- EndoCollector (to retrieve a representative sample of endometrial cells);
- Cocktail-GCI (to identify abnormal cells in the endometrial cytology sample); and
- One-Step Real-Time Reverse Transcription Polymerase Chain Reaction ([RT-PCR, qPCR] to identify abnormal cells in the cervical cytology sample using **ribonucleomics** criteria).

Figure 1 illustrates each component of the InPath™ System, as well as the Endometrial Cancer Scan.

Figure 1
CytoCore, Inc.

CYTOCORE'S COMPREHENSIVE INPATH™ SYSTEM AND ENDOMETRIAL CANCER SCAN



Source: CytoCore, Inc. and Crystal Research Associates, LLC.

Market Overview

The current cost of cervical cancer screening programs (Pap tests) is between \$5 billion to \$6 billion annually, according to the American Social Health Association. In addition, cervical cancer treatment incurs costs in the U.S. of more than \$2 billion a year. A market research firm, BCC Research (formerly Business Communications Company, Inc. [www.bccresearch.com]), estimated in May 2005 that the U.S. market for new therapeutics and diagnostics for women's disorders is likely to grow at an average annual growth rate (AAGR) of 10.3% to reach nearly \$41 billion by 2009. Within this market, female-specific cancer treatments are predicted to rise at the greatest rate, with an AAGR of 12.6%.

Studies have shown that 70% to 80% of a person's healthcare expenditures occur in the last four to six months of life. As a result, increased emphasis is being given to developing early detection methods for potentially fatal diseases. Accordingly, the FDA recently announced that it would devote 60% of its approvals for the coming period toward diagnostic-related products to catch diseases before they become life-threatening and costly to treat. CytoCore is designing its products to address this emphasis and focus on early detection.

Target Markets

Cervical Cancer

Cervical cancer is the second leading cause of female cancer mortality worldwide, with approximately 250,000 deaths globally each year. The American Cancer Society, Inc. (ACS) estimates that in 2006, there will likely be 9,710 new cases of **invasive cervical cancer** (cancer that has spread into surrounding healthy tissue) in the U.S. alone, proving fatal in approximately 3,700 cases. Cervical cancer begins as a cell change in the lining of the cervix. In most cases, it takes a number of years for normal cells to turn precancerous and then cancerous, but it is possible for the change to occur in under a year, making early detection particularly important. When found and treated early, cervical cancer can typically be cured.

The most significant risk factor for developing cervical cancer is persistent infection with high-risk **HPV Types 16 and 18**. Approximately 20 million women in the U.S. are currently infected with HPV, and by age 50, at least 80% of women have acquired a genital HPV infection. Existing treatments for cervical cancer include surgery, **radiation therapy**, and **chemotherapy**. CytoCore is developing a new treatment modality (the DDS, described on pages 36-38) for mild-, moderate-, and potentially some high-grade lesions. The DDS is designed to apply therapeutic drugs directly to the surface of the cervix.

Endometrial Cancer

Endometrial cancer starts in the **endometrium** (the inner lining of the uterus). The ACS estimates that approximately 41,200 new cases of uterine corpus cancer (cancer of the body of the uterus) will likely be diagnosed in the U.S. in 2006, and that more than 95% of these will be endometrial cancers. Uterine corpus cancer is expected to be fatal in 7,350 women in the U.S. during 2006. A majority of endometrial cancers are diagnosed in postmenopausal women aged 50 to 70 years, according to the Mayo Foundation for Medical Education and Research, and 70% are expected to be found in women between the ages of 45 and 74.

The primary risk factor for developing endometrial cancer is increased **estrogen** levels within the uterus. Once the cancer has spread beyond the pelvis, the chance of the patient surviving another five years is at most 26%. This percentage is much higher when cancer is found at an early stage. However, typically, it is only after symptoms appear, such as abnormal bleeding, that invasive biopsies are performed (which are only 80% to 90% accurate), followed by a histological evaluation of the tissue sample by a pathologist. To date, the chance that a woman is diagnosed with endometrial cancer in her lifetime is 1 in 38, according to the ACS. There are currently four standard treatment options: radiation therapy, chemotherapy, **hormone therapy**, and surgery.



Corporate History

CytoCore, Inc. (formerly known as Molecular Diagnostics, Inc.) was incorporated in Delaware in December 1998 as the successor to Bell National Corporation, which was incorporated in California in 1958. Bell acquired InPath, LLC—a development-stage company engaged in the design and development of products to screen for cervical and other cancers—in December 1998. Bell then merged into Ampersand Medical Corp. in May 1999 and changed its state of incorporation to Delaware. Ampersand acquired 100% of the outstanding stock of AccuMed International, Inc. in September 2001 through another merger. Subsequently, Ampersand changed its name to Molecular Diagnostics, Inc. From 2001 to 2002, Molecular Diagnostics conducted research and product development for the InPath™ System, and in May 2002, the Company received FDA approval to market its e² Collector™ (CytoCore's cell collection device). Research studies were suspended during the latter half of 2002 due to capital limitations, but from 2003 to 2005, the Company was able to refine and optimize its Cocktail-CVX™ biochemical assay, as well as initiate development of its AIPS platform (both described briefly on page 4 and described in greater detail on pages 30-31 and 35-36, respectively).

In September 2005, a new management team was installed who resumed CytoCore's existing projects (the e² Collector™, Cocktail-CVX™, and AIPS platform), established a valuable research relationship with the University Hospitals Case Medical Center ([UHCMC] formerly the University Hospitals of Cleveland) and Dr. George Gorodeski (biography on pages 12-13), licensed the P2X₇ biomarker and the DDS, and began preparations to open a research laboratory facility at the UHCMC.

CytoCore has reduced its debt from \$13.4 million at June 30, 2005, to \$3.6 million as of December 11, 2006. In addition, the Company recently announced the removal of an additional \$1.7 million from long-term debt by paying off their last Senior Note holder. Furthermore, the new management has settled approximately 19 legal matters (an estimated \$2.5 million in claims) involving CytoCore since August 31, 2005, and reduced accounts payable and accrued expenses by approximately \$4.2 million and Notes payable by \$5 million.

The Company's current management team is focused on propelling products into research studies, development, and production, and intends to further reduce the debt balance to reflect only trade liabilities needed for working capital purposes. The Company formally changed its name to CytoCore, Inc. on June 22, 2006, to better reflect its expanded product line and target markets, and to demonstrate its renewed impetus and focus. CytoCore's trading symbol changed to CYCR.OB (formerly "MCDG.OB") on August 17, 2006.

Headquarters and Employees

CytoCore, Inc. occupies approximately 2,540 square feet of leased space at 414 North Orleans Street, Suites 502 and 503, Chicago, IL 60610, under a five-year lease that expires in October 2008. This space houses executive offices, a research laboratory, and engineering development facilities. The Company employs a total of four full-time individuals and five part-time individuals supplemented by additional consultants in the U.S. The staff reductions from prior years were undertaken in order to conserve limited operating funds. CytoCore continues to upgrade its management team as it seeks individuals with the experience and knowledge in which to bring the Company's products from development to market.

Growth Strategy

CytoCore's InPath™ System is based on a core of protein antibodies (biomarkers) that enable the rapid detection of abnormal or suspicious cells. Varying the antibody combinations can allow the Company to use its System for multiple applications. As such, CytoCore intends to expand its focus beyond cervical and endometrial cancers to the detection and diagnosis of additional cancer and cancer-related diseases in the future. The Company also plans to develop products through internal development processes, strategic partnerships, licenses, and acquisitions of products/companies. While CytoCore does not expect to develop its own distribution, manufacturing, or sales organizations, it does intend to utilize the operations, quality systems, and facilities of contract manufacturers who specialize in medical products manufacturing.

Expanding into markets outside of North America is an important component of CytoCore's growth strategy. As the Company begins to market and sell its InPath™ System, it anticipates closely reviewing its foreign operational practices and attempting to adopt strategies that minimize the risk of changing economic and political conditions within foreign countries.

Marketing Strategy

In the U.S. and Canada, CytoCore's initial marketing strategy is based on first bringing the e² Collector™ to market, building distribution for its products through laboratories that support Pap testing within the obstetrics and gynecology (OB/GYN) market, and gaining exposure for its products and brand name.

Outside of the U.S. and Canada, CytoCore does not intend to develop any sales or distribution infrastructure. Instead, the Company expects to rely on existing channels through strategic partnerships and licensing relationships. A number of strategic partnerships and alliances are currently being considered with global leaders in the sales and marketing of medical technologies. Differing market needs and medical-political environments may necessitate multiple distribution partners.

CytoCore's specific growth strategies are more fully outlined below.

- *CytoCore's initial strategy involves bringing the e² Collector™ to market, followed by subsequent products that are currently completing development and clinical trials.* The Company is led by a physician, Dr. Augusto Ocana (biography on page 12), and advised by several practicing physicians, including Dr. George Gorodeski, director of the Scientific-Medical Advisory Board, chief scientist, and lead researcher; Drs. Steven Waggoner, Floyd Taub, and Stephen Raab—all Scientific-Medical Advisory Board members (biographies are on pages 15-16). CytoCore recognizes that once a distributor has one product in the physician's office that the physician finds useful and beneficial, it is then much easier to get follow-up products into that same physician's standard treatment protocol. With that in mind, the Company is developing a multi-level treatment plan with the InPath™ System that, ideally, can build off the acceptance of its first product, the e² Collector™. CytoCore intends to use the same distribution channels and doctors for its additional products as will likely be used with the e² Collector™. Therefore, once they complete development and clinical trials, these products can be added into the InPath™ System as components for the cervical cancer screening market as seamlessly as possible. Ultimately, CytoCore believes that these products can upgrade the Pap test entirely. The Company intends to apply to obtain insurance coverage for the e² Collector™ and expects to receive a **current procedural terminology (CPT) code** within the next 12 to 18 months.
- *CytoCore expects to build distribution for its products through laboratories that distribute Pap test supplies to doctors.* The Company expects to make both its assays and AIPS platform available to laboratories upon completion of the early clinical trials for Cocktail-CVX™. CytoCore aims to offer its components to laboratories as **Analyte Specific Reagents (ASRs)**. ASRs are composed of chemicals or antibodies that can be considered the active ingredients of in-house developed tests, and thereby purchased from manufacturers under this label. The majority of ASRs are exempt from FDA approval or clearance. Consequently, manufacturers of ASRs are prohibited from making claims of analytical or clinical performance (Source: College of American Pathologists). CytoCore believes that laboratories using ASRs may be able to offer the Company's products. For instance, the



Cocktail-CVX™ assay and AIPS system could be offered as an adjunctive, secondary test for women and physicians in conjunction with the Pap test—possibly becoming commercially referred to as the “Super Pap.” After the laboratories have utilized the system for a period of time, and upon FDA clearance, the laboratories would be able to approach customers with “local” data and request a conversion from the Pap test to the InPath™ System exclusively. In addition, upon successful completion of the recently launched Phase I trials, CytoCore intends to offer its Endometrial Cancer Scan as an ASR for sale through laboratories while waiting for the completion of its Phase II trials.

- *CytoCore intends to identify and initiate discussions with pharmaceutical companies that are interested in using off-patent drugs or unique new compounds for cancer treatment via CytoCore’s Drug Delivery System (DDS).* The DDS represents a unique opportunity for companies with compounds or therapeutic drugs that have expired patents. By partnering with CytoCore, companies can provide these drugs as cancer treatments with a novel delivery system, thus allowing these companies to acquire “new use” patents for their off-patent products. CytoCore believes that pursuing this avenue can provide it with cost savings since these other companies will likely supply some of the research and development costs. In addition, CytoCore expects this to double as a marketing strategy, as these larger companies already have established marketing processes that can aid in the introduction and distribution of CytoCore’s products to the market.

The unique capabilities of the DDS may allow the Company to also offer it as a delivery platform for other compounds—such as anti-viral or **immunostimulant** compounds—that could effectively treat cervical lesions or HPV. In each case, CytoCore’s DDS offers a unique potential product and method for delivering treatment compounds to the cervical area.

Financial Strategy

CytoCore has had more than \$40 million invested to develop its technology and products, and has recently completed a comprehensive financial and capital restructuring. The Company now believes that it requires only a small amount of funding in order to bring to market its first product, the e² Collector™, and to achieve cash flow breakeven. The e² Collector™ has a unique market opportunity that could lead to rapid adoption. CytoCore’s other products offer revenue opportunities as well, such as the Endometrial Cancer Scan and the other components of the InPath™ System. Current capital investment is anticipated to achieve the following:

- complete financial restructuring;
- complete the e² Collector™ confirmation trial;
- bring the e² Collector™ into production, marketing, and sales;
- establish domestic and international distribution agreements for the e² Collector™;
- complete high-volume production capability for the e² Collector™ by mid-year 2007;
- scale-up e² Collector™ sales during the summer and early fall of 2007, enabling the Company to reach its cash flow breakeven point;
- complete the AIPS development project by customizing it to recognize the P2X₇ Endometrial Cancer Scan marker;
- complete the Endometrial Cancer Scan Phase I trial;
- upon successful completion of the Phase I trial, offer the Endometrial Cancer Scan as an ASR through laboratory partners;
- further the development and integration of the Cocktail-CVX™ with the AIPS Platform and prepare each for clinical trials; and
- begin development of the prototype handle and patch for the DDS and set up parameters for its trials.

Intellectual Property

CytoCore relies on a combination of licenses, trade names, trademarks, patents, know-how, proprietary technology, and policies and procedures to protect its intellectual property. The Company considers security and protection an important aspect of successful product development and marketing in both the U.S. and worldwide.

Trademarks and Licenses

CytoCore owns the trade names for InPath™, e² Collector™, and Cocktail-CVX™, and may file additional U.S. and foreign trademark applications in the future. CytoCore also has a license for the P2X₇ biomarker, the Drug Delivery System (DDS), and the Endometrial Cancer Scan through a strategic partnership with Dr. George Gorodeski, which is detailed on pages 10-11.

Patents

CytoCore's patent portfolio includes three issued U.S. patents and six U.S. and foreign pending patent applications. These patents and patent applications cover all aspects of the InPath™ System including, but not limited to, the union of hardware, software, and proteomic-based assays creating a point-of-service (POS) instrument; the personal and physicians' collectors; and the Company's **slide-based tests**. In addition, Dr. Gorodeski and the University Hospitals Case Medical Center (UHCMC) have filed patents assigned to CytoCore for the P2X₇ biomarker, the DDS, and the Endometrial Cancer Scan. CytoCore intends to prepare additional patent applications for processes and inventions arising from its research and development process. Its future technology acquisition efforts are expected to be focused toward technologies with solid patent or trade secret protection. A snapshot of the Company's patent portfolio is provided in Table 1.

Table 1
CytoCore, Inc.
PATENT PORTFOLIO

Title	Description	Status
Method and Apparatus for Collecting and Analyzing Tissue	POS System: System patent covering the staining and analysis of cytological specimens on the surface of a cervical cell collection device	Issued
Physician's Cervical Cell Collector	Cervical cell collection device for use in clinical environments	Issued
Personal Cervical Cell Collector	Cervical cell collection device for use by individual patients	Issued
Title	Description	Status
Detection and Differentiation of Cancerous Cells	Detection of abnormal cells using three-color analysis of cytological specimens	Pending
Marker Cocktail and Use in Identifying Cervical Cell Abnormalities	Detection of abnormal cells using three-color analysis of cytological specimens	Pending
Truncated Proteins as Cancer Markers	Using the P2X ₇ as a marker for detection of cancer	Pending
Cancer and Cancer Potential Marker, Target, Antibody, and Therapeutic	Using the P2X ₇ as a marker for detection of cancer	Pending
Method and Apparatus for Applying Medication to Internal Tissue	Drug Delivery System based upon the e ² Collector™ for depositing patch on surface of cervix	Pending
Cell Collection and Disease Screening	Using a flushing technique and the P2X ₇ marker for detection of uterine cancer	Pending

Source: CytoCore, Inc.



Strategic Partnerships

Strategic Research Partnership and Technology Transfer Agreement

University Hospitals Case Medical Center (UHCMC)

On January 27, 2006, CytoCore entered into a strategic research partnership and technology transfer agreement with the University Hospitals Case Medical Center (UHCMC) and one of UHCMC's leading researchers in the area of women's health, Dr. George Gorodeski. Under the terms of the transfer agreement, CytoCore licensed the P2X₇ cancer biomarker and Drug Delivery System (DDS), detailed on pages 31 and 36-37, respectively. The addition of these products to CytoCore's portfolio enhanced and expanded its InPath™ System. The partnership also provided for the establishment of a new CytoCore laboratory within UHCMC's Center for Clinical Research. Research at this location is expected to focus on the P2X₇ biomarker and its capabilities for the identification and treatment of certain gynecological disorders, including cervical dysplasia and all forms of endometrial cancer.

This agreement provides CytoCore with a number of strategic advantages, some of which are listed below.

- It licenses all development rights for the P2X₇ to CytoCore, allowing the Company to develop commercial products based on the P2X₇ biomarker.
- The P2X₇ biomarker has shown that it can accurately detect both cervical and endometrial cancers. It is being tested for several other cancers. The Company recently announced that the P2X₇ accurately identified bladder cancer tissue from normal bladder tissues (See Recent Events, page 56, 12/04/2006).
- Local research on the P2X₇ biomarker has produced test evidence that it is well suited for the Endometrial Cancer Scan.
- The new P2X₇ biomarker, when combined with CytoCore's Cocktail-CVX™ assay, has demonstrated to significantly improve the accuracy of cervical cancer screening.
- Additional screening applications based on the P2X₇ are expected to be developed for other types of **epithelial cancers**.
- CytoCore has been granted rights to commercialize a unique DDS that can apply FDA-approved therapeutic drugs directly to existing cervical lesions. The DDS could provide physicians for the first time with a non-surgical therapeutic treatment option for cervical lesions.
- The acquired DDS leverages CytoCore's technology that was previously developed for the e² Collector™ handle.
- The agreement positions CytoCore to grow with a focus on cytology screening and treatment for an expanding group of cancers.

CytoCore intends to conduct all of its basic research work at the UHCMC's Center for Clinical Research. The annual budget for operating the new laboratory is anticipated to be 25% to 30% less than the budget requirements of a stand alone facility. In addition, the laboratory space is located within Dr. Gorodeski's existing research space inside the Center for Clinical Research, thereby providing the Company with access to the full capabilities of the clinic as well as increasing the overall effectiveness and productivity of this facility versus a stand alone location. This space also offers access to additional scientists and clinicians at the UHCMC, the Case Western Reserve University (CASE) School of Medicine, and potentially other CASE departments that may be needed to move CytoCore's research forward, as well as offers recognition for the Company and its efforts.

The UHCMC is also providing the principal sites and administrative support for CytoCore's current and future clinical trials designed to test the Company's new biotechnology products. Through the UHCMC, CytoCore is able to organize and conduct multiple clinical trials simultaneously or individually, as well as initiate timely and effective FDA trials to bring new products to market quickly. The Company believes that its strategic relationship with the UHCMC could increase the likelihood of successful development and commercialization of its product portfolio. The UHCMC is a 947-bed **tertiary medical center** specializing in adult and pediatric medical and surgical specialties. It is also the primary affiliate of CASE. Together, these institutions form the largest center for biomedical research in Ohio.

Dr. George Gorodeski

Dr. George Gorodeski joined CytoCore as the director of the Scientific-Medical Advisory Board, chief scientist, and principal investigator of the CytoCore-UHCMC Research Program. Dr. Gorodeski facilitates the Company's research being performed at the UHCMC. Under the partnership, Dr. Gorodeski licensed two products that he developed to CytoCore —the P2X₇ biomarker and the DDS. He is also the creator of CytoCore's e² Collector™ and is the force behind combining multiple biomarkers into cocktails to increase screening precision and diagnostic response (a process described in greater detail on pages 30-35).

Dr. Gorodeski has agreed to devote a significant amount of his time to the following four activities for CytoCore: (1) directing the Company's overall basic research; (2) directing CytoCore's research and development (R&D) efforts at the UHCMC; (3) coordinating commercial R&D at CytoCore's existing research facility in Chicago, Illinois; and (4) acting as medical director of the clinical trials. Dr. Gorodeski's role also includes assisting with staffing for the new laboratory.



Leadership

Management

CytoCore is currently upgrading its management team, bringing on additional professionals before the end of 2006. The Company currently employs a total of four full-time and five part-time individuals. Several of these individuals have recently joined the Company (see Recent Events, pages 56-59). Table 2 summarizes the Company's current management team, followed by detailed biographies.

Table 2
CytoCore, Inc.
MANAGEMENT

Augusto Ocana, M.D., J.D.	Chief Executive Officer and Director, Board of Directors
Robert McCullough, Jr., CPA	Chief Financial Officer and Director, Board of Directors
George Gorodeski, M.D., M.Sc., and Ph.D.	Director, Scientific-Medical Advisory Board, Chief Scientist, and Lead Researcher
Daniel Kusswurm, Ph.D.	Vice President, Image Engineering
Frank Mancuso	Chief Engineer

Source: CytoCore, Inc.

Augusto Ocana, M.D., J.D., Chief Executive Officer and Director, Board of Directors

Dr. Augusto Ocana has more than 20 years of international marketing and general and sales management experience. He has worked with both large multinational corporations and Corporate 500 companies, including Abbott Laboratories (ABT-NYSE) and Group Taper, S.A. Multilingual, he has successfully built businesses on four continents, establishing corporate partnerships, acquisitions, mergers, strategic alliances, and initial public offerings (IPOs) in clinical fields such as pharmaceuticals, cardiology, diagnostics, surgery, and orthopedics. He has also worked with a broad range of products, including implants, disposables, and capital equipment. Most recently, he was senior vice president and general manager of CH-Werfen, S.A. and a member of the Board of Directors. Over the past five years under Dr. Ocana's leadership, this division has grown from \$500 million to approximately \$1 billion in sales. Dr. Ocana holds a J.D. in international law, and a Certificate in International Trade from Northwestern University's School of Management. He received a B.S. in international trade and business administration from Pace University, New York; a Certificate in Accounting from Merchant Bankers School, New York; and a Certificate from Conferencia Internacional Del Sida, Universidad Menéndez Pelayo, Spain. Dr. Ocana earned a diploma as a medical doctor from the Universidade Haveriana de Bogotá.

Robert McCullough, Jr., CPA, Chief Financial Officer and Director, Board of Directors

Mr. Robert McCullough, Jr. has an MBA in finance and is a Certified Public Accountant (CPA). He was an executive at Ernst & Young LLP and served as chief financial officer (CFO) at two privately owned healthcare companies—American Homecare Inc. and Value Care. Mr. McCullough has been in the investment business for the past 20 years. He was a portfolio manager/security analyst for the first 18 years and is currently president of Summitcrest Capital, Inc., a registered investment advisor located in San Francisco, California.

