Breakthrough Bowel Cancer Diagnostic

Rhythm Biosciences (RHY) has developed its first diagnostic test, ColoSTAT®, to detect colorectal (CRC) or bowel cancer. Its readying for launch. Its recent Clinical Study 6 confirmed the test kit design and commercial production capability. The study also showed ColoSTAT® outperformed the current CRC screening market leader, Faecal Immunochemical Test (FIT). ColoSTAT®'s Clinical Trial 7 is in progress. Positive results will initiate the steps to market approval, with early revenues expected to commence during FY23.

Current choices dissuade test candidates

While CRC has a high rate of cure if diagnosed early, current screening programs are not well utilised. Many candidates reject the faecal tests because of the test protocols and their relatively poor accuracy. In the US, health payers endorse colonoscopy as the preferred testing regimen as it offers higher accuracy. However, it requires sedation and carries risk of serious adverse effects such bowel perforation. The higher cost excludes many participants.

ColoSTAT® potential

ColoSTAT® is a blood test, offering convenience. It can be slotted into current blood screening tests programs such as cholesterol, prostate cancer and glucose. In our view, many will prefer a blood test to a faecal test. In terms of efficacy, data to date has shown ColoSTAT® had ~40% higher detection of CRC to FIT. It effectively identified 88 cases in every 100 CRC samples versus FIT with 63. It may also expand the current market by enticing those who reject the faecal tests and offer a role as an adjunct to colonoscopy screening programs.

Later stage asset offering near term catalysts

RHY has commenced the final stage of development. Positive results of its Clinical Study 7 will see it apply for approval in Australia and support its commercialisation in the other target markets of US, EU, China and Japan. Full recruitment for Clinical Study 7 is expected by end CY21. RHY has commenced engagement with the Australian regulator and will follow with the EU and US.

Valuation of $2.08 includes usual industry risk weighting

MST's DCF valuation of A$420.6m, $2.08 ps is risk adjusted at 70% to reflect industry standards for ColoSTAT®'s late stage of development. It is also supported by peers, BARD1 Life Sciences (BD1.AX) at $143m and Volpara Health(VHT.AX) at $302m. Both are developing cancer screening diagnostics. The valuation is subject to the usual upside/downside risks of medical device development including trial failure, timing differences, non-approval, commercial uptake variations and competitor behaviours.

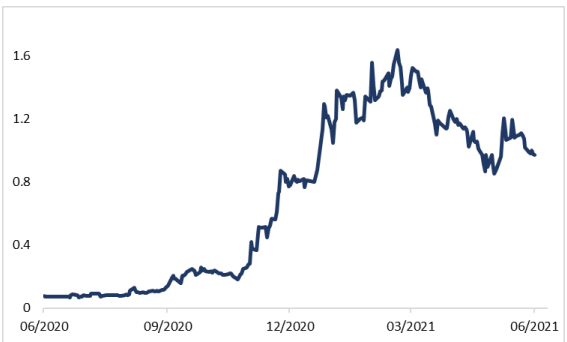
Rhythm Biosciences is an Australian medical diagnostics company. Its protein-based technology platform is being trialled in its first indication, colorectal cancer. Other tests are expected to follow. The work is well credentialled. The technology reflects 13+ years of CSIRO research and to date 3+ years of RHY development. Management brings experience in both development and commercialisation of new medical products.

www.rhythmbio.com

Stock	RHY.ASX
Price	A$1.00
Market cap	A$202m
Valuation	A$420.6m
Valuation (per share)	A$2.08

Next steps	
H2CY21	Full enrolment Clinical Study 7
H2CY21	File for EU CE Mark
CY21	US CLIA laboratory initial steps

RHY Share Price (A$)



Source: FactSet

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Financial Summary

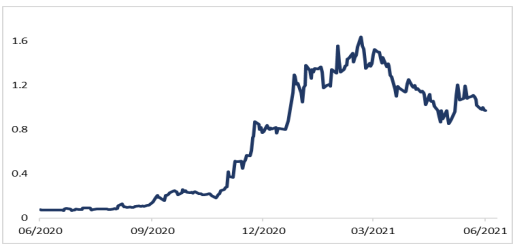
RHYTHM BIOSCIENCES — RHY.AX

Year end 30 June

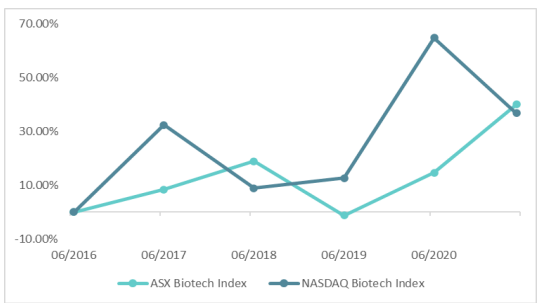
MARKET DATA

Share price	**$**	**1.00**
52 week high / low	$	0.063 - 1.68
Valuation (12 month forward)	**$**	**$2.08**
Market capitalisation	**$m**	202.2
Shares on issue	m	202
Options	m	7
Other equity	m	-
Potential Share Issue FY22	m	5.3
Potential shares on issue	m	215

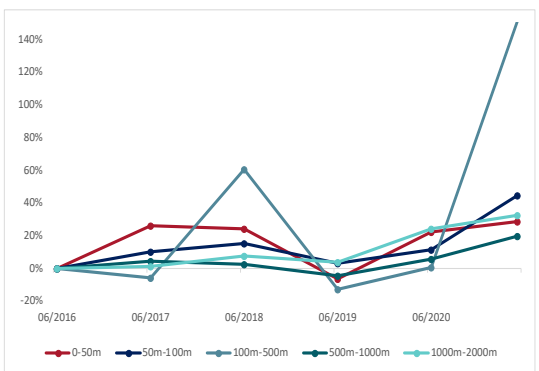
12 month share price performance



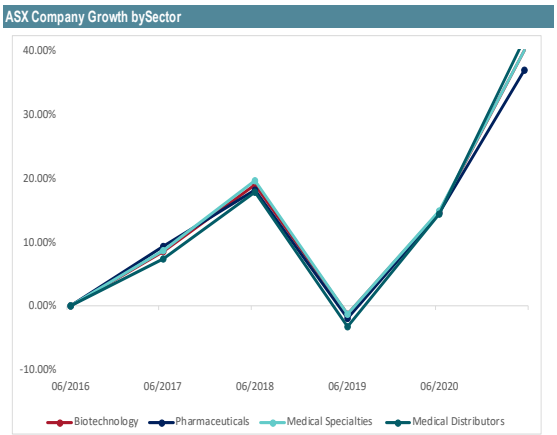
ASX and NASDAQ Biotechnology Indices



Biotechnology Company Growth by Market Capitalisation



ASX Company Growth bySector



PROFIT AND LOSS (US$)		FY20	FY21E	FY22E	FY23E	FY24E
R&D Tax Refund	000s	-	843.7	1,406.4	1,200.0	1,305.0
Interest Income	000s	46.3	63.4	108.6	96.7	51.3
Other Income	000s	100.0	-	-	-	-
Licensing Royalties	000s	-	-	-	5,462.8	17,065.3
Total Revenue	000s	**146.3**	**907.1**	**1,515.0**	**6,759.5**	**18,421.6**
Research and development costs	000s	(1,939.4)	(4,688.0)	(4,000.0)	(3,000.0)	(2,000.0)
Other expenses	000s	(2,229.8)	(1,634.8)	(1,653.0)	(1,668.7)	(1,684.6)
Underlying NPAT	000s	**(4,023.0)**	**(5,415.7)**	**(4,138.0)**	**2,090.8**	**14,737.0**

BALANCE SHEET (US$)		FY20	FY21E	FY22E	FY23E	FY24E
Cash and cash equivalents	000s	1,798.0	1,208.6	1,242.9	3,300.1	17,867.1
Trade and other receivables	000s	139.2	139.2	139.2	139.2	139.2
Other financial assets	000s	45.0	45.0	45.0	45.0	45.0
Prepayments	000s	23.2	23.2	23.2	23.2	23.2
Total current assets	000s	2,005.4	1,416.0	1,450.3	3,507.5	18,074.5
Intangible assets	000s	498.0	498.0	498.0	498.0	498.0
Right of use assets	000s	40.0	40.0	40.0	40.0	40.0
Property, plant and equipment	000s	102.5	102.5	102.5	102.5	102.5
Total Non-Current Assets	000s	640.5	640.5	640.5	640.5	640.5
Total Assets	000s	2,645.9	2,056.6	2,090.9	4,148.0	18,715.0
Trade and other payables	000s	676.1	489.1	582.6	535.9	535.9
Provisions	000s	75.9	75.9	75.9	75.9	75.9
Lease liabilities	000s	42.4	42.4	42.4	42.4	42.4
Total current liabilities	000s	794.4	607.4	700.9	654.2	654.2
Provisions	000s	8.4	8.4	8.4	8.4	8.4
Total non-current liabilities	000s	8.4	8.4	8.4	8.4	8.4
Total liabilities	000s	802.9	615.9	709.4	662.6	662.6
Net Assets	000s	1,843.1	1,440.7	1,381.5	3,485.4	18,052.4
Issued capital	000s	10,037.2	15,846.5	20,846.5	20,846.5	20,846.5
Reserves	000s	194.0	194.0	194.0	194.0	194.0
Accumulated losses	000s	(8,388.2)	(14,599.8)	(19,659.0)	(17,555.1)	(2,988.1)
Total shareholders' equity	000s	**1,843.1**	**1,440.7**	**1,381.5**	**3,485.4**	**18,052.4**
Total liabilities and equity	000s	**2,645.9**	**2,056.6**	**2,090.9**	**4,148.0**	**18,715.0**

