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Zacks Small-Cap Research

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VolitionRx Ltd (VNRX-NYSE)

Reenginenred Nu.Q assays; Initial data from animal studies are promising; Anticipate upcoming data readouts

Based on our DCF model which goes out to year 2029 and uses a 9.5% discount rate (based on CAPM) and 2% terminal growth rate, VNRX is valued at $6.70/share. Our model and assumptions will be updated if appropriate based on news flow which could also influence valuation

Current Price (05/18/20)	$3.47
Valuation	**$6.70**

OUTLOOK

A key highlight is the company's acquisition of Octamer which has enabled them to move manufacturing inhouse. The COVID-19 pandemic presents a potential opportunity for Volition as Nu.Q assay can be used to detect minute quantities of nucleosomes in COVID-19 patients.

In addition to the compelling lung and colorectal cancer data announced in 2019, we could see data from several ongoing and just-commenced clinical studies. This potentially includes data from the three Fosun March studies in CRC, lung and ovarian cancers, lung cancer data from the University of Taiwan study. Initial data from the NuQ Vet program are promising and offers a significant opportunity in the veterinary space.

Data from proof-of-concept studies could also be forthcoming in a variety of programs. This includes CRC, lung, prostate and pancreatic cancers.

SUMMARY DATA

52-Week High	**$6.42**
52-Week Low	**$2.47**
One-Year Return (%)	**7.83**
Beta	**1.90**
Average Daily Volume (sh)	**128,306**
Shares Outstanding (mil)	**41**
Market Capitalization ($mil)	**$150**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**8**
Insider Ownership (%)	**23**
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 2019 Estimate	**N/A**
P/E using 2020 Estimate	**N/A**
Zacks Rank	**N/A**

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

ZACKS ESTIMATES

Revenue
(in '000 of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	$0.0 A	$0.0 A	$17.1 A	$0.0 A	$17 A
2020	$0.5 A	$0.0 E	$60.0 E	$125.0 E	$186 E
2021					$6,260 E
2022					$14,043 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.12 A	-$0.12 A	-$0.09 A	-$0.07 A	-$0.41 A
2020	-$0.14 A	-$0.10 E	-$0.09 E	-$0.09 E	-$0.42 E
2021					-$0.42 E
2022					-$0.26 E

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

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WHAT'S NEW

VNRX: Q1 2020 Financial and Business Update

Financial Update

On May 7th VolitionRx reported financial results for their fiscal 2020 first quarter ending March 31st. Q1 OpEx was $5.8M, and significantly higher than Q4 2019. Net income and EPS were ($5.5) M and ($0.14).

Although VNRX is conducting several studies related to COVID-19 and veterinary medicine, guidance is for expenses to remain flattish as the company maintains their diligence on expense and cash control. We continue to model little to no revenue until end of 2020 although if all the pieces fall squarely in place relative to completing these studies and tying up any other loose ends, it is not unreasonable that VNRX could recognize initial COVID revenue in the current year.

Cash used in operating activities was $4.8M. Management is guiding for near-term burn (operating and investing) of ~$4M per quarter. The firm exited the quarter with $12M in cash and cash equivalents.

Equity at quarter end consisted of approximately 41.2 million common shares outstanding. In addition, there were approximately 4.2 million warrants and options outstanding (of which approximately 1.3 million are in-the-money at the current $3.47/share price).

Business Update

- ***Octamer:*** In early 2020, Volition acquired Octamer GmbH for approximately $725k consisting of both cash and restricted shares of Volition's common stock. This strategic acquisition provided Volition with the capability to manufacture recombinant nucleosomes, one of the key components of Volition's Nu.Q tests, in-house. By internalizing the process of chemiluminescence antibody labeling and coating of magnetic beads, Volition has secured its supply chain which, in turn, provides flexibility to speed up assay development work. From this strategic business collaboration, Volition is able to leverage the extensive expertise of Dr. Adrian Schomburg while combining the cost benefits of inhouse manufacturing. Since the beginning of the year, Volition's team has been undergoing intensive training with Octamer's team. The firm plans to produce histones and DNA templates that can be used for custom applications in epigenetic research and drug discovery. We expect this to be the long-term driver of revenue and earnings.

- ***Canine cancer diagnostic:*** In early 2019, VolitionRx partnered with Texas A&M University (TAMU) and formed a new U.S. subsidiary, Vetco, which focuses on the veterinarian diagnostics market. As per the agreement, TAMU will receive an equity stake in Vetco. Currently, there is a dearth in the availability of accurate, simple and affordable cancer screening tests in veterinary medicine. The goal is to provide all veterinarian clinics with blood tests that can help identify disease early.

  Currently, VNRX is working with TAMU's College of Veterinary Medicine to conduct a study of Nu.Q Vet. Preclinical work with Nu.Q Vet is completed. At a specificity of 90%, a single Nu.Q Vet assay detected almost 70% of two cancers, Canine Hemangiosarcoma and Canine Lymphoma. These two diseases represent a third of all canine cancers. The development strategy is to process the samples in Q2 and have the data readout in Q3. Management believes that a canine cancer test could be a relatively fast-moving program given the less-stringent U.S. regulatory pathway for animal diagnostics (via USDA versus FDA's PMA or 510k). If all goes as per plan, management believes they could have a Nu.Q test for the diagnosis of animal cancers (initially canines but potentially also other animals including cats, horses) on the market before end of 2020.

