Zacks Small-Cap Research

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# DiagnoCure Inc. (T.CUR)

**T.CUR: *Q1 2012 Earnings - No Major Surprises***

| | |
|---|---|
| **Current Recommendation** | **Outperform** |
| Prior Recommendation | N/A |
| Date of Last Change | 03/19/2012 |
| Current Price (04/04/2012) | $0.70 |
| **Target Price** | **$2.25** |

## OUTLOOK

DiagnoCure's flagship PCA3 test received FDA approval in February 2012. The test, marketed by Gen-Probe, could provide significantly greater clinical utility than the standard prostate cancer test (i.e. - PSA). PSA is infamously unreliable and, coupled with a huge unmet demand for a better prostate cancer test, provides a potentially attractive opportunity for DiagnoCure. The company also recently sold its CLIA lab and brought on Signal Genetics to sell its proprietary colon cancer test. With a restocked balance sheet, DiagnoCure restarted their previously mothballed lung cancer program.

We are maintaining our Outperform rating and $2.25/share price target.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$1.30** |
| **52-Week Low** | **$0.49** |
| **One-Year Return (%)** | **-22.22** |
| **Beta** | **1.01** |
| **Average Daily Volume (sh)** | **61,668** |
| **Shares Outstanding (mil)** | **43** |
| **Market Capitalization ($mil)** | **30** |
| **Short Interest Ratio (days)** | **N/A** |
| **Institutional Ownership (%)** | **42** |
| **Insider Ownership (%)** | **N/A** |
| **Annual Cash Dividend** | **N/A** |
| **Dividend Yield (%)** | **N/A** |
| **5-Yr. Historical Growth Rates** | |
| **Sales (%)** | **N/A** |
| **Earnings Per Share (%)** | **N/A** |
| **Dividend (%)** | **N/A** |
| **P/E using TTM EPS** | **N/A** |
| **P/E using 2012 Estimate** | **N/A** |
| **P/E using 2013 Estimate** | **N/A** |
| **Zacks Rank** | **N/A** |

| | |
|---|---|
| **Risk Level** | **N/A** |
| **Type of Stock** | **Large-Growth** |
| **Industry** | **Med Products** |

## ZACKS ESTIMATES

**Revenue**
(in '000 of $U.S.)

| | Q1 (Jan) | Q2 (Apr) | Q3 (Jul) | Q4 (Oct) | Year (Oct) |
|---|---|---|---|---|---|
| 2011 | | | | | 1.2 A |
| 2012 | 0.6 A | 0.3 E | 0.4 E | 0.6 E | 1.9 E |
| 2013 | | | | | 3.7 E |
| 2014 | | | | | 6.9 E |

**Earnings per Share**
(EPS is operating earnings before non recurring items)

| | Q1 | Q2 | Q3 | Q4 | Year |
|---|---|---|---|---|---|
| 2011 | | | | | -$0.09 A |
| 2012 | -$0.02 A | -$0.02 E | -$0.02 E | -$0.02 E | -$0.08 E |
| 2013 | | | | | -$0.07 E |
| 2014 | | | | | -$0.03 E |

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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## WHAT'S NEW....

### Q1 2012 Financial Results

On March 30th DiagnoCure Inc. reported results for the fiscal first quarter ending January 31, 2012. Revenue of $556k was slightly ahead of our $381k estimate as a result of higher than modeled ($269k A vs. $60k E) payments from Signal Genetics related to the R&D services agreement. As a reminder, the mid-2011 transaction in which Signal acquired CUR's clinical lab and exclusive rights to Previstage GCC also calls for DiagnoCure to be paid $2.5 million related to funding of R&D projects, including for studies related to the Previstage test (including phase 2 of the VITAR study) as well as for continued development of a lung cancer test. Payments under this R&D agreement may be somewhat irregular quarter-to-quarter - for simplicity purposes our model assumes ~ $500k/year over the next several years.

Q1 royalties from Gen-Probe related to Progensa PCA3 were $145k while royalties from Signal Genetics related to Previstage GCC were $10k - both slightly below our estimates. Management noted on the call that there is a several-month lag between when Gen-Probe makes sales of Progensa PCA3 and when DiagnoCure books the related royalties. Also noted was that Signal Genetics has recently added sales reps which may help the acceleration in Previstage sales. We continue to model sequential growth in royalties from both Progensa and Previstage throughout 2012.

Q1 net income and EPS were ($816k) and ($0.02), in-line with our ($859k) and ($0.02) estimates. Cash balance (including investments) stood at $7.8MM at 1/31/12, compared to $8.9MM at 10/31/2011. Management noted that they expect cash burn to be approximately $2MM - $3MM in fiscal 2012. The balance sheet remains very healthy.

We have made some slight but relatively immaterial adjustments to our model following the Q1 2012 earnings release. We are maintaining our Outperform rating and $2.25/share price target.

## BUSINESS

DiagnoCure Inc. (CUR.TO) is a Quebec, Canada-based developer of molecular diagnostic tests for the detection and quantification of various forms of cancer, including colorectal, prostate, lung and bladder. The company was founded in 1994 and commercialized its first test, for bladder cancer, in Europe in 1998 and in 2000 the test received FDA approval. In 2003 they brought an analyte specific reagent (ASR) prostate cancer test to the U.S. market which used their proprietary PCA3 marker. The company is looking to capitalize on the rapidly growing demand for more accurate and quantifiable cancer tests - which is being driven by molecular diagnostics, a segment experiencing 15%+ annual growth.

The company's current focus is on prostate and colorectal cancer and includes its flagship PCA3 test (Gen-Probe's Progensa PCA3), for prostate cancer. The test was approved in Europe in 2006 but had only been available in the U.S. in ASR format until receiving FDA approval in mid-February 2012. FDA approval allows commercialization partner Gen-Probe to explicitly market Progensa PCA3 which could greatly expand its use. The test, which uses the proprietary biomarker PCA3, could provide significantly greater clinical utility than the standard prostate cancer test (i.e. - PSA). PSA is infamously unreliable and, coupled with a huge unmet demand for a better prostate cancer test, provides a potentially attractive opportunity for DiagnoCure. The FDA approved indication (supported by clinical trial data) is to assess the risk of a future positive biopsy (i.e. - risk of diagnosing cancer in the future) following a prior negative biopsy - a worldwide market estimated at about $180MM (DiagnoCure receives royalties on sales). We believe Progensa PCA3 may also have utility outside of its indicated use including potentially prior to an initial biopsy, which would greatly expand the market opportunity for the test.

The company's colorectal cancer test, Previstage GCC, uses the marker Guanylyl Cyclase C (GUCY2C or more commonly, GCC) to stratify the risk of colon cancer recurrence by more accurately determining the stage of the disease, which is considered the best determinant of predicting cancer recurrence and survival. As staging is used to determine the most appropriate course of treatment, mis-diagnosis can result in compromised patient care and outcomes. DiagnoCure, which had been selling Previstage GCC through its own sales force until June 2011, expects uptake of the test to accelerate as a result of a recent out-licensing agreement and a regular flow of peer-reviewed publications supporting the utility of the test. The target market are the ~70k patients in North America that have been diagnosed by traditional methods as having Stage I or II colorectal cancer but may actually have more advanced progression of the disease. DiagnoCure estimates this market represents ~ $200MM in sales (of which DiagnoCure would receive royalties on).

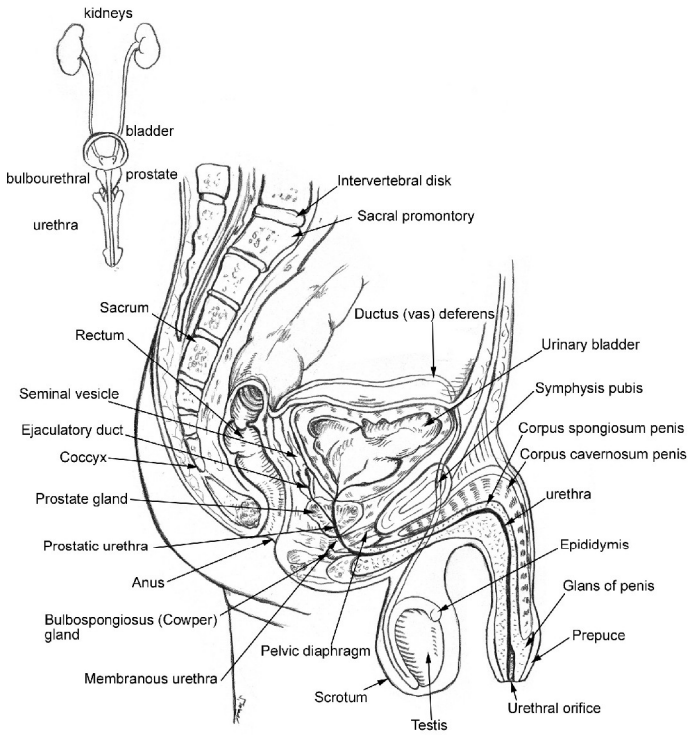
In the year 2003 DiagnoCure licensed development and commercialization rights to their PCA3 marker to Gen-Probe, which sells their current (and will sell their follow-on test) Progensa PCA3 tests. In return DiagnoCure received an upfront payment and continues to receive sales royalties. DiagnoCure had been selling their Previstage GCC test themselves but in mid-2011 they restructured operations, selling their CLIA-certified lab and granting worldwide rights to the Previstage test to Signal Genetics. DiagnoCure received upfront cash and will receive ongoing sales royalties as well as some R&D funding. The move was driven by DiagnoCure's desire to more rapidly expand growth of the GCC test via a partner with greater distribution reach, reduce operating expenses and to restock their cash balance, providing more opportunity to advance pipeline projects. DiagnoCure had previously mothballed their lung cancer program but now with additional financial flexibility and funding afforded by the Signal Genetics deal, the company announced that it will resume the program which is expected to include the development of a multiplex PCR-based test.

DiagnoCure's future now largely hinges on execution by their commercialization partners and their ability to capture as much of the target markets of each of these two cancer tests. The recent Signal Genetics deal provides the company with much greater selling resources and reach. While Previstage GCC has had only limited success to date, it's possible with Signal Genetics now onboard that sales could start to show more substantial growth in the U.S. Similarly, Gen-Probe has not had much success in moving the needle on Progensa sales in Europe but FDA approval of the test offers a new opportunity to spark revenue growth. U.S. regulatory approval now opens up the door to explicitly market the test with a potentially compelling message to a wide audience - including directly to the patient which could help uptake in the absence of widespread insurance reimbursement. The rate of ramp in sales of the test may be determined by a number of things, many of which are out of the company's control including coverage decisions by private payers and the utility of the test in clinical practice. Perhaps the most influential factor that may shape the near and intermediate term success of PCA3, however, will be the level of effort and resources that Gen-Probe dedicates to marketing and sales of the test.