George Gorodeski, M.D., M.Sc., and Ph.D., Director, Scientific-Medical Advisory Board, Chief Scientist, and Lead Researcher

Dr. George Gorodeski is a gynecologist and reproductive endocrinologist at the Department of Obstetrics and Gynecology at University Hospitals Case Medical Center (UHCMC) and a tenured professor in the Department of Reproductive Biology at Case Western Reserve University (CASE) School of Medicine. He is also a professor of oncology and a professor of physiology and biophysics at the CASE School of

Medicine. Dr. Gorodeski served as president of the North American Menopause Society from 2005 to 2006, and is chairperson of a National Institutes of Health (NIH) Study Section and of the obstetrics and gynecology (OB/GYN) departmental Investigational Review Board. Dr. Gorodeski has been lead or co-investigator on over 40 basic science projects and FDA-approved clinical trials. He has written over 200 publications, including 100 peer-reviewed articles in his areas of research and has five patents filed. Dr. Gorodeski developed and patented CytoCore's e² Collector™ product, originated the combination of multiple biomarkers into the "cocktail" approach, and developed the P2X₇ and the DDS, and the concept of using the e² Collector™ for mapping cervical lesions. Dr. Gorodeski combines an academic career of a busy clinical practice and active basic and clinical research with applied research towards products and procedures that address issues of the detection and prevention of cervical cancer. He earned a M.D. from the Sackler School of Medicine at Tel Aviv University, Israel, a M.Sc. from Sackler School of Continuing Medical Education at Tel Aviv University, Israel, and a Ph.D. in cell physiology from CASE.

Daniel Kusswurm, Ph.D., Vice President, Image Engineering

Dr. Daniel Kusswurm is vice president of image engineering at CytoCore. With over 20 years of experience developing software for medical devices and analytical instruments, his areas of expertise include image processing, pattern recognition, computer graphics, real-time systems, and software engineering. At CytoCore, Dr. Kusswurm is responsible for developing the image analysis software designed to analyze specimen slides on the AIPS platform, including slides prepared using the Company's P2X₇-based assay. Prior to joining CytoCore, Dr. Kusswurm was employed by AccuMed as an imaging scientist. At AccuMed, he developed software for microscopy-based imaging systems used to detect and analyze proteins associated with cancer. Dr. Kusswurm has also held lead software engineering positions at Baxter Healthcare (BAX-NYSE) and PerkinElmer, Inc. (PKI-NYSE). While at Baxter, he designed software for drug delivery systems and intravenous therapy devices. At PerkinElmer, he developed application software for a series of spectrometer products. Dr. Kusswurm holds a B.S. in electrical engineering technology from Northern Illinois University and an M.S. and Ph.D. in computer science from DePaul University.

Frank Mancuso, Chief Engineer

Mr. Frank Mancuso is chief engineer at CytoCore. He has more than 15 years of experience managing, designing, and developing embedded systems for medical, industrial, and telecommunications applications. Mr. Mancuso also has five years of experience developing custom digital video solutions for many medical applications, such as Hologic, Inc.'s (HOLX-NASDAQ) Fluoriscan mini C-arm imaging systems and Stratagene Corp.'s (STGN-NASDAQ) and FOTODYNE Inc.'s **gel electrophoresis** imaging applications. He was a senior level engineer for AccuMed, where he assisted in developing the AcCell and TracCell Automated Microscopy Workstations. Currently, Mr. Mancuso is in a project management/engineering role at CytoCore to develop and commercialize the e² Collector™ and AIPS automated microscopy workstation.

Board of Directors

CytoCore's Board of Directors oversees the conduct of and supervises the Company's management. As the Company completes its turnaround, it intends to upgrade its Board of Directors to include additional female perspective. Table 3 summarizes CytoCore's Board members, followed by biographies (page 14).

Table 3
CytoCore, Inc.
BOARD OF DIRECTORS

Augusto Ocana, M.D., J.D.	Chief Executive Officer and Director
Robert McCullough, Jr., CPA	Chief Financial Officer and Director
Alexander M. Milley	Director
John H. Abeles, M.D.	Director
Clinton H. Severson	Director

Source: CytoCore, Inc.



Augusto Ocana, M.D., J.D., Chief Executive Officer and Director

Biography on page 12.

Robert McCullough, Jr., CPA, Chief Financial Officer and Director

Biography on page 12.

Alexander M. Milley, Director

Mr. Alexander M. Milley has been a director of CytoCore since 1989. Mr. Milley is president and chairman of the Board of ELXSI Corp. (ELXS.PK-OTC), a holding company with subsidiaries operating in the restaurant and environmental inspection equipment industries. He is also president and chairman of the Board of Azimuth, a holding company with subsidiaries operating in the trade show exhibit, retail environment design, and distribution of electrical components and fasteners industries. Mr. Milley was chairman of the Board and chief executive officer (CEO) of Bell National Corporation, a predecessor of CytoCore, until December 1998 and was president of Bell from August 1990 until December 1998. Mr. Milley is the founder, president, sole director, and majority shareholder of Milley Management, Inc., a private investment and management consulting firm. Mr. Milley is also the president of Cadmus, a private investment and management consulting firm. Mr. Milley was senior vice president of acquisitions from December 1983 until July 1986 of the Dyson-Kissner-Moran Corporation, a private investment company.

John H. Abeles, M.D., Director

Dr. John H. Abeles has been a director of CytoCore since May 1999. Dr. Abeles is president of MedVest, Inc., a venture capital and consulting firm he founded in 1980. He is also general partner of Northlea Partners, Ltd., a family investment partnership. Dr. Abeles was a senior medical executive at Sterling Drug, Pfizer Inc. (PFE-NYSE), and Revlon Healthcare, Inc., and subsequently was a medical analyst at Kidder, Peabody & Co. Dr. Abeles is a director of a number of companies operating in the medical device or healthcare fields, including I-Flow Corporation (IFLO-NASDAQ), Oryx Technology Corp. (ORYX.PK), Encore Medical Corporation (ENMC-NASDAQ), and DUSA Pharmaceuticals, Inc. (DUSA-NASDAQ). Dr. Abeles received a medical degree and degree in pharmacology at the University of Birmingham in England and is currently a director at the Higuchi BioSciences Institute at the University of Kansas.

Clinton H. Severson, Director

Mr. Clinton H. Severson has served as president, CEO, and a director of Abaxis, Inc. (ABAX-NASDAQ)—a northern California-based provider of portable technology, tools, and services used for medical diagnostics sold to customers and distributors worldwide—since June 1996. He was appointed chairman of the Board of Abaxis in May 1998. From February 1989 to May 1996, Mr. Severson served as president and CEO of MAST Immunoseystems, Inc., a privately held medical diagnostic company.

Scientific-Medical Advisory Board

CytoCore's scientific-medical advisors bring a diverse viewpoint and the ability to maximize the market potential of CytoCore's products. Table 4 (page 15) summarizes these individuals, followed by detailed biographies (pages 14-16).

George Gorodeski, M.D., M.Sc., and Ph.D., Director, Scientific-Medical Advisory Board, Chief Scientist, and Lead Researcher

Biography on pages 12-13.

Table 4
CytoCore, Inc.
SCIENTIFIC-MEDICAL ADVISORY BOARD

George Gorodeski, M.D., M.Sc., and Ph.D.	Director, Scientific-Medical Advisory Board, Chief Scientist, and Lead Researcher
Jorge Leon, Ph.D.	Member
Steven Waggoner, M.D.	Member
Floyd Taub, M.D.	Member
Stephen Raab, M.D.	Member

Source: CytoCore, Inc.

Jorge Leon, Ph.D., Member

Dr. Jorge Leon was one of the founders of the Molecular Diagnostic and Applied Genomics businesses at Quest Diagnostics Inc. (DGX-NYSE) where, as the vice president of applied genomics, he helped build and drive the strategy for Quest Diagnostics' Molecular Diagnostics business, now the largest in the country. Dr. Leon is recognized internationally within the investment and scientific communities as an industry leader for molecular diagnostics. Currently, he is founder and president of Leomics Associates, Inc., a consulting company that develops diagnostic strategies for companies seeking to enter the diagnostics space. Some of Dr. Leon's clients are Digene Corp. (DIGE-NASDAQ), Laboratory Corp. of America Holdings (LH-NYSE), and the Mayo Clinic. Dr. Leon has over 20 years of experience in evaluating and developing new technologies and scientific innovations and then commercializing those into successful diagnostic products. He is the holder of several patents, has been published extensively, and serves on the Boards of various leading technology companies. Dr. Leon has a Ph.D. in cellular and molecular biology from New York University.

Steven Waggoner, M.D., Member

Dr. Steven Waggoner is chief of the Division of Gynecologic Oncology at UHCCM, vice chairman of clinical affairs of the Department of Obstetrics and Gynecology at MacDonald Women's Hospital, and associate professor at CASE School of Medicine. Dr. Waggoner has been recognized as one of the best physicians in his field, receiving a variety of "Top Doctor" and "Top Women's Doctor in America" citations. Dr. Waggoner is active in clinical research at UHCCM and the CASE Comprehensive Cancer Center. He has extensive experience in the design and conduct of human subject clinical trials and holds leadership positions in the National Cancer Institute (NCI)-sponsored Gynecologic Oncology Group and the Society of Gynecologic Oncologists. Dr. Waggoner serves as a peer reviewer for major publications in the field: *Obstetrics and Gynecology*, *Gynecologic Oncology*, *Cancer*, *International Journal of Gynecological Cancer*, *The Lancet*, and *Clinical Cancer Research*. He received a B.S. in biology from the University of Puget Sound and a M.D. from the University of Washington.

Floyd Taub, M.D., Member

Dr. Floyd Taub is a founder of Digene, the only company with an FDA-approved test (the Digene[®] HPV Test) to detect cancer-causing cervical viruses. As Digene's first CEO, Dr. Taub's expertise encompasses early NanoDrug[™] development, clinical trials, and distribution, as well as the use of DNA technology in the detection and treatment of patients with a range of infectious stages of cervical cancer. He has also founded and currently works with a number of cutting-edge biomedical organizations, including Dovetail Technologies, Inc., LifeTime Pharmaceuticals Inc., and CureImmune Corp. Prior to his leadership work in the commercial sector, Dr. Taub was head of a pathology unit in the NIH, focusing on immunopathology. Under his direction, the unit analyzed some of the first human monoclonal antibodies. Earlier in his tenure at NIH (late 1970's), while in the Laboratory of Biochemistry of the NCI, he devised and implemented the first computerized image processing analysis of array hybridizations. Computerized analysis of array hybridizations today is one of the major tools of genomics. An honors graduate of Northwestern Medical School, Dr. Taub studied pathology at the University of Colorado Medical Center, and was awarded the first Surgical Pathology Fellowship at George Washington University Medical Center. Dr. Taub is Board Certified in pathology and licensed to practice medicine in Maryland and California.



Stephen Raab, M.D., Member

Dr. Stephen Raab is chief of pathology at University of Pittsburgh Medical Center (UPMC) Shadyside Hospital, medical director of research at the UPMC Center for Quality Improvement and Innovation, and director of the Division of Pathology Quality and Healthcare Research. Dr. Raab is a practicing pathologist and health services researcher, and his area of interest is quality improvement and patient safety of diagnostic testing and screening.

Consultants

Table 5 lists CytoCore’s consultants, followed by a brief description of each individual.

Table 5 CytoCore, Inc. CONSULTANTS	
Richard Domanik, Ph.D.	Biomolecular Consultant
Roberta Speyer	CEO of OBGYN.net and Founder of medispecialty, inc.
Beaufort Advisors LLC	FDA Regulatory Consultants
SIPR LLC	Public Relations Firm

Source: CytoCore, Inc.

Richard Domanik, Ph.D., Biomolecular Consultant

Dr. Richard Domanik is the principal in R. Domanik Consulting, Inc., which provides services in the areas of product development and intellectual property management. He is also director of commercialization for Xomix, Ltd., a consultancy specializing in technology commercialization and workforce development in the biotechnology arena. Dr. Domanik has previously served as vice president, technology for ZelleRx Corporation, a cellular therapy company, and as vice president, engineering and chief technology officer (CTO) for Molecular Diagnostics and AccuMed, developers of clinical laboratory instruments, devices, and reagents. During his 15 years with the Diagnostics Division of Abbott, Dr. Domanik managed a multi-department, advanced technologies group that was responsible for identifying and evaluating novel technologies, developing them to the product prototype stage, and supporting their development into commercial products. He has over 20 issued patents and has publications in areas ranging from biophysics and environmental chemistry to optical engineering.

Roberta Speyer, CEO of OBGYN.net and Founder of medispecialty, inc.

Ms. Roberta Speyer is the CEO of OBGYN.net, one of the largest gynecology websites on the internet. She is a marketing specialist to the gynecology sector and founder of medispecialty, inc. (www.medispecialty.com)—an online medical company which began in 1995 and is still operated today by Roberta and Bruce Speyer, as well as a core team of veterans in the field. Medispecialty, inc. specializes in optimizing online investment in the medical professional field and to the consumer market.

Beaufort Advisors LLC, FDA Regulatory Consultants

Beaufort Advisors LLC (www.beaufortadvisors.com) are FDA regulatory consultants specializing in biomolecular and medical device companies. Beaufort was hired to provide CytoCore with senior regulatory advice and guidance for the next phase of the Company’s development activities—clinical trials and product manufacturing.

SIPR LLC, Public Relations Firm

SIPR LLC (www.sipr.com) is a “Strategic Implementation in Public Relations” firm hired to help CytoCore’s platform and launch the Company’s early detection test for uterine/endometrial cancers. SIPR has two decades of experience supporting emerging technologies, and its strategic campaign experience is expected to advance CytoCore’s product portfolio.

Core Story

CytoCore, Inc. (“CytoCore” or “the Company”) is a biomolecular and medical device company engaged in the design, development, and commercialization of cost-effective screening systems for the early detection of cancer and cancer-related diseases, as well as for the local delivery of drugs to sites affected by disease. The Company is currently developing the InPath™ System, which combines a biomolecular screen with medical devices to identify patients who have developed a treatable cervical dysplasia or cancer condition. The System is expected to deliver faster, easier, more accurate, and more cost-effective test results than the traditional Papanicolaou (“Pap”) or human papillomavirus (HPV) test. The InPath™ System aims to provide a complete testing method for widespread use, including in locations that lack a laboratory infrastructure. CytoCore believes that the InPath™ System has the potential to provide a novel technology for cervical cancer and precancer screening and treatment on a global basis. Additionally, the Company hopes to bring to market a revolutionary early detection test for endometrial (uterine) cancer—the Endometrial Cancer Scan. The InPath™ System’s components are expected to improve the accuracy and administration of current Pap tests, while providing a new therapeutic treatment option for mild-, moderate-, and potentially some high-grade cervical lesions. One component of the InPath™ System—the e² Collector™—is already U.S. Food and Drug Administration (FDA) approved and is currently in preparation for production. This product is expected to be ready for unit sales by the end of the first quarter 2007. In addition, the Endometrial Cancer Scan has begun its Phase I trials.

CANCER

Cervical Cancer

Cervical cancer is the second leading cause of female cancer mortality worldwide, with 250,000 deaths globally each year from the disease, according to the World Health Organization (WHO). Furthermore, the American Cancer Society (ACS) states that in 2006, there is likely to be 9,710 new cases of invasive cervical cancer (cancer that has spread into surrounding healthy tissue) in the U.S. alone, with approximately 3,700 mortalities. Fortunately, following the introduction of the Pap test in 1955, which enabled early detection of cervical cancer, the number of patients dying from the disease has decreased sharply. A number of researchers estimate that **non-invasive cervical cancer** (still confined to the surface of the cervix) is four times more common than invasive cervical cancer. According to the Centers for Disease Control and Prevention (CDC), most women who do develop invasive cervical cancer have not had regular cervical cancer screenings.

Figure 2 illustrates the female reproductive system—showing the location of the cervix in relation to the other organs. The cervix is the lower part of the uterus, connecting the upper part of the uterus (where a baby would grow) to the vagina (the birth canal). Cervical cancer begins as a cell change in the lining of the cervix. In most cases, it takes a number of years for normal cells to turn precancerous and then cancerous, though it is possible for the change to occur in less than a year, making early detection particularly important.

Figure 3 (page 18) illustrates the stages of abnormal cell growth as they turn into cervical cancer. In approximately 50% of patients, the slightly abnormal cell growth, called cervical dysplasia, will vanish on its own. However, abnormal cells can become cancerous. Should this occur, immediate treatment is necessary. Eliminating the cancer while it is still non-invasive makes a complete cure much more likely. However, if the cancer continues to invasive stages (attacking deeper layers of tissue), the odds of the growth stopping become minimal.

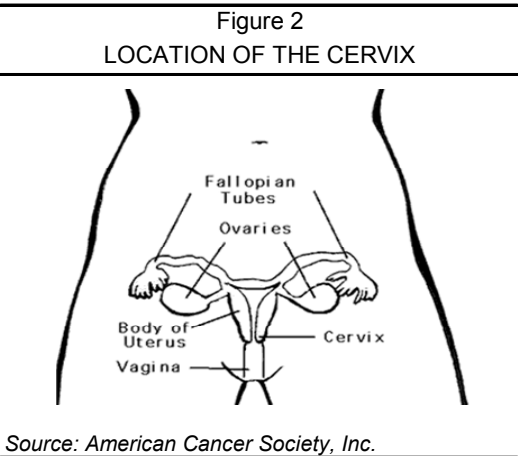
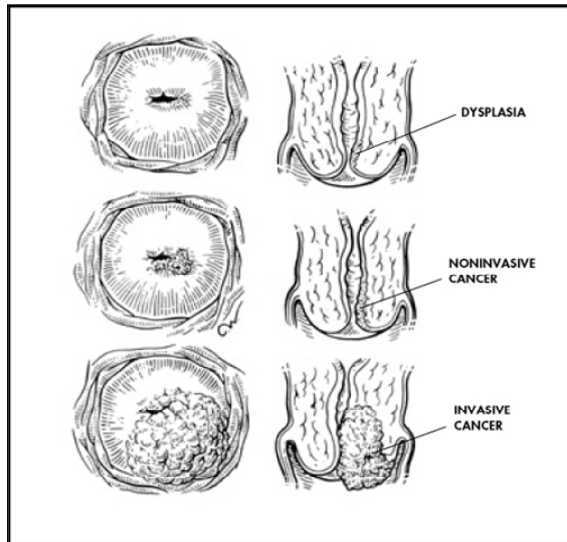


Figure 3
THREE STAGES OF ABNORMAL CELL GROWTH



Source: PDR Family Guide to Women's Health.

The two main types of cervical cancer are **squamous cell carcinoma** (approximately 80% to 90% of cervical cancers) and **adenocarcinoma** (approximately 10% to 20% of cervical cancers). A cancerous combination of these is called a **mixed carcinoma**.

Risk Factors for Developing Cervical Cancer

There are many risk factors that can increase the likelihood of a woman developing cervical cancer. While rarely appearing before age 15, its risk does not decrease with age. In 2003, the average age of women newly diagnosed with cervical cancer was between 50 and 55 years. Therefore, it is important for women to continue to have Pap tests as they age. Women are encouraged to have a Pap test every year if they exhibit any of the following risk factors:

- **Positive for Human Papillomavirus (HPV).** The most significant factor for developing cervical cancer is an HPV infection. HPV is a group of more than 100 virus types. Many of its virus

strains are relatively harmless and do not affect the genital area. The body's immune system can often fight these strains on its own. However, approximately 30 HPV types do affect the genital area, and one-third of these can lead to cervical cancer.

Persistent infection with high-risk HPV Types 16 and 18 is the main cause of cervical cancer, and low-risk Types 6 and 11, can cause genital warts and **benign** (abnormal, but noncancerous) changes in the cervix. According to the CDC, for approximately 90% of women, cervical HPV infection becomes undetectable within two years. Roughly 20 million people are currently infected with HPV, and by age 50, at least 80% of women have acquired a genital HPV infection. Additionally, about 6.2 million people in the U.S. contract a new genital HPV infection annually.

- **Smoking.** The ACS reports that women who smoke are twice as likely as non-smokers to develop cervical cancer. Tobacco smoke can produce chemicals in the body that damage the **Deoxyribonucleic Acid (DNA)** in cervical cells and increase the likelihood of cancer.
- **Human Immunodeficiency Virus (HIV).** HIV is the virus that causes **Acquired Immune Deficiency Syndrome (AIDS)**. Women who are HIV positive may have a weaker immune system that is unable to fight off viruses and early cancers.
- **Birth Control Pills.** Long-term use of birth control pills (five or more years) can increase the risk of cervical cancer.
- **Low Income.** Women with lower incomes correlate to a greater risk of cervical cancer, possibly due to an inability to afford healthcare, Pap tests, or treatment of precancerous cervical disease.
- **Multiple Pregnancies.** Many full-term pregnancies can increase the risk of cervical cancer.
- **Diet.** According to the ACS, diets low in fruits and vegetables are linked to an increased risk of cervical and other cancers. Women who are overweight have a higher risk as well.
- **Family History and Diethylstilbestrol (DES).** Women whose mother or sisters have had cervical cancer are more likely to develop the disease. Additionally, daughters of women who have taken DES have higher risks as well. DES is a hormone drug that was taken between 1940 and 1971 to prevent miscarriages.

- *Chlamydia*. A chlamydia infection consists of bacteria that can infect the female sex organs. The direct relationship of chlamydia to cervical cancer is still being researched, but some studies suggest that this infection can put women at a greater risk for developing cervical cancer.

Current Treatment Options for Cervical Cancer

Existing treatment options for cervical cancer include surgery, radiation therapy, and chemotherapy. In situations where a cure is unlikely, the goal of treatment becomes keeping the cancer from growing and spreading by removing or destroying as much of the cancer as possible. Surgical options range from **laser surgery** (using a laser beam to burn off cells in pre-invasive cervical cancer) to a **pelvic exenteration** in which the uterus, surrounding tissues, pelvic lymph nodes, bladder, vagina, rectum, and part of the colon may all be removed. The pelvic exenteration is used when cancer returns after an earlier treatment. Other common surgery options that are used include **cryosurgery**, **cone biopsy**, **simple hysterectomy**, and **radical hysterectomy** with a **pelvic lymph node dissection**. A **radical trachelectomy** is a relatively new surgery that may allow some women to still have children by using a special stitch as an artificial cervix. This technique requires additional long-term studies to verify the eradication of cancer through the surgery, though some cancer centers are currently performing this operation.

Radiation therapy may also be used to treat cervical cancer. The two types of radiation therapy—external (from outside of the body) and internal or implant (from radioactive materials placed in the tumor)—use high-energy rays to kill or shrink cancer cells. Side effects associated with radiation therapy include changes in skin coloration in the treated area that may last for 6 to 12 months, vaginal narrowing due to scar tissue, pain during sexual activity, early menopause, and urination problems. Smoking increases side effects, but occasionally medicines or other methods may reduce them.

Chemotherapy is the use of chemical substances to treat disease; more specifically, drugs to treat cancer. Chemotherapeutic drugs are typically administered through the vein or the mouth and spread throughout the body via the bloodstream. This form of treatment is currently associated with the following side effects: upset stomach, nausea and vomiting, loss of appetite, mouth sores, constipation, diarrhea, temporary loss of hair, pain, numbness and tingling, cognitive deficits (forgetfulness, difficulty concentrating), increased chance of infection resulting from decreased white blood cell counts (**neutropenia**), bleeding or bruising after minor cuts or injuries due to diminished blood platelets (**thrombocytopenia**), shortness of breath from lowered red blood cell counts (**anemia**), fatigue, and a variety of reproductive and sexual side effects such as menopause and infertility.

