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Motif Bio Plc

(MTFB-NASDAQ)

MTFB: REVIVE-1 Results Published in Clinical Infectious Diseases…

Based on our probability adjusted DCF model that takes into account potential future revenues from Iclaprim, MTFB is valued at $31 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 (02/01/18)	$10.50
Valuation	**$31.00**

OUTLOOK

Motif Bio Plc recently announced the publication of results from the REVIVE-1 Phase 3 clinical trial of iclaprim in patients with acute bacterial skin and skin structure infections (ABSSSIs). The company had previously announced positive topline data from the study in April 2017. The results showed 80.9% of iclaprim-treated patients and 81.0% of vancomycin-treated patients achieved the primary endpoint of early clinical response. The rates of treatment emergent adverse events were similar between iclaprim- and vancomycin-treated patients. We continue to anticipate a new drug application (NDA) for iclaprim before the end of the first quarter of 2018, and with priority review iclaprim could be approved before the end of 2018.

SUMMARY DATA

52-Week High	**$11.84**
52-Week Low	**$5.88**
One-Year Return (%)	**57.42**
Beta	**N/A**
Average Daily Volume (sh)	**3,145**
Shares Outstanding (mil)	**13**
Market Capitalization ($mil)	**$137**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**43**
Insider Ownership (%)	**16**
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)
2016	0.0 A	0.0 A	0.0 A	0.0 A	0.0 A
2017	0.0 A	0.0 A	0.0 E	0.0 E	0.0 E
2018					0.0 E
2019					11.0 E

Earnings per ADS

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2016	-$1.21 A	-$1.40 A	-$1.90 A	-$2.41 A	-$6.92 A
2017	-$1.50 A	-$1.50 A	-$1.15 E	-$1.15 E	-$5.20 E
2018					-$3.38 E
2019					-$2.30 E

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WHAT'S NEW

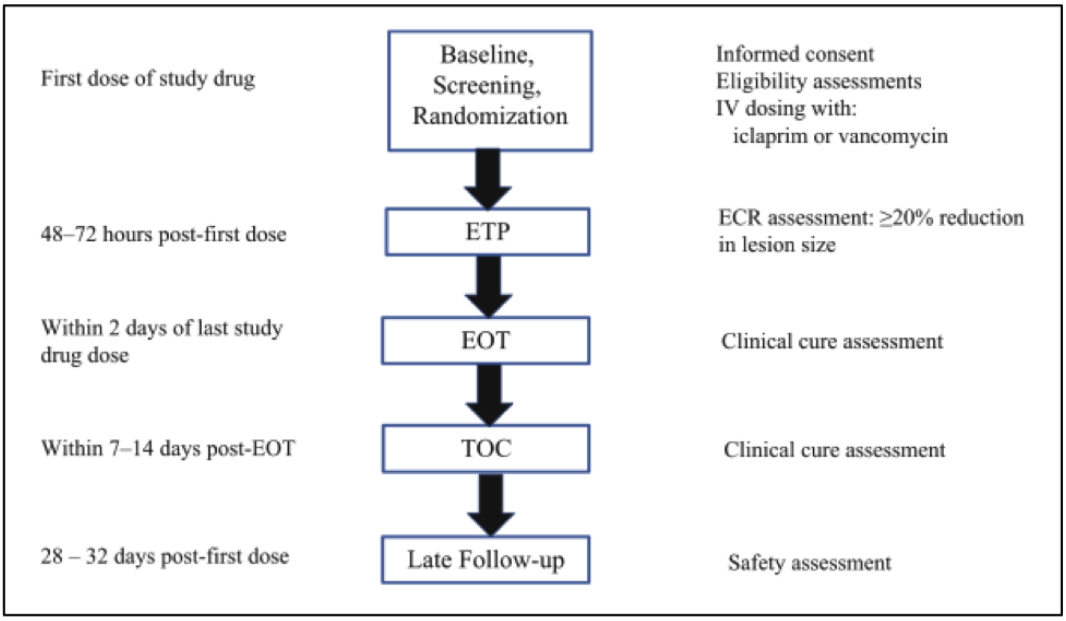
Business Update

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. We anticipate a New Drug Application (NDA) to be submitted for iclaprim in first quarter of 2018 and a regulatory submission in Europe in the second quarter of 2018. 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*.

REVIVE-1 Results Published

On December 21, 2017, Motif announced the publication of results from the Phase 3 REVIVE-1 study in the journal *Clinical Infectious Diseases* (Huang *et al*., 2017). The company had previously announced positive topline results from the study in April 2017.