## PROSTATE CANCER: *Progensa PCA3*

According to the National Cancer Institute, it is estimated that ~ 241k men will be diagnosed with and ~34k men will die of prostate cancer in the U.S. Prostate cancer is most prevalent in the elderly, with the vast majority of cases in men over the age of 65. Prostate cancer develops (the cause of which is not fully understood) in the male reproductive system and while it is typically slow growing and may never be life-threatening, it may spread to other parts of the body, particularly the lymph nodes and bones. While prostate cancer can be deadly if metastasized, when the cancer remains contained to the prostate or in nearby areas, the five-year survival rate is almost 100%. As prostate cancer is the most frequent cancer in men, an accurate test to regularly screen for the disease is in high demand. An important point to note, however, is that due to prostate cancer's typically slow-growing nature, a positive diagnosis does not necessarily mean that treatment (including surgery and radiation which can have deleterious side-effects) is the safest and best course of action. The real key to improving prostate cancer diagnosis and patient outcomes is being able to accurately (i.e. – minimize false-positives/false-negatives and determine the extent of progression) diagnose the disease at an early stage which in-turn will allow physicians to better determine the most appropriate course of treatment (if any) and reduce patient anxiety related to false-positive diagnoses.

*SOURCE: Medscape*




The current standard screening method for prostate cancer is a digital rectal exam (DRE) along with the prostate-specific antigen (PSA) test, which measures a protein released by prostate cells to determine the presence of cancer. Despite its widespread use (~20MM PSA tests done every year in North America and ~45MM worldwide, representing markets worth ~$200MM U.S. and ~$500MM worldwide), PSA's accuracy in detecting prostate cancer as well as its effectiveness in reducing mortality (the ultimate goal) is highly controversial and has recently come under increasing scrutiny. Among the evidence that detractors cite as support against the use of PSA is the results of a meta-analysis of clinical trial data on over 400k patients which were published in the British Medical Journal in 2010. The study found that while PSA increases cancer detection, it is not associated with a "significant effect of screening on death from prostate cancer or overall mortality." The authors concluded that, "The existing evidence from randomized controlled trials does not support the routine use of screening for prostate cancer with PSA with or without digital rectal exam."

In a well publicized announcement, based on the results several large clinical trials in the U.S. and Europe, in late 2011 the U.S. Preventative Services Task Force recommended that healthy men without any symptoms of prostate cancer not receive a PSA test. The draft recommendation, which is expected to be finalized shortly, carries significant weight and can determine whether public (including Medicare) and private health insurers will reimburse for the test. Per the chairwoman of the task force relative to the recommendation, “Unfortunately, the evidence now shows that this test does not save men’s lives. This test cannot tell the difference between cancers that will and will not affect a man during his natural lifetime. We need to find one that does.” The Task Force gave the PSA test its lowest rating, D, noting that it does more harm than good.

Meanwhile there continue to be resolute advocates of PSA testing which dismiss the conclusions cited by the Task Force including Dr. Eric Klein, an expert on prostate cancer from the Cleveland Clinic who notes that a substantial amount of clinical data does indicate that PSA testing does indeed save lives.

Studies have shown that PSA testing has a sensitivity and specificity of approximately 85% and 30%, respectively - indicating that while it is fairly good at detecting cancer (detects 85% of cases) it is very poor at differentiating between what is, and what is not cancer (i.e. - very low specificity, resulting in high false-positive rate). The heart of the accuracy problem with PSA testing is that levels of the PSA protein can be elevated (and result in the test

indicating positive for cancer) under fairly common circumstances when cancer may not actually be present – which could result in a false-positive diagnosis. The most common of these is when there is an enlargement of the prostate (called benign prostate hyperplasia or BPH). While the majority of men will experience some enlargement of the prostate as they age, only a very small percentage of them will develop prostate cancer. The correlation between BPH and increased levels of PSA results in only about 30% of positive PSA tests (i.e. – PSA elevated beyond what is considered normal, >4ng/ml) actually turning out to be cancer. And of those accurately diagnosed as having cancer (as confirmed by biopsy) with PSA, most have slow-growing cancers that would never become life-threating. There is also no definitive evidence that the presence of BPH increases the chances of eventually developing prostate cancer.

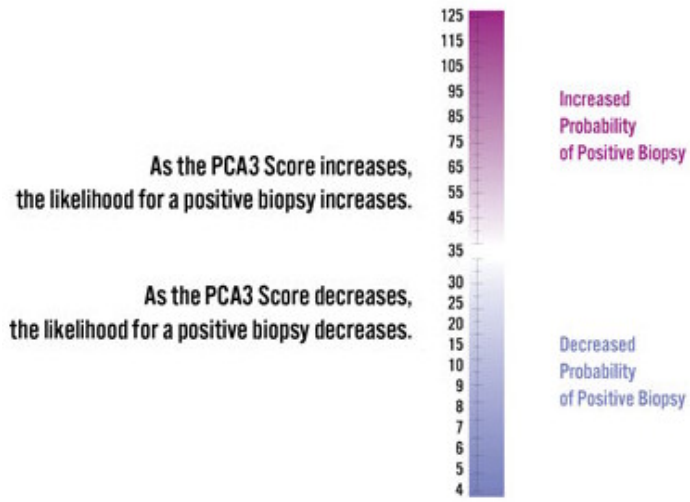
In the event of a positive PSA test showing, a biopsy will be done to confirm the diagnosis. If cancer cells are found in the tissue a Gleason score is assigned which is a measure of the severity or aggressiveness of the cancer. Prostate cancer biopsy involves the insertion of needles into different regions of the prostate gland to extract tissue which are then examined under a microscope. As a result of the low specificity of the PSA test, almost 75% of biopsies for prostate cancer turn out to be negative for the disease. Consequences of this include unnecessary mental anxiety associated with the thought of having a potentially deadly disease (this mental stress, especially with the elderly, can also result in physical health risks such as heart stress) and the risks inherent with biopsy such as infection. And even if the biopsy comes back negative, there still can be lingering mental anxiety from wondering if the biopsy was wrong and cancer is actually present. Instead of what might be a more appropriate course of action such as watchful-waiting (i.e. –monitoring including future follow-up testing), this anxiety can prompt the patient to undergo unnecessary treatments such as surgery, radiation, and hormone-blocking medication which can expose them to further negative side effects such as persistent blood in the semen, impotence, erectile dysfunction, urinary incontinence, bowel dysfunction, and even death (the latter, a result of complications from surgery). The unnecessary mental anxiety and over-treatment associated with PSA testing was a major reason for the recent recommendations by the U.S. Preventative Services Task Force against use of the test.

## PROGENSA PCA3

### Progensa PCA3

Unlike PSA, DiagnoCure's PCA3 (Prostate CAncer gene 3) marker is prostate cancer-specific and is not influenced by enlargement of the prostate. The test detects cancerous cells with high levels of PCA3 which are shed into the urine following a standard digital rectal exam. A higher level of PCA3 detected by the test indicates that there is a greater likelihood of a positive biopsy.

*SOURCE: www.pca3.org*



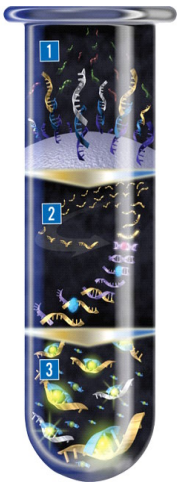

The PCA3 test's biomarker is a gene that was discovered in the 1990's by a Holland biologist while doing work at Johns Hopkins University. Originally known as DD3, DiagnoCure obtained patent rights to the marker from Nijmegen University (Netherlands) and John Hopkins University and used it initially to develop a qualitative assay. DiagnoCure began commercializing a PCA3 test named uPM3 in the U.S. in 2003 in ASR format – in November of that same year the company signed a deal with Gen-Probe to use the marker to develop a second generation, quantitative test and to distribute it throughout a network of laboratories. Gen-Probe, with worldwide development and commercialization rights, launched PCA3 in the U.S. in ASR format in 2005 and began selling the test under the Progensa PCA3 name in Europe and Canada following regulatory approval (CE Marking came November 2006, Health Canada approval came August 2011).

The test had only been available in the U.S. in ASR format until finally receiving FDA approval in mid-February 2012. FDA approval allows full commercialization of the test beyond the much more limited ASR format - which entails development of in-house tests (often called "home-brews") by labs, using the "ingredients" supplied by Gen-Probe. While ASR tests are widely accepted as scientifically valid and are an important part of diagnostic testing, unlike an FDA approved test (supported by clinical trial data), ASR ingredients can not be packaged and marketed as specific tests or kits for specific indications or applications and can not include labeling stating analytical or

clinical performance – all of this limits their marketability and potential profitability. FDA approval of Progensa PCA3 was obtained in February 2012 which is a major milestone for DiagnoCure.

***How It Works…***

The quantitative PCA3 that Gen-Probe developed uses a combination of technologies (Target Capture, Transcription Mediated Amplification, and Hybridization Protection Assay) to capture the target marker, amplify it, and allow for it to be detected. The PCA3 test is a dual-assay which uses the ratio of PCA3 (numerator) and PSA (denominator) to determine an overall PCA3 score. A PCA3 score of 25 is used as it has been shown to provide the greatest diagnostic accuracy, or balance between sensitivity and specificity as determined during the clinical evaluation of the Gen-Probe PMA submission approved by the FDA. As we note below, a number of studies with various designs and protocols have been done with PCA3 in prostate cancer. Based on various studies, sensitivity and specificity at the 35 cut-off were generally in the range of 50% - 60% (sensitivity) and 70% - 75% (specificity). Patients in clinical trials with PCA3 scores above 35 have been shown to be between 2 and 3 times more likely to have a positive biopsy than those with scores below 35. PCA3 is also linear, so the higher the score, the greater the likelihood of positive biopsy. And unlike PSA, PCA3 is not affected by BPH.