Hycamtin[®], developed by GlaxoSmithKline plc (GSK-NYSE) and in conjunction with chemotherapy agent cisplatin, is an FDA-approved combination chemotherapy treatment for patients whose cervical cancer is not amenable to surgery or radiation therapy. Hycamtin[®] with cisplatin has shown to extend patient survival beyond that of cisplatin alone.

The HPV Vaccine's Effect on Cervical Cancer

Several companies have developed or are developing cervical cancer vaccines, most notably Merck & Co. Inc. (MRK-NYSE) and GlaxoSmithKline. Merck's cervical cancer vaccine, GARDASIL[®], is FDA approved but is not intended as treatment for cervical cancer and has not been shown to protect against disease due to non-vaccine HPV types. It is only effective against HPV Types 16 and 18, which cause approximately 70% of cervical cancers. Therefore, the vaccination does not substitute for routine cervical cancer screening. Women who receive an HPV vaccine must still continue to undergo cervical cancer screening per standard of care.



Endometrial (Uterine) Cancer

Endometrial (uterine) cancer starts in the endometrium (the inner lining of the uterus). It is not the same disease as uterine **sarcoma**, which is cancer of the muscle of the uterus. Ninety-five percent of endometrial cancers are considered to be typical adenocarcinomas. In some cases, a woman can have a **papillary serous adenocarcinoma** or a **clear cell adenocarcinoma** that tends to grow and spread more quickly than a typical adenocarcinoma, but these are considered rare types of endometrial cancer.

The ACS estimates that approximately 41,200 new cases of uterine corpus cancer (cancer of the body of the uterus) will likely be diagnosed in 2006, with more than 95% of these estimated to be endometrial cancers. Uterine sarcomas only account for approximately 4% of uterine cancers. Uterine corpus cancer is expected to be fatal in 7,350 women in the U.S. during 2006.

A majority of endometrial cancers are diagnosed in postmenopausal women aged 50 to 70 years according to the Mayo Foundation for Medical Education and Research, with approximately 70% of these cancers found in women between the ages of 45 and 74. When all cases of endometrial cancer are examined together, the chance of surviving five years past the diagnosis is 84%, though the percentage is much higher when cancer is found at an early stage. To date, the chance a woman may be diagnosed with endometrial cancer in her lifetime is 1 in 38.

Early Detection

Endometrial cancer is the most common cancer of the female reproductive organs, and the fourth leading cancer among women in the U.S.—primarily due to a lack of early detection methods to catch uterine precancers before they become cancers.

When cancer is detected early, there are often more treatment options available and survival rates are generally higher since the cancer can often be contained and eliminated before it has spread to other organs. Early detection can also substantially reduce the billions of dollars spent on cancer treatment each year. Unfortunately, to date, there are no early detection tests specifically available for endometrial cancer. According to the ACS, both regular pelvic exams and Pap tests can find *some* cancers, but neither method is considered effective for early detection of endometrial cancer. Most women are diagnosed only after they have already shown the following symptoms of cancer: irregular or unusual vaginal bleeding, spotting, or discharge; pelvic pain; pain during sexual activity, difficult or painful urination, or weight loss. Irregular vaginal bleeding, occurring in approximately 90% of women, is the most common symptom.

Stage I	90% to 95%
Stage II	75%
Stage III	60%
Stage IV	15% to 26%

**the percentage of patients who live at least five years after their cancer is diagnosed*

Source: American Cancer Society, Inc.

Endometrial cancer often develops as a result of less serious abnormalities of the endometrium, such as **endometrial hyperplasia**—an increased growth of the endometrium. Hyperplasia has a small risk of becoming cancerous, but if not detected or treated, simple atypical hyperplasia can become cancerous in approximately 8% of cases, and **complex atypical hyperplasia** can become cancerous in approximately 29% of cases. As depicted in Table 6, allowing endometrial cancer to progressively worsen before detection and treatment results in significantly decreased chances of patient survival. If cancer is caught while it is still confined to the uterus (Stage I), the chance of surviving five years past the initial diagnosis is very high at 90% to 95%. Once the cancer has spread beyond the pelvis (Stage IV), the chance of the patient surviving another five years is at most 26%. The

staging system used is the International Federation of Gynecology and Obstetrics (FIGO) system. It is based on the examination of tissue removed during surgical treatment.

Risk Factors for Developing Endometrial Cancer

The root of most of these risk factors is an increase in estrogen levels within the uterus. Two hormones—estrogen and progesterone—are produced by the **ovaries**. The hormonal balance shifts during the course of the female menstrual cycle, producing monthly ovulations and keeping the endometrium healthy. When too much estrogen is produced, the risk of endometrial cancer is increased. Risk factors such as an early onset of menstruation, late onset of menopause, few pregnancies or infertility, and obesity all relate to estrogen levels. **Tamoxifen**, while actually an anti-estrogen drug used to treat breast cancer, can have adverse effects in the uterus and act like estrogen, causing growth of the endometrium and increasing the risk of cancer.

Obesity also increases the risk of endometrial cancer by two to five times. Diabetes can make a woman four times more likely to develop the disease. Additionally, women who have taken solely estrogen to offset menopause have multiplied their risk by five times. Women with or at risk for **hereditary nonpolyposis colon cancer (HNPCC)** should have an annual endometrial biopsy beginning at age 35, as their incidence of endometrial cancer ranges from 20% to 60%. Caucasian women have a higher incidence of endometrial cancer, but Black women have higher mortality rates due to the cancer. Table 7 summarizes some of the factors that can put females at an increased risk for developing endometrial cancer.

<ul style="list-style-type: none"> ▪ Increased estrogen levels ▪ Starting menstrual cycles before age 12 ▪ Starting menopause after age 52 ▪ Infertility or few pregnancies ▪ Obesity ▪ Taking tamoxifen ▪ Possessing the HNPCC gene ▪ Hypertensive 	<ul style="list-style-type: none"> ▪ Ovarian diseases and cancers ▪ Diet high in animal fat ▪ Diabetes ▪ Family history ▪ Breast cancer ▪ Prior pelvic radiation therapy ▪ Caucasian ▪ Estrogen replacement therapy to offset menopause
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Source: American Cancer Society, Inc. and the National Cancer Institute.

Current Treatment Options for Endometrial Cancer

Treatment options for endometrial cancer are very similar to those for cervical cancer. Women with endometrial cancer have four standard options: radiation therapy, chemotherapy, hormone therapy, and surgery. The treatment or any combination of treatments used depends upon many factors, including cancer type and stage and the patient's medical condition. Radiation therapy and chemotherapy are detailed under Current Treatment Options for Cervical Cancer (page 19). Hormone therapy halts the growth of cancer cells by removing or blocking the hormone that causes the cells to grow.

Surgery is the most common of the available treatments. The surgeon aims to remove all of the cancer at the time of the operation. However, radiation or hormone therapy may be prescribed after surgery to destroy any remaining cancer cells that may have been left behind. The type of surgery performed depends upon the location of the cancer. A **total hysterectomy** removes the uterus and the cervix; a **bilateral salpingo-oophorectomy** removes the ovaries and fallopian tubes; and a radical hysterectomy removes the uterus, cervix, part of the vagina, and possibly the ovaries, fallopian tubes, or nearby lymph nodes.

Additionally, a procedure known as **dilatation and curettage (D&C)**, which is typically used as a method to diagnose endometrial cancer, can be performed to treat many conditions that cause abnormal bleeding in the uterus. It involves dilating the cervix to insert an instrument—a spoon-shaped surgical device called a curette—that scrapes the uterine wall, collecting tissue. D&C takes approximately an hour and usually requires general anesthesia.



Furthermore, there are additional potential treatment options for endometrial cancer that are still in clinical trials. As of September 2006, the National Cancer Institute (NCI) could refer women to 46 different clinical trials testing new treatment options ranging from radiation therapy in combination with chemotherapy to 30- to 90-minute weekly infusion sessions of **trastuzumab** (Herceptin[®], marketed by Genentech, Inc. [DNA-NYSE]), which was originally used for the treatment of metastatic breast cancer).

PAPANICOLAOU (PAP) TESTS

The Papanicolaou test, also known as the Pap test or Pap smear, was developed by Dr. George Papanicolaou of Cornell University in the 1940s. It is used to screen for cervical cancer by detecting precancerous changes (which may develop into cancer if left untreated) and cancerous cells before they spread or are visible to the naked eye. The test has used almost the same basic technology for the past 50 years, except for the addition of liquid-based cytology post-cell collection and the Digene[®] HPV Test (marketed by Digene). The Pap test currently costs between \$70 to \$350, depending on the laboratory and doctor.

Typically, to collect a cell sample from the cervix, the physician uses a **speculum** to widen the vagina and a spatula and brush to scrape cells off of the cervix. After the cells are collected, the sample is sent to the laboratory via a liquid preservative (liquid-based cytology), such as CYTYC Corp.'s (CYTC-NASDAQ) ThinPrep[®] solution, for preparation of a slide. Using white light, cytologists view the slides under a microscope and look for differences in cell shapes that might indicate an abnormality. This is known as a morphologic examination.

According to the NCI, as of February 2003, approximately 55 million Pap tests are given each year in the U.S., and approximately 10% of these are considered abnormal and require medical follow-up. More than five million Pap tests are performed annually in Canada, and approximately 8% of these have abnormal results. Globally, approximately 180 million Pap tests are performed each year, according to the International Consensus Conference on the Fight Against Cervical Cancer. Aside from the U.S., a large portion of these are in developed countries such as Europe, Japan, Canada, and Australia.

Despite the large number of Pap tests that are performed, the International Consensus Conference estimated that there are between 1.5 to 1.8 billion women around the world who require annual Pap tests. In the U.S. alone, between 60% to 80% of women with cervical cancer have not had a test in the past five years, and many have not had the test at all—particularly among the elderly, African-Americans, and women in low-income brackets.

Current guidelines stipulate that all women should have a Pap test at least once every three years. Women should begin testing three years after the onset of sexual intercourse but no later than 21 years of age. At about 65 to 70 years of age, women who have had at least three normal Pap tests within the last ten years may safely decide to discontinue testing. Additionally, women who have had their cervix removed for reasons unrelated to precancer or cancer treatment do not need the Pap test.

Abnormal Pap Test Results and Treatment Options

Table 8 (page 23) classifies the possible abnormal Pap test results that a patient may experience according to the **Bethesda System**—a classification system developed by the NCI for providing detailed information about Pap test results. The table also includes the possible test and treatment options available for the varying result stages. CytoCore's Drug Delivery System (DDS) is designed to provide a therapeutic treatment option in the form of a **transdermal** polymer patch seated directly on the cervix that delivers a compound for the treatment of all forms of cervical lesions except cancerous tissues. Greater details on this DDS are provided on pages 36-38.

Table 8
PAP TEST ABNORMALITIES AND TREATMENT OPTIONS

Pap Test Result	Abbrev.	Also Known As	Tests and Treatments May Include
Atypical squamous cells—undetermined significance	ASC-US		HPV testing Repeat Pap test Colposcopy and biopsy Estrogen cream
Atypical squamous cells—cannot exclude HSIL	ASC-H		Colposcopy and biopsy
Atypical glandular cells	AGC		Colposcopy and biopsy and/or endocervical curettage
Endocervical adenocarcinoma <i>in situ</i>	AIS		Colposcopy and biopsy and/or endocervical curettage
Low-grade squamous intraepithelial lesion	LSIL	Mild dysplasia or cervical intraepithelial neoplasia-1 (CIN-1)	Colposcopy and biopsy
High-grade squamous intraepithelial lesion	HSIL	Moderate dysplasia, severe dysplasia, CIN-2, CIN-3, or carcinoma <i>in situ</i> (CIS)	Colposcopy and biopsy and/or endocervical curettage Further treatment with LEEP, cryotherapy, laser therapy, conization, or hysterectomy

Source: National Cancer Institute.

Accuracy of the Pap Test

In the past four decades, widespread use of the Pap test in the U.S. has reduced deaths from cervical cancer—once a leading cause of death in women—by almost 75% (Source: *Postgraduate Medicine*). Outside of the U.S., rates of cervical cancer deaths are estimated to have dropped by 20% to 60% since the introduction of the Pap test (Source: National Center for Chronic Disease Prevention and Health Promotion). Despite these achievements, the accuracy of the Pap test is perpetually disputed. The Brigham and Women’s Hospital, a teaching affiliate of Harvard Medical School, reports that approximately 20% of the time, abnormal cells in the cervix do not show up on a Pap test. Digene reports that the Pap test misses precancerous cells between 15% to 50% of the time. CytoCore believes that the current Pap test has an accuracy rate of 50% to 70%. Ideally, multiple Pap tests can identify what may have been missed on a previous test.

The Pap test is composed of two basic steps: (1) a collection of a sample of cervical and endocervical cells from the patient, and (2) an examination of the slide by a cytotechnician for cells showing any abnormalities. It is believed among the scientific community, clinicians, and physicians that the principal cause for inaccuracy and variability in Pap tests is due to inadequate sampling or gathering of cervical cells for the slide examination. If a representative collection of cervical cells is not obtained, the laboratory examination becomes much less relevant. This has placed physicians in a difficult position, with patients suing over erroneous results, leading to an uneasy balance between physician, patient, and provider. Accordingly, OB/GYNs have some of the highest insurance coverage rates in the medical profession because of the “unknowns” or risks associated with the inherently inaccurate Pap test.

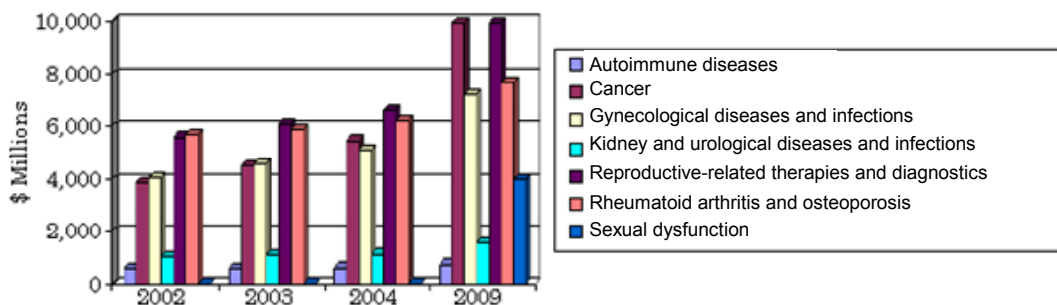
Since the Pap test has become the standard of care, there is now a need for improved devices, enhanced methodologies, and increased accuracy. CytoCore believes that its e² Collector™, described in greater detail on pages 27-30, could improve the process. With the e² Collector™, the physician can develop a degree of confidence that this cell collection device can provide a consistently more thorough collection of all the cells—ectocervical and endocervical. Patients can also feel more comfortable that physicians have done their jobs to the best of their ability with the “best available” tools at hand. CytoCore’s e² Collector™ and Cocktail-CVX™/AIPS System are designed to address both steps of the Pap test and combine to increase the accuracy of the test to between 85% and 90%.



MARKET OVERVIEW

CytoCore is focused on meeting needs within the cervical and endometrial cancer screening markets, such as those presented below. The CDC estimates that cancer costs in the U.S. were \$210 billion in 2005, including nearly \$136 billion for lost productivity and more than \$70 billion for direct medical costs. On its own, cervical cancer treatment incurs costs in the U.S. of more than \$2 billion per year, and the cost of cervical cancer screening programs (Pap tests) is \$5 to \$6 billion annually. Market research firm BCC Research estimated in May 2005 that the U.S. market for new therapeutics and diagnostics for women’s disorders is likely to grow at an average annual growth rate (AAGR) of 10.3% to reach nearly \$41 billion by 2009. Within this market, female-specific cancer treatments are predicted to increase the greatest, with an AAGR of 12.6%. Figure 4 illustrates this market by segment (2002-2009).

Figure 4
U.S. MARKET FOR NEW THERAPEUTICS AND DIAGNOSTICS FOR WOMEN'S DISORDERS
BY SEGMENT, 2002-2009



Source: BCC Research.

Studies have shown that 70% to 80% of a person’s healthcare expenditures occur in the last four to six months of life. As a result, increased emphasis is being placed on developing early detection methods for potentially fatal diseases. The FDA recently announced that it would devote 60% of its approvals for the coming period toward diagnostic-related products to catch diseases before they become life-threatening and more costly to treat. Accordingly, CytoCore’s technology is focused on the early detection of cancer and cancer-related diseases.

Need for an Accurate, Cost-effective, and Accessible Pap Test and Cervical Cancer Screen

An article published in the June 7, 2006, issue of the *Journal of the National Cancer Institute* detailed a European research study that found that testing for cervical cancer using HPV tests and liquid-based Pap tests increased the **sensitivity**—accurate identification of abnormal cells—47% above the rate of conventional Pap tests (pre-liquid cytology where cell samples are placed directly on a slide and are not submerged in a liquid preservative first). However, the combination of an HPV test and the newer Pap test also increased the **false positive** rate by 60%. This means that many women have unnecessary follow-up procedures, such as a **colposcopy**. After the study, experts agreed that an ideal cervical cancer screen has yet to be found.

Roughly 80% of the world’s cervical cancer deaths occur in developing countries, where deaths average approximately 600 women per day. In Latin America and the Caribbean, the incidence of cervical cancer is double and mortality rates are triple versus those rates in developed countries. The main reason for these high rates in developing nations is the lack of early detection capabilities. When cancer is detected in these populations, it is usually already in advanced stages. Women in these countries need a cost-effective system that can improve access to screening services.

Need for Single-Visit Screening and Treatment Options

A study performed in India, Kenya, Peru, South Africa, and Thailand and published in the *New England Journal of Medicine* asserts that the most cost-effective strategy for combating cervical cancer in developing nations would be the system that requires the fewest visits on behalf of the patient, such as a single-visit strategy that screens and treats in the same day. Such a system could result in improved follow-up testing and treatment, and using it only once, for example in 35-year-old women, could possibly reduce the lifetime risk of cancer by 25% to 36% and cost less than \$500 for each year of life saved. Two screenings per lifetime (35 and 40 years of age) could decrease relative cancer risk by an additional 40%. The study also found that the most clinically effective strategies relied less on laboratory infrastructure than did conventional cytologic methods (*New England Journal of Medicine* November 17, 2005).

A similar trial published in the *Journal of the American Medical Association* tested the feasibility of single-visit systems in the U.S. The trial found that women in underserved populations—low incomes and minorities—who had a higher incidence of cervical cancer due to a lack of Pap tests or a lack of follow-up had a high degree of acceptability for single-visit programs. In addition, women with high-grade lesions (10/16; 63% [in the study]) that were treated through a single-visit process were significantly more likely to have a follow-up Pap test 12 months later than women with similar lesions (4/19; 21% [in the study]) treated by the standard care methods (*Journal of the American Medical Association* November 2, 2005).

CytoCore's Estimated Worldwide Potential for Cervical Cancer Screens

CytoCore believes that its technology could dramatically expand the number of annually performed cervical screening tests worldwide. The Company is introducing its InPath™ System in stages as each component becomes available for use. CytoCore readied the first component, the e² Collector™ (detailed on pages 27-30), for manufacturing in September 2006 and expects to have units delivered and ready for sale during the first quarter 2007. The Company anticipates that the visibility and success from sales of the e² Collector™ to OB/GYN physicians will likely open distribution and sales channels for future InPath™ products, such as the DDS and the Endometrial Cancer Scan (described on pages 36-40). Each of these products could be used by the same OB/GYN physicians to treat all (or appropriate groups) of their patients. CytoCore intends to bring its products to market in the U.S. first and to other developed countries next. Table 9 illustrates CytoCore's perceived global market potential.

Table 9
CytoCore, Inc.

ESTIMATED WORLDWIDE POTENTIAL FOR CERVICAL CANCER SCREENS

Market Segment	Current Number of Pap Tests	Potential Number of Tests Using InPath™	Potential Market for Cervical Cancer Screens
North America	80 million	90 million	\$1,080 million
Western Europe, Australia, Japan	90 million	150 million	\$1,050 million
Rest of World	<10 million	1,600 million	\$5,250 million
Total	~180 million	~1,840 million	\$7,380 million

Source: CytoCore, Inc.



THE INPATH™ SYSTEM

CytoCore’s InPath™ System is designed to detect cancer and cancer-related diseases of the cervix and uterus in its early stages. The System is expected to provide physicians and women around the world with the following:

- increased efficiency and accuracy compared to the currently available Pap test;
- a method for cervical cancer screening combined with an automated testing platform, particularly for populations without access to the Pap test;
- a means to treat mild- to moderate- and potentially some high-grade cervical lesions therapeutically without the need for surgery; and
- a means of cost-effective endometrial cancer screening for women.

The InPath™ System is an automated, portable, and comprehensive system being developed to provide test results at the point-of-service (POS)—a laboratory, a clinic, or the doctor’s office—within 30 minutes, giving physicians the capability to obtain test results in the office as a patient waits. These results can then be accompanied by immediate therapeutic treatment if warranted. In lesser-developed countries, where there may be little to no infrastructure that can accommodate laboratories or few properly trained cytotechnicians, the InPath™ System could be a feasible option. Its components can be transported to remote locations and utilized with a limited amount of training—thereby requiring little infrastructure.

The InPath™ System is based on a core of protein antibodies (biomarkers)—the Cocktail-CVX™ and the Cocktail-GCI assays—that enable the rapid detection of abnormal or suspicious cells. Varying the antibody combinations could allow CytoCore to use its System in multiple applications, and accordingly, the Company intends to use the InPath™ System to focus on the detection and diagnosis of additional forms of cancer and cancer-related diseases in the future, beyond the initial targets of cervical and endometrial cancers.

Table 10 summarizes many of the advantages that CytoCore believes the InPath™ System can offer to women over current screening technologies.

Table 10 CytoCore, Inc. ADVANTAGES TO THE INPATH™ SYSTEM	
▪ Expands precancer screening applications	▪ Reduces human error
▪ User friendly	▪ Requires minimal operator training
▪ Provides a rapid test result	▪ Improves accuracy
▪ Cost-effective	▪ Improves patient care/standard of care
▪ Offers early detection of cancer	▪ Designed to handle multiple cancer applications
▪ Provides POS capabilities	▪ Incorporates a screen for endometrial cancer
▪ Has built-in safety and operating checks	▪ Full system for testing, diagnosis, and treatment
▪ Widens availability of screening and treatment to undertreated populations in overseas markets such as China, India, Southeast Asia, Latin America, Africa, and the Middle East	

Source: CytoCore, Inc. and Crystal Research Associates, LLC.

Components of the InPath™ System

The InPath™ System is composed of a vertically integrated family of related products that may be utilized separately or as a complete, comprehensive system. It has four components: the e² Collector™, the Cocktail-CVX™ and Cocktail-GCI biochemical assays and P2X₇ biomarker, the AIPS platform, and the DDS. The Company is also developing an Endometrial Cancer Scan in addition to the InPath™ System, which may be the first of its kind to enter the market. Together, these products represent an end-to-end system for the detection, diagnosis, and treatment of cervical cancer, as well as early detection of endometrial cancer.

