Zacks Small-Cap Research

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VolitionRx Ltd (VNRX-NYSE)

VNRX: More Details On Triage Strategy, Launch Still Expected in 2017

Based on our DCF model which goes out to year 2026 and uses a 9.5% discount rate (based on CAPM) and 2% terminal growth rate, VNRX is valued at $7/share. Our model and assumptions will be updated if appropriate based on news flow which could also influence valuation

Current Price (11/17/16)	$3.40
Valuation	**$7.00**

OUTLOOK

Data from the various clinical trials continues to be consistently positive. Based on the number of studies anticipated to read out over the near term, this should be a telling year in terms of the potential utility of the NuQ assays in a variety cancers. Still expect CE Marking of the initial CRC assay this year. Commercial introduction in Europe slated for early 2017. VNRX to announce more details on launch, mktg and branding strategy in Jan 2017. We will be eagerly awaiting additional clinical data in several cancers which, assuming positive, could prompt upward revisions to our modeled revenue and related valuation. For example, we have yet to model any contribution from a potential pancreatic cancer panel but will likely do so if high accuracy of the diagnostic is maintained in subsequent studies including recently initiated 750-patient study.. We feel the current market price remains cheaper than warranted and undervalues the company. Our price target is $7/share. We think additional and ongoing positive clinical data should further benefit appreciation of the share price.

SUMMARY DATA

52-Week High	**$5.64**
52-Week Low	**$3.08**
One-Year Return (%)	**5.77**
Beta	**-1.51**
Average Daily Volume (sh)	**21,529**
Shares Outstanding (mil)	**26**
Market Capitalization ($mil)	**$107**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**12**
Insider Ownership (%)	**30**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
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 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in '000)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	$0 A	$0 A	$0 A	$0 A	$0 A
2016	$0 A	$0 A	$0 A	0 E	$0 E
2017					$1481 E
2018					$4517 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$0.12 A	-$0.10 A	-$0.16 A	-$0.15 A	-$0.54 A
2016	-$0.13 A	-$0.13 A	-$0.15 A	-$0.15 E	-$0.55 E
2017					-$0.51 E
2018					-$0.43 E

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

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Q3 Results / Operational and Milestones Update:

VNRX reported Q3 financial results and provided an operational and milestones update. On the financials side, results continue to come in very close to our estimates. We continue to expect zero revenue in the current year with initial contribution beginning in the first half of 2017 following launch of NuQ Triage, the initial CRC panel that will be positioned as an adjunct to FIT and expected to be initially introduced in five European countries early next year.

Q3 OpEx was $3.5M, mostly inline with our $3.3M estimate and up slightly from Q2. We expect operating expenses to continue to trend higher on additional clinical trial and regulatory activities, some initial (moderate) spend on sales, marketing and launch preparations and activities related to initiation of a U.S. regulatory program. Management continues to guide for Triage to be CE Marked by the end of this year and anticipates launch in one or more of their initially targeted European countries sometime in the first half of next year. Meanwhile, the company's clinical pipeline remains very active with programs ongoing in CRC as well as several other cancers. This now also includes a new, very large study (30k patients, 90k samples) being conducted in collaboration with Hvidovre. And on the horizon is implementation of an FDA-clearance/approval strategy which will include preparations for a U.S.-based colorectal cancer study to support a potential future 510(k) de novo submission.

Q3 net income and EPS were ($3.5)M and ($0.15), compared to our ($3.3)M and ($0.14) estimates. Cash used in operating activities was $2.1M and $6.7M in the three and nine months ending September 30th. As we have noted in the past, we think the company has done an impressive job with efficient use of cash as evidenced by the reams of clinical data, ongoing studies, CE Marking of several CRC assays and completing validation of Triage (among other successes) that they have accomplished over the last ~2 years on a cash budget of less than $20M.

Pro forma for the October equity raise (2.48M shares @ $5/share, net proceeds of ~$11.7M) cash balance at Q3 quarter end was approximately was $24.2M which management noted is the highest cash position in company history. At the current burn rate this represents over 30 months worth of operating funds. And while we expect cash burn to increase, the current stockpile should provide more than a sufficient runway for launch of Triage and funding of the various clinical programs as well as for general operating activities at least well into 2018. By that time VNRX could have at least one more product on the market (potentially including in the U.S.) and possibly several more. And if the clinical activity remains as robust and results as successful as it has been over the recent past, the shares could be trading at significant higher levels if and when VNRX again looks to tap the equity markets.

Triage Update:

In early September VNRX announced that their first commercialized test is expected to be a single 'normalized' assay - consisting of two of the three assays that have already received CE Mark - called Nu.Q Triage Colorectal Cancer Screening Test. VNRX expects Nu.Q Triage, which will be positioned for use following a positive result from a fecal immunochemical test (FIT), to be CE Marked later this year and launch in their initial targeted European territories sometime in the first half of 2017. These initial countries are Ireland, Scotland, the Netherlands, France and Denmark.

