Zacks Small-Cap Research

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Motif Bio Plc

MTFB - NASDAQ

MTFB: Additional Preclinical Data Presented on Iclaprim; Up to $20 Million in Financing Secured…

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 (11/29/2017)	$8.08
Valuation	**$31.00**

OUTLOOK

Motif Bio Plc recently presented additional preclinical data for iclaprim showing activity against MRSA in a preclinical model of cystic fibrosis. The company has reported positive Phase 3 data in acute bacterial skin and skin structure infections (ABSSSI), thus this data supports the potential use of iclaprim in additional indications. The company also presented data on the ability of sub-inhibitory doses of iclaprim to inhibit toxin production in MRSA clinical isolates, an important clinical consideration when deciding what treatment to use.

Motif has secured up to $20 million in debt financing with Hercules Capital, which the company intends to use for pre-commercialization activities ahead of an anticipated 2019 launch of iclaprim in the U.S.

SUMMARY DATA

52-Week High	**$11.84**
52-Week Low	**$5.29**
One-Year Return (%)	**43.09**
Beta	**N/A**
Average Daily Volume (sh)	**1,794**
Shares Outstanding (mil)	**13**
Market Capitalization ($mil)	**$101**
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 #Lin Estimate	**N/A**
P/E using #Lin Estimate	**N/A**

Risk Level	**N/A**
Type of Stock	**Large-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*.

New Preclinical Data Presented at IDWeek 2017

Motif recently presented new preclinical data for iclaprim at IDWeek 2017. The data show iclaprim's activity in a rat model of cystic fibrosis (CF) along with an ability to suppress toxin production in methicillin-resistant *Staphylococcus aureus* (MRSA) isolates at sub-inhibitory doses.

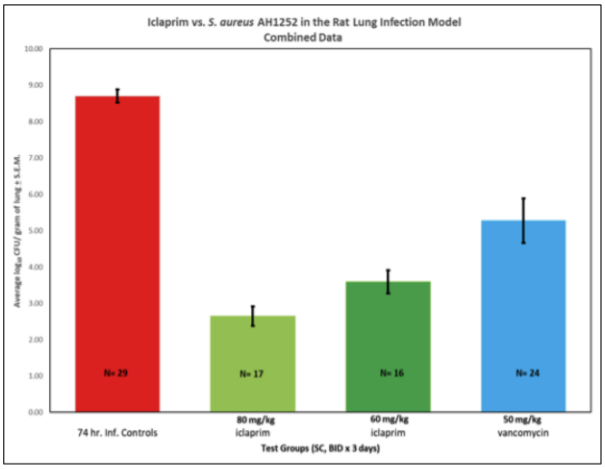
Poster #1: *Efficacy Evaluation of Iclaprim in a Neutropenic Rat Lung Infection Model with Methicillin-Resistant Staphylococcus aureus Entrapped in Alginate Microspheres*

This study was performed to determine the efficacy of iclaprim in a neutropenic rat chronic lung infection model using MRSA entrapped in alginate beads. The bacteria are encapsulated in alginate in order to produce a chronic infection model and allow for the development of biofilms in the lung, similar to what is seen in CF patients (Pedersen *et al*., 1990). Beginning two hours after infection, rats were treated with iclaprim (80 mg/kg or 60 mg/kg) or vancomycin (50 mg/kg) by subcutaneous injection every 12 hours for three days. The following table shows that both doses of iclaprim were more effective than vancomycin (80 mg/kg vs. vancomycin *P*=0.0002; 60 mg/kg vs. vancomycin *P*=0.05), while untreated animals showed decreased survival with only 48.3% (14/29) surviving to the end of the experiment. In contrast, all iclaprim-treated animals survived while 91.7% (22/24) of vancomycin-treated animals survived.

Group	Dose (mg/kg)	Route / regimen	Survival > 60h	Log_{10} Change in CFU at 74 hr
Control	vehicle	SC/BID	48.3%	NA
Iclaprim	80	SC/BID	100%	-6.05
Iclaprim	60	SC/BID	100%	-5.11
Vancomycin	50	SC/BID	91.7%	-3.42

Source: Huang *et al*., 2017

In addition to improving survival, iclaprim was more effective at decreasing the amount of bacteria in the lungs, as shown in the following graph. Compared to untreated controls, there was an approximate 6-log reduction in bacterial colony forming units (CFU) per gram of tissue in rats treated with 80 mg/kg iclaprim. Treatment with 60 mg/kg iclaprim and vancomycin resulted in 5- and 4-log reductions, respectively, compared to untreated controls.