CASH FLOW (US$)		FY20	FY21E	FY22E	FY23E	FY24E
Licensing Royalties	000s	-	-	-	5,462.8	17,065.3
Interest received	000s	47.2	63.4	108.6	96.7	51.3
R&D Expenses	000s	(1,939.4)	(4,688.0)	(4,000.0)	(3,000.0)	(2,000.0)
Interest paid	000s	(7.8)	-	-	-	-
R&D tax fund	000s	743.8	-	843.7	1,406.4	1,200.0
Other items	000s	(1,586.4)	(1,634.8)	(1,653.0)	(1,668.7)	(1,684.6)
Net cash flows from operating activitie	000s	**(2,742.6)**	**(6,259.3)**	**(4,700.7)**	**2,297.2**	**14,632.0**
Purchases of P&E	000s	(45.5)	(15.0)	(15.0)	(15.0)	(15.0)
Net cash flows from investing	000s	**(45.5)**	**(15.0)**	**(15.0)**	**(15.0)**	**(15.0)**
Repayment of lease liabilities	000s	(59.9)	(50.0)	(50.0)	(50.0)	(50.0)
Repayment of other borrowings	000s	(82.4)	(75.0)	-	-	-
Proceeds from issue of ord shares	000s	-	6,034.0	5,000.0	-	-
Payment of share issue costs	000s	-	(224.0)	(200.0)	(175.0)	-
Net cash flow from financing	000s	**(142.2)**	**5,685.0**	**4,750.0**	**(225.0)**	**(50.0)**
Change in Cash	000s	(2,930.4)	(589.3)	34.3	2,057.2	14,567.0
Year end cash	000s	1,798.0	1,208.6	1,242.9	3,300.1	17,867.1

Comparable Companies

Company	**BARD1 Life Sciences (BD1.AX)**	**Company**	**Volpara Health Technologies Ltd (VHT.AX)**
Description	BD1 develops and commercialises diagnostics to detect/support detection of cancer	**Description**	VOL is developing a software-as-a-service company that utilises AI to improve early detection of breast cancer
Market Cap - 143m		**Market Cap - 302m**	

Investment Thesis

Rhythm Biosciences (RHY) has developed a platform technology to offer simple, low cost, mass market cancer screening tests. The 'lead' cancer biomarker is highly expressed in a range of cancers, opening the potential for multiple applications. RHY has also developed three biomarkers which identify the recognised 'cancer' cells as CRC. Its first product, ColoSTAT®, is in late-stage development with plans to enter US, Europe, Australia, New Zealand, China and Japan markets. MST investment thesis is built around CRC only, although it recognises further upside. ColoSTAT® presents opportunity through:

1. CRC is the second largest cause of US cancer related death. Screening for early diagnosis draws strong support from the key health and regulatory bodies and governments with funding for programs available in many countries. The general awareness coupled with established programs should expedite ColoSTAT®'s market penetration.
2. Trial data to date has shown clear superiority to the SOC faecal test, Faecal Immunochemical Test (FIT).
3. Utilisation of current tests is low due to poor efficacy and protocols of the faecal tests and the higher cost of colonoscopy. As a blood test, ColoSTAT® can be incorporated into current screening tests for cholesterol, glucose. The format and potential higher efficacy are likely to be well received and expand the current markets.
4. ColoSTAT® is in its final stage of trialling, offering lower risk and near term market entry.

Valuation, Risks, Sensitivities

Based on a risk adjusted DCF, MST attributes RHY a value of $420.6m or $2.08 ps. The valuation is supported by peer comparison to Volpara Health Technologies (VHT.AX) and BARD1 Life Sciences (BD1.AX). Both companies are diagnostic technology based and targeting global markets. The companies vary in terms of stage of development and targeted markets.

The key risks to the MST DCF valuation include positive trial data and supporting documentation to meet the regulatory standards of the targeted markets. The DCF recognises the need for further funding to complete the planned program. Assumptions have been made regarding approval and commercial uptake in the nominated markets. Many of the countries offer government funded CRC screening programs. Our forecasts assume RHY will be accepted as an alternative. The valuation focuses on the key commercial markets of the US, Australia and the EU. RHY is yet to provide detail on its path to the rest of world markets such as Japan and China. Review of ColoSTAT®'s market potential will be undertaken as the plans are confirmed.

Upcoming Milestones

CY 21 - Full enrolment of Clinical Study 7, an efficacy study to confirm ColoSTAT®'s diagnostic capability.

CY21 – Filing of Conformité Européenne (CE) mark to allow sales within the European Economic Area (EEA).

CY21 - Commence initial steps to confirm and establish US CLIA laboratory

CY21 - Commence initial steps to confirm FDA approval pathway

CY22 –Establish partnerships in the US, EU, Australia markets to commercialise ColoSTAT®

CY22 – Filing with Therapeutic Goods Administration (TGA) for Australian approval

CY22 – Identify and develop other cancer tests

Answer to Clear and Present Need

ColoSTAT® looks to offer the key characteristics of a mass market screening test – efficacious, simple, affordable, widely available and generally participant 'acceptable'. CRC is an attractive target. Screening programs are well supported by key health and regulatory bodies as early diagnosis results in higher survival rates and lower health costs. The current tests are not well utilised. ColoSTAT® looks to offer a cost-effective alternative that is likely to find greater acceptance within the screening population. Clinical trial data to date are supportive.

Early Diagnosis of CRC = High Survival Rate

CRC survival rates decrease rapidly with advancement of the disease. In addition, treatment costs escalate as more intensive therapy is required. The need for early diagnosis is thereby well recognised, with many countries offering subsidised CRC screening programs.

Exhibit 1 – Stage of CRC and associated survival rates

Stage	0	I	II	III	IV
5-year % survival rate	>96%	93%	82%	59%	8%

Source: SEER

Diagnosis at Stage 0 or 1, when the tumour is confined within the bowel wall, sees a 5-year survival rate of 93%- 96%. In contrast, when the cancer has spread outside the bowel in Stage IV, the survival rate drops to 8%. Treatment is relatively simple in Stage 0 with pre-cancerous polyps and Stage 1 with early cancerous lesions. They can be removed during colonoscopy and result in survival rates of 90% or higher. If the cancer has metastasised and spread to other parts of the body, treatment is more complex, commonly involving extensive surgery and chemotherapy. Late-stage diagnosis brings additional cost, patient hardship and commonly shorter survival. In the US, CRC is the second highest cause of death by cancer with ~ 53,000 people dying annually [1] and incurs significant medical cost.

Opportunity: Current Diagnostic Tests Don't Provide the Answer

The mainstays of the current screening programs are the Faecal Occult Blood Test (FOBT) and the Faecal Immunochemical Test (FIT). The FOBT detects faecal occult blood, ie micro amounts of blood in the faeces. It can indicate bleeding from polyps or cancer. However, a positive test, the presence of blood in the faeces, can arise from other causes such as haemorrhoids, bleeding from the stomach or the upper gastro-intestinal tract or simply eating rare meat or other foods. Similarly, a negative test is not definitive. Polyps and cancers do not bleed continuously, so FOBTs must be repeated more frequently than other test to increase probability of detecting blood in the faeces.

FIT is also a faecal test, which detects minute amounts of blood in faeces. In keeping with FOBT, a positive result is not definitive as the blood may arise from a number of conditions. However, it is more specific for CRC than FOBT as it is based on antibodies that only detect human blood in the faeces. A diet including meat will not trigger a positive test as it may with FOBT. Its superiority to FOBT has seen it as the preferred option for screening programs. Studies have shown it can reduce ~30% of deaths from colorectal cancer if performed yearly and 18% if undertaken every other year[2]. However, many candidates are dissuaded by the need to handle faeces. The combination of test regimen and high rate of false test results see poor uptake.

[1] SEER
[2] Cancer.net

The main alternative is colonoscopy. The procedure entails the insertion of a colonoscope, a flexible tube with a camera/microscope, to examine the bowel wall to identify cancer or precancerous polyps. Colonoscopy requires a bowel preparation and fasting from the preceding day as well as sedation for the procedure. It also carries the risk of bowel perforation with potentially serious side effects. Higher costs generally exclude it from nationalised health screening programs.

Other Screening Options include:

- **Cologuard -** is a faecal DNA test, which also screens for blood and abnormal genetic material that may indicate CRC. In addition to screening, it is commonly used as a follow up to confirm positive results from the other screening tests. It is only available in the US.
- **Computed tomography (CT) colonography,** otherwise known as a virtual colonoscopy, is a CAT scan examination of the bowel.
- **Sigmoidoscopy -** A procedure in keeping with colonoscopy however only the rectum and lower part of the colon are examined. It is commonly interspersed with annual FIT testing.

The majority of government funded CRC screening programs are based on FOBT or FIT, due to the lower cost. The higher costs of the colonoscopy, sigmoidoscopy and faecal DNA tests limit their uptake. Generally, CRC screening colonoscopies are funded by Private Health Insurance (PHI) or the individual. The US is an exception where colonoscopy is the SOC screening method and is funded by PHI and the government funded Medicare program for >65 year olds.

RHY Poised to Fill the Need

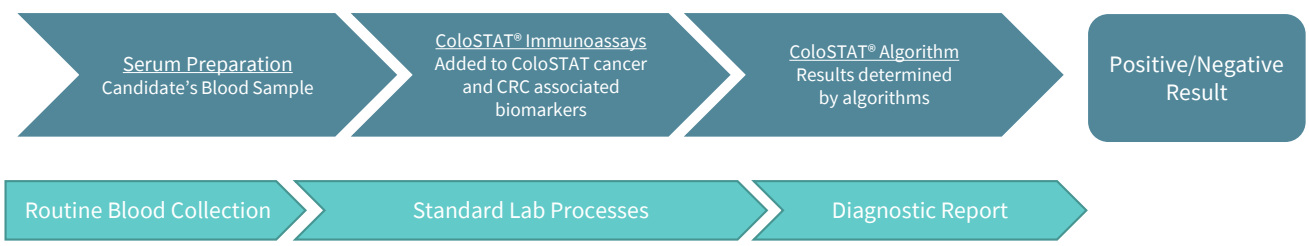
RHY's ColoSTAT® presents as a cost-effective, low risk and patient-friendly alternative.