Management indicated the recent change in plans regarding the composition of their initial CRC test was opportunity-based, made after significant market analysis and provides the fastest route towards generating significant initial revenue. The company points to market feedback that indicates the greatest current unmet need in CRC screening is to reduce bottlenecks in colonoscopy screening (up to 14 weeks in some places) in parts of Europe caused in part by the high false positive rates of FIT - which are often used as a first-line diagnostic, positive results of which are then referred for colonoscopy.

As envisioned by VNRX, Triage would be used following positive FIT results which would reduce the number of colonoscopy referrals for people that do not have CRC - this in-turn will reduce bottlenecks and increase throughput of colonoscopy screening for those people that are most likely to have cancer. Being able to reduce the number of unnecessary colonoscopies could be highly appealing to both the individual and the healthcare systems. On the individual level, colonoscopies are invasive, uncomfortable and time consuming - so being able to safely avoid them is a potentially potent message for Triage. And for the healthcare system, Triage may be able to reduce colonoscopy bottlenecks for more of the people that are most likely to benefit from them while possibly reducing overall healthcare costs.

In a prospective screening study (n=2,000) conducted with Hvidovre Hospital, Triage demonstrated the potential to reduce colonoscopies by 25% while maintaining a 97% detection rate for CRC. The study includes a total of 8,000 patients. Management noted on the Q3 call that the validation study is now completed, results of which will be presented at ENDO 2017 World Congress of GI Endoscopy in mid-February. Results will support CE Marking, and perhaps even more importantly, marketing of the test to the national health care systems and/or screening programs in Europe.

We think Triage may provide for easier entry into and less disruption to existing CRC screening programs as compared to a first-line screen. This is because Triage is not replacing another current test (such as FIT) and therefore is not asking clinicians and screening programs to make an either/or decision, like a NuQ first line screen might. So it may allow easier foot-in-the-door opportunity. And if Triage can provide foot-in-the-door opportunity, it may help facilitate entry of VNRX's expected follow-on CRC tests, including those for symptomatic populations and a stand-alone first-line screen.

On the potential negative side is that Triage will add incremental cost (i.e. in addition to FIT) to screening programs - although management indicated that expected pricing of ~50 Euro is relatively insignificant to the budgets of these screening programs. And certainly in a bigger-picture view, Triage has the potential to reduce overall cost of colorectal cancer diagnosis and care if it reduces the number of unnecessary colonoscopies and improves detection, particularly at the more treatable early stages of the disease.

VNRX expects effective marketing can be done with a fairly bare-bones program given that European CRC screening programs are largely nationalistic in nature. Targeting KOL's (influential clinicians and screening program leaders) in each of the targeted countries may be a part of the effort. Decideum, VNRX's market access consultants, helped with advising the company on the initial target countries and penetration strategies. These first five countries should also provide somewhat of a litmus test in terms of utility and adoption as well as potentially learning experiences related to steps, procedures and policies for access to national health and screening programs. VNRX expects to reveal more about their marketing and branding strategy as well as launch expectations at the JP Morgan health care conference in January (which we will be attending).

Larger Facility, New 30k Hvidovre Study, Follow-On Products, Pancreatic Cancer…

VNRX continues to have several irons in the fire as they simultaneously move closer to launch of their first assay. Recent activities and milestones, in addition to Triage-related progress, includes securing a new and larger office and R&D facility, further beefing up of the IP portfolio and commencement of their largest study to-date. Upcoming milestones include completion of the larger Germany-based pancreatic cancer study, presentation of data from both the 4,800 retrospective and 14k prospective CRC studies as well as the 27-cancer Bonn study. VNRX also expects to announce additional studies in lung and pancreatic cancers;

- IP: VNRX received a fourth U.S. patent for their NuQ technology, "Method For Detecting Nucleosomes Containing Histone Variants", which relates to the ability to detect nucleosomes in the blood
- Validation: study, "Pre-analytical variables of circulating cell-free nucleosomes containing 5-methylcytosine DNA or histone modification H3K9me3", published in the Scandinavian Journal of Clinical Laboratory Investigation demonstrated that certain pre-analytical variables related to collection and handling of blood samples, including stasis (vs. no stasis), different time and day of collection, variability in temperature, collected pre vs. post colonoscopy and collected pre and post surgery, had no influence on the stability of the NuQ test. Demonstration of stability and replication under various conditions is critical as real-world testing does not have the homogeneity or structure that a typical clinical trial would

- Triage Commercialization: timelines for expected CE Mark of the full panel (late 2016/early 2017) and launch in Europe (early 2017) remain largely intact. Expect to provide more details about launch, marketing and new branding strategy at JPM conference in January. Full results of validation study expected to be presented at ENDO 2017 in February.
- 30k Patient study: Prospective seven year study in collaboration with Hvidovre Hospital announced in early November. Total of 90k blood samples will be taken from 30k patients that tested negative in national fecal colorectal cancer screening test. Samples will be taken at three timepoints, two years apart. Study will determine how early NuQ can detect cancer prior to a definitive diagnosis. In addition, up to 120 points of data will be collected including risk factors such as smoking, obesity, etc. This could provide a massive amount of information relative to utility of NuQ in different population subsets as well as how soon the technology can detect cancer. VNRX believes they will have initial data by the end of 2018
- New, larger facility: VNRX acquired a larger facility for office and lab space which is expected to expansion of the scientific team, greater R&D capabilities and help expedite commercialization of Triage and follow-on products. VNRX expects the facility to be fully operational by the end of Q1 2017 which should closely coincide with Triage launch timelines
- Pancreatic cancer: While we expect VNRX will look to bring a follow-on CRC test to market – likely a stand-alone for symptomatic population, management noted again on the Q3 call that pancreatic cancer is next in line in terms of the next cancer target. Initial (small) studies have indicated potentially high accuracy of NuQ in detection of pancreatic cancer. The 750-patient German study, while delayed from earlier expectations, is expected to read out sometime next year. A larger more 'pivotal' study could follow and potentially support commercialization