  Canine cancer represents a sizeable market as more than four million cases of canine cancer are diagnosed each year in the U.S., which is nearly 2.5x as many human cancers. Pricing is likely to be similar to a human Nu.Q test (~$100-$200 per test). The canine cancer opportunity could be in the many hundreds of millions of dollars.

- ***Nu.Q re-engineered:*** In the beginning of the year, the company announced that it has completely re-engineered its Nu.Q assays. The assay was previously using the ELISA plate format that provided a traditional colorimetric endpoint but now uses a magnetic particle-based assay format that gives a luminescent endpoint. Luminescent assays are known to be very sensitive and have a wide dynamic range. Further, the benefits of using blood plasma instead of serum has aided in reducing interferences. When compared to Volition's ELISA plate Nu.Q assay format,

the magnetic particle-based assay format shows a 10 to 20-fold improvement in analytical sensitivity. It also shrinks the turnaround time of test results to one hour and 20 minutes from six hours, allowing much higher throughput. The within-day reproducibility of the test results is excellent; now is just below 3% as compared to previous test which yielded below 10%. The magnetic particle-based chemiluminescence assay format offers significant merits such as high sensitivity, improved specificity, reproducibility, reduced background noise and reduced assay time, all of which translates into improved clinical performance. The new format has enabled the use of Nu.Q on a wide range of commercial, fully-automated platforms. The FDA approved automated immunoassay analyzer with all of the above improvements for clinical use in the U.S. and Europe. Currently, the company has developed eight different bead-based Nu.Q assays that will be used in clinical studies. We expect to see data forthcoming from these studies in 2Q 2020.

- ***Expanded Scientific Advisory Board:*** Volition expanded its Scientific Advisory Board to include Dr. Adrian Schomburg, an epigenetics entrepreneur and the founder and CEO of Octamer. Dr. Schomburg has over a decade of experience in histone and nucleosome production. He was at the NIH, Bethesda and the Max Planck Institute in Göttingen. Dr. Schomburg was instrumental in developing candidates in oncology and neuroscience.

Clinical Update

COVID-19 could be a new opportunity: Nu.Q assay has already demonstrated its ability to detect epigenetically altered circulating nucleosomes in the blood of cancer patients. In patients with Severe Acute Respiratory Syndrome (SARS) and pneumonia, the body elicits an inappropriate hyperimmune response to the virus that causes white blood cells to produce a very high level of Neutrophil Extracellular Traps (NETs), which are made of nucleosomes. Therefore, Nu.Q assay can be used to detect even minute quantities of nucleosomes in COVID-19 patients. The ongoing pandemic caused by coronavirus presents a potential opportunity for Volition.

A proof of concept study was conducted to investigate if the Nu.Q blood test could be used as a diagnostic or prognostic tool against SARS-CoV-2, the novel coronavirus causing COVID-19. On the earnings call, Management noted that the study involving 34 polymerase chain reaction (PCR) COVID-19 positive subjects and 50 control subjects tested with the Nu.Q assay showed that nucleosomes were highly elevated in the PCR positive subjects (area under the curve (AUC) for a single Nu.Q assay of 98.7% for PCR positive COVID versus control subjects). The results of the study are very encouraging as they demonstrated 100% sensitivity and 94% specificity. A second Nu.Q assay also showed promising results with an AUC of 86.2%.

Preliminary studies are underway in Belgium and Germany. Volition believes the Nu.Q blood test may be able to predict the progression of SARS-CoV-2 pneumonia and complications including Acute Respiratory Distress Syndrome (ARDS) in COVID-19 patients. Volition is working with collaborators to investigate whether existing Nu.Q epigenetic assays can provide early insight into which patients with COVID-19 may require higher levels of monitoring, including hospitalization and critical care resources, versus those who will not develop serious symptoms. Subject to successful results from these initial proof of concept studies that are currently underway, Volition plans to conduct further studies using its fully automated Nu.Q assay platform to ascertain the best use of these tests in different geographies. Also, management believes Nu.Q has the potential to detect in other respiratory infections such as flu and pneumonia given the similarity of having elevated levels of NETs.

The regulatory path for triage test related to COVID-19 may be somewhat dynamic and largely driven by knowing the clinical utility of the test, whether it will be used as a diagnostic, prognostic or predictive test. We may hear more on the regulatory pathway on future calls. While COVID-19 could be a potential opportunity for Volition, we are not sure if this is a near-term opportunity to grow revenues. We are keeping a close watch on the progress of Nu.Q assay's investigation against COVID-19.

Lung Cancer studies: In an initial proof-of-concept data with 76 subjects, the Nu.Q assay detected lung cancer, including stage 1 cancer, with an AUC of 85% as compared to healthy tissue. The same (single) Nu.Q assay, when used in a confirmatory cohort of 152 subjects detected lung cancer with an AUC of 79%.

As noted, VNRX signed a formal contract with the National University of Taiwan to conduct the first large-scale lung cancer study. The study will include 1,200 participants receiving low-dose CT scan, 1,000 of which have lung cancer. The study could provide the first statistically-powered evidence of the potential utility of Nu.Q diagnostics as a screen for lung cancer or as an adjunct/triage test for low-dose CT. LDCT, currently the only recommended screening test for lung cancer, has drawbacks including its relatively high cost, patient exposure to radiation, overdiagnosis and a potential for meaningful rates of false-positives. As such, an adjunct or triage test that could

improve accuracy of lung cancer screening and/or reduce the need for LDCT (without compromise to diagnosis) could have massive appeal, in our opinion. VNRX currently expects to announce preliminary data from this study in 2H2020.