- As ColoSTAT® is a blood test, it avoids the 'unpleasantness' of preparing the faecal sample on multiple occasions. The test can be performed as part of any routine 'wellness' programs for cholesterol, anaemia, Prostate Specific Antigen (PSA). The higher acceptability and efficacy of the ColoSTAT® promises substitution in existing markets. In addition, it has the potential to increase the market through persuading people who currently don't participate in the faecal test program or undertake the high cost of colonoscopies.
- From a payer's view it is also attractive. Higher efficacy may reduce health system costs by reducing unnecessary colonoscopies and/or may assist with the prioritisation of patients for colonoscope investigations.
- The test kit design offers low costs and wide availability as it is analysed through highly automated equipment, common to most pathology labs.
- Data to date are supportive that ColoSTAT® is more effective test than SOC faecal tests, FIT and FOBT.

RHY cancer technology platform – ColoSTAT® is the first test

ColoSTAT®'s biomarkers detect the cancer and the test kit and algorithms signal their presence.

Exhibit 2 – ColoSTAT® blood test based on proprietary biomarkers and algorithms for analysis



Source: MST adaption from Rhythm Biosciences

A diagnostic test requires:

- a signal or marker to indicate the presence of the disease
- a test kit to identify the presence of the signal.

The signal

Biomarkers are molecules, such as DNA (genes), proteins or hormones, that are found in the blood, other body fluids, and/or tissues. Disease can give rise to abnormal biomarkers and/or different concentrations of the biomarkers. The gene mutations in cancer commonly can lead to production of abnormal proteins. The body recognises the cancer cells as abnormal and mounts an immune reaction triggering inflammatory changes. Cancer diagnostic tests can be designed to detect the changes in the genes, the changes in proteins or other molecules they encode and/or the induced inflammatory changes.

Diagnostic tests are commonly developed around molecules that are associated with the disease state. ColoSTAT® 'biomarkers' emerged from studies by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) of ~68 proteins that vary in concentration in the blood serum of patients with and without colorectal cancer.

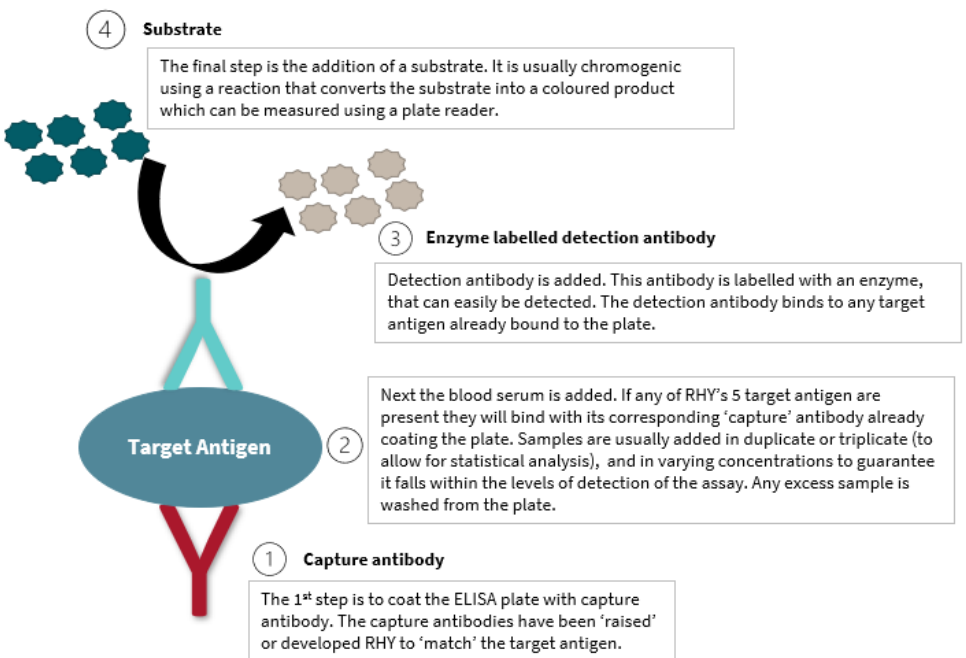
CSIRO conducted five clinical studies which included > 1,000 patient samples and the results refined the biomarkers to a panel of ten lead markers for further development. In 2017, RHY's fully owned subsidiary, Vision Tech, entered a Licence Agreement with CSIRO which granted the company an exclusive right to the patents and patent applications.

In 2019, RHY announced that it had identified a protein that enabled differentiation between cancer and healthy samples. The work established the key component of the test, the ability to detect the presence of cancer. Further work has seen confirmation of three complementary or adjunct markers that identify the cancer as CRC. Ongoing R&D has refined the use of the biomarkers. RHY continues to optimise the algorithms leading to continued improvement in the test results.

The test

In addition to confirmation of the biomarkers, RHY has developed a test kit to 'present' the biomarkers in an 'environment' to demonstrate their presence. RHY's test is an Enzyme-Linked Immunosorbent Assays (ELISA). It has developed in-house protein reagents and monoclonal antibodies to identify and measure the five target proteins. From a commercial perspective, ELISA tests are attractive.

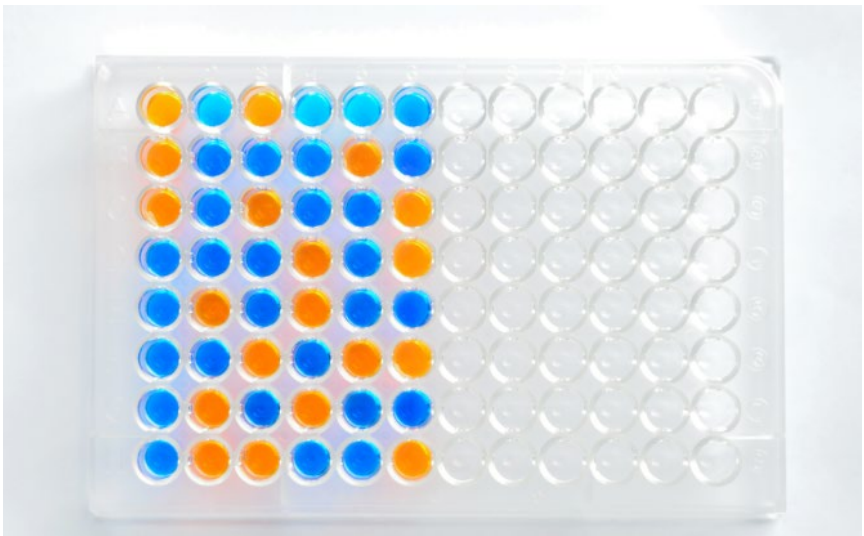
Exhibit 3 – Four component test of a Sandwich ELISA test



Source: MST Adaption from standard ELISA formats

RHY testing kit comprises the different reagents with labelled antibodies and substrate to detect the CRC antigen and software program of proprietary algorithms to calculate the concentration of each target CRC antigen to deliver a positive or negative result.

Exhibit 4 – A 96 well plate demonstrating a positive result



Source: Shutterstock

The serum samples are placed in 96-well plates lined with the 'capture' antibodies. The blood serum sample is added allowing the target CRC antigens, if present, to bind with the capture antibodies. Another antibody, carrying an enzyme is added which also binds to the target antigens. The final step is the addition of a substrate that targets the enzyme label. The plate is processed or 'read' by the ELISA scanner which can detect the colour enzyme presence and record the presence of the CRC antigens. The results are analysed by reiterative algorithms based on the presence of the different biomarkers.

The type of test is important in screening programs. Ideally they should be capable of managing high volumes and offer low cost. ELISA is one of the most commonly used laboratory techniques in clinical medicine. ELISA tests include HIV, and pregnancy diagnosis and conducted in most diagnostic pathology laboratories promising wide application. As a highly automated test platform, it can process high volumes efficiently. The automation requires little training and input from trained pathology staff, allowing for a low cost implementation.

The Path to Market

Regulatory Requirements

Confirmation that ColoSTAT can be manufactured at commercial volumes

With the research test kit defined, RHY has engaged a manufacturing partner for commercial production. As part of the regulatory requirements for approval, a company must demonstrate that the test kits' results are reproducible at commercial production levels, with the robust and consistent manufacturing processes. In December 2020, RHY appointed French company, Biotem, as the global manufacturer of its ColoSTAT® test-kit. Biotem offers a long history in the custom development of antibodies and immunoassays for ELISA tests.

As part of the commercial production programs, Clinical Study 6 was undertaken to confirm the commercially manufactured test kits were able to reproduce the results of the laboratory-based kits. The study of 300 samples of

cancerous and healthy specimens confirmed the commercial kits' efficacy. It also trialled ColoSTAT® against FIT. ColoSTAT® outperformed in both sensitivity and specificity with its 84% sensitivity and 95% specificity comparing to FIT sensitivity of 63% and specificity of 92%.

Confirmation of efficacy

As part of its submissions for regulatory approval, RHY will be required to submit clinical evidence of ColoSTAT®'s performance. More recently, RHY has reported improvement of ColoSTAT®'s performance in comparison to the Clinical Study 6, through ongoing enhancements of its algorithms. Lifestyle Related Factors (LRF) such as diet, weight, exercise, smoking and Type 2 Diabetes have been linked to the risk of CRC. The inclusion of a number of LRFs resulted in further gains in accuracy. ColoSTAT®'s sensitivity improved by ~4% to 88%. Specificity remained at 95%. RHY expects continued improvement through the iterative processes leading to on-going machine learning which will continue to refine the underlying algorithms.