Snapshot of Ongoing Programs…

- Colorectal Cancer:
  - **4,800** sample retrospective trial expected to have full and final results in 2017. May be used to support development of next CRC panel
  - **14k** sample prospective trial. This study is comparing NuQ to FIT test, the market standard for CRC in Europe. Additional data expected to be presented in early 2017
  - Additional data from (pre-cancerous) adenomas in 2017
  - FDA – expect to meet with FDA regarding proposed 510(k) de novo pathway seeking clearance for use as an adjunct to standard of care in high-risk symptomatic patients
    - Hope to begin 510(k) supporting studies in 2017. Initial indication will be CRC
    - Anticipate ~600 patient study at cost of $1M - $1.5M per indication
    - Hope to file for first 510(k) clearance in 2017
    - Follow-on indications in other cancers would follow including potentially lung and pancreatic cancer in 2018
    - PMA – may also look to initiate PMA supporting studies in 2017 for NuQ as a screening test for CRC. Pivotal PMA study would likely be significantly larger than those for 510(k) clearance – if all goes well PMA studies might complete in 2018
    - LDT – will continue to investigate the CLIA lab route. We think LDT would be a fall-back if for some reason 510(k) de novo proves not viable.

- Pancreatic Cancer:
  - Recently announced data from 59-patient study showing pancreatic panel demonstrated 92% sensitivity @ 90% specificity. Study published in Clinical Epigenetics.
  - Shortly after the 59-patient data, VNRX announced NuQ was able to correctly detect 19 of 20 (95% sensitivity) pancreatic cancers with an 84% specificity in patients from their 4,800-sample retrospective colorectal cancer study using two NuQ assays along with carcino-embryonic antigen (CEA) test
  - Subsequent to the positive data from the (above) two smaller pilot studies, in May 2016 VNRX announced 750-patient pancreatic cancer study will be done with DKFZ, the German Cancer Research Center. Will use assays from two pilot studies as well as new assays (as well as CEA test). This 750-patient study has been slower than anticipated but we think could have data in 2017
  - Assuming further positive data, CE Mark for pancreatic cancer might be possible in 2017

- Lung Cancer:

- Expect full analysis of **240-patient** lung cancer study in 2017. As a reminder VNRX announced interim results, on 73 patients (29 with NSCLC, 22 with COPD and 22 healthy controls), in November 2015 which showed a panel of four NuQ assays detected 93% of lung cancer cases (27/29) with 91% specificity (2 false positives among 22 healthy controls).
- The larger **600-patient** lung cancer trial, being conducted at University Hospital in Bonn Germany, is also expected to read out
- May initiate other studies in lung cancer in 2017
- If all goes well CE Mark for lung cancer may also be a possibility in 2017

- Prostate Cancer:
  - Results from retrospective study using **537 blood samples** from hospital patients in collaboration with Surrey Cancer Research Institute (Univ of Surrey, UK) announced in April 2016 and presented at AACR. Showed a single NuQ assay detected 71% of early stage I (and 86% of late stage IV) prostate cancer cases at 93% specificity – this is significantly more accurate than that of the widely used PSA test. These results are particularly encouraging given that the study used just one NuQ assay. Follow-on studies incorporating more than one NuQ assay and/or in combination with PSA may further improve on this already highly positive data
  - Prospective **120-patient** study being done by Immune Health. Recruiting patients – shooting to have data completed in 2017
  - May initiate other studies in prostate cancer in 2017
  - Given the highly encouraging 537-sample data, prostate cancer is also a front-runner to follow colorectal cancer as next assay for commercialization

- 27-Cancer (Pan-Cancer): 4,700 patients looking at 27 of the most prevalent cancers. Analysis will be conducted with several (~25) NuQ assays. Expected to complete in 2017

- Non-Cancers: in March 2016 VNRX announced the first data from a non-cancer study. Preliminary data showed NuQ was able to detect 86% of patients with Idiopathic Pulmonary Fibrosis (IPF), a fatal lung disease. The study, being conducted at Liege University Hospital in Belgium, included 30 healthy subjects and 47 IPF patients; 21 which had not been treated and 27 which had. Interim data showed NuQ detected IPF in 18 of the 21 non-treated (86%) from the healthy cohort at 80% specificity (6 false positives). VNRX expects to move into a larger study to help confirm results. While IPF affects only about 100k in the U.S., it is usually fatal and diagnosis options are limited and costly. As such, an accurate blood-based IPF test could have real appeal.

