Market entries in sight

As the development program for Rhythm Biosciences (RHY)'s bowel or colorectal cancer (CRC) diagnostic screening test, ColoSTAT®, nears its close, investor focus is turning to the market opportunity. RHY is expecting to receive approval to market ColoSTAT® in the EU in Q4CY21. The results of its Clinical Study 7, which is designed to support Australian approval, are expected over H1CY22. Positive results will also facilitate discussions with potential laboratory partners as RHY seeks to launch ColoSTAT® in the US and to support licensing and marketing activities in the EU and other markets.

More effective, participant-friendly test

Bowel cancer carries a high burden if not diagnosed early. However, the current Standard of Care (SOC) screening test, the Faecal Immunochemical Test (FIT), sees global participation rates of only ~32%.[1] Contributing factors include the need to handle faecal samples, poor test efficacy and cultural reasons.

RHY's studies have indicated ColoSTAT® may offer a 33%[2] higher rate of detection than FIT. As a blood test, ColoSTAT® is likely to be more 'participant friendly', opening the opportunity to increase current screening uptake rates.

Pipeline to offer further value

RHY's platform technology is designed to offer a range of simple, low cost, mass market cancer screening tests. It is based on a 'lead' cancer biomarker that is highly expressed in a range of cancers to identify the presence of cancer. In combining the 'lead' with cancer-specific biomarkers, the technology aims to detect and specify the cancer. The technology offers a strong pipeline.

Full Valuation Recognition

Over the next 12 months, RHY is expected to receive confirmation of its application for EU approval; obtain Clinical Study 7 results with Australian approval potentially to follow; and commence US market entry initiatives. In view of the strength of the supporting data to date, MST has de-risked the 12-month valuation. The unweighted 12-month forward valuation is A$600m, or $2.90 per share. The former valuation of A$420m/$2.03ps carried a 70% probability to reflect the R&D risk.

Our 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.

Further detail on RHY.AX - MST Initiation Report
https://www.mstaccess.com.au

RHYTHM BIOSCIENCES

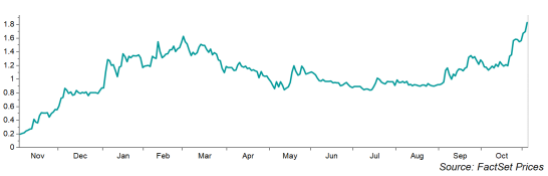
Rhythm Biosciences is an Australian medical diagnostics company. Its protein-based technology platform is being trialled in its first indication, colorectal cancer. Other tests are expected to follow. The work is well credentialled. The technology reflects 13+ years of CSIRO research and to date 3+ years of RHY development. With its initial development program completed, RHY is undertaking the regulatory processes to gain approval in its first markets: the US, EU and Australia. Management brings experience in both development and commercialisation of new medical products.

www.rhythmbio.com

Stock	RHY.ASX
Price	A$1.90
Market cap	A$403m
12 month valuation	A$600m
12-month valuation (per share)	A$2.90

Potential near-term milestones	
Q4CY21	Approval of CE Mark for the EU market
H1CY22	Positive Clinical Study 7 results to support Australian approval
CY22	Commence US market entry initiatives

RHY share price (A$)



Source: FactSet.

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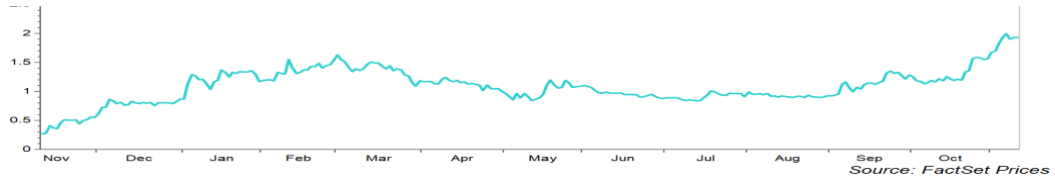
[1] Refer Exhibit 5, MST Initiation Report 17 June 2021.