Colorectal cancer studies: The proof-of-concept data from an in 123 subjects using a single Nu.Q assay detected CRC with an AUC of 72%. A two-assay panel, which included this initial product grade Nu.Q assay and an inflammatory biomarker test, had an AUC of 84%. These are relatively tiny POC studies but the data is certainly encouraging. The goal will be to replicate these results with reproducible product grade assays in larger, fully powered studies.

As a reminder, VolitionRx already has a relationship with National Taiwan University and previously finalized agreements to conduct two large CRC studies; 5k-sample asymptomatic screening study and a 2ksample symptomatic study.

Blood Cancer Studies: A single pre-clinical Nu.Q assay was used to investigate whether it could detect hematopoietic cancer. In 54 subjects, the same Nu.Q assay detected blood cancer with an AUC of 91% (cancer vs healthy). More specifically, the test detected 80% of newly diagnosed Non-Hodgkins Lymphoma and Leukemia cases (mixture of Acute Lymphocytic Leukemia and Acute Myeloid Leukemia) at 95% specificity among healthy subjects. A number of other assays in development also demonstrated promising individual assay results with AUCs ranging from 79% to 91%.

The Nu.Q assay has overcome the limitation of relying on multiple assay panels to detect different cancer types. It is now possible to screen for three different hematopoietic cancers using a single assay, which decreases both the overall costs as well as samples required to detect mutations. This single assay seems to have high sensitivity and specificity that offers a much-needed effective diagnostic technique. The results of this preliminary study suggest that the Nu.Q assay could be potentially used to screen people for early detection of a wide variety of cancers.

Data on enhanced Nu.Q Capture technology:
Recently, Volition shared data at the ASCO meeting from studies conducted to detect lung and blood cancers using the newly enhanced Nu.Q assay.

Enrichment of circulating tumor DNA from cell-free DNA of hematopoietic origin
The research team at Volition used the Nu.Q Capture technology to enrich tumor-derived nucleosomes. Chromosomes from healthy cells differ from those in cancer cells based on the genetic sequence and protein structure. The key difference between the DNA of the healthy nucleosomes (background cell free DNA) is slightly longer than the ones from tumor cells (circulating tumor DNA (ctDNA)). The Nu.Q Capture technology is designed to remove this healthy nucleosomes so that the sample has enriched cancer-derived nucleosomes which have cancer specific mutations. After isolation the sample can undergo mass spectrometry to help identify biomarker targets or the DNA can be sequenced for diagnostic applications, treatment selection as well as to monitor the disease. This methodology offers the benefit of higher sensitivity to detect different types of cancers.

Volition's team tested this process on samples obtained from CRC patients and the clearly showed the separation of short and long nucleosomes from cancer cell lines and no difference in samples from healthy controls. The Nu.Q Capture offers a simple way to enrich the samples used for testing. has the potential

Performance in lung cancer detection
Dr Mark Eccleston, scientist at Volition, explained how the removal of healthy nucleosomes creates an enriched sample that allows for detection of cancer nucleosomes with greater accuracy. A pilot study was conducted with Dr Anne Sibille and the team at Liege University Hospital in Belgium, to assess the performance of a Nu.Q assay to discriminate lung cancer and Chronic Obstructive Pulmonary Disease (COPD) patients from normal subjects.

A total of 142 samples were collected, comprising of 45 from normal subjects, 44 from lung cancer and 53 from COPD patients. The circulating level of intact nucleosomes containing the histone H3.1 isoform (Nu.Q^{a}-H3.1) was individually tested as well as in combination with cytokines for its performance in discriminating subjects for their underlying condition. The results demonstrated that the Nu.Q assay was able to discriminate between lung cancer and normal samples with an Area Under the Curve (AUC) of 88%. Further, the test also revealed a difference between lung cancer and COPD samples with an AUC of 85%.

Circulating nucleosomes in hematological malignancy
The pilot study investigated the circulating levels of intact nucleosomes containing the histone H3.1 isoform (Nu.Q-H3.1) in a variety of solid tumors including Non Hodgkin Lymphoma (NHL), Acute Myeloid Leukemia (AML), Acute Lymphocytic Leukemia (ALL) and in healthy subjects. Blood cancers are generally difficult to detect as they can present non-specific symptoms. In order to be definitive about the diagnosis whether it is indeed cancer or not requires the patient to undergo biopsy. Having a test that is able to discriminate blood cancer from other infections, not only speeds up the time to obtain treatment for cancer but also saves the patient from undergoing invasive biopsy tests unnecessarily and get the required treatment for their underlying condition.

A drop of blood is about 50-60 µl. only a fraction of this amount, about 20µl of plasma samples, were taken from 62 healthy controls and 329 patients (271 solid tumor, 25 NHL, 25 AML and 8 ALL) diagnosed with various types of cancer and analyzed. The results were very encouraging as they revealed elevated levels of the Nu.Q assay in patients diagnosed with different types of cancers. To be specific, the median levels of circulating nucleosomes were more than 275ng/ml in NHL, AML and ALL patients and more than 200ng/dl in 14 solid tumor patients, while the healthy control patients averaged only 40ng/ml. All other solid tumor patients exhibited higher level of circulating nucleosomes than normal control subjects. The exceptionally exciting about this study was the extremely high level, of circulating nucleosomes, 7x-14x that of healthy subjects.