CLINICAL TRIAL DETAILS:

- **Prostate Cancer:** feasibility study assessing NuQ in detecting prostate cancer done in collaboration with Surrey Cancer Research Institute (Univ of Surrey, UK) showed very encouraging data. Data, announced in April 2016 and presented at AACR, showed a single NuQ assay detected 71% of early stage I (and 86% of late stage IV) prostate cancer cases at 93% specificity (detailed results below) – this is significantly more accurate than that of the widely used PSA test. The retrospective study used 537 blood samples (266 prostate cancer, 271 age-matched healthy samples) from hospital patients. Evaluated groupings were patients with; aggressive prostate cancer, slow-growth prostate cancer and age-matched healthy individuals (control group). We view this 537-sample results as particularly encouraging given that the study used just one NuQ assay. Follow-on studies incorporating more than one NuQ assay and/or in combination with PSA (similar to VNRX's pancreatic cancer studies which use NuQ in combo with CEA) may further improve on this already highly positive data

AACR Poster Presentation of 537-Sample Data

Cancer Stage	Sensitivity (@ 93% specificity)	N=
Stage I	71%	93 / 131
Stage II	63%	22 / 35
Stage III	79%	11 / 14
Stage IV	86%	12 / 14

We think eventual pursuit of prostate cancer was almost a given based on the relatively high incidence of the disease (~250k U.S. diagnoses each year) and widespread testing despite the poor accuracy of current non-invasive diagnostics. There's significant debate about the benefits of prostate cancer testing as onset of the disease mostly occurs in older age, it is relatively slow-growing and usually is not the cause of death. Prostate serum antigen (PSA) tests are the most widely used front-line diagnostic with ~20 million tests performed each year in U.S. and ~45 million worldwide. But PSA is fraught with accuracy issues as 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).

PSA's lack of 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. In fact the USPSTF recommends that healthy men without any symptoms of prostate cancer not receive a PSA test with the USPSTF chairwoman at the time of the decision noting that, "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." This 537-sample feasibility study provides initial support that NuQ may eventually provide the technology backbone of a test that USPSTF is looking for.

VNRX is also working with the MD Anderson Cancer Center on a retrospective study to determine NuQ's ability to distinguish anaplastic prostate cancer, a particularly aggressive form of the disease, from typical castration resistant prostate cancer.

- **Colorectal Cancer:**

  - **30k Patient study**: Prospective seven year study in collaboration with Hvidovre Hospital announced in November 2016. Total of 90k blood samples will be taken from 30k patients that tested negative in national fecal colorectal cancer screening test. Samples will be taken at three timepoints, two years apart. Study will determine how early NuQ can detect cancer prior to a definitive diagnosis. In addition, up to 120 points of data will be collected including risk factors such as smoking, obesity, etc. This could provide a massive amount of information relative to utility of NuQ in different population subsets as well as how soon the technology can detect cancer. VNRX believes they will have initial data by the end of 2018

  - **Hvidore Retrospective**: in September 2015 VNRX reported additional positive interim data. The presentation supports earlier data that found the NuQ technology has better than 80% sensitivity at 78% specificity with high accuracy at all stages of the disease, including Stage I (i.e. earliest) – we discuss more fully below. VNRX expects to have full data, including early-stage pre-cancerous lesions, from the 4,800-patient retrospective colorectal cancer study in 2017. May be used as support for development of next CRC panel

  - **Hvidore Prospective**: additional data from 14,000 sample prospective colorectal cancer study expected in 2017.

  - **Pre-Cancerous Colorectal Study:** a subset of the Hvidore retrospective study included patients with precancerous lesions, or adenomas. NuQ was able to detect 60% of these lesions. This prompted VNRX to initiate a study, which will is also being conducted at Hvidore Hospital, for the detection of precancerous polyps. Data was announced in mid-February which showed highly promising accuracy in this difficult to diagnose population. The double-blinded trial was and designed to detect adenomas before they become cancerous, as well as early stage colorectal cancer. It included 430 samples who either had symptoms of colorectal cancer or were at high risk. This included 42 with stage I CRC, 46 with stage II CRC and 181 with adenomas. The healthy cohort included 160 patients. A panel of five NuQ assays detected 75% of adenomas and 86% of stage I CRCs at 78% specificity. VNRX may include additional assays in this other early stage CRC studies in order to try and further improve on accuracy. The company expects to release additional data from this study. The current thinking is that an adenoma assay/panel could be layered into a colorectal cancer assay or as a stand-alone product. As precancerous polyps have proven difficult to detect, relatively high accuracy in this indication could be a meaningful differentiator compared to other colon cancer tests.

