PRIVATE COMPANY PROFILE:

METABOLON

MOLECULAR DIAGNOSTICS FOR THE MASSES

Research 2.0
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Stephen Waite
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OVERVIEW

Nano-enabled healthcare technology is finally entering the mainstream of commercial healthcare technology. Nanotech penetration of therapeutics and diagnostics is still relatively small today at around 15%, or $70 billion. However, in the decade ahead, as nano-enabled medicine and healthcare commercialization ramps up, we are likely to see that share rise sharply to 50% or more.[1]

Diagnostics is one area of healthcare that is ripe for technology disruption, as Clayton Christensen notes in his book, *The Innovator's Prescription*. "The technologies that enable precise diagnosis and subsequently predictably effective therapy," says Christensen, "are those that have the potential to transform healthcare through disruption." Such is the promise of nano-enabled diagnostic technology.

One of the companies pioneering advances in molecular diagnostics is Metabolon. Based in The Research Triangle and led by a talented and experienced management team that includes co-founder and CEO John Ryals, privately-held Metabolon is developing mechanism-based molecular diagnostics and providing broad service business solutions based on its innovative biochemical profiling technology. Founded in 2003 and having raised $32 million in venture capital to date from investors, including H&H, Metabolon is building a scalable services business based around metabolomics and is in the early stages of launching an innovative and potentially lucrative molecular diagnostic business.

B2B METABOLOMICS

To date, Metabolon's primary source of revenue generation has come from a B2B service model based on metabolomics. Metabolomics is the systematic study of the unique chemical fingerprints that particular cellular processes leave behind – specifically, the study of their small-molecule metabolite profiles. The metabolome represents the collection of all metabolites in a biological cell, tissue, organ or organism, which are the end products of cellular processes. Unlike RNA gene expression data and proteomic analanalyses, which do not tell the whole story of what might be happening in a cell, metabolic profiling can give an instantaneous snapshot of the physiology of that cell.

There are about 2,400 small molecules in the human body, compared with about 25,000 genes and tens of thousands of proteins. Using proprietary software in conjunction with mass spectrometry instruments, Metabolon extracts small molecules out of samples and then processes the information contained within them. The emerging field of metabolomics is benefitting significantly from the expanding availability of user-friendly and affordable mass spec instruments.

Metabolon is leveraging the increasing power of mass spectrometry instruments and developing innovative software to advance the field of metabolomics. Mass spec instruments are critical to metabolomics, but Metabolon's secret sauce lies in its proprietary data processing software. The company has a growing patent portfolio – over 100 patents filed and 17 granted – that includes data analysis and software patents that cover critical aspects of its metabolomics platform. In addition, Metabolon has pending patents directed to small molecule biomarkers related to drug action, toxicity, carcinogens, aging and numerous diseases and disorders.

This software allows for the extraction of relevant small molecule information in processes that typically produce massive amounts of noise – on the order of 90%. Think of pulling the proverbial needle out of a haystack and you can appreciate the sophistication of the software.

Metabolon is employing metabolomics investigations to clarify the mechanism of action of several new

[1] See Mihail C. Roco, The Long View of Nanotechnology Development: The NNI at 10 Years. http://www.wtec.org/nano2/docs/ChaptersPdf/Ch0_2_LTV_10-1121.pdf

compounds. The company is using its metabolomics platform technology in a range of studies, including following the global effects of disease processes on metabolism with the aim of uncovering new biomarkers.

The discovery of new biomarkers through Metabolon's metabolmics platform technology has fostered the development of its B2B service model. The company has over 275 clients today that include many of the major pharmaceutical, biotechnology, nutritional and consumer product companies as well as universities. Customers use Metabolon's technology to create innovative products and enhance or reengineer existing products. Employing Metabolon's technology, customers can solve complex problems in a matter of weeks that previously would have taken months, if not years.

Metabolon's B2B service business is cash flow positive and has been growing at a healthy clip over the past several years. It generated $14 million in revenues last year and some 90% of the business is repeat business from existing customers. The B2B service has given Metabolon a solid foundation to expand its operations and seek out new business opportunities. A major opportunity for the company lies in the area of healthcare diagnostics, which we will explore in the next section.

DISRUPTIVE DIAGNOSTICS

There is a paradigm shift occurring in the field of clinical diagnostics in which high-resolution biochemical characterization of body fluids, by targeted metabolomics, is being used to assist the development of function-oriented diagnostics, moving from expensive immunoassays to cheaper, more specific, and more accurate mass spec assays. These new diagnostics are much more than just a positive or negative test for the condition. They also allow detailed subtyping and staging, which will direct personalized therapeutic regimens.

Metabolon is in the early stages of building out a molecular diagnostics business based on its metabolomics platform technology. Metabolon's diagnostics technology seeks to address some large markets where there are currently unmet needs, including insulin resistance and cancer.