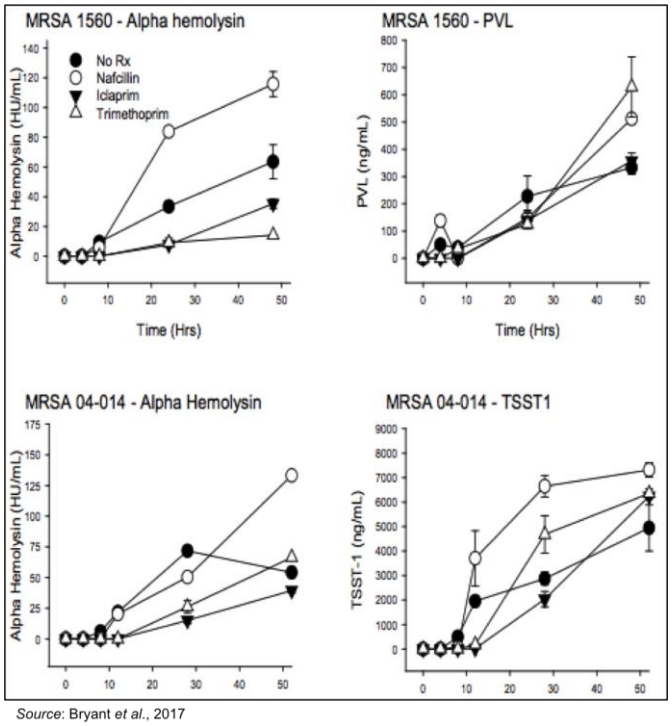
Source: Huang *et al*., 2017

These data are consistent with the results of a Phase 2 clinical trial of iclaprim in patients with nosocomial pneumonia caused by Gram-positive pathogens where patients treated with iclaprim had higher clinical cure rates than those treated with vancomycin (Huang *et al*., 2017).

Poster #2: *Effects of Iclaprim and Trimethoprim on Exotoxin Production by Methicillin-Resistant Staphylococcus aureus*

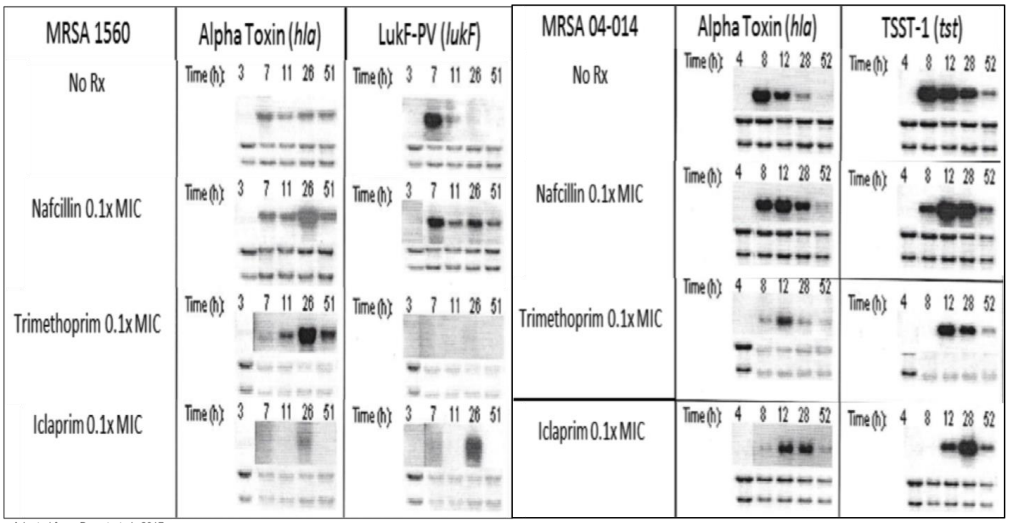
Antibiotic therapy that can limit or inhibit toxin production (e.g., alpha hemolysin [AH], panton valentine leukocidin [PVL], toxic shock syndrome toxin-1 [TSST-1]) is advantageous, however antibiotics vary widely in regards to their ability to do so. Sub-inhibitory concentrations of beta-lactam antibiotics increase and prolong toxin gene expression and protein production in both methicillin-sensitive *S. aureus* (MSSA) and MRSA (Stevens *et al*., 2007). Protein synthesis inhibitors also increase toxin gene expression, but block protein production. This study investigated whether folic acid synthesis inhibitors (e.g., iclaprim and trimethoprim) had any effect on toxin production in two MRSA clinical isolates (MRSA 1560 – produces both AH and PVL; MRSA 04-014 – produces both AH and TSST-1) compared to nafcillin and vancomycin.

The following graphs show that treatment with iclaprim resulted in decreased or similar toxin production compared to no drug treatment. This is in contrast to nafcilllin, which resulted in increased production of AH, PVL, and TSST-1. Trimethoprim treatment resulted in a statistically significant increase in PVL production.



Source: Bryant *et al*., 2017

Gene expression of AH, PVL, and TSST-1 was also examined. In strain MRSA 1560, nafcillin and trimethoprim induce expression of AH while iclaprim inhibits its expression, and nafcillin and iclaprim delay expression of PVL while trimethoprim inhibits its expression. In strain MRSA 04-014, nafcillin slightly delays expression of AH and TSST-1, while iclaprim and trimethoprim both delay expression of AH and TSST-1 while also decreasing their expression.



Adapted from: Bryant *et al.*, 2017

The data presented by Motif show that an antibiotic's effects on toxin production are highly strain- and toxin-dependent, however both iclaprim and trimethoprim were more effective than the beta-lactams in suppressing toxin gene expression and production, with iclaprim being more effective overall.

Financial Update

On November 15, 2017, Motif announced it had entered into an agreement with Hercules Capital, Inc. (HTGC) whereby Motif could acquire up to $20 million in debt financing. The first tranche of $15 million was drawn down immediately, with the second tranche of $5 million available upon the company achieving certain milestones in 2018. There is a 15-month interest only period (which may be extended up to 21 months if certain milestones are achieved) followed by a 30-month repayment period. The interest rate is 10% and is tied to the US prime rate. The company issued warrants to Hercules to purchase 73,452 ADSs at an exercise price of $9.53 per ADS. The funds will be utilized for pre-commercialization activities ahead of an anticipated 2019 launch of iclaprim, assuming approval by the FDA.

Valuation

We continue to anticipate an NDA being filed for iclaprim for the treatment of ABSSSI in 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, 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.

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. Even following the release of positive data from REVIVE-2, Motif 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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