The design of the e² Collector™ allows a physician to gather a more comprehensive cell sample; the assays and biomarker activate and identify cancerous cells; the Automated Imaging Proteomic System (AIPS) platform automatically screening cells, identifying abnormal cells on the slides, and returning test results; and the Drug Delivery System (DDS) provides a therapeutic treatment option to remedy any discovered dysplasia or lesions. In addition, the Endometrial Cancer Scan consists of three components: an EndoCollector (an endometrial cell collection device), a Cocktail-GCI assay, and the test method (a One-Step Real-Time Reverse Transcription Polymerase Chain Reaction—a GCI-qPCR assay), detailed under Ongoing Laboratory Results for the P2X₇ on pages 34-35.

e² Collector™

CytoCore's e² Collector™ is the first component of the Company's InPath™ System. The design of the e² Collector™ offers more rapid and accurate specimen collection than conventional methods by reducing the possibility of physician error during the cell collection procedure. Currently, physicians use a two-step process that harvests cells from the outer cervix (**ectocervix**) with a spatula and from the less-accessible cervical canal (**endocervix**) with a brush. Accurate Pap tests require the precise placement and maneuvering of the spatula and brush to scrape the entire cervix. Physician technique, which results in a wide range of cell collection thoroughness, is recognized as the single greatest variable in the accuracy of the Pap test. The e² Collector™, due to its shape and design characteristics, offers greater ease of use for physicians than the spatula and brush combination, and establishes a consistency in cell collection versus the spatula and brush, which relies entirely on physician technique.

The most critical step in the conventional Pap test collection is harvesting the endocervical cells. A poor collection may result in an inadequate sample of cells for diagnosis. False negative tests can lead to an undetected cancerous condition and potential liability problems for the physician.

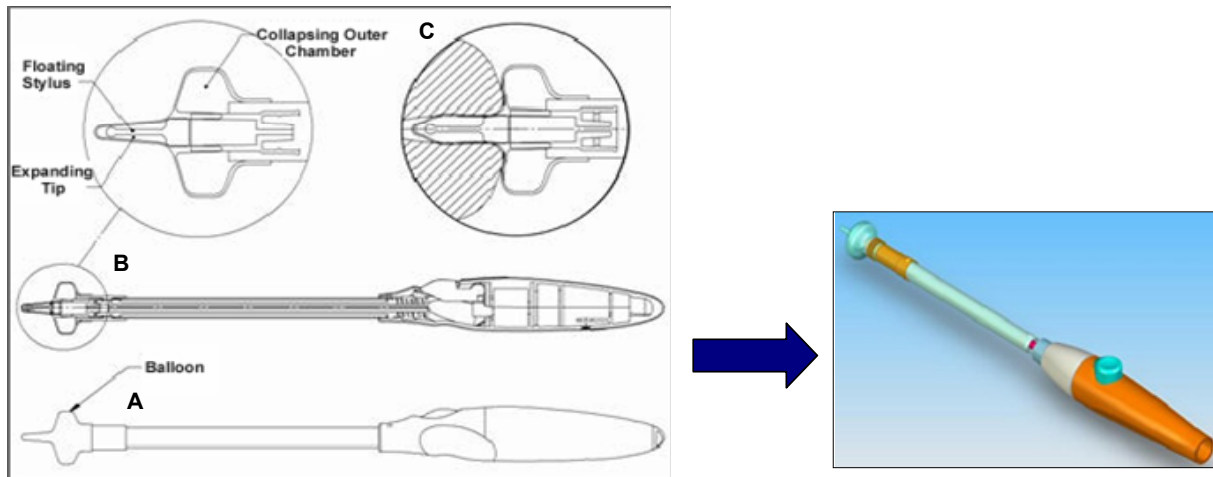
It has been reported that in an effort to minimize patient discomfort and improve collection time, approximately 30% of physicians do not use both devices (Sources: CytoCore and Independent 3rd Party survey over 125 Obstetricians and Gynecologists at the 49th Conference of the American College of Obstetrics and Gynecology May 2000). A possible explanation for this is that an increasing number of physicians only use the brush because it can collect an "adequate" quantity of endocervical cells, which is considered to meet the legal requirements for an adequate cell collection. It has also been estimated that upwards of 50% of **false negative (FN)** Pap tests collected using the conventional spatula and brush technique result from "inadequate" collections due to limitations in brush and spatula design and dependency on physician technique.

Design

The e² Collector™ is designed to consistently gather a sample of cells from the entire cervix in a single step. Figure 5 (page 28) illustrates both a rendering (right) and a diagram (left) of the e² Collector™. The device has an inflatable, single-use, pliable, **dimethylsilicone** balloon, shaped to mirror the surface of the ectocervix and endocervix (*Letter A*, Figure 5). The Company uses medical-grade dimethylsilicone to create a tacky balloon surface. The balloon has a narrow tip at the end and is attached to the handle of the e² Collector™ via a long neck (*Letter B*). The handle is covered by a disposable sheath that is replaced, along with the balloon apparatus, for each patient. As the e² Collector™ is inserted through a speculum into the cervix, the narrow tip of the balloon is inserted into the patient's endocervix, while the top of the balloon's wider base is positioned against the ectocervix (*Letter C*).

Figure 5
CytoCore, Inc.

RENDERING AND DIAGRAM OF THE e² COLLECTOR™



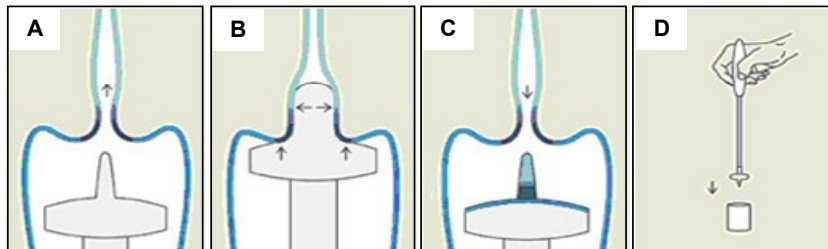
Source: CytoCore, Inc.

Collection Process

The collection process of the e² Collector™ is illustrated in Figure 6 and described in detail below.

Figure 6
CytoCore, Inc.

INFLATION AND INSERTION OF THE e² COLLECTOR™ BALLOON INTO THE CERVIX AND SOLUTION



Source: CytoCore, Inc.

- **Step 1.** After the device has been inserted (*Box A*), the physician presses a button on the handle of the e² Collector™ to release air pressure into the balloon for it to inflate. (Over- and under-inflation cannot occur due to the device's fixed air volume.)
- **Step 2.** The narrow tip of the balloon penetrates one-third of the endocervix and expands the most during inflation—growing wider not longer—to press itself against the endocervical walls and collect cells (*Box B*). The tip is designed to accommodate the range of the endocervical canal diameters commonly encountered in clinical practice. The length of the tip is constrained to limit excessive depth penetration into the cervical canal. This portion of the balloon is 3 millimeters (mm) in diameter and 12 mm in length when not inflated. The wider base of the balloon expands forward to press against the ectocervix. This portion is sized to collect cells from an area approximately 23 mm in diameter on the ectocervix. Rotation of the device is not necessary because as the balloon inflates, its tacky surface contacts all the walls of the cervix, opens the tissue folds, and retrieves cells by touch in 360 degrees around the ectocervix. The current spatula and brush method retrieves cells by scraping the cervix, an uncomfortable process for women that, depending upon the physician's technique, can result in bleeding, an incomplete cell sample, and an inaccurate and ineffective Pap test.

- *Step 3.* As air pressure in the balloon gradually releases, cervical cells adhere to the surface of the balloon through surface tension (*Box C*). The entire collection process takes roughly five to six seconds.
- *Step 4.* Once removed from the cervix by the physician, the balloon is detached from the handle and immediately placed into a liquid preservative vial, depositing the cervical cells in the preservative (*Box D*). The preservative used with the e² Collector™ is the same solution that the physician would have typically used with the spatula and brush technique (e.g. CYTYC Corp.'s ThinPrep®). The vial is then transferred to a laboratory for analysis.

Success of Device

Proven conclusively through a clinical trial at CASE, cell collection using the e² Collector™ has demonstrated to result in a better cell sample for a more accurate analysis and Pap test. The initial trial results yielded zero false positives and half the false negatives of the spatula and brush. The trial also found that a greater density of cells was captured by the e² Collector™, thereby reducing inadequate specimens and enhancing the sensitivity of screening.

In addition, by employing a soft balloon, the e² Collector™ has been shown to increase patient comfort and improve physician ease-of-use, reducing trauma to the cervix initiated by conventional brush and spatula scraping techniques. Test participants from Dr. Gorodeski's trial preferred the e² Collector™ over the spatula and brush. The e² Collector™ further reduced the incidence of post-collection bleeding or cramping, as well as the number of Pap tests that are diagnosed as "inadequate" due to obscuring blood. Because this product has demonstrated the ability to deliver a more accurate Pap test, the Company believes it could provide an important solution to reducing physician errors and potential physician liability.

Status of Device

The patented e² Collector™ received **510(K)** FDA approval for marketing and sale on May 31, 2002. In September 2006, CytoCore engaged two Wisconsin-area manufacturers to begin production of the e² Collector™. Initial units are expected for delivery and sale during the first quarter 2007. The selected manufacturers, Plas-Tech Engineering (Lake Geneva, Wisconsin) and ATP Rubber and Plastics (Elk Horn, Wisconsin), have each been involved in the e² Collector™ development process since its early stages. Plas-Tech is responsible for production of the e² Collector™ handle, and ATP is manufacturing the disposable balloons.

Manufacturing is on track to have the device ready for production by end of 2006. This device is expected to be put through a confirmation trial starting in December 2006. The objective of the trial is to confirm the performance advantages against the currently used spatula and brush. The trial is expected to be completed during the first quarter 2007, with FDA approval to initiate product sales by the end of the first quarter 2007 or beginning of the second quarter 2007. High volume, multi-cavity production capability is expected to be ready by late summer.

CytoCore believes that a future application of its e² Collector™ involves capturing cervical cells *in situ*—on the surface of the e² Collector™—by using a methodology to identify biomarkers expressed by **dysplastic** and neoplastic cells on the balloon portion of the e² Collector™ in a manner that provides information about the location of lesions on the cervix.

e² Collector™ Marketing Strategy

The e² Collector™ will likely be initially targeted toward women who have tested positive for HPV, since CytoCore believes that these women are very alert to issues concerning Pap tests. Reports from gynecologists indicate that women who test positive with the Digene® HPV test (especially for the more active strains of the virus) are increasing their Pap testing to twice per year, and some choose to be tested every 90 to 180 days. In addition, the Company believes that the upcoming trial for the e² Collector™ could provide conclusive results that could be used in CytoCore's product advertising. Given that the inaccuracy of the current Pap test creates anxiety for both the physician and patient, CytoCore



believes the e² Collector™ could be brought onto the market based upon the increased accuracy of Pap tests using the e² Collector™.

The spatula and brush, the current standard for Pap test cell sample collection, are provided to physicians free of charge; therefore, the Company does not have to compete against a competitor defending market share. CytoCore believes that HPV-positive women may elect to pay the out-of-pocket charges for the e² Collector™ for the confidence of a more accurate Pap test. CytoCore intends to apply to obtain insurance coverage for this product and expects to receive a current procedural terminology (CPT) code within 12 to 18 months. The Company hopes to have the e² Collector™ recognized and adopted as a “best standard of care” both domestically and abroad.

Biochemical Assays and Biomarkers

Presently, after the cell sample has been collected and deposited into a liquid preservative vial, the cells are removed via centrifuge in a laboratory and a slide is prepared. Cytotechnicians then study the slides for regular microscopy and morphological criteria, such as the shape and size of cells and their nuclei, to identify changes that could indicate an abnormality. The cytotechnician usually screens between 50,000 and 300,000 cells per slide to find 20 to 30 potentially abnormal cells. Due to the burden this process places on the cytotechnicians, limits have been placed on the number of hours and slides per day that can be evaluated. Moreover, the slide evaluation process uses subjective points of reference; therefore, it is not uncommon for standard Pap test results to have a 30% to 50% range of inaccuracy.

CytoCore has developed an alternative method that has demonstrated the ability to improve Pap test accuracy from a range of 50% to 70% to a range of 85% to 90%. In the InPath™ System, after being removed from the preservative via centrifuge, cells are exposed to a biochemical assay that “tags” the abnormal cells and enables easy identification by the Company’s AIPS screening program (detailed on pages 35-36) of these abnormal cells. CytoCore’s biochemical assays fluorescently tag protein antibodies, which can detect select cell-surface proteins associated with a cell’s decline into a cancerous state. The assays then turn cells that indicate cancerous properties a different color. This type of fluorescent protein tagging is known as proteomics.

It is generally accepted that there are two forces acting upon cells. One force stimulates cell growth, and the other force inhibits cell growth. Under normal conditions, both of these work together to establish a normal cell growth process. However, if there is an overgrowth of cells, due to either the first factor—too much stimulation or proliferation of the cells—or due to the second factor, the inhibitory forces, cancer could arise. One of these inhibitory forces is the P2X₇ (described on page 31)—an apoptosis biomarker (a biochemical with particular features that are expressed in cells containing high or low levels of essential cell components, such as DNA, **ribonucleic acid [RNA]**, and proteins) that controls the growth of cells. If this mechanism is **down-regulated** (diminished), it could be signaling the inhibition of apoptosis and a resulting uncontrolled cell growth.

CytoCore’s assays utilize biomarkers, in particular the P2X₇, that are useful in measuring the progression of disease or the effects of treatment. CytoCore has two such assays: the initial Cocktail-CVX™ assay (described below) and the newly developed Cocktail-GCI assay (page 32). The Cocktail-CVX™ assay is intended to improve CytoCore’s cervical cancer screen, and the Cocktail-GCI centers on the characteristics of the unique P2X₇ biomarker to form the basis of an endometrial cancer screen.

Cocktail-CVX™

Current biochemical assays typically use **up-regulated biomarkers**, which include proteins or nucleic acids that have higher levels in cancer cells than in normal cells. The increased amounts are usually associated with a greater rate of cell proliferation. Since rapid, uninhibited cell proliferation is a distinctive characteristic of a cancerous cell, up-regulated proliferation biomarkers can help cytotechnicians identify abnormal cells that have increased proliferation proteins. Determinations of these molecules can be done using **immunofluorescence** techniques, and their identification may indicate the presence of cancer cells. The Cocktail-CVX™ assay consists of a proprietary combination of proliferation biomarkers, and focuses on detecting cells that have an increased expression of these biomarkers.

Status and Potential Market Size of the Cocktail-CVX™ Assay

The Cocktail-CVX™ assay for cervical cancer screening is expected to enter trials lasting 15 to 18 months during early 2007. CytoCore expects to use the Cocktail-CVX™ assay in laboratories early on as a parallel test to the existing Pap test. The Company aims to customize the software that enables the AIPS platform to read the Cocktail-CVX™ assay during the second quarter 2007 and follow customization with Phase I and II trials.

CytoCore estimates that the use of the Cocktail-CVX™ for a cervical cancer screen could have significant worldwide market opportunity, depending upon the successful development of the InPath™ System as a cost-effective test capable of use in developing countries and as an automatic and quick procedure that tests and delivers results to the physician and the patient in one visit. CytoCore believes that with these two capabilities, the InPath™ System could be adopted worldwide.

Approximately 180 million Pap tests are given annually, mostly in developed countries such as the U.S., Canada, Europe, and Japan, with what CytoCore believes to be an accuracy rate of 50% to 70%. These tests are the target market for the first phase of the Cocktail-CVX™ assay and AIPS platform. Since the new P2X₇ biomarker (described below) combines with the Cocktail-CVX™ to greatly improve Pap test accuracy, CytoCore estimates that the U.S. market for its Cocktails could be as high as 40 to 60 million Pap tests per year. Through use of the P2X₇ biomarker and the AIPS platform, Pap test accuracy could increase to 85% to 90%.

P2X₇ Biomarker

Another characteristic of cancerous cells is the slowing of the natural programmed cell death process—apoptosis. Discovered by Dr. George Gorodeski and licensed by CytoCore is a unique set of nucleic acids and proteins (P2X₇) which is down-regulated in cancer cells, rather than up-regulated like the proliferation proteins. Normally, one of the main functions of the P2X₇ is the regulation of apoptosis in tissues that line body surfaces. Dr. Gorodeski has determined through his research that this mechanism is significantly down-regulated in precancerous and cancerous cells, thereby contributing to decreased apoptosis and to an increased chance of these cells becoming cancerous. Dr. Gorodeski found that the P2X₇ biomarker closely correlates with the change in the apoptosis process that results as epithelial cells begin to turn dysplastic (abnormal) or cancerous.

The P2X₇ occurs on the surface of virtually all forms of epithelial (or skin) cells. Dr. Gorodeski's hypothesis is that three long chains of the P2X₇ proteins combine, and when they do, begin to open portals on the cell surface for other chemicals, such as calcium, to enter the cell and contribute to apoptosis. However, also on the cell surface is a short chain version, a variant of the P2X₇, the P2X_{7j}. When cancer is present or immanent, the P2X_{7j} aligns with the three-part P2X₇ and prevents the opening of portals into the cell, thereby stopping apoptosis.

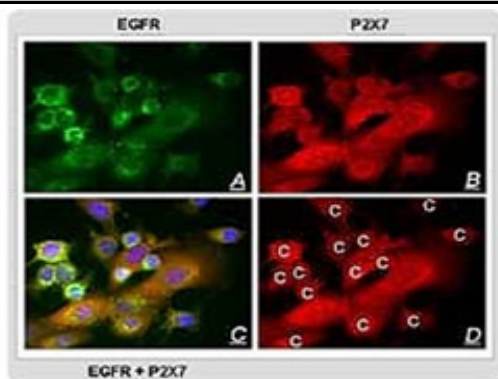
Laboratory testing by Dr. Gorodeski demonstrates a very high correlation between decreased expression of this apoptotic biomarker and the accurate detection of cancer and precancerous cells. The results have been published in two leading journals (Feng, Li, Wang, Zhou, and Gorodeski [*Journal of Biological Chemistry* 281:17228, 2006] and Li, Zhou, Feng, Abdul-Karim, and Gorodeski [*Cancer Epidemiology Biomarkers & Prevention*, 15:1, 2006]). Dr. Gorodeski determined through his research that the P2X₇ may be the first biomarker to make this correlation, as well as the first to detect and signal the cell's potential to develop cancer. Results from Dr. Gorodeski's laboratory testing are on pages 33-35. Accordingly, he is developing the P2X₇ to be used with CytoCore's AIPS platform. A patent has been filed on the concept and commercial use of this P2X₇ gene as a biomarker for cancer identification.

Cocktail-GCI

In an innovative approach, CytoCore licensed the newly discovered P2X₇ biomarker, and based on Dr. Gorodeski's studies, combined this down-regulated biomarker, the P2X₇, with an up-regulated proliferation biomarker (e.g. the **epidermal growth factor receptor [EGFR]**), to create the Cocktail-GCI assay. The combination shows greater accuracy in differentiating precancerous and cancer cells from normal cells, allowing the Company to better triangulate and identify cancerous cells. The proprietary combination of the Cocktail-CVX™ and the P2X₇ biomarker, designated the Cocktail-GCI assay, is intended to detect cervical and endometrial precancerous and cancer cells using proteomics criteria. The Cocktail-GCI assay can be applied to tissue and cellular samples and is designed to integrate with existing laboratory work-flow procedures and reduce the propensity for inaccurate cytology evaluations. The Cocktail-GCI assay is anticipated to be effective at detecting abnormalities within 30 to 60 minutes of use. Eventually, CytoCore believes that its Cocktail-GCI could be effective in a completely automated fashion.

This assay provides a unique method of protein detection resulting in clinically proven high levels of sensitivity and **specificity** (measures of biomarker accuracy) in cytology samples. Initial laboratory results demonstrate that the P2X₇ biomarker used in the new assay significantly outperforms standard Pap testing. To date, a Pap test can range from 50% to 70% accurate in terms of sensitivity and specificity, while the P2X₇ biomarker has demonstrated initial figures of 87% and 100% accuracy.

Figure 7
CytoCore, Inc.
EGFR AND P2X₇ BIOMARKER VISUALS



Source: CytoCore, Inc.

One example for the unique potential of combining a proliferation marker (e.g. the EGFR) with the apoptosis marker P2X₇ is shown in Figure 7. The EGFR and P2X₇ biomarkers used in this example assay contain a fluorescent component that enables visual identification of normal versus cancerous cells after the biomarker has attached to the cells. Figure 7 shows an image sequence of normal and cancerous cells that have been tagged with the EGFR and P2X₇ biomarkers and highlighted through the biomarkers' fluorescent components. Frame A illustrates cells targeted by the EGFR proliferation marker. Frame B shows cells that were targeted through the apoptosis marker, the P2X₇. When used together, the biomarkers produce a composite image such as the one in Frame C. Based on that data, the subsequent classification of cancerous cells, labeled "c", can be seen in Frame D.

Status and Market for the Cocktail-GCI Assay

CytoCore intends for the Cocktail-GCI assay to be used as a screen for endometrial cancer. Since there is currently no available screening test for endometrial cancer, the Company expects this screen to be the first known test of its kind. CytoCore's Endometrial Cancer Scan is detailed on pages 38-40.

Utilizing the P2X₇ biomarker for the Endometrial Cancer Scan, the Cocktail-GCI has begun a Phase I trial and will likely require seven to nine months to complete both the trial and development. If the Phase I trial is successful, the Endometrial Cancer Scan may be prepared for market by late 2007 for use as an Analyte Specific Reagent ([ASR] described on page 7) through **Clinical Laboratory Improvement Amendment (CLIA)** laboratories, also known as "reference" laboratories. Completion of Phase II trials and FDA approval is expected to require approximately 18 to 24 months.

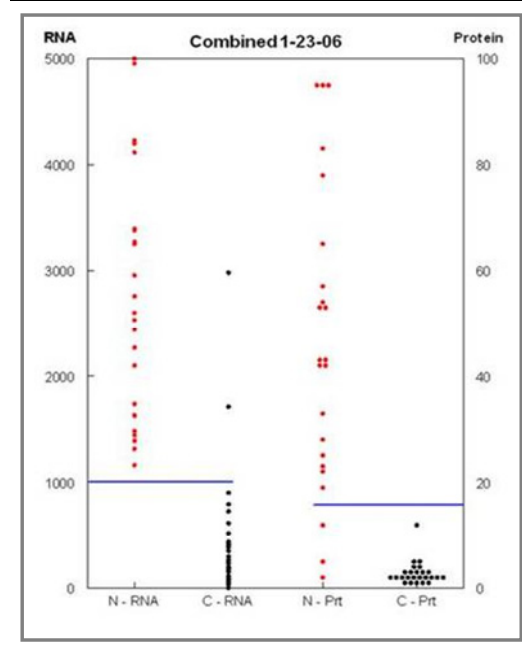
The Company estimates the U.S. market potential for the Endometrial Cancer Scan is between 20 and 28 million women who have high-risk characteristics and who could receive the Endometrial Cancer Scan in conjunction with the Pap test.

Initial Laboratory Results for the P2X₇

Dr. Gorodeski performed a series of laboratory tests to statistically investigate the ability of the P2X₇ biomarker to accurately identify cancerous cells in human tissue samples. The tests used uterine tissue samples containing both cancerous and noncancerous cells from the same patient tissue source. Doing so enabled each sample to return both a normal and a cancer reading. Dr. Gorodeski compared the normal tissue and the cancerous tissue to the cancer/non-cancer results returned by the P2X₇ biomarker. Figure 8 and Table 11 illustrate the results of this laboratory study.