The AUC (accuracy of the test) for all patients diagnosed with cancer vs healthy volunteers was 91% with 74% sensitivity and 95% specificity. This study showed far better results than widely accepted cancer detection tests. Samples collected from newly diagnosed patients revealed even better results. The AUC was 92.6% with 80.6% sensitivity and 95% specificity. This result is key as it is extremely difficult to diagnose blood cancer in a patient who has shown no history of cancer in the past. Analyzing the subgroup only from NHL patients revealed that AUC was ~94% with very low variability, 80% sensitivity and 95% specificity. The above results have demonstrated that the Nu.Q technology may be a useful diagnostic tool in detecting cancers early. However, we think this technology needs to be further investigated. Management intends to file for regulatory approval to commence clinical studies for NHL as it is the most commonly occurring blood cancer.

Volition in Asia: In addition to the studies in Taiwan, VNRX has made a significant stride towards conducting large studies in China. Asia is a market which we have always viewed as holding significant potential value for blood-based cancer diagnostics (given a cultural aversion to fecal handling and relatively high rates of lung cancer in certain areas of that continent).

Volition signed a memorandum of understanding (MOU) with Shanghai Fosun Long March Medical Science Co, Ltd, a diagnostics division of Chinese pharmaceutical company, Shanghai Fosun Pharmaceutical (Group) Co., Ltd. Per the MOU, Fosun is expected to be instrumental in the development and subsequent regulatory activities and commercialization of the company's colorectal cancer assays in China. Initially this will include conducting clinical studies in colorectal, lung and ovarian cancers in China. Per the press release, it will also include evaluating the development of Nu.Q assays on Fosun's existing chemiluminescence platform (LUMIART-II Automated Chemiluminescence Immunoassay System). The fully-automated, high throughput system is commercialized in China.

While development timelines related to the large studies in colorectal and lung cancer in Taiwan have remained on track, despite the COVID-19 pandemic, they have slipped a bit in the U.S. (with EDRN) from guidance provided on the previous earnings call. However, we think the studies in the U.S. are having a temporary pause in the interest of helping ensure safety of clinical staff and patients. While we think this pause could likely be a temporary one, we are eagerly awaiting updates on all of VNRX's programs. Given the recent highly encouraging data in blood studies, we think this Nu.Q blood cancer assay could be another commercial opportunity. Whether that may still be in the cards, we don't know, but will be something we hope to know more about as well.

VolitionRx's updated program timelines

Institution	Condition	Sample Collection	Cohort	Timing
Early Detection Research Network of the U.S. National Cancer Institute	Colorectal cancer	9000 Prospective 4,600 Retrospective	13,500 screening population	Collection Ongoing
Hvidore Hospital, University of Copenhagen	Colorectal cancer	Retrospective	4,800 symptomatic	Collection completed and Analysis Ongoing
Hvidore Hospital, University of Copenhagen	Colorectal cancer	Prospective	14,000 screening population	Collection completed and Analysis Ongoing
Hvidore Hospital, University of Copenhagen	Colorectal cancer and other	Prospective, longitudinal	30,000 screening population to provide 3 samples (90,000 samples total)	Collection completed and Analysis Ongoing
University of Bonn	27 most prevalent cancers	Prospective	4,500	Collection completed and Analysis Ongoing
German Cancer Research Center (DKFZ)	Pancreatic	Restrospective	750	Collection completed and Analysis Ongoing

NuQ Compelling Asymptomatic Detection of Pre/Early Cancers:
In early 2018 VNRX announced results of a 680-subject study, which included ~100 with cancer. A panel of three NuQ assays detected 80% of stage 1 cancers and 66% of high-risk pre-cancer adenomas at 78% specificity. Data of the later-stage cases and detection across all cancers was not released, although we expect that more comprehensive data will be included in future announcements.

For context of the performance of some of the leading non-invasive CRC screening diagnostics in detecting precancers; Exact Sciences (stool-based) ColoGuard showed 42% sensitivity in detection of advanced precancerous adenomas at 87% specificity, FIT showed 24% sensitivity in detection of advanced precancerous adenomas at 94% specificity and Septin9 showed 18% sensitivity in detection of advanced precancerous adenomas at 80% specificity. While the differences in specificity of all of the studies makes head-to-head performance comparison difficult, we think this at least provides some insight into the relatively poor pre-cancer detection abilities of currently available non-invasive diagnostics and helps illustrate the unmet need for a more accurate test.

As it relates to performance in detecting CRC (of any stage) published studies showed sensitivity / specificity of these tests at; ColoGuard 92% / 87%, FIT 79% / 94% and Septin9 68% / 80%. Again, we provide this only for some context and also note that, as we have discussed in detail in prior reports, all non-invasive CRC diagnostics suffer from one or more meaningful drawbacks some of which include low accuracy, high cost and requisite fecal handling. As such, sensitivity / specificity, while important, is not the only criteria in gauging the potential utility of a CRC screen instead as long NuQ can increase compliance of CRC screening at an acceptable cost, it should have commercial appeal.

And while Exact Sciences ColoGuard has had solid uptake since its launch in early 2015, compliance of it is also lacking to some extent. Approximately 10k ColoGuard tests were sold during the first full quarter (Q1 2015) on the market and this has grown at an average quarterly rate of approximately 25%. In the most recent quarter (Q1 2019) 334k tests were completed. But, EXAS reports that (as of their most recent reporting) their compliance was 65% (which is actually down slightly from 68% in Q1 19). Compliance in their context relates to the percentage of test kits that were used and sent to EXAS lab for processing as compared to the total number prescribed (insurers are charged once a ColoGuard kit is ordered). So, despite relative ease-of-use and in the privacy of the home, ColoGuard also appears to have a certain level of compliance issues (despite EXAS dedicated efforts to improve compliance rates). We think that this further highlights the potential opportunity for VNRX s frontline screen.

