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Motif Bio Plc

(MTFB-NASDAQ)

MTFB: Additional Data for Iclaprim Presented at ESCMID/ASM …

Based on our probability adjusted DCF model that takes into account potential future revenues from Iclaprim, MTFB is valued at $28 per share. This model is highly dependent upon continued clinical and commercial success of Iclaprim and will be adjusted accordingly based upon future clinical results and the company's execution.

Current Price (10/03/18)	$8.70
Valuation	**$28.00**

OUTLOOK

In Sep. 2018, Motif Bio Plc (MTFB) announced a number of presentations on iclaprim data were presented at the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)/American Society for Microbiology (ASM) Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance. One of those presentations was based on diabetes patients in the REVIVE-1 and REVIVE-2 Phase 3 trials. Results showed that overall adverse events in diabetic patients were lower with iclaprim than with vancomycin. In addition, no diabetic patients developed acute kidney injury compared to three diabetic patients taking vancomycin.

The PDUFA date for iclaprim is Feb. 13, 2019 and in the run-up to that the company is continuing to increase awareness of iclaprim with potential commercialization powers, physicians, and investors.

SUMMARY DATA

52-Week High	**$11.84**
52-Week Low	**$7.90**
One-Year Return (%)	**-13.95**
Beta	**0.07**
Average Daily Volume (sh)	**1,527**
Shares Outstanding (mil)	**15**
Market Capitalization ($mil)	**$129**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**7**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2018	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
2019					11.0 E
2020					49.0 E

Earnings per ADS

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-$1.50 A	-$1.50 A	-$1.07 A	-$1.07 A	-$3.87 A
2018	-$0.29 A	-$0.28 A	-$0.58 E	-$0.59 E	-$1.77 E
2019					-$1.85 E
2020					-$0.48 E

Business Update

Motif Bio Plc (MTFB) is a biopharmaceutical company focused on the development of antibiotic compounds for difficult to treat bacterial infections. The company's lead asset, iclaprim, is a novel diaminopyrimidine molecule that has completed Phase 3 testing for the treatment of acute bacterial skin and skin structure infections (ABSSSI), with the company announcing positive results from the two studies earlier in 2017. Following submission of a new drug application (NDA), the drug was assigned a PDUFA date of Feb. 13, 2019. In addition, the U.S. Food and Drug Administration (FDA) has granted iclaprim orphan drug designation (ODD) for the treatment of bacterial infections in patients with cystic fibrosis caused by *Staphylococcus aureus*.

Presentations at ESCMID/ASM

On September 5, 2018, Motif announced multiple presentations at the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)/American Society for Microbiology (ASM) Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance. We highlight some of these presentations below.

The Safety of Iclaprim among Diabetic Patients for the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI): Pooled REVIVE Studies

A post-hoc analysis was performed on pooled data from the two Phase 3 clinical trials (REVIVE-1 and REVIVE-2) of iclaprim in patients with acute bacterial skin and skin structure infections (ABSSSI). 11% (127/1198) of the intent to treat (ITT) patients in the REVIVE studies had diabetes, with more treated with vancomycin (n=71) than with iclaprim (n=56). There was a similar level of renal impairment among both groups of patients with 22/56 (39.2%) diabetic patients in the iclaprim group having mild or moderate to severe renal impairment compared with 26/71 (36.6%) in the vancomycin group. This data is shown in the table below.

	REVIVE-1		REVIVE-2		Pooled REVIVE	
Creatinine Clearance, n (%)*	Iclaprim (n=20)	VAN (n=35)#	Iclaprim (n=36)#	VAN (n=36)	Iclaprim (n=56)#	VAN (n=71)#
≥ 90 ml/min	11 (55.0)	20 (57.1)	22 (61.1)	23 (63.8)	33 (58.9)	43 (60.5)
60-89 ml/min	8 (40.0)	7 (20.0)	8 (22.2)	8 (22.2)	16 (28.5)	15 (21.1)
15-59 ml/min	1 (5.0)	6 (17.1)	5 (13.8)	5 (13.8)	6 (10.7)	11 (15.4)

Abbreviations: VAN, vancomycin

Source: Huang *et al*., 2018

*No patients had creatinine clearance <15 mL/min.

#Data on renal function is missing on 1 iclaprim-treated patient and 2 vancomycin-treated patients.

