Research Note

MDxHealth

Leader in Molecular Diagnostic Solutions for Urologic Cancers

Chief Research Analyst

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Name:	**MDxHealth SA**
Country:	**Belgium**
Price:	**EUR 3.66**
ISIN Code:	**BE0003844611**
Reuters Code:	**MDXH.BR**
Market Cap (AUD m):	**165.2**
EV (AUD m):	**130.1**
Cash & cash eq. (AUD m):	**35.1**
Shares outstanding (m):	**45.2**
Volume:	**105,277**
Free float:	**73%**
52-week Range:	**3.21-5.88**

	2013A	2014A	2015E
Total Revenues	7.554	11.671	18.000
Net (Loss)/Profit	(16.175)	(15.256)	(13.500)
Net loss per share (cents)	(0.54)	(0.44)	(0.31)
R&D costs	4.567	2.376	2.200
Cash increase/(decrease)	8.924	(5.786)	11.103
Cash and marketable sec.	24.683	18.897	30.000

Executive Summary

- MDxHealth is a molecular diagnostics company that develops and commercializes advanced, accurate and scalable molecular diagnostic products to improve the diagnosis of urological cancers. The Company is a market leader in the fast growing field of molecular testing focused on identification of DNA or RNA imprints, which can turn a healthy cell into a cancer cell. MDxHealth has a proven track record of developing and delivering molecular diagnostic assays in the urologic oncology field and a proprietary portfolio of molecular biomarkers and know-how, validated by leading partners.

- MDxHealth's proprietary technology platform is called MSP (Methylation-Specific-PCR), which is a proprietary DNA-based technology that functions on standard commercial PCR equipment. MSP is extremely powerful and accurate with the ability to detect a single cancer cell among 10,000 healthy cells in any type of bodily fluid or tissue.

- The main commercial focus of the Company is on urologic cancers, including prostate and bladder cancer, and it currently commercializes its proprietary ConfirmMDx® for Prostate Cancer test on the U.S. market and SelectMDx™ for Prostate Cancer on the European market. To date, over 35,000 ConfirmMDx® tests have been ordered by approximately 2,500 US urologists since its launch in mid-2012. MDxHealth markets the ConfirmMDx test in the US via its direct sales force, which has grown to 33 representatives, and via co-marketing agreements with national urology-focused laboratories including Bostwick and Miraca.

- For other cancer types, the Company has established licensing agreements to commercialize its molecular diagnostic technologies, e.g. with the launches of Cologuard® for colon cancer by licensee Exact Sciences and PredictMDx® for

Glioblastoma by licensee Laboratory Corporation of America (Labcorp). We especially feel that these license agreements offer rather low risk cash flow stream for MDxHealth, and the market considers the prospect for successful commercialization of Cologuard® to be very high. Partner Exact Sciences in its 10Q statement of October30 2015, estimates its US market at USD 2 billion and its global market opportunity to be greater than USD 3 billion, well above the USD 1 billion considered by analysts. As it represents a rather low risk cash flow stream for MDxHealth, the market may underestimate the true value of the Cologuard® royalty stream for MDxHealth.

- Recently the company acquired the privately held Dutch molecular diagnostics company NovioGendix for a price of USD 8.8 million. The acquisition strengthened MDxHealth's position in uro-oncology and provides the Company access to the fast growing market for liquid biopsies with a CE-marked non-invasive urine test for prostate cancer. In November 2015, the test was launched as SelectMDx™ for Prostate Cancer in the Benelux region and it will be launched as an IVD kit on the European market in early 2016. MDxHealth also plans to launch SelectMDx as a laboratory developed test (LDT) on the US market in 2016. Besides, NovioGendix brings a range of diagnostic tests for prostate, bladder, kidney and other urologic cancers in various stages of development to MDxHealth.

- The Company's current cash position is EUR 35 million, after it raised USD 31 million in June 2015. Revenues for the first nine months of 2015 grew 44% to USD 11.9 million, primarily due to an increase in ConfirmMDx® test sales. Based on the company's guidance for 2015 projected revenues of USD16-20 million, we estimate full year revenues of USD 18 million, including increasing royalty amounts from Exact Sciences on its Cologuard® test. Our forecasts reflect an outlook for a strong increase in sales

volume and an ongoing high reimbursement rate for Cologuard for 2016 (USD 484). We expect ongoing strong sales if Cologuard® will be in the finalized screening guidelines.