Importantly, we do not view certain recently commercialized novel technologies, including Exact Sciences ColoGuard and EpiGenomics Epi proColon, as significant potential competitive threats to VNRX in most European markets. National screening programs are highly budget sensitive, which largely excludes the relatively expensive ($300 - $500 per test) ColoGuard while relatively poor accuracy of Epi proColon means it is unlikely to unseat FIT as the non-invasive testing standard. See our Appendix for a detailed discussion about Exact and Epi proColon. If VNRX can develop a frontline screen that is competitive with FIT in accuracy and manufacture it at a cost that will qualify it for national screening programs, that could be a true game-changer for CRC screening. The added benefit of NuQ versus that of FIT is ease of use and the fact that fecal handling is completely avoided.

Upcoming Milestones
We expect the company to accomplish some of the near-term milestones below:

- Q2 Clinical performance data from individual assays and in the panel combinations across the range of cancers
- Q2/3 Clinical data from COVID-19 studies currently underway
- Advance large-scale colorectal and lung cancer trials in Europe, Asia and the U.S.
- Determine the level of tumor associated nucleosomes using mass spectrometry and identify NEW biomarker targets
- Q2 Utilize Nu.Q sequencing to identify tumor of origin and specific mutations
- Q3 Utilize in conjunction with Nu.Q immunoassay approach to enhance performance
- Q4 Launch Nu.Q Vet

IP protection: The company currently has 23 patent families related to diagnostic test, with a total of 44 patents granted, including eight in the U.S., nine in Europe and a further 27 worldwide. The company has 105 patent applications pending including 13 in the U.S., 10 in Europe, and further 82 worldwide. The patent portfolio also covers veterinary medicine applications.

VALUATION

Based on updates to our financial model and DCF methodology, which forecasts out to year 2030, uses a 9.5% discount rate (based on CAPM) and 2% terminal growth rate, **VNRX is valued at $6.70/share**. Our model and assumptions will be updated if appropriate based on news flow which could also influence valuation.

FINANCIAL MODEL

VolitionRx Ltd.

VNRX	2019 A	Q1 A	Q2 E	Q3 E	Q4 E	2020 E	2021 E	2022 E
Revenue	$17.1	$0.5	$0.0	$60.0	$125.0	$185.5	$6,260.2	$14,043.2
YOY Growth	-	-	-	-	-	*985.3%*	*3274.0%*	*124.3%*
Cost of Goods Sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1,250.0	$2,907.0
Gross Income	$17.1	$0.5	$0.0	$60.0	$125.0	$185.5	$5,010.2	$11,136.2
Gross Margin	*100.0%*	-	-	-	-	-	*80.0%*	*79.3%*
SG&A	$5,696.8	$1,977.5	$1,785.6	$1,571.0	$1,623.4	$6,957.5	$8,476.4	$9,717.9
%SG&A	*33322.2%*	-	-	*2618.3%*	*1298.7%*	*3749.8%*	*135.4%*	*69.2%*
R&D	$10,363.3	$3,895.0	$2,550.0	$2,453.7	$2,475.1	$11,373.8	$13,585.7	$15,287.4
% R&D	*60618.0%*	-	-	*4089.5%*	*1980.1%*	*6130.0%*	*217.0%*	*108.9%*
Operating Income	($16,060.0)	($5,871.9)	($4,335.6)	($3,964.7)	($3,973.5)	($18,145.7)	($17,051.9)	($13,869.1)
Operating Margin	-	-	-	-	-	-	-	-
Total Other Expense (Income)	($56.1)	$12.6	$36.8	$35.7	$35.9	$121.0	$140.0	$174.0
Pre-Tax Income	($16,099.1)	($5,859.3)	($4,298.8)	($3,929.0)	($3,937.6)	($18,024.7)	($17,191.9)	($14,043.1)
Taxes (benefit)	$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%*	*35.0%*	*35.0%*
FXtranslation	$0.0	$373.9	$0.0	$0.0	$0.0	$373.9	$0.0	$0.0
Net Income	($16,099.1)	($5,485.4)	($4,298.8)	($3,929.0)	($3,937.6)	($17,650.7)	($17,565.8)	($14,043.1)
Net Margin	-	-	-	-	-	-	-	*17.1%*
EPS	($0.41)	($0.14)	($0.10)	($0.09)	($0.09)	($0.42)	($0.42)	($0.26)
YOY Growth	-					-		
Diluted Shares O/S	39,180	41,197	41,580	42,000	43,550	42,082	53,500	56,500

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Appendix

Large U.S. Prospective Trial Could Support Eventual Asymptomatic FDA Filing

In July 2017 VNRX announced that it will participate in a large U.S. study that could potentially serve as primary support for an eventual FDA filing seeking U.S. regulatory approval for a NuQ technology-based blood test in the primary diagnosis of colorectal cancer. Such a test would be aimed at the asymptomatic U.S. population - a market size estimated at approximately 90M individuals and, per our estimate, valued at over $4B. Given the relative enormous and valuable market, coupled with drawbacks of currently available non-invasive CRC testing options - including low accuracy, required fecal-handling, dietary restrictions and high cost, eventual FDA approval would likely be a highly substantial value driver.

