EDISON

VolitionRx

Company update

Shifts in US CRC screening; major catalysts in H2

Pharma & biotech

VolitionRx has broad R&D programme and expects to announce major milestones in the coming months, culminating with CE marking and launch of both colorectal cancer (CRC) triage and frontline screening tests in Europe, potentially in 2019. Other recent positive developments include a recommendation to reduce age to start CRC screening in the US and a new legislative initiative that could help increase reimbursement coverage in the US. Our valuation is $243m or $7.02 per share (vs $6.93 per share).

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/16	0.0	(12.5)	(0.54)	0.0	N/A	N/A
12/17	0.0	(15.1)	(0.57)	0.0	N/A	N/A
12/18e	0.1	(17.0)	(0.54)	0.0	N/A	N/A
12/19e	1.4	(17.3)	(0.53)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles and exceptional items.

Start of commercial phase with research use sales

In May 2018, VolitionRx announced a global sales and distribution agreement with Active Motif that will distribute kits based on VolitionRx's technology for research use. While VolitionRx focuses on cancer (CRC screening primarily), the Nu.Q™ assays can be used in other conditions. This is not likely to lead VolitionRx to break even; however, the benefits of such business include a high-margin royalty stream, increasing awareness of the Nucleosomics technology within the research community and obtaining insights into various other applications for Nu.Q assays.

Shifts in US CRC screening market

The US CRC screening market has seen several major recent developments. The American Cancer Society has lowered the recommended age to start screening for CRC from 50 to 45 in its updated guidelines in May 2018, which theoretically increases the US target population from 93 million to 114 million. Separately, a bipartisan initiative, the Colorectal Cancer Detection Act of 2018, was introduced to the Senate in March 2018, aiming to provide coverage under the Medicare programme for FDA-approved CRC blood-based screening tests. If passed, the law would increase the likelihood of novel tests achieving reimbursement.

Approaching major R&D milestones

VolitionRx's expects to deliver several R&D milestones over the next 12 months. These include launch of research-use kits and sales potentially from Q318; results of the updated Nu.Q CRC triage test in Q318 and CE marking in Q418; and final panel for the Nu.Q CRC frontline screening test based on 4,300 samples in H218, which will be validated in a 12,000+ sample study and CE mark obtained in Q119. The triage and frontline screening tests could be launched in 2019.

Valuation: Increased to $243m or $7.02 per share

Our valuation of VolitionRx has increased slightly to $243m or $7.02 per share from $212m or $6.93 per share due to the inclusion of modest research-use sales, a reduction in near-term costs and rolling our model forward. Our other assumptions remain unchanged. Our updated model suggests a $9.5m funding gap in 2019.

18 July 2018

Price	**US$1.95**
Market cap	**US$59m**

Net cash ($m) at end Q118 + $700k non-dilutive funding in July 2018	13.2
Basic shares in issue	30.0m
Free float	70%
Code	VNRX
Primary exchange	NYSE American
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(18.8)	(10.6)	(39.1)
Rel (local)	(19.6)	(13.8)	(46.7)

52-week high/low	US$4.0	US$1.9

Business description

VolitionRx is a life sciences company developing novel, simple-to-use, blood-based tests to diagnose a broad range of cancers and other conditions by identifying and measuring nucleosomes in the blood stream. The primary focus is to develop the Nu.Q family of blood-based diagnostics tests for colorectal cancer.

Next events

Triage test finalised	Q318
Triage test CE mark	Q418
4,300 sample training study results	H218
12,000+ sample blinded study initiation	Q119

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Active Motif deal: Entering the commercial phase

The research use-only kits that Active Motif will be distributing are based on the Nu.Q immunoassay technology and can be used to investigate epigenetic modifications to cell-free nucleosomes. While VolitionRx focuses on cancer, the Nu.Q assays can potentially be used in a variety of conditions beyond cancer, such as inflammatory and infectious diseases in preclinical or clinical studies. Active Motif is a US-based private company, therefore its financial details are not publicly released. However, the company specialises in supplying the research community with products for epigenetic and gene regulation research, so it appears to be a good distribution partner for VolitionRx.