- Based on NPV based valuation, we believe that MDxHealth is substantially undervalued at the current share price of EUR 3.66. Using our valuation model and taking into account the future revenues of ConfirmMDx®, SelectMDx® and the growing income from royalties derived from its out-licensed products, the company's current total value should be EUR 350 million, or EUR 7.95 per share. This represents a substantial upside from the current share price.

Company Profile & Technology

MDxHealth is a multinational healthcare company that provides actionable epigenetic and molecular information to personalize the diagnosis and treatment of cancer. The company's tests are based on proprietary gene methylation (epigenetic) technology and assist physicians with the diagnosis of cancer, prognosis of recurrence risk, and prediction of response to a specific therapy. The term epigenetics refers to heritable changes in gene expression (active versus inactive genes) that does not involve changes to the underlying DNA sequence; a change in phenotype without a change in genotype. Epigenetic change is a regular and natural occurrence but can also be influenced by several factors including age, the environment/lifestyle, and disease state. Epigenetic modifications can manifest as commonly as the manner in which cells terminally differentiate to end up as skin cells, liver cells, brain cells, etc. Or, epigenetic change can have more damaging effects that can result in diseases like cancer. At least three systems including DNA methylation, histone modification and non-coding RNA (ncRNA)-associated gene silencing are currently considered to initiate and sustain epigenetic change.

MDxHealth's ConfirmMDx® for Prostate Cancer was launched mid-2012 and has enjoyed increasing commercial uptake. ConfirmMDx has been shown to help distinguish patients who have a true negative biopsy from those who may have undetected cancer, thereby helping to reduce unnecessary repeat biopsies. To date, over 35,000 ConfirmMDx tests have been ordered by approximately 2,500 urologists since launch. The final Medicare LCD for coverage of ConfirmMDx became effective in November 2014 with a reimbursement price of USD 2,030.

Business Strategy: Focus on Urologic Cancers, successfully out-licensing others

Over the past several years, MDxHealth has built a proprietary portfolio of hundreds of epigenetic biomarkers and related expertise. Its focus is on urologic cancers, namely prostate, bladder, and kidney. The Company's lead product is the ConfirmMDx® for Prostate Cancer test which has been validated to help prevent unnecessary invasive repeat prostate biopsies on prostate cancer-free men, while also helping to identify men at increased risk for aggressive disease who may benefit from early detection and treatment. The Company's second marketed product is its non-invasive liquid biopsy SelectMDx™ for Prostate Cancer test, which the company obtained via its acquisition of NovioGendix. On page 12 we elaborate further on the liquid biopsy test. In bladder cancer, MDxHealth has developed an epigenetic assay named AssureMDx™ for Bladder Cancer that helps identify patients at risk for bladder cancer. MDxHealth will offer the AssureMDx test, a urine-based liquid based biopsy test, as a Laboratory Developed Test (LDT) on the US market, and as a CE-marked IVD kit in Europe. The Company plans to launch the AssureMDx LDT service test by the end of 2016 in the US.

For cancer outside of its urologic focus, the Company's strategy is to partner or out-license the commercialization of biomarkers and technologies. So far, MDxHealth has addressed the following key cancer types:

- **Colon:** In 2010, MDxHealth entered into an exclusive licensing agreement with Exact Sciences Corporation for stool-based screening of colorectal cancer. Under the terms of the agreement, Exact Sciences obtained exclusive, worldwide rights to use MDxHealth's NDRG biomarker in stool-based detection of colorectal cancer, as well as non-exclusive access to MDxHealth's MSP platform technology for use with those biomarkers. Exact Sciences has obtained FDA approval and CMS coverage, and launched its Cologuard® test in H2 2014. With the 2015Q3 figures, Exact Sciences published that is it has sold for