Figure 8 lists RNA and protein on the y-axes. Dr. Gorodeski used the P2X₇ biomarker to test the tissue samples for levels of both RNA and protein. The x-axis is divided into four groups: normal tissues tested for RNA (N-RNA), cancerous tissues tested for RNA (C-RNA), normal tissues tested for protein (N-Prt), and cancerous tissues tested for protein (C-Prt). The N-RNA column of data points illustrates the N-RNA samples that produced an RNA reading above 1000 units. All but two of the C-RNA data points in the next column to the right had RNA measures of less than 1000 units. The opposite side of the graph illustrates a similar phenomenon. The N-Prt and C-Prt data points were tested for protein. The cancerous tissue, and only three cases of normal tissue, registered at less than 15 units. The remaining normal tissues measured above the baseline. The lines drawn at RNA 1000 units and Protein 15 units on the graph are arbitrary. They can be moved and were added to the test in order to perform the confidence level calculations listed in Table 11.

Figure 8
CytoCore, Inc.
GRAPHICAL REPRESENTATION OF
LABORATORY TEST RESULTS



Source: CytoCore, Inc.

Table 11 interprets the RNA and protein data of Figure 8. The sections are divided by: RNA, protein, cancer, and normal categories. C-RNA had 36 samples total. By measuring the tissue's RNA, the P2X₇ biomarker indicated that 34 of these samples were **true positive (TP)**—cancerous tissues with RNAs of less than 1000—and that two were false negatives (FN)—cancerous tissues with RNAs greater than 1000 (the two data points in the C-RNA column of Figure 8 above the baseline). By measuring above the baseline, these two FNs indicate that they were not cancerous.

Table 11
CytoCore, Inc.

INITIAL LABORATORY TESTING RESULTS

True Positive and False Negative Totals for RNA and Protein in Both Cancer and Normal Cells as Identified by the P2X ₇ Biomarker			
RNA	Cancer	Normal	Total
Positive	34 TP	0 FP	34
Negative	2 FN	15 TN	17
Total	36	15	51
Protein	Cancer	Normal	Total
Positive	25 TP	3 FP	28
Negative	0 FN	20 TN	20
Total	25	23	48

Measures of P2X ₇ Biomarker Accuracy				
	RNA		Protein	
Sensitivity	(34/36)	94%	(25/25)	100%
Specificity	(15/15)	100%	(20/23)	87%
Positive Predictive Value	(34/34)	100%	(25/28)	89%
Negative Predictive Value	(15/17)	88%	(20/20)	100%
False Positive	(0/34)	0	(3/28)	11%
False Negative	(2/17)	12%	(0/20)	0
Likelihood Ratio	(94/[100-100]) ∞		(100/[100-87]) 7.7	
95% Confidence Interval	2.31-31.26		- ∞ to + ∞	
χ ² (Fisher's Exact test)	p<0.0001		p<0.0001	

Source: CytoCore, Inc.



Knowing that all 36 samples were cancerous and that the P2X₇ biomarker accurately identified 34 samples results in a sensitivity measure (the accurate identification of abnormal cells) of 94% (recorded on the right side of Table 11, page 33). Likewise, the normal tissues tested for RNA were all correctly classified as true negatives (15 TN's out of 15 samples) with RNA measures above the baseline, giving the P2X₇ biomarker a specificity measure (the probability of correctly identifying a non-diseased person) of 100%. The protein data is interpreted in the same manner. The normal tissues tested for protein had three data points below the baseline (false positives that would have indicated the presence of cancer), and the cancerous tissues had no markers above the baseline, thus all true positives. The sensitivity for protein is 100% and the specificity is 87%. The best possible combined score for sensitivity and specificity is 200%, 100% for each measure. In order for the biomarker to be meaningful, it must have a score above 150%. The P2X₇ biomarker had scores of 194% and 187% for RNA and protein, respectively. The "X² (Fisher's Exact test)" row at the bottom of Table 11 summarizes all of the data into a confidence factor. The test can be considered statistically significant when the p-value is less than 0.01; the results of Dr. Gorodeski's laboratory testing give a p-value of less than 0.0001, indicating a correlation or confidence factor of 99.99.

Additional details about this study can be found in the October 2006 issue of the American Association for Cancer Research's (AACR) journal, *Cancer Epidemiology Biomarkers & Prevention*, available online at <http://cebp.aacrjournals.org/>. The article, written by Dr. Gorodeski, is titled "The P2X₇ Receptor: A Novel Biomarker of Uterine Epithelial Cancers." The first article Dr. Gorodeski published on the underlying science of the P2X₇ receptor's behavior was published in the *Journal of Biological Chemistry* in April 2006. That paper can be found at <http://www.jbc.org/cgi/reprint/M602999200v1>.

Ongoing Laboratory Results for the P2X₇

Dr. Gorodeski's laboratory testing has demonstrated that the P2X₇ biomarker is equally as accurate in detecting cervical lesions as it is in detecting the various forms of endometrial cancers. Due to the effectiveness of the biomarker for both cervical and endometrial cancer, CytoCore is developing accurate assay and screen tests, which could be useful to women throughout their lives. In particular, the Company is testing the P2X₇ as an Endometrial Cancer Scan. CytoCore anticipates that the proprietary Cocktail-GCI assay could supplement the Cocktail-CVX™ assay in the detection of cervical and endometrial precancerous and cancer cells.

A third P2X₇-related assay—the One-Step Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR, GCI-qPCR) assay—was recently developed by Dr. Gorodeski and licensed to CytoCore. This assay uses ribonucleomics criteria for the detection of endometrial precancerous and cancer cells, and utilizes technology developed in Dr. Gorodeski's laboratory specifically for measuring P2X₇ **messenger RNA (mRNA)** in endometrial and cervical tissues. The GCI-qPCR assay builds on three discoveries: (1) the finding that in endometrial and cervical epithelial cells, changes in cellular P2X₇ protein correlate with changes in mRNA levels; (2) that P2X₇ mRNA and protein molecules are expressed predominantly by epithelial cells; and (3) that tissue levels of the epithelium-specific background marker, **cytokeratin-18 (CK-18)**, are not affected by the presence of precancerous or cancer cells. The GCI-qPCR assay determines P2X₇ mRNA levels relative to CK-18 mRNA levels, thereby providing a reading of P2X₇ mRNA that is specific to the epithelial component of the tissue. As such, the GCI-qPCR assay is very sensitive to the presence of P2X₇ mRNA and is less sensitive to contaminating components in the tissue sample. The GCI-qPCR assay is anticipated to be effective at detecting abnormalities within five to six hours of use, and its potential advantage is its high sensitivity. The GCI-qPCR with the P2X₇ biomarker began Phase I trials for the Endometrial Cancer Scan with the Cocktail-GCI in November 2006. A paper by Gorodeski et al. on the GCI-qPCR has been submitted for publication.

Additional recent preliminary studies in Dr. Gorodeski's laboratory have suggested that the P2X₇ biomarker can accurately identify apoptotic deficiencies in other types of epithelial cells, not only cervical and endometrial cells. CytoCore recently announced that the P2X₇ biomarker has accurately identified bladder cancer tissue from normal bladder tissue, offering the potential to develop a urine-based bladder cancer screen that could potentially detect low-grade bladder tumors. This unique screen could also point to the P2X₇'s potential in identifying other types of epithelial cancer tissues.

Dr. Gorodeski has also tested a limited number of tissues from other epithelial cancer cells. Continued positive results in tests on other epithelial cells could prove his initial hypothesis that the P2X₇ biomarker is potentially a generic mechanism on many other forms of epithelial cells. To date, the hypothesis also appears to relate to female breast tissue. Furthermore, initial accuracy levels of the P2X₇ suggest that this biomarker could be used as a diagnostic tool as well as a screening tool. If proven through the next level of trials, this could open additional markets for CytoCore.

Automated Imaging Proteomic System (AIPS)

The next component within CytoCore's InPath™ System is the AIPS platform. AIPS is a second-generation, fully automated microscope platform designed to analyze specimen slides which have been exposed to a biochemical assay. The AIPS accomplishes this by reading the fluorescent tags attached to the biomarkers. AIPS sweeps the slide looking for cells with bandwidth changes that indicate that the cell underwent a color change due to the assays identifying it as potentially cancerous. In doing so, the software automatically recognizes those cells that could be cancerous, and notates the cell location on the slide in its database. Slides with cells that have positive indicators are brought to the attention of the cytopathologist, who is then guided to the exact location and cell on the slide generating the color change. The cytopathologist can then examine the cell for shape change as well. This workstation is key to CytoCore's research process and clinical trials, as well as to the InPath™ System's laboratory-based tests.

The second-generation AIPS has the capacity to hold 120 slides and a bar code reader, as well as user controls for examining a single slide with zoom capability. Optimized for high-volume analysis of specimen slides, the platform is highly integrated, customizable, and requires little human intervention. The AIPS includes a computer-controlled microscope, automated slide handling abilities, advanced image analysis software, and a data management interface. The platform allows users to produce test results in the laboratory or ultimately at the POS, thereby providing Pap and cervical cancer screens to undertreated populations without access to laboratory facilities.

The AIPS image analysis module can be customized to either quantitatively or qualitatively analyze specimen slides prepared using a wide variety of biomarkers. CytoCore believes that a customizable, automated scanning microscope may provide partnering opportunities for some of the array of biomarkers that are emerging from laboratories and trials. The platform may be utilized as an automatic slide scanning instrument or as an independent review workstation. Its advanced image analysis software highlights abnormal cells detected by the assay and is capable of performing image acquisition using either fluorescent or white light and automatically switching between the two.

The platform's data management software executes specimen review, patient record management, and electronic data transfer. AIPS is also enabled to support network-oriented applications such as **telepathology**, virtual slide, and service-oriented functions using a web browser. Its shell is designed to fit major microscope brands (e.g. Olympus by Olympus America Inc., Zeiss by Carl Zeiss, Inc., and Nikon by Nikon Corp. [NINOF.PK]). Figure 9 (page 36) illustrates a rendering of the AIPS platform, both opened and closed.

Status

Initial hardware and software product development of the AIPS platform was completed during the summer of 2006. During the first quarter 2007, the platform is expected to be customized for the P2X₇ biomarker in support of the Endometrial Cancer Scan. It is scheduled to enter trial tests by the end of the first quarter 2007 with CytoCore's other products, as well as be customized for the new Cocktail-GCI assay. Customization is a process of developing a library of images and "dialing in or teaching" the program to recognize the biomarker's characteristics as they express their changes in the presence of cancer. Once finished, the device with the software can be integrated into CytoCore's trial sites to support the second and third objectives of the Phase I Endometrial Cancer Scan trial (as bulleted on page 39). The platform could be ready for manufacturing and sales or partnering by the second quarter 2007. The Company aims to market the platform through either a distribution partner or, in select instances, as placement in customers' facilities on a fee-for-use basis.



Figure 9
CytoCore, Inc.
RENDERING OF AIPS PLATFORM



Source: CytoCore, Inc.

Drug Delivery System (DDS)

CytoCore's Drug Delivery System (DDS) completes the comprehensive InPath™ System by offering therapeutic treatment for cervical lesions or dysplasia detected through the previous components of the system, or the conventional Pap test. The DDS could present the first treatment option for mild-, moderate-, and potentially some high-grade cervical lesions. Based on the prevalence of dysplasia in women, the Company estimates that 85% to 90% of cervical lesions can be treated therapeutically.

This device is designed to allow physicians to apply FDA-approved chemotherapy, immuno-enhancement, and antiviral (anti-HPV) compounds directly to the cervix. Currently, physicians are not able to provide localized medical therapeutic treatments to the cervix due to its complex topographical and environmental characteristics. As a result, the primary treatment has often been surgery. At present, women who have mild- to moderate-grade lesions are not considered candidates for surgery, and are typically advised to maintain follow-up visits at intervals of three to six months. With a decreasing average age of start of dysplasia and uncertainty about the progression of lesions, it is not unusual to have patients reporting for repeated Pap tests and exams for up to 8 to 12 years.

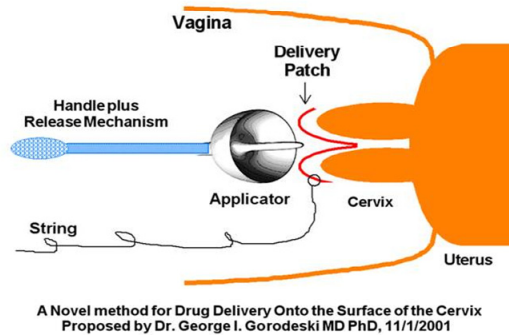
The DDS—initially intended for use in cases of cervical dysplasia—is to provide localized treatment to the cervix directly targeting the lesions. The DDS is being developed as an alternative to the currently prevailing follow-up expectant management, which dictates no action until disease progression. CytoCore believes that the novel DDS concept backed by its unique technology may alter the natural course of the disease and reduce the rate of progression to high-grade lesions and invasive cervical cancer.

An additional potential benefit of the DDS concept and technology relates to the role of dysplasia on a woman's pregnancy potential. Dr. Gorodeski has indicated that along with the decreasing average age of start of dysplasia, surgical treatments for cervical lesions also tend to begin at an earlier age. This practice is intended foremost to diagnose and remove high-grade lesions in order to prevent progression into invasive cancer; however, since there is currently no known effective method to eradicate the disease and cervical dysplasia tends to recur, women are being exposed to repeated surgical procedures at an ever decreasing age. A concern of repeated surgeries is that greater parts of the cervix are permanently removed or scarred, thereby potentially limiting a woman's ability for future pregnancies. The DDS could provide an effective treatment option to these types of conditions in the younger population of women.

Design

Figure 10 (page 37) illustrates the DDS. In its current stage, the DDS is designed to provide treatment only to the cervix. However, CytoCore believes that the technology can be generalized for additional body surfaces and various drug types. The DDS is derived from the same technology used in the e² Collector™.

Figure 10
 CytoCore, Inc.
 DRUG DELIVERY SYSTEM (DDS)



Source: CytoCore, Inc.

The key component of the DDS, a compound-saturated transdermal polymer patch, is attached to the tip of an applicator in a collapsed state. The applicator is an evolution of the e² Collector™ designed to enter easily through a standard gynecological speculum. The patch contains the select compound for treatment and when seated on the cervix, it adheres and releases the compound from the patch in one direction directly to the lesion on the surface of the cervix. The patch is deposited onto the cervix through the use of a second-generation e² Collector™ handle, which, once the balloon is inflated and the patch is seated, is then withdrawn. The treatment compound is released gradually over the next three to seven days from time of application. After the treatment period, the patch is removed via a string attached to the patch, similar to the process of removing a standard vaginal tampon. By providing targeted localized delivery and treatment through direct application to the cervix, the Company anticipates requiring smaller amounts of compounds to address the lesions present on the cervix.

Status

CytoCore licensed the DDS from Dr. Gorodeski and the UHCMC, and a patent has been filed on the System. The Company expects to develop the specialized prototype handle within the next 6 to 12 months while also testing, in parallel with the handle development, various compounds with the polymer patch over the next 12 months. The trial process for the DDS could take 12 to 18 months. Following testing, CytoCore believes that it can market the DDS domestically and internationally in conjunction with the other components of the InPath™ System.

CytoCore expects to seek the assistance of pharmaceutical companies to aid in development and testing compound options, as well as the funding of clinical trials for this technology. Since the patent filed on the DDS is generic for the process of applying a therapeutic patch, companies with an interest in working with CytoCore can file patents on select compounds used with the polymer patch. The DDS could then allow pharmaceutical companies to file “new use” patents for select drugs that are no longer protected through patents.

Market Size

The initial market for the DDS consists of patients with abnormal Pap tests. Approximately 10% of Pap tests administered each year are considered abnormal, consisting of approximately six million in the U.S. and a total of 18 million worldwide. CytoCore believes its DDS can provide effective therapeutic treatment for 90% to 95% of abnormal lesions that are not considered high grade or cancerous. A complete listing of Pap test abnormalities and their respective treatment options can be found in Table 8 (page 23).

The DDS could present the first therapeutic option of its kind for treating cervical lesions. CytoCore estimates the DDS could capture market share in the U.S. and worldwide, and have a market potential based on 180 million annual Pap tests, 10% of which are abnormal. As doctors and patients become



acquainted with the accuracy and ease of use of the Company's e² Collector™, market adoption of CytoCore's follow-on products, in this case the DDS, could accelerate. The DDS has the potential to treat abnormal Pap tests on a worldwide basis. In underdeveloped countries, the DDS may offer the only viable treatment option for women diagnosed with cervical lesions.

THE ENDOMETRIAL CANCER SCAN

Endometrial cancers contribute significantly to the morbidity and mortality of women. In the U.S., approximately 6% of all cancer deaths in women are caused by endometrial cancers (Source: American College of Obstetricians and Gynecologists, Practice bulletin number 65, August 2005). The clinical significance of the problem is even greater because risk factors and symptomatology compatible with endometrial cancer are prevalent among one-third to one-half of women. These conditions include obesity, glycemic index, diabetes, hypertension, and a failure to ovulate, as well as symptoms such as irregular uterine bleeding in the pre- and perimenopausal periods and uterine bleeding in postmenopausal women (Weiss et al., *American Journal of Epidemiology* 164:56, 2006).

Although only a small percentage of women will likely develop endometrial cancer, the prevalence of symptoms and greater awareness for risk factors has created a demand by women and caregivers for screening and early detection tests for the cancer. Currently, there is no known effective screening test for endometrial cancer. At present, suspected cases are either watched by follow-up or referred for endometrial biopsy or curettage. The endometrial biopsy that is commonly used to diagnose an endometrial abnormality tends to be accurate in 80% to 90% cases (Dijkhuizen et al., *Cancer* 89:1765, 2000).

CytoCore's preliminary studies indicate that the P2X₇ biomarker (described on page 31) can effectively detect all three forms of uterine cancer—endometrial, ectocervical, and endocervical—using either a protein-based or RNA-based test. Since endometrial cancers represent more than 95% of uterine cancers, this could open a significant new market opportunity for the Company. Laboratory results have shown sensitivity and specificity for the detection of both cervical and endometrial cancers, potentially providing CytoCore with an accurate marker forming the basis of what could be the first endometrial cancer screen. The Company's Endometrial Cancer Scan has three components: (1) the EndoCollector (described on pages 38-39); (2) the Cocktail-GCI (described on page 32); and (3) the One-Step Real-Time Reverse Transcription Polymerase Chain Reaction ([RT-PCR, qPCR] also known as the GCI-qPCR assay), described under Ongoing Laboratory Results for the P2X₇ (page 34).

Current Technology: Biopsies

CytoCore intends to utilize its P2X₇ biomarker in an endometrial cancer screening test that can detect uterine cancer earlier, more accurately, and more comfortably than a biopsy. Currently, biopsies are performed with a device called the Pipelle Endometrial Biopsy Instrument—a 25 cm long, 3 mm in diameter tube with an interior plastic rod and a cap at the end. Near the end of the tube is a small opening approximately 1.5 mm wide. The physician inserts the Pipelle through the cervical canal into the uterus, and by removing the rod, creates a powerful suction inside the tube. The suction pulls uterine tissue glands from inside the uterus into the tube, essentially tearing off the glands. The physician rotates the tube inside the uterus to obtain tissue samples from as much area as possible; however, due to the asymmetrical shape of the Pipelle, such maneuvers may not provide an accurate sampling of the endometrial lining. Once the samples are collected and the tube is removed, the sample is sent to the laboratory where it is examined by a pathologist for the presence of cancer. This entire process is usually performed only in symptomatic women, primarily after the patient has shown abnormal uterine bleeding. In cases where cancer causes the bleeding, it is likely that the patient has already developed a significant degree of disease.

CytoCore's Cancer Screen Using an EndoCollector and the Cocktail-GCI Assay

CytoCore plans to develop a novel endometrial cell collector known as the EndoCollector—a minimally invasive collection device to obtain a representative sample of endometrial cells. Combined with the novel Cocktail-GCI or GCI-qPCR assays, this could create a test capable of screening (providing a positive or negative result) for the presence of cancer cells within one to six hours. The EndoCollector is a thin

catheter-like tube that is designed to collect cells from the uterus by a flushing process, where the physician introduces and retrieves saline solution from the uterus. The retrieved solution with the uterine cells is placed into a liquid preservative and sent to a laboratory for testing. The uterine endometrial cells contained in the saline solution are then examined either via the Cocktail-GCI using CytoCore's methodology with the AIPS system or via the GCI-qPCR assay using CytoCore's P2X₇ mRNA method—a proprietary One-Step Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR or qPCR). The qPCR method was recently developed in Dr. Gorodeski's laboratory, and it can accurately measure tissue P2X₇ mRNA levels.

CytoCore's Endometrial Cancer Scan Using the Cocktail-GCI/AIPS method

Cells obtained by the EndoCollector and placed in the preservative are removed via centrifuge and assayed by the Cocktail-GCI method. Cells tagged with a fluorescent probe are then analyzed using the AIPS platform to identify cancerous cells on the slide. Slides with positive indicators would be reexamined by a pathologist. CytoCore's Endometrial Cancer Scan test does not incorporate anything that a laboratory could not implement during its normal course of business, as laboratories are currently preparing Pap test slides using this methodology.

This screen could be a dramatic improvement for both physicians and patients whose current alternative when confronting a questionable uterine condition is to have an invasive biopsy procedure performed. Equally important, an Endometrial Cancer Scan could allow physicians earlier detection of uterine cancer than is currently available, and an earlier initiation of treatment with an improved overall prognosis.

Status

CytoCore initiated a Phase I trial for the Endometrial Cancer Scan on November 10, 2006, at the UHCMC. The Company expects the trial to last approximately six to eight months and plans to incorporate additional medical institutions into the trial as it progresses. The Phase I trial is expected to demonstrate the following "essential equivalencies" for the Endometrial Cancer Scan:

- identification of uterine cancer by the P2X₇ as accurately as by the pathologic biopsy;
- recognition of P2X₇-marked cancer tissues by the AIPS platform as accurately as using the pathologic biopsy; and
- recognition by the AIPS of dispersed P2X₇-tagged cancer cells retrieved from the uterus with a flushing technique as accurately as using the pathologic biopsy.

The Phase I trial aims to produce results demonstrating that the P2X₇ biomarker used with a flushing technique in the Endometrial Cancer Scan is at least equivalent in accuracy to the current Pipelle biopsy (described on page 38). After completing the Phase I trial and obtaining results, CytoCore intends to offer its screen as an ASR through one of its trial laboratory partners. Laboratories that meet specific government standards (CLIA laboratories) may offer products for sale under their own laboratory guidance. These laboratories may sell the products; however, they must perform the product testing at their laboratory. By offering the Endometrial Cancer Scan as an ASR, the Company may be able to take this product to the marketplace as an ASR product by mid-year 2007 while it parallels a Phase II trial.

A Phase II trial is scheduled to commence in the second half of 2007. CytoCore anticipates being able to conclude the trial, receive FDA approval, and bring the product to market within approximately 24 months.

Dr. Gorodeski and the UHCMC have filed a patent for the Endometrial Cancer Scan based on the process of using a saline flush to retrieve cells and a biomarker to screen the cells for cancer. The patent has been assigned to CytoCore and is currently under review.