  - **CHU Dinant Godine Colon Cancer Study:** NuQ continues to show high accuracy in colon cancer trials. Some of the most recent data comes from a small study conducted at the university hospital, CHU Dinant Godinne - UCL Namur, in Belgium. 121 patients which either had symptoms of colon

cancer or were at high risk were given a colonoscopy and 23 were found to have colon cancer. The same subjects' blood samples were tested with a panel of four NuQ tests which detected 90% of colon cancer cases at 90% specificity and 67% of precancerous polyps. The panel was able to detect cancer at all stages. The results (below) are inline with earlier findings (and larger studies) which have shown NuQ to be able to detect colon cancer at specificity of at least 80% and in some cases, better than 90% and precancerous polyps at 60% or better. Additional data from VNRX's two large colon cancer studies being conducted at Hvidore hospital which combined includes almost 20k samples as well as an 800-sample precancerous polyp study, are expected in 2017. These announcements should provide even greater insight into the detection ability of NuQ in colon cancer.

	4 NuQ® biomarker assays*		5 NuQ® biomarker assays**	
	% detected	Number cases	% detected	Number cases
CRC (all stages)	91%	21 of 23 cases	87%	20 of 23 cases
CRC stage I	100%	4 of 4 cases	75%	3 of 4 cases
CRC stage II	83%	5 of 6 cases	83%	5 of 6 cases
CRC stage III	86%	6 of 7 cases	86%	6 of 7 cases
CRC stage IV	100%	4 of 4 cases	100%	4 of 4 cases
CRC unknown stage	100%	2 of 2 cases	100%	2 of 2 cases
Dysplastic pre-cancers	67%	6 of 9 cases	67%	6 of 9 cases
At 90% specificity against healthy subjects.				
*age adjusted				
**not age adjusted				

- **Lung Cancer:** In December 2014 VNRX announced that they were pursuing a larger lung cancer study, which followed positive data from a pilot study, announced in November of that year. 46 individuals were included in the pilot study, including 21 with non-small cell lung cancer, 12 with COPD and 13 healthy subjects. Both sputum and blood samples were tested. With sputum, NuQ was able to detect 18 of the 21 (85%) lung cancer cases with no false positives for healthy individuals. In addition, NuQ was able to differentiate between lung cancer and COPD.

  With blood samples, NuQ identified 76% (16 of 21) patients with lung cancer with only one false positive (1 of 13) of a healthy individual. With blood, NuQ was also able to differentiate between lung cancer and COPD.

  VNRX since initiated a larger prospective study – which includes 240 patients and is being conducted at Liege University Hospital in Belgium. Interim results, on 73 patients (29 with NSCLC, 22 with COPD and 22 healthy controls), were announced in November 2015 which showed a panel of four NuQ assays detected 93% of lung cancer cases (27/29) with 91% specificity (2 false positives among 22 healthy controls). VNRX expects the full data set from this trial as well as interim data from the company's larger 600-patient lung cancer trial being conducted at University Hospital in Bonn Germany. We think if NuQ can confirm accuracy at this 90%+ level in larger studies, particularly in early-stage cancers, that this should be a catalyst to the stock price given the dearth of reliable testing options, high mortality of lung cancer and significant incidence of the disease.

- **27-Cancers Study**: 4,700 patients looking at 27 of the most prevalent cancers at the U of Bonn. Study could complete in 2017. The study has the potential to produce an enormous amount of data given the number of assays (~25) that may be included as well as the diverse sample set. It is still a question mark as to how the output will applied, although if the data supports it, a home-run would be eventual development of an assay/panel that could detect and differentiate between several cancer types

- **Pancreatic Panel Shows 92% Sensitivity @ 90% Specificity:** *Study Published in Clinical Epigenetics. Could It Become The New "Gold Standard"???….*

  In mid-October 2015 VNRX announced that results of their pancreatic cancer pilot study were published in the online version of Clinical Epigenetics. The study included 59 individuals; 25 with stage IIa or stage IIb pancreatic cancer (i.e. early-stage, operable cancers), 24 healthy subjects and 10 with other pancreatic non-cancer disorders (i.e. benign pancreatic disease). Blood samples were taken from patients prior to being treated at Skane University Hospital in Lund, Sweden. Healthy samples came from a local blood bank.

In January VNRX announced interim results which showed a five-assay NuQ panel correctly identified 21 of the 25 cancer cases (**84% sensitivity**) at a **90% specificity** among the healthy subjects (i.e. - two false positives). This panel was also able to distinguish 18 of the pancreatic cancer cases from healthy individuals or those with other pancreatic non-cancer disorders with a 72% sensitivity at 90% specificity (three false positive results; one from healthy group and two from benign group).

As we noted in January 2015, we characterized the interim results as highly encouraging given the impressive accuracy seen with the interim data. However, we are even more inspired with the results of the full data set which included, in addition to the initial five-assay panel, a four-NuQ assay panel in combination with a generic CA19-9 ELISA test. Carbohydrate antigen 19-9 (CA 19-9) is considered the current gold-standard diagnostic for pancreatic cancer testing and is used as a benchmark for comparing novel pancreatic cancer diagnostics. This is despite it not being particularly accurate – with reported sensitivity/specificity of 79%/82%.