[2] Symonds EL, et al A Blood Test for Methylated BCAT1 and IKZF1 vs. a Fecal Immunochemical Test for Detection of Colorectal Neoplasia. Clinical and Translational Gastroenterology (2016) 7, e137; doi:10.1038/ctg.2015.67

Financial Data

RHYTHM BIOSCIENCES		RHY.AX
Year end 30 June		
MARKET DATA		
Share price	**$**	**1.90**
52 week high / low	$	0.21-1.94
Valuation (12 month forward)	**$**	**2.90**
Market capitalisation	**$m**	**403**
Shares on issue	m	209
Options	m	17
Potential shares on issue	m	226

12 month share price performance



Source: FactSet Prices

PROFIT AND LOSS (US$)	000s	FY20	FY21	FY22E	FY23E	FY24E
R&D Tax Refund		-	1,108.5	1,366.4	1,200.0	1,305.0
Interest Income		46.3	14.0	108.6	96.7	51.3
Other Income		100.0	-	-	-	-
Licensing Royalties		-	-	-	5,462.8	17,065.3
Total Revenue		**146.3**	**1,122.5**	**1,475.0**	**6,759.5**	**18,421.6**
Research and development costs		(1,939.4)	(4,554.7)	(4,000.0)	(3,000.0)	(2,000.0)
Other expenses		(2,229.8)	(3,178.7)	(3,084.9)	(3,115.3)	(3,146.1)
Underlying NPAT		**(4,023.0)**	**(6,610.9)**	**(5,609.9)**	**644.2**	**13,275.5**

BALANCE SHEET (US$)	000s	FY20	FY21	FY22E	FY23E	FY24E
Cash and cash equivalents		1,798.0	2,228.3	349.9	874.8	13,934.6
Trade and other receivables		139.2	163.9	163.9	163.9	163.9
Other financial assets		45.0	45.0	45.0	45.0	45.0
Prepayments		23.2	56.5	56.5	56.5	56.5
Total current assets		2,005.4	2,493.7	615.3	1,140.2	14,200.0
Intangible assets		498.0	462.0	462.0	462.0	462.0
Right of use assets		40.0	-	-	-	-
Property, plant and equipment		102.5	113.8	113.8	113.8	113.8
Total Non-Current Assets		640.5	575.8	575.8	575.8	575.8
Total Assets		2,645.9	3,069.5	1,191.1	1,716.0	14,775.8
Trade and other payables		676.1	1,206.2	941.1	1,073.7	1,073.7
Provisions		75.9	137.0	137.0	137.0	137.0
Lease liabilities		42.4	-	-	-	-
Total current liabilities		794.4	1,343.2	1,078.2	1,210.7	1,210.7
Provisions		8.4	19.7	19.7	19.7	19.7
Total non-current liabilities		8.4	19.7	19.7	19.7	19.7
Total liabilities		802.9	1,362.9	1,097.9	1,230.4	1,230.4
Net Assets		1,843.1	1,706.6	93.2	485.6	13,545.4
Issued capital		10,037.2	15,981.4	20,981.4	20,981.4	20,981.4
Reserves		194.0	531.6	531.6	531.6	531.6
Accumulated losses		(8,388.2)	(14,806.4)	(21,419.8)	(21,027.4)	(7,967.6)
Total shareholders' equity		**1,843.1**	**1,706.6**	**93.2**	**485.6**	**13,545.4**
Total liabilities and equity		**2,645.9**	**3,069.5**	**1,191.1**	**1,716.0**	**14,775.8**