Insulin resistance is the number one health problem in the world, affecting some 800 million people. Insulin is a hormone that regulates blood sugar in the body. After a meal, the pancreas produces insulin to move glucose from the blood into cells for fuel. People with type 2 diabetes either do not secrete enough insulin or their cells are resistant to its effects. The body's resistance to insulin is a precursor to diabetes, a debilitating condition that requires management. Managing the disease and its complications can last for many decades. Long-term complications from diabetes include cardiovascular disease, retinopathy, neuropathy, and nephropathy. Type 2 diabetes has a huge impact on patient quality of life and healthcare costs.

Metabolon is identifying biomarkers for insulin resistance, with the objective of developing a test that can measure the level of insulin resistance in non-diabetic at-risk patients. The company has discovered a number of significant biochemical markers indicative of Type 2 diabetes. These markers are currently being incorporated as part of Metabolon's *Quantose* series of diagnostic products. The *Quantose* products are targeted at different stages of diabetes: pre-diabetes, drug efficacy and complications of the disease.

Metabolon's diagnostic test for insulin resistance is relatively inexpensive at $100-$125 per test and is easily administered by physicians. According to the company, there is scope to do up to 20 million diagnostic tests per year on humans so there is a $2 billion-plus market opportunity in the U.S. alone. The company is in the process of identifying a partner to assist with the sales of the insulin resistance diagnostic test, and will be establishing six beta test sites later this year.

Metabolon's technology can also be used to detect insulin resistances in pets, such as cats. Some 10% of the 80 million cats in the U.S. are diabetic. We expect to see some announcements from Metabolon in the months ahead related to its insulin resistance diagnostic technology for pets. It could become another sizable market opportunity for the company in the future.

In terms of potential competition in the diabetes diagnostics market, there is another company to keep an eye on: Kleiner Perkins-backed Tethys Bioscience. Tethys is developing a diabetes risk test called *PreDx*. *PreDx* is a quantitative test that employs a complex algorithm to analyze a defined set of biomarkers im-

plicated in the development of diabetes. Unlike Metabolon's test, *PreDx* does not monitor insulin resistance. And at around $600 per test, Tethys' product is considerably more expensive that Metabolon's.

The other major opportunity in diagnostics for Metabolon is cancer. There is little question that there is huge potential value in cancer diagnostic technology, which in many cases is still at a primitive stage today. Cancer is a metabolic problem. Metabolon is developing novel diagnostic tests to detect various types of cancer.

One of the areas Metabolon is focusing on is prostate cancer. The company believes there is a $550 million addressable market for prostate cancer diagnostics. There is a large gray area related to conventional diagnostics for prostate cancer – some 60% of people tested fall within a PSA level between 4 and 10.

Metabolon has identified biomarkers that would complement PSA, a protein long used for detection of prostate cancer, to guide the decision on whether to biopsy a patient or not. Researchers screened a large number of metabolites in normal, benign, and malignant cells. They found sarcosine to be a marker for aggressive prostate cancer and preliminary investigations indicate that sarcosine may be a useful marker of prostate cancer invasion and aggressivity. If this is correct, sarcosine may have potential both as a biomarker and as a therapeutic target.

Metabolon is developing two diagnostics tests for prostate cancer. One test complements the PSA in helping a physician/patient decide whether to move forward to a prostate biopsy while the second is a test performed with the biopsy to help assess how aggressive an individual patient's cancer is to aid in treatment decisions.

Metabolon is also exploring diagnostics for detecting liver and kidney damage in chemotherapy patients. The company believes their metabolomic technology platform can be used to create powerful diagnostics with other types of cancer, including urological (i.e., bladder), colorectal and early lung cancer. These are relatively large and growing areas and represent a combined $400 million-plus addressable market opportunity.

There is little question that clinical diagnostics is an important piece of winning the battle against cancer. Early detection is critical. If a cancer is caught at an early stage, there is a much higher likelihood of it becoming manageable. It is with cancer and other life-threatening diseases where there is tremendous potential for nano-enabled diagnostics technology to have a positive impact on humanity and health care in the years ahead.

Metabolon's molecular diagnostic business will commence later this year when the company launches tests for insulin resistance and urological cancers. Metabolon's new facility on Davis Drive in Research Triangle Park, NC has received receipt of a Certificate of Registration from the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Amendment (CLIA). The CLIA registration allows Metabolon's clinical laboratory to perform high-complexity tests on patient samples. Additional tests will be added in 2012 as the

METABOLON CANCER DIAGNOSTIC PIPELINE

Product	Market Size	Unmet Clinical Need	Test Description
Bladder Cancer Aggressiveness	$165 mm	Guide treatment decision: active surveillance, cystectomy, adjuvant chemotherapy	Distinguish aggressive hi-grade tumors from less aggressive, biopsy
Nephrotoxicity of Cisplatin in Bladder Cancer	$100 mm	Prevention of AKI	Monitoring test for targeted therapy nephrotox in RCC, blood
Hepatotoxicity of Taxotere in Prostate Cancer	$60 mm	Prevention of DILI	Monitoring test for taxotere hepatotoxicity in HRPC, blood
Nephrotoxicity of Targeted Agents in RCC	$70 mm	Prevention of AKI	Monitoring test for targeted therapy nephrotox in RCC, blood

Source: Metabolon

company builds out its molecular diagnostics business.