From a safety standpoint, there were numerically lower adverse events (AEs) and treatment-related AEs in the iclaprim group compared to the vancomycin group. Three of the diabetic patients treated with vancomycin developed acute kidney injury compared to no patients taking iclaprim. Lastly, there was a higher number of discontinuations due to an AE in diabetic patients taking vancomycin (10.0%; 7/70) compared to those taking iclaprim (3.6%; 2/56). Since diabetics are known to be at a greater risk of ABSSSI and kidney related toxicity, a drug like iclaprim could be an important treatment for this cohort. All of this data is summarized in the following table.

n (%)	REVIVE-1		REVIVE-2		Pooled REVIVE-1/2	
	Iclaprim (N=20)	VAN (N=34)	Iclaprim (N=36)	VAN (N=36)	Iclaprim (N=56)	VAN (N=70)
Deaths	0	1 (2.9)	0	0	0	1 (1.4)
Serious AEs	1 (5.0)	3 (8.8)	4 (11.1)	2 (5.6)	5 (8.9)	5 (7.1)
AEs leading to discontinuation	0	4 (11.8)	2 (5.6)	3 (8.3)	2 (3.6)	7 (10.0)
Drug-related AEs	2 (10.0)	7 (20.6)	3 (8.3)	4 (11.1)	5 (8.9)	11 (15.7)
Any AEs	7 (35.0)	19 (55.9)	20 (55.6)	18 (50.0)	27 (48.2)	37 (52.9)
Pyrexia	0	3 (8.8)	0	1 (2.8)	0	4 (5.7)
Phlebitis	0	0	2 (5.6)	1 (2.8)	2 (3.6)	1 (1.4)
Blood glucose increased*	0	0	0	1 (2.8)	0	1 (1.4)
Acute kidney injury/ Blood creatinine increased#	0	1 (2.9)	0	2 (5.6)	0	3 (4.3)
Hypo-magnesemia*	0	0	2 (5.6)	1 (2.8)	2 (3.6)	1 (1.4)
AST increased*	0	0	1 (2.8)	0	1 (1.8)	0
ALT increased*	0	0	1 (2.8)	1 (2.8)	1 (1.8)	1 (1.4)
QTc prolongation (QTcF >500 ms or >60 ms from BL)	0	0	0	0	0	0

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; ms, milliseconds; VAN, vancomycin.

*Investigator reported.

#Patients who have a confirmed increase in serum creatinine (SCr) of 0.5mg/dL from baseline, if SCr was normal at baseline or a 50% increase in SCr from baseline, if the upper limit of SCr was not normal at baseline.

Source: Huang *et al*., 2018

Iclaprim Activity Against Clinical Isolates Causing Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in the Phase 3 REVIVE-1 and REVIVE-2 Studies

This study was designed to test the in vitro potency of iclaprim against clinical isolates obtained during a patient's initial visit in the REVIVE-1 and REVIVE-2 trials. A total of 803 isolates were collected, which included 593 isolates of *S. aureus* (322 MSSA and 272 MRSA), 12 isolates of *Staphylococcus haemolyticus*, 83 isolates of beta-hemolytic streptococci, and 113 isolates of viridans streptococci. Each of the isolates was tested against iclaprim, trimethoprim (TMP), trimethoprim-sulfamethoxazole (TMP-SMX), vancomycin, linezolid, and daptomycin.

Results showed that iclaprim was more potent (as judged by $MIC_{50/90}$) against MRSA than vancomycin (8-fold), linezolid (16-fold), and daptomycin (4-fold). In addition, iclaprim was more potent than TMP and had similar potency as TMP-SMX. Iclaprim was also more potent than TMP (4-fold) and TMP-SMX (2-fold) against *S. pyogenes*. This data is summarized in the following table.

Pathogen	Antimicrobials ($MIC_{50/90}$ µg/mL)											
	Iclaprim		TMP		TMP-SMX*		VAN		Linezolid		DAP	
	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
S. aureus (n=594)	0.06	0.12	1	2	≤0.12	≤0.12	1	1	2	2	0.5	0.5
MRSA (n=272)	0.03	0.25	0.5	4	≤0.12	≤0.12	1	1	2	2	0.5	0.5
MSSA (n=322)	0.06	0.12	1	2	≤0.12	≤0.12	1	1	2	2	0.5	0.5
S. haemolyticus (n=12)	0.25	>8	4	>16	1	>8	1	2	1	1	0.5	0.5
S. pyogenes (n=52)	0.015	0.12	0.25	0.5	0.12	0.25	0.5	0.5	1	1	0.06	0.06
S. agalactiae (n=11)	0.25	0.5	2	4	0.25	0.25	0.5	0.5	1	2	0.25	0.25
S. dysgalactiae (n=20)	0.06	0.12	1	1	0.12	0.25	0.25	0.5	1	2	0.06	0.12
S. anginosus group (n=113)	≤0.004	0.008	≤0.12	≤0.12	≤0.06	0.06	1	1	1	2	0.5	0.5

Source: Noviello *et al*., 2018

Financial Update

On September 25, 2018, Motif announced financial results for the first half of 2018. As expected, the company did not report any revenues. Net loss for the first half of 2018 was $7.8 million, compared to $29.7 million in the first half of 2017. General and administrative expenses were $4.1 million for the first half of 2018 compared to $4.6 million for the first half of 2017. The decrease was primarily due to a reduction in stock-based compensation, legal costs, and investor relations costs partially offset by an increase in employee compensation. Research and development expenses were $6.9 million in the first half of 2018 compared to $23.6 million in the first half of 2017. The decrease was mostly due to a reduction in Phase 3 clinical trial expenses due to the trials being complete in 2017.