Clinical Study 7

RHY has commenced Clinical Study 7. Positive results are planned to support application to Australia's Therapeutic Goods Administration (TGA) for approval. The data is also likely to support commercialisation strategies for EU, US and other jurisdictions. The results of Clinical Study 6 and more recently, the LRF testing, provide confidence in a positive outcome of Clinic study 7.

The purpose of Clinical Study 7 is to demonstrate that the studies to date translate from the 'lab' setting to the clinical arena – effectively that it works in the real world. It is an Australian based, prospective, cross sectional, multi centred study. Cohort 1 will include CRC-diagnosed patients who are progressing to surgery. Cohort 2 will include patients who are referred for colonoscopy by their physician. The patient cohorts are designed to provide sufficient positive and negative cancer samples to confirm ColoSTAT®'s ability to accurately identify the disease. Each patient will receive a ColoSTAT® blood test, FIT and a colonoscopy.

As a screening test, the primary aim is to demonstrate ColoSTAT®'s ability to detect the presence of CRC. The trial also aims to demonstrate non-inferiority to FIT - in other words, that ColoSTAT® is at least as effective as FIT. From a commercial view, the comparison to FIT as the SOC for screening is a key outcome. FIT is currently used in most national screening programs outside the US. A similar or superior performance to FIT, opens the opportunity for ColoSTAT® to become the SOC, given its other advantages. As discussed, a blood test performed as part of other blood-based investigations is likely to be preferred to the faecal test protocols.

The study will also look at the ability of ColoSTAT® to identify early-stage disease, advanced adenomas and clinically actionable neoplasia. While not central to the trial's purpose, confirmation of the earlier stage disease may create the opportunity for further refinement. It is also likely to increase health regulators' interest and the market opportunity from a competition perspective.

Recruitment for Study 7 continues to accelerate as Australia's COVID impact lessens. Recruitment is expected to be completed by the end of CY21. The blood samples for ColoSTAT® will be tested at the end of the recruitment period with the most updated and appropriate ColoSTAT® test-kit and algorithms. The FIT and colonoscopy results are being collected as they become available. RHY is working with the TGA to determine the final number of patients required to demonstrate ColoSTAT®'s performance. Positive results will underpin application for approval in Australia and may assist ColoSTAT®'s uptake in the US and EU.

Regulatory Processes

The key markets have structured regulatory pathways for approval of medical devices which include diagnostic tests. Commonly referred to as In vitro diagnostic devices (IVDs), the classification is generally based on risk. The regulatory requirements will reflect the health risk (either to the public or an individual) that may arise from an incorrect result. The level of risk is commensurate with the level of assessment and the need to demonstrate ongoing compliance with the standards. As a test with no predicate, ColoSTAT® is likely to undergo greater scrutiny.

Australian Regulatory Pathway

ColoSTAT® is likely to be classified as an IVD Class 3, a moderate public health risk or high personal risk. Under the TGA guidelines, as a test kit manufactured outside Australia, RHY will be required to have a copy of the manufacturer's evidence, with a declaration of Conformity to Australian standards to be submitted if required. It has commenced engagement with TGA. The results of Clinical Study 7 are expected to meet the clinical data as required by the TGA requirements.

EU Regulatory Pathway

The EU system is based on Conformité Européene" (CE) marking. The addition of the administrative mark, CE, indicates manufacturer's declaration of conformity with health, safety, and environmental protection standards for products sold within the European Economic Area (EEA). As a screening IVD to detect cancer, ColoSTAT® is likely to fall into Class 1 self-assessment where the manufacturer attests to the conformity of the product themselves.

RHY is expected to file for its CE Mark in late 2021 after confirmation of the next batch of test kits from Biotem. RHY may undertake a 'soft' product launch, with wider market adoption to follow after confirmation of positive results of Study 7.

US Market

The US offers two pathways, Laboratory-developed tests (LDT) and commercial tests. The majority of marketed clinical tests are 'commercial', manufactured and sold in volume as kits for pathology laboratories or other healthcare facilities. 'Laboratory' tests are sometimes called 'home-brewed' tests which are usually developed and used in one pathology centre. These two types of tests are governed by different regulatory bodies and carry different validation and approval processes.

Historically, Laboratory-developed tests (LDTs) were developed to meet a particular need when there was no commercial test available. They are developed within a single laboratory. The US Centers for Medicaid and Medicare Services, (CMS) have oversight of laboratory tests and they must be performed in a 'Clinical Laboratory Improvement Amendment (CLIA 88)' accredited medical laboratory. LDTs are not required to have FDA approval. The system can offer a faster route to market with earlier revenues and lower costs. However, it potentially limits market penetration.

Commercial tests are regulated by the FDA. A classification system of Class I, II and III reflects the increasing need of oversight from the FDA. Tests that have a high level of sophistication, significant differentiation from already approved tests or have a new use will be required to undergo more scrutiny and submission of supporting data and testing.

The FDA filing may require a '510 (K)' a premarket submission or the more rigorous PMA (Pre-Marketing Approval). A 510(K) must demonstrate that the device to be marketed is safe and effective and is substantially equivalent to a legally marketed device. PMA approval is based sufficient valid scientific evidence to assure that the device is safe and effective for its intended use. FDA approval must be granted prior to marketing the device. Exact Sciences which developed the faecal based DNA test, Cologuard, filed under PMA for approval.

RHY has announced it will undertake a dual process. It will utilise the LDTs' expedited path to market to establish the test on the market and receive early revenues. In tandem, it will seek approval under the FDA path. While it incurs a higher cost and longer time frame, FDA approval opens the total US market and greater sales.

CRC Market – current and potential

The toll of CRC coupled with the benefit of early intervention sees strong support from key medical and national health bodies for screening programs. Generally, recommendations for CRC include regular screening for people between the ages of 50 and 75 years, which accounts for ~33% of the population. There is emerging support to extend

cohort to include 45-49 year olds, as the incidence of CRC increases in this age group. While the recommendations across the different jurisdictions are similar, uptake varies significantly from country to country.

Current market + unscreened cohort = Total eligible market

Exhibit 5 – Participation Rate in RHY's Main Screening Regions

Market	Screened Population	Unscreened Population	Total Population	Participation Rate	Current Screening Market	Unrealised Market	Total Market
US	64.95m	29.46m	94.41m	68.8%	US$ 2,468m	US$ 1,119m	US$ 3,588m
EU	52.64m	49.0m	101.64m	51.7%	US$2,000m	US$1,862m	US$3,862m
Australia	2.78m	3.57m	6.35m	43.8%	US$106m	US$135m	US$241m
China	76.34m	331.66m	408m	18.71%	US$2,901m	US$12,603m	US$15,504m
Japan	15.84m	25.9m	41.74m	37.95%	US$602m	US$984m	US$1,586m
Overall	212.55m	439.59m	652.14m	32.6%	US$8,077m	US$16,703m	US$24,781m

Source: Participation rates – USPTF, EIHS, AIHW, International Journal of Environmental Research & Public Health, NCBI; Population – ABS, Europa, Statistics Bureau of Japan, Statista

MST market estimates are based on RHY's key targeted countries, Australia, US, EU, China and Japan. The target markets have been derived by accounting for each local CRC screening age range guidelines and participation rates. The unscreened markets, those who do not participate in current screening programs, have also been included. We believe they represent a potential market for ColoSTAT®. Value has been assigned by applying MST estimated price of ColoSTAT® of US$38 (A$50). In the EU, while our review of the current screening practices includes all countries, we include only the 'Big 5' in the valuation. We believe the UK, France, Italy, Spain and Germany will be the key drivers over the short- medium term.

Our analysis shows that ColoSTAT®'s key targeted global market represents a total potential US$ $24.8bn (screened and unscreened) based on an eligible cohort of 652m people and a price of US$38 per ColoSTAT® test. Analysis of the current screening rates rate shows a ~33% participation. The three initial targets of US, EU and Australia represent a potential market of US$7.8bn, of which the current utilisation represents ~US$4.6b.

ColoSTAT®'s likely performance

ColoSTAT®'s market performance will reflect its ability to compete with the SOC tests and to persuade those who currently don't participate.

Exhibit 6 – Comparison between Main CRC Screening Methods

	ColoSTAT®	FOBT/FIT	Colonoscopy
Efficacy*	√√	√	√√√
Cost	√	√	√√√
Patient Experience	√√√	√√	√

Source: MST Assumptions

Our review of ColoSTAT® examines its competitive position from the perspectives of

- Efficacy - sensitivity and specificity
- Cost – payers will want to see a value proposition
- Patient experience –RHY's blood test versus faecal tests, colonoscopies and radiological tests

Faecal tests

Most government funded public programs are based on the lower cost faecal tests, FIT and FOBT. In our view, ColoSTAT® presents strongly as a potential alternative offering higher efficacy, greater patient acceptability and a comparative cost.

Efficacy

From an efficacy viewpoint two measures are key, sensitivity and specificity.

Sensitivity and Specificity - assessment of test

The two parameters used to assess the performance of the test are sensitivity - the ability to detect the presence of the disease - and specificity - the ability to only detect the target disease.

Sensitivity measures the ability to **capture all those who have the disease**– It is the proportion of people WITH Disease X that have a POSITIVE blood test. A test that is 100% sensitive means all diseased individuals are correctly identified as targeted disease i.e., there are no false negatives.

Specificity test is used to **exclude those who don't have the disease**. Specificity is the proportion of people WITHOUT Disease X that have a NEGATIVE blood test. A test that is 100% specific means all healthy individuals are correctly identified as healthy, i.e., there are no false positives.