**In step No.1 (top), target capture of the mRNA is performed, using magnetic bead (purple).**

**In step No. 2, the captured gene is amplified using Transcription Mediated Amplification, a process that generates some 10 billion copies of PCA3 in one hour.**

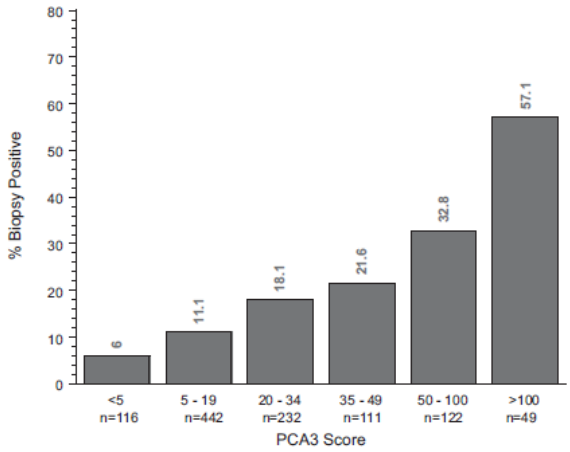
**In step No. 3, the Hybridization Protection Assay is performed using DNA probes tagged with a chemiluminescent substance that is activated upon contact with detection reagents.**

*SOURCE: usrf.org*

There's been a substantial amount of research done with PCA3 and over 80 peer-reviewed articles have been published supporting use of the marker as a diagnostic for prostate cancer. While results of the 495-patient multi-site study used as support for FDA approval were not submitted for publication, other trial data, published in prominent medical journals provide insight into PCA3's clinical utility as a diagnostic for prostate cancer. This includes;

*SOURCE: J Urol. 2010 Nov:184(5):1947-52*

A subset of GlaxoSmithKline's four-year, ~8,000-patient REDUCE trial which tested the ability of Glaxo's BPH drug Avodart to reduce the risk of prostate cancer in patients that had previously had a negative (i.e. – no cancer) biopsy within the preceding 6 months. The subset included ~2,400 patients (1,100 placebo, 1,300 Avodart) whose urine was tested for PCA3. All patients had a biopsy done two and four years following enrollment. Results, which were presented at the American Society of Clinical Oncology (ASCO) conference in 2010, showed that;




- **Placebo arm:** 94% of urine specimens yielded sufficient RNA for PCA3 testing. 18% of these patients were biopsy positive for prostate cancer with cancer found in only 6% of men with very low PCA3 scores (i.e. <5) but in 57% of those with very high (i.e. >100) PCA3 scores. The study concluded that PCA3 was associated with a positive biopsy rate and PCA3 at year-2 was a significant predictor of year-4 biopsy outcome (this relates directly to DiagnoCure's initial commercial target indication as a predictor of repeat biopsy), while PSA was not predictive of this. Results also showed that PCA3 was significantly correlated with biopsy Gleason score – which is indicative of the aggressiveness of the cancer.
- **Avodart arm:** the goal of this was to test the effect of Avodart on PCA3. Post-Avodart urine specimens were collected prior to year-2 and year-4. Results showed that PCA3 significantly predicted biopsy outcomes at year-4 while PSA was not predictive. The study concluded that PCA3 can be used to predict

biopsy outcome in men taking Avodart (i.e. - Avodart does not impair the performance of the PCA3 test) and PCA3 outperformed PSA for prostate cancer detection and improved diagnostic accuracy when combined with PSA. As Avodart is one of the most commonly prescribed medications for the treatment of BPH and almost all men will eventually have some form of enlarged prostate in their lifetime, it was important that the Avodart arm in this trial showed PCA3 performance is not affected by the medication.

Another trial that DiagnoCure points to is a 516-patient European study which was presented at the annual European Association of Urology meeting in April 2010. The trial studied PCA3's usefulness in predicting the outcome of initial prostate biopsies and cancer aggressiveness. The study showed that patients with a PCA3 score of over 35 were almost 3x as likely to have a positive initial biopsy compared to those with a score under 35. In addition, it showed (with a cutoff PCA3 score of 20), 40% of patients could have avoided a biopsy, with only 5% of the high-grade cancers (Gleason $\leq$ 7) being missed.

***PCA3 Commercialization Strategy…***

The test has been available in the use in ASR format in about 13 laboratories in the U.S. (including Quest, Lab Corp of America, and Bostwick) and fully commercialized in over 40 labs in Europe. It is just beginning roll-out in Canada. FDA approval now opens up the door to explicitly market the test with a potentially compelling message to a wide audience - including directly to the patient which could help uptake in the absence of widespread insurance reimbursement. The rate of ramp in sales of the test may be determined by a number of things, many of which are out of the company's control including coverage decisions by private payers and the utility of the test in clinical practice - which are both closely related. Despite FDA approval and coverage under existing CPT codes, more robust reimbursement for the test may be a progressive process related to evidence from clinical practice that it can actually improve patient care and/or reduce unnecessary procedures and the related costs - which may take some time. One positive factor is that healthcare reform measures have put greater focus on more rapid adoption and reimbursement of tests that can save money and improve patient care - which could potentially bode well for even more favorable reimbursement of Progensa PCA3. FDA approval will also hopefully facilitate more widespread reimbursement throughout Europe (which is a country-by-country decision), lack of which has hampered sales of the test (the test launched in Europe in late 2006). Perhaps the most influential factor that may shape the near and intermediate term success of PCA3, however, will be the level of effort and resources that Gen-Probe dedicates to marketing and sales of the test. A dedicated marketing effort will be key to maximize potential sales of the test.

Gen-Probe currently sells the test in North America and Europe and is expected to eventually be run on Gen-Probe's fully-automated PANTHER system, a next-generation instrument complementing their older TIGRIS system. PANTHER was CE Marked in late 2010 and received Health Canada approval in August 2011 - it is already available in Europe and Canada. Gen-Probe filed for 510(k) approval of PANTHER in May 2011 - approval is expected to come in the first half of 2012.

The recently approved FDA indication for Progensa PCA3 is "for use in conjunction with other patient information to aid in the decision for repeat biopsy in men 50 years or older who have had one or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended by a urologist based on standard of care". It is contra-indicated for men with atypical small acinar proliferation (ASAP). As a negative Progensa PCA3 result is associated with a lower chance of a positive biopsy, the expected value-added by using the test is to reduce the number of unnecessary repeat biopsies.

There are approximately 1 million prostate biopsies done every year in the U.S. and a similar number done in Europe. Worldwide, about 3 million prostate biopsies are done every year. As roughly 70% of prostate biopsies are negative for cancer, based on the indicated use of the test, this means the maximum combined U.S. and European markets are roughly 1.5 million people. While we note that not all patients with initial negative biopsies will be recommended for a repeat biopsy and ASAP is present in about 5% of biopsies - both of which mean that the indicated target markets may be slightly smaller than 1.5 million, for our financial model-building and forecasting purposes we think 1.5 million is a fair gauge of the indicated target market (U.S. and Europe combined).

Based on $100/test, this represent a total indicated U.S./European (i.e. - where the test is currently available) market size of approximately $150 million. Per terms of the development and commercialization agreement with Gen-Probe, DiagnoCure will receive royalties equal to 8% of worldwide sales of the PCA3 test up to the first (cumulative) $62.5MM in sales and 16% royalties beyond $62.5MM (cumulative). Approximately $29MM in sales have been generated to date (i.e. - ~ 1/2 to the $62.5MM mark when royalties of 16% kick in), including approximately $1.8 million in the most recent quarter (fiscal Q1 2012).

Based on an assumed $150 million total market (not including off-label use), this represents potential peak royalties to DiagnoCure of $24 million - more realistic peak penetration of the total market is probably closer to 50% (reached

several years after launch) however, equal to peak royalties to DiagnoCure of $12 million. However, if also used outside of the FDA-approved indication (i.e. - off-label), especially prior to a first biopsy, this could potentially expand the market for the test to many times the size of the indicated market. DiagnoCure believes the expanded market opportunity for the test is represented by the 9 million people worldwide that are screened with a PSA test and show elevated PSA (>2.5ng/ml). Progensa PCA3 could potentially be used to with these individuals to help determine whether an initial biopsy should be done. Based on a $100/test, this represents an expanded annual market size of approximately $900 million. This market is relatively large and potentially offers significant upside to our model depending on success of Progensa PCA in penetrating this market segment as we currently model only very modest sales of the test related to use prior to first biopsy - we will update our model accordingly.

Our model assumes the $62.5 million in cumulative sales watermark (moving the royalty rate to 16%) is attained around mid-to-late fiscal 2013.

2011 full-year (ending 10/31/2011) and Q1 2012 royalty revenue from Gen-Probe were $605k and $145k, roughly flat compared to the year earlier periods, respectively. $605k in royalties translates to about $7.6 million in PCA3 revenues to Gen-Probe - which (assuming a total market of $150MM) equals just over 5% of the target market. Approximately 65% of Gen-Probe's PCA3 revenue currently comes from Europe - although with FDA approval, a greater percentage may now shift towards the U.S.

## COLORECTAL CANCER: *Previstage GCC*

While regular screening has helped reduce the overall incidence of colon cancer since the mid-1980's, current screening programs and procedures may not be enough as the disease remains the second leading cause of cancer death in the U.S., behind only lung cancer. It is the third most commonly diagnosed cancer (behind only prostate and lung), with approximately 5% of people developing colon cancer at some point in their lifetime. The American Cancer Society estimates that about 160k Americans will be diagnosed with the disease during 2011 and almost 50k will die from it. Over 1 million Americans currently have colon cancer.

Colon cancer rarely afflicts younger people and is usually (although not always) first discovered in middle-aged or older individuals. In fact, 90% of new cases and 95% of deaths from colon cancer are with people 50 years of age or older. Although the overall incidence rate of colon cancer has been declining, as has the rates in people 50 years of age and older, the incidence rate for those younger than 50 has actually been on the rise. Despite a decline in the overall incidence of colon cancer, colon cancer screening is expected to grow by as much as 20% per year over the next 10 years, largely as a result of significant growth in the proportion of the population over the age of 50.

Treatment of colon cancer is most effective when the disease is discovered at an early stage - if found and managed at the earliest stage, five-year survival rate is over 90%. Once the cancer has reached the lymph nodes and distant organs, the rate of survival decreases significantly. At stage IV, the most severe, five-year survival rate falls to less than 10%. Regular screening is advised in order to increase the chances of finding and removing polyps before they become cancerous. Unfortunately, current screening and staging techniques fail to either find or accurately characterize the risk of most cancers at a point when they are most manageable, resulting in approximately 20%+ (~ 32k of the ~160k diagnosed in the U.S. each year) of cases advancing to stage IV and likely to be fatal. The initial step in guiding appropriate treatment is to first determine whether cancer is actually present (i.e. - **diagnoses**). The second step is to accurately **stage** the cancer (characterize the severity of the disease). The third step is to decide what is appropriate **treatment** based on the stage of the cancer. DiagnoCure believes their Previstage GCC Staging test can more accurately stage localized cancers (i.e. - stage I / II), which will in-turn, provide better treatment decisions.

### DIAGNOSING COLON CANCER

Colon cancer is usually initially diagnosed during regular screening. A variety of screening methods are regularly used including:

- **Colonoscopy:** a small flexible tube with a camera on the end is used to look at the interior walls of the rectum and the entire colon. During a colonoscopy, tissue samples may be collected and polyps removed so they can be microscopically examined. It is widely agreed that colonoscopies should be done as a screening procedure

at least once every 10 years beginning at the age of 50 and as a confirmatory diagnosis when the results of another screening test are positive. Weakness of colonoscopies is that they can miss small polyps and diagnosis involves a significant amount of interpretive skill - this not only increases the risk that cancerous polyps are left to grow, it also can result in unnecessary biopsies from benign polyps being mistakenly suspected of being cancerous. While smaller polyps, in general, typically present a lower risk of cancer, as small (< 1 cm) polyps account for approximately 85% of all polyps, it's imperative that screening can accurately detect these. Approximately 3.1 million colonoscopies are performed in the U.S. each year, with another ~ 4.1 million performed in Europe.