But when four of the five NuQ assays in the original panel (the least incrementally additive assay was excluded) were combined with CA 19-9, VNRX was able to achieve higher accuracy as compared to both their initial five-assay panel as well as to CA 19-9. This four NuQ panel plus CA 19-9 achieved **92% sensitivity** using a **90% specificity** (identified 23 of 25 cancer cases) on discriminating cancer versus healthy subjects as well as versus healthy and benign subjects. This is significantly higher than CA 19-9 alone. The table below illustrates the superiority of the four NuQ panel plus CA 19-9 as compared to CA 19-9 alone, the four NuQ assay panel alone and the original five NuQ assay panel. In addition to the high accuracy of the four NuQ panel plus CA 19-9, it is also noteworthy that all of the three false positives were from the benign group, with none coming from the healthy group (i.e. – 100% specificity versus healthy group).

Table 3 Performance of cfnucleosome biomarker panels with and without CA 19-9

	CA 19-9		4 NuQ® assays		5 NuQ® assays		4 NuQ® assays + CA 19-9	
Clinical question	AUC	Sensitivity (%) (90 % specificity)	AUC	Sensitivity (%) (90 % specificity)	AUC	Sensitivity (%) (90 % specificity)	AUC	Sensitivity (%) (90 % specificity)
Cancer vs. healthy	0.87	80	0.91	68	0.95	84	0.98	92
Cancer vs. healthy and benign	0.84	72	0.90	64	0.92	72	0.94	92

SOURCE: Bauden et al. Clinical Epigenetics (2015) 7:106

Despite CA 19-9's high risk of false negative results and the American Society of Clinical Oncology discouraging its use, it remains the gold standard for diagnosis of pancreatic cancer. However, its main use has mostly been relegated to determine whether a tumor is secreting carbohydrate antigen 19-9 and to monitor the level following treatment. The results of this small pilot study suggest NuQ assays in combination with CA 19-9 could have more than high enough accuracy as a clinical pancreatic cancer diagnostic and would be the only test able to identify early stage pancreatic cancer with relatively very high sensitivity.

And additional data, from a separate study, further supported the findings of high accuracy of NuQ in detection of pancreatic cancer. Later in October 2015 VNRX announced that NuQ was able to correctly detect 19 of 20 (**95% sensitivity**) pancreatic cancers with an **84% specificity** in patients from their 4,800-sample retrospective colorectal cancer study (while it is a colorectal cancer study, it also picked up patients with other cancers, including 20 with pancreatic cancer). Two NuQ assays along with carcino-embryonic antigen (CEA) test were used in the analysis.

Subsequent to these results, in May 2016 VNRX announced a 750-patient pancreatic cancer study will be done with DKFZ, the German Cancer Research Center. The study will use assays from the two pilot studies as well as new assays (as well as CEA test). This 750-patient study is expected to rwad out in 2017. Could form the basis for a CE Mark filing for pancreatic cancer – potentially in 2017.

Diagnosis of pancreatic cancer is almost always a death sentence given that no tests currently on the market can reliably identify early-stage pancreatic cancer. Currently only about 6% of people diagnosed with pancreatic cancer survive five years or more. The USPSTF has a grade D recommendation on pancreatic cancer screening, recommending "against routine screening for pancreatic cancer in asymptomatic adults using abdominal palpitation, ultrasonography, or serological markers." The USPSTF notes that they "found no evidence that screening for pancreatic cancer is effective in reducing mortality. There is a potential for significant harm due to the very low prevalence of pancreatic cancer, limited accuracy of available screening tests, the invasive nature of diagnostic tests, and the poor outcomes of treatment. As a result, the USPSTF concluded that the harms of screening for pancreatic cancer exceed any potential benefits."

As such a test that could identify pancreatic cancer at an early stage may allow for more effective clinical intervention and vastly improve mortality rates. If VNRX can demonstrate similar results of this pilot study in larger trials, we think eventual FDA approval would be almost a given and believe it is reasonable that this panel could one day become the new gold standard for pancreatic cancer diagnosis. Importantly, CA 19-9 is a generic ELISA test so it is easily available with no intellectual property protection and, therefore, can be freely combined and commercialized in a VNRX panel.