VNRX is required to contribute just $3M (paid in equal quarterly installments over 3 years), with most of the funding borne by the study's main sponsor, the U.S. National Cancer Institute's (NCI) Early Detection Network (EDRN), which is the leading cancer research organization in the U.S. The Great Lakes New England Clinical Validation Center and the University of Michigan are also major participants and, along with EDRN, focused on the pursuit of technologies for the early detection of cancer.

While complete details of the study have yet to be made public (although we think the study design may be publicly available later this year), we do know the following:

- will include ~13.5k asymptomatic screening samples from subjects $\geq$ 50 years of age who have not previously undergone colonoscopy or CRC screening. This "non-adherent" (to CRC screening guidelines) population is at particular risk and a focus for organizations such as EDRN in improving screening compliance
- 4,677 samples have already been collected (retrospective collection). The remainder (~8.8k) will be prospectively collected at multiple sites prior to participants undergoing colonoscopy
- 2 to 3 years is the expected timeframe for collection to be completed
- samples will be tested with a panel of NuQ colorectal cancer assays
- samples will also be tested with other (non-VNRX) diagnostics - while specifics were not provided, this could presumably include traditional FIT/gFOB (i.e. fecal) tests as well as potentially more recently commercialized diagnostics such as Exact Sciences' ColoGuard stool DNA test. This could provide a unique opportunity for a true head-to-head comparison of results against (potential) competing products from the same study and samples

Given that this is a third-party study in which VNRX is a participant but not the main sponsor, they did not have the benefit of direct consultation with and feedback from FDA relative to the study design. But, management stressed that the study was developed by NCI for the purpose of acting as a pivotal study which could be used as primary support by VNRX for an eventual FDA PMA filing seeking U.S. regulatory clearance for a NuQ-based blood test as a first line CRC screen (i.e. for asymptomatic patients). Whether this study will be 'sufficient' in the eyes of FDA as a pivotal study is something that we may not know for quite some time - VNRX expects their first significant interaction with FDA to be a pre-submission meeting which likely would not be scheduled until after this study is largely completed and initial results are compiled.

But, we think that there are certain aspects that should play in VNRX's favor in that regard. Most notably is the large size of the study - 13.5k samples, including ~9k collected prospectively. This compares to ~10k total (prospective) samples for Exact Sciences' ColoGuard pivotal FDA study. And as it relates to the inclusion criteria of non-compliant subjects - we think that is another (positive) key point as the goal for VNRX will be to demonstrate that their test can improve screening compliance (National Colorectal Cancer Roundtable is leading an initiative to improve compliance to 80% by 2018). The lack of an appropriate study population (i.e. enrollment was not confined to only non-compliant subjects) ultimately created an issue for Epigenomics in their FDA studies with Epi proColon - this resulted in FDA requesting an additional clinical study and delayed U.S. approval by ~2 years. Another aspect that we think bodes well for VNRX is the reputation and expertise of NCI, EDRN and Great Lakes and their focus on facilitating the development (and eventual commercialization) of cancer detection technologies - clearly the most efficient way to do that would be to design their studies to meet anticipated FDA requirements and protocol.

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The most significant benefit of participating in this study versus designing their own study (in which case they would have pre-study interaction with FDA) is cost. VNRX contributes just $3M over three years and will have access to over 13k blood samples for validation - that compares to management's estimates of $30M to $40M (cost of Exact's pivotal study as a proxy) that it would cost to design and conduct their own study. The valuable data and ~$30M or more that they will save by participating in this NCI study, in our opinion, is more than worth the risk that they will need to conduct additional clinical work to support an eventual FDA filing.

Additional Salient Points…

Below we discuss what we think are some of the most salient points relative to VNRX's potential opportunity in the U.S. in the context of the current environment of screening and diagnosis of CRC including available non-invasive methods/modalities and the opportunity to address unmet needs.

- **Non-Compliance Provides Opportunity**: The United States Preventive Services Task Force (USPSTF) recommends screening for CRC beginning at age 50 and until age 75. Currently, only about 65% of screening-age Americans adhere to recommended CRC screening guidelines. A consortium of healthcare and other organizations have a goal of increasing that to 80% by the year 2018, which they estimate will prevent 277k new cases of CRC and 203k deaths within 20 years. With approximately 90M Americans of screening age, that means over 30M are non-compliant. While organizations such as USPSTF and FDA are not part of this consortium, they are undoubtedly aware of the benefits of improving compliance.

  The reasons for lack of adherence to screening guidelines vary and include a lack of access to care, concerns specific to the testing modality such as risks associated with invasive screening methods (such as risk of bowel perforation during colonoscopy) or handling feces with gFOB/FIT tests, cultural barriers, lack of insurance or financial resources and general lack of awareness of the benefits of screening. Additional screening options, such as what VNRX hopes to bring market, have the potential to address some of these barriers, particularly as they relate to concerns of other modalities such as colonoscopy and FIT/gFOB but also, possibly, as they relate to other factors such as cost.

  Noteworthy is evidence which has indicated that screening by any available means is more important than the specific screening modality in reducing rates of CRC. To this point, USPSTF mentions in their CRC guidelines that screening with Hemoccult II, compared with no screening, consistently resulted in a 9% to 22% reduction in CRC-specific mortality. This is despite the fact that Hemoccult II, a guaiac-based FOBT test, is relatively very inaccurate (sensitivity between 13% and 50%) - in fact it is no longer recommended as a CRC screening test. We think this may also provide some context for how motivated (and potentially lenient) U.S. regulators may be in improving CRC screening compliance.