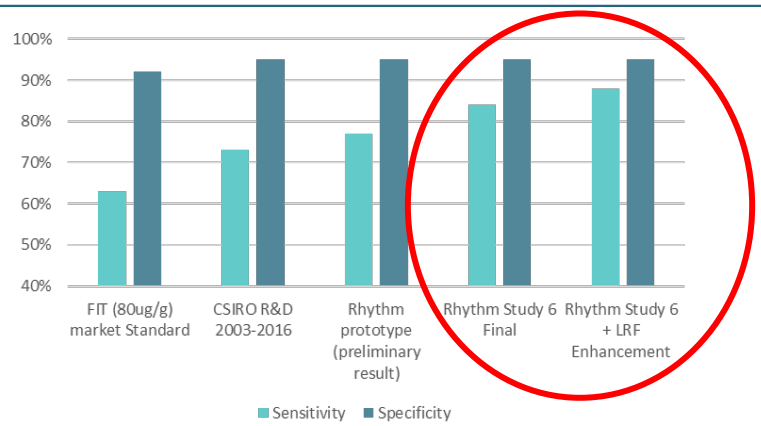
Diagnostic tests are rarely 100% accurate. Although a screening test is ideally both highly sensitive and highly specific, a balance is often required as most tests cannot do both to their highest levels. The balance is an arbitrary cut-off point, a trade-off of one characteristic against the other. To increase sensitivity to include all true positives, there will be a rise in false positives, decreasing the specificity level. Similarly, higher specificity sacrifices sensitivity, losing some of those with the condition.

As a test to detect CRC, sensitivity may outweigh specificity as the priority. RHY has options to further optimise the test as a screening test by decreasing specificity.

	Has Disease	Doesn't Have Disease
Sensitivity Blood Test Positive +	True Positive	False Positive
Specificity Blood Test Negative -	False Negative	True Negative

As discussed, Clinical Study 6 of 300 samples of cancerous and healthy specimens showed that ColoStat had a clear advantage over FIT, outperforming in both sensitivity and specificity. ColoSTAT®'s 84% sensitivity and 95% specificity compare to FIT's sensitivity of 63% and specificity of 92%. Further testing has included Lifestyle Related Factors (LRF) that have been linked to the risk of CRC. They included diet, weight, exercise, smoking and Type 2 Diabetes. Inclusion of the LRF analysis delivered further improvement taking sensitivity to 88% with specificity remaining at 95%. RHY expects further improvement as the iterative processes result in on-going machine learning and refinement of the underlying algorithms.

Exhibit 7 – ColoSTAT® test-kit performance vs faecal immunochemical (FIT), CSIRO tests and RHY prototype



	FIT (80ug/g) Market Standard	CSIRO R&D 2003-2016	Rhythm Prototype (preliminary result)	Rhythm Study 6 Final	Rhythm Study 6 + LRF Enhancement
Sensitivity	63%	73%	77%	84%	88%
Specificity	92%	95%	95%	95%	95%

Source: Rhythm Biosciences

In our view, if Clinical Study 7 confirms ColoSTAT®'s superiority over FIT, it will see ready take up in FIT/FOBT markets from an efficacy view.

Cost

From a payer's perspective, ColoSTAT® is likely to be attractive. The use of colonoscopy is restricted as a screening tool in many programs. Its higher cost, even when apportioned over longer testing intervals, presents a significant barrier, except in the US. The faecal based tests are generally the SOC for government funded programs. Data to date supports ColoSTAT®'s higher efficacy while still competitive with FIT from a price perspective. ColoSTAT®'s estimated price of US$38(A$50) price compares to FOBT/FIT tests at ~US$15-32. Under the government funded programs, the tests are usually not patient requested. They are sent to the candidates at home by automatic programming. Poor utilisation rates see most kits unused and wasted. As a doctor administered test, ColoSTAT® will only be undertaken on demand.

Participant perspective

From the participant perspective, we believe a blood test will be more acceptable than the faecal tests. As discussed, resistance to current FOBT/FIT programs is attributed to the need to handle faecal matter and low sensitivity, the test's poor ability to detect CRC. The process is quite involved and over some days. We include a sample instructions list to demonstrate the room for error with possible test invalidation and the propensity for the candidate to allocate it the 'too hard basket'.

Faecal Test instructions generally include

- For a complete investigation, this test ideally requires three separate faeces specimens collected on three separate days.
- If your doctor requests only one specimen, this can also be performed.
- All specimens must be returned within five days of the first collection.
- If you are taking iron tablets, you may continue this therapy before and during the test period.
- Avoid alcohol and the following medications (Indomethacin, Reserpine, Phenylbutazone and Corticosteroids) as these may cause gastrointestinal irritation and subsequent bleeding in some patients. Consult your doctor before ceasing any medication.
- Seven days prior to taking the sample, avoid Aspirin or anti- inflammatory drugs.
- Two days prior to taking the sample, stop using rectal medicines and tonics.

Do not collect a faeces sample if:

- You are menstruating
- You have bleeding haemorrhoids
- You are constipated

ColoSTAT® testing does require a visit to the doctor, potentially adding inconvenience and cost. However, we believe there are a number of drivers that should see high utilisation. Medical visits are more frequent in the aged population allowing the test to be part of another visit. 'Wellness' programs have become a key focus for many general practitioners/primary care physicians. The programs commonly include cholesterol, prostate cancer and glucose blood tests. The addition of ColoSTAT® is unlikely to add significantly to the burden.

In contrast, the current SOC faecal tests generally rely on the participant to be responsible for the testing process. We believe transition to the physician' s surgery is likely to see higher uptake with the doctor driving the process. Ongoing doctor visits will provide opportunity to give reminders and follow up. MST forecasts assume there will be significant uptake in the markets with a formal FIT/FOBT program with some conversion of those currently not being tested.

Colonoscopy

From an efficacy view, colonoscopy is likely to continue as the gold standard with 94.7 ± 4.6%, sensitivity and 99.8 ± 0.2%, specificity.[3] For many participants, colonoscopy carries greater appeal to faecal tests. However, at an average US cost US$2,750[4], the additional cost and need for specialised clinicians and medical facilities present barriers that restrict its use in many screening programs. The US is the only major market that sees significant use with some 61% of the eligible cohort undertaking colonoscopy. We believe, ColoSTAT® is unlikely to take significant share from colonoscopy market. Colonoscopies are commonly recommended to be undertaken every 10 years. Many are taken more frequently. There may be a role for ColoSTAT® to be offered in the intervening years as a 'check-up' and defer the colonoscopies to 10-year intervals.

Program metrics

We also consider structural elements of the markets, such as the presence formal screening programs and/ or whether it is patient or other funding source.

- Formalised screening programs - better utilisation versus self-initiated participation
- External/ participant funded – programs funded by a third party attract higher utilisation.

The lack of a formal program and/or self-funding are generally associated with poorer uptake. The ability of the GP to initiate testing and the appeal of an additional blood test may see increased utilisation in these groups. However, we do not factor in a material change in these market sectors.

Opportunity by market

US CRC Screening Opportunity

Under the current guidelines of screening for 45-75 year olds, MST estimates the potential US CRC screening market to represent US$3.6bn based on 95m eligible cohort and at US$38(A$50) per ColoSTAT® test. As part of its mandate, the US Preventive Services Task Force (USPSTF) oversees screening programs. Its recommendation for routine CRC screening includes six tests:

1) FOBT
2) FIT
3) multitarget stool DNA (FIT-DNA)
4) computed tomographic colonogram
5) sigmoidoscopy and FIT
6) colonoscopy.

[3] Sensitivity and Specificity of Colorectal Cancer Mass Screening Methods: A Systematic Review of the Literature January 2011 Iranian Journal of Cancer Prevention. Zahra Allemah

[4] Cost of a colonoscopy in the U.S.: what you need to know (newchoicehealth.com)

The Centre for Disease Control and Prevention (CDC) 2018 Behavioural Risk Factor Surveillance System survey reported that 68.8% of eligible cohort was current with the screening guidelines of USPSTF.

Exhibit 8 – CRC screening - US Test and Market Share

Test	Colonoscopy	Colonography	FOBT	DNA
Market Share	61%	1%	4.2%	2.7%

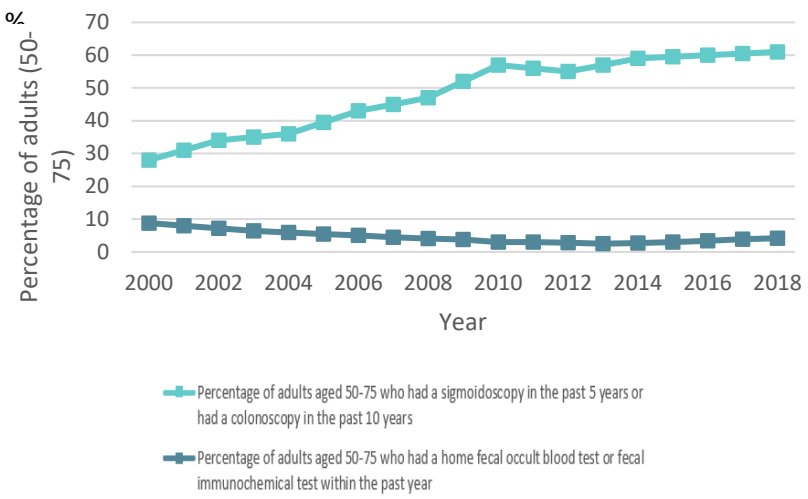
Source: National Cancer Institute Progress Report

Current Practices

Generally, US health authorities recommend CRC screening from 50-74 years excepting the USPSTF and the American Cancer Society which recently extended their recommendations to include 45 –49-year olds. The change potentially adds ~21m[5] to the eligible cohort. Colonoscopies are commonly performed every 10 years, sigmoidoscopies every 5 years while FOBT/FIT are recommended yearly.

US market shows that payers will support a premium for efficacy.

Exhibit 9 – Preference of colonoscopy/sigmoidoscopy over FOBT/FIT



Source: Centre for Disease Control and Prevention

The cost of a colonoscopy in the US ranges US$1,250 – $4,800+ with national average of US$2,750[6]. On an annualised basis, assuming a 10-year testing interval, the average cost is US$275 versus ~US$20 for FOBT. Despite the higher cost, there is a clear preference for colonoscopy over the other tests used.