Management has not yet provided guidance due to the products' early stage of commercialisation of the products, but has indicated that end-user pricing is likely to be <$1,000 per kit. VolitionRx will receive around $150-200 of that, but will not incur any additional costs as Active Motif will manufacture and distribute the kits and manage customer service. Therefore, this will be high-margin revenue for VolitionRx. Active Motif planned to start commercialising the kits by end Q218, so Q318 will be the first full 'in market' period. When it comes to long-term potential, we believe this could generate a modest income for VolitionRx that would help to offset some of the operating costs; however, the clinical application of Nu.Q technology is still the ultimate goal and path to profitability. To a large extent, VolitionRx considers the sale of kits to third-party researchers as further validation of its Nucleosomics platform and of increasing awareness. A potentially lucrative opportunity could be companion diagnostics. If VolitionRx's assays are used during drug development by a third party and pass regulatory approval, such companion diagnostics would be tied to the drug securing royalties or other licensing income for VolitionRx. Therapeutics, however, can takes years of development.

Major developments in the US CRC screening market

The US CRC screening market has seen several recent major developments. The American Cancer Society has lowered the recommended age to start screening for CRC from 50 to 45 years old in its updated screening guidelines released in May 2018.[1] This has increased the target population for screening in the US from 93 million to 114 million people. VolitionRx's competitor Exact Sciences' share price, which markets Cologuard, jumped 11% after the news. Cologuard was included in the updated guidelines and is approved by the FDA for screening for the over 50s, but the company plans to expand the label for the over 45s, in line with the new guidelines. In total, 186,000 Cologuard tests were carried out in Q118, bringing in revenue of $90.3m for Exact Sciences, where the test price is $485. The company expects to reach a total of 900-920k tests for 2018. Cologuard is a stool-based DNA screening test, which is expensive and likely to still be posing compliance issues, similar to other stool-based screening methods.

Another peer close to VolitionRx is Epigenomics, which developed Epi proColon, a blood-based DNA screening test (this is likely to be more expensive than VolitionRx's solution). Epigenomics has found itself in a less favourable situation because the new guidelines did not include its Epi proColon test as an option for screening and its share price fell c 43% on the same day. Epigenomics is securing reimbursement through a national coverage determination (NCD) and inclusion into guidelines was perceived as key stepping stone. While guidelines are subject to regular updates, this has introduced uncertainty for the company in the near term and shows the

[1] Andrew M. D. Wolf et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin, May 2018.*

need to gain approval from clinical consensus to convince payors of reimbursement. Another potential path to achieve reimbursement coverage for CRC screening in the US has opened up via legislation. A bipartisan initiative, the Colorectal Cancer Detection Act of 2018, was introduced to the Senate in March 2018, aiming to provide coverage under the Medicare programme for FDA-approved CRC screening blood-based tests. Epi proColon was approved by the FDA in April 2016, therefore if the law is passed, Epi proColon could potentially qualify for reimbursement. The law appears to increase the likelihood of novel, FDA-approved tests achieving reimbursement, so potentially positive for VolitionRx as well.

Pathway to market

As we detailed in our last outlook report, VolitionRx's Nu.Q technology centres on the detection and characterisation of circulating nucleosomes. The company has developed a series of 39 different ELISA-based assays to characterise and quantify these nucleosome-based biomarkers in the hope of identifying signatures indicative of different cancers. The main competitive advantage of VolitionRx's technology compared with other novel and established CRC screening methods is its simple use and minimal invasiveness (a blood sample is obtained via a regular blood draw). This could lead to increased compliance in CRC screening. In addition, the tests are based on ELISA, which makes them inexpensive and widely available in laboratories.

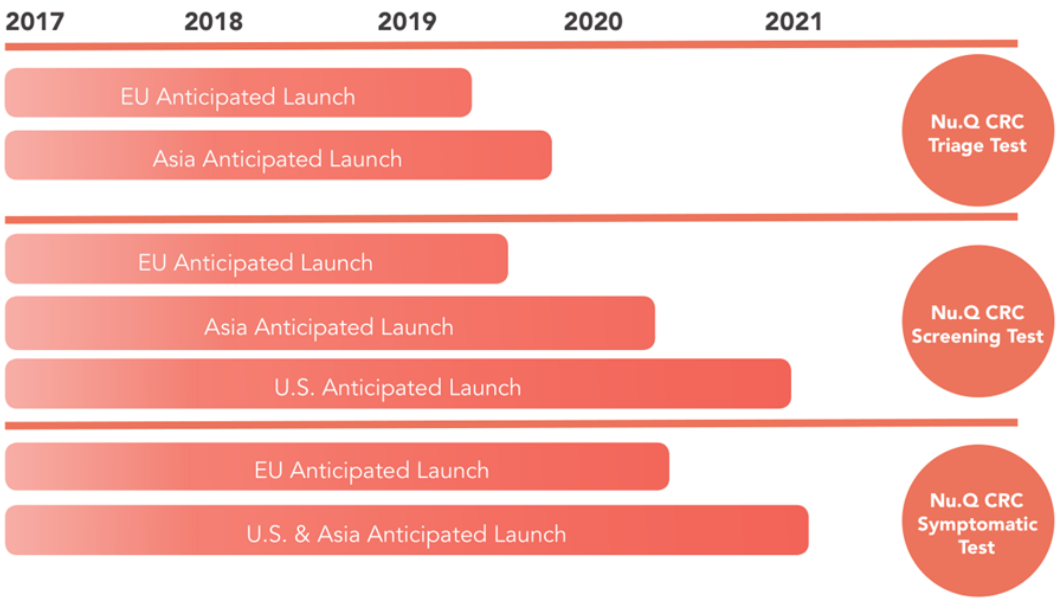
VolitionRx is running a broad R&D programme to establish the feasibility of various applications for its technology (Exhibit 1). Leading programmes are in CRC, but the company has also tested the technology in lung, pancreatic and prostate cancers, and has an ongoing study examining its assays in 27 common cancers (also presented in detail in our last outlook report). The primary focus in CRC is on the triage test and frontline screening (Exhibit 2), the latter being the largest opportunity due to market size (145 million in EU28, 114 million in the US); VolitionRx is also working on the strategy in Asia. In addition, VolitionRx is exploring how to position the Nu.Q test for symptomatic CRC patients.