- **Flexible sigmoidoscopy:** similar to colonoscopy except sigmoidoscopy looks at only the rectum and lower part (~ final 2 feet) of the colon. It is generally recommended once every 5 years beginning at the age of 50 as a screening procedure. If suspicious areas are identified, a colonoscopy is typically ordered for supporting diagnosis and to remove any polyps. Weaknesses of flexible sigmoidoscopies are that they view only about 1/3 of the colon, they can miss small polyps, it involves subjective diagnosis and polyps can not be removed during this procedure.

- **Double-contrast barium enema:** patient receives an enema with barium sulfate, a contrast agent, followed by x-rays of the colon and rectum. The contrast agent highlights the intestines which allows the x-rays to pick up abnormal growths. If suspicious areas are identified, a colonoscopy is typically ordered for supporting diagnosis and to remove any polyps. The American Cancer Society recommends a double-contrast enema is done once ever five years beginning at the age of 50. Weaknesses of double-contrast enemas are that they can miss small polyps, false positives can be an issue and polyps can not be removed during this procedure.

- **Fecal occult blood test:** blood vessels of large polyps can be easily damaged by the passage of feces. The small amount of blood released into the feces is usually not visible by the naked eye but can be detected by a stool test. If the test comes back positive, a colonoscopy is needed to determine the cause of the bleeding. Fecal occult blood (FOC) tests are generally recommended once every year beginning at the age of 50. These guaiac-based FOC tests have been the primary screening method for colon cancer since the 1970's (and continue to be so today). Roughly 140 million FOC tests are performed worldwide every year. Weaknesses of the test are that it can miss many polyps, can produce false positives, can be influenced by diet and should be done frequently (i.e. - every year).

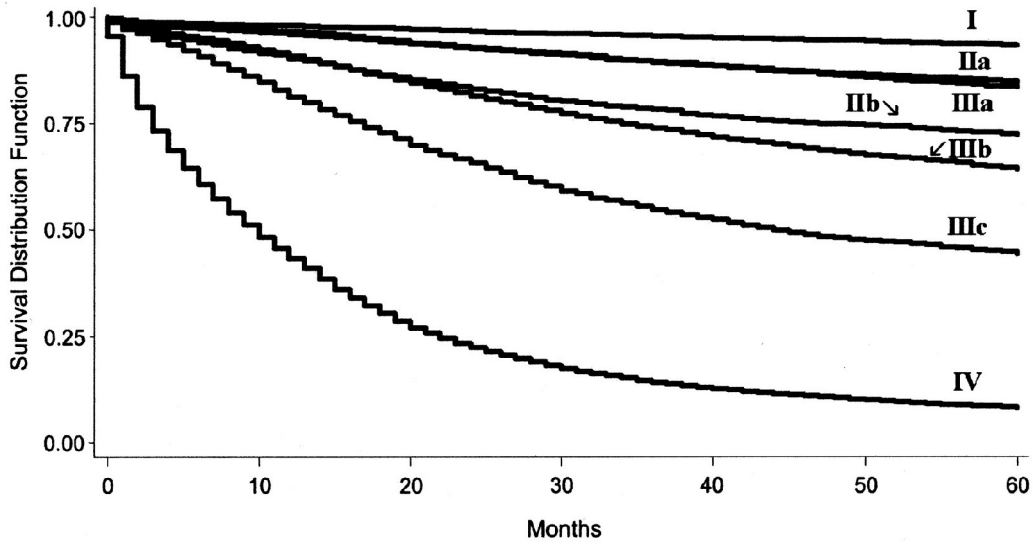
- **Polyp Biopsy:** if these screening methods suspect the presence of cancer, suspicious polyps are removed during colonoscopy and microscopically examined which provides a definitive diagnosis whether cancerous cells are present.

## STAGING COLON CANCER

When cancer is confirmed, the next step is to stage the severity of the disease to determine whether is has spread to other parts of the body. This will determine the appropriate course of treatment. Prior to surgery, staging is typically accomplished with imaging techniques such as CT and MRI scans. CT and MRI provide pictures of the inside of the body, including the colon, and have the advantage of being non-invasive but offer only limited diagnostic capability. Colon surgery and lymph nodes removal are considered the most effective and accurate way to stage colon cancer. During surgery, tumor and lymph node tissues are removed and sent to a pathology laboratory for examination to determine the pathological stage - the stage is based on how far the cancer has grown into the wall of the intestine, whether or not it has reached nearby structures, and whether or not it has spread to the lymph nodes.

During surgery, parts of the colon and surrounding lymph nodes will be removed which will then be examined under a microscope (histopathology). While histopathology is useful for determining whether or not there are cancer cells in a tissue, it sometimes fails in accurately determining the stage of the disease (e.g. - incorrectly diagnoses stage III as stage II) and the risk of recurrence because it may not detect low levels of cancer which may be present in the lymph nodes. Presence of cancer cells in the lymph nodes, if undetected and not removed or properly treated, can be particularly prone to progressing further to later, less treatable and more deadly stages (i.e. - stage III / IV). Prognostic risk stratification in early stage colon cancer remains a very clinically important issue due to the continuing challenge of attempting to identify those patients most likely to benefit from adjuvant chemotherapy. DiagnoCure believes their Previstage GCC test may be a more accurate staging method to address the issue of inaccurate staging and mis-diagnosis / inappropriate-treatment. Specifically, they believe it can be used as a treatment decision guide following surgery and lymph node removal by identifying patients in which likelihood of colon cancer recurrence is very low and could be safely managed without chemotherapy.

# 5-Year Colon Cancer Survival By TNM System



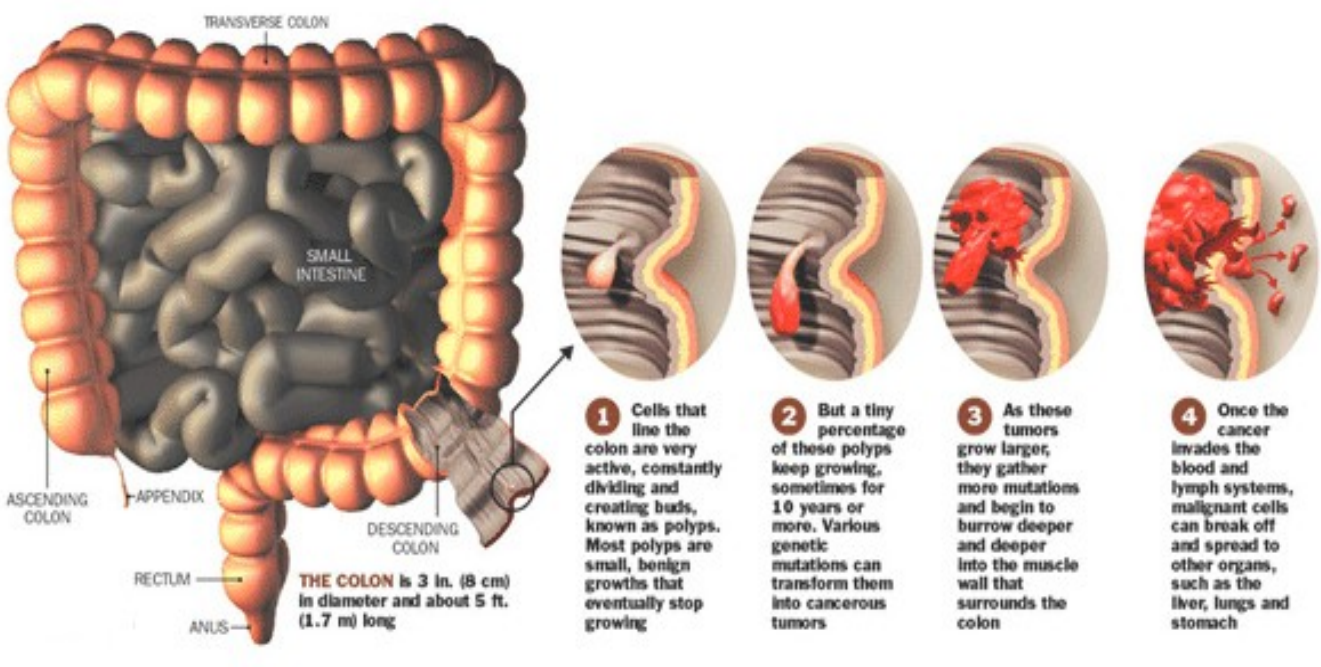

Five-year survival by the American Joint Committee on Cancer sixth edition system stages I–IV. *P* value determined by the log-rank test refers to the corresponding stage and the stage in the row above, unless otherwise indicated. All statistical tests were two-sided. * = IIIa versus IIb; † = IIa versus IIIa; ‡ = IIb versus IIIb; NS = not statistically significant.

| Stage | 0 mo | | 30 mo | | | 60 mo | | |
|---|---|---|---|---|---|---|---|---|
| | Survival, % | No. | Survival, % | No. | *P* | Survival, % | No. | *P* |
| I | 100 | 14500 | 96.1 | 8,581 | — | 93.2 | 4514 | — |
| IIa | 100 | 28535 | 91.0 | 2,105 | <.001 | 84.7 | 8494 | <.001 |
| IIb | 100 | 5826 | 80.2 | 3,060 | <.001* | 72.2 | 1611 | <.001* |
| IIIa | 100 | 1989 | 91.4 | 1,120 | NS† | 83.4 | 551 | NS† |
| IIIb | 100 | 15946 | 77.3 | 7,786 | <.001‡ | 64.1 | 3579 | <.001‡ |
| IIIc | 100 | 8600 | 59.1 | 3,039 | <.001 | 44.3 | 1250 | <.001 |
| IV | 100 | 20802 | 17.3 | 1,832 | <.001 | 8.1 | 432 | <.001 |

*SOURCE:* http://jnci.oxfordjournals.org/content/96/19/1420/F2.expansion.html

"Staging" is used to characterize the degree of severity of the disease - in particular, how far the cancer has grown into the wall of the intestine, whether it has reached nearby structures and whether it has penetrated nearby organs or the lymph nodes. Staging, which is especially focused on the involvement of cancer in the lymph nodes, is considered the most important factor in determining patient prognosis and treatment. In colon cancer, lymph node metastasis (i.e. - how many, if any, lymph nodes have cancer in them) has been shown to be the most important prognostic characteristic. Below we have included an illustration of the general staging groups (i.e. - I through IV) as well as the detailed staging classifications (which includes sub-categories within the general groupings):