MST attributes the wide funding of colonoscopies and subsequent increase in screening rates from 2001 to recognition of higher efficacy of colonoscopy in a disease that carries significant treatment costs and poor survival rates in late-stage diagnosis. The expansion was driven by payer funding of colonoscopy by private health funds and importantly in 2001, Medicare. Medicare provides health care cover for all US citizens over 65 years old. The US experience implies FIT/FOBT's poorer efficacy and need to deal with faecal matter are serious hurdles in the CRC screening market.

[5] Source: Statista
[6] Cost of a colonoscopy in the U.S.: what you need to know (newchoicehealth.com)

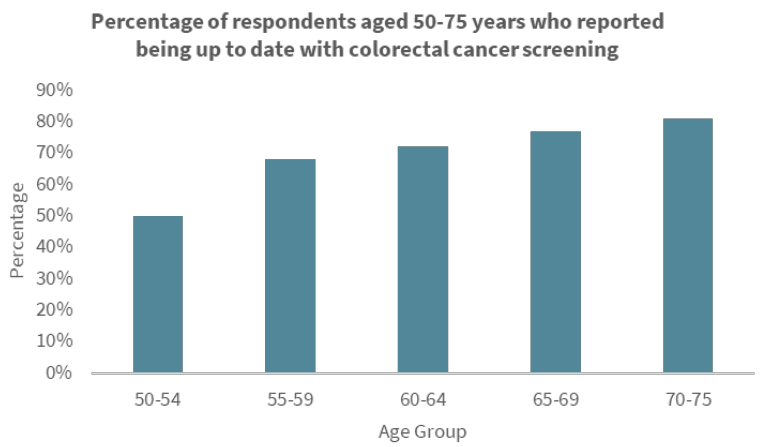
The funding experience has implications for ColoSTAT®. ColoSTAT® at an expected US$38 per test will carry a modest price premium over FOBT/FIT(US$15-32). Confirmation of higher efficacy in comparison to FOBT/FIT is likely to

attract health payers support despite the premium. MST believes that the combination of funding and ColoSTAT®'s patient focused features will see it gain significant share of the US FOBT/FIT market. However, in our view, there will be limited penetration of colonoscopy sector.

The introduction of colonoscopies grew the overall market

The shift to colonoscopy was not simply product substitution. Among adults aged 50 years and older, colonoscopy use tripled from 20% in 2000 to 61% in 2018. The decline in FIT and FOBT was not commensurate. Penetration of the unrealised market rose significantly. The preference of colonoscopy has seen it grow the overall market and become the clear test of choice.

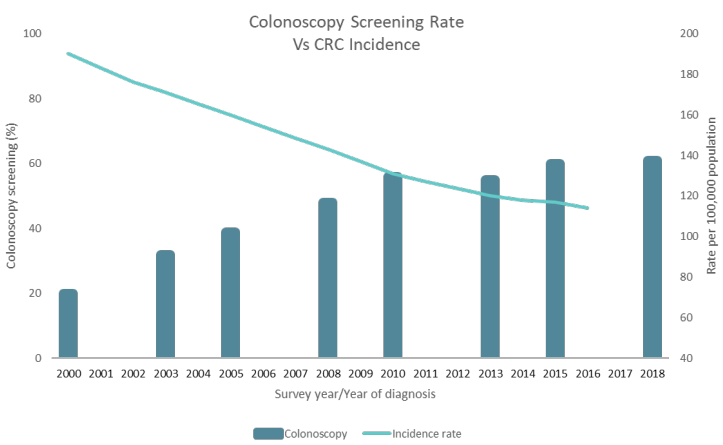
Exhibit 10 – Percentage of Respondents up to date with colorectal cancer screening



Source: Centre for Disease Control and Prevention

As discussed, Medicare is generally available to all US residents over the age of 65 and includes colonoscopy screening. The 32% 'unrealised' cohort is likely to include a number of 50-64 year olds who account for ~64m. These age brackets are likely to include employees. Their employer health schemes may not cover the higher priced colonoscopy CRC screening. The lower cost of ColoSTAT® combined with its more patient friendly characteristics compared to FIT/FOBT may find support in these groups.

Exhibit 11 – Colonoscopy Screening Rate and CRC Incidence Rate



Source: National Cancer Control Indicators

Efficacy will engender ongoing support

The increase in colonoscopy testing tracks the fall in rate of CRC. Accelerated decline of CRC since 2000 is thought to reflect the rapid dissemination of colonoscopy screening. MST believes the 'proof' of an efficacious CRC screening program in reducing the incidence is likely to reinforce ongoing health payers' support, particularly in reaching those still not being screened.

Home screening program versus doctor test

In contrast to the current home-based CRC screening programs offered by a number of governments, the ColoSTAT® test requires a visit to the doctor, adding cost and time. However, in the ageing population, medical visits tend to be more frequent and are increasing in a society conscious of health risks and clinicians promoting regular check-ups. As discussed, ColoSTAT®, can be added to other blood tests being ordered. Review of physician visits show there is likely to be a number of opportunities to include ColoSTAT® with other screening blood tests, minimising injection load and additional visits. MST believes ColoSTAT® will be well supported, with the doctor to encourage the screening process.

Exhibit 12 – Percentage of doctor visits

Percentage of doctor visit for any reason in past 12 months for adults, U.S 2019				
Year	18-34	35-49	50-64	65 and over
2019	77.1	81.2	88.4	95.8
Percentage of doctor visit for wellness checks in past 12 months for adults, U.S. 2019				
Year	18-34	35-49	50-64	65 and over
2019	69.1	73.9	83.6	92.8

Source: Centres for Disease Control and Prevention

European CRC Screening Opportunity

In 2003, the EU Council of Health Ministers recommended that all Member States implement population-wide screening for colorectal cancer for all citizens between 50 and 74 years old using the faecal occult blood test (FOBT and FIT) or other newer tests if they have demonstrated evidence of being effective. The implementation continues, varying cross the member states. The 2016 European Health Interview Survey (EHIS) provided an overview of the screening programs.

Exhibit 13 – European CRC Screening Data Review

EU Countries	Average Age Span	FOBT/FIT Test offered	Faecal with Colonoscopy offered	Screening Interval	Population based	Screening Test Free	FOBT mailed
25	50-74 years old	100%	20%	2-year FIT/ FOBT, 5- 10 year Colonoscopy	100%	100%	68%

Source: European Commission

The key conclusions include;

1. The screening programs are generally publicly funded with 50-74 year olds covered.
2. All programs provide the testing for free.

3. All programs offer FIT /FOBT, usually on a biennial basis. 20% also offer colonoscopy at intervals spanning every 5 – 10 years.
4. Most programs are population based and part of a national screening policy.
5. ~70% of the FOBT/FIT testing kits are mailed out.

Exhibit 14 – Type of CRC Screening Offering

Use of Faecal tests within 2 years of colonoscopy within 10 years (%)	Colonoscopy and faecal test offered in programs	Faecal Test only in organised programs	Faecal test in partial regional program	Faecal Test with no program
	Utilisation Rate Range: 23% - 71%	**Utilisation Rate Range: 29% - 66%**	**Utilisation Rate Range: 24% - 46%**	**Utilisation Rate Range: 5% - 31%**
	Germany (50-74) – 71%	UK (60-74) -66%	Denmark (50-74) -46%	Norway (50-74) – 31%
	Austria (50-74) – 68%	Slovenia (50-74) – 64%	Ireland (60-74) – 43%	Latvia (50-74) – 28%
	Luxembourg (50-74) – 55%	France (50-74) – 60%	Italy (50-74) – 42%	Ireland (50-59)– 24%
	Portugal (50-74) – 54%	Croatia (50-74) – 29%	Finland (60-74) – 35%	UK (50-59) – 23%
	Czech Republic (50-74) – 53%		Belgium (50-74) – 32%	Hungary (50-74) -22%
	Iceland (50-74) – 42%		Malta (55-69) – 31%	Finland (50-59) – 21%
	<30% Slovakia, Greece		<30% Sweden, Lithuania, Spain, Holland (55-74)	<20% Poland, Sweden, Malta, Cyprus, Estonia, Holland (50-54), Bulgaria, Romania

Source: PMC[7] Cancers (Basel). 2020 Jun; 12(6): 1409.Rafael Cardoso et al Utilisation of Colorectal Cancer Screening Tests in European Countries by Type of Screening Offer: Results from the European Health Interview Survey

Overall, jurisdictions with formal programs see higher uptake. Germany posts a 71% participation rate in its program that offers periodic colonoscopy and FIT. Norway posts only 31% as the highest participant in the 'no' program group. The presence of screening programs shows strong government support and funding and participant familiarity with the need to undertake CRC screening. The path to establishing a market in these countries is likely to be expedited.

Exhibit 15 – Colonoscopy Screening Rate and CRC Incidence Rate by Age Group

	Programs	No Program		
Age	**60-74 yrs**	**55-74 yrs**	**50-59 yrs**	**50-54yrs**
UK	66%	23%		
Ireland	43%	24%		
Netherlands		24%		16%

Source: European Health Interview Survey

In the UK, Ireland and Netherlands, the authorities offer CRC testing as a formal program for an older aged group and ad hoc for a younger cohort. The younger cohorts showed significantly lower testing rates. It is likely to reflect the

[7] Cardoso, R. et al. Utilisation of Colorectal Cancer Screening Tests in European Countries by Type of Screening Offer: Results from the European Health Interview Survey. Cancers 2020, 12, 1409. https://doi.org/10.3390/cancers12061409

lack of a program to remind the candidates and a lower general health concern in this group. The role of the medical practitioner in the ColoSTAT® model is likely to help compliance and increase testing rates.[8]

MST initial EU market

As discussed below, review of the current market dynamics gives insight to the likely parameters for ColoSTAT®.