Exhibit 1: VolitionRx clinical programmes

Indication	Sponsor	Patients	Notes
Colorectal cancer	NCI Early Detection Research Network	13,500	Registration trial, 4,600 retrospective samples, up to 9,000 prospective; ongoing to 2020.
Colorectal cancer	VolitionRx, Hvidovre Hospital (Denmark)	14,000+	4,300 sample prospective training set (results H218); 12,000+ prospective validation set (results Q119); CE mark Q119.
Colorectal cancer	Hvidovre Hospital (Denmark)	4,800	Biomarker analysis of samples from symptomatic patients; results expected in 2018.
Colorectal cancer	Hvidovre Hospital (Denmark)	30,000	Longitudinal study, each person to provide three samples totaling 90,000 samples. Ongoing to 2022.
Colorectal cancer	National Taiwan University	5,000	Frontline screening. Expected to start sample collection in 2018.
Colorectal cancer	National Taiwan University	2,000	Diagnostic test in symptomatic patients. Expected to start sample collection in 2018.
27 most prevalent cancers	Bonn University Hospital (Germany)	4,500	Broad, prospective screen of 27 most prevalent cancers to identify differences in nucleosome modification; results expected in 2018.
Pancreatic cancer	German Cancer Research Center (DKFZ)	750	Retrospective study to detect of pancreatic cancer; results expected H218/H119.

Source: VolitionRx

Exhibit 2: VolitionRx's colorectal cancer platform



Source: VolitionRx

While the R&D programme is broad, the main value drivers for VolitionRx are the large CRC trials in Europe (with Hvidovre Hospital in Denmark) and the US (with the National Cancer Institute's (NCI's) Early Detection Research Network), which include retrospective or prospective training sets and a subsequent prospective validation sets, as detailed in Exhibit 1. These trials, if successful, will allow VolitionRx to seek regulatory approval and gain marketing claims in the respective geographies. The triage test, while a smaller opportunity, could potentially reach the market sooner, as VolitionRx has been developing the test for longer. Current plans include CE marking the triage test in Q418, the CRC screening test in Q119 and launch of both tests in 2019 in Europe. VolitionRx is also looking to expand in Asia and is initiating two prospective trials in Taiwan in a partnership with the National Taiwan University.

Clinical trials update and upcoming milestones

According to the most recent update, the upcoming milestones include:

- **Frontline CRC screening in Europe**. The results from the 4,300-sample prospective training set in CRC screening are due imminently. VolitionRx expects this will allow identification of the final set of assays to be used in the test, which will be locked and validated in the 12,000 prospective sample set. According to the company, it is likely that the test will include five to six Nu.Q assays and generic markers such as well-known carcinoembryonic antigen.
- **Frontline CRC screening in US**. Collection of samples is ongoing and VolitionRx expects to select a panel for screening over the coming months. In total 4,600 retrospective samples, up to 9,000 prospective sample sets are expected to be collected by 2020. As a reminder, the company announced this 13,500-person trial in July 2017. At this scale, this is one of the largest-ever trials for a CRC screening product. The study is being run in collaboration with the NCI's Early Detection Research Network and the Great Lakes New England (of the University of Michigan) Clinical Validation Center, which will provide substantial resources for the trial, while VolitionRx's contribution is only c $3m. VolitionRx believes this trial should support a regulatory approval in the US, although it has not confirmed this with the FDA.
- **Triage test**. VolitionRx is updating the original version of its first product – a triage test for patients who had a positive FIT test to reduce unnecessary colonoscopies (as explained in the

outlook report). Management expects to announce the results of the updated Nu.Q CRC triage test during the third quarter of 2018. A significant step towards understanding how to position the novel triage test in this setting was the recently completed (Logistics and Pathway Design Study). The study explored the correct implementation of the triage test into the Danish Screening Programme, as an example, and involved 750 people. The February 2018 announcement from VolitionRx concluded that the logistics and feasibility of a triage concept seem plausible.