METABOLON VALUATION ANALYSIS

Looking at the clinical diagnostic market overall, we believe there is $100 million-plus revenue opportunity for Metabolon over the next five years. While the B2B Metabolomics business is generating positive cash flow and is likely to continue growing at a healthy pace, the molecular diagnostics business will require additional financial capital.

Most of that capital will likely be used to build out a sales and distribution channel for Metabolon's cancer diagnostics business. The company is likely to partner with an established company to distribute its insulin resistant diagnostic product so there will be little capital required for that part of the business. We assume the company will require $20-$30 million of new capital to seed the molecular diagnostics business.

Our base case intrinsic value (IV) model assumes a successful $20-$30 million capital raise later this year. We have projected a 5-year average revenue growth rate of 45% driven by increasing sales associated with the insulin resistance and cancer diagnostics business, with gross margins expanding to 76% by 2015 from around 62% currently. Importantly, we are using a 30% discount rate to compute present value, which is double the value we typically use in our technology company valuation analysis. We believe the higher discount rate is justified by the evolutionary stage of the company and the fact that the diagnostics business has yet to be launched. Based on these assumptions, we estimate Metabolon's IV around $350 million.

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Long Term Intrinsic Value: We use a more reliable model for determining company valuation that is very effective over multi-quarter periods. It also avoids the noise of small quarterly fluctuations. It enables investors to exploit volatility.

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Metabolon Intrinsic Valuation Model

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Base Case

Dec YE	2007	2008	2009	2010	2011	2012	2013	2014	2015
YoY Change $		1.4	0.8	6.1	4.0	12.0	26.5	39.2	54.5
Total Revenue	$6	$7	$8	$14	$18	$30	$56	$96	$150
YoY Growth		24.5%	11.7%	79.2%	29.0%	67.4%	88.9%	69.6%	57.1%
COGS %	48.9%	44.5%	46.8%	38.4%	37.1%	30.5%	26.3%	24.1%	24.0%
COGS $	$2.7	$3.1	$3.6	$5.3	$6.6	$9.1	$14.8	$23.0	$36.0
Gross Profit	$2.8	$3.8	$4.1	$8.5	$11.2	$20.7	$41.5	$72.5	$114.0
Gross Margin	51.1%	55.5%	53.2%	61.6%	62.9%	69.5%	73.7%	75.9%	76.0%
SG&A %		54.5%	187.9%	66.7%	67.4%	73.8%	51.5%	32.5%	22.0%
SG&A	$3.3	$3.8	$14.5	$9.2	$12.0	$22.0	$29.0	$31.0	$33.0
R&D %	23.2%	10.7%	8.1%	5.1%	11.2%	13.4%	14.2%	10.5%	10.0%
R&D $	$1.3	$0.7	$0.6	$0.7	$2.0	$4.0	$8.0	$10.0	$15.0
Operating Margin	-61%	-18%	-268%	-16%	-25%	-26%	11%	43%	58%
Operating Income	-$2	-$1	-$11	-$1	-$3	-$5	$5	$32	$66
Other Income (expense)	0	0.3	-0.9	-0.2	0	0	0	0	0
Taxes	-$0.5	-$0.2	-$3.3	-$0.4	-$0.8	-$1.6	$1.4	$9.5	$19.8
30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Net Income	-$1	$0	-$9	-$1	-$2	-$4	$3	$22	$46
Net Margin	-22%	-2%	-112%	-9%	-11%	-12%	6%	23%	31%
Market Value Using P/E	-$24	-$3	-$172	-$24	-$39	-$74	$63	$441	$924
Cash Position				$9	$7	$3	$6	$29	$75
Shares (M)	27	27	27	27	38	38	38	38	38
Period Share Price	-$1	$0	-$6	-$1	-$1	-$2	$2	$11	$24
PV of MV 4 Years Out	-$14	-$26	$22	$154	$324				
PV of Cash 4 Years Out	$2	$1	$2	$10	$26				
PV MV + Cash	-$11	-$25	$24	$164	$350				
PV Value Per Share	-$0.42	-$0.92	$0.90	$6.09	$9.20				

NA	Ticker
Private	Exchange
45%	Rev Growth
$5.00	Current Price
27	Shares Out
1%	Avg. Dilution
$135	Cap (M)
$9	Cash
$5	Debt
30%	Tax Rate
20	P/E Multiple
30%	Discount Rate
$9.20	Intrinsic Value
84%	Up/Downside