COMMERCIALIZATION

- **CE Mark / European Commercialization**: NuQ X001S was the first assay to receive CE Mark, which happened in September 2015. A second and third (NuQ V001 and NuQ T003) assay received CE Mark in April 2016. Despite some delay in expected release of data from the Hvidore studies, VNRX continues to expect that additional assays and the initial panel will be approved and launch sometime in 2016. Initial panel will be supported by 4,800-sample colorectal cancer study. Follow on CRC screen could also come in 2017 and be supported by 14K-sample study.
    - o Follow-ons…: VNRX will then look to strengthen both the clinical support for their technology as well as the performance. Follow-on data from the two large Hvidore studies should provide support for both – as noted, additional data should be available fairly quickly. The 14k sample prospective trial expected to have preliminary data in late 2016. This study is comparing NuQ to FIT test, the market standard for CRC in Europe. Positive results could provide support for NuQ as a CRC screen which could significantly broaden its appeal. The data should help drive development of new and higher performing assays on a regular basis and, combined into panels, can further enhance performance, providing opportunity for the next iteration of CE Marked products. Providers and payers are also interested in seeing as much data as possible to make informed use and reimbursement decisions – so a regular flow of positive trial data will be key to maximizing initial chances of success in the marketplace
    - o Commercialization: VNRX does not expect to launch into Europe until they have more supporting data and the full panel CE Marked – which they think can happen in late 2016. VNRX had previously been guiding for launch to happen in late 2016 but has since revised to an early 2017 timeline. VNRX recently brought on two consulting firms to guide the European commercialization strategy which includes advice on market selection, reimbursement expectations, distribution, etc. They also recently brought on a Chief Marketing and Communications Officer to help lead the roll-out in Europe as well as (eventually) the U.S.
    - o Piggy-back as an adjunct: despite clinical evidence demonstrating relatively high accuracy in detecting cancer, the novel nature of NuQ all but guarantees uptake and adoption among clinicians will be drawn out. VNRX recently provided some particularly interesting insight relative to initial foot-in-the-door strategy. By initially commercializing as an adjunct to standard diagnostics (or gold-standard in many cases), clinicians aren't making a 'replace' decision but instead an 'in addition to' decision, the latter which they will almost certainly be more receptive to. This piggy-backing off of the industry standard test allows a foot-in-the-door opportunity, initial revenue and chance to build greater awareness while pursuing the eventual goal of positioning NuQ as a first-line screen. And NuQ has demonstrated in clinical studies that it provides incremental decision-making value to gold standard cancer diagnostics. This includes in a pancreatic cancer study where a panel of NuQ assays plus CA 19-9 (considered the current gold-standard diagnostic for pancreatic cancer testing) achieved 92% sensitivity using a 90% specificity, which was better than CA 19-9 alone
    - o More follow-ons: with the plethora of data expected to come out of the various studies, VNRX hopes to further enhance the performance of their tests and bring further iterations of cancer panels through CE Marking. Clearly the initial focus is colorectal cancer but pancreatic, prostate, lung and others could potentially follow in short-order. And possibly, eventually a multi-cancer panel Pancreatic and lung looks to be the two next indications that VNRX will pursue after colorectal, both of which the company hopes to have CE Marking for in 2017.
    - o Our Comments: Epigenomics has had a tough go of it in Europe with their IVD Epi proColon colon cancer blood test. While the test has been available since 2012 product revenue from Europe remains at roughly $1 million per year.. They cite a difficult reimbursement environment and high barriers to get into the government level screening programs. Part of the difficulty is most likely pricing as government programs are tight-fisted and to be competitive pricing needs to be near the EUR 20 – 30 range (~$20 - $30). And if Epigenomics can't or won't come in near there, then it is reasonable they may not qualify. VNRX indicated that they believe they can meet that price point and

maintain reasonable margins. They brought on the two consulting firms (one focused on the U.K. and the other the rest of Europe) to help navigate the intricacies and difficulties – one potentially major one being reimbursement – of the European market. VNRX may also have an advantage in accuracy – the data to-date has suggested NuQ may have superior accuracy as compared to the 79% sensitivity / 68% specificity Epi proColon demonstrated in their PMA-supporting studies. This could be particularly true in pre-cancerous lesions – a much more difficult population to identify but one which NuQ has shown impressive accuracy. If confirmed in larger studies, this could draw particularly strong appeal. As more data is announced, it should provide greater insight.

We think it is reasonable to expect revenue from Europe will not be overly significant in the first year of launch, particularly as the process to obtain reimbursement under government programs can be drawn out.

- **U.S. Pathway**: initial U.S. introduction had until recently expected to be in the form of licensing rights to the technology to CLIA certified labs to develop LDT tests. However VNRX is now clearly leaning towards the 510(k) de novo (FDA clearance) route. Concurrent with that VNRX would work to bring an FDA approved test (i.e. PMA) to market.

  VNRX has brought on another consultant to guide them in their U.S. plans. VNRX's Chief Medical Officer, Dr. Terrell will lead their U.S. FDA strategy and commercialization plan. Timelines for the possible CLIA lab route are uncertain although management indicated on the Q4 2015 call that they will continue to investigate this along with the more recent strategy to potentially pursue 510(k) clearance. They will first meet with FDA regarding proposed 510(k) de novo pathway seeking clearance for use as an adjunct to standard of care in high-risk symptomatic patients. Assuming that route remains feasible, current expectations include;

  - FDA – expect to meet with FDA regarding proposed 510(k) de novo pathway seeking clearance for use as an adjunct to standard of care in high-risk symptomatic patients
  - Hope to begin 510(k) supporting studies in 2017. Initial indication will be CRC
  - Anticipate ~600 patient study at cost of $1M - $1.5M per indication
  - Hope to file for first 510(k) clearance in 2017
  - Follow-on indications in other cancers would follow including potentially lung and pancreatic cancer which could potentially begin PMA studies in 2017/2018

  LDT – will continue to investigate the CLIA lab route. This could be in lieu of or in parallel with 510(k) pursuit – we think LDT is likely more of a fall-back proposition and one VNRX may pursue if 510(k) de novo is deemed unviable.

  Timelines for an eventual FDA approved product are highly uncertain right now as there still needs to be clarification from FDA on what they will require to support a filing. VNRX may also look to initiate a PMA-supporting study – if so, likely the earliest that would complete is in late 2018. If that timeline is feasible, the earliest that an FDA approved (i.e. PMA pathway) assay/panel could likely come to the U.S. market is 2019. We think it is not unlikely that it would be later than 2019, however.