Market Size

Taking into account that Digene charges \$100 per HPV test, which is not a cancer screen, CytoCore believes that its Endometrial Cancer Scan priced at \$100 per test wholesale could see wide market adoption, particularly since the screen would likely be the first of its kind. CytoCore estimates that the U.S. market for endometrial cancer screening tests could be between 20 and 28 million women who may take this test every other year. The Company further believes that its test could be offered at a competitive price for a cancer screen, and that millions of women could incorporate this screen into their regular preventative healthcare regimen. The test is expected to require approximately six to eight hours of laboratory time and a result could be available within two days.

CytoCore believes that its Endometrial Cancer Scan has the potential to reach the market as a fast, non-invasive, accurate, and low-cost screening tool. There are between 25 to 28 million women, aged 35 to 70 years, within the U.S. alone that are considered to have “at risk” characteristics for endometrial cancer and that could benefit from this test. High-risk women (35% to 45% of all women) include those who are obese, diabetic, hypertensive, prone to polyps, prone to abnormal bleeding, or undergoing hormonal therapy. Additional risk factors for endometrial cancer are listed in Table 7 (page 21).

Dr. Steven Waggoner (biography on page 15), member of CytoCore’s Scientific-Medical Advisory Board and well-recognized gynecological oncologist, has indicated that this test could be used as a regular assessment of his at-risk patients. There is potential for a rapid adoption of the Endometrial Cancer Scan due to the fact that the distribution channels, OB/GYN physicians, and users for the screen are expected to be similar, if not the same as those for the e² Collector™ and the DDS.

Competition

CytoCore's competition currently comes from the cervical cancer screening and Pap test markets. Companies operating within these spheres that have marketed products currently in use, or that are developing products, are depicted in Table 12, along with key financial information. The companies are further described in the accompanying section. In addition, organizations working to promote improvements in healthcare, disease treatment, and vaccine and drug distribution are summarized in Table 12 and described thereafter. To date, there is no known competition in the endometrial cancer screening market of which the Company is aware, because a functional and effective endometrial cancer screen has not yet been developed to reach the market.

Table 12
CytoCore, Inc.
COMPETITION

Company Name	Symbol (Exchange)	Last Trade (12/08/06)	52-Week Range	Avg Vol (3 Month)	P/E	Market Cap
CYTYC Corporation	CYTC (NASDAQ)	\$27.26	22.79 - 30.77	884,666	25.1	3.07B
Digene Corporation	DIGE (NASDAQ)	48.42	27.80 - 52.15	377,991	91.3	1.15B
TriPath Imaging, Inc.	TPTH (NASDAQ)	9.22	5.11 - 9.24	386,197	63.1	359.09M
GlaxoSmithKline plc	GSK (NYSE)	52.52	50.03 - 58.40	1,505,600	19.2	147.42B
Merck & Co. Inc.	MRK (NYSE)	43.93	27.99 - 46.37	10,825,600	18.9	95.44B
Ventana Med. Sys. Inc.	VMSI (NASDAQ)	41.39	35.18 - 49.54	431,829	48.5	1.52B
Clariant Inc.	CLRT (NASDAQ)	1.43	0.70 - 1.44	135,768	N/A	100.30M
Grant Life Sciences, Inc.	GLIF.OB (OTC BB)	0.13	N/A	N/A	13.4	16.50M
MediSpectra, Inc.	private	N/A	N/A	N/A	N/A	N/A

Organization Name	Mission
Program for Appropriate Technology in Health (PATH)	Improving healthcare in communities worldwide; recently launched a five-year effort to provide HPV vaccines to women in the developing world
Penn State Milton S. Hershey Medical Center, College of Medicine	Currently performing a research study into the development of a screening test for endometrial cancer in at-risk women

Source: Yahoo! Finance and Crystal Research Associates, LLC.

Companies

CYTYC Corporation

CYTYC Corporation's ThinPrep[®] System for Pap tests is a method for improved preservation of cervical cells gathered by the physician for the laboratory cytologist. The System collects the cells through the standard method, using a spatula and brush, and deposits the collected cells into a vial of preservative liquid for transport to the laboratory. The preservative prevents the cells from clumping and allows the cytotechnician access to almost the entire sample, rather than just a portion. According to CYTYC, more than 205 million ThinPrep[®] Pap tests have been performed since the product was introduced in 1996, and 87% of physicians use the test for their patients. CYTYC's liquid-based cytology method is approved by the FDA for human papillomavirus (HPV), chlamydia, and gonorrhea testing, and is widely used to test for cervical cancer detection. Some of the company's other products include the NovaSure[®] System to treat excessive menstrual bleeding, the MammoSite[®] Radiation Therapy System to deliver radiation from inside the breast following tumor removal, and the FirstCyte[®] Breast Test to aid in breast cancer risk assessment.

*Digene Corp.*

Digene Corp. develops, manufactures, and markets proprietary DNA and RNA tests focused on women's cancers and infectious diseases. The company's flagship product, The Digene[®] HPV Test (also known as the DNAwithPap[®] Test or the hc2 High-Risk HPV DNA Test[®]), is an FDA-approved test for HPV—the primary cause of cervical cancer—and was developed and patented by Dr. Floyd Taub (biography on page 15). Digene's commercial products and research and development (R&D) efforts focus on detection of high-risk strains of HPV. This allows clinicians to identify women at risk and monitor them carefully for abnormal cells that can lead to cervical cancer if not treated early. Digene's product portfolio also includes DNA tests for the detection of other sexually transmitted infections, including chlamydia and gonorrhea, as well as tests for blood viruses such as **cytomegalovirus (CMV)**. Through its own staff or affiliated distributors, Digene markets its tests in more than 40 countries. One of Digene's R&D projects is a partnership with the Program for Appropriate Technology in Health ([PATH] described on page 44) to develop a low cost, easily used, culturally acceptable HPV test customized for developing countries. The project is part of PATH's Screening Technologies to Advance Rapid Testing (START) program, which was initiated with a grant from the Bill & Melinda Gates Foundation.

TriPath Imaging, Inc.

TriPath Imaging, Inc. develops, manufactures, markets, and sells solutions to improve clinical management of cancer, including detection, diagnosis, staging, and treatment. TriPath was formed in September 1999 through the merger of AutoCyte, Inc. and NeoPath, Inc., and the acquisition of technology and intellectual property from Neuromedical Systems, Inc. Each of these companies was a pioneer in the application of computerized image processing and analysis to detect subtle cellular abnormalities associated with cancer and its precursors. The company's U.S. product line includes the following process for cervical cell collection and screening: (1) the SurePath[®] liquid-based Pap test, approved for use by the FDA, which collects the cells and uses an ethanol-based, non-carcinogenic, proprietary preservative to transfer the sample to the laboratory; (2) the PrepMate[™] automated processor, which handles 1 to 12 samples per cycle, mixes and removes the cell sample from the preservative vial, and layers it onto a density reagent in a centrifuge tube; (3) the PrepStain[™] slide processor, which is capable of handling 48 samples, can prepare and stain cervical cytology samples using automation, and results in a uniform, homogeneous cell layer only 13 millimeters thick that represents the entire specimen; and (4) the FocalPoint[™] slide profiler, which is FDA-approved to screen both conventional and PrepStain[™] processed slides. On September 8, 2006, TriPath announced that it had signed a merger agreement with Becton Dickinson and Co. (BDX-NYSE). Becton is to acquire the approximately 93.5% of TriPath's outstanding shares that it does not currently own.

GlaxoSmithKline plc

GlaxoSmithKline plc is a global research-based pharmaceutical and healthcare company, commanding an estimated 7% of the world's pharmaceutical market, ranging from asthma and mental health treatments to developments in vaccines and cancer. Its biologicals division, GSK Biologicals, is a leading vaccine manufacturer with more than 1,500 scientists headquartered in Rixensart, Belgium. In 2005, GSK Biologicals distributed more than 1.2 billion doses of vaccines to 165 countries. In June 2006, the FDA approved the company's Stage IV-B (non-amenable to curative treatment with surgery or radiation therapy) cervical cancer treatment, Hycamtin[®] in combination with cisplatin. Hycamtin[®] in combination with cisplatin demonstrates a survival advantage over cisplatin alone. Hycamtin[®] was originally approved for the treatment of small cell lung cancer sensitive disease after failure of first-line chemotherapy and for the treatment of metastatic carcinoma of the ovary after failure of initial or subsequent chemotherapy.

In addition to developing a cervical cancer treatment, GlaxoSmithKline is creating a vaccine for HPV to prevent cervical cancer. Its GSK Biologicals division is an industry partner to PATH and is expected to provide PATH with the cervical cancer vaccines needed for demonstration projects in India, Peru, Uganda, and Vietnam. Data presented at the 2006 American Society of Clinical Oncology annual meeting in Atlanta, Georgia, illustrated that the company's vaccine candidate, Cervarix[™], is highly immunogenic and well tolerated. In its Phase III study, 100% of women from 15 to 55 years of age vaccinated with Cervarix[™] demonstrated an antibody response against HPV Types 16 and 18, the two most common cancer-causing HPV types, one month after completion of the vaccination course. Regulatory filings were

submitted to the European Agency for the Evaluation of Medicinal Products (EMA) in March 2006, in Australia and parts of Asia and Latin America since March 2006, and are targeted for submission to the FDA by the end of 2006.

Merck & Company, Inc.

Merck & Company, Inc. is a global, research-driven pharmaceutical company. Merck has partnered with PATH and is expected to deliver an approved HPV vaccine to the organization for use in the demonstration projects. On June 8, 2006, the FDA approved GARDASIL[®], the company's cervical cancer vaccine, for the prevention of cervical cancer and vaginal and vulvar precancers caused by HPV Types 16 and 18 and the prevention of low-grade and precancerous lesions and genital warts caused by HPV Types 6, 11, 16, and 18 in females aged 9 to 26. On September 22, 2006, Merck announced that GARDASIL[®] was granted a license by the European Commission that made it the first vaccine in the European Union for females aged 9 to 26 for the prevention of cervical cancer, high-grade cervical dysplasias/precancers, high-grade/precancerous vulvar dysplastic lesions, and external genital warts caused by HPV Types 6, 11, 16, and 18.

Ventana Medical Systems Inc.

Ventana Medical Systems Inc. supplies diagnostic instruments and reagent systems to healthcare providers around the world. Ventana's business is focused on tissue and the management of chemical reactions on glass slides used in the diagnosis of cancer and other disease. Its instrument-reagent systems are designed to automate and standardize the preparation and staining of patient tissue or cells mounted on a microscope slide for subsequent examination by a pathologist. Most of the work done with Ventana's instruments and products is done in anatomical pathology laboratories that focus mainly on histology and cytology.

Clariant Inc.

Clariant Inc. is a comprehensive cancer services company in advanced cancer diagnostics. The company offers laboratory services, bioanalytical services, and imaging. In terms of laboratory services, in December 2004, Clariant announced the opening of a new advanced cancer laboratory, Clariant Diagnostic Services, to serve pathologists' cancer testing needs and services. Clariant Diagnostic Services intends to meet pathologists' needs for accurate and reliable test results. Clariant's BioAnalytical Services group is involved in the ongoing development of new diagnostic assays that are expected to assist biopharmaceutical and pharmaceutical researchers in selecting the targets and patients for future therapeutics. Regarding imaging, Clariant's Automated Cellular Imaging System (ACIS[®]) has been used for more than 200,000 patients and has broad regulatory clearance. The System detects, counts, and classifies cells of clinical interest based on recognition of cellular objects of particular color, size, and shape. Additionally, the company is engaging in collaborative partnerships with pharmaceutical companies to help develop the pharmaceutical companies' leading drug candidates. On October 3, 2006, Clariant announced that it had received \$5 million in financing from GE Healthcare Financial Services (a unit of the General Electric Co. [GE-NYSE]) to support the working capital requirements of its rapidly growing diagnostic services business.

Grant Life Sciences, Inc.

Grant Life Sciences, Inc. is developing blood-based screening tests to screen women for cervical cancer and precancerous conditions. The company's tests detect the presence of certain antibodies that appear only when cervical cancer or certain precancerous conditions are present in the body. Grant's tests are performed by analyzing a small amount of the patient's blood. One version of the company's test (the AbREACT[™]) analyzes the blood sample in a clinical setting using standard laboratory equipment (the Enzyme Linked Immunosorbent Assay [ELISA]) and analytic software. This test can generally produce completed results in approximately two hours. Grant's rapid test (QuickStrip[™]) provides easy-to-read results in approximately 15 minutes and is designed to be administered by a health professional in the physician's office, hospital, clinic, or at home. The company holds worldwide rights to diagnostic devices for HIV-1, HIV-2, and **dengue fever** testing, as well as a proprietary diagnostic reagent, an ingredient used by manufacturers of rapid tests.



MediSpectra, Inc.

MediSpectra, Inc. is a privately held medical device company founded in 1996. The company aims to develop proprietary optical detection technology for enhanced accuracy and real-time results in the detection of cancer and other human tissue abnormalities. MediSpectra's technology is based on multimodal optical interrogation of tissue with light, where a combination of native fluorescence and white light backscatter spectroscopies are coupled with video imaging methods to more accurately detect tissue abnormalities. The company's first product, the LUMA™ Cervical Imaging System, was designed and developed to improve the detection of high-grade precancerous cervical abnormalities that have the potential of progressing to invasive cancer. The LUMA™ product is intended for use as an adjunct to colposcopy in identifying high-grade disease in patients referred to colposcopy by a cervical cytology test result. MediSpectra has been awarded 16 patents for its core technology. On March 16, 2006, MediSpectra's Premarket Approval (PMA) application for the LUMA™ Cervical Imaging System was approved by the FDA.

Organizations

Program for Appropriate Technology in Health (PATH)

PATH (www.path.org) is an international, nonprofit organization creating sustainable, culturally relevant solutions that enable communities worldwide to break longstanding cycles of poor health. The organization was originally founded as the Program for the Introduction and Adaptation of Contraceptive Technology (PIACT) in 1977. PIACT transitioned to PATH in 1980. With more than 400 employees, it is headquartered in Seattle, Washington, and has 23 offices in 14 countries—Cambodia, China, France, India, Indonesia, Kenya, Nicaragua, Senegal, South Africa, Thailand, Uganda, Ukraine, Vietnam, and the U.S. PATH is supported by foundations, the U.S. government, other governments, multilateral agencies, corporations, and individuals. The organization's programs include children's health, infectious diseases, maternal and reproductive health, and vaccines and immunization.

PATH has been working to prevent cervical cancer since the mid-1990s, when the organization first began researching the problem and raising awareness in international forums. From 1999 to 2004, PATH served as the coordinating agency for the International Alliance for Cervical Cancer Prevention and conducted pilot projects on innovative ways to bring screening and treatment to low-resource settings in Kenya and Peru. Since 2005, PATH has been working with vaccine manufacturers, the World Health Organization (WHO), and other global agencies, researchers, and country officials to identify the issues that must be addressed to introduce an HPV vaccine into the developing world.

On June 6, 2006, PATH launched a five-year effort to provide the new cervical cancer (HPV) vaccines to women in the developing world. The Bill and Melinda Gates Foundation supplied \$27.8 million to conduct research in India, Peru, Uganda, and Vietnam concerning the regional and global introduction of the vaccine, as well as international financing plans. PATH expects to conduct extensive research on issues specific to introducing an HPV vaccine in the developing world, such as contacting groups with little access to health systems, convincing communities that the vaccine does not condone early sexual activity (because HPV is believed to be a common sexually transmitted infection), and overcoming the reluctance associated with adopting a "girls-only" vaccine. While conducting this work, PATH intends to also coordinate closely with the WHO, the International Agency for Research on Cancer, Harvard University, the Catalonian Institute of Oncology, and other key partners.

Penn State Milton S. Hershey Medical Center, College of Medicine

The Penn State Milton S. Hershey Medical Center, College of Medicine is currently performing a research study into the development of a screening test for endometrial cancer in at-risk women. The College hopes to fill the current void in screening for gynecologic-related cancers. The study is directed by Dr. Richard S. Legro of the Department of Obstetrics and Gynecology at the Medical Center and has been approved by the Institutional Review Board under federal regulations at the Medical Center. The study aims to identify the effectiveness of two different methods by which to screen for endometrial cancer—a trans-vaginal ultrasound and an endometrial biopsy. The ultrasound uses a probe that is inserted into the vagina to examine the lining of the uterus. Dr. Legro believes that women in menopause should not have

a thick endometrial lining and that overgrowth of the lining could be an initial step towards the development of cancer. The biopsy uses a small, flexible catheter inserted into the vagina to obtain a small piece of tissue from the lining of the uterus. The tissue is then examined under a microscope for cell change. Both methods under investigation aim for early detection of endometrial cancers, before bleeding in women begins. The Penn State College of Medicine opened its doors to the first class of students in 1967, and Penn State Milton S. Hershey Medical Center accepted the first patients in 1970. Basic and clinical research is conducted at the Medical Center and is supported by \$60.1 million in awards from federal, state, and private agencies, businesses, and individuals.



Recent Milestones

Since the introduction of CytoCore's new management team in September 2005, the Company has achieved the following milestones (listed chronologically, beginning with the most recent).

- Announced that the P2X₇ has shown accuracy in identifying bladder tumors and precancerous tissues, thereby expanding the biomarker's range as a unique cancer screen.
- Announced the addition of a new CEO, Dr. Augusto Ocana (biography on page 12).
- Announced two new members of the Scientific-Medical Advisory Board, Dr. Floyd Taub and Dr. Stephen Raab (biographies on pages 15 and 16, respectively).
- Announced a new Board of Directors member, Mr. Clinton H. Severson (biography on page 14), who is currently CEO of Abaxis.
- Began testing the P2X₇ biomarker as a breakthrough Endometrial Cancer Scan.
- Began manufacturing the e² Collector™. Initial units are expected to be ready for delivery and sale by the end of the first quarter 2007.
- Published two of Dr. Gorodeski's papers on the P2X₇ biomarker in the American Society for Biochemistry and Molecular Biology's journal, *The Journal of Biological Chemistry*, and the American Association for Cancer Research's (AACR) journal, *Cancer Epidemiology Biomarkers & Prevention*, as well as presented the second paper at the 2006 AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development. The papers are available online at www.jbc.org/cgi/reprint/M602999200v1 and <http://cebp.aacrjournals.org/>, respectively.
- Finalized the process of changing the Company's name to CytoCore, Inc. from Molecular Diagnostics, Inc. by changing its ticker symbol to CYCR.OB from MCDG.OB and launching its new website at www.cytocoreinc.com.
- Demonstrated high levels of sensitivity and specificity with the P2X₇ biomarker for cervical and uterine cancer, as well as initial levels of sensitivity for other forms of epithelial cancers.
- Opened a basic research laboratory facility at University Hospitals Case Medical Center's (UHCMC) Center for Clinical Research to be run by Dr. Gorodeski. The research is intended to focus on clinical applications developed at UHCMC for the identification and treatment of certain gynecological disorders, including cervical dysplasia and cervical cancer.
- Obtained unrestricted licenses on two new products—the P2X₇ biomarker and the DDS—from Dr. Gorodeski and the UHCMC.
- Reduced accounts payable and accrued expenses by approximately \$4.2 million and Notes payable by \$5 million.
- Settled an estimated 19 legal matters (roughly \$2.5 million in claims) involving CytoCore since August 31, 2005.
- Reduced CytoCore's debt to \$3.6 million at December 11, 2006, from \$13.4 million at June 30, 2005, with an additional \$1.7 million reduction in debt announced the week of December 11, 2006, by repaying the Company's last Senior Note holder.
- Relunched development projects for the e² Collector™ and the AIPS platform.

Key Points to Consider

- CytoCore's InPath™ System is a fully integrated screening, diagnostic, and treatment system for cervical cancer, and could provide a revolutionary early detection screen for endometrial cancer. The InPath™ System is expected to provide cost-effective, biomolecular products for cancer coverage in women at the point-of-service (POS) around the world.
- The InPath™ System consists of a vertically integrated family of products, each with differing market potential and timelines, which can be used separately or as a comprehensive system.
 - The e² Collector™ is clinically proven to collect a better cervical cell sample, thus improving the existing Pap test technology. This product is FDA approved, currently being prepared for manufacturing, and is expected to be ready for sale by the end of the first quarter 2007.
 - The biochemical assays significantly improve Pap test performance to 85% to 90% accuracy. The assays are expected to be ready for trial by mid-year 2007 and be market ready by late 2008.
 - The Automated Imaging Proteomic System (AIPS) platform is capable of reading slides prepared with the Cocktail-CVX™ assay and is anticipated to be tested soon for the Cocktail-GCI assay. The platform could be ready for manufacturing and sales or partnering by the second quarter 2007. CytoCore expects the platform to be marketed through a distribution partner or, in select instances, placed in customers' facilities on a fee-for-use basis.
 - The DDS offers a therapeutic treatment option for cervical lesions as an alternative to waiting for cancer to progress to the point of surgery or having surgery as a first option. CytoCore expects to develop its prototype handle within approximately 6 to 12 months while testing compounds with its polymer patch at the same time over 12 to 18 months. The trial process for the DDS is also expected to take approximately 12 to 18 months.
- The Company believes that once sales channels are opened with the e² Collector™, sales of the biochemical assays, Drug Delivery System (DDS), and additional products could scale up rapidly due to the strategy of selling these new products to the same OB/GYNs who are already using the e² Collector™.
- CytoCore has commenced a Phase I clinical trial for a screening test for endometrial/uterine cancer that is expected to last seven to eight months. To the Company's knowledge, this is a unique product. CytoCore estimates the market for its Endometrial Cancer Scan could be a potential U.S. patient population of 23 to 28 million women valued at \$100 per test. The Company has filed a patent on the process for this test.
- CytoCore's upcoming clinical projects include basic research at UHCCM's Center for Clinical Research with the P2X₇ biomarker and its capabilities, and the launching of the e² Collector™ confirmatory trial.
- CytoCore has licensed a unique cancer marker—the P2X₇ biomarker. Not only does it appear to be highly sensitive and specific for endometrial and cervical cancers, but CytoCore has begun to demonstrate the P2X₇'s accuracy with other forms of epithelial tissue cancers as well, specifically for bladder cancer. An important characteristic of the P2X₇ is its ability to identify precancerous cells. This capability could give physicians the ability to explore early treatment options for these types of cells, potentially using the body's own immune system, before more aggressive treatment forms are required to treat the cancer, such as chemotherapy or surgery.
- The Company anticipates support from companies with an interest in helping develop, test, and fund clinical trials for various drug options to be used with CytoCore's DDS technology. The DDS could allow pharmaceutical companies to file "new use" patents for select compounds that are no longer



protected through patents. The patent filed on the DDS is generic; therefore, companies with an interest in using CytoCore's technology can file patents on select agents used with the polymer patch. Additionally, new treatments requiring minimal compound amounts could be developed as a result of the direct sustained application via the DDS's polymer patch.