- **Refine Panel**: the 2+ year collection time and large ongoing (and upcoming) OUS clinical trials provides VNRX with the ability to further refine the accuracy of their technology (actual testing, once the specific biomarkers have been chosen and the panel developed, can be done in only a matter of months). All else equal, the higher the sensitivity/specificity, the greater the chance of eventual FDA approval, inclusion as a recommended CRC screening option, reimbursement and for uptake of the test. And while we have not included colonoscopy in our review of alternative screening methods as it is (today) considered as a definitive diagnosis, level of sensitivity/specificity (across all cancer stages) could also determine how potentially competitive VNRX's test could be against invasive modalities.

  In May 2017 VNRX announced results of a small (n = 58) study which showed a panel of four NuQ assays detected 74% of all stages of CRC cancer at a 90% specificity. When incorporating an age-adjusted scoring system, 91% of CRC's were detected at a 90% specificity. Detection of early-stage cancers was also high, with 62% of pre-cancer polyps detected at 90% specificity. While the study was too small to presume replicability of detection at these levels, VNRX will be working to bring the highest performing test into this large NCI study.

- **Sensitivity / Specificity Threshold**: the threshold that may be required for FDA approval can be gleaned from Epigenomics' pivotal trial data. The FDA PMA filing for Epigenomics' Epi proColon blood-based (Septin 9) DNA test was supported by two clinical studies (n = ~2k in aggregate) which demonstrated sensitivity / specificity in detection (across all levels) of CRC of 68.2% / 78.8% in one study and 72.2% / 80.8% (versus FIT sensitivity of 68.0% at 97.4% specificity) in the other. The data was less then overwhelming, resulting in an adverse vote (5 in favor, 6 against) by an FDA advisory panel relative to the question of effectiveness of the test which ultimately required Epigenomics to conduct another clinical trial - this one aimed at assessing how their test would be received in a real-world situation (i.e. could the test improve adherence to CRC testing). Epi proColon finally received FDA approval in April 2016 but as a result of the less than compelling clinical data, it came with a relatively narrow label (discussed below). So while we think the Epi proColon pivotal trial data provides a goal for FDA approval purposes, meaningful adoption, competitiveness and ability to increase

compliance of CRC screening may require VNRX to demonstrate a level of sensitivity / specificity that is more in-line with that of FIT and Exact's ColoGuard (FIT-DNA).

- **Target Market**: we think certain characteristics of VNRX's test may appeal differently to two somewhat distinct U.S. target markets; the non-compliant population (~30M people) and the compliant population (~60M people). Assuming $50 per test and recommended annual testing, this values the non-compliant and compliant U.S. markets at approximately $1.5B and $3B per year, respectively. We suspect that the non-compliant market may be less concerned with superior accuracy than aspects such as cost or concerns over exposure to feces handling or risks of invasive screening methods. And while these potential benefits (i.e. lower cost, lack of exposure to feces and invasive risks) may also appeal to a certain portion of the compliant population, relative sensitivity/specificity will undoubtedly be a significant determinant in choice of screening modality for these people and their physicians. The design of this NCI study clearly focuses on improving non-adherence, although should also provide insight into competitiveness versus current, non-invasive screening methods, which we discuss below.
    - **Epi proColon**: labeling was ultimately restricted to a relatively narrow indication - that is, for only those individuals (average risk, age 50 years and older) who are first offered, and decline, a USPSTF-recommended screening test (such as FIT/gFOB or colonoscopy). It is contraindicated as a replacement for (guideline-recommended) CRC screening tests. While Epi proColon was not included in the updated (2016) USPSTF recommended CRC screening guidelines, that may have to do with (inferior) data from a prior version of the test being used in the determination. Updated clinical and longitudinal data as well as evidence supporting an increase in screening compliance could be favorable for inclusion in future USPSTF updates. Nonetheless, as Epi proColon is not currently covered by Medicare (although legislation has been introduced in the U.S. House for Medicare coverage of FDA-approved blood-based CRC screening tests) and its label essentially relegates it to a second-line option to FIT/FOB (which are covered by Medicare and included as recommended CRC screens), we think its competitiveness and ability to meaningfully address the non-compliant population are compromised. Epigenomics was taken private earlier in 2017 and information relative to the market performance of Epi proColon since its launch is largely unavailable.