CASH FLOW (US$)	000s	FY20	FY21	FY22E	FY23E	FY24E
Licensing Royalties		-	-	-	5,462.8	17,065.3
Interest received		47.2	20.2	108.6	96.7	51.3
R&D Expenses		(1,939.4)	(4,554.7)	(4,000.0)	(3,000.0)	(2,000.0)
Interest paid		(7.8)	(0.8)	-	-	-
R&D tax fund		743.8	1,108.5	1,108.5	1,366.4	1,200.0
Other items		(1,586.4)	(1,975.7)	(3,084.9)	(3,115.3)	(3,146.1)
Net cash flows from operating activities		**(2,742.6)**	**(5,402.5)**	**(5,867.8)**	**810.6**	**13,170.5**
Purchases of P&E		(45.5)	(68.3)	(68.3)	(68.3)	(68.3)
Net cash flows from investing		**(45.5)**	**(68.3)**	**(68.3)**	**(68.3)**	**(68.3)**
Repayment of lease liabilities		(59.9)	(42.4)	(42.4)	(42.4)	(42.4)
Repayment of other borrowings		(82.4)	-	-	-	-
Proceeds from issue of ord shares		-	6,168.8	4,300.0	-	-
Payment of share issue costs		-	(225.1)	(200.0)	(175.0)	-
Net cash flow from financing		**(142.2)**	**5,901.2**	**4,057.6**	**(217.4)**	**(42.4)**
Change in Cash		(2,930.4)	430.4	(1,878.5)	524.9	13,059.8
Year end cash		1,798.0	2,228.4	349.9	874.8	13,934.6

Source: Company data, MST estimates.

Investment Thesis

Rhythm Biosciences (RHY) has developed a platform technology to offer simple, low cost, mass market cancer screening tests. MST's investment thesis is built around bowel cancer, RHY's first product, ColoSTAT®. It is in late-stage development and plans to enter the US, Europe, Australia, New Zealand, China and Japan markets. The test is based on a 'lead' cancer biomarker which is highly expressed in a range of cancers, opening the potential for multiple applications. ColoSTAT® includes the lead biomarker as well as three colorectal or bowel specific biomarkers to identify the cancer as bowel cancer. RHY intends to develop a pipeline of cancer diagnostic tests.

ColoSTAT® to offer efficacy, participant acceptability and affordability

1. Participant and cost 'friendly' – The faecal immunochemical test (FIT) is the mainstay of most screening programs. Utilisation of current tests is low (~32% across the global markets) due to their low efficacy, protocols that require participant handling of the faecal samples and cultural reasons. Colonoscopy, while more participant-acceptable and efficacious, sees wide use only in the US due to its high cost.
   ColoSTAT® potentially offers higher efficacy, participant acceptability and affordability. Trial data to date have shown clear superiority, offering ~33% higher detection rate to the SOC faecal test, FIT. As a blood test, ColoSTAT® can be incorporated into current screening tests, such as cholesterol and glucose. While pricing is still to be determined, ColoSTAT® presents as a competitive alternative to FIT. In MST's view, ColoSTAT® has the potential the grow the current markets.
2. Large, established markets - 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.
3. Near term revenues- With the enrolment of Clinical Study 7 now completed, and requirements to apply for the EU market approval satisfied, RHY is preparing for market entry. Investor focus is turning to revenues.

Valuation, Risks, Sensitivities

Our 12-month DCF valuation of $600m ($2.90 per share) is based on the expected EU approval, positive results in Clinical Study 7 and US market initiatives over CY21/22. The previous valuation of $420m carried a risk weighting of 70% to reflect the development risk.

The key catalysts to the MST DCF valuation include positive trial data and supporting documentation to meet regulatory standards of its initial targeted markets: the EU, US and Australia. The valuation is subject to the usual upside/downside risks of medical devices: trial failure, failure to gain approval, competition, poor market uptake, pricing, and market entry timing. The price of ColoSTAT® is yet to be confirmed. MST forecasts are built on US$38/A$50. The price is likely to reflect its clinical performance as established initially in Clinical Study 7.

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 to these programs.

Upcoming Milestones

- Q4CY21 –Approval of Conformité Européenne (CE) Mark to allow sales within the European Economic Area (EEA)
- H1CY22 – Results for Clinical Study 7
- CY22 – Potential TGA approval for Australian market (on positive Study 7 results)
- CY22 –Establish partnerships in the US, EU, Australia markets to commercialise ColoSTAT®
- CY22 – Confirm next target test

Focus Turns to First Revenues

Investor focus is moving to RHY's commercial opportunities as the company looks to transition from the R&D stage to 'on market' with the company expecting EU approval by end CY21. We look at the steps to market entry for the first three markets: the EU, Australia and the US (see Exhibit 1).