- CytoCore's patent portfolio includes three issued U.S. patents and six U.S. and foreign pending patent applications. In addition, CytoCore owns the trade names for InPath™, e² Collector™, and Cocktail-CVX™, and has licenses for the P2X₇ biomarker and the DDS.
- CytoCore has a valuable strategic research partnership and technology transfer agreement with the University Hospitals Case Medical Center (UHCMC) and one of UHCMC's leading researchers in the area of women's health, Dr. Gorodeski. The agreement provides CytoCore with the license for the P2X₇ biomarker and the DDS, as well as with a new laboratory within the UHCMC's Center for Clinical Research, administrative support for CytoCore's future clinical trials, and the assistance of Dr. Gorodeski and additional scientists and clinicians at the UHCMC.
- CytoCore's new management has kept a solid focus on financially restructuring the Company. Since the new team joined the Company in September 2005, they have reduced the Company's debt from \$13.4 million at June 30, 2005, to \$3.6 million at September 30, 2006, settled approximately 19 legal matters (roughly \$2.5 million in claims) involving CytoCore since August 31, 2005, and reduced accounts payable and accrued expenses by roughly \$4.2 million and Notes payable by \$5 million. The week of December 11, 2006, the Company announced that it had reduced debt by an additional \$1.7 million by paying off the last Senior Note holder. With the conversion of debt and the settlement and payment of liabilities, the majority of CytoCore's future cash resources can be devoted to clinical operations and the development and marketing of its products.
- As of September 30, 2006, CytoCore had cash and cash equivalents of approximately \$873,000.
- CytoCore secured \$4 million in new equity financing during the quarter ended June 30, 2006, as it neared the end of its financial restructuring and turnaround. The financing has allowed the Company to settle most of its legal claims and a majority of its significant liabilities, move forward with new clinical trials, and begin manufacturing the e² Collector™. During the first six months of 2006, the Company raised net proceeds of approximately \$4.9 million through the private sale of unregistered, restricted Common Stock.

Historical Financial Results

Tables 13, 14, and 15 provide a summary of CytoCore's key historical financial statements—its Statements of Operations, Balance Sheets, and Statements of Cash Flows.

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2006	2005	2006	2005
Net revenues	\$ 21	\$ 24	\$ 70	\$ 93
Operating expenses				
Cost of revenues (includes impairment charge of property assets of \$169 for the nine months ended September 30, 2006, net of settlement of trade debt of \$81 and \$177 for three and nine months ended September 30, 2006, respectively)	(81)	—	19	—
Research and development (net of settlement of trade debt of \$141 and \$279 for the three and nine months ended September 30, 2006, respectively)	193	31	486	128
Selling, general, and administrative (net of settlement of trade debt, lease obligation, and Note payable of \$386 and \$1,045 for the three and nine months ended September 30, 2006, respectively, and \$80 and \$853 for the three and nine months ended September 30, 2005, respectively)	1,193	(55)	2,906	1,047
Total operating expenses	1,305	(24)	3,411	1,175
Operating income (loss)	(1,284)	48	(3,341)	(1,082)
Other income (expense):				
Interest expense —related party	—	(2)	(14)	(7)
Interest expense (net of interest settlement of \$11 and \$69 for the three and nine months ended September 30, 2006, respectively)	(51)	(124)	(1,686)	(932)
Interest income	11	—	12	—
Total other income (expense)	(40)	(126)	(1,688)	(939)
Net loss	\$ (1,324)	\$ (78)	\$ (5,029)	\$ (2,021)
Preferred Stock dividend	—	(230)	(648)	(683)
Net loss applicable to Common Stockholders	\$ (1,324)	\$ (308)	\$ (5,677)	\$ (2,704)
Basic and diluted net loss per Common Share	\$ (0.00)	\$ (0.00)	\$ (0.03)	\$ (0.02)
Basic and diluted weighed average number of Common Shares outstanding	275,509,600	118,669,134	224,293,002	111,137,400

Source: CytoCore, Inc.



Table 14
 CytoCore, Inc. (Formerly Molecular Diagnostics, Inc.)
 CONSOLIDATED BALANCE SHEETS
 (Dollars in thousands, except per share amounts)

	September 30, 2006	December 31, 2005
	(Unaudited)	
Assets		
Current Assets:		
Cash and cash equivalents	\$ 873	\$ —
Accounts receivables, net of allowance for doubtful accounts of \$0 at September 30, 2006 and December 31, 2005	28	38
Inventories	—	26
Prepaid expenses and other current assets	226	73
Total current assets	<u>1,127</u>	<u>137</u>
Fixed Assets, net	54	233
Licenses, patents, and technology, net of amortization	20	20
Other assets		16
Total assets	<u><u>\$ 1,217</u></u>	<u><u>\$ 390</u></u>
Liabilities and Stockholders' Deficit		
Current Liabilities:		
Checks issued in excess of amounts on deposit	\$ —	\$ 5
Accounts payable	1,461	3,714
Accrued payroll costs	354	643
Accrued expenses	1,838	2,292
Deferred revenue	25	25
Due to stockholder	37	37
Lease obligation	—	96
Notes payable—related party	—	70
Notes payable	1,586	3,557
Total current liabilities	<u>5,301</u>	<u>10,439</u>
Stockholders' Deficit:		
Preferred Stock, \$0.001 par value; 10,000,000 shares authorized; 578,653 and 1,102,192 shares issued and outstanding at September 30, 2006 and December 31, 2005, respectively (Liquidation value of all classes of Preferred Stock \$5,038 at September 30, 2006)	3,008	7,716
Common Stock, \$0.001 par value; 375,000,000 shares authorized; 288,342,264 and 154,665,084 shares issued and 288,150,176 and 154,472,995 shares outstanding at September 30, 2006 and December 31, 2005, respectively	288	155
Additional paid-in-capital	68,611	52,386
Treasury Stock: 192,088 shares at September 30, 2006 and December 31, 2005	(327)	(327)
Accumulated deficit	(75,589)	(69,911)
Accumulated comprehensive loss—		
Cumulative translation adjustment	(75)	(68)
Total stockholders' deficit	<u>(4,084)</u>	<u>(10,049)</u>
Total liabilities and stockholders' deficit	<u><u>\$ 1,217</u></u>	<u><u>\$ 390</u></u>

Source: CytoCore, Inc.

Table 15
 CytoCore, Inc. (Formerly Molecular Diagnostics, Inc.)
 CONSOLIDATED STATEMENTS OF CASH FLOWS (Unaudited)
 (Dollars in thousands)

	Nine Months Ended September 30,	
	2006	2005
Operating Activities:		
Net loss	\$ (5,029)	\$ (2,021)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of debt discount	173	575
Depreciation and amortization	31	92
Amortization of prepaid consulting fees	—	79
Impairment charge of property asset	169	—
Interest charge on Note conversion settled in stock	1,321	—
Loss on sale of fixed assets	—	3
Gain on settlements of trade indebtedness	(1,569)	—
Notes issued in payment of an expense	48	82
Warrant-related expenses issued in settlement of debt	166	421
Stock, Warrants, and Options issued to non-employees for services	857	—
Non-cash compensation expense	1,099	—
Changes in assets and liabilities:		
Accounts receivable	10	14
Inventories	26	—
Due from stockholder	—	(1)
Prepaid expenses and other current assets	(169)	(107)
Accounts payable	(699)	(229)
Accrued expenses	(454)	(135)
Net cash used in operating activities	<u>(4,020)</u>	<u>(1,227)</u>
Investing activities:		
Purchases of fixed assets	(20)	(27)
Net cash used in investing activities	<u>(20)</u>	<u>(27)</u>
Financing activities:		
Net proceeds from issuance of Common Stock	5,040	1,378
Proceeds from exercise of Warrants	44	—
Lease obligation	(96)	—
Payment of notes payable	(75)	(5)
Net cash provided by financing activities	<u>4,913</u>	<u>1,373</u>
Net increase in cash and cash equivalents	<u>873</u>	<u>119</u>
Cash and cash equivalents at the beginning of period	<u>—</u>	<u>11</u>
Cash and cash equivalents at end of period	<u>873</u>	<u>130</u>
Supplemental disclosure of cash flow information:		
Cash paid during the period for:		
Interest	\$ —	\$ 28
Financing costs	—	58
Non-cash transactions during the period for:		
Financing costs	\$ 239	\$ 93
Convertible Promissory Notes and accrued interest converted into Common Stock	\$ 3,557	\$ 6,884
Preferred Stock and cumulative dividends converted into Common Stock	\$ 4,217	\$ 71

Source: CytoCore, Inc.



Risks

Some of the information in this Executive Informational Overview[®] (EIO[®]) relates to future events or future business and financial performance. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in CytoCore's statements on Forms 10-KSB, 10-QSB, and 8-K, as well as other forms filed from time to time. The content of this EIO[®] with respect to CytoCore has been compiled primarily from information available to the public released by the Company through news releases, Annual Reports, and Securities and Exchange Commission (SEC) filings. CytoCore is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by CytoCore. Certain summaries of activities have been condensed to aid the reader in gaining a general understanding. For more complete information about CytoCore, please refer to the Company's website at www.cytocoreinc.com.

Investors should carefully consider the risks and information about CytoCore's business described below. Investors should not interpret the order in which these considerations are presented as an indication of their relative importance. The risks and uncertainties described below are not the only risks that the Company faces. Additional risks and uncertainties not presently known to CytoCore or that CytoCore currently believes to be immaterial may also adversely affect its business. If any of the following risks and uncertainties develops into actual events, the business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company's shares could decline.

There is a limited market for “penny stocks” such as CytoCore's Common Stock.

CytoCore's Common Stock is considered a “penny stock” because, among other things, its price is below \$5.00 per share, it trades on the Over-the-Counter Bulletin Board (OTC.BB), and the Company has net tangible assets of less than \$2 million. As a result, there may be little or no coverage by security analysts; the trading price may be lower; and it may be more difficult for stockholders to dispose of or to obtain accurate quotations as to the market value of the Common Stock. Being a penny stock also could limit the liquidity of CytoCore's Common Stock.

The historically volatile market price of CytoCore's Common Stock may affect the value of its stockholders' investments.

The market price of CytoCore's Common Stock, like that of many other medical products and biotechnology companies, has been highly volatile in the past. This volatility is likely to continue for the foreseeable future. Factors affecting potential volatility include:

- general economic and other external market factors;
- announcements of mergers, acquisitions, licenses, and strategic agreements;
- announcements of private or public sales of securities;
- announcements of new products or technology by the Company or its competitors;
- ability to finance its operations;
- fluctuations in operating results; and
- announcements by the U.S. Food and Drug Administration (FDA) relating to products.

CytoCore's Common Stock is unlikely to produce dividend income in the foreseeable future.

CytoCore has never paid a cash dividend on its Common Stock, and it does not anticipate paying cash dividends for the foreseeable future. Its ability to declare dividends on its Common Stock is further limited by the terms of certain of the Company's other securities, including several series of its Preferred Stock.

The Company intends to reinvest any funds that might otherwise be available for the payment of dividends in further development of its business.

The Company's Common Stock is subject to dilution, and an investor's ownership interest and related value may decline.

CytoCore is authorized to issue up to 10,000,000 shares of Preferred Stock. As of December 31, 2005, the Company had 82,655 shares of Series A Convertible Preferred Stock outstanding, which convert into approximately 36,102 shares of its Common Stock; 365,106 shares of Series B Convertible Preferred Stock outstanding, which convert into approximately 1,460,424 shares of its Common Stock; 245,833 shares of Series C Convertible Preferred Stock outstanding, which convert into approximately 1,229,165 shares of its Common Stock; 175,000 shares of Series D Convertible Preferred Stock outstanding, which convert into approximately 1,750,000 shares of its Common Stock; and 233,598 shares of Series E Convertible Preferred Stock outstanding, which convert into approximately 6,423,938 shares of its Common Stock. There are cumulative dividends due on the Series B, Series C, Series D, and Series E Convertible Preferred Stock, which may be paid in kind in shares of CytoCore's Common Stock. CytoCore's Certificate of Incorporation (as amended to date) gives its Board of Directors authority to issue the remaining undesignated shares of Preferred Stock with such voting rights, if any, designations, rights, preferences, and limitations as the Board may determine.

At December 31, 2005, the Company had outstanding Warrants to purchase an aggregate 32,558,111 shares of its Common Stock, outstanding Options to purchase approximately 4,003,991 shares of its Common Stock, and 450,000 stock appreciation rights, which are convertible into approximately 289,286 shares of Common Stock.

At December 31, 2005, outstanding Convertible Promissory Notes were convertible into approximately 22,735,000 shares of CytoCore's Common Stock. Under the provisions of certain outstanding Convertible Promissory Notes, the holders have the right to receive a Warrant to purchase additional shares of Common Stock upon exercise of the conversion right. CytoCore is unable to determine the exact number of additional Warrants to purchase shares of its Common Stock that will be issuable upon conversion of the Notes, although it could be approximately 5,684,000 shares.

At December 31, 2005, the Company had approximately 15,123,000 shares of Common Stock reserved for future stock options under its 1999 Equity Incentive Plan and 160,000 shares of Common Stock reserved for future sale to employees under its 1999 Employee Stock Purchase Plan.

The issuance of shares of CytoCore's Common Stock upon the conversion of its Preferred Stock or Notes, or upon exercise of outstanding Options and Warrants, would cause dilution of existing stockholders' percentage ownership of the Company. Holders of the Company's Common Stock do not have preemptive rights, meaning that current stockholders do not have the right to purchase any new shares in order to maintain their proportionate ownership in the Company. Such stock issuances and the resulting dilution could also adversely affect the price of CytoCore's Common Stock.

CytoCore has a limited operating history, and there are doubts as to the Company being a going concern.

CytoCore has a limited operating history. Its revenues, from inception in March 1998 through 2003, were derived almost entirely from sales by Samba Technologies SARL ("Samba"), its former wholly owned subsidiary. The assets of Samba were sold in December 2003 as part of the French Commercial Court ordered liquidation and CytoCore lost all rights and title to the assets, including Samba's software. CytoCore has sold only a very limited amount of its InPath™ System products to date and cannot be certain as to when sales of the Company's products might occur in the future.

The Company expects to devote substantial resources to product development. It anticipates that it will continue to incur significant losses unless and until some or all of its products have been successfully introduced, if ever, into the marketplace.



The Company has incurred substantial losses and has limited financial resources. Consequently, its independent auditors have noted that these conditions raise substantial doubt as to its ability to continue as a going concern. CytoCore's financial statements do not include any adjustments relating to the recoverability and classification of asset carrying amounts or the amount and classification of liabilities that may result from the outcome of this uncertainty. Moreover, the going concern explanatory paragraph may make obtaining additional financing more difficult or costly.

CytoCore continues to have severe liquidity problems.

CytoCore has a history of losses and continues to experience severe liquidity problems, which affects its overall ability to operate its business, including the ability to employ adequate staff and conduct ongoing studies and clinical trials of its products. Failure to raise adequate financing to meet its business needs could materially jeopardize CytoCore and its ability to conduct business. There can be no assurance that the Company will be able to secure necessary funds.

CytoCore may not be able to meet its short-term capital requirements.

CytoCore believes that its existing capital resources are not sufficient to meet the short-term requirements of the Company. These short-term requirements include a significant amount of liabilities and Promissory Notes in arrears. It is unlikely that CytoCore will be able to meet its short-term funding requirements through the sale of its products and services. CytoCore anticipates that these short-term funding needs will require the sale or issuance of additional shares of Common Stock or instruments convertible into Common Stock. Such sales or issuances, if any, would have a dilutive effect on the holdings of CytoCore's stockholders and the value of its Common Stock. The Company cannot be certain what level of dilution, if any, may occur or if it will be able to complete any such sales of Common Stock or other securities in the future.

The Company's operating business plan for 2005 anticipated that it would need to raise new equity. It was not able to raise the necessary level of new equity and had to reduce its operations significantly during the year. A failure to raise sufficient additional funds would adversely affect CytoCore's ability to meet short-term capital requirements, resume clinical tests, meet product timelines, and/or continue as a going concern.

The Company may not be able to meet its long-term capital requirements.

The Company does not know if it will be able to sustain its long-term operations through future revenues. Whether it will need to raise additional funds to support its long-term operations is influenced by many factors, including the costs, timing, and success of efforts to develop products and market acceptance of products.

CytoCore's products are subject to government regulation, and they may not receive necessary government approvals.

The sale and use of CytoCore's products in the U.S. is regulated by the FDA. The Company must meet significant FDA requirements before it can receive clearance to market its products. Included in these FDA requirements is the conduct of lengthy and costly clinical trials to prove the safety and efficacy of the products. Until CytoCore completes such clinical trials, its products may be used only for research purposes or to provide supplemental diagnostic information in the U.S. The Company has FDA approval for one of its products, the e² Collector™; began a clinical trial for the P2X₇ as an Endometrial Cancer Scan in November 2006; and plans to start a clinical trial for the Cocktail-CVX™ and Cocktail-GCI assays in 2007 (although such trials are contingent on the receipt of adequate capital).

The Company cannot be certain that its product development plans will allow these additional trials to commence or be completed according to plan or that the results of these trials, or any future trials, when submitted to the FDA along with other information, will result in FDA clearance to market CytoCore's products in the U.S. The Phase I Endometrial Cancer Scan trial is expected to last seven to eight months. The e² Collector™ marketing trial is expected to start in December 2006 and last 60 to 90 days with FDA approval for the Special Investigational Device Exemption (IDE) submission to take another 30 days.

Sales of medical devices and diagnostic tests outside the U.S. are subject to foreign regulatory requirements that vary from country to country. The time required to obtain regulatory clearance in a foreign country may be longer or shorter than that required for FDA marketing clearance. Export sales of certain devices that have not received FDA marketing clearance may be subject to regulations and permits, which may restrict the Company's ability to export the products to foreign markets. If CytoCore is unable to obtain FDA clearance for its products, it may need to seek foreign manufacturing agreements to be able to produce and deliver its products to foreign markets. CytoCore cannot be certain that it will be able to secure such foreign manufacturing agreements on acceptable terms, if at all.

The Company may be unable to compete with larger companies that have more resources.

CytoCore competes in the medical device and diagnostics marketplace with companies that are much larger and have greater financial resources than the Company. It may not succeed in developing technologies and products that are more effective than those being developed by its competitors. Its technologies and products may be rendered obsolete or noncompetitive as a result of products introduced by its competitors. Most of CytoCore's competitors have substantially greater financial and technical resources, production and marketing capabilities, and related experience, which may enable them to develop, manufacture, and market their products more successfully and at a lower cost. In addition, many of the Company's competitors have significantly greater experience in conducting preclinical testing and clinical trials of products and obtaining regulatory approvals to market such products. Accordingly, its competitors may succeed in obtaining FDA approval for products more rapidly, which may provide an advantage in achieving market acceptance of their products.

CytoCore may not be able to market its products.

CytoCore does not intend to maintain a direct sales force to market and sell its products. Therefore, in order to successfully market and sell its products, CytoCore must be able to negotiate profitable marketing and sales agreements with organizations that have direct sales forces calling on domestic and foreign market participants that may use its products. If it is not able to successfully negotiate such agreements, the Company may be forced to market its products through its own sales force. CytoCore cannot be certain that it will be successful in developing and training such a sales force, should one be required, or that it will have the financial resources to carry out such development and training. It is noteworthy that CytoCore's new chief executive officer (CEO), Dr. Augusto Ocana (biography on page 12), is seasoned in the area of distribution, with special capabilities in international distribution.

The Company may not be able to adequately protect its intellectual property.

CytoCore holds a variety of patents and trademarks and has applied for a significant number of additional patents and trademarks with the U.S. Patent and Trademark Office (USPTO) and foreign patent authorities. The Company intends to file additional patent and trademark applications as dictated by its research and development projects and business interests. CytoCore cannot be certain that any of the currently pending patent or trademark applications, or any of those which may be filed in the future, will be granted or that they will provide any meaningful protection for the Company's products or technologies.

CytoCore protects much of its core technology as trade secrets because its management believes that patent protection would not be possible or would be less effective than maintaining secrecy. CytoCore cannot be certain that it will be able to maintain secrecy or that a third party will not be able to develop technology independently. The cost of litigation to uphold the validity of a patent or patent application, prevent infringement, or protect trade secrets can be substantial, even if the Company is successful. Furthermore, CytoCore cannot be certain that others will not develop similar technology independently or design around the patent aspects of its products.

Management turnover could cause CytoCore's business to suffer.

CytoCore has experienced significant turnover in its senior management in the past, and there can be no assurance that it will be able to attract and retain key personnel.



Recent Events

12/12/2006—CytoCore announced that it has tendered payment of principal and accrued interest to its last senior debt holder, resulting in the reduction of approximately \$1.7 million in liabilities.

12/06/2006—Announced that Dr. Floyd Taub (biography on page 15), founder and first chief executive officer (CEO) of Digene Corp., the only company with a U.S. Food and Drug Administration (FDA)-approved DNA-based test to detect cervical cancer-causing viruses (the Digene[®] HPV Test), has joined the Scientific-Medical Advisory Board at CytoCore.

12/04/2006—Announced highly accurate results in using the P2X₇ biomarker to detect bladder cancer—suggesting broader implications for its use in the early detection of cancer in all epithelial cells. Following recent test results that confirmed the efficacy of the P2X₇ biomarker in the early identification of endometrial and cervical cancers, this new finding indicates the biomarker's potential effectiveness in early screening for bladder cancer—confirming the presence of bladder cancer in diagnostically difficult cases and perhaps in predicting the biologic potential of an individual tumor in terms of recurrence and progression to more advanced disease.

11/30/2006—Dr. George Gorodeski (biography on pages 12-13) appeared on the nationally distributed cable program “Your Cancer Today” to discuss the Company's breakthrough suite of cervical and endometrial (uterine) cancer screening, diagnostic, and treatment products. Dr. Gorodeski highlighted CytoCore's current clinical trials on the Endometrial Cancer Scan, which could potentially save the lives of tens of thousands of women diagnosed with the disease each year. He also discussed his work with the P2X₇ biomarker, a sensitive and accurate indicator of cancerous and precancerous epithelial cells, as well as CytoCore's e² Collector™, an innovative and non-invasive method of collecting cervical cell samples. Further information and local programming details about Dr. Gorodeski's appearance on “Your Cancer Today” are available at www.yourcancertoday.com.

11/29/2006—Announced the start of clinical trials to support its non-invasive uterine cancer screening method that are expected to become a standard gynecological wellness test available worldwide. Phase I trials is expected to be complete in six months. Phase II trials are expected to begin immediately, with a product market release anticipated during 2008. Trials began at University Hospitals Case Medical Center (UHCMC), and additional sites will likely be added as their approval process is completed.

11/28/2006—Announced the addition of Mr. Clinton H. Severson (biography on page 14) to its Board of Directors, one of a series of key executive moves driving the Company's move toward broad distribution of its line of products for the early detection and treatment of reproductive cancers. Mr. Severson is CEO of Abaxis. He brings to the CytoCore Board an understanding of the challenges and opportunities associated with launching diagnostic products.

11/21/2006—Named Dr. Augusto Ocana (biography on page 12) as its new CEO and driver behind the Company's line of early testing and treatment products for cervical, uterine, and endometrial cancers. Following a global search, Dr. Ocana was chosen for his experience with the U.S. and international pharmaceutical and medical device industries. Over a 20-year career leading both start-up and mature multi-million dollar companies, Dr. Ocana has developed a special expertise in the area of market distribution, as well as in strategic partnering, financing, and business development.

11/20/2006—Announced financial results for the third quarter ended September 30, 2006. The Company recorded a third quarter loss of \$1.325 million or (\$0.00) per share versus a loss of \$308,000 or (\$0.00) per share during the same quarter ended September 30, 2005. For the nine-month period ending September 30, 2006, the Company reported an operating loss of \$3.341 million versus a loss of \$1.082 million for the period ended September 30, 2005. After interest, preferred dividends, and one-time, non-recurring, non-cash charges, the Company incurred a net loss of \$5.677 million or (\$0.03) per share for the nine-month period ended September 30, 2006.