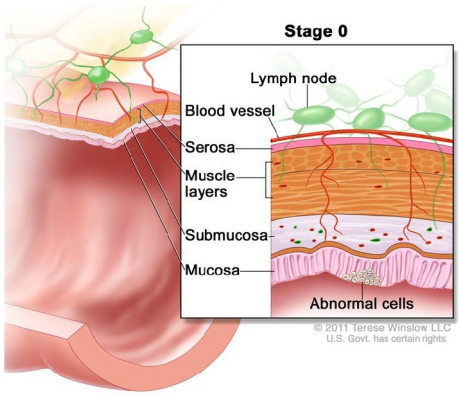
# General Staging Groups of Colon Cancer




*SOURCE: http://www.helpfulhealthtips.com/stages-colon-cancer/*

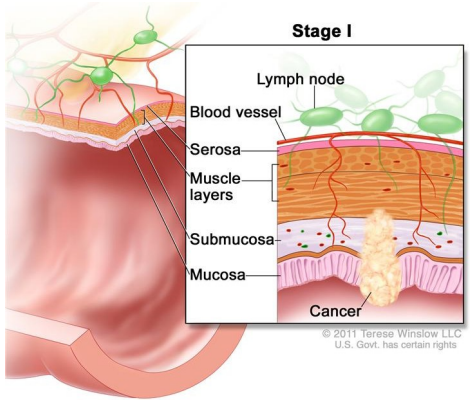
# Detailed Staging of Colon Cancer

**Stage 0:** abnormal cells are found in the mucosa (innermost layer) of the colon and/or rectal wall. These abnormal cells may become cancer. About 10% of all new U.S. colon cancer cases are thought to be at stage 0 (= ~ 16k people).
*SOURCE: National Cancer Institute*

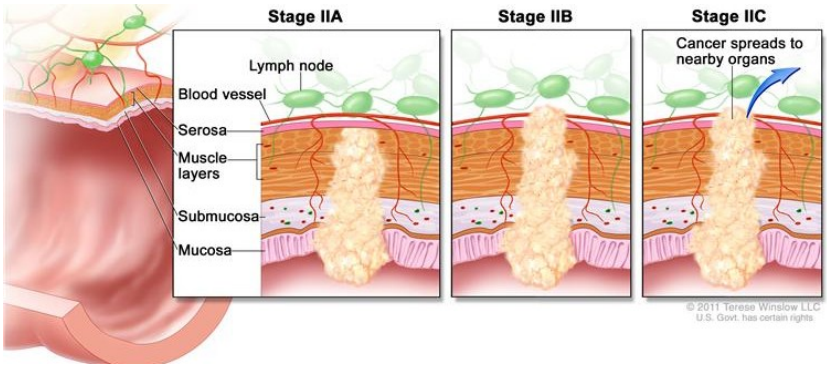



*SOURCE: Terese Winslow, LLC / U.S. Gov't*

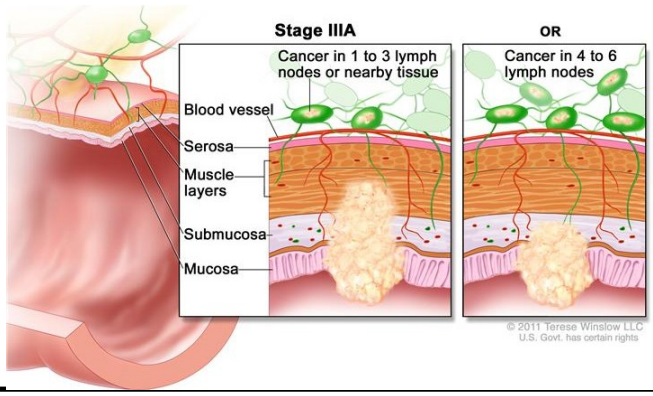
**Stage I:** cancer has spread from the mucosa (innermost layer) of the colon and/or rectal wall to the submucosa (layer of tissue under the mucosa) of the colon and/or rectal wall. Cancer may have spread to the muscle layer of the colon and/or rectal wall. Also called Dukes A colorectal cancer. About 15% of all new U.S. colon cancers are thought to be at stage I (= ~ 24k people).



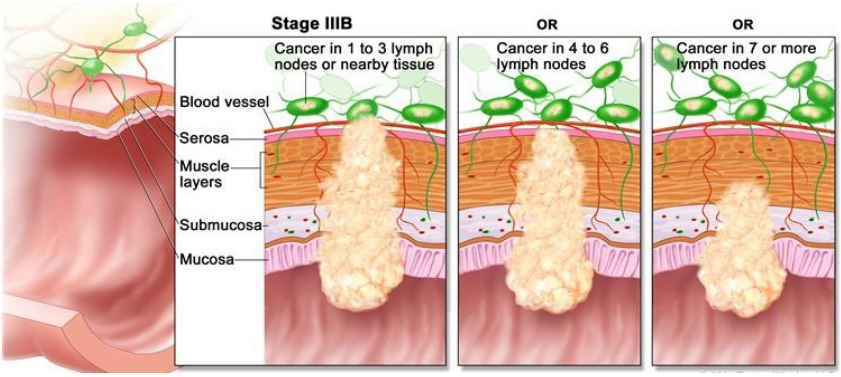

**Stage II:** colorectal cancer is divided into stage IIA, stage IIB, and stage IIC. In stage IIA, cancer has spread through the muscle layer of the colon and/or rectal wall to the serosa (outermost layer) of the colon and/or rectal wall. In stage IIB, cancer has spread through the serosa of the colon and/or rectal wall but has not spread to nearby organs. In stage IIC, cancer has spread through the serosa of the colon and/or rectal wall to nearby organs. Also called Dukes B colorectal cancer. About 25% of all new colon cancers are thought to be at stage II (= ~ 40k people).



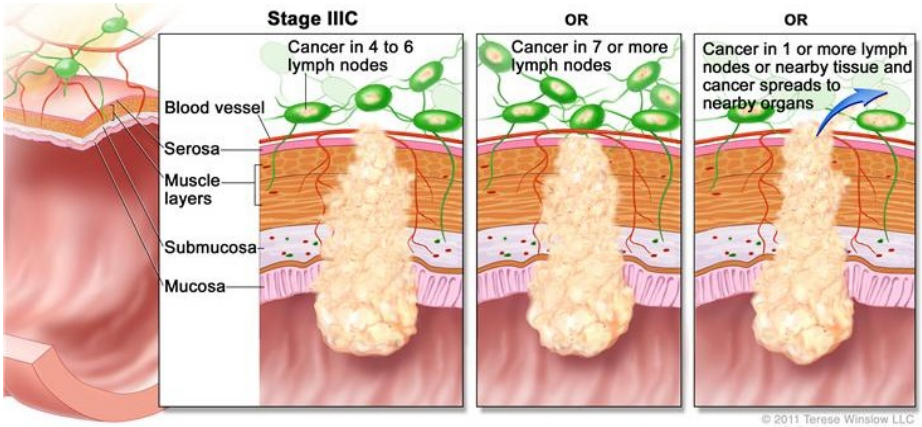

**Stage III**: colorectal cancer is divided into stage IIIA, stage IIIB, and stage IIIC. In stage IIIA, (1) cancer may have spread through the mucosa (innermost layer) of the colon and/or rectal wall to the submucosa (layer of tissue under the mucosa) and may have spread to the muscle layer of the colon and/or rectal wall. Cancer has spread to at least one but not more than 3 nearby lymph nodes, or cancer cells have formed in tissues near the lymph nodes; or (2) cancer has spread through the mucosa of the colon and/or rectal wall to the submucosa. Cancer has spread to at least 4 but not more than 6 nearby lymph nodes. About 30% of all colon cancers are thought to be at stage III (= ~ 48k people).



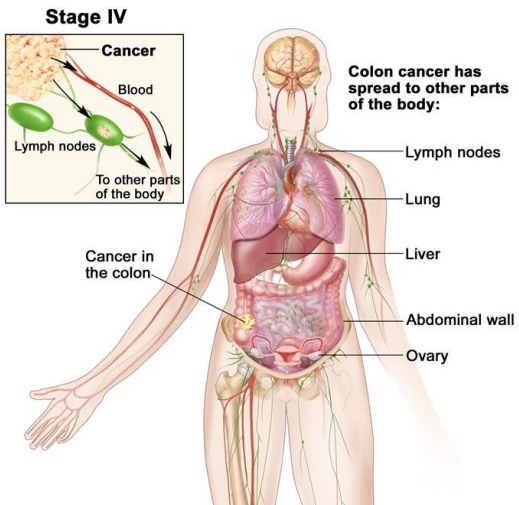
In stage IIIB, (1) cancer has spread through the muscle layer of the colon and/or rectal wall to the serosa (outermost layer) of the colon and/or rectal wall or has spread through the serosa but not to nearby organs. Cancer has spread to at least one but not more than 3 nearby lymph nodes, or cancer cells have formed in tissues near the lymph nodes; or (2) cancer has spread to the muscle layer of the colon and/or rectal wall or to the serosa of the colon and/or rectal wall. Cancer has spread to at least 4 but not more than 6 nearby lymph nodes; or (3) cancer has spread through the mucosa of the colon and/or rectal wall to the submucosa and may have spread to the muscle layer of the colon and/or rectal wall. Cancer has spread to 7 or more nearby lymph nodes.




In stage IIIC, (1) cancer has spread through the serosa of the colon and/or rectal wall but has not spread to nearby organs. Cancer has spread to at least 4 but not more than 6 nearby lymph nodes; or (2) cancer has spread through the muscle layer of the colon and/or rectal wall to the serosa of the colon and/or rectal wall or has spread through the serosa but has not spread to nearby organs. Cancer has spread to 7 or more nearby lymph nodes; or (3) cancer has spread through the serosa of the colon and/or rectal wall and has spread to nearby organs. Cancer has spread to one or more nearby lymph nodes, or cancer cells have formed in tissues near the lymph nodes. Also called Dukes C colorectal cancer.




**Stage IV**: colorectal cancer is divided into stage IVA and stage IVB. In stage IVA, cancer may have spread through the colon and/or rectal wall and may have spread to nearby organs or lymph nodes. Cancer has spread to one organ that is not near the colon and/or rectum, such as the liver, lung, or ovary, or to a distant lymph node. In stage IVB, cancer may have spread through the colon and/or rectal wall and may have spread to nearby organs or



lymph nodes. Cancer has spread to more than one organ that is not near the colon and/or rectum or into the lining of the abdominal wall. About 20% of all colon cancers are thought to be at stage IV (= ~ 32k people).