    - **ColoGuard**: ColoGuard was the first technology approved through the FDA-CMS parallel review program - resulting in FDA approval and Medicare coverage coming on the same day in August 2014. It is indicated for the screening of individuals 50 years and older at average risk of CRC. Pivotal study (n = 10k) demonstrated 92.3% sensitivity and 86.6% specificity in CRC. ColoGuard was included in USPSTF's updated (2016) CRC screening guidelines although does note that while single-test sensitivity of ColoGuard is higher than that of FIT, specificity is lower, resulting in more false positives. Medicare reimburses ColoGuard at a rate of approximately $510 every 3 years for those 50 - 85 years old who do not have symptoms and are not at increased risk of CRC. ColoGuard sales have ramped quite rapidly since its launch in late 2014. Approximately 10k tests were sold during the first full quarter (Q1 2015) on the market and this has grown at an average quarterly rate of almost 25%. In the most recent quarter (Q1 2019) 334k tests were completed. We think the relatively strong market performance of ColoGuard may be the product of a number of factors including; reimbursement at time of launch, relatively high accuracy, inclusion in USPSTF guidelines and a robust direct-to-consumer marketing campaign. And while fecal handling is a widely cited headwind to FIT adoption, that may be somewhat offset by the convenience of at-home sample collection (which is then shipped directly to the lab). In addition to (USPSTF's citing of) risk of false positives, the high cost is a drawback, particularly for the uninsured or under-insured. But, EXAS reports that (as of their most recent reporting) their compliance was 65%. 'Compliance' in their context relates to the percentage of test kits that were used and sent to EXAS' lab for processing as compared to the total number prescribed (insurers are charged once a ColoGuard kit is ordered). So, despite relative ease-of-use and in the privacy of the home, ColoGuard also appears to have a certain level of compliance issues. This further highlights the potential opportunity for VNRX's frontline screen.

    - **FIT:** USPSTF recommends fecal immunochemical testing every year. Medicare reimburses FIT at a rate of approximately $25 every 12 months. Given the various FIT test choices available by different manufacturers there is a lot of heterogeneity among performance. In evaluating FIT for their guidelines, USPSTF focused on those tests that had available data from at least two clinical studies. Among three clinical studies (encompassing ~26k samples) of OC-Light, a qualitative test, and five studies (encompassing ~13k samples) of OC FIT-CHEK, a quantitative test, the lowest sensitivity was 73% at 96% specificity while the highest sensitivity was 88% with 92% specificity. In the largest study (n =

9,989), sensitivity was 74% at 93% specificity – this was also the FIT (OC FIT-CHEK) comparator arm of ColoGuard's pivotal study.

One of the drawbacks of stool-based testing is fecal handling which can affect compliance – although evidence of rates of compliance varies widely depending on the source. Two separate studies[1,2] indicated FIT compliance between 60% and 62%, while (3 stool-sample) gFOB compliance was between 47% and 50% . Those rates are much higher than results from a retrospective study sponsored by Exact Sciences which used claims data from over 150k patients and found a compliance rate of just 0.3% (i.e. compliance in 3 of 1,000) using either FIT or FOB.[3]

- **gFOB**: similar to FIT, USPSTF recommends guaiac-based fecal occult blood testing annually. While legacy gFOB tests suffered from low sensitivity, this has improved with the next generation (such as Hemoccult SENSA) which have demonstrated in clinical studies to have a sensitivity of between 62% and 79% and specificity of 87% to 96%. In addition to fecal handling, other drawbacks of gFOB testing is it require sample collection of three consecutive stools (which can result in low compliance), generally considered to be less accurate than FIT and may require dietary restrictions.

[1] van Rossum LG, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. Gastroenterology. 2008 Jul;135(1):82-90. doi: 10.1053/j.gastro.2008.03.040. Epub 2008 Mar 25.
[2] Hol L, et al. Screening for colorectal cancer: randomised trial comparing guaiac-based and immunochemical faecal occult blood testing and flexible sigmoidoscopy. Gut. 2010 Jan;59(1):62-8. doi: 10.1136/gut.2009.177089.
[3] Anissa Cyhaniuk, MA, and Megan E. Coombes, MSc. Longitudinal Adherence to Colorectal Cancer Screening Guidelines. AJMC Feb 2016

Table. Characteristics of Colorectal Cancer Screening Strategies[a]

Screening Method	Frequency[b]	Evidence of Efficacy	Other Considerations
Stool-Based Tests			
gFOBT	Every year	RCTs with mortality end points: High-sensitivity versions (eg, Hemoccult SENSA) have superior test performance characteristics than older tests (eg, Hemoccult II)	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT[c]	Every year	Test characteristic studies: Improved accuracy compared with gFOBT Can be done with a single specimen	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every 1 or 3 y[d]	Test characteristic studies: Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test	There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test
Direct Visualization Tests			
Colonoscopy[c]	Every 10 y	Prospective cohort study with mortality end point	Requires less frequent screening Screening and diagnostic follow-up of positive findings can be performed during the same examination
CT colonography[e]	Every 5 y	Test characteristic studies	There is insufficient evidence about the potential harms of associated extracolonic findings, which are common
Flexible sigmoidoscopy	Every 5 y	RCTs with mortality end points: Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies	Test availability has declined in the United States
Flexible sigmoidoscopy with FIT[c]	Flexible sigmoidoscopy every 10 y plus FIT every year	RCT with mortality end point (subgroup analysis)	Test availability has declined in the United States Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

Abbreviations: FIT, fecal immunochemical test; FIT-DNA, multitargeted stool DNA test; gFOBT, guaiac-based fecal occult blood test; RCT, randomized clinical trial.

[a] Although a serology test to detect methylated *SEPT9* DNA was included in the systematic evidence review, this screening method currently has limited evidence evaluating its use (a single published test characteristic study met inclusion criteria, which found it had a sensitivity to detect colorectal cancer of <50%).[1] It is therefore not included in this table.

[b] Applies to persons with negative findings (including hyperplastic polyps) and is not intended for persons in surveillance programs. Evidence of efficacy is not informative of screening frequency, with the exception of gFOBT and

[c] Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling.[2]

[d] Suggested by manufacturer.

[e] Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling when lifetime number of colonoscopies is used as the proxy measure for the burden of screening, but not if lifetime number of cathartic bowel preparations is used as the proxy measure.[2]

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