As of June 30, 2018, the company had approximately $19.8 million in cash and cash equivalents. In May 2018, the company raised net proceeds of $12.7 million through a conditional placing with new and existing investors of 32.3 million shares at a price of 31 pence per share.

As of June 30, 2018, the company had 272,199,780 common shares outstanding that trade on the London stock exchange. The company also has American Depository Shares (ADSs) that trade on the Nasdaq Capital Market. Each ADS represents 20 of the company ordinary shares. When factoring in stock options and warrants the fully diluted share count is approximately 339.0 million, or 17.0 million ADSs.

Conclusion

The company is fully focused on building awareness of iclaprim among potential commercialization partners, physicians, and investors in the lead up to the PDUFA date of Feb. 13, 2019. Partnering discussions are ongoing, however during this time the company is also working on potentially building up a sales team. It is still uncertain whether the company will launch iclaprim on its own, assuming it is approved, or sign an agreement with a commercialization partner, however we anticipate learning more about the company's strategy post-PDUFA over the next few months.

There are an estimated 3.6 million people hospitalized with ABSSSI every year. We conservatively estimate that 20% of patients have renal insufficiency, based on published data (Halilovic *et al*., 2012). We believe iclaprim could attain peak market share among these patients of 20%. We model for a full course of treatment costing $3000 and an inflation rate of 2%, which leads to peak sales of approximately $500 million in the U.S. Outside the U.S., we believe Motif will sign a commercialization agreement that will result in an average 15% royalty on net sales, which we estimate will peak at approximately $225 million. Using a 90% probability of approval and a 15% discount rate leads to a net present value for iclaprim in ABSSSI of $475 million. After factoring in the company's cash position, potential cash from the exercise of outstanding warrants, estimated capital requirements, and dividing by the fully diluted ADS share count of 17.0 million leads to a valuation of $28 per share. The stock continues to trade at a significant discount to our valuation, thus offering investors plenty of upside at the current price.

PROJECTED FINANCIALS

Motif Bio Plc
Income Statement

Motif Bio Plc	2017 A	1H18 A	2H18 E	2018 E	2019 E	2020 E
Iclaprim (ABSSSI)	$0	$0	$0	$0	$11	$49
YOY Growth		-	-			
Iclaprim (HABP)	$0	$0	$0	$0	$0	$0
YOY Growth		-	-			
Iclaprim (CF)	$0	$0	$0	$0	$0	$0
YOY Growth		-	-			
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0
YOY Growth		-	-			
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$11**	**$49**
YOY Growth		-	-			
Cost of Sales	$0	$0	$0	$0	$2	$8
Product Gross Margin		-	-			
Research & Development	$29.5	$6.9	$8.0	$14.9	$18.0	$20.0
General & Administrative	$8.5	$4.1	$8.0	$12.1	$25.0	$30.0
Other Expenses	$0	$0	$0	$0	$0	$0
Operating Income	($38.02)	($11.0)	($16.0)	($27.0)	($34.0)	($9.0)
Operating Margin		-	-			
Non-Operating Expenses (Net)	($6.8)	$3.2	($1.5)	$1.7	($3.0)	($3.0)
Pre-Tax Income	($44.8)	($7.8)	($17.5)	($25.3)	($37.0)	($12.0)
Income Taxes Paid	$0	($0)	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($44.8)**	**($7.8)**	**($17.5)**	**($25.3)**	**($37.0)**	**($12.0)**
Net Margin		-	-			
Net Loss per Share	**($0.19)**	**($0.03)**	**($0.06)**	**($0.09)**	**($0.09)**	**($0.02)**
Net Loss per ADS	**($3.87)**	**($0.57)**	**($1.17)**	**($1.77)**	**($1.85)**	**($0.48)**
YOY Growth		-	-			
Basic Shares Outstanding	231.5	272.2	300.0	286.1	400.0	500.0
ADS Oustanding	11.6	13.6	15.0	14.3	20.0	25.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

HISTORICAL STOCK PRICE

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