## TREATING COLON CANCER

Physicians use staging to guide treatment decision-making which can involve surgery, chemotherapy, drugs and radiation. Surgery is required in almost all cases when colon cancer is found and not terminal. If the cancer is found at a very early stage, it may only involve removal of polyps (polypectomy) or local excision where a tube is put through the rectum and the cancer cut out of the colon. If the cancer is larger a partial colectomy may be done where the cancer and parts of the adjacent tissue and lymph nodes are removed - these lymph nodes are then examined for the presence of cancer cells. In cases where the cancer is more advanced and more of the colon needs to be removed, a colostomy is performed in which the colon is emptied outside of the body into a colostomy bag.

DiagnoCure believes their Previstage GCC test may be a more accurate staging method to address the issue of inaccurate staging and mis-diagnosis / inappropriate-treatment. Specifically, they believe it shows that many patients that are staged using traditional methods are underdiagnosed as current methods can miss cancer cells in lymph nodes. This can result in a Stage III patient being mis-diagnosed as Stage II. Chemotherapy has been shown to reduce the risk of cancer recurrence in Stage III patients but has much less utility in less severe (i.e. - Stage II or lower) cases. DiagnoCure / Signal Genetics point to the fact that ~20% of Stage II patients (a portion of which may actually be Stage III) have recurring cancer but only ~5% benefit from treatment as evidence that this patient population is both mis-diagnosed and treated inappropriately. The application for the test is as a guide following surgery and lymph node removal to determine the risk of cancer recurrence and to identify patients that are most likely to benefit from adjuvant chemotherapy and which ones can be safely managed without chemotherapy.

**Stage 0**: Recommended treatment is typically local excision and polypectomy. About 95% of Stage 0 patients have surgery. Chemotherapy is almost never administered.

**Stage I**: Recommended treatment is typically a resection which involves a partial colectomy and anastomosis where the colon is sewn back together. About 95% of Stage I patients have surgery. Chemotherapy is administered in less than 10% of cases (~2k Stage I patients get chemo every year in U.S.).

**Stage II**: Recommended treatment can include resection, anastomosis and sometimes chemotherapy. Over 95% of Stage II patients have surgery. Chemotherapy is administered in approximately 35% of cases (~15k Stage II patients get chemo every year in U.S.). Based on studies with Previstage GCC, chemotherapy may be overutilized in these patients.

**Stage III**: Recommended treatment can include resection, anastomosis and chemotherapy. Over 95% of Stage III patients have surgery. Chemotherapy is administered in approximately 45% of cases (~25k Stage III patients get chemo every year in U.S.).

**Stage IV**: Recommended treatment can include resection, anastomosis, colostomy, removal of other organs, radiation therapy, drugs, and chemotherapy. About 75% of Stage IV patients have surgery. Chemotherapy is administered in approximately 50% of cases (~20k Stage IV patients get chemo every year in U.S.).

# PREVISTAGE GCC

DiagnoCure gained worldwide rights to the Guanylyl Cyclase C (GCC or GUCY2C) marker from Targeted Diagnostics & Therapeutics, Inc. in April 2007. DiagnoCure completed development of a test using the GCC marker for colon cancer and in 2008 launched the Previstage GCC Colorectal Cancer Staging test from its Pennsylvania-based CLIA lab (the lab has since been divested with the June 2011 consummation of a

development/commercialization agreement). The test is covered by 11 U.S. patents and patent applications until 2030. Previstage GCC is marketed as an adjunct to histopathology to help determine which patients that have been histologically diagnosed as stage II (i.e. - lymph node-negative for cancer) may actually have stage III colon cancer (i.e. - lymph node-positive for cancer) and which patients are more likely to experience cancer recurrence. The basis for this is that 1) lymph node metastasis (i.e. - how many, if any, lymph nodes have cancer in them) has been shown to be the most important prognostic characteristic for colon cancer and 2) up to 25% of people histologically node-negative (i.e. - stage II or earlier) experience recurrent disease.

Following surgery and lymph node removal, the Previstage GCC test analyzes the nodes for levels of GCC to determine if the levels are consistent with Stage III colon cancer. DiagnoCure / Signal Genetics note that the GCC test is able to detect cancer cells in some lymph nodes which histopathology misses because the test is 100,000 times more sensitive and uses 375 times more lymph node tissue than histopathology, which evaluates less than 1% of the node.

***Guanylyl Cyclase C…***

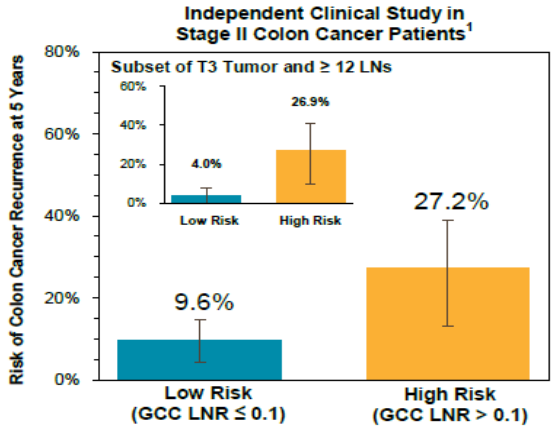
GCC (or GUCY2C) is a protein found only in the lining of the intestines which is responsible for activities such as water transport, crypt (glands in the intestine) morphology and the suppression of tumor creation. GCC should be confined to the intestines and if found in other parts of the body (such as the lymph nodes), it is an indication that cancer may be present. In addition, its expression is commonly found in metastatic colorectal cancer, indicating that this highly conserved intestinal receptor might contribute to malignant transformation by promoting tumor cell proliferation and genomic instability.

***Clinical Studies…***

GCC as a marker for colon cancer was initially discovered about 20 years ago by a researcher at Thomas Jefferson University. Since then over 50 peer-reviewed journal articles including studies on over 1,000 patients have been published on the relationship between GCC and colon cancer. Signal Genetics lists the catalog of articles and studies on its website. Some of the studies that DiagnoCure and Signal Genetics cite as support for use of Previstage GCC in colon cancer are:

- The initial study on GCC lymph node testing for determining the risk of colon cancer recurrence. Results of the study were published in November 2009 in an article in The Journal of the American Medical Association titled, *Association of GUCY2C Expression in Lymph Nodes With Time to Recurrence and Disease-Free Survival in pN0 Colorectal Cancer.* Primary and secondary outcomes were the time to recurrence of cancer and disease-free survival, respectively. The prospective study included 257 patients with pN0 colon cancer as determined by histology. N0 means no cancer cells detected in the lymph nodes - which is consistent with Stage II and lower. Median follow-up for all patients was 24 months and ranged from 2 - 63 months. Results showed that 1) all but 2 of the 32 patients with lymph nodes negative for GUCY2C remained disease-free at follow-up and 2) 47 of the 225 patients with lymph nodes positive for GUCY2C developed recurrent cancer and these GUCY2C-positive patients experienced an earlier time to recurrence than GUCY2C-negative patients. The authors concluded that "expression of GUCY2C in histologically negative lymph nodes appears to be independently associated with time to recurrence and disease-free survival in patients with pN0 colorectal cancer." The authors also note suggest that larger studies should be done to support these findings. Relative to the fact that only about 21% (47 of 225) GUCY2C node-positive patients recurred, the authors note that nodal metastases does not ensure recurrence but only indicates risk and this 21% recurrence rate is "nearly identical to (the rate) for patients with Stage III pN1, the lowest stage which all patients have histopathological detectable metastases" - which supports the theory (and Previstage GCC's indication) that GCC can determine which patients that have been histologically diagnosed as Stage II are actually have Stage III.

- A study published in the *Journal of Clinical Pathology* in 2010. The study compared the assessment of node-positivity by histopathology with that of GCC testing. Results showed that GCC was detected in 8% of the 560 nodes initially identified as histologically negative for cancer. In histologically-positive nodes, the GCC detection rate was between 90% and 95% (depending on how much of the node was tested for GCC). The study also showed that patients that were histologically negative but GCC positive had an earlier time to recurrence. The authors concluded that "Molecular detection of tumor cells in lymph nodes may have prognostic value in identifying




[1] *Sargent DJ, et al. Evaluation of Guanylyl Cyclase C Lymph Node Status for Colon Cancer Staging and Prognosis. Annals of Surgical Oncology; May 1, 2011.*

patients diagnosed as having pN0 colon cancer who will relapse following surgery."

- A study of the prognostic value of GCC for disease recurrence in chemotherapy-untreated Stage II colon cancer patients. The study, titled *Validating Indicators To Associate Recurrence Risk* (VITAR), includes two phases (an initial and a confirmation study). Phase 1 included 241 patients with Stage II colon cancer which were classified as either high or low risk based on the percentage of lymph nodes positive for GCC (LNR ratio). The results, presented at ASCO-GI 2011 and published online in May 2011 in the Annals of Surgical Oncology, showed LNR significantly predicted higher recurrence risk for 84 patients (34.9%) classified as high risk. The estimated five-year recurrence rates were 10% and 27% for the low and high-risk groups, respectively. DiagnoCure / Signal Genetics note that the 27% high-risk recurrence rate is comparable to that of Stage III colon cancer (which lends support to the ability of Previstage GCC to identify which patients that have been histologically diagnosed as Stage II as actually being Stage III). In a subset of 181 patients considered histologically low-risk, the phase 1 data showed the risk of five-year recurrence in these patients was 4%, indicating a "significant association between the GCC LNR and recurrence risk". Regarding the phase 1 results, the authors concluded, "Our prelimary results suggest that detection of GCC mRNA in LNs is associated with risk of disease recurrence in patients with untreated Stage II colon cancer." The phase 2 portion of VITAR, details of which have yet to be announced, will be a larger study which the companies hope will confirm the phase 1 results. Data from the phase 2 study is expected to be available sometime in 2012.

  A pooled analysis of the phase 1 study plus data on 69 additional patients was also done and presented at ASCO-GI in January 2012. Clinical endpoints included time to recurrence (TTR), overall survival (OS), and disease-free survival (DFS). The pooled analysis showed that high-risk patients had significantly higher risk of TTR, OS, and DFS. The estimated five-year recurrence rates were 11% and 32% for the low and high-risk groups, respectively. A secondary analysis of low risk patients showed "a strong relationship between GCC LNR and each endpoint remained". The authors concluded that "patients with GCC LNR high risk status have significantly poorer outcomes compared to patients with low risk status, particularly among those traditionally considered to be low risk."

***Signal Genetics Agreement…***

DiagnoCure had been selling their Previstage GCC test themselves but in mid-2011 they restructured operations, selling their Pennsylvania-based CLIA-certified lab and granting worldwide exclusive rights to the Previstage test to Signal Genetics. The move was driven by DiagnoCure's desire to more rapidly expand growth of the GCC test via a partner with greater distribution reach, reduce operating expenses and to restock their cash balance, providing more opportunity to advance pipeline projects.