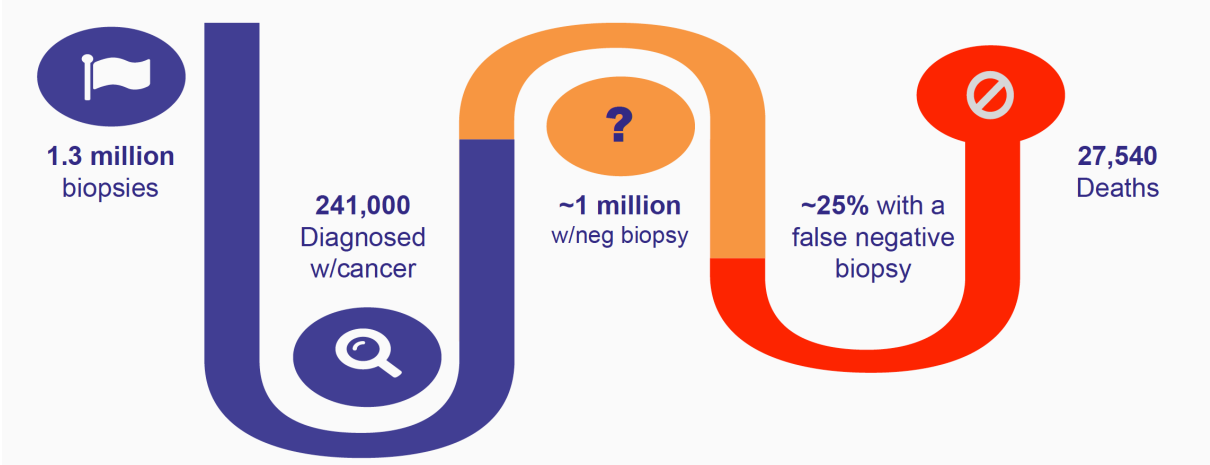
around USD 25 million in 2015 year-to-date. We expect a strong fourth quarter, with total revenues near USD 50 million. MDxHealth receives a low to mid single digit royalty on sales of Cologuard.

- **Brain:** MDxHealth holds exclusive rights to the MGMT biomarker, which has been extensively studied in glioblastoma and related brain cancers. Studies on thousands of clinical trial patients have demonstrated that methylation of MGMT can help oncologists identify newly diagnosed glioblastoma patients that are likely to respond to the most commonly used class of brain cancer drugs (alkylating agents). MDxHealth's PredictMDx® for Glioblastoma (MGMT) test was included in the 2013 National Comprehensive Cancer Network (NCCN) Senior Adult Oncology Guidelines and has been awarded a Tier 1 reimbursement code, 81287, by American Medical Association (AMA), which provides a clear basis for comprehensive reimbursement. MDxHealth's strategy has been to partner with leading pathology service providers, such as the Laboratory Corporation of America (LabCorp) in the US, Teva Pharmaceutical Industries in Israel, and HistoGeneX in Belgium, to distribute the MGMT test to clinicians.

- **Cervical:** In 2014, MDxHealth granted oncgnostics GmbH of Jena, Germany, a limited, non-transferable, non-exclusive, worldwide license for its patented methylation specific PCR (MSP) technology for diagnostic applications in cervical cancer. In return, MDxHealth will receive upfront and milestone payments, and royalties on net sales. oncgnostics will utilize MDxHealth's epigenetic technology for the accurate and sensitive assessment of DNA methylation markers included in its GynTect® test, which is intended for the early detection of cervical neoplasias that may progress to cancer.

Prostate Cancer: High unmet clinical need

Prostate cancer is globally recognised as the greatest unmet clinical need for men over 40. A number of compelling clinical factors make it imperative to improve the diagnostic toolset. Prostate cancer is now viewed as not one disease, but a spectrum of diseases. It presents in many different forms, its onset controlled by small genetic changes, which may vary from male to male. The disease spectrum ranges from non-life threatening (indolent) forms to life threatening illnesses, with variations occurring because genetic differences between individuals make for differences in their cancers. Since 1990 treatment has relied on the Prostate-Specific Antigen (PSA) test, biopsies and Gleason scores to diagnose and stage prostate cancers. The global market for the PSA test is currently in excess of 100 million tests per annum. However, the PSA screening test has been roundly criticised by medical opinion leaders as flawed, inconclusive and even dangerous. Approximately 70-75% of men diagnosed with prostate cancer through PSA screening have an indolent form of prostate cancer, which needs no treatment, and 25-30% have life-threatening illnesses, which require treatment.