10/12/2006—Announced that Dr. Gorodeski has identified the unique protein P2X₇ biomarker as a highly accurate early indicator of uterine, endometrial, and cervical cancer, as reported in the October 2006 issue of the American Association for Cancer Research (AACR) journal, *Cancer Epidemiology Biomarkers & Prevention*.

10/12/2006—Announced plans to begin trials for a quick, accurate, inexpensive screening test for endometrial and uterine cancers using a specialized computer-guided image recognition microscope system and the new P2X₇ genetic biomarker to identify precancerous cell changes.

10/04/2006—Announced that the Company has engaged a public relations firm, SIPR LLC (www.sipr.com), to help platform and launch a reliable and cost-effective early detection test for uterine/endometrial cancers. SIPR's strategic campaign experience is expected to advance CytoCore's product portfolio, which includes the e² Collector™ and the new InPath™ System, which incorporates a highly accurate cancer scan designed to prevent deaths through early diagnosis of the more than 40,000 cases of uterine cancer reported every year. With an estimated price of \$100 per test, the Company expects that many millions of women could eventually incorporate uterine screening in their regular preventative healthcare routine.

09/19/2006—Announced that the Company has engaged two manufacturing firms in the Chicago Midwest area to begin the process of development for the e² Collector™. The Company expects to have production units of the e² Collector™ delivered and ready for sale in the first quarter 2007. The two manufacturers responsible for the development of the e² Collector™ are Plas-Tech Engineering (Lake Geneva, Wisconsin), producing the e² Collector™ handle, and ATP Rubber and Plastics (Elk Horn, Wisconsin), producing the disposable balloon apparatus. Both companies have been involved with CytoCore for a number of years in early development and prototyping of the e² Collector™.

09/13/2006—Announced that Dr. Gorodeski's abstract of his recent paper, "The P2X₇ Receptor: A Novel Biomarker of Uterine Epithelial Cancers," was presented at the 2006 AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development on September 13, 2006, in Chicago, Illinois.

08/28/2006—Announced that the Company secured \$4 million in new equity financing during the quarter ended June 30, 2006. The Company has neared completion of its financial restructuring and prepared for clinical trials and manufacturing. The financing has permitted the Company to settle most of its legal claims and a majority of its significant liabilities, to move forward aggressively with two new clinical trials, and to prepare the e² Collector™ for manufacturing. The majority of CytoCore's future cash resources is to be devoted to clinical operations and the development and marketing of its products. The Company's clinical projects include basic research at Dr. Gorodeski's laboratory with the P2X₇ biomarker and its capabilities, and the launching of two short clinical trials this fall that are expected to be completed by the year's end.

08/21/2006—Reported a loss of (\$0.01) per share for the quarter ended June 30, 2006, and a loss of (\$0.02) per share for the six months ended June 30, 2006. The Company continued its progress toward successfully restructuring its financial position as it increased its cash balance to \$2.1 million through the sale of equity, reduced stockholders' deficit by 54% or \$5.3 million through the conversion of debt to equity, and reduced liabilities by 34% or \$3.5 million by payment and settlement of accounts payable and accrued liabilities. The Company raised approximately \$4.9 million in new funding through the sale of equity and converted \$6.2 million of Notes with accrued interest and Preferred Stock into equity. This was accomplished while CytoCore restarted clinical research operations, moved the e² Collector™ toward manufacturing, and organized two clinical trials set to begin this fall.

08/17/2006—Announced that the Company, formerly listed on the Over-the-Counter Bulletin Board (OTC.BB) market as MCDG.OB, has changed its ticker symbol to CYCR.OB to finalize the process of changing its name to CytoCore, Inc. and has launched its new website, www.cytocoreinc.com.

08/04/2006—Announced that Dr. Gorodeski had his most recent paper on the P2X₇ biomarker, "The P2X₇ Receptor: A Novel Biomarker of Uterine Epithelial Cancers," accepted for publication by the AACR's journal, *Cancer Epidemiology Biomarkers & Prevention*. The article was published in the October issue



and is available online at www.cebpaacrjournals.org/. The paper discusses the clinical aspects of the P2X₇ as a marker for uterine epithelial cancers.

07/24/2006—Announced the development of the InPath™ System, a cervical/uterine cancer screening and treatment system that can provide a rapid answer and reassurance to women who test negative and equip physicians with the ability to advise additional treatment in cases of a suspected positive result. CytoCore has received approval from the FDA to sell the first of the Company's products from the InPath™ System—the e² Collector™. Testing is to begin on InPath™ System products in the fall.

07/17/2006—Announced that CytoCore has engaged Beaufort Advisors LLC as its FDA regulatory consultants.

07/06/2006—Announced that it had signed an agreement with MMI Associates, Inc. for public relations, media relations, and product marketing support, as well as to increase brand recognition regarding CytoCore's newest products for cervical and uterine cancer screening.

06/22/2006—Announced the following results from its annual shareholders meeting held on Friday, June 16, 2006. First, shareholders voted to officially change the name of the Company to CytoCore, Inc. The name change application is being submitted to the state registrar where CytoCore is incorporated. Following the state's acceptance of the name change, the Company applied to NASDAQ for a change in the Company's stock symbol. Second, the Board of Directors was elected to serve another term.

06/12/2006—Announced in its first quarter financials that interest expense was reduced by 59% from \$401,000 in the first quarter 2005 to \$164,000 for the first quarter 2006. Preferred dividends were reduced by 100% from \$225,000 in the first quarter 2005 to \$0 in the first quarter 2006. These results reflect continued improvement in the capital structure of the Company. The first quarter 2006 results reflect expenses associated with the Company's agreement with Dr. Gorodeski and UHCMC to begin the product research work and associated trials. There were legal costs associated with ongoing arbitration against a former chairman and CEO, Peter Gombrich. CytoCore reported a loss of (\$0.01) per share for the first quarter ended March 31, 2006.

05/17/2006—Announced that a large European institutional investor in CytoCore, Monsun AS, chose to convert its Note into equity in CytoCore. The conversion eliminates a substantial amount of debt in the Company's restructuring and cleanup work and helps strengthen its balance sheet.

05/04/2006—Announced that Dr. Gorodeski presented two papers on the P2X₇, the unique apoptotic biomarker he discovered and licensed to CytoCore, at the 8th International Symposium on Adenosine and Adenine Nucleotides in Ferrara, Italy, the last weekend in May.

05/01/2006—Announced that the first paper on the workings of the P2X₇ biomarker submitted by Dr. Gorodeski was accepted for publication by *The Journal of Biological Chemistry*. The full paper can be found at <http://www.jbc.org/cgi/reprint/M602999200v1>.

04/27/2006—Announced the addition of Jorge A. Leon, Ph.D. (biography on page 15) to the Scientific-Medical Advisory Board and his company, Leomics Associates, Inc., a consulting company developing diagnostic strategies for companies wanting to enter the diagnostics space, as consultants to CytoCore.

04/25/2006—Announced that Dr. Gorodeski assumed the role of both lead research scientist and head of the Company's Scientific-Medical Advisory Board. Dr. Gorodeski is a gynecologist and reproductive endocrinologist in the Department of Obstetrics and Gynecology at UHCMC, and professor of reproductive biology, oncology, physiology, and biophysics at CASE.

04/19/2006—Announced that the Company is to hold its annual shareholders meeting at the Hyatt Regency Embarcadero Center in San Francisco, California, at 10 a.m. PDT on Friday, June 16, 2006.

04/17/2006—Announced year end 2005 and fourth quarter 2005 financial results and operating highlights. The Company continued to increase its positive financial momentum with improvement in operating results along with the recent announcement of new equity capital to provide for the launch and development of new products.

04/11/2006—Announced that it has secured an excess of \$1 million in new equity financing from institutional sources through the issuance of Common Stock at current market prices. The funding is intended to be used to immediately implement key aspects of the Company's product development plans, including hiring key personnel for its research laboratory with Dr. Gorodeski and its product development laboratory with the Automated Image Proteomic System (AIPS) project in Chicago, Illinois, putting the e² Collector™ into manufacturing development, and bringing together resources and people to develop the strategic distribution strategy for the e² Collector™.

03/30/2006—Announced that Steven Waggoner, M.D. (biography on page 15), joined the Company's Scientific-Medical Advisory Board. Dr. Waggoner is to assist Dr. Gorodeski and the Company's research teams in the development, activation, conduct, and analysis of clinical trials designed to test the accuracy and practicality of the Cocktail-CVX™/GCI assays, the Endometrial Cancer Scan, and the Drug Delivery System (DDS).

03/22/2006—Announced that with its recent product licenses, CytoCore has assembled four product components altogether called the InPath™ System NG, a unique and complete system to address the various aspects of the traditional Pap test. The four components are the e² Collector™, the Cocktail-CVX™/GCI assays, the AIPS automated microscopy platform, and a new DDS. Each product is an enhancement or upgrade to the current methods being used with the Pap test today.

02/23/2006—Announced that it licensed a new DDS developed by physician Dr. Gorodeski from UHCMC. This DDS could, for the first time, give physicians the ability to apply FDA-approved drugs to existing cervical lesions. The Company anticipates entering trials on this product before the end of the year.

02/17/2006—Announced that it has licensed a new cancer biomarker from Dr. Gorodeski, the inventor, and UHCMC. The new biomarker, labeled CGI5 (P2X₇), is unique among the few apoptosis markers that were found in preliminary experiments to distinguish precancerous and cancer cells from the corresponding normal cells. CytoCore's CGI5 (P2X₇) biomarker tracks the changes in the dying or apoptotic process, and initial laboratory results have produced excellent sensitivity and specificity (measures of biomarker accuracy) in testing for both cervical and endometrial cancers.

02/13/2006—Announced the signing of a technology transfer agreement between itself and UHCMC, CASE, and Dr. Gorodeski. With this agreement, CytoCore is expanding and strengthening its partnership with these two organizations, which together form a world-class medical teaching and research partnership.

02/09/2006—Announced that CytoCore intends to open a research facility within UHCMC's Center for Clinical Research. The research at UHCMC will likely focus on clinical applications developed at UHCMC for the identification and treatment of certain gynecological disorders including cervical dysplasia and cervical cancer.

02/06/2006—Announced that the Company is changing its name to CytoCore, Inc. The Company's Board approved the name change during the January Board meeting. The Company will be "doing business as" CytoCore, Inc. until the name is officially ratified by a vote of the shareholders at the annual shareholders meeting in June 2006.



Glossary

510(K)—Section 510(k) of the Food, Drug and Cosmetic Act requires device manufacturers who must register to notify the FDA, at least 90 days in advance of their intent to market a medical device. This is known as Premarket Notification—also called PMN or 510(k). This allows the FDA to determine whether the device is equivalent to a device already placed into one of the three classification categories. Thus, “new” devices (not in commercial distribution before May 28, 1976) can be properly identified.

Acquired Immune Deficiency Syndrome (AIDS)—The late stage of human immunodeficiency virus (HIV), which kills or impairs cells of the immune system and progressively destroys the body’s ability to fight infections and certain cancers. HIV is most commonly spread by sexual contact with an infected partner.

Adenocarcinoma—Cancer that begins in cells that line certain internal organs that have glandular (secretory) properties.

Analyte Specific Reagents (ASRs)—Antibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reaction with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens. The majority of ASRs are exempt from FDA approval or clearance, and manufacturers of ASRs are prohibited from making claims of analytical or clinical performance.

Anemia—A shortage of red blood cells that causes symptoms of fatigue, weakness, pallor, and shortness of breath. Approximately two-thirds of cancer patients undergoing chemotherapy become anemic as chemotherapy or radiotherapy treatments often result in a decrease of erythrocytes in the general circulation.

Apoptosis—Programmed cell death; this physiological process is necessary for the elimination of superfluous, diseased, or damaged cells and the formation of new cells.

Assay—A biological test, measurement, or analysis to determine whether compounds have the desired effect either in a living organism, outside an organism, or in an artificial environment.

Benign—Noncancerous or not malignant. Benign tumors do not invade surrounding tissue or spread throughout the body, but rather stay in a localized area. Benign tumors do, however, have the capacity to grow.

Bethesda System—Classifications and terminology used by laboratories and doctors to describe the results of Pap tests.

Bilateral salpingo-oophorectomy—Surgery to remove both ovaries and both fallopian tubes.

Biomarker—A substance sometimes found in the blood, other body fluids, or tissues that can be used to assess the presence of cancer. Some biomarkers are up-regulated (increased), and some can be down-regulated (diminished).

Cancer—A term for diseases in which abnormal cells divide without control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body.

Cervical cancer—Cancer that occurs when abnormal cells in a woman’s cervix—the lowest part of the uterus (womb) through which babies pass when they are born—divide and grow out of control.

Chemotherapy—Treatment with drugs that kill cancer cells.

Clear cell adenocarcinoma—A rare type of tumor, usually of the female genital tract, in which the inside of the cells look clear when viewed under a microscope. Also called clear cell carcinoma and mesonephroma.

Clinical Laboratory Improvement Amendment (CLIA)—A program set up by the Centers for Medicare and Medicaid Services (CMS) to set minimum standards for all laboratories to follow and to determine if laboratories are achieving those standards.

Colposcopy—Examination of the vaginal and cervical epithelia by means of a colposcope.

Complex atypical hyperplasia—Characterized by crowded glands showing cellular stratification, piling of epithelium into tufts, and atypia in the form of enlarged, pleomorphic, and hyperchromatic nuclei and prominent nucleoli.

Cone biopsy—The removal, under general anesthetic, of a cone-shaped section of the cervix so that the tissue can be examined in a laboratory. The same procedure is used as a treatment in some cases.

Cryosurgery—A surgical procedure that uses extreme cold to destroy abnormal tissue by freezing. A general anesthetic is not required.

Current procedural terminology (CPT) code—The official coding system for physicians to report their professional services and procedures to third parties for payment. It is produced and maintained by the American Medical Association.

Cytokeratin-18 (CK-18)—Cytokeratin is the generic name for the intermediate filament proteins of epithelial cells.

Cytology—The study of cells taken as samples during procedures such as a Pap smear.

Cytomegalovirus (CMV)—A type of virus which can cause unapparent infections in healthy individuals but is dangerous to immunosuppressed patients. CMV is a member of the herpes family of viruses. The virus may manifest itself as pneumonia, colitis, or hepatitis.

Dengue fever—A serious infectious disease caused by a virus carried by *Aedes aegyptii* mosquitoes and most often found in hot climates. Symptoms include rash, fever, headaches, and severe muscle and joint pain.

Deoxyribonucleic acid (DNA)—The genetic material of all living organisms (except for RNA-carrying viruses, such as HIV). DNA is a double-stranded, helical molecular chain found within each cell. DNA contains the information necessary for cells to produce proteins, which enable cells to reproduce and carry out their functions.

Dilatation and curettage (D&C)—A gynecological procedure in which the lining of the uterus (endometrium) is scraped away.

Dimethylsilicone—An oil which may be used as a transport medium for specimens containing anaerobic microorganisms.

Down-Regulated—This term usually denotes proteins or nucleic acids that begin to decline with the cell's impending change to a cancerous state and are absent when cancer is present. The P2X₇ is an example of a down-regulated biomarker.

Dysplasia—Abnormal cells that are not cancer.

Dysplastic—Abnormally developed.

Ectocervix (ectocervical)—The part of the cervix closest to the vagina.



Endocervix (endocervical)—The inner part of the uterine cervix.

Endometrial cancer—Cancer of the uterine lining.

Endometrial hyperplasia—Abnormal thickening of the endometrium caused by excessive cell growth.

Endometrium—The layer of tissue that lines the uterus.

Epidermal growth factor receptor (EGFR)—A protein found on the surface of some breast cancer cells that allows epidermal growth factor to stimulate cell growth. Also called HER-2/neu or c-erb B-2.

Epithelial cancer—A malignant growth containing epithelial cells, also called epithelioma.

Epithelial cells—Cells that cover the surface of the body and line its cavities.

Estrogen—A type of hormone made by the body that helps develop and maintain female sex characteristics and the growth of long bones. Estrogens can also be made in the laboratory. They may be used as a type of birth control and to treat symptoms of menopause, menstrual disorders, osteoporosis, and other disorders.

False negative (FN)—Test result implying a condition does not exist when in fact it does.

False positive—A test result that is read as positive but actually is negative; a test that shows evidence of a disease when it not present.

Fast Track—A designation that the U.S. Food and Drug Administration (FDA) reserves for products intended to treat a serious or life threatening condition and have the potential to address an unmet medical need. The FDA takes appropriate actions to expedite the development and review of the approval applications for fast track products.

Gel electrophoresis—A technique for separating protein molecules of varying sizes in a mixture by moving them through a block of gel, as of agarose or polyacrylamide, by means of an electric field, with smaller molecules moving faster and therefore farther than larger ones.

Hereditary nonpolyposis colon cancer (HNPCC)—An inherited disorder in which affected individuals have a higher-than-normal chance of developing colorectal cancer and certain other types of cancer, often before the age of 50. Also called Lynch syndrome.

Histological—Of or relating to histology, which is the study of cells and tissue on the microscopic level.

Hormone therapy—Treatment that adds, blocks, or removes hormones. For certain conditions (such as diabetes or menopause), hormones are given to adjust low hormone levels. To slow or stop the growth of certain cancers (such as prostate and breast cancer), synthetic hormones or other drugs may be given to block the body's natural hormones. Sometimes surgery is needed to remove the gland that makes a certain hormone. Also called hormonal therapy, hormone treatment, or endocrine therapy.

HPV Types 16 and 18—High-risk forms of the HPV virus, known to add to the possibility of developing cervical cancer.

Human Papillomavirus (HPV)—A member of a family of viruses that can cause abnormal tissue growth (for example, genital warts) and other changes to cells. Infection with certain types of HPV may increase the risk of developing some types of cancer.

Immunofluorescence—Any of various techniques for detecting an antigen or antibody in a sample by coupling its specifically interactive antibody or antigen to a fluorescent compound, mixing with the sample, and observing the reaction under an ultraviolet-light microscope.

Immunostimulant—An agent that stimulates an immune response.

In situ—A Latin term meaning “in place” or not removed.

Invasive cervical cancer—Cancer that has spread from the surface of the cervix to tissue deeper in the cervix or to other parts of the body.

Laser surgery—A surgical procedure that uses the cutting power of a laser beam to make bloodless cuts in tissue or to remove a surface lesion such as a tumor.

Lesions—Any localized, abnormal structural change in the body. Lesions start very small and then progress. The medical community agrees that there are basically five categories of lesions: mild, moderate, high-grade, cancer, and invasive cancer. High-grade lesions must be treated; mild and moderate are up to the physician.

Messenger RNA (mRNA)—A form of RNA that carries the genetic code for a particular protein from the DNA in the cell’s nucleus to a ribosome in the cytoplasm and acts as a template, or pattern, for the formation of that protein.

Mixed carcinoma—The combination of two types of cancers, such as adenocarcinoma (epithelial cancer) and sarcoma (mesenchymal cancer).

Neoplastic—Pertaining to the neoplasia process; the formation of new cell types with atypical features and uncontrolled growth as in neoplasms (cancers).

Neutropenia—Marked by the deficiency of neutrophils, a type of white blood cell that kills microorganisms through phagocytosis.

Non-invasive cervical cancer—Cancer where the abnormal cells are limited to the surface of the cervix.

Ovary—One of a pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus.

Pap test—A procedure in which cells are scraped from the cervix for examination under a microscope. It is used to detect cancer and changes that may lead to cancer. A Pap test can also show noncancerous conditions, such as infection or inflammation. Also called a Pap smear.

Papillary serous adenocarcinoma—A rare mullerian tumor type that is histologically similar to ovarian serous carcinoma. Distinguished from clear cell carcinoma by the absence of a clear cell component, its appearance is suggestive of ovarian carcinoma, and the tumor cells are supported on thin, fibrovascular cores forming delicate papillary fronds.

Pelvic exenteration—Surgery to remove the lower colon, rectum, and bladder, and create openings (stomata) through which urine and stool are passed out of the body. In women, the cervix, vagina, ovaries, and nearby lymph nodes are also removed.

Pelvic lymph node dissection—Removal of some lymph nodes from the pelvis.

Point-of-service (POS)—A business or place where a product or service can be obtained.

Proteomics—The large-scale study of protein, particularly their structures and functions.

Radiation therapy—The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy.



Radical hysterectomy—Surgery to remove the uterus, cervix, and part of the vagina. The ovaries, fallopian tubes, and nearby lymph nodes may also be removed.

Radical trachelectomy—A surgery which removes the cervix, but preserves the uterus.

Ribonucleic Acid (RNA)—A single-stranded molecule composed of chemical building blocks similar to those in DNA. RNA is the sole genetic material of retroviruses and an intermediary in making proteins in all living things.

Ribonucleomics—A new branch of genetics focusing on the study of RNA and its properties.

Sarcoma—A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Sensitivity—A measure of the probability of correctly diagnosing a condition and is calculated as the number of true positive results divided by the number of true positive and false negative results.

Simple hysterectomy—Surgery where at least one ovary is conserved.

Slide-based test—A test where a small sample of cells (such as from the surface of the cervix) is spread onto a glass slide, treated, and read under a microscope. Results are reported if any abnormal cells are found.

Specificity—A measure of the probability of correctly identifying a non-diseased person.

Speculum—A metal or plastic instrument used to widen the vagina slightly so that the cervix can be seen more easily.

Squamous cell carcinoma—Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts.

Tamoxifen—A drug used to treat certain types of breast cancer in women and men. It is also used to prevent breast cancer in women who have had ductal carcinoma *in situ* (abnormal cells in the ducts of the breast) and are at a high risk of developing breast cancer. Tamoxifen is being studied in the treatment of other types of cancer. It blocks the effects of the hormone estrogen in the breast. Tamoxifen belongs to the family of drugs called anti-estrogens. Also called tamoxifen citrate.

Telepathology—The ability to transmit test data via telecommunication from a remote location to cancer hospitals or laboratories around the world for the purposes of diagnosis or consultation.

Tertiary medical center—A medical center which, in addition to providing traditional hospital care, provides training to healthcare providers, performs research, and provides high-level services (such as organ transplantation).

Thrombocytopenia—A decrease in the number of platelets in the blood, potentially resulting in increased bleeding and poor clotting function.

Total hysterectomy—Surgery to remove the entire uterus, including the cervix. Sometimes, the entire cervix is not removed. Also called complete hysterectomy.

Transdermal—Applied to the skin, usually as part of an adhesive patch, for absorption into the bloodstream.

Trastuzumab—A monoclonal antibody used to treat estrogen-receptor positive breast cancer that has spread after treatment with other drugs. It is also being studied in the treatment of other types of cancer. Monoclonal antibodies are made in the laboratory and can locate and bind to cancer cells. Trastuzumab

binds to HER-2, a human epidermal growth factor receptor, and can kill HER-2-positive cancer cells. Also called Herceptin[®] by Genentech.

True positive (TP)—A result or definition that accurately reflects the true status as positive.

Up-Regulated biomarker—This term usually relates to increased expression of certain proteins or nucleic acids, which correlate with rapid cell/tumor growth.

Uterus—The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a baby grows. Also called the womb.



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