The REVIVE-1 study was a multicenter, double blind, randomized trial where suffering from acute bacterial skin and skin structure infections (ABSSSI) received either 80 mg iclaprim or 15 mg/kg vancomycin intravenously (IV) every 12 hours. The study design followed both the U.S. FDA and European Medicines Agency guidance. The primary endpoint was an analysis of early clinical response (ECR) at the early time point (ETP, 48-72 hours after the first infusion of drug) comparing response to iclaprim with response to vancomycin. Secondary analyses included response to treatment at the end of therapy (EOT), at test of cure (TOC, 7-14 days after the last dose of study drug), and safety and tolerability. The following chart shows the schedule of visits for study subjects.



Source: Huang *et al*., 2017

A total of 598 patients were randomized into the study to receive either iclaprim (n=298) or vancomycin (n=300) and the baseline and demographic characteristics were comparable between the two groups. The baseline mean lesion sizes of iclaprim and vancomycin groups were 333 cm^2 and 337 cm^2, respectively. In the intent-to-treat (ITT) population, which consisted of all randomized subjects, an ECR was reported for 80.9% (241/298) of iclaprim-treated patients and 81.0% (243/300) of vancomycin-treated patients (% difference, -0.13; 95% CI, -6.42, 6.17), thus iclaprim demonstrated non-inferiority (within 10% margin) compared to vancomycin. The clinical cure rates at the EOT were 92.3% (275/298) and 90.7% (272/300) for the iclaprim and vancomycin groups, respectively. Clinical cure at the TOC was 83% (248/298) and 87% (262/300) for the iclaprim and vancomycin groups, respectively. Lastly, the ECR at ETP was comparable between iclaprim and vancomycin groups when stratifying by lesion type, pathogen, diabetes, and renal impairment. The results are summarized in the following table.

Clinical Response	Iclaprim (n = 298)	Vancomycin (n = 300)	Treatment Difference (%; 95% Confidence Interval)
Primary endpoint			
ECR at ETP in intent-to-treat	241 (80.9%)	243 (81.0%)	–0.13 (–6.42, 6.17)
Secondary analyses			
ECR at ETP among major cutaneous abscess	35/40 (87.5)	49/55 (89.1)	–1.59 (–14.74, 11.56)
ECR at ETP among cellulitis/erysipelas	54/76 (71.1)	68/87 (78.2)	–7.11 (–20.50, 6.28)
ECR at ETP among wound infections	152/182 (83.5)	126/158 (79.7)	3.77 (–4.50, 12.04)
ECR at ETP among methicillin-resistant *Staphylococcus aureus* infected	59/73 (80.8%)	50/61 (82.0%)	–1.15 (–17.94, 15.80)
ECR at ETP among methicillin-susceptible *S. aureus* infected	81/97 (84.4%)	88/104 (85.4%)	–1.06 (–14.94, 12.85)
ECR at ETP among *Streptococci pyogenes* infected	20/25 (80.0%)	18/25 (72.0%)	8.00 (–32.98, 33.86)
ECR at ETP among diabetics	16/20 (80.0%)	26/35 (74%)	5.71 (–21.94, 32.74)
ECR at ETP among mild renal impairment (CrCl of 60–89 mL/min)	24/30 (80%)	35/44 (80%)	0.45 (–22.43, 23.52)
ECR at ETP among moderate and severe renal impairment (CrCl of <60 mL/min)	5/6 (83%)	9/12 (75%)	8.00 (–46.02, 52.44)
ECR at ETP in per-protocol	228 (84.8%)	232 (86.2%)	–1.49 (–7.44, 4.46)
Clinical cure at TOC	248 (83.2%)	262 (87.3%)	–4.11 (–9.78, 1.56)
Modified clinical cure[a] at TOC	227 (76.2%)	240 (80.0%)	–3.83 (–10.45, 2.80)

Abbreviations: CrCl, creatinine clearance; ECR, early clinical response; ETP, early time point; TOC, test-of-cure.

[a] Modified clinical cure defined as a ≥90% reduction in lesion size compared to baseline, no increase in lesion size since ETP, and no requirement for additional antibiotics (except aztreonam or metronidazole) or unplanned significant surgical procedures after ETP.

Source: Huang *et al*., 2017

Iclaprim was safe and well tolerated as drug-related treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (SAEs) were similar between treatment groups. There were slight increases in the incidence of headache (10.2% and 2.4%), nausea (9.9% and 5.7%), and fatigue (6.1% and 3.0%) in the iclaprim group compared to the vancomycin group. Importantly, there were no drug-related TEAEs related to nephrotoxicity reported for iclaprim compared to 3 (1.0%) for vancomycin. TEAEs led to discontinuation in 2.7% and 4.4% of patients in the iclaprim and vancomycin groups, respectively. A summary of the safety findings is shown in the following table.