OUTLOOK / VALUATION

We model launch in Europe in 1H 2017. Initial introduction as an adjunct should provide foot-in-the-door opportunity as well as the chance to build early awareness. Broadening the label in Europe to include as a CRC screen could have the effect of accelerating interest in demand. We continue to expect data from the large Danish CRC studies as well as pre- and early-stage cancer to provide greater insight into the utility of the assays for CRC. The anticipated announcement in January 2017 regarding more details about the launch, marketing and branding strategy should also be informative.

With studies ongoing in several other cancer types, including pancreatic and breast, among several others, subsequent CE Marking in other cancers could potentially come in fairly short order – as noted, we think pancreatic could emerge as a very formidable indication if larger studies confirm the early highly encouraging data. We also expect VNRX will look to continually enhance the performance of their commercialized panels. Ongoing study data will also be used to support reimbursement.

Relative to the U.S. market, we think VNRX's current game-plan – that is, to initially tap the LDT channel via licensing agreement(s) with established CLIA lab(s) and/or 510(k), makes a lot of sense. Not only are these earlier revenue opportunities in the U.S. as the company continues to pursue FDA (PMA) approval, it also provides additional and valuable clinical experience and awareness benefits.

In terms of the road towards eventual FDA approval – which is the ultimate quest and one which we think could rapidly steepen VNRX's revenue curve – this could be a years-long process and require U.S.-based clinical studies.

Valuation Remains Attractive…

Based on our DCF model which goes out to year 2026 and uses a 9.5% discount rate (based on CAPM) and 2% terminal growth rate, VNRX is valued at $7/share. Our model and assumptions will be updated if appropriate based on news flow which could also influence valuation.

We will be eagerly awaiting additional clinical data in several cancers which, assuming positive, could prompt upward revisions to our modeled revenue and related valuation. For example, as we noted, we have yet to model any contribution from a potential pancreatic cancer panel but will likely do so if high accuracy of the diagnostic is maintained in subsequent studies (particularly the recently announced 750-patient Germany-based study).

As it is now, we value VNRX at $7/share. We feel the current market price ($4.10) remains cheaper than warranted and undervalues the company. We think additional and ongoing positive clinical data should further benefit appreciation of the share price towards our target.

FINANCIAL MODEL

VolitionRx Ltd.

	2015 A	Q1 A	Q2 A	Q3 A	Q4 E	2016 E	2017 E	2018 E	2019 E
Revenue	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1,481.4	$4,517.3	$12,403.4
YOY Growth	-	-	-	-	-	-	*#DIV/0!*	*204.9%*	*174.6%*
Cost of Goods Sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$743.1	$2,032.8	$5,072.6
Gross Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$738.3	$2,484.5	$7,330.8
Gross Margin	-	-	-	-	*#DIV/0!*	*#DIV/0!*	*49.8%*	*55.0%*	*59.1%*
SG&A	$3,903.8	$1,029.8	$1,183.2	$1,484.3	$1,561.0	$5,258.3	$6,740.0	$7,820.0	$8,660.0
%SG&A	-	-	-	-	-	*#DIV/0!*	*455.0%*	*173.1%*	*69.8%*
R&D	$6,101.7	$1,462.8	$1,792.1	$1,994.8	$2,215.0	$7,464.7	$9,250.0	$9,550.0	$9,400.0
% R&D	-	-	-	-	-	*#DIV/0!*	*624.4%*	*211.4%*	*75.8%*
Asset Impairment	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($10,005.5)	($2,492.6)	($2,975.3)	($3,479.1)	($3,776.0)	($12,723.0)	($15,251.7)	($14,885.5)	($10,729.2)
Operating Margin	-	-	-	-	-	-	*-1029.5%*	*-329.5%*	*-86.5%*
Total Other Expense (Income)	($502.2)	$0.0	($25.9)	$0.0	$4.5	($21.4)	$23.2	$23.2	$23.2
Pre-Tax Income	($9,503.3)	($2,492.6)	($2,949.4)	($3,479.1)	($3,780.5)	($12,701.6)	($15,274.9)	($14,908.7)	($10,752.4)
Taxes (benefit)	($4.6)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
FX translation	$12.0	($18.4)	$67.4	$0.0	$0.0	$49.0	$0.0	$0.0	$0.0
Net Income	($9,510.6)	($2,474.2)	($3,016.8)	($3,479.1)	($3,780.5)	($12,750.7)	($15,274.9)	($14,908.7)	($10,752.4)
Net Margin	*#DIV/0!*	-	-	-	-	*#DIV/0!*	*-1031.1%*	*-330.0%*	*-86.7%*
EPS	($0.54)	($0.13)	($0.13)	($0.15)	($0.15)	($0.55)	($0.51)	($0.43)	($0.28)
YOY Growth	-	-	-	-	-	-	-	-	
Diluted Shares O/S	17,734	19,289	23,412	23,525	25,800	23,007	30,000	35,000	39,000

Brian Marckx, CFA

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