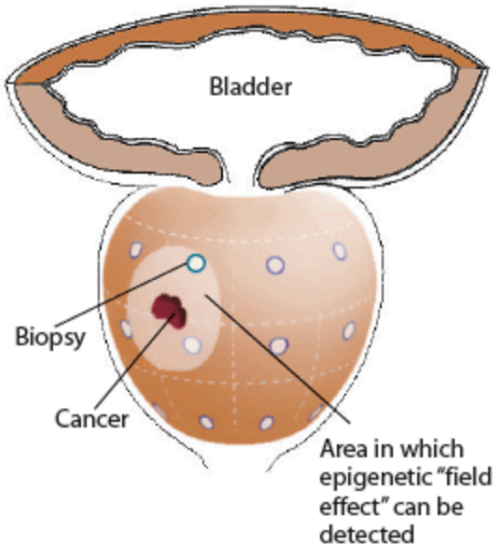


Source: MDxHealth

Annually, there are approximately 30 million men screened by the PSA test resulting in approximately 4.5 million abnormal PSA test results (>4.0) leading to over 1.3 million biopsy procedures, of which 240,000 are diagnosed with prostate cancer with 28,000 annual deaths.[1] Approximately USD 4.4 billion is spent annually on screening, diagnosing and staging and an additional USD 9.9 billion is spent annually on treatment of these patients, totaling nearly USD 15 billion being spent annually on prostate cancer in the US alone. Annually, over USD 4 billion is spent on pharmaceuticals for prostate cancer, which is expected to increase to USD 8.7 billion by 2019.[1]

Over 975,000 American men are diagnosed with a negative prostate biopsy each year; however approximately 25% of those men receive false-negative results. Under the current standard of care, prostate biopsy procedures consisting of 10-12 needle biopsy cores only sample approximately 1% of a man's prostate. This approach leaves men at risk of undetected cancer, leading to a high rate of repeat biopsies, even on cancer-free men. There is an unmet medical need for a clinically effective diagnostic test to address this dilemma. ConfirmMDx® for Prostate Cancer is able to detect an epigenetic field effect or "halo" associated with the cancerization process at the DNA level. This "halo" around a cancer lesion can be present despite cells having a normal appearance under the microscope. Thus, ConfirmMDx aids urologists in identifying truly negative men who may forego an unnecessary repeat biopsy procedure. Performance of the proprietary ConfirmMDx genes and technology has been published in 45 studies on over 5,000 patients tested. The ConfirmMDx test has qualified for Medicare reimbursement as of November 3, 2014 and is also available to more than 152 million insured lives via private health insurance plans. To date over 35,000 ConfirmMDx tests have been ordered by approximately 2,500 urologists since launch in 2012.

[1]Aubry et al; Budget Impact Model-Epigenetic Assay Can Help Avoid Unnecessary Repeated Prostate Biopsies and Reduce Healthcare Spending, American Health and Drug Benefits 2013



ConfirmMDx® for Prostate cancer is instrumental to distinguish men with a true negative biopsy from those men that may have undetected cancer missed in a previous biopsy. It provides urologists with information to take action on by firstly ruling out cancer free men from undergoing unnecessary repeat biopsies and screening procedures and secondly ruling in high risk men with a previous negative biopsy result who may be harboring undetected cancer. These men would benefit from a repeat biopsy and treatment. ConfirmMDx is an assay that consists of three biomarkers that detects the level of methylation in three separate genes (GSTP1, APC and RASSF1) that are associated with the presence of prostate cancer cells. GSTP1 is the most studied epigenetic biomarker associated with prostate cancer diagnosis due to its high sensitivity and specificity. Methylation of APC and RASSF1 genes are often found in prostate cancer and have demonstrated a field effect, aiding in the identification of biopsies with false negative histopathological results.