- **Study in 27 most prevalent cancers.** This cooperation with the Bonn University Hospital began in 2015. Most recent confirmation from the management is that the results from the analysis of the 4,500 samples collected by the university hospital are expected later this year. This will be a discovery study and will analyse cell-free nucleosome modification across the 27 most prevalent cancers. Therefore, for the first time the study will establish the breadth of the platform technology to such level.
- **New Asian initiatives.** VolitionRx has begun preparations for two clinical trials in Taiwan for approximately 7,000 patients and expects to start them later in 2018. The company believes that both CE mark data and the trial results will be accepted by the local country authorities. Although the markets are large throughout Asia and incidence of CRC is high, screening is underpenetrated. Part of that issue is either inconvenient screening methods (FIT, colonoscopies) or expensive novel DNA tests. VolitionRx believes its cheaper ELISA-based screening test could deliver convincing value proposition in these countries.

Other application areas emerging

Circulating tumour DNA enrichment

Together with its Q118 results, VolitionRx described its progress with one of its internal projects, which explores Nu.Q technology's potential in enriching nucleosomes of tumour origin for use in circulating tumour DNA (ctDNA) detection. ctDNA research has expanded substantially since the advent of cheaper next-generation sequencing techniques and now constitutes a significant research area in liquid biopsy, followed by circulating tumour-cell harvesting technologies. The main hurdle in ctDNA research is the very small amount of tumour DNA. Another layer of complexity is that there can be other types of DNA in the bloodstream, such as in post-myocardial infarction patients or pregnant women with DNA from the baby (collectively ctDNA and other types are called cell-free DNA). For these reasons the ctDNA enriching idea is intriguing, although so far VolitionRx has not released much information about how its Nucleosomics platform could achieve it.

Animal health

During the Q118 results call, VolitionRx provided details on another initiative it has been exploring in animal health. The company has undertaken a pilot veterinary study, where it was able to detect nucleosomes in samples from dogs that were diagnosed with cancer using the same assays as in humans. VolitionRx does not intend to carry this programme further by itself, but is keen to establish collaborations with parties specialising in the area. If this initiative gains traction, animal health will represent a whole new area for VolitionRx; we will revisit this if there are updates in the future.

Financials

As expected, VolitionRx reported no income and an operating loss of $4.6m in Q118, compared to $3.3m a year ago. The increase mainly was due to higher R&D costs of $2.4m from $1.7m. VolitionRx had cash of $14.3m at end Q118 after it raised $8.4m gross in March. The company reiterated its guidance that cash burn is likely to stay at $3m per quarter in the near future. Adding

$700k in non-dilutive financing from the Walloon regional government announced in June 2018, the guidance suggests that runway extends well into 2019 and past several R&D catalysts. VolitionRx had $1.8m in gross debt at end Q118.

Our estimate changes include a modest downward revision to our near-term operating expenses to reflect the steady guidance. In addition, we include small initial research use sales of $50k in 2018 and $100k in 2019. Notably, there is little visibility of the potential of research-use sales and we will revise our estimates once more data points are reported. As a result, our operating loss has improved to $16.9m (from $18.9m) and $17.2m (from $21.5m) in 2018 and 2019 respectively. We calculate a $9.5m funding gap in 2019 (shown as long-term debt in Exhibit 4).

Valuation

Our VolitionRx valuation has increased slightly to $243m or $7.02 per share from $212m or $6.93 per share due to the inclusion of modest research use sales, reduction in near-term costs and rolling our model forward. Our assumptions for the development programmes remain almost unchanged. For now we have not increased the target screening population in the US as recommended in the screening guidelines, which were announced in May 2018. We will revisit this once the awareness spreads and data emerge to suggest CRC screening in under 50-year-olds is increasing. Near-term catalysts for the share price include:

- Progress of Active Motif's launch of a range of research-use kits (we do not expect any tangible financial effect for VolitionRx until Q318)
- Results of the updated Nu.Q CRC triage test in Q318 and CE marking in Q418
- Results and final panel for the Nu.Q CRC frontline screening test based on 4,300 samples in H218; validation of the panel in a 12,000+ sample study and CE mark in Q119
- Preliminary data from study in 27 cancers due in H218
- If the trials are successful, the triage and frontline screening tests could be launched in 2019

Exhibit 3: Valuation of VolitionRx

Product	Main indication	Status	Probability of success	Launch year	Peak sales ($m)	Patent protection	Economics	rNPV ($m)
NuQ	Colorectal	Development	30%	2018	404	2034	56% peak margin	158
	Colorectal triage	Development	40%	2018	42	2034	50% peak margin	16
	Lung	Development	20%	2020	132	2034	61% peak margin	31
	Pancreatic	Development	20%	2020	42	2034	58% peak margin	8
Total								212
Cash (Q118 + non-dilutive funding in June 2018) ($m)								15.0
Total firm value ($m)								227
Total basic shares (m)								30.0
Value per basic share ($)								7.57
Warrants and options (m)								4.7
Weighted average exercise price ($)								3.45
Cash on exercise ($m)								16.1
Total firm value ($m)								243
Total diluted number of shares (m)								34.7
Diluted value per share ($)								7.02

Source: Edison Investment Research, VolitionRx reports

Exhibit 4: Financial summary

$'000s	2016	2017	2018e	2019e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS				
Revenue	0	0	50	1,429
Cost of Sales	0	0	(14)	(170)
Gross Profit	0	0	36	1,260
Research & Development	(7,905)	(8,906)	(8,242)	(8,736)
Sales, General & Administrative	(4,525)	(6,140)	(8,673)	(9,756)
EBITDA	(12,430)	(15,046)	(16,879)	(17,233)
Operating profit (before amort. and except.)	(12,430)	(15,046)	(16,879)	(17,233)
Intangible Amortisation	0	0	0	0
Other	0	0	0	0
Exceptionals	0	0	0	0
Operating Profit	(12,430)	(15,046)	(16,879)	(17,233)
Net Interest	(20)	(73)	(90)	(115)
Other	436	414	0	0
Profit Before Tax (norm)	(12,450)	(15,119)	(16,969)	(17,348)
Profit Before Tax (FRS 3)	(12,014)	(14,705)	(16,969)	(17,348)
Tax	0	0	0	0
Deferred tax	(0)	(0)	(0)	(0)
Profit After Tax (norm)	(12,450)	(15,119)	(16,969)	(17,348)
Profit After Tax (FRS 3)	(12,014)	(14,705)	(16,969)	(17,348)
Average Number of Shares Outstanding (m)	23.0	26.4	31.2	32.5
EPS - normalised ($)	(0.54)	(0.57)	(0.54)	(0.53)
EPS - FRS 3 ($)	(0.52)	(0.56)	(0.54)	(0.53)
Dividend per share ($)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	2,721	4,057	3,222	2,601
Intangible Assets	602	576	576	576
Tangible Assets	2,119	3,481	2,646	2,025
Other	(0)	(0)	(0)	(0)
Current Assets	21,846	10,319	5,227	653
Stocks	0	0	1	8
Debtors	0	0	9	255
Cash	21,679	10,116	5,015	188
Other	167	202	202	202
Current Liabilities	(2,033)	(2,290)	(3,002)	(3,220)
Creditors	(2,003)	(1,847)	(2,558)	(2,776)
Short term borrowings	(31)	(444)	(444)	(444)
Long Term Liabilities	(1,524)	(2,376)	(2,376)	(11,876)
Long term borrowings	(432)	(1,313)	(1,313)	(10,813)
Other long term liabilities	(1,092)	(1,063)	(1,063)	(1,063)
Net Assets	21,009	9,709	3,071	(11,842)
CASH FLOW				
Operating Cash Flow	(8,865)	(12,193)	(12,997)	(14,313)
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	(415)	(1,425)	(1)	(14)
Acquisitions/disposals	0	0	0	0
Financing	25,302	998	7,896	0
Dividends	0	0	0	0
Other	(553)	(136)	0	0
Net Cash Flow	15,470	(12,756)	(5,101)	(14,327)
Opening net debt/(cash)	(5,916)	(21,216)	(8,360)	(3,258)
HP finance leases initiated	0	0	0	0
Exchange rate movements	146	(89)	0	0
Other	-316	-12	0	0
Closing net debt/(cash)	(21,216)	(8,360)	(3,258)	11,069

Source: VolitionRx accounts, Edison Investment Research. Note: Please see the company's discussion of risk factors in its annual report on certain identified material weaknesses, which could impact financial reporting and remediation efforts.

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