Under the agreement, DiagnoCure received $5.7 million upfront for the lab and will receive $5.1 million in minimum royalty payments over the first five years. In addition, the deal calls for DiagnoCure to be paid $2.5 million related to R&D projects, including for studies related to the Previstage test (including phase 2 of the VITAR study) as well as for continued development of a lung cancer test (DiagnoCure booked $82k and $287k in revenue in 2011 and Q1 2012, respectively related to this R&D collaboration agreement). DiagnoCure received the $5.7 million upfront payment during the quarter ending 7/31/2011 (fiscal Q3). The installment/royalty piece is structured where DiagnoCure is paid a "high single digit" (the specific rate was not disclosed - we estimate ~7.5%) royalty on sales of Previstage GCC and will receive at least $5.1 million over five years. The aggregate royalties are essentially a carve-out of a total of $5.1 million in installment payments and DiagnoCure receives any royalties above this amount as well. Royalty payments have already started - DiagnoCure did not disclose whether or not the installments are equal annual payments but did indicate that they are expected to begin around the second year (i.e. ~ mid-2013).

***Marketing / Distribution…***

DiagnoCure expects Signal Genetics' greater marketing and distribution muscle to result in a faster ramp in sales of the test than what they were able to accomplish alone. Signal Genetics was formed in early/mid 2010 with an initial focus on genetic testing for multiple myeloma (cancer of the plasma cells) and in December 2010 launched MyPRS (Myeloma Prognostic Risk Signature) and in January launched MyPRS-plus, proprietary molecular multiple myeloma tests performed at their Little Rock, AR CLIA lab. In January 2011 Signal Genetics entered into an agreement with Caris Life Sciences, a privately-held national lab company with ~ 100 sales people, to distribute the MyPRS tests to its network of U.S. community-based hematologists/oncologists. In May 2011 Signal Genetics brought on NeoGenomics, to sell the tests to the hospital segment in the U.S. NeoGenomics is a pure-play cancer genetics lab company which performed an estimated 75 million tests for customers throughout the U.S. in 2011. Neogenomics has about 25 sales reps throughout the U.S.

DiagnoCure views the target application for Previstage GCC to help determine, following surgery, whether histologically diagnosed Stage I and Stage II patients actually have more advanced cancer and whether chemotherapy is appropriate in these patients. The specific target market are the ~70k colon cancer patients in the U.S. that are diagnosed as Stage II or earlier. Based on the Medicare reimbursement rate of ~ $3k per test, this equates to a peak annual market worth ~$210 million - or in terms of royalties (based on our 7.5% estimate), a peak annual market worth ~ $16 million to DiagnoCure. The realistic attainable market may, however be smaller than this.

While the $5.1 million minimum in installments/royalties provides a floor on Previstage GCC revenues over the first five years, the ultimate success and upside in revenue of Previstage may be most influenced by the effort and ability of DiagnoCure's commercialization partner (i.e. - Signal Genetics and their partners) to sell the test and grow the customer base.

In Q4 2011 DiagnoCure recorded $9.6k in royalties, the first royalties under this agreement with Signal Genetics for Previstage. Royalties were $10.2k in Q1 2012. We approximate the royalty rate is about 7.5% - which implies Signal Genetics' Previstage revenue was about $136k in the most recent quarter (~$540k+ annualized). Our model assumes that now with Signal onboard, sales of the test grow to about $3 million in fiscal 2012 (~$200k in royalties to DiagnoCure) and to approximately $14 million (~$1MM in royalties to DiagnoCure) in 2015. DiagnoCure noted on the Q1 2012 conference call that Signal has recently added sales reps which may help the acceleration in sales. We also assume the installment payments begin around mid-2013.

## PIPELINE: *Lung Cancer Test / GCC Blood Test*

***Lung Cancer…***

DiagnoCure began research on markers for lung cancer about 10 years ago and a couple years later completed a small study with various that showed potential promise in reducing false negatives in diagnosis of lung cancer. They then mothballed the program to conserve resources and focus on the prostate and colon cancer tests. Now, with additional financial flexibility and growing revenues from the PCA3 test, the company announced that it will resume their lung cancer project which is expected to eventually include the development of a multiplex PCR-based test in bronchiole aspiration as an adjunct to cytology. As this is still in a relatively early stage, we do not currently incorporate any contribution into our financial model from a lung cancer test.

The company also has stated that it will continue to look for additional M&A and partnering deals in order to help facilitate its R&D strategy. In connection with the R&D collaboration agreement, in 2011 DiagnoCure sold $82k of clinical samples to Signal Genetics to support its lung cancer program. In Q1 2012 $287k was received under the R&D agreement with Signal (although it wasn't disclosed what portion, if any, was related to the lung cancer program - continued development of Previstage is also funded by Signal).

Lung cancer is the number one leading cause of cancer death. In the U.S. there are approximately 220k new cases of lung cancer and 160k deaths every year. Worldwide, there are about 1.5 million new cases and 1.3 million deaths. The standard diagnostic methods for lung cancer are a bronchoscopy (thin tubular instrument inserted into the airway used to view bronchial tubes) followed by a histology or cytology test. There are an estimated 600k+ bronchoscopy procedures done every year in the U.S. and Europe, approximately 50% of which result in a positive diagnosis for lung cancer. The other 50% are either negative or inconclusive - of these negative/inconclusive results, about one-half actually have lung cancer but it is not detected - DiagnoCure views this as the potential early adopter market for their future lung cancer diagnostic test. This represents a market size of approximately 300k annual procedures and at an estimated $1k per test, a potential early adopter market worth ~$300 million combined for the U.S. and Europe. If expanded to all patients prior to bronchoscopy, the market size is about 600k patients, or roughly $600 million.

***Colon Cancer Blood Test…***

DiagnoCure notes that Signal Genetics, with exclusive rights to the GCC marker, may pursue a blood test for colon cancer in the future. DiagnoCure has not provided much in the way of details of if or when development a blood test would be pursued but it presumably is an option. If found viable as a screening (or even future surveillance after cancer is initially detected), an FDA-approved GCC blood test would target a signficantly larger market

segment than the current Previstage GCC staging test (targeting post-diagnosis, post-surgery market). As an example, it is estimated that there are ~135 million fecal occult blood tests performed every year in the U.S. Commercialization of a GCC blood test is also not likely to be a near-term event, however.

## BALANCE SHEET

The balance sheet is very healthy, with a relatively large cash balance (bolstered by the infusion from the Signal Genetics deal) and little debt. Shedding the CLIA lab also reduced cash burn. CapEx has historically been minimal. Barring any sizeable capital investments or unforeseen significant increases in operating expenses, we expect little stress on the balance sheet in the near-to-intermediate term.

**Cash**
As of their most recent reporting period (01/31/2012), DiagnoCure had $7.8 million in cash, short-term, and long-term investments.

**Debt**
Debt (at 10/31/2011) is immaterial at $140k ($26k ST, $114k LT) and consists entirely of a loan with the landlord of the company's headquarters to finance improvements to the property.

**Cash Flow**
Cash flow from operations was $173k and ($1,100k) in the three and twelve months ending 10/31/2011 compared to ($465k) and ($3,596k) in the comparable periods in 2010. Excluding changes in working capital, cash flow from operations was ($341k) and ($2,120k) in the three and twelve months ending 10/31/2011 compared to ($169k) and ($3,296k) in the comparable periods in 2010. DiagnoCure most recently noted that they expect cash burn to be about $2 million to $3 million in fiscal 2012.

CapEx was $343k in fiscal 2011 (10/31/2011).

**Preferred Stock**
4.9 million shares of convertible preferred stock are outstanding and owned by Gen-Probe which acquired the shares in May 2009 as part of an amended agreement between the two parties related to FDA submission milestones for the Progensa PCA3 test. The preferred shares have a cumulative 6% dividend and are convertible into an equal number of common shares at any time at the option of the holder.

## OUTLOOK / RECOMMENDATION / VALUATION

We model $1.2 million in royalty revenue in fiscal 2012, including about $1.0 million in PCA3-related royalties from Gen-Probe and $130k in royalties from Signal Genetics for Previstage GCC. We also include ~$500k in R&D payments from Signal Genetics. FDA approval of PCA3 in February (early fiscal Q2 2012), means the $500k in annual installments from the amended license agreement with Gen-Probe related to FDA submission milestones now goes ($124k received in Q1 2012 was the final payment). With the CLIA lab shed, we model SG&A expenses to remain fairly stable from the level in Q3/Q4 2011. R&D expenses will likely tick up with activity related to the lung cancer program and phase 2 of VITAR, although this should be offset from R&D revenue from Signal. We model EPS of ($0.08) in fiscal 2012.

As FDA approval of Progensa PCA3 just came, it's very difficult right now to gauge what the resulting ramp in sales will look like, especially in later years. The steepness in the ramp as well as peak sales will likely be highly influenced by the rate of penetration in what we characterize as the (very large) expanded market for Progensa PCA3. As it is now, we assume Progensa PCA3 sales (and the related royalty to CUR) exhibit somewhat of an

elongated rising slope during fiscal 2012 as Gen-Probe gets fully geared up to detail the test. Our model assumes the $62.5 million royalty-rate hurdle (moving the royalty rate from 8% to 16%) is met during fiscal 2013 and sales of the test related to the indicated market increase by an approximate 35% CAGR from 2012 through 2015. Our model also assumes that penetration in the expanded market remains relatively modest but, as we indicated earlier in this report, depending on the uptake in this segment, our royalty estimates could prove conservative. We will update our model accordingly.

We look for revenue to grow to about $10.2 million in 2015, which includes ~$9 million in Progensa PCA3 royalties (which equates to ~ $54 million in Progensa PCA3 related revenue to Gen-Probe) and about $1 million from Previstage royalties/installment payments (we model Signal Genetics to generate about $14 million in Previstage product sales in 2015). We model EPS of $0.02 in 2015.

We use a DCF model through 2022 to value CUR. Key inputs to our DCF model include DiagnoCure's revenue growing to approximately $42 million in 2022 and a 12% discount rate. Our DCF model calculates a valuation of approximately $2.25/share. We think it bears repeating, however, that our revenue estimates, especially over the long-term, may be conservative at this stage as it's too early following FDA approval to gauge what the U.S. demand will be for Progensa PCA3 and, as we noted earlier, our model does not currently incorporate any contribution from DiagnoCure's pipeline. If our revenue estimates prove conservative, so likely would our valuation - both of which are subject to change.