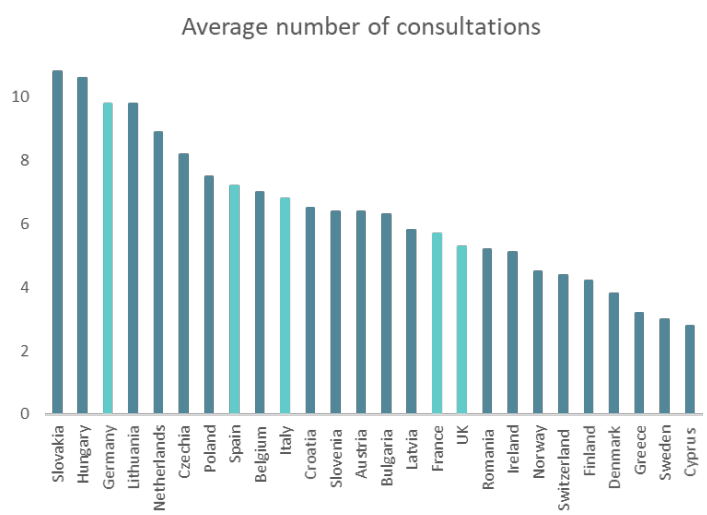
Exhibit 16 – CRC Screening Rate in Main Regions

Country	Screening Test Type	Nationwide / Regional	Rollout	Target age (years)	Screening Interval (years)	Participation Rate	Total Value (US)
UK	gFOBT	Nationwide	Complete	60 - 74	2	46%	$748m
	FS	Regional	Ongoing	55-59	2		
France	gFOBT	Regional	Complete	50-74	2	60%	$749m
	FIT	Regional	Complete	50-74	2		
Spain	FIT	Nationwide	Ongoing	50-74	2	25%	$544m
Italy	FIT	Nationwide	Ongoing	50-69	2	42%	$766m
	FS + FIT	Regional	Complete	50-69	2		
Germany	FIT	Nationwide	Planning	50-74	1 (50-54); 2 (55+)	71%	$1,055m
	TC	Nationwide	Planning	50-74	10		

Source: Europe Commission

The MST valuation model is based on the current populations in the five major countries, UK, Germany, France, Italy and Spain. Together these countries represent a notional US$3.8bn market, based on current screening criteria. Those currently undergoing CRC screening represent a U$2bn market. All countries have subsidised health care systems and offer CRC screening. Faecal tests are used predominantly. Age ranges span 50-74 years. If the advantages of ColoSTAT® over FIT/FOBT are confirmed, it promises to see penetration of the existing market. The high rate of the unscreened cohort suggests the potential for a significant increase in uptake on a two-yearly basis. Rhythm may undertake studies to demonstrate cost saving benefits from annual testing.

Exhibit 17 – Average Number of Doctor Consultations in Europe



Source: Eurostat

[8] T R Levin et al , Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population Gastroenterology2018 Nov;155(5):1383-1391. h**ttps**
https://ec.europa.eu/health/sites/default/files/major_chronic_diseases/docs/2017_cancerscreening_2ndreportimplementation_en.pd

Review of annual physician visits is also supportive. The data are based on total population, so it is likely that the visits are higher in the elderly.

Australian CRC Screening Opportunity

In Australia, the CRC screening program is based on the FIT test and includes Australians aged 50-74 years biennially. There are 6.35m 50-74year old Australians, presenting an opportunity of 3.18m tests pa. At a cost of US$38(A$50), this represents a US$241m (A$318m) annual market value. In 2018-19, the Australian Institute of Health and Welfare reported that 43.8% of the population eligible for the participated in the program, implying some 2.78m of the eligible cohort availed themselves of the test. This represents US$106m, leaving a potential additional market of US$135m.

Exhibit 18 – Australian Colorectal Screening Market

Market	Population (50-74 years old)	Participation Rate	Screened Population	Unrealised population	Total market	Current Screening Market	Unrealised Market
Australia	6.35m	43.8%	2.78m	3.57m	US$241m	US$106m	US$135m

Source: National Cancer Control Indicators

Japanese Market

In Japan, the incidence of CRC has been increasing where it is the fourth most common cancer among men and the second most common cancer among women. In 1992, a CRC screening program using FIT was incorporated into public health policy. CRC screening targets individuals 40 years and older with a screening interval of one year. Participation rate in the CRC program has been 41.4% for men and 34.5% in women, totalling ~16m people.

Chinese market

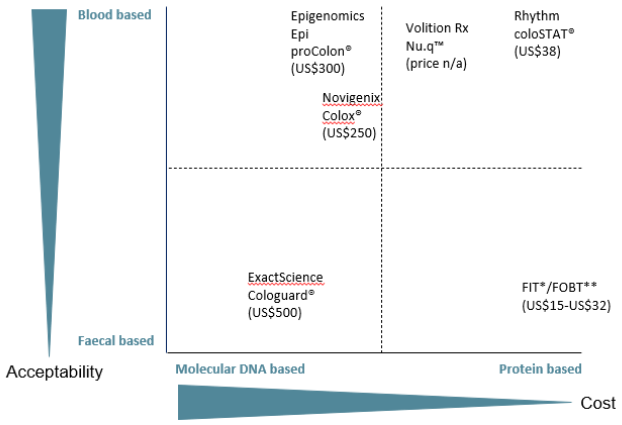
The China Anti-Cancer Association recommends regular colorectal cancer screening for the urban population, aged between 40 and 74. Currently, the participation rate for China is at 18.9%. The low penetration rate in China is primarily due to low awareness, lack of effective screening methods, low compliance and insufficient capacity of colonoscopy. The penetration rate is forecast to reach 39.8% in 2030[9] through the Government's *Healthy China Action-Cancer Prevention and Control Implementation Plan (2019-2022.* It includes a two-step screening strategy comprising FIT and a quantitative high-risk factor questionnaire as the primary screening test, and a full colonoscopy for follow-up screening.

Competitive landscape

Cancer diagnostics have seen significant expansion as R&D has created a greater understanding of the diseases coupled with the development of new investigative methods. The CRC presents an attractive market, and it has been a beneficiary of extensive R&D with a number of new tests developed or in development. While the field looks busy, in MST's view the only current 'true' competitors for ColoSTAT® are the existing faecal tests. The cost of the newer DNA technologies are likely to exclude their use from the general mass screening markets.

[9] Frost and Sullivan; Colorectal Cancer Screening Industry in China. 2019

Exhibit 19 – Novel CRC diagnostic tests in development or on market



Source: Rhythm Biosciences

There is a strong R&D focus on DNA based tests. In MST's view, the higher cost will see their role more as diagnostic test for higher risk candidates as a 'personalised' screening program. They may also have a role in confirmation of FIT/FOBT results or potentially to monitor for recurrence.

Exhibit 20 – ColoSTAT®'s Competitive Landscape

Product	Company	Test type	Test biomarkers	Sensitivity	Specificity	Price (USD)
ColoSTAT®	Rhythm Biosciences	Blood	Protein	88%	95%	$38*
FOBT[10]	Various	Faecal	Protein	50-68%	90%	$15-$32
FIT[11]	Various	Faecal	Protein	69%	94%	$20
Cologuard®[12]	Exact Science	Faecal	Molecular/DNA	92%	87%	$500
Colox®[13]	Novigenix	Blood immune	Molecular/DNA	78%	92%	$250
Epi proColon® [14]	Epigenomics	Blood	Molecular/DNA	73%	80%	$300
Nu.Q™[15]	Volition	Blood	Molecular/DNA	81%	78%	N/A

Source: National Cancer Control Indicators, *MST estimate

The tests' specificity and sensitivity performance is given as a guide as the results show variation over the different tests. Closer examination of the different CRC tests shows different intended roles. Pricing is likely to limit a number from screening roles.

1. Epigenomics' Epi proColon - Epi proColon is the first and to date the only FDA approved blood test for colon cancer screening. It is a genetic based test, aiming to detect the gene mutation changes that induce CRC.

[10] FOBT - U.S. Preventive Services Task Force Screening for Colorectal Cancer: Recommendation Statement American Family Physician Apr 15 2010
[11] Stonestreet, J. et al. FIT-Systematic review and meta-analysis: diagnostic accuracy of faecal immunochemical testing for haemoglobin (FIT) in detecting colorectal cancer for both symptomatic and screening population. Acta Gastroenterol Belg. Apr-Jun 2019; 82(2):291-299.
[12] Oliver, E. 4 gastroenterologists share their thoughts on Exxact sciences Cologuard. https://www.beckersasc.com/gastroenterology-and-endoscopy/4-gastroenterologists-share-their-thoughts-on-exact-sciences-cologuard-2.html
[13]Ciarloni, L. et al. Development and Clinical Validation for a Blood Test Based on 29-Gene Expression for Early Detection of Colorectal Cancer. American Association for Cancer Research. Sep 2016; 10.1158/1078-0432.CCR-15-2057.
[14] Pickhardt, P. Emerging stool-based and blood-based non-invasive DNA tests for colorectal cancer screening: The importance of cancer prevention in addition to cancer detection Abdom Radiol (NY). 2016 Aug; 41(8): 1441–1444.
[15] Volition www.Conditions | Volition RX Conditions

2. Methylation of the gene is common cancer genetic change. Its Methylation Core Technology amplifies the target biomarker to enable easier detection. It identifies CRC in all cancer stages and throughout the colon and rectum. Its studies demonstrated 73% sensitivity and 80% efficacy. A separate study of samples from 290 people compared the accuracy of Epi proColon to FIT. Epi proColon was found to be statistically non-inferior to FIT (72% vs 68%) but inferior with respect to specificity (81% vs 97%). The cost at US$300 is prohibitive as a screening test.