Exhibit 1 – Key market approval requirements

Path to Market - Approval requirements

Jurisdiction	Technical and Clinical Data Requirements	Timing	MST Market Estimates
EU	Conformité Européenne (CE) Mark		
	Assessment of the test componentry and procedure	Submission and approval in Q4CY21	US$3.9bn
	No Formal Clinical trials required		
	Supporting clinical data important for medical uptake		
Australia			
	Manufacturer's Evidence Documentation	Accepted Q3CY21	US$0.4bn
	Australian Register Therapeutics Goods Listing	Clinical Study 7 results in H1CY22	
US			
LDT* pathway	Validation of ColoSTAT® in the designated laboratory		US$3.6bn
	Sale of test confined to laboratory network		
	Clinical data supportive for reimbursement submissions		
FDA	US Clinical trials and regulatory process	Commence CY22	
	Total US market access		

Source: Rhythm Biosciences, MST estimates, relevant websites.

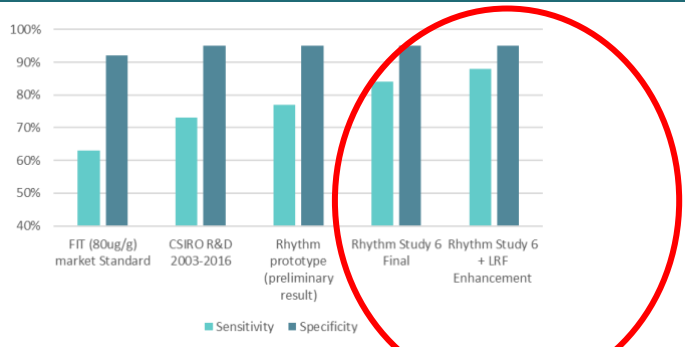
EU Markets

Under EU regulations, a company must receive its Conformité Européenne (CE) Mark to commence sales/marketing within the European Economic Area. RHY has completed the testing and validation requirements and plans to submit its CE Mark application for approval. The company expects approval by end-CY21. While not a requirement for the CE Mark and market entry, RHY's Clinical Study 7 data will be important to support its marketing activities with clinicians and possible negotiations with the national authorities responsible for the bowel cancer screening programs. The results of the study are planned for over H1CY22.

Australian Market

The Australian Therapeutic Goods Administration (TGA) approval of a diagnostic test is a two-step process. RHY has already met the first stage, the Manufacturer's Evidence Documentation. The results of its Clinical Study 7, if positive, are planned to support the second stage, listing on the Australian Register of Therapeutic Goods. Clinical Study 7 is based on 'real-world data' with ColoSTAT®'s performance being assessed by its correlation with the results of the patient's colonoscopy, the 'gold standard' of CRC diagnosis. The trial will also include a FIT. While not part of the clinical trial result, a superior performance to FIT will support its marketing activities. Results of previous ColoSTAT® studies, based on laboratory bowel cancer blood samples, have shown 88% sensitivity and 95% specificity. While it is difficult to compare directly, ColoSTAT® promises to offer superiority to published FIT data, which has shown sensitivity and specificity of 63% and 92%, respectively (see Exhibit 2).

Exhibit 2 – ColoSTAT® offers more effective test than FIT



	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.

US Market

RHY has commenced the steps to US market entry. The US offers two pathways, Laboratory Developed Tests (LDTs) and FDA approved tests. RHY plans to initially enter the US market under the classification of an LDT. Most tests are FDA approved, sold in 'commercial' volumes by the larger pathology laboratories and/or other healthcare facilities. LDTs, which are developed for use in one pathology centre/network, are referred to as 'home-brewed' tests.

While the majority of marketed clinical tests are FDA approved, many developers choose the LDT path to enter the market. It offers a faster route and lower costs. As revenues can be restricted in more limited market access, many will go on to seek FDA approval and full market access once a market presence is established. Under the LDT path, RHY will be required to validate its test in the nominated laboratory. Positive Clinical Study 7 data are likely to strengthen licensing partnership negotiations.