## MANAGEMENT

### Dr. Yves Fradet, M.D., FRCS(c)

***President and Chief Medical Officer***

Dr. Fradet is co-founder of the Company and Chairman of the Board of Directors of DiagnoCure. He graduated from Medical School at Université Laval in 1976 and is member of the Royal College of Physicians and Surgeons of Canada since 1981. He has been full professor of surgery/urology at Université Laval since 1992. He is also Director, Urology Services, and Director of the Experimental Uro-Oncology Laboratory at the CHUQ - Hôtel-Dieu de Québec. Dr. Fradet studied at the Memorial Sloan-Kettering Cancer Center in New York from 1981 to 1983, where he sub-specialized in urologic oncology. He is a member of several national and international associations and was the first Canadian member of the Urology Research Society. This society is limited to 100 members from all around the world admitted by invitation from the most recognized researchers in urology. He serves as consultant for numerous national and international organizations and he is a frequent invited speaker around the world. He was the founding President of the Canadian Urological Oncology Group, which conducts clinical trials in the field of genito-urinary cancers in Canada. He has published over 180 articles and more than 300 abstracts. Dr. Fradet was appointed Chairman of the Board in January 2010 and President of DiagnoCure in February 2010.

### Chantal Miklosi, MBA

***Chief Financial Officer***

Mrs. Miklosi brings over 15 years experience in investment banking and finance. She holds a BBA in finance from HEC Montreal (1993) and a MBA from the University of Western Ontario, Ivey School of Business (1998). Mrs. Miklosi spent five years as an investment banker at Thomas Weisel Partners, Montgomery Securities and Nesbitt Burns. She then served as Senior Director of Financial Planning and Analysis at Versata (2000-2003), a publicly traded software company, where-in addition to overseeing finance functions she was responsible for investor relations and sales operations. At Orrick, Herrington & Sutcliffe LLP (2003-2004), a national U.S. law firm, she was a Senior Finance Executive responsible for financial statement analysis, budgeting, treasury and M&A. She then spent four years as Managing Director and Chief Financial Officer at JMP Securities in San Francisco (2004-2008), a publicly traded investment bank and asset management firm, where she was responsible for the firm's accounting and financial operations. During her tenure at JMP, the firm successfully completed its initial public offering converting from a partnership to a C-Corporation and implemented Sarbanes Oxley within budget and timeline. Mrs. Miklosi joined DiagnoCure in July 2010 as Chief Financial Officer.

### Frédéric Boivin

***Senior Director, Finance and Administration***

Frédéric Boivin holds a Bachelor's Degree in Business Administration from Université Laval since 1996. From 1996 to 2001, he was controller at four private companies managed by the same shareholder. Mr. Boivin joined DiagnoCure in March 2001 as

Coordinator, Finance & Administration. On November 2003, Mr. Boivin was appointed as Director, Finance & Administration. He is currently Senior Director, Finance & Administration.

## FINANCIAL MODEL

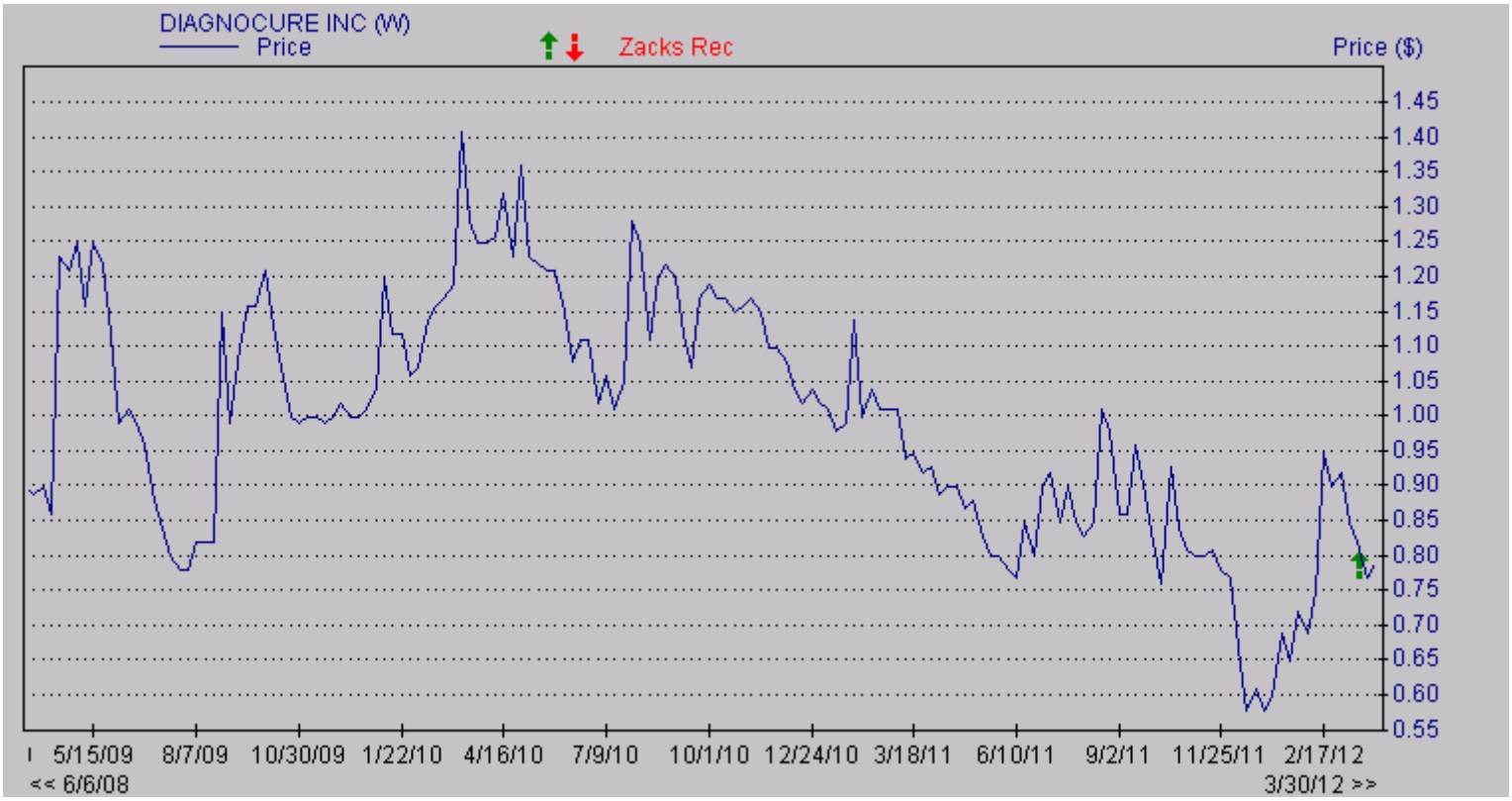
DiagnoCure Inc.

| | 2011 A | Q1A | Q2E | Q3E | Q4E | 2012 E | 2013 E | 2014 E | 2015 E |
|---|---|---|---|---|---|---|---|---|---|
| **Royalty revenue total** | $659.1 | $163.8 | $257.8 | $336.5 | $452.8 | $1,210.8 | $3,254.0 | $6,383.0 | $9,734.0 |
| *y-o-y growth* | *2.2%* | *1.2%* | *37.8%* | *100.0%* | *218.9%* | *83.7%* | *168.7%* | *96.2%* | *52.5%* |
| **Total other revenue** | $585.1 | $392.4 | $70.0 | $75.0 | $125.0 | $662.4 | $500.0 | $500.0 | $500.0 |
| *y-o-y growth* | *-7.1%* | *120.7%* | *-52.9%* | *-39.4%* | *-39.4%* | *13.2%* | *-24.5%* | *0.0%* | *0.0%* |
| Revenue | $1,244.2 | $556.2 | $327.8 | $411.5 | $577.8 | $1,873.2 | $3,754.0 | $6,883.0 | $10,234.0 |
| *y-o-y growth* | *-2.4%* | *63.8%* | *-2.4%* | *40.9%* | *65.8%* | *50.5%* | *100.4%* | *83.4%* | *48.7%* |
| Cost of Goods Sold | $2.5 | $0.0 | $4.6 | $5.8 | $7.6 | $17.9 | $55.2 | $113.3 | $172.8 |
| Gross Income | $1,241.8 | $556.2 | $323.2 | $405.7 | $570.2 | $1,855.3 | $3,698.8 | $6,769.7 | $10,061.2 |
| *Gross Margin* | *99.8%* | *100.0%* | *98.6%* | *98.6%* | *98.7%* | *99.0%* | *98.5%* | *98.4%* | *98.3%* |
| R&D | $1,235.6 | $802.2 | $481.0 | $467.5 | $522.5 | $2,273.2 | $2,405.0 | $2,600.0 | $2,750.0 |
| *% R&D* | *99.3%* | *144.2%* | *146.8%* | *113.6%* | *90.4%* | *121.4%* | *64.1%* | *37.8%* | *26.9%* |
| SG&A | $3,897.6 | $576.6 | $840.0 | $895.0 | $900.0 | $3,211.6 | $4,525.0 | $5,450.0 | $6,375.0 |
| *% SG&A* | *313.2%* | *103.7%* | *256.3%* | *217.5%* | *155.8%* | *171.5%* | *120.5%* | *79.2%* | *62.3%* |
| Restructuring Charges | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| Operating Income | ($3,891.4) | ($822.7) | ($997.8) | ($956.8) | ($852.3) | ($3,629.6) | ($3,231.2) | ($1,280.3) | $936.2 |
| *Operating Margin* | *-312.8%* | | | | | *-193.8%* | *-86.1%* | *-18.6%* | *9.1%* |
| Financial income, net | $47.9 | $0.0 | $37.0 | $32.0 | $30.0 | $99.0 | $50.0 | ($50.0) | ($100.0) |
| Pre-tax Income | ($3,843.5) | ($822.7) | ($960.8) | ($924.8) | ($822.3) | ($3,530.6) | ($3,181.2) | ($1,330.3) | $836.2 |
| Taxes (benefit) | ($111.5) | ($6.5) | $0.0 | $0.0 | $0.0 | ($6.5) | $0.0 | $0.0 | $0.0 |
| *Tax Rate* | *-9.0%* | | | | | *-0.3%* | *0.0%* | *0.0%* | *0.0%* |
| Net Income (continuing ops) | ($3,732.0) | ($816.2) | ($960.8) | ($924.8) | ($822.3) | ($3,524.1) | ($3,181.2) | ($1,330.3) | $836.2 |
| *Net Margin* | *-299.9%* | | | | | *-188.1%* | *-84.7%* | *-19.3%* | *8.2%* |
| EPS (continuing ops) | ($0.09) | ($0.02) | ($0.02) | ($0.02) | ($0.02) | ($0.08) | ($0.07) | ($0.03) | $0.02 |
| *YOY Growth* | *-57.7%* | | | | | *-5.7%* | *-11.7%* | *-60.0%* | *-160.2%* |
| Diluted Shares O/S | 42,993 | 43,013 | 43,025 | 43,050 | 43,100 | 43,047 | 44,000 | 46,000 | 48,000 |

*Brian Marckx, CFA*

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