Liquid Biopsy: The new "holy grail" in diagnostics

Liquid biopsy tests are gaining traction within the industry as a viable alternative to traditional screening methods for cancer. Although liquid biopsy applications are still in their early days, the potential uses for the technology is expected to grow quickly in the next few years. The SelectMDx™ test was designed to address an unmet need in the identification of men at risk for prostate cancer and importantly, the stratification of patients at risk for potentially lethal high-grade prostate cancer compared to those with low-grade cancer. In clinical studies, SelectMDx has been shown to outperform the existing PCA3 assay, improving the information available to urologists seeking to further reduce unnecessary invasive biopsy procedures.

Liquid biopsy technology has a lot of potential applications and study results have shown promise for these new testing options. A liquid test could provide a less-expensive and less-invasive way to monitor patients throughout treatment, help individuals avoid additional surgeries and help clinicians make better decisions about which drugs are the best fit for patients. The total market for liquid biopsies is estimated to be more than USD 32 billion, with oncology applications taking more than USD 28 billion. Within oncology, early cancer detection would be the largest opportunity with a expected market size of USD 15 billion based on USD 300 per test and 50 million people eligible for testing yearly. Oncologists would then employ such liquid biopsy tests to patients with clinical risk factors for cancer and could potentially expand utilisation with lower risk populations over time.

Liquid biopsies are already commercially available for therapy selection and treatment monitoring with an increasing number of laboratories launching cancer recurrence monitoring tests in the near future. To date, MDxHealth has entered into an agreement with Dutch based DDL Diagnostic Laboratory for SelectMDx. DDL has been the largest service provider of the existing prostate cancer PCA3 test in the Netherlands, and recently announced its decision to discontinue processing of the PCA3 assay.

As a result, MDxHealth anticipates that it will be the principal provider of urine-based prostate cancer testing for patients with elevated PSA levels in the Netherlands. The novel biomarkers that make up SelectMDx™ were discovered by Prof. Dr. Jack Schalken, original developer of the PCA3 assay.

Assay Characteristics	SelectMDx for Prostate Cancer	PROGENSA PCA3
Company	MDxHealth	Hologic
Specimen	Urine	Urine
Assay Characteristics	qPCR Assay	mRNA PCR
	2 mRNA Biomarkers	1 Biomarker
	DLX1, HOXC6	PCA3
Regulatory	LDT/CLIA/CE	FDA/CE
PCR Instrument	All open PCR instruments	Only of DTS from Hologic
List price ($)	$500	$500
Assay Performance (AUC)	AUC 0.90	AUC 0.65
Comments	Indicates risk for high grade cancer	Indicates risk for cancer (any grade)

In clinical studies, SelectMDx has been shown to outperform PCA3 in the identification of men at increased risk for aggressive prostate cancer, thereby improving the information available to urologists deciding on the need for a prostate biopsy while also aiding to identify men a sufficiently low risk for prostate cancer who may avoid unnecessary invasive biopsy procedures. See also the table above.

Concurrent to SelectMDx, the Company is developing the urine based liquid biopsy test AssureMDx for Bladder Cancer. It has entered into a license and collaboration agreement with Erasmus University Medical Center Rotterdam (Erasmus MC) in The Netherlands.

AssureMDx is being validated in a, multi-center, two-arm, prospective randomized clinical trial financed by by three organisations, including Erasmus MC. A total 435 patients will be enrolled into this trial (2,000 urine samples). The study is designed to assess the test's ability to safely reduce the number of invasive cystoscopies performed during follow-up of patients with NMIBC with a low/intermediate risk of recurrence or progression. The study will also examine whether the addition of urine tests to follow-up of patients with higher risk of recurrence and progression leads to earlier detection of potentially dangerous recurrences. All urine samples will be tested using AssureMDx assay. Earlier this year, MDxHealth already announced positive topline data on its biopsy test for bladder cancer. In a cohort of 154 patients with hematuria, shown that the company's liquid biopsy urine test for bladder cancer had a negative predictive value (NPV) of 98.3%. The will be offered as an LDT service on the US market and a CE-marked IVD kit in Europe.

Analyst: Marcel Wijma MSc

Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.