Category	Iclaprim (N = 293)	Vancomycin (N = 297)
Any drug-related TEAE	151 (51.5%)	128 (43.1%)
Study drug–related TEAE	57 (19.5%)	53 (17.8%)
TEAE leading to discontinuation of study drug	8 (2.7%)	12 (4.4%)
TEAE-related SAEs[a]	8 (2.7%)	12 (4.0%)
QTc prolongation	1 (0.4)	0 (0)
Mean serum creatinine (μmol/L) change from baseline to test-of-cure	2.9 (13.1)	7.2 (25.3)
Deaths	0	1 (0.3%)
TEAE by system organ class		
Headache	30 (10.2%)	7 (2.4%)
Nausea	29 (9.9%)	17 (5.7%)
Secondary acute bacterial skin and skin structure infection (skin bacterial infection or wound infection)	20 (6.8%)	10 (3.3%)
Fatigue	18 (6.1%)	9 (3.0%)
Vomiting	14 (4.8%)	15 (5.1%)
Pyrexia	12 (4.1%)	12 (4.0%)
Peripheral edema	8 (2.7%)	9 (3.0%)
Increased alanine aminotransferase*	6 (2.0%)	5 (1.7%)
Increased aspartate aminotransferase*	6 (2.0%)	1 (4.3%)
Chills	6 (2.0%)	6 (2.0%)
Pain in extremity	6 (2.0%)	5 (1.7%)
Peripheral swelling	4 (1.4%)	8 (2.7%)

The order of the TEAE by system organ class was listed in the order of most frequent (top) to least frequent (bottom) for iclaprim.

Abbreviations: QTc, corrected QT; SAE, severe adverse event; TEAE, treatment emergent adverse events. *Investigator reported.

Source: Huang *et al*., 2017

In summary, REVIVE-1 met the primary endpoint of demonstrating non-inferiority between iclaprim and vancomycin for the treatment of ABSSSI with respect to ECR at the ETP 48-72 hours after the first dose of drug. In addition, TEAEs were similar between the two treatments. As shown in the results table above, approximately 20-25% of patients in each treatment group had infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), with the ECR at ETP almost identical to the result for the treatment group as a whole. The International Disease Society of America (IDSA) guidelines for the treatment of ABSSSI include the use of vancomycin, linezolid, or daptomycin in patients with risk factors for MRSA (Stevens *et al*., 2014). However, both safety issues and resistance have been reported for these drugs (Hanai *et al*., 2016; Nannini *et al*., 2010). Thus, iclaprim may be an appropriate treatment option for ABSSSI caused by or suspected to be caused by MRSA given its efficacy, lack of nephrotoxicity, and no need for therapeutic drug monitoring or renal dosing adjustments.

NDA Filing in 1Q18

We continue to anticipate an NDA being filed for iclaprim for the treatment of ABSSSI before the end of the first quarter of 2018. The FDA then has up to two months to determine whether or not to accept the application for review. If accepted, we anticipate iclaprim will receive a priority review (the FDA has designated it a Qualified Infectious Disease Product, QIDP), which will result in a PDUFA date six months following acceptance of the NDA as opposed to the usual 10-month review time period. Thus, iclaprim could be approved before the end of 2018, with a commercial launch likely in the beginning of 2019. Upon approval, iclaprim would be eligible to receive 10 years of market exclusivity (five years for new molecular entity status and 5 years for QIDP).

Valuation

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, and dividing by the fully diluted ADS share count of 16.9 million leads to a valuation of $31 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	2016 A	1H17	2H17	2017 E	2018 E	2019 E
Iclaprim (ABSSSI)	$0	$0	$0	$0	$0	$11
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**	**$0**	**$11**
YOY Growth	-	-	-			
Cost of Sales	$0	$0	$0	$0	$0	$2
Product Gross Margin	-	-	-			
Research & Development	$34.8	$23.8	$25.0	$48.8	$35.0	$30.0
General & Administrative	$4.9	$4.4	$5.0	$9.4	$20.0	$25.0
Other Expenses	($0)	$0	$0	$0	$0	$0
Operating Income	($39.6)	($28.2)	($30.0)	($58.22)	($55.0)	($46.0)
Operating Margin	-	-	-			
Non-Operating Expenses (Net)	($0.7)	($1.5)	($0.2)	($1.7)	$0.0	$0.0
Pre-Tax Income	($40.3)	($29.7)	($30.2)	($59.9)	($55.0)	($46.0)
Income Taxes Paid	($0)	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($40.3)**	**($29.7)**	**($30.2)**	**($59.9)**	**($55.0)**	**($46.0)**
Net Margin	-	-	-			
Net Loss per Share	**($0.35)**	**($0.15)**	**($0.11)**	**($0.26)**	**($0.17)**	**($0.11)**
Net Loss per ADS	**($6.92)**	**($3.00)**	**($2.30)**	**($5.20)**	**($3.38)**	**($2.30)**
YOY Growth	-	-	-			
Basic Shares Outstanding	116.6	198.1	262.9	230.5	325.0	400.0
ADS Oustanding	5.8	9.9	13.1	11.5	16.3	20.0

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

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HISTORICAL STOCK PRICE



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