Commercial Potential

Commercialisation Opportunity

Exhibit 3 – Participation rate in RHY's main screening regions

Market	Screened Population (m)	Unscreened Population (m)	Participation Rate	Current Screening Market ($USm)*	Unrealised Market ($USm)	Total Market ($USm)
US	64.95	29.46	68.8%	$2,468	**$1,119**	$3,587
EU	52.64	49	51.8%	$2,000	**$1,862**	$3,862
Australia	2.78	3.57	43.8%	$106	**$135**	$241
Overall	120.37	82.03	41%	4574	**$3,116**	7690

* Assumes ~US$38 ColoSTAT® price

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

MST market estimates for the first three key markets are based on the current bowel cancer screening guidelines applied to the local populations, current uptake and an MST assumed price of US$38. It also flags the 'unrealised' market, those who are eligible but currently do not participate.

Market Penetration

Exhibit 4 – Comparison between main CRC screening methods

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

Source: MST assumptions.

ColoSTAT®'s market performance will reflect its ability to compete with the SOC tests and to persuade those who currently don't participate. There is good cause to believe many who currently don't undertake screening will choose to participate. Confirmation of higher efficacy is also likely to drive uptake.

ColoSTAT® may also find a role with those who currently choose colonoscopy. The expense of colonoscopy sees its use generally restricted as a screening tool apart from in the US. In the US, ~61% of eligible participants undergo colonoscopy versus ~4% faecal tests. Colonoscopies are recommended to be undertaken every 10 years, but many opt for more frequent testing. ColoSTAT® may offer a role in the intervening years as a 'check-up' and obviate the need for more frequent colonoscopies.

Valuation, Risks and Sensitivities

CY21/CY22 Potential Valuation Upside as R&D Risk Abates

Exhibit 5 –Impact of Potential Positive Newsflow on MST Risk Weighted DCF Valuation

Potential Newsflow Effect on Valuation

Previous Risk Adjusted Valuation		**New De Risked Valuation**	
per Share	$2.03	per Share	$2.90
Market Cap	$420m	Market Cap	$600m

Expected Newsflow

Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July →
CE MARK		Clinical Study 7 Results, Establish US CLIA Laboratory						TGA Approval
EU Market Approval		Support Australian Approval Application, EU market penetration, CLIA Laboratory revenues						Aust Market Entry
CY21		CY22						

Source: MST assumptions.

Over the next 6-8 months, RHY offers a number of significant value inflexion points as it seeks approval in the key markets. We expect that positive news of EU approval through the CE Mark, Clinical Study 7 results to support Australian approval and US market entry will negate the development risk. As a result, we are de-risking our DCF-based valuation on a 12-month view, lifting it to $2.90 per share from $2.03 previously (which incorporated a 70% probability of approval during the R&D stage) (see Exhibit 5). Over this period, on positive newsflow, we expect the share price to rise to meet this 'de-risked' level.

MST forecasts assume RHY will partner with pathology service provider/s. Royalty streams are commonly in the 5%-15% range. The MST model assumes licensing agreements will be based on a 12% royalty stream for the Australian, US and EU markets. Royalties of 2% of all net sales are payable to CSIRO under the agreements. The valuation is based on a net ~10% to RHY. We forecast revenues of A$5.5m and A$17.0m for FY22 and FY23, recognising that time will be needed to establish supply and commercial partnerships and gain market acceptance.

The valuation is subject to the usual upside/downside risks of medical devices: trial failure, failure to gain approval, competition, poor market uptake, royalty streams, timing and pricing. The price of ColoSTAT® is yet to be confirmed. MST forecasts are built on US$38/A$50. The price is likely to reflect its clinical performance as established initially in Clinical Study 7.

MST forecasts assume RHY will participate in the current national/regional funded programs. Generally, the products used in national programs demand pricing discounts. There is a risk that the price will fall below our 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.

Overall, we see significant near-term upside in RHY, on the assumption that the testing results to date are reflected in Clinical Study 7. We expect the share price to increase as 'development' risk decreases over the next six months+. Commercial performance and new test developments will then become the key ongoing driver of the share price.

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