3. Volition Nu.Q
   Nu.Q is also DNA or gene based technology aiming to detect nucleosomes in the blood. It plans to include off-patent low cost cancer markers such as carcinoembryonic antigen (CEA) to improve accuracy. As an ELISA test also it offers wide applicability across the pathology testing facilities. Results of four Nu.Q assays, have shown sensitivity of ranging 81% sensitivity and 78% specificity in a cohort of 4,800 CRC symptomatic patients. It has also shown 74% sensitivity at 90% specificity, in 58 asymptomatic patients, detecting 75% of early stage I cancers. There is no indication of price.

4. Novigenix Colox®
   Colox® is a molecular test that measures the immune system response to colorectal lesions, aiming to detect earlier stage CRC. In both preclinical and clinical stage CRC, Peripheral Blood Mononuclear Cells (PBMC) modify their gene expression profile. Colox® aims to measure the modification of the PBMCs expression profile using an algorithm to give a positive or negative result. In its 782-subject study, Colox®showed sensitivity of 78% CRC patients with specificity of 92%.

5. Exact Sciences Cologuard®
   Cologuard®is the only stool-DNA screening test for detecting colon cancer that is approved by the Food and Drug Administration (FDA). It detects abnormal DNA and traces of blood in the stool that can indicate precancerous polyps and colon cancer. In a trial of 9,989 asymptomatic subjects at average risk for colorectal cancer, the multitarget stool DNA testing detected significantly more cancers than FIT but had more false positive results.

Exhibit 21 – IP Patents Filed

Region	Patent Status
United States	√
Australia	√
China (x2)	√
Japan	√
United Kingdom	√
Europe*	√
Brazil	Pending
India	Pending

*Patents in Europes are granted in Austria, Belgium, Denmark, Finland, France, Germany, Italy, Luxembourg, Netherlands, Norway, Spain, Sweden, Switzerland & Liechenstein

Source: Rhythm Biosciences

RHY's current patents offer protection to 2031 in the major markets including all its current targeted countries, with ongoing filing to extend market protection.

Management and Board

Otto Buttula; Chairman

Otto Buttula has had extensive experience in investment research, funds management and has held directorships in a number of public companies. Otto's executive experience includes co-founder and CEO of IWL Limited, a company taken over by Commonwealth Bank of Australia for $373 million in 2007. Otto also founded and was Managing Director of Investors Mutual and was a director of Lonsdale Securities prior to that. Otto has also held non-executive roles on Imugene Limited (ASX: IMU) and Investorfirst Limited and led the acquisition of HUB24 Limited (ASX: HUB).

Glenn Gilbert; CEO

Glenn Gilbert has had over 17 years of experience in the healthcare sector across domestic and international markets, with expertise in strategy, manufacturing and sales. Prior to Rhythm, Glenn held leadership roles at CSL's biotherapeutics arm (ASX: CSL) known as Seqirus and Medical Development International (ASX: MVP) where he gained extensive experience across Europe, Asia and America. His senior roles have included both medical devices and pharmaceuticals with responsibility across product development, commercialisation, sales and marketing in both domestic and international markets. Glenn holds a Master of Business Administration (MBA), Graduate Certificate in Corporate Management and a Bachelor of Science degree.

Trevor Lockett; Technical Executive Director

Dr Lockett brings over 30 years of research experience, predominantly at the CSIRO, leading multidisciplinary research efforts in in prostate cancer gene therapy, colorectal cancer prevention and the promotion of gastrointestinal health. Trevor received his PhD in biochemistry from the University of Adelaide and postdoctoral experience at Rockefeller University in New York. Trevor is an inventor of seven commercially licensed patent families. Trevor also brings strong leadership experience from serving on the leadership executive team of business units within CSIRO.

Lou Panaccio; Non-Executive Director

Lou Panaccio is a chartered accountant with extensive management experience in business and healthcare services. Lou currently serves on the boards of Sonic Healthcare Limited (ASX: SHL) and Avita Medical Limited (ASX: AVH). Lou is also on the board of NeuralDX Limited and Unison Housing Limited and was previously the CEO of Melbourne Pathology and Monash IVF.

David White; Non-Executive Director

David is the Vice President of Business Development, North America for Bluechiip Limited. David brings over 18 years of experience covering strategic and tactical marketing, medical device sales and the commercialisation of diagnostic products where he was the Group Marketing Manager of Advanced Staining for Leica Biosystems followed by molecular sales for GenMark DX.

Eduardo Vom; Non-Executive Director

Eduardo is a Co-Founder and Executive Director of Planet Innovation. Eduardo has over 20 years' experience in technology development and commercialisation in the biotech industry, having held leadership roles at cancer diagnostics manufacturer Vision BioSystems and molecular diagnostics company Genetic Technologies.

Top 20 Shareholders FY21

#	Shareholder	Shares ('000)	Issued Capital (%)
1	Webinvest Pty Ltd	16,666,667	8.27
2	Newfound Investments Pty Ltd	10,733,333	5.33
3	Ferndale Securities Pty Ltd	10,400,000	5.16
4	Loumea Investments Pty Ltd	9,915,000	4.92
5	Northern Star Nominees Pty Ltd	7,200,000	3.57
6	Mrs Sarah Cameron	6,751,781	3.35
7	Rojo Nero Capital Pty Ltd	4,166,668	2.07
8	Giokir Pty Ltd	3,400,000	1.69
9	Jawaf Enterprises Pty Ltd	3,150,000	1.56
10	Mr Hsien Michael Soo	3,000,000	1.49
11	Mr Daniel Eddington & Mrs Julie Eddington	2,560,000	1.27
12	Commonwealth Scientific and Industrial Research Organisation	2,500,000	1.24
13	Ms Natalie Louise Patterson	2,416,666	1.20
14	Dr Gavin James Shepherd & Mrs Catherin Shepherd	2,150,000	1.07
15	E & W Nominee Pty Ltd	2,144,668	1.06
16	MOWBRICK PTE Limited	2,130,000	1.06
17	Garnsworthy Pension Fund Pty Ltd	2,050,000	1.02
18	Ardroy Securities Pty Ltd	1,760,000	0.87
19	DC & PC Holdings Pty Ltd	1,750,000	0.87
20	HSBC Custody Nominees (Australia) Limited	1,672,277	0.83

Valuation, Risks and Sensitivities

Based on a risk adjusted DCF, MST attributes RHY a value of $420.6m, $2.08 ps. The valuation is supported by peer comparison to Volpara Health Technologies (VHT.AX) and BARD1 Life Sciences (BD1.AX). Both companies are diagnostic technology based and targeting global markets. The companies vary in terms of stage of development and targeted markets. In MST view, given its stage of development, initial target markets and

The key risks to the MST DCF valuation include

i) Regulatory Approval
ii) Commercial performance

Regulatory Approval

Industry data for drug development shows a new drug in Phase 3 trial carries an average probability of ~60% of approval. MST's DCF valuation of ColoSTAT® reflects a probability of approval of 75%. The higher value reflects:

i) In-Vitro-Diagnostics (IVDs) are usually assigned a higher rate of approval as safety is not a concern, with only efficacy to be confirmed.
ii) In terms of efficacy, ColoSTAT® is in its final stage of clinical trials. Clinical data to date have consistently shown superior performance to the SOC FIT, giving confidence of a positive outcome.

Clinical Study 7 is the first 'real-world' trial of ColoSTAT®. The trial data may not be supportive, resulting in the need for further trials and potentially additional funding. Such delay is likely to impact the forecast market entries dates. The trials may fail leading to product abandonment.

Commercial performance

In terms of market size, MST has determined the nominated target population of the US, EU and Australia, by recommended screening criteria. The estimates include both those already undertaking CRC screening and those who do not. The data to date support a superior performance to FIT. As noted, we believe ColoSTAT® will be preferred to the faecal tests. We have assumed its uptake will grow to 80% in the faecal testing groups and up to 25% in those who currently don't participate in faecal testing programs. We have assumed only minimal in the colonoscopy CRC cohorts in a role to support testing in the periods in between colonoscopies.

Our assumptions are based on a price of A$50. Reimbursement is yet to be negotiated. We note that pricing is likely to vary in the different markets. RHY has also nominated New Zealand, China and broader Asian markets. Plans for these markets are yet to be disclosed. They present upside to the valuation.

In terms of timing, Clinical study 7 is expected to reach full enrolment by end CY21. Positive results are expected to support market entry in Australia and a 'soft' product launch is the EU. It plans a dual regulatory approach in the US. The data may provide support of early marketing activities. First revenues are forecast for FY23.

To realise its full market access, our forecasts assume RHY will negotiate acceptance into the current national/regional funded programs. Generally, the products in national program demand pricing discounts so may fall below the A$50 assumption. There is also timing risk. The MST valuation is based on annual increments in market uptake to maturity. There may be timed entry points based on existing contracts.

We have assumed RHY will partner with a commercial entity/ies. Royalty streams are commonly range 5%-15%. MST model assumes licensing agreement will be based on a 12% royalty stream for the Australian, US and EU markets. Royalties of 2% of all gross sales are payable to CSIRO under the agreements. The valuation is based on a net 10% to RHY. The timing and nature of any agreements are yet to be determined. They may vary region to region.
RHY may not be able to reach a satisfactory agreement or may choose market ColoSTAT® directly or adopt a model that a combination of both approaches presenting differences in timing and revenue forecasts.
We also believe that RHY is at high risk of acquisition.

Intellectual Property

RHY has patent coverage granted in the key targeted markets until 2031. Our forecast assumes generic versions of ColoSTAT® will enter the markets on expiry, taking market share and reducing pricing.

Financial

MST forecasts assume further funding will be required given its cash of $6m at 31.03.21 and forecast expenditure of ~$6m over FY22. RHY may enter a licensing agreement or may choose to raise funding from a capital raising. The valuation assumes it will raise need $5m during FY22. There is risk that it will not be able to source the funds to complete the planned program.

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